Vaccination as an Alternative to Non-Drug Interventions to Prevent Local Resurgence of COVID-19

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Research Article

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Abstract

Background

While a COVID-19 vaccine protects people from serious illness and death, it remains concern when and how to relax from the high cost strict non-pharmaceutical interventions (NPIs).

Methods

We developed a stochastic calculus model to identify the level of vaccine coverage that would allow safe relaxation of NPIs, and the vaccination strategies that can best achieve this level of coverage. We applied Monto Carlo simulations more than 10,000 times to remove random fluctuation effects and obtain fitted/predicted epidemic curve based on various parameters with 95% confidence interval (95% CI) at each time point.

Results

We found that a vaccination coverage of 50.42% was needed for the safe relaxation of NPIs, if the vaccine effectiveness was 79.34%. However, with the increasing of variants transmissibility and the decline of vaccine effectiveness for variants, the threshold for lifting NPIs would be higher. We estimated that more than 8 months were needed to achieve the vaccine coverage threshold in the combination of accelerated vaccination strategy and key groups firstly strategy.

Conclusion

If there are sufficient doses of vaccine then an accelerated vaccination strategy should be used, and if vaccine supply is insufficient then high-risk groups should be targeted for vaccination first. Sensitivity analyses results shown that the higher the transmission rate of the virus and the lower annual vaccine supply, the more difficult the epidemic could be under control. In conclusion, as vaccine coverage improves, the NPIs can be gradually relaxed. Until that threshold is reached, however, strict NPIs are still needed to contain the epidemic. The more transmissible SARS-CoV-2 variant lead to higher resurgence probability, which indicates the importance of accelerated vaccination and achieving the vaccine coverage earlier.

Trial registration

We did not involve clinical trial.

Introduction

Coronavirus disease 2019 (COVID-19) was first reported in Wuhan (Hubei Province) in early December 2019, and the causative virus was subsequently identified as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1–3]. On March 11, 2020, COVID-19 had spread to 114 countries and the WHO characterized it as a pandemic [4]. Due to the lack of effective drugs and vaccines at that time, non-pharmaceutical interventions (NPIs) played a significant early role in control of the COVID-19 outbreak in China and other countries [5–8]. However,

long-term and strict NPIs can lead to significant economic and social costs, and a second wave of infections is likely if they are relaxed too early [9, 10].

COVID-19 was under control in China at the end of March 2020, but China faced a new challenge of recontamination due to close contact with foreign visitors because of increased travel to China [11, 12]. The National Health Commission of China recommended that foreign personnel should be subject to nucleic acid testing and centralized quarantine or household quarantine for 14 days upon entry. They also recommended that foreigners with confirmed or suspected COVID-19 identified in local customs quarantine should receive treatment in designated hospitals [13]. However, from the end of March 2020 there were some sporadic and local outbreaks in the regions of Suifenhe, Harbin [14], Shulan [15], Beijing [16], Urumqi [17], Dalian [18], Qingdao [19], Kashgar, Chengdu [20], and Shanghai [21]. Some of these outbreaks were related to imported cases [22, 23] and others to cold-chain foods [24, 25]. Quarantine, treatment of confirmed cases, comprehensive close contact tracking, large-scale nucleic acid detection, and community lockdown are NPIs that have greatly prevented COVID-19 transmission and helped to control local outbreaks [26–30]. Although these measures are effective, they are also costly and disruptive.

Vaccines save millions of lives each year and are powerful tools for controlling infectious diseases. An effective vaccine is considered the key for preventing further morbidity and mortality from COVID-19 [31]. As of May 28, 2021, there were 184 vaccine candidates in pre-clinical development, and 102 candidate vaccines currently undergoing clinical trials worldwide [32]. By the end of 2021, the global total production capacity of the 12 currently approved COVID-19 vaccines was estimated to reach about 10 billion doses [33]. As of December 31, 2020, 14 COVID-19 vaccines developed in China were undergoing clinical trials, including 5 in Phase III trials. The National Medical Products Administration granted conditional approval for first COVID-19 vaccine in China on December 30, 2020 [34]. China now provides COVID-19 vaccines free-of-charge to all citizens [35]. The vaccination strategy of China gives priority to those with high risk (including doctors and individuals engaged in the import of cold chain foods, public transportation, etc.), followed by eligible members of the general population [36]. China had a production capacity of 610 million doses in 2020 and was projected to produce at least one billion doses by the end of 2021 [37]. However, China's large and heterogeneous population has made it difficult to achieve herd immunity. Thus, NPIs are still important for the prevention and control of imported COVID-19 cases and local outbreaks.

We developed a stochastic calculus model to determine the role of vaccination and NPIs on COVID-19 prevention and control at the city level. We focused on the relationship of vaccine coverage with the timing of the relaxation of different NPIs.

Materials And Methods

A stochastic calculus model of SARS-CoV-2 transmission, with the population of a city stratified into 6 compartments, was developed (Fig. 1). The model city had a population size similar to Beijing and demographics similar to the general population of China, although the results are generalizable to other populations. The model assumed that vaccine-induced immunity lasted at least 2 years (model time horizon).

Data collection

Large-scale test data were from the website of the National Health Commission, which had data on sporadic cases in Beijing [38], Dalian [39], Qingdao [19], Chengdu [20], and Shanghai [21].

The compartmental model

The stochastic calculus model analyzed a population stratified into 6 compartments by extension of the classic SIRS model [40] to a BSIQDRS model (Fig. 1). This model incorporates three additional compartments to account for individuals with adverse reactions (B), quarantined cases (Q) and deaths due to COVID-19(D) (where S: susceptible people, I: infected people, R: recovered people, and N: total population (S+I+Q+R)). Dynamics of these compartments across time t were described in Fig. 1. The differential equations of dynamic model as followed.

$$\frac{dS}{dt} = -\frac{\beta SI}{N} - eV + \sigma R$$
$$\frac{dI}{dt} = \frac{\beta SI}{N} - hI - \gamma_1 I - d_1 I + C\frac{dA}{dt}$$
$$\frac{dQ}{dt} = hI - \gamma_2 Q - d_2 Q$$
$$\frac{dR}{dt} = \gamma_1 I + \gamma_2 Q + eV - \sigma R$$
$$\frac{dB}{dt} = bV$$
$$\frac{dD}{dt} = d_1 I + d_2 Q$$

In addition, A represented a Poisson process to simulate sporadic foreign imported COVID-19 arrival times with a parameter C (number of patients selected randomly from a discrete uniform distribution each time). Furthermore, β was the transmission rate of COVID-19 cases, defined as the average number of individuals that a case can infect per day [12], V was the daily vaccination number, e was the vaccine effectiveness, σ^{-1} was the immunity duration, h was the rate of an infectious cases to isolated cases (h^{-1}: actual infectious period), γ_1^{-1} and γ_2^{-1} were the rate of patients recovered, d_1 and d_2 were case fatality rates, and b was the adverse reaction rate. Additionally, β was a time-varying coefficient which was simulated as the quotient of randomly selected basic reproduction number and mean infectious period without quarantine. Parameters e, V, σ, h, γ_1, γ_2, d_1, d_2 and b were time-varying coefficients (fixed constant with 10% perturbation). Since the infectious disease stochastic modelling was too complicated theoretical analysis, we applied Monte Carlo (MC) simulations to extract numerical results.

Monto Carlo simulations

In this study, we made efforts to do numerical analysis on infectious disease stochastic modelling. In addition, since stochastic process were included in the model and most of parameters were time-varying and time-dependent, we applied Monto Carlo simulations more than 10,000 times to remove random fluctuation effects and obtain fitted/predicted epidemic curve based on various parameters with 95% confidence interval (95% CI) at each time point.

Parameter settings and initial states

Parameter settings for the main analysis were summarized in Table S1. We constructed a BSIQDRS infectious disease stochastic modelling to simulate three-year results in this study. We set $\beta = R_0/\tau$ according to [41, 42], where R_0 was basic reproduction number which varied around 2.5 [43, 44]. and τ was mean infectious time, and it was 9 days according to previous papers reported [1, 45]. We set the vaccine effectiveness e=0.7934 according to the results of phase III clinical trials of the vaccine in China [46, 47]. We set up two vaccination scenarios situations. In addition, this study assumed that 10% of the people in the city were the key population (held higher chance to contact foreign imported patients and had higher transmission rate). We compared simulation results based on key group vaccinated firstly with slow situations in this article. We assumed that vaccine-induced immunity last around two years (our time horizon), thus the σ was 1/730. h was the rate of an infectious cases to isolated cases (MEAN DETECTION TIME, MDT), which refers to both pharmacological and non-pharmacological interventions, including but not limited to large-scale nucleic acid testing, which can reduce the detection time of patients. We used h to represent intensity of the non-pharmacological intervention. The average incubation period of COVID-19 is around 5.18 days [48] Since COVID-19 was very hard be detected in the first several days until onset [49], we assumed that the most stringent non-pharmacological interventions were detected on day 5, with a mean detection time, h of 5. Additionally, the average duration from symptom onset to isolated was 4.1 ± 3.7 days [50], thus, the largest mean detection time, h, should be around 10 days. We assumed that infected cases in this city would recover 14 days after infections, and γ_1^{-1} and γ_2^{-1} were 14. We assumed the infectious cases and the quarantined cases shared the same case fatality rate in this city, and for our results are generalizable to other populations, we set d_1 and d_2 =0.005/21, which were similar to the normal city like Shanghai [21], Beijing [38] and Qingdao [19]. A was represented as a Poisson process to simulate sporadic foreign imported COVID-19 arrival times with a parameter C, which is the number of patients selected randomly from a discrete uniform distribution (1 to 7 patients) each time. We assumed the frequency of sporadic cases in this city is similar to that in Beijing, China, which was around 5 times from September to December, 2020 in 120 days.

Estimated scenarios in which vaccines can replace current NPIs

The stochastic simulations described above were used to estimate the daily number of infected cases, death rate, and probability of resurgence under different scenarios. First, vaccine coverage was assumed to range from 0 to 60% of the total population in 5% increments (the proportion in compartment R). In this analysis, b represented the daily vaccination rate, assuming that after a certain vaccination coverage is reached, the rate of vaccination is consistent with the rate of vaccine failure. Second, to model different levels of nucleic acid detection, we used mean detection time, h was used to represent the intensity of nucleic acid detection, h was the rate of an infectious cases to isolated cases, defined h^{-1} as the actual infectious period. It was assumed that h^{-1} varied from 5 days to 10 days in 0.5-day increments; an h^{-1} of 5 days meant that the person was identified and isolated on the first day of symptom onset [49]. An individual is infectious during the four days before symptom onset, but nucleic acid testing is insufficiently sensitive during this time due to the low viral titer, and it represents the NPIs were not rigorous when h^{-1} was 10 days. There were 143 combinations of parameters and each combination run Monte Carlo simulations for more than 10,000 times.

Predicting the risk of resurgence after cessation of NPIs

The risks of halting NPIs on the probability of resurgence, daily number of infections, and number of deaths were determined. This included relaxing all NPIs at t days after the first day of vaccination. Time to resurgence was

defined as the number of days from lifting controls to when the number of active cases above 7 patients in some day. It was assumed necessary to consider NPIs and vaccination rates when the resurgence probability exceeded 20%.

We performed Monte Carlo simulations for more than 10,000 times with different parameter combinations. The probability of resurgence was the proportion of simulations in which resurgence occurred, and we simulated the following three years from the day of vaccination. Several vaccination scenarios were considered. First, it was assumed that 5 million doses of vaccine were available every year, and the city could choose to vaccinate high-risk individuals or to vaccinate everyone (no priorities). Second, it was assumed the government could provide 16 million vaccine doses in the first year and 2 million doses in each subsequent year, and the city could choose to vaccinate high-risk individuals or to vaccinate everyone (no priorities). Then, these two plans were combined to create four different vaccination scenarios. The slow vaccination plan was that the city had an annual supply of 5 million vaccine doses and the city chose to vaccinate everyone (no priorities). The high-risk individuals were workers may be exposed to dangerous occupation of COVID-19, such as workers in the Centers for Disease Control and Prevention (CDC), hospital workers, delivery workers, cold food chain workers, and so on. This study assumed high-risk individuals accounted for 10% of the total population of the city.

Sensitivity analyses for the real data

We designed four sensitivity analyses to test the robustness of our results from real data. For each of the sensitivity analyses, we fixed parameters and initial states to be the same as the main analysis except for those mentioned below. According to COVID-19 Weekly Epidemiological Update Reports Edition 43, published 8 June 2021 of World Health Organization (WHO) [51], some variants of SARS-CoV-2 have resulted in changes in transmissibility, for instance, Alpha (B.1.1.7) variant first detected in United Kingdom may increase 45%-71% transmissibility, Beta (B.1.351) variant first detected in South Africa may increase 50% transmissibility, and the transmissibility of Gamma (P.1) variant which first detected in Brazil may be 1.4-2.2 times as the original transmissibility of SARS-CoV-2. Therefore, for analysis (S1), we set different scenarios of transmission rate of SARS-CoV-2 under the slow vaccination strategy. The different cases of transmission rate settings are assumed to be how many times the transmission rate is increased from the original basis, respectively 0%, 25%, 50%, 75% and 100%. For analysis (S2), we set different total number of vaccinations scenarios per year: 3 million, 4 million, 5 million, 6 million, 7 million. For analysis (S3), vaccine effective rate was assumed to range from 60–100% of the total population in 10% increments. For analysis (S4), we set different vaccination effectiveness times scenarios: 1 year, 1.5 years, 2 years, 2.5 years, 3 years (2 years was our baseline scenario in the main analysis). For analysis (S5), we assume this city have 30, 60, 90, 120, 150 sporadic foreign imported COVID-19 cases per year (60 sporadic foreign imported COVID-19 cases per year was our baseline scenario in the main analysis).

Results

Scenarios in which vaccines can lead to relaxation of NPIs

We assumed the mean detection time was 5 days and the vaccination rate was 0% (strictest NPIs without vaccination) as a basic scenario because of the low probability of an outbreak (resurgence probability: 51%, Fig. 2.a). This meant that when the vaccine introduced in this scenario, we can relax the NPIs gradually. If the vaccination rate was 10% (vaccine coverage: 12.60%), prolonging the detection time to 5.5 days led to the same outcome. The same outcome also occurred if the vaccination rate was 20% (vaccine coverage: 25.21%) and the

detection time was more than 6.5 days; if the vaccination rate was 30% (vaccine coverage: 37.81%) and the detection time was more than 8 days; and if the vaccination rate was 40% (vaccine coverage: 50.42%) and the detection time was more than 10 days. Thus, when vaccine coverage reaches 50.42%, no matter whether the large-scale detection was strict or not, we can obtain the same effect of basis scenario (because we can prolong the detection time to longest 10 days), Which means we can fully lift the NPIs.

Under the same intervention intensity, the probability of resurgence declined as vaccine coverage increased. When effective vaccination coverage was 40 to 60%, the probability of resurgence was low regardless of the extent of detection. When effective vaccination coverage was 40%, NPIs could be relaxed (i.e., mean time interval from infection to isolation was longer), and the resurgence probability was the same as when there were strict NPIs without vaccination (resurgence probability: 51%). Strict NPIs were still needed when the vaccine coverage was 10 to 30%. If there was no vaccine, there was a high probability of resurgence if NPIs were relaxed. We observed the same trends in terms of maximum daily infected cases and deaths (Fig. 2.b and c). In particular, when effective vaccine coverage was less than 40%, the daily number of infected cases and deaths increased exponentially as the NPIs were relaxed; when 40% of the population was vaccinated (vaccine coverage: 50.42%), NPIs may be safely relaxed.

Predicting the risk of resurgence after relaxation of NPIs

We assessed the effect of relaxing NPIs under no priority vaccination strategy (Fig. 3.a) and high-risk population first vaccination strategy (Fig. 3.b) on resurgence probability, daily infections, and total deaths when there were 5 million vaccine doses per year. Under these scenarios, when the mean detection time (MDT) was 10 days and regardless of vaccination strategy, there was a high initial probability of resurgence and this continued over time. For a vaccination strategy with no prioritized individuals, a continuing relaxation of NPIs, and a continuous increase of vaccination, the probability of resurgence was still high. Only after 27 months, when vaccination coverage reached 26.11%, was there a decline in the probability of resurgence (Fig. 3.a). Thus, when the NPIs are least stringent, the decline in the number of cases is mainly due to vaccination, and it will take 27 months to achieve a reduced probability of resurgence. When high-risk individuals had priority for vaccination, this time could be shorter, and the effect of the vaccine was evident after 21 months when the NPIs were most relaxed. If NPIs were in place at the time of vaccination, there was a significant reduction in the probability of resurgence, the number of infections, and the number of deaths. Moreover, stricter interventions led to a sharper decline. Thus, maintaining the strictest scenario (MDT = 5) led to a low risk of resurgence. However, if the MDT increased to 6, there was a sharp increase in the probability of resurgence. Finally, after the third year of vaccination, the most relaxed NPIs (MDT = 10) was also associated with a probability of resurgence that was less than 20%.

We also assessed the effect of relaxing NPIs under no priority vaccination strategy (Fig. 4.a) and high-risk population first vaccination strategy (Fig. 4.b) on resurgence probability, daily infections, and total deaths when there were 16 million vaccine doses in the first year and 2 million doses in the following two years. In these cases, even if when the MDT was 10 days, the probability of resurgence gradually declined, and the effect of vaccination appeared during the first month (Fig. 4.a and b). In addition, for the same intervention intensity, the risk of resurgence is lower for the high-risk population first vaccination strategy than for the no priority vaccination strategy. Moreover, when this large vaccine supply was available, if priority was given to high-risk individuals then the greater effectiveness of vaccination was obvious, even with the greatest relaxation of NPIs. After 9 months, the risk of resurgence was less than 20% (Fig. 4.b). If slightly intensified NPIs were implemented at this time, the epidemic was controlled (Fig. 4.b).

We then compared the effects of multiple strategies (Fig. 5). During the first 21 months, there were far fewer COVID-19 cases in the accelerated vaccination scenario than the slow vaccination scenario, the decline percentage were nearly 100% (Fig. 5.a). This indicated that the impact of rapid mass vaccination was very significant. These results also emphasize that when all NPIs were withdrawn, the reduction in the number of cases was entirely due to vaccination. We also determined the effect of prioritizing vaccines for high-risk individuals when 5 million doses were available (Fig. 5.b), the number of COVID-19 cases was reduced by about 60% over three years These results indicated that, the targeting of COVID-19 vaccinations provides an important benefit. Finally, prioritizing COVID-19 vaccinations for high-risk individuals and accelerating vaccination led to a very dramatic decline in total incidence (Fig. 5.c). We then assessed that how long can we lift all NPIs (Fig. 5.d). We estimated that 8 months are needed to achieve the vaccine coverage threshold for the fully relaxation of NPIs in the combination strategy of accelerated vaccination and key groups firstly. However, if we conduct a slow vaccination strategy, NPIs would not be fully liberalized in three years (Fig. 5.d).

Sensitivity analyses

We performed a series of sensitivity analyses to test the robustness of our results by varying the transmission rate, the number of vaccinations per year, the vaccination effectiveness rate, the lengths of vaccination effective time and the imported patients per year. Consistent with simulations, sensitivity analyses results shown that the total incidence number were negatively correlated with the vaccination number per year, vaccination effectiveness rate, the specified vaccination effective time, while the total incidence number were positively correlated with the number of imported patients per year, and transmission rate. One of the most sensitive parameters is the transmission rate, followed by annual vaccine supply. We could see that the higher the transmission rate, the more difficult the slow vaccination strategy is to control the epidemic, and it is necessary to accelerate the vaccination rate to control the epidemic (Fig. 6.a). When the vaccine supply reaches 7 million doses per year, the total incidence number is significantly less than that when the vaccine supply is 3 million doses per year, and 32.86% patients can be reduced in three years in that scenario (Fig. 6.b). In addition, we found that vaccination effectiveness rate and vaccine duration had less impact on the total number of cases compared to the number of vaccinations (Fig. 6.c and d). The imported patients had few influences on the total number of patients (Fig. 6.e). With the increasing of vaccination number per year, vaccination effectiveness rate and the vaccination effectiveness time, the resurgence probability decreased (Fig. S1).

Discussion

The major result of this modeling study is that gradual relaxation of NPIs, such as large-scale detection and quarantine, would be safe as vaccine coverage increased. In particular, for the transmission of wild strain in a city with a population of 20 million, NPIs can be relaxed when vaccine coverage reaches 50.42%. The outcomes will be improved if the vaccination strategy was accelerated or high-risk groups were given priority.

Consistent with previous studies [52–55], our results suggested that the relaxation of NPIs before establishment of sufficient immunity increased the probability of COVID-19 resurgence (maximum daily infected cases and the number of deaths). In particular, our model indicated that if vaccine effectiveness was 79.34%, vaccine coverage must be 50.42% before NPIs can be fully relaxed. Before vaccine coverage reaches 50.42%, NPIs still had a significant impact in preventing resurgence, and some NPIs were still needed even if vaccine coverage increased. However, once vaccine coverage reached 50.42%, almost all NPIs can be relaxed, and when coverage reached 75.62%, resurgence was very unlikely. We also estimated that 8 months are needed to achieve the vaccine

coverage threshold for the fully relaxation of NPIs in the combination of accelerated vaccination strategy and key groups firstly strategy. However, if we conduct a slow vaccination strategy, NPIs would not be fully liberalized in three years. The vaccination coverage threshold 50.42% was estimated based on the transmissibility of wild strain and the vaccine efficacy against wild strain infection. Although there were some variants of SARA-CoV-2, such as the Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1) and Delta (B.1.617) variant, the protection of COVID-19 vaccine seems to retain against the disease [51]. While some study found that the COVID-19 vaccine effectiveness against the Beta variant was lower [56–58]. As our results suggested that with the increasing of transmissibility of variants and the possible decreasing of vaccine effectiveness, the vaccine coverage threshold for safely relaxing NPIs would be higher. As scientists around the world learn more about the Delta variant of the novel coronavirus, they have been finding that it is more transmissible than the variants that have preceded it [51, 59], further implying the need of speeding up vaccination.

A localized COVID-19 outbreak occurred in Guangzhou on May 21, 2021 and on May 31, 2021, there were 34 symptomatic cases and 8 asymptomatic infections [60]. According to public data, we estimated that vaccine coverage was 40% (effective vaccinated population: 31.74%) in Guangzhou on May 23, 2021. If Guangzhou implemented moderate NPIs, in particular if the MDT was 7 to 8 days, the probability of resurgence was 30–60%. This suggested that NPIs, such as the social distancing, large-scale nucleic acid testing, close contact tracking, and centralized isolation, still played a significant role in reducing the probability of resurgence and controlling local resurgences before the vaccine coverage threshold was attained. On 29 May 2021, there were 12 COVID-19 asymptomatic infections in Guangzhou [60], which had met the criteria of resurgence. However, even if Guangzhou lifted all NPIs, the resurgence probability was estimated about 90%. Those facts suggested that the virus might be more infectious, or the efficiency of vaccine may be not high enough for the variants. As vaccine coverage increased, the NPIs can be gradually relaxed without increasing the risk of resurgence.

The results of the present study suggested that acceleration of vaccination and targeting high-risk groups could reduce the probability of COVID-19 resurgence, especially when implemented early during the vaccination program. This is consistent with the results of previous studies [55, 61]. Accelerating vaccination is also necessary to prevent the transmission and spread of more contagious SARS-CoV-2 variants [61]. When a high-risk group was given priority, an accelerated vaccination had a greater effect on reducing the number of cases, indicating that rapidly achieving high vaccine coverage was more important. High vaccine coverage and effectiveness provides long-lasting protection and greatly reduces the probability of resurgence [53]. And compared with no vaccination, introducing vaccination had high cost-effectiveness [53].

Vaccine hesitancy is a complex public health issue, and obviously hinders vaccination programs. At the end of March 2020, when the first wave of the COVID-19 outbreak was controlled in China, 67.1 to 91.3% of people were willing to accept the available COVID-19 vaccine [62, 63]. However, in May 2020, 83.5% of people said they had the intent intended to get vaccinated in China, and only 28.7% reported they definitely intended to get vaccinated [64]. Because of the successful control of the COVID-19 outbreak and the low incidence rate of COVID-19 in China, many people believed that vaccination was unnecessary [62]. Our results suggested that there is a high probability of resurgence if the NPIs are relaxed before the target vaccine coverage is achieved. Therefore, to reduce vaccine hesitancy, it is necessary to educate the general public about the safety, benefits, and importance of vaccination. There are evidences that individuals at high-risk have greater acceptance of the vaccine [62]. Our results indicated it is essential to improve vaccine coverage for these high-risk individuals as soon as possible to prevent resurgence.

There are some limitations of the current study. Our model did not consider the characteristics of the population, such as age, sex, and occupation. A heterogeneous population might influence vaccine coverage. Thus, a more sophisticated model, such as an agent-based model, is more suited for addressing the issue of population heterogeneity.

In conclusion, our study estimated that vaccine coverage of 50.42% was needed before NPIs can be fully relaxed. As vaccine coverage increases, the NPIs can be gradually relaxed. Until that threshold is reached, however, strict NPIs are still needed to contain the epidemic. An accelerated vaccination strategy was the most effective measure for preventing resurgence, followed by providing vaccination to high-risk groups. Targeting of high-risk groups for vaccination may be the best approach if there are insufficient vaccine doses. The more transmissible SARS-CoV-2 variant lead to higher resurgence probability, which indicates the importance of accelerated vaccination and achieving the vaccine coverage earlier.

Conclusion

With the application of COVID-19 vaccine, people are concerned about when and how to relax from the high cost strict non-pharmaceutical interventions (NPIs). The study suggested that for the transmission of wild strain in a city with a large population, NPIs could be relaxed when vaccine coverage reached 50.42% (effective vaccine coverage reached 40%), if the vaccine effectiveness is 79.34%. Once the NPIs was lifted before the vaccine coverage reached 50.42%, the resurgence probability would increase. However, with the increasing of variants transmissibility and the decline of vaccine effectiveness for variants, the threshold for lifting NPIs would be higher. We estimated that more than 8 months were needed to achieve the vaccine coverage threshold in the combination of accelerated vaccination strategy and key groups firstly strategy. Without a robust COVID-19 vaccination program, NPIs would not be fully liberalized in three years. With the increasing of transmissibility of SARS-CoV-2 variants and the possible decreasing of vaccine effectiveness, the vaccine coverage threshold for safely relaxing NPIs would be higher, implying a need of speeding up vaccination to prevent and control the variants with increased transmissibility.

Abbreviations

COVID-19: Coronavirus disease 2019

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

NPIs: non-pharmaceutical interventions

SIRS: Susceptible Infectious Recovered Susceptible

MC simulation: Monte Carlo simulation

95%CI: 95% Confidence interval

MDT: Mean detection time

CDC: Centers for Disease Control and Prevention

WHO: World Health Organization

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

Authors declare that they have no competing interests.

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Authors' contributions

JHP, WLZ, YY, and WBW designed and conceived the study. JHP, YY, and WBW developed the stochastic calculus model and conducted the analysis. WLZ, JT, ZXL, and AX collected the data. JHP and WLZ drafted the manuscript, with all authors contributing to interpretation and critical revision of the work and approving the final manuscript. YY and WBW act as the guarantors.

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Figures

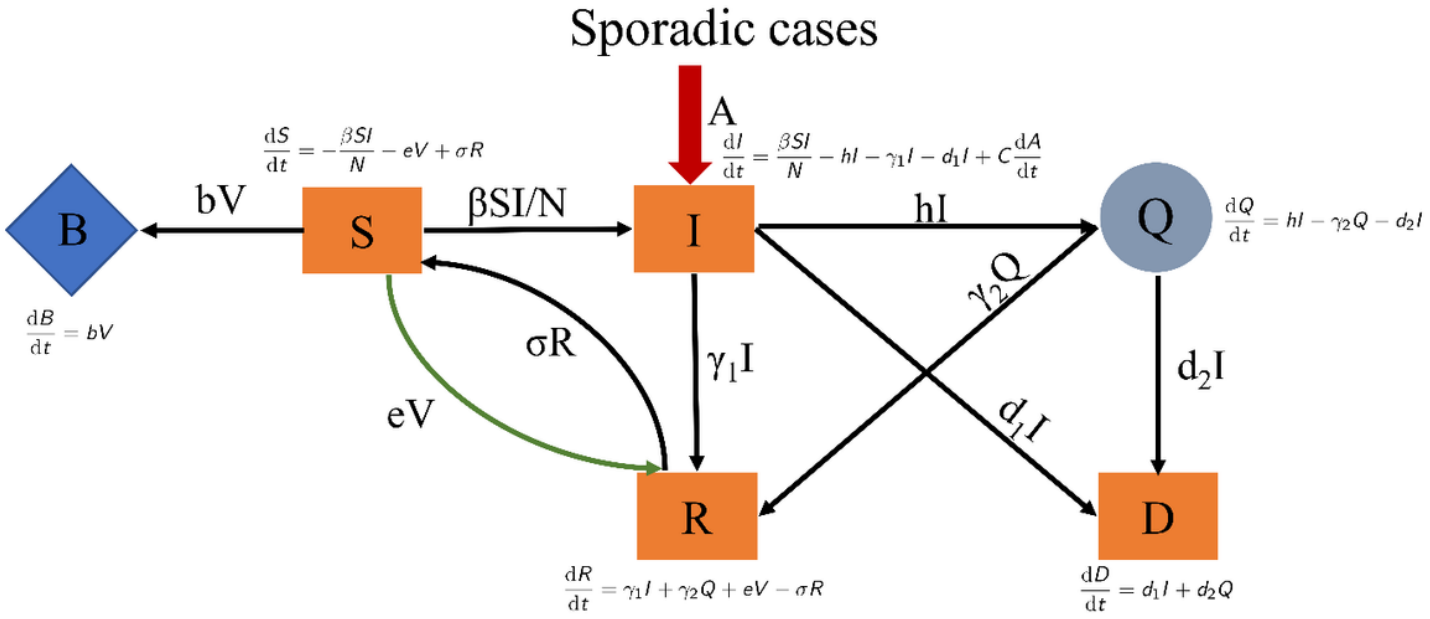

Figure 1

The BSIQDRS model. We extended the classic SIRS model to include six compartments: susceptible (S), adverse reactions (B), infectious (I), quarantined cases (Q), removed (R), and deaths due to COVID-19(D). Each compartment attached an equation in the model.

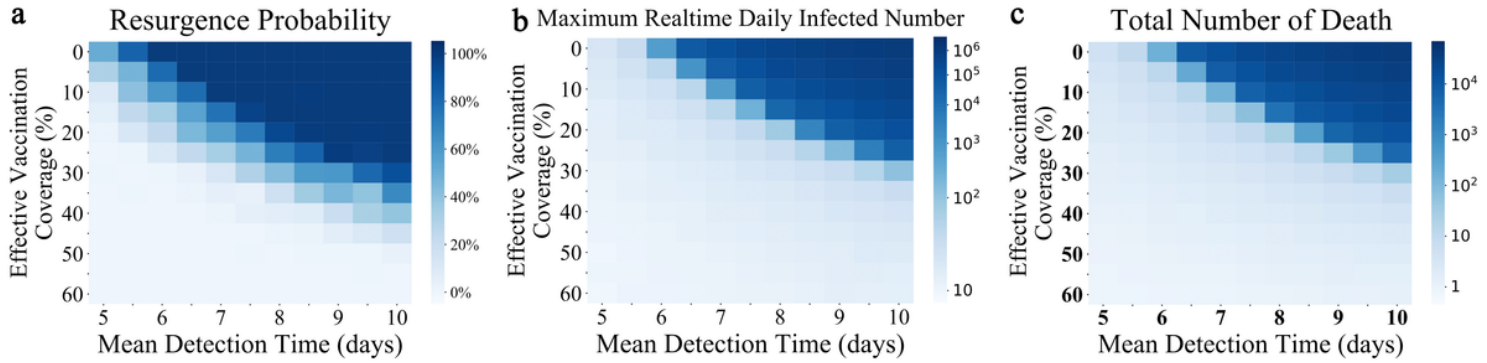

Figure 2

Joint effects of NPIs and vaccination on resurgence probability (a), daily infections (b), and total deaths (c). For each plot, each row represents a different NPIs intensity (Mean detection time) and each column represents effective vaccination coverage (percentage of the total population to be vaccinated multiply vaccine effective rate). Colors represent the probability of resurgence / maximum daily infected number / total death number, ranging from 0 (white) to 100% / 10^6 / 10^5 (blue).

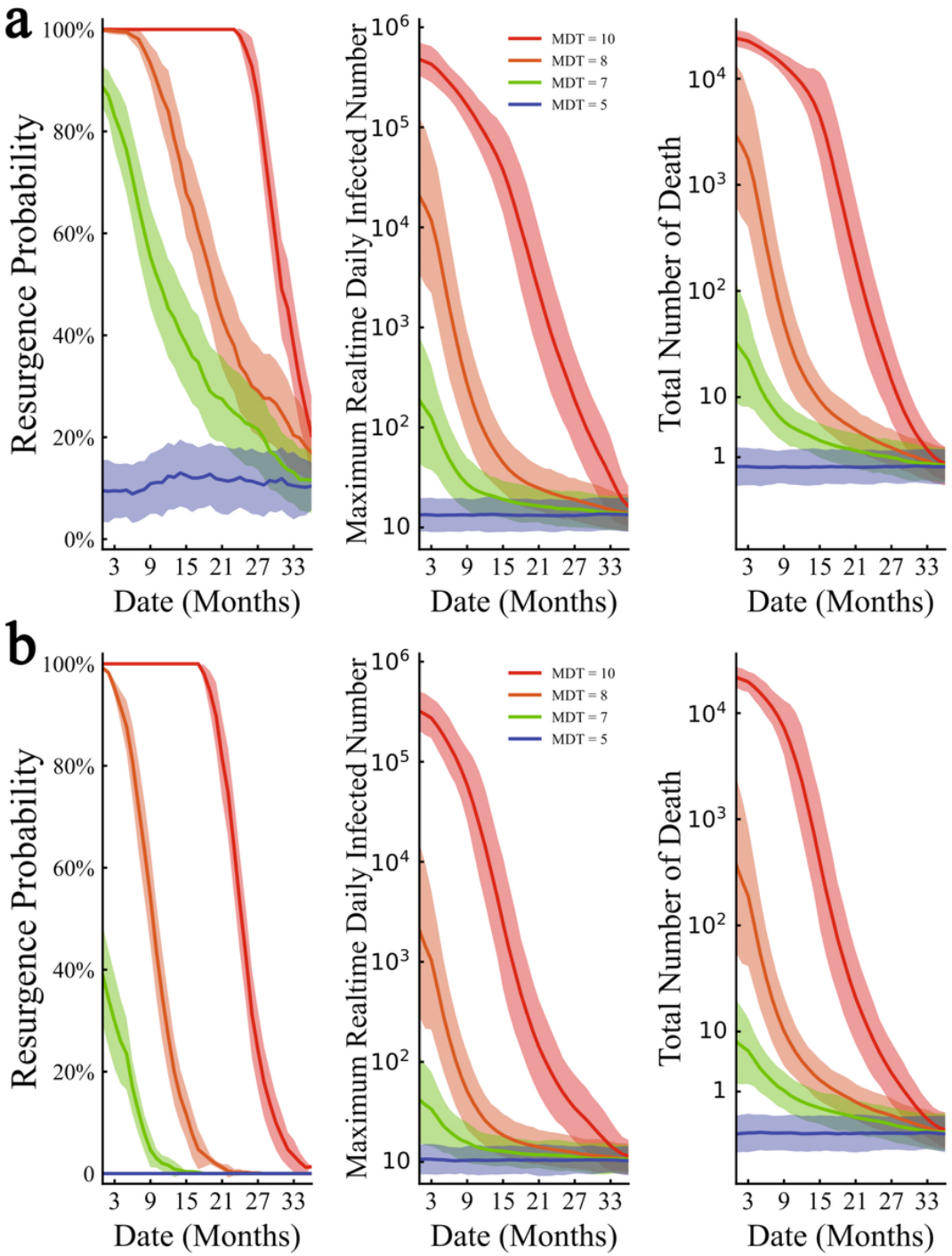

Figure 3

Effect of relaxing NPIs under no priority vaccination strategy (a) and high-risk population first vaccination strategy (b) on resurgence probability, daily infections, and total deaths when there were 5 million vaccine doses per year. Colors represent different NPIs intensity (Mean detection time), ranging from 5 (purple, “baseline”) to 10 (red). For each plot, each row represents the date to lift NPIs (months, from the day of vaccination) and each column represents resurgence probability, daily infections, and total deaths. The dashed line represents resurgence probability, daily infections, and total deaths when lifting NPIs, the shaded area represents averaged results of MC simulations with 95% confidence interval.

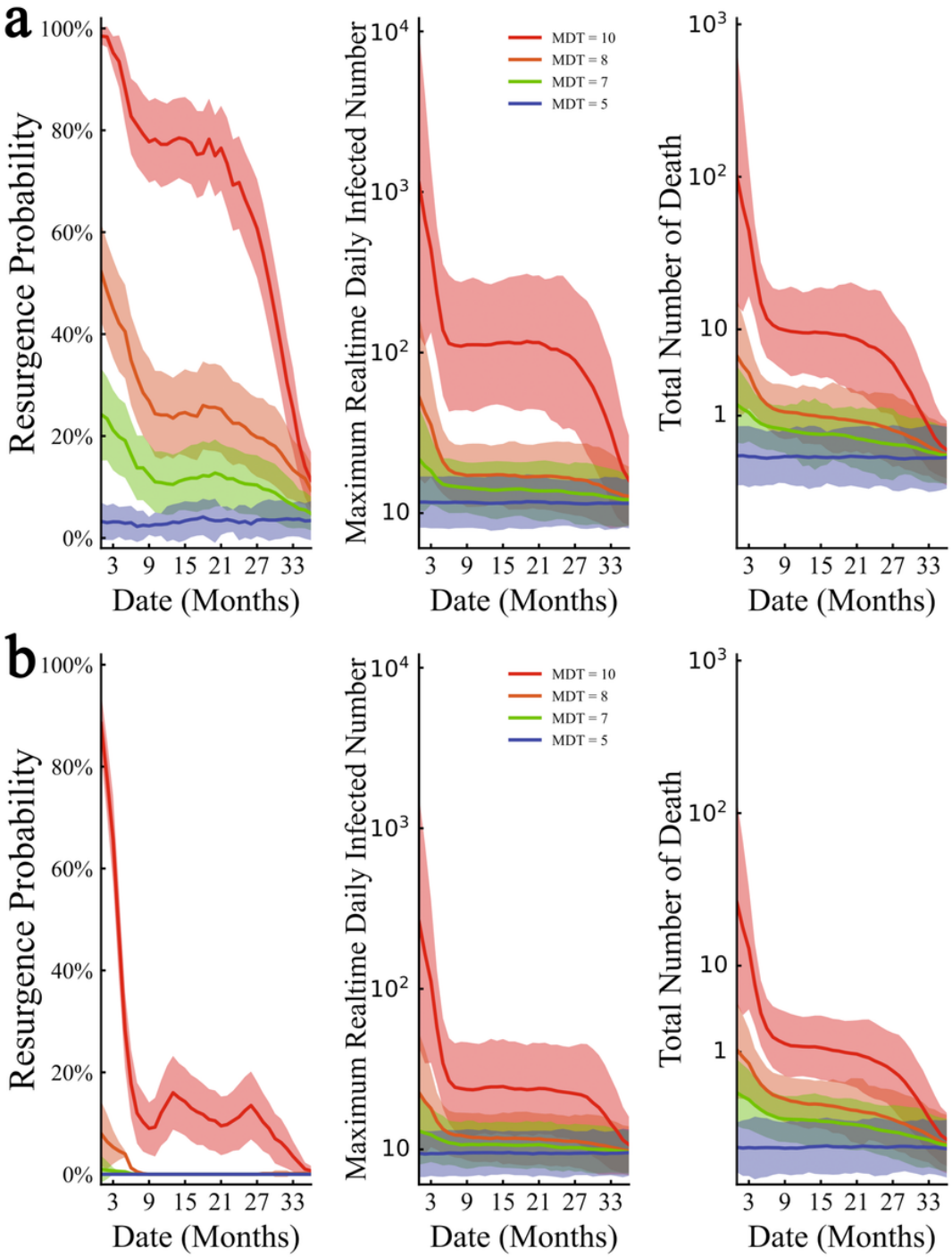

Figure 4

Effect of relaxing NPIs under no priority vaccination strategy (a) and high-risk population first vaccination strategy (b) on resurgence probability, daily infections, and total deaths when there were 16 million vaccine doses during the first year. Colors represent different NPIs intensity (Mean detection time), ranging from 5 (purple, “baseline”) to 10 (red). For each plot, each row represents the date to lift NPIs (months, from the day of vaccination) and each column represents resurgence probability, daily infections, and total deaths. The dashed line represents resurgence probability, daily infections, and total deaths when lifting NPIs, the shaded area represents averaged results of MC simulations with 95% confidence interval.

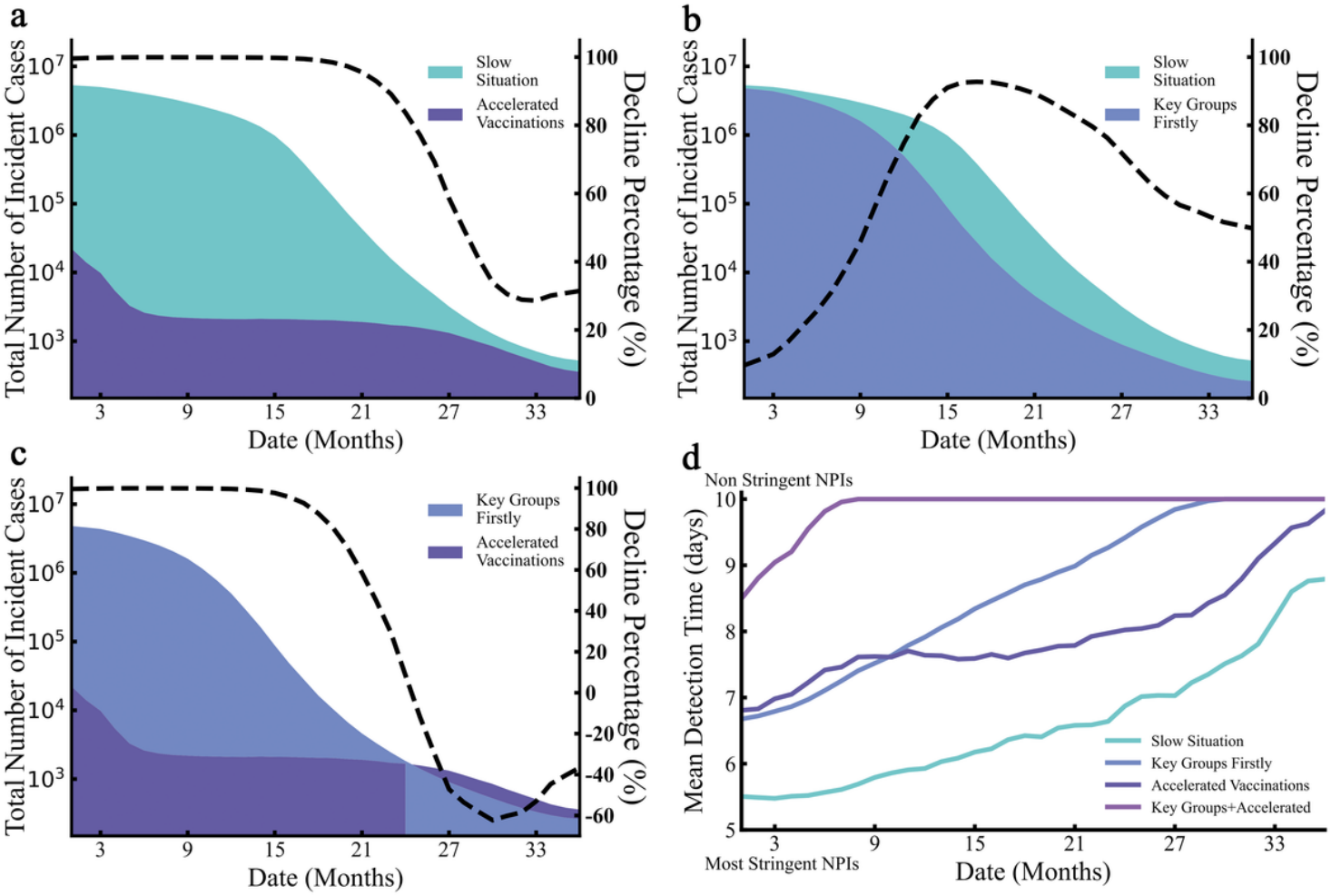

Figure 5

Comparison of different vaccination strategies. For each plot, each row represents the date to lift NPIs (months, from the day of vaccination) and each column represents total incidence number (a, b, and c), and different NPIs intensity (d). Colors represent different vaccination strategies.

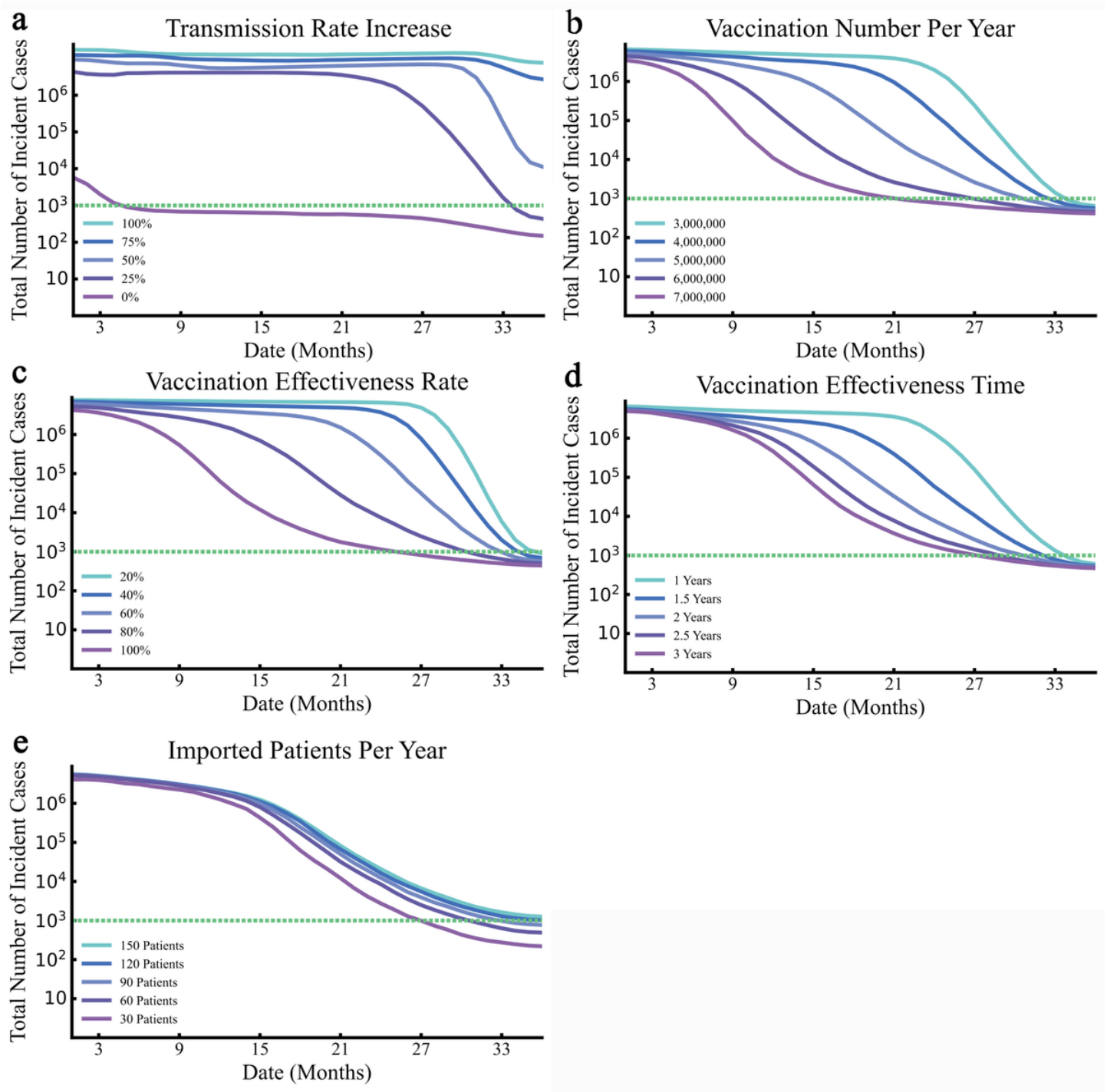

Figure 6

Sensitivity analyses on transmission rate (a), vaccination number per year (b), vaccination effectiveness rate (c), vaccination effectiveness time (d) and imported patients per year (e). For each plot, each row represents the date to lift NPIs (months, from the day of vaccination) and each column represents total incidence number. Colors represent different scenarios of every parameters. Horizontal dotted line in each plot represents the threshold of total incidence number (1000 cases).

Supplementary Files

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- SupplementaryMaterials.docx