Supplementary Information: The resurgence risk of COVID-19 in the presence of immunity waning and ADE effect: a mathematical modelling study

Weike Zhou[a,1], Biao Tang[b,1], Yao Bai[c,1], Yiming Shao[d,e], Yanni Xiao[b,*], Sanyi Tang[a,*]

[a]*School of Mathematics and Statistics, Shaanxi Normal University, Xi'an, 710119, P.R. China*
[b]*School of Mathematics and Statistics, Xi'an Jiaotong University, Xi'an, 710049, P.R. China*
[c]*Department of Infection Disease Control and Prevention, Xi'an Center for Disease Prevention and Control, Xi'an, 710043, P.R. China*
[d]*State Key Laboratory for Infectious Disease Prevention and Control, National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, 102206, P.R. China*
[e]*Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Hangzhou, 310058, P.R. China*

S1. Full structure model

The full modelling framework includes the infection and transmission dynamic of COVID-19 and the two-doses vaccination program and immunity waning dynamic.

Transmission progression: We used an *SEIAHR* model structure to describe the transmission dynamics of COVID-19. That is, according to the epidemic status of COVID-19 infections, the total population is divided into susceptible (S), exposed (E), symptomatic infected (I), asymptomatic infected (A), hospitalized (H), recovered (R) classes [1–4]. The susceptible population will enter into the exposed class (E) once they are infected by symptomatic or asymptomatic infected population. The exposed individuals move to I or A at a rate of σ. And we assume that the probability of showing symptoms is ρ. The recovery rates of I and A are set to be γ_I and γ_A, respectively. Given the immunity waning, the recovered population can become susceptible again. The transmission diagram with the mass vaccination program is shown in Fig. 1 in the main text.

Vaccination program for susceptible population: Susceptible population (S), will be firstly vaccinated by one-dose at a rate v_1. The effective protection rate by one-dose is p_1, hence, the part $p_1 v_1$ can be effectively protected and temporarily immune to COVID-19, and the class

*Corresponding author
Email addresses: yxiao@mail.xjtu.edu.cn (Yanni Xiao), sytang@snnu.edu.cn (Sanyi Tang)
[1]Equal Contributor

is denoted by V_1. The rest part ($(1-p_1)v_1$) remains in the susceptible class, which is denoted by S_{V_1}. The population vaccinated by one-dose will be further vaccinated by a second dose after a pre-set period since the first dose. Similarly, we set a protection rate of the second dose as p_2. Once vaccinated by the second dose, individuals will either move to the class effectively protected (denoted by V_2), or to the class susceptible to COVID-19 (denoted by S_{V_2}). We assume that the population effectively protected by one-dose (the persons in V_1), will all move to V_2 when they receive the second dose. It should be mentioned that the population vaccinated but not immune to COVID-19 (S_{V_1}, S_{V_2}) can be infected. Then according to the epidemic status, we further have the classes of $E_j, I_j, A_j, R_j, j \in \{V_1, V_2\}$.

Immunity waning and ADE effects: As we mentioned in the introduction, lots of evidence suggest that the neutralizing antibodies decay significantly since the onset of symptoms of COVID-19 patients, indicating the existence of immunity waning. Given the immunity waning, we assume that both the recovered and effectively vaccinated population can temporarily immune to COVID-19, and will return back to susceptible classes. In particularly, we assume that the individuals in V_1 will move to $S_{V_{1\omega}}$ due to the waning of immunity, and the population in R, R_{V_1}, R_{V_2}, V_2 will move to $S_{V_{2\omega}}$. Correspondingly, the rate of immunity waning are denoted by $\omega_i, i \in \{R, R_{V_1}, R_{V_2}, V_1, V_2\}$. On the other hand, as the decay of the neutralizing antibodies, the binding antibodies can dominant the immune response, which will enhance the infectivity of the virus (i.e. ADE effects). That is, compared with other susceptible population, the susceptibility of $S_{V_{1\omega}}$ and $S_{V_{2\omega}}$ is much higher as the pre-existing of immunity. Here, we denote κ as the modification factor of the susceptibility of the individuals who have lost their immunity.

Based on the above assumptions, the model equations can be written as:

$$
\begin{aligned}
\frac{dS}{dt} &= -\beta S\frac{I+I_{V_1}+I_{V_2}+\theta(A+A_{V_1}+A_{V_2})}{N} - v_1 S,\\
\frac{dE}{dt} &= \beta S\frac{I+I_{V_1}+I_{V_2}+\theta(A+A_{V_1}+A_{V_2})}{N} - \sigma E,\\
\frac{dI}{dt} &= \rho\sigma E - \gamma_I I - \delta_I I,\\
\frac{dA}{dt} &= (1-\rho)\sigma E - \gamma_A A,\\
\frac{dH}{dt} &= \delta_I I - \gamma_H H - \alpha H,\\
\frac{dR}{dt} &= \gamma_A A + \gamma_I I + \gamma_H H - \omega_R R,\\
\frac{dV_1}{dt} &= p_1 v_1 S - v_2 V_1 - \omega_{V_1} V_1,\\
\frac{dV_2}{dt} &= v_2 V_1 + p_2 v_2 S_{V_1} + p_3 v_2 S_{V_{1\omega}} - \omega_{V_2} V_2,\\
\frac{dS_{V_{1\omega}}}{dt} &= \omega_{V_1} V_1 - \kappa\beta S_{V_{1\omega}}\frac{I+I_{V_1}+I_{V_2}+\theta(A+A_{V_1}+A_{V_2})}{N} - v_2 S_{V_{1\omega}},\\
\frac{dS_{V_{2\omega}}}{dt} &= -\kappa\beta S_{V_{2\omega}}\frac{I+I_{V_1}+I_{V_2}+\theta(A+A_{V_1}+A_{V_2})}{N} + \omega_{R_{V_1}} R_{V_1} + \omega_{R_{V_2}} R_{V_2} + \omega_R R + \omega_{V_2} V_2,\\
\frac{dS_{V_1}}{dt} &= (1-p_1) v_1 S - \beta S_{V_1}\frac{I+I_{V_1}+I_{V_2}+\theta(A+A_{V_1}+A_{V_2})}{N} - v_2 S_{V_1},\\
\frac{dE_{V_1}}{dt} &= (\kappa\beta S_{V_{1\omega}} + \beta S_{V_1})\frac{I+I_{V_1}+I_{V_2}+\theta(A+A_{V_1}+A_{V_2})}{N} - \sigma E_{V_1},\\
\frac{dI_{V_1}}{dt} &= \rho\sigma E_{V_1} - \gamma_I I_{V_1} - \delta_I I_{V_1},\\
\frac{dA_{V_1}}{dt} &= (1-\rho)\sigma E_{V_1} - \gamma_A A_{V_1},\\
\frac{dH_{V_1}}{dt} &= \delta_I I_{V_1} - \gamma_H H_{V_1} - \alpha H_{V_1},\\
\frac{dR_{V_1}}{dt} &= \gamma_A A_{V_1} + \gamma_I I_{V_1} + \gamma_H H_{V_1} - \omega_{R_{V_1}} R_{V_1},\\
\frac{dS_{V_2}}{dt} &= (1-p_2) v_2 S_{V_1} + (1-p_3) v_2 S_{V_{1\omega}} - \beta S_{V_2}\frac{I+I_{V_1}+I_{V_2}+\theta(A+A_{V_1}+A_{V_2})}{N}\\
\frac{dE_{V_2}}{dt} &= (\kappa\beta S_{V_{2\omega}} + \beta S_{V_2})\frac{(I+I_{V_1}+I_{V_2}+\theta(A+A_{V_1}+A_{V_2}))}{N} - \sigma E_{V_2},\\
\frac{dI_{V_2}}{dt} &= \rho\sigma E_{V_2} - \gamma_I I_{V_2} - \delta_I I_{V_2},\\
\frac{dA_{V_2}}{dt} &= (1-\rho)\sigma E_{V_2} - \gamma_A A_{V_2},\\
\frac{dH_{V_2}}{dt} &= \delta_I I_{V_2} - \gamma_H H_{V_2} - \alpha H_{V_2},\\
\frac{dR_{V_2}}{dt} &= \gamma_A A_{V_2} + \gamma_I I_{V_2} + \gamma_H H_{V_2} - \omega_{R_{V_2}} R_{V_2}.
\end{aligned}
\tag{S1}
$$

Here, N is the whole population in the considered region. The equations for S, E, I, A, H, R represent the infection and transmission dynamic in the non-vaccinated population, the equations for $S_{V_1}, E_{V_1}, I_{V_1}, A_{V_1}, H_{V_1}, R_{V_1}$ represent the infection and transmission dynamic in the population vaccinated with the first dose vaccine, the equations for $S_{V_2}, E_{V_2}, I_{V_2}, A_{V_2}, H_{V_2}, R_{V_2}$ represent the infection and transmission dynamic in the population vaccinated with two doses vaccine. V_1 and V_2 are the population effectively protected by the first dose and two doses vaccine, respectively, who would not evolve in the transmission dynamic but will lose the immunity with rate ω_{V_1} and ω_{V_2}, respectively. $S_{V_{1\omega}}, S_{V_{2\omega}}$ are the population lost the immunity and are more susceptible to

the infection due to ADE effect. The detailed definitions of all the parameters are listed in Table 1.

Using the next generation matrix method, we can firstly calculate the basic reproduction number [5]. Then subsisting the time-varying parameters and variables into the basic reproduction number, we can obtain the effective reproduction number of model (S1), which is given by

$$R_t = R(t) = \beta \left(\frac{\rho}{\delta_I + \gamma_I} + \frac{\theta(1-\rho)}{\gamma_A} \right) \frac{S(t) + S_{v_1}(t) + S_{V_2}(t) + \kappa S_{V_{1\omega}}(t) + \kappa S_{V_{2\omega}}(t)}{N(t)}. \quad \text{(S2)}$$

S2. Data

We obtained the data of the COVID-19 epidemic, and the data of the mass vaccination program in mainland China from the National Health Commission of the People's Republic of China [6] and Our World in Data [7], which include the number of daily confirmed cases and deaths from January 23, 2020 to April 8, 2020 (Fig. S1 (a) and S1 (b)), the cumulative vaccine doses administered and the daily vaccine doses administered from December 15, 2020 to June 29, 2021 (Fig. S1 (c) and S1 (d)). It should be mentioned that the vaccination data is available from December 15, 2020 with a report of accumulative 1,500,000 doses used in the population. However, during the period from December 15, 2020 to March 23, 2021, the data was not released daily, hence is intermittent. Since March 23, 2021, the vaccination data was reported per day.

S3. Model calibaration

To calibrate the model, we firstly use the data of the COVID-19 epidemic from January 23, 2020 to April 8, 2020 in mainland China to estimate the parameters related to transmission dynamics. As there is no vaccination during this period, the full model can be reduced to a model without vaccination.

$$\begin{aligned}
\frac{dS}{dt} &= -\beta(t) S \frac{I+\theta A}{N}, \\
\frac{dE}{dt} &= \beta(t) S \frac{I+\theta A}{N} - \sigma E, \\
\frac{dI}{dt} &= \rho\sigma E - \delta_I(t) I - \gamma_I I, \\
\frac{dA}{dt} &= (1-\rho)\sigma E - \gamma_A A, \\
\frac{dH}{dt} &= \delta_I(t) I - \gamma_H H - \alpha H, \\
\frac{dR}{dt} &= \gamma_I I + \gamma_A A + \gamma_H H.
\end{aligned} \quad \text{(S3)}$$

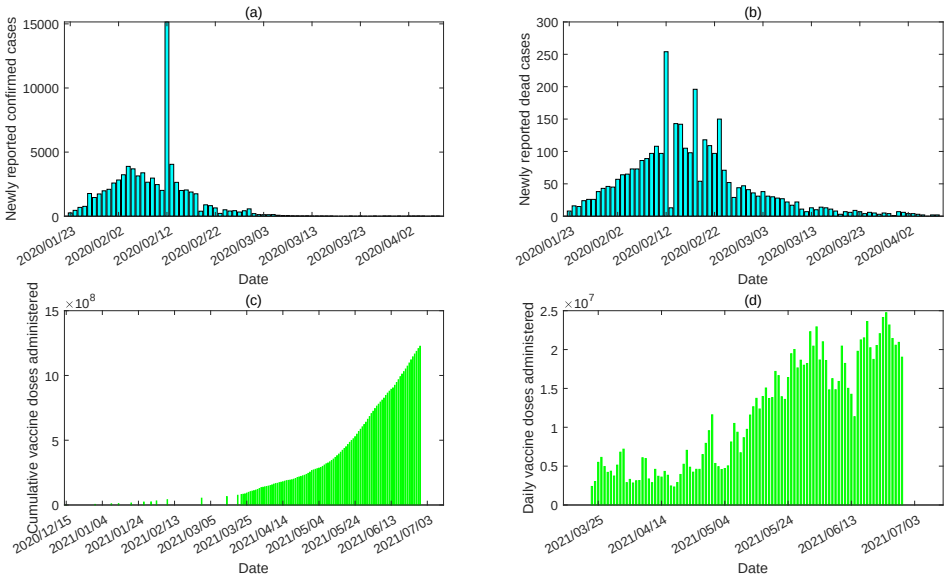

Figure S1: The epidemic data of COVID-19 in mainland China from January 23, 2020 to April 8, 2020 ((a)-(b)), and the vaccine doses administered in mainland China from December 15, 2020 to June 29, 2021 ((c)-(d)). (a) Daily reported confirmed cases; (b) Daily reported dead cases; (c) Cumulative vaccine doses administered; (d) Daily vaccine doses administered.

Note that, because the epidemic lasted less than four months and only a very small proportion of the whole population was infected, we didn't consider the immunity waning in the reduced model. Considering the continuously enhanced control interventions implemented by the government, we introduced a time-dependent transmission rate and diagnose rate. In detail, the transmission rate β is set to be a decreasing function of time t with the following form

$$\beta(t) = (\beta_0 - \beta_1)e^{-r_b t} + \beta_1, \tag{S4}$$

where β_0 is the initial transmission rate, β_1 is the minimum transmission rate, and r_b is the exponential decreasing rate of the transmission rate. Similarly, we set the diagnose rate is a increasing function of time t with the following form

$$\delta_I(t) = (\delta_{I_0} - \delta_{I_1})e^{-r_d t} + \delta_{I_1}. \tag{S5}$$

where δ_{I_0} is the initial diagnose rate, δ_{I_1} is the maximum diagnose rate, and r_d is the exponential increasing rate of the diagnose rate. t_0 corresponds to January 23, 2020.

Model (S3) with (S4) and (S5) can be used to describe the transmission dynamic of the

COVID-19 epidemics in mainland China in 2020, with the gradually improved and enhanced non-pharmaceutic interventions (NPIs), and without vaccination. Therefore, model (S3) can be used to fit the epidemic data of COVID-19 epidemic in mainland China in 2020, to obtain the values of parameters related to the disease transmission. To this end, we first fixed several parameters from the literature and initial values from the database, as listed in Table 1. Given the randomness of reported cases, we used a bootstrap method to generate 1000 time series of daily confirmed cases and deaths from a Poisson distribution with mean given by the reported data, hence we obtained 1000 data set. We then use the least square method to fit the model to each data set.

The fitting results of the transmission dynamic model (S3) to the epidemic data of mainland China in 2020 are shown in Fig. S2, with the best fitting curves marked as black. Based on the fitting results, we obtained the estimation of the unknown parameters (listed in Table 1), and also the estimated effective reproduction number (Fig. S2(c)).

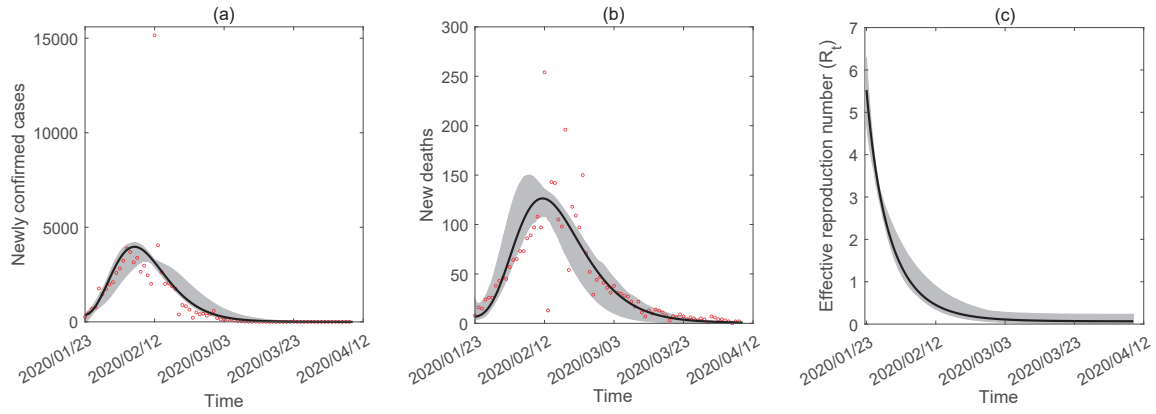

Figure S2: Model fitting results for the transmission dynamic model in mainland China in 2020. (a) The daily reported confirmed cases. (b) The daily reported dead cases. (c) The estimated effective reproduction number. The black curves are the estimated curves with the shadow areas as the corresponding 95% confidence intervals. The red circles in (a) and (b) are the observed data of the daily reported confirmed cases and the daily reported dead case from January 23, 2020 to April 8, 2020 in mainland China.

We further used the vaccination data in mainland China from December 15, 2020 to June 29, 2021 to estimate the parameters related to the mass vaccination program in China. Since the initiation of the vaccination program, it has already taken more than 9 months to vaccinate against COVID-19 in mainland China. Therefore, the vaccination program is also a dynamic process. To model the vaccination dynamic without the transmission dynamic, a three-compartment model reduced from the full modelling framework (S1) was derived. The three

compartments are the population without vaccination (S), the population got the first vaccine dose (S_1) and the population who have received the second vaccine dose (S_2), respectively. Then the model is given by:

$$\begin{aligned} \frac{dS}{dt} &= -v_1(t)S, \\ \frac{dS_1}{dt} &= v_1(t)S - v_2 S_1, \\ \frac{dS_2}{dt} &= v_2 S_1. \end{aligned} \tag{S6}$$

where $v_1(t)$ is the time-dependent vaccination rate, as it should be small initially since the availability of the number of vaccine doses was limited at the beginning, and then exponentially increased as the production of COVID-19 vaccines was accelerated, and finally it could plateau to a constant level depending on the daily vaccination capacity. Thus, we assume $v_1(t)$ as a logistic increasing function of time t with the following form:

$$v_1(t) = \frac{v_0 v_b}{v_0 + (v_b - v_0)e^{-r_v t}}. \tag{S7}$$

with t corresponds to the time when the initial time is assumed to be December 15, 2020.

Considering the initial accessability of vaccines and the capacity of daily vaccination population, we set the rate, at which the population receive the first dose, as a logistic function of time. In contrast, the rate at which the individuals get the second dose is fixed as a constant. Note that the second doses is requested to be vaccinated in 3-8 weeks in China [8], hence we set $v_2 = \frac{1}{35}$. Based on the vaccination data, the initial time is set as December 15, 2020, and the initial conditions are $S(0) = 1,400,000,000, S_1(0) = 1,500,000, S_2(0) = 0$. Then, by using the similar methods as in fitting the epidemic data, we fitted the vaccination dynamic model to 1000 vaccination data set.

S4. Immunity waning dynamic model without transmission dynamic

Note that immunity waning makes the people who have gained the immunity after vaccination become susceptible again, thus based on model (S1) and incorporating the natural immunity waning into model (S6), we can obtain the following system:

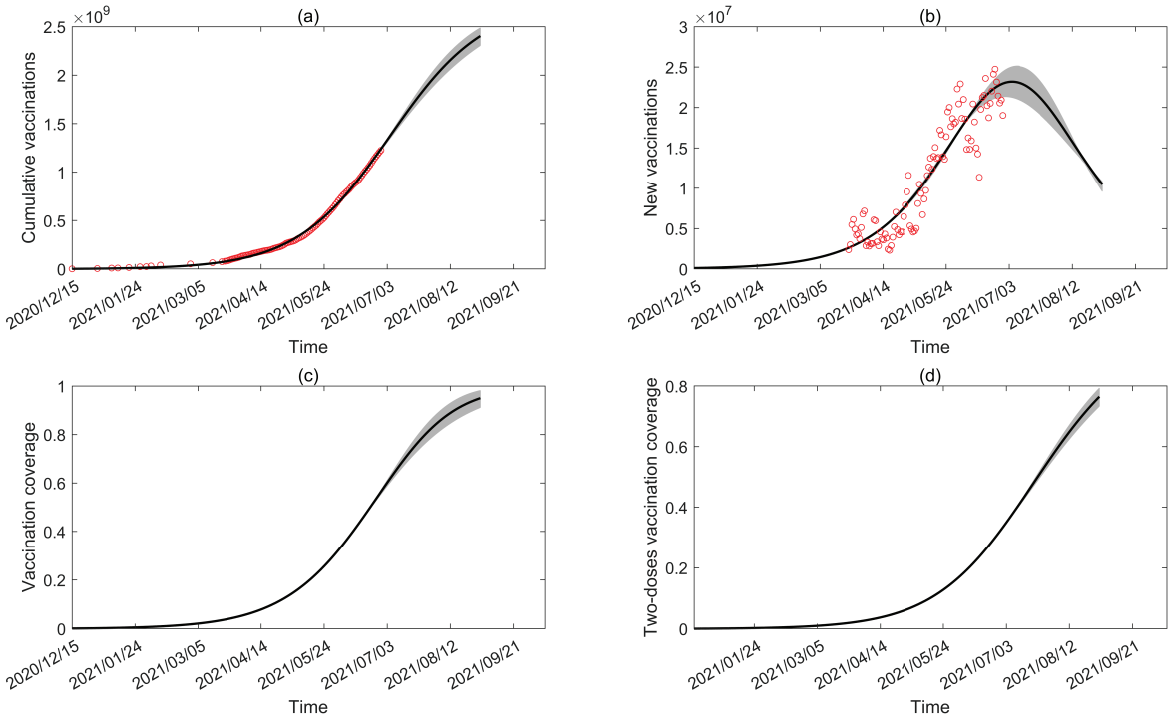

Figure S3: Model fitting results for the vaccination dynamic model. (a) The accumulative number of vaccine doses administered. (2) The daily number of vaccine doses administered. (c) Proportion of population vaccinated with at least one dose. (d) Proportion of population vaccinated with both two doses. The black curves are the estimated curves with the shadow areas as the corresponding 95% confidence intervals. The red circles in (a) and (b) are the reported data of the accumulative vaccine doses and daily vaccine doses administered from December 15, 2020 to June 29, 2021 in mainland China.

$$
\begin{aligned}
\frac{dS}{dt} &= -v_1 S, \\
\frac{dV_1}{dt} &= p_1 v_1 S - v_2 V_1 - \omega_{V_1} V_1, \\
\frac{dV_2}{dt} &= v_2 V_1 + p_2 v_2 S_{V_1} + p_3 v_2 S_{V_{1\omega}} - \omega_{V_2} V_2, \\
\frac{dS_{V_{1\omega}}}{dt} &= \omega_{V_1} V_1 - v_2 S_{V_{1\omega}}, \\
\frac{dS_{V_{2\omega}}}{dt} &= \omega_{V_2} V_2, \\
\frac{dS_{V_1}}{dt} &= (1-p_1) v_1 S - v_2 S_{V_1}, \\
\frac{dS_{V_2}}{dt} &= (1-p_2) v_2 S_{V_1} + (1-p_3) v_2 S_{V_{1\omega}}.
\end{aligned}
\tag{S8}
$$

Then, model (S8) combined the vaccination dynamic and the nature immunity wanning dynamic, but without the transmission dynamic of COVID-19. That is, model (S8) can be used to simulate the vaccination dynamics and the immunity waning dynamic during the pre-epidemic period.

S5. PRCCs of R_s

By plotting the partial rank correlation coefficients (PRCCs) [21], we conducted a sensitivity analysis of R_s with resect to the transmission related parameters $(\beta, \rho, \delta_I, \theta, \gamma_I, \gamma_A)$ and vaccination related parameters $(p_1, p_2, p_3, \omega_{V_1}, \omega_{V_2})$ and the ADE factor κ over time, as shown in Fig. S5 (a). As a results, we found that the transmission rate always have the most significant effect and is positive related to R_s. κ does not dominant before June 13, 2021, which means that ADE almost has no effect in the early stage of the vaccination program, mainly due to the high effectiveness of the vaccine and majority of the population had not been vaccinated. However, κ positively affects the reproduction number significantly after June 13, 2021, attributing to the fact that people vaccinated may lose the immunity and has the ADE after a period of time. In particular, the PRCCs with respect to the vaccination parameters and the ADE factor (Fig. S5)(b) showed that the immunity waning rate ω_{V_1} of those received the first dose is also positive related to R_s, which is high in the initial stage of the vaccination program. The PRCC of the immunity waning rate ω_{V_2} is high in the middle stage of the vaccination program, and the PRCC of the efficacy of two-doses p_2 becomes high in the late stage, illustrating the evolution of the vaccination and immunity waning dynamics.

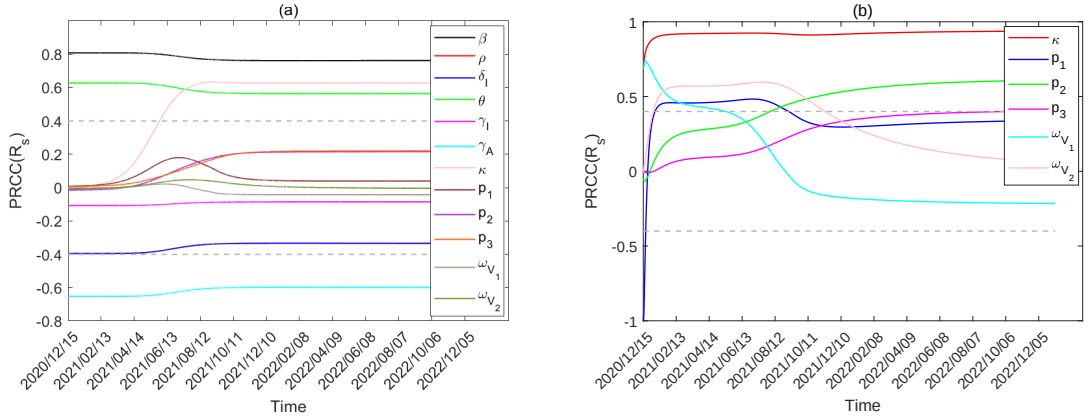

Figure S4: PRCCs of R_s at different introducing time s with respect to: (a) $\beta, \rho, \delta_I, \theta, \gamma_I, \gamma_A, \kappa, p_1, p_2, p_3, \omega_{V_1}, \omega_{V_2}$; (b) $\kappa, p_1, p_2, p_3, \omega_{V_1}, \omega_{V_2}$. Other parameters are fixed as in Table 1.

S6. Theoretical illustration

We will briefly illustrate that the time length it takes for the number of newly confirmed cases reaching kI_0 $(k \geq 1)$ is independent of the number of infected cases introduced, by using a simple *SEIAHR* model in the following. The total population N is divided into 6 classes

S, E, I, A, H, R, namely, $N = S + E + I + A + H + R$. Assume that several infected cases (I_0) are introduced at time s in a fully susceptible population, then the system

$$\begin{aligned}
\frac{dS}{dt} &= -\frac{\beta S(I+\theta A)}{N}, \\
\frac{dE}{dt} &= \frac{\beta S(I+\theta A)}{N} - \sigma E, \\
\frac{dI}{dt} &= \rho\sigma E - \delta_I I - \gamma_I I, \\
\frac{dA}{dt} &= (1-\rho)\sigma E - \gamma_A A, \\
\frac{dH}{dt} &= \delta_I I - \gamma_H H - \alpha H, \\
\frac{dR}{dt} &= \gamma_I I + \gamma_A A + \gamma_H H.
\end{aligned} \tag{S9}$$

has the initial condition $(S(s), E(s), I(s), A(s), H(s), R(s)) = (S_0, 0, I_0, 0, 0, 0)$ at the initial time s, and $I_0 \ll N_0 = S_0 + I_0$. Thus it is reasonable to assume $\frac{S}{N} \approx 1$ in the initial stage of the disease transmission. Then by omitting the equation of S and R, the model can be reduced to

$$\begin{aligned}
\frac{dE}{dt} &= \beta(I + \theta A) - \sigma E, \\
\frac{dI}{dt} &= \rho\sigma E - \delta_I I - \gamma_I I, \\
\frac{dA}{dt} &= (1-\rho)\sigma E - \gamma_A A, \\
\frac{dH}{dt} &= \delta_I I - \gamma_H H - \alpha H,
\end{aligned} \tag{S10}$$

with initial condition $(E(s), I(s), A(s), H(s)) = (0, I_0, 0, 0)$. Denote $e = \frac{E}{I_0}$, $i = \frac{I}{I_0}$, $a = \frac{A}{I_0}$, $h = \frac{H}{I_0}$, system (S10) is equivalent to the following system

$$\begin{aligned}
\frac{de}{dt} &= \beta(i + \theta a) - \sigma e, \\
\frac{di}{dt} &= \rho\sigma e - \delta_I i - \gamma_I i, \\
\frac{da}{dt} &= (1-\rho)\sigma e - \gamma_A a, \\
\frac{dh}{dt} &= \delta_I i - \gamma_H h - \alpha h,
\end{aligned} \tag{S11}$$

with initial value $(0, 1, 0, 0)$. Thus the solution of system (S11) is independent of I_0 and is unique. Assume that t_1 is the time when the number of newly confirmed cases increases to kI_0 for the first time, namely, $\delta_I I(t_1) = kI_0$, then we have $i(t_1) = \frac{k}{\delta_I}$, which is a constant. Thus t_1 as well as $t_1 - s$ is independent of the value of I_0.

[1] B. Tang, X. Wang, Q. Li, N. L. Bragazzi, S. Tang, Y. Xiao, J. Wu, Estimation of the transmission risk of the 2019-ncov and its implication for public health interventions, Journal of clinical medicine 9 (2) (2020) 462.

[2] B. Tang, N. L. Bragazzi, Q. Li, S. Tang, Y. Xiao, J. Wu, An updated estimation of the

risk of transmission of the novel coronavirus (2019-ncov), Infectious disease modelling 5 (2020) 248–255.

[3] B. Tang, F. Xia, S. Tang, N. L. Bragazzi, Q. Li, X. Sun, J. Liang, Y. Xiao, J. Wu, The effectiveness of quarantine and isolation determine the trend of the covid-19 epidemics in the final phase of the current outbreak in china, International Journal of Infectious Diseases 95 (2020) 288–293.

[4] B. Tang, F. Xia, N. L. Bragazzi, Z. McCarthy, X. Wang, S. He, X. Sun, S. Tang, Y. Xiao, J. Wu, Lessons drawn from china and south korea for managing covid-19 epidemic: Insights from a comparative modeling study, ISA Transactions 124 (2022) 164–175.

[5] P. Van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, Mathematical biosciences 180 (1-2) (2002) 29–48.

[6] National Health Commission of the People's Republic of China, Over 1.82 bln doses of covid-19 vaccines administered in china, http://en.nhc.gov.cn/2021-08/13/c_84379.htm (2021).

[7] Our World in Data, Coronavirus (covid-19) vaccinations, https://ourworldindata.org/covid-vaccinations#what-share-of-the-population-has-been-fully-vaccinated-against-covid-19 (2021).

[8] National Health Commission of the People's Republic of China, Infographic: All you need to know about taking covid-19 vaccines, http://en.nhc.gov.cn/2021-04/12/c_83463.htm (2021).

[9] National Bureau of Statistics of China, Main data of the seventh national population census, http://www.stats.gov.cn/english/PressRelease/202105/t20210510_1817185.html (2021).

[10] X. Hao, S. Cheng, D. Wu, T. Wu, X. Lin, C. Wang, Reconstruction of the full transmission dynamics of covid-19 in wuhan, Nature 584 (7821) (2020) 420–424.

[11] J. A. Backer, D. Klinkenberg, J. Wallinga, Incubation period of 2019 novel coronavirus (2019-ncov) infections among travellers from wuhan, china, 20-28 january 2020, Eurosurveillance 25 (5) (2020) 2000062.

[12] Q. Li, X. Guan, P. Wu, Early transmission dynamics in wuhan, china, of novel coronavir-uscinfected pneumonia, The New England Journal of Medicine 382 (13) (2020) 1199–1207.

[13] Sixth Tone, Chinese-developed covid-19 vaccine over 91% effective, turkey says, https://www.sixthtone.com/news/1006620/chinese-developed-covid-19-vaccine-over-91%25-effective%2C-turkey-says (2021).

[14] The University of MelBourne, What are the sinopharm and sinovac vaccines? and how effective are they? two experts explain, https://findanexpert.unimelb.edu.au/news/15054-what-are-the-sinopharm-and-sinovac-vaccines%3F-and-how-effective-are-they%3F-two-experts-explain (2021).

[15] M. D. Tanriover, H. L. Doanay, M. Akova, H. R. Gner, K. Aksu, Efficacy and safety of an inactivated whole-virion sars-cov-2 vaccine (coronavac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in turkey, The Lancet 398 (10296) 213–222.

[16] N. Ferguson, R. Anderson, S. Gupta, The effect of antibody-dependent enhancement on the transmission dynamics and persistence of multiple-strain pathogens, Proceedings of the National Academy of Sciences 96 (2) (1999) 790–794.

[17] D. A. Cummings, I. B. Schwartz, L. Billings, L. B. Shaw, D. S. Burke, Dynamic effects of antibody-dependent enhancement on the fitness of viruses, Proceedings of the National Academy of Sciences 102 (42) (2005) 15259–15264.

[18] B. Adams, E. Holmes, C. Zhang, M. Mammen, S. Nimmannitya, S. Kalayanarooj, M. Boots, Cross-protective immunity can account for the alternating epidemic pattern of dengue virus serotypes circulating in bangkok, Proceedings of the National Academy of Sciences 103 (38) (2006) 14234–14239.

[19] H. J. Wearing, P. Rohani, Ecological and immunological determinants of dengue epidemics, Proceedings of the National Academy of Sciences 103 (31) (2006) 11802–11807.

[20] M. Recker, K. B. Blyuss, C. P. Simmons, T. T. Hien, B. Wills, J. Farrar, S. Gupta, Immunological serotype interactions and their effect on the epidemiological pattern of dengue, Proceedings of the Royal Society B: Biological Sciences 276 (1667) (2009) 2541–2548.

[21] S. Marino, I. B. Hogue, C. J. Ray, D. E. Kirschner, A methodology for performing global uncertainty and sensitivity analysis in systems biology, Journal of theoretical biology 254 (1) (2008) 178–196.

Table S1: Definitions and values of variables and parameters

Variables		Description	Initial value	Resource
S		Susceptible population	1.4×10^9	[9]
E		Exposed population	5926	Estimated
I		Symptomatic infected population	3591	Estimated
A		Asymptomatic infected population	3459	Estimated
H		Hospitalized population	771	data
R		Recovered population	34	data
Parameters		**Description**	**Value**	**Resource**
Parameters related to the disease transmission				
$\beta(t)$	β_0	Transmission rate in the pre-pandemic era	2.8749	Estimated
	β_1	Minimum transmission rate with control strategies	0.0521	Estimated
	r_b	Exponential decreasing rate of the transmission rate	0.1232	Estimated
θ		Relative transmissibility of A to I	0.55	[10]
σ		Progression rate of exposed individuals to infectives	1/5.2	[11, 12]
ρ		Probability of symptomatic	0.4972	Estimated
$\delta_I(t)$	δ_{I_0}	Initial diagnosis rate of infected individuals	0.1	[10]
	δ_{I_1}	Maximum diagnosis rate of infected individuals	0.5848	Estimated
	r_d	Exponential decreasing rate of diagnosis rate from symptom onset to detection	0.1247	Estimated
γ_I		Recovery rate of symptomatic infectives	1/2.9	[10]
γ_A		Recovery rate of asymptomatic infectives	1/2.9	[10]
γ_H		Recovery rate of hospitalized infectives	0.2149	Estimated
α		Disease induced death rate	0.0087	Estimated
Parameters related to the vaccination program and immunity waning				
$v(t)$	v_0	Initial vaccination rate of the first dose	5.0437×10^{-5}	Estimated
	v_1	Minimum vaccination rate of the first dose	0.0585	Estimated
	r_v	Net increasing rate of the vaccination rate of the first dose	0.0338	Estimated
v_2		Vaccination rate of the second dose	1/35	[8]
p_1		Effective protection rate to S by one-dose vaccine	0.3	[13–15]
p_2		Effective protection rate to S_{V_1} by two-doses vaccine	0.9	[13–15]
p_3		Effective protection rate to $S_{V_{1\omega}}$ by two-doses vaccine	0.9	Assumed
ω_i		Immunity waning rate ($i = R, R_{V_1}, R_{V_2}, V_1, V_2$)	1/365	Assumed
κ		Modification factor of susceptibility	[1,3]	[16–20]