Getting jab or regular test: observations from an impulsive epidemic COVID-19 model

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Abstract

Several safe and effective vaccines are available to prevent individuals from experiencing severe illness or death as a result of COVID-19. Widespread vaccination is widely regarded as a critical tool in the fight against the disease. However, some individuals may choose not to vaccinate due to vaccine hesitancy or other medical conditions. In some sectors, regular compulsory testing is required for such unvaccinated individuals. Interestingly, different sectors require testing at various frequencies, such as weekly or biweekly. As a result, it is essential to determine the optimal test frequency and identify underlying factors. This study proposes a population-based model that can accommodate different personal decision choices, such as getting vaccinated or undergoing regular tests, as well as vaccine efficacies and uncertainties in epidemic transmission. The model, formulated as impulsive differential equations, uses time instants to represent the reporting date for the test result of an unvaccinated individual. By employing well-accepted indices to measure transmission risk, including the basic reproduction number, the peaking time, the final size, and the number of severe infections, the study shows that an optimal test frequency is highly sensitive to parameters involved in the transmission process, such as vaccine efficacy, disease transmission rate, test accuracy, and existing vaccination coverage. The testing frequency should be appropriately designed with the consideration of all these factors, as well as the control objectives measured by epidemiological quantities of great concern.

Keywords: Test frequency, epidemiological model, vaccine efficacy, vaccine hesitancy, impulsive differential equation

1 Introduction

⟨sec1⟩ Since the novel coronavirus (SARS-CoV-2) outbreak (COVID-19) was asserted by the World Health Organization (WHO) as a global pandemic in March 11, 2020, most countries have implemented mandatory non-pharmaceutical interventions (NPIs) including social distancing and lock-down strategies to control the transmission [18, 55]. This unforeseen pandemic brought global economic and social activities to a standstill. SARS-CoV-2 vaccines were expected to be the life-saving straw to release the restrictions caused by COVID-19 and get back to normal life. However, on-going COVID-19 mass vaccination failed to establish herd immunity due to imperfect vaccine efficacy and relatively low vaccine coverage in some regions, as well as emerging strains of SARS-CoV-2. In parallel with vaccination, COVID-19 testing can serve as an aided preventive measure during and post vaccination era. Existing COVID-19 tests mainly contain two types: viral test and antibody (serology) test, which can detect current and past infection respectively [22]. Nucleic acid amplification tests (NAAT) and antigen tests are now available viral tests, some of which can produce results in 15-30 minutes [6]. Polymerase chain reaction-based (PCR) tests as a type of NAAT are widely used in most countries. Besides, some types of NAAT and antigen tests can be produced into portable COVID testing kits, which offered a new option for self-testing at home. Before the implementation of mass vaccination, these convenient rapid tests for SARS-CoV-2 have exhibited indispensable roles in identifying infected population especially the asymptomatic and pre-symptomatic individuals [11, 21, 57]. To boost COVID-19 vaccination rate and timely mitigate the spread of constantly emerging new cases, a growing number of local governments have called for compulsory vaccination reporting or regular testing for unvaccinated frontline workers or other public event participants.

The Hong Kong Government recommended all government employees should get vaccine jab starting from August 2, 2021 [39]. Individuals who have contraindications for a particular type of COVID-19 vaccine or medical conditions, as per the guidance provided by the Hong Kong Centre for Health Protection [36], may choose to have regular tests in place of getting vaccinated. Those opting out of receiving vaccination are required to undergo PCR tests using combined nasal and throat swabs at community testing centers every two weeks [39]. All members in some sectors and companies are posed with similar arrangements. In order to resume normal teaching/learning and other campus activities from Semester 1 of 2021/22 academic year, most major universities in Hong Kong set similar arrangements, with surprisingly different testing frequencies, either on a weekly or biweekly basis: weekly testing for students in

The Hong Kong Polytechnic University for face-to-face classes [40] and dormitory residents in The University of Hong Kong [41], while biweekly testing for members in The Hong Kong University of Science and Technology [44], all members in The Chinese University of Hong Kong [42] and Hong Kong Baptist University [43] as well as student-residents in The Education University of Hong Kong [38].

In the global scale, other local governments worldwide have implemented similar compulsory policies regarding vaccination/regular testing. The Singapore government has initiated mandatory Vaccinate or Regular Testing (VoRT) Regime from 1 October 2021, which stipulates medically eligible employees either to be vaccinated against COVID-19 or to undergo regular testing [45]. The selected sectors covering health-care, education, social and food services are subjected to the VoRT regime. The testing frequency is twice a week for unvaccinated employees in selected sectors [45]. The White House have issued an announcement in late October 2021, which required all US federal workers and contractors should either receive coronavirus shots or get regular testing [28]. Before this announcement, some local governments including New York City, the state of California, Los Angeles and other localities have enacted similar policies on city employees [53]. The Occupational Safety and Health Administration (OSHA) have rolled out an emergency temporary standard for enterprises with 100+ employees [12]. Based on this standard, these employers must formulate mandatory vaccination policies to require employees fully vaccinated by January 4, 2022, and unvaccinated employees must get COVID-19 testing at least once per week. Many universities in US including Stanford University [37], UC Davis [47], Clark University [7] and University of Stirling [50] have complied with these requirements. In November 2021, the Canada government rolled out a framework on mandatory COVID-19 vaccination or testing requirements for employees in the core public administration [16]. Before the establishment of this framework, major universities in British Columbia including Simon Fraser University, the University of British Columbia, Thompson Rivers University and the University of Victoria already required their staff/students who did not disclose vaccination status to get regular tests [15]. Although there is no specific official compulsory policies on vaccination/regular testing for non-healthcare workers, the National Health Service (NHS) encouraged everyone (especially unvaccinated) in UK who do not display symptoms of COVID-19 to take regular free rapid COVID-19 testing twice a week from 9 April, 2021 [29]. Some universities in UK, such as University of Oxford [49] and University of Kent [48] have provided regular symptom-free testing per week and twice a week respectively for staff and students using or providing college or University on-site services. More regions with official policies on COVID-19 vaccination/regular testing requirements can refer to Table 1.

Based on comprehensive review of regional policies on vaccination/regular COVID-19 test, the difference in testing frequency poses interesting questions worthy of further exploration: how to judiciously choose the testing

Table 1 Regional policies on vaccination or regular testing for COVID-19

Regions	Policy on Vaccination/Regular testing	Fully vaccination coverage	Testing frequency
Hong Kong	Mandatory for government employees and members in some sectors and companies [39]	67.3 % [31]	per week/ biweekly
Singapore	Mandatory for frontline workers in selected sectors covering health-care, education, social and food services [45]	83.4 % [31]	per week/ twice a week
UK	Mandatory for NHS workers and other care-home workers [29]	69.6 % [31]	twice a week
United States	Mandatory for all federal workers and contractors [28]	59.5 % [31]	per week/ twice a week
Canada	Mandatory for employees in core public administration [16]	78.2 % [31]	regularly, no specific frequency
Egypt	Mandatory for public sector workers [34]	13.7 % [31]	per week
Kazakhstan	Mandatory for people working in groups of 20+ [34]	44.1 % [31]	per week
Philippines	Mandatory for in-office workers and employees in public transportation services [34]	41.1 % [31]	regularly, no specific frequency

⟨tab:policy⟩

frequency and which are the most influential factors determining this choice. Intuitively, the uncertainty in the transmission process, the efficacy of vaccines and the testing efficiency play joint roles in determining the testing frequency. To obtain more accurate answer, a population based model will be formulated in this manuscript. Indeed, a number of mathematical models have been proposed to investigate COVID-19 testing related issues. These model-based studies mainly focused on two topics. Some are seeking the optimal testing strategies for controlling COVID-19 by employing decision analysis approaches [35], statistical models [2], and stochastic individual-based chain-binomial models [10]. Others are investigating the combined effects of regular screening/testing strategy with vaccination and other NPI strategies. Study [17] proposed a mathematical model to compare different testing and isolation strategies and found that weekly screening/PCR testing of health-care workers and other groups with high-risk would effectively reduce the effective reproduction number. Authors in [54] explored the optimal testing time during quarantine that would reduce the probability of post-quarantine transmission. As mass-vaccination campaign was conducted, the study [5] proposed a stochastic compartmental model to evaluate the joint effects of vaccination and asymptomatic testing uptake on containing the spread of SARS-CoV-2 in a university setting.

Compared to previous modelling studies on testing, the novel modeling framework, by incorporating the result reporting date as the time instant of impulsive effect, makes the problem mathematically tractable. Various model parameters in terms of the virus transmission, vaccine efficacy and testing efficiency will be fed to project the optimal test frequency. Further sensitivity analysis will be conducted to illustrate the impact of various factors on determining a cost-effective test frequency.

2 Methodology

We will employ a model-based approach to the problem by first formulating an epidemiological model, and then perform the uncertainty and sensitivity analysis about the impact of test frequency on some epidemiological quantities, such as the basic reproduction number, the peak size of infections, the peaking time, the final epidemic size, and the number of severe cases.

2.1 The epidemiological model

We are going to formulate a compartmental model, by dividing the individuals into different classes or groups and describing how individuals in different compartments in a population interact, based on the feature of the question in the investigation. In the current problem, individuals in the whole population may experience distinct infection stages, vaccination states (vaccinated or unvaccinated), and different testing dates for unvaccinated ones.

It is recognized that COVID-19 vaccines have relative low effectiveness and recent studies showed that COVID-19 vaccines might have failed to generate antibody response in quite a few people including immunosuppressive drug users [51] and solid organ transplant recipients [3]. After getting the COVID-19 vaccine, the host may not get protection due to primary vaccine failure or all-or-nothingness, or vaccines only provide insufficient partial protection to prevent further infection, virus replication, and transmission. Therefore, the vaccinated population in the study sector can be stratified into two groups based on the protection level: vaccinated group V_f with failure efficacy (including individuals who receive no protection from the vaccine) and vaccinated group with partial protection V_p (including individuals who receive partial protection but the vaccine fails to prevent further infection and transmission). The unvaccinated susceptible individuals must have the regular test with a fixed frequency, i.e., one testing round of T days, and report the test result at the $(m+1)$-th day in one round with $m = 0, 1, \cdots, T-1$. Those with positive test results need to self-isolate. SARS-CoV-2 infected people may develop symptoms while some may remain asymptomatic. However, the exact proportions of asymptomatic and symptomatic infections remain uncertain. Therefore, we did not distinguish the asymptomatic and symptomatic infections and explore the well-accepted susceptible-exposed-infectious-removed (SEIR) compartmental structure to account separately for transmission characteristics of each subgroup. The transmission diagram is shown in Figure 1 and related parameters are given in Table 2. In what follows, we give details of the sub-models for different groups with subscripts p, f and m, respectively.

(i) The number of individuals in each compartment in the vaccinated group with partial protection (variables with subscript p) (see Figure 1(a) for the

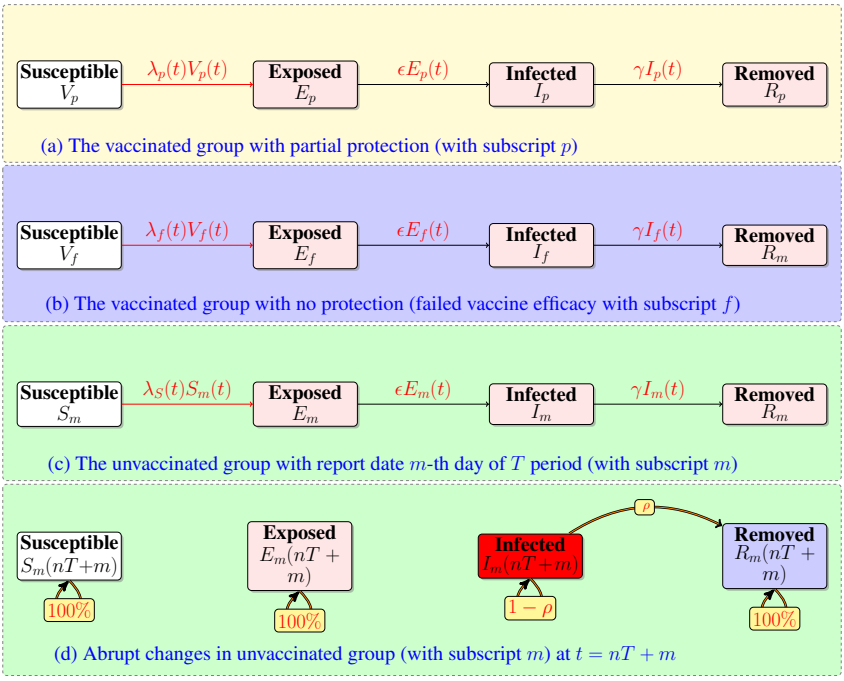

Fig. 1 The diagram for the transition rates of variables for each group with subscripts p, f and m. All parameters are shown in the Table 2 and $\lambda_j(t)$ represents the force of infection for each class $j = S, f, p$.

⟨fig:diagram⟩

transition diagram):

$$\begin{cases} \frac{dV_p(t)}{dt} = -\lambda_p(t)V_p(t), & \text{susceptible, vaccinated with partial protection} \\ \frac{dE_p(t)}{dt} = \lambda_p(t)V_p(t) - \epsilon E_p(t), & \text{latent, vaccinated with partial protection} \\ \frac{dI_p(t)}{dt} = \epsilon E_p(t) - \gamma I_p(t), & \text{infectious, vaccinated with partial protection} \\ \frac{dR_p(t)}{dt} = \gamma I_p(t), & \text{removed, vaccinated with partial protection} \end{cases} \quad (1)$$

Eq:Modelp

(ii) The number of individuals in each compartment in the vaccinated group with no protection (variables with subscript f) (see Figure 1(b) for the transition diagram):

$$\begin{cases} \frac{dV_f(t)}{dt} = -\lambda_f(t)V_f(t), & \text{susceptible, vaccinated with no protection} \\ \frac{dE_f(t)}{dt} = \lambda_f(t)V_f(t) - \epsilon E_f(t), & \text{latent, vaccinated with no protection} \\ \frac{dI_f(t)}{dt} = \epsilon E_f(t) - \gamma I_f(t), & \text{infectious, vaccinated with no protection} \\ \frac{dR_f(t)}{dt} = \gamma I_f(t), & \text{removed, vaccinated with no protection} \end{cases} \quad (2)$$

Eq:Modelf

(iii) The number of unvaccinated individuals receiving regular test (variables with subscript m) (see Figure 1(c) for the transition diagram): Assume that testing results of unvaccinated individuals in group m are reported at the same time instant $nT+m$, then we classify these unvaccinated individuals into T subgroups with subscript notation m, for $m = 0, 1, \cdots, T-1$. Note that here $n \in \mathbb{N}$ represents the $(n+1)$-th round of testing. After getting test, some but possibly not all individuals with high virus loads will be screened out and isolated. Suppose ρ measures the testing efficiency, which represents the proportion of positive cases identified out of all tested individuals, then a proportion of ρ of infected individuals in I_m will be isolated from the community to the removed class R_m. There are abrupt changes in these variables, as sketched in the diagram Figure 1(d), and can be described by impulsive terms mathematically as follows

$$I_m((nT+m)^+) = (1-\rho)I_m(nT+m)$$

while

$$R_m((nT+m)^+) = R_m(nT+m) + \rho I_m(nT+m).$$

However, we should mention that individuals in the same infected status may have distinct testing efficiency rates, which will be determined by the test sensitivity [27], a measure of how well an individual assay can detect viral protein or RNA molecules.

The remaining variables S_m and E_m, stay unchanged, that is

$$S_m((nT+m)^+) = S_m(nT+m) \text{ and } E_m((nT+m)^+) = E_m(nT+m).$$

When $t \neq nT+m$, the number of individuals in each compartment in the unvaccinated group with regular test results reported in the $m+1$-th day for $m = 0, 1, \cdots, T-1$ can be described by the following system (see Figure 1(c) for the transition diagram):

$$\begin{cases} \frac{dS_m(t)}{dt} = -\lambda_S(t)S_m(t), & \text{unvaccinated susceptible} \\ \frac{dE_m(t)}{dt} = \lambda_S(t)S_m(t) - \epsilon E_m(t), & \text{unvaccinated latent} \\ \frac{dI_m(t)}{dt} = \epsilon E_m(t) - \gamma I_m(t), & \text{unvaccinated infectious} \\ \frac{dR_m(t)}{dt} = \gamma I_m(t), & \text{unvaccinated removed} \end{cases} \tag{3}$$

Eq:Modelm

The baseline infection force is assumed as

$$\lambda(t) = \beta \frac{I_f(t) + \sum_{m=0}^{T-1} I_m(t) + \phi_I I_p(t)}{N},$$

where β represents effective transmission rate. Therefore,

$$\lambda_p(t) = \phi_S \lambda(t) \text{ and } \lambda_f(t) = \lambda_S(t) = \lambda(t).$$

Parameters ϕ_S and ϕ_I are used to measure the effects of vaccines on reducing susceptibility and infectiousness of a vaccinated individual.

In summary, the system consisting of (1), (2) and (3) becomes the following one when time $t \neq nT + m$:

$$\begin{cases} \frac{dV_p(t)}{dt} = -\phi_S\beta\frac{(I_f(t)+\sum_{m=0}^{T-1} I_m(t)+\phi_I I_p(t))}{N}V_p(t), \\ \frac{dE_p(t)}{dt} = \phi_S\beta\frac{(I_f(t)+\sum_{m=0}^{T-1} I_m(t)+\phi_I I_p(t))}{N}V_p(t) - \epsilon E_p(t), \\ \frac{dI_p(t)}{dt} = \epsilon E_p(t) - \gamma I_p(t), \\ \frac{dR_p(t)}{dt} = \gamma I_p(t), \\ \frac{dV_f(t)}{dt} = -\beta\frac{(I_f(t)+\sum_{m=0}^{T-1} I_m(t)+\phi_I I_p(t))}{N}V_f(t), \\ \frac{dE_f(t)}{dt} = \beta\frac{(I_f(t)+\sum_{m=0}^{T-1} I_m(t)+\phi_I I_p(t))}{N}V_f(t) - \epsilon E_f(t), \\ \frac{dI_f(t)}{dt} = \epsilon E_f(t) - \gamma I_f(t), \\ \frac{dR_f(t)}{dt} = \gamma I_f(t), \\ \frac{dS_m(t)}{dt} = -\beta\frac{(I_f(t)+\sum_{m=0}^{T-1} I_m(t)+\phi_I I_p(t))}{N}S_m(t), \\ \frac{dE_m(t)}{dt} = \beta\frac{(I_f(t)+\sum_{m=0}^{T-1} I_m(t)+\phi_I I_p(t))}{N}S_m(t) - \epsilon E_m(t), \\ \frac{dI_m(t)}{dt} = \epsilon E_m(t) - \gamma I_m(t), \\ \frac{dR_m(t)}{dt} = \gamma I_m(t). \end{cases} \quad (4)$$ Eq:Model

However, at the time instant $t = nT + m$ in the $(n+1)$-th testing round, we have

$$\begin{aligned} I_m((nT+m)^+) &= (1-\rho)I_m(nT+m), \\ R_m((nT+m)^+) &= R_m(nT+m) + \rho I_m(nT+m), \end{aligned}$$

and other variables remain unchanged. The initial values are set as

$$\begin{aligned} V_p(0) &= p_V(1-p_f)(N(0) - \sum_{m=0}^{T-1} I_m(0)), \quad E_p(0) = 0, \ I_p(0) = 0, \ R_p(0) = 0 \\ V_f(0) &= p_V p_f(N(0) - \sum_{m=0}^{T-1} I_m(0)), \qquad\quad E_f(0) = 0, \ I_f(0) = 0, \ R_f(0) = 0 \\ S_m(0) &= p_m(1-p_V)(N(0) - \sum_{m=0}^{T-1} I_m(0)), \ E_m(0) = 0, \ I_m(0) > 0, \ R_m(0) = 0, \end{aligned}$$

for $m = 0, 1, \cdots, T-1$. Furthermore, we assume every unvaccinated individual must take one test in a particular day m in one round, and therefore, the sum of all proportions having test results reported in m-th day should be 100%, that is $\sum_{m=0}^{T-1} p_m = 1$. This is a reasonable assumption for the "getting

jab of regular test" policies posed by many sectors in Hong Kong during the COVID-19 pandemic, as discussed in the introduction Section 1.

Table 2 Parameters and their baseline values in the model equations.

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Parameter	Description	Baseline value
N	Population size	7000 (assumed)
β	Effective transmission rate of infectious cases	0.8 [33]
ϕ_S	Relative susceptibility of vaccinated individuals with partial protection	0.4 [26, 32, 46]
ϕ_I	Relative infectiousness of vaccinated individuals with partial protection	0.8 [26, 32, 46]
$1/\epsilon$	Latency period for those exposed individuals	2.5 days, [33]
$1/\gamma$	Infection period of infectious individuals	5.5 days, [20]
p_V	Proportion of vaccinated individuals	0.8 (assumed)
p_f	Proportion of vaccinated failure cases	0.15 (assumed)
p_m	Proportion of individuals whose testing result comes out at the m-th day among unvaccinated individuals	0-1 (assumed)
ρ	Testing efficiency, represents the proportion of positive cases identified out of all infected individuals	0.05 (assumed)
T	Regular test period	1-14 days

2.2 Well-posedness of the model

The uniqueness of solutions to model (4) through a given positive initial value can be argued by discussing the initial value problem for the system of differential equations on each time interval $[nT+j, nT+j+1]$ for all $j = 0, 1, \cdots, T-1$ and $n \in \mathbb{N}$ while considering the abrupt changes at the time instants $nT+m$ for I_m and R_m variables. Moreover, the non-negativeness of solutions can be checked through the system of differential equations on each time interval $[nT+j, nT+j+1]$ and the impulsive changes for I_m and R_m variables at the impulsive timing instants.

2.3 The basic reproduction number

We will mainly focus on defining the basic (control) reproduction number, $\mathcal{R}_0$, to illustrate the effectiveness of testing strategies. To evaluate the expected number of cases generated by one index case in a population where all individuals are susceptible to infection, one mathematically tractable approach, while epidemiologically reasonable, is to define a next generation operator [9] on a suitable space consisting of initial infection distributions. For compartmental epidemiological models in the form of autonomous differential equations, van den Driessche and Watmough [52] developed an easy to follow framework to define $\mathcal{R}_0$ by distinguishing the new infection process from transition

among infected compartments. The next generation operator approach has been substantially extended to other compartmental models in heterogeneous environment (see the reference in [24]). In this manuscript, we are going to employ the idea in [1] to define the basic reproduction number and present the numerical scheme to compute it.

As $\mathcal{R}_0$ measures the expected number of infected cases in a population where all individuals are susceptible to the infection, this number should be evaluated at the population consisting of susceptible individuals while the size of other compartments are negligible. Theoretically, the evolution of the sizes for infected compartments can be described by the linearized system of model (4) as follows:

$$\begin{cases} \dfrac{dE_p(t)}{dt} = \phi_S\beta p_V(1-p_f)\phi_I I_p(t) + \phi_S\beta p_V(1-p_f)I_f(t) \\ \qquad\qquad + \phi_S\beta p_V(1-p_f)\displaystyle\sum_{m=0}^{T-1} I_m(t) - \epsilon E_p(t), \\ \dfrac{dI_p(t)}{dt} = \epsilon E_p(t) - \gamma I_p(t), \\ \dfrac{dE_f(t)}{dt} = \beta p_V p_f \phi_I I_p(t) + \beta p_V p_f I_f(t) + \beta p_V p_f \displaystyle\sum_{m=0}^{T-1} I_m(t) - \epsilon E_f(t), \\ \dfrac{dI_f(t)}{dt} = \epsilon E_f(t) - \gamma I_f(t), \\ \dfrac{dE_m(t)}{dt} = \beta p_m(1-p_V)\phi_I I_p(t) + \beta p_m(1-p_V)I_f(t) \\ \qquad\qquad + \beta p_m(1-p_V)\displaystyle\sum_{m=0}^{T-1} I_m(t) - \epsilon E_m(t), \\ \dfrac{dI_m(t)}{dt} = \epsilon E_m(t) - \gamma I_m(t), \end{cases} \tag{5}$$

linearb

supplemented with impulsive effect for I_m compartment at the instant time $nT + m$:

$$I_m((nT+m)^+) = (1-\rho)I_m(nT+m). \tag{6}$$

eq:LinImpulsi

The next generation operator can be defined by system (5) with impulsive changes described by (6). For notational simplicity, we introduce a vector to describe the distribution of individuals in all compartments $u = (u_1, u_2, u_3, u_4, \cdots, u_{T+2})$, where

$$u_1 = (E_p, I_p), \quad u_2 = (E_f, I_f), \quad u_3 = (E_0, I_0), \quad \cdots, \quad u_{T+2} = (E_{T-1}, I_{T-1}),$$

where $u_j = (u_{j,1}, u_{j,2}) = (E_{j-3}, I_{j-3})$, $j = 3, 4, \cdots, T+2$. Please note that system (5) contains 4 equations for infected f and p classes ($E_p(t)$, $I_p(t)$, $E_f(t)$ and $I_f(t)$), as well as $2 \times T$ equations for infected unvaccinated classes. In total, there are $4 + 2T$ equations.

Following the notations of [52], we can introduce F and V matrices to describe the new infection process and transition of infected individuals among

different compartments. In particular, the new infection matrix F can be expressed as

$$F = \begin{pmatrix} F_{1,1} & F_{1,2} & \cdots & F_{1,T+2} \\ F_{2,1} & F_{2,2} & \cdots & F_{2,T+2} \\ \vdots & \vdots & \ddots & \vdots \\ F_{T+2,1} & F_{T+2,2} & \cdots & F_{T+2,T+2} \end{pmatrix}$$

with each element defined as

$$F_{1,1} = \begin{pmatrix} 0 & \phi_S \beta p_V (1-p_f)\phi_I \\ 0 & 0 \end{pmatrix}, \; F_{1,j} = \begin{pmatrix} 0 & \phi_S \beta p_V (1-p_f) \\ 0 & 0 \end{pmatrix},$$

$$F_{2,1} = \begin{pmatrix} 0 & \beta p_V p_f \phi_I \\ 0 & 0 \end{pmatrix}, \qquad F_{2,j} = \begin{pmatrix} 0 & \beta p_V p_f \\ 0 & 0 \end{pmatrix},$$

$$F_{i,1} = \begin{pmatrix} 0 & \beta p_{i-3} (1-p_V)\phi_I \\ 0 & 0 \end{pmatrix}, \quad F_{i,j} = \begin{pmatrix} 0 & \beta p_{i-3} (1-p_V) \\ 0 & 0 \end{pmatrix},$$

$i = 3, \cdots, T+2,$
$j = 2, 3, \cdots, T+2.$

The transition matrix to describe the evolution of remaining infected individuals can be described by the V-matrix as

$$V = \begin{pmatrix} V_{1,1} & V_{1,2} & \cdots & V_{1,T+2} \\ V_{2,1} & V_{2,2} & \cdots & V_{2,T+2} \\ \vdots & \vdots & \ddots & \vdots \\ V_{T+2,1} & V_{T+2,2} & \cdots & V_{T+2,T+2} \end{pmatrix}$$

where

$$V_{i,i} = \begin{pmatrix} \epsilon & 0 \\ -\epsilon & \gamma \end{pmatrix}, \quad i = 1, 2, \cdots, T+2; \text{ and } V_{i,j} = \begin{pmatrix} 0 & 0 \\ 0 & 0 \end{pmatrix}, \quad i \neq j.$$

However, the impulsive effect in (6) is not included in F and V matrices. On the other hand, the impulsive force applies to I_m compartment as removing from this compartment and plays a role in the evolution of the distribution of infected individuals. Therefore, the actual evolution of remaining infected individuals can be appropriately defined by the V-matrix subject to the impulsive effect, which is given by the evolution process $\Psi(t, s)$, $t \geq s$, associated with

the following system with $n = 0, 1, 2, \cdots$ being the $(n+1)$-th time round:

$$\begin{cases} \frac{du(t)}{dt} = -Vu(t), & t \in [nT, (n+1)T], \quad t \neq nT + i, \quad i = 0, 1, \cdots, T-1, \\ u_1(t^+) = u_1(t), & t = nT + i, \quad i = 0, 1, \cdots, T-1, \\ u_2(t^+) = u_2(t), & t = nT + i, \quad i = 0, 1, \cdots, T-1, \\ u_{j,1}(t^+) = u_{j,1}(t), & t = nT + i, \ j = 3, 4, \cdots, T+2, \quad i = 0, 1, \cdots, T-1, \\ u_{j,2}(t^+) = u_{j,2}(t), & t \neq nT + j - 3, \quad j = 3, 4, \cdots, T+2, \\ u_{j,2}(t^+) = (1-\rho)u_{j,2}(t), & t = nT + j - 3, \quad j = 3, 4, \cdots, T+2. \end{cases} \tag{7}$$

eq:EvoV

Introduce the space of piecewisely continuous and T-periodic functions PC_T as follows

$$PC_T = \left\{ \psi : \mathbb{R} \to \mathbb{R}^{4+2T} \;\middle|\; \begin{array}{l} \psi(t) \text{ is continuous except at } t = nT + m, \\ \forall n \in \mathbb{Z}, m = 0, 1, \cdots, T-1, \\ \psi(t^-), \psi(t^+) \text{ exists} \\ \text{and } \psi(t^-) = \psi(t) \text{ for } t = nT + m, \\ \psi(t) = \psi(t+T), \forall t \in \mathbb{R} \\ \text{and } \psi((nT+m)^+) = \psi([(n+1)T + m]^+) \end{array} \right\}$$

where $\psi(t^+) = \lim_{s \to t^+} \psi(s)$ and $\psi(t^-) = \lim_{s \to t^-} \psi(s)$. Please note that PC_T consists of T-periodic functions which are continuous except at impulsive time instants. Equip the linear space PC_T with the maximum norm $\|\cdot\|$, then $(PC_T, \|\cdot\|)$ is a Banach space. Based on the infection matrix F in (2.3) and the evolution process $\Psi(t, s)$ defined by (7), we can define the next generation operator on PC_T as follows. Suppose $v(\cdot) \in PC_T$ and $v(t-s)$ is the distribution of infected individuals introduced at time $t - s$, then $Fv(t - s)$ describes the distribution of newly infected individuals at time $t-s$ while $\Psi(t, t-s)Fv(t-s)$ represents the distribution of the individuals newly infected at time $t - s$ and remain in the infected compartments at time t. Taking the integral $\int_0^\infty \Psi(t, t-s)Fv(t-s)ds$ gives the distribution of all accumulated infected individuals at time t, and therefore, the next generation operator can be defined as

$$[\mathbb{L}v](t) = \int_0^\infty \Psi(t, t-s)Fv(t-s)ds, \quad \forall t \in \mathbb{R}, \ v \in PC_T.$$

The spectral radius of $\mathbb{L}$ is defined to be the basic reproduction number [9], that is,

$$\mathcal{R}_0 = r(\mathbb{L}).$$

As the basic reproduction number is defined as the spectral radius of the linear operator on a functional space PC_T, it is very challenging to obtain an explicit formula for this number. However, it is possible to quantify $\mathcal{R}_0$ numerically. Here, we employ numerical algorithm for $\mathcal{R}_0$ computation by developing an auxiliary system, which takes a similar form as the linear system (5), but

including a parameter $\lambda \in [0, \infty)$ as follows:

$$\begin{cases} \dfrac{du(t)}{dt} = \lambda F u(t) - V u(t), & t \in [nT, (n+1)T], \quad t \neq nT + i, \quad i = 0, 1, \cdots, T-1, \\ u_1(t^+) = u_1(t), & t = nT + i, \quad i = 0, 1, \cdots, T-1, \\ u_2(t^+) = u_2(t), & t = nT + i, \quad i = 0, 1, \cdots, T-1, \\ u_{j,1}(t^+) = u_{j,1}(t), & t = nT + i, \ j = 3, 4, \cdots, T+2, \quad i = 0, 1, \cdots, T-1, \\ u_{j,2}(t^+) = u_{j,2}(t), & t \neq nT + j - 3, \quad j = 3, 4, \cdots, T+2, \\ u_{j,2}(t^+) = (1-\rho) u_{j,2}(t), & t = nT + j - 3, \quad j = 3, 4, \cdots, T+2. \end{cases} \tag{8}$$

perturbation

Let $\{U(t, s, \lambda) : \ t \geq s\}$ be the evolution operator on $\mathbb{R}^{4+2T}$ of (8), and $r(U(T, 0, \lambda))$ be the spectral radius of $U(T, 0, \lambda)$. Using similar arguments as those in [1, Theorem 2], we can prove that $\lambda = \frac{1}{\mathcal{R}_0}$ is the unique solution of $r(U(T, 0, \lambda)) = 1$ whenever $\mathcal{R}_0 > 0$. Thus, we can obtain the value of λ_0 from solving $r(U(T, 0, \lambda)) = 1$ numerically by using the bisection method. Note that for any specific value of λ, $r(U(T, 0, \lambda))$ can be computed numerically via Lemma 2.5 in [24] (also see [1, Remark 1]).

3 Main results

In this section, we will explore the uncertainty analysis of some epidemiological quantities of great concern, such as the peaking size, peaking time of total infections, the basic reproduction number and final size. Different test frequencies characterized by T, and various factors in the transmission process and vaccine efficacy, including the effective transmission rate β, the relative infectiousness ϕ_I of vaccinated individuals acquiring partial protection, vaccination coverage p_V and testing efficiency ρ, will be considered. We further explore the effect of vaccine efficacy in preventing severe SARS-CoV-2 infections under different test frequencies. All baseline parameter values are taken from Table 2. Furthermore, the distribution of proportion p_m is assumed to be uniform, that is $p_m = 1/T$ for $m = 0, 1, \ldots, T-1$.

3.1 Epidemic peaks vs test frequencies

The impact of regular test on the spread of infections is depicted in Figure 2, where the curves of total infections and infections among unvaccinated persons under 4 different test frequencies are shown. Compared with the case of no regular test, the peaking size of infections is slightly lowered down and the peaking time is delayed when test period T is reduced from 14 days to 7 days. The reduction on the peaking infection size becomes more significant with increasing test frequency, i.e. shortening the test period to 3 days and 1 day.

The peak size and peaking time of total infections are also employed as indices to evaluate the joint impact of test frequencies T and other factors characterizing the transmission, vaccine and test efficiency. Compared with the case of no test, the absolute changes of peak size and peak time are computed respectively under 4 different test frequencies, i.e., $T = 1$, 3, 7 and 14 days.

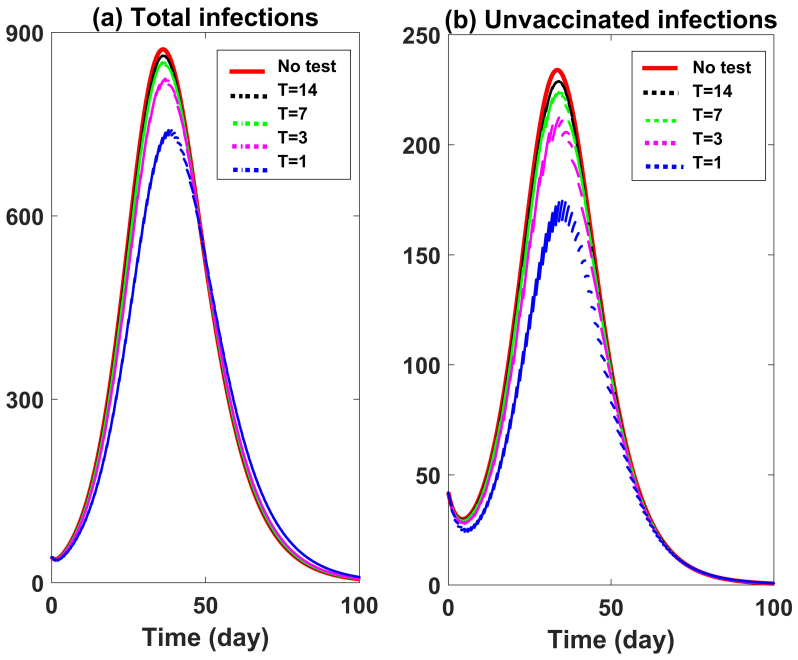

Fig. 2 (a) The profile of total infections with different testing frequencies. (b) The profile of infections for unvaccinated population with different testing frequencies.

⟨Fig6⟩

Figures 3 and 4 show respectively the absolute reduction of peak size and absolute delay of peak time varying with respect to above-mentioned parameters. The reduction of peaking size reported in Figure 3 is always positive, which indicates that regular test do reduce the peaking infection size.

With more uncertainties included, the negative correlation between the peaking size of total infection and test frequencies always holds (Figure 3), however the extent of correlation is changing when different factors are considered. For a wide range of effective transmission rates β and relative infectiousness ϕ_I, there seems no much reduction when increasing the test frequency from $T = 14$ days to $T = 3$ days. However, daily testing would greatly reduce the peaking size (Figures 3(a) and (b)). On the other hand, it is essential to increase the test frequency when the vaccination coverage p_V is very small or testing is very accurate (Figures 3(c) and (d)). However, intensive test frequency seems not necessary to reduce the peak infection size when the testing efficiency is very low or the vaccination coverage is very high (Figures 3(c) and (d)).

Generally speaking, Figure 4 shows that frequent testing may delay the time to attaining the peak size, which can be regarded as the positive role that an intensive testing schedule may have. However, the relationship between the peaking time and the test frequency T is variable, and therefore, more factors should be included to have an accurate prediction. It is interesting to observe that for some ranges of the effective transmission rate β, relative

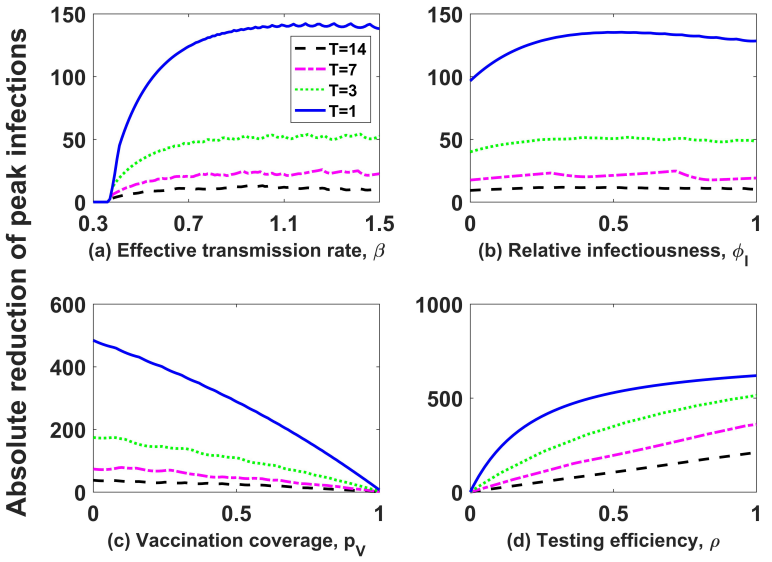

Fig. 3 Absolute reduction of peak infections varies with (a) β, (b) ϕ_I, (c) p_V, (d) ρ under four different testing frequencies $T = 1$, 3, 7 and 14 days.

⟨Fig7⟩

infectiousness ϕ_I and vaccination coverage p_V, increasing the frequency from $T = 14$ days to $T = 7$ days may not significantly change the peaking time (Figures 4(a), (b) and (c)). Similarly, changing the test frequency from $T = 14$ days to $T = 3$ days may not substantially delay the peaking time, however, the peaking time is greatly delayed if daily testing is applied, in particular, when the test efficacy is very high, or the effective transmission rate is very low (Figures 4(a) and (d)). It is surprising to observe that regular testing may put forward the peaking time, instead of delaying it (Figures 4(a), 4(b) and (c)) in some parameter regions.

The peak infection size and peaking time are explored in a wider region for parameters β and ρ under different test frequencies in Figures 5 and 6, respectively. In general, we can make the same conclusion on the relationship between the peaking size and test frequency: more frequent testing can reduce the peaking size of the total infection. However, the results for the peak time become more complicated since both positive and values in the absolute delay of peak time are observed, which are highly dependent on other model parameters (Figure 6). In particular, when the effective transmission rate β is very small (such that the basic reproduction number is very small), the compulsory test requirement with high test efficiency ρ may accelerate the peak time instead of delaying it. Only when the effective transmission rate β is very large, compulsory tests may delay the peak time.

It is interesting to observe that small oscillations appear in some plots of Figures 3-6 when parameter value varies. These oscillations may be attributed

to the joint effect of the parameter(s) in consideration and impulsive effects of the regular test.

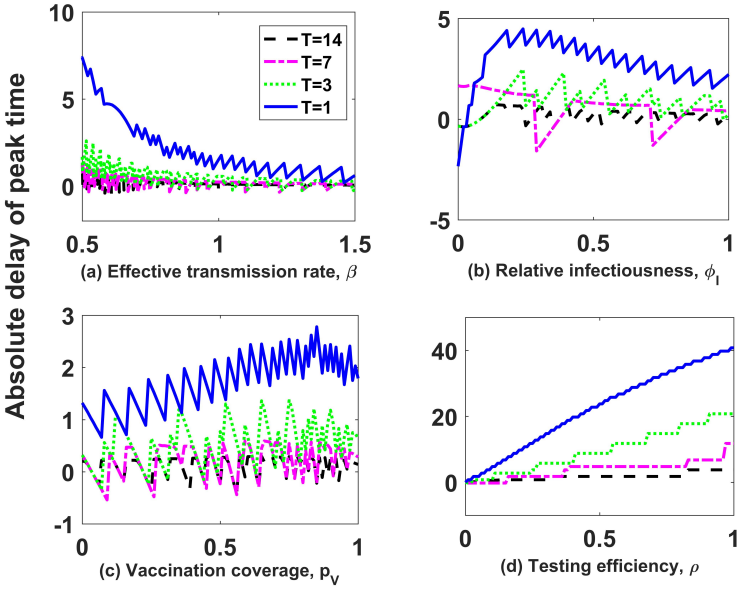

Fig. 4 Absolute delay of peak time (days) varies with (a) β, (b) ϕ_I, (c) p_V, (d) ρ under four different testing frequencies $T = 1$, 3, 7 and 14 days.

⟨Fig8⟩

3.2 R_0 vs test frequencies

For the given test frequency, the basic reproduction number is shown to be a decreasing function of the testing efficiency (Figure 7), which implies that accurate testing technique plays an important role in reducing the disease transmission risk. Furthermore, increasing the test frequency from $T = 14$ days to $T = 1$ day fails to greatly reduce the basic reproduction number. This conclusion generally holds in a wider range of parameter values (Figures 8 and 9), where test frequency seems to play a little role on the basic reproduction number. However, an intensive test schedule with $T = 1$ day may significantly reduce the basic reproduction number when the vaccination coverage p_v is low and the test efficiency ρ is very high (Figure 10(d)). Additionally, Figure 10 illustrates that despite relatively high vaccination coverage p_v and test efficiency, the basic reproduction number R_0 remains greater than one. This suggests that in order to further mitigate the risk of disease transmission, it is necessary to decrease the effective transmission rate through other effective means.

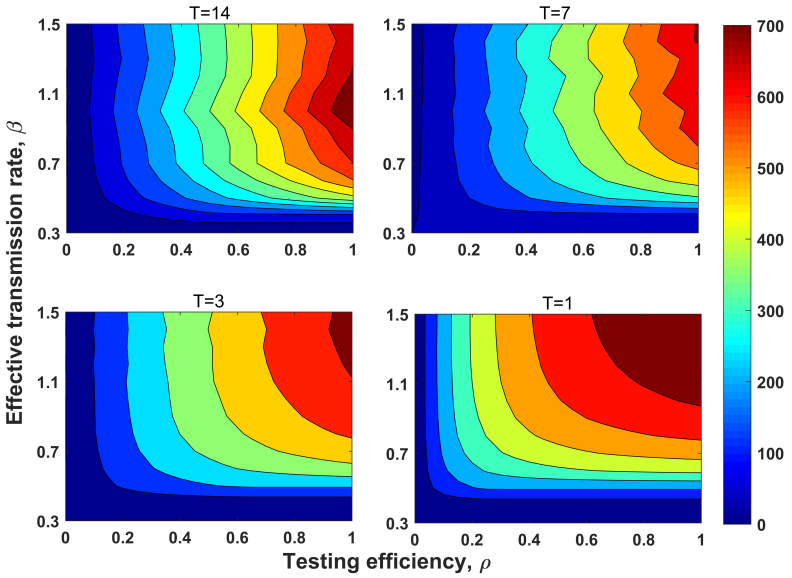

Fig. 5 Absolute reduction of peak infections varies with test efficiency ρ and effective transmission rate β under four different testing frequencies.
⟨Fig9d⟩

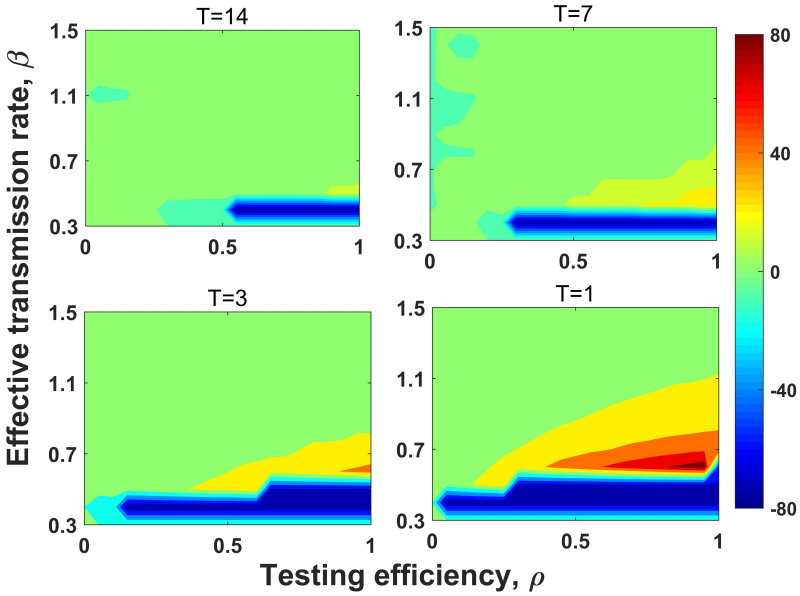

Fig. 6 Absolute delay of peak time (days) varies with test efficiency ρ and effective transmission rate β under four different testing frequencies.
⟨Fig9c⟩

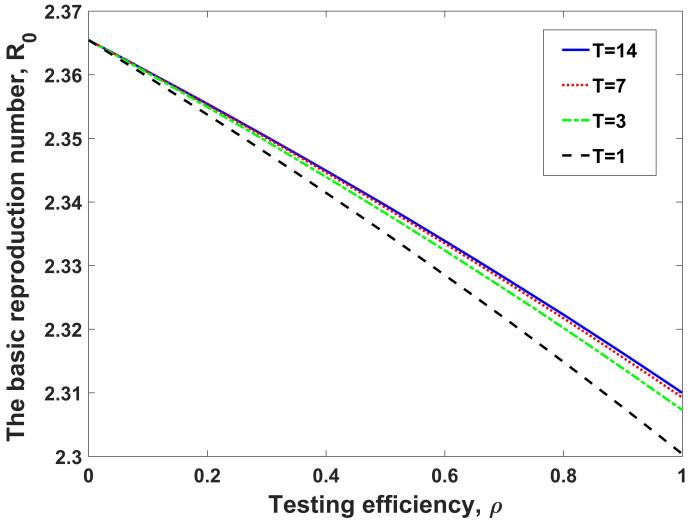

Fig. 7 The basic reproduction number $\mathcal{R}_0$ varies with test efficiency ρ under four different test frequencies.

⟨Fig10⟩

3.3 Final size vs test frequencies

Final size S_∞, which is defined as

$$S_\infty := \lim_{t\to\infty}(V_f(t) + \sum_{m=0}^{T-1} S_m(t) + V_p(t)),$$

is another important index for transmission severity, and it describes the number of individuals who are infected over the course of the epidemic through $N - S_\infty$ and the probability that an individual will get infection through the attack rate $1 - S_\infty/N$. By setting t very large, we can numerically compute S_∞ through the solution for susceptible individuals in different compartments, $V_p(t)$, $V_f(t)$ and $S_m(t)$. In comparison with the situation of no test, the absolute changes of final epidemic size under 4 different test frequencies are employed for sensitivity analysis of above-mentioned parameters in Figures 11 and 12. It can be observed from the positive increments in these plots that regular tests do protect individuals from infection. Generally speaking, testing more frequently can greatly increase the final size and therefore, protect more individuals from infection. Figure 11 depicts the relationship between the absolute increment of final size and test frequency. This reveals that increasing the test frequency has a more significant impact when the effective transmission rate is at an intermediate level, or the relative infectiousness is very high, or test efficiency is very high, or the vaccination coverage is not too high. When the vaccination coverage is low, it is essential to set a more frequent testing

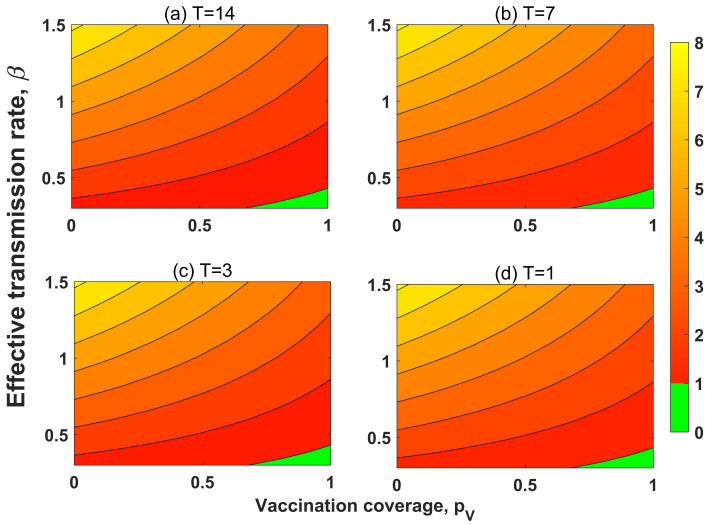

Fig. 8 The basic reproduction number $\mathcal{R}_0$ varies with effective transmission rate β and vaccination coverage p_V under (a) $T = 14$ days, (b) $T = 7$ days, (c) $T = 3$ days and (d) $T = 1$ day. Divergent color schemes are used to differ cases when R_0 is below (green) and above (red and yellow) one.

⟨Fig10a⟩

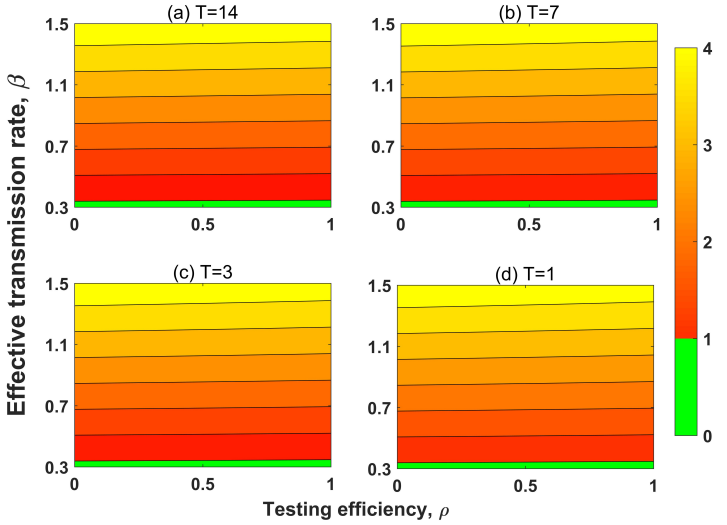

Fig. 9 The basic reproduction number $\mathcal{R}_0$ varies with testing efficiency ρ and effective transmission rate, β under (a) $T = 14$ days, (b) $T = 7$ days, (c) $T = 3$ days and (d) $T = 1$ day. Divergent color schemes are used to differ cases when R_0 is below (green) and above (red and yellow) one.

⟨Fig10c⟩

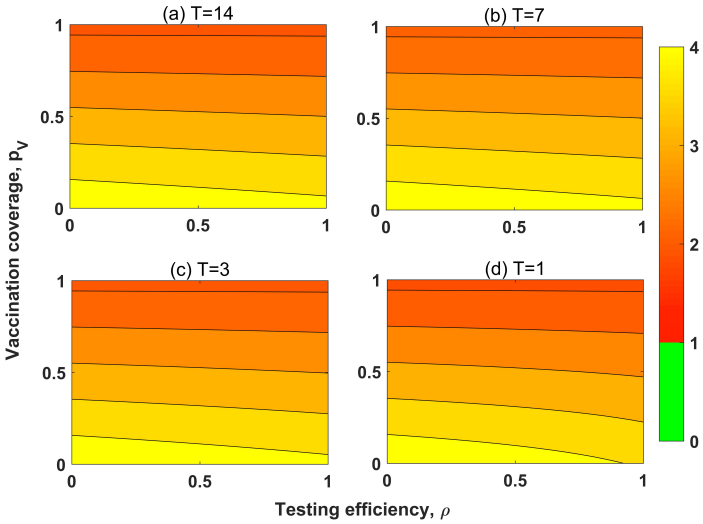

Fig. 10 The basic reproduction number $\mathcal{R}_0$ varies with test efficiency ρ and vaccination coverage p_V under (a) $T = 14$ days, (b) $T = 7$ days, (c) $T = 3$ days and (d) $T = 1$ day. Divergent color schemes are used to differ cases when R_0 is below (green) and above (red and yellow) one.

⟨Fig10b⟩

strategy to reduce the final size (Figure 11(c)). A more comprehensive uncertainty analysis of the impact of test frequency on the final size is presented in Figure 12. The four plots in the figure demonstrate that test frequency has a significant effect on the final size.

3.4 Severe infections vs vaccine efficacy under different test frequencies

Based on our model, the impact of vaccine efficacy on preventing severe SARS-CoV-2 infections can be investigated under 4 different test frequencies. Let v_e denote the efficacy of COVID-19 vaccines in preventing severe infections. Age-specific ratio of severe infections was estimated by using multi-country serology studies and public data about hospital admissions and death during the first half of 2020 (see Table 1 in [19]). In this paper, we take severe infections as all non-mild cases including severe, critical and fatal infections. In view of the data in [19], the average ratio of severe infections is roughly 13.67% among infected individuals from all age groups. Then, the number of severe infections, N_{SI} can be calculated as follows

$$N_{SI} = [(1 - v_e) * R_p(\infty) + R_f(\infty) + \sum_{m=0}^{T-1} R_m(\infty)] * 13.67\% \quad \text{for } T = 1,\ 3,\ 7,\ 14.$$

The number of severe infections with respect to the vaccine efficacy is explored under 4 test frequencies as shown in Figure 13. The illustration highlights an

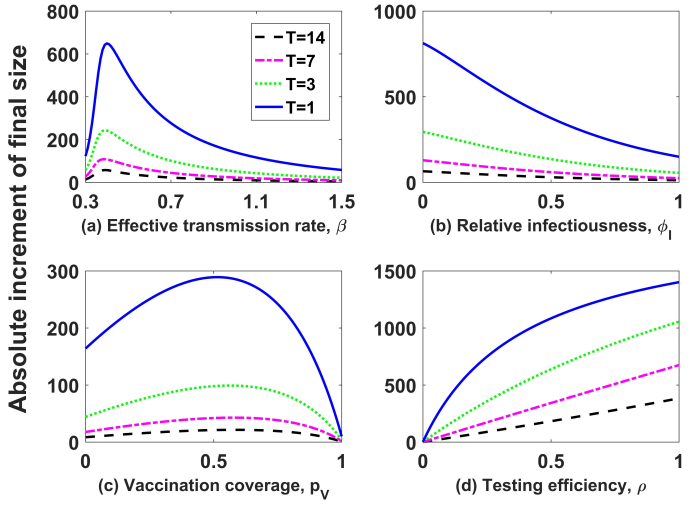

Fig. 11 Variations in the absolute increment of final epidemic size S_∞ (in comparison with no compulsory tests for unvaccinated individuals) are shown with respect to the changes of (a) β, (b) ϕ_I, (c) p_V, (d) ρ under four different testing frequencies.

⟨Fig11⟩

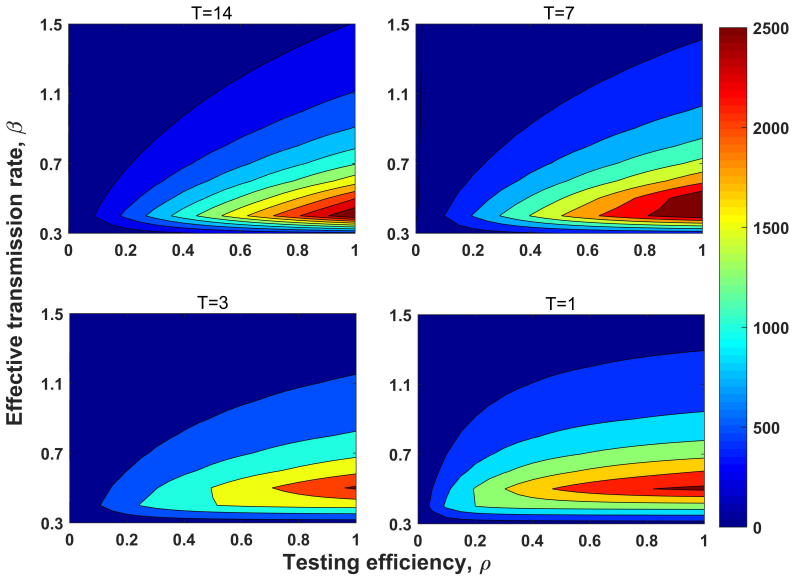

Fig. 12 Absolute increment of final size S_∞ (in comparison with no compulsory tests for unvaccinated individuals) varies with test efficiency ρ and effective transmission rate β under four different testing frequencies.

⟨Fig11b⟩

intuitive outcome: increasing vaccine efficacy can result in a reduction of severe infections, regardless of the test frequency. However, when vaccine efficacy and vaccination rate are both very high, altering the test frequency from $T = 14$ days to $T = 1$ has minimal impact on the reduction of severe infections.

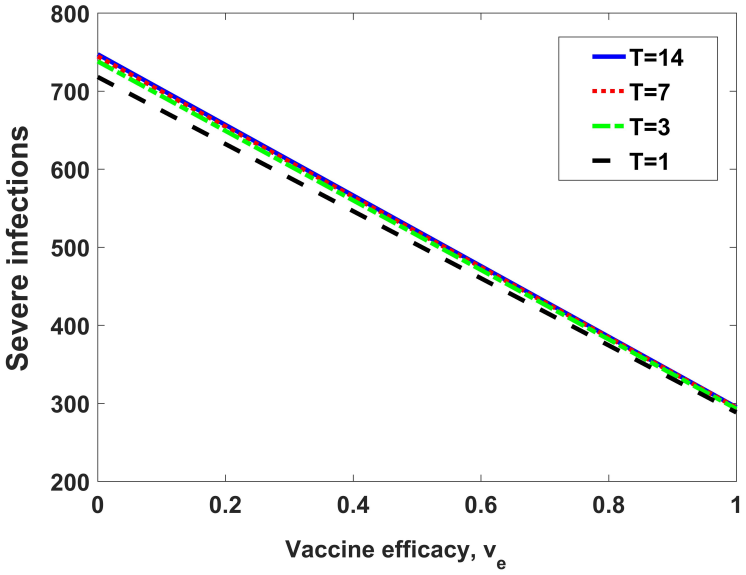

Fig. 13 Number of severe infections varies with vaccine efficiency v_e under four different testing frequencies.

⟨Fig12⟩

4 Conclusion and discussion

Motivated by the "getting jab or regular test" policy, this study proposes a mechanistic model to assess the effectiveness of compulsory testing requirements for unvaccinated individuals during the COVID-19 pandemic. The hypothetical model is suitable for companies or universities with mild heterogeneity in epidemiological characteristics and is formulated to investigate whether regular testing for unvaccinated individuals is a viable alternative to vaccination in mitigating the spread of SARS-CoV-2, particularly when vaccination rates are very low. The key objective is to balance the trade-offs between frequent testing and disease control. To naturally accommodate the test frequency and variable testing dates decided by different proportions of unvaccinated individuals, the model takes the form of compartmental differential equations with impulsive forces describing the removal of unvaccinated individuals whose test results are positive. The basic reproduction number is

rigorously defined. To evaluate the effectiveness of testing strategies and propose optimal test frequencies, further indices are simulated to describe the disease transmission risk, including the peaking size, peaking time, final size, and the number of severe infections.

The study's results suggest that regular testing of unvaccinated individuals can serve as a viable alternative to vaccination in suppressing the spread of SARS-CoV-2. Generally, frequent testing is advantageous in reducing the peaking size of total infections, delaying the timing of attaining the peak size, decreasing the basic reproduction number, and increasing the final size. However, the benefits of more frequent testing may be limited due to other factors involved in the transmission process, including the effective transmission rate, existing vaccination coverage, vaccine efficacy, and accuracy of testing techniques. Therefore, designing a cost-effective testing frequency for unvaccinated individuals requires careful consideration of these factors. Additionally, determining an optimal test frequency should be based on the specific index used to measure transmission risk.

In the model formulation, it is assumed that all vaccinated individuals can still contract the infection, and the vaccination only provides partial or no protection against infection. If the vaccine provides perfect protection to a fraction of individuals, those individuals can be placed in the removed class, and there is no need to include equations for this group of fully protected individuals. Although the model is general in some sense, as it considers the effects of imperfect vaccination and the distribution of test dates for unvaccinated individuals, it has a few limitations.

One key assumption is that only unvaccinated individuals with positive test results are isolated to prevent further transmission. However, in reality, vaccinated individuals who show symptoms may also take a test and self-isolate if the result is positive. Additionally, the virus can be spread by infected individuals who do not develop symptoms (asymptomatic transmission), those who are infected but have not yet developed symptoms (pre-symptomatic transmission), as well as those who have symptoms [13, 56]. To better evaluate transmission risk and develop effective public health strategies to contain transmission, it is important to distinguish between these three transmission routes. Therefore, the model should be extended by adding more classes, such as asymptomatic, presymptomatic, and symptomatic classes. However, as the primary goal of this study is to illustrate the approach of incorporating test frequency in model formulation, proposing theoretical methodologies for the model, and exploring the effect of test frequency on disease transmission risk, we keep the model as simple as possible by using the widely used susceptible-exposed-infectious-removed compartmental structure in COVID-19 studies.

Another limitation of the model formulation is that the impact of two important variables is not incorporated: result releasing time and test sensitivity. Result releasing time is the duration between sample collection and

diagnosis reporting, and faster reporting of results is beneficial for disease control. Test sensitivity measures how well a test can detect an infected sample. Although the test efficacy parameter measures the probability of false negatives, where the test result incorrectly indicates the absence of infection for an infected sample, test sensitivity determines the ability of the testing technique to correctly identify a true positive COVID-19 case [14]. Moreover, test sensitivity is dependent on the within-host kinetics of SARS-CoV-2 in an infected individual. To refine the model in the future, viral detection tests with different sensitivities [23] and limits of detection (LOD) of viral load in tested individuals could be considered, along with delays in reporting. One possible way to incorporate the test sensitivity, infectivity and symptom progression in a model would be introducing a variable, the age-since infection, and integrating viral kinetics into within- and between-host dynamics through age-structured modeling framework. The new age variable makes it possible to characterize the infectivity, the virus load (and therefore, the probability of being tested positive) and the symptom through various probability density functions in viral kinetics modeling [30].

Furthermore, in the current study, a uniform distribution of p_m was employed, but it would be interesting to evaluate the impact of the distribution of p_m on model predictions. Specifically, a data-driven and realistic distribution of p_m should be used for the hypothetical framework. In this study, we numerically compute S_∞ through the solution for susceptible individuals in different compartments. Analytical approaches have been developed for autonomous epidemic models to derive the final size relationship (see references [4, 8, 25] and therein) and it is appealing to extend these analytical results to non-autonomous systems, as the one in the current study.

We leave these interesting and important issues for further investigation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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