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Global stability and optimal control for a COVID-19 model with vaccination and isolation delays

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A B S T R A C T

COVID-19 pandemic remains serious around the world and causes huge deaths and economic losses. To investigate the effect of vaccination and isolation delays on the transmission of COVID-19, we propose a mathematical model of COVID-19 transmission with vaccination and isolation delays. The basic reproduction number is computed, and the global dynamics of the model are proved. When \( R_0 < 1 \), the disease-free equilibrium is globally asymptotically stable. The unique endemic equilibrium is globally asymptotically stable if \( R_0 > 1 \). Based on the public information, parameter values are estimated, and sensitivity analysis is carried out by the partial rank correlation coefficients (PRCCs) and the extended version of the Fourier amplitude sensitivity test (eFAST). Our results suggest that the isolation rates of asymptomatic and symptomatic infectious individuals have a significant impact on the transmission of COVID-19. When the COVID-19 is epidemic, the optimal control strategies of our model with vaccination and isolation delays are analyzed. Under the limited resource with constant and time-varying isolation rates, we find that the optimal isolation rates may minimize the cumulative number of infected individuals and the cost of disease control, and effectively contain the transmission of COVID-19. Our study may help public health to prevent and control the COVID-19 spread.

Introduction

Coronavirus disease 2019 (COVID-19) is a novel coronavirus disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Since the first case was reported in December 2019, the confirmed cases of COVID-19 increase rapidly and cause the deaths of millions of people and huge economic losses. The later research shows that COVID-19 is more contagious than both severe acute respiratory syndrome coronavirus (SARS-CoV) and middle east respiratory syndrome coronavirus (MERS-CoV) [1]. On March 11, 2020, the World Health Organization (WHO) classified COVID-19 as a pandemic [2]. As of June 6, 2022, the cumulative reported number of confirmed cases and deaths of COVID-19 reaches over 531 million and 6.29 million worldwide, respectively [2].

In the early stage of the COVID-19 outbreak, non-pharmaceutical interventions (NPIs) such as quarantine, contact tracing and isolation, wearing masks and other personal protection, social distancing, restrictions on the movement of people, closure of public places and school closures play important roles in controlling the spread of COVID-19 because there were no available vaccines [3,4]. Since the emergence of new variants of SARS-CoV-2 changed dramatically the nature of the pandemic [5], then the current vaccines could not provide complete protection and only reduce the risk of infection [6]. Besides, the antibody-dependent enhancement is deemed to be a major problem in the development and use of COVID-19 vaccines [7]. Thus it is necessary to combine other interventions with vaccination to prevent and control the spread of COVID-19.

Currently, a large proportion of COVID-19 patients are asymptomatic when they are infectious [8,9], and then large-scale nucleic acid testing is an effective way to screen asymptomatic infectious people and prevent the follow-up epidemic. In the initial stage of virus invasion, the virus in the human body could not be detected, and then multiple sample tests are performed. Therefore, timely detection and isolation of cases could effectively control the transmission of COVID-19 [10] and reduce the risk of COVID-19 spread.

Mathematical modeling is an important method to particularly explore the transmission of diseases and dynamically predict the process of diseases by the public information. Lai et al. [11] established a
travel network-based SEIR model to simulate the spread of COVID-19 in mainland China, and assessed the effectiveness of NPIs in various scenarios. Giordano et al. [12] established a mathematical model, and predicted the peak time and epidemic size of COVID-19 in Italy. Given presymptomatic infectivity and population migration, Hao et al. [13] investigated the impact of unidentified cases on ongoing surveillance and interventions. Song et al. established a SIFR (susceptible-unfound infected-found-removed) model to evaluate the scale of the COVID-19 epidemic in Harbin [14], and established a mathematical model with population mobility from Wuhan to Henan Province to estimate the spread of COVID-19 in Wuhan [15]. Since the adjustment of interventions may lead to changes in human behavior, Tang et al. [16] analyzed the effect of time-varying contact rate and diagnosis rate on the transmission of COVID-19. Using the reported deaths and mathematical model, Song et al. [17,18] predicted the COVID-19 spread in India as well as southeast Asian countries. Besides, patch model [19] and network model [20] are used to study the COVID-19 spread. However, the effect of vaccine and isolation delays on the model are analyzed. Based on the real data and mathematical model, parameter values are estimated. Sensitivity analysis and numerical simulations are performed. Finally, we investigate the optimal isolation problem under the limited resource for the constant and variant isolation resources.

The rest of this paper is organized as follows. In Section “Model formulation”, a mathematical model of COVID-19 with vaccination and isolation delays is established. In Section “Threshold dynamics”, we calculate the basic reproduction number and prove the global stability of the equilibria. In Section “Parameters estimation”, parameter estimation and numerical simulations are performed. In Section “Numerical simulations”, sensitivity analysis is performed. Section “Control strategy” investigates the optimal isolation strategies. The discussion and conclusion are given in Section “Conclusion and discussion”.

Model formulation

We divide the population into six groups: susceptible individuals \(S(t)\), exposed individuals (infected but not infectious) \(E(t)\), asymptomatic infectious individuals \(A(t)\), symptomatic infectious individuals \(I(t)\), isolated individuals \(Q(t)\) and recovered individuals \(R(t)\). We assume that the people in the recovered class will not be infected again.

Assume that the vaccination rate is \(\varphi\), and vaccine efficacy is \(\epsilon\). The susceptible individuals can become exposed individuals by contact with the asymptomatic or symptomatic infectious individuals. \(\beta\) is the transmission rate, and the asymptomatic individuals are assumed to transmit virus at a reduced rate given by \(\sigma\). Then the incidence is \(\beta(1-\phi)(1-\epsilon)S(t)(\sigma A(t) + I(t)) = \beta(1-\phi)S(t)(\sigma A(t) + I(t))\). After the exposed period \(1/\alpha\), the proportion \(1 - \rho\) become symptomatic and asymptomatic infectious individuals, respectively. Asymptomatic (symptomatic) infectious individuals recover at the rate \(\gamma_1\) (\(\gamma_2\)), and \(f_1\) (\(f_2\)) is the isolation rate of asymptomatic (symptomatic) infectious individuals. \(\gamma_1\) is the recovery rate of isolated individuals. We assume that \(b\) is the natural birth rate and \(d\) is the natural mortality rate. \(d_1\) is the death rate due to the disease. The isolation delay is \(\tau_1\) (\(\tau_2\)) of asymptomatic (symptomatic) infectious individuals due to the limited resources. The flow chart is shown in Fig. 1.

Based on the transmission mechanism of COVID-19 and previous work [13,16–18], the transmission dynamics model of COVID-19 with vaccination and isolation delays is established as the following equations

\[
\begin{align*}
\frac{dS(t)}{dt} &= b - \beta(1-\epsilon)S(t)(\sigma A(t) + I(t)) - dS(t) \\
\frac{dE(t)}{dt} &= \beta(1-\epsilon)S(t)(\sigma A(t) + I(t)) - \alpha E(t) - dE(t) \\
\frac{dA(t)}{dt} &= (1-p)eE(t) - f_1A(t) - \gamma_1A(t) - dA(t) \\
\frac{dI(t)}{dt} &= paE(t) - f_2A(t) - \gamma_2I(t) - dI(t) \\
\frac{dQ(t)}{dt} &= f_1A(t - \tau_1) + f_2I(t - \tau_2) - \gamma_3Q(t) - dQ(t) \\
\frac{dR(t)}{dt} &= \gamma_1A(t) + \gamma_2I(t) + \gamma_3Q(t) - dR(t)
\end{align*}
\]

Let \(\mathbb{R}_+^6 = \{(S(t), E(t), A(t), I(t), Q(t), R(t)) : S(t) \geq 0, E(t) \geq 0, A(t) \geq 0, I(t) \geq 0, Q(t) \geq 0, R(t) \geq 0\}\), and \(\mathbb{C}([-r,0],\mathbb{R}_+^6) = \{x = \max\{t_1, t_2\}\} \) is a Banach space of continuous mapping the interval \([-r,0]\) into \(\mathbb{R}_+^6\) with the induced norm from \(\mathbb{C}([-r,0],\mathbb{R}_+^6)\). The initial conditions are

\[
\begin{align*}
S(\theta) &= \varphi_1(\theta), E(\theta) = \varphi_2(\theta), A(\theta) = \varphi_3(\theta), I(\theta) = \varphi_4(\theta), \\
Q(\theta) &= \varphi_5(\theta), R(\theta) = \varphi_6(\theta), \varphi_5(\theta), \varphi_6(\theta) \geq 0 (i = 1, 2, 3, 4, 5, 6), \theta \in [-r,0].
\end{align*}
\]

Lemma 1. The solutions of system (1) with initial conditions (2) are nonnegative and ultimately bounded.

Proof. By the theory 5.2.1 in [21] and the model (1) with initial conditions (2), it is easy to show that \(S(t) \geq 0, E(t) \geq 0, A(t) \geq 0, I(t) \geq 0, Q(t) \geq 0, R(t) \geq 0\). So we can derive that the nonnegative cone \(\mathbb{R}_+^6\) is positively invariant for system (1). Define the function

\(G(t) = S(t) + E(t) + A(t) + I(t)\).

Differentiating \(G(t)\) along the solutions of system (1), we get

\[
\frac{dG(t)}{dt} = b - dG(t) - (f_1 + f_2)A(t) - (f_2 + f_4)I(t) \leq b - dG(t).
\]

Then

\[
\lim_{t \to \infty} \sup G(t) \leq \frac{b}{d},
\]

which means that \(S(t), E(t), A(t)\) and \(I(t)\) are ultimately bounded. From the fifth equation of system (1), we have

\[
\lim_{t \to \infty} \sup Q(t) \leq \frac{b(f_1 + f_3)}{d(f_2 + d + d_1)}.
\]

Hence, the solutions of system (1) are ultimately bounded for all \(t \geq 0\). □
The feasible region of model (1)
\[ \Omega = \left\{ (S, E, A, I, Q, R) \in \mathbb{R}_+^6 : S + E + A + I \leq \frac{b}{d}, Q \leq \frac{b(f_1 + f_3)}{d(f_3 + d + d_1)} \right\} \]

is positively invariant for system (1).

Threshold dynamics

It is easy to see that there always exists a disease-free equilibrium \( E_0(S_0, 0, 0, 0, 0) \), where \( S_0 = b/d \). By determining the basic reproduction number [22], we can derive the basic reproduction number of system (1)

\[ R_0 = \frac{\beta(1 - \gamma_1)S_0}{\sigma(1 - \alpha)A} \frac{\beta(1 - \gamma_2)S_0}{\sigma(1 - \alpha)A} \]

The endemic equilibrium of (1) satisfies

\[ 0 = b - \beta(1 - \gamma_1)S(\sigma A^* + I^*) - dS^*, \]
\[ 0 = b - \beta(1 - \gamma_2)S(\sigma A^* + I^*) - dE^*, \]
\[ 0 = (1 - \rho)A^* - f_2A^* - \gamma_3A^* - dA^*, \]
\[ 0 = paE^* - \gamma_3E^* - df_1^* - dI^*, \]
\[ 0 = f_4^*f_2^*A^* - \gamma_5dQ^* - dQ^*, \]
\[ 0 = \gamma_1A^* + \gamma_2I^* - \gamma_3Q^* - dR^*. \]

When \( R_0 > 1 \), there exists an endemic equilibrium \( E_1 = (S^*, E^*, A^*, I^*, Q^*, R^*) \), where

\[ S^* = \frac{S_0}{R_0}, \quad E^* = \frac{b}{a + d}(1 - \frac{1}{R_0}), \quad A^* = \frac{1 - \rho}{\sigma(1 - \alpha)}E^*, \]
\[ I^* = \frac{paE^*}{\gamma_3 + d + d_1}, \quad Q^* = \frac{f_4^*f_2^*A^*}{\gamma_1A^* + \gamma_2I^* + \gamma_3Q^*}, \quad R^* = \frac{\gamma_1A^* + \gamma_2I^* + \gamma_3Q^*}{d}. \]

Since the first five equations do not contain \( R(t) \), then it is sufficient to consider the sub-system of (1) including \( S(t), E(t), A(t), I(t), Q(t) \) equations

\[
\begin{align*}
\frac{dS(t)}{dt} &= -\beta(1 - \gamma_1)S(t)(\sigma A(t) + I(t)) - dS(t) \\
\frac{dE(t)}{dt} &= -\beta(1 - \gamma_2)S(t)(\sigma A(t) + I(t)) - dE(t) \\
\frac{dA(t)}{dt} &= (1 - \rho)A(t) - f_2A(t) - \gamma_3A(t) - dA(t) \\
\frac{dI(t)}{dt} &= \rho E(t) - f_3I(t) - dI(t) \\
\frac{dQ(t)}{dt} &= f_4(I(t) - \gamma_3Q(t) - dQ(t) - dI(t).
\end{align*}
\]

(3)

Theorem 1. For system (3),

(i) If \( R_0 < 1 \), the disease-free equilibrium \( E_0 \) is locally asymptotically stable in \( \Omega \).

(ii) If \( R_0 > 1 \), the disease-free equilibrium \( E_0 \) is globally asymptotically stable in \( \Omega \).

Proof. The Jacobi matrix of system (3) at \( E_0 \) is given by

\[
J(E_0) = \begin{pmatrix}
-d & \sigma\beta(1 - \gamma_1)S_0 & -\beta(1 - \gamma_2)S_0 & 0 \\
0 & -\sigma(1 - \alpha)A & -\beta(1 - \gamma_2)S_0 & 0 \\
0 & 0 & -\sigma(1 - \alpha)A & -\beta(1 - \gamma_2)S_0 \\
0 & -\sigma(1 - \alpha)A & 0 & -\gamma_3 + df_4 \\
0 & 0 & -\gamma_3 + df_4 & 0 \\
0 & 0 & 0 & 0 \\
\end{pmatrix}
\]

Obviously, the characteristic equation with respect to \( J(E_0) \) always have negative real roots \( \lambda_1 = -d, \lambda_2 = -\gamma_3 + d_1 \), and other roots satisfy the following equation

\[ (\lambda + a + d)\lambda + f_3 + \gamma_1 + d)\lambda + f_3 + \gamma_1 + d) \]

Assume that there is an \( \lambda \) with nonnegative real part \( Re(\lambda) \geq 0 \). Then we can divide by \((\lambda + a + d)(\lambda + f_3 + \gamma_1 + d)(\lambda + f_3 + \gamma_1 + d)\) and take the absolute value of both sides of the equation, and we have

\[ 1 = \frac{pa\beta(1 - \gamma_1)S_0}{(\lambda + a + d)(\lambda + f_3 + \gamma_1 + d)} + \frac{(1 - \rho)\alpha\beta(1 - \gamma_2)S_0}{(\lambda + a + d)(\lambda + f_3 + \gamma_1 + d)} \]

If \( \lambda = x + yi \), where \( i \) is the imaginary unit, then

\[ \left| (\lambda + a + d)(\lambda + f_3 + \gamma_1 + d) \right| \geq (x + a + d)(x + f_3 + \gamma_1 + d) \geq (a + d)(x + f_3 + \gamma_1 + d) \]

Hence, we have

\[ 1 \leq \frac{pa\beta(1 - \gamma_1)S_0}{(\lambda + a + d)(\lambda + f_3 + \gamma_1 + d)} + \frac{(1 - \rho)\alpha\beta(1 - \gamma_2)S_0}{(\lambda + a + d)(\lambda + f_3 + \gamma_1 + d)} \]

which contradicts with \( R_0 < 1 \). Thus all roots of the characteristic equation have negative parts if \( R_0 < 1 \), which means that the disease-free equilibrium \( E_0 \) is locally asymptotically stable.

The method in [23] is applied to prove the global stability of the disease-free equilibrium. System (3) is rewritten in the form

\[ \begin{align*}
\frac{dX}{dt} &= F(X, Z) \\
\frac{dZ}{dt} &= G_1(X, Z) + G_2(X, Z_t) + G_3(X, Z_{t}), \\
G_1(X, 0) &= 0 \quad (i = 1, 2, 3),
\end{align*} \]

(4)

where \( X = (t, A(t), I(t), Q(t)), Z_t = (t - \tau, A(t - \tau), I(t - \tau), Q(t - \tau)) \)

\[ F(X, Z) = \begin{pmatrix}
\beta(1 - \gamma_1)S(\sigma A(t) + I(t)) - aE(t) - dE(t) \\
\beta(1 - \gamma_2)S(\sigma A(t) + I(t)) - aE(t) - dE(t) \\
(1 - \rho)A(t) - f_3A(t) - \gamma_3A(t) - dA(t) \\
\rho E(t) - f_3I(t) - dI(t) \\
\gamma_3A(t) + \gamma_2I(t) - \gamma_3Q(t) - dQ(t) - dI(t).
\end{pmatrix} \]

\[ G_1(X, Z) = \begin{pmatrix}
0 \\
0 \\
0 \\
0 \\
0 \\
0
\end{pmatrix}, \quad G_2(X, Z_t) = \begin{pmatrix}
0 \\
0 \\
0 \\
0 \\
0 \\
0
\end{pmatrix}, \quad G_3(X, Z_{t}) = \begin{pmatrix}
0 \\
0 \\
0 \\
0 \\
0 \\
0
\end{pmatrix} \]

\[ U_0 = (X_0, 0) = (S_0, 0) \text{ denotes the disease-free equilibrium of system. Thus we have the following two conditions} \]

\[ H_1 \quad \text{For} \quad \frac{dX}{dt} = F(X, Z) = b - dS(t), \text{ X_0 is globally asymptotically stable.} \]

\[ H_2 \quad G_1(X, Z) = AZ - G_1(X, Z), G_2(X, Z_t) = BZ_t - G_2(X, Z_t), G_3(X, Z_{t}) = CZ_t - G_3(X, Z_{t}), G_1(X, Z) \geq 0, G_2(X, Z_t) \geq 0, G_3(X, Z_{t}) \geq 0, \text{ where} \quad A = Dz_1G_1(X_0, 0), B = Dz_1G_2(X_0, 0), \quad C = Dz_1G_3(X_0, 0), \quad D = Dz_1G_3(X_0, 0), \]

\[ \begin{pmatrix}
-a + d \\
\sigma\beta(1 - \gamma_1)S_0 \\
\beta(1 - \gamma_2)S_0 \\
-\sigma(1 - \alpha)A \\
0 \\
0
\end{pmatrix} \]

\[ A \begin{pmatrix}
0 \\
0 \\
0 \\
0 \\
0 \\
0
\end{pmatrix} \]
\[ \dot{G}_2(X, Z_1) = G_3(X, Z_2) = \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}. \]

Define
\[ D = A + B + C = \begin{pmatrix} -(\alpha + d) & \sigma(1 - c\phi)S_0 & \beta(1 - c\phi)S_0 \\ -(f_1 + \gamma_1 + d) & \rho S_0 & 0 \\ 0 & f_1 & 0 \end{pmatrix}. \]

Note that \( D \) is an Metzler matrix, \(-D\) is an M-matrix, and all eigenvalues with respect to \( D \) have negative real parts when \( R_0 < 1 \). According to the theory in [24], we derive that \( Z(t) \) is globally asymptotically stable, which means
\[ \lim_{t \to \infty} Z(t) = 0. \]

Theorem 2. For system (3),

(i) If \( R_0 > 1 \), the endemic equilibrium \( E_1 \) is locally asymptotically stable in \( \mathbb{R}^3 \).

(ii) If \( R_0 > 1 \), the endemic equilibrium \( E_1 \) is globally asymptotically stable in \( \mathbb{R}^3 \).

Proof. The Jacobi matrix of system (3) at \( E_1 \) is given by
\[ J(E_1) = \begin{pmatrix} -\beta(\sigma A^* + I^*) - d & -\sigma S^* & -\beta S^* \\ \beta(\sigma A^* + I^*) & -(\alpha + d) & \beta S^* \\ 0 & 0 & -(f_1 + \gamma_1 + d) \end{pmatrix}. \]

where \( \beta = \beta(1 - c\phi) \). Obviously, the characteristic equation with respect to \( J(E_1) \) always has a negative real root \( \lambda_1 = -(\gamma_1 + d + d_1) \), and other roots satisfy the following equation

\[ \lambda + \beta(\sigma A^* + I^*) + d||[(\lambda + a + d)(\lambda + f_1 + \gamma_1 + d)(\lambda + \gamma_2 + f_2 + d)] - \lambda(\alpha + d) + d|| + (1 - p)a\sigma \lambda S^*/(\lambda + a + d)(\lambda + f_1 + \gamma_1 + d) \]

Using the similar discussion with Theorem 1, we assume that there exists an \( \lambda \) with nonnegative real part \( \text{Re}(\lambda) \geq 0 \). Then we can divide by \( (\lambda + a + d)(\lambda + f_1 + \gamma_1 + d)(\lambda + \gamma_2 + f_2 + d) \) and take the absolute value of both sides of the equation, and we have
\[ \left| \frac{\lambda + \beta(\sigma A^* + I^*) + d}{\lambda + d} \right| > 1. \]

For the left hand side of equality, we find that
\[ \left| \frac{\lambda + \beta(\sigma A^* + I^*) + d}{\lambda + d} \right| \leq \frac{pa\beta S^*}{(\lambda + a + d)(\lambda + f_1 + \gamma_1 + d)} + \frac{1 - p)a\sigma \lambda S^*/(\lambda + a + d)(\lambda + f_1 + \gamma_1 + d) \]

which leads to a contradiction. Then all roots of the characteristic equation have negative real parts when \( R_0 > 1 \). Thus, the endemic equilibrium \( E_1 \) is locally asymptotically stable.

Denote \( F(x) = x - 1 - \ln x(x > 0) \). It is obviously that \( F(x) \geq 0 \) and \( F'_{\max}(x) = F(1) = 0 \). Since the variables \( S(t), E(t), A(t), I(t) \) are decoupled from the \( Q(t) \) and \( R(t) \) equations, we only consider the sub-system of (1) including \( S(t), E(t), A(t), I(t) \) equations.

Define a Lyapunov function
\[ V(t) = S^*F \left( \frac{S(t)}{S^*} \right) + E^*F \left( \frac{E(t)}{E^*} \right) + \sigma \beta S^* \left( \frac{A(t)}{A^*} \right) + \frac{\beta S^*}{\gamma_2 + f_2 + d} \left( \frac{I(t)}{I^*} \right).
\]

Calculating the derivation of \( V(t) \) along the solutions of system (3), we get
\[ \frac{dV(t)}{dt} = \left( 1 - \frac{S^*}{S(t)} \right)(b - \beta S^*(\sigma A(t) + I(t)) - dS(t)) + \left( 1 - \frac{E^*}{E(t)} \right) \beta S^*(\sigma A(t) + I(t)) - aE(t) - dE(t)) + \frac{\beta S^*}{\gamma_2 + f_2 + d} \left( 1 - \frac{I^*}{I(t)} \right)(paE(t) - \gamma_2 I(t) - f_q I(t) - dI(t)) \]

Note that
\[ b = \beta S^*(\sigma A^* + I^*) + dS^*, (a + d) = \frac{\beta S^*(\sigma A^* + I^*)}{E^*}, \]

Then we can derive that
\[ \frac{dV(t)}{dt} = -d \left( \frac{S(t) - S^*}{S(t)} \right)^2 + \beta S^* A^* \left( \frac{3 - \frac{S^*}{S(t)} - \frac{A^*}{A(t)E^*}}{S^* I^* E(t)} \right) \]

Data source

Our data including confirmed COVID-19 cases from December 18, 2021 to January 20, 2022 in Xi’an are obtained from the Health Commission of Shannxi Province [26]. The data includes new confirmed cases, the cumulative number of confirmed cases, new cured cases and death cases. All data are used are from publicly available data sources.

Parameter estimation

Xi’an is an important central city in western China with a population of 12.9529 million. The first case in this outbreak was reported on December 9, 2021, and then the first round of nucleic acid testing in
Xi’an was launched. The results of genetic sequencing showed that the outbreak was caused by the delta variant.

The exposed period $1/\alpha$ is about 3.86 days for the delta mutant strain [27]. The vaccination rate of Xi’an is over 95% [28], and the overall vaccination effectiveness for two-dose vaccination was 59.0% [29]. The infectivity of symptomatic individuals is 3.85 times higher than asymptomatic individuals [30]. The nature recovery rate of symptomatic individuals is 59.0% [29]. The infectivity of symptomatic individuals is 3.85 times higher than asymptomatic individuals [30]. The vaccination rate of Xi’an is over 95% [28], and the overall vaccination effectiveness for two-dose vaccination was 59.0% [29]. The infectivity of symptomatic individuals is 3.85 times higher than asymptomatic individuals [30].

### Table 1
Parameter values and source.

| Parameter | Description | Mean | 95% CI | Source |
|-----------|-------------|------|-------|--------|
| $b$       | The number of newborn per day | 300  | –     | [32]   |
| $d$       | The natural mortality rate     | $2.06 \times 10^{-5}$ | –     | [32]   |
| $\beta$   | The transmission rate of COVID-19 by contacting with symptomatic infectious individuals | $5.18 \times 10^{-4}$ | [1.85 $\times 10^{-4}$, 8.52 $\times 10^{-4}$] | Fitted |
| $\phi$    | Vaccination rate of susceptible individuals | 0.95 | –     | [28]   |
| $c$       | Vaccine efficacy                | 0.59 | [0.160, 0.816] | [29]   |
| $\sigma$  | Reduced rate of the infection from asymptomatic infectious individuals | 0.2597 | [0.1391, 0.4854] | [30] |
| $1/\alpha$| The exposed period              | 3.86 | –     | [27]   |
| $\rho$    | The proportion of exposed       | 0.12 | –     | [31]   |
| $f_s$     | Isolation rate of asymptomatic infectious individuals | 0.1478 | [0.1068, 0.1888] | Fitted |
| $f_a$     | Isolation rate of symptomatic infectious individuals | 0.6599 | [0.5443, 0.7755] | Fitted |
| $r_s$     | Recovery rate of asymptomatic infectious individuals | 0.037 | –     | [31]   |
| $r_a$     | Recovery rate of symptomatic infectious individuals | 0.037 | –     | [31]   |
| $r_i$     | Recovery rate of isolated individuals | 1/21 | –     | Data   |
| $d_i$     | The death rate due to the disease | 0    | –     | Data   |
| $t_s$     | Isolation delay of asymptomatic infectious individuals | 4.0626 | [3.9070, 4.2181] | Fitted |
| $t_a$     | Isolation delay of symptomatic infectious individuals | 1.2945 | [1.2179, 1.3710] | Fitted |

### Table 2
Initial values in Xi’an.

| Initial values | Description | Mean | 95% CI | Source |
|----------------|-------------|------|-------|--------|
| $S(0)$         | Initial number of susceptible individuals | $12.9529 \times 10^5$ | –     | Data   |
| $E(0)$         | Initial number of exposed individuals | 1470 | [919, 2021] | Fitted |
| $A(0)$         | Initial number of asymptomatic infectious individuals | 15   | [7, 100] | Fitted |
| $I(0)$         | Initial number of symptomatic infectious individuals | 18   | [1, 34] | Fitted |
| $Q(0)$         | Initial number of isolated individuals | 19   | –     | Data   |
| $R(0)$         | Initial number of recovered individuals | 0    | –     | Data   |

### Fitting results

Given the uncertainty of the initial values and parameters, we use the LSM method to evaluate the model (1) with the estimated parameters and initial values in Tables 1 and 2. Fig. 2 shows the new confirmed cases and the cumulative number of confirmed cases in Xi’an with real data. The simulations are consistent with the real data, which verifies the accuracy of our model.

### Numerical simulations

In this section, we perform uncertainty and sensitivity (US) analysis, and calculate the sensitivity indexes of the basic reproduction number $R_0$, and state variables $E$, $A$, $I$, $Q$. These indexes reveal the important factors that might influence the spread of COVID-19. Then numerical simulations are implemented to illustrate our theoretical results. All simulations are implemented by Matlab.

Here we use partial rank correlation coefficients (PRCCs) and an extended Fourier amplitude sensitivity test (eFAST) to carry out sensitivity analysis. Based on sampling and rank transforms, PRCCs provide a measure of monotonicity of the linear effect on one variable but no other variables. Based on variance decomposition, eFAST provides a measure of the size of the effects of a single variable and the sum size of effects on its interactions with other variables, but the monotonicity of the effect is not obtained [33]. To have a more complete US analysis, we calculate PRCCs and eFAST sensitivity indexes of $R_0$, $E$, $A$, $I$, $Q$.

### Sensitivity analysis of $R_0$

The PRCCs and eFAST sensitivity analysis results of $R_0$ are shown in Fig. 3. The PRCCs show the correlation among the input and output variables. PRCCs values range from $-1$ to $1$, where the value $+1$ denotes a positive linear relationship of perfection, the value $-1$ denotes a negative linear relationship of perfection, and the value 0 denotes no relationship. Considering only $p < 0.01$, Fig. 3(a) reveals that the parameters $\beta$, $c$, $\phi$, $\sigma$, $r_i$, and $f_s$ have a significant effect on the basic reproduction number $R_0$.

In Fig. 3(b), the blue bar represents the sensitivity of the independent effects of a single parameter, denoted as $S_i$ (first-order sensitivity index), and the red bar represents the sum of the effects of a single parameter and the interactions between it and other parameters, denoted as $S_{Ti}$ (total-order sensitivity index). Considering only $p < 0.01$,
Fig. 2. The fitting results of our model with real data from December 18, 2021 to January 20, 2022 in Xi’an. (a) New confirmed cases. (b) The cumulative number of confirmed cases.

Fig. 3. (a) PRCCs for $R_0$. (b) eFAST for $R_0$.

The size relationship of $S_i$ is $\beta > \epsilon > \phi > f_i > \sigma > \gamma_1 > f_q$, and the size relationship of $S_T$ is $\beta > \epsilon > f_i > \phi > \sigma > \gamma_1 > f_q$.

The results of PRCCs and eFAST indicate that parameters $\beta$ and $\sigma$ have significantly positive effect on $R_0$, while parameters $\epsilon$, $\phi$, $f_T$, $\gamma$, $f_q$ have significantly negative effect on $R_0$.

Sensitivity analysis of $E$, $A$, $I$ and $Q$

To evaluate the importance of the parameter that appears at a certain time of the disease transmission process, we focus on the state variables $E$, $A$, $I$ and $Q$. Using Matlab, we calculate the PRCCs and eFAST ($S_i$) sensitivity indexes at multiple time points and plot time series in Figs. 4–7. Where the gray area indicates that there is no significant difference from zero.

Fig. 4(a) finds that the parameters $\beta$ and $\sigma$ are positively related to $E$, which means that the increase of infectivity may contribute to the exposed individuals. The parameters $\phi$, $\epsilon$ are negatively related to $E$, which means that the increase in vaccination rate and vaccine efficacy may contribute to the decrease of exposed individuals. Then we can see that a prolonged exposed period goes against the control of the disease. From Fig. 4(b), we can see that parameter $f_i$ has a strong sensitivity to $E$, which indicates that large-scale testing and rapid isolation of asymptomatic infectious individuals are conducive to controlling the spread of the disease.

From Fig. 5, we see that the parameters $\gamma_1$, $\beta$ and $f_i$ are negatively related to $A$ in the early stage. The most significant parameter $f_i$ suggests that we focus on the isolation of asymptomatic infectious individuals, which means that conducting large-scale nucleic acid testing is required when confirmed cases occur.

From Fig. 6, we note that the parameter $\alpha$ is positively related to $I$ at the initial stage, then rapidly decreases to negative correction and finally becomes no significant difference with zero. The phenomenon indicates that the longer the exposed period, the more individuals are infected. Parameter $\epsilon$ is also positively related to $I$, which means that more symptomatic infectious individuals may lead to more infection. The phenomenon indicates that the longer the exposed period, the more individuals are infected. Parameter $\phi$ is also positively related to $I$, which means that more symptomatic infectious individuals may lead to more infection. Fig. 7 indicates that the parameter $f_i$ is positively related to $Q$.

Numerical simulations

In this paper, we mainly focus on the impact of the vaccination rate, the isolation rate of the asymptomatic infectious individuals, and delay on the spread of the disease. Numerical simulations are carried out using Matlab.

Firstly, we set the parameters $b = 300, d = 2.06 \times 10^{-5}, \beta = 5.18 \times 10^{-5}, \epsilon = 0.59, \phi = 0.2597, \alpha = 0.2591, \rho = 0.12, f_i = 0.12, \gamma_1 = 0.037, \gamma_2 = 0.037, \gamma_3 = 1/21, f_q = 0.66, d_1 = 0.01, \epsilon_1 = 1, \epsilon_2 = 1$, and initial values $S(0) = 1.4 \times 10^7, E(0) = A(0) = 10^7, I(0) = 100, Q(0) = R(0) = 0$. Let $\phi = 0.5, 0.65, 0.8, 0.95$, respectively. Fig. 8 shows that the vaccination rate could reduce the peak value of asymptomatic and isolated individuals and peak time of disease.

Secondly, we set $f_i = 0.1, 0.3, 0.5$ and 0.8, respectively. Fig. 9 derives that the testing rate can reduce the peak value and peak time of the
asymptomatic and isolated individuals. Rapid and large-scale testing and isolating asymptomatic infectious individuals could contribute to the control of the disease. Finally, we set $r_2 = 1$ and $r_1 = 1, 2, 3, 4$ respectively. Also, we set $r_1 = 4$ and $r_2 = 0.5, 1, 2, 3, 4$ respectively. Fig. 10 shows that decrease of isolation delays contributes to the control of disease.

**Control strategy**

In this section, we consider the two different isolation strategies. Inspired by the control strategies in [34], we first consider the disease control with constant isolation rates $f_1$ and $f_2$ under the limited resources. Then we investigate the optimal isolation strategies, in which the isolation rates are time-varying.

**Disease control with constant isolation strategies**

In this subsection, we mainly focus on the isolation implementation policy of COVID-19 when the isolation resource is limited. We assume that our resource is $m$, and isolating an asymptomatic person or symptomatic person consumes one resource. Thus the resource occupied by isolated individuals could be denoted as

$$c(t) = \int_0^t (f_1A(t-r_1) + f_2I(t-r_2)) dt$$

Our goal is to ensure $c(t) \leq m, t \in [0, T]$. Fig. 11 shows the cumulative number of infected individuals of model (1) with constant isolation rates $f_1$ and $f_2$ in different resource $m$. Fig. 11 indicates that when the resource is less than 2200, the bigger $f_1$ is not the better, and there exists a best choice to minimize the cumulative number of infected individuals. Isolating asymptomatic infectious individuals takes resources away from isolating symptomatic infectious individuals, which leads to a wider spread of disease. This situation does not happen when resources are plentiful. For example, if the total resource is 2400, the cumulative number of infected individuals with $f_1 = 1$ arrives at the least. Our results are consistent with the COVID-19 treatment protocol of the ninth edition [35]. The asymptomatic infectious individuals and mild cases are centralized to isolate, and the general and severe cases are treated intensively in the hospital.
Fig. 6. (a) Time-varying PRCCs sensitivity analysis indexes of $I$. (b) Time-varying first-order eFAST sensitivity analysis indexes of $I$.

Fig. 7. (a) Time-varying PRCCs sensitivity analysis indexes of $Q$. (b) Time-varying first-order eFAST sensitivity analysis indexes of $Q$.

Fig. 8. The effect of vaccination rate on the COVID-19 transmission.
Disease control with optimal isolation strategies

In this subsection, we investigate an optimal control model for the COVID-19 transmission by replacing the isolation rate for asymptomatic infectious individuals with \( u_1(t) \) and the isolation rate for symptomatic infectious individuals with \( u_2(t) \). Our objective here is to study the optimal isolation strategies with the minimum cost. The optimal control system of differential equations is given by

\[
\begin{aligned}
\frac{dS(t)}{dt} &= b - \beta (1 - c\phi)S(t)(\sigma A(t) + I(t)) - dS(t) \\
\frac{dE(t)}{dt} &= \beta (1 - c\phi)S(t)(\sigma A(t) + I(t)) - aE(t) - dE(t) \\
\frac{dA(t)}{dt} &= (1 - \rho)\alpha E(t) - u_1(t)A(t) - \gamma_1 A(t) - dA(t) \\
\frac{dI(t)}{dt} &= \rho\alpha E(t) - u_2(t)I(t) - \gamma_2 I(t) - dI(t) \\
\frac{dQ(t)}{dt} &= u_1(t)A(t - \tau_1) + u_2(t)I(t - \tau_2) - \gamma_3 Q(t) - dQ(t) - \delta Q(t)
\end{aligned}
\]

with initial conditions

\[
S(\theta) = \varphi_1(\theta),
E(\theta) = \varphi_2(\theta),
A(\theta) = \varphi_3(\theta),
I(\theta) = \varphi_4(\theta),
Q(\theta) = \varphi_5(\theta),
\varphi_i(\theta) \geq 0(i = 1, 2, 3, 4, 5, 6), \theta \in [-\tau, 0], \text{ and } 0 \leq t \leq T.
\]

Where \( T \) is the final time. We suppose that the time-varying control functions \( u_i(t) \in [0, 1], i = 1, 2 \) are Lebesgue integrable on the interval \([0, T]\). We aim to reduce the number of infected individuals and minimize the cost for isolated individuals. Our objective function \( J(u_1, u_2) \) is defined as

\[
J(u_1, u_2) = \int_0^T \left[ E(t) + A(t) + I(t) + Q(t) + \frac{B_1}{2}u_1^2(t) + \frac{B_2}{2}u_2^2(t) \right] dt.
\]

The above integrand reflects the cumulative level over the time \([0, T]\) that we implement isolation measures and the cost of isolation, where \( B_i(t) = 1, 2 \) denote the weight constant which means the importance of implementing isolation measures. According to the meaning of \( u_i(t) \) and \( u_2(t) \), it is reasonable to assume that the upper bound is 1 and the lower bound is 0. Our goal is to find the optimal control \( u_1^* \) and \( u_2^* \) such that

\[
J(u_1^*, u_2^*) = \min_{(u_1, u_2) \in A} J(u_1, u_2),
\]

where \( A = \{(u_1, u_2) \in L^1[0, T] : 0 \leq u_1(t) \leq 1, 0 \leq u_2(t) \leq 1\} \). By the Filippov–Cesari Existence Theorem and the Mangasarian Theorem [36], an unique solution \((u_1^*, u_2^*)\) which is the optimal control exists. Then we could find this solution by Pontryagin’s Minimum Principle [37].
The necessary conditions of optimal control problem could be obtained by dealing with the Hamilton function

\[
H(t) = E(t) + A(t) + I(t) + Q(t) + \frac{B_1}{2} u_1^2(t) + \frac{B_2}{2} u_2^2(t)
\]

\[
\begin{aligned}
&+ \lambda_1(t)[b - \beta(1 - c\phi)(\sigma A(t) + I(t)) - dS(t)] \\
&+ \lambda_2(t)[\beta(1 - c\phi)(\sigma A(t) + I(t)) - dE(t) - dE(t)] \\
&+ \lambda_3(t)[(1 - \rho)aE(t) - u_1(t)A(t) - \gamma_1 A(t) - dA(t)] \\
&+ \lambda_4(t)[\alpha_{1}(t)A(t - \tau_1) - u_2(t)I(t) - \gamma_2 I(t) - dI(t)] \\
&+ \lambda_5(t)[u_1(t)A(t - \tau_1) + u_2(t)I(t - \tau_2) - \gamma_3 Q(t) - dQ(t) - d_{\lambda} Q(t)].
\end{aligned}
\]

(7)

where \(\lambda(t) = (\lambda_1(t), \lambda_2(t), \lambda_3(t), \lambda_4(t), \lambda_5(t))^T\) is the adjoint variable satisfying

\[
\begin{aligned}
\frac{d\lambda_1(t)}{dt} &= -\frac{\partial H}{\partial S}(t) \\
\frac{d\lambda_2(t)}{dt} &= -\frac{\partial H}{\partial A}(t) \\
\frac{d\lambda_3(t)}{dt} &= -\frac{\partial H}{\partial E}(t) - \chi_{[0,T-\tau_1]}(t)\frac{\partial H}{\partial \alpha_1}(t - \tau_1) \\
\frac{d\lambda_4(t)}{dt} &= -\frac{\partial H}{\partial I}(t) - \chi_{[0,T-\tau_2]}(t)\frac{\partial H}{\partial \alpha_2}(t - \tau_2) \\
\frac{d\lambda_5(t)}{dt} &= -\frac{\partial H}{\partial Q}(t) \\
\end{aligned}
\]

(8)

with the transversality conditions \(\lambda_i(T) = 0 (i = 1, 2, 3, 4, 5)\). Here \(A_{\tau_i}\) represents the delayed state variable of \(A\) by \(A_{\tau_1} = A(t - \tau_1)\), \(I_{\tau_2}\) represents the delayed state variable of \(I\) by \(I_{\tau_2} = I(t - \tau_2)\), and \(\chi_{[0,T-\tau]}(t)\) is indicator functions on \([0,T-\tau]\) satisfying

\[
\chi_{[0,T-\tau]}(t) = \begin{cases} 1, & t \in [0,T-\tau], \\ 0, & \text{Otherwise.} \end{cases}
\]

The adjoint equation

\[
\frac{\partial H}{\partial u_1}(t) = \frac{\partial H}{\partial u_2}(t) = 0.
\]

(9)

Theorem 3. Assume that \(u^*(t) = (u_1^*(t), u_2^*(t))\) and \((S(t), E(t), A(t), I(t), Q(t))\) are the solutions of system (5), and there exist adjoint variable \(\lambda^*(t) = (\lambda_1^*(t), \lambda_2^*(t), \lambda_3^*(t), \lambda_4^*(t), \lambda_5^*(t))^T\) of adjoint Eqs. (8) and optimal control \(u^*(t)\) of optimality Eq. (9) such that

\[
H(S(t), \dot{E}(t), \dot{A}(t), \dot{I}(t), \dot{Q}(t), u^*(t), \lambda^*(t))
\]

\[
= \min_{u \in \mathcal{A}} H(S(t), E(t), A(t), I(t), Q(t), u(t), \lambda(t)).
\]

Furthermore, the optimal control can be expressed as

\[
\begin{aligned}
u_1^*(t) &= \min \left\{1, \frac{1}{B_1} \left[\frac{\lambda_1^*(t) - \lambda_2^*(t)}{\lambda_1^*(t) A(t)} \right] \right\}, \\
u_2^*(t) &= \min \left\{1, \frac{1}{B_2} \left[\frac{\lambda_4^*(t) - \lambda_5^*(t)}{\lambda_4^*(t) I(t)} \right] \right\}.
\end{aligned}
\]

(10)

Proof. Computing the adjoint system, we derive

\[
\begin{aligned}
\frac{d\lambda_1(t)}{dt} &= \lambda_1(t) - \lambda_2(t) - \beta(1 - c\phi)(\sigma A(t) + I(t)) - dS(t), \\
\frac{d\lambda_2(t)}{dt} &= -1 + (a + \gamma_1 \alpha_1)(A(t) - \gamma_1 A(t)), \\
\frac{d\lambda_3(t)}{dt} &= -1 + \sigma(1 - c\phi)S(t)[\lambda_1(t) - \lambda_2(t)] + (u_1(t) + \gamma_1 + \gamma_2 A(t)), \\
\frac{d\lambda_4(t)}{dt} &= -1 + \beta(1 - c\phi)S(t)[\lambda_1(t) - \lambda_2(t)] + (u_2(t) + \gamma_2 I(t) + \gamma_3 Q(t)), \\
\frac{d\lambda_5(t)}{dt} &= -1 + (\gamma_3 + \gamma_4 + \gamma_5 I(t)) - dI(t).
\end{aligned}
\]

(10)

According to the optimality condition, we get

\[
\begin{aligned}
B_1 u_1(t) - \lambda_1(t) A(t) + \lambda_2(t) A(t - \tau_1) &= 0, \\
B_2 u_2(t) - \lambda_4(t) I(t) + \lambda_5(t) I(t - \tau_2) &= 0.
\end{aligned}
\]

Then we obtain an unique solution \(\bar{u}(t) = (\bar{u}_1(t), \bar{u}_2(t))\) in terms of state variables and adjoint variables, where

\[
\begin{aligned}
\bar{u}_1(t) &= \frac{1}{B_1} \left[\lambda_1(t) A(t) - \lambda_2(t) A(t - \tau_1)\right], \\
\bar{u}_2(t) &= \frac{1}{B_2} \left[\lambda_4(t) I(t) - \lambda_5(t) I(t - \tau_2)\right].
\end{aligned}
\]

Since \(u^*(t)\) belongs to \(\mathcal{A}\), then we have

\[
\begin{aligned}
\bar{u}_1^*(t) &= \min \left\{1, \max \left\{0, \bar{u}_1(t)\right\}\right\} \\
\bar{u}_2^*(t) &= \min \left\{1, \max \left\{0, \bar{u}_2(t)\right\}\right\}.
\end{aligned}
\]

Substituting \(u^*(t) = (\bar{u}_1^*(t), \bar{u}_2^*(t))\) into systems (5) and (10), combining the initial conditions and the transversality conditions, and using the forward–backward sweep method [37], then we obtain the corresponding state variables \((S(t), E(t), A(t), I(t), Q(t))\) and adjoint variables \((\lambda_1^*(t), \lambda_2^*(t), \lambda_3^*(t), \lambda_4^*(t), \lambda_5^*(t))\). \(\square\)
In the optimal control, we choose the parameter values $b = 300$, $d = 2.06 \times 10^{-5}$, $\beta = 5.18 \times 10^{-8}$, $\phi = 0.95$, $\epsilon = 0.59$, $\sigma = 0.2597$, $\alpha = 0.2591$, $p = 0.12$, $\tau_1 = 0.037$, $\tau_2 = 0.037$, $\tau_3 = 1/21$, and $d_1 = 0.01$. Initial values are $S(0) = 10^7$, $E(0) = 10^3$, $A(0) = 200$, $I(0) = 100$, $Q(0) = R(0) = 0$, delays $\tau_1 = 4$ and $\tau_2 = 1$, and the weights in the objective function $B_1 = 10$ and $B_2 = 15$. Fig. 12 shows the time-varying control values during 50 days in model (5). Fig. 13 shows the time series for exposed individuals, asymptomatic infectious individuals, symptomatic infectious individuals, isolated individuals over time with and without optimal control. Fig. 14 shows the cumulative number of infected people and the consumed resource with and without optimal control. The results in Figs. 12–14 suggest that the optimal control is effective in reducing the number of infected people and controlling the spread of the disease. From Figs. 12–14, we find that taking the strongest possible controls in the first ten days could drastically reduce the number of exposed individuals, asymptomatic infectious individuals, symptomatic infectious individuals, isolated individuals over time with and without optimal control. Fig. 14 shows the cumulative number of infected people and the consumed resource with and without optimal control.

The results in Figs. 12–14 suggest that the optimal control is effective in reducing the number of infected people and controlling the spread of the disease. From Figs. 12–14, we find that taking the strongest possible controls in the first ten days could drastically reduce the number of exposed individuals, asymptomatic infectious individuals, symptomatic infectious individuals, isolated individuals over time with and without optimal control. Also, the cumulative number of infected people decreases significantly. Besides, improving the detection coverage rate and frequency in the early stage of the epidemic effectively contains the COVID-19 spread. Meanwhile, the results suggest that testing on the high-risk population and decreasing the testing frequency may minimize the economic loss of the epidemic. Fig. 14 gives that the resource consumption of optimal control is reduced by 17.6% compared to the constant control, while the cumulative number of infected individuals decreases by 30%. Therefore, we can conclude that optimal control plays an important role in controlling the spread of the disease.

**Conclusion and discussion**

Since the first case was reported in December 2019, COVID-19 rapidly spread across the world and cause over 6 million death and enormous economic losses. To study the effect of vaccination and isolation delays on the transmission of COVID-19, we develop a mathematical model of COVID-19 transmission with vaccination and isolation delays. We calculate the basic reproduction number, and the global dynamics of the mathematical model are proved. Parameters are estimated, and sensitivity analysis is carried out. The effect of vaccination and isolation delays on the transmission of COVID-19 is assessed. The optimal isolation problem under the limited resource for the constant and variant isolation resources is investigated.

This is the first study to prove the global dynamics of the mathematical model of COVID-19 transmission with vaccination and isolation delays. The basic reproduction number is calculated, and the global dynamics are completely determined by the basic reproduction number $R_0$. When $R_0 < 1$, the disease-free equilibrium is globally asymptotically stable, which means that the disease dies out. The unique endemic equilibrium is globally asymptotically stable when $R_0 > 1$, which means that the disease persists.

Our results find that the isolation rates of asymptomatic and symptomatic infectious individuals have a significant impact on the transmission of COVID-19. PRCCs and eFAST are applied to assess the effect of parameters on $R_0$ and $E, A, I, Q$. PRCCs show the monotonicity relation between input and output factors, but eFAST could assess the magnitude of parameters sensitivity. Firstly, the results show that parameters
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Our findings show that the optimal control strategies of our model with vaccination and isolation delays are analyzed. When the limited isolation resource is constant, the optimal isolation rates of asymptomatic and symptomatic infectious individuals are obtained to minimize the cumulative number of infected individuals and effectively contain the transmission of COVID-19. When the resources are abundant, the isolation rates could be as large as possible. When the isolation rates are time-varying, the optimal isolation strategies with the minimum cost are acquired in the system (5). The results show that the resource consumption of optimal control is reduced by 17.6% compared to the constant control, while the cumulative number of infected individuals decreases by 30%. To minimize the cumulative number of infected individuals and the cost of disease control, testing on the high-risk population and decreasing the testing frequency may minimize the economic loss of the epidemic.

It is of great significance to investigate the effect of contact tracing on the transmission of COVID-19. Contact tracing is an intervention where close contacts at risk of infection are required to quarantine themselves when a confirmed case is detected [11]. Contact tracing has a big influence on reducing the transmission of COVID-19. For future work, we may assess the effect of contact tracing on the transmission of COVID-19. Our findings in this paper may help public health to prevent and control the transmission of COVID-19.

CRediT authorship contribution statement

Haitao Song: Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing. Ruifeng Wang: Formal analysis, Writing – original draft, Writing – review & editing. Shengqiang Liu: Writing – original draft, Writing – review & editing. Zhen Jin: Writing – original draft, Writing – review & editing. Daihai He: Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing.

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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Fig. 14. (a)The cumulative number of infected individuals with and without control. (b)The consumed resources with and without control.
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