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Optimal control and cost-effectiveness analysis of a new COVID-19 model for Omicron strain
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A B S T R A C T
Omicron, a mutant strain of COVID-19, has been sweeping the world since November 2021. A major characteristic of Omicron transmission is that it is less harmful to healthy adults, but more dangerous for people with underlying disease, the elderly, or children. To simulate the spread of Omicron in the population, we developed a new 9-dimensional mathematical model with high-risk and low-risk exposures. Then we analyzed its dynamic properties and obtain the basic reproduction number $R_0$. With the data of confirmed cases from March 1, 2022 published on the official website of Shanghai, China, we used the weighted nonlinear least square estimation method to estimate the parameters, and get the basic reproduction number $R_0 \approx 1.5118$. Finally, we considered three control measures (isolation, detection and treatment), and studied the optimal control strategy and cost-effectiveness analysis of the model. The control strategy $G$ is determined to be the optimal control strategy from the purpose of making fewer people infected. In strategy $G$, the three human control measures contain six control variables, and the control strength of these variables needs to be varied according to the pattern shown in Figure 11, so that the number of infections can be minimized and the percentage of reduction of infections can reach more than 95%.

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1. Introduction

The novel coronavirus pneumonia is named “COVID-19” by WHO, which refers to pneumonia caused by 2019 new corona virus infection. In the current, the global epidemic situation of COVID-19 is still very severe. As of May 26, 2022, there are more than 527 million confirmed cases and nearly 6.29 million deaths worldwide [1]. COVID-19 is highly infectious, and it has a great impact on human health and life, and on the global economy. COVID-19 will damage the respiratory system, immune system and even the reproductive system [2]. Many people cannot work normally and the pressure of life is increasing. The global economy suffered the worst recession last year, since the great depression of the 30s of last century. In the future, COVID-19 may inhibit the global economic development for a long time.

Omicron (No. B.1.1.529), a variant of the novel 2019 coronavirus. It was first detected in South Africa on November 9, 2021. On November 26, 2021, the World Health Organization defined it as the fifth “variant of concern” with the Greek letters Omicron. On November 29, WHO said that the overall global risk assessment for the Omicron variant of the new coronavirus was “very high” and that it could spread widely around the world. On January 4, 2022, WHO said that by the Christmas and New Year holidays, 128 countries and territories had reported the detection of the Omicron variant. On

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1 March 2022, the website of Shanghai Municipal Health Commission reported that 2 cases of Omicron were found [3]. From this point on, Omicron began widespread transmission in Shanghai, China.

Since the outbreak of COVID-19 in 2020, many scholars have begun to study the spread of COVID-19 by establishing epidemic dynamics model. They have done a lot of work in modeling, prediction and control, which provide a lot of valuable references for later people.

Many scholars have established a series of different dynamic models for different reasons. Wickramararachchi and Perera [4] used a classic SEIR model with standard incidence to simulate the spread of COVID-19 in Sri Lanka. Considering that the incidence would change with the increase of the infected people, Rohith and Devika [5] established a SEIR model with saturation incidence to simulate the transmission of COVID-19. Kwuimy et al. [6] considered a SEIRD model with public and government behavior intervention, analyzed the dynamic properties of the model, and studied the impact of these behavior on disease dynamics in South Korea. There are also some important COVID-19 models, please see Refs. [7–10].

In the simulation of the propagation of COVID-19, the parameters of the model need to be selected. Many scholars used different parameter estimation methods to fit different warehouses in different areas and different time periods. With the help of the estimated parameters, further prediction or control can be done. Awais et al. [11] used the nonlinear least square estimation method to fit the cumulative number of confirmed cases in China from January 21 to April 9, 2020, and obtained the estimated values of each parameter, and calculated the $R_0 = 4.95$. Sun et al. [12] used an extended MCMC algorithm to fit the cumulative number of confirmed cases from January 15 to March 30, 2020 in Wuhan City, Hubei Province, China. Similar applications can also refer to [13–18].

The above scholars fitted the number of confirmed cases, and some scholars noted that other data are also very important. Tsay et al. [19] used the nonlinear least square estimation method to simulate the number of confirmed, recovered and asymptomatic cases in the United States from January 22 to April 16, 2020. Zhu et al. [20] used a two-step iterative optimization algorithm to fit the number of confirmed cases and recovered cases in Wuhan.

Many scholars added specific control measures of local government in a certain area to the mathematical model to analyze its control effect. Tchepmo et al. [21] considered the blockade protection measures in South Africa in the model, and studied the protection effect and prediction of the policy on healthy people. Khan et al. [22] considered a fractional order COVID-19 model with quarantined and isolation in the model, and got a better fitting result. Alota et al. [23] considered the effect of testing, contact tracing and household quarantine on reducing the spread of the disease in Boston during the second wave of COVID-19 pandemic. Silva et al. [24] considered the impact of the emergency lockdown order on people’s lives during COVID-19, proposed a SAIRP model with protected groups, and simulated case data for Portugal from March 2 to July 29, 2020. They then applied optimal control theory to maximize the number of people returning to “normal life” and to minimize the number of active infections at minimal economic cost while ensuring low levels of hospitalization. This work allows testing various control scenarios during a disease pandemic (closure of economic sectors, partial/full compliance of citizens with protective measures, number of intensive care unit beds, etc.) and becomes a tool to support public health decisions. Yuan et al. [25] considered the importance of personal protection awareness among susceptible individuals during the COVID-19 epidemic and proposed a 6-dimensional deterministic compartment model for a group of susceptible individuals with self-protection awareness. Through global sensitivity analysis of parameters in the basic reproduction number, the authors proposed three control means (personal protective measures, vaccination, and awareness programs) to curb the spread of COVID-19. The results of the study showed that awareness-raising controls could further reduce the number of COVID-19 infections. There are also many important literatures about COVID-19, please refer to [26–33].

Inspired by the above literatures, the differences between this paper and previous literatures are as follows.

(i) Based on the characteristics of Omicron and its propagation law, a new 9-dimensional deterministic compartment model is developed.
(ii) In the parameter estimation process, the weighted least squares estimation method was used to fit the data in order to make full use of the reported data.
(iii) In addition to the control strategies considered by the above scholars, we also consider the treatment measure that plays an important role in the control of the epidemic in the real world.

The rest of this paper is organized as follows. The model formulation is presented in Section 2. The basic reproduction number and all equilibria are obtained in Section 3. Stability analysis of disease-free equilibrium is proved in Section 4. Optimal control problem is analyzed in Section 5. All numerical simulation are carried out in Section 6. Finally, the conclusions are presented in Section 7.

2. The model formulation

2.1. System description

Before modeling, we considered some of the following facts related to COVID-19.

(1) The Omicron strain is compared to other COVID-19 variant strains. It is a much weaker strain and is a self-limiting disease that is strongly related to the body’s resistance [34]. Among those exposed, the elderly, children and some younger people with diseases such as diabetes or AIDS, who are less resistant, are at greater risk of contracting COVID-19 [35,36].
Because of the significant difference in risk between them and normal young adults, we divided the exposed individuals into high-risk $E_1$ and low-risk $E_2$.

(2) Because asymptomatic, mild and severely infected people have different amounts of virus in their bodies, they have different rates of transmission when they come into contact with susceptible people [37]. Therefore, we divided the infected persons into three categories: asymptomatic infected $I_1$, mild infected $I_2$ and severe infected $I_3$.

(3) After being tested and confirmed by the hospital, COVID-19 patients will be sent to different places for treatment according to their symptoms of infection [38]. Asymptomatic and mild, will be arranged to Fangcang hospital for treatment. Severe cases are transferred to the ICU for treatment. Their cure rates are different. So we divide the treated population into $T_1$ and $T_2$.

Based on the analysis of the characteristics of Omicron strain, we divided the total population denoted by $N(t)$ into 9 compartments, namely: $S(t), E_{1}(t), E_{2}(t), I_{1}(t), I_{2}(t), I_{3}(t), T_{1}(t), T_{2}(t), R(t)$, and their meanings are shown in Table 1. Thus, the total population is given by:

$$N(t) = S(t) + E_{1}(t) + E_{2}(t) + I_{1}(t) + I_{2}(t) + I_{3}(t) + T_{1}(t) + T_{2}(t) + R(t).$$  (1)

The population flow among those compartments is shown in Fig. 1. The transfer diagram leads to the following system of ordinary differential equations:

$$S'(t) = \Lambda - \mu S - \beta S \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{N},$$

$$E'_{1}(t) = \theta \beta S \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{N} - (v_1 + v_2 + v_2 + \mu)E_1,$$

$$E'_{2}(t) = (1 - \theta)\beta S \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{N} - (v_4 + v_5 + v_6 + \mu)E_2,$$

$$I'_{1}(t) = v_1 E_1 + v_4 E_2 - (w_1 + w_2 + \mu)I_1,$$

$$I'_{2}(t) = v_2 E_1 + v_5 E_2 - (w_3 + w_4 + \mu)I_2,$$

$$I'_{3}(t) = v_6 E_1 + v_6 E_2 - (w_5 + w_6 + \mu)I_3,$$

$$T'_{1}(t) = w_1 I_1 + w_2 I_2 + w_3 I_3 + \eta_1 T_1 - (\eta_1 + \xi_1 + \mu)T_1,$$

$$T'_{2}(t) = w_4 I_1 + w_5 I_2 + w_6 I_3 + \eta_2 T_1 - (\eta_2 + \xi_2 + \mu + d)T_2,$$

$$R'(t) = \xi_1 T_1 + \eta_2 T_2 - \mu R.$$  (2)
For the convenience of the following expression, we will make the following abbreviations. $\lambda_0 = \frac{\alpha_1 + \alpha_2 + \alpha_3}{N}$,  
$k_1 = v_1 + v_2 + v_3 + \mu$,  
k_2 = v_4 + v_5 + v_6 + \mu$,  
k_3 = w_1 + w_2 + \mu$,  
k_4 = w_3 + w_4 + \mu$,  
k_5 = w_5 + w_6 + \mu$,  
k_6 = \eta_1 + \xi_1 + \mu$,  
k_7 = \eta_2 + \xi_2 + \mu + d$.

By adding all the equations of system (2), we get

$$\frac{dN}{dt} = \Lambda - \mu N - dT_2 \leq \Lambda - \mu N,$$

which yields that

$$\limsup_{t \to \infty} N(t) \leq \frac{\Lambda}{\mu}.$$ 

Therefore, we get the following biologically feasible region for the COVID-19 model given by (2) is

$$\Omega = \{(S, E_1, E_2, I_1, I_2, I_3, T_1, T_2, R) \in \mathbb{R}^9_+ : S + E_1 + E_2 + I_1 + I_2 + I_3 + T_1 + T_2 + R \leq \frac{\Lambda}{\mu}\},$$

and it is a positive invariant set of system (2).

3. The basic reproduction number and existence of equilibria

3.1. The basic reproduction number

Through the analysis of system (2), we can get the Disease-Free Equilibrium $D_0$

$$D_0 = \left(\frac{\Lambda}{\mu}, 0, 0, 0, 0, 0, 0, 0, 0\right).$$

(3)

From the perspective of biomathematics, the basic reproduction number is a crucial concept, which involves whether the disease will spread or die out [39]. Thus, the basic reproduction number of system (2) will be obtained by the next
generation matrix method. Let $x = (E_1, E_2, I_1, I_2, I_3, T_1, T_2, R, S)^T$, then the system (2) can be rewritten as
\[
\frac{dx}{dt} = \mathcal{F}(x) - \mathcal{V}(x),
\]
where
\[
\mathcal{F}(x) = \begin{pmatrix}
\theta \beta S \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{N} \\
(1 - \theta) \beta S \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{N} \\
0 \\
0 \\
0 \\
0 \\
0 \\
0
\end{pmatrix},
\]
\[
\mathcal{V}(x) = \begin{pmatrix}
k_1 E_1 \\
k_2 E_2 \\
k_3 I_1 - v_1 E_1 - v_4 E_2 \\
k_4 I_2 - v_2 E_1 - v_5 E_2 \\
k_5 I_3 - v_3 E_1 - v_6 E_2 \\
-w_1 I_1 - w_3 I_2 - w_5 I_3 - \eta_2 T_2 + k_6 T_1 \\
-w_2 I_1 - w_4 I_2 - w_6 I_3 - \eta_1 T_1 + k_7 T_2 \\
-\xi_1 I_1 - \xi_2 T_2 + \mu R \\
-\Lambda + \mu S + \beta S \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{N}
\end{pmatrix}.
\]

The Jacobian matrices of $\mathcal{F}(x)$ and $\mathcal{V}(x)$ at the Disease-Free Equilibrium $D_0$ are
\[
D\mathcal{F}(D_0) = \begin{pmatrix}
F_{7 \times 7} \\
0 \\
0
\end{pmatrix},
D\mathcal{V}(E_0) = \begin{pmatrix}
V_{7 \times 7} \\
J_1 \\
J_2
\end{pmatrix},
\]
where
\[
F_{7 \times 7} = \begin{pmatrix}
0 & 0 & \theta \beta \alpha_1 & \theta \beta \alpha_2 & \theta \beta \alpha_3 & 0 & 0 \\
0 & 0 & (1 - \theta) \beta \alpha_1 & (1 - \theta) \beta \alpha_2 & (1 - \theta) \beta \alpha_3 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0
\end{pmatrix},
\]
\[
V_{7 \times 7} = \begin{pmatrix}
k_1 & 0 & 0 & 0 & 0 & 0 & 0 \\
k_2 & 0 & 0 & 0 & 0 & 0 & 0 \\
-v_1 & -v_4 & k_3 & 0 & 0 & 0 & 0 \\
-v_2 & -v_5 & 0 & k_4 & 0 & 0 & 0 \\
-v_3 & -v_6 & 0 & 0 & k_5 & 0 & 0 \\
0 & 0 & -w_1 & -w_3 & -w_5 & k_6 & -\eta_2 \\
0 & 0 & -w_2 & -w_4 & -w_6 & -\eta_1 & k_7 \\
\end{pmatrix},
\]
\[
J_1 = \begin{pmatrix}
0 & 0 & 0 & 0 & -\xi_1 & -\xi_2 \\
0 & \alpha_1 \beta & \alpha_2 \beta & \alpha_3 \beta & 0 & 0
\end{pmatrix},
J_2 = \begin{pmatrix}
\mu & 0 \\
0 & \mu
\end{pmatrix}.
\]
The basic reproduction number, denoted by $R_0$, is given by
\[
R_0 = \rho(FV^{-1}) = \frac{\beta(1 - \theta) + \frac{\alpha_1}{k_3} v_4 + \frac{\alpha_2}{k_4} v_5 + \frac{\alpha_3}{k_5} v_6}{\alpha_1 + \frac{\alpha_2}{k_4} v_5 + \frac{\alpha_3}{k_5} v_6} + \frac{\beta \theta}{k_1} \left( \frac{\alpha_1}{k_3} v_1 + \frac{\alpha_2}{k_4} v_2 + \frac{\alpha_3}{k_5} v_3 \right)
\]
\[
\triangleq R_1 + R_2,
\]
where
\[
R_1 = \frac{\beta(1 - \theta)}{k_2} \left( \frac{\alpha_1}{k_3} v_4 + \frac{\alpha_2}{k_4} v_5 + \frac{\alpha_3}{k_5} v_6 \right),
R_2 = \frac{\beta \theta}{k_1} \left( \frac{\alpha_1}{k_3} v_1 + \frac{\alpha_2}{k_4} v_2 + \frac{\alpha_3}{k_5} v_3 \right).
\]

3.2. Existence of endemic equilibrium

The Endemic Equilibrium $D^*(S^*, E_1^*, E_2^*, I_1^*, I_2^*, I_3^*, T_1^*, T_2^*, R^*)$ of system (2) is determined by equations:
\[
\Lambda - \mu S - \beta S \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{N} = 0,
\]
\[
\theta \beta S \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{N} - k_1 E_1 = 0,
\]
\[
(1 - \theta) \beta S \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{N} - k_2 E_2 = 0,
\]
\[
v_1 E_1 + v_4 E_2 - k_3 I_1 = 0,
\]
\[
v_2 E_1 + v_5 E_2 - k_4 I_2 = 0,
\]
\[
v_3 E_1 + v_6 E_2 - k_5 I_3 = 0.
\]
By adding all equations of (5)–(13), we have

\begin{align}
    w_1I_1 + w_3I_2 + w_5I_3 + \eta_2T_2 - k_5T_1 &= 0, \quad (11) \\
    w_2I_1 + w_4I_2 + w_6I_3 + \eta_1T_1 - k_7T_2 &= 0, \quad (12) \\
    \xi_1T_1 + \eta_2T_2 - \mu R &= 0. \quad (13)
\end{align}

By solving the above equations, we can get the following relations.

\begin{align*}
    S^* &= \frac{N^*}{R_0}, \\
    E_1^* &= \frac{\theta \mu N^*}{k_1} (\frac{A}{\mu N^*} - \frac{1}{R_0}), \\
    E_2^* &= \frac{(1 - \theta) \mu N^*}{k_2} (\frac{A}{\mu N^*} - \frac{1}{R_0}), \\
    I_1^* &= \frac{v_1}{k_1} + \frac{v_4}{k_3} (\frac{A}{\mu N^*} - \frac{1}{R_0}), \\
    I_2^* &= \frac{v_2}{k_2} + \frac{v_5}{k_4} (\frac{A}{\mu N^*} - \frac{1}{R_0}), \\
    I_3^* &= \frac{v_3}{k_3} + \frac{v_6}{k_5} (\frac{A}{\mu N^*} - \frac{1}{R_0}), \\
    T_1^* &= \frac{k_3w_1 + \eta_2w_2}{k_6k_7 - \eta_3k_2} I_1^* + \frac{k_3w_3 + \eta_2w_4}{k_6k_7 - \eta_3k_2} I_2^* + \frac{k_3w_5 + \eta_2w_6}{k_6k_7 - \eta_3k_2} T_1^*, \\
    T_2^* &= \frac{k_6w_1 + \eta_1w_1}{k_6k_7 - \eta_3k_2} I_1^* + \frac{k_6w_4}{k_6k_7 - \eta_3k_2} I_2^* + \frac{k_6w_6 + \eta_1w_5}{k_6k_7 - \eta_3k_2} T_2^*, \\
    R^* &= \frac{\xi_1}{\mu} T_1^* + \frac{\xi_2}{\mu} T_2^*.
\end{align*}

By adding all equations of (5)–(13), we have \( A - \mu N^* - dT_2^* = 0 \). Combining the expressions of \( I_1^* \), \( I_2^* \), \( I_3^* \) and \( T_2^* \) in the above relations, we can get that

\begin{align*}
    \Lambda[1 - d(M_1N_1 + M_2N_2 + M_3N_3)] &= \mu N^* [1 - \frac{d}{R_0}(M_1N_1 + M_2N_2 + M_3N_3)],
\end{align*}

where

\begin{align*}
    M_1 &= \frac{k_6w_2 + \eta_1w_1}{k_6k_7 - \eta_3k_2}, \quad M_2 = \frac{k_3w_3 + \eta_2w_4}{k_6k_7 - \eta_3k_2}, \quad M_3 = \frac{k_3w_5 + \eta_2w_6}{k_6k_7 - \eta_3k_2}, \\
    N_1 &= \left[ \frac{v_1}{k_1} + \frac{v_4}{k_3} (\frac{1}{\mu N^*} - \frac{1}{R_0}) \right], \quad N_2 = \left[ \frac{v_2}{k_2} + \frac{v_5}{k_4} (\frac{1}{\mu N^*} - \frac{1}{R_0}) \right], \quad N_3 = \left[ \frac{v_3}{k_3} + \frac{v_6}{k_5} (\frac{1}{\mu N^*} - \frac{1}{R_0}) \right].
\end{align*}

The next thing we want to prove is that

\begin{align*}
    1 - d(M_1N_1 + M_2N_2 + M_3N_3) &= 1 - \frac{d}{R_0}[(k_6w_2 + \eta_1w_1)k_4k_5[k_2v_1 + v_1v_4(1 - \theta)] \\
    + k_6w_4k_3[k_2v_2 + k_1v_5(1 - \theta)] + (k_6w_6 + \eta_1w_5)k_3k_4[k_2v_3 + k_1v_6(1 - \theta)]] \\
    > 0.
\end{align*}

Because

\begin{align*}
    d[(k_6w_2 + \eta_1w_1)k_4k_5[k_2v_1 + v_1v_4(1 - \theta)] + k_6w_4k_3[k_2v_2 + k_1v_5(1 - \theta)] \\
    + (k_6w_6 + \eta_1w_5)k_3k_4[k_2v_3 + k_1v_6(1 - \theta)]] \\
    = d[\theta k_6(w_2v_1k_3k_4k_5 + w_4v_2k_3k_5 + w_6v_3k_3k_4) \\
    + (1 - \theta)k_6(w_2v_4k_1k_3k_4k_5 + w_4v_5k_1k_3k_4 + w_6v_5k_1k_3k_4) \\
    + \theta \eta_1(w_1v_1k_3k_4 + w_3v_2k_3k_5 + w_5v_3k_2k_4) \\
    + (1 - \theta)\eta_1(w_1v_4k_1k_3k_4 + w_3v_5k_1k_3k_4 + w_5v_5k_1k_3k_4)] \\
    < d[\theta k_6[(w_1 + w_2)v_1k_3k_4k_5 + (w_3 + w_4)v_2k_3k_5 + (w_5 + w_6)v_3k_2k_4] \\
    + (1 - \theta)k_6[(w_1 + w_2)v_4k_1k_4k_5 + (w_3 + w_4)v_5k_1k_4k_5 + (w_5 + w_6)v_5k_1k_4k_5]]
\end{align*}
< \{ \theta k_5 [v_1 k_2 k_3 k_4 k_5 + v_2 k_2 k_3 k_4 k_5 + v_3 k_2 k_3 k_4 k_5] \\
+ (1 - \theta) k_5 [v_4 k_1 k_3 k_4 k_5 + v_5 k_1 k_3 k_4 k_5 + v_6 k_1 k_3 k_4 k_5] \}
< d(\theta k_5 k_1 k_2 k_3 k_5 + (1 - \theta) k_5 k_1 k_2 k_3 k_5] \\
= dk_5 k_1 k_2 k_3 k_5.

and

\[ k_6 k_7 - \eta_1 \eta_2 - d k_6 \]

\[
\eta_1 + \xi_1 + \mu)(\eta_2 + \xi_2 + \mu + d) - \eta_1 \eta_2 - d(\eta_1 + \xi_1 + \mu) > 0.
\]

there is a unique positive \( N^* \) when \( R_0 > 1 \). Thus, we obtain the following theorem.

**Theorem 1.** In the system (2), there is always a Disease-Free Equilibrium \( D_0 = (\frac{\mu}{N}, 0, 0, 0, 0, 0, 0, 0) \). When \( R_0 > 1 \), the system has a unique Endemic Equilibrium \( D^*(S^*, E^*_1, E^*_2, I^*_1, I^*_2, T^*_1, T^*_2, R^*) \).

**4. Stability analysis of disease-free equilibrium**

**Theorem 2.** For the system (2), the Disease-Free Equilibrium \( D_0 \) is globally asymptotically stable if \( R_0 < 1 \).

**Proof.** A continuous differentiable and positive definite Lyapunov function constructed by us for the COVID-19 model (2) is as follows.

\[ L(t) = x_1 E_1 + x_2 E_2 + x_3 I_1 + x_4 I_2 + x_5 I_3 + x_6 T_1 + x_7 T_2 + x_8 R, \]

where, \( x_i, (i = 1, 2, \ldots, 8) \) are nonnegative constants to be determined.

The time derivative of \( L(t) \) along the solution path of system (2) is given by

\[
\frac{dL(t)}{dt} = x_1 \theta \beta S \frac{\alpha I_1 + \alpha_2 I_2 + \alpha_3 I_3}{N} - k_1 E_1 + x_2 \{ (1 - \theta) \beta S \frac{\alpha_1 I_1}{N} - k_2 E_2 \}
+ x_3 (v_1 E_1 + v_4 E_2 - k_3 I_1) + x_4 (v_2 E_1 + v_5 E_2 - k_4 I_2)
+ x_5 (v_3 E_1 + v_6 E_2 - k_5 I_2) + x_6 (w_1 I_1 + w_3 I_2 + w_5 I_3 - k_6 T_1)
+ x_7 (w_2 I_1 + w_4 I_2 + w_6 I_3 + \eta_1 T_1 - k_7 T_2) + x_8 (T_1 + \eta_2 T_2 - \mu R)
\]

\[
\leq x_1 \theta \beta (\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3) - k_1 E_1 + x_2 \{ (1 - \theta) \beta (\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3) - k_2 E_2 \}
+ x_3 (v_1 E_1 + v_4 E_2 - k_3 I_1) + x_4 (v_2 E_1 + v_5 E_2 - k_4 I_2)
+ x_5 (v_3 E_1 + v_6 E_2 - k_5 I_2) + x_6 (w_1 I_1 + w_3 I_2 + w_5 I_3 + \eta_1 T_1 - k_6 T_1)
+ x_7 (w_2 I_1 + w_4 I_2 + w_6 I_3 + \eta_1 T_1 - k_7 T_2) + x_8 (T_1 + \eta_2 T_2 - \mu R)
\]

\[
= E_1 x_1 k_1 \left( \frac{x_3 v_1 + x_4 v_2 + x_5 v_3}{x_1 k_1} - 1 \right) + E_2 x_2 k_2 \left( \frac{x_3 v_4 + x_4 v_5 + x_5 v_6}{x_2 k_2} - 1 \right)
+ I_1 [x_1 \theta \beta \alpha_1 + x_2 (1 - \theta) \beta \alpha_1 - x_3 k_3 + x_6 w_1 + x_7 w_2]
+ I_2 [x_1 \theta \beta \alpha_2 + x_3 (1 - \theta) \beta \alpha_2 - x_4 k_4 + x_6 w_3 + x_7 w_4]
+ I_3 [x_1 \theta \beta \alpha_3 + x_4 (1 - \theta) \beta \alpha_3 - x_5 k_5 + x_6 w_5 + x_7 w_6]
+ T_1 (-x_6 k_6 + x_7 \eta_1 + x_8 \xi_1) + T_2 (x_6 \eta_2 - x_7 k_7 + x_8 \xi_2) + R(-x_8 \mu).
\]

Then choosing

\[
x_1 = \frac{1}{\beta \theta} \frac{R_2}{R_1 + R_2}, \quad x_2 = \frac{1}{\beta (1 - \theta)} \frac{R_1}{R_1 + R_2}, \quad x_3 = \frac{\alpha_1}{k_3}, \quad x_4 = \frac{\alpha_2}{k_4}, \quad x_5 = \frac{\alpha_3}{k_5}, \quad x_6 = x_7 = x_8 = 0.
\]

after simplification we can get

\[
\frac{dL(t)}{dt} \leq E_1 \frac{k_1}{\beta \theta} \frac{R_2}{R_1 + R_2} (R_0 - 1) + E_2 \frac{k_2}{\beta (1 - \theta)} \frac{R_1}{R_1 + R_2} (R_0 - 1).
\]

So if \( R_0 < 1 \) then \( dL(t)/dt < 0 \). By the LaSalle’s invariant principle [40], the Disease-Free Equilibrium \( D_0 \) is globally asymptotically stable in \( \Omega \).
5. Optimal control

In order to find the best way to alleviate the spread of COVID-19 in the population, we apply the optimal control theory to the COVID-19 model (2). This is achieved by introducing three groups of time related control variables, which are described as follows.

1. Isolation $u_1(t)$: Isolating possible infected cases at home to reduce their contact with others. The main means to achieve the effect of isolation are: media coverage, education, case tracking and legal restrictions.

2. Detection $(u_2(t), u_3(t), u_4(t))$: It represents the improvement of nucleic acid detection ability and rational allocation of resources in the case of limited medical resources.

On the one hand, we should try our best to improve the ability of nucleic acid detection, so that possible infected cases can be quickly diagnosed, and then isolated for treatment. On the other hand, we should allocate medical resources reasonably. We let the confirmed cases in possible asymptomatic compartment $(I_1)$ and mild compartment $(I_2)$ as many as possible transfer to the shelter hospital $(T_1)$ for centralized treatment, and $(u_2)$ and $(u_3)$ represent the strength of this control measure respectively. We let the confirmed cases in possible severe compartment $(I_3)$ transfer to the hospital $(T_2)$ for treatment as much as possible, and $u_4$ represents the strength of this control measure. $\varphi_1$ represents the efficiency of nucleic acid detection.

3. Treatment $(u_5(t), u_6(t))$: $u_5(t)$ and $u_6(t)$ represent the intensity of the increased treatment, respectively. These are mainly achieved through the support of medical equipment and medical staff in other places. $\varphi_2$ and $\varphi_3$ represent the effective rate of treatment respectively.

The goal of control is not only to minimize the number of infected people, but also to minimize the cost of control. Through the above analysis, we consider the following function as our objective function.

$$J(u_1, u_2, u_3, u_4, u_5, u_6) = \int_0^T \left( A_1E_1 + A_2E_2 + A_3I_1 + A_4I_2 + A_5I_3 + A_6T_1 + A_7T_2 ight.$$ 
$$+ \frac{B_1}{2} u_1^2 + \frac{B_2}{2} u_2^2 + \frac{B_3}{2} u_3^2 + \frac{B_4}{2} u_4^2 + \frac{B_5}{2} u_5^2 + \frac{B_6}{2} u_6^2 \right) dt$$

(14)

where $A_1, A_2, A_3, A_4, A_5, A_6, A_7$ are the weight coefficients of the exposed, infected and treated people. The constants $B_1, B_2, B_3, B_4, B_5, B_6$ are the weight coefficients of the control variables $u_1, u_2, u_3, u_4, u_5, u_6$.

Thus, the state system becomes

$$S(t) = \Lambda - \mu S - \left( 1 - u_1 \right) \beta S \frac{I_1 + I_2 + I_3}{N}$$
$$E_1(t) = \left( 1 - u_1 \right) \left( 1 - \beta S \frac{I_1 + I_2 + I_3}{N} \right) - (v_1 + v_2 + v_3 + \mu) E_1$$
$$E_2(t) = \left( 1 - u_1 \right) \left( 1 - \beta S \frac{I_1 + I_2 + I_3}{N} \right) - (v_4 + v_5 + v_6 + \mu) E_2$$
$$I_1(t) = v_1 E_1 + \varphi_1 I_1 + \mu I_1$$
$$I_2(t) = v_2 E_1 + \varphi_2 I_1 + \mu I_2$$
$$I_3(t) = v_3 E_1 + \varphi_3 I_1 + \mu I_3$$
$$T_1(t) = (\xi_1 + \mu + \eta_1 + \eta_2) T_1$$
$$T_2(t) = (\xi_2 + \mu + \eta_3) T_2$$
$$R^R(t) = (\xi_2 + \mu + \eta_3) T_2 - \mu R$$

(15)

Then we want to look for an optimal control such that

$$J(u_1^*, u_2^*, u_3^*, u_4^*, u_5^*, u_6^*) = \min \left\{ J(u_1, u_2, u_3, u_4, u_5, u_6) : u_1, u_2, u_3, u_4, u_5, u_6 \in U \right\}$$

Here, $u_i(t) \in (0, 1)$, for all $t \in [0, t_f]$, $i = 1, 2, 3, 4, 5, 6$. The control set is given by

$$U = \{(u_1, u_2, u_3, u_4, u_5, u_6) | u_i(t) \text{ is Lebesgue measurable on } [0, 1], i = 1, 2, 3, 4, 5, 6\}.$$  

(16)

(17)

According to Pontryagin’s maximum principle, we can transform the optimal control problem into the problem of finding the minimum value of a Hamiltonian function. So we set the Hamiltonian function as follows

$$H = A_1E_1 + A_2E_2 + A_3I_1 + A_4I_2 + A_5I_3 + A_6T_1 + A_7T_2$$
$$+ \frac{B_1}{2} u_1^2 + \frac{B_2}{2} u_2^2 + \frac{B_3}{2} u_3^2 + \frac{B_4}{2} u_4^2 + \frac{B_5}{2} u_5^2 + \frac{B_6}{2} u_6^2$$
$$+ \lambda_1 \left( \Lambda - \mu S - \left( 1 - u_1 \right) \beta S \frac{I_1 + I_2 + I_3}{N} \right)$$
$$+ \lambda_2 \left( \left( 1 - u_1 \right) \left( 1 - \beta S \frac{I_1 + I_2 + I_3}{N} \right) - (v_1 + v_2 + v_3 + \mu) E_1 \right)$$
$$+ \lambda_3 \left( \left( 1 - u_1 \right) \left( 1 - \beta S \frac{I_1 + I_2 + I_3}{N} \right) - (v_4 + v_5 + v_6 + \mu) E_2 \right)$$
$$+ \lambda_4 \left( v_1 E_1 + v_2 E_2 - (w_1 + w_2 + \varphi_1 I_1 + \mu) E_1 \right)$$
$$+ \lambda_5 \left( v_3 E_1 + \varphi_3 I_1 + \mu I_3 \right)$$
$$+ \lambda_6 \left( v_4 E_1 + \varphi_2 I_1 + \mu I_2 \right)$$

(18)

According to Pontryagin’s maximum principle, we can transform the optimal control problem into the problem of finding the minimum value of a Hamiltonian function. So we set the Hamiltonian function as follows

$$H = A_1E_1 + A_2E_2 + A_3I_1 + A_4I_2 + A_5I_3 + A_6T_1 + A_7T_2$$
$$+ \frac{B_1}{2} u_1^2 + \frac{B_2}{2} u_2^2 + \frac{B_3}{2} u_3^2 + \frac{B_4}{2} u_4^2 + \frac{B_5}{2} u_5^2 + \frac{B_6}{2} u_6^2$$
$$+ \lambda_1 \left( \Lambda - \mu S - \left( 1 - u_1 \right) \beta S \frac{I_1 + I_2 + I_3}{N} \right)$$
$$+ \lambda_2 \left( \left( 1 - u_1 \right) \left( 1 - \beta S \frac{I_1 + I_2 + I_3}{N} \right) - (v_1 + v_2 + v_3 + \mu) E_1 \right)$$
$$+ \lambda_3 \left( \left( 1 - u_1 \right) \left( 1 - \beta S \frac{I_1 + I_2 + I_3}{N} \right) - (v_4 + v_5 + v_6 + \mu) E_2 \right)$$
$$+ \lambda_4 \left( v_1 E_1 + v_2 E_2 - (w_1 + w_2 + \varphi_1 I_1 + \mu) E_1 \right)$$
$$+ \lambda_5 \left( v_3 E_1 + \varphi_3 I_1 + \mu I_3 \right)$$
$$+ \lambda_6 \left( v_4 E_1 + \varphi_2 I_1 + \mu I_2 \right)$$

(18)
where \( \lambda_i \) (i = 1, 2, 3, 4, 5, 6, 7, 8, 9) are the adjoint variables. And the adjoint variables \( \lambda_i \) satisfying the following adjoint system

\[
\frac{d\lambda_i}{dt} = -\frac{\partial H}{\partial s_i} = \mu \lambda_i + [(1 - u_1)\lambda_1 - (1 - u_1)\theta \lambda_2 - (1 - u_1)(1 - \theta)\lambda_3] \beta \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{N}
\]

The transversality condition of adjoint equations is given by

\[
\lambda_i(T) = 0, \quad i = 1, 2, 3, 4, 5, 6, 7, 8, 9.
\]

By the Pontryagin’s maximum principle, \((u_1^*, u_2^*, u_3^*, u_4^*, u_5^*)\) satisfy the condition

\[
\frac{\partial H}{\partial u_i} = 0, \quad i = 1, 2, 3, 4, 5, 6.
\]

Thus the optimal controls are given by

\[
\begin{align*}
    u_1^* &= \max \{0, \min \{u_{1\text{max}}, (\lambda_2 \theta + \lambda_3 (1 - \theta) - \lambda_1) \beta S \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{B_1 N}\} \}, \\
    u_2^* &= \max \{0, \min \{u_{2\text{max}}, (\lambda_4 - \lambda_7 \beta S I_1) \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{B_2} \} \}, \\
    u_3^* &= \max \{0, \min \{u_{3\text{max}}, (\lambda_5 - \lambda_7 \beta S I_2) \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{B_3} \} \}, \\
    u_4^* &= \max \{0, \min \{u_{4\text{max}}, (\lambda_6 - \lambda_8 \beta S I_3) \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{B_4} \} \}, \\
    u_5^* &= \max \{0, \min \{u_{5\text{max}}, (\lambda_7 - \lambda_9 \beta S T_1) \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{B_5} \} \}, \\
    u_6^* &= \max \{0, \min \{u_{6\text{max}}, (\lambda_8 - \lambda_9 \beta S T_2) \frac{\alpha_1 I_1 + \alpha_2 I_2 + \alpha_3 I_3}{B_6} \} \}.
\end{align*}
\]

6. Numerical simulation

6.1. Data collection and parameter estimation

Whether or not an infectious disease spreads among the population and how quickly it spreads are related to the specific location of transmission. If people are aware of the transmission characteristics of the disease and take precautions
in their daily lives, the rate of transmission in the local population will be greatly reduced. To study the spread of Omicron variant strain of COVID-19 under prevention and control measures in China, we chose the spread of Omicron cases starting from March 1, 2022 in Shanghai, China as an example.

We collected the daily data of mild and severe confirmed cases published on the website of Shanghai Municipal Health Commission from Mar 1, 2022 to Apr 19, 2022 as the research sample [3]. Fig. 2 shows a histogram of the cumulative number of confirmed cases during this period.

From Fig. 2, we can see that the cumulative number of confirmed cases has shown an explosive and rapid increase. This can show that although people were already aware of the precautions when the epidemic started to appear, it is still not enough. If control measures are not taken in time, it will cause widespread infection in a short period of time, putting people's lives at serious risk.

In order to make full use of the statistical data to estimate the parameters, we use the weighted nonlinear least square method to fit the statistical data. Compared with the nonlinear least square method, the weight can effectively reduce the fitting deviation caused by the different orders of magnitude between the data, and the value of the weight is usually the reciprocal of the variance of the time series. Before that, some parameters can be selected through the existing literature. In 2021, the population statistics report showed that the average life expectancy of Shanghai is 84 years old [41]. Therefore, we choose \( \mu = 1/(84 \times 365) \) per day. According to the population statistics report, the total number of Shanghai is 24894300 [41], so \( \Lambda = 811.9471 \) per day. We use the cumulative number of deaths reported per day divided by the cumulative number of severe confirmed cases [3], and then take its mean value as the estimation of the death rate in severe cases is 6.85%.

Then we set the objective function in the fitting process as follows.

\[
K = W_1 \sum_{i=1}^{n} [(T_1)_i - (\tilde{T}_1)_i]^2 + W_2 \sum_{i=1}^{n} [(T_2)_i - (\tilde{T}_2)_i]^2, \tag{20}
\]

where \( T_1, T_2 \) are the estimated number of mild treated and severe treated cases; \( \tilde{T}_1, \tilde{T}_2 \) are the reported number of mild treated and severe treated; \( W_i (i = 1, 2) \) are the weight coefficients of the error square sum in each compartment, and the value of \( W_i \) is the reciprocal of the variances of various real data sequences. To obtain the estimation of the parameters in model (2), we need to minimize the following objective function.

\[
\begin{align*}
\text{min} \quad K \\
\text{subject to} \quad \text{system (2)}. \tag{21}
\end{align*}
\]

Our fitting results are compared with the reported data in Fig. 3. The values of the fitted parameters are shown in Table 2, and the basic reproduction number \( R_0 = 1.5118 \).

From Fig. 3, we can see that the simulated results are very close to the reported real data. The simulated results are more reliable and it can be used in the next step to analyze the trend of COVID-19 under some control measures. Before taking control measures, it is necessary to study the sensitivity analysis of each parameter in the basic reproduction number of the model in order to determine which parameters will play an important and critical role, which is helpful for our analysis of control measures.
### Table 2
Estimation of parameters.

| Parameters | Descriptions                      | Values            | Source     |
|------------|-----------------------------------|-------------------|------------|
| $\Lambda$  | Recruitment rate                  | 811.9471          | Estimated  |
| $\mu$      | Natural death rate $\frac{1}{14}$ | $\frac{1}{365}$ day$^{-1}$ | [42]      |
| $\theta$   | Proportion of $S$ who become $E_1$| 0.310696          | Fitted     |
| $\beta$    | The transmission coefficient      | 0.89764           | Fitted     |
| $\alpha_1$ | Proportion of $I_1$ who are in contact with $S$ | 0.686165          | Fitted     |
| $\alpha_2$ | Proportion of $I_2$ who are in contact with $S$ | 0.458246          | Fitted     |
| $\alpha_3$ | Proportion of $I_3$ who are in contact with $S$ | 0.861165          | Fitted     |
| $v_1$      | Rate of moving from $E_1$ to $I_1$| 0.564536          | Fitted     |
| $v_2$      | Rate of moving from $E_1$ to $I_2$| 0.597458          | Fitted     |
| $v_3$      | Rate of moving from $E_1$ to $I_3$| 0.828898          | Fitted     |
| $v_4$      | Rate of moving from $E_2$ to $I_1$| 0.505740          | Fitted     |
| $v_5$      | Rate of moving from $E_2$ to $I_2$| 0.645081          | Fitted     |
| $v_6$      | Rate of moving from $E_2$ to $I_3$| 0.899525          | Fitted     |
| $w_1$      | Proportion of $I_1$ assigned to $T_1$ after diagnosis | 0.246770          | Fitted     |
| $w_2$      | Proportion of $I_1$ assigned to $T_2$ after diagnosis | 0.047458          | Fitted     |
| $w_3$      | Proportion of $I_2$ assigned to $T_1$ after diagnosis | 0.260097          | Fitted     |
| $w_4$      | Proportion of $I_2$ assigned to $T_2$ after diagnosis | 0.013579          | Fitted     |
| $w_5$      | Proportion of $I_3$ assigned to $T_1$ after diagnosis | 0.644552          | Fitted     |
| $w_6$      | Proportion of $I_3$ assigned to $T_2$ after diagnosis | 0.020362          | Fitted     |
| $\eta_1$  | Proportion of severe $T_2$ to mild $T_1$ | 0.005115          | Fitted     |
| $\eta_2$  | Proportion of mild $T_1$ to severe $T_2$ | 0.806286          | Fitted     |
| $\xi_1$   | Recovery rate of $T_1$            | 0.894377          | Fitted     |
| $\xi_2$   | Recovery rate of $T_2$            | 0.868972          | Fitted     |

![Fig. 3. Model fitting to the COVID-19 infected cases using system (2).](image)
6.2. Global sensitivity analysis

In this subsection, we will study the global sensitivity analysis (SA) of the basic reproduction number $R_0$ of the model to analyze those model parameters that have a large impact on the disease dynamics. The most effective way to quantify uncertainty in mathematical models using global sensitivity analysis is to use numerical simulation results from Latin hypercube sampling (LHS) and partial rank correlation coefficients (PRCC). LHS is a stratified sampling technique with no alternative that can effectively analyze the variation of each parameter over a range of uncertainties [42]. PRCC measures the strength of the relationship between the output results of the model and the parameters, and can be expressed numerically as the degree of influence of each parameter [43]. To generate the LHS matrix, we assumed that all parameters of the model obeyed a uniform distribution. We then performed a total of 5000 simulations of the model for each LHS run using the estimated values of the parameters in Table 2. We obtained a total of 5000 values of the basic reproduction number, and their distribution is shown in Fig. 4. Fig. 5 shows, in the basic reproduction number $R_0$, the PRCC values of each parameter. The corresponding $P$-values for each parameter are listed in Table 3. The results are significant when the $p$-value is less than 0.1.

From the results in Fig. 5, we can see the PRCC values of all parameters. When the PRCC value is greater than 0, it means that, increasing the parameter, the basic reproduction number $R_0$ also increases. When the PRCC value is less than ...
0, increasing the parameter, the basic reproduction number decreases. Therefore, we can reduce the basic reproduction number $R_0$ by decreasing those parameters $(w_2, w_4, w_6)$ whose PRCC values are positive or increasing those parameters $(v_1, v_3, v_2, v_5, v_6, w_1, w_3, w_5)$ whose PRCC values are negative. In conjunction with practical control measures in reality, we considered three important means of controlling the spread of COVID-19: isolation, detection, and treatment.

6.3. Optimal control strategies

In this section, we use the forward–backward sweep method with fourth order Runge–Kutta method to find the optimal control solution. The main process of the algorithm is as follows.

Step 1: starting from a reasonable control initial value, the fourth order Runge–Kutta method is used to solve the state equations according to the time from front to back.

Step 2: the obtained state solution is substituted into the adjoint system, and the fourth order Runge–Kutta method is used to solve the adjoint equations from back to front according to time.

Step 3: the obtained state variables and adjoint variables are substituted into the control expression, and the control variables are updated in a convex combination way, and the first step is continued for iteration.

Step 4: checking the two adjacent optimal solutions. When they are close enough, the iteration stops, otherwise, the iteration continues.

For more introduction and application of the algorithm, please refer to Ref. [44–47]. In order to explore the control effect of control measures, we designed the following control scenarios, namely single, coupled and threefold control strategies.

Scenario 1: Single control strategies

Strategy A: Isolation only ($u_1$).
Strategy B: Detection only ($u_2$, $u_3$, $u_4$).
Strategy C: Treatment only ($u_5$, $u_6$).

Scenario 2: Double control strategies

Strategy D: Isolation ($u_1$) + Detection ($u_2$, $u_3$, $u_4$).
Strategy E: Isolation ($u_1$) + Treatment ($u_5$, $u_6$).
Strategy F: Detection ($u_2$, $u_3$, $u_4$) + Treatment ($u_5$, $u_6$).

Scenario 3: Triple control strategies

Strategy G: Isolation ($u_1$) + Detection ($u_2$, $u_3$, $u_4$) + Treatment ($u_5$, $u_6$).

Because many control measures in the process of implementation will be affected by many factors, it is difficult to achieve 100% of the ideal control effect, so we set the upper limit of each control variable as 0.8. When selecting the weight constant in the objective function (14), in order to ensure that no item will seriously affect other items, equal weight constants are selected, $\alpha_i = 1.0$ ($i = 1, 2, 3, 4, 5, 6, 7$). After many experiments, the rest of the weight coefficients are selected as $B_1 = 250$, $B_2 = 250$, $B_3 = 250$, $B_4 = 250$, $B_5 = 2500$ and $B_6 = 2500$. The values of the remaining parameters are shown in Table 2. Control measures will be in place for 30 days.

### Table 3

| Parameters | PRCC  | P-value | Parameters | PRCC  | P-value |
|-----------|-------|---------|------------|-------|---------|
| $\mu$     | 0.151453 | 0.000000 | $\alpha_1$ | 0.035629 | 0.011894 |
| $\beta$   | -0.035896 | 0.011273 | $\alpha_1$ | -0.021669 | 0.126156 |
| $\alpha_2$| -0.006746 | 0.633989 | $\alpha_3$ | -0.030121 | 0.033484 |
| $v_1$     | -0.199214 | 0.000000 | $v_2$      | -0.174982 | 0.000000 |
| $v_3$     | -0.176723 | 0.000000 | $v_4$      | -0.155313 | 0.000000 |
| $v_5$     | -0.168334 | 0.000000 | $v_6$      | -0.157089 | 0.000000 |
| $w_1$     | -0.098770 | 0.000000 | $w_2$      | 0.072350  | 0.000000 |
| $w_3$     | -0.080817 | 0.000000 | $w_4$      | 0.057064  | 0.000055 |
| $w_5$     | -0.044702 | 0.001597 | $w_6$      | 0.042295  | 0.002824 |

From Fig. 6 (b–e), we can see that the effect of strategy A and strategy B on the reduction of the number of infections is relatively significant, and the reduction of infections in strategy C is very small. These results show that both isolation and timely detection can quickly interrupt the spread of the disease. Treatment alone, without stopping it at the source, has very poor results.
**Scenario 2:** Double control strategies.

The population change patterns of all bins under the three control strategies of Scenario 2 are shown in Fig. 8. The change patterns of the control variables for the three control strategies are shown in Fig. 9. In control strategy D, \( u_1, u_2, u_3 \), and \( u_4 \) were required to maintain a maximum control effort of 0.8 from day 1 until day 13, 10, 11, and 8, respectively, when they were reduced to 0. In control strategy E, \( u_1, u_5 \) and \( u_6 \) need to maintain the maximum strength of 0.8 from the beginning and gradually decrease to 0 at 29, 21, and 7 days, respectively. In the control strategy F, \( u_2, u_3, u_4, u_5 \), and \( u_6 \) maintain a maximum strength of 0.8 at the beginning and gradually decrease to 0 on days 10, 11, 8, 29, and 27, respectively.

In Fig. 8 (b-e), we can see that strategies D and F can rapidly reduce the number of exposed individuals and possible cases, but bring about a rapid rise in confirmed cases. Strategy E can also rapidly reduce the number of infections. In addition, we can see from Fig. 8(a) that the final number of susceptible persons is the highest among these three control strategies, and then it will have the lowest number of infections during the control period.

**Scenario 3:** Triple control strategies.

In strategy G of scenario 3, the change of the number of all compartments are shown in Fig. 10 (a-f), and the optimal control is shown in Fig. 11. As can be seen from Fig. 10 (b-e), the control result of strategy G is satisfactory. The number of possible and confirmed cases decreases rapidly, achieving a very good control effect. It is not easy to compare the specific infection cases under each strategy graphically, so it is necessary for us to further compare the cost-effectiveness analysis of these strategies.
6.4. Cost-effectiveness analysis

To facilitate the analysis, we need to quantify the cost-effectiveness of the control strategy [46,47]. So we consider the incremental cost-effectiveness ratio (ICER) of strategy A relative to strategy B:

\[ ICER = \frac{TC(B) - TC(A)}{TA(B) - TA(A)} \]

where \( TC(B) \) represents the cost of implementing control strategy B, \( TA(B) \) represents that the total number of averted infected people in strategy B compared with that without control. The definition of the total cost (TC) is as follows.

\[ TC = \int_0^{t_f} \left[ C_1 u_1 (E_1 + E_2 + I_1 + I_2 + I_3) + C_2 (u_2 I_1 + u_3 I_2 + u_4 I_3) + C_3 u_5 T_1 + + C_4 u_6 T_2 \right] dt, \]

where

- \( C_1 \): the daily cost of isolation measures for each person. It mainly including the tracking of close contacts and suspected cases, and making them insist on wearing masks and keeping social distance through media reports, education and laws and regulations. So we choose \( C_1 = 5 \) (unit: $).
- \( C_2 \): the cost of nucleic acid testing per person. According to the actual situation, we choose \( C_2 = 10 \) (unit: $).
- \( C_3 \): the daily cost per person for mild treatment in Fangcang hospital. In the treatment of mild cases in Fangcang hospitals, only some common testing equipment and medicines are needed. Thus, we choose \( C_3 = 20 \) (unit: $).
- \( C_4 \): the daily cost per person for severe treatment in ICU. Expensive ventilators are almost always used to help treat severe cases in the ICU. Let us assume that severe cases cost $2,000 a day to treat. Thus, we choose \( C_4 = 2000 \) (unit: $).

The definition expression of the total infected cases (TI) is as follows \( TI = S(0) - S(t_f) \), where \( S(0) \) denotes the number of susceptible people at the beginning of the control, \( S(t_f) \) denotes the number of susceptible people at the end of the
control. $TA = TI_0 - TI_A$ is the number of total averted people ($TA$) in the implementation of control strategy $A$, where $TI_0$ is the number of people who are infected without control, $TI_A$ is the number of people infected during the implementation of control strategy $A$. We get the value of IAR and ICER under all control strategies (A to G) in Table 4.

From the ICER in the last column of Table 4, we can know that ICER(D) = 2.1885 is the smallest, which means that more people can avoid being infected to COVID-19 with the least cost. When the policy budget is limited, we should consider a combination of isolation and detection strategies so that more people can avoid COVID-19 at the least cost.

From the IAR of each strategy in Table 4, we can see that in the case of relatively abundant finance, we should implement the three control measures at the same time according to the control intensity shown in Fig. 11, so as to minimize the number of infected people. Implementation of strategy $G$ can prevent 95% of people from contracting COVID-19. From the people-oriented perspective, we believe that strategy $G$ is the optimal control strategy. Although this will cost a lot of money, it will save many precious lives.

7. Conclusion

In March 2022, the Omicron mutant strain of COVID-19 spread rapidly through Shanghai, China with its strong infectiousness, causing a huge number of infections in a short period of time. Although the Shanghai government has
taken certain preventive and control measures, the number of infections continues to rise every day, which shows that the prevention and control efforts are not sufficient. Therefore, more effective measures should be taken in a timely manner to curb the spread of Omicron.

In this study, we built a more objective and detailed 9-dimensional mathematical model of COVID-19 to simulate its propagation. We analyzed its dynamic properties and obtained the expression of the basic reproduction number. Then we considered the three most important control measures (isolation, detection and treatment) and established an optimal control system. Through the classical Pontryagin maximum principle, the expression of optimal control pairs was obtained.
In the numerical simulation, in order to make full use of the data provided by the official website, we used the weighted nonlinear least square estimation method to estimate the parameters of the model. The basic reproduction number was obtained as $R_0 = 1.5118$, which is far beyond the threshold of 1, so COVID-19 will spread in the population at a very fast speed.

Then we combined the control measures in three scenarios and got seven control strategies. We used the forward–backward sweep method with fourth order Runge–Kutta to obtain the optimal control and the change of the number of warehouses under each strategy. Then, by the cost-effectiveness analysis of all strategies, the IAR and ICER values of all strategies were obtained. The results showed that when the budget of the policy is limited, we can use strategy D to increase the detection as much as possible, so that more people can avoid infection at the same cost. When the policy budget is adequate, we should adopt strategy G, which can minimize the number of infected people to the greatest extent.
Fig. 11. The strength of the control variables in each strategy of scenario 3.

CRediT authorship contribution statement

Tingting Li: Conceptualization, Methodology, Software, Formal analysis, Resources, Data curation, Writing – original draft, Writing – review & editing. Youming Guo: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Supervision.

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.

Data availability

No data was used for the research described in the article.

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