Mathematical modeling for COVID-19 with focus on intervention strategies and cost-effectiveness analysis

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Abstract The realistic assessments of public health intervention strategies are of great significance to effectively combat the COVID-19 epidemic and the formation of intervention policy. In this paper, an extended COVID-19 epidemic model is devised to assess the severity of the pandemic and explore effective control strategies. The model is characterized by ordinary differential equations with seven-state variables, and it incorporates some parameters associated with the interventions (i.e., media publicity, home isolation, vaccination and face-mask wearing) to investigate the impacts of these interventions on the spread of the COVID-19 epidemic. Some dynamic behaviors of the model, such as forward and backward bifurcation, are analyzed. Specifically, we calibrate the model parameters using actual COVID-19 infected data in Brazil by Markov Chain Monte Carlo algorithm such that we can study the effects of interventions on a practical case. Through a comprehensive exploration of model design and analysis, model calibration, sensitivity analysis, implementation of optimal control problems and cost-effectiveness analysis, the rationality of our model is verified, and the effective strategies to combat the epidemic in Brazil are revealed. The results show that the asymptomatic infected individuals are the main drivers of COVID-19 transmission, and rapid detection of asymptomatic infections is critical to combat the COVID-19 epidemic in Brazil. Interestingly, the effect of the vaccination rate associated with pharmaceutical intervention on the basic reproduction number is much lower than that of non-pharmaceutical interventions (NPIs). Our study also highlights the importance of media publicity. To reduce the infected individuals, the multi-pronged NPIs have considerable positive effects on controlling the outbreak of COVID-19. The infections are significantly decreased by the early implementation of media publicity complemented with home isolation and face-mask wearing strategy. When the cost of implementation is taken into account, the early implementation of media publicity complemented with a face-mask wearing strategy can significantly mitigate the second wave of the epidemic in Brazil. These results provide some management implications for controlling COVID-19.

Keywords COVID-19 · Parameter estimation · Bifurcation · Sensitivity analysis · Optimal control · Cost-effectiveness analysis

1 Introduction

The emergence of COVID-19 in 2019 has led to an unprecedented global public health crisis [1]. In the face of this crisis, scientists constantly look for effective intervention strategies aimed at reducing the number of COVID-19 infections and containing the fast spread of SARS-CoV-2. Since January 23, 2020, a range of non-
pharmaceutical interventions (NPIs) were adopted by the Chinese government, including close contact tracing, quarantine, home isolation, and face-mask wearing. With the implementation of NPIs, there have been few local COVID-19 epidemic outbreaks in China since March 19th, 2020, which indicates the high effectiveness of these interventions [2]. Similar interventions were implemented by other countries, but with varying outcomes. Some of these countries failed to prevent the subsequent wave of outbreaks, causing the continuation of the epidemic. According to the WHO [3], as of January 2022, there were reported 306,839,580 cumulative confirmed cases of COVID-19 infections with 5,505,643 deaths worldwide. Therefore, the realistic assessments of proposed public health intervention strategies play a vital role in disease control and the formation of intervention policy.

Generally, modeling dynamical behavior for an epidemic relies on the population dynamics, where individuals are assigned with the certain states to denote the diseases, reflecting their interplay and evolution [4]. Kermack et al. construct three compartments in epidemic dynamic models, namely, susceptible, infected, and recovered, that is the famous SIR model [5]. Anderson et al. modify the SIR model by adding an extra compartment: exposed (E), named SEIR model [6]. Presently, most of the COVID-19 epidemic models originate from the SEIR structure.

To explore the COVID-19 pandemic, some researchers propose different models to delineate the disease transmission dynamics and assess the course or severity of COVID-19 [7–14]. Hao et al. [15] present a compartmental mathematical model to reconstruct the full-spectrum dynamics of COVID-19 in Wuhan. Bulut et al. [16] present a compartmental mathematical model that incorporates the importance of personal cautiousness to study the spread of COVID-19 in Turkey and Italy. To deal with the doubly-censored data model appearing in COVID-19 fields, Yin et al. [17] propose a novel algorithm (i.e., ECIMM algorithm) to estimate the parameters of the incubation period of COVID-19 with success, thereby providing some suggestions for the prevention and control of COVID-19. Note that individual’s infection or transmission of COVID-19 tends to be age-related. For this reason, the age-structure models [18, 19] based on partial differential equations are studied to capture the transmission dynamics in detail. But such models may be too complicated to analyze theoretically and solve numerically. Recent works of solutions to nonlinear evolution equations provide an alternative to the preceding model [20, 21].

With the introduction of public health interventions for inhibiting COVID-19, some mathematical models begin to consider the impact of interventions to re-estimate the course of COVID-19 [22–31]. Zhou et al. [32] use a deterministic dynamical model to study the interaction between media publicity and disease progression so as to investigate the effectiveness of media publicity in combating the COVID-19 epidemic. To explore the impact of isolation and contact-tracing strategies on the transmission of COVID-19, Hellewell et al. [33] present a stochastic model. Ngonghala et al. [34] devise a mathematical model to address the key issue of whether the use of face masks can halt the resurgence of the COVID-19 pandemic. Acuña-Zegarra et al. propose an optimal control problem to explore the optimal vaccination policies [35]. In combating the COVID-19 epidemic, the roles of non-pharmaceutical interventions and pharmaceutical interventions are indispensable and complementary. Hence, we design an extended epidemic model to explore the co-inhibitory effects of these interventions, which contains some model parameters associated with the main interventions being implemented in practice (i.e., media publicity, home isolation, vaccination and face-mask wearing). Based on the epidemiological status of the individuals, clinical progression of the disease, the model involves the seven-state compartments, namely, conscious susceptible (S₁), unconscious susceptible (S₂), exposed (E), symptomatic infected (I), asymptomatic infected (A), hospitalized (H) and recovered (R), which can better describe the epidemiological status of the individuals, and realistically assess the effectiveness of interventions. Some basic mathematical properties of this model are explored in detail. We calibrate the model parameters using actual COVID-19 infected data in Brazil by Markov Chain Monte Carlo algorithm (MCMC). The influential model parameters related to the basic reproduction number are determined by global sensitivity analysis. Through qualitative analysis and numerical simulation of the dynamic behavior in our model, we can estimate the causes and critical factors of the COVID-19 outbreak.

Meanwhile, the optimal control problem is employed to explore effective control strategies for combating the COVID-19 epidemic. Asamoah et al. [36] present a cost-effectiveness analysis based on the
work of Alqarni [37], where they propose a nonlinear deterministic model to reveal the economic health and cost outcomes associated with COVID-19. Inspired by that, we are motivated to formulate an optimal control problem and take a case study in Brazil to explore effective control strategies for curtailing the progression of COVID-19. Further, we present a cost-effectiveness analysis to unravel the cost and the infections averted by focusing on assessing their consequences of some interventions.

The rest of the paper is organized as follows. The general description and some dynamic behaviors of the proposed model are established in Sect. 2. Section 3 gives baseline values of model parameters based on the actual infected data in Brazil. Section 4 decides the influential model parameters which greatly affect the basic reproduction number by global sensitivity analysis. Section 5 presents the formulation and characterization of the control model, and the numerical simulations for seven control strategies. Section 6 assesses the previous control strategies by the cost-effectiveness analysis. Section 7 gives the conclusive remarks.

2 The model formulation

2.1 System description

To delineate the transmission dynamics of COVID-19, we investigate an extended SEIR-type epidemic model that incorporates seven compartments, namely, the conscious susceptible (S1): educated individuals and aware of their status, the unconscious susceptible (S2): uneducated individuals and unaware of their status, exposed (E), symptomatic infected (I), asymptomatic infected (A), hospitalized (H) and recovered (R). Such educated individuals are those who have received health enlightenment through media publicity. On the other hand, the uneducated individuals are those who do not receive such enlightenment. Thus, the total population N(t) is given by

\[ N(t) = S_1(t) + S_2(t) + E(t) + I(t) + A(t) + H(t) + R(t). \]

We incorporate the main interventions implemented to combat the COVID-19 epidemic into this model, including media publicity, home isolation, vaccination and face-mask wearing. Therefore, we suppose that, \( p \) is the transfer rate from \( S_2 \) to \( S_1 \) reflecting the impact of media publicity, \( \epsilon_1 \) is the voluntary home isolation rate, \( \epsilon_2 \) is the face-mask wearing rate, and \( \mu \) is the vaccination rate. We make the following hypotheses:

(H-1) Only the conscious susceptible individuals choose to be vaccinated and become vaccinated at \( \mu \) rate.

(H-2) The recovered individuals return to the conscious susceptible group at \( \omega \) rate after an immunity period.

(H-3) The unconscious susceptible individuals (S2) can be transformed into the conscious susceptible group (S1) at p rate through media publicity.

The COVID-19 transmission dynamics over last more than one year is explored. We assume the natural mortality rate is \( d \) of individuals in the seven compartments. Further, we include the net inflow per unit time of susceptible individuals at the rate \( \Lambda \). This parameter represents the new immigration and births of the individuals. We name these individuals as the newly recruited individuals. The fraction \( \lambda \) of these recruited individuals who are not educated enter \( S_2 \) and the remaining \( (1 - \lambda) \) individuals will enter \( S_1 \). In conscious susceptible individuals, only the individuals \( (1 - \epsilon_1)(1 - \epsilon_2)S_1 \), who do not carry out home isolation and do not wear face-mask effectively) will come into contact with infected individuals \( I \) and \( A \) at the transmission coefficients \( \beta_I \) and \( \beta_A \), respectively, thus become exposed (E). The unconscious susceptible individuals (S2) without self-protection consciousness will unconsciously contact infected individuals \( I \) and \( A \) with the transmission coefficients \( \beta_I \) and \( \beta_A \), respectively, and become exposed (E). The exposed individuals (E) will move to the infected groups \( I \) or \( A \) after being infected. The symptomatic infected individuals (I) either recover directly or are sent to the hospital for treatment and then recover, or die at the mortality rate \( d_I \) after the treatment fails. Whereas the asymptomatic infected individuals (A) will move to group \( R \) at \( \tau \) rate after a period of time. Additionally, the recovered individuals \( R \) will return to the conscious susceptible group \( S_1 \) after an immunity period. The schematic diagram of model (1) is illustrated in Fig. 1, which describes the movement of individuals from one compartment to another. The descriptions of the model parameters are shown in Table 1. The dynamics of these compartments are formulated by model (1):

\[ \frac{dS_1}{dt} = \lambda N(t) - \beta_I I(t)S_1(t) - \beta_A A(t)S_1(t) - \sigma S_1(t) - \mu S_1(t) - \nu S_1(t). \]

\[ \frac{dS_2}{dt} = \lambda N(t) - \beta_I I(t)S_2(t) - \beta_A A(t)S_2(t) - \sigma S_2(t) - \mu S_2(t) - \nu S_2(t). \]

\[ \frac{dE}{dt} = \beta_I I(t)S_1(t) + \beta_A A(t)S_1(t) + \sigma S_1(t) + \mu S_2(t) + \nu S_2(t) - \sigma E(t) - \mu E(t). \]

\[ \frac{dI}{dt} = \beta_I I(t)S_1(t) + \beta_A A(t)S_1(t) + \sigma S_1(t) + \mu S_2(t) + \nu S_2(t) - \sigma I(t) - \mu I(t) - \gamma I(t). \]

\[ \frac{dA}{dt} = \beta_I I(t)S_2(t) + \beta_A A(t)S_2(t) + \sigma S_2(t) + \mu S_1(t) + \nu S_1(t) - \sigma A(t) - \mu A(t) - \gamma A(t). \]

\[ \frac{dH}{dt} = \beta_I I(t)S_1(t) + \beta_A A(t)S_1(t) + \sigma S_1(t) + \mu S_2(t) + \nu S_2(t) - \sigma H(t) - \mu H(t). \]

\[ \frac{dR}{dt} = \beta_I I(t)S_1(t) + \beta_A A(t)S_1(t) + \sigma S_1(t) + \mu S_2(t) + \nu S_2(t) - \sigma R(t) - \mu R(t). \]
Table 1 The descriptions of model parameters

| Parameters | Description |
|-----------|-------------|
| $\Lambda$ | Recruitment rate |
| $\lambda$ | Proportion of recruitment with unconscious susceptible individuals $S_2$ |
| $\alpha$ | Latency rate |
| $d$ | Natural mortality rate |
| $d_1$ | Mortality due to illness |
| $\tau$ | Recovery rate of asymptomatic infected individuals |
| $\theta$ | Recovery rate of symptomatic infected individuals |
| $\gamma_H$ | Recovery rate of hospitalized individuals |
| $v$ | Vaccine efficacy |
| $\mu$ | Vaccination rate |
| $\rho$ | The transfer rate from $S_2$ to $S_1$ reflecting the impact of media publicity |
| $\beta_I$ | Transmission coefficient of the symptomatic infected individuals |
| $\beta_A$ | Transmission coefficient of the asymptomatic infected individuals |
| $\epsilon_1$ | The voluntary home isolation rate |
| $\epsilon_2$ | The face-mask wearing rate |
| $\rho$ | Proportion of symptomatic infected individuals |
| $\kappa$ | Proportion of hospitalized individuals |
| $\omega$ | Waning rate of vaccine efficacy |

\[
\frac{dS_1}{dt} = (1 - \lambda)\Lambda - \frac{(\beta_I(1 - \epsilon_1)(1 - \epsilon_2)I + \beta_A(1 - \epsilon_1)(1 - \epsilon_2)A)S_1}{N} - \mu v S_1 + p S_2 + \omega R - d S_1,
\]

\[
\frac{dS_2}{dt} = \lambda \Lambda - p S_2 - \frac{(\beta_A + \beta_I I) S_2}{N} - d S_2.
\]

\[
\frac{dE}{dt} = \frac{(\beta_I(1 - \epsilon_1)(1 - \epsilon_2)I + \beta_A(1 - \epsilon_1)(1 - \epsilon_2)A)S_1}{N} + \frac{(\beta_A A + \beta_I I) S_2}{N} - (\alpha + d) E,
\]

\[
\frac{dI}{dt} = \rho \alpha E - (\theta + d) I,
\]

\[
\frac{dA}{dt} = (1 - \rho) \alpha E - (\tau + d) A,
\]

\[
\frac{dH}{dt} = \kappa \theta I - (\gamma_H + d_1 + d) H,
\]

\[
\frac{dR}{dt} = (1 - \kappa) \theta I + \gamma_H H + \tau A + \mu v S_1 - (\omega + d) R,
\]

where $\gamma_I = \beta_I (1 - \epsilon_1)(1 - \epsilon_2)$, $\gamma_A = \beta_A (1 - \epsilon_1)(1 - \epsilon_2)$.

2.2 Analysis of the model

Considering that model (1) describes the real-life infectious disease in the population, it is necessary to study on the premise of meeting the ecological significance. Therefore, we need to claim the following results.

2.2.1 Positive invariant region

**Theorem 1** Define the closed set

\[
D = \left\{ (S_1, S_2, E, I, A, H, R) \in \mathbb{R}_+^7 : S_1, E, I, A, H, \frac{\Lambda}{d + d_1} \leq N \leq \frac{\Lambda}{d}, 0 \leq S_2 \leq \frac{\lambda \Lambda}{p + d} \right\}.
\]

The solution trajectories of model (1) are bounded, and set $D$ is positive invariant. Specially, $S_1(t), S_2(t), E(t), I(t), A(t), H(t), R(t)$ are positive for all $t > 0$ if
the initial values $S_1(0) > 0$, $S_2(0) > 0$, $E(0) > 0$, $I(0) > 0$, $A(0) > 0$, $H(0) > 0$ and $R(0) > 0$.

**Proof** First, we can get the nonnegativity of the solutions of model (1). Under the initial values $S_1(0) > 0$, $S_2(0) > 0$, $E(0) > 0$, $I(0) > 0$, $A(0) > 0$, $H(0) > 0$ and $R(0) > 0$, we define

$$G(t) = \min\{S_1(t), S_2(t), E(t), I(t), A(t), H(t), R(t)\}, \quad \text{for all } t > 0.$$ (2)

It’s obviously that $G(0) > 0$. Suppose there exists a $t_1 > 0$ such that $G(t_1) = 0$ and $G(t) > 0$, for all $t \in [0, t_1)$. If $G(t_1) = S_2(t_1)$, and $S_1(t) \geq 0$, $E(t) \geq 0$, $I(t) \geq 0$, $A(t) \geq 0$, $H(t) \geq 0$ and $R(t) \geq 0$ for all $t \in [0, t_1]$. Therefore, according to the second equation in model (1), we have

$$\frac{dS_2}{dt} = \lambda \Delta - pS_2 - \frac{(\beta_A A + \beta_I I) S_2}{N} - dS_2$$

$$\geq -pS_2 - \frac{(\beta_A A + \beta_I I) S_2}{N} - dS_2$$

$$> -pS_2 - \frac{(\beta_A N + \beta_I N) S_2}{N} - dS_2$$

$$> -pS_2 - (\beta_A + \beta_I) S_2 - dS_2,$$

for all $t \in [0, t_1]$. (3)

Then, we can obtain

$$S_2(t) > S_2(0) e^{-(\beta_A + \beta_I + d)t} > 0,$$

for all $t \in [0, t_1]$. (4)

so, $G(t_1) = S_2(t_1) > 0$, which contradicts the hypothesis above. Hence, $S_2(t) > 0$ for all $t \geq 0$. Similarly, we have $S_1(t) > 0$, $E(t) > 0$, $I(t) > 0$, $A(t) > 0$, $H(t) > 0$ and $R(t) > 0$ for all $t \geq 0$.

Second, the uniform and ultimate boundedness of the solution can be proved. From model (1), we have

$$N(t) = S_1(t) + S_2(t) + E(t) + I(t) + A(t) + H(t) + R(t),$$

that is

$$\frac{dN}{dt} = \frac{d(S_1 + S_2 + E + I + A + H + R)}{dt} = \Lambda - dN - d_1 H,$$

$$\Lambda - (d + d_1) N \leq \frac{dN}{dt} \leq \Lambda - dN.$$ (6) (7)

By a standard comparison theorem, we have

$$N(0) e^{-(d + d_1)t} + \frac{\Lambda}{d + d_1} (1 - e^{-(d + d_1)t})$$

$$\leq N(t) \leq N(0) e^{-dt} + \frac{\Lambda}{d} (1 - e^{-dt}),$$

(8)

therefore, $N(t)$ is bounded by $\frac{\Lambda}{d + d_1} \leq N(t) \leq \frac{\Lambda}{d}$ as $t \to \infty$. According to the second equation in model (1), we can obtain

$$\frac{dS_2}{dt} = \lambda \Delta - pS_2 - \frac{(\beta_A A + \beta_I I) S_2}{N} - dS_2$$

$$\leq \lambda \Delta - (p + d) S_2,$$

that is

$$0 < S_2(t) \leq S_2(0) e^{-(p + d)t} + \frac{\lambda \Delta}{p + d} (1 - e^{-(p + d)t}),$$

(9)

hence, $S_2(t)$ is bounded by $\frac{\lambda \Delta}{p + d}$ as $t \to \infty$. The positive invariant set of model (1) can be obtained as

$$\mathcal{D} = \left\{ (S_1, S_2, E, I, A, H, R) \in \mathbb{R}_+^7 : S_1, E, I, A, H, R \geq 0, \frac{\lambda \Delta}{d + d_1} \leq N \leq \frac{\lambda \Delta}{d}, 0 \leq S_2 \leq \frac{\lambda \Delta}{p + d} \right\}.$$ (11)

\[\square\]

2.2.2 **Disease-free equilibrium (DFE) and the basic reproduction number**

For the epidemic system, there often exists a special equilibrium, i.e., the disease-free equilibrium (DFE), which corresponds to a steady state of the population without disease. There are no infectious individuals or no immigration of infections in the population at this stage [38]. The basic reproduction number $R_0$ is an indicator to measure whether an infectious disease is prevalent. To obtain $R_0$, it is first necessary to obtain disease-free equilibrium $E_0$ of model (1), so we have

$$E_0^* = (S_1^0, S_2^0, E^0, I^0, A^0, H^0, R^0)$$

$$= \left( \frac{\Lambda (\omega + d)(p + d - \lambda d)}{d(p + d)(\mu \nu + \omega + d)}, \frac{\lambda \Delta}{d + d_1}, 0, 0, 0, \frac{\mu \nu \Lambda (p + d - \lambda d)}{d(p + d)(\mu \nu + \omega + d)} \right).$$ (12)

Let $X = (E, I, A, H, S_1, S_2, R)^T$. By using the method of the next generation matrix proposed in [39], the terms with the new infection $\mathcal{F}$ and the outflow terms $\mathcal{V}$ are defined by

$$\frac{dX}{dt} = \mathcal{F}(X) - \mathcal{V}(X).$$
terms and the non-singular matrix $V$ are given by

$$\frac{(\gamma I + \gamma A)S_1}{N} + \frac{(\beta A + \beta I)S_2}{N}$$

The disease-free equilibrium of model (1) can be established.

By using Theorem 2 in [39], the following theorem can be obtained as follows

$$R_0 = \rho (F V^{-1}) = \frac{[(d + \tau)\rho \beta_I + (d + \theta)(1 - \rho)\beta_A] \cdot [\alpha(1 - \epsilon_1)(1 - \epsilon_2)(\omega + d)(p + d - \lambda d) + \alpha \lambda d(\mu v + \omega + d)]}{(\alpha + d)(\theta + d)(d + \tau)(p + d)(\mu v + \omega + d)}.$$  \hspace{1cm} (13)

By using Theorem 2 in [39], the following theorem can be established.

**Theorem 2** The disease-free equilibrium of model (1), given by (12), is locally asymptotically stable whenever $R_0 < 1$, and unstable if $R_0 > 1$.

### 2.2.3 The existence of endemic equilibrium

For the epidemic system, there may exist endemic equilibrium, which corresponds to a steady state of the disease persistence [41]. We will explore the existence of endemic equilibrium in this section. The possible equilibrium solutions of model (1) are defined by

$$\mathbb{E}^* = (S_1^*, S_2^*, E^*, I^*, A^*, H^*, R^*),$$

where $\mathbb{E}^*$ can be considered as any equilibrium of model (1). Furthermore, we let

$$r^* = \frac{\beta_A(1 - \epsilon_1)(1 - \epsilon_2)A^* + \beta_I(1 - \epsilon_1)(1 - \epsilon_2)I^*}{N^*}.$$  \hspace{1cm} (14)

Hence, at steady state of model (1), we have
A unique endemic equilibrium if $b_1 < 0$ and $b_2 = 0$ or $b_1^2 - 4b_0b_2 = 0$.

(c) two endemic equilibria if $b_2 > 0$, $b_1 < 0$ and $b_1^2 - 4b_0b_2 > 0$.

(d) no endemic equilibrium otherwise.

Case (c) of Theorem 3 indicates the existence of backward bifurcation in model (1) provided that $R_0 < 1$. To check that, we set the discriminant $b_1^2 - 4b_0b_2$ to zero, and the critical value of $R_0$ as follows

$$R_0^c = 1 - \frac{b_1^2}{4c}$$

Based on Theorem 3, we study the occurrence of forward and backward bifurcation with respect to the different parameter $b_1$. As shown in Fig. 2a, the backward bifurcation occurs for the values of $R_0$ when $0 < R_0^c < R_0 < 1$ with $R_0^c = 0.9775$. At this time, two endemic equilibria coexist with a locally asymptotically stable disease-free equilibrium. When $R_0 < R_0^c$, there exists a unique locally asymptotically stable disease-free equilibrium, which indicates that there is no outbreak of infectious diseases. The locally asymptotically stable endemic equilibrium coexists with an unstable disease-free equilibrium provided that $R_0 > 1$, which indicates that infectious diseases tend to be stable over time.

As seen in the forward bifurcation diagram of Fig. 2b, when $R_0 < 1$, the model has a unique locally stable disease-free equilibrium. When $R_0 > 1$, there exists a unique locally stable endemic equilibrium. Hence, we have the following conclusions
Theorem 4 Model (1) exhibits backward bifurcation when Case (c) of Theorem 3 holds and $R_0^c < R_0 < 1$. The epidemiological significance of the backward bifurcation phenomenon above is that the reproduction threshold ($R_0$) is less than unity, which is necessary but not sufficient to eliminate the COVID-19 epidemic (since two stable endemic equilibria coexist when $R_0^c < R_0 < 1$). In this case, effective disease control or elimination depends on the initial values of the model [42].

3 Baseline values of model parameters

To assign the model parameters with practical meaning and address the proposed model in a real case to verify the rationality of our model, we calibrate the model with the weekly confirmed data from March 22, 2020 to January 2, 2022 in Brazil. The information on weekly confirmed cases of COVID-19 is extracted from the COVID-19 Data Repository designed by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU) [43], as shown in Fig. 3. The important events, information on specific COVID-19 control measures and their timelines are derived from the Brazilian government website and the literature [44]. According to the critical event, the epidemic in Brazil can be divided into two stages corresponding to the different levels of public health interventions implemented in Brazil. The first wave occurred ahead of the first round of the Brazilian 2020 Municipal Elections, and its peak occurred in July and August. After the first round of the Brazilian Municipal Elections, the epidemic rebounded with a second wave and rapidly spread in Brazil.

We model the outbreak from March 22, 2020 to January 2, 2022 over two time periods, i.e., March, 22 to November 15, 2020 (before the first round of Brazilian Municipal Elections), and November 15, 2020 to January 2, 2022 (after the first round of Brazilian Municipal Elections). We mainly concentrate on the weekly confirmed cases (denoted by $I_C(t)$) and the cumulative confirmed cases per week (denoted by $N_C(t)$) in Brazil. The cumulative confirmed cases can be expressed by

$$\frac{dN_C(t)}{dt} = \rho \alpha E(t),$$

the weekly confirmed cases can be defined as follows
\[ I_C(t) = N_C(t) - N_C(t - 1). \] (17)

Some parameters of our proposed model can be obtained according to existing literature and research experience. The other unknown parameters can be estimated based on the infected data by Markov Chain Monte Carlo (MCMC) algorithm. We simulate the infected curves over two time periods by MCMC algorithm for 20,000 iterations with a burn-in of 10,000 times to obtain our parameter estimation. Tables 2 and 3 summarize the parameter calibration values. The fitting results of the weekly confirmed cases over two time periods are shown in Fig. 4a, b, and the fitting results of the cumulative confirmed cases over two time periods are shown in Fig. 4c, d. Pearsons correlation coefficients between the number of the weekly confirmed cases and estimated cases over two time periods are given in Fig. 4e, f. The fitting results confirm a good fitting between the actual data and model estimation.

It is evident from Tables 2 and 3 that the fitted values of the transmission coefficients for asymptomatic infected individuals (\( \beta_A \)) exceed the transmission coefficients for symptomatic infected individuals (\( \beta_I \)) over two time periods. This shows that the asymptomatic infected individuals are the main drivers of COVID-19 transmission in Brazil (this is also demonstrated by Fig. 10 in Appendix 1), and rapid detection of asymptomatic infections is critical to combat the COVID-19 epidemic in Brazil. According to Table 2, the fitted values of the voluntary home isolation rate \( \epsilon_1 \), the trans-
Fig. 4 Curve fitting of the weekly confirmed cases in Brazil. The black square curves represent the confirmed cases, and the pink regions indicate 95% confidence interval (CI)
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Table 3 Baseline parameter values of model (1) for the second period

| Parameters | Mean       | 95% CI       | Source         |
|------------|------------|--------------|----------------|
| $\Lambda$  | 20,759     | [45]         |                |
| $d$        | $\frac{1}{\tau}$ | [46]         |                |
| $\sigma$   | 7/5.2      | [47]         |                |
| $\tau$     | 7/8        | [48]         |                |
| $\theta$   | 7/14       | [49]         |                |
| $\gamma_H$ | 7/13       | [50,51]      |                |
| $\rho$     | 40%        | [53]         |                |
| $\omega$   | 13.9%      | [54]         |                |
| $\nu$      | 0.7122     | [55–57]      |                |
| $p$        | 0.0119     | [0.0070 0.0179] | MCMC calibration |
| $\beta_I$  | 0.7972     | [0.5048 1.2892] | MCMC calibration |
| $\beta_A$  | 1.4105     | [0.7756 1.8046] | MCMC calibration |
| $\epsilon_1$ | 0.2581     | [0.0929 0.4692] | MCMC calibration |
| $\epsilon_2$ | 0.1167     | [0.0044 0.4358] | MCMC calibration |
| $\mu$      | 0.3018     | [0.1026 0.5833] | MCMC calibration |
| $\kappa$   | 0.6735     | [0.1413 0.9817] | MCMC calibration |
| $d_1$      | 0.2211     | [0.1051 0.4300] | MCMC calibration |
| $\lambda$  | 0.0911     | [0.0064 0.2592] | MCMC calibration |

The proposed model based on an extension of the SEIR model shows good universality, which is applicable to analyze the COVID epidemics in other countries. Provided that new infected data is available, we can follow the procedure of parameter estimation to make this model fit the concrete condition of a new country.

It is known that the second COVID-19 wave began in November 2020, which coincided with the local elections in Brazil. The elections are characterized by mass gatherings and political rallies, which lead to the relaxation of public health measures. Moreover, there is a skepticism emerging in Brazil about the disease as well as non-pharmaceutical interventions to prevent the pandemic crisis. The digital era has facilitated access to information but also magnified the scale of fake news and distorted facts, leading to the spread of misinformation [58]. Consequently, safe and effective protective strategies such as face-mask wearing and home isolation are not taken seriously in Brazil.

In order to improve the implementation of these strategies in the public, the key is to eliminate this new skepticism. Therefore, it is more convincing to assess the effectiveness of implementation measures from the perspective of actual data, which will be discussed next.

4 Sensitivity analysis and efficacy of interventions

The aim of the global sensitivity analysis is to determine certain significant parameters that have a large impact on the basic reproduction number $R_0$, and some interventions related to these parameters may greatly affect the transmission dynamics of COVID-19. We perform a sensitivity analysis to determine the influence of related parameters on the basic reproduction number by a combination of Partial Rank Correlation Coefficient (PRCC) and Latin Hypercube Sampling (LHS) methods. PRCC is a common method used to measure the nonlinear monotonic relationship between two variables. The analysis shows the PRCC values and the corresponding $p$ values, which are used to evaluate the uncertainty level of the certain model parameters. The sign “+” or “−” of the PRCC value represents the qualitative relationship between the input and output variables. Generally, the parameter with the highest PRCC value and a corresponding lowest $p$ value ($p < 0.01$) is considered to take the most influence on the output variable.

The asterisk ($*$) in Fig. 5 highlights the four most influential parameters (i.e., with four highest PRCC values) related to $R_0$. We summarize the PRCC values...
of all 14 parameters related to \( R_0 \) and their \( p \) values in Table 4. The transmission coefficient \( \beta_A \) for asymptomatic infected individuals has a positive influence on \( R_0 \) (that is, as \( \beta_A \) increases, the value of \( R_0 \) increases). The parameters \( \epsilon_1, \epsilon_2, \) and \( p \) have negative influence on \( R_0 \) (that is, as these parameters increase, the value of \( R_0 \) decreases). The parameter \( \beta_A \) is the most influential parameter with the leading PRCC value, followed by \( \epsilon_1, \epsilon_2 \) and \( p \). It also implies that the asymptomatic infected individuals are the main drivers of COVID-19 transmission in Brazil. The voluntary home isolation rate \( (\epsilon_1) \), the face-mask wearing rate \( (\epsilon_2) \) and the transfer rate \( (p) \) are identified as the critical parameters, and the non-pharmaceutical interventions (NPIs) related to these parameters can greatly affect the COVID-19 pandemic. The PRCC value of the parameter \( \mu \) is \(-0.0988\), and the PRCC values of the parameters \( \epsilon_1, \epsilon_2 \) and \( p \) are \(-0.4211, -0.4063, -0.2502\), respectively. Hence, the effect of vaccination rate \( \mu \) associated with pharmaceutical intervention on the basic reproduction number \( R_0 \) is much lower than that of three NPIs (i.e., home isolation, face-mask wearing and media publicity). In order to explore the impacts of these NPIs on the COVID-19 pandemic, we pay more attention to these three highly sensitive parameters to predict the spread of COVID-19.

Next, we use the baseline parameter values given by fitting the actual data to perform numerical simulations so as to assess the impacts of home isolation, face-mask wearing and media publicity on the COVID-19 pandemic. We mainly alter the critical parameters (i.e., the voluntary home isolation rate \( (\epsilon_1) \), the face-mask wearing rate \( (\epsilon_2) \), and the transfer rate \( (p) \)) to observe the corresponding effects.

We first examine the variations of COVID-19 progression with the voluntary home isolation rate \( \epsilon_1 \) and the face-mask wearing rate \( \epsilon_2 \), as presented in Fig. 6a, b. In panel (a), the other parameters remain the same as the baseline values in Table 3, and \( \epsilon_1 \) varies. In panel (b), the other parameters remain the same as the baseline values in Table 3, and \( \epsilon_2 \) varies. It is observed that
the implementation rate of home isolation or face-mask wearing increases, and the number of infections in the second wave will be greatly reduced. When the implementation rate of home isolation or face-mask wearing reaches 60%, the peak number of infections in the second wave will be lower than that in the first wave. The higher the implementation rate of these two strategies, the more infections averted.

To explore the impact of media publicity on COVID-19 infections, we examine the effect of the parameter $p$ on the weekly infected cases, as shown in Fig. 6c. The other parameters remain the same as the baseline values in Table 3, and $p$ varies. It demonstrates that as
the transfer rate $p$ increases, the number of infections decreases, and the size of the outbreak decreases. The increase of the parameter value $p$ results in a significant decrease in the number of infections. With the implementation rate of media publicity reaching 60%, Brazil can largely avoid a second wave of the pandemic. When the implementation of home isolation, the face-mask wearing and media publicity can greatly decrease the number of infections. Generally speaking, home isolation, the face-mask wearing rate, and media publicity maintains the largest number of infections. Generally speaking, home isolation, the face-mask wearing and media publicity can greatly affect the spread of the COVID-19, and the impact of media publicity is more significant.

5 Optimal control analysis

In the previous section, the critical model parameters that affect the dynamics of COVID-19 greatly are given, including the voluntary home isolation rate, $\epsilon_1$, the face-mask wearing rate, $\epsilon_2$, and the transfer rate through media publicity, $p$. Here, we incorporate the following control measures in terms of these three parameters into model (1) to study the effective intervention strategies in combating COVID-19:

- $u_1$: practising media publicity, and educating unconscious susceptible individuals by media,
- $u_2$: practising the voluntary home isolation,
- $u_3$: practising the face-mask wearing.

In combination with model (1), we replace the constant-value parameters $p$, $\epsilon_1$ and $\epsilon_2$ by the time-dependent control factors $u_1(t)$, $u_2(t)$ and $u_3(t)$, respectively, so as to generate the control model. The optimal control problem is investigated by the control model along with the minimization of the objective function, as follows

\[
\dot{S}_1 = (1 - \lambda)A - \frac{(\beta_I I + \beta_A A)(1 - u_2)(1 - u_3)S_1}{N} - \mu \nu S_1 + u_1 S_2 + \omega R - dS_1,
\]

\[
\dot{S}_2 = \lambda \Lambda - u_1 S_2 - \frac{\beta_A A + \beta_I I S_2}{N} - dS_2,
\]

\[
\dot{E} = \frac{(\beta_I I + \beta_A A)(1 - u_2)(1 - u_3)S_1}{N} + \frac{\beta_A A + \beta_I I S_2}{N} - (\alpha + d)E,
\]

\[
\dot{I} = \rho \alpha E - (\theta + d)I,
\]

\[
\dot{A} = (1 - \rho)\alpha E - (\tau + d)A,
\]

\[
\dot{H} = \kappa \theta I - (\gamma_H + d_1 + d)H,
\]

\[
\dot{R} = (1 - \kappa)\theta I + \gamma_H H + \tau A + \mu \nu S_1 - (\omega + d)R,
\]

subject to minimize the objective function

\[
\mathcal{J}(u_1, u_2, u_3) = \min \int_0^T \left( B_1 E + B_2 I + B_3 A + B_4 H + \frac{1}{2} \sum_{i=1}^3 W_i u_i^2 \right) \, dt,
\]

where $T$ is the terminal time, $B_1, B_2, B_3, B_4 \in \mathbb{R}^+$ are the weight coefficients on the infectious population. The values of $W_i$ (for $i = 1, 2, 3$) are the balancing cost factors on the respective controls. Our control goal is to reduce the number of infected individuals and minimize the cost of the controls, i.e., the minimization of the infectious groups $E$, $I$, $A$, $H$, while keeping the low cost of the controls $u_1(t)$, $u_2(t)$, $u_3(t)$. We set $B_1 = 0.012$, $B_2 = 0.028$, $B_3 = 0.015$, $B_4 = 0.2$, $W_1 = 45,000$, $W_2 = 6000$, $W_3 = 5000$. The admissible set for three control variables $u_1(t), u_2(t)$ and $u_3(t)$ is defined as follows

\[
\mathcal{U} = \{(u_1, u_2, u_3) : u_i \text{ Lebesgue measurable,} \quad 0 \leq u_i \leq u_{i,\text{max}}, \text{ for } i = 1, 2, 3, \, t \in [0, T]\},
\]

where $u_{i,\text{max}}(i = 1, 2, 3)$ are fixed positive constants. Hence, it is important to seek an optimal control $u^* = (u_1^*, u_2^*, u_3^*)$ to make

\[
\mathcal{J}(u^*) = \min \{ \mathcal{J}(u_1, u_2, u_3) : u_1, u_2, u_3 \in \mathcal{U} \}.
\]

5.1 Characterization of the optimal control

The necessary conditions for optimal control are provided by Pontryagin’s maximum principle (PMP). According to PMP, the optimal control problem consisting of the objective function $\mathcal{J}$ (19) and the optimal
system (18) can be converted into the problem of minimizing a Hamiltonian (denoted by $\mathcal{H}$). Hence, we construct the Hamiltonian $\mathcal{H}$, which is defined for all $t \in [0, T]$, as follows

$$
\mathcal{H} = B_1 E + B_2 I + B_3 A + B_4 H + \frac{1}{2} \sum_{i=1}^{3} W_i u_i^2
$$

$$
+ \lambda_{S_1} \left[ (1 - \lambda) \lambda + \frac{(\beta_1 I^* + \beta A^*)(1 - u_2)(1 - u_3) S_1}{N} \right]
$$

$$
- \mu \nu S_1 + u_1 S_2 + \rho \omega - d S_1
$$

$$
+ \lambda_{S_2} \left[ \lambda A - u_1 S_2 - \frac{\beta A + \beta I S_2}{N} - d S_2 \right]
$$

$$
+ \lambda_E \left[ \frac{(\beta_1 I + \beta A)(1 - u_2)(1 - u_3) S_1}{N} \right]
$$

$$
+ \frac{(\beta A + \beta I S_2)}{N} - (\alpha + d) E \right]
$$

$$
+ \lambda_I[\rho \alpha E - (\theta + d) I]
$$

$$
+ \lambda_A[(1 - \rho) \alpha E - (\tau + d) A]
$$

$$
+ \lambda_H[\kappa \theta - (\gamma_H + d_1 + d) H]
$$

$$
+ \lambda_R[1 - (1 - \kappa) \theta I + \gamma_H H + \tau A
$$

$$
+ \mu \nu S_1 - (\omega + d) R
$$

$$
\text{(22)}
$$

where $\tilde{\lambda} = [\lambda_{S_1}, \lambda_{S_2}, \lambda_{E}, \lambda_I, \lambda_A, \lambda_H, \lambda_R]^{T}$ are costate variables, and $N = S_1 + S_2 + E + I + A + H + R$.

**Theorem 5** There exists an optimal control $(u_1^*(t), u_2^*(t), u_3^*(t))$, and corresponding solution $x^* = [S_1^*, S_2^*, E^*, I^*, A^*, H^*, R^*]^{T}$ that minimizes $J(u_1(t), u_2(t), u_3(t))$ over $U$. Further, there also exist the adjoint functions, $\lambda_{S_1}, \lambda_{S_2}, \lambda_{E}, \lambda_I, \lambda_A, \lambda_H$ and $\lambda_R$ [36], such that

$$
\dot{\lambda}_{S_1} = -\mu \nu \lambda_R
$$

$$
+ \lambda_{S_1} \left[ \frac{(\beta_1 I^* + \beta A^*)(1 - u_2)(1 - u_3) S_1}{N^2} \right]
$$

$$
+ \frac{(\beta I^* + \beta A^*)S_1}{N^2}
$$

$$
+ \lambda_{S_2} \left[ u_1 + \frac{(\beta_1 I^* + \beta A^*)}{N^2} \right]
$$

$$
+ \lambda_{E} \left[ \frac{(\beta I^* + \beta A^*)(1 - u_2)(1 - u_3) S_1}{N^2} \right]
$$

$$
- \frac{(\beta I^* + \beta A^*)(1 - u_2)(1 - u_3) S_1}{N^2}
$$

$$
\dot{\lambda}_{S_2} = -\lambda_{S_1} \left[ \frac{(\beta_1 I^* + \beta A^*)(1 - u_2)(1 - u_3) S_1}{N^2} \right]
$$

$$
- \lambda_{S_2} \left[ u_1 + \frac{(\beta_1 I^* + \beta A^*)}{N^2} \right]
$$

$$
+ \lambda_{E} \left[ \frac{(\beta I^* + \beta A^*)(1 - u_2)(1 - u_3) S_1}{N^2} \right]
$$

$$
- \frac{(\beta I^* + \beta A^*)(1 - u_2)(1 - u_3) S_1}{N^2}
$$

$$
\dot{\lambda}_{E} = -\frac{(\beta_1 I^* + \beta A^*)(1 - u_2)(1 - u_3) S_1}{N^2}
$$

$$
- \frac{(\beta I^* + \beta A^*)(1 - u_2)(1 - u_3) S_1}{N^2}
$$

$$
- \frac{(\beta_1 I^* + \beta A^*)}{N^2}
$$

$$
- \frac{(\beta I^* + \beta A^*)}{N^2}
$$

$$
\dot{\lambda}_{I} = -\frac{(\beta_1 I^* + \beta A^*)(1 - u_2)(1 - u_3) S_1}{N^2}
$$

$$
+ \lambda_{I}[\theta + (\theta + d) I]
$$

$$
+ \lambda_{A}[1 - (1 - \rho) \alpha E - (\tau + d) A]
$$

$$
+ \lambda_{H}[\kappa \theta - (\gamma_H + d_1 + d) H]
$$

$$
+ \lambda_{R}[1 - (1 - \kappa) \theta I + \gamma_H H + \tau A
$$

$$
+ \mu \nu S_1 - (\omega + d) R
$$

$$
= \frac{(\beta_1 I^* + \beta A^*)(1 - u_2)(1 - u_3) S_1}{N^2}
$$

$$
- \frac{(\beta I^* + \beta A^*)(1 - u_2)(1 - u_3) S_1}{N^2}
$$

$$
+ \frac{(\beta_1 I^* + \beta A^*)}{N^2}
$$

$$
+ \frac{(\beta I^* + \beta A^*)}{N^2}
$$

$$
\text{(23)}
$$

**With the transversality conditions**

$$
\lambda_{S_1}(T) = \lambda_{S_2}(T) = \lambda_{E}(T) = \lambda_{I}(T)
$$

$$
= \lambda_{A}(T) = \lambda_{H}(T) = \lambda_{R}(T) = 0
$$

the following characterizations hold
\[ u_1^* = \max \left\{ 0, \min \left\{ \frac{\lambda_{S_2} S_2^* - \lambda_{S_1} S_2^*}{W_1}, u_{1\text{max}} \right\} \right\}, \]  
\[ u_2^* = \max \left\{ 0, \min \left\{ \frac{(\beta A^* + \beta I^*) (1 - u_3) \left( \lambda_E S_1^* - \lambda_{S_1} S_1^* \right)}{W_2 N^*}, u_{2\text{max}} \right\} \right\}, \]  
\[ u_3^* = \max \left\{ 0, \min \left\{ \frac{(\beta A^* + \beta I^*) (1 - u_2) \left( \lambda_E S_1^* - \lambda_{S_1} S_1^* \right)}{W_3 N^*}, u_{3\text{max}} \right\} \right\}. \]  

**Proof** According to Pontryagin’s Maximum Principle, we give the proof of Theorem 5. By differentiating the Hamiltonian function (22) partially with respect to the state variables \( S_1, S_2, E, I, A, H, R \), we can obtain the adjoint state equations (23) as follows

\[
\begin{align*}
\frac{d\lambda_{S_1}}{dt} &= -\frac{\partial H}{\partial S_1}, \quad \lambda_{S_1}(T) = 0, \\
\frac{d\lambda_{S_2}}{dt} &= -\frac{\partial H}{\partial S_2}, \quad \lambda_{S_2}(T) = 0, \\
\frac{d\lambda_E}{dt} &= -\frac{\partial H}{\partial E}, \quad \lambda_E(T) = 0, \\
\frac{d\lambda_I}{dt} &= -\frac{\partial H}{\partial I}, \quad \lambda_I(T) = 0, \\
\frac{d\lambda_A}{dt} &= -\frac{\partial H}{\partial A}, \quad \lambda_A(T) = 0, \\
\frac{d\lambda_H}{dt} &= -\frac{\partial H}{\partial H}, \quad \lambda_H(T) = 0, \\
\frac{d\lambda_R}{dt} &= -\frac{\partial H}{\partial R}, \quad \lambda_R(T) = 0,
\end{align*}
\]  

(28)

and the optimality condition of control variable is

\[
\frac{\partial H}{\partial u_1} = 0, \quad \frac{\partial H}{\partial u_2} = 0, \quad \frac{\partial H}{\partial u_3} = 0,
\]  

(29)

where \( u_1 \) needs to satisfy \( 0 < u_1 < u_{1\text{max}} \). By solving (29), the optimal control \( u_1^* \) can be obtained as follows

\[
u_1^* = \begin{cases} 0 & \phi_1^* \leq 0 \\
\phi_1^* & 0 \leq \phi_1^* \leq u_{1\text{max}} \\
u_{1\text{max}} & \phi_1^* \geq u_{1\text{max}} \end{cases}
\]  

where

\[
\phi_1^* = \frac{\lambda_{S_2} S_2^* - \lambda_{S_1} S_2^*}{W_1},
\]  

that is

\[
u_1^* = \max \left\{ 0, \min \left\{ \frac{\lambda_{S_2} S_2^* - \lambda_{S_1} S_2^*}{W_1}, u_{1\text{max}} \right\} \right\}.
\]  

(30)

By similar arguments, the optimal controls \( u_2^* \) and \( u_3^* \) are characterized as

\[
\begin{align*}
u_2^* &= \max \left\{ 0, \min \left\{ \frac{(\beta A^* + \beta I^*) (1 - u_3) \left( \lambda_E S_1^* - \lambda_{S_1} S_1^* \right)}{W_2 N^*}, u_{2\text{max}} \right\} \right\}, \\
u_3^* &= \max \left\{ 0, \min \left\{ \frac{(\beta A^* + \beta I^*) (1 - u_2) \left( \lambda_E S_1^* - \lambda_{S_1} S_1^* \right)}{W_3 N^*}, u_{3\text{max}} \right\} \right\},
\end{align*}
\]  

(32)

5.2 Numerical simulation

In this section, we conduct some numerical simulations for seven possible combinations of the three intervention strategies \((u_1, u_2, u_3)\) to explore the most effective intervention strategies. The numerical simulations are implemented by system (18) forward in time and an adjoint system (23) backward in time until convergence reaches, which are known as the fourth-order Runge-Kutta forward-backward sweep simulations [36]. To solve the control system and the corresponding adjoint system, we adopt the parameters set in Table 3. We divide the seven possible combinations of the intervention strategies into three cases, namely, Case 1 involving the single control, Case 2 involving the dual controls, and Case 3 involving the triple controls.
(1) Case 1 involving the single control measure

- Strategy 1: educating unconscious susceptible individuals by media publicity only \((u_1 \neq 0, u_2 = u_3 = 0)\),
- Strategy 2: practising the voluntary home isolation only \((u_2 \neq 0, u_1 = u_3 = 0)\),
- Strategy 3: practising the face-mask wearing only \((u_3 \neq 0, u_1 = u_2 = 0)\).

(2) Case 2 involving the dual control measures

- Strategy 4: educating unconscious susceptible individuals by media publicity and practising the voluntary home isolation \((u_1 \neq 0, u_2 \neq 0, u_3 = 0)\),
- Strategy 5: educating unconscious susceptible individuals by media publicity and practising the face-mask wearing \((u_1 \neq 0, u_2 = 0, u_3 \neq 0)\),
- Strategy 6: practising the voluntary home isolation and the face-mask wearing \((u_1 = 0, u_2 \neq 0, u_3 \neq 0)\).

(3) Case 3 involving the triple control measures

- Strategy 7: educating unconscious susceptible individuals by media publicity, practising the voluntary home isolation, and practising the face-mask wearing \((u_1 \neq 0, u_2 \neq 0, u_3 \neq 0)\).

According to Sect. 3, we know that the implementation intensity of the intervention strategies remains at a moderate level before the first round of Brazilian Municipal Elections, since the implementation level of home isolation and face-mask wearing reaches more than 50%. However, the implementation of these strategies is relaxed after the Brazilian Municipal Elections, which then leads to an obvious increase in the number of infections. Consequently, it is more significant and constructive to evaluate the control strategy over this period, i.e., from November 15, 2020 to January 2, 2022. We predict the trend of the infection curve under the given control strategy.

5.2.1 Case 1: implementation of single control measures

Considering the implementation cost of each strategy, and in order to make the implementation rate of each strategy acceptable to the public, we set the maximum implementation rate of each strategy to 0.3. Figure 7 presents the numerical simulations with the implementation of single control measures. Figure 7a suggests the optimal control configuration over time for strategy 1, and Fig. 7b, c give the optimal control configurations over time for strategy 2 and strategy 3. Figure 7d presents the infections averted by single control strategies, where strategy 1 is the most effective, followed by constant control, strategy 2, and strategy 3. The number of infections averted by strategy 2 is equal to that averted by strategy 3. Compared with the counterfactual scenario, the infection averted ratio of strategy 1 reaches 88%, and the infection averted ratio of strategy 2 and strategy 3 reaches 30%. According to Fig. 7e, f, strategy 1 has the highest number of cumulative infections averted and the minimum objective functions. In general, strategy 1 (i.e., practising media publicity only) has a significant effect on reducing the infections of COVID-19. The optimal control configuration of strategy 1 suggests that the early implementation level of media publicity should be kept at 0.3 for 11 weeks (i.e., from November 15, 2020 to January 31, 2021) and then slowly reduced to 0 for the rest of the simulation time.

5.2.2 Case 2: the implementation of dual control measures

The maximum implementation rate of each dual control measure is also set to 0.3. Figure 8 presents the numerical simulations with the implementation of dual control measures. Figure 8a–c gives the optimal control configurations over time for strategies 4, 5, 6 respectively. Figure 8d presents the infections averted by dual control strategies, where strategy 4 and strategy 5 have the highest number of the infections averted, followed by constant control, strategy 6. Compared with the counterfactual scenario, the infection averted ratio by strategy 4 and strategy 5 reaches 92%, and the infection averted ratio by strategy 6 reaches 48%. According to Fig. 8e, f, strategy 4 and strategy 5 also have the highest number of cumulative infections averted and the minimum objective functions. In general, strategy 4 and strategy 5 have a significant effect on reducing the infections of COVID-19. The optimal control configuration of strategy 4 suggests that the early implementation of media publicity is complemented with the implementation of home isolation. The early implementation level of media publicity should be kept at 0.3 for 8 weeks (i.e., from November 15, 2020 to January 10, 2021) and then slowly reduced to 0, and the implementation level of home isolation should be kept at 0.3.
Fig. 7  Simulation results of single control measures. a optimal solution of strategy 1; b optimal solution of strategy 2; c optimal solution of strategy 3; d weekly confirmed individuals; e weekly cumulative confirmed individuals; f the value of objective function $J$. The solid blue lines represent the counterfactual scenario with no single control strategy implemented. Baseline constant control is denoted by the solid green line, which represents the actual situation of prevention control in Brazil. (Color figure online)
Fig. 8 Simulation results of dual control measures. a optimal solution of strategy 4; b optimal solution of strategy 5; c optimal solution of strategy 6; d weekly confirmed individuals; e weekly cumulative confirmed individuals; f the value of objective function $J$. The solid blue lines represent the counterfactual scenario with no dual control strategy implemented. The denotations of counterfactual scenario and baseline constant control are the same as that in Fig. 7. (Color figure online)
for 23 weeks (i.e., from November 15, 2020 to April 25, 2021) and then slowly reduced to 0. The optimal control configuration of strategy 5 shows that the early implementation of media publicity is complemented with the implementation of the face-mask wearing. The early implementation level of media publicity should be kept at 0.3 for 8 weeks (i.e., from November 15, 2020 to January 10, 2021) and then slowly reduced to 0, and the implementation level the face-mask wearing should be kept at 0.3 for 23 weeks (i.e., from November 15, 2020 to April 25, 2021) and then slowly reduced to 0.

5.2.3 Case 3: the implementation of triple control measures

Here, we carry out numerical simulations with the implementation of triple control measures simultaneously. The maximum implementation rate of the triple control measure is set to 0.3. Figure 9a presents the optimal control configuration over time for strategy 7.

In order to intuitively evaluate the effectiveness of the seven optimal strategies in restraining the COVID-19 epidemic, we propose a cost-effectiveness analysis, which is discussed in the next section.

6 Cost-effectiveness analysis

To assess the cost associated with intervention strategies, we propose the cost-effectiveness analysis. Here, we adopt two indexes, i.e., infection averted ratio (IAR) [59] and average cost-effectiveness ratio (ACER) [36]. Infection averted ratio can be defined by

\[
\text{IAR} = \frac{\text{Number of infections averted}}{\text{Number of recovered}},
\]

where the difference between the total number of disease infections under no control strategy and the total number of infections with the implementation of the control strategy, which is calculated as the number of infections averted. The number of recovered is equal to the total number of individuals who have recovered from disease infection with the implementation of the control strategy. The most cost-effective control strategy usually has the highest IAR value.

Average cost-effectiveness ratio is usually expressed by

\[
\text{ACER} = \frac{\text{Total cost incurred on the implementation of a particular control strategy}}{\text{Total number of infections averted by the control strategy}},
\]

where the most cost-effective control strategy usually has the lowest ACER value, and the total cost of the implementation of a particular control strategy is estimated as

\[
C(u) = \frac{1}{2} \int_0^T \sum_{i=1}^3 W_i u_i^2 \, dt.
\]

6.1 Cost-effectiveness analysis in Case 1

Using the optimal control results as presented in Fig. 7, the IAR and ACER among three single control strategies can be calculated. According to the results of IAR in Table 5, strategy 1 (practising media publicity only) has the most cost-effectiveness, followed by strategy 2 and strategy 3, both of which are equally cost-effective.

The results of the ACER cost-effectiveness analysis in Table 6 demonstrate that strategy 1 is more effective in infections averted than strategy 2 and strategy 3,
**Fig. 9** Simulation results of triple control measures. **a** optimal solution of strategy 7; **b** weekly confirmed individuals; **c** weekly cumulative confirmed individuals; **d** the value of objective function $J$. The solid blue lines represent the counterfactual scenario with no triple control strategy implemented. The denotations of counterfactual scenario and baseline constant control are the same as that in Fig. 7. (Color figure online)

**Table 5** IAR for Case 1

| Strategy        | Total infection averted | Total recovered   | IAR    |
|-----------------|-------------------------|-------------------|--------|
| $u_1(t)$        | 1.3921e+08              | 1.0927e+09        | 0.1274 |
| $u_2(t)$        | 4.0392e+07              | 5.6285e+08        | 0.0718 |
| $u_3(t)$        | 4.0392e+07              | 5.6285e+08        | 0.0718 |
6.2 Cost-effectiveness analysis in Case 2

According to the results obtained from the numerical simulation as presented in Fig. 8, we can obtain the IAR and ACER among three dual control strategies in Case 2. A review of Table 7 indicates that strategy 4 and strategy 5 have the highest IAR value. Hence, strategy 4 (which combines the implementation of media publicity and home isolation) and strategy 5 (which combines the implementation of media publicity and face-mask wearing) are considered as the most cost-effective in Case 2. According to ACER value in Table 8, strategy 5 with the lowest ACER value, which can be treated as the most cost-effective in Case 2, followed by strategy 4 and strategy 6.

6.3 Cost-effectiveness analysis in Case 3

Using the simulation results of strategy 7 as presented in Fig. 9, the cost-effectiveness analysis of strategy 7 is given in Tables 9 and 10. Besides, we present the sorting IAR and ACER values of the seven strategies in Tables 11 and 12, respectively.

A review of Table 11 indicates that strategy 7 (which combines the implementation of media publicity, home isolation and the face-mask wearing) has the highest IAR value, followed by strategy 5 and strategy 4. Hence, the multi-pronged control strategies have a con-
Table 11 The sorting IAR of each strategy

| Strategy | Total infection averted | Total recovered | IAR   |
|----------|-------------------------|----------------|-------|
| Strategy 7: $u_1(t) + u_2(t) + u_3(t)$ | 1.4350e+08          | 1.0655e+09     | 0.1347|
| Strategy 5: $u_1(t) + u_2(t)$ | 1.4248e+08          | 1.0792e+09     | 0.1320|
| Strategy 4: $u_1(t) + u_3(t)$ | 1.4248e+08          | 1.0790e+09     | 0.1320|
| Strategy 1: $u_1(t)$ | 1.3921e+08          | 1.0927e+09     | 0.1274|
| Strategy 6: $u_2(t) + u_3(t)$ | 6.3443e+07          | 5.1956e+08     | 0.1221|
| Strategy 2: $u_2(t)$ | 4.0392e+07          | 5.6285e+08     | 0.0718|
| Strategy 3: $u_3(t)$ | 4.0392e+07          | 5.6285e+08     | 0.0718|

Table 12 The sorting ACER of each strategy

| Strategy | Total infection averted | Cost   | ACER   |
|----------|-------------------------|--------|--------|
| Strategy 5: $u_1(t) + u_3(t)$ | 1.4248e+08          | 2.5432e+04 | 1.7849e--04|
| Strategy 1: $u_1(t)$ | 1.3921e+08          | 2.5329e+04 | 1.8195e--04|
| Strategy 7: $u_1(t) + u_2(t) + u_3(t)$ | 1.4350e+08          | 2.6434e+04 | 1.8421e--04|
| Strategy 4: $u_1(t) + u_2(t)$ | 1.4248e+08          | 2.6429e+04 | 1.8549e--04|
| Strategy 3: $u_3(t)$ | 4.0392e+07          | 1.3275e+04 | 3.2865e--04|
| Strategy 2: $u_2(t)$ | 4.0392e+07          | 1.5930e+04 | 3.9438e--04|
| Strategy 6: $u_2(t) + u_3(t)$ | 6.3443e+07          | 2.9205e+04 | 4.6034e--04|

Fig. 10 The transmission percentage generated by asymptomatic $\beta_A$ and symptomatic $\beta_I$ infectious individuals over two time periods in Brazil
considerable positive impact on epidemic control. According to Table 12, strategy 5 has the lowest ACER value, followed by strategy 4 and strategy 7. Further, strategy 5 shows the competitive cost advantage as compared to strategies 7. Hence, when the cost of implementation is taken into account, strategy 5 appears to be preferred in inhibiting the COVID-19 outbreak.

7 Conclusion

Since the outbreak of COVID-19, many countries have adopted different interventions to lower the risk of COVID-19 transmission. The transmission dynamics of COVID-19 are affected to some extent by the interventions. To explore effective interventions in combating COVID-19, we propose an extended COVID-19 epidemic model with consideration of the main interventions. We describe the realistic transmission dynamics of COVID-19 by extending the SEIR model to the model with seven-state variables.

Positivity and boundedness of the model indicate the biological significance as well as the rationality of this model. The dynamic behaviors of the model, such as forward and backward bifurcation, are analyzed. We conduct a sensitivity analysis to determine the influence of related parameters on the basic reproduction number. Meanwhile, numerical simulations also validate the impacts of the three non-pharmaceutical interventions related to critical parameters on the spread of COVID-19. The results find that the voluntary home isolation, the face-mask wearing and media publicity can greatly affect the COVID-19 pandemic, and the impact of media publicity is more significant. The asymptomatic infected individuals are the main drivers of COVID-19 transmission in Brazil. The effect of vaccination rate \( \mu \) associated with pharmaceutical intervention on the basic reproduction number \( R_0 \) is lower than that of non-pharmaceutical interventions.

To obtain effective interventions, an optimal control problem is established based on the proposed epidemic model. Further, we present a cost-effectiveness analysis to unravel the cost and the infections averted effectiveness of the intervention strategies. When the effectiveness in terms of infections averted is taken into account, strategy 7 averts the highest number of disease infections. The multi-pronged NPIs have considerable positive effects on controlling the outbreak of COVID-19. The infections are significantly decreased by the early implementation of media publicity complemented with home isolation and a public face-mask wearing strategy. When the cost of implementation is taken into account, strategy 5 appears to be preferred. The infections can also be significantly decreased by the early implementation of media publicity complemented with a public face-mask wearing strategy.

Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Yang Deng, Yi Zhao. The first draft of the manuscript was written by Yang Deng, Yi Zhao, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability The datasets generated and/or analyzed during the current study are available in the COVID-19 Data Repository designed by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU), https://github.com/CSSEGISandData/COVID-19.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Appendix 1: Supplemental figures

The transmission percentage generated by the asymptomatic and symptomatic infectious individuals in Brazil is illustrated in Fig. 10. The blue part represents the infections caused by the asymptomatic infectious individuals, and the red part represents the infections caused by the symptomatic infectious individuals. Infections caused by asymptomatic infectious individuals far exceed those caused by symptomatic infectious individuals. Hence, the asymptomatic infected individuals are the main drivers of COVID-19 transmission in Brazil.

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