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Study on SEAI Model of COVID-19 Based on Asymptomatic Infection

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Abstract: In this paper, an SEAI epidemic model with asymptomatic infection is studied under the background of mass transmission of COVID-19. First, we use the next-generation matrix method to obtain the basic reproductive number R_0 and calculate the equilibrium point. Secondly, when $R_0 < 1$, the local asymptotic stability of the disease-free equilibrium is proved by Hurwitz criterion, and the global asymptotic stability of the disease-free equilibrium is proved by constructing the Lyapunov function. When $R_0 > 1$, the system has a unique endemic equilibrium point and is locally asymptotically stable, and it is also proved that the system is uniformly persistent. Then, the application of optimal control theory is carried out, and the expression of the optimal control solution is obtained. Finally, in order to verify the correctness of the theory, the stability of the equilibrium point is numerically simulated and the sensitivity of the parameters of R_0 is analyzed. We also simulated the comparison of the number of asymptomatic infected people and symptomatic infected people before and after adopting the optimal control strategy. This shows that the infection of asymptomatic people cannot be underestimated in the spread of COVID-19 virus, and an isolation strategy should be adopted to control the spread speed of the disease.

Keywords: asymptomatic infection; stability; consistent persistence; optimal control; numerical simulation; sensitivity analysis

MSC: 34A34; 34A37

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1. Introduction

Infectious diseases [1,2] are one of the biggest threats to human survival. The frequent outbreaks and epidemics of infectious diseases not only affect people's health and hinder economic development, but also threaten social stability and damage social interests to a greater extent. Therefore, experts in the field of epidemiology and related biology are deeply studying infectious diseases, and their goal is to expose the spread dynamics and patterns of diseases and predict the future development trend by analyzing and understanding various infectious disease models [3–5].

Since the end of 2019, COVID-19 [6], caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread all over China and the world. This virus shows symptoms such as dry cough, fever and fatigue, and may further develop into pneumonia and renal failure, which may lead to death in severe cases [7–10]. The disease is mainly spread by bodily contact and sneezing and coughing droplets [11], and more and more evidence shows that asymptomatic infected people play an important driving role in its rapid spread [12]. Therefore, in order to prevent the rapid spread of COVID-19, many researchers in the field of biology aimed to understand it, and wanted to expose the epidemic law of diseases through the study of models, so as to provide theoretical basis and strategies for the detection, prevention and management of disease outbreaks. For example, Zhang et al. [13] combined the transmission mechanism of COVID-19 with preventive

measures, put forward a new stochastic dynamic model, and estimated and predicted the epidemic trend and control opportunity abroad. In addition, Tang et al. [14] considered medical follow-up quarantine, hospital isolation, treatment and other control and management measures, and evaluated the impact of public health interventions on the spread of COVID-19.

Asymptomatic infected people are contagious, but have no clinical symptoms. They are hidden in the crowd and are not easy to find found. Therefore, this group plays a great role in the spread of COVID-19. This characteristic of asymptomatic infected people is the main reason why COVID-19 has become a pandemic. Several studies have found that asymptomatic infection accounts for about 40% of patients in COVID-19, and individuals with asymptomatic infection are more likely to cause a larger epidemic than imported cases [15–17]. In order to understand more deeply how asymptomatic infected people promote the rapid spread of new pneumonia, many experts and scholars have established relevant infectious disease models. For example, Khan et al. [18] studied the dynamics of a stochastic SAIR mathematical model. Tan et al. [19] estimated the spread of symptomatic and asymptomatic COVID-19 with contact information. Dobrovolny [20] researched the role of asymptomatic individuals in the spread of infection. This study shows that even if asymptomatic infection does not necessarily account for a large proportion of infections, it can still change the scale and lethality of epidemics. Sun et al. [21] established an SCIRA model to estimate the impact of asymptomatic infected people. Their research shows that the potential impact of these hidden cases greatly promoted the outbreak of COVID-19 because asymptomatic infected people are contagious.

As an important method to study the transmission mechanism of infectious diseases, dynamic modeling has always been one of the hot issues in the field of infectious diseases. At present, the spread theory and modeling of infectious diseases have been extensively studied [22,23]. Scholars have established an infectious disease model based on the characteristics of COVID-19 to predict the epidemic spread trend, but there are still some limitations. In order to make up for the deficiency of the existing research, this paper used the actual transmission characteristics of COVID-19 to improve the classic SEAI infectious disease model, so as to accurately reveal the transmission mechanism of asymptomatic infected people in COVID-19, explore how asymptomatic infected people affect the outbreak of COVID-19 epidemic, and put forward some strategies to control the spread of COVID-19.

In this paper, we establish an SEAI model of COVID-19 with asymptomatic infection, and make a dynamic analysis to determine the influence of asymptomatic infection in the spread of COVID-19. The rest is organized as follows: Section 1 introduces the research background of COVID-19. Section 2 establishes the model. Sections 3 and 4 calculate the basic reproduction number and the equilibrium point of the model and prove the stability of the equilibrium point. In Section 5, the optimal control theory is put forward and the optimal control solution is obtained. In Section 6, the stability of the equilibrium point is numerically simulated, the sensitivity of the parameters affecting R_0 is analyzed, and the number of asymptomatic infected people and symptomatic infected people before and after adopting the optimal control strategy is further simulated. Section 7 gives the conclusion of this paper.

2. Model Formulation

At present, scholars at home and abroad have begun to study the influence of limited resources on the spread of diseases. For example, Zhou et al. [24] proposed a continuously differentiable treatment function

$$h(I) = \frac{rI}{1+\alpha I},$$

to describe the "saturation" phenomenon of limited treatment. r represents the maximum cure rate, α describes the effect of the delayed treatment of the infected person. Obviously, r/α represents the maximum supply of therapeutic resources, while $1/(1+\alpha I)$ describes the supply efficiency of medical resources, which has an important impact on the spread and control of diseases.

In this paper, the total population N is divided into four different parts: S stands for susceptible person, E stands for the infiltrator, A stands for asymptomatic infected person, I stands for symptomatic infected person. Considering that the treatment of COVID-19 is saturated, the saturated treatment function $h(I)$ is introduced into the classical infectious disease model, and the SEAI model is established. A flow chart of the model is shown in Figure 1.

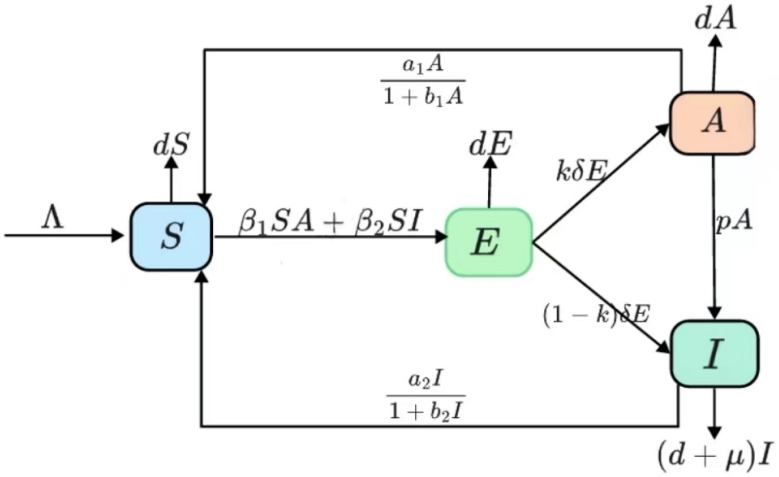

Figure 1. Flow chart of SEAI transmission.

The propagation dynamics model corresponding to the flow chart is as follows:

$$\begin{cases} \frac{dS}{dt} = \Lambda - \beta_1 SA - \beta_2 SI - dS + \frac{a_1 A}{1+b_1 A} + \frac{a_2 I}{1+b_2 I}, \\ \frac{dE}{dt} = \beta_1 SA + \beta_2 SI - (\delta + d)E, \\ \frac{dA}{dt} = k\delta E - (p+d)A - \frac{a_1 A}{1+b_1 A}, \\ \frac{dI}{dt} = (1-k)\delta E + pA - (d+\mu)I - \frac{a_2 I}{1+b_2 I}. \end{cases} \tag{1}$$

Assuming that all the parameters and variables involved in the above model are non-negative, please refer to Table 1 for the dynamic significance of infectious diseases of the corresponding parameters. Note that the expressions $\frac{a_1 A}{1+b_1 A}$ and $\frac{a_2 I}{1+b_2 I}$ represent limited medical resources.

Table 1. Parameter definitions for model (1).

Parameter	Definition	Unit
Λ	the constant input of population	$\text{people}^{-1}\text{day}^{-1}$
d	the natural death rate of population	day^{-1}
μ	the morbidity and mortality of symptomatic infected persons	day^{-1}
p	the rate of transformation from asymptomatic infection to symptomatic infection	day^{-1}
a_1	the maximum cure rate for asymptomatic patients	day^{-1}
a_2	the maximum cure rate for an infected person	day^{-1}
b_1	resource constraints for treating asymptomatic patients	day^{-1}
b_2	resource constraints for treating infected people	day^{-1}
β_1	the infection rate of asymptomatic infected people to susceptible people	$\text{people}^{-1}\text{day}^{-1}$
β_2	the infection rate of infected people with symptoms to susceptible people	$\text{people}^{-1}\text{day}^{-1}$
δ	the transfer rates of latent to infected persons	day^{-1}
$k\delta$	the rate at which latent persons develop asymptomatic infections	day^{-1}
$(1-k)\delta$	the rate at which latent persons become infected with symptoms	day^{-1}

It follows from model (1) that $N = S + E + A + I$ and $\frac{dN}{dt} = \Lambda - dN - \mu I \leq \Lambda - dN$. When $N > \frac{\Lambda}{d}$ approaches infinity, such that $\frac{dN}{dt} < 0$, for the sake of generality, the feasible domain is

$$X = \left\{ (S, E, A, I) \in R_+^4 : S + E + A + I \leq \frac{\Lambda}{d} \right\}. \tag{2}$$

3. Basic Regeneration Number and Equilibrium

By simple calculation, the only disease-free equilibrium of system (1) is $E_0 = (\frac{\Lambda}{d}, 0, 0, 0)$, where $S_0 = \frac{\Lambda}{d}, E_0 = A_0 = I_0 = 0$.

By the next generation matrix method [25,26], we will derive the basic regeneration number of model (1). Let

$$\mathcal{F} = \begin{bmatrix} \beta_1 SA + \beta_2 SI \\ 0 \\ 0 \end{bmatrix}, \mathcal{V} = \begin{bmatrix} Q_1 E \\ -k\delta E + Q_2 A + \frac{a_1 A}{1+b_1 A} \\ -(1-k)\delta E - pA + Q_3 I + \frac{a_2 I}{1+b_2 I} \end{bmatrix}$$

be the input rate of newly infected individuals and the rate of transfer of individuals, where

$$Q_1 = \delta + d, Q_2 = p + d, Q_3 = d + \mu.$$

Respectively, then we obtain

$$F = \begin{bmatrix} 0 & \beta_1 \frac{\Lambda}{d} & \beta_2 \frac{\Lambda}{d} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}, V = \begin{bmatrix} Q_1 & 0 & 0 \\ -k\delta & Q_2 + a_1 & 0 \\ -(1-k)\delta & -p & Q_3 + a_1 \end{bmatrix}.$$

Thus, we have

$$FV^{-1} = \begin{bmatrix} \frac{\beta_1 \Lambda k\delta}{dQ_1(Q_2+a_1)} + \frac{\beta_2 \Lambda k\delta p}{dQ_1(Q_2+a_1)(Q_3+a_2)} + \frac{\beta_2 \Lambda(1-k)\delta}{dQ_1(Q_3+a_2)} & \frac{\beta_1 \Lambda(Q_3+a_2)+\beta_2 \Lambda p}{d(Q_2+a_1)(Q_3+a_2)} & \frac{\beta_2 \Lambda}{d(Q_3+a_2)} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}.$$

Therefore, the basic regeneration number is

$$R_0 = \rho(FV^{-1}) = r_1 + r_2 + r_3, \tag{3}$$

where

$$r_1 = \frac{k\delta\beta_1\Lambda}{dQ_1(Q_2 + a_1)}, r_2 = \frac{(1-k)\delta\beta_2\Lambda}{dQ_1(Q_3 + a_2)}, r_3 = \frac{k\delta p\beta_2\Lambda}{dQ_1(Q_2 + a_1)(Q_3 + a_2)}.$$

The endemic equilibrium of system (1) is denoted as $E^* = (S_1, E_1, A_1, I_1)$. To solve the endemic equilibrium, we set the right side of model (1) to 0, that is

$$\begin{cases} \Lambda - \beta_1 S_1 A_1 - \beta_2 S_1 I_1 - dS_1 + \frac{a_1 A_1}{1+b_1 A_1} + \frac{a_2 I_1}{1+b_2 I_1} = 0, \\ \beta_1 S_1 A_1 + \beta_2 S_1 I_1 - (\delta + d)E_1 = 0, \\ k\delta E_1 - (p + d)A_1 - \frac{a_1 A_1}{1+b_1 A_1} = 0, \\ (1-k)\delta E_1 + pA_1 - (d + \mu)I_1 - \frac{a_2 I_1}{1+b_2 I_1} = 0, \end{cases} \tag{4}$$

where

$$\begin{cases} A_1 &= A_1, \\ E_1 &= \frac{Q_2(1+b_1A_1)+a_1}{(1+b_1A_1)k\delta}A_1, \\ I_1 &= \frac{(R_0-1)(\Lambda-dN)W}{R_0\mu[W-dQ_1(Q_2+a_1)(Q_3+a_2)]}, \\ S_1 &= \frac{\mu Q_1[Q_2(1+b_1A_1)+a_1]A_1}{(1+b_1A_1)k\delta[\mu\beta_1A_1+\beta_2(\Lambda-dN)]}, \end{cases}$$

and $W = k\delta\beta_1\Lambda(Q_3+a_2)+(1-k)\delta\beta_2\Lambda(Q_2+a_1+p)$.

If $R_0 > 1$, then I_1 is positive, and A_1 satisfies the following equation

$$w_1A_1^2 + w_2A_1 + w_3 = 0,$$

where

$$\begin{aligned} &w_1 = b_1kp+(1-k)Q_2b_1 > 0, w_2 = kp+(1-k)Q_2+(1-k)a_1 > 0, \\ &w_3 = -H < 0, H = \tfrac{a_2(\Lambda-dN)}{\mu+b_2(\Lambda-dN)} > 0, A_1 = -w_2/(2w_1), \\ &\Delta = w_2^2-4w_1w_3 = [kp+(1-k)Q_2+(1-k)a_1]^2+4(b_1kp+(1-k)Q_2b_1)H > 0. \end{aligned}$$

So there is only root $A_1 > 0$. When $R_0 > 1$, S_1, E_1, A_1, I_1 are positive and system (1) has a unique endemic equilibrium $E^* = (S_1, E_1, A_1, I_1)$.

3.1. Stability of Disease-Free Equilibrium

Theorem 1. *When $R_0 < 1$, the disease-free equilibrium E_0 of system (1) is locally asymptotically stable in X; When $R_0 > 1$, the disease-free equilibrium is unstable.*

Proof of Theorem 1. The Jacobian matrix of system (1) at E_0 is

$$J_* = \begin{bmatrix} -d & 0 & -\beta_1\frac{\Lambda}{d}+a_1 & -\beta_2\frac{\Lambda}{d}+a_2 \\ 0 & -Q_1 & \beta_1\frac{\Lambda}{d} & \beta_2\frac{\Lambda}{d} \\ 0 & k\delta & -Q_2-a_1 & 0 \\ 0 & (1-k)\delta & p & -Q_3-a_2 \end{bmatrix}.$$

The characteristic equation of matrix J_* is

$$(\lambda+d)(\lambda^3+\mathcal{A}_1\lambda^2+\mathcal{A}_2\lambda+\mathcal{A}_3) = 0. \tag{5}$$

Obviously, $\lambda_1 = -d$ is a negative real root of equation, and

$$\begin{aligned} \mathcal{A}_1 &= Q_1+Q_2+Q_3+a_1+a_2 > 0, \\ \mathcal{A}_2 &= (Q_3+a_2)(Q_1+Q_2+a_1)+Q_1(Q_2+a_1)-\beta_2(1-k)\delta\tfrac{\Lambda}{d}-\beta_1k\delta\tfrac{\Lambda}{d} \\ &= Q_1(Q_3+a_2)(1-r_2)+Q_1(Q_2+a_1)(1-r_1)+(Q_3+a_2)(Q_2+a_1) > 0, \\ \mathcal{A}_3 &= Q_1(Q_2+a_1)(Q_3+a_2)-(Q_2+a_1)\beta_2\tfrac{\Lambda}{d}(1-k)\delta-(Q_3+a_2)\beta_1\tfrac{\Lambda}{d}k\delta-k\delta p\beta_2\tfrac{\Lambda}{d} \\ &= Q_1(Q_2+a_1)(Q_3+a_2)(1-R_0) > 0. \end{aligned}$$

Then, we obtain

$$\begin{aligned} \mathcal{A}_1\mathcal{A}_2-\mathcal{A}_3 &= Q_1^2[(Q_3+a_2)(1-r_2)+(Q_2+a_1)(1-r_1)] \\ &\quad +(Q_2+Q_3+a_1+a_2)[Q_1(Q_3+a_2)(1-r_2)+Q_1(Q_2+a_1)(1-r_1) \\ &\quad +(Q_3+a_2)(Q_2+a_1)]+Q_1(Q_2+a_1)(Q_3+a_2)R_0 > 0. \end{aligned}$$

Therefore, according to the Hurwitz criterion [27,28], when $R_0 < 1, \mathcal{A}_3 > 0$, system (1) is locally asymptotically stable at the disease-free equilibrium point E_0. When $R_0 > 1$ $\mathcal{A}_3 < 0$, the disease-free equilibrium point is unstable. The proof is complete. □

Theorem 2. *When $R_0 \le 1-\frac{W}{\beta_1A+\beta_2I} < 1$, the disease-free equilibrium point E_0 of system (1) is globally asymptotically stable in X, where*

$$W = \left[\frac{\beta_1(Q_3+a_2)+p\beta_2}{(Q_2+a_1)(Q_3+a_2)}\frac{a_1b_1A^2}{1+b_1A} + \frac{\beta_2}{Q_3+a_2}\frac{a_2b_2I^2}{1+b_2I}\right].$$

Proof of Theorem 2. Construction of Lyapunov function

$$\begin{aligned} V &= \frac{\Lambda}{d}\left[\frac{k\delta}{Q_1(Q_2+a_1)}\beta_1 + \frac{k\delta p+(1-k)\delta(Q_2+a_1)}{Q_1(Q_2+a_1)(Q_3+a_2)}\beta_2\right]E \\ &\quad + \frac{\Lambda}{d}\left[\frac{\beta_1}{Q_2+a_1} + \frac{p\beta_2}{(Q_2+a_1)(Q_3+a_2)}\right]A + \frac{\Lambda}{d}\frac{\beta_2}{Q_3+a_2}I > 0. \end{aligned}$$

When $R_0 \le 1 - \frac{W}{\beta_1 A+\beta_2 I} < 1$,

$$\begin{aligned} \frac{dV}{dt} &= \frac{\Lambda}{d}\left[\frac{k\delta}{Q_1(Q_2+a_1)}\beta_1 + \frac{k\delta p+(1-k)\delta(Q_2+a_1)}{Q_1(Q_2+a_1)(Q_3+a_2)}\beta_2\right]E' \\ &\quad + \frac{\Lambda}{d}\left[\frac{\beta_1}{Q_2+a_1} + \frac{p\beta_2}{(Q_2+a_1)(Q_3+a_2)}\right]A' + \frac{\Lambda}{d}\frac{\beta_2}{Q_3+a_2}I' \\ &= \frac{\Lambda}{d}\left[\frac{k\delta}{Q_1(Q_2+a_1)}\beta_1 + \frac{k\delta p+(1-k)\delta(Q_2+a_1)}{Q_1(Q_2+a_1)(Q_3+a_2)}\beta_2\right][\beta_1 SA + \beta_2 SI - (\delta+d)E] \\ &\quad + \frac{\Lambda}{d}\left[\frac{\beta_1}{Q_2+a_1} + \frac{p\beta_2}{(Q_2+a_1)(Q_3+a_2)}\right][k\delta E - (p+d)A - \frac{a_1A}{1+b_1A}] \\ &\quad + \frac{\beta_2}{Q_3+a_2}[(1-k)\delta E + pA - (d+\mu)I - \frac{a_2I}{1+b_2I}]\frac{\Lambda}{d} \\ &= (R_0-1)(\beta_1A+\beta_2I) + \left[\frac{\beta_1(Q_3+a_2)+p\beta_2}{(Q_2+a_1)(Q_3+a_2)}\frac{a_1b_1A^2}{1+b_1A} + \frac{\beta_2}{Q_3+a_2}\frac{a_2b_2I^2}{1+b_2I}\right] \\ &= (R_0-1)(\beta_1A+\beta_2I) + W \le 0. \end{aligned}$$

Let $\Omega = \left\{(S,E,A,I)|\frac{dV}{dt} = 0\right\} = \{(S,E,A,I)|A = I = 0\}$, within Ω , when $t \to \infty$, there is $S \to \frac{\Lambda}{d}$. Therefore, E_0 is the maximal w-invariant set of Ω. According to LaSalle's invariant set principle [29], any trajectory within X converges to E_0, where E_0 is the disease-free equilibrium and is globally asymptotically stable within X. The proof is complete. □

3.2. Stability of the Endemic Equilibrium

Theorem 3. *When $R_0 > 1$, if $\mathcal{B}_1\mathcal{B}_2 - \mathcal{B}_3 > 0$ and $\mathcal{B}_3(\mathcal{B}_1\mathcal{B}_2 - \mathcal{B}_3) > \mathcal{B}_1^2\mathcal{B}_4$, then the endemic equilibrium E^* of system (1) is locally asymptotically stable in X. Among them,*

$$\begin{aligned} \mathcal{B}_1 &= a_{11} + a_{12} + d, \\ \mathcal{B}_2 &= a_{11}(a_{12}+d) + a_{13} + a_{14} - a_{15}, \\ \mathcal{B}_3 &= (a_{12}+d)(a_{13}+a_{14}-a_{15}) + a_{12}a_{17} + a_{16} + a_{18} - k\delta p\beta_2 S_1, \\ \mathcal{B}_4 &= (a_{12}+d)(a_{16} - \beta_2 S_1 k\delta p - a_{18}) \\ &\quad + a_{12}\{\delta(\beta_2 S_1 + N)[kp + (1-k)(Q_2+M)] + k\delta(Q_3+N)(\beta_1 S_1 + M)\} \end{aligned}$$

and have

$$\begin{aligned} &a_{11} = Q_1+Q_2+Q_3+M+N, a_{12} = \beta_1A_1 + \beta_2I_1, \\ &a_{13} = (Q_2+M)(Q_3+N), a_{14} = Q_1(Q_2+Q_3+M+N), \\ &a_{15} = [\beta_2(1-k) - k\beta_1]S_1\delta, a_{16} = Q_1(Q_2+M)(Q_3+N), \\ &a_{17} = (1-k)\delta(\beta_2S_1+N) + k\delta(\beta_1S_1+M), \\ &a_{18} = (1-k)\delta\beta_2S_1(Q_2+M) + k\delta\beta_1S_1(Q_3+N), \end{aligned}$$

where

$$M = \frac{a_1}{(1+b_1A_1)^2}, N = \frac{a_2}{(1+b_2I_1)^2}.$$

Proof of Theorem 3. The Jacobian matrix of system (1) at E^* is

$$J_{|E_*} = \begin{bmatrix} -\beta_1A_1 - \beta_2I_1 - d & 0 & -\beta_1S_1 - \frac{a_1}{(1+b_1A_1)^2} & -\beta_2S_1 - \frac{a_2}{(1+b_2I_1)^2} \\ \beta A_1 + \beta_2 I_1 & -Q_1 & \beta_1S_1 & \beta_2S_1 \\ 0 & k\delta & -Q_2 - \frac{a_1}{(1+b_1A_1)^2} & 0 \\ 0 & (1-k)\delta & p & -Q_3 - \frac{a_2}{(1+b_2I_1)^2} \end{bmatrix},$$

then

$$\lambda Identity - J_{|E_*} = \begin{bmatrix} \lambda+\beta_1 A_1+\beta_2 I_1+d & 0 & \beta_1 S_1+\frac{a_1}{(1+b_1 A_1)^2} & \beta_2 S_1+\frac{a_2}{(1+b_2 I_1)^2} \\ -\beta A_1-\beta_2 I_1 & \lambda+Q_1 & -\beta_1 S_1 & -\beta_2 S_1 \\ 0 & -k\delta & \lambda+Q_2+\frac{a_1}{(1+b_1 A_1)^2} & 0 \\ 0 & -(1-k)\delta & -p & \lambda+Q_3+\frac{a_2}{(1+b_2 I_1)^2} \end{bmatrix},$$

then

$$det(\lambda Identity - J_{|E_*}) = \lambda^4 + \mathcal{B}_1\lambda^3 + \mathcal{B}_2\lambda^2 + \mathcal{B}_3\lambda + \mathcal{B}_4 = 0.$$

If $R_0 > 1$, it can be determined that

$$\mathcal{B}_1, \mathcal{B}_2, \mathcal{B}_3, \mathcal{B}_4 > 0, \tag{6}$$

then we have

$$\mathcal{B}_1\mathcal{B}_2 - \mathcal{B}_3 > 0, \mathcal{B}_3(\mathcal{B}_1\mathcal{B}_2 - \mathcal{B}_3) > \mathcal{B}_1^2\mathcal{B}_4. \tag{7}$$

The proofs of (6) and (7) are given in Appendix A and Appendix B, respectively. Therefore, according to Hurwitz criterion [30], the equilibrium E^* of system (1) is locally asymptotically stable. The proof is complete. □

4. Persistence

Theorem 4. *When $R_0 > 1$, the system (1) is uniformly persistent.*

Proof of Theorem 4. To prove persistence, we first give the following notation and definition

$$X_0 = \{(S, E, A, I) \in X | E, A, I > 0\}, \partial X_0 = X \setminus X_0.$$

We obtain from system (1)

$$E(t) \geq E(t_0)e^{-(\sigma+d)(t-t_0)}, A(t) \geq A(t_0)e^{-(p+d)(t-t_0)}, I(t) \geq I(t_0)e^{-(\mu+d)(t-t_0)}. \tag{8}$$

Therefore, X and X_0 are positively invariant sets, where ∂X_0 is a relatively closed set of X. Next, we will prove that system (1) is uniformly persistent. Let

$$M_\partial = \{(S(0), E(0), A(0), I(0)) | (S(t), E(t), A(t), I(t)) \in \partial X_0, \forall t \geq 0\}.$$

Now we prove

$$M_\partial = (S(0), 0, 0, 0) | S(t) \geq 0,$$

we clearly have

$$\{(S(0), 0, 0, 0) | S(t) \geq 0\} \subseteq M_\partial,$$

and now we just need proof

$$M_\partial \subseteq \{(S(0), 0, 0, 0) | S(t) \geq 0\}.$$

Let $(S(0), E(0), A(0), I(0)) \in M_\partial$ be a statement. We need to prove that for statement $\forall t \geq 0$, have $E(t) = 0, A(t) = 0, I(t) = 0$, there exists the statement $E(t) = 0, A(t) = 0$, $I(t) = 0$. By using proof by contradiction, let us assume that the conclusion is not true. In that case, there exists the statement $t_0 \geq 0$ such that one of the following equations holds:

$$(i) E(t_0) > 0;\ (ii) A(t_0) > 0;\ (iii) I(t_0) > 0.$$

For case (i), solving Equation (8) for all $t > t_0$ yields statement $A(t) > 0$. Furthermore, from system (1), we have $E(t) > 0, I(t) > 0$. Hence, we have statement $(S(t), E(t), A(t), I(t)) \notin \partial X_0$, which leads to a contradiction. For case (ii) , a similar approach leads to a contradiction with statement $(S(0), E(0), A(0), I(0)) \in M_\partial$. In the case of (iii), that is $E(t_0) > 0$, when $t > t_0$ holds, we can obtain

$$A(t) = A(t_0)e^{-(p+d)(t-t_0)} + \int_{t_0}^{t}(k\delta E - \frac{a_1 A}{1+b_1 A})e^{p+d}dt.$$

Clearly, when $E(t_0) > 0$, for $\forall t > t_0$ have $A(t) > 0$ holds. Similarly, by applying the same method, the formal solutions for $I(t)$ can be obtained. When $t > t_0$, we have $I(t) > 0$. Therefore, statement $(S(t), E(t), A(t), I(t)) \notin \partial X_0$ leads to a contradiction. Thus, it is concluded that $M_\partial = \{(S(0), 0, 0, 0)|S(0) \geq 0\}$ holds. The system (1) has a globally asymptotically stable disease-free equilibrium $E(0)$, and there is only one equilibrium $E(0)$ in M_∂.

The following will prove that E_0 is weakly repulsive with respect to the set X_0, that is, proving $\lim\limits_{t\to\infty} supd(\Phi(t), E_0) > 0$ is sufficient by demonstrating $W^s(E_0) \cap X_0 = \varnothing$. Using proof by contradiction, let us assume this conclusion is not true. Then there exists a positive solution $(S(t), E(t), A(t), I(t))$ for system (1) such that

$$\lim_{t\to\infty}(S(t), E(t), A(t), I(t)) = (S^0, 0, 0, 0).$$

Define $M = F - V$. Due to $R_0 > 1$, therefore $s(M) > 0$. For a small enough value of $\varepsilon > 0$, there exists $s(M - M_\varepsilon) > 0$, where

$$M_\varepsilon = \begin{bmatrix} 0 & \beta_1\varepsilon & \beta_2\varepsilon \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}.$$

There exists $T > 0$ such that for any $t > T$, have $S^0 - \varepsilon < S(t) < S^0 + \varepsilon$. Thus, the following differential equation inequality can be obtained:

$$\begin{cases} \frac{dE}{dt} \geq \beta_1(S^0 - \varepsilon)A + \beta_2(S^0 - \varepsilon)I - (\delta + d)E, \\ \frac{dA}{dt} = k\delta E - (p + d)A - \frac{a_1 A}{1+b_1 A}, \\ \frac{dI}{dt} = (1 - k)\delta E + pA - (d + \mu)I - \frac{a_2 I}{1+b_2 I}. \end{cases}$$

Auxiliary system

$$\begin{cases} \frac{dE}{dt} = \beta_1(S^0 - \varepsilon)A + \beta_2(S^0 - \varepsilon)I - (\delta + d)E, \\ \frac{dA}{dt} = k\delta E - (p + d)A - \frac{a_1 A}{1+b_1 A}, \\ \frac{dI}{dt} = (1 - k)\delta E + pA - (d + \mu)I - \frac{a_2 I}{1+b_2 I}. \end{cases} \tag{9}$$

Because of $s(M - M_\varepsilon) > 0$, when $t \to \infty$, $E(t) \to \infty, A(t) \to \infty, I(t) \to \infty$. This contradicts the assumption that when $t \to \infty$,$E(t) \to 0, A(t) \to 0, I(t) \to 0$. Thus, it is proved that $W^s(E_0) \cap X_0 = \varnothing$ holds. In summary, it can be concluded that the system (1) with respect to $(X_0, \partial X_0)$ is uniformly persistent. The proof is complete. □

5. Optimal Control Strategy

The maximum principle proposed by Pontryagin is one of the three cornerstones of optimal control theory. It can be applied to solve interdisciplinary problems, formulate rational and effective control strategies in mathematical models, and effectively prevent the spread of COVID-19. Given the complexity of infectious disease modeling, which typically involves numerous parameters, the use of optimal control measures to analyze the dynamics of diseases is crucial. The application of optimal control theory contributes to improving the predictive accuracy of models and designing the most effective strategies to reduce the impact of diseases on populations [31].

In this section, the Pontryagin maximum principle is employed to identify optimal control strategies for addressing COVID-19, with the aim of minimizing the number of infected individuals and minimizing the associated control costs. Applying the Pontryagin

maximum principle from optimal control theory allows for the identification of rational and effective strategies for controlling infectious diseases, necessitating the exploration of optimal control conditions within the model.

Rewrite system (1) as the following set of nonlinear differential equations:

$$\begin{cases} \frac{dS}{dt} = \Lambda - \beta_1(1-u_1)SA - \beta_2(1-u_2)SI - dS + \frac{a_1A}{1+b_1A} + \frac{a_2I}{1+b_2I}, \\ \frac{dE}{dt} = \beta_1(1-u_1)SA + \beta_2(1-u_2)SI - (\delta+d)E, \\ \frac{dA}{dt} = k\delta E - (p+d+u_3)A - \frac{a_1A}{1+b_1A}, \\ \frac{dI}{dt} = (1-k)\delta E + pA - (d+\mu+u_4)I - \frac{a_2I}{1+b_2I}, \end{cases} \tag{10}$$

where u_1 signifies the strategy of isolating to reduce interaction between susceptible and asymptomatic infected individuals, u_2 indicates the strategy of isolating to lessen contact between susceptible and symptomatic infected individuals, u_3 denotes the approach to enhance treatment and recovery of asymptomatic infected individuals, and u_4 corresponds to the strategy of improving treatment and recovery of symptomatic infected individuals.

Define the control set

$$U = \{(u_1(t), u_2(t), u_3(t), u_4(t)) | 0 \le u_i(t) \le 1, i = 1, 2, 3, 4\},$$

and $u_i(t)$ is Lebesgue measurable at $[0, 1]$.

By applying the method of Ahmad et al. [32] to construct the objective function, we have completed additional research on the basis of their work and constructed the following objective function

$$J(u_1, u_2, u_3, u_4) = \int_0^T (P_1A + P_2I + \frac{w_1}{2}u_1^2 + \frac{w_2}{2}u_2^2 + \frac{w_3}{2}u_3^2 + \frac{w_4}{2}u_4^2)dt, \tag{11}$$

where: P_1 and P_2, respectively, represent the weight coefficients of asymptomatic infected persons and symptomatic infected persons; w_1, w_2, w_3, w_4 respectively represent the weight coefficients corresponding to each control strategy; $\frac{w_1}{2}u_1^2$, $\frac{w_2}{2}u_2^2$, $\frac{w_3}{2}u_3^2$, $\frac{w_4}{2}u_4^2$ respectively indicate the cost required for the corresponding control policy.

The optimal control strategy problem is now described as

$$OCP : \begin{cases} minJ(u), \\ s.t.u = (u_1, u_2, u_3, u_4) \in U. \end{cases} \tag{12}$$

5.1. Existence of Optimal Control Solutions

Theorem 5. *System* (10) *has optimal control* $\overrightarrow{u^*} = (u_1^*, u_2^*, u_3^*, u_4^*) \in U$, *such that*

$$J({u_1}^*, {u_2}^*, {u_3}^*, {u_4}^*) = \min_{u_1,u_2,u_3,u_4 \in U} J(u_1, u_2, u_3, u_4). \tag{13}$$

Proof of Theorem 5. According to the theory of optimal existence [33], it is established that

(1) For any control variable $u_i \in U$, the initial values of system (10) are all negative;
(2) The control set is a closed and convex set;
(3) The right-hand linear function of system (10) satisfies the initial conditions, ensuring boundedness on the control set U;
(4) The integrand of the objective function (11) is convex on the control set U, and there exist constants c_1 and c_2, such that

$$P_1A + P_2I + \tfrac{w_1}{2}u_1^2 + \tfrac{w_2}{2}u_2^2 + \tfrac{w_3}{2}u_3^2 + \tfrac{w_4}{2}u_4^2 \ge c_1 \parallel u \parallel^{c_2},$$

where $P_1A + P_2I \ge 0, c_1 = \frac{1}{2}min(B_i)(i = 1, 2, 3, 4), c_2 = 2$.

Therefore, the optimal control solution for system (10) exists. The proof is complete. □

5.2. Optimal Control Solution

Next, the Pontryagin's Maximum Principle is employed to determine the solution for optimal control [34]. For $\forall t \in [0, T]$, the Hamiltonian function H is defined as

$$\begin{aligned} H(Y, U, \lambda) &= P_1 A + P_2 I + \frac{w_1}{2}u_1^2 + \frac{w_2}{2}u_2^2 + \frac{w_3}{2}u_3^2 + \frac{w_4}{2}u_4^2 + \lambda_1 \frac{dS}{dt} + \lambda_2 \frac{dE}{dt} + \lambda_3 \frac{dA}{dt} + \lambda_4 \frac{dI}{dt} \\ &= P_1 A + P_2 I + \frac{w_1}{2}u_1^2 + \frac{w_2}{2}u_2^2 + \frac{w_3}{2}u_3^2 + \frac{w_4}{2}u_4^2 \\ &\quad +\lambda_1[\Lambda - \beta_1(1-u_1)SA - \beta_2(1-u_2)SI - dS + \tfrac{a_1 A}{1+b_1 A} + \tfrac{a_2 I}{1+b_2 I}] \\ &\quad +\lambda_2[\beta_1(1-u_1)SA + \beta_2(1-u_2)SI - (\delta + d)E] \\ &\quad +\lambda_3[k\delta E - (p + d + u_3)A - \tfrac{a_1 A}{1+b_1 A}] \\ &\quad +\lambda_4[(1-k)\delta E + pA - (d + \mu + u_4)I - \tfrac{a_2 I}{1+b_2 I}], \end{aligned}$$

where $\lambda_1(t), \lambda_2(t), \lambda_3(t), \lambda_4(t)$ represent the adjoint variables corresponding to each state. And there is the following:
$\mathcal{H}_1$: control system satisfaction

$$\frac{dS}{dt} = \frac{\partial H}{\partial \lambda_1}, \frac{dE}{dt} = \frac{\partial H}{\partial \lambda_2}, \frac{dA}{dt} = \frac{\partial H}{\partial \lambda_3}, \frac{dI}{dt} = \frac{\partial H}{\partial \lambda_4};$$

$\mathcal{H}_2$: adjoint system satisfaction

$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S}, \frac{d\lambda_2}{dt} = -\frac{\partial H}{\partial E}, \frac{d\lambda_3}{dt} = -\frac{\partial H}{\partial A}, \frac{d\lambda_4}{dt} = -\frac{\partial H}{\partial I};$$

$\mathcal{H}_3$: minimum condition

$$H(Y^*(t), U^*(t), \Lambda^*(t)) = \min_{0 \le u_i \le u_{imax}} H(Y^*(t), U^*(t), \Lambda^*(t)).$$

In addition, the following cross-sectional conditions also hold true.

$$\lambda_i(T) = 0, i = 1, 2, 3, 4.$$

Theorem 6. *There exists an optimal control $U(t)$, suppose $(S^*(t), E^*(t), A^*(t), I^*(t))$ is the optimal control solution for the system (11), where $\lambda_1^*(t), \lambda_2^*(t), \lambda_3^*(t), \lambda_4^*(t)$ is the adjoint function. According to Pontryagin's Maximum Principle, the derivative of the adjoint variables is obtained as*

$$\begin{cases} \frac{d\lambda_1^*}{dt} = [\beta_1(1-u_1)A + \beta_2(1-u_2)I](\lambda_1^* - \lambda_2^*) + d\lambda_1^*, \\ \frac{d\lambda_2^*}{dt} = (\delta + d)\lambda_1^* - k\delta\lambda_3^* - (1-k)\delta\lambda_4^*, \\ \frac{d\lambda_3^*}{dt} = -P_1 + \beta_1(1-u_1)S(\lambda_1^* - \lambda_2^*) + \frac{a_1}{(1+b_1 A)^2}(\lambda_3^* - \lambda_1^*) + (p + d + u_3)\lambda_3^* - p\lambda_4^*, \\ \frac{d\lambda_4^*}{dt} = -P_2 + \beta_2(1-u_2)S(\lambda_1^* - \lambda_2^*) + \frac{a_2}{(1+b_2 I)^2}(\lambda_4^* - \lambda_1^*) + (d + \mu + u_4)\lambda_4^*, \end{cases} \tag{14}$$

and there is a cross-sectional condition $\lambda_i^*(T) = 0, i = 1, \ldots, 4$. Additionally, the optimal control must satisfy

$$\frac{\partial H}{\partial u_1}\Big| u_1^* = 0, \frac{\partial H}{\partial u_2}\Big| u_2^* = 0, \frac{\partial H}{\partial u_3}\Big| u_3^* = 0, \frac{\partial H}{\partial u_4}\Big| u_4^* = 0. \tag{15}$$

Furthermore, the optimal control solution is expressed in the following form:

$$u_1^*(t) = min\left\{max\left\{0, \frac{(\lambda_1^* - \lambda_1^*)\beta_1 S^* A^*}{w_1}\right\}, 1\right\},$$

$$u_2^*(t) = min\left\{max\left\{0, \frac{(\lambda_2^* - \lambda_1^*)\beta_2 S^* I^*}{w_1}\right\}, 1\right\},$$

$$u_3^*(t) = min\left\{max\left\{0, \frac{\lambda_3^* A^*}{w_1}\right\}, 1\right\},$$

$$u_4^*(t) = min\left\{max\left\{0, \frac{\lambda_4^* I^*}{w_1}\right\}, 1\right\}.$$

6. Numerical Simulation

6.1. Stability of Balance Point

Assuming $\Lambda = 100$ people/day, $\beta_1 = 0.01$/people/day, $\beta_2 = 0.014$/people/day, $d = 0.05$/day, $a_1 = 0.15$/day, $b_1 = 0.25$/day, $a_2 = 0.2$/day, $b_2 = 0.3$/day, $\delta = 0.4$/day, $p = 0.3$/day, $k = 0.6$, $\mu = 0.07$/day, we obtain $R_0 \approx 0.588$ people < 1, as shown in Figure 2, which verifies that the disease-free equilibrium point is globally asymptotically stable.

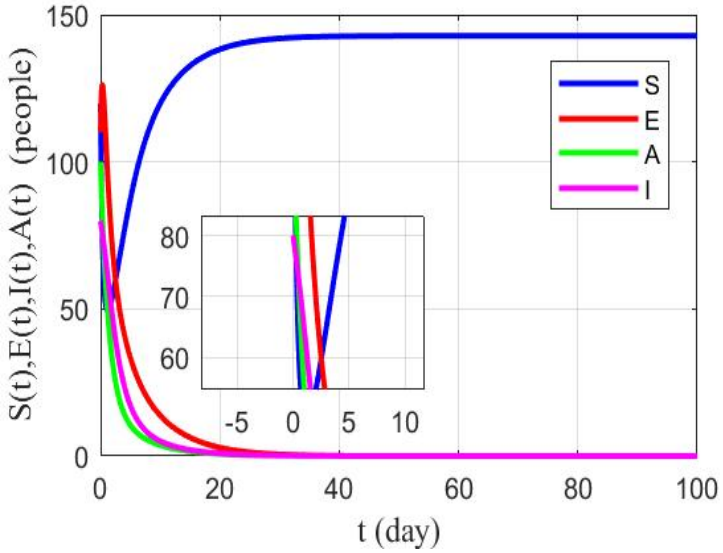

Figure 2. Time series of $S(t), E(t), I(t), A(t)$.

Assuming $\Lambda = 100$ people/day, $\beta_1 = 0.015$/people/day, $\beta_2 = 0.0145$/people/day, $d = 0.05$/day, $a_1 = 0.15$/day, $b_1 = 0.25$/day, $a_2 = 0.2$/day, $b_2 = 0.3$/day, $\delta = 0.4$/day, $p = 0.3$/day, $k = 0.6$, $\mu = 0.066$/day, we obtain $R_0 \approx 1.527$ people > 1, as shown in Figure 3, the endemic equilibrium point is globally asymptotically stable.

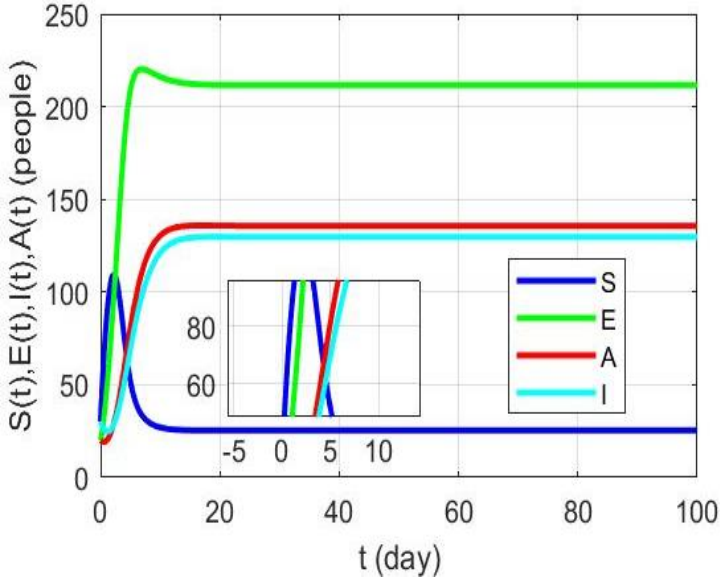

Figure 3. Time series of $S(t), E(t), I(t), A(t)$.

6.2. Sensitivity Analysis

Sensitivity analysis [35] is a method to evaluate the influence of various input parameters on the output. Simply put, it is a technique for determining which input parameters have a significant impact on the results of the model. Through sensitivity analysis, we can find out the most important factors, which can help to optimize model design, improve model precision and provide a more reliable basis for decision making.

Specific methods and applications of sensitivity analysis may vary in different fields and applications, but the core objective is to better understand the behavior and predictive results of models. Sensitivity analysis is a common tool for model verification, risk assessment and decision support in the fields of statistics, engineering, economics, and environmental science. One of the most important methods is the Partial Rank Correlation Coefficient method, which is a very useful statistical sampling technique and has been widely used in the analysis of infectious disease models [36,37].

This method first generates a large number of parameter combinations through Latin Hypercube Sample (LHS), and then calculates the model output corresponding to these parameter combinations (e.g., base generation R_0). Finally, the influence of each parameter on the model output is evaluated by calculating the partial correlation coefficient between each parameter and the model output. This method can reveal the key parameters that affect the output of the model and provide important information for the further study and application of the model.

This article employs Latin hypercube sampling to conduct sensitivity analysis on various parameters affecting the basic reproduction number R_0 of the system (1), thereby determining the degree of influence of each parameter on R_0. Through the analysis, it is found that among the selected parameters, d, a_2 and μ are significantly negatively correlated with R_0, while Λ, β_1 and β_2 are significantly positively correlated with R_0.

As can be seen from Figure 4, among these parameters that have different degrees of influence on the outbreak of COVID-19, the infection rate of asymptomatic infected people to susceptible people is β_1. It has a significant effect on R_0. Therefore, it can be reduced by reducing β_1 to reduce and control the spread of COVID-19; one can also increase the maximum cure coefficients a_1 and a_2 of asymptomatic infected persons and symptomatic infected persons can shorten the cure cycle of COVID-19; or, the constant input Λ of the reduced population can reduce the population mobility, thus reducing the spread speed of COVID-19.

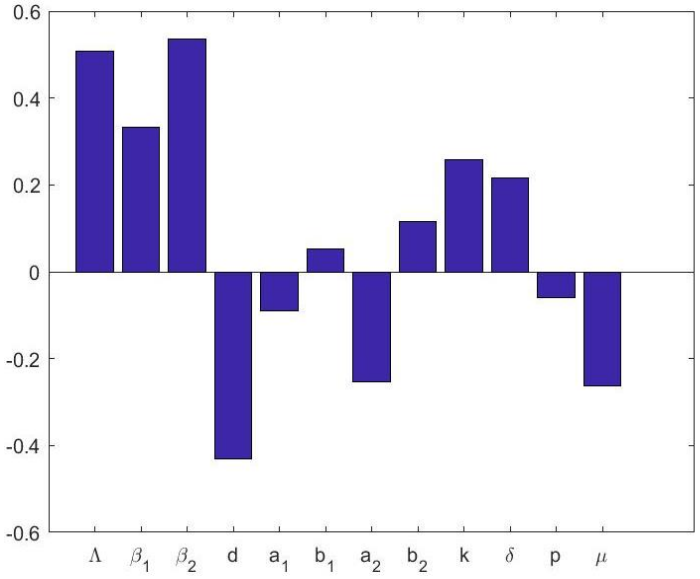

Figure 4. Correlation between R_0 and parameters. The units of each parameter are shown in Table 1.

6.3. Optimal Control

Suppose $\Lambda = 100$ people/day, $\beta_1 = 0.0015$/people/day, $\beta_2 = 0.002$/people/day, $d = 0.06$/day, $a_1 = 0.15$/day, $b_1 = 0.25$/day, $a_2 = 0.02$/day, $b_2 = 0.03$/day, $\delta = 0.0068$/day, $p = 0.94$/day, $k = 0.86$, $\mu = 0.07$/day. Each control strategy has its limitations, so the maximum values of u_1, u_2, u_3 and u_4 are $0.8, 0.9, 0.6$ and 0.7 respectively. As shown in Figure 5, and all control strategies will gradually decrease with the change of time. In Figures 6 and 7, we obtain the comparison of the number of asymptomatic infected people and symptomatic infected people before and after adopting the optimal control strategy. Obviously, due to adopting the control strategy, the number of infected people quickly approaches zero. This shows that the control strategy studied can play a very good role in controlling the spread of COVID-19, which proves the effectiveness of the control strategy. This practice keeps both asymptomatic and symptomatic infected people in COVID-19 at a relatively low level.

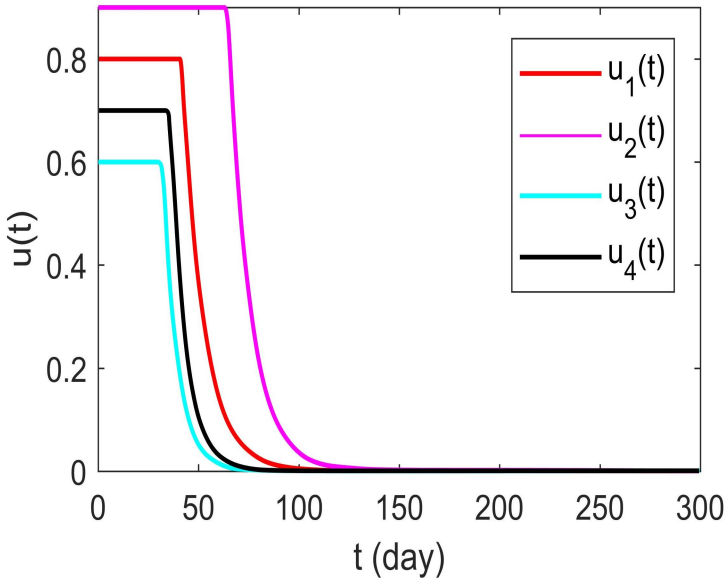

Figure 5. The functional relationship between the control variable $u(t)$and time t.

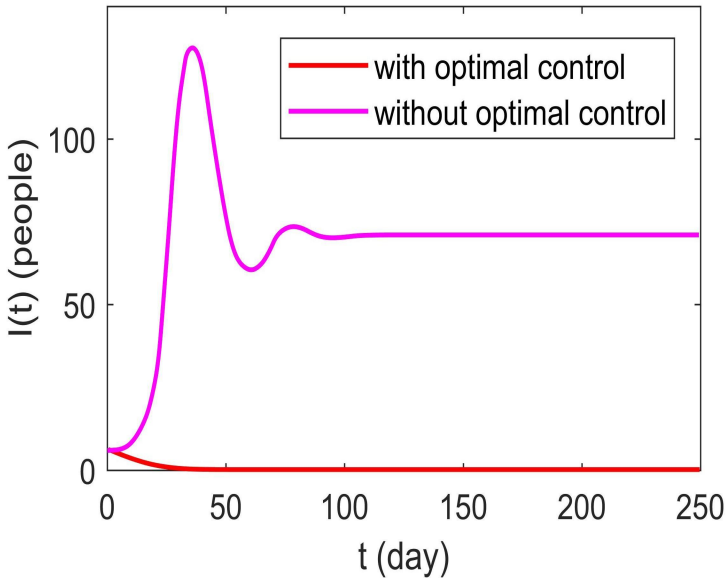

Figure 6. Comparing the number of asymptomatic infectives before and after implementing the control measures.

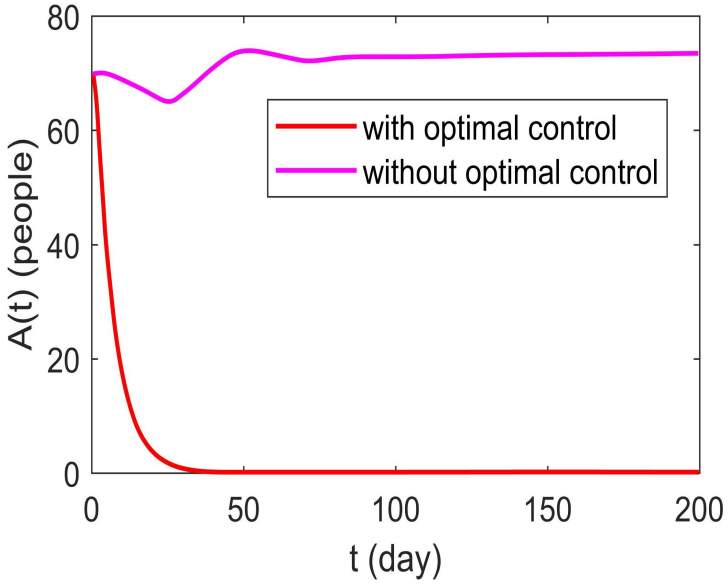

Figure 7. Comparing the number of symptomatic infectives before and after implementing the control measures.

7. Conclusions

This paper proposes an SEAI model of COVID-19 with asymptomatic infection. This paper mainly studies the influence of asymptomatic infected people on the rapid spread of novel coronavirus. Firstly, the basic regeneration number R_0 and equilibrium point of the model are calculated. Then, the local asymptotic stability of disease-free equilibrium and endemic equilibrium is proved by Hurwitz criterion, and the stability of disease-free equilibrium is proved by constructing Laplace function, and the uniform persistence of the system is proved. Then, the Pontryagin maximum principle is applied to solve the optimal control problem. Finally, the theoretical results are verified by numerical simulation, and the sensitivity of parameters is analyzed by PRCC technology, which shows that the influence of asymptomatic infected people on the spread of COVID-19 should not be underestimated.

In the current COVID-19 epidemic, isolation and keeping social distance are the main measures to control the spread of the virus. The state can start with this aim and implement a perfect isolation policy by taking appropriate measures. For asymptomatic infected people, the state can use advanced technology to identify them and then isolate them to prevent the outbreak of diseases. In addition, the state can also reduce the mobility of the population by raising people's awareness of COVID-19, including prevention measures such as washing hands frequently, wearing masks when going out, avoiding gatherings of crowds, reducing the contact between susceptible people and infected people, and reducing the constant input of population, so as to slow down and eventually control the spread of this disease.

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Appendix A

Proof of Equation (6). It follows from the Theorem 3 that we have the following expressions of $\mathcal{B}_1, \mathcal{B}_2, \mathcal{B}_3$ and $\mathcal{B}_4$

$$\begin{aligned}
\mathcal{B}_1 &= a_{11} + a_{12} + d \\
&= Q_1 + Q_2 + Q_3 + M + N + \beta_1 A_1 + \beta_2 I_1 + d, \\
\mathcal{B}_2 &= a_{11}(a_{12} + d) + a_{13} + a_{14} - a_{15} \\
&= (Q_1 + Q_2 + Q_3 + M + N)(\beta_1 A_1 + \beta_2 I_1 + d) + (Q_2 + M)(Q_3 + N) \\
&+ Q_1(Q_2 + Q_3 + M + N) - [\beta_2(k-1) - k\beta_1]S_1\delta \\
&= (Q_1 + Q_2 + Q_3 + M + N)(\beta_1 A_1 + \beta_2 I_1 + d) + (Q_2 + M)(Q_3 + N) \\
&+ Q_1(Q_2 + Q_3 + M + N) + [k\beta_1 + (1-k)\beta_2]S_1\delta, \\
\mathcal{B}_3 &= (a_{12} + d)(a_{13} + a_{14} - a_{15}) + a_{12}a_{17} + a_{16} + a_{18} - k\delta p\beta_2 S_1 \\
&= \{(\beta_1 A_1 + \beta_2 I_1 + d)[(Q_2 + M)(Q_3 + N) + Q_1(Q_2 + Q_3 + M + N)] \\
&+ (\beta_1 A_1 + \beta_2 I_1)[(1-k)\delta(\beta_2 S_1 + N) + k\delta(\beta_1 S_1 + M)] \\
&+ Q_1(Q_2 + M)(Q_3 + N) + [k\beta_1 + (1-k)\beta_2]S_1\delta(\beta_1 A_1 + \beta_2 I_1 + d)\} \\
&dQ_1(Q_2 + a_1)(Q_2 + a_2)(R_0 - 1), \\
\mathcal{B}_4 &= (a_{12} + d)(a_{16} - \beta_2 S_1 k\delta p - a_{18}) \\
&+ a_{12}\{\delta(\beta_2 S_1 + N)[kp + (1-k)(Q_2 + M)] + k\delta(Q_3 + N)(\beta_1 S_1 + M)\} \\
&= (\beta_1 A_1 + \beta_2 I_1 + d)\{Q_1(Q_2 + M)(Q_3 + N) + \delta\beta_2 S_1[k(d + M) + (Q_2 + M)] \\
&+ k\delta\beta_1 S_1(Q_3 + N)\} + (\beta_1 A_1 + \beta_2 I_1)\delta(\beta_2 S_1 + N)[kp + (1-k)(Q_2 + M)] \\
&+ (\beta_1 A_1 + \beta_2 I_1)k\delta(Q_3 + N)(\beta_1 S_1 + M).
\end{aligned}$$

Since $Q_1 = \delta + d, Q_2 = p + d, Q_3 = d + \mu$, $M = \frac{a_1}{(1+b_1 A_1)^2}, N = \frac{a_2}{(1+b_2 I_1)^2}$, the parameters $\delta, p, d, \mu, a_1, a_2, b_1, b_2$ are all positive integers, and A_1, I_1 are all greater than 0, so the expressions Q_1, Q_2, Q_3, M, N are all greater than 0, then we have $\mathcal{B}_1 > 0, \mathcal{B}_2 > 0, \mathcal{B}_4 > 0$. Meanwhile, the expression $\mathcal{B}_3 > 0$ as $R_0 > 1$. The proof is complete. □

Appendix B

Proof of Equation (7). Similar to the proof of Appendix A, we first derive the following expressions

$$\begin{aligned}
\mathcal{B}_1\mathcal{B}_2 - \mathcal{B}_3 &= (a_{11} + a_{12} + d)[a_{11}(a_{12} + d) + a_{13} + a_{14} - a_{15}] \\
&- [(a_{12} + d)(a_{13} + a_{14} - a_{15}) + a_{12}a_{17} + a_{16} + a_{18} - k\delta p\beta_2 S_1] \\
&= (Q_1 + Q_2 + Q_3 + M + N + \beta_1 A_1 + \beta_2 I_1 + d)(Q_1 + Q_2 + Q_3 + M + N) \\
&(\beta_1 A_1 + \beta_2 I_1 + d) + (Q_2 + Q_3 + M + N)(Q_2 + M)(Q_3 + N) \\
&+ (Q_1 + Q_2 + Q_3 + M + N)\{Q_1(Q_2 + Q_3 + M + N)\} \\
&+ [k\beta_1 + \beta_2(1-k)]S_1\delta\} + (1-k)\delta\beta_2 S_1(Q_2 + M) + k\delta\beta_1 S_1(Q_3 + N) \\
&+ k\delta P\beta_2 S_1 + (\beta_1 A_1 + \beta_2 I_1)[(1-k)\delta(\beta_2 S_1 + N) + k\delta(\beta_2 S_1 + M)], \\
\mathcal{B}_1\mathcal{B}_2\mathcal{B}_3 - \mathcal{B}_3^2 - \mathcal{B}_1^2\mathcal{B}_4 &= (a_{11} + a_{12} + d)[a_{11}(a_{12} + d) + (a_{13} + a_{14} - a_{15})][(a_{12} + d)(a_{13} + a_{14} - a_{15}) \\
&+ a_{12}a_{17} + a_{16} - a_{18} - k\delta P(\beta_2 S_1] - [(a_{12} + d)(a_{13} + a_{14} - a_{15}) + a_{12}a_{17} \\
&+ a_{16} + a_{18} - k\delta p\beta_2 S_1]^2 - (a_{11} + a_{12} + d)^2\{(a_{12} + d)(a_{16} - \beta_2 S_1 k\delta p - a_{18}) \\
&+ a_{12}\delta(\beta_2 S_1 + N)[kp + (1-k)(Q_2 + M)] + a_{12}k\delta(Q_3 + N)(\beta_1 S_1 + M)\}
\end{aligned}$$

Noting that all the parameters and variables are non-negative, then $Q_1, Q_2, Q_3, M, N > 0$, so we can easily deduce $\mathcal{B}_1\mathcal{B}_2 - \mathcal{B}_3 > 0$.

Furthermore,

$$\begin{aligned}\mathcal{B}_1\mathcal{B}_2\mathcal{B}_3 - \mathcal{B}_3^2 - \mathcal{B}_1^2\mathcal{B}_4 > {} & (Q_1+Q_2+Q_3+M+N)(\beta_1A_1+\beta_2I_1+d)[(Q_2+M)(Q_3+N)\\ & + Q_1(Q_2+Q_3+M+N)+k\beta_1S_1\delta(1-k)\beta_2S_1\delta]^2+(Q_1+Q_2+Q_3\\ & + M+N)(\beta_1A_1+\beta_2I_1)[(1-k)\delta(\beta_2S_1+N)+k\delta(\beta_1S_1+M)][(Q_2+M)\\ & (Q_3+N)+Q_1(Q_2+Q_3+M+N+k\beta_1S_1\delta+(1-k)\beta_2S_1\delta)]\\ & + (Q_1+Q_2+Q_3+M+N)(\beta_1A_1+\beta_2I_1+d)^3[(Q_2+M)(Q_3+N)\\ & + Q_1(Q_2+Q_3+M+N)+k\beta_1S_1\delta+(1-k)\beta_2S_1\beta_1\delta+(Q_1+Q_2+Q_3\\ & + M+N)(\beta_1A_1+\beta_2I_1)[(1-k)\delta(\beta_2S_1+N)+k\delta(\beta_1S_1+M)](\beta_1A_1\\ & + \beta_2I_1+d)^2+(k\delta p\beta_2S_1)^2>0.\end{aligned}$$

Therefore, we prove that $\mathcal{B}_3(\mathcal{B}_1\mathcal{B}_2-\mathcal{B}_3) > \mathcal{B}_1^2\mathcal{B}_4$. The proof is complete. □

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