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Optimal quarantine and isolation strategies in epidemics control*

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Abstract. In the absence of valid medicines or vaccine, quarantine and isolation strategies are the most important and effective measures against the SARS outbreaks. This paper discusses the application of the optimal and sub-optimal control for SARS outbreak control via the Pontryagin's Maximum Principle and genetic algorithm, respectively. To this end, a pair of control variables representing the quarantine and isolation strategies is incorporated into our improved SARS transmission model. The simulation results demonstrate that the maximum implementation of quarantining and isolation strategies in the early stage of the epidemic are of very critical impacts in the both cases of optimal and sub-optimal control. This gives a theoretical interpretation to the practical experiences that the early quarantine and isolation strategies are critically important to control the outbreaks of epidemics. Furthermore, our results also show that the proposed sub-optimal control can lead to performances close to the optimal control, but with much simpler strategies for long periods of time in practical use.

Keywords: optimal control, epidemics control, quarantine and isolation, SARS model, genetic algorithm

1 Introduction

In the human history from ancient times to the present, quarantine and isolation strategies have been widely adopted against the natural disease, especially in the early stage of the epidemics outbreak without valid medicines or vaccine, such as the Black Death in the mid 14th century, influenza outbreak of 1918 and SARS (Severe acute respiratory syndrome) in late 2002 and 2003. The emergence of SARS challenged the global public health community to confront a novel epidemic that spread rapidly from its origins in southern China until it had reached more than 25 other countries within a matter of months. In addition to the number of patients infected with the SARS virus, totaling more than 8000 cases and 774 known deaths[16], the disease had profound economic and political repercussions in many of the affected regions. Since there are no valid medicines or vaccine for SARS, measures to control the spread of SARS had to take two major forms: isolation of symptomatic individuals and quarantine and close observation of asymptomatic individuals[27]. It had been shown that quarantine and isolation of the diseased individuals was a critically important strategy that can control SARS outbreaks because of the effective reduction in the contact rate between susceptible and diseased individuals[4, 11, 27]. SARS represents the most recent challenge to the well being of our species posed by microbes and viruses. In order to better prepare ourselves against future epidemics, we must learn from both our achievements and mistakes in dealing with SARS.

Mathematical models have recently been used to examine the transmission dynamics and model the control of SARS in the literature[4, 24]. But most of them are mainly in the pure curve fitting and simulative levels[22, 24]. Dye and Gay[9] and Lipsitch[17] proposed a typical SEIR model consists of four subpopulations, namely susceptible, exposed (latent), infectious, and recovered. Wnag and Ruan[26] proposed a mathematical

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model consists of six subpopulations, namely susceptible, exposed, quarantined, suspect, probable and removed, to simulate the SARS outbreak in Beijing. Shi[23] and Lloyd-Smith[18] presented stochastic dynamic models, while the discrete case had been studied by Zhou and Ma[28]. In addition, small-world networks had been introduced to study the propagation of the SARS by Naoki Masuda[19] and Small[24]. It has been obtained that if all infectious individuals are isolated as rapidly as they are identified the severity of the outbreak would be minimal[19]. Furthermore, Chowell[4] attempted to obtain a threshold for the basic reproductive number R_0 for assessing the strategies of quarantine and isolation, and discussed control of SARS by looking at the role of disease transmission parameters in the reduction of R_0 and the prevalence of the disease. Uncertainty and sensitivity analysis of R_0 to assess the role that model parameters play in outbreak control had been studied and the results showed that the transmission rate and isolation effectiveness have the largest fractional effect on R_0[3]. Moreover, Gumel and Ruan[11] examined mathematically the impact of isolation and quarantine on the control of SARS during the outbreaks in Toronto, Hong Kong, Singapore and Beijing. The results showed the importance of quarantine and isolation strategies for SARS outbreak control.

However, those models did not consider the dynamical control strategies since their discussions are based on prevalence of disease at equilibrium. In Swan's work[25], the optimal control theory is applied to obtain maximal benefits in terms of social benefits from the parsimonious use of insufficient public funds in the control of epidemics. Moreover, the Pontryagin's Maximum Principle[21] and the time dependent control strategies are also applied for the studies of HIV models[15], mosquito-borne diseases[6], insect transmitted diseases[7], dengue models[1], tuberculosis models[14] and others[12].

In this paper, we consider the optimal and sub-optimal control strategies associated with quarantining asymptomatic individuals and isolating symptomatic individuals for our improved SARS transmission model based on Chowell[4] and Gumel[11]. The model monitors the dynamics of eight sub-populations (classes), namely susceptible with high infection risk, susceptible with reduction of infection risk, asymptomatic, quarantined, symptomatic, isolated, recovered and disease-induced dead individuals. We introduce into the model two control variables representing the rate of quarantining of the asymptomatic individuals who have been exposed to the virus, but have not yet developed clinical symptoms and the rate of isolating of symptomatic individuals, respectively.

The rest of the paper is organized as follows. Section 2 describes our improved SARS transmission model with control variables. The analysis of optimization problems and the sub-optimal solution are presented in section 3 and section 4, respectively. In section 5, we present the numerical method and the simulation results. Finally, the conclusions are summarized in Section 6.

2 Improved dynamic transmission model for SARS

In this section, we present our improved dynamic SARS transmission model based on Chowell[4] and Gumel[11]. The host population consists of eight sub populations: namely susceptible with high infection risk $(S_1(t))$, susceptible with reduction of infection risk $(S_2(t))$, asymptomatic $(E(t))$, quarantined $(Q(t))$, symptomatic $(I(t))$, isolated $(J(t))$, recovered $(R(t))$ and disease-induced dead individuals $(D(t))$. The detailed descriptions see Tab. 1 and Fig. 1. Our SARS transmission model with quarantine and isolation controls is given by the following nonlinear system of differential equations:

$$\dot{S} = -\beta S_1 \frac{I + qE + \varepsilon Q + lJ}{N} \tag{1}$$

$$\dot{S} = -\beta p S_2 \frac{I + qE + \varepsilon Q + lJ}{N} \tag{2}$$

$$\dot{E} = -\beta(S_1 + pS_2)\frac{I + qE + \varepsilon Q + lJ}{N} - (u_1(t) + k_1)E \tag{3}$$

$$\dot{Q} = u_1(t)E - \sigma Q \tag{4}$$

$$\dot{I} = -kE - (u_2(t) + \gamma_1 + \delta)I \tag{5}$$

$$\dot{J} = u_2(t)I + \sigma Q - (\gamma_2 + \delta)J \tag{6}$$

$$\dot{R} = \gamma_1 I + \gamma_2 J \tag{7}$$

$$\dot{D} = \delta I + \delta J \tag{8}$$

where $S_1(0), S_2(0), E(0), Q(0), I(0), J(0), R(0)$ are given and the definitions of above model parameters are listed in Tab. 2.

Table 1. Epidemiological classes definitions

Class	Definition
S_1	Susceptible individuals with high infection risk ($S_1 = \rho N$)
S_2	Susceptible individuals with reduction of infection risk ($S_1 = (1-\rho)N$)
E	Asymptomatic individuals who have been exposed to the virus but have not yet developed clinical symptoms of SARS
Q	Quarantined individuals
I	Symptomatic individuals (infected, infectious and undiagnosed)
J	Isolated individuals (for special diagnosis and treatment)
R	Recovered individuals
D	SARS disease-induced death
N	Total population $N = S_1 + S_2 + E + Q + I + J + R + D$

Table 2. Parameter definitions

Parameter	Definition
β	Transmission rate per day
q	Relative measure of infectiousness for the asymptomatic class E
ε	Relative measure of reduced risk among quarantined SARS cases
l	Relative measure of reduced risk among isolated SARS cases
p	Reduction in risk of SARS infection for class S_2
k	Rate of normal progression to the infectious state per day
σ	Rate of progression to the isolated class for treatment per day
γ_1	Rate at which individuals in the infectious class recover per day
γ_2	Rate at which diagnosed individuals recover per day
δ	SARS-induced mortality per day
ρ	Initial proportion of the population at higher risk of SARS infection

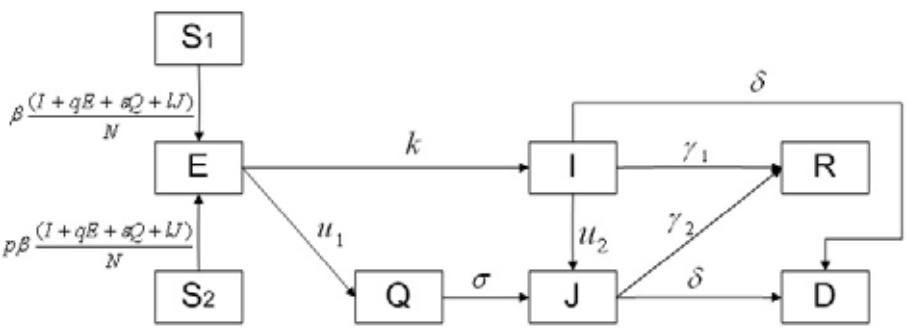

Fig. 1. A schematic representation of the flow of individuals between the different classes

The susceptible is divided into two distinct classes: S_1, the most susceptible, and S_2, less so [4]. We assume that a susceptible individual may be infected through contacts with an asymptomatic individual, a quarantined individual, an infected individual or an isolated individual.

The control variables, $u_1(t)$ and $u_2(t)$, are bounded, Lebesgue integrable functions[14]. The control $u_1(t)$ represents the rate of quarantining of people who have been in contact with an infected individual by a quarantine program and educational campaigns for close observation. The control $u_2(t)$ represents the rate of isolating of symptomatic individuals by an isolation program for special medical treatment. Furthermore, from epidemiological modeling view, the transfer rate u_1E corresponds to an exponential waiting time $e^{u_1 t}$ as the fraction that is still in the asymptomatic class t units after entering this class and to $1/u_1$ as the mean waiting time[13]. And the interpretation of $u_2 I$ is similar to $u_1 E$.

3 The optimal control problems

The problem is to minimize the cost function

$$J(u_1, u_2) = \int_0^{t_f} [B_1 E(t) + B_2 Q(t) + B_3 I(t) + B_4 J(t) + \frac{C_1}{2} u_1^2(t) + \frac{C_2}{2} u_2^2(t)] dt \tag{9}$$

subject to the differential equations (1)-(6), where t_f is the final time. This performance specification involves the numbers of individuals of symptomatic, asymptomatic, quarantined, or isolated, respectively, as well as the cost for applying quarantine control (u_1) and isolations control (u_2). The total cost includes not only the consumption for every individual but also the cost of organization, management, and cooperation etc. Hence, the cost function should be nonlinear. In this paper, a quadratic function is implemented for measuring the control cost by referenced to many literatures in epidemics control[1, 6, 7, 14, 15]. The coefficients, $B_{1,3}$, B_4, C_1 and C_2, are balancing cost factors due to scales and importance of the six parts of the objective function. We seek to find an optimal control pair, u_1^* and u_2^*, such that

$$J(u_1^*, u_2^*) = \min_{\Omega} J(u_1, u_2) \tag{10}$$

Here $\Omega = \{(u_1, u_2) \in L^1(0, t_f) | a_i \le u_i \le b_i, i = 1, 2\}$ and $a_i, b_i, i = 1, 2$, are fixed positive constants.

Pontryagin's Maximum Principle[21] provides the necessary conditions for an optimal control problem. This principle converts (1) - (6), (9) and (10) into a problem of minimizing a Hamiltonian, H, pointwisely with respect to u_1 and u_2:

$$H = B_1 E(t) + B_2 Q(t) + B_3 I(t) + B_4 J(t) + \frac{C_1}{2} u_1^2(t) + \frac{C_2}{2} u_2^2(t) + \sum_{i=1}^{6} \lambda_i f_i \tag{11}$$

where f_i is the right hand side of the differential equation of i-th state variable. By applying Pontryagin's Maximum Principle[21] and the existence result for the optimal control pairs from [10], we obtain the following theorem.

Theorem 1. *There exists an optimal control pair u_1^*, u_2^* and corresponding solution, S_1^*, S_2^*, E^*, Q^*, I^* and J^*, that minimizes $J(u_1, u_2)$ over Ω. Furthermore, there exists adjoint functions, $\lambda_1(t)$, $\lambda_2(t)$, $\lambda_3(t)$, $\lambda_4(t)$, $\lambda_5(t)$, $\lambda_6(t)$, such that*

$$\begin{aligned}
\dot{\lambda_1} &= \lambda_1 \frac{\beta(I^* + qE^* + \varepsilon Q^* + lJ^*)}{N} - \lambda_3 \frac{\beta(I^* + qE^* + \varepsilon Q^* + lJ^*)}{N} \\
\dot{\lambda_2} &= \lambda_2 \frac{\beta(I^* + qE^* + \varepsilon Q^* + lJ^*)}{N} - \lambda_3 \frac{\beta(I^* + qE^* + \varepsilon Q^* + lJ^*)}{N} \\
\dot{\lambda_3} &= -B_1 + \lambda_1 \frac{\beta q S_1^*}{N} + \lambda_2 \frac{\beta q p S_2^*}{N} - \lambda_3 \frac{\beta q (S_1^* + pS_2^*)}{N} + \lambda_3 [k + u_1^*(t)] - \lambda_4 u_1^*(t) - \lambda_5 k \\
\dot{\lambda_4} &= -B_2 + \lambda_1 \frac{\beta \varepsilon S_1^*}{N} + \lambda_2 \frac{\beta \varepsilon p S_2^*}{N} - \lambda_3 \frac{\beta \varepsilon (S_1^* + pS_2^*)}{N} + \lambda_4 \sigma - \lambda_6 \sigma \\
\dot{\lambda_5} &= -B_3 + \lambda_1 \frac{\beta S_1^*}{N} + \lambda_2 \frac{\beta p S_2^*}{N} - \lambda_3 \frac{\beta (S_1^* + pS_2^*)}{N} + \lambda_5 [u_2^*(t) + \gamma_1 + \delta] - \lambda_6 u_2^*(t) \\
\dot{\lambda_6} &= -B_4 + \lambda_1 \frac{\beta l S_1^*}{N} + \lambda_2 \frac{\beta l p S_2^*}{N} - \lambda_3 \frac{\beta l (S_1^* + pS_2^*)}{N} + \lambda_6 (\gamma_2 + \delta)
\end{aligned} \tag{12}$$

with transversality conditions

$$\lambda_i(t_f) = 0, i = 1, \cdots, 6 \tag{13}$$

The optimal control is given by

$$u_1^*(t) = \min\{\max\{a_1, \frac{1}{C_1}(\lambda_3 - \lambda_4)E^*\}, b_1\} \tag{14}$$

and

$$u_2^*(t) = \min\{\max\{a_2, \frac{1}{C_2}(\lambda_5 - \lambda_5)E^*\}, b_2\} \tag{15}$$

Proof: Due to the convexity of integrand of J with respect to (u_1, u_2), a priori boundedness of the state solutions, and the Lipschitz property of the state system with respect to the state variables. The existence of an optimal control pair has been given by [21] (see Corollary 4.1). The adjoint equation (12) can be obtained by using Pontryagin's Maximum Principle such that

$$\frac{d\lambda_1}{dt} = -\frac{\partial H}{\partial S_1}, \lambda_1(t_f) = 0,$$
$$\cdots$$
$$\frac{d\lambda_6}{dt} = -\frac{\partial H}{\partial J}, \lambda_6(t_f) = 0,$$

The optimal control u_1^* and u_2^* can be solve from the optimality conditions,

$$\frac{\partial H}{\partial u_1} = 0, \frac{\partial H}{\partial u_2} = 0$$

That is

$$\frac{\partial H}{\partial u_1} = C_1 u_1 - \lambda_3 E + \lambda_4 E = 0; \quad \frac{\partial H}{\partial u_2} = C_2 u_2 - \lambda_5 E + \lambda_6 E = 0$$

By the bounds in Ω of the controls, it is easy to obtain u_1^* and u_2^* in the form of (14) and (15), respectively.

Remark 1: Due to the a priori boundedness of the state and adjoint functions and the resulting Lipschitz structure of the ODEs, we obtain the uniqueness of the optimal control for small[14]. The uniqueness of the optimal control pair follows from the uniqueness of the optimality system, which consists of (1)-(6) and (9), (10) with characterizations (14) and (15). There is a restriction on the length of the time interval in order to guarantee the uniqueness of the optimality system. This smallness restriction on the length on the time interval is due to the opposite time orientations of (1)-(6), (9), and (10); the state problem has initial values and the adjoint problem has final values. This restriction is very common in control problems (see [15] and [14]).

Remark 2: The problem described above is a Two Point Boundary Value Problem (TPBVP), with specified initial condition for state equation (1)-(6) and terminal boundary conditions (13) for adjoint equation (12). It can be numerically solved by iteration method presented in section 5.

4 Sub-optimal solution

In this section, the sub-optimal solution is obtained by genetic algorithm follows the idea of [1]. Let the class of admissible controls be restricted to the collection of functions of type

$$u_k^*(t) = \begin{cases} u_k^i & if\ t \in I_i \\ 0 & otherwise \end{cases}, k = 1, 2 \tag{16}$$

where $u_k^i \in \Omega$ are constants and I_i are closed intervals $[t_i, t_i + \Delta_i]$ such that $I_i \cap J_i = \emptyset$ if $i \neq j$. Therefore, the restricted class admissible controls consist of pulses of height $u_k^i (k = 1, 2)$ and width Δ_i, starting at time t_i.

In order to simplify the actual policy implementation, we assume that the two controls are to be of pulsed form. Let $u_k(t) = u_k^N(t)(k = 1, 2)$ be admissible controls with N pulses, characterized by $(t_1, \Delta_1, u_1^1, u_2^1, t_2, \Delta_2, u_1^2, u_2^2, \cdots, t_N, \Delta_N, u_1^N, u_2^N)$. Therefore, the sub-optimal control problem is to minimize

$$J'(t_1, \Delta_1, u_1^1, u_2^1, t_2, \Delta_2, u_1^2, u_2^2, \cdots, t_N, \Delta_N, u_1^N, u_2^N) := J[u_1^N(\cdot), u_2^N(\cdot)]$$

where $J[\cdot, \cdot]$ is the same as defined in (2).

Let $\Pi = t_1, \Delta_1, u_1^1, u_2^1, t_2, \Delta_2, u_1^2, u_2^2, \cdots, t_N, \Delta_N, u_1^N, u_2^N) := J[u_1^N(\cdot), u_2^N(\cdot) \in R^{4N}$ for the case of N pulses, the sub-optimal control problem is simply

$$\min_{\pi = R^{4N}} J'(\Pi)$$

In this work, the search for a global minimum of $J'(\pi)$ is implemented by an extended method based on Genetic Algorithm[5]. This extension admits the constraints $t_i + \Delta_i = t_{i+1}$, $t_N + \Delta_N = t$, $t_i \geq 0$, $\Delta_i \geq 0$ and $a_k \leq u_k^i \leq b_k$, $k = 1, 2$.

5 Numerical simulation

In the simulation, we study the impact of optimal quarantine and isolation control on SARS during the outbreaks in Hongkong. The numerical solution for this TPBVP problem by the multiple shooting method[1, 2, 20].

We choose the upper bound of u_1 equals 0.50 according to the reasonable case in China that it took at least average 2 days to quarantine the asymptomatic individuals who have been exposed to the virus, but have not yet developed clinical symptoms. And the choice of upper bound of u_2 is similar to u_1. The sub-optimal control was computed for the case $N = 3$ and specified time intervals: $\Delta_1 = 60$, $\Delta_2 = 240$ and $\Delta_2 = 60$. Parameters such as population size for the genetic algorithm, generation gap and others were adjusted ad hoc[1]. The data and parameters we used, in Table 3, are mainly from the published data [4, 11, 26]. In order to evaluate the effect of the uncertainty on the model parameters, simulations were repeated with values of $\beta, \varepsilon, l, p, k, \sigma, \gamma_2, \delta$ and ρ altered by random values in the range 10% (normal distribution), while the inputs and were kept identical to the computed optimal values.

Considering the four weight factors associated with E, Q, I and Jwe choose $B_1 = B_2 = B_3 = B_4 = 1$, $C_1 = 300$ and $C_2 = 600$ to illustrate the optimal strategies.

Remark 3: We assume that the weight factor C_2 associated with control u_2 is much larger than C_1 which associated with control u_1. This assumption is based on the following facts: The cost associated with u_1 mainly includes the cost of monitoring and quarantining programs, while the cost associated with u_2 includes the cost of monitoring and isolating programs, and the hospital treatment resource. The ideal weights are very hard to obtain in practice. It needs a lot of work on data mining, analyzing, and fitting. Hence, the acquirement of appropriate practical weights is a difficult problem and it still remains for further investigations. It should be pointed that the weights in the simulations here are of only theoretical sense to illustrate the control strategies proposed in this paper.

Fig. 2 shows the time dependent optimal and sub-optimal quarantine and isolation control laws. In order to minimize the total infected individuals, $E + Q + I + J$, the optimal control u_1 is at its upper bound during the first two months of the year and then u_1 is steadily decreasing to a lower level value (0.13), while the optimal control u_2 stays at its upper bound for a short time, about 55 days and then steadily decreases to the lower bound over the rest simulated time. The sub-optimal control laws u_1 and u_2 both stay at the upper bound during the first time interval.

In fact, at the beginning of simulated time, both the optimal control and sub-optimal control are staying at their upper bound in order to quarantining and isolating as many as asymptomatic individuals (I) and symptomatic individuals (E) to prevent the increasing of the number of the infected individuals. For both u_1 and u_2, the steadily decreasing to lower values in the optimal control case and staying at proper values in the sub-optimal case are determined by the balance between the cost of the infected individuals and the cost of the controls.

Table 3. Values of the model parameters

Parameters	Values	Computational	Parameters Values
β	0.75	$S_1(0)$	3million
q	0.1	$S_2(0)$	4.5million
ε	0.2	$E(0)$	500
l	0.1	$Q(0)$	110
p	0.1	$I(0)$	660
k	0.125	$J(0)$	350
σ	0.125	Final timet_f	1 year
γ_1	0.125	Time step duration dt	1 day
γ_2	0.2	Upper bounder for u_1	0.50
δ	0.006	Lower bound for u_1	0.05
ρ	0.4	Upper bounder for u_2	0.50
		Lower bound for u_2	0.05

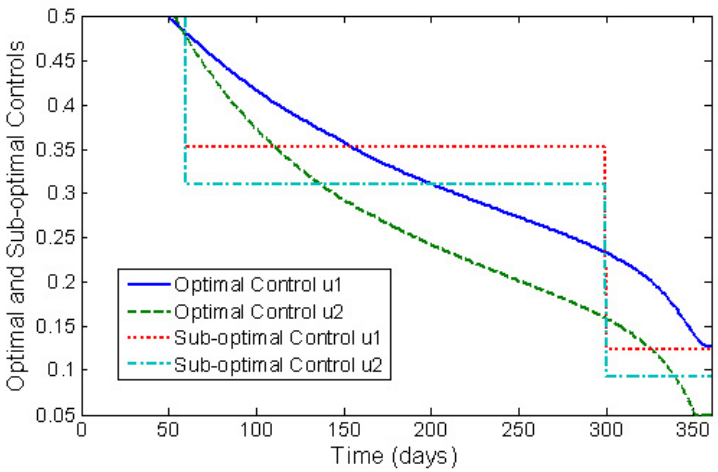

Fig. 2. The optimal and sub-optimal control laws

Comparison of the optimal control, the sub-optimal control and the constant controls ($u_1 \equiv 0.2$ and $u_2 \equiv 0.2$) throughout the simulated time are also implemented (Fig. 3 (a)). It is easy to see that the optimal control and sub-optimal control are much more effective for reducing the number of infected individuals and decreasing the time-span of the epidemic. As normally expected, in the early phase of the epidemic breakouts, keeping the quarantining and isolation controls at their upper bounds will directly leads to the decreasing of the number of the infected people. Moreover, Fig. 3 (b) shows that if we take the lower bound values for each control throughout the simulated time, the number of infected individuals would reach about 5.9731105 (nearly 7.96% of the total population). This illustrates that the quarantine and isolation strategies is critically important to control the outbreak of SARS. In addition, in order to illustrate the overall of picture of the epidemic, the number of susceptible individuals under the optimal control, the sub-optimal control, the constant control and the lower bound control are shown Fig. 4.

The costs achieved by the optimal control and sub-optimal control are much less than the constant control, as seen in Fig. 5. It is interesting to note that the cost achieved by the sub-optimal control is very close to that by the optimal control, despite the fact that the sub-optimal control is much easier to be implemented than the optimal control.

6 Conclusions

As we known, highly contagious and viral diseases are significant threats to the future of human being. SARS represents the most recent challenge to the well being of our species posed by microbes and viruses. In order to better prepare ourselves against future catastrophic epidemics, quarantine and isolation strategies,

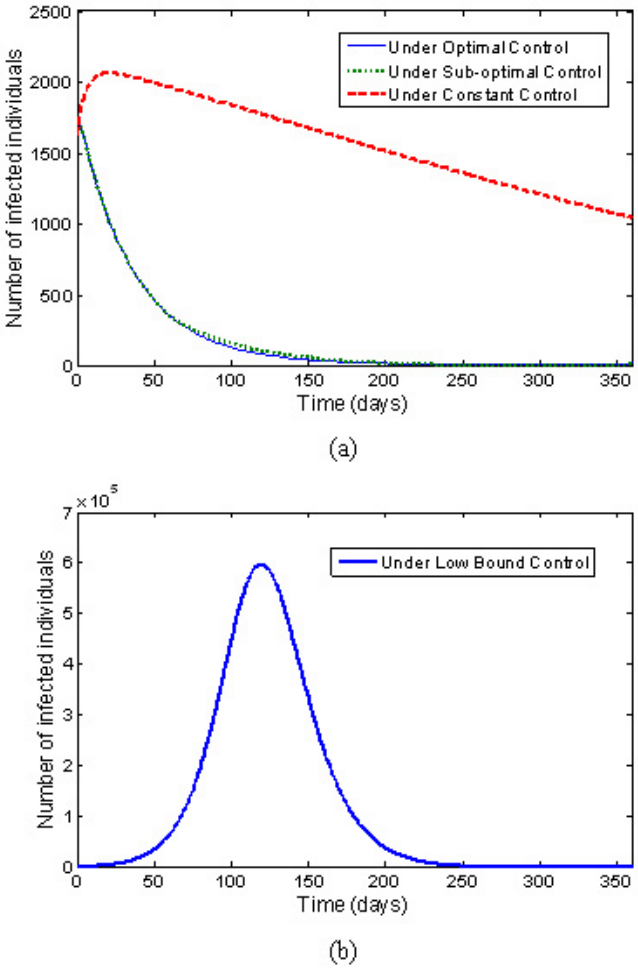

Fig. 3. The optimal and sub-optimal control laws

as the most effective measures in SARS outbreaks control, have been studied in this paper. A pair of control variables representing quarantine and isolation strategies has been proposed. The optimal and sub-optimal quarantine and isolation control for our improved SARS transmission model has been studied. The numerical results show the effectiveness of both the optimal and sub-optimal strategies for SARS epidemics control. It should be pointed out that, as was mentioned in [12], the ideal time-varying optimal strategy might not be applied in practice easily. Nevertheless, it does provide a reference basis on which to design the practical quasi-optimal control strategies or policies and assess their effectiveness. However, the proposed sub-optimal control in this paper can provides much simpler strategies, which, as verified by numerical simulations, can also lead to a performance very similar to that achieved by the optimal control. In practical implementations, it is considerably easier to use the sub-optimal control.

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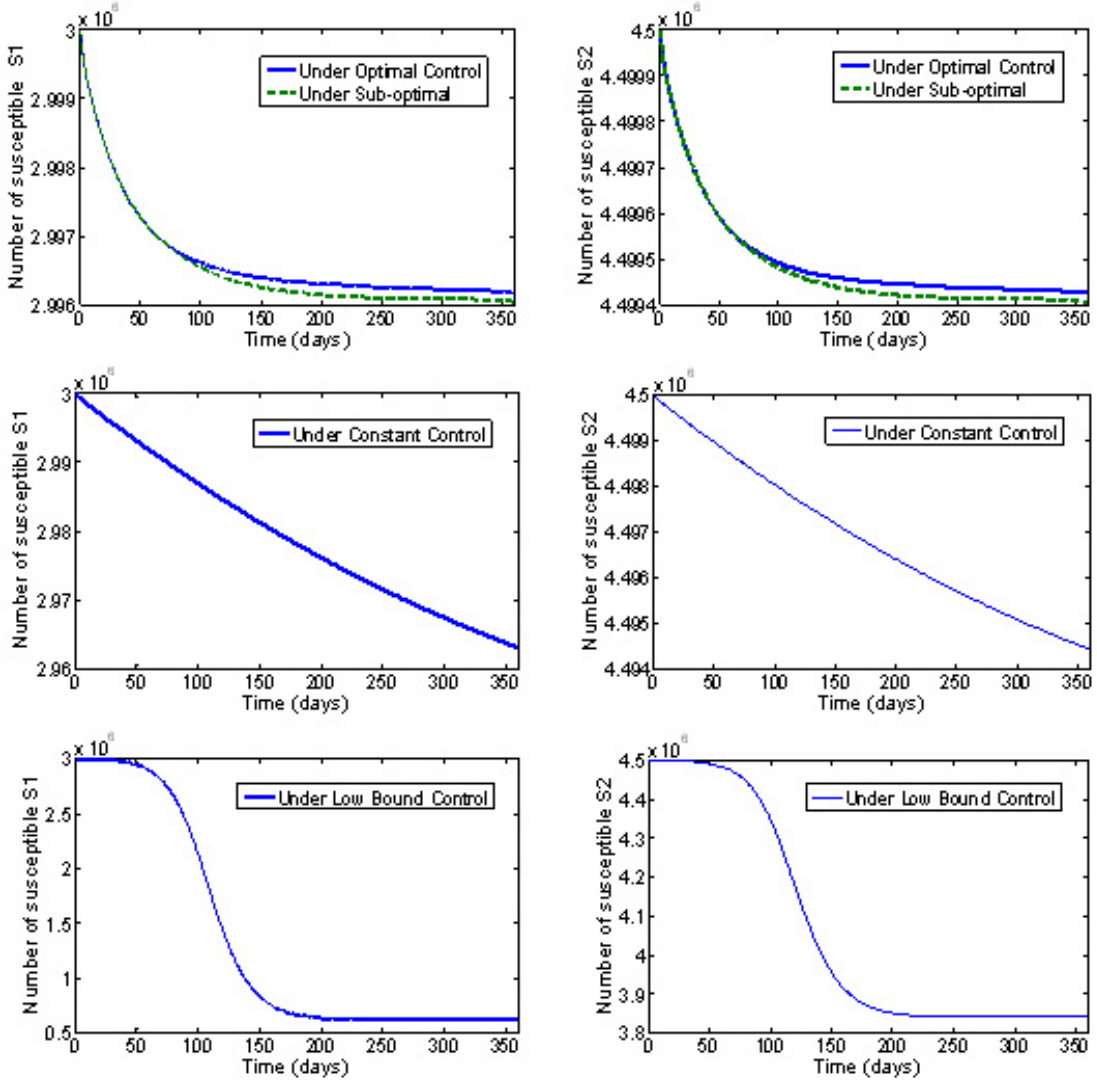

Fig. 4. Number of susceptible individuals under the optimal control, the sub-optimal, the constant control and the lower bound control

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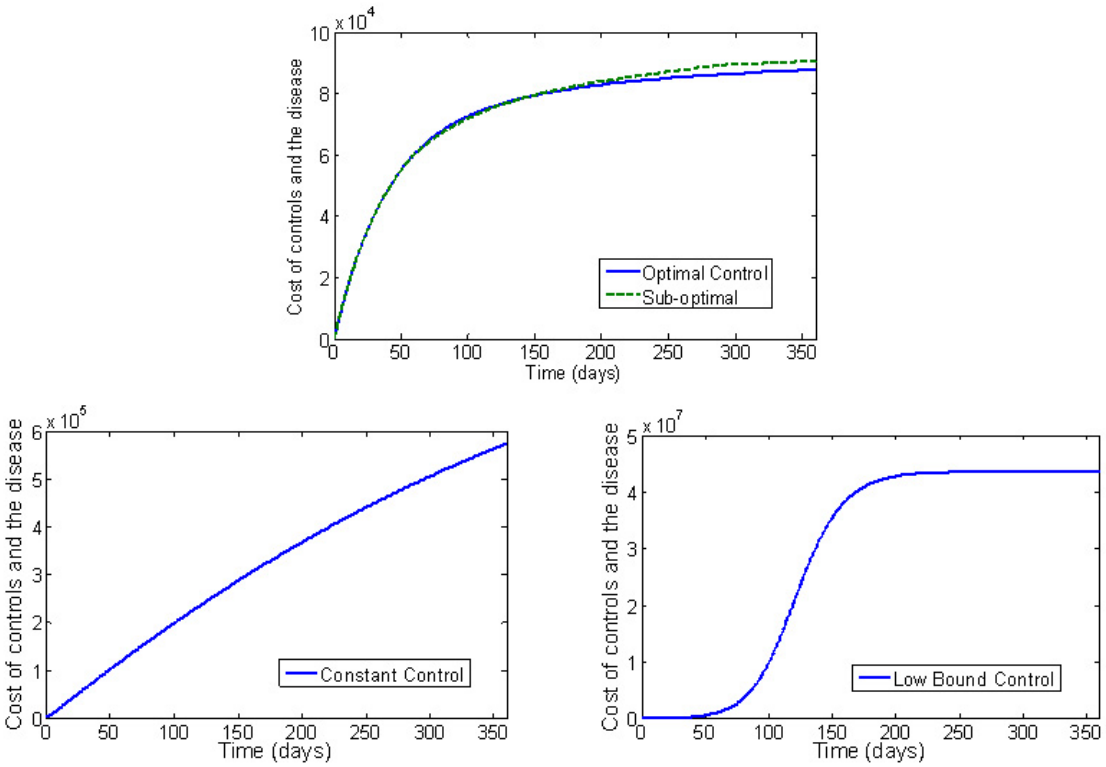

Fig. 5. Cost of the controls and the disease under the optimal control, the sub-optimal control, the constant control and the lower bound control

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