The optimal vaccination strategy to control COVID-19

Department of Systems Informatics, Graduate School of System Informatics, Kobe University
Huaiyu Teng

Toshikazu Kuniya *

Abstract

Models of infectious disease dynamics suggest that treatment, vaccination, and isolation are required for the control of infectious diseases. Considering that vaccination is one of the most effective methods to control infectious diseases, it is often not possible to rapidly vaccinate all susceptible populations in the early stages of the spread of infectious diseases due to the limitation of the number of vaccines, insufficient medical personnel, or the slow progress of vaccination efforts. Our simulation analysis by building an SVIWRD model found that the degree of negative impact of infectious diseases shown when young and old people were divided into two populations and vaccinated at different rates was different.Therefore, for the current problem of continued spread of COVID-19, we consider the infectious disease dynamics model to achieve the goal of making the risk of COVID-19 infection lower by controlling the proportion of vaccination of elderly and young people. In this paper, we divided young and old people into two groups, established an SVIWRD model, performed single-objective optimization using Pontryagin's maximum principle, and used the Runge-Kutta method for numerical calculation and simulation, so as to arrive at a certain vaccination ratio that plays the effect of reduced negative impact of COVID-19.

1 Introduction

The COVID-19 pandemic has severely impacted populations and economies worldwide, with global cases reaching 704,753,890, deaths 7,010,681, and recoveries 675,619,811 as of April 13, 2024 [24]. Despite prevention efforts, new infection waves persist, highlighting uncertainty about the pandemic's resolution [19].

Researchers are working to develop vaccines, prevention strategies, and treatments against the coronavirus. The emergence of virus variants necessitates more effective vaccines to curb infections. Mathematical models play a critical role in predicting infection trends and designing optimal control strategies [10, 25, 26, 1, 23, 21]. These models underscore the importance of combining treatment, vaccination, and isolation measures, with vaccination being the most effective. However, limitations like vaccine shortages and logistical challenges often impede rapid vaccination.

Vaccines are not fully effective, and infections may still occur post-vaccination. Paper [18] explored optimal vaccination coverage to minimize costs and infection losses. Building on this, our study employs the SVIWRD (Susceptible-Vaccinated-Infected-Waned-Removed-Death) model to analyze the impact of vaccination rates on young and elderly populations. Using Pontryagin's maximum principle [9] and numerical methods like the Runge-Kutta method [3], we identified an optimal vaccination ratio to reduce COVID-19 transmission [7, 16, 8, 4, 11, 17]. This paper is structured as follows:

- **Section 2** introduces the SVIWRD model and age-based population groups.
- **Section 3** derives the disease-free equilibrium and the basic reproduction number R_0 under constant control.

*E-mail:toukaiu1215@gmail.com

- **Section 4** investigates the sensitivity of R_0 to parameters.
- **Section 5** applies Pontryagin's maximum principle to determine the optimal control using adjoint functions.
- **Section 6** provides numerical simulations for vaccine allocation strategies.
- **Section 7** concludes with discussions and implications.

2 SVIWRD model

The SVIWRD model, a variation of common epidemic models, assumes constant mortality and birth rates, maintaining a steady population during the epidemic. Given the higher mortality risk for the elderly (60+ years) and the greater infection spread risk among the non-elderly (below 60 years), the population is divided into these two groups. This study constructs the following SVIWRD dynamic system model:
Elderly:

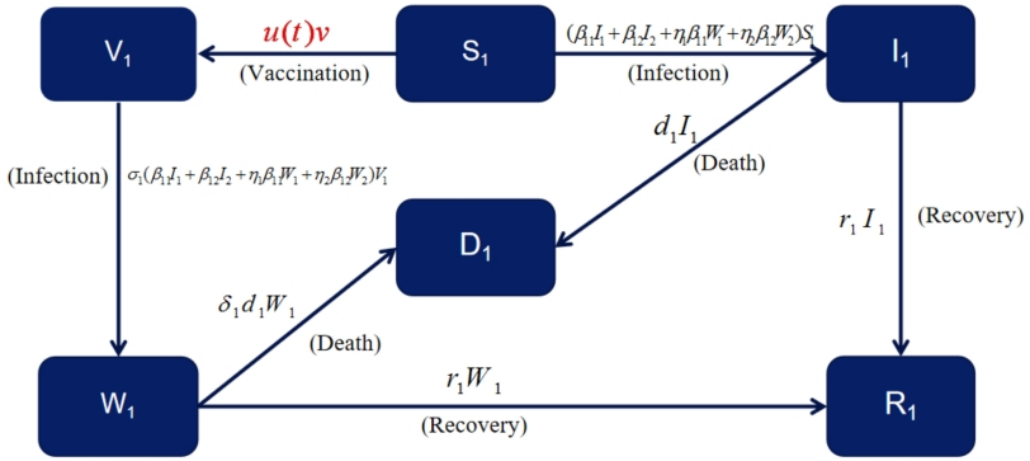
$$\begin{aligned}
S_1'(t) &= aS_2(t) - \left[\beta_{11}I_1(t) + \beta_{12}I_2(t) + \eta_1\beta_{11}W_1(t) + \eta_2\beta_{12}W_2(t)\right] S_1(t) - \mu_1 S_1(t) - u(t)v,\\
V_1'(t) &= aV_2(t) + u(t)v - \sigma_1\left[\beta_{11}I_1(t) + \beta_{12}I_2(t) + \eta_1\beta_{11}W_1(t) + \eta_2\beta_{12}W_2(t)\right] V_1(t) - \mu_1 V_1(t),\\
I_1'(t) &= aI_2(t) + \left[\beta_{11}I_1(t) + \beta_{12}I_2(t) + \eta_1\beta_{11}W_1(t) + \eta_2\beta_{12}W_2(t)\right] S_1(t) - (\mu_1 + \gamma_1 + d_1)\, I_1(t),\\
W_1'(t) &= aW_2(t) + \sigma_1\left[\beta_{11}I_1(t) + \beta_{12}I_2(t) + \eta_1\beta_{11}W_1(t) + \eta_2\beta_{12}W_2(t)\right] V_1(t) - (\mu_1 + \gamma_1 + \delta_1 d_1)W_1(t),\\
R_1'(t) &= aR_2(t) + \gamma_1 I_1(t) + \gamma_1 W_1(t) - \mu_1 R_1(t),\\
D_1'(t) &= d_1 I_1(t) + \delta_1 d_1 W_1(t).
\end{aligned}$$

Non-elderly:

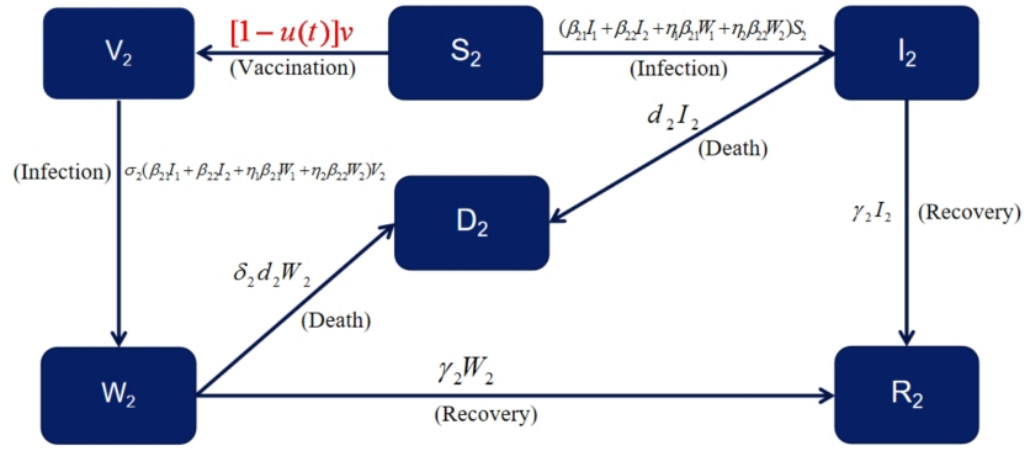
$$\begin{aligned}
S_2'(t) &= b - \left[\beta_{21}I_1(t) + \beta_{22}I_2(t) + \eta_1\beta_{21}W_1(t) + \eta_2\beta_{22}W_2(t)\right] S_2(t) - (\mu_2 + a)\, S_2(t) - [1-u(t)]v,\\
V_2'(t) &= [1-u(t)]\, v - \sigma_2\left[\beta_{21}I_1(t) + \beta_{22}I_2(t) + \eta_1\beta_{21}W_1(t) + \eta_2\beta_{22}W_2(t)\right] V_2(t) - (\mu_2 + a)\, V_2(t),\\
I_2'(t) &= \left[\beta_{21}I_1(t) + \beta_{22}I_2(t) + \eta_1\beta_{21}W_1(t) + \eta_2\beta_{22}W_2(t)\right] S_2(t) - (\mu_2 + \gamma_2 + d_2 + a)I_2(t),\\
W_2'(t) &= \sigma_2\left[\beta_{21}I_1(t) + \beta_{22}I_2(t) + \eta_1\beta_{21}W_1(t) + \eta_2\beta_{22}W_2(t)\right] V_2(t) - (\mu_2 + \gamma_2 + \delta_2 d_2 + a)W_2(t),\\
R_2'(t) &= \gamma_2 I_2(t) + \gamma_2 W_2(t) - (\mu_2 + a)\, R_2(t),\\
D_2'(t) &= d_2 I_2(t) + \delta_2 d_2 W_2(t),
\end{aligned} \tag{1}$$

with the initial conditions $S_i(0) > 0, V_i(0) \geq 0, I_i(0) \geq 0, W_i(0) \geq 0, R_i(0) \geq 0$ and $D_i(0) \geq 0$, $i = 1, 2$. Here, S is the susceptible population, V is the vaccinated population, I is the infected population, W is the infected population after vaccination, R is the recovered population, and D is the dead population due to disease. a is the natural growth rate of age. When the model spans a longer time period, the natural growth rate should be considered as non-elderly individuals transition into the elderly group. However, since this study focuses on the early stage of the epidemic (0.2 years), $a = 0$ is assumed. b is the natural birth rate, β_{ij} is the rate of disease transmission from I_j to S_j, η_i is the reduction ratio of infectivity of people who are infected after vaccination. μ is the natural mortality rate, d is the disease-induced mortality rate, γ is the recovery rate. v is the number of vaccination done per unit time. $u \in [0, 1]$ is the control function representing the ratio of vaccine allocation to the elderly people: $u(t)v$ and $[1 - u(t)]v$ are the numbers of vaccination allocated at time t to the elderly and non-elderly populations, respectively. In this model, we assume that the vaccine efficacy can not be perfect, so $\sigma \in [0, 1]$ is the efficacy in reducing the disease transmission rates ($\sigma = 0$ implies the perfect efficacy, i.e., no infection occurs in the vaccinated population), and $\delta \in [0, 1]$ is the efficacy in reducing the disease-induced death rate ($\delta = 0$ implies that no disease-induced death occurs in

the vaccinated population). Moreover, η in [0,1] is the efficacy in reducing the infectivity of infected individuals. Among them, the subscripts 1 and 2 represent the elderly and non-elderly populations, respectively. For the flowchart of the model, see Figure 1.



(a) Elderly population



(b) Non-elderly population

Figure 1: Flowchart of the SVIWRD model with elderly and non-elderly populations

3 Disease-free equilibrium and basic reproduction number

In this section, we derive the disease-free equilibrium and basic reproduction number R_0 of model (1) in the case where the control function is constant ($u(t) = u$). "Disease-free equilibrium" is the state in a disease model where there are no infected individuals present. The disease-free equilibrium can formally be expressed as

$$(S_1^0, V_1^0, 0, 0, 0, 0, S_2^0, V_2^0, 0, 0, 0, 0),$$

where

$$\begin{aligned} S_1^0 &= \frac{-uv + aS_2^0}{\mu_1} = \frac{ab - (a + \mu_2 u)v}{\mu_1(\mu_2 + a)}, \quad V_1^0 = \frac{uv + aV_2^0}{\mu_1} = \frac{(a + \mu_2 u)v}{\mu_1(\mu_2 + a)}, \\ S_2^0 &= \frac{b - (1 - u)\, v}{\mu_2 + a}, \quad V_2^0 = \frac{(1 - u)\, v}{\mu_2 + a}. \end{aligned} \tag{2}$$

Hence, the disease-free equilibrium exists uniquely if $S_1^0, S_2^0 > 0$, which is equivalent to

$$v < \min\left(\frac{b}{1-u},\ \frac{ab}{a+\mu_2 u}\right).$$

In what follows, unless otherwise noted, we assume that this inequality holds and the disease-free equilibrium uniquely exists. The basic reproductive number (R_0) of an infectious agent is defined as the average number of secondary infections produced by an infected individual in a disease-free host population [5]. R_0 determines whether a pathogen can persist in such a population and is valuable for assessing control options. When R_0 is less than 1, on average each infectious individual infects less than one other individual, and the pathogen will die out in the population. In contrast, when R_0 exceeds 1, numbers of cases will on average rise over time, and an epidemic can occur [8].

In order to verify how effective this model is in controlling infectious diseases through vaccination, we need to calculate the value of the basic reproduction number R_0 and analyze its stability. Following [6], we consider the linearized equations around the disease-free equilibrium as follows:

$$\begin{bmatrix} I_1'(t) \\ I_2'(t) \\ W_1'(t) \\ W_2'(t) \end{bmatrix} = \begin{bmatrix} (\beta_{11}I_1 + \beta_{12}I_2 + \eta_1\beta_{11}W_1 + \eta_2\beta_{12}W_2)\, S_1^0 \\ (\beta_{21}I_1 + \beta_{22}I_2 + \eta_1\beta_{21}W_1 + \eta_2\beta_{22}W_2)\, S_2^0 \\ \sigma_1\,(\beta_{11}I_1 + \beta_{12}I_2 + \eta_1\beta_{11}W_1 + \eta_2\beta_{12}W_2)\, V_1^0 \\ \sigma_2\,(\beta_{21}I_1 + \beta_{22}I_2 + \eta_1\beta_{21}W_1 + \eta_2\beta_{22}W_2)\, V_2^0 \end{bmatrix} - \begin{bmatrix} (\mu_1+\gamma_1+d_1)\, I_1 - aI_2 \\ (\mu_2+\gamma_1+d_2+a)\, I_2 \\ (\mu_2+\gamma_1+\delta_1 d_1)\, W_1 - aW_2 \\ (\mu_2+\gamma_2+\delta_2 d_2+a)\, W_2 \end{bmatrix}.$$

Using the general theory in [6], R_0 can be calculated as $R_0 = \rho\left[FV^{-1}\right]$ (ρ denotes the spectral radius), where

$$F = \begin{bmatrix} \beta_{11}S_1^0 & \beta_{12}S_1^0 & \eta_1\beta_{11}S_1^0 & \eta_2\beta_{12}S_1^0 \\ \beta_{21}S_2^0 & \beta_{22}S_2^0 & \eta_1\beta_{21}S_2^0 & \eta_2\beta_{22}S_2^0 \\ \sigma_1\beta_{11}V_1^0 & \sigma_1\beta_{12}V_1^0 & \sigma_1\eta_1\beta_{11}V_1^0 & \sigma_1\eta_2\beta_{12}V_1^0 \\ \sigma_2\beta_{21}V_2^0 & \sigma_2\beta_{22}V_2^0 & \sigma_2\eta_1\beta_{21}V_2^0 & \sigma_2\eta_2\beta_{22}V_2^0 \end{bmatrix}$$

and

$$V = \begin{bmatrix} \mu_1+\gamma_1+d_1 & -a & 0 & 0 \\ 0 & \mu_2+\gamma_2+d_2+a & 0 & 0 \\ 0 & 0 & \mu_1+\gamma_1+\delta_1 d_1 & -a \\ 0 & 0 & 0 & \mu_2+\gamma_2+\delta_2 d_2+a \end{bmatrix}.$$

Note that $F - V$ is the Jacobian matrix at the disease-free equilibrium. From [6, Theorem 2], we see that if $R_0 < 1$, then the disease-free equilibrium is locally asymptotically stable, whereas if $R_0 > 1$, then it is unstable. In other words, $R_0 < 1$ means that the infectious disease will stop spreading and $R_0 > 1$ means that the infectious disease will continue to spread.

4 Optimal control in the SVIWRD model with vaccination

4.1 Problem Definition

Let $u(t)$ represent the proportion of the population vaccinated among the elderly at time t. The objective is to minimize the following cost functional:

$$J(u) = \int_0^{t_f} \left(k_1 I_1 + k_2 I_2 + l_1 D_1 + l_2 D_2 + \frac{m_1}{2}(uv)^2 + \frac{m_2}{2}\left((1-u)v\right)^2\right) dt, \tag{3}$$

where

- k_1, k_2 are the cost coefficients for infections of the elderly and non-elderly, respectively.
- l_1, l_2 are the cost coefficients for deaths of the elderly and non-elderly, respectively.
- m_1, m_2 are the cost coefficients for distributing vaccines to the elderly and non-elderly, respectively.
- $u(t) \in [0, 1]$ is the control variable, representing the fraction of the vaccine allocated to the elderly at time t.

The dynamic equations of the system are described by the SVIWRD model, which accounts for the changes in susceptible (S), vaccinated (V), infected (I), waned (W), recovered (R), and deceased (D) populations.

4.2 Hamiltonian Definition

Using Pontryagin's Maximum Principle [9], we define the Hamiltonian function as:

$$H = k_1 I_1 + k_2 I_2 + l_1 D_1 + l_2 D_2 + \frac{m_1}{2}(uv)^2 + \frac{m_2}{2}\left((1-u)v\right)^2 + \sum_{i=1}^{12} \lambda_i f_i, \tag{4}$$

where

- λ_i are the adjoint variables.
- f_i are the right-hand side functions of the state equations.

4.3 Existence and Uniqueness of the Optimal Control

(i) Existence and Uniqueness of the Solution to the State and Adjoint Equations

The right-hand side of the SVIWRD model is Lipschitz continuous with respect to the state variables in any bounded closed region $\Omega \subset R_+^{12}$. That is, there exists a positive constant $L > 0$ such that

$$\|f(t, x_1, u) - f(t, x_2, u)\| \leq L\|x_1 - x_2\| \quad \text{for all } x_1, x_2 \in \Omega, \quad u \in [0, 1] \quad \text{and} \quad t > 0, \tag{5}$$

where $f = (f_1, f_2, \ldots, f_{12})$ and $\|\cdot\|$ denotes the Euclidean norm. This ensures the existence and uniqueness of the solution to the state equations. Similarly, we can verify the existence and uniqueness of the solution to the adjoint equations by virtue of the Lipschitz continuity of the system.

(ii) Strict convexity of the Cost Function and the Hamiltonian

The cost functional $J(u)$ is strictly convex in u because it includes terms like $(uv)^2$ and $((1-u)v)^2$, both of which ensures that $\partial^2 J/\partial u^2 > 0$. By a similar reason, the Hamiltonian H is also strictly convex in u.

(iii) Existence and Uniqueness of the Optimal Control

The control variable $u(t)$ is bounded, meaning $u(t) \in [0, 1]$ and is Lebesgue measurable. According to the optimal control theory [9], such constraints guarantee the existence of the optimal control. By applying Pontryagin's Maximum Principle [3, 7], we can obtain the optimal control $u^*(t)$ by solving the condition:

$$\frac{\partial H}{\partial u} = 0 \quad \text{at the optimal solution.} \tag{6}$$

This gives us an expression for $u^*(t)$. Specifically, the optimal control $u^*(t)$ is given by

$$u^*(t) = \min\left(\max\left(0, \frac{v(\lambda_1 - \lambda_2 + \lambda_8 - \lambda_7)}{m_1 v^2 + m_2 v^2}\right), 1\right). \tag{7}$$

This form guarantees the uniqueness of the optimal control $u^*(t)$.

5 Numerical simulation

In this section, we perform numerical simulation adopting the optimal control u^*. For solving ordinary differential equations (ODEs), we use the standard fourth-order Runge-Kutta method. In the simulation, we use the parameters as shown in Table 1, which are chosen considering the COVID-19 in Japan for 0.2 year from April 2021, when the vaccine distribution started in Japan.

Table 1: The summary of parameters used in simulation

Parameter	Value	Description	Reference
$(\beta_{11}, \beta_{12}, \beta_{21}, \beta_{22})$	$q(0.25, 1, 1, 4)$	Disease transmission rate	Assumed
q	40	Scaling parameter for intensity of disease spread	Calculated
a	0	Transfer rate from the non-elderly group to the elderly group	Assumed
b	0.0219	Birth rate	Calculated
(μ_1, μ_2)	$(1/20, 1/80)$	Natural mortality	[12]
(d_1, d_2)	$(2.4, 0.024)$	Disease-induced mortality	[13]
(γ_1, γ_2)	$(24, 24)$	Recovery rate	[2]
v	0.8	Number of vaccination shots per unit time	[14]
(σ_1, σ_2)	$(0.4, 0.4)$	Vaccine efficacy ($1 - \sigma_1$, $i = 1, 2$) to reduce the susceptibility	[20]
(δ_1, δ_2)	$(0.2, 0.2)$	Vaccine efficacy ($1 - \delta_i$, $i = 1, 2$) to reduce the disease-induced mortality	[20]
(η_1, η_2)	$(0.5, 0.5)$	Vaccine efficacy ($1 - \eta_i$, $i = 1, 2$) to reduce the infectivty	[15]
(k_1, k_2)	$(1, 2)$	Cost coefficient of being infected	Assumed
(l_1, l_2)	$(100, 200)$	Cost coefficient of being dead	Assumed
(m_1, m_2)	$(0.1, 0.2)$	Cost coefficient of distributing vaccines	Assumed

The biological justification for them is as follows:

- The unit time is 1 year.
- Based on [12], we assume that the average life expectancy is 80 years. The people aged more than 60 is categorized as elderly, and thus, the average life expectancies for each group are $1/\mu_1 = 20$ and $1/\mu_2 = 80$, respectively. Moreover, the average sojourn time in the non-elderly group is $1/a = 60$.
- In the absence of disease and vaccination, the total population is calculated as

  $$S_1^0 + S_2^0 = \frac{aS_2^0}{\mu_1} + S_2^0 = \frac{\mu_1 + a}{\mu_2 + a}\frac{b}{\mu_1}.$$

  Under the assumption that the total population is normalized as 1, the parameter b can be calculated as

  $$b = \frac{(\mu_2 + a)\mu_1}{\mu_1 + a} \approx 0.0219.$$

- Based on [2], we assume that the average infection period $(1/\gamma_i,\ i = 1, 2)$ for both of the elderly and non-elderly people is 1/2 month = 1/24 year.

- Based on [13], we assume that the disease-induced mortality in elderly people is 100 times higher than that in non-elderly people, and about 10 percent of the infected elderly people become severe. Regarding the severe individuals as removed individuals, we assume that $d_1 = 0.1\gamma_1 = 2.4$ and $d_2 = 0.01d_1 = 0.0024$.

- Based on [14], we assume that 80 percent of total population has been vaccinated after 1 year passed, and thus, $v = 0.8$.

- We assume that the vaccine efficacy is the same for two age groups. By [20], we assume that the reduction effect in infection risk is 60 percent ($1 - \sigma_i = 0.6$, $i = 1, 2$) and that in disease-induced death is 80 percent ($1 - \delta_i = 0.8$, $i = 1, 2$). Moreover, by [15], we assume that the reduction effect in disease transmission is 50 percent ($1 - \eta_i = 0.5$, $i = 1, 2$).

- We assume that $\beta_{ij} = q\phi_i\psi_j$, $i = 1, 2$, where q is a scalling parameter for intensity of disease spread, and ϕ_i and ψ_i are the susceptibility and infectivity in group i, respectively. We can consider that elderly people is more careful and more likely to reduce the contact opportunity because the disease-induced mortality is quite high. Hence, we assume that $\phi_1 = \psi_1 = 0.5$ and $\phi_2 = \psi_2 = 2$. The scalling parameter q is set to be 40 so that the basic reproduction number in the absence of vaccination approximates 5, which is close to the estimated value for the delta variant [22].

- We assume that the cost of disease-induced death is 100 times higher than that of infection ($l_i = 100k_i$, $i = 1, 2$). Moreover, from the perspective of remaining life, we assume that the cost in non-elderly people is 2 times higher than that in elderly people. Thus, setting $k_1 = 1$, we obtain $k_2 = 2$, $l_1 = 100$ and $l_2 = 200$. Moreover, we assume that the cost of vaccine distribution is 10 times less than that of infection. Here, we can consider that distributing vaccines in non-elderly people is much harder than in elderly people because the disease-induced death rate is lower in non-elderly people, and therefore, some of the non-elderly people often show the vaccine hesitancy.

The initial condition is fixed as follows

$$S_1(0) = 0.33, \quad S_2(0) = 0.65, \quad I_1(0) = I_2(0) = 0.01, \quad V_i(0) = W_i(0) = R_i(0) = D_i(0) = 0, \quad i = 1, 2.$$

The optimal control u^* can be calculated as shown in Figure 2.

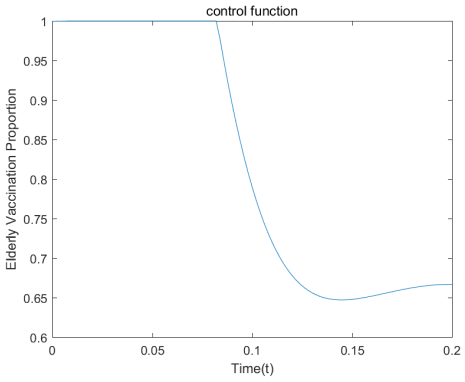
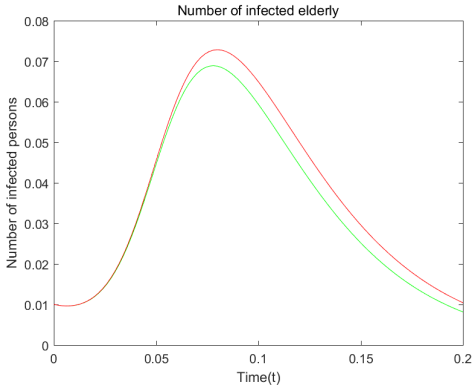
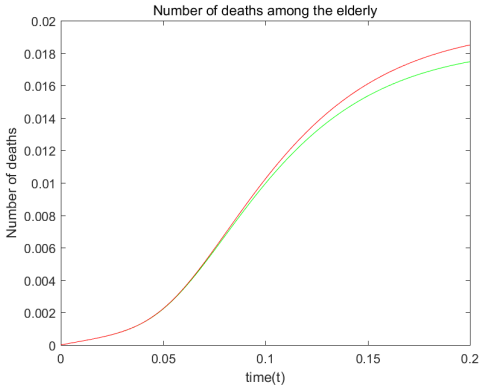


Figure 2: The optimal control u^*

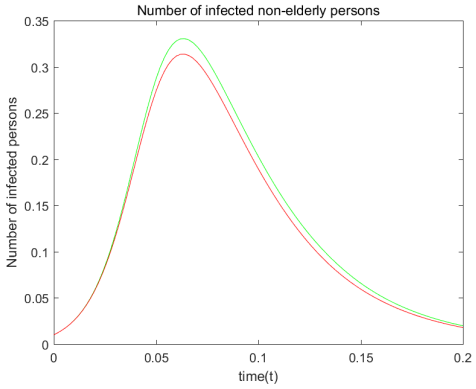
Moreover, Figure 3 shows that the infected and dead populations in the optimal case $u = u^*$ (green) and the uncontrolled case $u = 0.5$ (red).



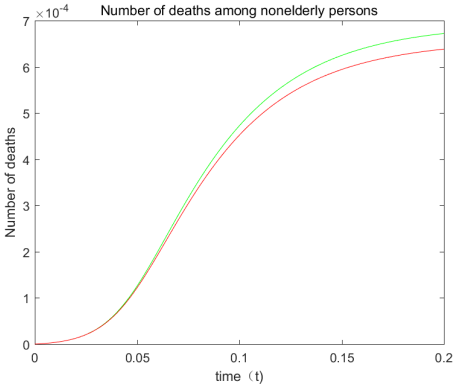
(a) Infected elderly population $I_1 + W_1$



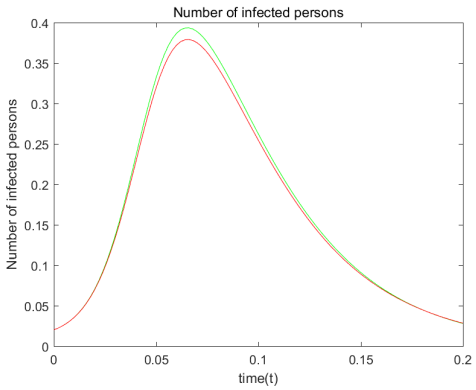
(b) Dead elderly population D_1



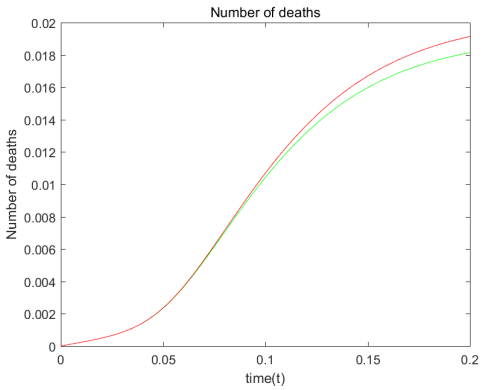
(c) Infected non-elderly population $I_2 + W_2$



(d) Dead non-elderly population D_2



(e) Total infected population $I_1 + I_2 + W_1 + W_2$



(f) Total dead population $D_1 + D_2$

Figure 3: The infected and dead populations in the optimal case ($u = u^*$, green) and the uncontrolled case ($u = 0.5$, red)

From these figures, we obtain the following insights:

1. Adopting the strategy of giving priority to the elderly for vaccination will result in the lowest cost.

2. Due to the adoption of a priority vaccination strategy for the elderly, the number of infections and deaths in the elderly population will decrease, but the number of infections and deaths in the non-elderly population will increase.

3. After adopting the strategy of giving priority to the elderly for vaccination, the number of deaths in the total population will decrease, but the number of infections will increase. If the infection weight parameter is adjusted higher, the simulation results will change. As the infection weight parameter increases, the number of deaths might gradually increase and the number of infections will gradually decrease. At this time, priority might be given to non-elderly people for vaccination.

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