Optimal Control of Infectious Disease Transmission Dynamics

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Abstract

In this paper, we develop a deterministic model of an infectious disease that can be managed with vaccination. The goal of this paper is to find a vaccination strategy that maximizes net benefits of managing the disease over a finite time horizon. We use Pontryagin's Maximum Principle to characterize the optimal level of vaccination analytically and then solve the resulting system numerically. Numerical results suggest that an early round of vaccination is a key part of disease management. A typical optimal vaccination schedule includes vaccinating at a maximum level in the early stages of the disease.

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1 Introduction

During the early stage of controlling a highly contagious infectious disease, policymakers rely on non-pharmaceutical interventions (e.g., restricting international travel, closing schools and restaurants, imposing curfews) to curtail disease spread. These strict non-pharmaceutical interventions come with serious concerns about their social and economic impacts. However, easing national lockdowns to alleviate those impacts can cause resurgence of confirmed cases and fatality rates. Therefore, achieving the right balance between controlling the spread of a disease and maintaining economic growth is a difficult yet urgent task for policy makers.

In addition to any lockdown policies that policy makers impose at the early stages of a pandemic, the development and implementation of vaccines can also effectively mitigate the spread of disease. Implementation of vaccination programs can shorten the lockdown period and limit its negative impact on a nation's wellbeing. However, the challenge is to propose a suitable intervention strategy while taking disease dynamics into account. Optimal control theory can be used to solve for an optimal mitigation strategy that efficiently balances the costs of vaccination with its benefits.

Optimal control theory has become an important area of mathematics used extensively to model the management of infectious diseases. It is a powerful tool used to make decisions involving complex biological situations. Researchers have formulated deterministic models of epidemiological systems and have considered both pharmaceutical approaches (such as vaccination) and non-pharmaceutical interventions (such as quarantine) as control measures. One of the earliest contributions from Sethi [1] includes a deterministic SI (Susceptible-Infected) epidemiology model with a quarantine ratio (number of those in quarantine over the number of susceptible) as the control measure. Sethi solves for the optimal quarantine ratio over time. Papers by Yusuf and Benyah [2] and Yusurf and

Olayinka [3] study the transmission and progression of infectious diseases using both vaccination and recovery rates as control measures. Both papers use Pontryagin's Maximum Principle to characterize the optimal levels of the two controls, albeit with different epidemiological models.

When setting up optimal control problems, researchers need to consider the most appropriate model specification. Solution types depend on whether the control variable enters linearly or nonlinearly. A nonlinear specification for the control variable facilitates an interior solution, whereas the alternative (using a linear control term in objective function) involves either a bang-bang or a singular solution. An interior solution for the control variable tends to lead to a smooth path of the control over time. However, a solution to a problem that is linear in the control may involve discontinuities in the optimal control. For example, Sethi [1] proposed an optimal control problem in which the quarantine ratio entered the objective function linearly. The analytical solution from Sethi is one in which the optimal policy is binary: to quarantine or not. A more recent contribution from Rowthorn and Toxvaerd [4] proposes an optimal control problem that considers both prevention and treatment, incorporated within a SIS (Susceptible-Infected-Susceptible) epidemiology model. Both control variables enter the objective function linearly. The result is that there is a singular solution with control variables at their extremes until the solution is reached.

In addition to considering the linearity of control variables, researchers also need to consider whether to solve their optimality system analytically or numerically. To construct a problem that can be solved analytically, researchers often need to impose strong assumptions on the model, necessitating a relatively simple model of infectious disease dynamics. Without restricting the number of state and control variables, detailed characterization of the disease dynamics may result in a complicated system of ordinary differential equations which is unsolvable with analytical methods. However, more complicated systems involving more realistic models of disease transmission dynamics can be solved using numerical methods such as in papers Yusurf and Olayinka [3] and Yusuf and

Benyah [2]. Their simulation results show that the optimal combination of vaccination and treatment required to achieve the set objective will depend on the relative costs of the two control measures.

In this paper, we use optimal control theory where disease dynamics are governed by the Susceptible, Exposed, Infected, and Recovered (SEIR) model proposed by Lenhart [5] to solve for an optimal vaccination policy. After solving the model numerically, we explore the implications of changes in parameters to shed light on optimal policy under various conditions.

The paper proceeds as follows. Section 2 introduces the infectious disease transmission dynamics. Section 3 formulates the optimal control problem subject to the SEIR model dynamics proposed by Lenhart [5] and derives the optimality system. Section 4 solves the optimal control problem numerically and presents simulation results. Section 5 illustrates some of the main points through simulation and concludes.

2 Model

2.1 Proposed Model with Vaccination

In this paper, we use a model that was proposed by Lenhart [5]. Susceptible individuals (S) become exposed (E) through contact with infected individuals (I) and some fraction of exposed individuals become infected. A proportion of infected individuals recover (R). The total number of individuals in the population (N) is the sum of individuals in all the categories. The model includes a control policy for the fraction of the population being vaccinated, u. It also includes natural births and deaths as well as deaths caused by the disease. This model is represented below.

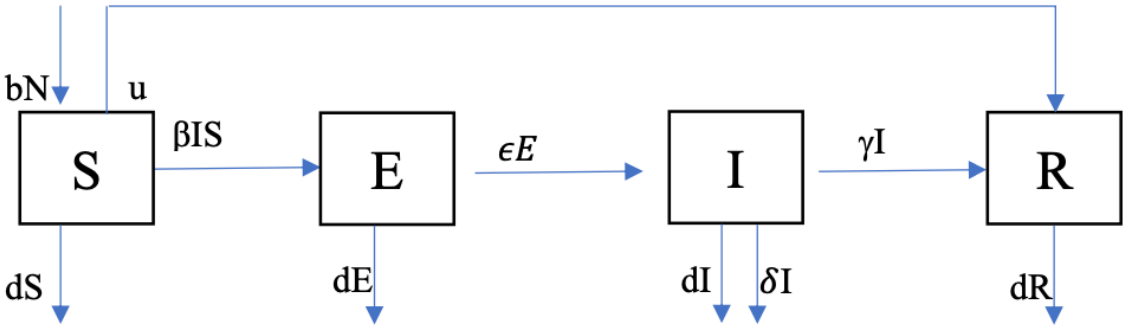


Figure 2.1 SEIR Model with Vaccination

From this flow chart we can notice that population inflow comes from natural births, denoted as "bN." Outflow due to natural death occurs from each group, represented by "d." Vaccination reduces the Susceptible population and places them in the Recovered group. Population movements between groups depend on few key disease transmission parameters, such as contact rate β, progression rate ϵ, and recovery rate γ. As proposed by Lenhart [5] the above flow chart with vaccination can be described by the following system of ordinary differential equations (ODEs):

$$\dot{S} = bN - dS \ - \beta S(1-u)I - uS \qquad (2\text{-}1)$$

$$\dot{E} = \beta(1-u)SI - (\epsilon + d)E$$

(2-2)

$$\dot{I} = \epsilon E - (d + \delta + \gamma)I$$

(2-3)

$$\dot{R} = \gamma I - dR + uS$$

(2-4)

$$\dot{N} = (b-d)N - \delta I$$

(2-5)

- S(t), Susceptible – healthy individuals who have not been exposed to the disease yet at time t
- E(t), Exposed – people are exposed to the virus but not yet infectious at time t. The Exposed group allows for an incubation period for the disease inside its host, where an infected person remains latent without clinical symptoms or signs of infection before becoming infectious (Lenhart and Workman [2007]).
- I(t), Infectious – the group infected with the disease after exposure, with symptoms.
- R(t), Recovered– individuals recovered from the disease or immune due to immunization

The parameter β measures the average number of contacts made by one person per unit of time and is assumed to be constant over time. So, βSI is the total number of Susceptible individuals that become exposed (new cases). The progression rate ϵ is the rate at which exposed individuals become infectious. The recovery rate γ reflects the rate at which infected individuals recover. The death induced rate δ is the death rate caused by the disease. As mentioned by Lenhart [5], 1/ δ measures the average length of infection period before recovery and 1/ϵ measures the incubation period: a higher recovery rate or progression rate means a shorter infection period or incubation period. Note that there are no reinfections. Once in the recovered group, there is no chance of becoming infected.

All parameters, as listed in Table 2.1 below, are assumed to be positive and to remain constant over time.

Parameter	Description
b	Natural birth rate
d	Natural death rate
$\boldsymbol{\beta}$	Contact rate
$\boldsymbol{\epsilon}$	Progression rate (exposed become infected)
$\boldsymbol{\delta}$	Disease induced death rate
$\boldsymbol{\gamma}$	Recovery rate

Table 2.1 Parameters used in SEIR model

The vaccination rate u may be modeled as fixed or a variable function of time, t. The total population N(t) can be obtained from $N(t) = S(t) + E(t) + I(t) + R(t)$, resulting in $\dot{N}(t) = \dot{S}(t) + \dot{E}(t) + \dot{I}(t) + \dot{R}(t)$.

2.2 Basic Reproduction Number

Now we can use the proposed disease transmission dynamics to derive the basic reproduction number of the infectious disease. $\mathcal{R}_0$ can be used as the threshold quantity that helps to determine whether an outbreak of infectious disease dies out or spreads in a community. In epidemiology, the basic reproduction number is the expected number of secondary infections produced in a population of susceptible individuals. In this section, we first explore basic reproduction numbers with and without vaccination intervention, noting that the vaccination rate *u* is fixed here. Then, sensitivity analysis is carried out in order to understand the relative importance of different factors responsible for disease transmission and prevalence.

We obtain $\mathcal{R}_0$ by following the next-generation matrix approach proposed by Van den Driessche and Watmough [6]. Using their notation, we have

$$\mathcal{F} = \begin{bmatrix} 0 & \frac{\beta b N}{d+u} \\ 0 & 0 \end{bmatrix}$$

(2-6)

$$\upsilon = \begin{bmatrix} (\epsilon + d) & 0 \\ -\epsilon & d + \delta + \gamma \end{bmatrix}$$

(2-7)

where the matrix $\mathcal{F}$ represents transmission and the matrix υ represents transitions. Hence, all epidemiological events that lead to new infections are incorporated in the model via $\mathcal{F}$ and all other events via υ. The reproduction number is given by the dominance eigenvalue of a next-generation matrix $\rho(\mathcal{F}\upsilon)^{-1}$:

$$\mathcal{R}_{\upsilon} = \frac{b\beta\epsilon N}{(d+u)(d+\epsilon)(d+\delta+\gamma)}$$

(2-8)

The threshold quantity $\mathcal{R}_{\upsilon}$ from this equation represents the average number of infected people produced by one infected individual when introduced into a host population in the presence of vaccination. Figure 2.2 shows the relationship between $\mathcal{R}_{\upsilon}$ and the vaccination rate when the parameters take on various vaccination rates while keeping transmission parameter values (natural death rate d, disease progression rate ϵ, contact rate β, recovery rate γ, disease mortality rate δ) constant. This figure shows that increases in vaccination reduce the value of $\mathcal{R}_{\upsilon}$. The figure also indicates that, when vaccination rates are lower, secondary infections are higher. From a social planner's perspective, the negative relationship between $\mathcal{R}_{\upsilon}$ and the vaccination level suggests a trade-off between vaccination intensity and confirmed cases.

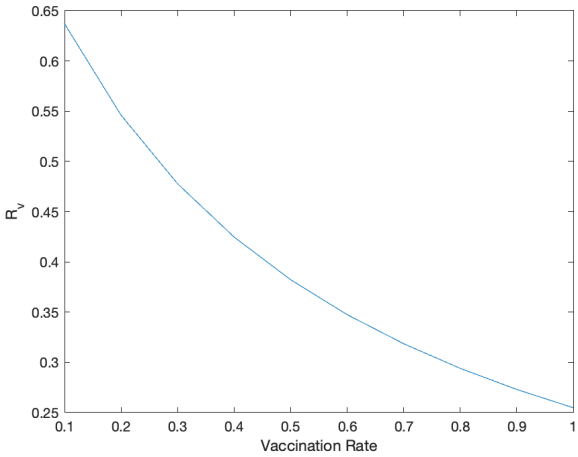


Figure 2.2 Vaccination-induced reproduction number ($\mathcal{R}_v$) versus the Vaccination Rate, u.

Parameter values used to calculate $\mathcal{R}_v$ are provided below. They are consistent with parameter values used in the baseline scenario in Section 4. Note that these parameter values are proposed by Lenhart and Workman as reflecting a micro-parasitic infectious disease.

Natural birth rate	Contact rate	Progression rate	Natural death rate	Disease mortality rate	Recovery rate	Vaccination rate
b	β	ϵ	d	δ	γ	u
0.525	0.001	0.5	0.5	0.2	0.1	0.1 - 1

Table 2.2 Parameter values used to calculate $\mathcal{R}_v$

In the absence of vaccination (u = 0), the basic reproduction number is:

$$\mathcal{R}_0 = \frac{b\beta\epsilon N}{d(d+\epsilon)(d+\delta+\gamma)}$$

(2-9)

Assuming constant levels of natural birth/death rate and unchanged total population (holding *b, d*, and *N* constant), we evaluate the sensitivity of the basic reproduction number to some key disease transmission parameters: contact rate β, progression rate ϵ, mortality rate δ, and recovery rate γ. When $\mathcal{R}_0$ < 1, the disease dies out without any medical intervention. But when $\mathcal{R}_0$ > 1, the disease

becomes endemic, requiring certain pharmaceutical or non-pharmaceutical interventions to control the spread of the disease.

In the figures below, $\mathcal{R}_0$ increases when β and ϵ increase, meaning secondary infections will be higher if contact rates and/or progression rates increase. This makes sense, as the contact rate measures the rate at which susceptible individuals have contact with other individuals, and the progression rate measures how many exposed individuals become infectious. If both contact and progression rates are high, then the basic reproduction number becomes higher. This means that when people have close contacts to virus hosts and quickly become infectious, the disease can spread at a faster rate. In addition, we can also observe that $\mathcal{R}_0$ is reduced when δ and γ increase, meaning secondary infections caused by a single infected individual become lower if disease mortality rates and/or recovery rates are high. This also makes sense, as more infected people are removed from transmission dynamics due to disease induced mortality or recovery, then the secondary infection likely to decline. Comparing sensitivity analysis results presented in both figures below, we can also see that $\mathcal{R}_0$ is more sensitive to the incremental movements of values in contact rate and progression rate β and ϵ than to mortality and recovery rates δ and γ.

The indication from the sensitivity analysis is that controlling the contact rate β and progression rate ϵ has more direct impact on reducing the basic reproduction number. In other words, preventive measures are more effective than reactive measures to reduce secondary infections. For example, preventive measures such as practicing social distancing or wearing masks can effectively reduce or prevent the spread of disease in early stages. On the other hand, reactive measures such as developing medical treatments or drugs (affecting the death rate and recovery rate) require significant resources to develop and become effective. Assume the costs of changing parameter values are equal, we would prefer changing the contact rate β and the progression rate ϵ as they have more direct impact on reducing the basic reproduction number than changing either the death rate or the recovery rate. Therefore, from social planner's perspective, it is important to

implement preventive measures during early stages of an epidemic to curtail the spread of disease.

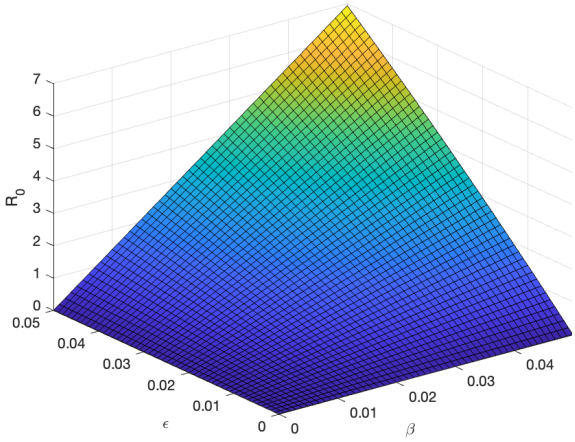


Figure 2.3 Effect of parameters in basic reproduction number for β and ϵ with fixed natural birth and death rate: b = 0.525, d = 0.5; and fixed mortality and recovery rate: δ = 0.2, $\gamma = 0.1$

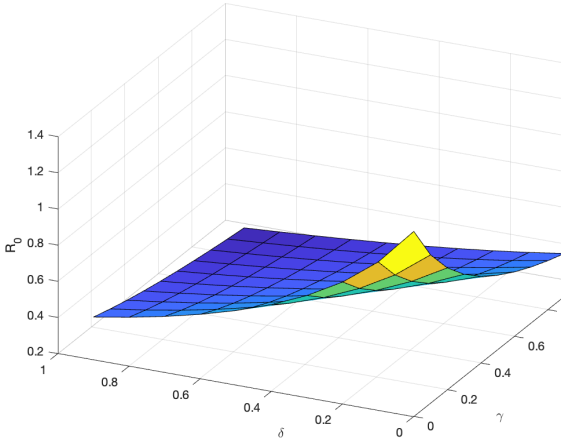


Figure 2.4 Effects of parameters in basic reproduction number for δ and γ with fixed natural birth and death rate: b = 0.525, d = 0.5; and fixed contact rate and progression rate: $\beta = 0.01, \epsilon = 0.5$

3 Optimal Control Problem

3.1 Formulation of the problem

Now, instead of using a fixed vaccination rate, we allow the vaccination rate to be determined by a social planner in a vaccination campaign and to vary over time. The goal of a vaccination campaign is to strategically reduce the Susceptible population through enhancing public immunity to the virus. In this case, $u(t)$, represents the proportion of susceptible people receiving vaccinations per unit of time at t. The goal then becomes to look for the optimal level of $u(t)^*$ that would maximize net benefits over a finite time horizon. Although the exact end date for an epidemic is not likely to be known, a finite time horizon is chosen for the optimal control problem because it is reasonable for a social planner to implement the vaccination plan within a fixed period of time (e.g., by the end of a presidential administration).

To model the dynamics of disease transmission in a population, we used the SEIR model with a vaccination policy proposed by Lenhart. The goal is to maximize the benefits of maintaining the size of the population minus the costs of implementing the vaccination program, subject to the disease transmission dynamics. Next, we specify the costs of vaccination as a quadratic function of u(t). This formulation reflects the idea that a stringent vaccination policy is much more expensive to be implemented than a relaxed policy: costs rise quickly when many vaccinations need to be administered at the same time. In summary, the problem is written:

$$Max\ J(u) = \int_0^T A * N(t) - c * u(t)^2\, dt \qquad (3\text{-}1)$$

Subject to

$$\dot{S}(t) = bN(t) - dS(t) - \beta S(t)I(t) - u(t)S(t)$$

(3-2)

$$E\dot{(t)} = \beta S(t)I(t) - (\epsilon + d)E(t)$$

(3-3)

$$\dot{I}(t) = \epsilon E(t) - (d + \delta + \gamma)I(t)$$

(3-4)

$$\dot{N}(t) = (b - d)N(t) - \delta I(t)$$

(3-5)

$$S(0) = S_0, E(0) = E_0, I(0) = I_0, N(0) = N_0$$

(3-6)

$$u(t) \in [0,0.9]$$

$$S(T), E(T), I(T), N(T)\ are\ free$$

(3-7)

The differential equations governing the state variables, $\dot{S}(t), \dot{E}(t), \dot{I}(t), \dot{N}(t)$, are represented in the form of SEIR framework introduced in previous section. Notice that *R* does not appear in the other differential equations of $\dot{S}(t), \dot{E}(t), \dot{I}(t), \dot{N}(t)$. Therefore, R can be ignored while developing the necessary conditions. R can be solved separately using its own differential equation $\dot{R}(t)$. The optimal control problem aims to find the optimal path of vaccinations, $u(t)^*$, that maximizes the objective functional subject to the system of differential equations governing disease dynamics.

3.2 Solution of the problem

To determine the optimal level of the vaccination rate and associated state variables that would yield optimal value for the objective functional, I apply Pontryagin's Maximum Principle. The necessary conditions on the optimal control problem are derived by first setting up the Hamiltonian:

$$\mathrm{H}\,(\mathrm{S(t)},\mathrm{E(t)},\mathrm{I(t)},\mathrm{N(t)},\mathrm{u(t)},\mathrm{t})$$
$$= \mathrm{A}N - cu^2 + \lambda_1(bN - dS - \beta SI - uS) + \lambda_2[\beta SI - (\epsilon + d)E]$$
$$+ \lambda_3[\epsilon E - (d + \delta + \gamma)I] + \lambda_4[(b - d)N - \delta I]$$

(3-8)

where $\lambda_1, \lambda_2, \lambda_3, \lambda_4$ are time dependent costate variables that capture the marginal variation in the value function with respect to each state at each instant or period. The shadow price can be interpreted as the contribution to the value of the program from having marginal increase in the state variable at a particular date, t. Costate variables satisfy the conditions below

$$\dot{\lambda_1} = -\frac{\partial H}{\partial S} = (d + u^* + \beta I)\lambda_1 - \beta I\lambda_2$$

(3-9)

$$\dot{\lambda_2} = -\frac{\partial H}{\partial E} = (\epsilon + d)\lambda_2 - \epsilon\lambda_3$$

(3-10)

$$\dot{\lambda_3} = -\frac{\partial H}{\partial I} = \beta S\lambda_1 - \beta S\lambda_2 + (d + \delta + \gamma)\lambda_3 + \delta\lambda_4$$

(3-11)

$$\dot{\lambda_4} = -\frac{\partial H}{\partial N} = -1 - b\lambda_1 - (b - d)\lambda_4$$

(3-12)

In addition, we define transversality conditions as $\lambda_1(T) = 0$, $\lambda_2(T) = 0, \lambda_3(T) = 0, \lambda_4(T) = 0$. These transversality conditions arise because we are allowing the terminal states to be freely chosen. In other words, $S(T)$, $E(T)$, $I(T)$, $N(T)$ are not required to have fixed values at the terminal time. As t moves towards the terminal time T, the shadow value for each state variable must go to zero. Thus, the terminal value of costate variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4$ are zero at time T. These conditions can be interpreted as saying that none of the state variables have any inherent forward-looking marginal value or cost at the end of the planning horizon.

The optimal control $u(t)^*$is obtained by invoking the optimality condition, which is achieved by differentiating the Hamiltonian with respect to the control variable:

$$let\ \frac{\partial H}{\partial u} = 0$$

(3-13)

$$u(t)^* = -\frac{\lambda_1(t)S(t)}{2c}$$

(3-14)

Taking the bounds into account, we have

$$u(t)^* = \min\left[0.9, \max\left[0, -\frac{\lambda_1(t)S(t)}{2c}\right]\right]$$

(3-15)

In an interior solution, we observe the marginal cost of vaccination as

$$-\lambda_1(t) = \frac{2cu(t)^*}{S(t)}$$

(3-16)

This equation indicates that the optimal level of vaccination depends on the number of Susceptible individuals, $S(t)$, as well as the marginal value $\lambda_1(t)$ at time *t* of any additions to S(t). The marginal cost of vaccination for an individual is $\frac{2cu(t)^*}{S(t)}$. $\lambda_1(t)$ is negative, indicating that a marginal increase in the Susceptible population at time t will reduce the forward-looking value of net benefits by $\lambda_1(t)$ at time *t*. Therefore, -λ_1 is the marginal cost of increasing the susceptible population. When we have an interior solution, the marginal cost of vaccination $-\lambda_1(t)$ is thus equal to the marginal cost of increasing the number of susceptible individuals ($\frac{2cu(t)^*}{S(t)}$). A higher marginal cost of increasing the number of susceptible individuals leads to a higher optimal vaccination rate $u^*(t)$. This makes sense: the higher the damage caused by additional individuals being susceptible to the disease, the more effort should be put into prevention through vaccination.

To summarize, the differential equation system that characterizes the optimal paths of the variables of interest, along with constraints on the control and boundary conditions, is shown below:

$$\dot{S} = bN - dS\ - \frac{\beta SI}{N} - uS$$

(3-17)

$$\dot{E} = \frac{\beta SI}{N} - (\epsilon + d)E$$

(3-18)

$$\dot{I} = \epsilon E - (d + \delta + \gamma)I$$

(3-19)

$$\dot{N} = (b - d)N - \delta I$$

(3-20)

$$S(0) = S_0, E(0) = E_0, I(0) = I_0, N(0) = N_0$$

(3-21)

$$\dot{\lambda_1} = \ -\frac{\partial H}{\partial S} = \left(d + u^* + \frac{\beta I}{N}\right)\lambda_1 - \frac{\beta I}{N}\lambda_2$$

(3-22)

$$\dot{\lambda_2} = \ -\frac{\partial H}{\partial E} = (\epsilon + d)\lambda_2 - \epsilon\lambda_3$$

(3-23)

$$\dot{\lambda_3} = \ -\frac{\partial H}{\partial I} = \frac{\beta S}{N}\lambda_1 - \frac{\beta S}{N}\lambda_2 + (d + \delta + \gamma)\lambda_3 + \delta\lambda_4$$

(3-24)

$$\dot{\lambda_4} = \ -\frac{\partial H}{\partial N} = -1 - \left(\frac{\beta SI}{N^2} + b\right)\lambda_1 + \frac{\beta SI}{N^2}\lambda_2 - (b - d)\lambda_4$$

(3-25)

$$\lambda_1(T) = 0\ ,\ \lambda_2(T) = 0, \lambda_3(T) = 0, \lambda_4(T) = 0$$

(3-26)

$$u(t)^* = \min\left[0.9, \max\left[0, -\frac{\lambda_1(t)S(t)}{2c}\right]\right]$$

(3-27)

In the appendix, we also discuss the optimal control problem that considers the impact of including discounting, i.e.

$$J(u) = \int_0^T [A * N(t) - c * u(t)^2] e^{-\rho t} dt$$

(3-28)

Alternatively, instead of assuming free terminal conditions, which is suggested by Lenhart's paper, we can define a terminal condition such as $I(T) = 0$. In this case, all states are free at the terminal time, except for the Infected state, which is fixed at both starting and terminal times. Doing so enables us to explore the optimal control solution when no more infected individuals are left by the end of time T. Therefore, we can modify the terminal conditions for adjoint variables $\lambda_1(T) = 0$, $\lambda_2(T) = 0, \lambda_4(T) = 0,$ but $\lambda_3(T)$ is unknown and will be solved numerically in the next section.

4 Simulation of optimal solutions

To find the numerical solution of optimal vaccination ratio, we use the fourth order Runge-Kutta method in MATLAB. First, all state variables are solved simultaneously forward in time, then all adjoint variables are simultaneously solved backward in time. Each control is updated according to its individual characterization. This process is called forward-backward sweeping and is repeated until convergence occurs.

Table 4.1 summarizes the initial values of all parameters, defined as Scenario 1, as well as other scenarios with different parameter values. The source of parameter values is from Lenhart [5]. The choice of parameters was suggested by a micro-parasitic infectious disease, which includes any viruses, bacteria, or fungi. Such diseases can be characterized by their small size, ability to reproduce directly within an individual host, and relatively short duration of infection, see Neilan and Lenhart [6]. Note that vaccination rate is capped at 90% rather than 100% due to vaccine hesitancy. We assume a small proportion of the total population is not able to receive vaccines due to medical reasons. For example, vaccines can be harmful to receivers if they have already been receiving other medical treatments. Another reason is that children under a certain age are not allowed to receive vaccines.

Using initial values as the baseline scenario, we explore other scenarios by varying parameter values one at a time. The goal is to understand how the optimal path of vaccination varies when parameters change. These parameter values were not chosen to represent a particular disease, but just to illustrate the control techniques, see discussions by Neilan and Lenhart [6]

Parameter	Scen.1 Baseline	Scen.2 Low Contact rate	Scen.3 High Recovery rate	Scen.4 No Recovery rate	Scen.5 High Mortality rate	Scen.6 Short Latency	Scen.7 High Benefit	Scen. 8 Low cost	Description
b	0.525								Natural birth rate

Parameter	Scen.1 Baseline	Scen.2 Low Contact rate	Scen.3 High Recovery rate	Scen.4 No Recovery rate	Scen.5 High Mortality rate	Scen.6 Short Latency	Scen.7 High Benefit	Scen. 8 Low cost	Description
d	0.5								Natural death rate
β	0.001	0.0001							Contact rate
ϵ	0.5					0.1			Latency
δ	0.2				0.4				Disease induced death rate
γ	0.1		0.4	0					Recovery rate
A	1								Weight parameter
S_0	1000								Initial population size of group S
E_0	100								Initial population size of group E
I_0	50								Initial population size of group I
R_0	15								Initial population size of group R
A	0.1						2		Weight parameter for Total Population N
c	1							0.5	Weight parameter for vaccination "u"

Note that $u(t) \in [0, 0.9]$ condition is applied across all scenarios to eliminate the case where the entire susceptible population is vaccinated

Table 4.1 Parameters used in each scenario

4.1 Numerical Results for the Optimal Control Problem

We now present the numerical solution of the formulated optimal control problems posed above. Figures display the optimal trajectory of the state variables, optimal control functions, the basic reproduction numbers, and co-state variables (shadow prices).

Outcomes for the Baseline Scenario are shown in Figure 4.1 and Figure 4.2. We can see that vaccination rate is at its maximum level for the first three years. Figure 4.1 and Figure 4.2 also show that the recovered population increases

significantly and the susceptible population decreases during early stage of an epidemic when the vaccination is fully implemented at the highest percentage. As the vaccination rate drops after the initial period, the exposed population also drops. Meanwhile, the susceptible population starts to grow and quickly makes up most of the total population.

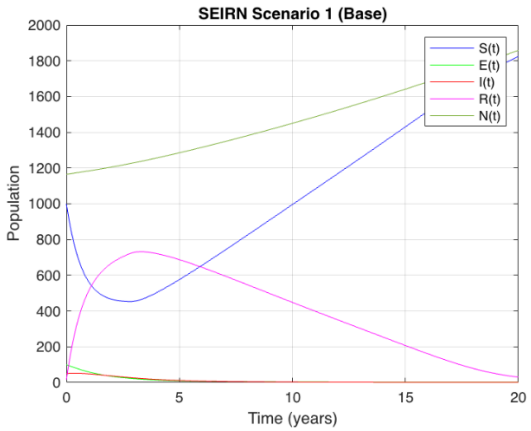


Figure 4.1 Simulation results for Scenario 1, the baseline scenario

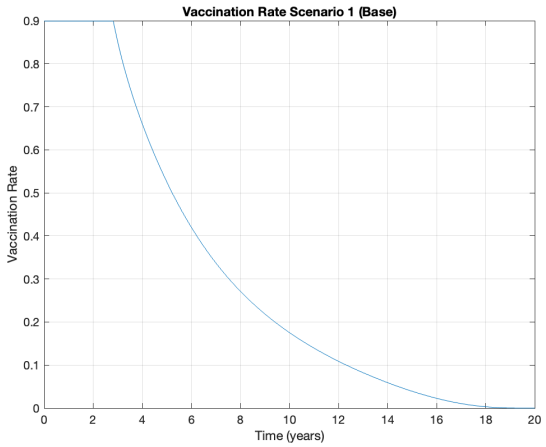


Figure 4.2 Optimal vaccination rate for Scenario 1

Figure 4.3 and Figure 4.4 shows the outcome of the Low Contact Rate Scenario (Scenario 2) where the incidence level is low (β = 0.0001). Compared to outcomes in the Baseline Scenario (Figure 4.2) where a normal incidence level is assumed, the vaccination strategy in the Low Contact Rate Scenario (Figure 4.4) is significantly less aggressive when the disease incidence level is low. As vaccination starts, the infected population drops significantly. By year 5, the vaccination rate remains at a low level as the spread of disease is under control. The recovered population grows rapidly during the first two years and then gradually decreases as vaccination ends. The susceptible population drops significantly for the first two years due to the vaccination implementation, and then starts to grow closer towards the total population, eventually making up the entire population towards the end of the horizon.

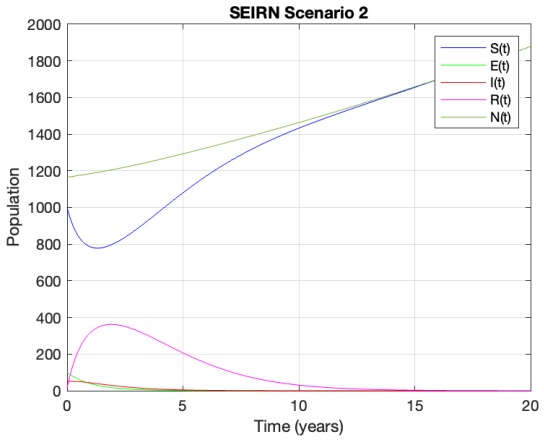


Figure 4.3 Simulation results for Scenario 2 with low disease incidence level

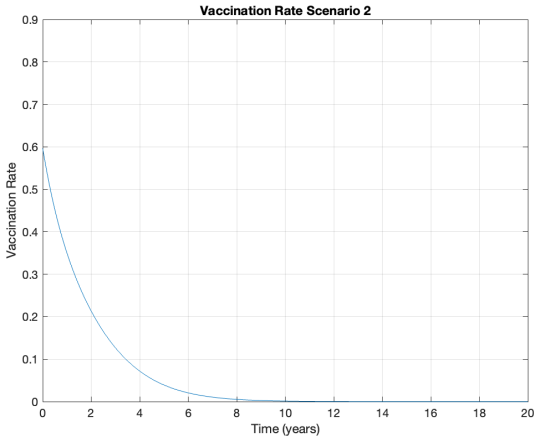


Figure 4.4 Optimal vaccination rate for Scenario 2

In the High Recovery Rate Scenario (Scenario 3), we investigate a scenario with a higher recovery rate, but with all other parameters unchanged from the Baseline Scenario. We can see from Figures 4.5 and 4.6 that, with a higher recovery rate (γ = 0.4 vs γ = 0.1), we can shorten the period for maximum vaccination level from three years to less than two years. The Recovered population initially increases when vaccination is fully implemented and then decreases quickly as vaccination percentage drops after one year. We can observe similar patterns but opposite directions for the Susceptible: the population for susceptible group drops quickly during the initial year of epidemic, as most people are vaccinated and removed from the Susceptible category. However, the Susceptible size rebounds quickly as the vaccination rate drops. Infection rates are so low that the Susceptible population does not become exposed to infection.

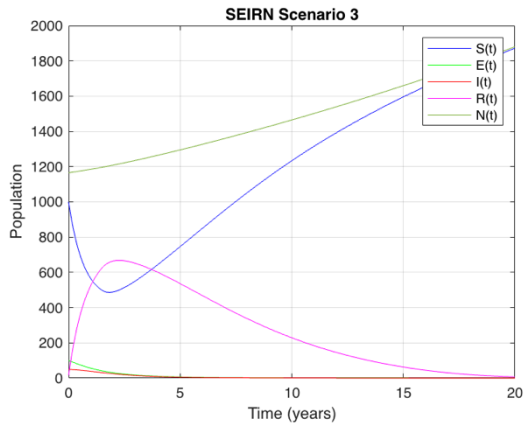


Figure 4.5 Simulation results for Scenario 3 with high recovery rate

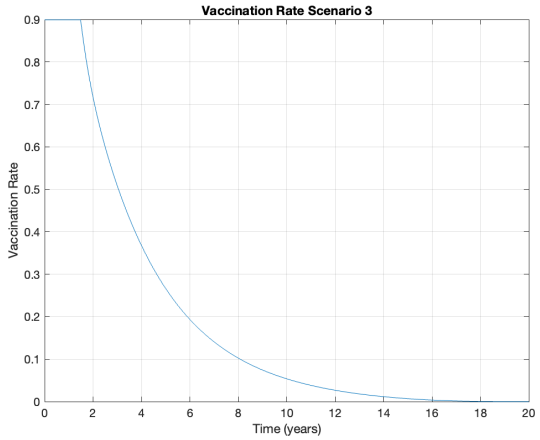


Figure 4.6 Optimal vaccination rate for Scenario 3

In the No Recovery Rate Scenario (Scenario 4), we assume there's zero recovery rate, which is the opposite extreme of the High Recovery Rate Scenario. In this case, the optimal level of vaccination is at the maximum rate for almost four years. In addition, after the initial four years of maximum vaccination, the vaccination rate drops much more slowly in this scenario than in the High Recovery Rate Scenario. As shown in Figure 4.8, the intensity of vaccination program is the strongest (i.e., longer implementation period at maximum level and slower declining rate) for the No Recovery Scenario where recovery rate is assumed to be zero, compared with all other scenarios. This makes sense as nobody recovers and the decline in infected group is due only to death.

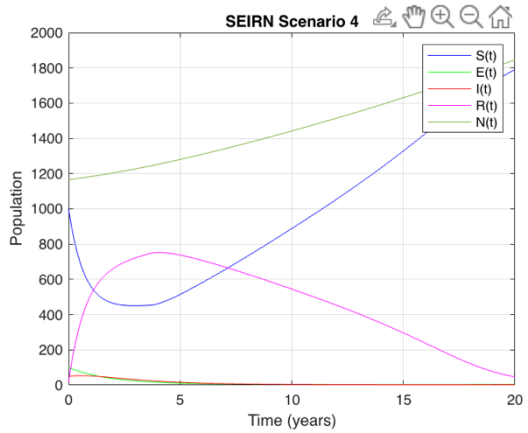


Figure 4.7 Simulation results for Scenario 4 with zero recovery rate

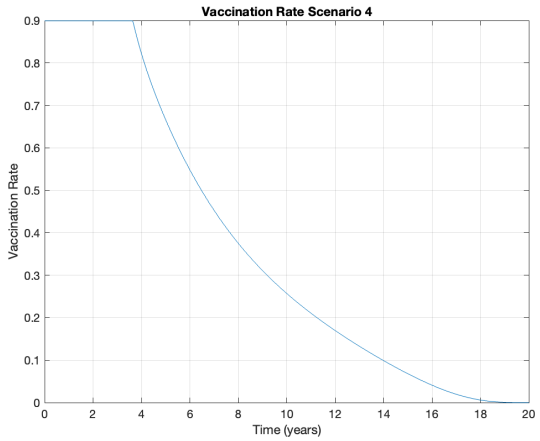


Figure 4.8 Optimal vaccination rate for Scenario 4

The contrasts among Scenarios 1 (Baseline), Scenario 3 (High Recovery Rate Scenario) and Scenario 4 (No Recovery Rate Scenario) demonstrate that, if it is possible to increase the recovery rate, the implications are dramatic. If the recovery rate for the infectious disease is low, *ceteris paribus*, the optimal vaccination strategy becomes more aggressive with a prolonged implementation period at the maximum level and slowly declining vaccination rates afterwards. If the recovery rate for the infectious disease is high, then a less intense vaccination plan can be implemented. Thus, to understand the relative importance of the recovery rate to the vaccination strategy, additional sensitivity analysis is carried out.

As shown in Figure 4.9 below, assuming other disease transmission parameters are held constant over time, a lower recovery rate requires a longer period of maximum level of vaccination, and vice versa. Also, as shown in Figure 4.10, overall net benefits increase with higher recovery rates. The overall net benefit is calculated as the integral $\int_0^T AN(t) - cu(t)^2\, dt$. From Figure 4.10 we can observe a non-linear relationship between overall net benefit and the recovery rate: when recovery rates are within a low range, i.e. less than 0.5, the increase of overall net benefits is more obvious with every unit increase of recovery rate. Thus, the level of the recovery rate parameter can have a direct impact on the intensity of the optimal vaccination plan. A high recovery rate can effectively reduce the optimal intensity of vaccination program, limiting the cost of vaccine implementation. Observations from the recovery rate assumption suggests that social planners can take the recovery rate of infectious disease into account when determining the optimal vaccination strategy.

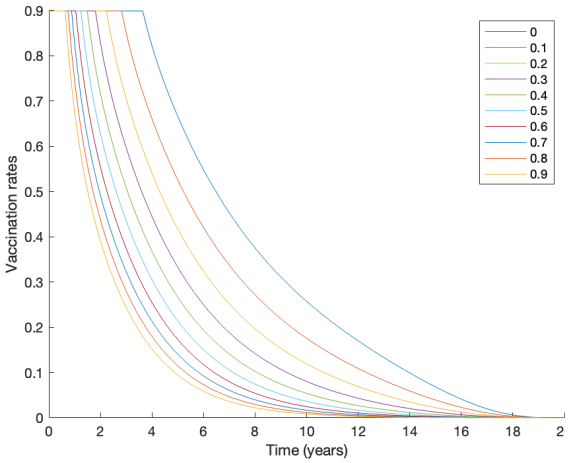


Figure 4.9 Vaccination Strategy with different level of recovery rates

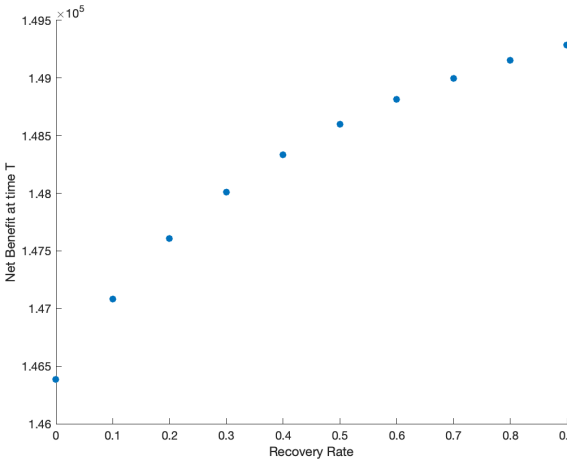


Figure 4.10 Cumulative Net Benefits with different recovery rates

In the High Mortality Rate Scenario (Scenario 5), we show simulation results with a high mortality rate caused by the disease. In this case, we investigate a scenario with higher disease-induced death rate but keep all other parameters unchanged from the baseline. As shown in Figure 4.12, the optimal path of vaccinations, however, is highly comparable to the one in the Baseline Scenario (shown in Figure 4.2).

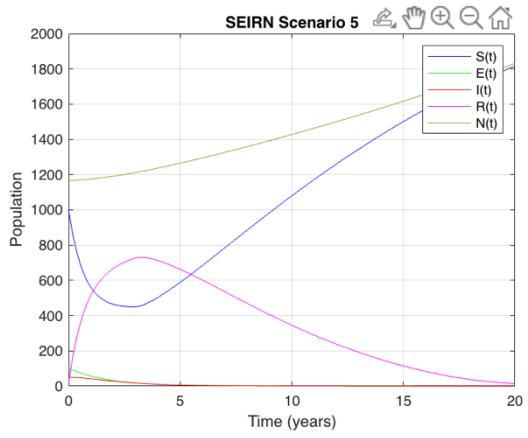


Figure 4.11 Simulation results for Scenario 5 with high disease mortality rate

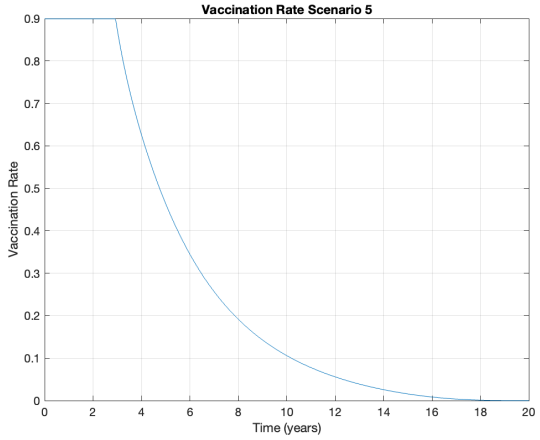


Figure 4.12 Optimal vaccination rate for Scenario 5

Figure 4.13 shows the optimal paths for all scenarios. We see that, by comparing the High Mortality Rate Scenario (Scenario 5, green line) with the Baseline Scenario (Scenario 1, blue line), the early vaccination plan remains at

maximum for the initial three years for both high and low mortality rates. However, the vaccination rate declines faster for the High Mortality Rate Scenario (Scenario 5, green line) than for the Baseline Scenario (Scenario 1, blue line) as more individuals are removed from the population due to the high mortality rate.

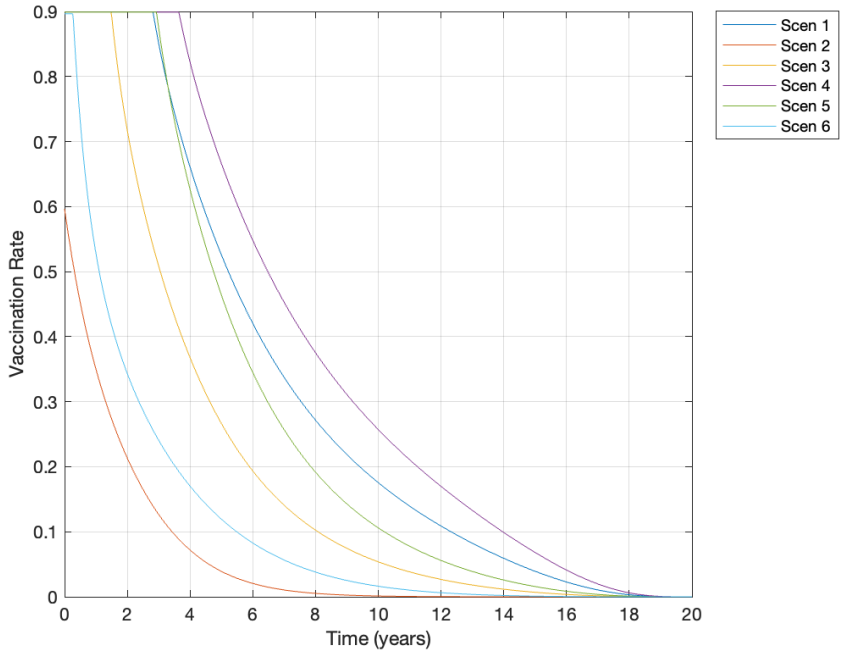


Figure 4.13 Simulation results of vaccination rates for all scenarios

Similarly, we can observe from Figure 4.15, Figure 4.16 and Figure 4.17 that Exposed, Infected, and Recovered populations decline faster in the High Mortality Rate Scenario (Scenario 5, green line) than in the Baseline Scenario (Scenario 1, blue line) due to the high mortality rate. Figure 4.14 shows that Susceptible populations for both scenarios drop at the same speed, as the vaccination level remains at maximum level. However, the Susceptible population rebounds at a faster pace for the High Mortality Rate Scenario (Scenario 5, green line) than in the Baseline Scenario (Scenario 1, blue line), which corresponds to the change in vaccination plans shown in Figure 4.13: when the mortality rate is high, fewer people need to be vaccinated and removed from the Susceptible group after the initial period of the pandemic.

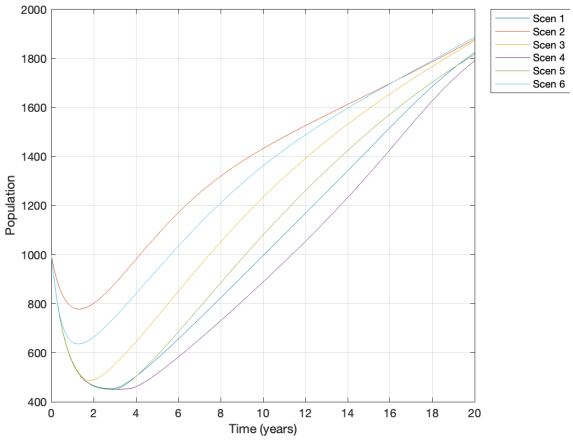


Figure 4.14 Simulation results of Susceptible population for all scenarios

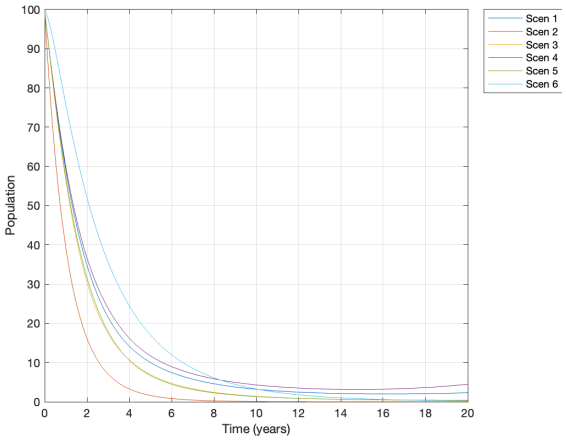


Figure 4.15 Simulation results of Exposed population for all scenarios

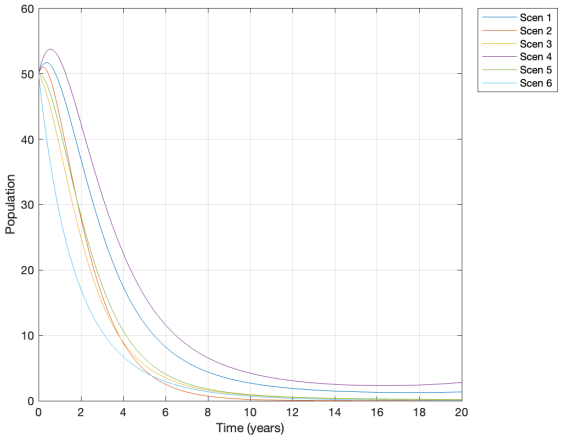


Figure 4.16 Simulation results of Infected population for all scenarios

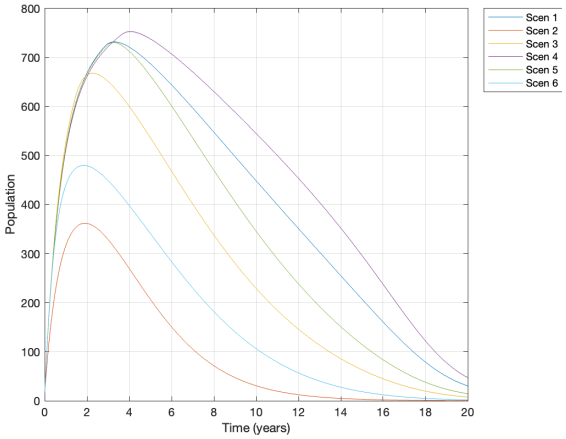


Figure 4.17 Simulation results of Recovered population for all scenarios

In the Long Incubation Period Scenario (Scenario 6), we assume a lower rate (ϵ = 0.1) at which the exposed individuals become infectious than in the baseline scenario (ϵ = 0.5). The latency period is defined as 1/ ϵ. Therefore, a lower progression rate from exposed to infected group represents a longer incubation period. In this scenario, by changing the progression rate from 0.5 to 0.1, we assume the disease has an incubation period five times as long as in the baseline. In other words, the exposed group takes five times longer to develop symptoms in the Long Incubation Period Scenario than in the baseline scenario. The contrast between simulation results shown in Figure 4.19 (Long Incubation Period Scenario) and Figure 4.4 (Baseline Scenario) indicates that initial round of

maximum level of vaccination is not as extensive when the incubation period is long. If the incubation period is long, *ceteris paribus*, the vaccination strategy can become less aggressive. Figure 4.18 shows that when the vaccination rate drops, the exposed population also drops, but the Susceptible group starts to grow and quickly makes up most of the total population.

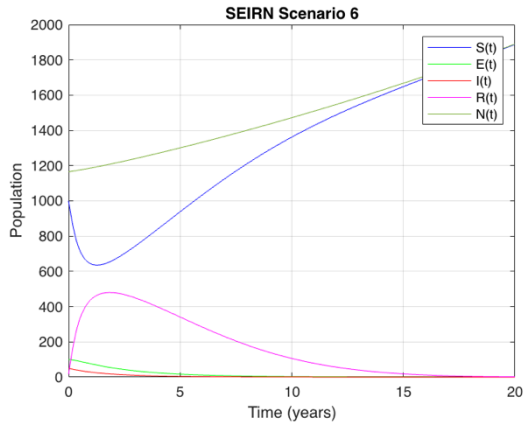


Figure 4.18 Simulation results for Scenario 6 with long incubation period

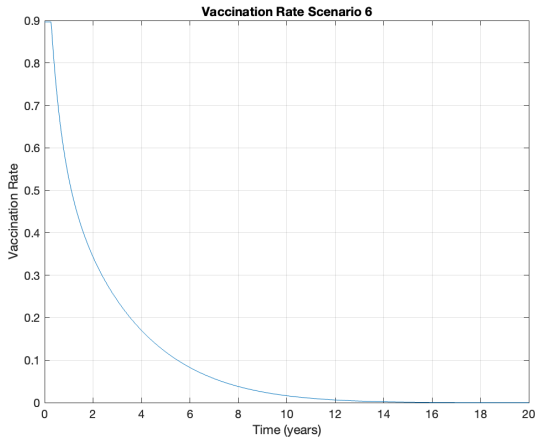


Figure 4.19 Optimal vaccination rate for Scenario 6

In addition to testing the sensitivity of key transmission parameters, we also explore sensitivity of weight parameters. Compared to baseline, when the parameter value for total population becomes 1 (High Benefit Scenario, Scenario 7), the maximum vaccination rate will be extended until year 9, the longest period of time among all scenarios, as shown in Figure 4.21. When the value of maintaining the population increases, the vaccination level should be at its maximum for an extended period. This makes sense, as maintaining the population can be interpreted as maintaining high level of the nation's wellbeing. Thus, to reach high level of total population, an intense vaccination effort is required for an extended period, limiting the infection and death rates.

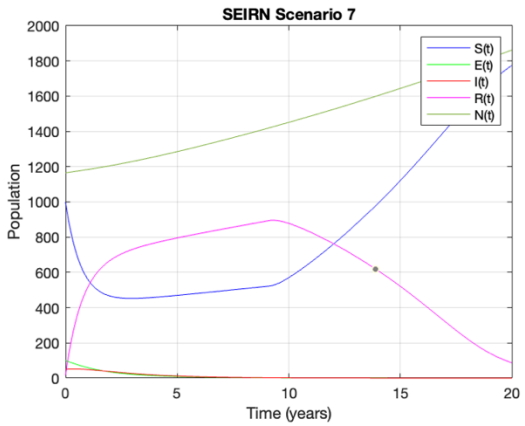


Figure 4.20 Simulation results for Scenario 7 with long incubation period

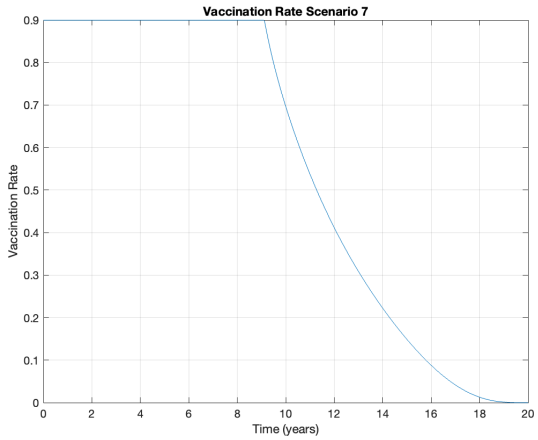


Figure 4.21 Optimal vaccination rate for Scenario 7

Next, we explore sensitivity of weight parameter on vaccination cost. Compared to the Baseline Scenario, when the cost parameter value for vaccination drops from 1 to 0.5 in the Low Vaccination Cost Scenario (Scenario 8), the maximum vaccination rate will be extended until year 8, as shown in Figure 4.23, which is longer than the three year period of maximum vaccination effort in the Baseline scenario, as shown in Figure 4.2. The comparison between high and low vaccination costs implicates that if vaccination cost drops, assuming all other parameters are the same, the vaccination plan can be carried out for an extended period of time.

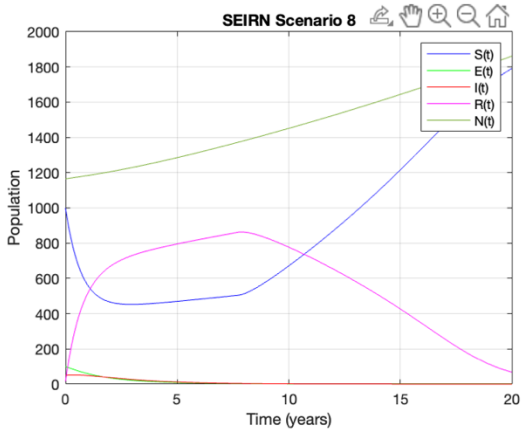


Figure 4.22 Simulation results for Scenario 8 with long incubation period

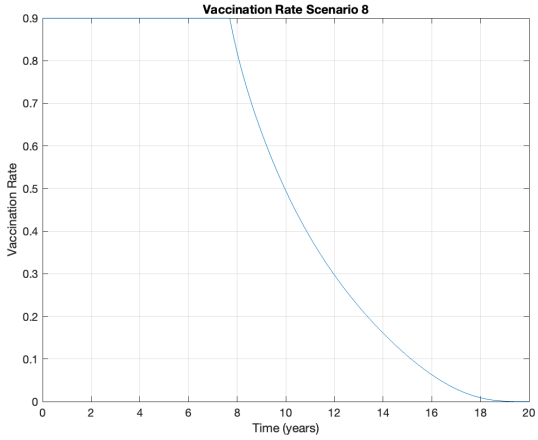


Figure 4.23 Optimal vaccination rate for Scenario 8

To summarize, there are several important indications from the above simulation results. First, from a disease control perspective, an early round of vaccination is a key part of disease management. The vaccination schedule needs to be carried out at its maximum level for initial period when necessary. Only when the disease is less infectious with a low incidence rate, as shown in the Low Contact Rate Scenario (Scenario 2), should only a small proportion of population be vaccinated.

Second, if the recovery rate of the infectious disease is known to be high, then a less aggressive vaccination plan can be considered. These results are indicated in Figure 4.13, where the maximum level of vaccination only needs to be carried out for fewer than two years in the High Recovery Rate Scenario (Scenario 3, yellow line), instead of three years in the Baseline Scenario (blue line). Therefore, from disease control and cost control perspective, the intensity of vaccination campaign can be reduced when the recovery rate is high.

In contrast, the Zero Recovery Rate Scenario (Scenario 4) requires the most aggressive vaccination strategy. When no recovery can occur, significant amount of immunization through vaccines is needed to maintain survival. In this extreme scenario, the maximum level of vaccination needs to be carried out for the longest period (purple line) and declines at slowest speed afterwards among all other scenarios, as shown in Figure 4.13.

Third, assume all else equal, if the benefit of maintaining total population is high or the cost of implementing vaccination plan is low, then it makes sense to have an extended vaccination period, as shown in Figure 4.21 and Figure 4.23. Therefore, from disease control and cost control perspectives, a social planner can take the weight parameter on total population and vaccination cost into account when determining the optimal vaccination strategy.

4.2 Numerical Results for Shadow price

Constraints in the optimal control problem also have important economic interpretations. As shown in Figure 4.24, Figure 4.25, Figure 4.26, and Figure 4.26, shadow prices ($\lambda_1, \lambda_2, \lambda_3, \lambda_4$) indicate the marginal variation in the value function with respect to each state variable at each point in time. Previously defined transversality conditions $\lambda_1(T) = 0$, $\lambda_2(T) = 0, \lambda_3(T) = 0, \lambda_4(T) = 0$ in Section 3.1, equations (3-7), are all met. Transversality conditions dictate that as t moves towards the terminal time T, shadow values of the state variable must go to zero. In other words, the marginal variation of additional increase in the state variable becomes zero towards the end of horizon.

Figures show that, in general, during the early stage of the pandemic when vaccination plan is carried out at maximum effort, the marginal value of reducing population in disease transmission such as Exposed, Infected, and Recovered keeps growing and eventually flattens out towards the end of horizon. Among all scenarios, the marginal value of reducing Susceptible, Exposed, and Infected population grows most rapidly in Scenario 5 (High Mortality Rate Scenario, green line) when disease mortality is high. This makes sense, as fewer people are exposed or infected, higher marginal benefits in the value function can be achieved. This is especially the case when the disease mortality rate is the highest. In contrast, the marginal value of increasing total population becomes smaller at each point in time as more people are removed from the disease transmission system, such as the Exposed, Infected, and Recovered groups. Note that the shadow price for the Recovered population is not presented, as R(t) does not appear in the other differential equations of $\dot{S}(t), \dot{E}(t), \dot{I}(t), \dot{N}(t)$.

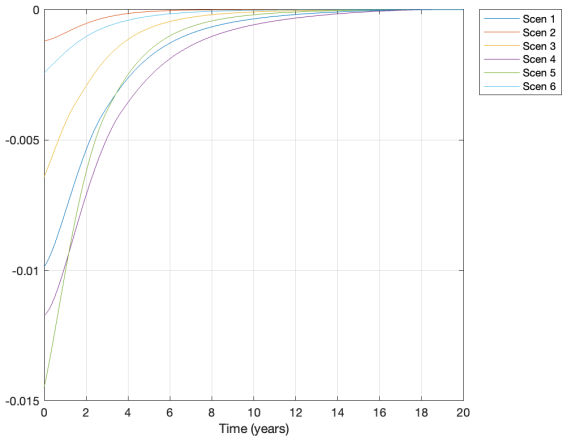


Figure 4.24 Shadow price for the Susceptible (λ_1)

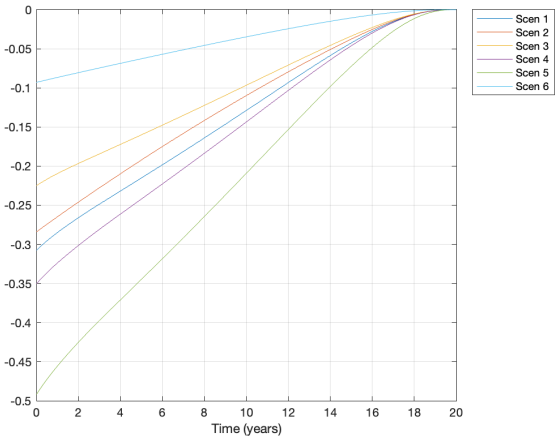


Figure 4.25 Shadow price for the Exposed (λ_2)

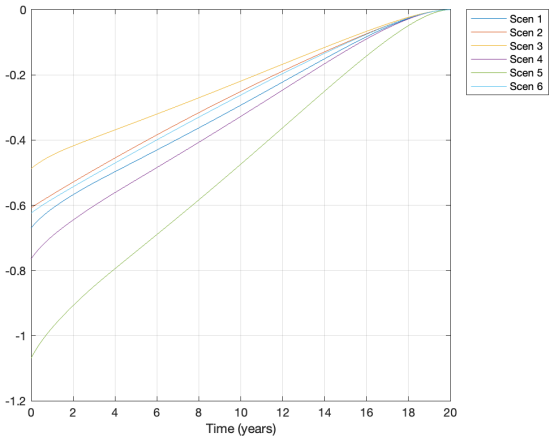


Figure 4.26 Shadow price for the Infected (λ_3)

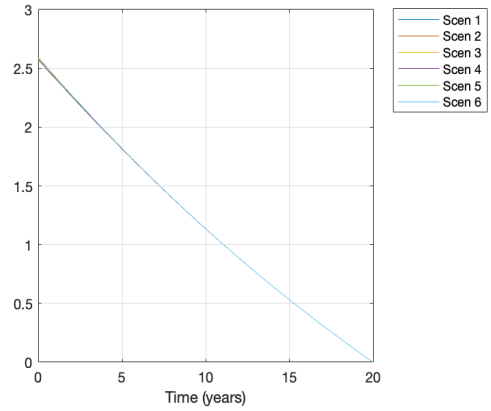


Figure 4.27 Shadow price for total population (λ_4)

4.3 Numerical Results for Basic Reproduction Number:

In this section, we evaluate the impact of optimal control strategies on the total infection number under various baseline reproduction numbers. Recall that the baseline reproduction number is an indicator of virulence—the higher the $\mathcal{R}_0$, the more secondary infections can result from a single primary infection. We calculate different basic reproduction numbers (Equation 2.8) by varying the key disease transmission parameters one at a time. Meanwhile, the optimal control solution is recalibrated numerically with different disease transmission parameter values. Additionally, the SEIR transmission dynamics derived in section 2.1, are also solved without optimal control (u = 0) via the “ode45” function in MATLAB,

using Equation (2-9). Then we explicitly focus on the total infected population numbers with and without optimal control, and these are presented with the corresponding basic reproduction numbers. Figures below are graphical representations of $\mathcal{R}_0$ against total infected population with (red dots) and without optimal control (blue dots). Furthermore, the 3D plots below highlight the sensitivity of $\mathcal{R}_0$ with respect to each of the transmission parameters.

As presented in the figures below, among all key disease transmission parameters, namely contact rate β, progression rate ϵ, mortality rate δ, and recovery rate γ, $\mathcal{R}_0$ is most sensitive to changes in the contact rate β. Therefore, $\mathcal{R}_0$ changes significantly with changes in contact rate β, as shown in Figure 4.28. Values for $\mathcal{R}_0$ only vary within a limited range (mostly below 1) with changes in progression rate ϵ, mortality rate δ, and recovery rate γ.

Figure 4.28 shows that the infected population size increases as $\mathcal{R}_0$ increases. Figure 4.29 shows that the increase of $\mathcal{R}_0$ is driven by the increasing contact rates. However, Figure 4.28 also shows that the infected population size increases much slower when optimal control is applied (red dots) and when $\mathcal{R}_0 <$ 4. In the absence of any vaccination (blue dots), the infected population increases significantly when $\mathcal{R}_0$ is below 4 but slows down when $\mathcal{R}_0$ becomes even larger. Intuitively, if the secondary infection is out of control, then implementing vaccination alone is not enough to prevent the outburst of case numbers. Thus, this result suggests that vaccination strategy needs to be carried out in a timely manner during the early stage of a pandemic when the spread of disease is still under control. In case of a pandemic, the reasonable range for the basic reproduction number should be 1.5-6.49. If a vaccination plan is implemented when $\mathcal{R}_0 <$ 4, then the case number is likely to grow at a slower pace than with no vaccination. However, if $\mathcal{R}_0 >$ 4, suggesting much severe spread of infectious disease, then the social planner needs to consider stronger preventive measures than vaccination alone. In this case, when $\mathcal{R}_0 >$ 4, the growth of case numbers

flattens even without any vaccination, which is possible due to the decreasing population from high mortality.

As shown in Figure 4.30, Figure 4.32, and Figure 4.34, when $\mathcal{R}_0$ is low ($\mathcal{R}_0$ < 0.5), implementing a vaccination program is not as meaningful as when $\mathcal{R}_0$ becomes higher ($\mathcal{R}_0$ > 0.5) because the infected population with control grows at slower pace only when $\mathcal{R}_0$ is high enough. This suggests that a social planner needs to consider existing secondary infection status prior to implementing a vaccination strategy. For example, if $\mathcal{R}_0$ is within a very low range (i.e. $\mathcal{R}_0$ < 0.5), then no vaccination action needs to be taken. But when $\mathcal{R}_0$ reaches a certain range (i.e. 0.4 < $\mathcal{R}_0$ < 4), the effect of vaccination plan can effectively slow down the growth of infected population and therefore limit the infection population size. However, if secondary infection is out of control, i.e. $\mathcal{R}_0$ > 4 in this case, then a vaccination strategy alone is not effective enough to curtail the growth of case numbers and therefore other control measures should be considered.

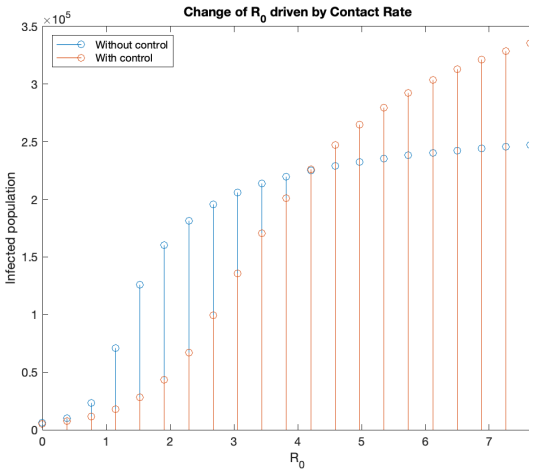


Figure 4.28 Basic Reproduction Number by Contact Rate

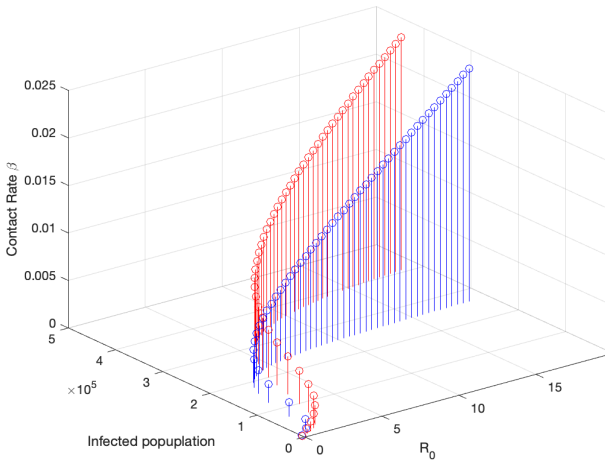


Figure 4.29 3D plot of Basic Reproduction Number by Contact Rate and total Infected Population

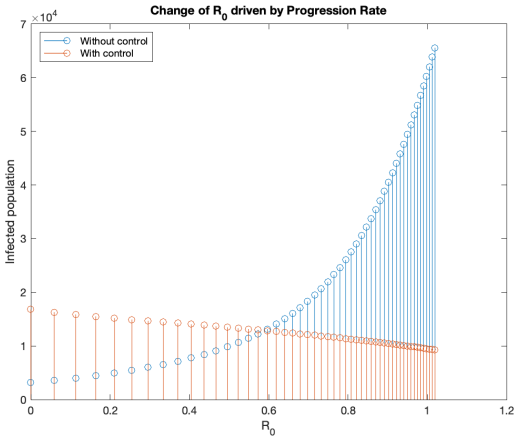


Figure 4.30 Basic Reproduction Number by Progression Rate

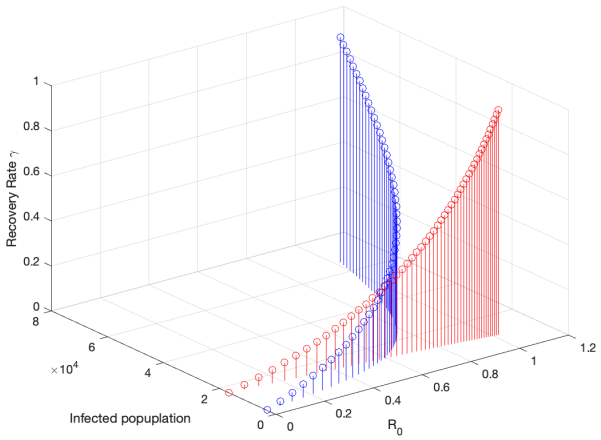


Figure 4.31 3D plot of Basic Reproduction Number by Recovery Rate and total Infected Population

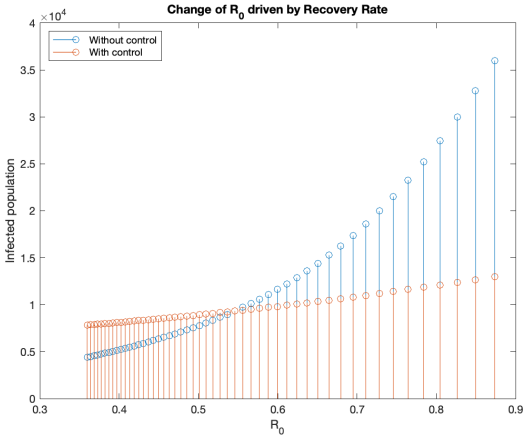


Figure 4.32 Basic Reproduction Number by Recovery Rate

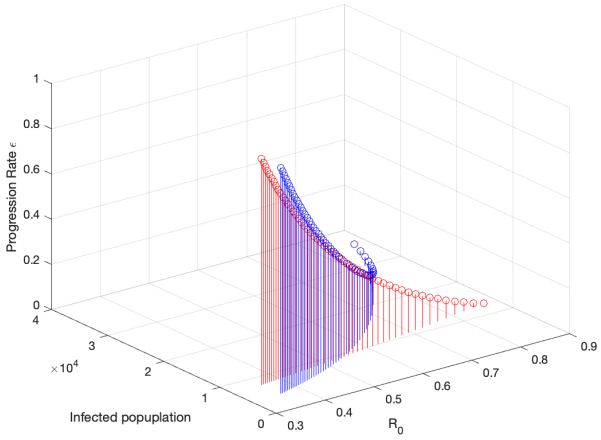


Figure 4.33 3D plot of Basic Reproduction Number by Progression Rate and total Infected Population

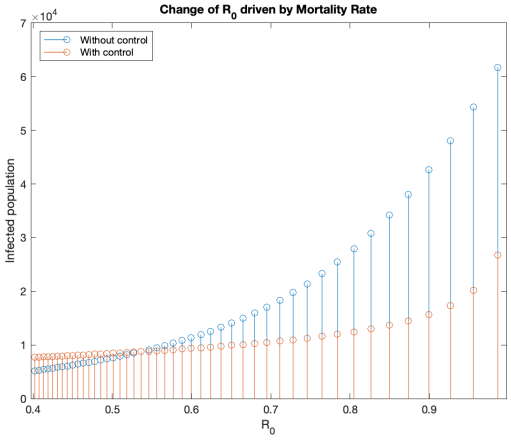


Figure 4.34 Basic Reproduction Number by Mortality Rate

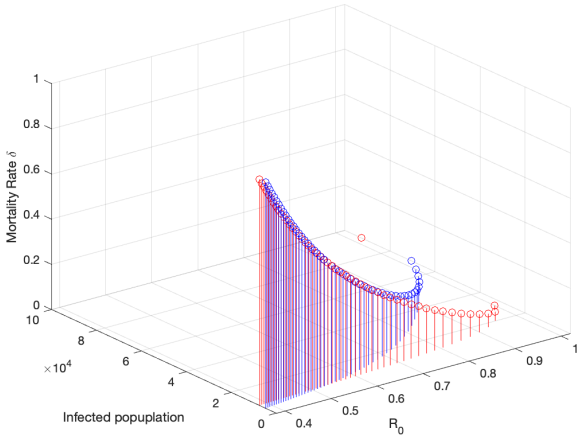


Figure 4.35 3D plot of Basic Reproduction Number by Mortality Rate and total Infected Population

4.4 Numerical Results for Using Terminal Condition

As discussed in section 3.1, equation (3-7), instead of assuming free terminal conditions, we can use a terminal condition such as $I(T) = 0$. In this case, all states are free at the terminal time except for the Infected state. The Infected state is instead fixed at terminal time:

$$\lambda_1(T) = 0\ ,\ \lambda_2(T) = 0, \lambda_4(T) = 0, \text{ but } \lambda_3(T) = k$$

where k is an unknown constant. The value of k directly affects the terminal value of $I(T)$. Note that the normal Forward-Backward Sweep method cannot be used to find the appropriate value of k that ensures terminal value of $I(T)$. Therefore, we use a secant code, a type of shooting method, to find the appropriate value of k that satisfies the endpoint conditions.

From a social planner's perspective, the optimal vaccination schedule should be arranged based on certain goals that need to be achieved at the terminal time. For example, the total infected population should be controlled under a certain threshold by the end of a presidential administration. Therefore, we present a few terminal conditions for $I(T)$ and their corresponding optimal controls and state values below. Note that $I(T) = 0$ was not considered because it is reasonable to assume a small size of infected population remains at the endpoint; total eradication of an infectious disease may be extremely hard to achieve.

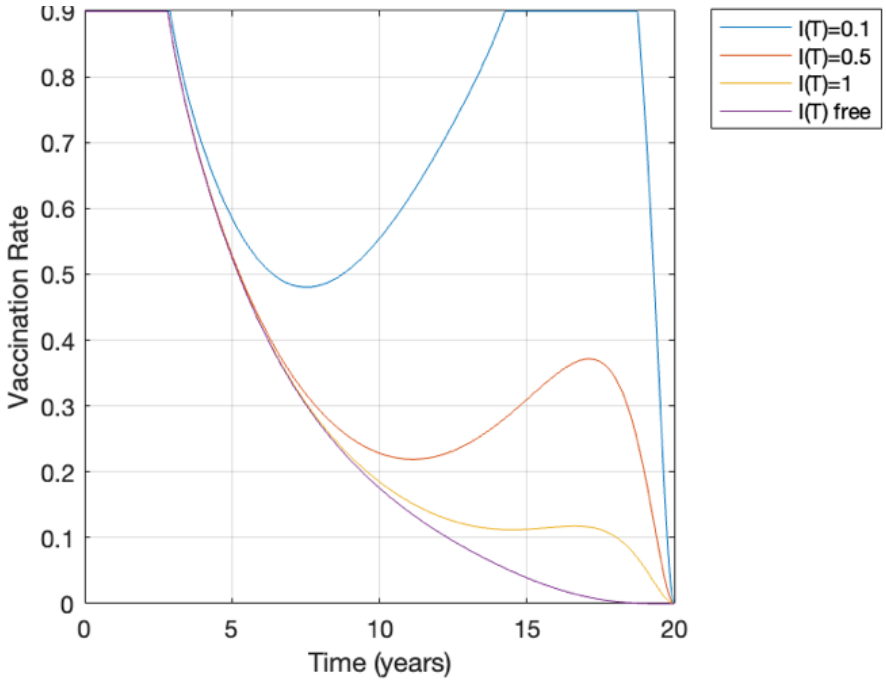
Using the same parameter values in the Baseline Scenario defined at the beginning of this chapter, we compare optimal control solution when $I(T)$ is specified with the optimal control solution to when $I(T)$ is free.

Parameter	Baseline Scenario	Description
b	0.525	Natural birth rate
d	0.5	Natural death rate
$\boldsymbol{\beta}$	0.001	Contact rate
$\boldsymbol{\epsilon}$	0.5	Latency
$\boldsymbol{\delta}$	0.2	Disease induced death rate
$\boldsymbol{\gamma}$	0.1	Recovery rate
A	1	Weight parameter
$\boldsymbol{S_0}$	1000	Initial population size of group S

Parameter	Baseline Scenario	Description
E_0	100	Initial population size of group E
I_0	50	Initial population size of group I
R_0	15	Initial population size of group R
A	0.1	Weight parameter for Total Population N
c	1	Weight parameter for vaccination "u"

Table 4.2 Parameter values in the Baseline Scenario

Figure 4.36 below shows numerical solutions for vaccination rates based on different terminal condition for the infected state at end point. Compare the optimal vaccination schedules across different endpoint assumptions. We can see that when terminal conditions $I(T) = X$ are imposed, all schedules require maximum vaccination initially, then a gradual decrease over a certain period until vaccinations increase later in the time horizon. Smaller endpoint values $I(T) = X$ require a stronger effort in the second surge of vaccinations.



Note that S(T), E(T), and N(T) are free in the above scenarios. The only difference across scenarios is the terminal condition for I(T)

Figure 4.36 Vaccination Rate with different terminal conditions for I(T)

As shown in Figure 4.36, $I(T)$ = 0.1 requires the strongest second-round vaccination effort which is at maximum level for few years prior to the end of the terminal time for those who did not receive vaccination during the first few years. For $I(T) = 0.5$ and $I(T) = 1$, the second-round vaccination effort is still necessary but only proportional to the susceptible population who has not been vaccinated yet. For free $I(T)$ condition, second round of vaccination is not needed, which is equivalent to the optimal control problem in equation (3-7).

The terminal condition of $I(T)$ indicates that, if the social planner wants to ensure only limited infected population can be left out by the end of an administration period, then a second round of vaccination should be considered. Driving $I(T)$ lower requires stronger effort devoted to vaccination later in the time horizon. Note that the second-round vaccination means that people who did not get vaccinated early will receive vaccinations later.

5 Conclusion

This paper first reviews the classic SIR model and then introduces a deterministic SEIR model proposed by Lenhart [5] that considers an incubation period for the disease inside its host. Compared to the classic SIR model, an "exposed" group is introduced into the transmission dynamics. The consideration of an "exposed" group introduces incubation period as one of the key diseases' transmission parameters in the optimal control model. In addition, a vaccination policy is also introduced into the SEIR model as proposed by Lenhart.

To understand the role of vaccination policy in controlling the spread of an infectious disease through a finite time horizon, we set up the Optimal Control problem as proposed by Lenhart. The goal of the optimal control is to find the best vaccination strategy that maximizes net benefits over time with a finite time horizon. We use Pontryagin's Maximum Principle to characterize the optimal level of vaccination. The optimality system is solved using Runge-Kutta of order four scheme (RK4) with the forward-backward sweep algorithm in MATLAB.

Using initial parameter values suggested by Lenhart as the baseline scenario, we explore other scenarios by varying parameter values one at a time. The goal of the simulation is to understand how optimal trajectories of vaccination vary under different assumptions. There are several important observations from the above simulation results.

First, from a disease control perspective, an early round of vaccination is a key part of disease management. The vaccination schedule needs to be carried out at maximum level at the beginning of the pandemic if necessary. As emphasized by sensitivity analysis results for reproduction number, implementing a vaccination plan can effectively slow down the growth of infected population and therefore limit the infection population size in a timely way.

Second, a high recovery rate can effectively reduce the optimal intensity of a vaccination program, limiting the overall cost of vaccine implementation. From a social planner's perspective, if the recovery rate of the disease is already high, then a high-intensity vaccination plan may not be needed, as shown in the simulation results in section 4.1. However, if the disease has no available medical cure and recovery rate is low, then the social planner should consider more intense level of vaccination implementation.

Third, compared to the classic SIR model, the inclusion of an Exposed group in SEIR model allows for an incubation period for the disease inside its host, where an infected person remains latent without clinical symptoms or signs of infection before becoming infectious. As shown in the simulation results, the length of incubation period has a direct impact on optimal vaccination plans: a longer incubation period leads to less stringent vaccination level, and vice versa. Therefore, it is more meaningful and realistic to include an Exposed group when analyzing infectious diseases. From a social planner's perspective, the vaccination plan can be relaxed or tightened, depending on the time that passes between being exposed to a virus and having symptoms.

Fourth, in addition to assuming free terminal conditions, we also explore optimal vaccination trajectories by setting the terminal condition of $I(T)$ to fixed conditions. Comparing the optimal vaccination schedules across different endpoint assumptions of $I(T) = X$, we can see that when terminal conditions are imposed, all schedules require maximum vaccination initially, then a gradual decrease over a certain period until the next round of vaccination is required. A smaller endpoint value $I(T) = X$ requires a stronger vaccination effort later in the time horizon. From social planner's perspective, to ensure only limited infected population left by the end of an administration period, it is necessary to vaccinate a remaining group of individuals who did not receive vaccinations the first time.

Finally, this paper can be further enhanced by considering the dynamic relationships among the key factors for disease transmission and prevalence. For example, as a future enhancement of this paper, we could introduce a second control variable such as a recovery rate into the model. Dual control variables of both recovery rate and vaccination rate will be more meaningful for social planners to maintain the balance between intensity of vaccination level and recovery rate dynamically based on existing treatment plan. In addition, we can also consider a time optimal control model that drives the disease transmission and prevalence from any given initial states to the desired terminal state in minimum amount of time. In this case, the objective function only has a linear term, and the optimal solution can be either Bang-Bang or singular or both. Different from what we are showing in this paper, the solution to a linear problem will involve discontinuities, switching between boundary extreme values of the control set.

6 Bibliography

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7 Appendix

7.1 Optimal Control Problem with Discounting

In section 3.1, we formulated the optimal control problem without considering discounting in objection function equation (3-1). Now we introduce the discounting term $e^{-\rho t}$ into the objective function of the optimal control problem. In addition, we also assign weight parameters into the objective functions.

$$\text{Max: J(u)} = \int_0^T [A * N(t) - c * u(t)^2] e^{-\rho t} dt \quad (7\text{-}1)$$

Subject to

$$\dot{S}(t) = bN(t) - dS(t) - \frac{\beta S(t) I(t)}{N(t)} - u(t)S(t) \quad (7\text{-}2)$$

$$\dot{E}(t) = \frac{\beta S(t) I(t)}{N(t)} - (\epsilon + d)E(t) \quad (7\text{-}3)$$

$$\dot{I}(t) = \epsilon E(t) - (d + \delta + \gamma)I(t) \quad (7\text{-}4)$$

$$\dot{N}(t) = (b - d)N(t) - \delta I(t) \quad (7\text{-}5)$$

The current-value Hamiltonian for this problem is

$$\begin{aligned} &\mathrm{H^C(S(t), E(t), I(t), N(t), u(t), t)} \\ &= AN - cu^2 + \mu_1 \left(bN - dS - \frac{\beta SI}{N} - uS \right) + \mu_2 \left[\frac{\beta SI}{N} - (\epsilon + d)E \right] \\ &+ \mu_3[\epsilon E - (d + \delta + \gamma)I] + \mu_4[(b - d)N - \delta I] \end{aligned} \quad (7\text{-}6)$$

where $\mu_1, \mu_2, \mu_3, \mu_4$ are current-value shadow prices

$$\dot{\mu_1} = \rho\mu_1 - \frac{\partial H^C}{\partial S} = \rho\mu_1 + \left(d + u^* + \frac{\beta I}{N}\right)\mu_1 - \frac{\beta I}{N}\mu_2$$

(7-7)

$$\dot{\mu_2} = \rho\mu_2 - \frac{\partial H^C}{\partial E} = \rho\mu_2 + (\epsilon + d)\mu_2 - \epsilon\mu_3$$

(7-8)

$$\dot{\mu_3} = \rho\mu_3 - \frac{\partial H^C}{\partial I} = \rho\mu_3 + \frac{\beta S}{N}\mu_1 - \frac{\beta S}{N}\mu_2 + (d + \delta + \gamma)\mu_3 + \delta\mu_4$$

(7-9)

$$\dot{\mu_4} = \rho\mu_4 - \frac{\partial H^C}{\partial N} = \rho\mu_4 - A - \left(\frac{\beta SI}{N^2} + b\right)\mu_1 + \frac{\beta SI}{N^2}\mu_2 - (b - d)\mu_4$$

(7-10)

The optimal control $u(t)^*$is obtained by invoking the optimality condition, which is achieved by differentiating the Hamiltonian with respect to the control variable:

$$Let\ \frac{\partial H^C}{\partial u} = 0,$$

$$-S * \mu_1 - 2c * u(t) = 0$$

$$u(t)^* = -\frac{\mu_1(t)S(t)}{2c}$$

Parameter	Scenario 7 Baseline	Scenario7 Low Discount rate (new base)	Scenario8 High Discount rate	Scenario9 High Benefit	Scenario10 High cost	Description
b	0.525					Natural birth rate
d	0.5					Natural death rate
β	0.001					Disease transmission rate
ϵ	0.5					Latency
δ	0.2					Disease induced death rate
γ	0.1					Recovery rate
A	1			2		Weight parameter for Total Population N

Parameter	Scenario 7 Baseline	Scenario7 Low Discount rate (new base)	Scenario8 High Discount rate	Scenario9 High Benefit	Scenario10 High cost	Description
S_0	1000					Initial population size of group S
E_0	100					Initial population size of group E
ρ	NA	0.05	0.2			Discount rate
c	1				0.5	Weight parameter for vaccination "u"
I_0	50					Initial population size of group I
R_0	15					Initial population size of group R

Table 7.1 Parameter values use in each scenario

Without discount rates, patterns for SEIRN paths are smooth overtime, as shown in the simulation results in section4.1. As shown in the figures below, with 2% discount rate (scenario 7), the maximum vaccination rate will be extended until year 7. With 20% discount rate (scenario 8), the extended period for maximum vaccination rate drops to 4 years. Patterns for SEIR paths are also smoother in when discount rate is 20%. When parameter value for total population becomes 2 (scenario 9), the maximum vaccination rate will be extended until year 8. When parameter value for vaccination becomes 0.5 (scenario 10), the maximum vaccination rate will be extended until year 10, the longest period of time among all other scenarios. The implication is that, if vaccination cost drops, a more powerful vaccination plan can be carried out for an extended period of time.

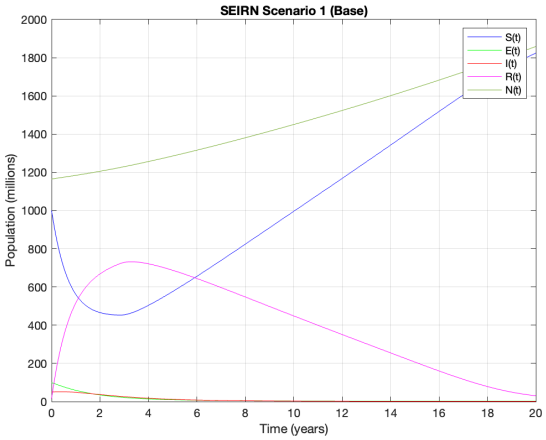

Figure 7.1 Simulation results for Scenario 1, the baseline scenario

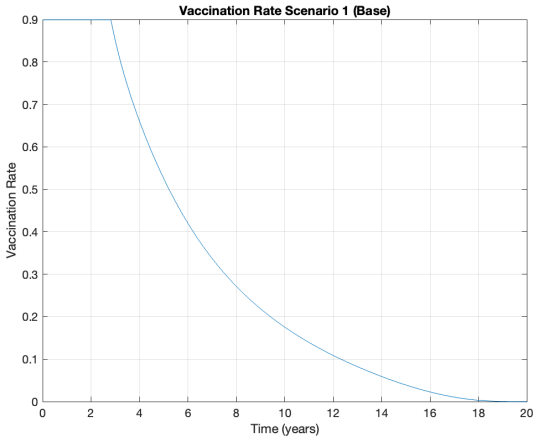

Figure 7.2 Optimal vaccination rate for Scenario 1

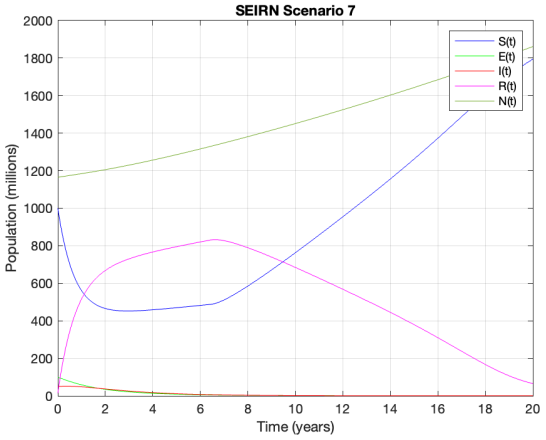

Figure 7.3 Simulation results for Scenario 7, with 2% discount rate

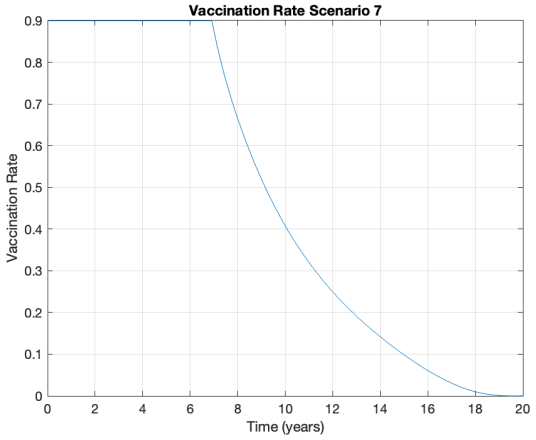

Figure 7.4 Optimal vaccination rate for Scenario 7

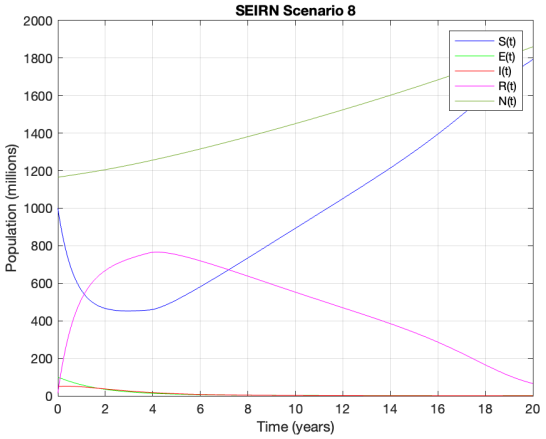

Figure 7.5 Simulation results for Scenario 8, with high discount rate

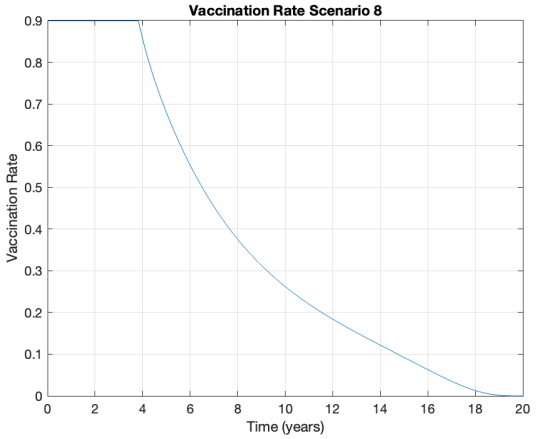

Figure 7.6 Optimal vaccination rate for Scenario 8

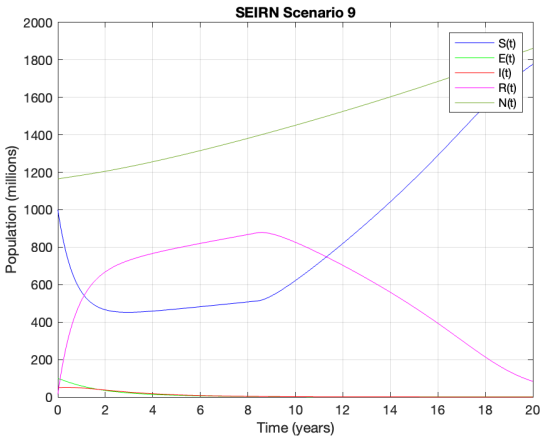

Figure 7.7 Simulation results for Scenario 9 with A = 2

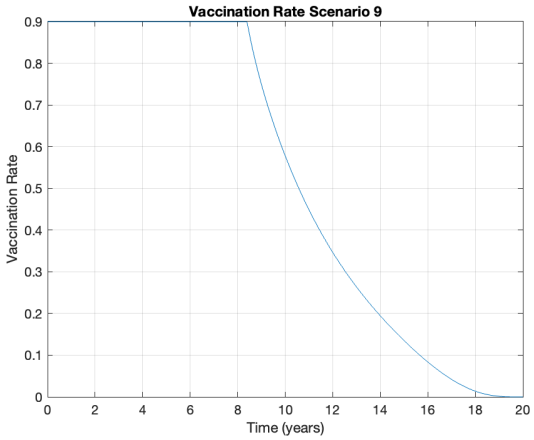

Figure 7.8 Optimal vaccination rate for Scenario 9

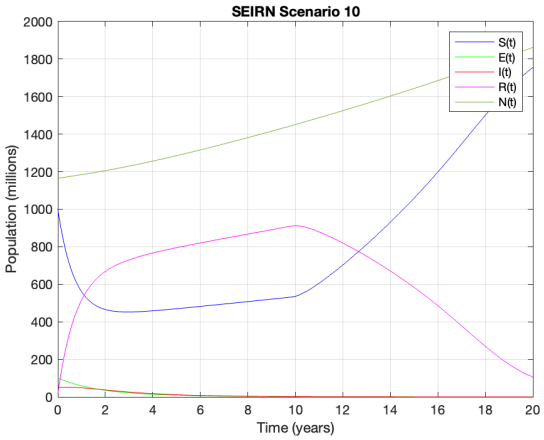

Figure 7.9 Simulation results for Scenario 10 with c = 0.5

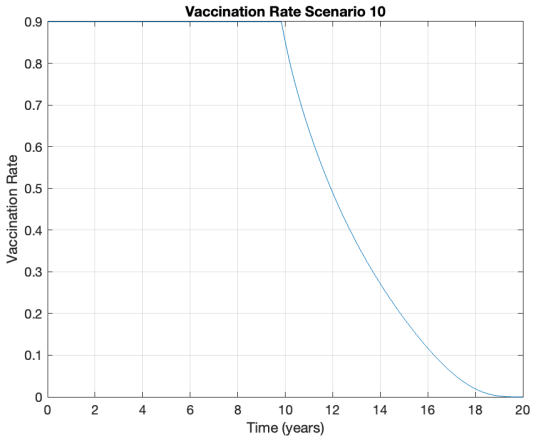

Figure 7.10 Optimal vaccination rate for Scenario 10