Chapter 1

Mathematical Model

1.1 Problem description and assumptions

We incorporate the widely used epidemiological compartmental model, Susceptibles Infected Recovered (SIR) model. In this model, births and deaths are neglected, and the recovered population is assumed to no longer infect others and cannot be reinfected. Here, the SIR model captures the importation of infected non-resident travellers. Our model and analysis follow from Hansen and Day (2011) [4]. We address epidemics with no vaccination, where the possible controls are community isolation and traveller isolation measures. We model these measures via finite time controls $(u_1(t), u_2(t)) \in [0, u_{1\max}] \times [0, u_{2\max}]$, where 0 corresponds to no control and $u_{1\max}, u_{2\max}$ correspond to when we have maximum daily rate of community isolation and traveller isolation respectively. We denote S, I_1, I_2 the number of susceptibles, community prevalence, and traveller's prevalence, respectively, and their evolution is governed by the following system of nonlinear ordinary differential equations.

$$\frac{dS}{dt} = -\beta S(I_1 + cI_2), \tag{1.1}$$

$$\frac{dI_1}{dt} = \beta S(I_1 + cI_2) - (\mu + u_1(t))I_1, \tag{1.2}$$

$$\frac{dI_2}{dt} = \theta - (\gamma + u_2(t))I_2, \tag{1.3}$$

with $S(t_0) > 0, I_1(t_0) \geq 0, I_2(t_0) \geq 0,\ \beta, \mu, \theta, \gamma, c \geq 0$, where β is the transmission rate, μ is the per capita loss rate of infected community members through both mortality and recovery, θ is the baseline number of infected non-resident travellers per unit time, γ is the removal rate of non-resident travellers and c is the relative transmissibility of travellers. We assume that non-resident travellers who are infected have contracted the infection before entering the community, and therefore are promptly either recovered or removed from the community, i.e. $\gamma > \mu$.

Moreover, $u_2(t)$ is defined as a post-arrival traveller isolation (daily rate) representing the post-arrival travel isolation measure. This is implemented after travellers arrive to reduce the spread of infection from incoming cases. It Includes actions like quarantine, isolation, and testing of travellers. $u_2(t)$ is integrated into the model as a control variable affecting the rate of change of I_2 (infected non-resident travellers).

1.2 Objectives and contributions

The modelling and assumptions in the present work are motivated by epidemics, which are mainly managed through broad NPIs with limited resources and without vaccines. To understand the effects of NPIs on an entire population, we stick to model (1.1)-(1.3) with isolation of infected community members and travellers.

Our primary objective is to understand the timing and best control strategies for implementing isolation and travel restrictions. That is;

1. Identify when different public health strategies are optimal, as defined by optimal control theory.

2. Extend existing results to consider imported infections and travel measures.

To this end, we also investigate solutions in specific scenarios (such as isolation-only (no importation), isolation-only (with importations), traveller isolation-only, and mixed strategies).

1.3 Defining an outbreak end-point

One aspect of this work is that the problem is posed in terms of the infinite time limit but formulated in a way that only requires a solution over a finite time interval. We assume that the interventions last a finite time T, the maximum time that the population will adhere. The selection of the terminal time T is one possible issue with optimal control [4]. Hansen and Day defined an outbreak as over at $t = T$ if prevalence is less than a small value, $I_{\min}$. This approach prevents a second wave of infection arising from a fractional individual [4]. Defining an outbreak end-point in this way is necessary to consider elimination strategies as a possible recommended strategy [6].

1.4 Resource Constraints (Optimal Control Problem)

Let $U_{1[u_1,u_2]}(T)$, $U_{2[u_1,u_2]}(T)$ denote the total number of community residents and travellers that need to be isolated at time T respectively and $U_{1\max}, U_{2\max}$ the total resources available for community isolation and traveller isolation respectively. Examples of such resources include healthcare provisions like well-equipped isolation centers and quarantine facilities stocked with essential medical supplies. This also encompasses a robust supply of rapid and accurate testing kits for detecting infections, as well as personal protective equipment (PPE) such as masks, gloves, gowns, face shields, and sanitizers for both healthcare workers and the general public. Financial resources are crucial as well, as they involve allocating funds to bolster healthcare systems and provide financial assistance to individuals in isolation. Moreover, basic necessities such as food, water, and essential supplies must be made available to those in isolation.

In keeping with [4], we assume that these resources are limited, such that,

$$U_{1[u_1,u_2]}(T) = \int_0^T u_1(t) I_{1[u_1,u_2]} \, dt \leq U_{1\max} \tag{1.4}$$

and

$$U_{2[u_1,u_2]}(T) = \int_0^T u_2(t) I_{2[u_1,u_2]} \, dt \leq U_{2\max}. \tag{1.5}$$

The aim of public health measures is assumed to minimize the number of new infections,

$$J = \int_0^T \beta S_{[u_1,u_2]} (I_{1[u_1,u_2]} + c I_{2[u_1,u_2]}) \, dt \tag{1.6}$$

subject to the resource constraints (1.4)-(1.5).

Without constraints, thus when we have no resource limitations on the controls, we get,

$$U_{1[u_1,u_2]}(T) = \int_0^T u_1(t) I_{1[u_1,u_2]} \, dt \tag{1.7}$$

and

$$U_{2[u_1,u_2]}(T) = \int_0^T u_2(t) I_{2[u_1,u_2]}\ dt. \tag{1.8}$$

To apply the Pontryagin's Maximum Principle (PMP), we define the Hamiltonian as

$$H(t) = \lambda_0 \beta S(I_1 + I_2) + \lambda_{I_1}\frac{dI_1}{dt} + \lambda_{I_2}\frac{dI_2}{dt} + \lambda_{U_1}\frac{dU_1}{dt} + \lambda_{U_2}\frac{dU_2}{dt}. \tag{1.9}$$

1.5 Bang-Bang Optimal Controls

Now we concentrate on scenarios characterized by linearity in the controls. The linear optimization problem is defined as that class of optimal control problems in which the control function appears only linearly [3]. In these cases, optimal solutions often incorporate discontinuities in the control variables [5]. Notice that equations (1.1) - (1.3) and the integrand in (1.6) are both linear functions of the controls $u_1(t), u_2(t)$. Thus, the Hamiltonian (1.9) is also a linear function of the controls; hence, the optimality condition contains no information on the controls [5]. The PMP, when applied to bounded control problems that are linear in the control variable, explicitly defines the bang-bang control. However, the bang-bang control is undefined when the switching function is identically singular. The consequence of this problem is that we are not able to find a characterization of the optimal controls.

Remarks 1.5.1. *Hansen and Day [4] show that the optimal control for our problem is bang-bang. Bang-bang control involves switching between two extreme values, typically represented as u_{max} and 0.*

$$u_1^*(t) = \begin{cases} u_{1max}, & \textit{maximum rate of community isolation} \\ 0, & \textit{no community isolation} \end{cases} \tag{1.10}$$

$$u_2^*(t) = \begin{cases} u_{2max}, & \textit{maximum rate of traveller isolation} \\ 0, & \textit{no traveller restrictions} \end{cases} \tag{1.11}$$

1.6 Problem Classification

Next, we classify our general problem into the following four parts:

Problem	**Description**	**Special values of parameters**
1	Community member isolation only, no importations	$\theta = 0, I_2(0) = 0, U_{2\max} = 0$
2	Community member isolation, with importations	$U_{2\max} = 0.$
3	Travel measures only	$U_{1\max} = 0.$
4	Both community member isolation and travel measures	None

Table 1.1: The four problems that we analyze

1.7 Problem 1: Community Isolation Only (no case importation)

The derivation and proof of the theorems of Problem 1 is a direct result of the work of Hansen and Day 2011 [4].

Considering community isolation as the only control in the model, our model now becomes;

$$\frac{dS}{dt} = -\beta S I_1 \tag{1.12}$$

$$\frac{dI_1}{dt} = \beta S I_1 - (\mu + u_1(t)) I_1 \tag{1.13}$$

Our objective function is,

$$\min J = \min \int_0^T \beta S_{[u_1]} I_{1[u_1]} \, dt, \tag{1.14}$$

subject to equations (1.12)-(1.13), $T = \inf\{t | I_{[u_1]}(t) = 1\}, u_1(t) \in [0, u_{1\max}]$ for all $t \in [0, T]$ and subject to the resource constraint

$$U_{1[u_1]}(T) = \int_0^T u_1(t) I_{1[u_1]} \, dt \leq U_{1\max}. \tag{1.15}$$

From equation (1.12), we have

$$dS = \beta S I_1 \, dt \tag{1.16}$$

integrating both sides, we get

$$\int_0^T dS = -\int_0^T \beta S I_1 \, dt, \tag{1.17}$$

$$S(T) - S(0) = -\int_0^T \beta S I_1 \, dt, \tag{1.18}$$

$$S(0) - S(T) = \int_0^T \beta S I_1 \, dt. \tag{1.19}$$

Rearranging equation (1.12), we get

$$\frac{1}{S} \, dS = -\beta I_1 \, dt. \tag{1.20}$$

Taking integral on both sides, we have

$$\int_0^T \frac{1}{S} \, dS = -\beta \int_0^T I_1 \, dt, \tag{1.21}$$

$$-\frac{1}{\beta} \ln\left(\frac{S(T)}{S(0)}\right) = \int_0^T I_1 \, dt. \tag{1.22}$$

We observe from equations (1.19) and (1.22) that the terms on the right-hand side are both minimized by maximizing $S(T)$ since S_0 is a fixed quantity. Next, we state and prove the main result of the community isolation only problem.

Theorem 1.7.1. ***(Optimal Community Isolation Strategy)*** *If $U_{1[u_{1max}]}(T) \leq U_{1max}$, then the optimal community isolation strategy for Problem 1 is $u_1^*(t) \equiv u_{1max}$. If $U_{1[u_{1max}]}(T) > U_{1max}$, then the optimal control $u_1^*(t)$ is any bang-bang control $u_1(t)$ such that $U_{1[u_1^*]}(T) = U_{1max}$.*

The optimal isolation policy, as outlined in theorem (1.7.1), is to implement maximal isolation efforts throughout the epidemic, provided sufficient resources are available. Without adequate resources, the optimal policy defaults to any strategy that utilizes all available resources [4].

Proof **(Theorem** (1.7.1): Following equations (1.12), (1.13) and (1.15), the isolation model with limited resources is described by the system of ordinary differential equations:

$$\frac{dS}{dt} = -\beta S I_1 \tag{1.23}$$
$$\frac{dI_1}{dt} = \beta S I_1 - (\mu + u_1(t)) I_1 \tag{1.24}$$
$$\frac{dU_1}{dt} = u_1(t) I_1 \tag{1.25}$$

Next, we formulate Problem 1 (Sec.1.7) as a maximization problem and apply the PMP. The objective function now becomes,

$$\max J = \max \left(- \int_0^T \beta S_{[u_1]} I_{1[u_1]} \, dt \right) \tag{1.26}$$

We derive the necessary conditions for optimality and the associated adjoint variables. The Hamiltonian is,

$$H(t) = -\lambda_0 \beta S I_1 - \lambda_S \beta S I_1 + \lambda_{I_1} \beta S I_1 - \lambda_{I_1}(\mu + u_1 I_1) + \lambda_{U_1} u_1 I_1 \tag{1.27}$$
$$= -\dot{\lambda}_{I_1} I_1 = -\dot{\lambda}_S S - \lambda_{I_1}\mu + (\lambda_{U_1} - \lambda_{I_1}) u_1 I_1 = 0 \tag{1.28}$$

There are associated adjoint variables, $\lambda_S, \lambda_{I_1}, \lambda_{U_1}$, which correspond to the states S, I_1, and U_1 respectively such that;

$$\dot{\lambda}_S = -\frac{\partial H}{\partial S} = -(\lambda_{I_1} - \lambda_0 - \lambda_S)\beta I_1, \tag{1.29}$$

$$\dot{\lambda}_{I_1} = -\frac{\partial H}{\partial I_1} = -(\lambda_{I_1} - \lambda_0 - \lambda_S)\beta S - (\lambda_{U_1} - \lambda_{I_1})u_1 + \lambda_{I_1}\mu, \tag{1.30}$$

$$\dot{\lambda}_{U_1} = -\frac{\partial H}{\partial U_1} = 0, \tag{1.31}$$

and the optimality condition is obtained as follows:

$$\frac{\partial H}{\partial u_1} = \psi_1(t) = (\lambda_{U_1} - \lambda_{I_1})I_1 \text{ at } u_1^*(t) \tag{1.32}$$

with the boundary conditions $(\lambda_0, \lambda_S(T), \lambda_{I_1}(T), \lambda_{U_1} = (\lambda_0, 0, \lambda_{I_1}(T), q)$ known as the transversality conditions, where $q \leq 0$, and $\psi_1(t)$ is called the switching function. Equations (1.27)-(1.32) form the necessary conditions that an optimal control must satisfy.

Remarks 1.7.2. *Pontryagin defines the Hamiltonian with two co-state variables λ_0 and $(\lambda_S, \lambda_{I_1}, \lambda_{U_1})$. Here, $(\lambda_S, \lambda_{I_1}, \lambda_{U_1})$ represents the adjoint variables with respect to our state variables (S, I_1, U_1) respectively. Subsequently, λ_0 turns out to be constant in time, and its value is determined in the Pontryagin theory as follows:*
$\lambda_0 = -1$ if $u_1(t)$ is feasible and the objective functional (1.26) is to be minimized.
$\lambda_0 = +1$ if $u_1(t)$ is feasible and the objective functional (1.26) is to be maximized.
$\lambda_0 = 0$ if $u_1(t)$ is unfeasible.

For our simplified problem, we have shown that all admissible controls are feasible, and we are to look for a maximum of the objective function, thus $\lambda_0 = +1$.

We now summarize the control characterization as follows:

$$u_1^*(t) = \begin{cases} u_{1\max}, & \text{if} \quad \lambda_{U_1} > \lambda_{I_1} \\ ?, & \text{if} \quad \lambda_{U_1} = \lambda_{I_1} \\ 0, & \text{if} \quad \lambda_{U_1} < \lambda_{I_1} \end{cases} \tag{1.33}$$

which follows from equation (1.10).

We observe the optimal control is either $u_1^*(t) \equiv 0, u_1^*(t) \equiv u_{1\max}$ or $u_1^*(t)$ is singular (i.e. $\lambda_{U_1} = \lambda_{I_1}$ over some interval).

We observe that without the constraint, Problem 1 (1.7) and equation (1.15) become an unconstrained optimal control problem, and its solution is $u_1^*(t) \equiv u_{1\max}$ where $u_{1\max} = \infty$.

Claim 1.7.3. *The Optimal control for Problem 1 with $U_{1max} = \infty$ is $u_1^*(t) \equiv u_{1max}$.*

Proof: substituting equation (1.29) into (1.30) with $\lambda_{U_1} = 0$ for $U_{1\max} = \infty$ and making $\dot{\lambda}_S$ the subject gives,

$$\dot{\lambda}_S = \dot{\lambda}_{I_1}\frac{I_1}{S} - \lambda_{I_1}(\mu + u_1)\frac{I_1}{S} \tag{1.34}$$

The optimal control will be determined once the sign of λ_{I_1} is determined. To determine the sign of λ_{I_1}, we use the transversality condition $\lambda_S(T) = 0$. Since $\lambda_{I_1}(T)$ is a constant, equation (1.30) gives

$$\lambda_{I_1}(T) = \frac{(\lambda_0 + \lambda_S(T))\beta S(T)}{\beta S(T) - u_1(T) - \mu} = \frac{\lambda_0 \beta S(T)}{\beta S(T) - u_1(T) - \mu}. \tag{1.35}$$

This implies that $\text{sign}(\lambda_{I_1}(T)) = \text{sign}\Big(S(T) - \frac{u_1(T)+\mu}{\beta}\Big)$. From equation (1.13), λ_{I_1} is negative if and only if $\frac{dI_1}{dt} < 0$. Since T is the smallest time that $I_1(t) = I_{\min}$ and $I(0) > I_{\min}$, it must be that $\frac{dI_1}{dt}$ is negative at T. Therefore, $u_1^*(t) \equiv u_{1\max}$. This concludes the proof of Claim (1.7.3).

Clearly, if $U_{1[u_{1\max}]}(T) \leq U_{1\max}$, then the optimal control is the unconstrained optimal control and $u_1^*(t) \equiv u_{1\max}$.

To prove that $u_1^*(t)$ is not singular but bang-bang for $U_{1[u_{1max}]}(T) > U_{1max}$, we need to analyze the behavior of the switching function $\psi_1(t)$ (1.32) over time. According to the PMP, the optimal control $u_1^*(t)$ switches between its extremal values based on the sign of the switching function $\psi_1(t)$.

For the control to be bang-bang, the switching function $\psi_1(t)$ should only take values that drive $u_1^*(t)$ to either 0 or $u_{1\max}$.

From (1.31), we find that λ_{U_1} is a constant. Since λ_{U_1} is constant, the behavior of $\psi_1(t)$ depends mainly on λ_{I_1}. That is,

1. If $\lambda_{U_1} > \lambda_{I_1}$, then $\psi_1(t) > 0$, which makes $u_1^*(t) = u_{1\max}$.

2. If $\lambda_{U_1} < \lambda_{I_1}$, then $\psi_1(t) < 0$, which makes $u_1^*(t) = 0$.

For $u_1^*(t)$ to be singular, $\psi_1(t)$ must be identically zero over some interval, i.e., $\lambda_{U_1} = \lambda_{I_1}$. Using the adjoint equation for λ_{I_1} (1.30), if $\lambda_{U_1} = \lambda_{I_1}$, the adjoint equation simplifies to:

$$\dot{\lambda}_{I_1} = -(\lambda_{I_1} - \lambda_0 - \lambda_S)\beta S + \lambda_{I_1}\mu. \tag{1.36}$$

This would imply a specific dynamic relationship between λ_{I_1}, S, and μ that should hold over time. However, given that λ_{U_1} is constant and λ_{I_1} is not, this situation is highly restrictive and unlikely. Specifically, λ_{I_1} is influenced by λ_S and other factors that vary in time due to the dynamic nature of S and $u_1(t)$. Given these influences, λ_{I_1} will generally not remain constant. Since the switching function $\psi_1(t)$ can only be zero at isolated points but not over an interval, $u_1^*(t)$ is not singular. Therefore, $u_1^*(t)$ is bang-bang.

Next, we observe that from equation (1.23), we can write $-\dot{S} = \beta S I_1$ and $I_1 = -\frac{\dot{S}}{\beta S}$. Substituting these two expressions into equation (1.24) gives

$$\dot{I} = -\dot{S} + \frac{\mu}{\beta}\frac{\dot{S}}{S} - u_1 I_1. \tag{1.37}$$

Rearranging equation (1.37) and integrating from 0 to T, we obtain the total number of isolated infected community members,

$$U_{1[u_1]}(T) = \int_0^T u_1 I_{1[u_1]}\, dt = S(0) - S_{[u_1]}(T) + I_1(0) - I_{1[u_1]}(T) + \frac{\mu}{\beta}\ln\left(\frac{S_{[u_1]}(T)}{S(0)}\right). \tag{1.38}$$

Equation (1.38) shows that the constraint value $U_{1[u_1]}(T) = \int_0^T u_1 I_{1[u_1]} dt$ depends on $S_{[u_1]}(T)$ since $S(0), I_1(0)$ in the equation are known initial conditions and β, μ are constant parameter values .

Again, the objective function can be rewritten as

$$\int_0^T \beta I_{1[u_1]} S_{[u_1]}\, dt = S(0) - S_{[u_1]}(T), \tag{1.39}$$

and therefore minimizing the objective function is equivalent to maximizing $S_{[u_1]}(T)$.

Now to determine the optimal control when $U_{1[u_{1\max}]}(T) > U_{1\max}$, we rewrite equation

(1.38) as

$$\frac{\mu}{\beta}\ln(S_{[u_{1\max}]}(T)) - S_{[u_{1\max}]}(T) = I_{1[u_{1\max}]}(T) - I_1(0) - S(0) + \frac{\mu}{\beta}\ln(S(0)) + U_{1[u_{1\max}]}(T). \tag{1.40}$$

There are two possible scenarios:

1. If $U_{1[u_{1\max}]}(T) > U_{1\max}$ and $S_{[u_{1\max}]}(T) < \frac{\mu}{\beta}$, then as long as $U_{1[u_1]}(T) \leq U_{1\max} < U_{1[u_{1\max}]}(T)$, $S_{[u_1]}(T)$ shows an upward trend concerning $U_{[u_1]}(T)$. This implies that any control strategy $u_1(t)$ utilizing the entire available resource set will be optimal.

2. If $U_{1[u_{1\max}]}(T) > U_{1\max}$ and $S_{[u_{1\max}]}(T) > \frac{\mu}{\beta}$, considering the convex downward function $f(S) = \frac{\mu}{\beta}\ln(S) - S$ with a maximum at $S = \frac{\mu}{\beta}$, for any $u_1(t)$ satisfying $U_{1[u_1]}(T) < U_{1\max}$, it must be that $S_{[u_1]}(T) < \frac{\mu}{\beta}$. Consequently, $S_{[u_1]}(T)$ increases with $U_{1[u_1]}(T)$ for any $U_{1[u_1]}(T) < U_{1\max}$. Therefore, $u_1(t)$ denotes any control strategy utilizing all available resources.

This concludes the proof of Theorem 1.7.1.

1.8 Problem 2: Community Isolation Only (with case importation)

In this model, we assume that there are case importations and the only control measure is community isolation.

$$\frac{dS}{dt} = -\beta S(I_1 + cI_2) \tag{1.41}$$

$$\frac{dI_1}{dt} = \beta S(I_1 + cI_2) - (\mu + u_1(t))I_1 \tag{1.42}$$

$$\frac{dI_2}{dt} = \theta - \gamma I_2 \tag{1.43}$$

$$\frac{dU_1}{dt} = u_1(t)I_1 \tag{1.44}$$

The optimal control is similar to Problem 1 [4] and the resulting theorem is Theorem 1.7.1. The problem of minimizing the total number of new cases becomes a problem of finding the control $u_1(t)$ that minimizes:

$$J = \int_0^T \beta S(I_1 + cI_2)\ \ dt \tag{1.45}$$

subject to the constraints $I_1(T) = I_{\min}$ and $U_1(T) \leq U_{1\max}$.

The Hamiltonian is given by

$$H(t) = (\lambda_0 - \lambda_S + \lambda_{I_1})\beta S(I_1 + cI_2) - \lambda_{I_1}(\mu + u_1(t))I_1 + \lambda_{I_2}(\theta - \gamma I_2) + \lambda_{U_1}u_1(t)I_1 \tag{1.46}$$

where the adjoint variables are defined by

$$\dot{\lambda}_S = -\frac{\partial H}{\partial S} = -(\lambda_0 - \lambda_S + \lambda_{I_1})\beta(I_1 + cI_2) \tag{1.47}$$

$$\dot{\lambda}_{I_1} = -\frac{\partial H}{\partial I_1} = -(\lambda_0 - \lambda_S + \lambda_{I_1})\beta S - (\lambda_{U_1} - \lambda_{I_1})u_1 + \lambda_{I_1}\mu \tag{1.48}$$

$$\dot{\lambda}_{I_2} = -\frac{\partial H}{\partial I_2} = -(\lambda_0 - \lambda_S + \lambda_{I_1})\beta S + \lambda_{I_2}\gamma \tag{1.49}$$

$$\dot{\lambda}_{U_1} = -\frac{\partial H}{\partial U_1} = 0 \tag{1.50}$$

The transversality conditions are $(\lambda_0, \lambda_S(T), \lambda_{I_1}(T), \lambda_{I_2}(T), \lambda_{U_1}) = (\lambda_0, 0, \lambda_{I_1}(T), 0, q)$ where $q \leq 0,\ \lambda_{I_1}(T) \geq 0$, which implies $\lambda_{U_1} \leq 0$.

The optimal control therefore satisfies

$$u_1^*(t) = \begin{cases} u_{1\max}, & \text{if} \quad \lambda_{U_1} - \lambda_{I_1} < 0 \\ ? & \text{if} \quad \lambda_{U_1} - \lambda_{I_1} = 0 \\ 0, & \text{if} \quad \lambda_{U_1} - \lambda_{I_1} > 0 \end{cases} \tag{1.51}$$

Since the optimal control is bang-bang [4], it implies that the optimal control is either $u_1^*(t) \equiv u_{1\max}$ or $u_1^*(t) \equiv 0$. To further constrain the form of the optimal control, let's consider the case when $\lambda_{U_1} = 0$. Since $\lambda_{I_1}(T) \geq 0$ and $\dot{\lambda}_{I_1} < 0$, it must be that $\lambda_{I_1}(t) > 0$ for all $t < T$. Therefore, if $\lambda_{U_1} = 0$, the optimal control $u_1^*(t)$ is to isolate with maximum effort for the entire epidemic.

Let's consider the case when $\lambda_{U_1} < 0$. If $\lambda_{U_1} < 0$, then all of the control resources are used before the epidemic ends, therefore the optimal control $u_1^*(t)$ is any bang-bang control that uses all of the available resources and then $u_1^*(t) = 0$.

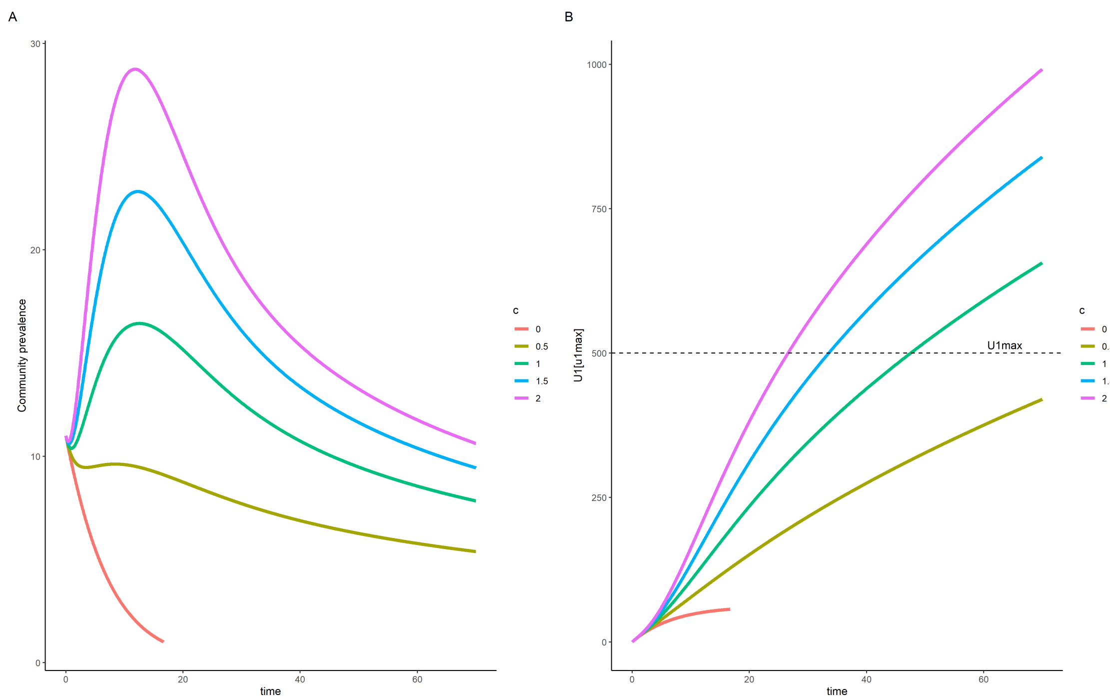

Figure 1.1: The effect of the infected travellers' relative transmissibility factor (c) on the dynamics of the community prevalence and the total resources used ($U_{1[u_{1\max}]}$). Figure 1.1 (A) illustrates the variation in community prevalence in response to different values of the transmissibility factor (c). It is evident that higher values of c result in an increase in the number of community infections. In contrast, Figure 1.1 (B) demonstrates that for lower values of c, the resource constraints are more easily met. The black dashed line represents the total resources available for community isolation. The figure shows that when the transmissibility rate is high, there is a likelihood of surpassing the total resource capacity for community isolation (i.e., $U_{1[u_{1\max}]}(T) > U_{1\max}$). As a result, resource limitations prevent the continuation of isolation measures throughout the entire outbreak. Consequently, the optimal control strategy is a bang-bang control approach that fully utilizes all available resources. Parameters are $u_{1\max} = 0.8,\ U_{1\max} = 500,\ \beta = 0.002,\ \mu = 0.334,\ \theta = 2$

.

1.9 Problem 3: Post-Arrival Traveller isolation Only

In Problem 3, we consider traveller isolation as the only control in the model. Our model now becomes

$$\frac{dS_1}{dt} = -\beta S(I_1 + cI_2) \tag{1.52}$$
$$\frac{dI_1}{dt} = \beta S(I_1 + cI_2) - \mu I_1 \tag{1.53}$$
$$\frac{dI_2}{dt} = \theta - (u_2(t) + \gamma)I_2 \tag{1.54}$$
$$\frac{dU_2}{dt} = u_2(t)I_2 \tag{1.55}$$

Our objective function now becomes;

$$\min J = \min \int_0^T \beta S_{[u_2]}(I_{1[u_2]} + cI_{2[u_2]})\ dt \tag{1.56}$$

subject to equations (1.52)-(1.55), $T = \inf\{t|I_{1[u_2]}(t) = I_{\min}\}, u_2(t) \in [0, u_{2\max}]$ for all $t \in [0,T]$ and subject to the resource constraint;

$$U_{2[u_2]}(T) = \int_0^T u_2 I_2\ dt \leq U_{2\max} \tag{1.57}$$

Theorem 1.9.1. ***(Optimal Traveller Isolation Strategy)*** *If $U_{2[u_{2max}]}(T) \leq U_{2max}$, then the optimal traveller isolation policy for Problem 3 is $u_2^*(t) \equiv u_{2max}$. If $U_{2[u_{2max}]}(T) > U_{2max}$, then the optimal control $u_2^*(t)$ is any bang-bang control $u_2(t)$ such that $U_{2[u_2^*]}(T) = U_{2max}$.*

The proof of the optimal traveller isolation strategy mirrors and adheres to the methodologies of Theorem 1.7.1 and Theorem 1.9.1, with the PMP relations for problem 3 outlined below.

The Hamiltonian is given by

$$H(t) = (\lambda_0 - \lambda_S + \lambda_{I_1})\beta S(I_1 + cI_2) - \lambda_{I_1}\mu I_1 + \lambda_{I_2}\theta - \lambda_{I_2}(u_2(t) + \gamma)I_2 + \lambda_{U_2}u_2(t)I_2 \tag{1.58}$$

where the adjoint variables are defined by

$$\dot{\lambda}_S = -\frac{\partial H}{\partial S} = -(\lambda_0 - \lambda_S + \lambda_{I_1})\beta(I_1 + cI_2) \tag{1.59}$$

$$\dot{\lambda}_{I_1} = -\frac{\partial H}{\partial I_1} = -(\lambda_0 - \lambda_S + \lambda_{I_1})\beta S + \lambda_{I_1}\mu \tag{1.60}$$

$$\dot{\lambda}_{I_2} = -\frac{\partial H}{\partial I_2} = -(\lambda_0 - \lambda_S + \lambda_{I_1})\beta S - (\lambda_{U_2} - \lambda_{I_2})u_2(t) + \lambda_{I_2}\gamma \tag{1.61}$$

$$\dot{\lambda}_{U_2} = -\frac{\partial H}{\partial U_2} = 0 \tag{1.62}$$

The transversality conditions are $(\lambda_0, \lambda_S(T), \lambda_{I_1}(T), \lambda_{I_2}(T), \lambda_{U_2}) = (\lambda_0, 0, \lambda_{I_1}(T), \lambda_{I_2}(T), p)$ where $p \leq 0$.

The optimal control therefore satisfies

$$u_2^*(t) = \begin{cases} u_{2\max}, & \text{if} \quad \lambda_{U_2} - \lambda_{I_2} < 0 \\ 0, & \text{if} \quad \lambda_{U_2} - \lambda_{I_2} > 0 \end{cases} \tag{1.63}$$

The conclusion drawn from Theorem 1.9.1 is that the optimal traveller isolation strategy is to isolate with maximum effort throughout the epidemic, provided sufficient resources are available. Without adequate resources, the optimal strategy is any strategy that fully utilizes all available resources. An intriguing insight from the theorem is that, in specific situations, stringent restrictions might be inefficient, leading to unnecessarily high costs [9]. This is exemplified by scenarios where the impact of traveller isolation is minimal due to the limited contribution of imported cases to local transmission [8] (see Figure 1.2). Hence, it is significant that policymakers consider the local incidence of the disease, the growth of local epidemics, and the volume of travel before implementing such strategies.

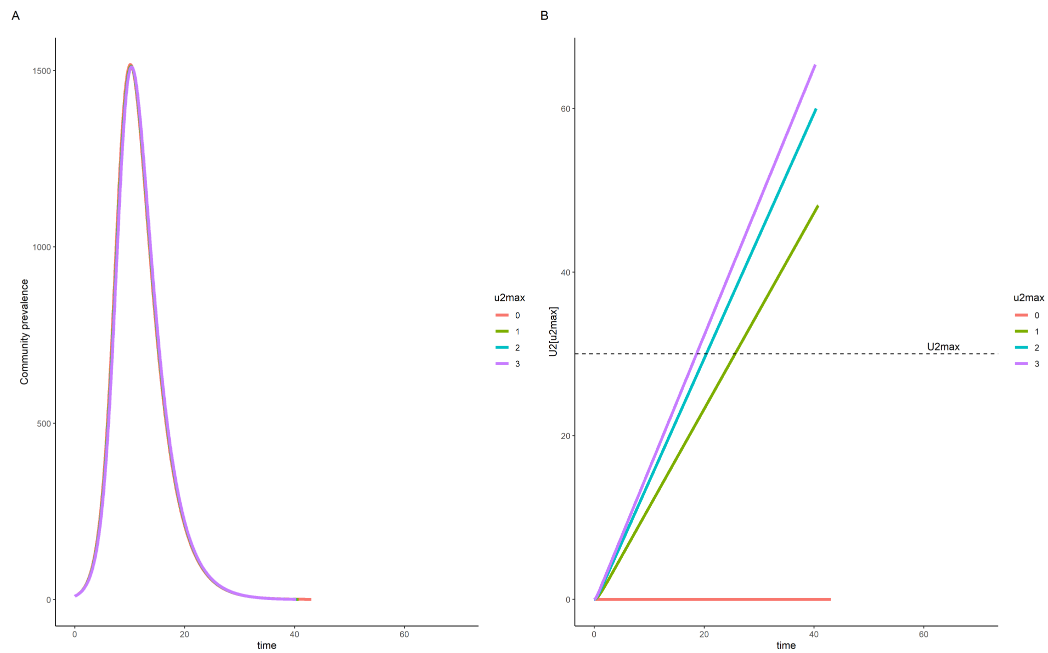

Figure 1.2: The impact of the post-traveller isolation rate ($u_{2\max}$) on the community prevalence dynamics and the total resources used ($U_{2[u_{2\max}]}$). Figure 1.2 (A) depicts the effect on community prevalence with varying values of the post-traveller isolation rate ($u_{2\max}$). It is clear that different post-traveller isolation rates do not significantly alter the dynamics of community infections. Figure 1.2 (B) indicates that when $u_{2\max}$ is elevated, there is a potential to exceed the total resource capacity allocated for traveller isolation (i.e., $U_{2[u_{2\max}]}(T) > U_{2\max}$). The black dashed line represents the total available resources for traveller isolation. Consequently, resource constraints limit the ability to maintain isolation measures throughout the entire outbreak. Therefore, the optimal control strategy is a bang-bang approach that fully utilizes all available resources. Parameters are $c = 1,\ U_{2\max} = 30,\ \beta = 0.002,\ \mu = 0.334,\ \theta = 2$.

1.10 Problem 4: Combined Strategies

The model for the combined strategies with limited resources is described by the system of ordinary differential equations:

$$\frac{dS}{dt} = -\beta S(I_1 + cI_2) \tag{1.64}$$
$$\frac{dI_1}{dt} = \beta S(I_1 + cI_2) - (\mu + u_1(t))I_1 \tag{1.65}$$
$$\frac{dI_2}{dt} = \theta - (\gamma + u_2)I_2 \tag{1.66}$$
$$\frac{dU_1}{dt} = u_1(t)I_1 \tag{1.67}$$
$$\frac{dU_2}{dt} = u_2(t)I_2 \tag{1.68}$$

Theorem 1.10.1. ***(Optimal Mixed Strategies)***
If $U_{1[u_{1max},u_{2max}]}(T) \leq U_{1max}$ and $U_{2[u_{1max},u_{2max}]}(T) \leq U_{2max}$, then the optimal control $u_1^*(t) \equiv u_{1max}$ and $u_2^*(t) \equiv u_{2max}$.
If $U_{1[u_{1max},u_{2max}]}(T) \leq U_{1max}$ and $U_{2[u_{1max},u_{2max}]}(T) > U_{2max}$, then the optimal control $u_1^*(t) \equiv u_{1max}$ and $u_2^*(t)$ is any bang-bang control such that $U_{2[u_1^*,u_2^*]}(T) = U_{2max}$.
...

Claim 1.10.2. *If there exists a $t_k \geq 0$ such that $u_1(t) = 0$ for all $t \in (t_k, T]$, then $u_2(t) = u_2^*(t)$ for all $t \in (t_k, T]$.*

Proof: Once $t > t_k$, the mixed strategies model becomes a traveller isolation-only model, and therefore, $u_2^*(t)$ is the optimal control for the traveller isolation-only model where $\tilde{U}_{2\max} = U_{2\max} - \int_{t_0}^{t_k} u_2\ I_2\ dt$.

Claim 1.10.3. *If there exists a $t_k \geq 0$ such that $u_2(t) = 0$ for all $t \in (t_k, T]$, then $u_1(t) = u_1^*(t)$ for all $t \in (t_k, T]$.*

Proof: Once $t > t_k$, the mixed strategies model becomes a community isolation-only model, and therefore, $u_1^*(t)$ is the optimal control for the community isolation-only model where $\tilde{U}_{1\max} = U_{1\max} - \int_{t_0}^{t_k} u_1\ I_1\ dt$.

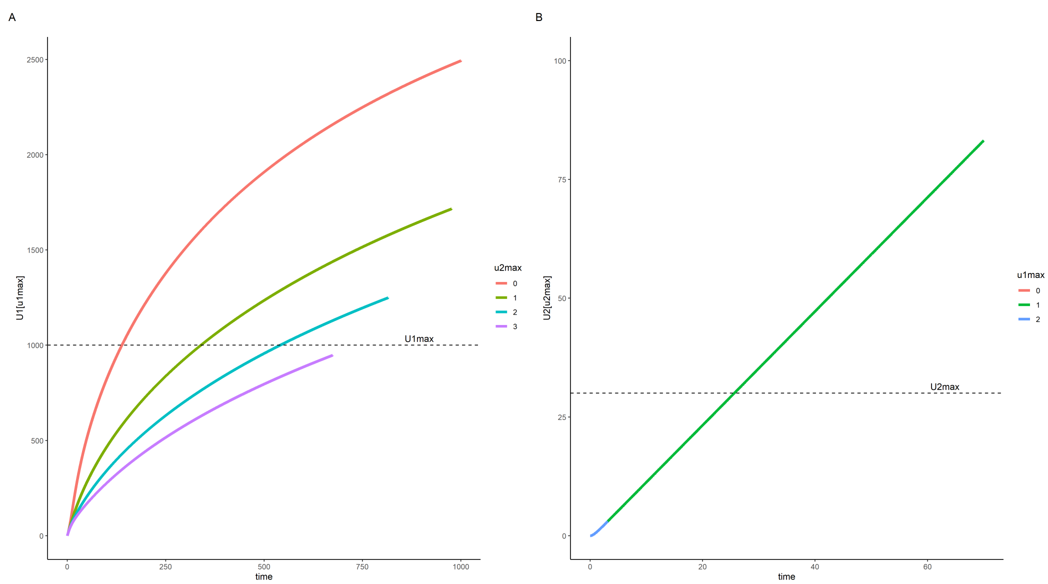

Figure 1.3: The influence of the post-traveller isolation rate ($u_{2\max}$) on the total resources allocated for community isolation ($U_{1\max}$), as well as the effect of the community isolation rate ($u_{1\max}$) on the total resources available for traveller isolation ($U_{2\max}$). Figure 1.2 (A) indicates that a higher post-traveller isolation rate ($u_{2\max}$) increases the likelihood of meeting the resource constraints for community isolation. Conversely, Figure 1.3 (B) demonstrates that the community isolation rate does not influence the resource constrain for post-traveller isolation and the total isolated infected travellers ($U_{2[u_{2\max}]}(T)$). Parameters are $c = 1,\ U_{1\max} = 1000,\ U_{2\max} = 30,\ \beta = 0.002,\ \mu = 0.334,\ \theta = 2$.

Chapter 2

Numerical Results and Discussion

In this chapter, we delve into our comprehensive findings on the optimal strategies for community and traveller isolation in the context of resource limitations. Our investigation is structured around the four distinct problem sets: community isolation only, community isolation with case importation, traveller isolation only, and mixed strategies incorporating both community and traveller isolation. These sets of problems act as the basis for our study, enabling us to assess and contrast the effectiveness of different public health strategies as defined below.

2.1 Definition of Public Health Strategies

To control disease outbreaks and protect the population from health risks, public health initiatives are crucial. The elimination, suppression, and circuit breakers stand out as three significant strategies. Safeguarding public health and reducing the impact of infectious diseases requires an understanding of and effective implementation of these strategies.

Public Health Strategy	**Description**	**Our Definition**
Elimination	Strict public health measures reduce infection prevalence to zero locally, but not in all regions, such that there remains a risk of disease importation [1], [7].	(a) The outbreak is eliminated by public health measures, i.e., $U_{1[u_{1\max}]}(T) \leq U_{1\max}$ and $U_{2[u_{2\max}]}(T) \leq U_{2\max}$. (b) $\frac{dI_1}{dt} < 0$ shortly after $u_1^*(t)$ and/or $u_2^*(t)$ are implemented.
Suppression	Infection is kept at low levels [1].	(a) The outbreak is eliminated by public health measures, i.e., $U_{1[u_{1\max}]}(T) \leq U_{1\max}$ and/or $U_{2[u_{2\max}]}(T) \leq U_{2\max}$; (b) $\frac{dI_1}{dt} \geq 0$ shortly after $u_1(t)$ and/or $u_2(t)$ are implemented.
Circuit Breaker	Public health measures are intermittent with breaks in between.	An optimal control involves at least two switches between public health measures of different intensities.

Table 2.1: Definitions of public health strategies

We provide a thorough presentation of the findings for each problem set, explaining the best controls and how they relate to the public health strategies. The underlying assumption of our study is that these strategies are shaped in large part by resource limitations. We examine how limited resources influence the implementation of these strategies and the effectiveness of community and post-traveller isolation measures. A significant insight from our findings is that, in most scenarios, the performance of the optimal strategy is largely independent of the timing of its implementation. This phenomenon is evident across the different problem sets, highlighting the equivalence of various circuit breakers. By presenting these insights, we contribute to the broader discourse on optimizing public health strategies during pandemics and other health crises.

Now rephrasing Theorem (1.10.1) in terms of public health terminology, the optimal control strategy is:

1. **Elimination:** if $U_{1[u_{1\max}]}(T) \leq U_{1\max}$ and $U_{2[u_{2\max}]}(T) \leq U_{2\max}$, and community infections decline shortly after the implementation of public health measures.

2. **Suppression:** if $U_{1[u_{1\max}]}(T) \leq U_{1\max}$ and $U_{2[u_{2\max}]}(T) \leq U_{2\max}$, and community infections increase shortly after the implementation of public health measures.

3. **Suppression/circuit-breaker (Supp/Circ):** if $U_{1[u_{1\max}]}(T) \leq U_{1\max}$ and $U_{2[u_{2\max}]}(T) > U_{2\max}$.

4. **Circuit-breaker/Suppression (Circ/Supp):** if $U_{1[u_{1\max}]}(T) > U_{1\max}$ and $U_{2[u_{2\max}]}(T) \leq U_{2\max}$.

5. **Circuit-breaker:** if $U_{1[u_{1\max}]}(T) > U_{1\max}$ and $U_{2[u_{2\max}]}(T) > U_{2\max}$.

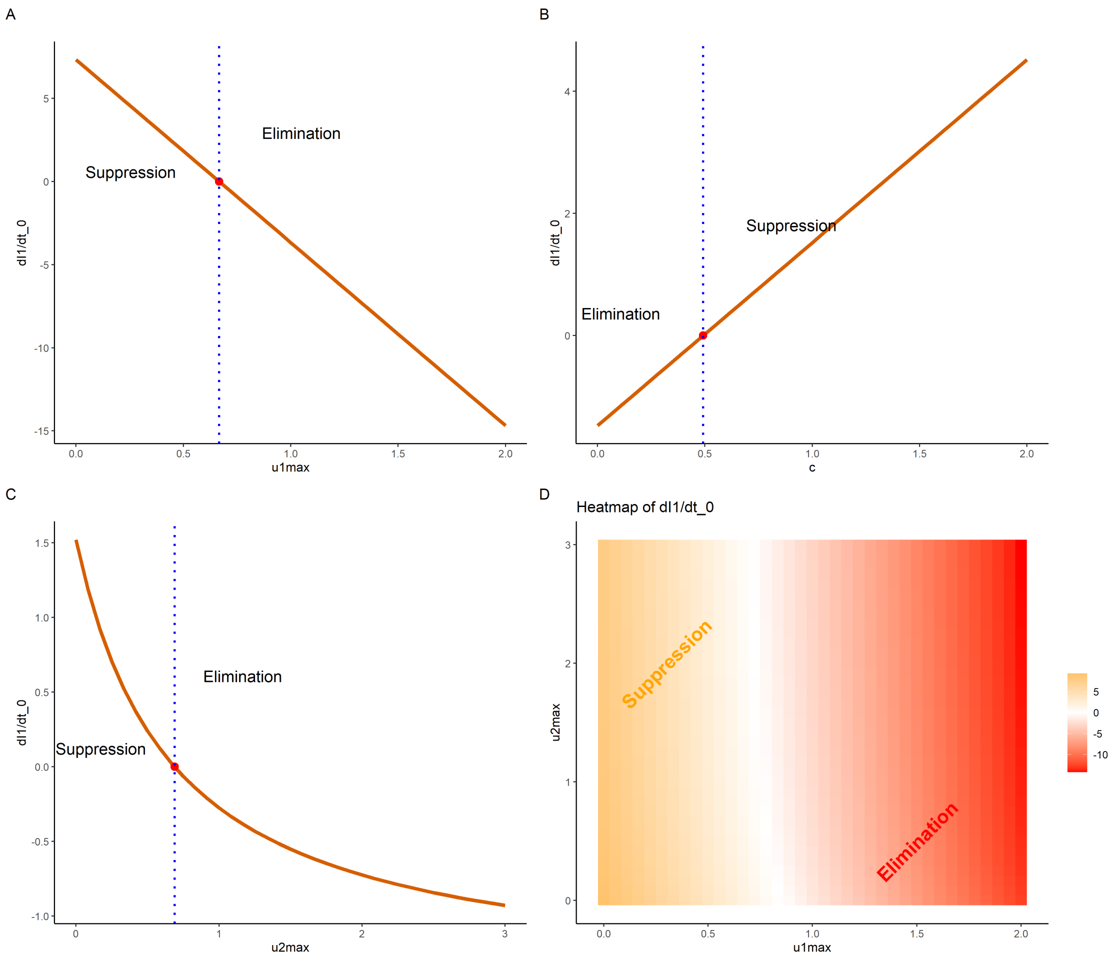

Figure 2.1: The state dynamics of community prevalence in response to varying rates of community isolation and post-arrival traveller isolation at the initial time are examined. The blue dotted line indicates the point on the x-axis where $\frac{dI_1}{dt}|_{t=0} = 0$. Parameters are $c = 1,\ U_{1\max} = 1000,\ U_{2\max} = 30,\ \beta = 0.002,\ \mu = 0.334,\ \theta = 2.$

Figure 2.1 (A) corresponds to Problem 1 (1.7), which considers community isolation only. It is observed that with low values of $u_{1\max}$, $\frac{dI_1}{dt}|_{t=0} > 0$, signifying an initial increase in community infections. In this scenario, elimination does not occur, and the observed public health strategy is limited to suppression. Conversely, higher values of $u_{1\max}$ result in a decrease in the number of infections (i.e., $\frac{dI_1}{dt}|_{t=0} < 0$), leading to elimination.

Figure 2.1 (B) represents Problem 2 (1.8), which includes the importation of infected travellers. Here, the dynamics are analyzed concerning the relative transmissibility of infected travellers. It is observed that elimination is more likely (i.e., $\frac{dI_1}{dt}|_{t=0} < 0$) when the transmissibility rate is low, while high transmissibility rates lead to suppression.

Figure 2.1 (C) addresses Problem 3 (1.9), focusing solely on post-arrival traveller isolation measures. It is observed that high values of $u_{2\max}$ increase the likelihood of elimination, while low values result in suppression.

Finally, Figure 2.1 (D) pertains to Problem 4 (1.10), which involves combined strategies. The heatmap illustrates various pairs of community isolation and post-arrival traveller isolation rates $(u_{1\max}, u_{2\max})$ and their effects on community prevalence. It is observed that elimination is more heavily influenced by the rate of community isolation. Therefore, high values of both $u_{1\max}$ and $u_{2\max}$ lead to elimination, whereas low $u_{1\max}$ values result in suppression.

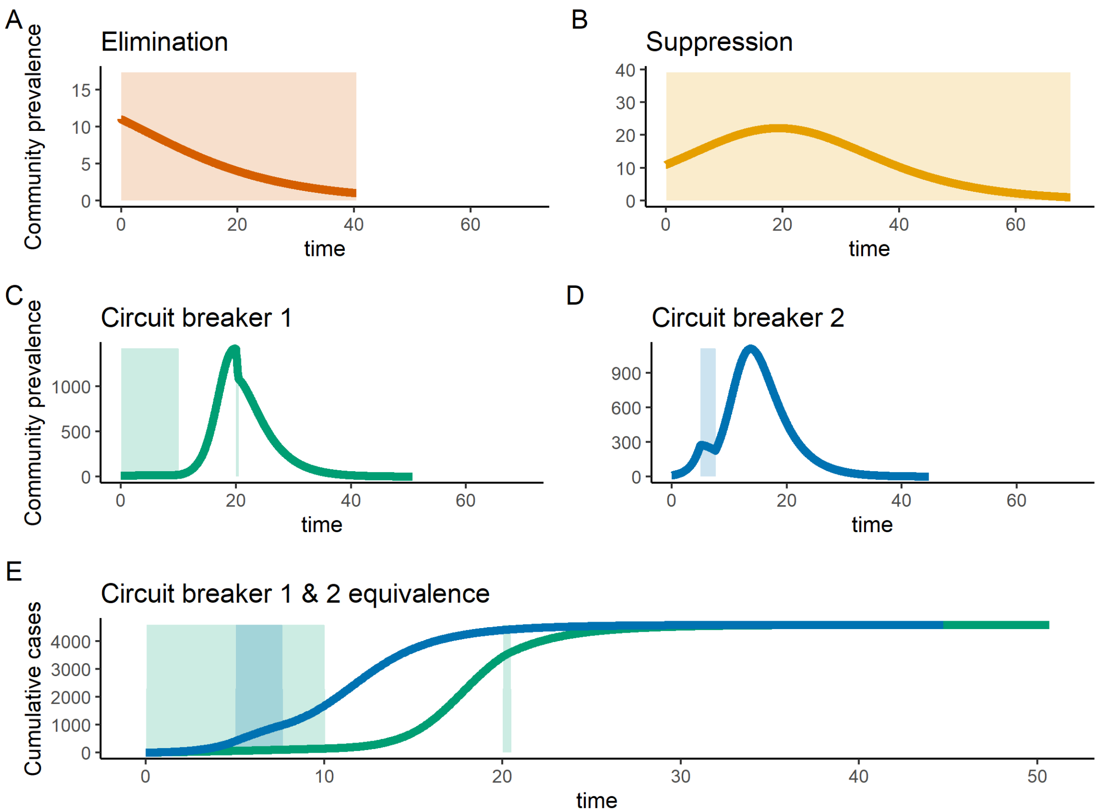

Figure 2.2: Optimal control for the community isolation-only model (Problem 1 (1.7)) described in terms of public health strategies. In Figure 2.2 (A and B), there are sufficient resources to implement the control for the entire outbreak. In C - D, resource limitations mean isolation measures cannot remain in place for the entire outbreak. Here, as shown in [4], the cumulative number of cases in the outbreak does not depend on when isolation requirements are implemented, and any strategy that uses all the resources is equivalent (E). Parameters are $u_{1\max} = 0.7$ (A) or 0.6 $(B-E); U_{1\max} = 500$ (A, B) or 400 $(C-E)$ and for all panels $\beta = 0.002, \mu = 0.334, S(0) = 5000$ and $I_1(0) = 10$, and all other initial conditions are zero. The optimal control is to isolate community members at the maximum rate (shaded region) or not at all (unshaded regions), and the outbreak is over when community infection prevalence (solid lines in A-D) is sufficiently low $(I_1(T) = 1)$.

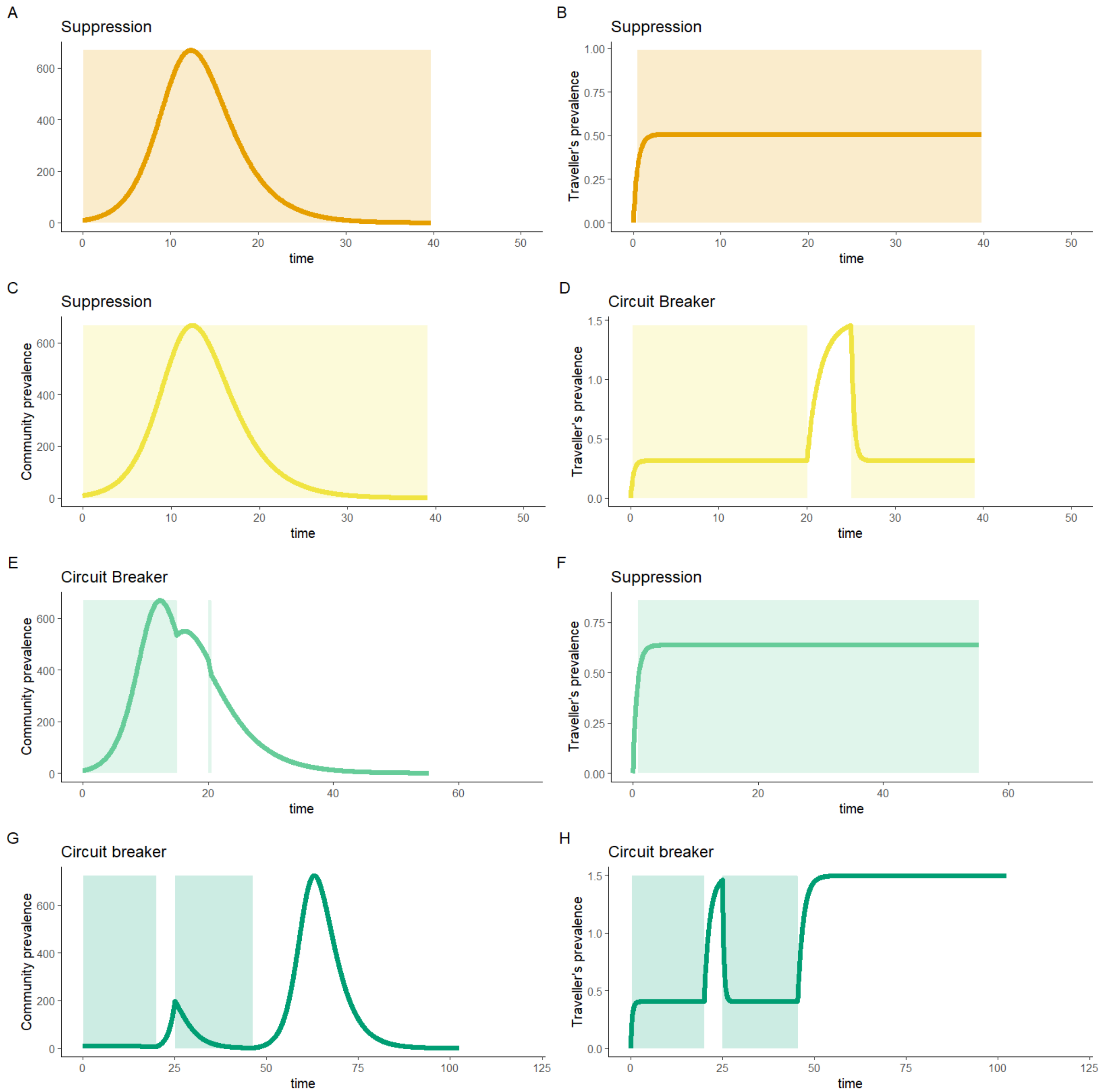

Figure 2.3: Optimal control for the mixed model (Problem 4 (1.10)) described in terms of public health strategies. Parameter values used are $u_{1\max} = 0.2, u_{2\max} = 1.3$ for (A-B), $u_{1\max} = 0.2, u_{2\max} = 2.5$ for (C-D), $u_{1\max} = 0.2, u_{2\max} = 0.9$ for (E-F), $u_{1\max} = 0.7, u_{2\max} = 1.8$ for (G-H).

The mixed strategies model (1.10) exhibits exceptional adaptability, especially when community isolation resources are exhausted first. In such cases, maintaining optimal traveller isolation proves to be the most effective approach. This adaptability emphasizes the advantage of the mixed strategies, which is not simply a combination of optimal community and traveller isolation measures, but a dynamic and responsive strategy tailored to varying resource constraints.

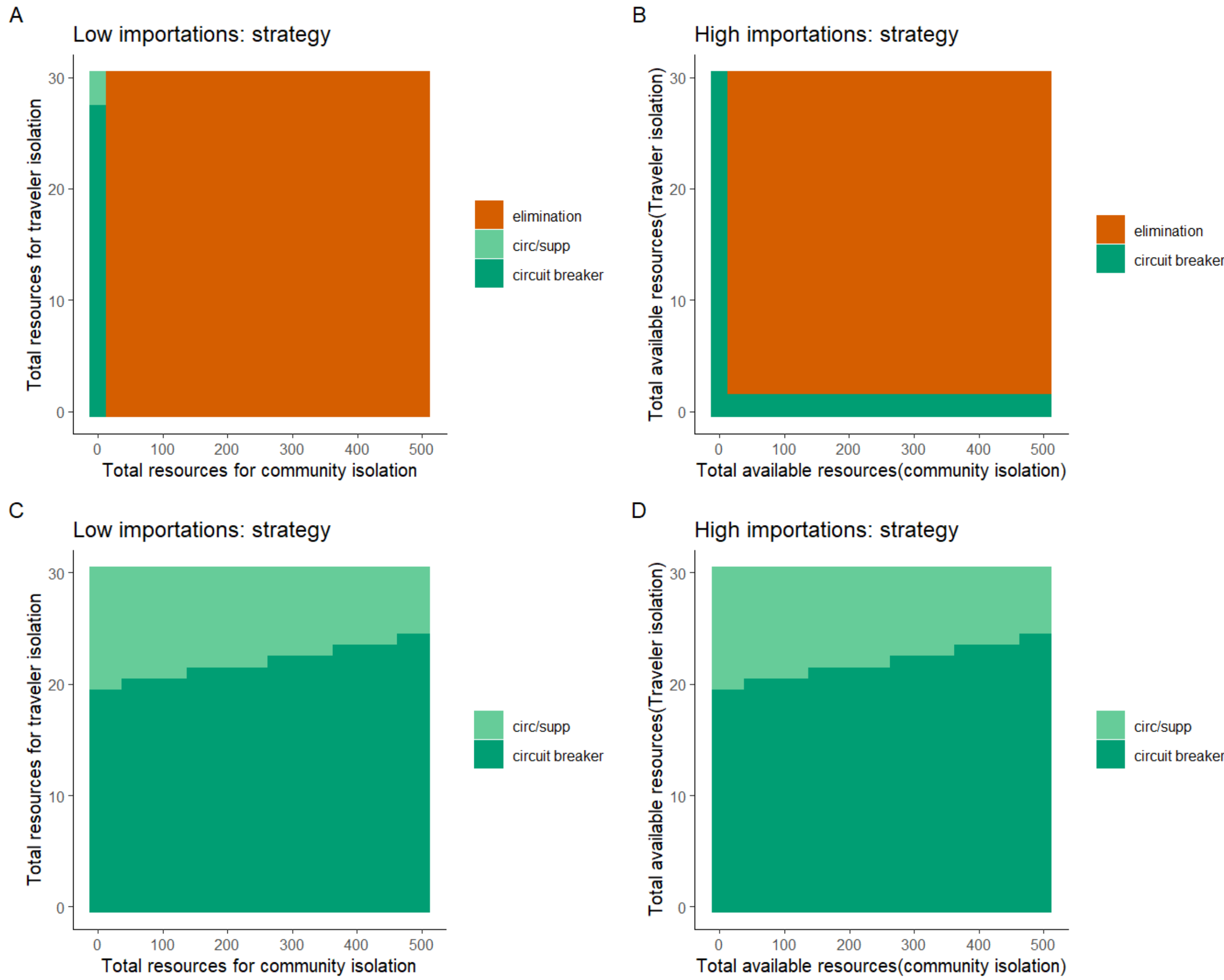

Figure 2.4: Heat map showing the different public health strategies corresponding to the total resources available for community and traveller isolation. Control Parameters are $u_{1\max} = 2.5$, $u_{2\max} = 1.2$ for (A-B) and $u_{1\max} = 0.3$, $u_{2\max} = 0.2$ for (C-D).

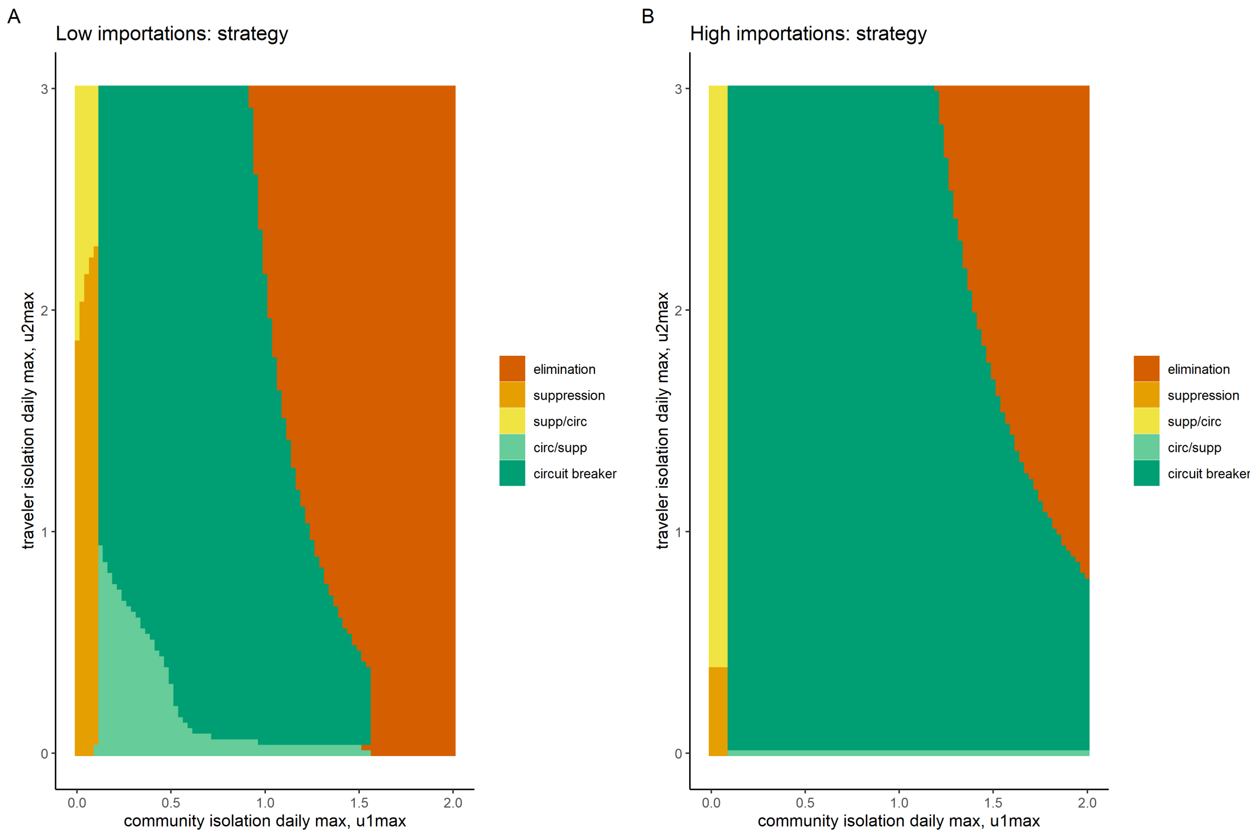

Figure 2.5: Heat map depicting the various public health strategies for community and traveller isolation.

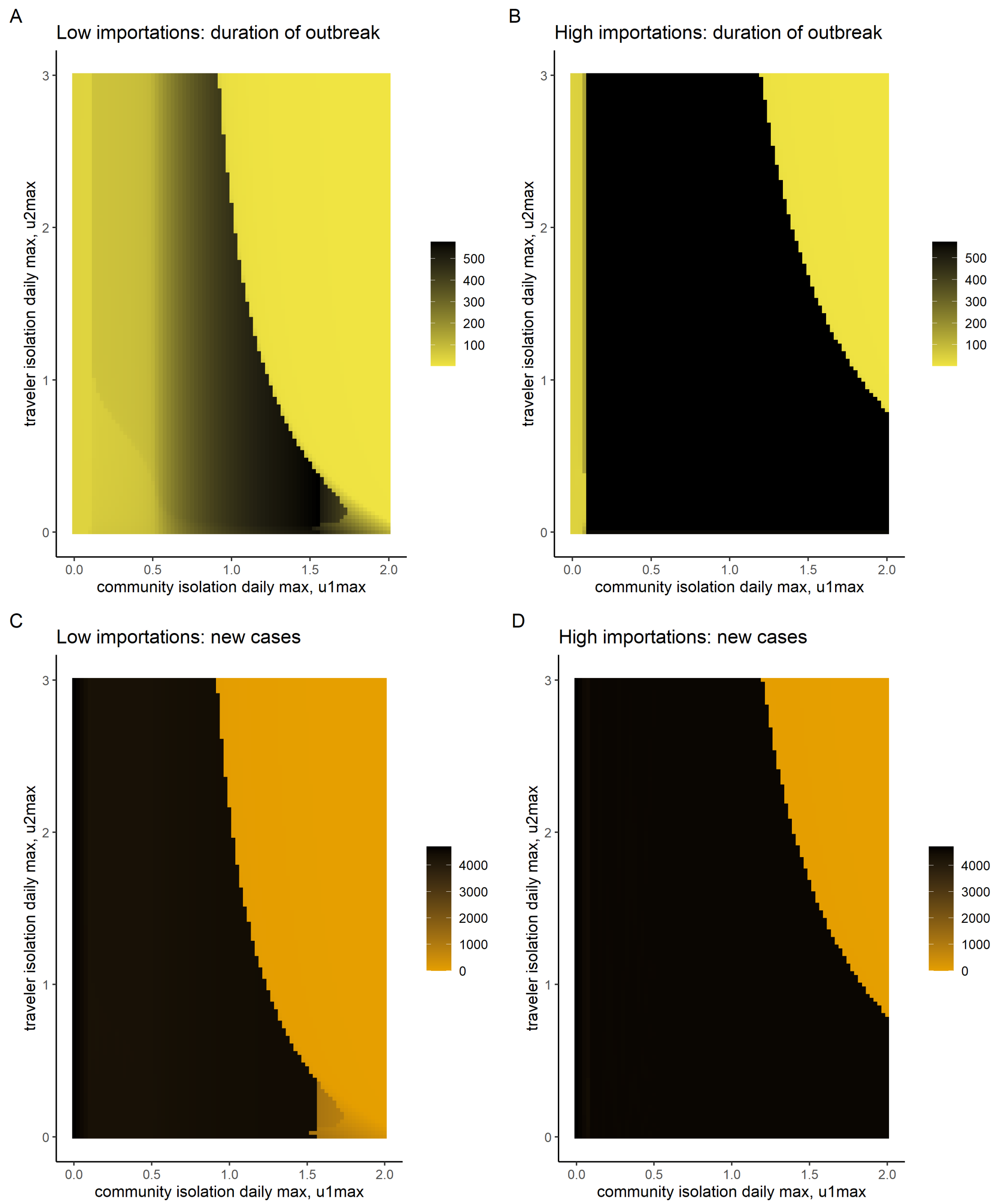

Figure 2.6: Heat map illustrating the effects of various public health strategies on the duration and incidence of new cases.

In problem 2 (1.8), which considers the importation of cases without traveller isolation, we observe that when the rate of case importation is relatively high, elimination of the outbreak becomes unfeasible due to the uncontrolled influx of infected travellers (Figure 2.5(B)). Consequently, the outbreak persists for a longer duration (Figure 2.6(B)), resulting in a higher number of new cases (Figure 2.6(D)). On the other hand, when importation rates are relatively low, elimination can be achieved with a higher community isolation rate, $u_{1\max}$ (Figure 2.5(A)). However, given our constraints on resources, it is likely that we will deplete available resources before the epidemic ends, leading to another peak in infections. This depletion results in a subsequent increase in infections (Figure 2.6(C)) after the exhaustion of the available resources.

In all the problems (1.7-1.10), we observe that elimination can be achieved with sufficient isolation resources and maximal efforts [1], resulting in a shorter outbreak duration and fewer new cases (see Figure 2.5 and 2.6). The goal of elimination is to achieve zero community transmission, rapidly escalating the stringency of control measures to break the chains of disease transmission [1].

For suppression and suppression/circuit strategies, public health measures have a minimal effect and do not delay the occurrence of infections. This causes the epidemic to grow rapidly and end swiftly. Suppression aims to flatten the epidemic curve more than circuit breaker does, but still without expecting to end community transmission [2].

For circuit breaker and circuit breaker/suppression strategies, the total number of cases is similar to those seen with suppression strategies. However, the number of cases is significantly higher compared to scenarios where the maximum daily isolation rates are adequate for elimination.

Hansen and Day [4] found that if resources are insufficient to maintain isolation throughout the entire outbreak, any strategy that maximizes the utilization of available resources is optimal.

Our results indicate that, given sufficient resources, initiating maximum isolation efforts immediately is the best action. Additionally, higher values of $u_{1\max}$ and $u_{2\max}$ are necessary to achieve elimination when the importation rate, θ, is elevated. If resources are insufficient for the entire duration of the outbreak, any strategy that maximizes the use of available resources remains optimal (Theorems 1.7.1 and 1.10.1). Despite the importation of cases, the optimal strategy aligns with the findings of Hansen and Day (2011) [4].

Even small increases in $u_{1\max}$ and $u_{2\max}$ can make elimination possible, significantly reducing the duration of the outbreak and the number of cases. Additionally, while the timing of interventions does not drastically alter the outcome, delaying actions can incur substantial costs.

A prominent finding of our research is the effectiveness of the mixed strategies model, which demonstrates that implementing both community and traveller isolation simultaneously from the outset can significantly reduce the number of new infections. Our results highlight that community isolation measures are considerably more effective than post-arrival traveller isolation. The model further indicates that the optimal mixed strategy involves applying maximal isolation efforts until either community or traveller isolation resources are depleted.

Chapter 3

Conclusion

We expanded on the work of Hansen and Day [4] by considering case importation from infected travellers and implementing post-traveller isolation as a control measure. Our model indicates that the most effective approach for managing an outbreak depends on the availability of isolation resources. When resources are abundant, we recommend putting in the highest effort to isolate infected individuals throughout the outbreak. Conversely, when resources are scarce, it's critical to employ a strategy that optimizes all available resources for isolation. This adaptable strategy guarantees the best possible outcome under resource-constrained conditions. For optimal results, we recommend initiating isolation efforts at the highest level of effort as soon as an epidemic begins and maintaining this stringent level until all resources are fully expended.

3.1 Study Limitations

This study has several limitations. First of all, our model makes the assumption that recovered individuals cannot be reinfected. This might not apply to diseases where immunity wanes over time or if the pathogen mutates, allowing for potential reinfection. Additionally, the model explicitly neglects vaccination as a control measure. In real-world situations, vaccination is a vital part of controlling epidemics, and excluding it may limit the model's relevance in comprehensive epidemic response strategies. Moreover, the accuracy of the model depends on the values of parameters like (β), removal rates (μ), and others. If these parameters are not well-estimated or vary significantly in real-world scenarios, the model's predictions may be unreliable. Again, the model uses finite time controls for community and traveller isolation. We used a terminal condition $I_1 = 1$, which might not capture the long-term dynamics and consequences of prolonged epidemics or control measures, and therefore using other thresholds would impact the duration of the outbreak and the control measures.

3.2 Future Work

Future research in this area could focus on exploring additional control measures like vaccination. Considering vaccination with different vaccination rates would make the model more comprehensive and applicable to a wider range of epidemic scenarios. Conduct thorough sensitivity analyses to understand how variations in parameters (e.g., transmission rates, removal rates) affect model outcomes. Modify the model to account for the possibility of recovered individuals being reinfected, especially for diseases where immunity is temporary or the pathogen changes over time. Incorporate stochastic elements or uncertainty quantification to reflect the real-world variability and uncertainty in these parameters. Integrate human behavioural responses to epidemics and interventions within the model. By addressing these areas, future research can significantly enhance the robustness and applicability of the epidemiological model, leading to more accurate predictions and effective control strategies for managing epidemics.

References

[1] Michael Baker, Nick Wilson, and Tony Blakely. Elimination could be the optimal response strategy for covid-19 and other emerging pandemic diseases. *BMJ*, 371:m4907, December 2020.

[2] N Ferguson, D Laydon, G Nedjati Gilani, N Imai, K Ainslie, M Baguelin, S Bhatia, A Boonyasiri, ZULMA Cucunuba Perez, G Cuomo-Dannenburg, A Dighe, I Dorigatti, H Fu, K Gaythorpe, W Green, A Hamlet, W Hinsley, L Okell, S Van Elsland, H Thompson, R Verity, E Volz, H Wang, Y Wang, P Walker, P Winskill, C Whittaker, C Donnelly, S Riley, and A Ghani. Report 9: Impact of non-pharmaceutical interventions (NPIs) to reduce COVID19 mortality and healthcare demand. Technical report, Imperial College London, March 2020.

[3] John Gibson and Carroll Johnson. Singular Solutions in Problems of Optimal Control. *Department of Electrical and Computer Engineering Technical Reports*, August 1963.

[4] Elsa Hansen and Troy Day. Optimal control of epidemics with limited resources. *Journal of Mathematical Biology*, 62(3):423–451, March 2011.

[5] Suzanne Lenhart and John T. Workman. *Optimal Control Applied to Biological Models*. Chapman and Hall/CRC, New York, May 2007.

[6] Maria M. Martignoni, Julien Arino, and Amy Hurford. Is SARS-CoV-2 elimination or mitigation best? Regional and disease characteristics determine the recommended strategy, February 2024. Pages: 2024.02.01.24302169.

[7] C. Jessica Metcalf, Soa Andriamandimby, Rachel Baker, Emma Glennon, Katie Hampson, T. Hollingsworth, Petra Klepac, and Amy Wesolowski. Challenges in evaluating risks and policy options around endemic establishment or elimination of novel pathogens. *Epidemics*, 37:100507, November 2021.

[8] Timothy W Russell, Joseph T Wu, Sam Clifford, W John Edmunds, Adam J Kucharski, and Mark Jit. Effect of internationally imported cases on internal spread of COVID-19: a mathematical modelling study. *The Lancet Public Health*, 6(1):e12–e20, January 2021.

[9] Wei Shi, Yun Qiu, Pei Yu, and Xi Chen. Optimal Travel Restrictions in Epidemics. 2022.