Optimal Control Strategies in Epidemic models: Analysis of Community and Traveler Isolation Strategies Under Resource Constraints

by

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Abstract

In response to infectious disease spread, health authorities allocate limited resources to support the implementation of control measures, such as the isolation of infected community members and travelers. These control measures may occur as: an elimination strategy, which reduces infection incidence to zero; a mitigation strategy, which reduces disease spread, but not so much as to achieve low levels of incidence; or a circuit-breaker strategy, which involves intermittent breaks from control measures. We consider an epidemic model, and characterize optimal controls that involve the isolation of infected community members, post-arrival isolation of infected travelers, and both of these measures in combination. When resources are not limiting, if the maximum daily isolation rate is high, the optimal control corresponds to an elimination strategy, which results in a small outbreak of short duration. However, if the maximum daily isolation rate is low, the optimal control corresponds to a mitigation strategy, which results in a large outbreak of short duration. When resources are limiting, the optimal control is any strategy that uses all available resources, including circuit breaker strategies of this type, which results in a large outbreak of a duration ranging from short to long. We recommend implementing control measures at the start of an outbreak, as this action is always optimal, and is consistent with the precautionary principle, which recommends action even when important information, such whether resources will be limiting, is unknown. The elimination strategy results in substantially smaller outbreaks of short duration, and increasing the maximum daily isolation rate, or increasing the total resources available so as to achieve elimination is likely optimal in some circumstances. Our modelling could be reformulated to consider multiple outbreaks over a fixed period of time, and would then serve as a suitable framework to characterize the conditions for when travel measures are an optimal control.

I dedicate this thesis to my family for their constant support and whose inspiration and vision continue to guide me.

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List of abbreviations

SIR	Susceptible-Infected-Recovered
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
PMP	Pontryagin's Maximum Principle
ODEs	Ordinary Differential Equations
IVP	Initial-Value Problem
SARS	Severe Acute Respiratory Syndrome

Chapter 1

Introduction

Optimal control theory is a mathematical framework for determining the application of control measures to a dynamical system to achieve the best possible outcome and is an effective tool for decision-making in complex biological situations [44]. Optimal control theory has been applied to epidemiology to identify the best strategies to control and mitigate infectious diseases [3], [5], [11], [22], [30], [40], [44], [47], [55]. To the best of our knowledge, optimal control theory has yet to be applied to problems involving infection importation, where infection importation refers to infected travelers that arrive at a destination from another region.

The arrival of an infected traveler into a susceptible destination population can trigger the onset of a local outbreak if the local conditions (population density, public health infrastructure, etc.) favour the spread of the disease [36]. Various approaches to modelling importation have been developed, each providing unique insights and applications for different epidemiological contexts [13], [63], [8], [43],[29], [1], [6]. Some previous work has found that imported infections are likely to contribute little to local epidemics [59], [34], [28],[7], [15], [69]. As part of the control measures available to public health authorities, some are specifically aimed towards reducing the risk of importations, i.e. travel restrictions or bans, self-isolation upon arrival and so forth. Since the effect of these measures vary, it is important to understand the importation process to evaluate the relative effectiveness of control measures that aim to reduce the importation rate [6].

Our analysis bridges the mathematical framework of optimal control theory with terminology used in public health to describe different types of infectious disease control strategies. Elimination is a strategy which aims to bring the incidence of disease down to zero [10], [53], [33], [70]. The elimination strategy, together with its challenges, has been studied in the context of vaccine-preventable diseases such as measles and polio [23], [9], [54], [20]. Mitigation strategies aim to slow the spread of an infectious disease to avoid overwhelming healthcare capacities [39], [70]. Research has demonstrated the application of mitigation strategies during flu pandemics, highlighting the role of targeted measures such as antiviral distribution, prioritization of high-risk groups, and public health communications [52]. A circuit breaker strategy involves the implementation of public health measures for a fixed, short period to reduce community transmission of a disease [42], [12] with intermittent breaks from public health measures to minimize the adverse impacts associated with extended restrictions [16]. The theoretical underpinnings of a circuit breaker strategy can be found in studies of disease dynamics, which highlight the non-linear benefits of temporarily halting transmission [41]. During the COVID-19 pandemic, short-term lockdowns implemented in numerous countries, including the United Kingdom, demonstrated that circuit breakers could effectively reduce transmission rates and provide a crucial respite for drained healthcare systems [17].

Significant progress has been made by proposing mathematical models, which offer valuable information for decision-making in global health [30], [68], [71], [67], [72],[61], [66], [14], [58], [4], [60], [65]. One common aim when modelling resource constraints is to describe how changes in intervention measures will affect the characteristics of the infection dynamics and consequently affect disease control. Hansen and Day (2011) provided optimal control policies for an isolation-only model, a vaccination-only model and a combined isolation–vaccination model, with analytic solutions for the controls that minimize the infectious burden under the assumption that there are limited control resources [30]. Our research builds upon the framework and analysis developed by Hansen and Day [30].

In this thesis, we extend the framework of Hansen and Day [30] by considering an epidemic model with infection of community members due to importations. We determine the optimal control when the control measures are: community isolation only; post-arrival isolation of infected travelers only; and the combination of both community isolation and post-arrival isolation of infected travelers. We characterize the optimal control as an elimination, mitigation, or circuit breaker strategy, and quantify the outbreak size and duration for the optimal controls corresponding to each strategy. Our work explores infectious disease control strategies using optimal control theory to consider resource limitations and minimize the number of cases in an outbreak. We answer the question of "when" and "how" control measures can be implemented within resource constraints.

Chapter 2

Basic fundamental properties of ODEs and the PMP

The foundation of our modelling involves using a system of ODEs, which provides a framework to describe the dynamic processes inherent in the spread of the disease [63]. The essence of using ODEs in this context is their ability to capture the continuous change in population compartments, which correspond to the disease states and other critical variables [19]. This is achieved through rate equations that combine various processes, including transmission rates, recovery rates, and death rates. By adjusting these rates, we can mimic real-world scenarios across diverse populations and conditions [41]. The resulting systems of ODEs yield rich dynamics that can be studied analytically and numerically to predict disease trajectories and evaluate the potential impact of health policies [32].

Understanding how solutions to ODEs depend on initial conditions and parameters, such as transmission coefficients or contact patterns, is central to using ODEs in infectious disease modelling [18], [51]. The system's ability to forecast future states stems from the existence and uniqueness of solutions, which hinges upon the initial conditions and parameters. With the notion of admissibility of control functions, we set a framework that ensures the system's responses remain within feasible bounds, aligning with realistic scenarios [44]. The practical application of this model rests on these controls being seamlessly adjustable within the compact set's constraints over the chosen time frame. Verifying the solutions' existence and uniqueness, which we will delve into in the upcoming section, is a critical step that reinforces the model's integrity and application to real-world systems [56].

We state some essential characteristics of the solutions to ordinary differential equations, including existence, uniqueness, continuous dependence on initial conditions, and continuous dependence on parameters. Consider the nonlinear dynamical control system

$$\dot{x}(t) = f(t, x(t), u(t), .); \quad x(t_0) = x_0, \tag{2.1}$$

where $x(t) = (x_1(t), \cdots, x_n(t)) \in \mathbb{R}^n, u(t) = (u_1(t), \cdots, u_m(t)) \in \mathbb{R}^m$. For the mathematical model to predict the system's future state from its current state, the Initial-Value Problem (IVP) (2.1) must have a unique solution. A trajectory of the system (2.1) corresponding to a control $u(t)$ is a continuous curve $x(t)$ solving (2.1) for almost all t. We also refer to $x(t) \in \mathbb{R}^n$ for some t as the state. An admissible control $u(t)$ will be a piecewise-continuous vector-valued function on time interval $\mathbb{I} = [0, T]$, which will have values at time $t \in \mathbb{I}$ in a nonempty compact set. We establish the question of existence and uniqueness in the next section.

2.1 Existence and uniqueness of solutions to ODEs

The first goal of this section is to establish the local existence and uniqueness of solutions.

Thus, we are interested in solutions to the differential equations (2.1) that appear to take a more general form. Let $\mathbb{I} \subset \mathbb{R}^n$ an interval of time, $U \subset \mathbb{R}^n$ and $\Theta \subset \mathbb{R}^m$ be open sets and let $f : \mathbb{I} \times U \times \Theta \to \mathbb{R}^n$ be a continuous function. We focus on solutions to the initial value problem

$$\dot{x} = f(t, x, \theta), \quad x(t_0) = x_0, \tag{2.2}$$

that is, the existence of a solution $x : \mathbb{I} \to U$ such that $t_0 \in \mathbb{I}$, $\theta \in \Theta$ and $x(t_0) = x_0$.

It is known from the theory of ordinary differential equations [64], [31] that under certain regularity assumptions, a (nonlinear) differential equation (2.2) has a unique solution passing through x_0 at $t = t_0$. The regularity conditions are

1. $f(t, x, \theta)$ is a continuous function.
2. $f(t, x, \theta)$ satisfies a global Lipschitz condition.

Definition 2.1.1. *Consider metric spaces (X, d_X) (Y, d_Y). A function $f : X \to Y$ is Lipschitz if there exists a real constant $K \geq 0$ such that, for all $x_1, x_2 \in X$*

$$d_Y(f(x_1), f(x_2) \leq K d_X(x_1, x_2)$$

The smallest K satisfying this inequality is denoted by $Lip(f) := K$ and is called the Lipschitz constant of f.

The corresponding existence and uniqueness theorem is as follows. The proofs can be found in [35],[49], [62].

Theorem 2.1.2. *Let $\mathbb{I} \subset \mathbb{R}$, $U \subset \mathbb{R}^n$ and $\Theta \subset \mathbb{R}^m$ be open sets, and assume $f : \mathbb{I} \times U \times \Theta \to \mathbb{R}^n$ is a Lipschitz function. If $(t_0, x_0, \theta_0) \in \mathbb{I} \times U \times \Theta$, then there exists an open neighbourhood of the form $\mathbb{I}_0 \times U_0 \times \Theta_0$ of (t_0, x_0, θ_0) and a Lipschitz continuous function $\varphi : \mathbb{I}_0 \times U_0 \times \Theta_0 \to \mathbb{R}^n$ such that for every $(t_0, x_0, \theta_0) \in \mathbb{I}_0 \times U_0 \times \Theta_0$*

$$\varphi(., t_0, x_0, \theta_0) : \mathbb{I}_0 \to \mathbb{R}^n$$

is a solution to the initial value problem

$$\dot{x} = f(t, x, \theta_0), \quad x(t_0) = x_0. \tag{2.3}$$

Furthermore, if $\psi(., t_0, x_0, \theta_0)$ is another solution to the initial value problem (2.3), then $\psi(t) = \varphi(t)$ on the intersection of their domains of definition.

By solving the relevant differential equation, we can use Gronwall's inequality (Theorem 2.1.3) to constrain a function known to meet a particular differential inequality [27]. It offers a comparison theorem, which can be utilized to demonstrate the uniqueness of a solution to the initial value problem (2.3).

Theorem 2.1.3. ***(The Gronwall's Inequality)*** *Let $\alpha, \beta : (a, b) \to [0, \infty)$ be continuous functions. Assume*

$$\alpha(t) \le C + \left| \int_{t_0}^{t} \alpha(s)\beta(s)ds \right|, \;\; t_0, t \in (a, b)$$

for some constant $C \ge 0$. Then,

$$\alpha(t) \le C \exp\left(\left| \int_{t_0}^{t} \beta(s)ds \right| \right)$$

Applying the Gronwall's inequality to our initial value problem (2.3), let $\alpha(t) := \|\varphi(., x_0) - \psi(., y_0)\|$, $C = \|x_0 - y_0\|$ and $\beta(t) = K$. We obtain the proposition below.

Proposition 2.1.4. *Let $U \subset \mathbb{R}^n$ be an open set and assume $f : U \to \mathbb{R}^n$ is a Lipschitz continuous function with Lip$(f) = K$. If $\varphi(., x_0) : \mathbb{I}_{x_0} \to \mathbb{R}^n$ and $\psi(., y_0) : \mathbb{I}_{y_0} \to \mathbb{R}^n$ are solutions to the initial value problem* (2.3) *with $x(t_0) = x_0$ and $x(t_0) = y_0$, respectively, then*

$$\|\varphi(t, x_0, \theta_0) - \psi(t, y_0, \theta_0)\| \leq \|x_0 - y_0\| e^{K|t-t_0|} \tag{2.4}$$

for all $t \in \mathbb{I}_{x_0} \cap \mathbb{I}_{y_0}$.

Remarks 2.1.5. *Proposition 2.1.4 guarantees the existence and uniqueness of solutions. To show that two solutions to the same initial value problem* (2.3) *agree on the intersection of their domains of definition, we let $\varphi : \mathbb{I}_0 \to \mathbb{R}^n$ and $\psi : \mathbb{I}_1 \to \mathbb{R}^n$ denote two solutions to the initial value problem* (2.3)*. Given that $x(t_0) = x_0 = y_0$, from equation* (2.4) *for all $t \in \mathbb{I}_0 \cap \mathbb{I}_1$,*

$$\|\varphi(t) - \psi(t)\| = 0,$$

which establishes the uniqueness of the solution to the initial value problem (2.3)*.*

2.2 PMP

The Pontryagin Maximum Principle is a fundamental mathematical principle in the field of optimal control theory. It provides necessary conditions that an optimal control and corresponding state trajectory must satisfy for a wide class of optimal control problems [57].

The PMP is applied to problems where the objective is to maximize a particular performance criterion or cost, typically expressed as the integral of a given performance index over a specified time interval, and subject to given constraints. The principle states that, under certain regularity conditions, an optimal control strategy and the corresponding state trajectory must satisfy a set of differential equations known as the canonical equations [45].

The canonical equations involve the system dynamics, the costate variables (Lagrange multipliers), and the partial derivatives of the Hamiltonian, which is a function combining the system dynamics and the cost function. The optimal control is determined by maximizing the Hamiltonian over the set of feasible controls.

The Pontryagin Maximum Principle is widely used to analyze and solve optimal control problems, where the goal is to find the best control strategy for a dynamic system.

The basic optimal control problem for ordinary differential equations consists of finding a piecewise control $u(t)$ and the associated state variable $x(t)$ to maximize the given objective functional below,

$$\max J = \int_{t_0}^{T} L(t, x(t), u(t))\, dt \tag{2.5}$$

$$\text{subject to } \; \dot{x} = f(t, x(t), u(t)), \quad x(t_0) = x_0. \tag{2.6}$$

where equation (2.6) models the system dynamics, and the term $L(t, x(t), u(t))$ is referred to as the integral cost. The function $L(t, x(t), u(t))$ is assumed to be non-negative and continuous in all arguments for $t \in [t_0, T]$. In solving the optimal control problem above (2.5)-(2.6), the first step is to form the Hamiltonian. The Hamiltonian is defined as

$$H(t, x(t), u(t), \lambda(t)) = \lambda_0 L(t, x(t), u(t) + \lambda f(t, x(t), u(t)) \tag{2.7}$$

The set of admissible controls is given by

$$\begin{aligned} U_{ad} = \{u = (u_1, u_2, \cdots, u_m) \text{ such that } (u_1, u_2, \cdots, u_m) \text{ measurable;} \\ (u_1(t), u_2(t), \cdots), u_m(t) \in [0, \infty]\} \end{aligned} \tag{2.8}$$

being a compact convex subset of $\mathbb{R}^m$ and the controls are bounded and Lebesgue measurable. Thus, all possible set u must be contained in the set of admissible controls U_{ad}.

Given the set of admissible controls U_{ad}, we have U_{ad} closed by the definition of a closed set. Further, let $u_1, u_2 \in U_{ad}$, then it follows from the definition of a convex set that

$$bu_1 + (1-b)u_2 \in [0, \infty]$$

for all $b \in [0, 1]$. Consequently $bu_1 + (1-b)u_2 \in U_{ad}$, implying the convexity of U_{ad}.

Theorem 2.2.1. *(PMP) If $u^*(t)$ and $x^*(t)$ are the optimal solution of the control problem, then there exist piecewise differentiable adjoint variables $\lambda(t)$ such that*

$$H(t, x^*(t), u(t), \lambda(t)) \leq H(t, x^*(t), u^*(t), \lambda(t)) \tag{2.9}$$

for all controls u at each time t, where H is the Hamiltonian and

$$\dot{\lambda}(t) = \frac{\partial H(t, x^*(t), u^*(t)}{\partial x} \tag{2.10}$$

$$\lambda(T) = 0 \tag{2.11}$$

are the costate and transversality conditions, respectively.

We focus on the application of the PMP theorem, excluding detailed proof. We refer [5], [57] for the proof.

Definition 2.2.2. *A triple (x^*, u^*, λ) is called extremal if (x^*, u^*) is admissible and the equations $\dot{x} = H_\lambda$ and $\dot{\lambda} = -H_x$ hold along (x^*, u^*).*

Theorem 2.2.3. *Suppose that $f(t, x, u)$ is a continuously differentiable function in its three arguments and concave in u. Suppose u^* is an optimal control with associated state x^*, and λ a piecewise differentiable function with $\lambda(t) \geq 0 \; \forall \; t$. Suppose for all $t_0 \leq t \leq T$*

$$0 = H_u(t, x^*(t), u^*(t), \lambda(t)) \;\; (\textit{optimality condition}). \tag{2.12}$$

Then for all controls u and each $t_0 \leq t \leq T$, we have

$$H(t, x^*(t), u(t), \lambda(t)) \leq H(t, x^*(t), u^*(t), \lambda(t)) \tag{2.13}$$

The same essential conditions are derived through similar reasoning when the problem involves minimizing rather than maximizing. In a minimization problem, we minimize the Hamiltonian pointwise and the inequality in PMP is reversed [44]. Indeed, for a minimization problem with f being convex in u, we can derive

$$H(t, x^*(t), u(t), \lambda(t)) \geq H(t, x^*(t), u^*(t), \lambda(t)) \tag{2.14}$$

by the same argument as in Theorem 2.2.3

This concludes our elementary derivation of the Pontryagin maximum principle.

2.2.1 Existence of optimal controls

The PMP only provides necessary conditions for optimality, and the fulfilment of necessary conditions alone does not guarantee optimality. For an optimal control to exist, we want to have compactness of feasible solution sets. We provide a result stating the existence of at least one optimal solution to the optimal control problem (2.5)-(2.6) under some appropriate compactness and convexity assumptions. Precisely, we follow the standard Filippov's approach [22]. Filippov's existence theorem is a result of the theory of differential inclusions, which are generalizations of ordinary differential equations that allow for multiple possible trajectories at a single point in the state space. Filippov's existence theorem addresses the existence of solutions for differential inclusions [21], [22].

Theorem 2.2.4. ***(Filippov's existence theorem)*** *Consider an optimal control problem defined by a differential inclusion $\dot{x} \in F(t, x, u)$, where $F : [t_0, T] \times \mathbb{R}^n \times \mathbb{R}^m \to \mathbb{R}^n$ is a set-valued mapping representing the dynamics, t is time, x is the state variable and u is the control input. Assume that the set-valued map F is upper semi-continuous in x and continuous in u for each fixed t. If the optimal control problem has nonempty, compact, and convex solution sets for all t, then an optimal control exists for almost every initial point in $\mathbb{R}^n$.*

To establish the existence of the optimal control, we rely on findings presented in [24] and [48]. Initially, we address the boundedness of the state variables in the system (2.5)-(2.6). In other words, the state variables of the system should be bounded. The assurance of the existence of an optimal control solution is ensured by satisfying the following conditions.

(a) The set of control variables and corresponding state variables are not empty.

(b) The admissible control set U_{ad} is compact and bounded.

(c) The vector function $f(t, x, u)$ is continuous.

Chapter 3

Mathematical Model

3.1 Problem description and assumptions

Our model and analysis follow from Hansen and Day (2011) [30], with an extension of the epidemiological model to consider imported infection, and to consider post-arrival travel measures as a control,

$$\frac{dS}{dt} = -\beta S(I_1 + cI_2), \tag{3.1}$$

$$\frac{dI_1}{dt} = \beta S(I_1 + cI_2) - (\mu + u_1(t))I_1, \tag{3.2}$$

$$\frac{dI_2}{dt} = \theta - (\gamma + u_2(t))I_2, \tag{3.3}$$

with $S(0) > 0, I_1(0) \geq I_{\min}$ (see Section 3.2 for an explanation), $I_2(0) \geq 0,\ \beta, \mu, \theta, \gamma, c > 0$, where S is the number of susceptible community members. The extension from Hansen and Day (2011) is to partition infections as infection prevalence in community members, I_1, and infection prevalence in travelers, I_2. The force of infection term considers that susceptible community members are either infected by community members at rate β (per infected community member) or at rate $c\beta$ (per infected traveller), where c is a constant that measures the relative transmissibility of infected travelers as compared to infected community members. The rate that infected travelers arrive in the community is $\theta > 0$, and the rate that travelers become uninfectious, relative to their arrival date at the community, is γ. We consider post-arrival travel measures that isolate infectious travelers from the community at a rate $u_2(t)$. The rate at which community members become uninfectious is γ, with γ less than μ, because community members were in the community from their first day of infectiousness, while travelers may have spent some time away from the community, while infectious, before arriving, or they may leave before their infectious period is over. The rate at which infectious community members are isolated is $u_1(t)$.

There are several different ways that importations might be included in an epidemic model. Our formulation assumes that travelers are a source of infection for susceptible members of the community, but does not explicitly consider the origin of the infected travelers or any infectious disease dynamics at the origin. Further, our formulation assumes that the community members themselves do not become travelers. This model formulation was chosen because we can examine the risk of infection from a non-community source without adding so much model complexity to the dynamics of the number of susceptible community members that the optimal control analysis becomes not possible. Further, we do not consider births and background mortality of community members. Vaccination, as a control variable, was considered in the analysis of Hansen and Day (2011) so we do not consider vaccination in our analysis.

3.2 Defining an outbreak end-point

Hansen and Day (2011) note that when a control that has reduced infection prevalence to a very low level is released, a second wave of infection may occur where this second wave of infection may be caused by a fractional number of individuals. This second wave of infection, which can be caused by a 'nano-individual' [25] is an artifact of the ordinary differential equation model formulation which necessarily describes infection prevalence as a continuous variable. A discrete state model formulation, such as a branching process model, would not have this limitation, however, optimal control for problems described as branching processes is substantially more challenging. To avoid this artificial second wave of infection, we use the approach of Hansen and Day (2011) and define an outbreak as over at $t = T$ if infection prevalence is less than some small value. Specifically, T is the smallest t such that $I_1(t) \leq I_{\min}$ where $I_{\min} \leq 1$ and $I_1(0)$ needs to be chosen as bigger than $I_{\min}$. We note that it is necessary to prevent such artificial waves of infection for our problem of interest as elimination may fail to be identified as the best strategy [50] in a model formulation where infection prevalence artificially increases form a very small number, when in practice infection prevalence was zero and no such 'second wave' could have occurred.

3.3 Resource constraints (Optimal control problem)

The control variables are $u_1(t)$ and $u_2(t)$, which are the daily isolation rates per infected community member and infected traveler, and $(u_1(t), u_2(t)) \in [0, u_{1\max}] \times [0, u_{2\max}]$, where 0 corresponds to no control and $u_{1\max}$ and $u_{2\max}$ correspond to the maximum daily rate of community member isolation and traveler isolation, respectively.

Let $U_{1[u_1,u_2]}(T)$, $U_{2[u_1,u_2]}(T)$ denote the total number of community residents and travelers that have been isolated up until time T where the square brackets denote the dependence of this quantity on the controls, $u_1(t)$ and $u_2(t)$. This dependence occurs both directly due to the total resources used, and indirectly as the controls being implemented impact infection prevalence and the duration of the outbreak, T. A quantity that appears in our subsequent analysis is $U_{1[u_{1\max},u_{2\max}]}(T)$ which is the total number of community members that are isolated if the isolation rate for community members and travelers is maximal for all time until the outbreak ends, and where $U_{2[u_{1\max},u_{2\max}]}(T)$ is defined similarly.

The optimal control problem is constrained at $U_{1\max}$ and $U_{2\max}$ which are defined as the total resources available for community isolation and traveler isolation respectively. Examples of such resources are funding to pay the staff employed in testing, tracing, and isolating infected community members, as well as the resources, such as testing facilities to complete these activities; and funding to pay the staff involved in developing, implementing, and enforcing post-arrival travel measures, as well as the necessary resources, such as isolation facilities or testing equipment to complete these activities.

In keeping with [30], we assume that these resources are limited, such that,

$$U_{1[u_1,u_2]}(T) = \int_0^T u_1(t) I_{1[u_1,u_2]}\, dt \leq U_{1\max} \tag{3.4}$$

and

$$U_{2[u_1,u_2]}(T) = \int_0^T u_2(t) I_{2[u_1,u_2]} \ dt \leq U_{2\max}. \tag{3.5}$$

The aim of public health measures is assumed to be to minimize the number of infections in the outbreak,

$$J = \int_0^T \beta S_{[u_1,u_2]} (I_{1[u_1,u_2]} + c I_{2[u_1,u_2]}) \ dt \tag{3.6}$$

subject to the resource constraints (3.4)-(3.5).

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

$$U_{1[u_1,u_2]}(T) = \int_0^T u_1(t) I_{1[u_1,u_2]} \ dt \tag{3.7}$$

and

$$U_{2[u_1,u_2]}(T) = \int_0^T u_2(t) I_{2[u_1,u_2]} \ dt. \tag{3.8}$$

To apply the PMP, we define the Hamiltonian as

$$H(t) = \lambda_0 \beta S (I_1 + c I_2) + \lambda_{I_1} \frac{dI_1}{dt} + \lambda_{I_2} \frac{dI_2}{dt} + \lambda_{U_1} \frac{dU_1}{dt} + \lambda_{U_2} \frac{dU_2}{dt}. \tag{3.9}$$

3.4 Bang-Bang optimal controls

Equations (3.1)-(3.6) are a linear optimization problem, which is a class of optimal control problems where the control function appears only linearly [26]. In these cases, optimal solutions often incorporate discontinuities in the control variables [44]. Notice that equations (3.1) - (3.3) and the integrand in (3.6) are both linear functions of the controls $u_1(t)$ and $u_2(t)$. Thus, the Hamiltonian (3.9) is also a linear function of the controls; hence, the optimality condition (2.12) contains no information on the controls [44]. The PMP (Sec. 2.2), when applied to bounded control problems that are linear in the control variable, explicitly defines the bang-bang control.

Remarks 3.4.1. *Hansen and Day [30] show that the optimal control for a special case of our model (i.e., see Problem 1 in Section 3.6) is bang-bang, where a bang-bang control is characterized by switching between two extreme values. Specifically, for our model:*

$$u_1^*(t) = \begin{cases} u_{1max}, & \textit{maximum rate of community isolation,} \\ 0, & \textit{no community isolation,} \end{cases} \tag{3.10}$$

and

$$u_2^*(t) = \begin{cases} u_{2max}, & \textit{maximum rate of traveler isolation,} \\ 0, & \textit{no traveler restrictions.} \end{cases} \tag{3.11}$$

We use the notation '$\equiv$' to indicate that a function is equal to the same value for all time, $t \in [0, T]$. For example, $u_1^*(t) \equiv u_{1\max}$ means that the optimal control is to isolate infected community members at the maximum rate for the entire outbreak.

3.5 Problem classification

We classify our general problem into the following four parts as described in Table 3.1.

Table 3.1: The four problems that we analyze

Problem	Description	Special values of parameters
1	Community member isolation only, no importations	$I_2(t) \equiv 0, U_{2\max} = 0$
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

3.6 Problem 1: Community Isolation-Only (no case importation)

The derivation and proof of the theorems of Problem 1 are a direct result of results shown in Hansen and Day 2011 [30].

Considering community isolation as the only control in the model, and with no importations, our model now becomes,

$$\frac{dS}{dt} = -\beta S I_1, \tag{3.12}$$

$$\frac{dI_1}{dt} = \beta S I_1 - (\mu + u_1(t)) I_1. \tag{3.13}$$

Our objective function is,

$$\min J = \min \int_0^T \beta S_{[u_1]} I_{1[u_1]} \, dt, \tag{3.14}$$

subject to equations (3.12)-(3.13), $T = \inf\{t | I_{1[u_1]}(t) = I_{\min}\}, u_1(t) \in [0, u_{1\max}]$ for all $t \in [0, T]$ and subject to the resource constraint,

$$U_{1[u_1]}(T) = \int_0^T u_1(t) I_{1[u_1]} \, dt \leq U_{1\max}. \tag{3.15}$$

Note that $S_{[u_1]} = S$, $I_{1[u_1]} = I_1$ are the number of susceptibles and community infections for a given $u_1(t)$ respectively, where the change in notation is to explicitly denote the dependence of these variables on the control being considered.

From equation (3.12), we have

$$dS = \beta S I_1 \, dt. \tag{3.16}$$

Integrating both sides, we get

$$\int_0^T dS = -\int_0^T \beta S I_1 \, dt, \tag{3.17}$$

$$S(T) - S(0) = -\int_0^T \beta S I_1 \, dt, \tag{3.18}$$

$$S(0) - S(T) = \int_0^T \beta S I_1 \, dt. \tag{3.19}$$

Rearranging equation (3.12), we get

$$\frac{1}{S} \, dS = -\beta I_1 \, dt. \tag{3.20}$$

Taking integral on both sides, we have

$$\int_0^T \frac{1}{S}\, dS = -\beta \int_0^T I_1\, dt, \tag{3.21}$$

$$-\frac{1}{\beta} \ln\left(\frac{S(T)}{S(0)}\right) = \int_0^T I_1\, dt. \tag{3.22}$$

We observe from equations (3.19) and (3.22) 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 3.6.1. ***(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 (3.6.1), 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 [30].

Proof **(Theorem** (3.6.1): Following equations (3.12), (3.13) and (3.15), the community isolation model with limited resources is described by the system of ordinary differential equations:

$$\frac{dS}{dt} = -\beta S I_1 \tag{3.23}$$

$$\frac{dI_1}{dt} = \beta S I_1 - (\mu + u_1(t)) I_1 \tag{3.24}$$

$$\frac{dU_1}{dt} = u_1(t) I_1 \tag{3.25}$$

Next, we formulate Problem 1 (Sec.3.6) as a maximization problem and apply the PMP. The objective function now becomes,

$$\max J = \max\left(-\int_0^T \beta S_{[u_1]} I_{1[u_1]}\ dt\right) \tag{3.26}$$

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

$$H(t) = -\lambda_0 \beta S I_1 - \lambda_S \beta S I_1 + \lambda_{I_1} \beta S I_1 - \lambda_{I_1}(\mu + u_1 I_1) + \lambda_{U_1} u_1 I_1, \tag{3.27}$$

$$= -\dot{\lambda}_{I_1} I_1 = -\dot{\lambda}_S S - \lambda_{I_1}\mu + (\lambda_{U_1} - \lambda_{I_1}) u_1 I_1 = 0. \tag{3.28}$$

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,

$$\dot{\lambda}_S = -\frac{\partial H}{\partial S} = -(\lambda_{I_1} - \lambda_0 - \lambda_S)\beta I_1, \tag{3.29}$$

$$\dot{\lambda}_{I_1} = -\frac{\partial H}{\partial I_1} = -(\lambda_{I_1} - \lambda_0 - \lambda_S)\beta S - (\lambda_{U_1} - \lambda_{I_1}) u_1 + \lambda_{I_1}\mu, \tag{3.30}$$

$$\dot{\lambda}_{U_1} = -\frac{\partial H}{\partial U_1} = 0, \tag{3.31}$$

and the optimality condition is obtained as follows:

$$\frac{\partial H}{\partial u_1} = \psi_1(t) = (\lambda_{U_1} - \lambda_{I_1}) I_1 \ \text{ at } \ u_1^*(t), \tag{3.32}$$

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 (3.27)-(3.32) form the necessary conditions that an optimal control must satisfy.

Remarks 3.6.2. *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* (3.26) *is to be minimized.*

$\lambda_0 = +1$ *if* $u_1(t)$ *is feasible and the objective functional* (3.26) *is to be maximized.*

$\lambda_0 = 0$ *if* $u_1(t)$ *is unfeasible.*

For our Problem 1 (3.6), 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:

$$u_1^*(t) = \begin{cases} u_{1\max}, & \text{if} \quad \lambda_{U_1} > \lambda_{I_1} \\ ?, & \text{if} \quad \lambda_{U_1} = \lambda_{I_1} \\ 0, & \text{if} \quad \lambda_{U_1} < \lambda_{I_1} \end{cases} \tag{3.33}$$

which follows from equation (3.10), however we know from Remarks 3.4.1 that $u_1^*(t)$ is bang-bang so $\lambda_{U_1} = \lambda_{I_1}$ does not occur for any interval of time.

We consider the optimal control for an unconstrained problem.

Claim 3.6.3. *The optimal control for Problem 1 with* $U_{1max} = \infty$ *is* $u_1^*(t) \equiv u_{1max}$.

Proof: substituting equation (3.29) into (3.30) with $\lambda_{U_1} = 0$ for $U_{1\max} = \infty$ and making $\dot{\lambda}_S$ the subject gives,

$$\dot{\lambda}_S = \dot{\lambda}_{I_1}\frac{I_1}{S} - \lambda_{I_1}(\mu + u_1)\frac{I_1}{S}. \tag{3.34}$$

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 (3.30) gives,

$$\lambda_{I_1}(T) = \frac{(\lambda_0 + \lambda_S(T))\beta S(T)}{\beta S(T) - u_1(T) - \mu} = \frac{\lambda_0 \beta S(T)}{\beta S(T) - u_1(T) - \mu}. \tag{3.35}$$

This implies that $\text{sign}(\lambda_{I_1}(T)) = \text{sign}\Big(S(T) - \frac{u_1(T)+\mu}{\beta}\Big)$. From equation (3.13), 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 (3.6.3).

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

Next, we observe that from equation (3.23), we can write $-\dot{S} = \beta S I_1$ and $I_1 = -\frac{\dot{S}}{\beta S}$. Substituting these two expressions into equation (3.24) gives

$$\dot{I}_1 = -\dot{S} + \frac{\mu}{\beta}\frac{\dot{S}}{S} - u_1 I_1. \tag{3.36}$$

Rearranging equation (3.36) and integrating from 0 to T, the total number of community members isolated during the outbreak for any $u_1(t)$ is,

$$U_{1[u_1]}(T) = \int_0^T u_1 I_{1[u_1]}\, dt = S(0) - S_{[u_1]}(T) + I_1(0) - I_{\min} + \frac{\mu}{\beta}\ln\left(\frac{S_{[u_1]}(T)}{S(0)}\right), \tag{3.37}$$

where we note that to observe the constraint $U_{1[u_1]}(T)$ must be less than or equal to $U_{1\max}$.

Again, the objective function can be rewritten as

$$\int_0^T \beta I_{1[u_1]} S_{[u_1]}\, dt = S(0) - S_{[u_1]}(T), \tag{3.38}$$

and, therefore, minimizing the objective function is equivalent to maximizing $S_{[u_1]}(T)$ which is a term that appears in equation (3.37).

The shape of equation (3.37) is illustrated in figure 3.1. For $S_{[u_1]}(T) > \mu/\beta$, the problem is unconstrained because achieving a very high number of susceptible community members at the end of the outbreak requires that the control is $u_{1\max}$ for all time, which means that $U_{1[u_1]}(T) \leq U_{1[u_{1\max}]}(T)$, which is that resources are sufficient, and the maximum rate of isolation of community members can occur for the entire outbreak.

When resources are limiting, i.e., $U_{1[u_1]}(T) < U_{1[u_{1\max}]}(T)$, then $S_{[u_1]}(T) < \mu/\beta$, and then $U_{1[u_1]}(T)$ and $S_{[u_1]}(T)$ are positively related (equation (3.37); figure 3.1), such that increasing $U_{1[u_1]}(T)$, increases $S_{[u_1]}(T)$. Therefore, any $u_1^*(t)$ that uses all available resources, $U_{1[u_1]}(T) = U_{1\max}$, and is a bang-bang control (see Remarks 3.4.1), minimizes equation (3.38). This concludes the proof of Theorem 3.6.1 and a detailed proof of this theorem is given in Hansen and Day (2011) [30].

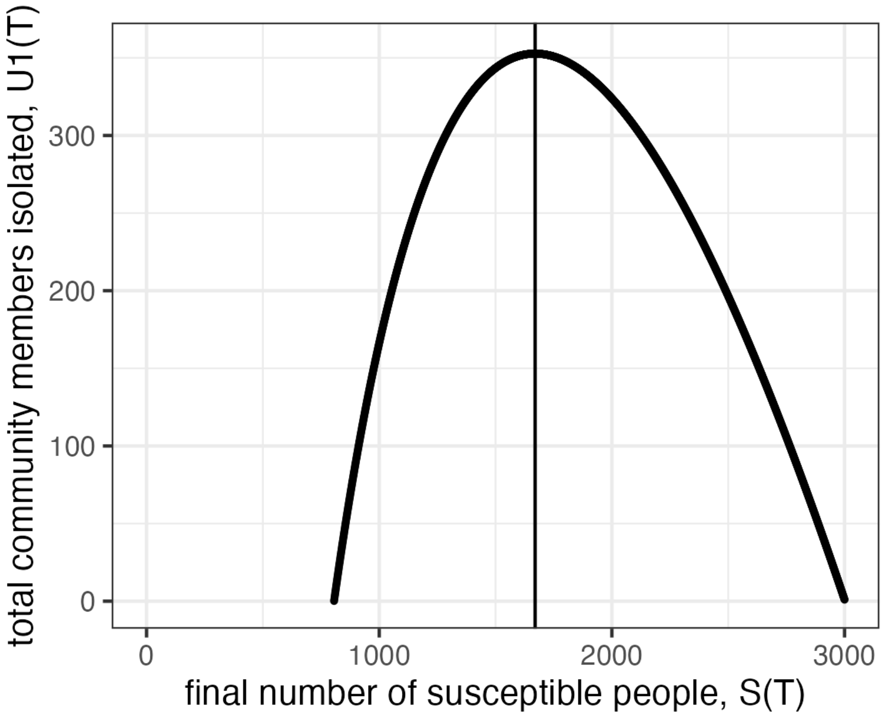

Figure 3.1: Equation (3.37) (black curve) describes the total community members isolated, $U_{1[u_1]}(T)$, as a function of the final number of susceptible people, $S_{[u_1]}(T)$ for a given $u_1(t)$. The region where $S_{[u_1]}(T)$ is to the right of μ/β (vertical line) corresponds to $U_{1[u_{1\max}]}(T) < U_{1\max}$, such that these very high numbers of community members still susceptible after the outbreak ends is achieved only by $u_1(t) \equiv u_{1\max}$, which corresponds to the unconstrained problem when resources are not limiting. Resources are limiting when $S_{[u_1]}(T) < \mu/\beta$ which is the region to the left of the vertical line at μ/β. In this region, $S_{[u_1]}(T)$ and $U_{1[u_1]}(T)$ are positively related such that a $u_1(t)$ that uses more resources results in more community members still susceptible after the outbreak, $S_{[u_1]}(T)$, which is equivalent to a larger value of the objective function (equation 3.26). Parameters are $u_{1\max} = 0.8$ day^{-1}, $\beta = 0.0002$ person^{-1} day^{-1}, $\mu = 0.334$ person^{-1} day^{-1}. Initial conditions are $S(0) = 5000$ people, $I_1(0) = 10$ people.

3.7 Problem 2: Community isolation-only (with imported infections)

For Problem 2, we assume that there are imported infections and the only control measure is community isolation. The epidemiological dynamics are,

$$\frac{dS}{dt} = -\beta S(I_1 + cI_2), \tag{3.39}$$

$$\frac{dI_1}{dt} = \beta S(I_1 + cI_2) - (\mu + u_1(t))I_1, \tag{3.40}$$

$$\frac{dI_2}{dt} = \theta - \gamma I_2, \tag{3.41}$$

$$\frac{dU_1}{dt} = u_1(t)I_1. \tag{3.42}$$

Problem 2 still describes a linear optimization problem such that the optimal control is bang-bang as described by Remarks 3.4.1. For Problem 2, the problem is to find the $u_1(t)$ that minimizes the number of community members that are infected,

$$J = \int_0^T \beta S(I_1 + cI_2)\ dt, \tag{3.43}$$

where susceptible community members (S) can be infected by either an infectious community member (I_1) or an infectious traveler (I_2) and subject to the terminal condition $I_1(T) = I_{\min}$, and the constraint $U_1(T) \leq U_{1\max}$.

As for Problem 1, for Problem 2 minimizing the total number of infected people is equivalent to maximizing the number of susceptible community members at the end of the outbreak. This is shown by integrating equation (3.39)

$$S(T) - S(0) = -\int_0^T \beta S(I_1 + cI_2)\, dt = -J. \tag{3.44}$$

Next, we observe that from equation (3.39), we can write $-\dot{S} = \beta S(I_1 + cI_2)$ and making I_1 the subject, we get $I_1 = -\frac{\dot{S}}{\beta S} - cI_2$. Substituting these two expressions into equation (3.40) gives,

$$\dot{I}_1 = -\dot{S} + \frac{\mu}{\beta}(1 + c\beta I_2) - u_1 I_1. \tag{3.45}$$

If we let $I_2(0) = \theta/\gamma$, then $I_2 \equiv \theta/\gamma$ is constant, rearranging equation (3.45) and integrating from 0 to T, we obtain the total number of isolated infected community members,

$$\begin{aligned} U_{1[u_1]}(T) &= \int_0^T u_1 I_{1[u_1]}\, dt, \\ &= S(0) - S_{[u_1]}(T) + I_1(0) - I_{\min} + \frac{\mu}{\beta} \ln\left(\frac{S_{[u_1]}(T)}{S(0)}\right) + \frac{\theta}{\gamma}\mu c T_{[u_1]}. \end{aligned} \tag{3.46}$$

Equation (3.46) is identical to (3.37) except for the $+\frac{\theta}{\gamma}\mu c T_{[u_1]}$ term, where $T_{[u_1]}$ is the duration of the outbreak and the subscript $[u_1]$ has been added to emphasize that this duration depends on the control, $u_1(t)$. This new term is positive, and so the impact of importations is to move the $U_{1[u_1]}(T)$ curve (as shown in Figure 3.1) upwards, although this upwards shift is not the same for all $S_{[u_1]}(T)$ due to the co-dependence of $S_{[u_1]}(T)$ and $T_{[u_1]}$ on the control strategy, $u_1(t)$.

We are not able to complete the proof that Problem 2 also satisfies Theorem 3.6.1, however, our numerical analysis (see Chapter 4) suggests that Theorem 3.6.1 also holds for Problem 2. Theorem 3.6.1 states that $u_1^*(t) \equiv u_{1\max}$ is the optimal strategy if resources are sufficient.

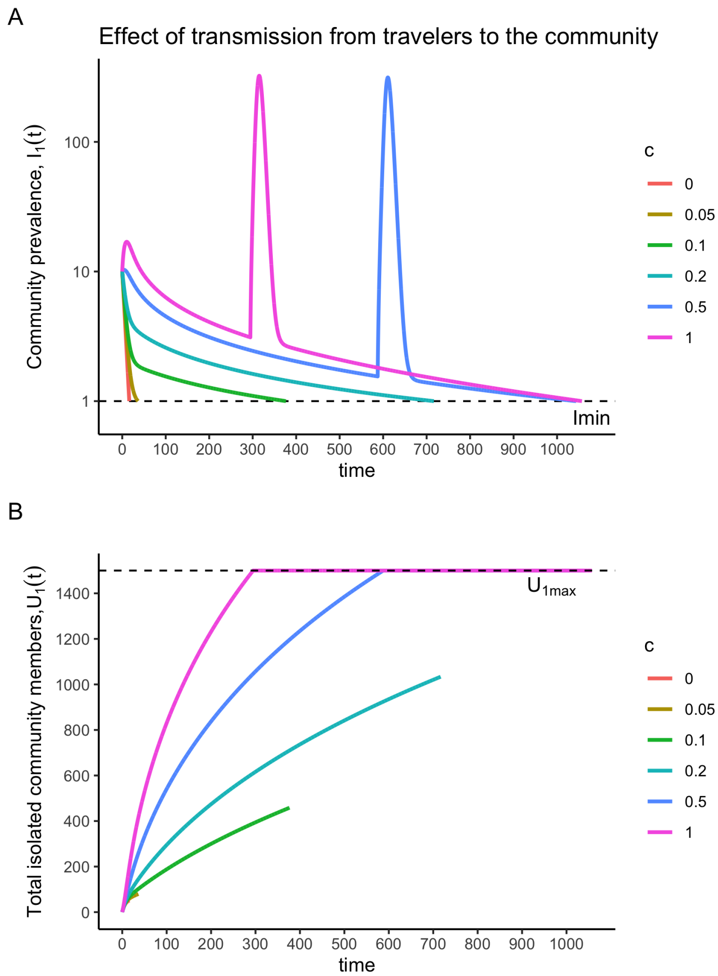

Figure 3.2: The effect of the relative transmissibility of infected travelers, c, on community infection prevalence when an optimal control is implemented. When c is large, resources are not sufficient to implement $u_1(t) = u_{1\max}$ for all time. In this case, when resources are used up, $u_1(t) = 0$, and community infections rebound. As this rebound can be large, community infection prevalence, $I_1(t)$, is shown on a logarithmic scale. For the successively increasing values of c shown, the outbreak ends at $T = 16, 36, 377, 717, 1044$ and 1057 days. Parameters and initial conditions are the same as in figure 3.1 except $\theta = 2$ people day^{-1}, $U_{1\max} = 1500$ people and $I_{\min} = 1$ person, $I_2(0) = \frac{\theta}{\gamma + u_{2max}}$ people. When resources are not sufficient, the optimal control is not unique. Here, the optimal control that we have considered is to implement $u_1(t) = u_{1\max}$ until all resources are used and to then implement $u_1(t) = 0$.

The impact that infected travelers spreading infections to community members ($c > 0$) can have on the optimal control is that more community infections occur, and this may mean that community isolation resources are not sufficient (figure 3.2 B, $c = 0.5$ and 1). In this case, when resources are exhausted and $u_1(t) = 0$ occurs, community infection prevalence can rebound (figure 3.2 B, $c = 0.5$ and 1). Further, when infected travelers spread infections to community members more readily the outbreak can last substantially longer (up to $T = 1057$ days for $c = 1$, as compared to $T = 16$ when there is no infection spread from travelers). However, these substantial effects of infection spread from travelers occur when the community outbreak initially declines. When the community outbreak initially increases, infection spread from travelers can have a negligible effect as will be discussed in the next section.

3.8 Problem 3: Post-Arrival Traveler isolation Only

In Problem 3, we consider post-arrival isolation of infected travelers as the only public health measure used to control infection prevalence in the community. Our model now becomes

$$\frac{dS}{dt} = -\beta S(I_1 + cI_2) \tag{3.47}$$
$$\frac{dI_1}{dt} = \beta S(I_1 + cI_2) - \mu I_1 \tag{3.48}$$
$$\frac{dI_2}{dt} = \theta - (u_2(t) + \gamma)I_2 \tag{3.49}$$
$$\frac{dU_2}{dt} = u_2(t)I_2 \tag{3.50}$$

The objective function is,

$$\min J = \min \int_0^T \beta S_{[u_2]}(I_{1[u_2]} + cI_{2[u_2]})\ dt \tag{3.51}$$

subject to equations (3.47)-(3.50), $T = \inf\{t | I_{1[u_2]}(t) = I_{\min}\}, u_2(t) \in [0, u_{2\max}]$ for all

$t \in [0, T]$ and subject to the resource constraint,

$$U_{2[u_2]}(T) = \int_0^T u_2 I_2 \ dt \leq U_{2\max}. \tag{3.52}$$

As for Problems 1 and 2, it is possible to show that min J is equivalent to maximizing $S_{[u_1]}(T)$, and Problem 3 is still a linear optimization problem such that $u_2^*(t)$ is a bang-bang control as described by Remark 3.4.1. For $u_2(t) \equiv u_{2\max}$ and $I_2(0) = \theta/(\gamma + u_{2\max})$, integrating equation (3.49) gives,

$$U_{2[u_{2\max}]}(T) = \frac{u_{2\max} \ \theta \ T_{[u_{2\max}]}}{u_{2\max} + \gamma}, \tag{3.53}$$

and this expression can be evaluated to determine if resources are limiting. Our numerical results suggest that a theorem similar to Theorem 3.6.1, likely applies for Problem 3. Specifically:

Claim 3.8.1. ***(Optimal Traveler Isolation Strategy)*** *If $U_{2[u_{2max}]}(T) \leq U_{2max}$, then the optimal traveler 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 $U_{2[u_2^*]}(T) = U_{2max}$.*

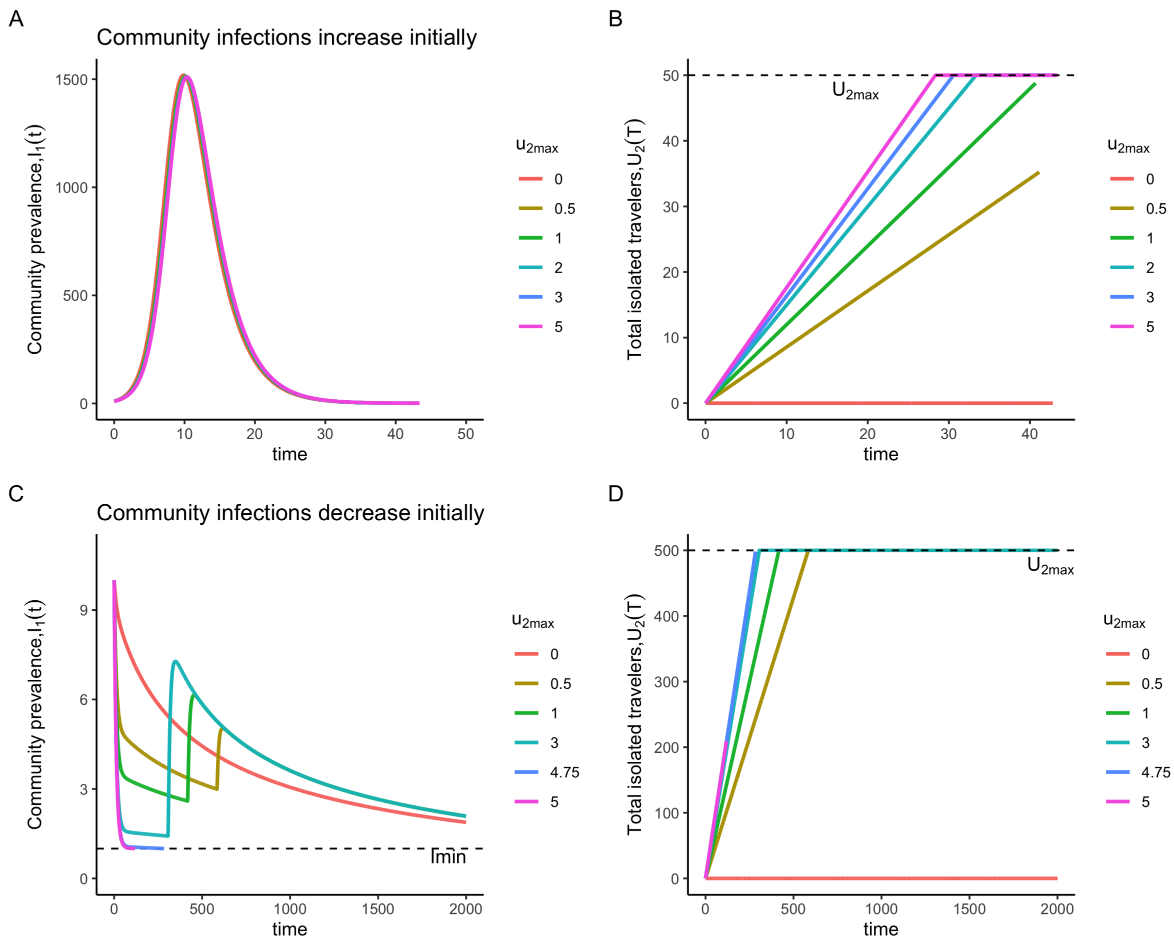

Figure 3.3: The effect of the post-arrival traveler isolation rate ($u_{2\max}$) on community infection prevalence, $I_1(t)$, when an optimal control is implemented. The strategies shown are $u_2(t) = u_{2\max}$ until all resources are used, and then $u_2(t) = 0$ (if resources are not sufficient). The scenarios considered are when community infections initially: decrease (A,B; $\beta = 0.0002$ person^{-1} day^{-1} with $U_{2\max} = 50$ people), or increase (C,D; $\beta = 0.00005$ person^{-1} day^{-1} with $U_{2\max} = 500$ people). For the increasing values of $u_{2\max}$ that are shown, the outbreak end times are $T = 42.8, 42.2, 40.7, 42.9, 43.2$ and 43.4 days (A,B); and $T > 2000$ days for $u_{2\max} = 0, 0.5, 1$ and 3 day^{-1}, and $T = 284$ and 119 days for $u_{2\max} = 4.75$ and 5 day^{-1} (C,D). $c = 1$ and all other parameters and initial conditions are as in figure 3.2.

The effect of post-arrival isolation of travelers is negligible for a community outbreak that increases initially (figure 3.3 A), but can be substantial for outbreaks that decrease initially (figure 3.3 C). When the post-arrival traveler isolation rate is high (i.e., $u_{2\max} = 4.75$ or 5 day^{-1}) the outbreak ends quickly (i.e., in 284 days or less, figure 3.3 C) and resources are sufficient to implement $u_2(t) \equiv u_{2\max}$ for the entire outbreak (figure 3.3 D). However, when the post-arrival traveler isolation rate is low (i.e., $u_{2\max} = 0, 0.5, 1$ or 3) then the community outbreak decreases more slowly and does not reach the terminal condition, $I_1(t) = I_{\max}$ before all the resources for traveler isolation are used (figure 3.3 D). Community infection prevalence, $I_1(t)$ then rebounds (figure 3.3 C) and the outbreak takes a very long time to terminate. In figure 3.3 C, for $u_{2\max} = 0, 0.5, 1$ and 3, the outbreak has still not concluded after 2000 days. However, the outbreak will eventually terminate because $S(t)$ is always decreasing, and dI_1/dt will be negative when $S(t)$ becomes small enough.

3.9 Problem 4: Combined Strategies

The model for the combined strategies: isolation of infected community members, $u_1(t)$, and post-arrival isolation of infected travelers, $u_2(t)$, is described by the system of ordinary differential equations:

$$\frac{dS}{dt} = -\beta S(I_1 + cI_2), \tag{3.54}$$

$$\frac{dI_1}{dt} = \beta S(I_1 + cI_2) - (\mu + u_1(t))I_1, \tag{3.55}$$

$$\frac{dI_2}{dt} = \theta - (\gamma + u_2)I_2, \tag{3.56}$$

$$\frac{dU_1}{dt} = u_1(t)I_1, \tag{3.57}$$

$$\frac{dU_2}{dt} = u_2(t)I_2. \tag{3.58}$$

Let,

$$u_1^{**}(t) = \begin{cases} u_{1\max}, & \text{if} \quad 0 \leq t \leq t_{1\max} \text{ and} \\ 0, & \text{if} \quad t > t_{1\max} \end{cases} \tag{3.59}$$

and,

$$u_2^{**}(t) = \begin{cases} u_{2\max}, & \text{if} \quad 0 \leq t \leq t_{2\max} \text{ and} \\ 0, & \text{if} \quad t > t_{2\max} \end{cases} \tag{3.60}$$

where $t_{1\max}$ and $t_{2\max}$ are the times when all resources are used if the controls are implemented from $t = 0$ onwards. If resources are not limiting for $[u_1^{**}, u_2^{**}]$ then set $t_{1\max} = t_{2\max} = T^{**}$, which is the duration of the outbreak when $[u_1^{**}, u_2^{**}]$ is implemented.

Consider the resources used when $u_1(t) = u_1^{**}(t)$ and $u_2(t) = u_2^{**}(t)$ are implemented. These are,

$$U_{1[u_1^{**}, u_2^{**}]}(T^{**}) = \int_0^{t_{1\max}} u_1^{**} I_1 \, dt \leq U_{1\max}, \tag{3.61}$$

and

$$U_{2[u_1^{**}, u_2^{**}]}(T^{**}) = \int_0^{t_{2\max}} u_2^{**} I_2 \, dt \leq U_{2\max}. \tag{3.62}$$

When both resources are not limiting, following from the results of Problems 2 and 3, we conjecture that $[u_1^{**}, u_2^{**}] \equiv [u_{1\max}, u_{2\max}]$, which is to use both resources maximally until the outbreak ends, is the unique optimal strategy for Problem 4.

When at least one resource is limiting, the results from Problems 2-3 suggest that the optimal control may not be unique. However, because all the resources are used, $u_1^{**}(t)$ and $u_2^{**}(t)$ are an optimal controls, just not the only optimal controls, when resources are limiting for Problems 1-3. Therefore, $[u_1^{**}, u_2^{**}]$ may be an optimal control for Problem 4, although not a unique optimal control, when at least one resource is limiting. We consider this possibility in more detail below.

Claim 3.9.1. *The optimal combined strategy when both resources are not limiting is* $[u_1^{**}(t), u_2^{**}(t)] \equiv [u_{1max}, u_{2max}]$. *If only one resource is limiting, we define an optimal preferred strategy, as satisfying the requirements of an optimal control, but this strategy is preferred because it uses the least amount of the non-limiting resource.*

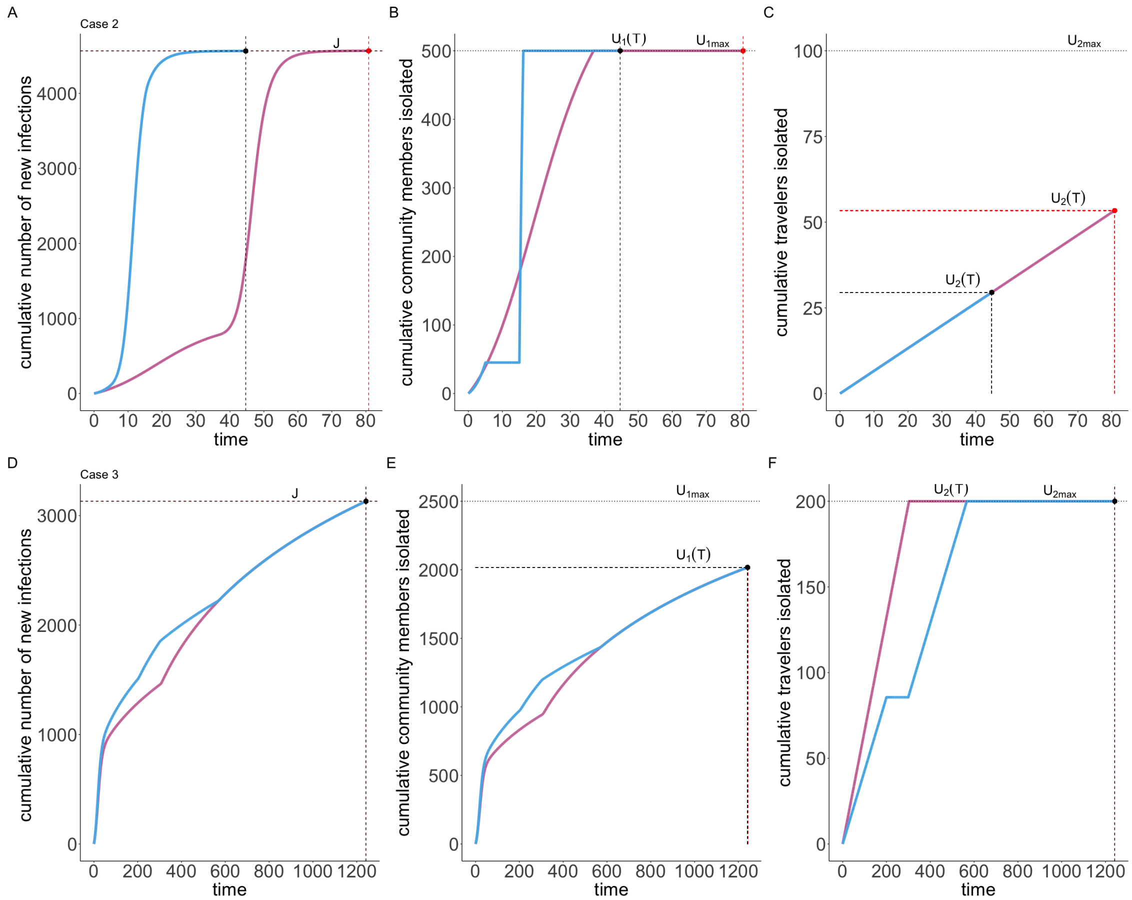

Figure 3.4: Comparison of two combined strategies when one resource is limiting (Case 2: traveler isolation resources are limiting, A-C; and Case 3: community isolation resources are limiting, D-F). The two strategies use resources maximally beginning at $t = 0$ until the limiting resource is exhausted (red) and delayed implemented of measures involving the limiting resource (blue). Note that the number of cases in the outbreak, J (A,D), is the same for the two strategies. For Case 3 (D-F), the outbreak ends at the same time for both strategies $T^{**} = \tilde{T} = 1143$ days. When community isolation resources are limiting, the strategy that delays the implementation of measures (blue) results in an outbreak that ends earlier ($\tilde{T} = 51$ days) and uses fewer traveler isolation resources (B) as compared to the strategy that implements community isolation measures from the beginning of the outbreak (red; $T^{**} = 82$ days). Parameters and initial conditions are the same as in figure 3.2 except $\theta = 1$ person day^{-1}, $u_{1\max} = 0.6$ $u_{2\max} = 1.3$ day^{-1}, $U_{1\max} = 500$, $U_{2\max} = 100$ people (A-C), $U_{1\max} = 2500$, $U_{2\max} = 200$ people, $u_{2\max} = 1.3$ day^{-1} (D-F).

Case 1: Both resources are not limited. See Claim 3.9.1.

Case 2: Community resources (limited); traveler resources (not limited). Resources for traveler isolation are not limited so the optimal control is $[u_1(t), u_2(t)] = [u_1^*(t), u_{2\max}]$ where $u_1^*(t)$ denotes an optimal strategy for community isolation resource use, which by definition uses all the available resources for community isolation. Consider two strategies that might meet the requirements for $u_1^*(t)$, which are $u_1^{**}(t)$ and $\tilde{u}_1(t)$ where the later is different from $u_1^{**}(t)$ and uses all the available resources for community isolation. Let $\tilde{T}$ be the duration of the outbreak when $[\tilde{u}_1(t), u_{2\max}]$ is implemented and let $U_{2[\tilde{u}_1,u_{2\max}]}(\tilde{T})$ be the amount of traveler isolation resources used.

Consider whether the total number of community infections, J (see equation 3.43) is smaller for $[u_1^{**}(t), u_{2\max}]$ or $[\tilde{u}_1(t), u_{2\max}]$. In general, we cannot determine this, but a numerical example (figure 3.4 A) shows that J (dashed horizontal line) is the same for $[u_1^{**}(t), u_{2\max}]$ (red line) and a $[\tilde{u}_1(t), u_{2\max}]$ (blue line) strategy. While both of these strategies satisfy the constraints and have the same value of the objective function, $[\tilde{u}_1(t), u_{2\max}]$ is preferred. This is because less of the non-limiting traveler isolation resource is used for $[\tilde{u}_1(t), u_{2\max}]$ (figure 3.4C, blue line). Less of the traveler isolation resource is used for $[\tilde{u}_1(t), u_{2\max}]$ because the outbreak ends more quickly ($\tilde{T}$= 51 days, while T^{**}=82 days). This may be surprising because it may seem that the strategy with the earliest implementation of maximum community isolation measures ($t = 0$ for $[u_1^{**}(t), u_{2\max}]$) would end first, however, this is not the case, likely because community infection prevalence is low initially, so few community members are isolated at this time. The delayed implementation of community isolation measures for $[\tilde{u}_1(t), u_{2\max}]$ are timed to correspond with high infection prevalence.

Case 3: Community resources (not limited); traveler resources (limited). Case 3 is similar to Case 2, except that traveler isolation measures do not noticeably impact community prevalence, and so both strategies, $[u_{1\max}, u_2^{**}]$ (red line) and $[u_{1\max}, \tilde{u}_2]$ (blue line) seem to end at the same time ($T^{**} = \tilde{T} = 1143$ days; figure 3.4 D-F) and require the same amount of the non-limiting resource ($U_{2[u_{1\max},\tilde{u}_2]}(\tilde{T}) = U_{2[u_{1\max},u_2^{**}]}(T^{**})$, figure 3.4 E).

Case 4: Both resources are limited. Numerical results suggest that any $[u_1^*(t), u_2^*(t)]$ that uses all available resources is optimal. Here, the exact form of $[u_1^*(t), u_2^*(t)]$ may affect the duration of the outbreak, T, but the total number of infections, J, will be the same and the number of individuals isolated will be $U_{1\max}$ and $U_{2\max}$ in all instances. The optimal strategy is likely any $[u_1(t), u_2(t)]$ that uses all available resources.

To summarize, our numerical results suggest that the combined optimal control is similar to the concurrent implementation of the optimal control when only one control is available (Problems 2 and 3). However, it should be noted that when traveler isolation resources are not limiting (Case 2), it is preferred to use an optimal community isolation strategy that ends the outbreak earlier, so as to require less of the non-limiting resource.

Chapter 4

Optimal controls and public health strategies

In this section, we provide mathematical definitions of the public health strategies so that the results of Chapter 3 can be discussed using public health terminology.

Table 4.1: Definition of public health strategies

Public Health Strategy	Description	Definition
Elimination	Infection prevalence is reduced to zero locally, but not in all regions, such that there remains a risk of disease importation [10], [53].	(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.
Mitigation	Mitigation aim to slow the spread of an infectious disease to avoid overwhelming healthcare capacities and to reduce overall morbidity and mortality [39], [70].	(a) Public health measures are implemented throughout the entire outbreak, i.e., $U_{1[u_{1\max}]}(T) \leq U_{1\max}$ 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.

Given these definitions (Table 4.1), Theorem 1 in Hansen and Day (2011) can be restated as,

(a) If resources for community isolation are not limited, then optimal control for Problem 1 is:

(i) elimination: if community infections decrease initially, or

(ii) mitigation, if community infections do not decrease initially.

(b) If resources for community isolation are limited, then an optimal control for

Problem 1 is:

(i) any circuit breaker strategy that uses all of the available resources. In this case, the circuit breaker strategy that uses all of the available resources is equivalent to a non-circuit breaker strategy that uses all of the available resources (for example, using community isolation resources at the maximum daily rate from $t = 0$ until they are all used up).

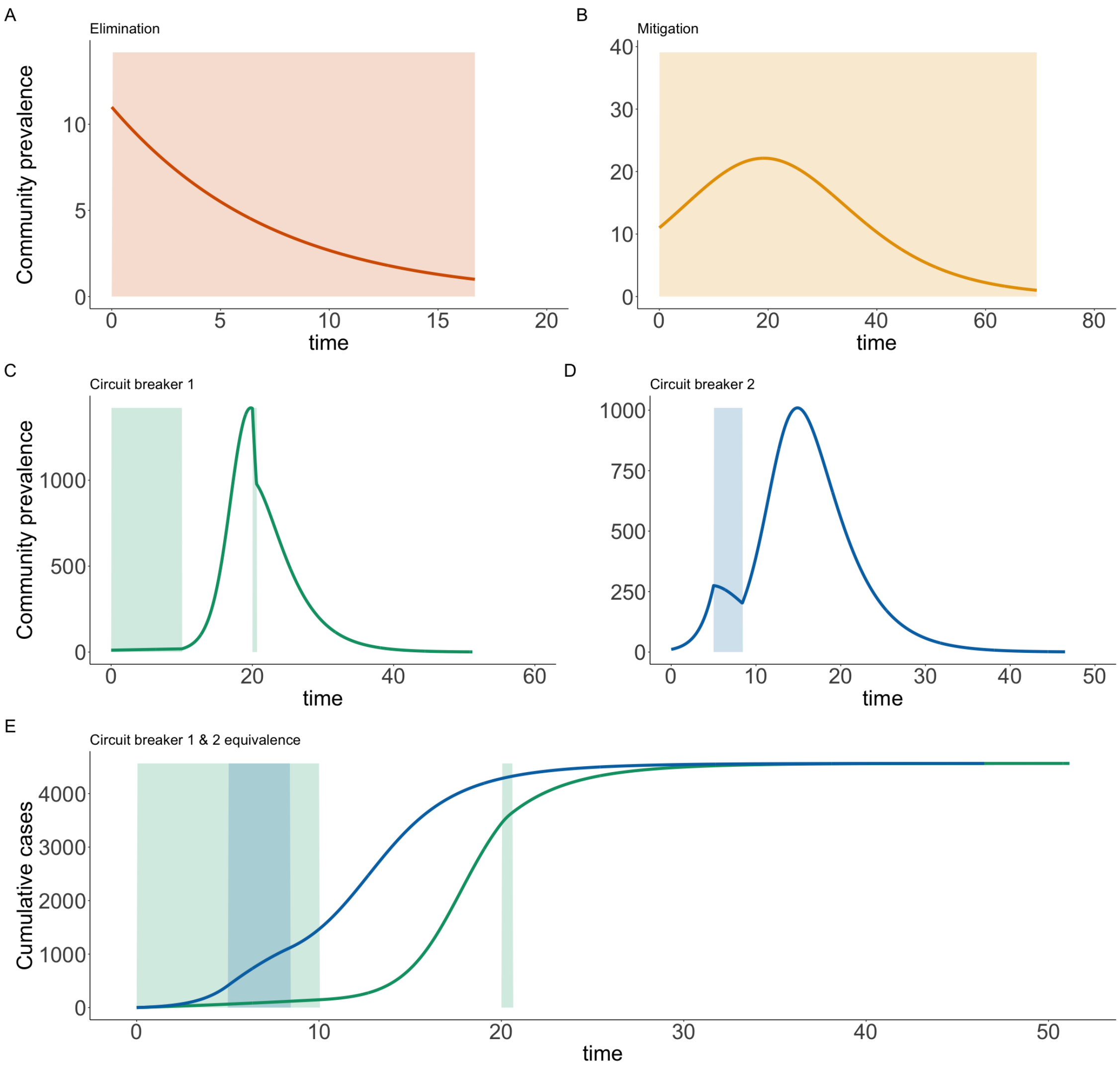

Figure 4.1: The optimal controls categorized as different types of public health strategies for the community isolation-only model (Problem 1 (Sec. 3.6)). The shaded regions correspond to $u_1(t) = u_{1\max}$ and the unshaded regions correspond to $u_1(t) = 0$ for the optimal control. The aim of the optimization problem is to minimize the number of cases in the outbreak, which is the final value (at $t = T$) in panel E. Parameters are $u_{1\max} = 0.7$ day^{-1} (A) or 0.6 day^{-1} (B-E), $U_{1\max} = 1500$ people (A, B) or 500 poeple (C-D) and for all panels all other parameters and initial conditions are the same as in figure 3.2.

Figure 4.1 (A-D) shows the dynamics of community infection prevalence, $I_1(t)$, for Problem 1 given these definitions of the public health strategies (Table 4.1). Note that for the elimination strategy, the outbreak is over more quickly (A, less than

17 days) than any of the other public health strategies (B-D, more than 45 days). Figure 4.1 (E) confirms numerically that any strategy that uses all available resources is equivalent when resources are limiting. Circuit breaker 1 and 2 are two optimal controls that have the same number of cases in the outbreak. Note that at any point during the outbreak, the cumulative number of cases may be different for circuit breaker 1 and 2, but when the outbreak ends, this total number of cases is the same.

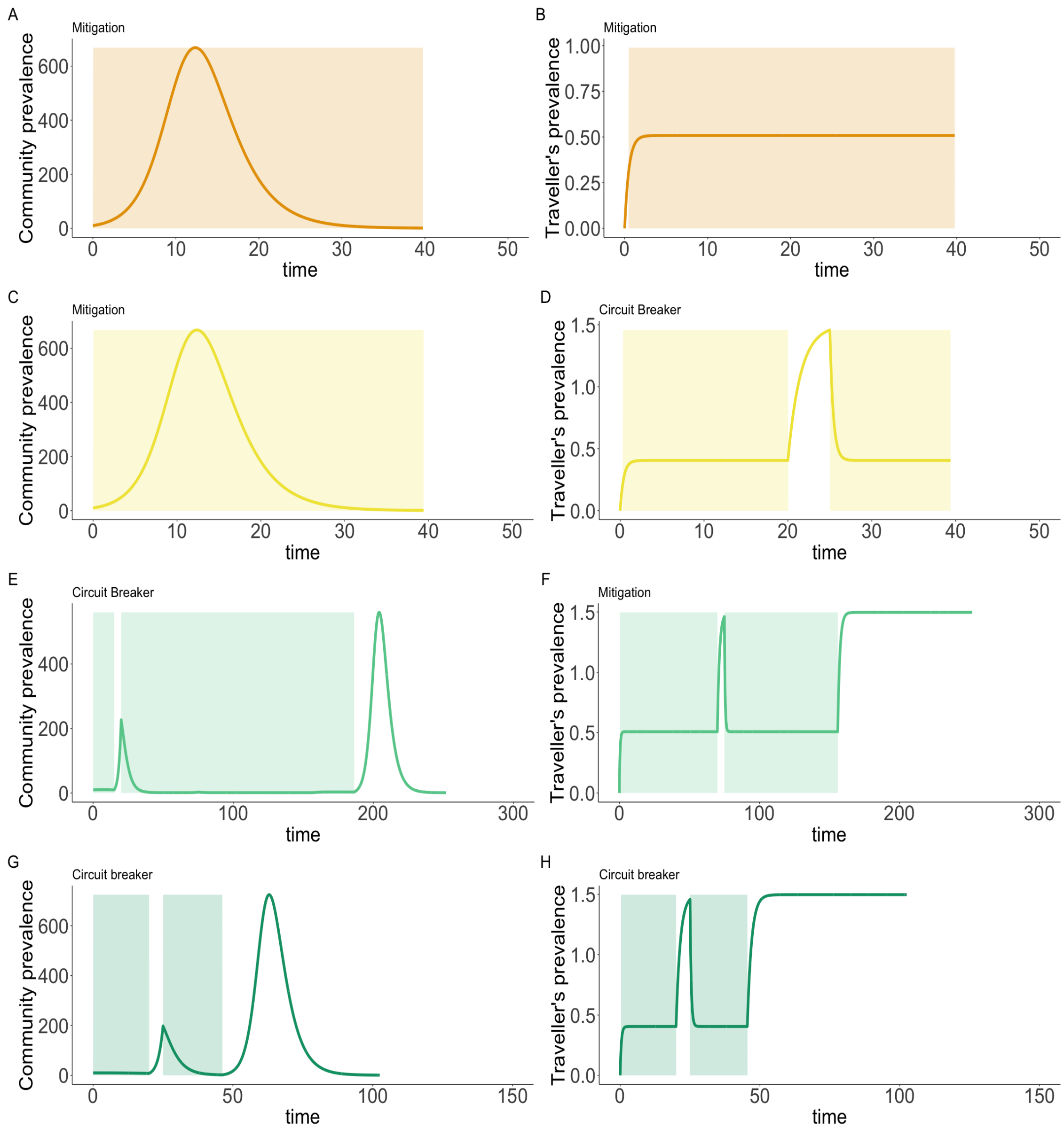

Figure 4.2: The optimal controls categorized as different types of public health strategies for the combined strategies (Problem 4 (Sec. 3.9)) with community infection prevalence, $I_1(t)$, shown in the left columns, and traveler infection prevalence, $I_2(t)$, shown in the right columns. The shading overlayed on $I_1(t)$ shows where $u_1(t) = u_{1\max}$ and the unshaded regions shows where $u_1(t) = 0$ for the optimal control (left columns), and the shading overlayed on $I_2(t)$ shows where $u_2(t) = u_{2\max}$ with the unshaded regions corresponding to $u_2(t) = 0$ for the optimal control (right columns). Parameter values are $u_{1\text{max}} = 0.2$ day^{-1}, $u_{2\text{max}} = 1.3$ day^{-1} for (A-B), $u_{1\text{max}} = 0.2$ day^{-1}, $u_{2\text{max}} = 1.8$ day^{-1} for (C-D), $u_{1\text{max}} = 0.7$ day^{-1}, $u_{2\text{max}} = 1.3$ day^{-1} for (E-F), $u_{1\text{max}} = 0.7$ day^{-1}, $u_{2\text{max}} = 1.8$ day^{-1} for (G-H), and all other parameters and intial conditions are the same as in figure 3.2.

Analogous rephrasing of the optimal controls is possible for Problems 2-3. For Problem 4, we need to specify whether the strategy corresponds to the community isolation control or the traveler isolation control and this is indicated with the notation, $[\mathrm{mit}, \mathrm{circ}]$ for example, to indicates that the optimal control involves community measures implemented as a mitigation strategy, and the travel measures implemented as a circuit breaker strategy that uses all of the available resources. The distinction between elimination and mitigation is a condition on the sign of the change in the number of community infections at $t = 0$. Therefore, when resources are not limiting for the combined controls the only possibilities are: $[\mathrm{elim}, \mathrm{elim}]$ or $[\mathrm{mit}, \mathrm{mit}]$. Notably, $[\mathrm{elim}, \mathrm{mit}]$ and $[\mathrm{mit}, \mathrm{elim}]$ is not possible.

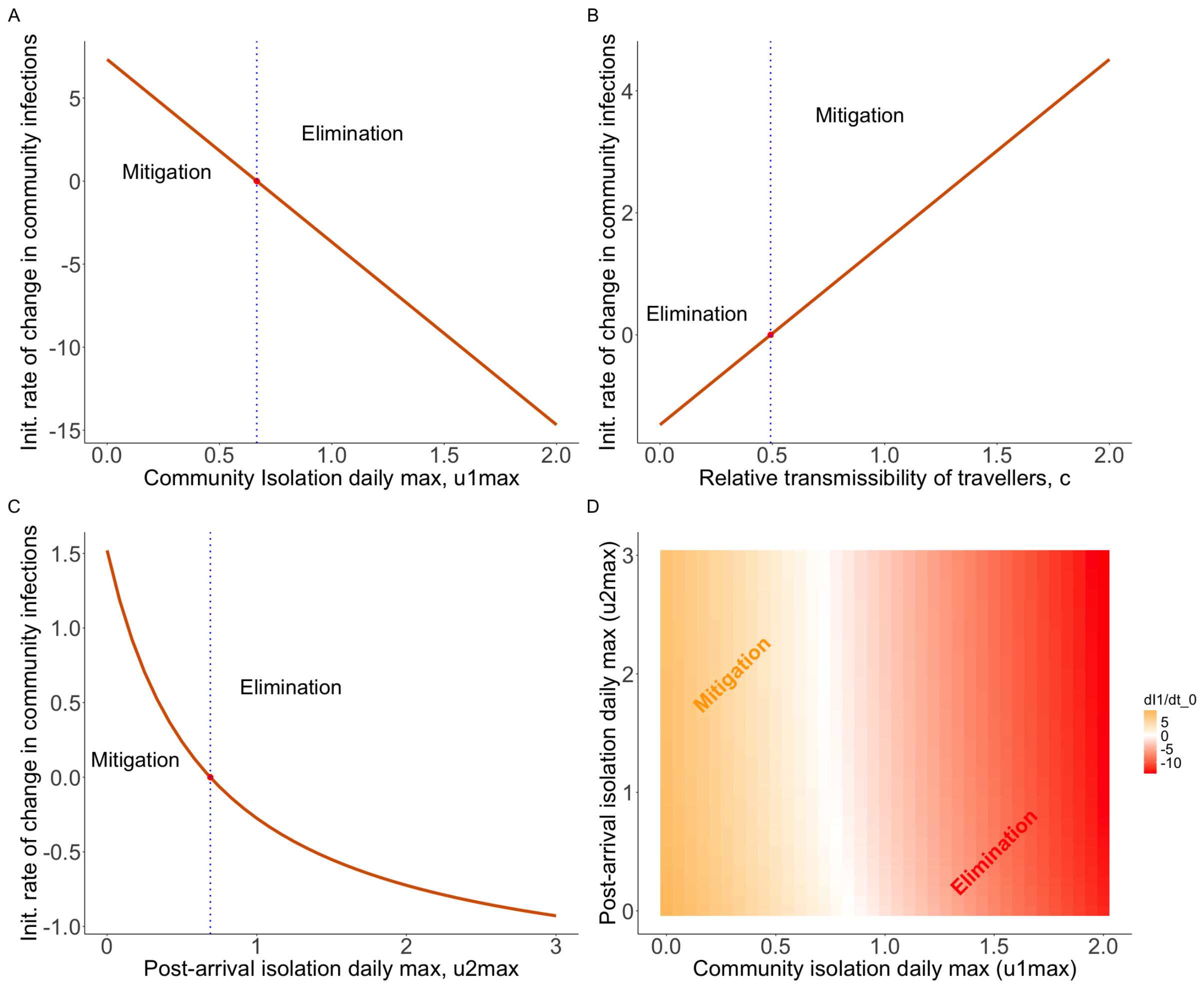

Figure 4.3: The effect of parameters on the initial change in the number of community infections, which determines whether the optimal control is an elimination strategy ($\frac{dI_1}{dt}|_{t=0} < 0$) or a mitigation strategy ($\frac{dI_1}{dt}|_{t=0} \geq 0$). The blue dotted line indicates the value of the parameter where $\frac{dI_1}{dt}|_{t=0} = 0$. Parameters and initial conditions are the same as in figure 3.2 except $U_{2\max} = 50$ people.

Next, we will determine how model parameters affect which public health strategies are the optimal controls. The characterization of a strategy as elimination or mitigation is due to the sign of $\frac{dI_1}{dt}|_{t=0}$. Numerical results (Figure 4.3) indicate that the optimal control corresponds to an elimination strategy when: the maximum daily isolation rate of community members, $u_{1\max}$ is high (A; Problem 1); the transmissibility of travelers relative to community members, c, is low (B; Problem 2); and the maximum daily isolation rate of infected travelers, $u_{2\max}$ is high (C; Problem 3). Further, a unit increase in the maximum daily rate that community members are isolated, $u_{1\max}$, decreases the slope, $\frac{dI_1}{dt}|_{t=0}$, more substantially than a unit increase in the maximum daily rate that travelers are isolated, $u_{2\max}$ (Figure 4.3 D; Problem 4).

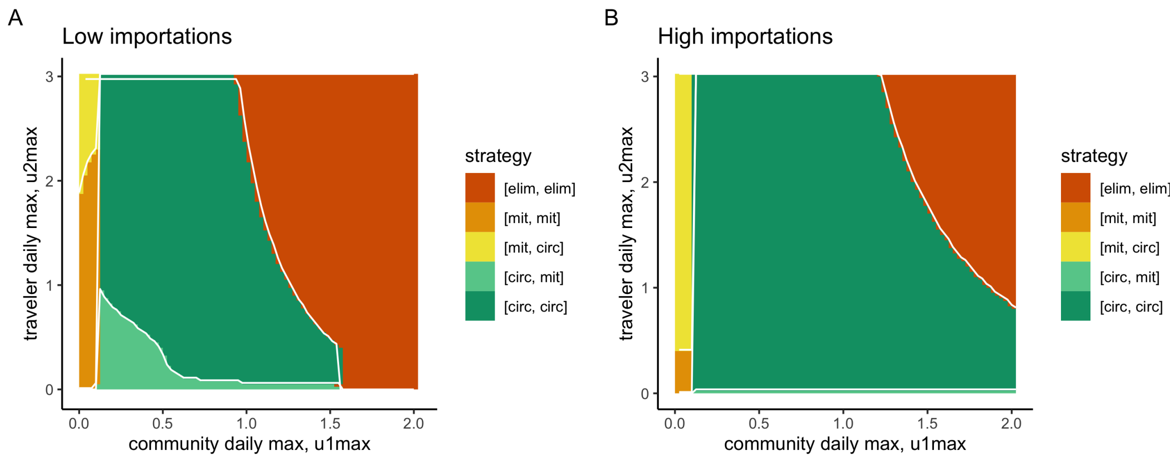

Figure 4.4: The effect of the maximum daily isolation rate of community members, $u_{1\max}$, and travelers, $u_{2\max}$ on the combined optimal control described in terms of public health strategies. The low importation scenario (A) has $\theta = 1$ and the high importation scenario has $\theta = 2$. All other parameters and initial conditions are the same as in figure 3.2.

When both community measures and travel measures can be used in combination to control the outbreak, if the maximum daily isolation rates for both community members, $u_{1\max}$, and travelers, $u_{2\max}$ is high, then the optimal control corresponds to an elimination strategy (Figure 4.4 A, B; red region). This is because the control measures are highly effective in decreasing the number of cases and quickly ending the outbreak (Figure 4.5 A, B; see the region labelled as [elim, elim]). When both of these daily maximum isolation rates are low, the optimal control corresponds to a mitigation strategy for both control measures (Figure 4.4 A, B; orange region) because the control measures have only a very small effect on the outbreak, with only a few people isolated, so that the total resources available are not used up. When the importation rate is high (Figure 4.4 B), larger maximum daily isolation rates are needed for the optimal control to correspond to elimination (i.e., the red region is smaller). The regions corresponding to a mitigation strategy for travel measures (Figure 4.4, light green and yellow) become smaller with higher importation rates as total traveller isolation resources are sufficient only when the maximum daily traveler isolation rate is very low.

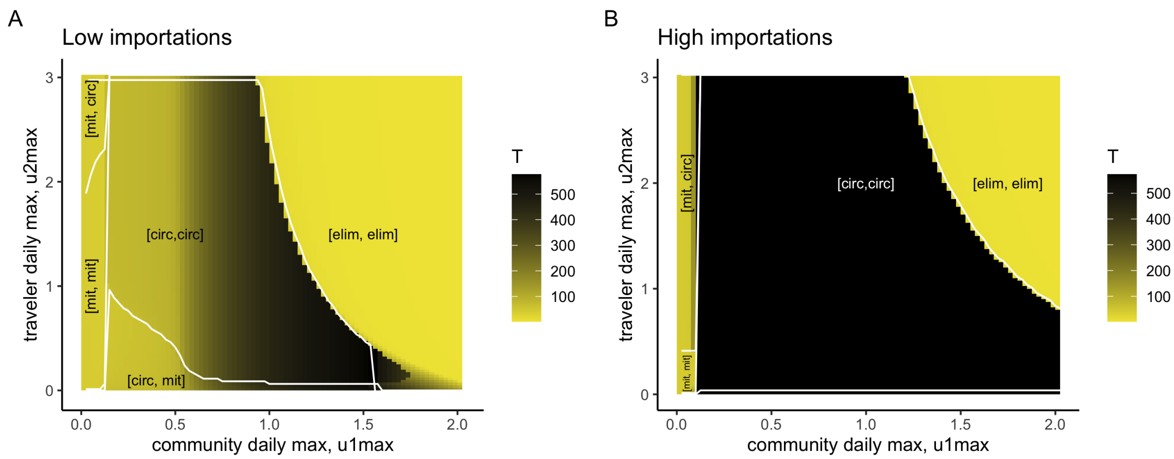

Figure 4.5: The duration of the outbreak, T, when the optimal control is implemented. All parameters are the same as figure 4.4 and the boundaries between regions corresponding to different public health strategies are shown with white lines.

Our categorization of the optimal controls into three different types of public health strategies correspond to substantial changes in the duration and number of cases in the outbreak. If resources are not limiting, and the control measures can stay in place until the outbreak ends (i.e., an elimination or mitigation strategy) then the outbreak shorter (figure 4.5). The longest duration outbreaks occur when resources are limiting and a circuit breaker strategy is needed. The outbreaks are particularly long, in these instances, when the importation rate is high, which slows the decline in community infection prevalence to the threshold for the outbreak to be defined as over, and when the maximum daily rates are just smaller than the values needed to achieve elimination.

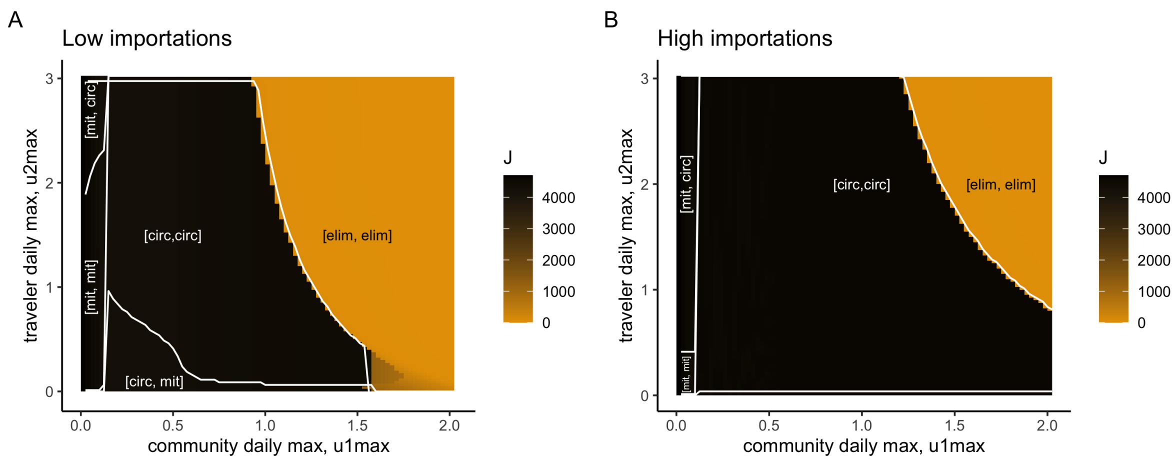

Figure 4.6: The number of cases in the outbreak, J, when the optimal control is implemented. All parameters are the same as figure 4.4 and the boundaries between regions corresponding to different public health strategies are shown with white lines.

When the conditions are such that an elimination strategy (labeled as [elim, elim]) is optimal the outbreak will be short (figure 4.5) and consist of relatively few cases (figure 4.5). When the conditions are such that the optimal strategy for community isolation is a mitigation strategy (labeled as [mit, mit] and [mit, circ]) the outbreak will be short (figure 4.5) and consist of many cases (figure 4.6). When the conditions are such that the optimal strategy for community isolation is a circuit breaker strategy (labelled as [circ, mit] and [circ, circ]) the outbreak will be long (figure 4.5) and consist of many cases (figure 4.6).

Chapter 5

Conclusion

We expanded on the work of Hansen and Day [30] by considering infection spread to community members from travelers, and implementing post-arrival traveler isolation as a control measure. Hansen and Day [30] had previously found that when isolation resources are limited, any strategy that uses all available resources is optimal. Our findings suggest that this result generalizes to situations that involve imported infections. We interpret the results that any strategy that uses all the available resources is optimal, as support for a circuit breaker strategy. The circuit breaker strategy involves precautionary breaks from public health restrictions [42], and such a strategy is optimal as long as the delays to implementing public health measures are not so long as to have the outbreak be nearly over by the time measures are implemented. When lengthy delays to implementing measures occurs, too few individuals remain to potentially be infected, and all of the isolation resources cannot be used, which is not optimal.

In some situations, circuit breaker (limited resources) and mitigation (low maximum isolation rates) strategies are optimal, however, in the situations where an elimination strategy is the optimal strategy, the elimination strategy performs substantially better, both in terms of smaller outbreaks (Figure 4.6) and shorter outbreaks (Figure 4.5). While not captured in our objective function, there is significant benefit to short duration outbreaks as this means that public health interventions need to be in place for a shorter duration. As the elimination strategy performs very well, in the situations where it is optimal, this suggests that future work might consider optimization problems where the control variables may allow the situation to become favorable for elimination. For example, the maximum isolation rates are fixed values in our optimizations problems, but future work could consider the maximum isolation rate as a control variable. Similarly, in our formulation the resource constraints are fixed, however in some situations, all the resources are used just before the outbreak was about to end. Releasing the public health measures results in a second wave of infection (i.e., see Figure 3.2 A) that would have been avoided if more resources could have been made available, such that the public health measures could have remained in place a short time longer.

While we find that circuit breaker strategies can be optimal, a simple recommendation from our results is that initiating maximum isolation efforts as soon as the outbreak is detected, i.e., 'don't wait, re-escalate' [37], is likely always a best action. If the outbreak ends before resources are exhausted, then this strategy is *the* best action. If resources are exhausted before the outbreak ends, then the 'don't wait' strategy results in the same number of infections in the outbreak as a circuit breaker strategy that uses all of the available resources, however, in this case, the 'don't wait' strategy was still one of many equivalent, and optimal, strategies. Further support for the 'don't wait' strategy comes from the precautionary principle, which states that even when information is lacking, actions should be taken to prevent catastrophes [38]. In the context of our problem, when the outbreak begins, it is likely not known if resources will be sufficient to remain in place for the entire outbreak, the precautionary principle would suggest the early, precautionary, implementation of public health measures, and our result further suggest that this approach would, at worst, perform the same as a different strategy.

5.1 Study Limitations and Future directions

The formalizations of the optimization problems that we consider follows closely from Hansen and Day [30], and is advantageous as the framework leads to clear descriptions of the qualitative characteristics of the optimal control that are likely applicable in many general settings. However, some aspects of the problem formulation are likely responsible for the results.

The model formulation does not consider a cost associated with resource use, but considers only a binary distinction between resources being limited or not limited. In reality, less resource use is likely to cost less and be preferred, and it is likely possible to increases the total resources available, although perhaps at some high cost. The results that, when resources are limited, any strategy that uses all available resources is optimal may be due to this assumption of a fixed constraint on the available resources. Furthermore, the objective function does not consider the duration of the outbreak, and shorter outbreaks may be more desirable as public health measures do not need to remain in place for an extended period.

Our study uses a terminal condition which defines the outbreak as over when community infection prevalence reaches some low value, $I_{1\min}$, which was necessary to prevent artificial second waves of infection when measures are released, and which occurs in the continuous dependent variable ordinary differential equation formulation. Considering the problem on a fixed interval of time may have been more instructive. The recent work of [50] contains important ideas on how to reconcile this challenge. Fully stochastic models can be difficult to analyze and questions considering elimination strategies can still be assessed if community outbreaks are modelled using deterministic Susceptible-Infected-Recovered type models that are ‘pieced together’ over some fixed time period, with zero incidence in the between-outbreak periods, with individual outbreak termination conditions as defined in this study, and with importations represented as discrete events that introduce infections and initiate the community outbreak. We refer to this as the ‘switch model’ because the community spread model is turned on when an importation occurs, and turned off when terminal condition is met, and this occurs repeatedly across the fixed period being considered.

Our study has not considered any mechanisms, other than infection, whereby the number of susceptible individuals could change. Such mechanisms could be births, waning immunity, vaccination, human behavior, and the evolution of the pathogen. Note that our optimal strategies require that if resources are limiting, all available resources need to be used. Therefore, if susceptible individuals are removed by a mechanism other other infection, it is necessary to implement public health measures earlier, to ensure that resources do not still remain after the outbreak ends, which is not optimal. This is similar to strategies implemented by some regions, i.e., Newfoundland and Labrador, during the COVID-19 pandemic, where relatively strict public health measures were implemented until the local community obtained substantial immunity through vaccination and the ‘Together.Again’ plan to relax these measures was proposed [2].

If the pathogen evolves new epidemiological characteristics, as the SARS-CoV-2 virus did during the pandemic, it remains an open problem to determine the optimal timing of public health measures, such as isolation of infected community members. 'Pandemic fatigue' [46] is an important consideration as compliance is likely to be lower after already prolonged periods of restrictions. Further, the pathogen may evolve, so as to be uncontrollable, for example evolving short generation times that make contact tracing difficult, and this would be an evolutionary reason why measures are less effective when timed later. Finally, public health measures are a component of the selection pressure that acts on the pathogen, and so the characteristics that pathogens evolve depends also on the public health strategy.

Our primary contributions have been to show that the results of Hansen and Day [30] generalize to problems that consider infection of community members of travelers. The framework of Hansen and Day [30] is amenable to future insights, and we recommend that future work continues to expand on this problem set-up. In this thesis, we also worked to unite the terminology used in public health with the results of optimal control problems. The value of the optimal control problem formulation is to tangibly describe the situations in which each public health strategy is recommended. While the problem set-up involves the assumptions typically associated with ordinary differential equation model formulations, the results are qualitative, i.e., elimination, mitigation or circuit breaker strategies are optimal, and the specific details of any specific application, might change quantitative nuances of the best public health strategies, but the general principles that we describe are likely applicable in many general settings.

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