Epidemiology Modeling

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Introduction: A Prelude to Epidemiological Models

The concept of threshold or tipping point, a mathematical expression that characterizes the

conditions needed for the occurrence of a drastic *transition* between epidemiological states, is central to the study of the transmission dynamics and control of diseases like dengue, influenza, SARS, and tuberculosis, to name a few. The quantification of tipping point phenomena goes back to the modeling and mathematical work of Sir Ronald Ross [86] and his "students" [72, 73]. The epidemiological modeling overview in this entry offers a *personal perspective* on the role of mathematical models in the study of the dynamics, evolution, and control of infectious diseases. The emphasis is on *epidemiological modeling thinking* which refers to the use of *contagion* models in the study of the transmission dynamics of infectious diseases as well as socio-epidemiological processes. Sir Ronald Ross was awarded the first Nobel Prize in Physiology or Medicine in 1902 for "his work on malaria, by which he has shown how it enters the organism and thereby has laid the foundation for successful research on this disease and methods of combating it." (http://nobelprize.org/nobel_prizes/medicine/laureates/1902/) Ross proceeded to confront the challenges associated with understanding and managing malaria patterns at the population level right after the completion of his fundamental research. His commitment to use his discoveries to improve the lives of those housed in malaria-infected areas brought him into the realm of dynamic mathematical models. Ross' writings implicitly emphasized the value of mathematical models as integrators of multi-level information. His malaria mathematical framework led to the development of the mathematical theory of infectious diseases (an outstanding review of the field can be found in Hethcote [65]). Ross' approach provides a wonderful cross-disciplinary example of the study of phenomena whose dynamics are intimately connected to processes across organizational, and temporal scales. We conclude, nearly a century after Ross' seminal contributions to the mathematical theory of infectious diseases (placed in the appendix of his 1911 paper), that the field of mathematics has been enriched by his use of models in addressing the biggest health challenge of his time (an excellent contemporary description of Ross' malaria model and its analysis is found in Aron and May [8]).

Malaria, a highly prevalent disease in many parts of the world, may become established following the arrival of few infected individuals to a malaria-free zone. Successful invasions are started by infectious founding cohorts capable of generating *sufficient* secondary infections before recovery (or death) from the disease. Sufficient is interpreted in many ways: the initial population of infected individuals manages to generate a pattern of exponential growth in the number of secondary infections during the initial phase of the outbreak or alternatively the average number of secondary infections generated, within a large disease-free population, exceeds the critical population threshold (critical population size of infected individuals) required for the establishment of the disease [4, 15]. The loss of susceptible individuals to infection can be thought of as a process of resource depletion as well [46]. Malariologists learned, from the pioneering work of Ross, that bringing the vector population below a minimal size is critical to malaria control. Unfortunately, the consequences of frontal attacks on malaria, such as those conducted in the past with DDT, can have unintended serious consequences [52].

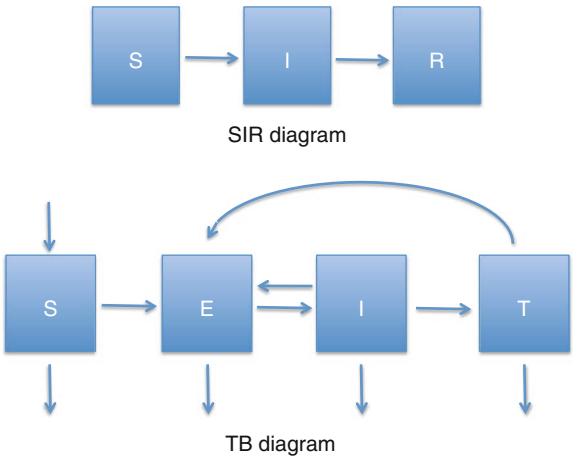
The effective use and dissemination of *epidemiological thinking* suggests that the "contagion" model is indeed part of our daily culture. For example, the use of epidemiological models and concepts helped journalist M. Gladwell [51] understand the reasons behind the dramatic reductions in car thefts and violent crimes in NY City in the 1990s. Gladwell sees "contagion" processes as engines capable of generating epidemics of criminal activity. In fact, through his use of epidemiological concepts, he identifies mechanisms capable of explaining the abrupt decline in criminal activity experienced over a relatively short period of time in NY City. "There is probably no other place in the country where violent crime has declined so far, so fast," Gladwell observes. The importance of these remarks is enhanced by a perspective that sees the growth of criminal activity as the result of "intense" interactions between susceptible and criminally active individuals. The introduction of a dynamic modeling framework in epidemiology increases the toolbox available to researchers that primarily rely on statistical methods. Contagion models, the generators of time-dependent patterns of disease spread, can be used to track a disease over time or evaluate the effectiveness of specific intervention measures. Gladwell's arguments support the view that the measures put in place in NY City (and the nation) were responsible for reductions in the number and/or in the quality of contacts between criminals and susceptible individuals.

Gladwell concludes (as Ross had done it in 1911) that the impact of such contact-reduction measures was sufficient to result in the dramatic reduction in the size of the population of criminals (the criminal core). In other words, the goal of putting policies in place, that brings the criminal core *below the minimal size* needed for the persistence of a sustainable culture of criminal activity, was achieved in NY City. The term *tipping point*, the subject of Gladwell's popular book [53], corresponds in this context, to the identification of the minimal critical size that an "infectious" subpopulation must maintain to thrive and survive. Related important theoretical work, in the context of sexuallytransmitted diseases, was carried out by Hethcote and Yorke [67]. The work of these researchers continues to have a significant impact on the development of public health policies in the context, for example, of gonorrhea and/or HIV/AIDS [19, 66].

The main goal of this entry is to provide an introductory, limited, and personal perspective on the role and use of epidemiological models in the study of infectious diseases and contagion processes in general. It is our hope that this brief entry will convince the reader of the value of epidemiological concepts and models in life and social sciences.

The Basic Contagion Model

W.O. Kermack (a statistician) and A.G. McKendrick (a medical doctor) applied Sir Ronald Ross' ideas to the study of the transmission dynamics of human infectious diseases. Specifically, these researchers applied Ross' ideas to diseases whose transmission dynamics depend on the frequency and intensity of the interactions between susceptible and infected individuals (handshakes or other forms of close intimate associations). Their foundational results published in their 1927 article [72] (with extensions in Kermack and McKendrick [73, 74]) continue to play a critical role in the mathematical theory of infectious diseases. We outline *some* of their ideas, the basic contagion model, and their threshold result in a rather idealized setting. It is assumed that the communicable disease under consideration does not cause a significant number of deaths (measles or chicken pox, or a mild strain of influenza, or a rhinovirus) and that the time scale of interest is so short, that the population's vital dynamics can be "safely" ignored. The disease's introduction is assumed to take place within a population of individuals with no prior history of infections. Individuals are found in three stages: uninfected and susceptible; infected (assumed infectious), and recovered (assumed to be permanently immune). Table 1 collects the state variables and parameters of the model. Figure 1 provides a diagram with the transitions that members of this population may experience as the disease spreads. It is assumed that individuals mix at "random," that is, the rate of encounters (contacts) between susceptible and susceptible, infectious and recovered individuals depends primarily on the frequency of each type.



Epidemiology Modeling, Fig. 1 Diagrams for SIR and TB model

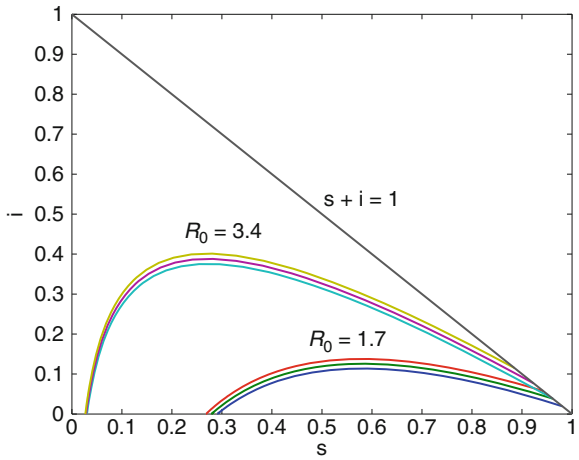
Epidemiology Modeling, Table 1 Parameter definitions

State variables	Description	Parameters	Description
$S(t)$	Susceptible population at time t	c	Average number of contacts per individual
$I(t)$	Infected population at time t	q	Average proportion of contacts with an infectious individual needed for transmission
$R(t)$	Recovered population at time t	γ	Per-capita recovery rate
$N(t)$	Total population size $(N(t) = S(t) + I(t) + R(t))$	$\beta = cq$	Per susceptible and per infective transmission rate

Hence, the average number of effective contacts per susceptible with infectious individuals is $\beta\frac{I}{N}$. The average rate of new infections per unit of time, or the so-called incidence rate, is modeled by $\beta S\frac{I}{N}$. The use of these definitions and assumptions lead to the following simple version of the Kermack–McKendrick model:

$$\begin{aligned}\frac{dS}{dt} &= -\beta S\frac{I}{N},\\ \frac{dI}{dt} &= \beta S\frac{I}{N} - \gamma I,\\ \frac{dR}{dt} &= \gamma I,\end{aligned} \tag{1}$$

with $S(0) = S_0$, $I(0) = I_0 > 0$, and $R(0) = 0$. It quickly follows that $\frac{d}{dt}(S + I + R) = 0$ which implies that N must be constant. Further, the introduction of a small number of infectious individuals, given that N is large, leads to the following reasonable approximation of the model dynamics (at the start of the outbreak): $\frac{dI}{dt} \approx (\beta - \gamma)I$ $[S(0) \approx N]$. Consequently, $I(t) = e^{(\beta-\gamma)t}I_0$ accounts for changes in the infectious class at the start of the outbreak (exponential growth or decay). This type of approximation (finding expressions that capture the dynamics generated by a small number of infectious individuals) is routinely used to asses, the potential for an epidemic outbreak. We conclude that if $\frac{\beta}{\gamma} > 1$ the disease will take off (an epidemic outbreak), while if $\frac{\beta}{\gamma} < 1$ the disease will die out. $\frac{\beta}{\gamma}$, known as the Basic Reproductive Number or R_0, defines a threshold that determines whether or not an outbreak will take place (crossing the line $R_0 = 1$). R_0, a dimensionless quantity, is the product of the average infectious period $(1/\gamma)$ (window of opportunity) *times* the average infectiousness (β) of the members of the *small initial* population of infectious individuals (I_0). β measures the average per-capita contribution of the infectious individuals in generating secondary infectious, per unit of time, within a population of mostly susceptibles $(S(0) \approx N)$. R_0 is *most* often defined as *the average number of secondary infectious generated by a "typical" infectious individual after its introduction in a population of susceptibles* [40, 58]. Computing R_0 is *central* in most instances to the study of the dynamics and control of infectious diseases (but see [45]). Hence, efforts to develop methods for computing R_0, in settings that involve the interactions between heterogenous individuals or subpopulations, are important [28, 40, 41, 43, 47, 58–61, 96].



Epidemiology Modeling, Fig. 2 The s-i phase diagram is plotted under two different values of R_0 ($R_0 = 1.7, 3.4$)

Since the population under consideration is constant, the state variables can be re-scaled (e.g., $s = S/N$). Letting s, i, and r denote the fraction of susceptible, infectious, and recovered, respectively, leads to the following relationship (derived by dividing the second equation by the first in Model (1)) between the s and i proportions:

$$\frac{di}{ds} = -1 + \frac{\gamma}{\beta s}. \tag{2}$$

Figure 2 displays the s-i phase diagram for two different values of R_0 ($R_0 = 1.7, 3.4$). For each value of R_0, three different initial conditions are used to simulate an outbreak and, in each case, the corresponding orbits are plotted. The parameter values are taken from Brauer and Castillo-Chavez [15]. A glance at Model (1) allows us to show that $s(t)$ is decreasing and that $\lim_{t\to 0} s(t) = s_\infty > 0$. The integration of (2) leads to the relationship:

$$ln\frac{s_0}{s_\infty} = R_0\Big[1 - s_\infty\Big], \tag{3}$$

where $1 - s_\infty$ denotes the fraction of the population that recovered with permanent immunity. Equation (3) is referred to as the final epidemic size relation [15, 63]. Estimates of the proportions s_0 and $1 - s_\infty$ can be

Epidemiology Modeling, Table 2 Parameter definitions

State variables	Definitions	Parameters	Definitions
S	Susceptible	Λ	Recruitment of new susceptible
E	Exposed (asymptomatic and noninfectious)	β	Transmission rate per susceptible and infectious
I	Infectious (active TB)	μ, d	Natural and disease-induced mortalities
T	Treated still partially susceptible	k, γ	Per-capita progression and treatment rates
N	Total population $N = S + E + I + T$	$\sigma\beta, 0 \leq \sigma \leq 1$	Transmission rate per treated and infectious
		$p, 0 \leq p \leq 1$	Susceptibility to reinfection

obtained from random serological studies conducted before and immediately after an epidemic outbreak. Independent estimates for the average infectious period $(1/\gamma)$ for many diseases are found in the literature. The use of priori and posteriori serological studies can be combined with independent estimates of the disease's infectious period to estimate β via (3) (see [64]). Efforts to develop methods for connecting models to epidemiological data and for estimating model parameters have accelerated, in part, as a result of the 2003 SARS outbreak [30]. Estimates of a disease's basic reproduction number are now routinely computed directly from data [32–34,36,37,62]. Efforts to identify final epidemic size relations like those in (3) have received considerable attention over the past few years as well (see [7, 17] and references therein). Most recently estimates of the basic reproductive number for A-H1N1 influenza were carried out by modelers and public health researchers at Mexico's Ministry of Health [35]. These estimates helped the Mexican government plan its initial response to this influenza pandemic. The value of these estimates turned out to be central in studies of the dynamics of pandemic influenza [62].

Backward Bifurcation: Epidemics When $R_0 < 1$

The question of whether epidemic outbreaks are possible when $R_0 < 1$ (backward bifurcation) has led to the study of models capable of sustaining multiple endemic states, under what appear to be paradoxical conditions. The study of hysteresis has received considerable attention in epidemiology particularly, after relevant theoretical results on mathematical models of infectious diseases appeared in the literatures [24,57,68]. The model for the transmission dynamics of tuberculosis (TB) provides an interesting introduction to the relevant and timely issue of hysteresis behavior [48]. A *brief* introduction to the epidemiology of TB is outlined before the model (in Feng et al. [48]) is introduced. Tuberculosis' causative agent is *mycobacterium tuberculosis*. This mycobacterium, carried by about one third of the world human population, lives most often within its host, on a latent state and, as a result, this mycobacterium often becomes dormant after infection. Most infected individuals mount effective immune responses after the initial "inoculation" [5, 6, 13, 79]. An effective immunological response most often limits the proliferation of the bacilli and, as a result, the agent is eliminated or encapsulated (latent) by the host's immune system. Tuberculosis was one of the most deadly diseases in the eighteenth and nineteenth centuries. Today, however, only about eight million individuals develop active TB each year (three million deaths) in the world, a "small" fraction in a world, where about two billion individuals live with this mycobacterium [91]. Latently infected individuals (those carrying the disease in a "dormant" state) may increase their own re-activation rate as a result of continuous exposure to individuals with active TB (exogenous re-activation). The relevance of exogenous re-activation on the observed TB prevalence patterns at the population level is a source of debate [48, 90, 93]. The model in Feng et al. [48] was introduced to explore the role that a continuous exposure to this mycobacterium may have in accelerating the average population TB progression rates [21, 23, 48, 90, 93]. It was shown that exogenous re-activation had indeed the potential for supporting backward bifurcations [48]. In order to describe a TB model that supports multiple positive endemic states, we proceed to divide the host population in four epidemiological classes: susceptible, exposed (latently infected), infectious, and treated. The possible epidemiological transitions of individuals in this population are captured in the second diagram in Fig. 1, while the definitions of the parameters and state variables are collected in Table 2.

The generation of new E-individuals per unit of time (E-incidence) comes from two subpopulations and therefore, it involves the terms: $B_S = \beta S\frac{I}{N}$ and $B_T = \sigma\beta T\frac{I}{N}$. The generation of new active cases, the result of reinfection, is modeled by the term $B_E = p\beta E\frac{I}{N}$. The definitions in Table 2 and the assumptions just described lead to the following model for the transmission dynamics of TB under exogenous reinfection:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - B_S(t) - \mu S,\\
\frac{dE}{dt} &= B_S(t) - B_E(t) - (\mu + k)E + B_T(t),\\
\frac{dI}{dt} &= kE + B_E(t) - (\mu + \gamma + d)I,\\
\frac{dT}{dt} &= \gamma I - B_T(t) - \mu T.
\end{aligned} \tag{4}$$

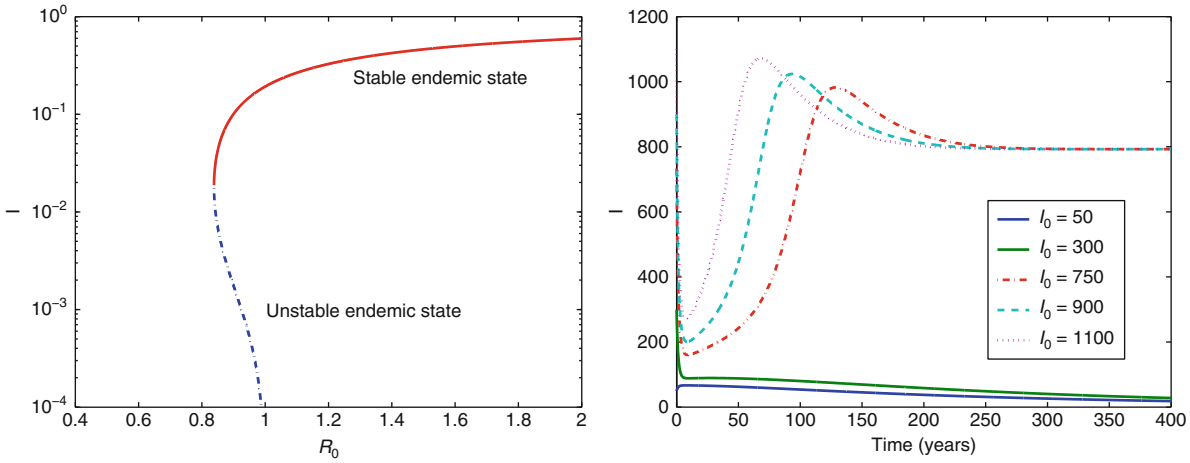
Model (4) indeed allows for the possibility of exogenous reinfection but only when $p > 0$. The basic reproduction number can be computed using various methods [28, 40, 43] all leading to

$$R_0 = \Big(\frac{\beta}{\mu + \gamma + d}\Big)\Big(\frac{k}{\mu + k}\Big). \tag{5}$$

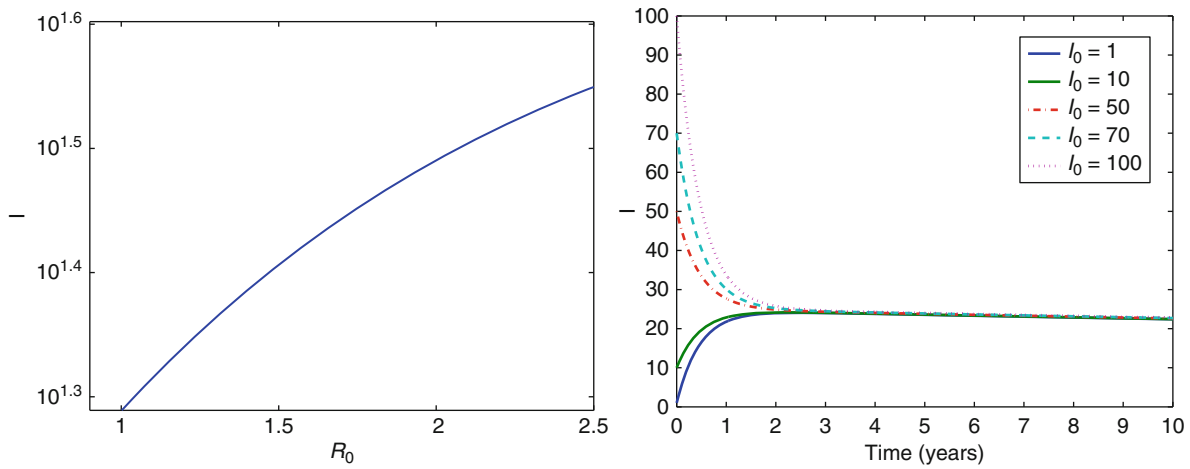
R_0 is the number of E individuals "generated" from contacts between S and typical I-individuals (when every body is susceptible, i.e., when $S(0) \approx \frac{\Lambda}{\mu}$) during the critical window of opportunity, that is, over the average length of the infectious period, namely, $\frac{\beta}{\mu+\gamma+d}$. R_0 is computed by multiplying the average infectious period *times* the proportion of latent individuals ($\frac{k}{\mu+k}$) that manage to reach the active TB-stage. $R_0 > 1$ means that the average number of secondary active TB cases coming from the S-population is greater than one, while $R_0 < 1$ corresponds to the situation when the average number of secondary active TB cases generated from the S population is less than one. In the absence of reinfection, one can show that if $R_0 \leq 1$ then $I(t)$ decreases to zero as $t \to \infty$ while if $R_0 > 1$ then $I(t) \to I_\infty > 0$. In the first case, the infection-freestate $(\Lambda/\mu, 0, 0, 0)$ is globally asymptotically stable, while in the latter there exists a unique locally asymptotically stable endemic state $(S^* > 0, E^* > 0, I^* > 0, T^* > 0)$. The dynamics of Model (4) are therefore " generic" and illustrated in Fig. 4 (bifurcation diagram and simulations). In the *generic* case, the elimination of the disease is feasible as long as the control measures put in place manage to alter the system parameters to the point that no TB outbreak is possible under the new (modified) parameters. In summary, if the model parameters jump from the region of parameter space where $R_0 > 1$ to the region where $R_0 < 1$ then the disease is likely to die out.

In the presence of exogenous reinfection ($p > 0$) the outcomes may no longer be "generic." It was established (in Feng et al. [48]) that whenever $R_0 < 1$ there exits a $p_0 \in (0, 1)$ and an interval $J_p = (R_p, 1)$ with $R_p > 0$ ($p > p_0$) with the property that whenever $R_0 \in J_p$, exactly two endemic equilibria exist. Further, only one positive equilibrium is possible whenever $R_p = R_0$ and no positive equilibria exists if $R_p < R_0$. The branch of endemic equilibria bifurcating "backward" from the disease-free equilibrium at $R_0 = 1$ is shown in Fig. 3 (left). Figure 3 (right) illustrates the asymptomatic behaviors of solutions when $p > p_0$ and $R_p < R_0 < 1$ ($p = 0.4$ and $R_0 = 0.87$). A forward bifurcation diagram of endemic steady states is also plotted in Fig. 4 (left). Figure 4 is generated from the model in the absence of exogenous reinfection ($p = 0$). Figure 4 (right) displays the asymptomatic behavior of solutions when $R_0 = 1.08$ under various initial conditions. The parameter values were taken from Feng et al. [48]. For an extensive review of TB models, see Castillo-Chavez and Song [22].

The identification of mechanisms capable of supporting multiple endemic equilibria in epidemic models was initially carried out in the context of HIV dynamics by Huang et al. [24, 45, 68]. These researchers showed that asymmetric transmission rates between sexually active interacting populations could lead to backward bifurcations. Hadeler and Castillo-Chavez [57] showed that in sexually active populations, with a dynamic core, the use of prophylactics or the implementation of a *partially* effective vaccine could actually increase the size of the core group. Further, such increases in the effective size of the core may generate abrupt changes in disease levels, that is, the system may become suddenly capable of supporting



Epidemiology Modeling, Fig. 3 Backward bifurcation ($p = 0.4$): a bifurcation diagram of endemic steady states is displayed (*left*). The numbers of infectious individuals as functions of time with various I_0 are plotted when $R_0 = 0.87$ (*right*). The outcomes ($I_\infty > 0$ or $I_\infty = 0$) of the simulation depend on the initial condition (value of $I(0)$)

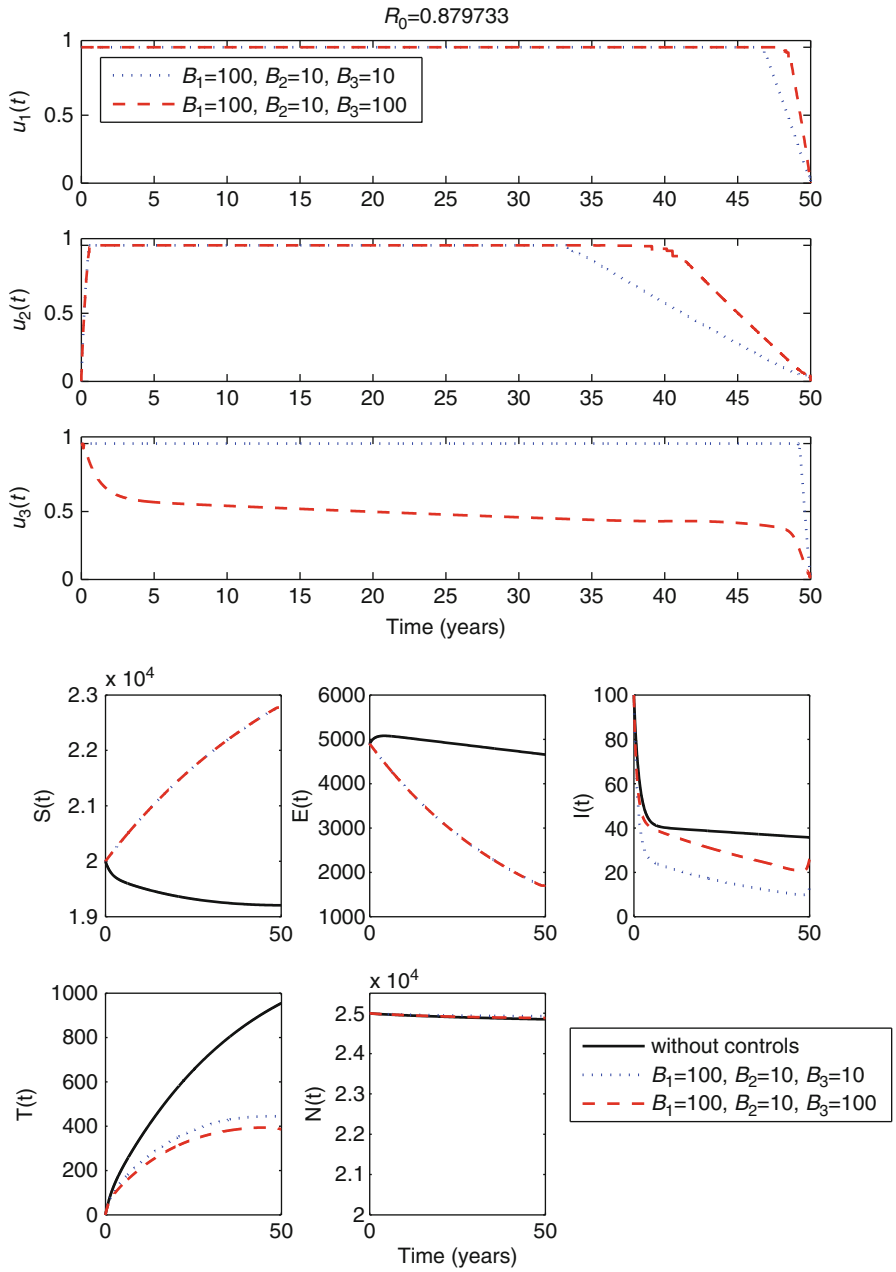


Epidemiology Modeling, Fig. 4 Forward bifurcation ($p = 0$): a bifurcation diagram of endemic steady states is displayed (*left*). The numbers of infectious individuals as functions of time with various I_0 are plotted when $R_0 = 1.08$ (*right*)

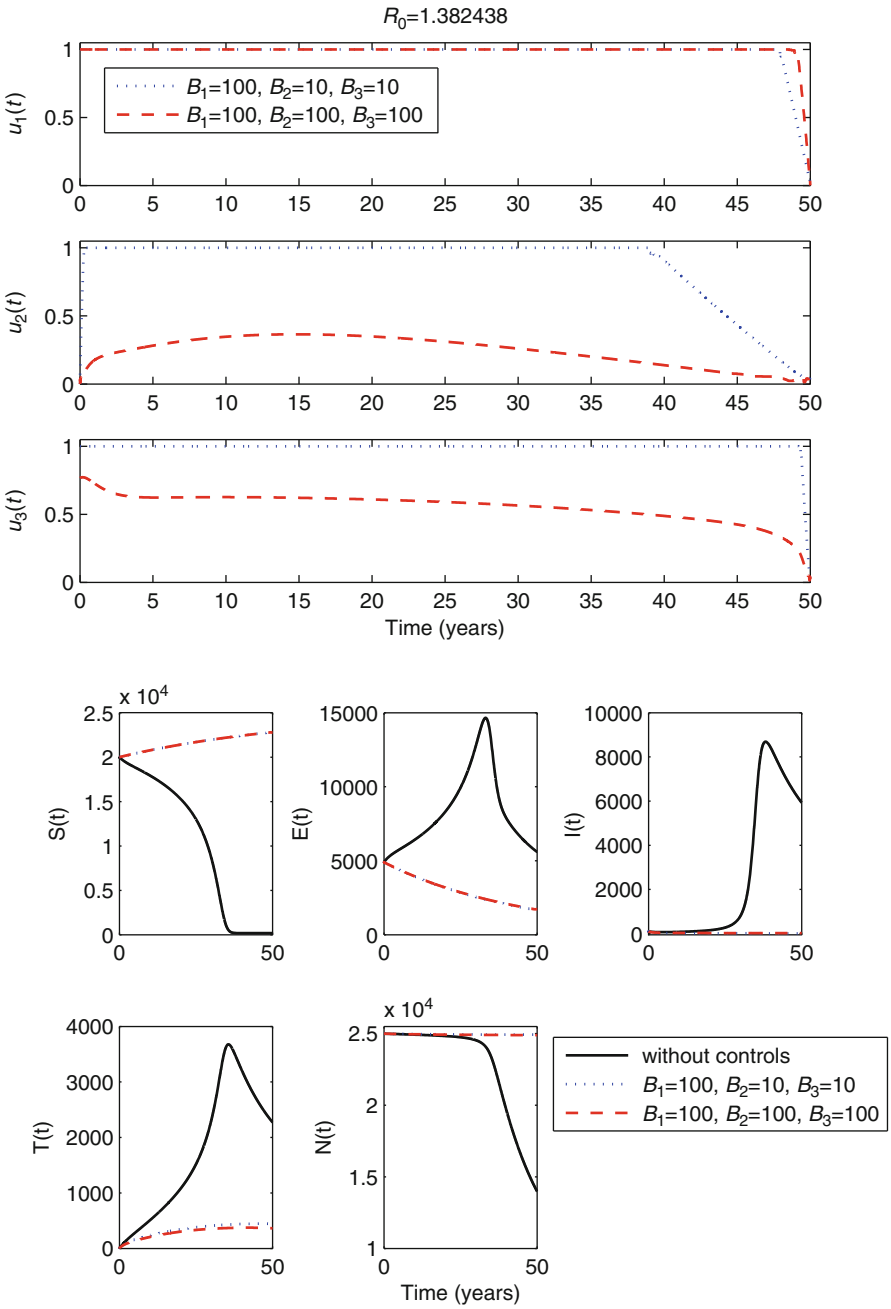
multiple endemic states (backward bifurcation). In the next section, control measures that account for the cost of interventions in an optimal way are introduced in the context of the TB model discussed in this section.

Optimal Control Approaches: The Cost of Epidemics

The use of optimal control in the context of contagion models has a long history of applications in life and social sciences. Recent contributions using optimal control approaches (from influenza to drinking) have generated insights on the value of investing on specific public health policies [55, 76–78]. Efforts to assess the relative effectiveness of intervention measures aimed at reducing the number of latently and actively TB infectious individuals at a minimal cost and over finite time horizons can be found in the literature [69]. We highlight the use of optimal control in the context of Model (4). *Three*, yet to be determined, control functions (policies): $u_i(t) : i = 1, 2, 3$ are introduced.



Epidemiology Modeling, Fig. 5 Low-risk TB community: the optimal controls ($u_1(t)$, $u_2(t)$, and $u_3(t)$) and state variables are displayed as functions of time. The *black solid*, *blue dotted*, and *red dashed curves* represent the cases of without controls, ($B_1 = 100$, $B_2 = 10$, $B_3 = 10$), and ($B_1 = 100$, $B_2 = 10$, $B_3 = 100$) with controls, respectively (Figures taken from [29])



Epidemiology Modeling, Fig. 6 High-risk TB community: the optimal controls ($u_1(t)$, $u_2(t)$, and $u_3(t)$) and state variables are displayed as functions of time. The *black solid*, *blue dotted*, and *red dashed* curves represent the cases of without controls, ($B_1 = 100$, $B_2 = 10$, $B_3 = 10$) and ($B_1 = 100$, $B_2 = 100$, $B_3 = 100$) with controls, respectively (Figures taken from [29])

These three policies are judged on their ability to reduce or eliminate the levels of latent- and active-TB prevalence in the population at a reduced cost. In this TB setup, exogenous reinfection plays a role and therefore the optimization process must account for such a possibility. It is important, therefore, to identify optimal strategies in low-risk TB communities where the disease is endemic, despite the existence of effective public health norms ($R_0 < 1$) as well as in high-risk TB communities, $R_0 > 1$ (the dominant scenario in parts of the world where TB is highly endemic). Three controls or time-dependent intervention policies yet to be computed are introduced as multipliers to the incidence and treatment rates: $B_S(t) = \beta(1 - u_1(t))SI/N$, $B_E(t) = p\beta(1 - u_1(t))EI/N$, $B_E(t) = \sigma\beta(1 - u_2(t))TI/N$, and $\gamma u_3(t)$. The first control, $u_1(t)$, works at reducing contacts with infectious individuals through policies of isolation, or social distancing, or through the administration (if available) of vaccines or drugs that reduce susceptibility to infection. The second control, $u_2(t)$, models the effort required to reduce or prevent the reinfection of treated individuals. This control is not identical to $u_1(t)$ since individuals with prior TB bouts are likely to react differently in the presence of active-TB cases. The treatment control, $u_3(t)$, models the effort directed at treating infected individuals. The goal of minimizing the number of exposed and infectious individuals while keeping the costs as low as possible requires access to data that is rarely available. Hence, the focus here is on the identification of solutions that only incorporate the *relative* costs associated with each policy or combination of policies. The identification of optimal policies is tied in to the minimization of a functional J (defined below), over the feasible set of controls $(u_i(t) : i = 1, 2, 3)$, subject to Model (4) over a finite time interval $[0, t_f]$. The objective functional is given by the expression:

$$J(u_1, u_2, u_3) = \int_0^{t_f} [E(t) + I(t) + \frac{B_1}{2}{u_1}^2(t) + \frac{B_2}{2}{u_2}^2(t) + \frac{B_3}{2}{u_3}^2(t)]dt \quad (6)$$

where the coefficients B_1, B_2, and B_3 model constant *relative* cost weight parameters. These coefficients account for the *relative* size and importance (including cost) of each integrand in the objective functional. It is standard to assume that the controls are nonlinear and quadratic. The objective, therefore, is to find numerically the optimal control functions, u_1^*, u_2^*, and u_3^* that satisfy

$$J(u_1^*, u_2^*, u_3^*) = \min_{\Omega} J(u_1, u_2, u_3), \quad (7)$$

where $\Omega = \{(u_1, u_2, u_3) \in (L^2(0, t_f))^3 | a_i \leq u_i \leq b_i, i = 1, 2, 3\}$ and $a_i, b_i, i = 1, 2, 3$ are lower and upper bounds for the controls, respectively. Pontryagin's maximum principle [50, 85] is used to solve the optimality system, which is derived and simulated following the approaches in Choi et al. [29], and Lee et al. [76]. We manage to identify optimal control strategies through simulations when $R_0 > 1$ and $R_0 < 1$ using reasonable TB parameters [29]. The optimal controls and corresponding states are displayed in Figs. 5 and 6 under two distinct scenarios: under a low-risk TB community ($R_0 = 0.87$) and under a high-risk TB community ($R_0 = 1.38$). It is observed that the social distancing control, $u_1(t)$, is the most effective when $R_0 < 1$, while the relapse control, $u_2(t)$, is the most effective when $R_0 > 1$. Further, simulation results suggest that when $R_0 < 1$, the control strategy cannot work without the presence of $u_1(t)$. Similarly, when $R_0 > 1$, $u_2(t)$ must be present. With the presence of $u_1(t)$ when $R_0 < 1$ and the presence of $u_2(t)$ when $R_0 > 1$, the identified optimal control programs will effectively reduce the number of exposed and infectious individuals.

Perspective on Epidemiological Models and Their Use

Epidemiological thinking has transcended the realm of epidemiological modeling and in the processes, it has found applications to the study of dynamic social process where contacts between individuals facilitate the buildup of communities that can suddenly (tipping point) take on a life of their own. This perspective has resulted in applications of the contagion model in the study of the dynamics of bulimia [54], or in the study of the spread of specific scientific ideas [11], or in the assessment of the emergence of new scientific fields [12]. Contagion models are also being used to identify population-level mechanisms responsible for drinking patterns [81, 87] or drug addiction trends [92]. Contagion models have also been

applied to the study of the spread of fanaticism [22] or the building of collaborative learning communities [38].

It is still in the context of the study of disease dynamics and in the evaluation of specific public policy measures that most of the applications of epidemiological models are found. Efforts to understand and manage the transmission dynamics of HIV [19, 24, 70, 95] or to respond to emergencies like those posed by the 2003 SARS epidemic [30], or the 2009 A-H1N1 influenza pandemic [35, 62], or to assess the potential impact of widely distributed rotavirus vaccines [88, 89] are still at the core of most of the research involving epidemiological mathematical models. The events of 9/11/2001 when our vulnerability to bioterrorism was exposed in fronts that included the deliberate release of biological agents has brought contagion and other models to the forefront of our battle against these threats to our national security (see [10]).

A series of volumes and books [1,3,9,15,16,20,26,27,36,39,56,71,94,97] have appeared over the past two decades that highlight our ever present concern with the challenges posed by the transmission dynamics and evolution of infectious diseases. The contagion approach highlighted here relies primarily on the use of deterministic models. There is, however, an extensive and comprehensive mathematical epidemiological literature that has made significant and far-reaching contributions using probabilistic perspectives [1, 2, 9, 36, 39]. The demands associated with the study of diseases like influenza A-H1N1 or the spread of sexually transmitted diseases (including HIV) in the context of social landscapes that change in response to knowledge, information, misinformation, or the excessive use of drugs (leading to drug resistance) have brought to the forefront of the use of alternative approaches including those that focus on social networks, into the study of infectious diseases [31, 42, 44, 82, 83]. Renewed interest in the characterization and study of heterogenous mixing patterns and their role on disease dynamics have also reemerged [14, 18, 25, 75, 80, 84]. Contagion models continue to contribute to our understanding of "contact" processes that change in response to behavioral decisions [49]. It is our hope that this idiosyncratic overview has captured the fundamental role that epidemiological models play and will continue to play in the study of human process of importance in life and social sciences.

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