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Priority Shifting and the Dynamics of Managing Eradicable Infectious Diseases

Radboud J. Duintjer Tebbens
Kids Risk Project, Harvard School of Public Health, Boston, Massachusetts 02115;
and Delft Institute of Applied Mathematics, Delft University of Technology,
2628 CD Delft, The Netherlands, r.j.duintjertebbens@tudelft.nl

Kimberly M. Thompson
Kid Risk, Inc., Newton, Massachusetts 02459; and Kids Risk Project, Harvard School of Public Health,
Boston, Massachusetts 02115, kimt@kidrisk.org

Public health budget constraints force policy makers to prioritize resources toward those interventions that yield the highest perceived benefits. Intuitively, it appears optimal to focus resources on affordable interventions against prevalent diseases. However, due to the dynamics of infectious disease eradication, policies focusing on a static perception of priorities may lead to economically suboptimal outcomes. Using a hypothetical two-disease dynamic transmission model, we explore several different decision rules with respect to vaccination policy for eradicable diseases. The simulations show that cost-effectiveness decreases as the extent of priority shifting increases. This model suggests the need for a longer-term dynamic perspective to appropriately recognize costs and benefits of different policies for eradicable diseases.

Key words: infectious diseases; disease eradication; health economics; stochastic model; system dynamics; perception delay; benefit-cost analysis
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1. Introduction

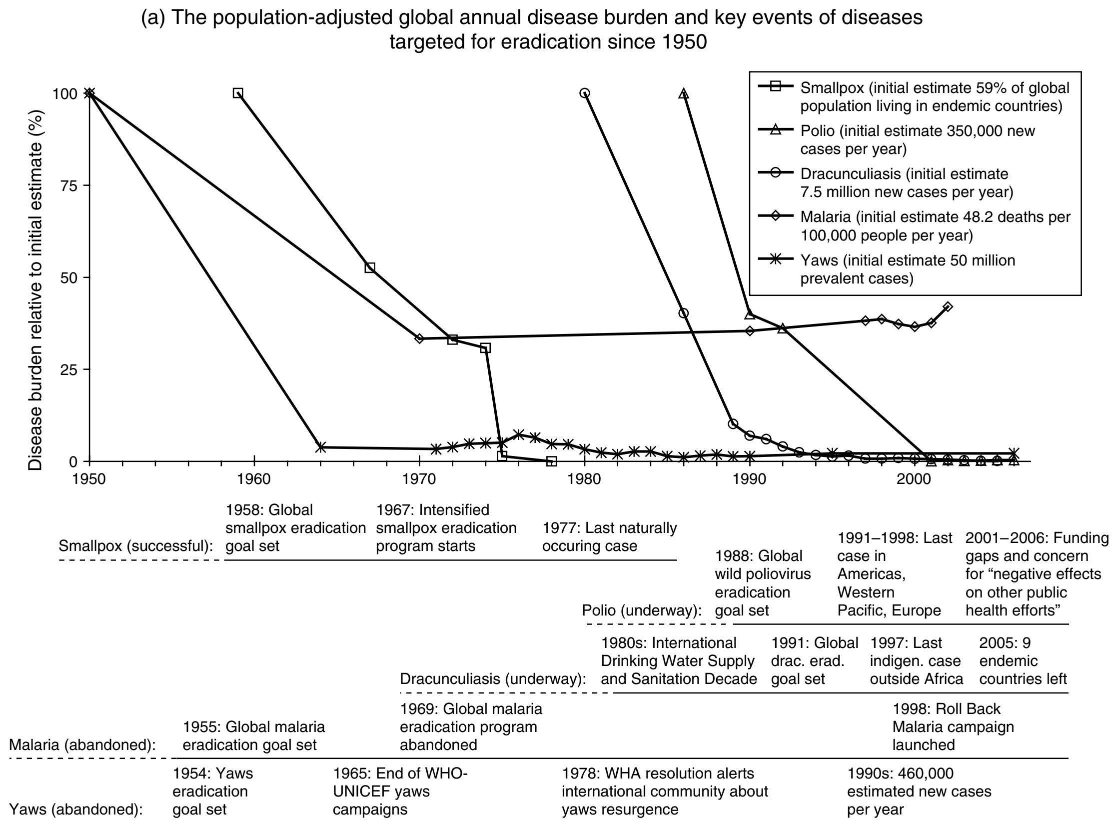
Economic evaluations represent well-accepted tools to help inform decision makers in public health. For example, standardized cost-effectiveness analyses for different public health interventions facilitate allocation of available resources toward those interventions that yield the highest expected societal utility per unit of monetary investment (Gold et al. 1996). However, economic evaluations typically provide a relatively static representation of the situation. In the context of infectious diseases, Edmunds et al. (1999) called for a more dynamic perspective and argued for the use of mathematical infection transmission models (Anderson and May 1991) in cost-effectiveness analyses (Edmunds et al. 1999). Researchers subsequently demonstrated the utility of these models in cost-effectiveness analyses for actual diseases, including varicella (Brisson and Edmunds 2003) and polio (Thompson and Duintjer Tebbens 2006). Furthermore, a growing body of work based on optimal control theory exists that explores the optimality of vaccination strategies in dynamic infection transmission models (see, for example, Greenhalgh 1988; Hadeler and Müller 1993; Müller 1998, 2000).

Eradicable diseases differ from other diseases with respect to the dynamics and economics of vaccination decisions. Geoffard and Philipson (1997) demonstrated the challenge of eradicating a disease if prevalence drives the demand for vaccines. Barrett and colleagues (Barrett 2004, Barrett and Hoel 2007) showed that when a vaccine-preventable disease is eradicable and offers financial dividends associated with the cessation of vaccination into the future, a policy of high control but no eradication is never economically optimal.

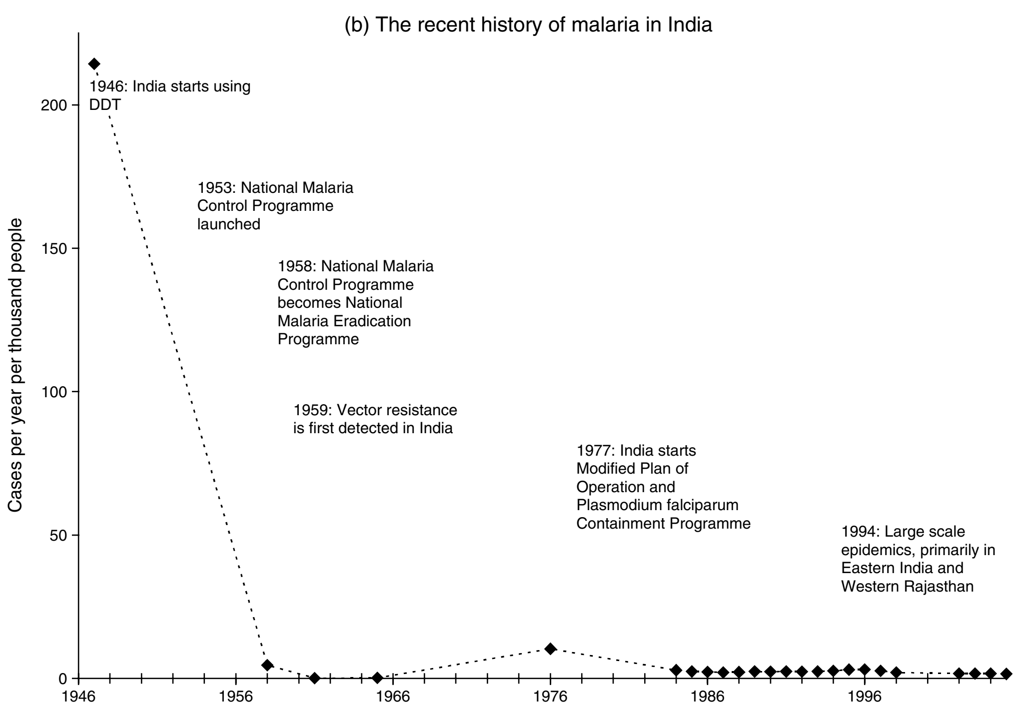
Figure 1 summarizes the history of several diseases targeted for global eradication since the establishment of the World Health Organization (WHO). Smallpox remains the only disease successfully eradicated to date, with the last naturally occurring case in 1977 (Fenner et al. 1988). Despite the estimated significant benefit:cost return for the investment by developed countries in the intensive smallpox eradication program that completed eradication in developing countries, a persistent lack of adequate funding jeopardized the eradication effort (Fenner et al. 1988, Barrett 2006).

Global wild poliovirus and dracunculiasis (Guinea worm) eradication efforts started in the late 1980s and resulted in very impressive reductions in incidence (i.e., new disease cases occurring per unit of time). Nevertheless, political, operational, and financial challenges plagued both eradication programs and resulted in setbacks in their progress. Watts (1998, p. 808) discussed "Ministry of Health officials thinking that they could take the eradication goal of December 1995 as an accomplished fact and

Figure 1 History of Selected Global and National Eradication Programs

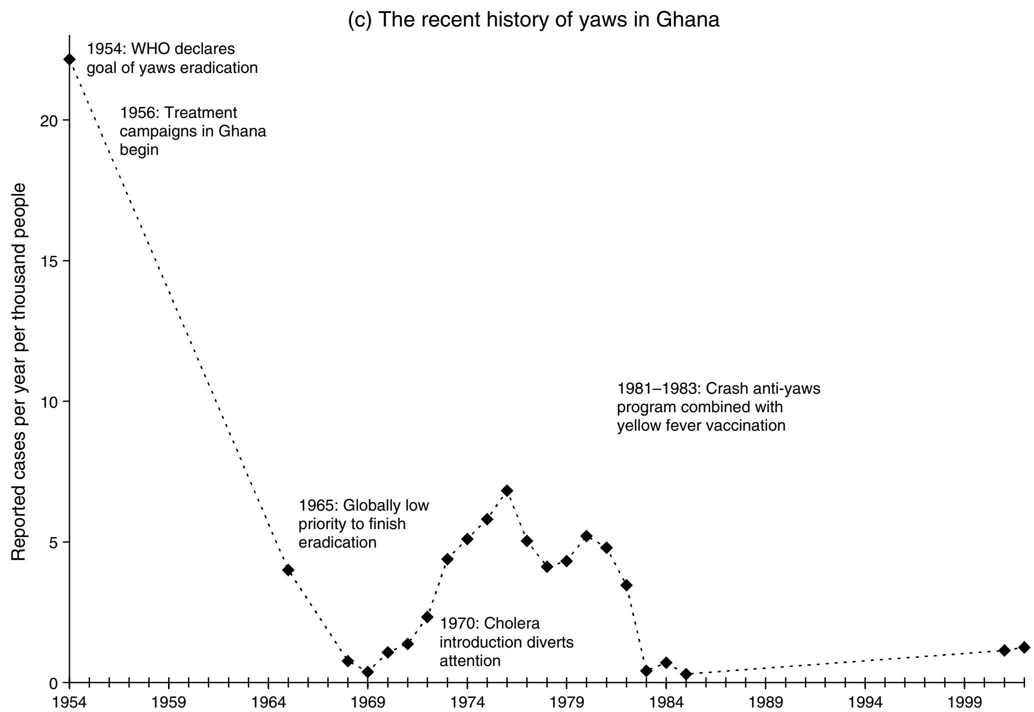


Disease burden data sources: smallpox, Fenner et al. (1988); polio, World Health Organization (2007b); dracunculiasis, Watts (1998), World Health Organization (2006); malaria, Carter and Mendis (2002), World Health Organization (2007a); yaws, Walker and Hay (2000), Antal et al. (2002), World Health Organization (2009); and population data, United Nations (2007). *Key events data sources*: Centers for Disease Control and Prevention (1993); smallpox, Fenner et al. (1988); polio, Arita et al. (2006), World Health Organization (2007b); dracunculiasis, Hopkins et al. (2005), World Health Organization (2006); malaria, World Health Organization (1999); and yaws, Walker and Hay (2000), World Health Organization (2009).



Source. Kakkilaya (2006).

Figure 1 (Continued)



Sources. Agadzi et al. (1983, 1985); Ghana Health Service (2004); World Health Organization (2009).

questioning the need to continue using scarce funds for dracunculiasis surveillance." Hopkins et al. (2005, p. 674) reported a "lack of urgency in responding to suspected cases . . . [and] inadequacy of surveillance for dracunculiasis in . . . [areas] that have reduced or apparently eliminated the disease at great cost." Similarly, the substantial financial commitment required to finish polio eradication has led some to suggest that "the time has come for the global strategy for polio to be shifted from 'eradication' to 'effective control,' " which they suggest would "benefit the fight against the many vaccine preventable diseases" (Arita et al. 2006, p. 853). However, assuming that wild poliovirus eradication is technically achievable, our recent analysis shows that abandoning eradication in favor of control out of a concern of high costs to eliminate the few remaining cases will lead to higher long-term economic and public health costs (Thompson and Duintjer Tebbens 2007).

Adopted as a goal by the World Health Assembly in 1955, the WHO abandoned global malaria eradication in 1969 after investing over $1 billion in external funding (converted to 2006 net present value from data in Fenner et al. 1988, p. 384). In hindsight, due to vector and parasite resistance and other factors, the feasibility of malaria eradication with the strategy in use at the time remains questionable (Centers for Disease Control and Prevention 1993, Carter and Mendis 2002). In 1998, the WHO launched the Roll Back Malaria Initiative to halt the resurgence of malaria in many developing countries. Although the geographical extent of malaria endemicity in tropical Africa has remained unchanged (Carter and Mendis 2002), other countries have experienced large changes. For example, Figure 1(b) shows the experience with malaria in the past six decades in India, where incidence decreased from an estimated 75 million cases in 1947 to less than 50,000 cases in 1961. Following shortages of DDT and then later technical, financial, and operational problems, the incidence of malaria in India resurged to almost 6.5 million cases in 1976, triggering modified control policies. In 1972, Scholtens, while acknowledging operational hurdles and problems with mosquito resistance in India, wrote that "the problem is one of near-success in an environment with an excess of problems clamoring for attention," and "as malaria recedes to a low level other pressing health and social problems exert irresistible demands for available resources" (Scholtens et al. 1972, p. 20). The malaria incidence in India currently equals approximately two million new cases per year.

In 1954, the WHO declared the goal of global yaws eradication and initiated efforts that successfully reduced the prevalence of yaws by over 95% (Antal et al. 2002). However, in the mid-1960s, following this success, the perception of yaws as a pressing public health problem waned, and advocates of integrating control efforts with other public health initiatives managed to shift resources away from yaws eradication. Hopkins (1985, p. S338) writes that "partly because of the great success of the mass campaigns of the 1950s and 1960s, the endemic treponematoses [including yaws] are widely thought to be under control" and that because they are "not fatal and usually restricted to poor, remote, rural populations, they are not perceived to be high-priority problems by many decision makers." The global yaws status has not been well documented, but the experience in Ghana provides an example of the dramatic consequences (Figure 1(c)). In the 1970s, following a cholera outbreak that diverted attention away from yaws, incidence surged and triggered renewed campaigns to bring yaws back under control (Agadzi et al. 1983, 1985). Incidence of yaws continues to creep up with yaws now prevalent in parts of sub-Saharan Africa and Asia, although it remains largely unrecognized as a serious public health problem (World Health Organization 2009).

In the context of scarce resources available to manage diseases, competition for resources seems inevitable, even between eradicable diseases. This paper focuses on the dynamics of disease control or eradication in the context of multiple eradicable diseases and builds on our prior modeling on polio that explored the dynamics of making decisions about control and eradication (Thompson and Duintjer Tebbens 2007). That paper considered the case of polio in isolation, showing that deciding about vaccination based on cost-per-case perceptions might lead to a failure to eradicate (Thompson and Duintjer Tebbens 2007). Here, we aim to investigate how changes in perceptions of priorities might play out in the context of multiple eradicable diseases competing for resources. To model this we need to consider the impact of decisions on at least two diseases. To keep the modeling as simple as possible without limiting the possibility of observing multiple-disease behavior, we model a hypothetical population in which two eradicable infectious diseases circulate and behave according to a stochastic infectious disease transmission model, which we adapted and modified from an existing model (Edmunds et al. 1999). Assuming a fixed budget exists for vaccination against these diseases, we evaluate policies that focus resources on the disease perceived as having the highest incidence at any particular time versus policies that pursue eradication. We emphasize that to keep the focus on identifying the key behavior for different policies we intentionally employ a very basic contagion model. Thus, the model is not appropriate to guide policy in the field for actual diseases, which would require much more detailed models. The next section describes the model with additional details provided in the e-companion.[1] The following section explores the behavior of the model for the different decision rules regarding the vaccination policies, and the last section discusses the insights. This paper aims to demonstrate the unintended consequences that might arise from employing apparently intuitive decision rules in the context of managing multiple eradicable diseases and to contribute to the literature related to challenges associated with using intuition when making decisions related to complex systems (Sterman 1989b, 2000, 2008; Güth et al. 1982; Tucker 1950; Hardin 1968). As with these other examples, the hypothetical disease epidemics used in this manuscript represent the class of general managerial problems for which frequent priority shifting may lead to nonoptimal outcomes due to nonlinear feedback dynamics. Focusing on the insights for hypothetical diseases, we only partially explore the impact of different model input choices, although we emphasize that in a real case the quantitative results must consider uncertainty in the model input values.

[1] An electronic companion to this paper is available as part of the online version that can be found at http://mansci.journal.informs.org/.

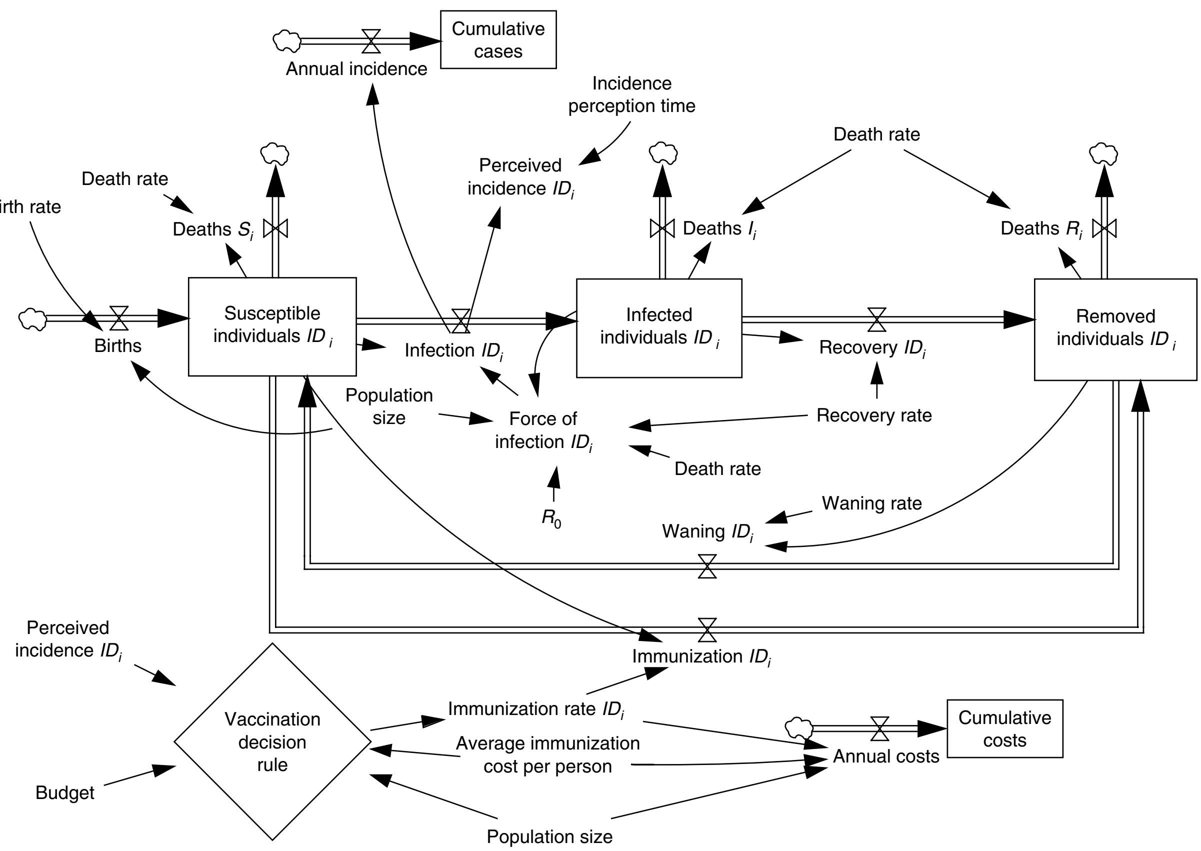
2. Methods

Edmunds et al. (1999) proposed a model for a hypothetical infectious disease with plausible, though hypothetical input values. We adapted their input values to include waning of immunity, not only of newborns but of any susceptible individual at the same rate. Combined with the lowered recovery rate (implying a longer duration of infectiousness), these changes ensure a more gradual impact of changes in vaccination rates than in the original model (Edmunds et al. 1999). Figure 2 shows the susceptible–infected–removed (SIR) model that forms the basis of our analysis. Table 1 lists the model inputs and symbols that we use throughout the paper. The equations for infectious disease ID_i of the deterministic SIR model with waning immunity and immunization of all susceptible individuals equal

$$\begin{aligned}\frac{dS_i(t)}{dt} &= bN - \left(\frac{(\mu+\gamma)R_0}{N} I_i(t) + \mu + u_i(t)\right) S_i(t) + wR_i(t),\\ \frac{dI_i(t)}{dt} &= \frac{(\mu+\gamma)R_0}{N} I_i(t) S_i(t) - (\mu+\gamma) I_i(t), \qquad (1)\\ \frac{dR_i(t)}{dt} &= \gamma I_i(t) - (\mu+w) R_i(t) + \mu_i(t) S_i(t).\end{aligned}$$

Here, the left-hand side of each equation corresponds to the stocks in Figure 2, and the terms on the right-hand side correspond to the flows. The term $(\mu+\gamma)R_0 I_i(t)/N$ is the force of infection (i.e., the rate at which susceptible individuals acquire infection). The assumption of homogeneous mixing means that the force of infection is proportional to the infected fraction $I_i(t)/N$ in the population. The proportionality constant (i.e., the transmission coefficient

Figure 2 Dynamic Infectious Disease Transmission Model with Stocks and Flows Indexed by Infectious Disease Number (ID_i)



$\beta = (\mu + \gamma)R_0$) is the number of potentially infectious contacts that individuals have per unit of time (i.e., years in our model). Through $\mu + \gamma$ (i.e., one over the average residence time in the stock of infected individuals), β relates to R_0, defined as the number of secondary infections caused by a single infectious person introduced into an entirely susceptible population (Anderson and May 1991). R_0 represents a theoretical measure of the transmissibility of the infectious agent in a given population. If the proportion of susceptible individuals $S_i(t)/N$ remain less than $1/R_0$, then the inflow to the stock of infected individuals equals less than its outflow $(\mu + \gamma) \times I_i(t)$, meaning that the number of infected individuals decreases and eventually tends to an equilibrium state of zero infected individuals. The immunization rate u represents the proportion

Table 1 List of Model Inputs

Model input	Symbol [unit]	Base case value	Description/note
Population size	N [people]	10,000	Constant due to assumed equal birth and death rate
Birth rate	b [1/year]	0.02	Fraction of population giving birth per year
Death rate	μ [1/year]	0.02	Fraction of population dying per year
Recovery rate	γ [1/year]	5	Reciprocal of average duration of infectiousness of 73 days
R_0	R_0 [dimensionless]	5	Basic reproductive number
Waning rate	w [1/year]	0.2	Reciprocal of average duration of immunity of five years
Incidence perception time	τ [year]	1	Reflects delay in reporting and altering incidence-based policy
Immunization rate for infectious disease i ($i = 1, 2$)	$u^i(t)$ [1/year]	Depends on decisions rule	Proportion of susceptible individuals successfully vaccinated per year
Threshold immunization rate	$\hat{u} = (R_0 - 1)(\mu + w)$ [1/year]	0.88	Theoretical threshold value above which infection prevalence permanently decreases
Average immunization cost per person	c [\$/people]	8.8	Average cost per person to achieve immunization rate $\hat{u}$
Budget	$B = N \times c \times 1.5$ [\$/year]	132,000	Available annual resources for vaccination against the two infectious diseases

Source. Adapted from Edmunds et al. (1999).

of susceptible individuals effectively immunized per year, which depends on vaccination rates and take rate of the vaccine (and in the case of live vaccines, also on immunization of contacts of vaccine recipients, which we ignore in this analysis). By setting all derivates in the set of equations (1) equal to zero and requiring that $S_i(t)/N$ equals $1/R_0$ at the equilibrium, one obtains four sets of equation with four unknowns (S, I, R, and u), yielding the equilibrium state and the theoretical threshold value $\hat{u} = (R_0 - 1)(\mu + w)$ (≈0.88 for values in Table 1) of the immunization rate above which infection prevalence permanently decreases and eventually tends to zero. For any value between zero and $\hat{u}$, the eventual equilibrium incidence follows from setting all derivatives in the set of equations (1) equal to zero without the extra condition, and equals

$$inc^{eq}(u) = \frac{(\gamma + \mu)N(\mu(R_0 - 1) - u - w + R_0 w)}{R_0(\gamma + \mu + w)}. \quad (2)$$

For the starting conditions, we set $u = 0$, yielding the prevaccine equilibrium incidence of $inc_{pv} = inc^{eq}(0) \approx$ 1,693 new infections (i.e., cases, assuming that each infection leads to disease) per year, with $S_i(0) = 2{,}000$, $I_i(0) \approx 337$, and $R_i(0) \approx 7{,}663$.

The term elimination refers to the "cessation of transmission" of an infectious agent in a given population (Miller et al. 2006, p. 1165). We define elimination in the model as the point in time when the number of infected individuals in the population reaches zero. Once elimination occurs, the infectious agent can never reappear from the same population, although it can get imported from a different population. In contrast, eradication requires simultaneous elimination of the infectious agent everywhere (Barrett 2003) and "absolute containment of any infectious source" (Miller et al. 2006, p. 1165). Although clearly eradication represents a global undertaking whereas elimination can be a local or national initiative, for simplicity, in this paper we ignore the difference between elimination and eradication by assuming that no exogenous introductions of the infectious agent can occur, or alternatively by assuming that the population under consideration is the last remaining population with indigenous transmission of the infectious agent. Deterministic models such as the original model (Edmunds et al. 1999) decrease stocks according to fractional rates, meaning that the number of infectious individuals never reaches absolute zero, and true elimination of the infectious agent does not occur. Although one can build a threshold into the deterministic model to capture elimination, a stochastic model avoids the need to assume this artificial threshold and more accurately captures the behavior near elimination (Eichner and Dietz 1996, Koopman 2004, Restif and Grenfell 2007, Rahmandad and Sterman 2008). Furthermore, in the context of studying policies involving two identical infectious diseases, a stochastic model allows analysis of the impact of small, random differences in the progression of both diseases. We made the deterministic and continuous time model presented above stochastic and discrete following Gillespie's (1976) numerical method (see the e-companion for details). In the stochastic model, elimination can occur by "chance," even with $u < \hat{u}$, especially if the population is small. We found that with a population size of $N = 10{,}000$ people, unexpected "chance" eliminations with $u < \hat{u}$ remained sufficiently rare for the purposes of this analysis. Recognizing that the size and structure of the population affects both the probability and time to reach zero prevalence (of infections), we keep the population size fixed at 10,000 for the base case analyses and further explore this issue in the e-companion. We assume that both infectious diseases (ID_1 and ID_2) behave according to the same model, and we assume that no cross-immunity exists between them such that transmission occurs independently. For the base case, we assume identical properties of both diseases. To account for delays in reporting and responding to changes in the incidence, we define the perceived incidence (*pinc*) as the first-order exponential smooth of the true incidence with a time constant of one year, i.e., the incidence perception time τ.

Assuming a linear cost model, the cost function corresponding to an immunization rate of u equals $(u/\hat{u}) \times N \times c$ per year, where c is the average cost per person in the population to achieve a collective immunization rate of $\hat{u}$ per year (the e-companion also considers the case of quadratic cost functions). To compare the different policy decision rules, we calculated the incremental cost-effectiveness ratio (CER) as the total cumulative costs of ID_1 and ID_2 vaccinations at the end of a 20-year time period divided by the total cumulative cases of ID_1 and ID_2 prevented compared to a policy of no vaccination. We assume a fixed annual budget exists that equals 0.75 times the budget needed to achieve $\hat{u}$ for both diseases, or $B = N \times c \times 0.75 \times 2 = 132{,}000$ dollars per year.

We implemented the stochastic model in Mathematica™ and based average results on 100 stochastic iterations.

3. Results

This section first presents the results of a single stochastic iteration for each decision rule to explain the behavior of the model. We then compare the decision rules by looking at the average results over all iterations. We recognize that other decision rules exist, such as for policies that mandate vaccination at a certain rate as long as vaccination appears cost-effective (Thompson and Duintjer Tebbens 2007). However, we focus on those decision rules that involve trade-offs between the different priorities resulting from a budget constraint because they may help explain possible behavior in relation to eradication programs.

3.1. Control Policies

We explored three different decision rules that focus on controlling the diseases without attempting to pursue eradication. We define decision rule C1 for the immunization rate u_i against infectious disease i (ID_i, $i = 1, 2$) such that the costs for infectious disease ID_i equal half the available budget at all times, or

$$(u_i/\hat{u}) \times N \times c = 0.5 \times B = 0.75 \times N \times c$$
$$\Leftrightarrow \quad u_i = 0.75 \times \hat{u} = 0.66 \text{ per year}, \quad i = 1, 2.$$

This very straightforward decision rule distributes the available resources evenly for the identical infectious diseases, without consideration of the level of priority of each disease over time. A deterministic model would give identical incidence for both diseases given our assumptions. In the stochastic model, we find that the trajectories differ, although the behavior remains similar. Figure 3(a) shows the perceived incidence and the proportion of the budget allocated toward each disease for the first stochastic iteration following decision rule C1. Clearly, the perceived incidence follows the actual incidence and smoothes out the peaks. The shaded areas indicate the proportion of the budget allocated toward ID_1 or ID_2, which for this decision rule equals 50% for each disease throughout. Because both immunization rates remain constant, this decision rule pushes the (perceived) incidence for each disease toward the equilibrium associated with the immunization rate of $u_i = 0.66$ per year (i.e., approximately 423 cases per year following Equation (2)), although random perturbations away from this level persist indefinitely.

We define decision rule C2 such that the costs for infectious disease ID_i equal the entire budget (i.e., $(u_i/\hat{u}) \times N \times c = B = 1.5 \times N \times c$) whenever the perceived incidence of ID_i is greatest, or

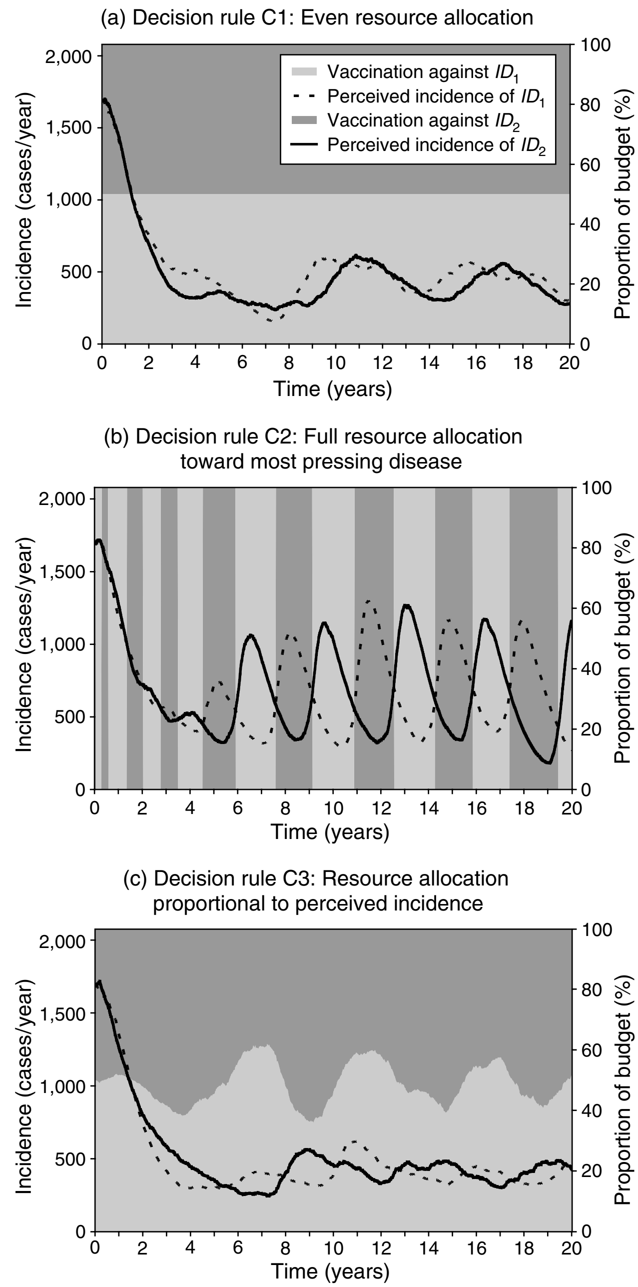
$$u_1 = 1.5 \times \hat{u} = 1.32 \text{ per year}$$
$$\text{if } pinc_1(t) \geq pinc_2(t), \text{ and 0 otherwise,}$$

and

$$u_2 = 1.5 \times \hat{u} = 1.32 \text{ per year}$$
$$\text{if } pinc_1(t) < pinc_2(t), \text{ and 0 otherwise.}$$

This decision rule mandates that we devote the entire budget to the perceived highest priority disease (i.e., toward the disease with the highest perceived incidence). Figure 3(b) shows the perceived incidence and the vaccination policy following decision rule C2 for the first stochastic iteration. Because $pinc_1(0) = pinc_2(0) = inc_{pv}$, the decision rule first

Figure 3 **Results of the First Stochastic Iteration for Decision Rules Corresponding to Policies of Disease Control**



steers all resources toward vaccination against ID_1. The immediate effect is a slightly lower $pinc_1$ than $pinc_2$, which switches the policy to vaccination only against ID_2, and this cycle rapidly repeats itself (in fact, the switches in policy initially occur too rapidly to show up in the shadings of the figure). Due to the delays in perceiving shifts in incidence, the time between policy shifts also increases, and consequently, the time without vaccination increases. More susceptible individuals accumulate, leading to further increases in the size of outbreaks and time needed to control them, which results in important fluctuations in incidence. This corresponds to operating in a "fire-fighting" mode of constantly responding to emerging priorities instead of structurally preventing them (Sterman 2000; Repenning 2000, 2001).

We define decision rule C3 such that the budget gets allocated proportional to the perceived incidence of each disease, or

$$(u_i/\hat{u}) \times N \times c$$
$$= B \times pinc_i(t)/(pinc_1(t) + pinc_2(t))$$
$$= 1.5 \times N \times c \times pinc_i(t)/(pinc_1(t) + pinc_2(t))$$
$$\Leftrightarrow \quad u_i = 1.5 \times \hat{u} \times pinc_i(t)/(pinc_1(t) + pinc_2(t)) \text{ per year}, \quad i = 1, 2.$$

This decision rule allocates resources according to the fraction of the total perceived incidence associated with each disease. Although $u_1 = u_2$ at time 0, randomness in the model leads to small differences in incidence (Figure 3(c)). The decision rule initially corrects the difference in incidence successfully. However, due to delays in the system, those corrections amplify future diversions from the path toward the equilibrium, with behavior similar to but less extreme than decision rule C2. We emphasize that despite completely symmetric diseases and policies, substantial shifting of resources emerges as a result of the stochastic nature of disease transmission.

3.2. Eradication Policies

We explore two different decision rules that pursue eradication, but use different criteria regarding the time of cessation of vaccination following eradication. Decision rule E1 involves sequential elimination of each infectious disease and subsequent immediate cessation of vaccination:

$$u_1 = 1.5 \times \hat{u} = 1.32 \text{ per year}$$
$$\text{if infection prevalence of } ID_1 > 0, \text{ and 0 otherwise,}$$

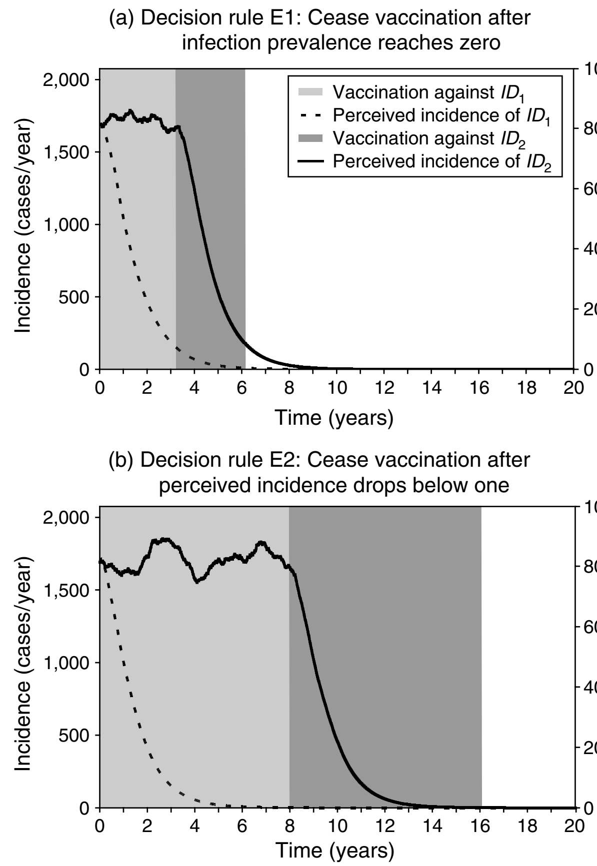
and

$$u_2 = 1.5 \times \hat{u} = 1.32 \text{ per year}$$
$$\text{if infection prevalence of } ID_1 = 0, \text{ and infection prevalence of } ID_2 > 0, \text{ and 0 otherwise.}$$

Figure 4(a) shows that elimination of ID_1 occurs within a little over three years of the start of vaccination for the first stochastic iteration. During those years, ID_2 hovers around its prevaccine equilibrium state, but as vaccination against ID_2 starts it takes approximately another three years for elimination of ID_2.

More realistically, vaccination can only cease after confirmation of eradication, which depends on a perception that the incidence reached sufficiently low

Figure 4 **Results of the First Stochastic Iteration for Decision Rules Corresponding to Policies Pursuing Disease Eradication**



levels for safe cessation. Thus, we define decision rule E2 as

$$u_1 = 1.5 \times \hat{u} = 1.32 \text{ per year}$$
$$\text{if } pinc_1(t) \geq 1, \text{ and 0 otherwise,}$$

and

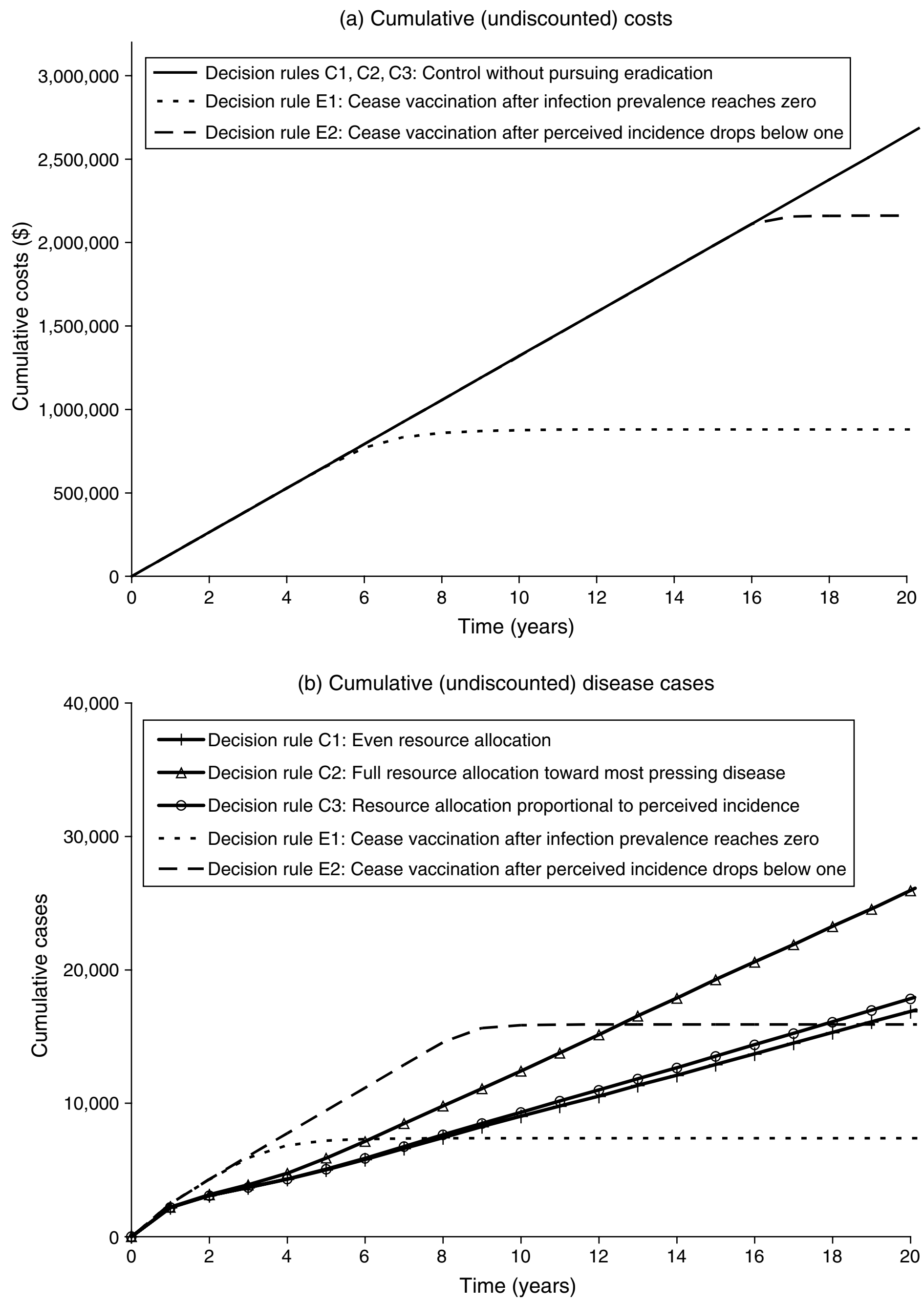
$$u_2 = 1.5 \times \hat{u} = 1.32 \text{ per year}$$
$$\text{if } pinc_1(t) < 1 \text{ and } pinc_2(t) \geq 1, \quad \text{and 0 otherwise.}$$

We note that the perceived incidence never reaches zero given exponential smoothing and that the threshold of one case per year remains artificial. Figure 4(b) shows that the slow exponential decay in perceived incidence following elimination means that, under decision rule E2, vaccination against ID_1 continues for five more years after elimination before the perceived incidence for ID_1 reaches the threshold of one case per year. With a similar delay for ID_2, complete cessation of vaccination occurs only a few years before the end of the 20-year time horizon.

3.3. Comparison of Decision Rules

Figure 5 shows the cumulative costs and cases with each decision rule, aggregated for ID_1 and ID_2 and

Figure 5 Average Cumulative Totals for Both Infectious Diseases with the Different Decision Rules



averaged over 100 iterations. Although the single iterations in Figure 3 show important cycles in response to the policy changes (as a deterministic model would), those cancel out in the averages, yielding smoother curves. All decision rules aimed at simultaneously controlling ID_1 and ID_2 utilize the full budget throughout, yielding a linear increase in cumulative costs. In terms of cumulative cases, we find higher numbers as the level of overreaction to shifts in perceived priorities increases, with decision rule C1 yielding the lowest cumulative cases, followed by C3 and then C2. Policies pursuing eradication, although requiring high resources in the short term for the disease with the lowest actual and perceived incidence, free up the budget to focus on the second disease and eventually no longer require resources. Over the 20-year time horizon, these policies yield both lower cumulative cases and lower cumulative costs. However, because in this model we fixed the available budget, the eradication policies controversially come with a higher aggregate disease burden in the short run.

Table 2 Evaluation of the Overall Cost-Effectiveness Performance of Each Decision Rule

Policy/decision rule	Incremental cost-effectiveness ratio after 20 years compared to no vaccination ($/prevented case)	
	No discounting	10% discount rate (of costs and prevented cases)
C1: Even resource allocation	52.0	53.6
C2: Full resource allocation toward most pressing disease	63.2	62.8
C3: Resource allocation proportional to perceived incidence	53.0	54.4
E1: Cease vaccination after infection prevalence reaches zero	14.6	27.6
E2: Cease vaccination after perceived incidence drops below one	41.7	57.7

Table 2 shows the incremental CERs of each policy compared to a policy of no vaccination based on the cumulative totals for the different decision rules and the prevaccine equilibrium incidence for the comparator. Despite operating on the same budget, the eradication policies yield much lower (i.e., better) incremental CERs than the control policies due to the possibility of cessation of vaccination and prevented cases. Rules C1 and C3 yield better results than firefighting (rule C2). Given the need to invest more in the short term, or in this example, to allow more cases, the eradication policies are more sensitive to the discount rate than the control policies. Consequently, we observe that decision rule E2 becomes less cost-effective than the control policies (except decision rule C2) at high levels of the discount rate of about 10%.

3.4. Expected Time Until the Last Case

Given the hypothetical nature of the population modeled and our focus on explaining possible behaviors, we did not conduct a full sensitivity analysis. However, we recognize that the time until eradication represents an important driver of the economics of control versus eradication on a limited (e.g., 20-year) time scale. In the e-companion, we explore how the average time until the last case depends on population size and structure and other factors. The results suggest a logarithmic relationship between total population size and time until the last case for immunization rates above $\hat{u}$. For context, if we assume that the world consists of one homogeneous global population and uniform immunization rates, this implies a mean time of approximately 11 years until the last case for a population of 6.5 billion people. Although the world more realistically consists of many small subpopulations that interact to some degree, we found that the estimated time until the last case appears robust to varying degrees of heterogeneity (i.e., with respect to probability that an individual's infectious contact is with another individual in another subpopulation; see the e-companion) as long as the same immunization rate applies to each subpopulation. Similarly, the CER of eradication versus control depends logarithmically on population size, such that control becomes more cost-effective than eradication for a large enough population size (see the e-companion for numerical results). Given the global scale of an eradication initiative, the optimal economics thus depend on the life cycle of the infectious disease, with control representing the most attractive option initially, and eradication becoming economically desirable once the global level of control is high (Barrett and Hoel 2007). Higher immunization rates mean shorter times until eradication, but also come at a higher cost. With all other inputs at the base case value, the immunization rate yielding the lowest cost-effectiveness of eradication following decision rule E1 and compared to no vaccination equaled approximately 1.25 times $\hat{u}$. We also found that the time until the last case decreased substantially when the initial values reflected prior immunization intensity close to $\hat{u}$, but there was a less important reduction for prior immunization intensities of less than 0.5 times $\hat{u}$.

4. Discussion

Our analysis of different decision rules explores the management of multiple infectious diseases within an integrated and generalizable model, and it leads to a number of important insights. First, the analysis confirms the potentially very attractive economics of eradication for any individual disease and the need to sustain commitment to eradication even when the perceived urgency of the disease declines (Barrett 2004, Barrett and Hoel 2007, Thompson and Duintjer Tebbens 2007). Second, we find that in the context of multiple diseases, chasing the "epidemic of the day" leads to firefighting behavior, with potentially very costly consequences in terms of financial and human costs. The more resources get diverted with each switch of perceived priority, the greater the costly oscillations in incidence. Third, the perception delay is an important factor in the economics; with a very short delay for decision rule C2, the rapid response to switches in the instantaneous incidence mitigates large oscillations, whereas with a very long delay, policy C2 effectively becomes more like an eradication policy (see the e-companion). Fourth, the nonlinear feedback process inherent in infectious diseases aggravates the suboptimality of firefighting. If we consider simultaneously managing one nonlinear process (e.g., management of an infectious disease) and one more linear process (e.g., a road construction project), we still find shifts in priority, but we only lose ground when we stop investments in the infectious disease after each switch in priority; even with interruptions, the completion of the road project will occur eventually, in the end freeing up resources to finish eradication of the infectious disease. The road does not recede back to a less finished state (at least not within a relevant time frame), whereas leaving a small reservoir of infections unchecked puts all previously achieved success in jeopardy. Thus, the competition for constrained resources of two (or more) processes with fast relative growth away from some desired equilibrium state (e.g., zero infected persons) gives rise to the very undesirable behavior demonstrated in this paper. Although this paper illustrates this behavior for infectious diseases, many other similar managerial applications exist with similar potential behavior, including new product development (Repenning 2001, Loch and Kavadias 2002), task management (Seshadri and Shapira 2001), emergency response (Green and Kolesar 2004), and organizational learning (Rahmandad 2008). For example, in new product development, underfunding of a project prior to completion can result in proportionally higher costs (e.g., for rework), leading to underfunding of other projects. In task management, firefighting can emerge whenever tasks compete for resources (e.g., time), and drawing away x amount of resources from a task causes a need for more than x additional resources to complete the task. Analogous to the two-disease example, sequential completion of the tasks becomes optimal when resources are insufficient to complete both tasks at the same time and resource requirements are substantially lower after completion of a task. Military strategy also provides an obvious parallel, with efforts to control insurgencies potentially quickly undone by any reduction in counterinsurgency intensity as long as an enemy foothold is present. Perhaps the most intuitively straightforward system that exhibits similar behavior is one consisting of two identical mechanical springs that lock in when completely compressed. If our goal is to lock both springs but we have enough force only to compress one spring at once, then obviously the optimal strategy is to compress the springs sequentially. Although the two-spring example demonstrates the simplicity of the core dynamic at work, we believe that in real managerial applications this dynamic may easily be lost due to the complexity of the system (e.g., delays, stochasticity, feedback structure) or ignored due to pressures resulting from misleading benchmarks for success (e.g., instantaneous perceived cost-effectiveness ratio or any benchmark that does not reflect the true state of a system). In this context, we highlight the counterintuitive result that allocating all resources based on information about the incidence (C2) emerges as a worse policy than acting based on no information at all (C1). With respect to infectious diseases, we also note that although the stochastic nature of transmission becomes similar to that of a deterministic model when averaged over a large number of iterations (Rahmandad and Sterman 2008), some degree of firefighting results purely from the stochastics for decision rule C3, which would be identical to C1 in the deterministic case. Fifth, this analysis provides another striking example of the danger of static yet apparently intuitive decision rules (Kleinmuntz 1985; Sterman 1989a, b, 1994; Booth Sweeney and Sterman 2000; Sterman 2000, 2008; Sterman and Booth Sweeney 2002; Cronin et al. 2009), which further underscores the importance of rigorous analytical applications to explore the optimality of vaccination strategies in dynamic infection transmission models (see, for example, Greenhalgh 1988; Hadeler and Müller 1993; Müller 1998, 2000). It is within the complex politics of resource allocation and execution of programs in the field that the larger dynamic perspective may get lost and the danger of reverting to simple decision rules becomes greatest.

Many challenges complicate the goal of disease eradication. This model does not address important challenges such as technical feasibility, logistical hurdles (i.e., conflict and poor public health infrastructure), free riding or lack of financing incentives for donor countries (Barrett 2006), the weakest link game inherent in the need to eliminate the agent simultaneously everywhere (which extends the time and costs of completing global eradication) (Barrett 2003), and the costs of risk management to ensure the safe discontinuation of vaccination (Sangrujee et al. 2003; Duintjer Tebbens et al. 2006a, b, 2008; Thompson et al. 2008). However, we believe that this model sheds light on the problem of shifting priorities in the face of eradication. To our knowledge, this work represents a first attempt to explicitly model the decision behavior that may complicate sustained commitment to eradication when managing multiple eradicable diseases and, by extension, to all disease management. By extension, this analysis also relates to any portfolio of investment problems for which shifts in resources may lead to nonlinear changes in results. The model demonstrates how shifting priorities will lead to a failure to eradicate and yields economically suboptimal outcomes. More extreme shifts in priorities will lead to greater long-run costs per prevented case, whereas pursuing eradication becomes more attractive as the time until safe cessation of vaccination decreases.

A model that supports actual decisions must include consideration of treatment and societal costs of disease cases, nonlinearity in costs as the immunization rate increases to high levels, and the impact of different time horizons or time preferences (i.e., discount rate). In general, simplifying model assumptions (e.g., about mixing, immigration, uniform versus targeted vaccination, stochastic versus deterministic approach, and continuous versus discrete stocks) are likely to have a greater impact at the end stages of epidemics than at the endemic stages. We briefly explored the role of heterogeneity in separate analyses (see the e-companion). We highlight that any two real diseases will not have the same properties. However, as long as the budget remains insufficient to increase immunization rates for all eradicable diseases above the eradication threshold ($\hat{u}$), control policies that do not pursue eradication risk cycles in incidence of all diseases and associated excess disease cases. The time until global eradication and subsequent cessation of vaccination represents a key determinant of the economics of managing actual eradicable diseases. Thus, the economic attractiveness of pursuing eradication depends on where we are in the life cycle of managing each disease. If we have achieved elimination of the infectious agent in many countries, or if immunization rates have previously been uniformly high, the economic case for eradication becomes stronger. A realistic life cycle of managing an eradicable infectious disease might include several phases (Thompson and Duintjer Tebbens 2006). For example, after a vaccine first becomes available, the societal willingness to pay (WTP) to prevent disease cases may generate economic support for a program to immunize at a certain rate below $\hat{u}$, but not yet for pursuing eradication given the long expected time until the last case. Once the incidence settles around the equilibrium associated with the control-level immunization rates, vaccination at a higher rate than the control level may at the surface appear less attractive given that it would prevent few additional cases. However, with the now reduced expected time until the last case, pursuing eradication may become economically attractive. Prior studies similarly found that the optimal control of epidemics depends on where the epidemic is in its life cycle for the control of HIV spread (Feichtinger et al. 2004) and related to policies to reduce illicit drug use (Tragler et al. 2001).

Because eradication requires simultaneous elimination everywhere, a process like this would have to occur on a global level. Initially, each country achieves a different level of control corresponding to its economically justified immunization rates based on the WTP, which may or may not exceed $\hat{u}$. After enough countries achieve sufficient levels of control, pursuing eradication may become an economically attractive goal given the reduced expected time until the last case and the desire to prevent importation of disease, even if the implied high immunization rates may not be economically sustainable in some countries (Barrett and Hoel 2007). Thus, global negotiations become an important part of the process (Thompson and Duintjer Tebbens 2008).

The experience with yaws provides the strongest indication that policy makers facing limited budgets may divert resources from an eradication attempt toward another disease only to later incur more costs and cases of the reemerging disease (Figure 1(c)). With polio and dracunculiasis eradication close to completion, it remains essential to understand the costs and opportunity costs of failing to eradicate. In our model, eradication policies for one disease require foregoing opportunities to prevent more cases of another disease with higher incidence in the short run to prevent more disease overall in the long term. If resources are truly constrained, this raises an important ethical dilemma that decision makers must discuss explicitly. It also raises questions about the basis for selection of the resource constraint and should lead to discussion about opportunities to expand resources. Without a resource constraint, the dilemma becomes one of low short-run costs versus eventual resource savings to help fight other diseases (Thompson and Duintjer Tebbens 2007).

Opponents of a vertical public health initiative, such as disease eradication, implicitly suggest that an integrated approach of investing in a better overall public health infrastructure will yield benefits in controlling multiple diseases (Scholtens et al. 1972, Arita et al. 2006), and indeed might facilitate their eventual eradication. In the context of our model, the integrated approach implies that investments out of the available budget might go toward interventions that reduce transmissibility or increase the immunization rate for both diseases *at the same time*, which will clearly change the dynamics. Although such an approach offers great potential, the potentially long time delays and uncertainty in impacts (both costs and cases) make it difficult to intuitively assess the benefits. Similar to our call for explicit consideration of the trade-offs associated with vertical approaches (Thompson and Duintjer Tebbens 2007), we suggest that quantification of the costs and benefits of the more integrated approaches over time will greatly facilitate decision making and that resource allocations should follow rigorous analysis.

5. Electronic Companion

An electronic companion to this paper is available as part of the online version that can be found at http://mansci.journal.informs.org/.

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