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Optimal disease eradication

SCOTT BARRETT
School of Advanced International Studies, Johns Hopkins University, 1619 Massachusetts Avenue NW, Washington, DC 20036-1984 USA. Tel: (202) 663-5761. Fax (202) 663-5769. Email: sbarrett@jhu.edu

MICHAEL HOEL
Department of Economics, University of Oslo, P.O. Box 1095 Blindern, N-0317 Oslo, Norway. Tel: 47 22858387. Fax 47 22855035. Email: michael.hoel@econ.uio.no

ABSTRACT. Using a dynamic model of the control of an infectious disease, we derive the conditions under which eradication will be optimal. When eradication is feasible, the optimal program requires either a low vaccination rate or eradication. A high vaccination rate is never optimal. Under special conditions, the results are especially stark: the optimal policy is either not to vaccinate at all or to eradicate. Our analysis yields a cost–benefit rule for eradication, which we apply to the current initiative to eradicate polio.

1. Introduction

The *eradication* of an infectious disease is an extreme – indeed, a singularly ambitious – policy goal. It is to be contrasted with a policy of *control*, which reduces incidence below the competitive level but not to zero, and a policy of *elimination*, which cannot stop disease imports but which can prevent a local epidemic. It is a goal that has been tried before (hookworm, yellow fever, yaws, malaria), but achieved only once (smallpox). It is a goal that is being attempted again now (poliomyelitis, dracunculiasis), and for which there exists a long wish list of future candidates (among them, mumps, rubella, lymphatic filariasis, cysticercosis, and measles).

Why eradicate? Suppose that a disease can be controlled – say, by means of vaccination. Suppose as well that the disease is already being controlled, and at a very high level – so high, in fact, that a slight increase in the vaccination rate would cause the disease to be eradicated. Eradication would increase costs in the short run, and prevent a few additional infections. But in making the pathogen disappear, eradication would also avoid the need ever to vaccinate in the future: a huge 'dividend'. A very high level of control will therefore never be optimal. Intuitively, the optimal policy will require no control, a modest level of control, or eradication. In this paper, we develop this intuition formally.

A disease can only be eradicated if it is eliminated everywhere in nature. Hence, our analysis applies to two kinds of situations: at the global level

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and at the level of the nation state after every other country has already eliminated the disease. If countries were symmetric, it might seem that the calculus of eradication would be the same for both of these situations. Barrett (2003), however, shows that, depending on the costs and benefits facing the 'last' country, global disease eradication – a global public good – may be either a coordination (weakest link) game or a prisoners' dilemma.[1] Though Barrett (2003) exposes the underlying incentive problem, his analysis relies on a static framework in which eradication is assumed to be instantaneous – an outcome that may not be optimal (or even feasible). Our paper focuses on the dynamics of eradication, solving explicitly for the conditions under which eradication (whether at the level of the globe or the 'last' country) will be optimal.[2]

Our approach is to solve a central planner's problem, where it is assumed that the planner can choose a sequence of vaccination rates directly. We ignore behavior in our model, either of individuals or of states acting independently. Our approach is thus more consistent with the optimal growth literature than with the emerging literature of economic epidemiology. Our interest is not in positive analysis or incentive mechanisms. It is in deriving a cost–benefit rule for eradication.[3]

Our approach is thus to be contrasted with Geoffard and Philipson (1997), who also develop a dynamic model of the economics of disease eradication, but with a focus on the positive analysis of public vaccination policy being (partially) crowded out by market behavior (under the assumption that the private demand for vaccination increases with prevalence). In contrast to our paper, Geoffard and Philipson (1997) do not solve explicitly for the conditions under which eradication is socially optimal, let alone the optimal path to eradication. Indeed, in their model, eradication can only be achieved in the limit as time goes to infinity (their analysis only compares steady states).

Our paper is closer in approach to Goldman and Lightwood (2002). In a model in which people are either susceptible or infected (never immune), and in which the control is treatment rather than vaccination, Goldman and Lightwood derive the conditions under which asymptotic eradication is an optimal steady state. Moreover, they show that the initial infection rate determines whether asymptotic eradication is optimal – a result also demonstrated here (see section 4.3). However, there is no dividend to eradication in the Goldman–Lightwood framework, the focus of our inquiry.

[1] Of course, eradication could also be globally inefficient or it could be in every country's interests to eliminate the disease unilaterally. Neither of these possible cases is economically interesting. In a related paper, Cooper (1989) examines international cooperation in the control of cholera and the eradication of smallpox, arguing that successful cooperation hinges on whether knowledge of cause and effect exists. Our analysis, and the literature summarized in this section, presumes such knowledge.

[2] Indeed, we shall show that, for the case of linear costs – the case actually studied by Barrett (2003) – it will be optimal to eradicate instantaneously, if allowed by the feasibility constraints.

[3] Olson and Roy (2003) develop cost–benefit rules for eradicating an invasive species – a situation that does not involve any health-related interactions with humans.

Such a dividend can only be realized if eradication is achieved in finite time. As noted by Gersovitz (2003), 'An important question would be whether settling for an internal steady state with positive infection is dominated by a push for eradication in finite time.' We address this question directly.[4]

The dividend from eradication can be enormous. According to Fenner *et al*. (1988), the annual global benefit of smallpox eradication was about $1.35 billion (using 1967 as a base year), while the total cost of eliminating smallpox from the remaining endemic countries was about $300 million. Assuming a 3 per cent discount rate, the benefit–cost ratio for smallpox eradication was thus about 150:1. Taking into account only the incremental costs needed to eliminate smallpox from the remaining endemic countries ($100 million), the benefit–cost ratio was even higher: about 450:1. Smallpox eradication was thus an astonishingly good deal for the world. It was also a good deal for individual countries. The United States saved about $150 million annually because of smallpox eradication (Fenner *et al.*, 1988), mainly in the form of avoided vaccination costs. Again, using a 3 per cent discount rate, the eradication dividend to the United States alone was about $5 billion, a small fraction of the (essentially, one-time) cost of eradication. Developing countries also gained hugely from the eradication effort. India, for example, gained more than the US (Fenner *et al.*, 1988).

Smallpox was the ideal candidate for eradication: there were no long-term carriers; smallpox survivors were immune for life; infected persons were easily detected; and only persons showing symptoms (probably) could transmit the disease. Moreover, the disease was only mildly infectious (relative to some other diseases; that is, the disease could be eliminated by mass vaccinating 'only' 80 per cent of a population), and the vaccine was relatively inexpensive (a single injection offered effective immunization). Being a live vaccine, immunization was risky, so that the rich countries had a strong incentive to eradicate. Poor countries also had a strong incentive to eradicate, for while vaccination levels were low in most poor countries before the eradication effort got underway, smallpox killed around a third of all infected individuals.[5]

Unfortunately, the eradication of other diseases is likely to be more difficult and less attractive in benefit–cost terms. For example, though measles kills about three-quarters of a million children every year in developing countries, in rich countries, where the disease has been eliminated, the measles vaccine is given as part of a combined vaccine (measles–mumps–rubella or MMR) and the savings from eliminating just the measles component may be relatively small.[6] As well, measles is more

[4] Related papers on the economics of vaccination, but not eradication, include Brito *et al*. (1991), Geoffard and Philipson (1996), Francis (1997), Gersovitz (2003), and Gersovitz and Hammer (2004).

[5] Despite these advantages, the effort to eradicate smallpox, and so to supply a global public good, came close to failing for lack of resources. See Barrett (2006) for an analysis.

[6] Estimates of the savings from measles eradication vary. According to Miller *et al*. (1998), the net benefits of measles eradication to the US would be between $500 million and $4 billion (1997 dollars). Savings estimates by Carabin and Edmunds (2003) are in the range of $10 million and $623 million for a selection of rich

infectious than smallpox, and eradication would require vaccination (in multiple doses) of a very high proportion of the population (probably 95 per cent or greater) – a problem if marginal costs increased in the vaccination rate. As explained in section 7, polio eradication also faces huge technical and biological challenges, even though the current campaign has already eliminated the disease from most parts of the world.

The threat of bioterrorism further weakens the economic case for eradication. Countries may now feel the need to continue to vaccinate, even if at a relatively low level (Carabin and Edmunds, 2003, for example, assume that vaccination for measles would be reduced but not stopped even after eradication), or to stockpile vaccine, and prepare for emergency distribution in the event of an attack (the approach being by a number of countries, including the United States, with respect to smallpox). These kinds of measures shrink the eradication dividend, while probably having no effect on the economics of control.[7]

In summary, the economic calculus for eradication of the most favorable remaining candidate diseases is likely to be more finely balanced than for smallpox – meaning that the framework used for benefit–cost analysis needs to be more carefully specified. Our paper is a contribution to this effort. We derive a cost–benefit rule for optimal eradication, and demonstrate its utility by applying it to the current global initiative to eradicate polio.

Our paper progresses as follows. Section 2 develops the epidemiological model that describes how eradication might be achieved in finite time, and section 3 specifies our economic model of eradication. Section 4 solves for the optimal eradication policy, and sections 5 and 6 analyze special cases. Section 7 applies our framework to the current effort to eradicate polio. Section 8 summarizes our main results.

2. Epidemiology

We take as our starting point Anderson and May's (1991) model of the dynamics of immunization, a standard in the epidemiology literature[8]

$$\dot{x}(t) = m - [m + \lambda(t)]x(t) - p(t), \tag{1}$$

$$\dot{\lambda}(t) = (v + m)\lambda(t)(R_0 x(t) - 1), \tag{2}$$

countries (Canada, Denmark, Finland, the Netherlands, Spain, Sweden, and the United Kingdom). One reason for the lower savings estimated by Carabin and Edmunds (2003) is the assumption that vaccination at some level would need to continue even after the wild virus had been eradicated because of the threat of bioterrorism – an issue discussed in the next paragraph.

[7] The rich countries would presumably be the target of a bioterrorist attack, but the rich countries are likely to eliminate candidate diseases for eradication unilaterally, making further measures to defend against a bioterrorist attack unnecessary.

[8] See, in particular, equations (7.1) and (7.2) in Anderson and May (1991: 145). Note that our equations (1) and (2) differ from these equations in two ways. First, our equation (2) corrects for a typo in Anderson and May's equation (7.2), which should be the same as their equation (6.6) on p. 123. Second, Anderson and May's equation (7.1) assumes that only newborns are vaccinated. We assume that any and all susceptible persons may be vaccinated, not just newborns.

where $x(t)$ is the fraction of the population that is susceptible, $\lambda(t)$ is the force of infection (the rate at which susceptible individuals become infected), and $p(t)$ represents the overall rate of vaccination (only susceptible individuals are vaccinated). This dynamical system assumes that population is constant (births equal deaths; we normalize by setting population equal to one), with m representing both the birth and mortality rate. It also assumes (as is customary in epidemiological modeling) that the disease is non-lethal. The parameter v represents the rate at which infected individuals become immune. Finally, R_0 is the basic reproductive rate of the microparasite (for a disease to spread, it is essential that $R_0 > 1$). A brief explanation is given in Appendix A.

For our purposes, this system of differential equations poses a problem: If the system (1)–(2) begins at $\lambda(t) > 0$, it can only converge to $\lambda(t) = 0$ as $t \to \infty$. This wouldn't matter if we only needed to study steady states. However, as noted in the introduction, the reason for pursuing a policy of eradication, rather than of high control, is to reap the benefits of not having to vaccinate post-eradication. If the aim is to study the optimality of eradication, the dynamics must permit eradication in finite time.[9]

Just how to model this is not so obvious. To Gersovitz (2003), moving 'away from the no-eradication property of the model would require a more cumbersome model of finite lives'. Our approach is much simpler. We solve for the steady state, $\lambda^{\infty} = m(R_0 - 1) - pR_0$, and assume that the dynamics can be represented by an adjustment equation

$$\dot{\lambda}(t) = \sigma[m(R_0 - 1) - p(t)R_0 - \lambda(t)] \tag{3}$$

for $\lambda(t) > 0$, where σ is the speed of adjustment parameter.[10] Conveniently, (3) captures (almost) everything we need in a single equation. For our purposes, $x(t)$ is not of direct importance. $x(t)$ is only important insofar as it affects $\lambda(t)$, and this effect is reflected in (3). Even more importantly, (3) allows eradication to be achieved in finite time. It therefore allows us to evaluate the conditions under which eradication will be optimal.

The differences between equations (1)–(2) and (3) need to be underlined. We know (1)–(2) is inappropriate for evaluating eradication. But (3) also behaves differently than (1)–(2) when $\lambda(t)$ is high. Equations (1)–(2) imply that a small increase in the vaccination rate will reduce the force of infection by more when λ is high than when λ is low (for a given value of x). In epidemiological terms, the number of follow-on infections prevented by a single vaccination increases with the force of infection. Our use of equation (3) fixes this effect. In economic terms, equation (3) makes the marginal benefit of vaccination independent of the vaccination level. When comparing a policy of high control versus eradication, use of (3) will not distort matters very much. The simplification matters more when comparing a policy of low control versus eradication. This is especially important for our linear model, presented in section 5, and we discuss

[9] We need hardly add that smallpox *was* eradicated, and in a period of just ten years. Empirically, (1)–(2) is invalid, at least for small λ.

[10] In Appendix A we discuss how the size of σ relates to the parameters in the original Anderson and May (1991) model.

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this assumption again in this section.[11] However, it is as well to note that eradication will not normally be contemplated unless and until $\lambda(t)$ is low. When the goal of eradicating smallpox was announced, the disease had already been eliminated in all industrialized countries; it remained endemic only in 59 developing countries. Similarly, the poliomyelitis eradication initiative was only launched after the disease had been eliminated in all of the Americas in addition to all industrialized countries. The main reason for this is that eradication must be demonstrated to be feasible before a policy to eradicate can be contemplated.

Before presenting our economic model, one further adjustment is required. Our main interest lies not in $\lambda(t)$ but in the proportion of the population that is infected under a control program. Denote this proportion $y(t)$. Assuming homogenous mixing, $\lambda(t)$ will be proportional to $y(t)$ (Anderson and May, 1991). In particular, we can write $\lambda(t) = \beta y(t)$ where β is a transmission parameter. We can thus rewrite (3) as

$$\dot{y}(t) = \sigma[\tilde{R}_0(K - p(t)) - y(t)], \tag{4}$$

where $\tilde{R}_0 \equiv R_0/\beta$ and $K \equiv m(1 - \frac{1}{R_0})$. Note that, since $R_0 > 1$ by assumption, K must be strictly positive. Note as well that K is proportional to $(1 - 1/R_0)$: a familiar term in the epidemiology literature; the critical proportion of the population that must be immunized in order for the disease to be eradicated (Anderson and May, 1991: 87).

3. The optimization problem

The socially efficient vaccination program maximizes the objective function

$$W = \int_0^T e^{-rt}[-c(p(t)) - by(t)]\,dt, \tag{5}$$

where $by(t)$ is the social cost at time t of having a proportion $y(t)$ of the population infected (b, a parameter, is thus the per unit social cost of infection), $c(p(t))$ is the social cost at time t of vaccinating susceptible persons at rate $p(t)$ per unit of time (e.g., per year), r is the rate of time discount, and T is the length of the vaccination program, which may be finite or infinite. If the disease is eradicated, T will be finite, and the integral of social welfare from T to infinity will be zero and so can be ignored.

We assume that $c(0) = 0$ and that $c(p)$ is strictly increasing and strictly convex. In sections 5 and 6 we consider special cases of linear and quadratic costs, respectively. Note that $c(p)$ includes more than just the costs of vaccine and of administering the vaccine. It also includes the costs of any side effects. The latter cost can be significant. For every million people given the

[11] We note here, however, that our approach can be shown to be robust even in this context. Assuming constant marginal costs, as in our linear model, but using (1)–(2) while assuming that eradication is achieved only when $\lambda(t)$ falls below some critical level, ε, Kenea Mideksa (2005) obtains results very similar to our own, even when ε is very small.

smallpox vaccine, for example, a few will die and many others will suffer severe reactions. Similarly, and as explained in section 7, the oral polio vaccine can cause paralysis in a very small percentage of cases. Worse, it can circulate in the community, infecting other susceptible persons. When a disease is prevalent, these associated effects are little noticed, but when control becomes very high, they become more prominent.

The government's problem is to maximize (5) subject to (4) and the additional constraints

$$p(t) \geq 0, \tag{6}$$

$$y(t) \geq 0, \tag{7}$$

$$y(0) > 0 \text{ given}, \tag{8}$$

and

$$y(T) = 0. \tag{9}$$

Except where stated otherwise, we shall assume $y(0) = \tilde{R}_0 K$. This is the steady state stock of infections when $p = 0$ (see equation (4)).

Equation (9) is of particular interest. It says that, once the disease is eradicated, there will be no more infections – and, therefore, no further need to vaccinate. The time T at which eradication is achieved is endogenous, determined as part of the solution to the optimization problem. As noted before, T may be infinite, implying that it is not optimal to eradicate the disease. In our formal mathematical treatment, however, it will prove convenient to assume that T is finite, i.e. that the choice of T is restricted to $T \in [0, \tau]$, where τ is very large (e.g., 5 million years). If we find that $T = \tau$ is optimal, this can be interpreted as saying that T is infinite.

4. The optimal policy

Taking the shadow price $\alpha(t)$ associated with (4) to be positive, the current value Hamiltonian may be written as

$$H = -c(p(t)) - by(t) - \alpha(t)\sigma[\tilde{R}_0(K - p(t)) - y(t)]. \tag{10}$$

Along the optimal program, the shadow price $\alpha(t)$ obeys the following differential equation (dropping the time argument when this causes no confusion)

$$\dot{\alpha} = r\alpha + \frac{\partial H}{\partial y} = (r + \sigma)\alpha - b. \tag{11}$$

At any point in time, $p(t)$ maximizes the Hamiltonian. For $p(t)$ positive, maximization requires

$$c'(p) = \sigma \tilde{R}_0 \alpha. \tag{12}$$

Along the optimal program, vaccination should be chosen at each instant in time such that marginal cost equals marginal benefit – the latter being equal to the shadow value on infections, α, times the change in the number of infections attributable to a small change in the vaccination rate.

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Equation (12) defines an increasing function, $p(\alpha)$, for $\alpha \geq c'(0)/\sigma\tilde{R}_0$. For $\alpha \leq c'(0)/\sigma\tilde{R}_0$, the constraint $p(\alpha) = 0$ applies.

From (4) and (12) we have

$$y = \tilde{R}_0(K - p(\alpha)) \quad \text{for } \dot{y} = 0 \tag{13}$$

and

$$\alpha = \frac{b}{r+\sigma} \quad \text{for } \dot{\alpha} = 0 \tag{14}$$

In $y - \alpha$ space, the $\dot{\alpha} = 0$ line is horizontal, whereas the $\dot{y} = 0$ line intersects the a-axis at $p(\alpha) = K$, decreases until $\alpha = c\prime(0)/\sigma\tilde{R}_0$, and then becomes vertical at $y = \tilde{R}_0 K$. Denote the intercept of the $\dot{y} = 0$ line α^0. Setting $p = K$, (12) gives

$$\alpha^0 = \frac{c'(K)}{\sigma\tilde{R}_0}. \tag{15}$$

There are two qualitatively different cases to consider. In the first, the $\dot{\alpha} = 0$ line lies above the $\dot{y} = 0$ line. In the second, these lines intersect in the interior. When solving both cases, we start by analyzing the optimal solution assuming that T is given. Later we solve for the optimal value of T.

4.1 Case 1

We first consider the case where the $\dot{\alpha} = 0$ line lies above the $\dot{y} = 0$ line, i.e. where a, defined by (14), is higher than a^0, defined by (15). Rearranging gives

$$\frac{b\sigma\tilde{R}_0}{r+\sigma} \geq c'(K). \tag{16}$$

Before proceeding with the mathematics, consider the economic implications of this condition. Begin at $t = 0$ with $y > 0$ given. Now, set $p = K$ and hold the vaccination rate at this level indefinitely. The marginal cost of this vaccination policy (at every moment in time) is given by the right-hand side of (16). From (4) we know that pursuit of this policy implies $y \to 0$ as $t \to \tau$ (recall that τ is very, very large). Equation (4) also tells us that the instantaneous effect of the policy is to reduce the number of infections by $\sigma\tilde{R}_0$. Each infection saved yields a social benefit, b, and so the marginal, instantaneous benefit of this vaccination policy is $b\sigma\tilde{R}_0$. The full marginal benefit is larger, however, because the effect of vaccination is long lasting. From (4) we know that, when $p = K$, $\dot{y}/y = -\sigma$. Hence, the infections saved by this policy (at each instant in time) degrade at constant rate σ. Of course, the economic benefit is also discounted (at rate r). The marginal benefit of following this policy at each instant in time is thus $\int_0^T b\sigma\tilde{R}_0 e^{-(r+\sigma)t}dt$. As already noted, pursuit of this policy eradicates the disease only in the limit (that is, the disease is not eradicated). Solving the integral (for $T \to \tau$, which is close to ∞) yields the LHS of (16): the present value marginal benefit of vaccination for this policy.

Inequality (16) is a kind of reference condition. For consider a small deviation in the policy described above. Suppose in particular that at some date the vaccination rate is increased very slightly above $p = K$ for a very

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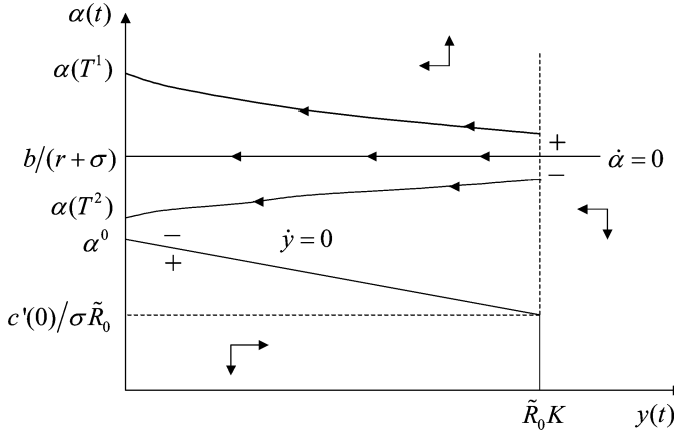

Figure 1. *Eradication in finite time*

short period of time and then set equal to K again. The cost of this one-time deviation will be approximately equal to the RHS of (16). The benefit, however, will strictly exceed the LHS of (16) because this tiny, one-time increase in vaccination will cause the disease to be eradicated in finite time. Hence, (16) is only a sufficient condition for eradication to be optimal (see Appendix B). It is not necessary.[12]

Case 1 is illustrated in figure 1. The optimal development of $y(t)$ and $\alpha(t)$ (and thus of $p(t)$) depends on the exogenously given value of T. We have drawn trajectories for three different values of T. For each trajectory we have assumed that $y(0) = \tilde{R}_0 K$ (this gives the steady state value of y when $p = 0$). The top trajectory in figure 1 is for a 'small' T, denoted T^1. Along this trajectory, $p(t)$ increases over time. The middle trajectory is for a value of T which implies that $p(t)$ must be constant over time. Finally, the bottom trajectory is for a 'large' T, denoted T^2. Along this trajectory, $p(t)$ declines over time. For $y(0)$ given, as the value of T increases, the terminal value of the shadow price, $\alpha(T)$, falls. It approaches α^0 as T approaches infinity (strictly speaking, τ).

As shown in Appendix B, $\alpha^* > \alpha^0$. So, if we can find a trajectory for $(y(t), \alpha(t))$ satisfying the differential equations (4) and (11), starting at $(y(0), \alpha(0))$ where $y(0)$ is given by (8) and ending at $(0, \alpha^*)$ at some time point T, then this T, denoted T^*, is the optimal end point. The optimal trajectory in figure 1 is thus the one that terminates at $\alpha(T) = \alpha^*$. All three of the paths shown in figure 1 are potential candidates. Which trajectory is optimal depends on the value of α^*, and thus on the factors that determine α^* (see Appendix B).

[12] Intuitively, eradication implies that the infections saved from a policy deviation do not degrade. Hence, it might seem that a necessary condition for eradication to be optimal should be given by (16) but with σ removed from the denominator. We are unable to prove this for the general model, but our analyses in sections 5 and 6 of two special cases confirm this intuition.

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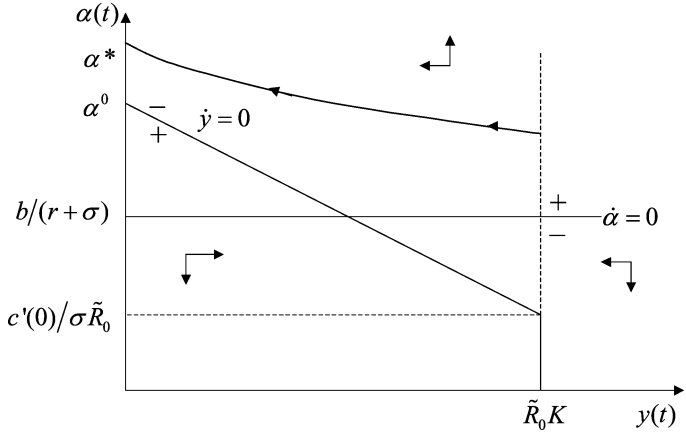

Figure 2. *Vaccination increasing over time prior to eradication*

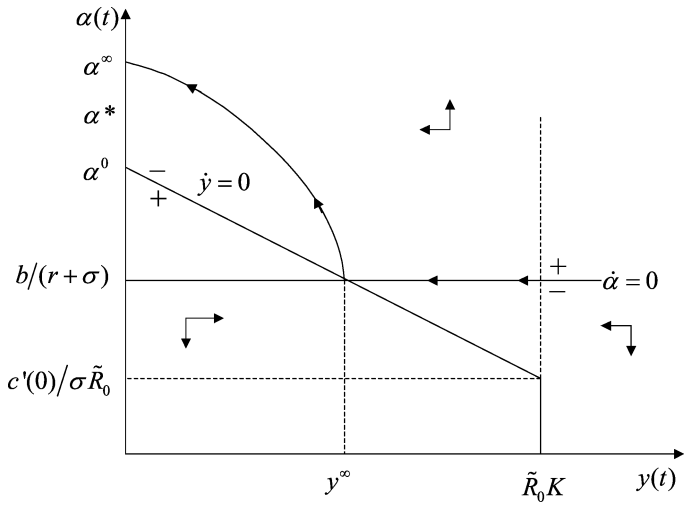

Figure 3. *Positive vaccination forever*

4.2 Case 2

Assume now that the inequality in (16) is reversed. Since (16) is a sufficient condition for eradication to be optimal, we should expect that, for Case 2, eradication may or may not be optimal. We confirm this intuition below.

Case 2 is illustrated in figures 2 and 3. Figure 2 assumes that there exists a trajectory for $(y(t), \alpha(t))$, starting at $(y(0), \alpha(0))$, where $y(0) = \tilde{R}_0 K$ and $\alpha(0) > b/(r+\sigma)$, and ending at $(0, \alpha^*)$ at $t = T^*$. This case is thus similar to Case 1. The only difference is that we can now be sure that $p(t)$ increases over time.

It is also possible that all trajectories starting at $y(0) = \tilde{R}_0 K$ and $\alpha(0) > b/(r+\sigma)$ reach $y = 0$ at a value of α that exceeds α^*. Under these conditions,

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no trajectory of the type illustrated in figure 2 will exist, and eradication in finite time will not be optimal.

However, there will always exist an unstable stationary point (y^∞, $b/(r+\sigma)$), where

$$y^\infty = \tilde{R}_0 \left[K - p\left(\frac{b}{r+\sigma}\right)\right]. \tag{17}$$

The trajectory starting at this point and moving in a northwest direction intersects the α-axis at a point labeled α^∞ in figure 3. If a trajectory of the type drawn in figure 2 does not exist, we have $\alpha^\infty > \alpha^*$. Under these conditions, and taking $y(0) = \tilde{R}_0 K$, we have $\alpha(T) > \alpha^\infty > \alpha^*$ for all $T \in [0, \tau]$. This means that $p(T) > p^*$ for all $T \in [0, \tau]$. From Appendix B it follows that $H(T) > 0$ for all $T \in [0, \tau]$. The optimal end point, therefore, is τ (in practical terms, infinity).[13] The optimal solution is to set $p(t) = b/(r+\sigma) \forall t$, arriving at y^∞ asymptotically.[14] That is, the disease is controlled but not eradicated. It is clear from figure 3 that p will be smaller, and y^∞ closer to $y(0) = \tilde{R}_0 K$, the smaller is $b/(r+\sigma)$ and the larger is $c'(0)/\sigma\tilde{R}_0$. If the marginal cost of vaccination exceeds the social marginal benefit when $p = 0$ – that is, if $c'(0) > b\sigma\tilde{R}_0/(r+\sigma)$ – then the optimal policy will be to set $p = 0$ always (technically, before τ is reached), unless eradication in finite time is optimal.

To sum up, we have thus far established a sufficient condition for eradication to be optimal, and we have characterized the other possible qualitative solutions. To derive more specific results – in particular, a necessary and sufficient condition for eradication to be optimal – we will have to work with explicit cost functions. We turn to this task in sections 5–6, but first it will prove helpful to consider the effect of the initial conditions on the results developed thus far.

4.3 Initial conditions

To this point we have assumed that the starting value of y is given by y's stationary value when $p = 0$ – that is, $\tilde{R}_0 K$. What would be the optimal policy at an early stage of a new disease when the initial infection rate is substantially below $\tilde{R}_0 K$?

Plainly, if eradication were optimal when $y(0) = \tilde{R}_0 K$, then it will also be optimal when $y(0) < \tilde{R}_0 K$. Indeed, the optimal program will require that vaccination proceed along the same optimal trajectory as derived above (that is, the optimal trajectory corresponding to the starting value $y(0) = \tilde{R}_0 K$). The only difference is that, since the starting value of y is different, the starting value of p must also be different. Our analysis thus applies equally well to a situation in which a disease has been controlled previously as to a situation in which a disease has not been controlled at all.

The initial conditions only really matter when eradication would not be optimal for $y(0) = \tilde{R}_0 K$. If $y(0)$ is small enough (relative to y^∞), then it can be shown that eradication will be optimal. This possibility is illustrated in

[13] See e.g. Theorem 1 in Seierstad (1988).

[14] Strictly speaking, since τ is finite, the trajectory lies infinitesimally above the trajectory going from ($\tilde{R}_0 K, b/(r+\sigma)$) to (0, α^∞) via (α^∞, $b/(r+\sigma)$), lying close to the latter point most of the time.

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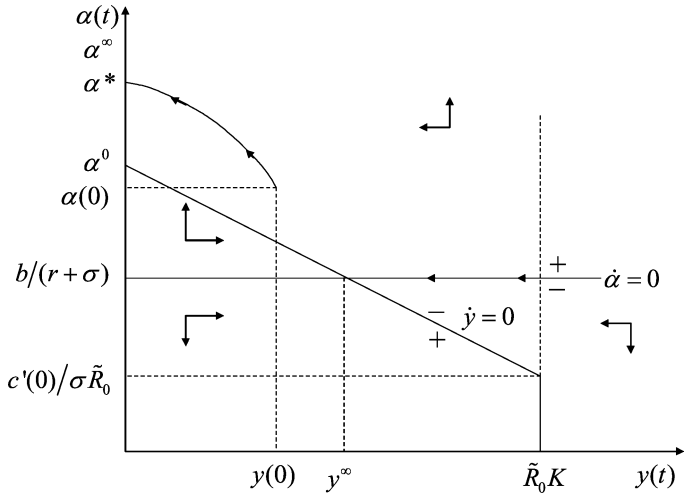

Figure 4. *Eradication only if the initial rate of infection is sufficiently low*

figure 4, which differs from figure 3 only with respect to the initial condition. For the starting values $(y(0), \alpha(0))$ in figure 4, the trajectory reaches $(0, \alpha^*)$, and so it is optimal to eradicate the disease at some time $T^* < \tau$. The reason that eradication will be optimal when the initial rate of infection is low is not that fewer people need to be vaccinated at any given time.[15] The reason is that people need be vaccinated for a shorter period of time.

Initial conditions are important in two different situations. The first concerns an emerging infectious disease. SARS (severe acute respiratory syndrome), we now know, emerged in late 2002 in China. In March 2003, the World Health Organization issued a global alert, and countries immediately began taking measures to control the disease. Some scientists argued that this was not enough, however, that the opportunity to eradicate the disease should be seized before SARS had a chance to become established. As Burke (2003) put it, 'epidemic-control efforts should not simply be maintained, but doubled, and redoubled again'. The epidemiological rationale for moving quickly was that there existed but a short window during which SARS could be readily distinguished from influenza. Wait too long, or act too

[15] In our model, control is achieved by means of mass vaccination. Only in a model with heterogeneous mixing would a strategy like 'ring vaccination' work, making it possible to isolate infected persons and to vaccinate only those susceptible persons who came into contact with infected individuals before quarantine. Boily *et al*. (2002) provide a related analysis of HIV epidemic phases. They show that, in an early phase of an HIV epidemic, robust intervention targeted at a high-risk group (a situation, therefore, involving heterogeneous mixing) can (theoretically) eradicate the disease, whereas efforts spent protecting the broader population require indefinite intervention. Also somewhat related to this point, Olson and Roy (2003) show that the economics of eradicating an invasive species may depend on the scale of the original invasion.

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passively, and eradication might cease to be feasible. This paper points to a further rationale: While a short, sharp response may be optimal at the early stage of the disease, a sustained effort at eradication may not be optimal after the disease has become established.[16]

The second situation concerns endemic diseases. As noted previously, eradication of these diseases never proceeds unless and until eradication can be shown to be feasible. This means that global incidence will already be reduced to a relatively low level before an eradication goal will be contemplated. Our analysis indicates that, the greater is the number of countries that eliminate a disease unilaterally, the more attractive will be the economics of eradication.

5. The special case of a linear cost function

To get sharper results, it will prove useful to consider the case of a linear cost function. Specifically, let

$$c(p) = cp, \tag{18}$$

where c is a positive parameter. To get a mathematically meaningful solution to our maximization problem, we assume instead of (6) that

$$p(t) \in [0, P], \tag{19}$$

where P is some large value (certainly large enough to make eradication possible). We shall in particular consider the limiting case in which $P \to \infty$.

Instead of (12) we now get

$$\begin{aligned} p(t) &= 0 \quad \text{for } \alpha(t) < \frac{c}{\sigma \tilde{R}_0}, \\ p(t) &= P \quad \text{for } \alpha(t) > \frac{c}{\sigma \tilde{R}_0}. \end{aligned} \tag{20}$$

The optimal vaccination program thus reaches the optimal steady state infection rate as quickly as possible. This result is not very surprising; we should expect to obtain a most rapid approach solution for the linear model. What is more surprising, however, is that, for the linear model, there are only two optimal steady states. It is optimal either not to vaccinate at all or to eradicate. A policy of disease control (short of eradication) is never optimal.

What is the reason for this result? Recall from section 2 that our simplification of the dynamics implies a constant marginal benefit of vaccination for any level of control short of eradication. With the linear model, marginal costs are also constant. Hence, if it is better to vaccinate many persons than one fewer, then it must also be better to vaccinate one person than none. We know that eradication is better than a policy of vaccinating many persons. For the linear model, therefore, eradication must also be better than a policy of vaccinating even one person. However,

[16] As well, for SARS the total effort required to isolate all infected individuals would be lower at any given time at an early stage of the disease than after the disease has become established. For a discussion of whether SARS is now eradicated, see Enserink (2003).

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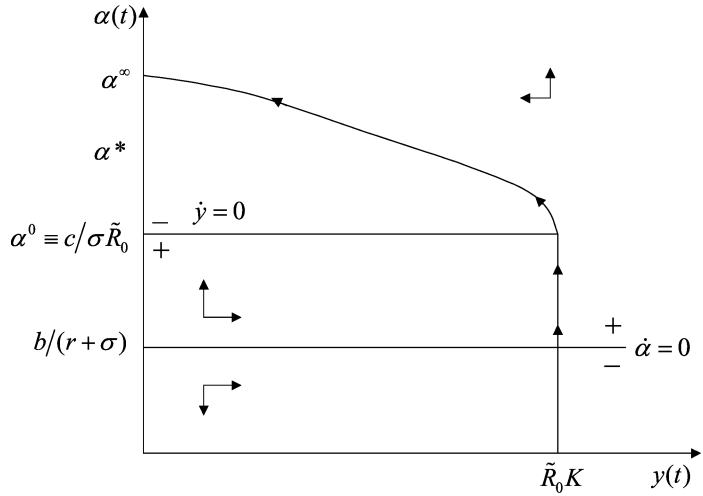

Figure 5. *Linear cost function and "high" costs, implying no vaccination*

eradication need not be welfare superior to a policy of zero control. Hence, with the linear model, only one of two extreme outcomes will be optimal: eradication or no control. It is important to emphasize that this result follows not only from the assumption about costs, but also from the way in which we have represented the dynamics of infection, as noted in section 2. Even with linear costs, positive vaccination short of eradication may be optimal if the number of follow-on infections prevented by each vaccination were decreasing in the vaccination rate.

When $a^0 < b/(r+s)$, the linear model yields an outcome qualitatively identical to the general model: eradication is optimal. The only noteworthy difference is that, for the linear model, eradication is achieved immediately for the limiting case of $P \to \infty$.

The more interesting case, drawn in figure 5, arises when $a^\circ > b/(r+\sigma)$. As was shown for the general case (see figure 3), we now have an unstable stationary point $(y^\infty, b/(r+\sigma))$. The difference is that, for the linear model, y^∞ will always equal $y(0) = R_0K$; partial control is never optimal. The trajectory rising from this point intersects the α-axis at α^∞. Assume first that $\alpha^\infty < \alpha^*$ (we have not illustrated this case). Then there will exist a trajectory for $(y(t), \alpha(t))$ starting at $(y(0), \alpha(0))$, where $y(0) = \tilde{R}_0K$ and $\alpha(0) > b/(r+\sigma)$, and ending at $(0, \alpha^*)$ at $t = T^*$. This solution is akin to the general case shown in figure 2. For the linear model, $p(t) = P$ for all $t \in [0, T^*]$. For the case illustrated in figure 5, $\alpha^\infty > \alpha^*$. Given $y(0) = \tilde{R}_0K$, $\alpha(T) > \alpha^\infty > \alpha^*$ for all $T \in [0, \tau]$. It is easily verified (from equations (B1) and (20)) that this implies $H(T) > 0$ for all $T \in [0, \tau]$. The optimal end point is therefore τ – in practical terms, infinity. [17] The optimal policy is never to vaccinate (strictly speaking, when τ is finite, we should have $p(t) = 0$ until just before τ, after which $p(t) = P$).

[17] See Theorem 1 in Seierstad (1988).

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The limiting case of $P \to \infty$ yields a particularly useful result (the proof is given in Appendix C): *For the linear model, and taking* $P \to \infty$, *eradication is optimal if and only if*

$$c < b\sigma \tilde{R}_0 / r. \tag{21}$$

Moreover, if condition (21) *holds, and if a policy of setting* $P \to \infty$ *is feasible, then eradication should be achieved instantaneously*.[18]

6. The special case of a quadratic cost function

For the general model, three qualitatively different outcomes may be optimal: no vaccination, control short of eradication, and eradication. With a linear cost function, only the two extreme outcomes of no vaccination and eradication may be optimal. For the quadratic cost function considered in this section (in which marginal cost is near zero for the first vaccination), it will be optimal either to eradicate the disease or to control it at some positive level; the outcome of no vaccination will not be optimal. Our aim here is thus to derive conditions under which it will be optimal to eradicate rather than to control a disease.

The cost function is

$$c(p) = \frac{g}{2} p^2, \tag{22}$$

where $g > 0$, giving a marginal cost $c'(p) = gp$. For the general model, we were only able to derive a sufficient condition for eradication to be optimal. For this specific quadratic function, however, we can give a necessary and sufficient condition. Appendix D derives explicit solutions for the differential equations (4) and (11), and solves for the conditions under which an optimal trajectory leading to $(0, \alpha^*)$ exists. These calculations imply that: *For the quadratic model, eradication is optimal if and only if*

$$gK < \frac{b\sigma \tilde{R}_0}{r}. \tag{23}$$

This condition is very similar to the condition for eradication for the case of a constant unit cost (see section 5). The only difference is that the relevant vaccination cost now is not the unit cost (constant for all vaccination rates), but the marginal cost at the minimum vaccination level necessary to achieve eradication (i.e., K; see (4)).

It is significant that the optimality condition for eradication should depend on this marginal cost, because the literature on vaccination routinely assumes (implicitly, at least) constant average costs. When R_0 is large, K will be large: a sizable proportion of the population must be vaccinated in order to reduce incidence to zero. Expanding coverage, however, is costly. It means reaching people in remote areas, the homeless, people with compromised

[18] It is interesting to compare this result with the corresponding condition given in Barrett (2003). Setting $n = \alpha = 1$ and $p^u = 0$ in Barrett's equation (7) gives the result that eradication is optimal if $bR_0/r \geq c$. This is equivalent to the condition given above once we set $\sigma = \beta = 1$. In Barrett's (2003) model p^u need not equal zero because the social benefit of vaccination is non-linear in the vaccination rate.

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immune systems, and people with religious objections to vaccination. The marginal cost of eradication can be substantially greater than the average cost.

7. Application to polio eradication

Our aim has been to characterize the optimal disease eradication program. In the course of doing so we have derived cost–benefit rules for eradication. In this section we apply these to the current effort to eradicate poliomyelitis.

The global polio eradication initiative – according to the World Health Organization (2001: 1), 'the largest public health initiative in history' – was launched in 1988 and was expected to have succeeded by now. Problems encountered have slowed the progress of the initiative, and even if transmission of wild polioviruses were to stop soon, it would take another three years before the eradication effort could be certified. Even then, a post-certification effort would be required. We describe this later in this section.

Two cost–benefit studies (Bart *et al*., 1996; Khan and Ehreth, 2003) have shown that polio eradication is economically attractive. However, both of these studies are deficient in a number of respects (Miller *et al*., 2006). Perhaps most importantly, neither of these studies compared eradication to the alternative of optimal control. That is an advantage of our framework.

Two vaccines are used today – the oral live-attenuated polio vaccine (OPV, developed by Albert Sabin) and the inactivated polio vaccine (IPV, developed by Jonas Salk). Both have positive and negative features.

OPV is inexpensive and easy to administer; it stimulates local immunity in the intestines, preventing spread of the disease; and when the vaccine virus is shed in areas with poor hygiene and sanitation, it immunizes the community. OPV also has one disadvantage: in a very small number of cases, the vaccine can cause paralysis, either in vaccinated persons (vaccine-associated paralytic polio or VAPP) or in susceptible individuals in the community (circulating vaccine-derived polioviruses or cVDPV). VAPP is especially problematic when vaccination coverage is high, for then the risk of VAPP can exceed the risk of infection by the wild virus. cVDPV, by contrast, is especially problematic when vaccination stops, for then susceptible persons are vulnerable to infection by cVDPV. Through mid-2005, cases of cVDPV have sparked polio outbreaks in six countries (Aylward *et al*., 2005).

IPV is more expensive than OPV, does not prevent transmission by vaccinated individuals, and does not spread immunity throughout the community. However, IPV is a killed poliovirus, and so cannot cause polio (VAPP). After polio had been eliminated from the United States, continued use of OPV caused about 10 cases of VAPP a year – a small number, perhaps, given the extent of vaccination coverage, but a sufficient risk to impel the US recently to switch from OPV to IPV, despite the higher cost.[19] Today, IPV

[19] There are about 250–500 cases of VAPP worldwide every year (WHO, 2003: 16). For a cost–benefit analysis of the decision by the US to discontinue OPV, see Miller *et al*. (1996).

is the vaccine of choice in rich countries, whereas poor countries continue to use OPV.

A number of strategies have been contemplated for the polio endgame – what to do after transmission of wild polioviruses has stopped and been certified (Kew *et al*., 2005). Rich countries have essentially decided to continue with IPV vaccination indefinitely. This is partly because of the risk of a bioterrorist release, but it is also because of the risks associated with the policy choices available to poor countries (described below). Given this decision, rich countries will not benefit substantially from polio eradication. The focus of our analysis is therefore on poor countries.

How can poor countries proceed from here? There are a few possibilities. One is to continue high rates of OPV vaccination indefinitely. This would reduce the risk of infection by cVDPV. It would also reduce the risk of infection by persons with primary immunodeficiency syndromes – people who can shed the virus for years (23 such persons, known as iVDPVs have so far been identified worldwide; Kew *et al*., 2005: 606). However, this approach would result in an increase in VAPP cases – and, of course, a high economic cost of continuing to vaccinate for a disease that has been 'eradicated'. It is unlikely that such a program could be sustained. A second possibility would be for the poor countries to follow the rich and switch to indefinite IPV vaccination. This would eliminate VAPP cases but would be much more costly. A third possibility would be for poor countries to choose independently when to stop using OPV. This, however, would pose huge risks of cVDPVs spreading in the countries that stop vaccination early. The final option considered here is for all countries still using OPV to initiate a coordinated pulse campaign for mass vaccination, and then to stop vaccination at the same time. This would reduce the risk of cVDPVs spreading, but it would not eliminate that risk. The risk of infection by iVDPVs would also remain, though so far no chronic shedders have been identified as living in poor countries. Finally, there is always the risk of polioviruses being introduced from samples held in medical laboratories, or released by terrorists (polioviruses can be constructed from raw materials, so that even safe containment cannot be sure to avoid a future release).

It is this last strategy that has been embraced by the World Health Organization. It has the best chance of actually achieving eradication, but is still risky. It may not even be politically achievable. If just one country refuses to stop using OPV, the entire plan would have to be shelved. And countries would also need to pledge not to use OPV in the event of an outbreak occurring. The WHO's plan is to build a large stockpile of monovalent OPV (vaccines that can respond to individual types of polio; there are three polioviruses), and to draw from this to suppress any outbreaks. The stockpile must be large enough to supply an insurance policy to all countries. Since OPV production will cease after eradication is certified, the stockpile must permit mass vaccination for a period of time long enough to allow OPV production to return to capacity. Finally, of course, surveillance would need to be maintained 'for the foreseeable future' (Kew *et al*., 2005: 622). Poliomyelitis is not an easy virus to detect in a population, not least because it causes paralysis in only about one in 200 cases. In poor countries surveillance problems are magnified. As an

illustration, polio was recently discovered in Sudan, more than three years after the last case had been reported.

Our model cannot accommodate all of these complexities. It can, however, uncover the basic economics. We turn to this now.

To know whether polio eradication is optimal, we need to ask if conditions like (21) and (23) hold for polio. Let us see. Begin by considering the RHS of these equations, since they are identical. From Appendix A (equation (A.7)), we know that $\sigma \tilde{R}_0$ can be approximated by $m(R_0 - 1)/(m + v)$. For polio, $R_0 \approx 6$ (Anderson and May, 1991: 70). The infectious period for polio lasts about 14–20 days (Anderson and May, 1991: 31), and the parameter v is approximately equal to the inverse of this duration (Anderson and May, 1991: 125).[20] Assuming that the duration of infection is 20 days, and taking time units to be years, implies that $v \approx 18.25$. Finally, we take it that $m = 0.02$ for poor countries, though our results will not be sensitive to this value.[21]

The parameter b represents the per person cost of infection, for the infections acquired in a given year. Estimates are available of the lifetime costs of paralysis due to polio (call this B), but these need to be adjusted for two reasons. First, our model assumes that losses due to infection apply only to the infectious period (about 20 days), and yet paralysis is long lasting. Second, polio results in paralysis only in about one in 200 infections. Let n denote the number of paralytic cases a year. The cost of polio infections is then Bn. In our model, this is given by by. Hence we have $Bn = by$. Let N denote the total number of infections in a year. Since our model assumes that the cost of infection only applies to the infections period, we also have $N/v = y$. Finally, $n = N/200$. Upon substituting in the relation $Bn = by$, we get $b = 0.09125B$. For the moment, we shall not attach a value to B. Letting the discount rate r be 3 per cent, the right-hand side of (21) and (23) reduces to $0.0166B$.

The left-hand side of conditions (21) and (23) represent the marginal costs of vaccination. Unfortunately, data are available only for average costs. In poor countries, vaccination involves a combination of routine and supplemental vaccination. Both are needed to ensure suppression of infection in a population. Sangrujee *et al*. (2004) assume three doses of OPV in routine immunization and two in supplemental vaccination for a total cost of $.95. Khan and Ehreth (2003) use higher values for costs per dose, implying a marginal vaccination cost of $4.16. There is an additional cost to OPV vaccination: the risk of VAPP. According to Kew *et al*. (2005: 603), the probability of VAPP is about 1:750,000 for the first dose of OPV, falling sharply with subsequent doses. We let the total probability of VAPP be 1:750,000 per person vaccinated and value this at B.

[20] Our model does not include a latent period, but for polio this is short – about 1–3 days (Anderson and May, 1991: 31). This means that a person who acquires poliovirus ceases to be infectious after about 15–23 days.

[21] Population growth rates for 1990–2003 in the six remaining polio-endemic countries range from 1.7 per cent (India) to 3.3 per cent (Niger); for all low income countries, population grew 2.0 per cent over the same period; see World Bank (2005).

Eradication is thus in the interests of poor countries provided $0.0166B > \$.95 + B/750{,}000$ or $B > \$58$ using the low estimates for dosage costs and $0.0166B > \$4.16 + B/750{,}000$ or $B > \$250$ using the high estimates for dosage costs. The literature does not offer estimates for B (the welfare cost of paralytic polio). Khan and Ehreth (2003: 703) only give estimates of medical care costs, assumed to equal $420 in poor countries. Taking this to be a lower bound on B, our analysis to this point leads to two conclusions. First, the risk of VAPP is quantitatively irrelevant to the decision to eradicate (as explained previously, it was relevant to the decision by rich countries to switch to IPV). Second, if achieving eradication were not subject to uncertainty, and did not require follow-up measures after transmission of wild polioviruses had been stopped, then the economics of polio eradication would be favorable, even for poor countries.[22]

We know, however, that polio eradication is uncertain. There is a good chance that transmission of wild polioviruses can be interrupted – and in our model that would suffice to eradicate the disease. But polio eradication is more complicated than that. According to Aylward *et al*. (2005), there is a 65–90 per cent chance of at least one outbreak of cVDPV within a year of OPV cessation. The recent spread of polio from northern Nigeria between 2003 and 2005 hints at the consequences of such an outbreak. In this case, against a background of high immunization, wild polio spread throughout sub-Saharan Africa, the Arab Gulf, and Asia. After OPV vaccination has ceased, the pool of susceptible persons will increase dramatically, making it likely that an outbreak in the post-eradication phase could spread even more rapidly. Of course, this is why a stockpile of vaccine is needed – to insure against such a risk, and to provide the assurance needed for countries to agree to stop OPV vaccination. But maintaining such a stockpile is costly, and cannot eliminate the risk of eradication failing – considerations that are not reflected in our cost–benefit calculations. There is also a longer-term risk of reintroduction by iVDPVs, from an IPV production facility, and by terrorists. And our analysis has also not accounted for the substantial fixed costs of eradication: the need to identify and secure all laboratory specimens of polio, to carry out surveillance indefinitely, and to maintain a stockpile of vaccine and the capacity to produce in the future, should the need arise.

8. Conclusions

Our analysis applies to infectious diseases for which eradication is epidemiologically feasible. At a minimum, these include global diseases like polio, measles, and rubella (Knobler *et al*., 2002) and tropical diseases like dracunculiasis. We have shown that eradication, when feasible, will often be preferable to control – and will always be preferable to high rates

[22] This is from the perspective of cost–benefit analysis. We note that money spent on polio eradication has an opportunity cost. Most analyses of health policies focus on cost-effectiveness (see Jamison *et al*., 2006). Our analysis is unable to determine whether health outcomes would improve if the money spent on polio eradication was spent instead on other health interventions. For discussions about the opportunity costs of polio eradication, see Taylor *et al*. (1997) and Sutter and Cochi (1997).

of control. We have also shown that rapid progress towards eradication will usually be preferred. Only when vaccination costs increase substantially with the rate of vaccination should a slower course be followed.

An implication of our analysis is that, when rich countries are observed to set a high level of control, this can be taken to be an economic indicator of eradication being possibly optimal as well as being technically achievable. Plainly, if a country would eliminate a disease even when eradication is infeasible (because of the risk of the disease being imported), then it would certainly eradicate the disease if eradication were feasible – eradication would cost no more than elimination but offer a huge dividend in avoided future vaccination costs. For the poor countries, the calculus is likely to be different, suggesting that achievement of an eradication goal may require financial transfers. A full, global cost–benefit analysis is needed to determine whether eradication is a good deal overall, but our optimality conditions provide a basis for making a first assessment of the economics of eradication versus control. We have demonstrated this in an application to the current effort to eradicate polio.

We end with a final observation. It is routine in health economics to rely on average benefit and cost estimates. For most policy analysis, this is probably satisfactory. For eradication, it is not. Eradication is an extreme goal, and our paper shows that our analysis of an eradication program needs to begin from the perspective of where the program will end. Eradication only succeeds if the last carrier of the disease is isolated, and the persons with whom he or she may have come into contact are vaccinated. It is fitting that our optimality rule should also focus on this last case.

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Appendix A

The relationship between our dynamic specification and the specification used by AM (Anderson and May, 1991):

At any point in time, the proportion of the population that is susceptible is $x(t)$, while the proportion that is infected is $y(t)$. The remaining proportion of the population, $1 - x(t) - y(t)$, is immune.

The interpretation of (1) is that the gross increase in the proportion of susceptibles is equal to the birth rate (m), while the gross reduction in the proportion of susceptibles is the sum of those who die naturally ($mx(t)$), those who become infected ($\lambda(t)x(t)$), and those who become immune due to vaccination ($p(t)$).

In addition to equation (1), AM assume that the proportion of infected persons develops according to

$$\dot{y}(t) = \lambda(t)x(t) - (v + m)y(t). \tag{A1}$$

The interpretation of (A1) is that those who have become infected either die naturally ($my(t)$) or recover into the immune class ($vy(t)$).

The 'force of infection', $\lambda(t)$, is the per capita rate of acquisition of the infection among susceptibles. In other words, $\lambda(t)\Delta t$ represents the probability that a given susceptible host will become infected in a small time interval Δt. AM argue that with homogenous mixing, $\lambda(t) = \beta y(t)$, where β is a transmission parameter that depends on various epidemiological, environmental, and social factors. Inserting $\lambda(t) = \beta y(t)$ into (A1) and defining the basic reproductive rate of the microparasite (according to 'Type II survival'; see AM: 75) by

$$R_0 = \frac{\beta}{v + m}, \tag{A2}$$

we can rewrite (A1) as (2).

The differential equations (1) and (2) have a stationary state (for a constant p) given by $x^{\mu} = 1/R_0$ and $\lambda^{\infty} = m(R_0 - 1) - pR_0$. Starting at the stationary state, consider the effect of a small increase ε in the proportion of infecteds, and a corresponding reduction in the proportion of susceptibles. Since $\lambda(t) = \beta y(t)$, this implies that λ increases by $\beta\varepsilon$. Immediately after such an increase, it is straightforward to see from (2) that we get

$$\dot{\lambda} = (v + m)\lambda^{\infty} R_0(-\varepsilon). \tag{A3}$$

With the differential equation (3) we would instead get

$$\dot{\lambda} = -\sigma\beta\varepsilon. \tag{A4}$$

Using (A2), it is clear that these two differential equations give the same value for $\dot{\lambda}$ if and only if

$$\sigma = \lambda^{\infty} = m(R_0 - 1) - pR_0. \tag{A5}$$

The RHS of (A5) depends on p, so that the value of $\dot{\lambda}$ following from AM and from (3) cannot be the same for all p. In the numerical application in section 7 we let σ be determined by (A5) with $p = 0$, i.e.

$$\sigma = m(R_0 - 1). \tag{A6}$$

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Using (A2) and the definition of $\tilde{R}_0$ given at the end of section 2, it follows that

$$\sigma \tilde{R}_0 = \frac{m}{m+v}(R_0 - 1). \tag{A7}$$

Appendix B

The eradication date when eradication is optimal:

The value of the Hamiltonian at time T, denoted $H(T)$, follows from (9) and (10)

$$H(T) = -c(p(T)) - \alpha(T)\sigma \tilde{R}_0[K - p(T)]. \tag{B1}$$

If we can find a T^* such that $H(T) \geq 0$ for $T \leq T^*$ and $H(T) \leq 0$ for $T \geq T^*$, then this will be an optimal solution to our optimization problem when T is endogenous.[23]

Differentiating (B1), remembering that $p(\alpha)$ maximizes H, and using the envelope theorem, we obtain

$$H'(T) = \sigma R_0[p(T) - K]\frac{\partial \alpha(T)}{\partial T} \tag{B2}$$

Since $y(t)$ approaches zero at $t = T$, it follows from (13) that the term in square brackets in (B2) is positive. Moreover, $\alpha(T)$ is decreasing in T (see the discussion in section 4.1). From (B2) it therefore follows that $H'(T) < 0$. Hence, if we can find a value T^* giving $H(T^*) = 0$, then this will be an optimal solution to our optimization problem.

Using the notation $p^T = p(\alpha(T))$, and inserting (12) into (B2), gives

$$H(T) = -c(p^T) + [p^T - K]c'(p^T). \tag{B3}$$

The RHS of (B3) is increasing in p^T for $p^T > p^*$. For $p^T > p^*$, as is the case in figure 3, we therefore must have $H(T) > 0$.

The value of p^T (denoted p^*) which makes $H(T) = 0$ is given by

$$c'(p^*) = \frac{c(p^*)}{p^* - K}. \tag{B4}$$

p^* thus depends on both the cost function and K (that is, on m and R_0).

The corresponding value of α, denoted α^*, is given by (see (12))

$$\alpha^* = \frac{c'(p^*)}{\sigma R_0}. \tag{B5}$$

The value of α^* depends on the factors determining p^* and on σ. Since $p^* > K$, it follows from (15) and (B5) that $\alpha^* > \alpha^\circ$. Since all paths leading to $\alpha^* > \alpha^\circ$ result in eradication, it follows that inequality (16) is a sufficient condition for eradication to be optimal, confirming the economic intuition given in the paper.

[23] See, e.g., Theorem 1 in Seierstad (1988). Notice that the Hamiltonian given by (10) with $p(\alpha)$ inserted is linear, and thus concave, in y.

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Appendix C

Proof that, for $P \to \infty$, if $c > b\sigma \tilde{R}_0/r$, then the optimal policy is never to vaccinate, whereas if $c < b\sigma \tilde{R}_0/r$, then eradication is optimal:

The $\dot{y} = 0$ line in figure 5 is now horizontal as it meets the vertical axis at $\alpha^0 = c/\sigma \tilde{R}_0$. Inserting $H(T^*) = 0$ into (B1) gives the value of $\alpha(T^*)$, i.e. α^*:

$$\alpha^* = \frac{cP}{\sigma \tilde{R}_0(P - K)}. \tag{C1}$$

As in the general case, $\alpha^* > a^\circ$. We also have $\alpha^* \to \alpha^0$ as $P \to \infty$.

Recall from (20) that it will either be optimal to do nothing or to vaccinate at the maximum feasible rate. The payoff from not vaccinating is

$$W^{do\ nothing} = \int_0^\infty e^{-rt}[-by(0)]dt = -\frac{b}{r}y(0). \tag{C2}$$

The payoff from immediate eradication (implying $T \to 0$) is

$$W^{eradication} = \int_0^T e^{-rt}[-cP]dt = cPT. \tag{C3}$$

As $P \to \infty$, the term including P will dominate the other terms in (4), so that

$$\dot{y}(t) = -\sigma \tilde{R}_0 P, \tag{C4}$$

which implies

$$y(T) = y(0) - \sigma \tilde{R}_0 PT \tag{C5}$$

or, since $y(\mathrm{T}) = 0$

$$PT = \frac{y(0)}{\sigma \tilde{R}_0}. \tag{C6}$$

Substitution into (C3) gives

$$W^{eradication} = \int_0^T e^{-rt}[-aP]dt = -c\frac{y(0)}{\sigma \tilde{R}_0}. \tag{C7}$$

A comparison of (C7) and (C2) proves the result.

Appendix D

Proof that, for the quadratic model, eradication is optimal if and only if $gK < b\sigma \tilde{R}_0/r$:

For the quadratic case, the function $p(\alpha)$ defined by (12) gives

$$p(t) = \frac{\sigma \tilde{R}_0}{g}\alpha(t). \tag{D1}$$

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Moreover, it follows from (15), (B4), and (B5) that, for the present case

$$\alpha^0 = \frac{gK}{\sigma \tilde{R}_0}, \tag{D2}$$

$$p^* = 2K, \tag{D3}$$

and

$$\alpha^* = \frac{2gK}{\sigma \tilde{R}_0}. \tag{D4}$$

Since $c'(0) = 0$, it is never optimal not to vaccinate. Moreover, we know from (16) that, if

$$gK < \frac{b}{r+\sigma}\sigma \tilde{R}_0, \tag{D5}$$

then eradication will be optimal. The interesting case is when the inequality in (D5) is reversed, in which case eradication may or may not be optimal.

Rather than derive conditions ensuring that $\alpha^* > \alpha^\infty$, our approach is to derive conditions under which an optimal path leading to $(0, \alpha^*)$ exists. To do this, it is useful to rewrite differential equations (11) and (4) as functions of the time variable h, which denotes the time remaining until T^* is reached. With this notation, (11) and (4) can be written as

$$\alpha'(h) + (r+\sigma)\alpha(h) = b,\ \alpha(0) = \alpha^* \tag{D6}$$

$$y'(h) - \sigma y(h) = A\alpha(h) + B,\ y(0) = 0, \tag{D7}$$

where

$$A = \frac{(\sigma \tilde{R}_0)^2}{g} \tag{D8}$$

and

$$B = -\sigma \tilde{R}_0 K. \tag{D9}$$

Solving (D6) gives

$$\alpha(h) = \left(\alpha^* - \frac{b}{r+\sigma}\right) e^{-(r+\sigma)h} + \frac{b}{r+\sigma}. \tag{D10}$$

Inserting (D10) into (D7) and solving gives

$$y(h) = e^{\sigma h}(J_1 + J_2) - e^{-(r+\sigma)h} J_1 - J_2, \tag{D11}$$

where

$$J_1 = \frac{A}{(r+2\sigma)}\left(\alpha^* - \frac{b}{(r+\sigma)}\right) \tag{D12}$$

and

$$J_2 = \frac{Ab}{\sigma(r+\sigma)} + \frac{B}{\sigma}. \tag{D13}$$

For the situation described by figure 2, $y(h)$ is positive (for $h > 0$) and increasing as we travel backwards in time. By inspection of (D11), $y(h)$

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will be positive (for $h > 0$) if $J_1 + J_2 > 0$. Since $y'(h) = \sigma e^{\sigma h}(J_1 + J_2) + (r + \sigma)e^{-(r+\sigma)h} J_1$, and since J_1 is positive for the situation described by figure 2, $y(h)$ will be increasing if $J_1 + J_2 > 0$. Hence, for the kind of situation depicted in figure 2, eradication will be optimal if and only if $J_1 + J_2 > 0$. Inserting A and B from (D8) and (D9) into (D12) and (D13) we find

$$J_1 + J_2 > 0 \Leftrightarrow gK < \frac{b}{r}\sigma \tilde{R}_0, \tag{D14}$$

which is the condition given in (23). Finally, note that, if (23) holds then (D5) will hold, confirming that (23) is the necessary and sufficient condition for eradication to be optimal for the quadratic model.

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