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Electronic Companion—"Priority Shifting and the Dynamics of Managing Eradicable Infectious Diseases" by Radboud J. Duintjer Tebbens and Kimberly M. Thompson, *Management Science*, DOI 10.1287/mnsc.1080.0965.

e-companion to Duintjer Tebbens and Thompson: *Priority shifting and the dynamics of managing eradicable infectious diseases*
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Model details and supplementary analyses

EC.1. Model details: Transformation from deterministic, continuous to stochastic, discrete model

We transform the model to a stochastic form following the approach first suggested by Gillespie (Gillespie 1976) and more recently described in the context of a polio transmission model by Eichner and Dietz (Eichner and Dietz 1996) by first initializing the state variable ($S^i(t)$, $I^i(t)$ and $R^i(t)$) to equal the integers closest to their pre-vaccine equilibrium values. To determine the time step $\Delta(j)$ until the next event (i.e., a birth, death, infection, recovery, vaccination, or waning of immunity), we first list all transfer flows for the current state of the system in one array. With $\xi(j)$ the sum of the flows in the current state and U_1 a random uniform number between 0 and 1, the step size equals $\Delta(j) = -Ln(U_1)/\xi(j)$ (Eichner and Dietz 1996). We then draw a second random uniform number between 0 and 1, U_2, to determine which event occurred in the step according to the probability distribution implied by the array of transfer flows. To simulate transfers, we increment or decrement state variables by 1. If the event is a death, we draw two additional random uniform numbers to determine the immunity status of the deceased with respect to each disease according to the proportions of susceptibles, infecteds, and removeds at step j. If the transfer at step j is an infection, the incidence $inc(j)$ for that step is 1 and we increment the cumulative incidence, which starts at 0, by 1. The perceived incidence at step j ($pinc(j)$) is a first order exponential smooth of the true incidence and follows from:

$$pinc(0) = inc^{eq}(0)$$

$$pinc(j) = pinc(j-1) + \frac{inc(j) - pinc(j-1)\Delta(j)}{\tau}$$

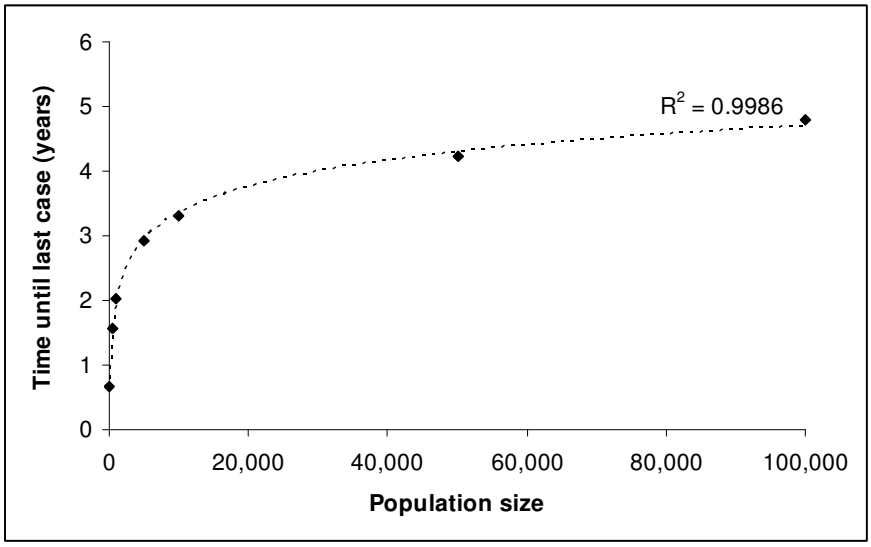
where $\tau = 1$ year is the perception delay time.

EC.2. Supplementary analyses

EC.2.1 Impact of population size and structure on time until elimination

The attractiveness of eradication policies depends on the time until elimination occurs. In this paper we assume a homogeneous population of 10,000 people. To explore the impact of population size and structure on the time until elimination, the following results focus on a single population with a single infectious disease. Figure EC1 depicts the relationship between the average time until the last case occurs (i.e., elimination) and the size of the (homogeneous) population, with all other inputs at their base case values.

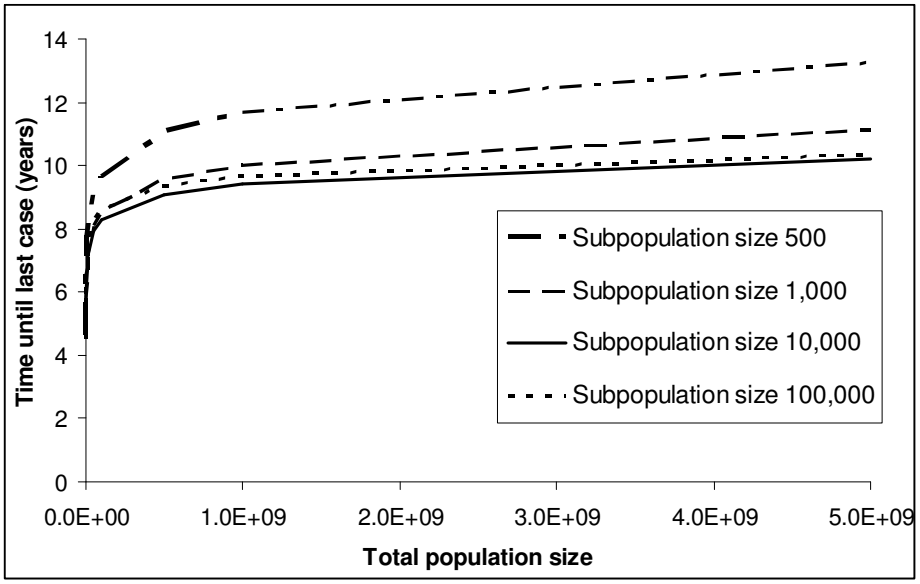
Figure EC1: The relationship between population size and average time until elimination (based on *n* = 100 iterations and homogeneous mixing) in the single-disease, single population stochastic model, with the dotted line showing the logarithmic regression.



Clearly, Figure EC1 suggests a logarithmic relationship (R^2>0.99). Extrapolating this relationship to a much larger population of 6.5 billion people, we obtain an average time until elimination of 11.2 years. More realistically, we can view the world as consisting of many subpopulation blocks in which transmission is homogeneous. Global eradication occurs after the last case occurred in the last subpopulation that still has transmission. If we assume that the world consists of *M* homogeneous subpopulations, then the time until global eradication equals $Y=\max(X_1, X_2, \ldots, X_M)$, where random variable X_i represents the time until the last case in subpopulation *i*. If we assume identical subpopulations, all subject to the same immunization rate, and that reintroductions into previously transmission-free populations do not take off (presumably due to sufficiently high population immunity achieved in the process of local elimination), then the X_is are i.i.d. and the expected time until global eradication is

$E(Y) = \int_0^\infty P(Y > x)dx = \int_0^\infty \left(1 - F_X(x)^M\right)dx$, with F_x the common probability distribution function of the X_is. Fitting lognormal distributions to the samples that generated the average elimination times in Figure EC1, we can estimate the expected time until global eradication for different global population sizes and sizes of the subpopulations, as shown in Figure EC2. This shows relationships between total population size and time until last case similar to Figure EC1. Note that dividing the world into increasingly larger subpopulations means larger expected values for each X_i, but smaller M, which together lead to a slightly decreasing E(Y). The results are sensitive to the estimated standard deviation of the lognormal distributions, which explains the ambiguous impact of the subpopulation size.

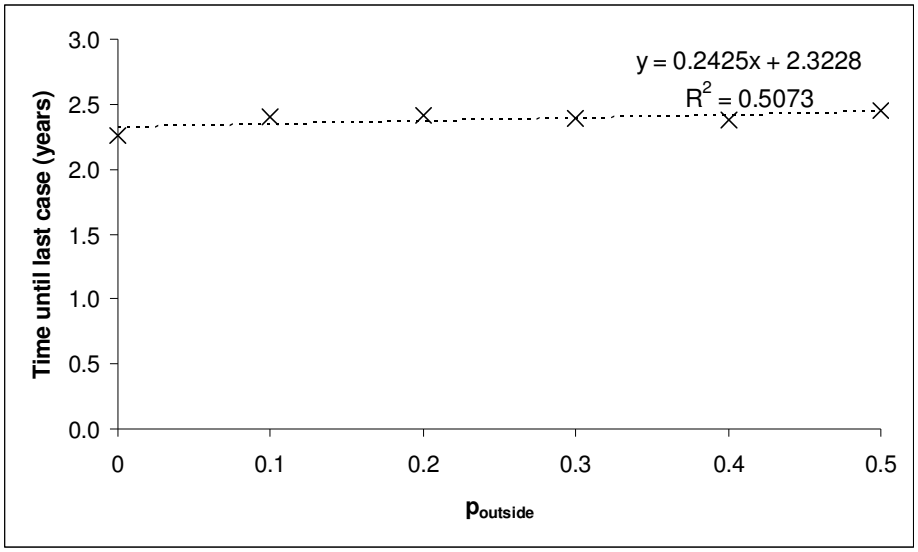
Figure EC2: The expected time until last case globally (E(Y)) as a function of subpopulation size and total population size, based on lognormal distributions fitted to samples obtained from running the single-disease, single-subpopulation stochastic model (*n* = 100 iterations for each subpopulation size).



More realistically, the X_is are not i.i.d. given the possibility of exportations delaying global eradication, and different properties of each subpopulation. Modeling a very large global population with assumptions that reflect the structure and properties of each for the disease in question implies very large computational costs and falls beyond the scope of this paper. However, Figure EC3 provides some insight into

the relationship between time until global eradication and the extent of transmission across subpopulations. The figure assumes a population consisting of 5 identical blocks of 500 people, each subject to the same immunization rates. We denote the probability that an individual's infectious contact is with another individual in another subpopulation as p_{outside} (see formulas for the transmission coefficients as a function of $p_{outside}$ elsewhere (Duintjer Tebbens et al. 2005)). Figure EC3 suggests that increasing this transmission heterogeneity increases the expected time until global eradication, although the increase remains minor even with as many as half of contacts occurring with individuals in other subpopulations. Thus, unless a very high proportion of infectious contacts occur outside of subpopulations, the relationship between expected time until global eradication and global population size in Figure EC2 remains a good approximation. The mean time until the last case of 2.34 for p_{outside}=0 remains consistent with an estimate of 2.26 based on the maximum of 5 draws from a lognormal fit to the elimination times for a single population of 500 people.

Figure EC3: The average time until the last case as a function of the probability of an infectious contact being with an individual in a different subpopulation (p_{outside}), based on 500 iterations. The results assume a total population consisting of 5 subpopulations of 500 people, all subject to the same immunization rate, and focus on elimination of a single disease.

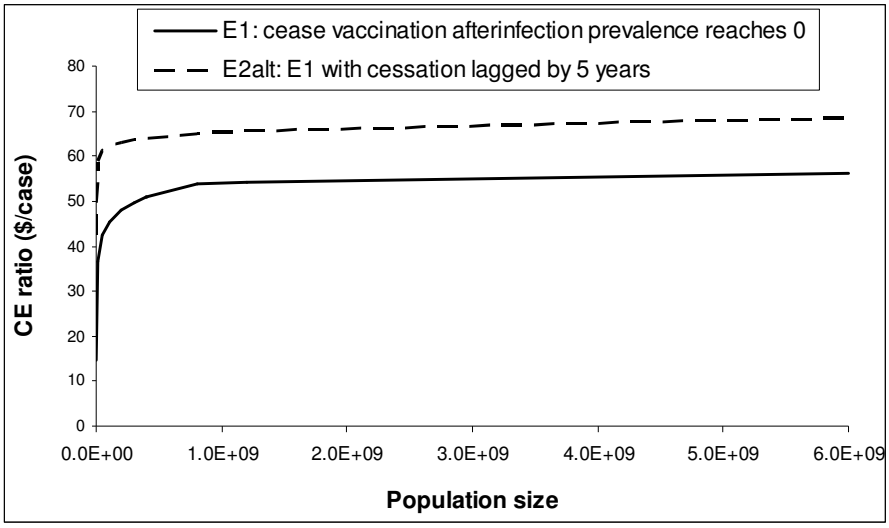


EC.2.2 Impact of population size on cost-effectiveness

Using a logarithmic relationship (see above), we can approximate the cost-effectiveness ratios for each decision rule as a function of population size. First, we note that unless elimination occurs, the model scales to population size, meaning that both the costs and cases are linear functions of population size. Thus, the cost-effectiveness ratios for the decision rules C1-C3 corresponding to control remain the same regardless of population size. For the eradication policies (decision rules E1 and E2), the costs depend on the time until cessation of vaccination. For decision rule E1, the time until cessation equals twice the expected time until the last case, which we determined above to be logarithmically related to population size. In spite of this logarithmic relationship, we found that the expected number of cases until eradication depends approximately linearly on population size (results not shown). This is not surprising given that the incidence curve scales to population size, with comparatively very few cases accumulating during the logarithmically-extended last phase of eradication associated with a larger population size. To estimate cost-effectiveness ratio for decision rule E1 versus no vaccination, we use the logarithmic fit of expected time until last case and population size from the previous paragraph and assume that for each disease the expected number of cases between equilibrium state and last case equals $k \times N$ for base case u=1.32, with k=0.0897 (determined in a separate simulation varying N between 100 and 1 million). To approximate the CER for decision rule E2, we alter the stopping criteria to exactly 5 years after the last case instead of a certain perceived incidence threshold, which would become a poor criterion for large population sizes. Figure EC4 shows the results. While the CER for E1 starts at about 14 $/case for small populations (as in Table 2), it increases to approximately 55 $/case for population sizes of 1 billion or more, similar to the CERs with C1 and C3. For such large populations, cessation of vaccination (i.e., elimination of both diseases) does not occur within the 20-year time horizon, meaning that the costs remain equal to those with the control policies while the cases approach or exceed those with the control policies. For decision rule E2, the CER starts at a higher level of 42 $/case (as in Table 2) and eventually exceeds the CER for the control policies at almost 70 $/case for a population of 6 billion people. This analysis shows that eradication becomes economically attractive only when the population that still has endemic transmission has already been reduced to a small enough geographic area. While the precise

economics will depend on the actual transmission model structure and input values, a policy of going from endemic transmission everywhere to global eradication at once is unlikely to emerge as cost-effective within a limited analytical time horizon. Rather, a more realistic scenario consists of a policy of control to eliminate transmission in most areas followed by eradication in the remaining areas (see comments in the next section).

Figure EC4: Approximate incremental cost-effectiveness ratio (without discounting) of decision rule E1 versus no vaccination as a function of population size, assuming a homogeneous population.



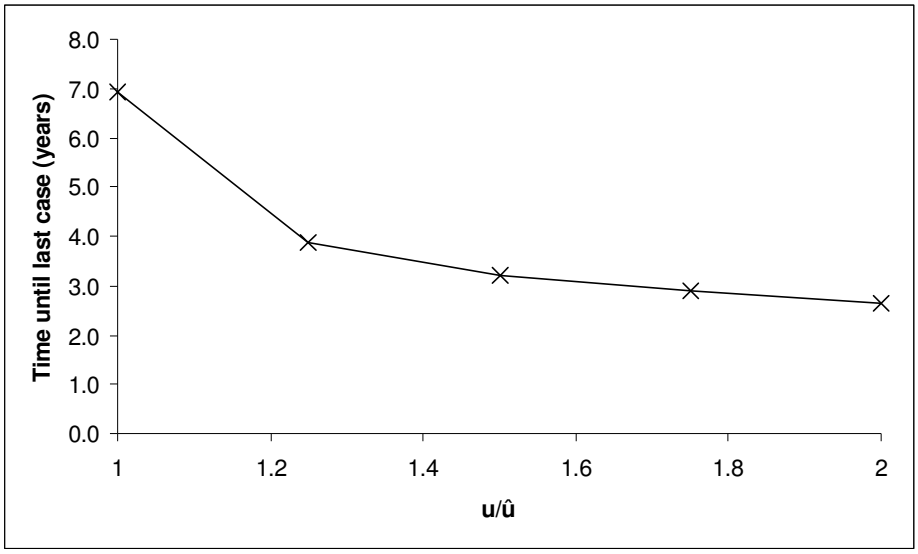
EC.2.3 Impact of (prior) vaccination intensity on time until elimination

The previous section demonstrated that the size of the total population substantially affects the expected time until global eradication, which potentially alters the balance in favor of control, depending on the time preference of future versus immediate benefits. In practice, this means that embarking on a global eradication initiative becomes economically attractive only if either: a) high immunization rates are attainable, or 2) substantial progress has already been made in controlling the disease.

Taking the base case assumptions from Table 1, Figure EC5 shows that the time until the last case in a single-disease model with a population of 10,000 people initially decreases rapidly as the immunization rate exceeds $\hat{u}$, with diminishing returns (i.e., in terms of time until last case) as the immunization

rate further increases. Consistent with that observation, Figure EC6 shows that the lowest (i.e., best) incremental cost-effectiveness of pursuing eradication compared to no vaccination occurs for an immunization rate of approximately 1.25 times û. Even with the linear cost function, the costs of very high immunization rates do not compare favorably with the associated benefits of being able to stop vaccination sooner.[1]

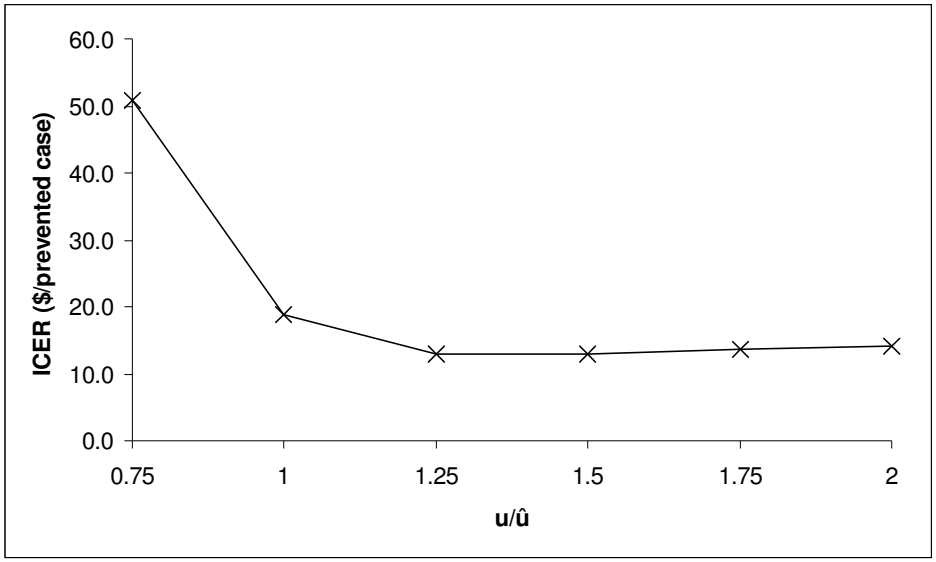
Figure EC5: The average time until elimination (based on *n* = 100 iterations) in the single-disease, single-population model as a function of the immunization rate relative to the theoretical threshold value (û) above which infection prevalence permanently decreases. [*]



[*]For the data point u/û=1, in 1 of the 100 iterations, elimination did not occur within 20 years. For the average shown in the figure, we artificially set the time of the last case at 20 years.

[1] We note that the theory developed by Barrett and Hoel (2007), which relies on a somewhat different transmission model (no waning of immunity and vaccination of susceptibles only) and including the costs associated with disease cases, suggests that "Only when vaccination costs increase substantially [i.e., more than linearly] with the rate of vaccination should a slower course be followed."

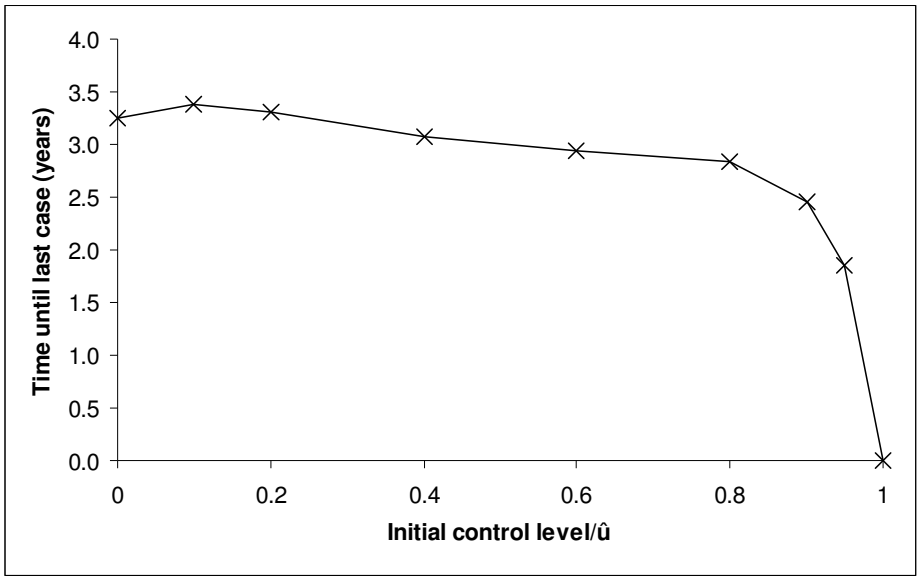
Figure EC6: The incremental cost-effectiveness ratio over a 20-year time horizon of pursuing eradication (assuming cessation of vaccination immediately after the last case) compared to no vaccination in the single-disease, single-population model as a function of the immunization rate of the eradication policy relative to the theoretical threshold value (û) above which infection prevalence permanently decreases.



All previous results assumed the pre-vaccine equilibrium as the starting point. Figure EC7 explores the impact of different levels of control already achieved before time 0. For a given immunization rate in the interval from 0 to $\hat{u}$, we assume as the initial control level the equilibrium state associated with the given immunization rate. Figure EC7 shows that for a control level less than approximately half of the elimination level $\hat{u}$, the time until the last case does not differ much from that associated with the pre-vaccine equilibrium initial values. However, as the initial control level approaches the elimination level, the expected time until the last case decreases rapidly. This implies that if a high level of control already exists, the expected time until the last case becomes low, and thus the economics of eradication become more attractive. Based on the single-disease results shown in Figure EC7, we estimated the incremental cost-effectiveness of pursuing eradication compared to maintaining the given initial control level (assuming cessation of vaccination immediately after the last case). For this example, we found that for a control level of approximately 25% of û or more, pursuing eradication economically dominated a policy of maintaining the control level, meaning that regardless of the economic value associated with prevented cases

eradication came out net beneficial. For initial control levels of less than approximately 25% of $\hat{u}$, the economic attractiveness depends on the economic value associated with prevented cases. For example, if the initial control level is no vaccination at all, the net benefits of eradication become positive for an economic value of approximately $13 per prevented case. This example illustrates the theory developed by Barrett and Hoel that states that if eradication is feasible, high control is never optimal and eradication always represents an economically better option (Barrett and Hoel 2007).

Figure EC7: The average time until elimination (based on n = 100 iterations) in the single-disease, single-population model as a function of the initial control level immunization rate relative to the theoretical threshold immunization rate (û) above which infection prevalence permanently decreases.



EC.2.4 Impact of heterogeneity of infectious disease properties

Our base case model assumes that both infectious diseases have identical properties. While this assumption remains helpful in the context of explaining shifts in priority and demonstrating that the behavior of interest is a property of the system and not a consequence of the input values selected, in practice infectious diseases will typically differ in many properties. Without fully exploring the impact of differences in each property, we provide one analysis of a possible asymmetry. For example, if we assume that the R_0 of ID_2 equals twice that of ID_1, this means that $\hat{u}$ for ID_2 becomes 1.98 per year and that

a budget of 2,145,000 (instead of 132,000 at the base case) supports vaccination at 1.5 times the average of $\hat{u}_1$ and $\hat{u}_2$. Clearly, decision rule C1, which mandates vaccination at half the available budget for both infectious diseases, would result in an immunization rate exceeding $\hat{u}_1$ (but not $\hat{u}_2$) and thus eradication of disease 1 would occur despite not explicitly pursuing eradication. For decision rules C2, E1, and E2 we found roughly the same behavior as in the base case, although with different time intervals between policy changes. For decision rule C3 (resource allocation proportional to perceived incidence), ID_2 was most often the disease with the highest incidence, and therefore the most often the target of high vaccination. When we computed the incremental CERs compared to no vaccination, we found higher ratios (consistent with the greater resource use), although the relative differences among the CERs for the different decision rules did not change substantially.

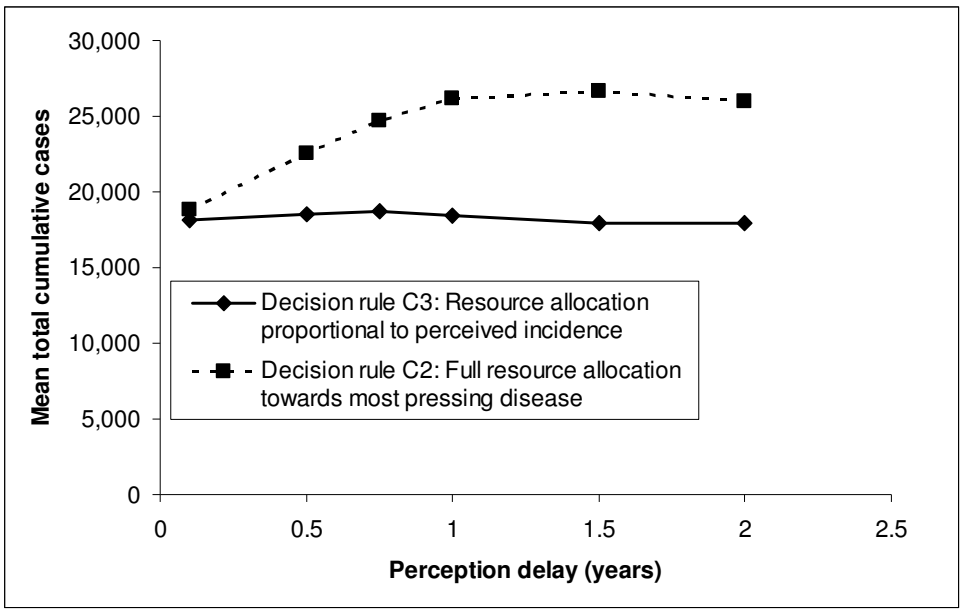
EC.2.5 Impact of the perception time

Our base case model characterizes the perceived priority based on the exponential smooth of the true incidence, with a perception delay time of $\tau = 1$ year. For simplicity, we assumed that τ reflects both the delay in observing incidence and the time it takes to shift resources and change policy. In reality, these two delays represent separate processes that each may vary substantially depending on the context. Further, one may argue that the delay until policy changes take effect behaves more like a fixed lag rather than an exponential smooth. Here, we briefly analyze alternative formulations and values.

Given that decision rules C1 and E1 do not depend on the perceived incidence, we focus on the other three rules. For decision rule E2, the impact of increasing τ or adding a lag is clearly a longer time until cessation of vaccination resulting in higher costs and more cases due to the later start of the eradication program for ID_2. In contrast, the impact of delays on decision rules C2 and C3 is less straightforward. Figure EC8 shows how τ influences the expected number of cases. For decision rule C2, which overreacts most heavily to perceived shifts in priorities, we see a rapid increase in total expected cases when increasing τ from 0 to 1 year. Apparently, if this policy responds very quickly to shifts in incidence, it

mitigates the size of the epidemics. However, if we further increase τ, we allow high immunization rates to persist longer, leading to a higher probability of eliminating one of the diseases. After eliminating one disease, all resources become available for the other and elimination of the other follows. Thus, we see a slight decrease in expected cases between τ=1.5 and τ=2 years. Based on the curve for decision rule C3, we find a much smaller impact of τ if we moderate the response to shifts in incidence by allocating resources in a proportional manner.

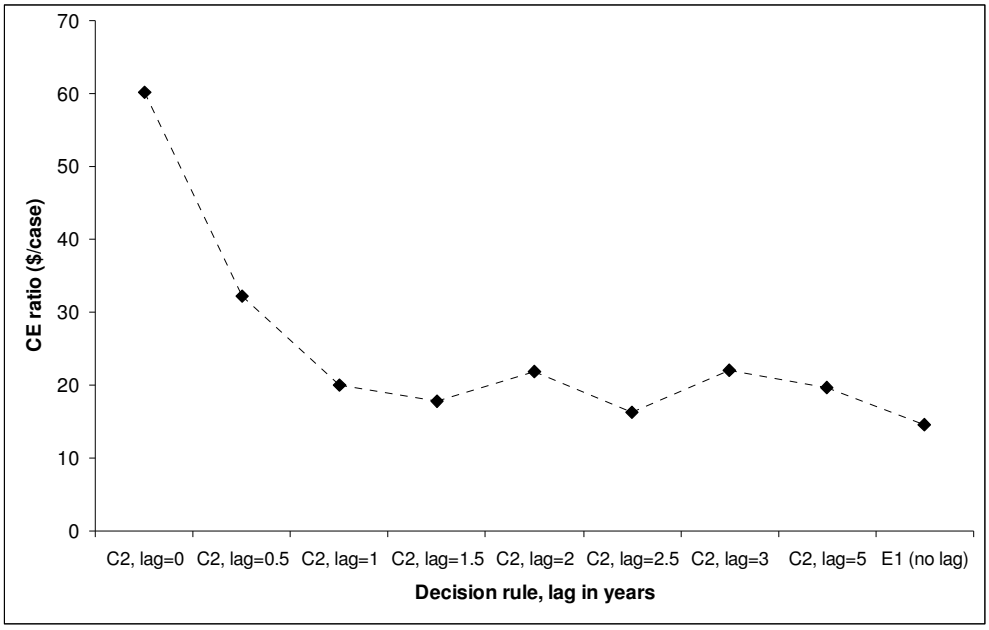
Figure EC8: The impact of varying the perception delay time (τ) on the expected number of cumulative cases for both diseases after 20 years for decision rules C2 and C3.



To explicitly consider a delay in shifting resources and implementing policy changes in response to changes in perceived incidence, the following analysis adds a fixed lag on top of the exponentially smoothed perceived incidence. The extra lag allows control against one disease to persist a fixed amount of time longer regardless of how much incidence of both diseases evolves, and thus increases the probability of "chance" eliminations with the control policy. In essence, this means that for long lags the control policy becomes more similar to the eradication policy, especially for decision rule C2. Figure EC9 shows how a lag time improves the cost-effectiveness of decision rule C2. In the event of elimination, we here assumed that vaccination would stop as soon as the prevalence for both infectious diseases becomes

0 (as with decision rule E1). While adding a short lag markedly improves the cost-effectiveness, further increasing the lag does not help since it means implies a longer time until vaccination switches from the first eliminated disease to the other. Therefore, the cost-effectiveness remains higher (i.e., less good) than decision rule E1.

Figure EC9: The impact of an added fixed lag (on top of the exponential perception delay) on the incremental cost-effectiveness ratio of decision rule C2 versus no vaccination (based on 20 iterations).



EC.2.6 Impact of a quadratic instead of a linear cost function

Arguably, the costs of vaccination rise more than linearly as the immunization rate reaches high levels. As an example, we here investigate the impact of a quadratic function $(u/\hat{u})^2 \times N \times c$ instead of the linear function $(u/\hat{u}) \times N \times c$ assumed for the analyses in the main paper. Given the model's assumption of a fixed budget, the change in cost function leads not to different costs but to different immunization rates for each decision rule. Thus, a budget allocation of p translates into an immunization rate as follows: $(u/\hat{u})^2 \times N \times c = p \times B = p \times 1.5 \times N \times c \Rightarrow u = \hat{u} \times (1.5 \times p)^{0.5}$. We applied this relationship to the budget allocations implied in each decision rule to generate results for the quadratic cost function. Table EC1 shows how the assumption of a quadratic cost function alters the expected number of cases for both diseases

with each decision rule. For C1, the immunization intensity becomes 0.76 instead of 0.66, leading to a drop in the number of cases by more than half. While the immunization intensity is still lower than $\hat{u}$, in 28% of the iterations "chance" elimination occurred within the 20-year time horizon. Similarly, with the quadratic cost function, decision rule C3 holds the immunization rate closer to $\hat{u}$ than with the linear cost function, leading to an even more dramatic drop in cases and "chance" elimination in 60% of iterations. In contrast, for decision rule C2 the immunization rate becomes either 0 or 1.22 $\hat{u}$ instead of either 0 or 1.5 $\hat{u}$ with the linear cost function, leading to an important increase in cases and "chance" elimination in 0% of iterations. Similarly, the eradication policies achieve a lower immunization rate with the same budget if the cost function is quadratic instead of linear, and thus incur greater numbers of cases, although elimination still occurs in every iteration. The quadratic cost function will lower the costs for decision rules C1 and C3, not affect the costs for decision rule C2, and raise the costs for decision rules E1 and E2. The difference in costs for the control policies depends on how long vaccination would continue after "chance" elimination. Overall, this supplementary analysis shows that the shape of the cost function may alter the economics in favor control policies that moderate resources between the two infectious diseases. Thus, it underscores the need to thoroughly study the nature of the cost function for any real-world case.

Table EC1: The impact of a non-linear cost function on the expected cumulative cases (undiscounted) for both diseases at the end of 20 years with each decision rule (based on 100 iterations).

Policy - decision rule	*Expected cumulative cases (both diseases) after 20 years*	
	Linear cost function	Quadratic cost function
C1: Even resource allocation	16,857	7,493
C2: Full resource allocation towards most pressing disease	25,926	32,370
C3: Resource allocation proportional to perceived incidence	17,818	7,361
E1: Cease vaccination after infection prevalence reaches 0	7,380	9,390
E2: Cease vaccination after perceived incidence drops below 1	15,913	16,956

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See references list in the main paper.

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