Group interest versus self-interest in smallpox vaccination policy

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The recent threat of bioterrorism has fueled debate on smallpox vaccination policy for the United States. Certain policy proposals call for voluntary mass vaccination; however, if individuals decide whether to vaccinate according to self-interest, the level of herd immunity achieved may differ from what is best for the population as a whole. We present a synthesis of game theory and epidemic modeling that formalizes this conflict between self-interest and group interest and shows that voluntary vaccination is unlikely to reach the group-optimal level. This shortfall results in a substantial increase in expected mortality after an attack.

Smallpox has reemerged recently as a public health issue. Because of the lack of information on smallpox transmission in contemporary populations, mathematical modeling has an especially important role to play in policy development. Suggestions for vaccination policy have ranged from preemptive mass vaccination (1) to post-outbreak ring vaccination (2). The policy of the current Bush administration calls for mandatory vaccination of the armed forces, voluntary vaccination of up to 10 million "first responders" thereafter, and some possibility of voluntary vaccination for the general public (3).

The level of vaccine coverage that is best for the population as a whole (the "group optimum") can be determined by minimizing a cost function $C(p)$ that expresses the impact on public health (from vaccination and/or bioterrorism) if a proportion p of the population is vaccinated preemptively. In contrast, under a voluntary policy, the coverage level will depend on a number of factors that influence individual behavior including self-interest, religious beliefs, and altruism. If acting according to pure self-interest, individuals would attempt to minimize their risks by weighing the risks of vaccine complications against the risks of bioterrorism. The preferred choice of an individual depends on the choices made by the rest of the population. In the scenario where individuals are motivated by self-interest, we refer to the level achieved under a voluntary program as the "individual equilibrium."

If there is a significant difference between the group optimum and individual equilibrium, then a policy dilemma results: On the one hand, voluntary vaccination does not protect the population as well as it should; on the other hand, imposing mandatory vaccination to group-optimal levels arguably violates civil rights. This potential dilemma motivates our investigation.

The individual equilibrium can be determined by using game theory, which predicts behavior in situations where the payoff to a strategy depends on the strategy chosen by others. Game theory was first applied to economics and international relations (4) and later to evolution (5). In the context of vaccination, a game-theoretical analysis should be able to predict the expected level of vaccine uptake in a population where individuals act to maximize their payoff (i.e., minimize their probability of death due to smallpox or vaccination).

Intuitively, high levels of voluntary vaccination may be difficult to maintain because an individual has little to gain from being vaccinated if everyone else is already immune. This situation is similar to the classical "prisoner's dilemma" in which cooperative behavior is not a stable strategy (6, 7). However, the "vaccination game" has the added dimension of epidemiological dynamics, which interplay with the self-/group-interest conflict in a potentially complex way. Even with complete knowledge of risks, the level of vaccine uptake that will result from this interaction is not obvious. In this article, we combine epidemic modeling with game theory to explore what differences, if any, exist between individual equilibria and group optima in smallpox vaccination policy.

The Individual Equilibrium

Our vaccination game is a population game (5) or nonatomic game (8), meaning that the payoff to an individual choosing a particular strategy depends on the average behavior of the population. The two basic strategies are "vaccinator" (obtain preemptive vaccination) and "delayer" (decline preemptive vaccination but seek vaccination in the event of an attack). For any strategy, the payoff to an individual is measured in terms of a cost function for the risks of death due to vaccination and/or smallpox bioterrorism.

To solve the game, we seek a Nash equilibrium strategy. In a population where all individuals play such a strategy, it is impossible for a few individuals to increase their payoffs by switching to a different strategy. Vaccinator cannot be a Nash equilibrium for the reason indicated in the introduction (an individual who chooses the delayer strategy when population coverage is at 100% reaps the benefits of high population immunity without suffering the risk of vaccine complications). By comparison, delayer can be a Nash equilibrium under certain conditions, such as when the attack risk is sufficiently low or the risk of death due to vaccination is sufficiently high. In other situations, it might be best for some individuals to be vaccinated preemptively and for others to delay. To allow for this we consider mixed strategies whereby individuals choose the vaccinator strategy with probability P ($0 < P < 1$) and the delayer strategy otherwise. If all individuals play the mixed strategy P, then a proportion $p = P$ of the population is preemptively vaccinated.

The payoff E_{vac} to an individual choosing the vaccinator strategy is

$$E_{\mathrm{vac}} = -d_{\mathrm{v}}, \qquad [1]$$

where d_{v} is the probability of death from vaccination. We take vaccine efficacy to be 100% [the efficacy of a course of repeated vaccination is nearly perfect (1)].

The effective level of preemptive vaccination will be slightly less than p (the proportion actually vaccinated) due to the death of some vaccinated individuals. Among survivors, the proportion vaccinated is

$$p_{\mathrm{eff}} = p \cdot \frac{1 - d_{\mathrm{v}}}{1 - p d_{\mathrm{v}}}. \qquad [2]$$

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However, because d_v is of order 10^{-6}, this effect is negligible, and we ignore it henceforth. With this approximation, the payoff $E_{del}(p)$ to an individual choosing the delayer strategy is

$$E_{del}(p) = -r[\phi_s(p)d_s + \phi_v(p)d_v], \quad [3]$$

where r is the risk of attack, $\phi_s(p)$ is the probability that a delayer becomes infected with smallpox after an attack, d_s is the probability of death due to a smallpox infection, and $\phi_v(p)$ is the probability that a delayer is vaccinated successfully after an attack (if d_v were not small, then we would need to replace p by p_{eff} on the right-hand side of Eq. **3**). We assume that postattack mass vaccination continues until all susceptibles have been vaccinated [a realistic assumption because full coverage can be accomplished within a single generation time of the infection (1)], and hence $\phi_v(p) = 1 - \phi_s(p)$. Note that $\phi_s(p)$ must be a strictly decreasing function of p.

If $E_{vac} > E_{del}(0)$, there is a unique Nash equilibrium p_{ind} ($0 < p_{ind} < 1$) that can be found by solving for p_{ind} in the equation

$$E_{vac} = E_{del}(p_{ind}). \quad [4]$$

If $E_{vac} \leq E_{del}(0)$, then the pure delayer strategy ($p_{ind} = 0$) is the unique Nash equilibrium (see *Existence and Uniqueness of Nash Equilibrium* in *Appendix*, which is published as supporting information on the PNAS web site, www.pnas.org).

The individual equilibrium p_{ind} predicted by this game-theoretical analysis corresponds to the level of coverage p_{ind} expected under a voluntary program where individuals act in a rational way to maximize their probability of survival.

The Group Optimum

From the perspective of group interest, we wish to minimize the total number of deaths expected from both vaccination and smallpox infection. If p is the proportion of the population that is preemptively vaccinated, we can express the expected cost $C(p)$ due to vaccination and a potential smallpox epidemic as

$$C(p) = N\{pd_v + r(1-p)[\phi_s(p)d_s + \phi_v(p)d_v]\}, \quad [5]$$

where N is the population size and the other symbols have the same meaning as in Eq. **3**. Because N is merely a scale factor (and therefore can be ignored for the purpose of minimization) and $\phi_v(p) = 1 - \phi_s(p)$, the cost can be written as

$$C(p) = pd_v + r(1-p)[(d_s - d_v)\phi_s(p) + d_v]. \quad [6]$$

We now minimize $C(p)$ on the unit interval ($0 \leq p \leq 1$) to determine the group optimum p_{gr}, which is the coverage level that would have to be imposed to minimize the total expected number of deaths.

SEIDV Epidemic Model

Both the individual equilibrium p_{ind} and the group optimum p_{gr} depend on the function $\phi_s(p)$, which gives the probability of death from smallpox for any given level of preemptive vaccination. To determine the function $\phi_s(p)$, an epidemiological model is required. We developed a compartmental epidemic model in which compartments reflect infection status and the rate of emergence of new cases is proportional to the product of the densities of susceptible and infectious individuals. Such models have been applied to a wide range of infectious diseases (9) including smallpox (1). Our model tracks the time evolution of the densities of individuals who are susceptible (S), infected but not yet infectious (E), infectious (I), removed (dead/immune) due to smallpox infection (D), and removed (dead/immune) due to vaccination (V) (the SEIDV model). The model equations are

$$\begin{aligned} \dot{S} &= -\beta SI - f(S,t) \\ \dot{E} &= \beta SI - \sigma E \\ \dot{I} &= \sigma E - \gamma I \\ \dot{D} &= \gamma I \\ \dot{V} &= f(S,t), \end{aligned} \quad [7]$$

where β is the mean transmission rate, $1/\sigma$ is the mean latent period, and $1/\gamma$ is the mean infectious period (here defined as the time between the onset of infectiousness and the isolation of the symptomatic patient). The effect of postattack intervention by health authorities is expressed through the function $f(S, t)$, which is the rate of mass vaccination of susceptible individuals. We assume that mass vaccination is initiated t_{res} days after the initial smallpox exposure (the "response time") and that susceptible individuals are vaccinated at a constant rate v until all have been vaccinated; hence

$$f(S,t) = \begin{cases} 0 & 0 < t < t_{res} \\ v & t > t_{res} \text{ and } S > 0. \\ 0 & t > t_{res} \text{ and } S = 0 \end{cases} \quad [8]$$

To estimate the initial attack size we assume that the attack takes the form of aerosolized dispersal in, for instance, a building or airport (10). Therefore the initial number α of individuals exposed to the virus is large, but a proportion p are immune due to preemptive vaccination. As a result, the initial number of infected individuals is $(1 - p)\alpha$.

Results

The key quantities for assessing policy are the difference in the proportion of the population preemptively vaccinated at the individual equilibrium versus the group optimum,

$$\Delta p \equiv p_{gr} - p_{ind}, \quad [9]$$

Table 1. Parameter values, intervals used in sensitivity analysis, and source references

Parameter	Definition	Estimated value	Range for sensitivity analysis	Ref.
$\mathcal{R}_0$	Basic reproductive ratio	5	[3.5, 6]	16
$1/\sigma$	Mean latent period	11 days	—	17
$1/\gamma$	Mean infectious period	3 days	—	17
t_{res}	Vaccinator response time	14 days	[7, 21]	n/a
v	Vaccination rate	0.10 day^{-1}	[0.05, 0.15]	1
d_v	Probability of death from vaccine	10^{-6}	—	17
d_s	Probability of death from smallpox	0.3	—	17
r	Attack risk (probability)	0.01	[0.001, 0.05]	n/a
α	Attack size (no. of individuals)	5,000	[100, 20,000]	10

The basic reproductive ratio $\mathcal{R}_0$ is the number of secondary infections produced by a typical infected individual in a wholly susceptible population; it determines the mean transmission rate β via the relation $\beta \simeq \gamma\mathcal{R}_0$ (9).

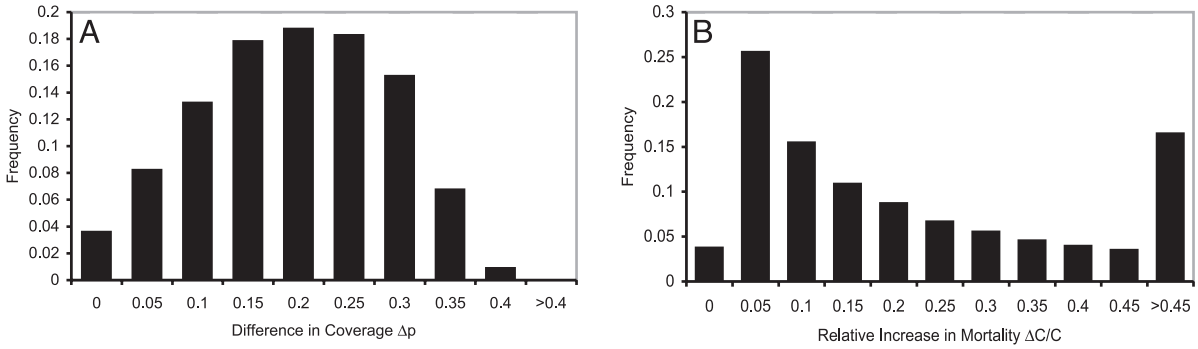

Fig. 1. Sensitivity analysis histograms for the difference in vaccine coverage, $\Delta p = p_{gr} - p_{ind}$ (*A*), and the relative increase in mortality at the individual equilibrium, $\Delta C/C = [C(p_{ind}) - C(p_{gr})]/C(p_{gr})$ (*B*). This analysis shows that, for a wide range of parameter values, self-interested decision making can cause coverage levels to fall short of the group-optimal levels, resulting in a significant increase in expected mortality. We analyzed 10^5 realizations of the model by randomly selecting parameter values from the ranges listed in Table 1. All horizontal axis labels except ''0'' give upper limits of corresponding bins; lower limits are given by the left adjacent label. The bin corresponding to the ''0'' label contains outcomes that were precisely zero.

and the corresponding relative difference in expected mortality,

$$\frac{\Delta C}{C} \equiv \frac{C(p_{ind}) - C(p_{gr})}{C(p_{gr})}. \quad [10]$$

All parameter values used in the analysis of our model are listed in Table 1. For the parameter values in the third column of that table, we found that the individual equilibrium is $p_{ind} = 0.19$ (corresponding to a situation where 19% of the population opts for preemptive vaccination). This falls well below the group optimum $p_{gr} = 0.47$. The corresponding relative increase in mortality $\Delta C/C$ was 0.54, i.e., 54% more deaths under a voluntary vaccination policy.

To determine the sensitivity of this result to parameter values we carried out a Monte Carlo sensitivity analysis by randomly selecting values from intervals with realistic bounds (Table 1, fourth column, and Fig. 1). We observed that both p_{ind} and p_{gr} usually fall strictly between 0 and 1, and that $p_{ind} \leq p_{gr}$ always (the individual equilibrium never exceeds the group optimum). Furthermore, the difference in the proportion preemptively vaccinated, Δp, was typically large, having an average value of 0.17 across all 10^5 realizations. The average values of p_{ind} and p_{gr} were 0.48 and 0.65, respectively (the variance was substantial in both cases). The ratio of the difference Δp to the group optimum p_{gr} averaged over all realizations was 35% (this is the expected "error" of the individual equilibrium relative to the group optimum). The relative increase in mortality at the individual equilibrium, $\Delta C/C$, averaged over all realizations was 22%. Both the group optimum and individual equilibrium respond in qualitatively similar ways as the basic reproductive ratio $\mathcal{R}_0$ (see Table 1 legend), postattack vaccination rate v, and attack risk r vary (Fig. 2); p_{ind} and p_{gr} exhibit thresholds below which vaccination is too risky and remains at zero.

We have assumed thus far that there is no residual immunity from the preeradication era; however, the inclusion of residual immunity has little effect on the results (see Fig. 3, which is published as supporting information on the PNAS web site, and *Impact of Inclusion of Residual Immunity* in *Appendix*). The impact of vaccine-induced morbidity (such as vaccinia) arising from vaccination can also be incorporated, although a weighting then must be chosen to express the cost of vaccine-induced morbidity relative to fatal complications. If vaccine-induced morbidity is incorporated, the results are again qualitatively unchanged (Fig. 4, which is published as supporting information on the PNAS web site, and *Impact of Inclusion of Vaccine-Induced Morbidity in Cost Function* in *Appendix*). Additionally, we carried out a sensitivity analysis with respect to the postattack vaccination rate v and the response time t_{res}, the two model parameters most readily controlled by the public health authorities (Fig. 5, which is published as supporting information on the PNAS web site, and *Sensitivity Analysis for Postattack Vaccination Rate v and Response Time* t_{res} in *Appendix*). This analysis confirmed that Δp and $\Delta C/C$ remain substantial across most of the two-dimensional (v, t_{res}) parameter space.

Discussion

Our results illustrate how the conflict between group interest and self-interest typically causes large differences between vaccine coverage levels that are best for the group and uptake levels that might actually be achieved under a voluntary vaccination program. Public health education should not ignore appeals to altruism, because, all else being equal, self-interested decision making could lead to seriously suboptimal vaccine uptake levels. More generally, our analysis highlights the potential value of game theory in the development and evaluation of public health policy.

Polls suggest that ≈60% of Americans would choose preemptive smallpox vaccination (11, 12), yet the proportion p_{ind} predicted by our model is typically <0.60. This apparent discrepancy may be caused by a number of factors. For example, individuals may have an inflated sense of attack risk (r), attack size (α), the rapidity with which a smallpox outbreak would spread (β) relative to the ability of public health authorities to stop the epidemic (v), or a distorted impression of the relationships among transmission potential, interventions, and the probability of being infected. However, building on the current results by using polls specifically designed to test game-theoretical predictions and adapting the models accordingly would help remedy this. For example, for the parameters in Table 1, a value of $p_{ind} = 0.60$ is produced by an attack risk r of 4.7%. This result could be compared with polls investigating the public perception of risk.

History details numerous examples of vaccine refusal (13–15). Some of these examples embody the prisoner's dilemma effect. The grounds for refusal vary widely but often are related to perceived risks of vaccination. In many cases, because of the success of the vaccination program itself, certain diseases are rarely seen, and hence individuals tend not to vaccinate because of a low perceived risk. A situation then can be created in which media coverage of potential vaccine risks may cause a scare that drags uptake below critical levels, making large outbreaks possible (14). A notable example was the pertussis vaccine scare of the 1970s in Britain, where a sustained drop in coverage preceded relatively large pertussis outbreaks. Such historical examples, together with the predictions of our game-theoretical model, suggest that persistently high levels of immunization will be difficult to maintain in countries with voluntary vaccination policies.

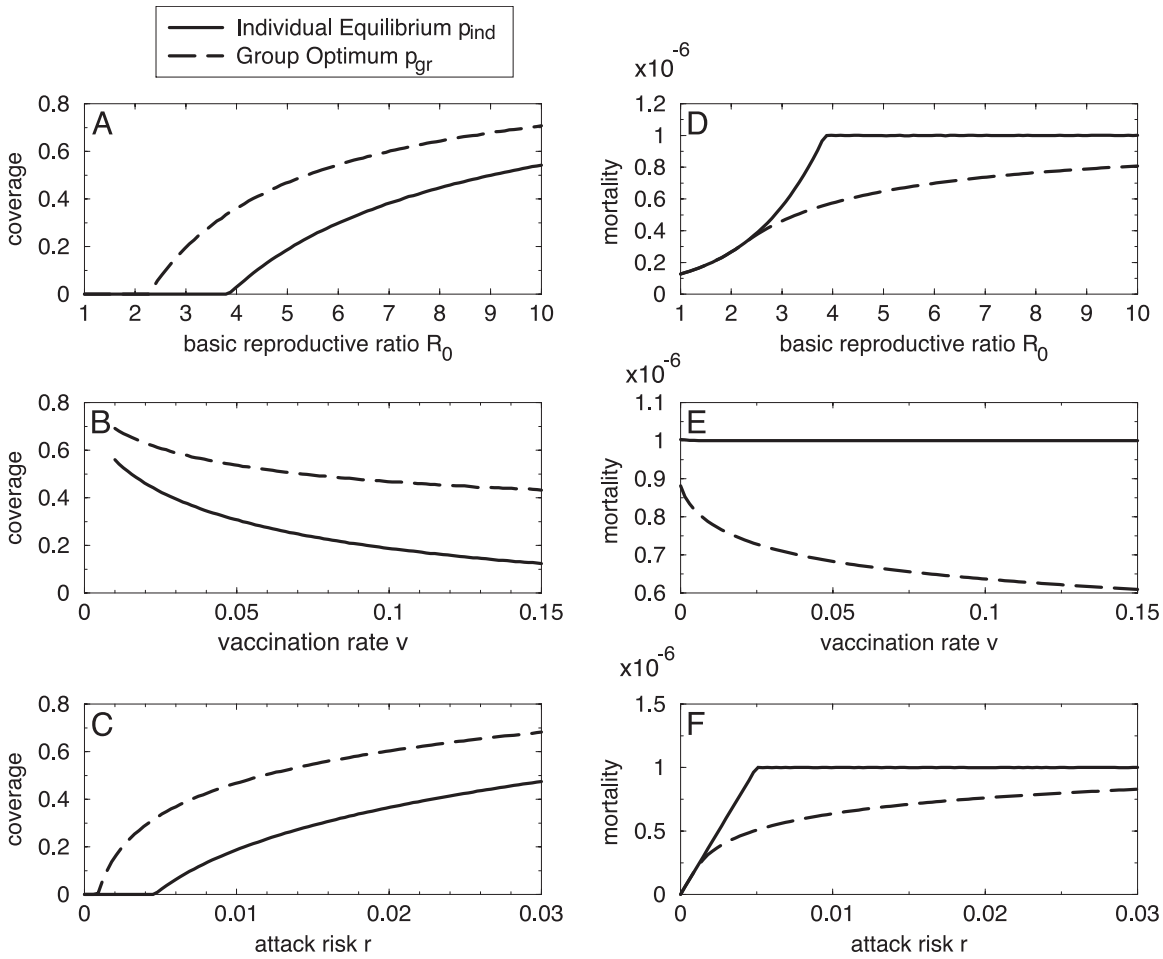

Fig. 2. Vaccination coverage levels (solid line, individual equilibrium p_{ind}; dashed line, group optimum p_{gr}) at various values of basic reproductive ratio $\mathcal{R}_0$ (*A*), postattack vaccination rate v (*B*), and attack risk r (*C*). The dependence of p_{ind} and p_{gr} on model parameters is qualitatively similar but quantitatively very different. (*D–F*) How the expected mortality $C(p)$ varies with model parameters at both the individual equilibrium [$C(p_{ind})$] and the group optimum [$C(p_{gr})$]. Other parameter values were set to the estimated values in Table 1. Because the payoffs for delayer and vaccinator are equal at the mixed Nash equilibrium [$E_{del}(p_{ind}) = E_{vac} = -d_v$, Eqs. **1** and **4**] and $C(p) = -pE_{vac} - (1 - p)E_{del}(p)$ (Eq. **5**), it follows that $C(p_{ind}) = d_v$ whenever the Nash equilibrium p_{ind} is a mixed strategy, which explains why $C(p_{ind}) = 10^{-6}$ over wide parameter ranges in *D–F*.

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Appendix

Existence and Uniqueness of Nash Equilibrium

Here we show that the vaccination game formulated in the main text always has a unique Nash equilibrium $p_{\rm ind} \in [0, 1)$. We assumed in the main text that all delayers are either vaccinated or infected in the case of an outbreak, i.e., $\phi_{\rm v}(p) = 1 - \phi_{\rm s}(p)$, so we can rearrange Eq. **3** to obtain

$$E_{\rm del}(p) = -r\left[\phi_{\rm s}(p)(d_{\rm s} - d_{\rm v}) + d_{\rm v}\right] . \qquad \textbf{[11]}$$

Therefore, because $\phi_{\rm s}(p)$ strictly decreases with p and $d_{\rm v} < d_{\rm s}$, $E_{\rm del}(p)$ strictly increases with p.

First consider the case where $E_{\rm vac} > E_{\rm del}(0)$. We identify a candidate Nash equilibrium as the mixed strategy $p_{\rm ind}$ corresponding to coverage levels where the payoff from playing vaccinator equals the payoff for playing delayer. Hence $p_{\rm ind}$ is given by the solution of the equation

$$E_{\rm vac} = E_{\rm del}(p_{\rm ind}) \qquad \textbf{[12]}$$

$$i.e., \qquad -d_{\rm v} = -r\left[\phi_{\rm s}(p_{\rm ind})(d_{\rm s} - d_{\rm v}) + d_{\rm v}\right] . \qquad \textbf{[13]}$$

Because $E_{\rm del}(p)$ is a strictly increasing function and $E_{\rm vac} > E_{\rm del}(0)$, there is a unique value of $p_{\rm ind}$ that satisfies Eq. **12** (or, equivalently, Eq. **13**).

To show this is a Nash equilibrium, suppose a fraction $\epsilon (0 < \epsilon < 1)$ of the population adopts the alternative mixed strategy of playing vaccinator with probability $p_{\rm alt} \in [0, 1)\backslash\{p_{\rm ind}\}$. For $p_{\rm ind}$ to be a Nash equilibrium, the payoff $E(p_{\rm alt})$ to individuals playing $p_{\rm alt}$ must be no greater than the payoff $E(p_{\rm ind})$ to individuals playing $p_{\rm ind}$, i.e., $E(p_{\rm alt}) \leq E(p_{\rm ind})$.

If a fraction ϵ of individuals play $p_{\rm alt}$, then the overall proportion $p_{\rm tot}$ of the population choosing preemptive vaccination is

$$p_{\rm tot} = (1 - \epsilon)p_{\rm ind} + \epsilon p_{\rm alt} . \qquad \textbf{[14]}$$

Under such conditions the payoff for playing p_{ind} is

$$E(p_{\text{ind}}) = p_{\text{ind}}E_{\text{vac}} + (1 - p_{\text{ind}})E_{\text{del}}(p_{\text{tot}}) \qquad \textbf{[15]}$$

while the payoff for playing p_{alt} is

$$E(p_{\text{alt}}) = p_{\text{alt}}E_{\text{vac}} + (1 - p_{\text{alt}})E_{\text{del}}(p_{\text{tot}})\,. \qquad \textbf{[16]}$$

Hence we must show that $E(p_{\text{alt}}) \leq E(p_{\text{ind}})$ for all $p_{\text{alt}} \neq p_{\text{ind}}$, i.e.,

$$\begin{aligned} & E(p_{\text{alt}}) \leq E(p_{\text{ind}}) \\ \iff \quad & p_{\text{alt}}E_{\text{vac}}(p_{\text{tot}}) + (1 - p_{\text{alt}})E_{\text{del}}(p_{\text{tot}}) \leq p_{\text{ind}}E_{\text{vac}}(p_{\text{tot}}) + (1 - p_{\text{ind}})E_{\text{del}}(p_{\text{tot}}) \\ \iff \quad & p_{\text{alt}}(E_{\text{vac}} - E_{\text{del}}(p_{\text{tot}})) \leq p_{\text{ind}}(E_{\text{vac}} - E_{\text{del}}(p_{\text{tot}})) \qquad \textbf{[17]} \end{aligned}$$

The following steps show that $E(p_{\text{alt}}) < E(p_{\text{ind}})$ when $p_{\text{alt}} < p_{\text{ind}}$:

$p_{\text{alt}} < p_{\text{ind}} \iff p_{\text{tot}} < p_{\text{ind}}$	Eq. **14**
$\iff \phi_{\text{s}}(p_{\text{tot}}) > \phi_{\text{s}}(p_{\text{ind}})$	because $\phi_{\text{s}}(p)$ is decreasing
$\iff E_{\text{del}}(p_{\text{tot}}) < E_{\text{del}}(p_{\text{ind}}) = E_{\text{vac}}$	Eqs. **11** and **12**
$\iff E_{\text{vac}} - E_{\text{del}}(p_{\text{tot}}) > 0$	
$\iff p_{\text{alt}}(E_{\text{vac}} - E_{\text{del}}(p_{\text{tot}})) < p_{\text{ind}}(E_{\text{vac}} - E_{\text{del}}(p_{\text{tot}}))$	because $p_{\text{alt}} < p_{\text{ind}}$
$\iff E(p_{\text{alt}}) < E(p_{\text{ind}})$	Eq. **17**

Hence the payoff to strategy p_{ind} is higher than the payoff to any alternative strategy $p_{\text{alt}} < p_{\text{ind}}$. The same approach shows that $E(p_{\text{alt}}) < E(p_{\text{ind}})$ when $p_{\text{alt}} > p_{\text{ind}}$. Therefore the mixed strategy p_{ind} identified by Eq. **13** is, in fact, a strict Nash equilibrium. It also follows immediately that p_{ind} is a unique Nash equilibrium. Any alternative strategy $p_{\text{alt}} \in [0, 1)\backslash\{p_{\text{ind}}\}$ cannot be a Nash equilibrium, because the arguments discussed above show that $E(p_{\text{ind}}) > E(p_{\text{alt}})$ for all values of ϵ, i.e., any proportion of individuals playing p_{ind} get a higher payoff when the rest of the population plays any other strategy.

In the second case, where $E_{\text{vac}} \leq E_{\text{del}}(0)$, there is no mixed strategy that satisfies Eq. **13** due to the fact that $E_{\text{del}}(p)$ is strictly increasing. However, it can be shown in a similar way that the pure delayer strategy $p_{\text{ind}} = 0$ is the unique, strict Nash equilibrium.

Impact of Inclusion of Residual Immunity

We repeated our analysis with the inclusion of residual immunity. Approximately 15% of the current U.S. population was immunized during the preeradication era (1), but exactly how much immunity remains from this era is unknown. To determine the potential impact of residual immunity, we assumed that a proportion p_{init} of the population had such residual immunity. Consequently $p_{\text{gr}} > p_{\text{init}}$ and $p_{\text{ind}} > p_{\text{init}}$ (we assumed that individuals with residual immunity do not presently seek and are not given the option of immunization). We repeated our Monte Carlo sensitivity analysis for the same intervals as in Table 1, additionally using the interval $[0, 0.15]$ for possible values of p_{init}.

The inclusion of residual immunity has little effect on the difference Δp between the group optimum and individual equilibrium for most parameter values (Fig. 3). The same is true for the relative increase in mortality rate, $\Delta C/C$. The average value of the difference between the group optimum and individual equilibrium Δp is 0.16, where the average values of p_{ind} and p_{gr} are 0.49 and 0.65, respectively. All these values are similar to the results for $p_{\text{init}} = 0$.

Impact of Inclusion of Vaccine-Induced Morbidity in Cost Function

It is reasonable to suppose that the risk of vaccine-induced morbidity such as vaccinia may also sway choice of strategy. Incorporation of vaccine-induced morbidity into the analysis necessitates the use of a weighting factor of the cost of vaccine-induced

morbidity relative to death. This allows both outcomes to be incorporated into the cost analysis for both the payoffs (for determining the individual equilibrium) and the cost function $C(p)$ (for determining the group optimum).

We included the risk of vaccine-induced morbidity in our model by replacing the term d_{v} everywhere by the term $d_{\mathrm{v}} + wc$, where $c = 0.00005$ is the risk of experiencing vaccine-induced morbidity (2) and w is the weighting factor (which was varied over the range $[0, 0.2]$ in the sensitivity analysis).

Although the group optimum and individual equilibrium are both lower when vaccine-induced morbidity is included, the average difference is essentially unchanged (Fig. 4). The average value of Δp is 0.19, where the average values of p_{ind} and p_{gr} are 0.17 and 0.36, respectively. As in the case where vaccine-induced morbidity is ignored, $\Delta C/C$ is typically substantial (but note that this quantity is now interpreted in terms of a generalized "health cost," not strictly in terms of expected mortality).

Sensitivity Analysis for Postattack Vaccination Rate v and Response Time t_{res}

We also carried out a sensitivity analysis with respect to the two parameters under most direct control of public health authorities, namely, the postattack vaccination rate v and the response time t_{res}. We explored the dependence of Δp and $\Delta C/C$ on these two parameters, where all other parameters were fixed at the values of Table 1 (third column). For most regions of this two-dimensional parameter space (Fig. 5), the values of Δp and $\Delta C/C$ are still substantial and often very high. Only for a very high postattack vaccination rate v and short response time t_{res} do the individual equilibrium and group optimum start to converge.

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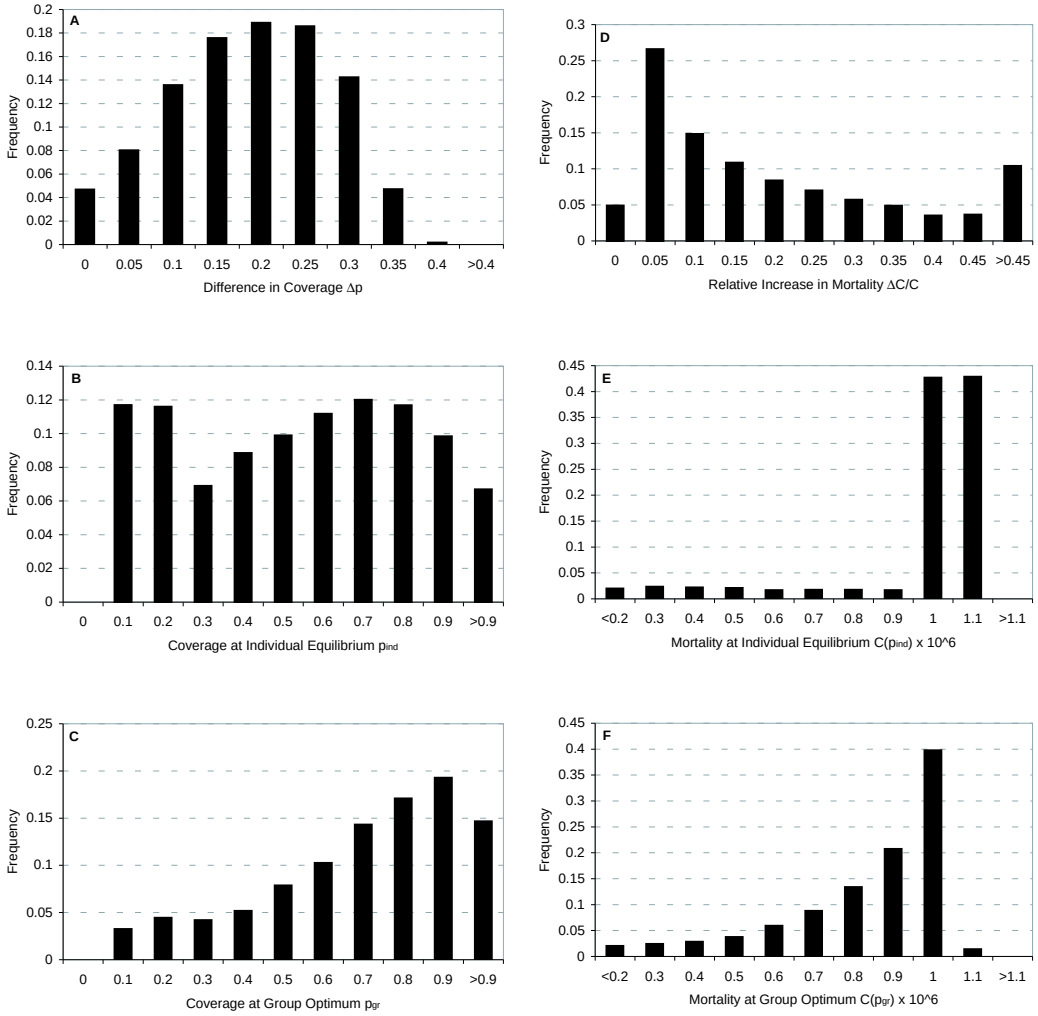

Fig. 3. Sensitivity analysis histograms for model with residual immunity. Difference in vaccine uptake Δp (A), $p_{\rm ind}$ (B), $p_{\rm gr}$ (C), relative difference in mortality cost $\Delta C/C$ (D), $C(p_{\rm ind})$ (E), and $C(p_{\rm gr})$ (F). Parameter ranges are as in Table 1. A total of 10^5 sets of parameter choices were randomly selected from the ranges listed to perform the Monte Carlo sensitivity analysis. The proportion of individuals who retain immunity to smallpox from previous vaccination, $p_{\rm init}$, was considered over the range $[0, 0.15]$ (only 15% of the present population were previously vaccinated). All horizontal axis labels except for "0" give upper limits of corresponding bins; lower limits are given by the left adjacent label. The bin corresponding to the "0" label contains outcomes that were precisely zero.

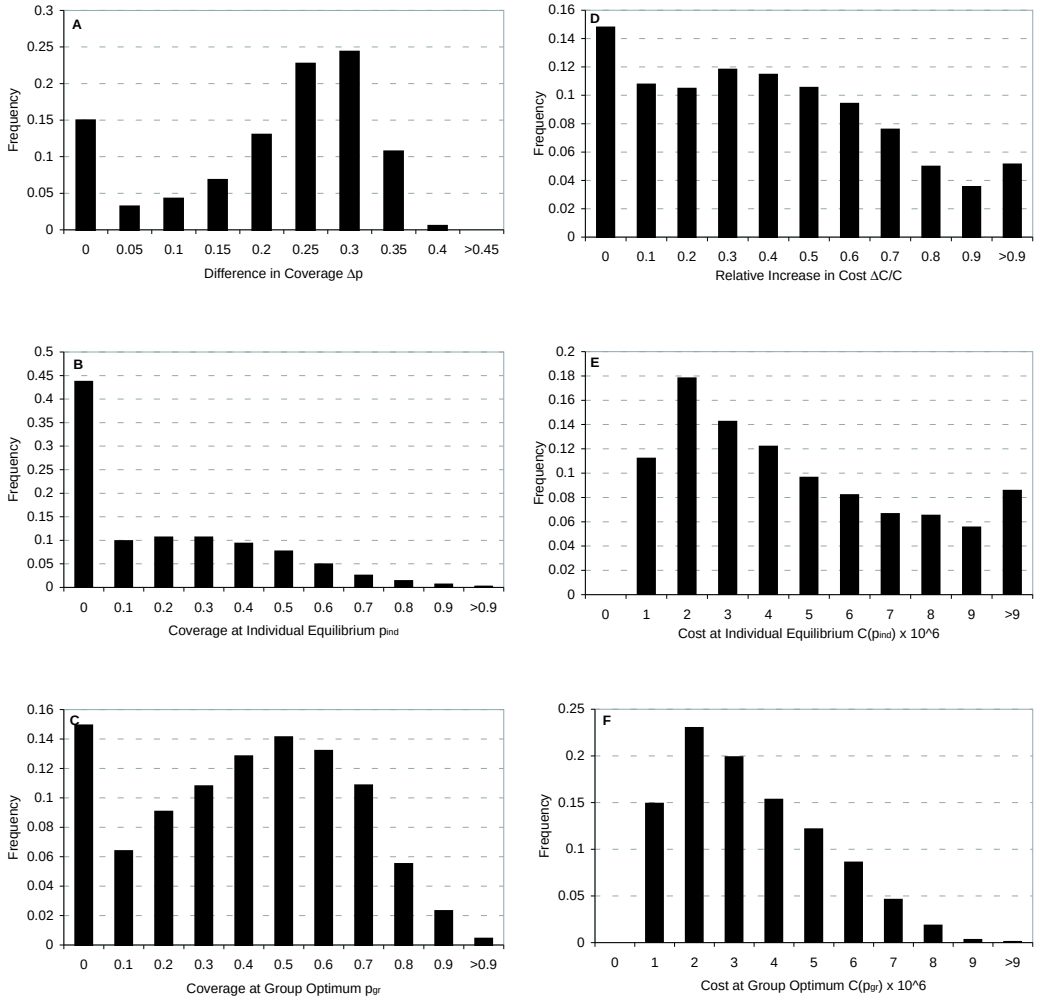

Fig. 4. Sensitivity analysis histogram for the case where vaccine-induced morbidity is included. Difference in vaccine uptake Δp (A), $p_{\rm ind}$ (B), $p_{\rm gr}$ (C), relative difference in health cost $\Delta C/C$ (D), $C(p_{\rm ind})$ (E), and $C(p_{\rm gr})$ (F). Parameter ranges are as in Table 1. A total of 10^5 sets of parameter choices were randomly selected from the ranges listed to perform the Monte Carlo sensitivity analysis. The weighting parameter ω, which determines the relative cost of vaccine-induced morbidity relative to death, was investigated in the range $[0, 0.2]$. All horizontal axis labels except for "0" give upper limits of corresponding bins; lower limits are given by the left adjacent label. The bin corresponding to the "0" label contains outcomes that were precisely zero.

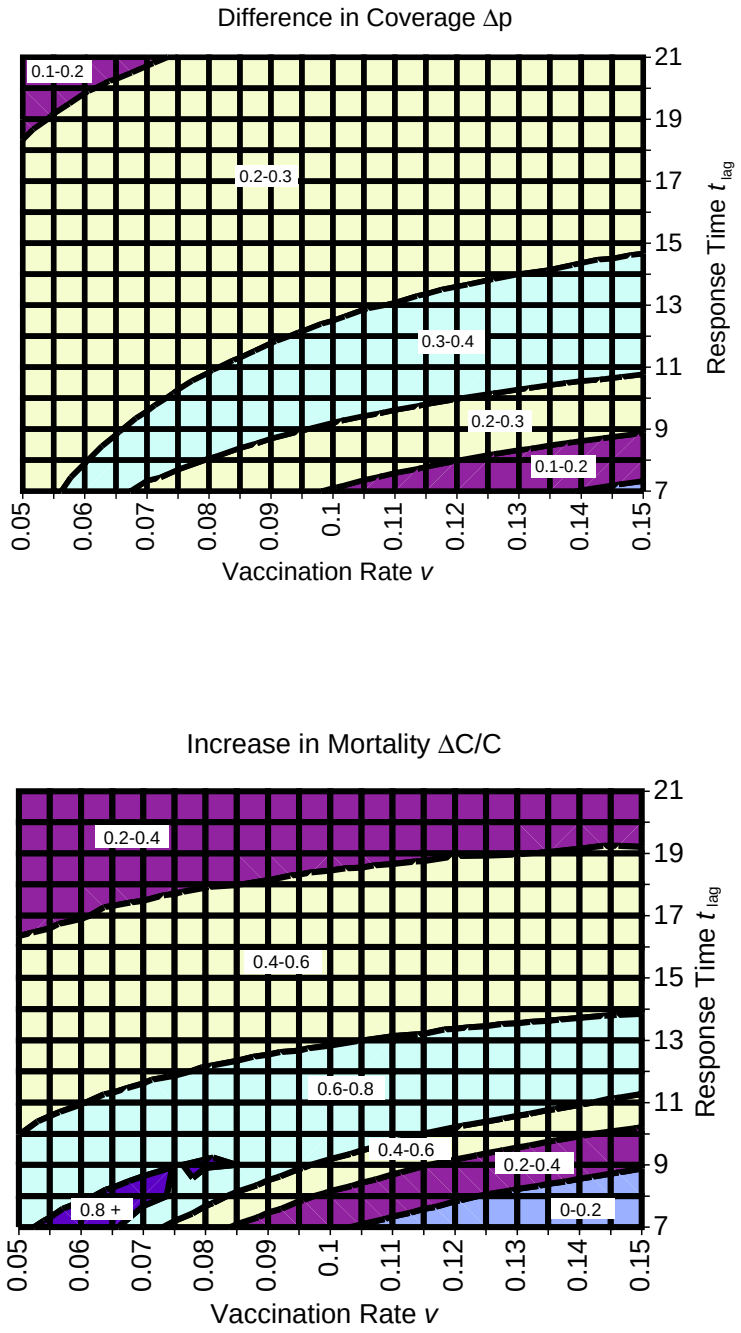

Fig. 5. Sensitivity analysis for postattack vaccination rate v and response time t_{res}, showing the difference in expected vaccine uptake Δp (A) and the relative difference in expected mortality cost $\Delta C/C$ (B). Parameters v and t_{res} vary according to the intervals given in the fourth column of Table 1, and all other model parameters are fixed at the values given in the third column of Table 1.