

Evolving public perceptions and stability in vaccine uptake

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Abstract

Recent vaccine scares and sudden spikes in vaccine demand remind us that the effectiveness of mass vaccination programs is governed by the public perception of vaccination. Previous work has shown that the tendency of individuals to optimize self-interest can lead to vaccination levels that are suboptimal for a community. We use game theory to relate population-level demand for vaccines to decision-making by individuals with varied beliefs about the costs of infection and vaccination. In contrast to previous work proposing that universal vaccination is impossible in a game theoretic context, we show that optimal individual behavior can vary between universal vaccination and no vaccination, depending on the relative costs and benefits to individuals. By coupling game models and epidemic models, we demonstrate that the pursuit of self-interest often leads to stable dynamics but can lead to oscillations in vaccine uptake over time. The instability is exacerbated in populations that are more homogeneous with respect to their perceptions of vaccine and infection risks. This research illustrates the importance of applying temporal models to an inherently temporal situation, namely, the time evolution of vaccine coverage in an informed population with a voluntary vaccination policy.

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1. Introduction

Vaccination is one of the most effective tools for reducing the burden of infectious diseases. Global vaccination programs for diphtheria, measles, pertussis, and polio have reduced the prevalence of these diseases dramatically over the last 25 years [1]. Despite their public health benefit, vaccination programs face obstacles. One obstacle is public perception of the relative risks and benefits of vaccination. Individuals often refuse or avoid vaccinations they perceive to be risky. A 1974 report linking pertussis vaccine to neurological disorders [2] preceded drops in vaccine coverage in several nations [3]. Recently, the report of a link between autism and the MMR (measles–mumps–rubella) vaccine in the United Kingdom precipitated a decline in vaccination coverage [4], and raised concerns over the reappearance of endemic measles [5]. Similarly, rumors that the polio vaccine could cause sterility and spread HIV have hampered polio eradication in Nigeria [6].

Demand for vaccination can also increase when individuals perceive limited vaccine supply or elevated infection risk. During a measles epidemic in Chicago in 1989–1990, for instance, physicians observed increased compliance in childhood measles vaccinations [7]. In October of 2004 the British government suspended the license of Chiron, the company contracted to produce half of the influenza vaccine used in the US [8]. Subsequent news reports indicate that demand for influenza vaccination spiked for a short period following announcements of the impending shortage [9–11], before receding toward normal levels [12–14].

The importance of vaccination in contemporary public health programs has motivated researchers to examine how the public's perceptions impact vaccination programs. Vaccination creates 'externalities': the individual's decision to vaccinate diminishes not only their own risk of infection, but also the risk for those people with whom the individual interacts. Thus, the total value of vaccination to a community is greater than the sum of the benefits accrued by each individual [15]. Stiglitz [16] cites the associated 'free rider' problem as justification for compulsory vaccination. Fine and Clarkson [17] quantify how differences in perspectives can lead to disparities between the vaccination levels in the best interest of the individual and the vaccination levels in the best interest of the community. Applying epidemiological models, other authors have used traditional [18,19] and game theoretic [20,21] methods to obtain related results.

A hitherto unrecognized challenge to vaccination programs is that the pursuit of self-interest may also destabilize a vaccination program, leading to oscillations in infection prevalence and vaccination coverage over time. In Section 2, we outline a general population game for vaccination. In Section 3, we summarize a simple extension of the SIR vaccination model of Geoffard and Philipson [19]. In Section 4, we couple the SIR model with our vaccination game using best-response dynamics or imitation dynamics and study how self-interested decision-making influences the stability of the equilibrium vaccine uptake and prevalence. The paper concludes with discussion of the importance of the dynamics of temporal relationships between disease prevalence and vaccine demand, the influence of the media on stability of vaccination coverage, and applications of our methods and results to other health policy issues.

2. A vaccination game with signaling

In this section, we describe how individual decision-making relates to population-level demand by extending the vaccination game introduced by Bauch and Earn [21] in a manner analogous to the work of Brito et al. [18]. We begin by considering a single-stage game with simultaneous play, in which every individual is given one opportunity to vaccinate, prior to the introduction of infection.

An individual has a choice of two behaviors: to accept vaccination or to refuse vaccination. With each choice, we can associate a perceived utility defined as the difference between the perceived benefits and the perceived costs. An individual who chooses to vaccinate may earn a small social benefit for their contribution to the public good but will incur the economic cost of vaccination and the risk of side effects. An individual who refuses to vaccinate does not incur any immediate costs and benefits, but runs the risk of future infection.

Formally, every individual of type y has a one-parameter family of strategies $p(\sigma, y)$. The signal $\sigma \in [0, 1]$ carries information about an individual's risk of infection: as σ increases so does the risk. All individuals receive the same signal. For a given signal the individual of type y will choose to vaccinate with probability $p(\sigma, y)$ but refuse to vaccinate with probability $1 - p(\sigma, y)$. The expected utility $U(\sigma, y)$ of a response p to the individual y can be expressed in terms of the individual's expected utility of vaccination U_v and utility of vaccine refusal U_r as

$$U(\sigma, y) = p(\sigma, y)U_v(y) + [1 - p(\sigma, y)]U_r(\sigma, \bar{p}, y), \quad (1)$$

where we define the population's average response under the given response set as

$$\bar{p} = \int_y p(\sigma, y) dy \quad (2)$$

with the integration carried out over all individuals of each type y in the population.

The utility of vaccination and vaccine refusal may differ among individuals because of age, sex, health history, nutrition, economic status, personal beliefs, and other factors. Because herd immunity provides greater protection to nonvaccinators at higher levels of vaccine coverage, the utility of refusal U_r is conventionally an increasing function of the average response \bar{p} , but a decreasing function of the signal σ . We could write $U_r(\sigma, y)$ rather than $U_r(\sigma, \bar{p}, y)$ because for a given response set there is an injective relation from σ to \bar{p} given by Eq. (2). However, expressing the utility of refusal as $U_r(\sigma, \bar{p}, y)$ emphasizes that the utility also depends on the strategies chosen by other players, and hence describes a game-theoretical problem.

Rational strategies $p(\sigma, y)$ will generally be increasing functions of σ . The best response strategies can be described by a set-valued mapping

$$p^*(\sigma, y; \bar{p}) = \begin{cases} 0 & \text{if } U_v(y) < U_r(\sigma, \bar{p}, y) \\ [0, 1] & \text{if } U_v(y) = U_r(\sigma, \bar{p}, y) \\ 1 & \text{otherwise.} \end{cases} \quad (3)$$

The theory of set-valued maps is less prominent in mathematics than that of single-valued functions, but it is an important tool in the continuing development of game theory. The interested reader should consult Aubin and Frankowska [22] for a full introduction. The set of Nash equilibria will consist of all response sets where each player is playing a best response and for every σ , the equilibrium average response

$$\bar{p}^* \in \int p^*(\sigma, y; \bar{p}^*) dy. \quad (4)$$

The righthand integral of Eq. (4) is a set-valued map returning the feasible values for the population's actual average response to a given signal σ and a perceived average response \bar{p}^* . The inclusion relation is interpreted such that

$$q \in \int p^*(\sigma, y; \bar{p}^*) dy \quad (5)$$

if and only if

$$\int \inf p^*(\sigma, y; \bar{p}^*) dy \leq q \leq \int \sup p^*(\sigma, y; \bar{p}^*) dy. \quad (6)$$

The graph

$$\{(u, v) : u \in [0, 1] \text{ and } v \in \int p^*(\sigma, y; u) dy, \} \quad (7)$$

is continuous and has a range restricted to the interval $[0, 1]$. Under these conditions, the contraction mapping principle ensures the existence of a solution to Eq. (4).

The integral is also decreasing in \bar{p} , in the sense that

$$p \geq \inf \int p^*(\sigma, y; \bar{p}_1) dy \quad (8)$$

implies that for every $\bar{p}_2 > \bar{p}_1$,

$$p \geq \sup \int p^*(\sigma, y; \bar{p}_2) dy. \quad (9)$$

This is sufficient to prove the uniqueness of a solution \bar{p}^* to Eq. (4). It follows that there exists a Nash equilibrium and that the population's average response is the same for all Nash equilibria. This generalizes the result of Brito et al. [18] to cases of non-smooth distribution functions.

What is best for individuals, however, is not necessarily best for the community. From a community's perspective, the best vaccination policy optimizes the community utility

$$\bar{U} = \int p(\sigma, y) U_v(y) + [1 - p(\sigma, y)] U_r(\sigma, \bar{p}^*, y) dy. \quad (10)$$

Brito et al. [18], and Geoffard and Philipson Fine and Clarkson [17], Brito et al. [18] and Geoffard and Philipson [19] have shown that coverage levels that optimize individual utilities will always be suboptimal for a community. Specifically, suppose that the population is sufficiently diverse for the community utility to be single-valued and differentiable and that there is a small proportional perturbation s in all strategies away from Nash equilibrium, so

$$\bar{U}(s) = \int s p^*(\sigma, y) U_v(y) + [1 - s p^*(\sigma, y)] U_r(\sigma, s \bar{p}^*, y) dy. \quad (11)$$

The change in the community utility is proportional to

$$\left. \frac{d\bar{U}}{ds} \right|_{s=1} = \int p^*(\sigma, y) [U_v(y) - U_r(\sigma, \bar{p}^*, y)] dy + \int [1 - p^*(\sigma, y)] \frac{\partial U_r(\sigma, \bar{p}^*, y)}{\partial \bar{p}} dy. \quad (12)$$

At a Nash equilibrium, only people for whom vaccination is more valuable than refusal will vaccinate, so

$$\int p^*(\sigma, y)[U_v(y) - U_r(\sigma, \bar{p}^*, y)] dy \geq 0. \quad (13)$$

Also, the value of refusal is an increasing function of the average response, so

$$\int [1 - p^*(\sigma, y)] \frac{\partial U_r(\sigma, \bar{p}^*, y)}{\partial \bar{p}} dy \geq 0. \quad (14)$$

Thus,

$$\left. \frac{d\bar{U}}{ds} \right|_{s=1} \geq 0. \quad (15)$$

Unless the Nash equilibrium is universal vaccination, a Nash equilibrium for individuals will always have less vaccination than is optimal for the community.

3. Dynamic models incorporating demand

To apply the vaccination game in a predictive context, we must relate the signal σ and the population's average response \bar{p} to the epidemiology of an infection. We will do this by coupling the vaccination game to an extension of the vaccination model of Geoffard and Philipson [19].

Geoffard and Philipson pose an SIR model with continuous population turnover where demand for vaccine varies over time. A population of size N is stratified into susceptible (S), infected (I), and removed (R) compartments. Individuals move from the susceptible compartment (S) to the infected compartment (I) at a rate proportional to the prevalence of infection I and the transmission rate β and at a rate ϵ from contacts to an external infection reservoir. Infected individuals recover at a rate γ and enter an immune compartment (R) that removes them from the epidemiological dynamics. The total population size is assumed to be constant, as population loss, occurring at rate μ due to emigration or death, is assumed to be equal to population gain due to immigration and birth. Values for the expected residence time $1/\mu$ can range from several years in a school system to several decades in a residential community. A proportion D of individuals entering the population are vaccinated and pass directly to the immune compartment, while the remaining proportion $1 - D$ enter the susceptible compartment. Here, D represents demand.

$$\dot{S} = \mu[1 - \min(D_{\max}, D)]N - (\epsilon + \beta \frac{I}{N})S - \mu S, \quad (16a)$$

$$\dot{I} = (\epsilon + \beta \frac{I}{N})S - \gamma I - \mu I, \quad (16b)$$

$$\dot{R} = \gamma I + \min(D_{\max}, D)N - \mu R, \quad (16c)$$

where $N = S + I + R$, and D_{\max} is the maximum rate of vaccine supply. The basic reproduction number \mathcal{R}_0 , defined as the ratio of new infections generated per infection in a naive closed population without contact to an external reservoir is given by

$$\mathcal{R}_0 = \frac{\beta}{\gamma + \mu}. \quad (17)$$

The basic reproduction number must be larger than one for the infection to be self-sustaining. Eq. (17) will be useful in our analysis of imitation dynamics.

4. Relating dynamics and game theory

Vaccine demand varies over time, depending on the difference in the population's perceived utilities of vaccination and vaccination refusal. Chapman and Coups [23], for instance, have shown that demand for influenza vaccine is positively correlated with past behavior and with perceived effectiveness in preventing influenza infection, but negatively correlated with perceived side effects. To describe the interdependence of vaccine demand, infection prevalence, and perceived utilities, we posit a set of relations between dynamic variables in Eq. (16), and game variables in Eqs. (1)–(4). Two common ways of doing this are the use of 'best-response' dynamics where individuals act in their immediate best interest, and the use of 'imitation' dynamics where individuals copy the behavior that is currently most successful.

4.1. Best-response dynamics

Let us assume that all individuals play their current best-response strategy when given an opportunity to vaccinate. As the population turns over, the probability that a newly susceptible individual will vaccinate is then the same as the population's average response. One may assume that the instantaneous demand for vaccine

$$D = \bar{p}, \quad (18)$$

where the average response \bar{p} is related to individual response choices by Eq. (2). We may also assume that individuals adopt responses corresponding to a Nash equilibrium, so that the average response \bar{p} solves Eq. (4). To close the system, we must express the risk signal σ and the perceived utilities in terms of the dynamic variables.

For example, if the utility of refusal is proportional to the risk and independent of the time until infection, we can express the perceived utilities to an individual of type y as

$$U_v = -C_v(y), \quad \text{and} \quad U_r = -\sigma C_s(y), \quad (19)$$

where C_v is the expected cost of vaccination and C_s is the expected cost of being infected assuming an individual does not vaccinate. In the simplest case, where demand depends only on the current hazard, the perceived risk of infection is

$$\sigma = \frac{\epsilon + \beta I/N}{\mu + \epsilon + \beta I/N}. \quad (20)$$

Each individual's best response is now given by Eq. (3), and, for a sufficiently diverse population, the unique average response \bar{p} given by Eq. (4) will be an increasing and differentiable function of I . Let (S^*, I^*, R^*, D^*) be a steady-state solution of Eq. (16). The prevalence I^* of infection at the interior steady-state is a nonnegative solution of the equation

$$\frac{\beta}{N}I^{*2} + \left(\mu + \epsilon - \mu \frac{\beta}{N} \frac{1 - \bar{p}(I^*)}{\mu + \gamma} \right) I^* - \epsilon \mu \frac{1 - \bar{p}(I^*)}{\mu + \gamma} = 0. \quad (21)$$

If demand saturates, such that $D^* = \bar{p} > D_{\max}$, the steady-state is locally stable independent of \bar{p} . Otherwise, linear stability analysis of Eq. (16) shows that if $d\bar{p}/dI \geq 0$, then an interior steady-state is stable, generalizing a result of Geoffard and Philipson [19].

In cases where changes in demand are delayed, the prevalence-demand relation specified by Eq. (18) is replaced with

$$\dot{D} = \alpha(\bar{p} - D), \quad (22)$$

where the adaptation rate α controls how quickly demand adjusts to changes in prevalence. The steady-state's location remains the same after this replacement, but the stability may change. When there is a positive steady-state solution, the linear stability in the special case of $\epsilon = 0$ is determined by the eigenvalues of the Jacobian matrix

$$\begin{bmatrix} -\frac{\beta}{N}I^* - \mu & -\gamma - \mu & -\mu \\ \frac{\beta}{N}I^* & 0 & 0 \\ 0 & \alpha \frac{d\bar{p}}{dI} & -\alpha \end{bmatrix} \quad (23)$$

Two of the three Routh–Hurwitz conditions for stability are always satisfied. The third condition is

$$(\mu + \alpha + \gamma) \frac{\beta^2}{N^2} I^{*2} + [(\mu + \alpha)^2 + \gamma\mu] \frac{\beta}{N} I^* + \mu\alpha(\alpha + \mu) - \mu\alpha \frac{\beta}{N} I^* \frac{d\bar{p}}{dI} \Big|_{I=I^*} > 0. \quad (24)$$

The left hand side is a linear increasing function of γ , so we can build a lower bound by taking $\gamma = 0$. If we then treat I^* as an independent variable and choose α and I^* to minimize the left argument, we can show that the steady-state is linearly stable provided

$$N \frac{d\bar{p}}{dI}(S^*, I^*, R^*, D^*) < 8. \quad (25)$$

On the other hand, there are certainly values for $d\bar{p}/dI$ so large that Eq. (24) is false. This suggests that greater homogeneity in a population's response increases the risk of instability because the response sensitivity to prevalence increases as homogeneity increases. Fig. 1 shows that in cases where the population's response to the proportional prevalence I^*/N approximates a Gauss distribution, variances larger than 0.05 guarantee local stability. Taylor series expansion suggests that small risks of infection from an external reservoir ($\epsilon > 0$) further stabilize the dynamics. Since Eq. (22) is closely approximated by Eq. (18) when α is very large, we surmise that the delay introduces a potential for instability, and that the instability must asymptotically weaken as the delay shortens. This can also be shown by asymptotic analysis of Eq. (24). Similarly, inspection of Eq. (24) shows that the steady-state must be stable for small α . Thus, only intermediate delays can lead to instability.

In cases where the population is approximately homogeneous and the utilities of vaccination and infection given by Eq. (19) are constant across all individuals, the optimal individual vaccination level at Nash equilibrium can be determined explicitly and compared to the response that optimizes the community utility (see Figs. 2 and 3). When there is no risk of infection from con-

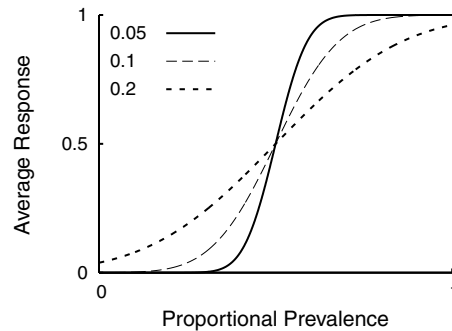


Fig. 1. Examples of the average response \bar{p} 's dependence on the proportional equilibrium prevalence I^*/N in cases of different degrees of homogeneity in response among individuals. We have assumed large populations where all individuals exhibit a 0,1 step response and the response thresholds are normally distributed over the proportional prevalence with mean 0.5 and variances 0.05, 0.1, or 0.2. In the case of a normal distribution, 0.05 is the smallest variance for which Eq. (25) is satisfied for all prevalence values.

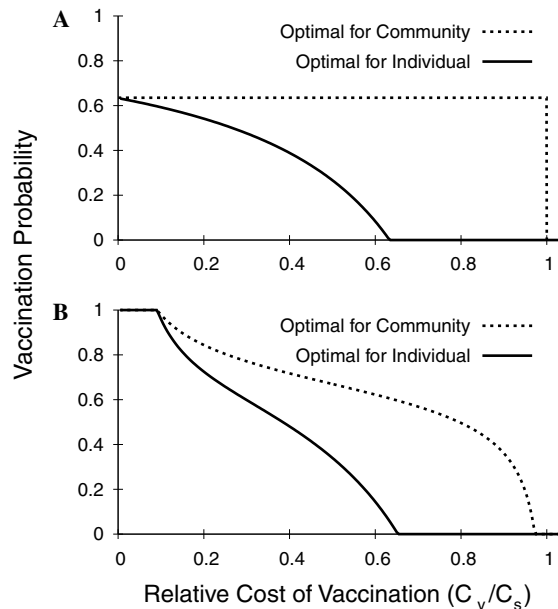


Fig. 2. A comparison of the optimal vaccination strategies in a homogeneous population depending on the cost of vaccination relative to the cost of infection (C_v/C_s) from the individual and the community perspectives when the population is closed (A) with $\epsilon = 0$ and when the population is open (B) with a reservoir infection rate $\epsilon = 0.1$. Vaccination probabilities that are optimal for the individual correspond to the Nash equilibria. When the cost of vaccination is small, there is a significant difference between the optimal behavior in open and closed populations. When the cost of vaccination is similar to the cost of infection, vaccine provides no benefits to the individual or the community in an open population. Parameters: $N = 1$, $\beta = 30$, $\gamma = 10$, $\mu = 1$.

tact with an external reservoir ($\epsilon = 0$), the community's utility is optimized by vaccinating just enough to eradicate infection as long as vaccination is less costly than infection. An individual's utility is optimized at a Nash equilibrium with lower levels of vaccination. Community-optimal

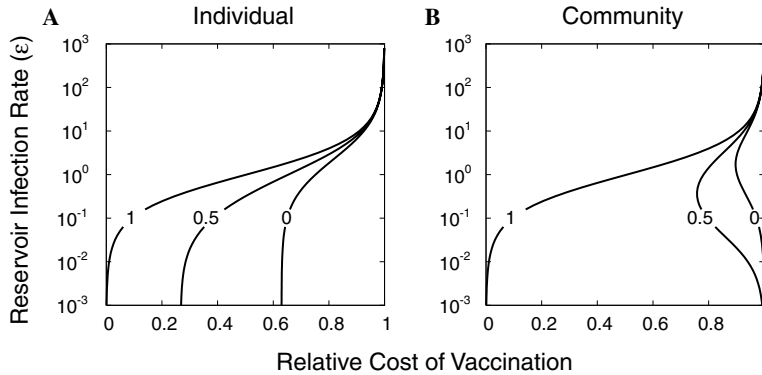


Fig. 3. Contour plots of the optimal vaccination levels p^* in a homogeneous population from the individual (A) and community (B) perspectives as functions of the external reservoir infection rate ϵ and the relative cost of vaccination (C_v/C_s). For high rates of reservoir infection, both individuals and the community prefer universal vaccination. In the absence of reservoir infection, individual preference depends on the cost of vaccination, while the community's preference is vaccination at the herd-immunity level independent of relative cost. Increases in reservoir infection can decrease optimal community vaccination levels because of an accompanying decline in the benefits of herd immunity. Parameters: $N = 1$, $\beta = 30$, $\gamma = 10$, $\mu = 1$.

and individual-optimal strategies only coincide when vaccination has no cost or vaccination is more costly than sickness. When infection is also transmitted by contact with an external reservoir ($\epsilon > 0$), optimal vaccination levels for the individual are greater than those in the comparable closed population. Universal coverage is optimal for both the individual and the community when vaccine costs are small because high vaccination levels do not eliminate the risk of infection. This is in contrast to suggestions that universal coverage is impossible [24]. However, if vaccination is costly, community-optimal levels of vaccination may actually decrease as transmission from an external reservoir increases, as seen in Fig. 3.

The analysis of local stability in a homogeneous population is more difficult than in a heterogeneous population because the average response is not a differentiable function of the signal. We will not address it in this paper.

4.2. Imitation dynamics

There are cases where vaccine uptake dynamics can more readily exhibit instability. In particular, populations with relatively uniform beliefs can have an average response that is sensitive to small changes in the signal σ . As an example, we consider the case of imitation dynamics [25] also studied in the context of voluntary vaccination by Bauch [24].

Let the rate of change in the demand for vaccination be proportional to the difference between the perceived utility of vaccination and the perceived utility of refusal, while the demand itself always remains between 0 and 1:

$$\dot{D} = \alpha \left[1 - \frac{v_r \mu}{\beta I + \mu} \right] D(1 - D), \quad (26)$$

where $v_r\mu/(\beta I + \mu) = U_r$ is a decreasing function of prevalence and we have adopted the convention that the utility of vaccination $U_v = 1$. The rate of adoption α describes how quickly the population switches to the behavior that is currently favored. At one extreme, large shifts in demand can occur instantly ($\alpha \rightarrow \infty$). At the other extreme, demand is independent of the utilities of the vaccination decisions ($\alpha = 0$). Although we have chosen to present results for an explicit prevalence-demand relation, the same qualitative stability characteristics can be shown to hold for more general relations of the form

$$\dot{D} = [U_v - U_r(I)]F(D) \quad (27)$$

where F is concave and has two roots on the interval $[0,1]$.

For the remainder of this section, we assume that there is no risk of infection from contact with an external reservoir ($\epsilon = 0$) in order to investigate the conditions where infection eradication is favored over the tolerance of endemic disease.

When vaccine supply cannot satisfy demand, vaccine uptake will be stable. However, when the vaccine is in abundant supply, the dynamics of vaccine uptake depend on the individual's perceived utilities of vaccination and vaccine refusal and upon infection prevalence. When the utility of vaccination is small and refusal is preferred even when infection is endemic, nobody will choose to vaccinate, and the dynamics are the same as those that would occur in the absence of vaccination. When the utility of vaccination is large and vaccination is preferred even when the infection is absent from the population, the entire population will choose to vaccinate. Social contracts, such as requiring vaccination for international travel or school admittance, or making refusal illegal can raise the utility of vaccination to this level. A large vaccination utility then implies that the vaccination coverage will be stable and sufficient for eradication.

In some cases, the utility of vaccination will lie between these extremes: when the infection is endemic, individuals may prefer vaccination, but when the infection is rare, individuals may prefer not to risk vaccination. This leads to a unique interior steady-state solution (S^*, I^*, R^*, D^*) where $I^* > 0$. In this circumstance, the steady-state corresponds to the traditionally perceived outcome of public health vaccination policy in an open market. Most individuals will be vaccinated, but some minimal level of infection risk will be tolerated. However, this steady-state solution is unstable when the population's rate of adoption and the basic reproduction number are large relative to the perceived utility of refusal,

$$\frac{\mu}{\alpha} + \frac{1}{\mathcal{R}_0} < \frac{1}{v_r} < 1. \quad (28)$$

This is proven using linear stability analysis of the positive steady-state to Eq. (16) and (26). Eq. (28) and the condition $\mathcal{R}_0 > 1$ are used to subdivide the parameter space into five regions shown in Fig. 4(A) with qualitatively distinct dynamics. Fig. 4(B) shows that faster adoption α enlarges the domain of instability. This contrasts our analysis of the best-response dynamics, where very large α improved stability. The difference may be caused by the tendency for imitation dynamics to over-react to changes in risk or by the synchrony of the population response. Both best-response and imitation dynamics are stable for small α .

Vaccine scares corresponding to increases in the relative perceived utility of refusal can contribute to instability, but can also stabilize an unstable system, depending on the initial perception of the utility of refusal (Fig. 4).

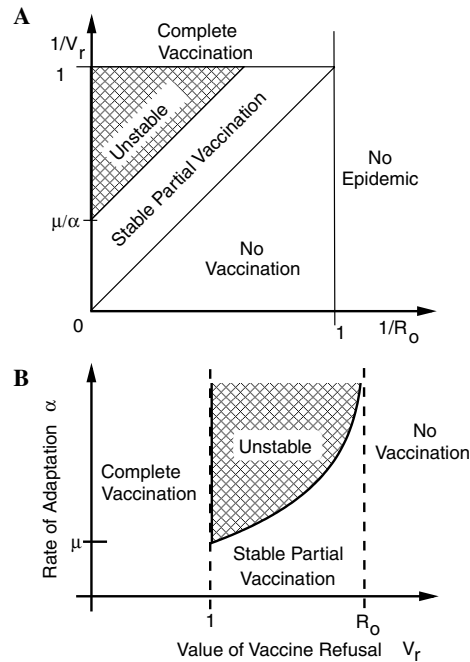


Fig. 4. Imitation dynamics of vaccination policy, depending on the utility of vaccine refusal v_r , the adoption rate α , and the basic reproduction number \mathcal{R}_0 , as given by Eq. (28) when $D_{\max} = 1$. The interior steady state can only be unstable if $\alpha > \mu$ (A). Unlike best-response dynamics, the interior steady state does not stabilize for large α when $v_r > 1$ because of imitation's tendency to overreact (B).

If the adoption rate and basic reproduction number are large, the prevalence and demand will oscillate (Figs. 5 and 6). When prevalence is low, individuals place greater value on refusal, and when prevalence is high, individuals place greater value on vaccination. Fig. 5(B) shows oscillations in demand on the order of 4 times the population's expected turnover time. This seems reasonable when studying vaccination in populations of school children where turnover is on a scale of several years, but it is less clear if this is reasonable when turnover is on the scale of a human lifetime.

5. Discussion

Most previous approaches to the relationship among risk perception, vaccinating behavior, and vaccine coverage under a voluntary policy have either been based on static models, or have analyzed only the equilibria of dynamic models [17,19,20]. However the supply and demand economics of vaccination unfold through time and in relation to infection prevalence. This work emphasizes the importance of dynamic relationships between prevalence and demand through a game-theoretic model.

The stability of vaccine uptake depends in part on the epidemiological characteristics of the infection in question. More interestingly, though, the degree of homogeneity in the population's response to infection prevalence is an important determinant of instability. The more

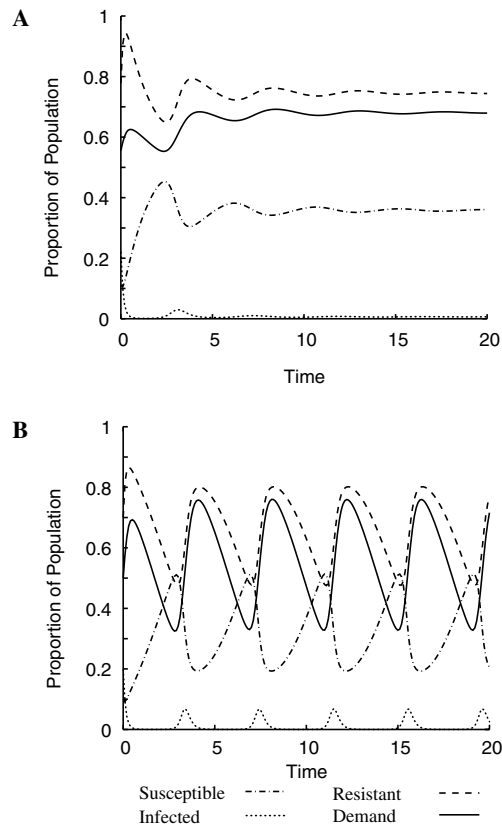


Fig. 5. Imitation dynamics of a vaccination policy for intermediate utility of vaccine refusal v_r ($1 < v_r < \mathcal{R}_0$) as described by Eqs. (16) and (26). (A) The time series exhibits stable dynamics when the demand for vaccine adapts slowly to changes in the perceived utility ($\alpha = 1.2$). (B) The time series shows periodic dynamics when the demand adapts quickly ($\alpha = 4$). Parameters: $\beta = 34.1$, $\gamma = 10$, $\mu = 1$, $U_r = 1.2$, $D_{\max} = 1$.

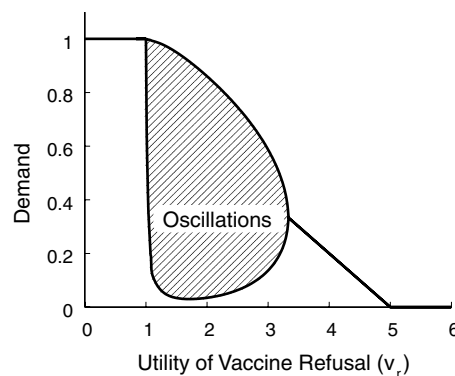


Fig. 6. Bifurcations in vaccine demand dynamics under varying utility vaccine refusal under imitation dynamics, as described by Eqs. (16) and (26). If $v_r < 1$, all individuals choose to vaccinate. If $1 < v_r < 3.3$, demand and infection prevalence oscillate. If $v_r > 5$, there is no demand for vaccine. Parameters: $\beta = 30$, $\gamma = 5$, $\mu = 1$, $\alpha = 10$.

homogeneous the response of a population, the less likely vaccine uptake is to be stable. We have also found that the stability of an implemented policy can depend on the rate at which individuals adapt to changes in the utility of vaccination versus vaccine refusal. The more rapidly individuals react, the more difficult it is to maintain consistently high levels of vaccination. Our work suggests that there may be limited windows of opportunity for disease eradication, where demand by individuals is strongly aligned with the community's interest in eradication, and that these windows close as individuals adapt to the reduced risks of infection. Our work also suggests that instability in vaccine coverage levels is inherent to voluntary vaccination policies under certain conditions.

Mass media might play an important role in shifting the public's perception of vaccination and potentially triggering epidemic instability. Conversely, independent decision-making can stabilize dynamics. The rapid dissemination of information may exacerbate the threat of vaccination scares by homogenizing public perception and increasing the rate at which individuals can adapt to changes in perception. On the other hand, some researchers have argued that the diversity of internet media sources creates more heterogeneity in public perception. A separate memetic model may be necessary for sorting out the relationship between media and vaccination behavior.

Human behavior can have important consequences for infection dynamics. Del Valle et al. [26] show that the size of an epidemic can be very sensitive to changes in behavior that alter the transmission rate. Haderler and Castillo-Chavez [27] show that education efforts to control sexually transmitted disease can increase or decrease disease prevalence, depending on education's effect on core group size. But as we have shown, behaviors that improve a community's welfare do not always yield improvements in the individual's welfare. Game-theoretic approaches help us account for these discrepancies, and will illuminate which behavior changes can make practical contributions to public health policy.

Our model framework is broadly applicable to vaccination in general and even to other health policy issues in which individuals must choose between risky behaviors. For example, our analysis is applicable to the transmission of many infectious diseases where individuals have a choice between risky and cautious behaviors, particularly when the risky behavior is rewarding. Sexually transmitted diseases are particularly likely to exhibit instability because of the high value placed on risky behavior by some individuals. Indeed, this may be the case in San Francisco, where there has been a dramatic increase in the number of cases of syphilis since the introduction of HAART (highly active anti-retroviral therapy) for the treatment of HIV [28].

Game theory explicitly formalizes the relationship between individual decision-making processes and population dynamics. Developing epidemiologic game theory in such a way that it can serve public health will require better data and improved social models of behavioral responses to transmission dynamics. It will also require continued efforts on the part of researchers to utilize increasingly sophisticated and realistic game theoretical techniques, many of which have already been developed and utilized in the fields of economics, social sciences and evolutionary biology.

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