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A game dynamic model for vaccine skeptics and vaccine believers: measles as an example

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Abstract

Widespread avoidance of Measles-Mumps-Rubella vaccination (MMR), with a consequent increase in the incidence of major measles outbreaks, demonstrates that the effectiveness of vaccination programs can be thwarted by the public misperceptions of vaccine risk. By coupling game theory and epidemic models, we examine vaccination choice among populations stratified into two behavioral groups: vaccine skeptics and vaccine believers. The two behavioral groups are assumed to be heterogeneous with respect to their perceptions of vaccine and infection risks. We demonstrate that the pursuit of self-interest among vaccine skeptics often leads to vaccination levels that are suboptimal for a population, even if complete coverage is achieved among vaccine believers. The demand for measles vaccine across populations driven by individual self-interest was found to be more sensitive to the proportion of vaccine skeptics than to the extent to which vaccine skeptics misperceive the risk of vaccine. Furthermore, as the number of vaccine skeptics increases, the probability of infection among vaccine skeptics increases initially, but it decreases once the vaccine skeptics begin receiving the vaccination, if both behavioral groups are vaccinated according to individual self-interest. Our results show that the discrepancy between the coverages of measles vaccine that are driven by self-interest and those driven by population interest becomes larger when the cost of vaccination increases. This research illustrates the importance of public education on vaccine safety and infection risk in order to maintain vaccination levels that are sufficient to maintain herd immunity.

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Keywords

measles; game theory; epidemiological model; vaccine

1. Introduction

The decision by parents to refuse vaccines poses a threat to vaccination policies. Refusing vaccination may increase the individual risk of infection, potentially leading to an outbreak and increased mortality from diseases preventable by vaccine. The effect of vaccine refusal on disease transmission and disease elimination has been exemplified by recent increases in the number of measles cases in the US (Omer et al., 2009). Although endemic transmission of measles was declared eliminated from the US in 2000 (Katz and Hinman, 2004; Sugerman et al.), lack of personal experience with measles has led certain parents to focus on vaccine-adverse events and to refuse measles vaccination (Gust et al., 2004; Sugerman et al.). Such refusals resulted in the decrease in the measles vaccine coverage (Sugerman et al.), leading to 38 measles outbreaks in the US during 2001–2008 (Parker Fiebelkorn et al.). A majority of such outbreaks were among those who exempted themselves from the vaccines (2008a; 2008b; 2008c; Dayan et al., 2005; Parker et al., 2006; Parker Fiebelkorn et al.). Specifically, during 2004–2008, 110 of 162 cases of measles infection among vaccine-eligible US residents were known to have been exempted from measles vaccination because of a personal or parental belief (Sugerman et al.).

The largest measles outbreak in the US since 1991 occurred in San Diego, CA, in 2008, when an intentionally unvaccinated 7-year-old boy who was infected with measles returned to the US from Switzerland (Sugerman et al.). Relatively high vaccine exemption rates in San Diego further attributed to the 2008 measles outbreak, which resulted in 839 exposed persons, 11 additional cases (all in unvaccinated children), and a net public sector cost of \$10,376 per case (Sugerman et al.). The vaccine exemption rate in San Diego was over 40% in 10 schools, and the second-dose of measles vaccine coverage was below 70% in 31 schools among the 643 schools surveyed (Sugerman et al.). In addition, schools and districts with high refusal rates tended to cluster, further attributing to the measles outbreak (Sugerman et al.).

The impact of vaccine refusal on herd immunity was also apparent during the recent MMR scare in the United Kingdom (Bhattacharyya and Bauch). During the past decade, the coverage level of one-dose measles vaccination among children two years of age in the UK decreased from 91% during 1997–1998 to 80% during 2003–2004 (Parker Fiebelkorn et al.). Similarly, during 1997–1998 in the UK, the coverage of two-dose measles vaccination among children five years of age was 73–76% (Parker Fiebelkorn et al.). Such a low level of measles vaccine coverage provided inadequate population immunity to sustain measles elimination in the UK (Choi et al., 2008). For instance, in England, 1.9 million school children and 300,000 pre-school children, including more than 800,000 children who were completely unvaccinated, were incompletely vaccinated against measles in 2004 and 2005 (Choi et al., 2008). As a result, approximately 1.3 million children aged 2–17 years were susceptible to measles, leading to an effective reproductive ratio exceeding 1.0 in 14 of the 99 districts in England (Choi et al., 2008).

Parents have various reasons for refusing or delaying vaccination, one of the most often cited of which is perception of high vaccine risk or low vaccine efficacy (Smith, May 1–4, 2010). Specifically, 26% of parents who refused or delayed vaccination in the US questioned whether vaccines really worked, 25% cited worries that measles vaccines might cause autism, and 24% worried about side effects (Smith, May 1–4, 2010). Perceived

adverse vaccine reactions, especially autism, were often cited as a primary deterrent to vaccination, although the numerous studies have failed to demonstrate such an association (Mitka, 2009). One study found that 34% of parents believed that measles vaccination is more dangerous than the childhood diseases themselves (Smailbegovic et al., 2003). As a result, the benefits of vaccination are mitigated by perceptions of vaccine risk, costs, or low vaccine efficacy, although vaccination has long provided direct protection against infection and reduced transmission in the population.

Anti-vaccination behavior poses a challenge to public health agencies that seek to achieve optimal vaccination level and public adherence. In addition, whenever there is a discrepancy between a public health strategy that is optimal for the population and a strategy that is perceived optimal for individuals, adherence to public health policies designed to benefit the population can be difficult to maintain (Brito et al., 1991). In order to understand the impact of the public's health-related perceptions on the success of interventions, several game-theoretical models in epidemiology have been proposed (Bauch and Earn, 2004; Bauch et al., 2003; Bauch et al., 2010; Chen, 2006; Cojocaru et al., 2007; Cornforth et al.; Fine and Clarkson, 1986; Francis, 2004; Galvani et al., 2007; Reluga, 2009; Reluga et al., 2006; Shim et al., 2009; Shim et al., 2010a; Shim et al., 2010b). In the case of vaccination, these studies have shown potential conflicts between individual incentives and population incentives. From the perspective of the population, vaccination reduces the transmission of infectious diseases and has the potential to eradicate diseases when herd immunity is achieved. From the perspective of the individual, vaccination reduces the probability of infections, but the benefit is mitigated by the risk of adverse effects and the potential to free-ride on herd immunity. The recent work by Manfredi et al. investigates the impact of vaccine refusal in the context of game theory (Manfredi et al., 2009), but their model did not incorporate the dynamics of disease transmission or the indirect protection of vaccination (Manfredi et al., 2009). The game-theoretic epidemiological model we propose incorporates an explicit dynamic relationship between disease incidence and vaccination decisions.

For individuals driven by self-interest, game-theoretic decisions are expected to tend toward the Nash strategy, where no player can increase his or her individual payoff by changing his or her own strategy. Thus, from the game-theoretic perspective, without public health intervention, an individual adopts a vaccination strategy that will maximize personal payoff, taking into account the disease incidence and risk of infection, which is determined by vaccination decisions made by the rest of the population. In contrast, the utilitarian vaccination strategy is defined as that which achieves the highest population payoff by considering a balance between the benefits and costs of vaccination, from the perspective of the population as a whole.

This paper proposes a game-theoretic dynamic model of measles transmission and examines the impact of perceived risks of measles vaccination on the vaccine uptake. Using our model, we explore how vaccine refusal may lead to the failure of herd immunity. Our model considers two behavioral groups, vaccine skeptics and vaccine believers, each of which has its own perceptions of the benefits and risks of vaccination. Our model is used to illustrate the effects of perceived vaccine risks on demand for the measles vaccination among vaccine skeptics and vaccine believers, the feasibility of achieving herd immunity, the size of potential epidemics, and the resulting morbidity of infection. We also present an epidemiological game theoretic analysis of individual versus population incentives in order to evaluate the impact of the discordance of incentives on vaccination coverage.

Our results highlight the role of vaccine skeptics in reducing overall vaccine coverage in populations, creating the discrepancies between the Nash and utilitarian strategies of vaccination. In contrast, the Nash and utilitarian strategies of vaccine believers are in

relative alignment when vaccination costs are low. Based on our results, we conclude that the probability and incidence of measles are more sensitive to the proportion of vaccine skeptics than to individual misperceptions about vaccine risks. Our study also highlights the impact of discrepancies between perceived and actual risks in the general population on the individual vaccine uptake. These results suggest that additional incentives or education about the safety of measles vaccination are required to raise vaccination levels among vaccine skeptics close to the utilitarian strategy.

2. Methods

To model the transmission of measles and vaccination, we developed a mathematical model that incorporates four epidemiological groups: susceptible, vaccinated, infectious, and recovered. The asymptotic dynamics of this epidemiological model are used to calculate the probability that individuals in two behavioral groups will become infected based on their vaccination decisions. These infection probabilities are then used to parameterize the expected payoffs of vaccination. Monte Carlo methods are employed to determine the optimal vaccination levels driven by self-interest versus the population's interest.

2.1 Epidemiological Population Model for Vaccine Refusal

We developed a model (Eqs. 1 – 8) of measles transmission and vaccination, dividing population into two behavioral groups—vaccine skeptics and vaccine believers—depending on individual attitudes toward vaccination. We assume that vaccine skeptics and vaccine believers have different perceptions of the cost of infection and the cost of vaccine side effects. Based on their perceptions of the benefits and risks of vaccination, parents decide whether to give measles vaccination to their children at the time of birth. Vaccine skeptics and vaccine believers are denoted by subscripts 1 and 2, respectively. We define $\bar{\varphi}_k$ as the average vaccination coverage of group k , while φ_k is defined as vaccination strategy of a specific individual in behavioral group k ($k=1, 2$). The overbar notation indicates the aggregate vaccination behavior in the population. In sufficiently large populations, the disease dynamics depend on the population strategy ($\bar{\varphi}_k$), not on one individual's behavior (φ_k), because one person's vaccination strategy will have little effect on the population's overall vaccine coverage. The probability of vaccination among vaccine skeptics is assumed lower than that among vaccine believers ($\bar{\varphi}_1 < \bar{\varphi}_2$).

Within each behavioral group, individuals may be susceptible (S_1 and S_2), infected (I_1 and I_2), recovered (R_1 and R_2), or vaccinated (V_1 and V_2). Children are born and enter the model at a constant rate per capita, μ . We also assume a constant natural mortality rate, μ , such that the population size is asymptotically constant. Based on our assumptions about the vaccine propensity in each behavioral group, a portion of newly born children in group k ($\bar{\varphi}_k q_k$) is vaccinated and enters V_k class, while the rest, $(1 - \bar{\varphi}_k)q_k$, enter a susceptible class, S_k ($k=1, 2$), where q_1 and q_2 represent relative sizes of vaccine skeptics and vaccine believers, respectively ($q_1 + q_2 = 1$). Since two measles vaccine doses administered after twelve months of age are 95–100% effective, we assume a perfectly efficacious vaccine against measles that confers lifelong immunity, as does recovery (Parker Fiebelkorn et al.).

Given these assumptions, the epidemiological model of vaccination behavior can be expressed by the following deterministic system of ordinary differential equations:

$$S_1' = \mu(1 - \bar{\varphi}_1)q_1N - \beta(I_1 + I_2)S_1/N - \mu S_1, \quad \text{Eq. 1}$$

$$I_1' = \beta(I_1 + I_2)S_1/N - (\gamma + \mu)I_1, \quad \text{Eq. 2}$$

$$R_1' = \gamma I_1 - \mu R_1, \quad \text{Eq. 3}$$

$$V_1' = \mu \bar{\varphi}_1 q_1 N - \mu V_1, \quad \text{Eq. 4}$$

$$S_2' = \mu(1 - \bar{\varphi}_2) q_2 N - \beta(I_1 + I_2) S_2 / N - \mu S_2, \quad \text{Eq. 5}$$

$$I_2' = \beta(I_1 + I_2) S_2 / N - (\gamma + \mu) I_2, \quad \text{Eq. 6}$$

$$R_2' = \gamma I_2 - \mu R_2, \quad \text{Eq. 7}$$

$$V_2' = \mu \bar{\varphi}_2 q_2 N - \mu V_2, \quad \text{Eq. 8}$$

where $N = \sum_{k=1}^2 (S_k + V_k + I_k + R_k) := K$ is the population size. We assume that individuals mix homogeneously, and the transmission rate (β) is assumed to be constant (i.e. no seasonal forcing). Here, γ represents recovery rate. In addition, we denote the size of two groups, vaccine skeptics and vaccine believers, by $N_1 = S_1 + V_1 + I_1 + R_1 := K_1$ and $N_2 = S_2 + V_2 + I_2 + R_2 := K_2$, respectively. Consequently, the number of vaccine skeptics and vaccine believers is asymptotically constant. Thus, without loss of generality (Thieme and Castillo-Chavez, 1995), we assume that $N_1 = q_1 N$ and $N_2 = q_2 N$.

Eqs. (1)–(8) can be rescaled by introducing following variables: $s_j = S_j / K$, $i_j = I_j / K$, $r_j = R_j / K$, and $v_j = V_j / K$:

$$s_1' = \mu(1 - \bar{\varphi}_1) q_1 - \beta(i_1 + i_2) s_1 - \mu s_1, \quad \text{Eq. 9}$$

$$i_1' = \beta(i_1 + i_2) s_1 - (\gamma + \mu) i_1, \quad \text{Eq. 10}$$

$$r_1' = \gamma i_1 - \mu r_1, \quad \text{Eq. 11}$$

$$v_1' = \mu \bar{\varphi}_1 q_1 - \mu v_1, \quad \text{Eq. 12}$$

$$s_2' = \mu(1 - \bar{\varphi}_2) q_2 - \beta(i_1 + i_2) s_2 - \mu s_2, \quad \text{Eq. 13}$$

$$i_2' = \beta(i_1 + i_2) s_2 - (\gamma + \mu) i_2, \quad \text{Eq. 14}$$

$$r_2' = \gamma i_2 - \mu r_2, \quad \text{Eq. 15}$$

$$v_2' = \mu \bar{\varphi}_2 q_2 - \mu v_2, \quad \text{Eq. 16}$$

Using $s_j = q_j - i_j - r_j - v_j$ and the conditions for steady states, we can rewrite the equations, $i_1' = 0$ and $i_2' = 0$, as

$$\beta(i_1 + i_2)(q_1 - i_1 - \bar{\varphi}_1 q_1 - \frac{\gamma}{\mu} i_1) = (\gamma + \mu) i_1 \quad \text{Eq. 17}$$

and

$$\beta(i_1 + i_2)(q_2 - i_2 - \bar{\varphi}_2 q_2 - \frac{\gamma}{\mu} i_2) = (\gamma + \mu) i_2. \quad \text{Eq. 18}$$

By solving Eqs. (17) and (18) simultaneously, one can determine the stationary solutions to Eq. (9)–(16). The disease-free steady state distribution of Eqs. (9)–(16) is

$$E_0 = (0, 0, 0, 0, 0, 0, 0, 0), \quad \text{Eq. 19}$$

and a non-uniform endemic steady state distribution is

$$E_1 = (s_1^*, i_1^*, r_1^*, v_1^*, s_2^*, i_2^*, r_2^*, v_2^*) \quad \text{Eq. 20}$$

where

$$s_k^* = \frac{(1 - \bar{\varphi}_k) q_k (\gamma + \mu)}{\beta(1 - q_1 \bar{\varphi}_1 - q_2 \bar{\varphi}_2)}, \quad i_k^* = q_k (1 - \bar{\varphi}_k) \left\{ \frac{\mu}{\gamma + \mu} - \frac{\mu}{\beta(1 - q_1 \bar{\varphi}_1 - q_2 \bar{\varphi}_2)} \right\}, \quad r_k^* = (1 - \bar{\varphi}_k) q_k \left\{ \frac{\gamma}{\gamma + \mu} - \frac{\gamma}{\beta(1 - q_1 \bar{\varphi}_1 - q_2 \bar{\varphi}_2)} \right\},$$

and $v_k^* = \bar{\varphi}_k q_k$ ($k=1, 2$). When calculating the cost of infection and vaccination, we assume the endemic steady state, Eq. (20). One can derive the effective reproductive ratio of Eqs.

$$(9)–(16), \quad R_c = \frac{\beta(1 - q_1 \bar{\varphi}_1 - q_2 \bar{\varphi}_2)}{\gamma + \mu}, \quad \text{as well as the basic reproductive ratio,}$$

$R_0 = R_c(\bar{\varphi}_1 = \bar{\varphi}_2 = 0) = \frac{\beta}{\gamma + \mu}$, using Eq (20). For measles, the estimate of a basic reproductive ratio ranges between 15 and 17 (Berger and Omer, 2010), and we set $R_0 = 15$ as a baseline parameter.

2.2 Utility Calculation for Measles Vaccination

From a game-theoretic perspective, an individual is expected to adopt a strategy that will maximize personal net payoff. An individual's decision is also subject to his or her perceptions of the costs and benefits of the vaccine, although these perceptions may deviate from epidemiological and economic reality. Consequently, our model is parameterized using the perceived costs of infection and the perceived costs of measles vaccines to determine the payoffs of a range of vaccination probabilities for individuals of each behavioral group, which amounts to the vaccination coverage for the population. Specifically, we define $c_{I,k}$ as the perceived cost per day of measles infection by an individual in group k , while $C_{V,k}$ is defined as the perceived cost of the measles vaccination, including possible adverse effects. The perceived costs of measles vaccination are likely to be greater for vaccine skeptics than for vaccine believers because of this group's perception of a greater risk of side effects ($C_{V,1} > C_{V,2}$). Similarly, the perceived costs of measles infection for vaccine skeptics are assumed to be no greater than that for vaccine believers, so $c_{I,1} \leq c_{I,2}$. Thus it follows that $c_{I,1}/C_{V,1} < c_{I,2}/C_{V,2}$ if $C_{V,k} > 0$ for $k=1, 2$. This asymmetry in perceived costs is reflected in our payoff calculation. Thus, when we calculate the Nash strategy for vaccine believers, we use the best estimates of vaccine cost. By contrast, the Nash strategy among vaccine skeptics is

calculated using vaccine cost that is assumed to be larger than the normative cost. For illustration purpose, we set the vaccine cost among vaccine skeptics to be twice as large as the normative cost; however, for sensitivity analysis, we vary the perceived cost of measles vaccination among vaccine skeptics in order to find the impact of misperceptions about the risks of vaccine on the demand for vaccine.

In our game-theoretic model of disease transmission and vaccination, vaccination behavior is modeled at the scales of both the population and the individual. We formulate our model as a population game, where the payoff of measles vaccination depends on both the individual's decision and the population's average behavior. Thus, the net payoff of measles vaccination is dependent on the probability of infection (determined by disease incidence), which is governed by the vaccination decisions made by the rest of the population. It is worth to note that increased infections are autocatalytic, but also lead to changed calculation of vaccine benefits, resulting in increased vaccination.

We define $\mathbf{n}_k(t)$ as the distribution of individuals who belong to behavioral group k in each of the four possible epidemiological states ($k=1, 2$). The population-scale dynamics satisfy a system of ordinary differential equations G (Eqs. 9–16), where the rates of change in the states of the population depend on the average vaccination decision of behavioral group k , $\bar{\varphi}_k$ ($k=1, 2$). Thus, the vaccination state (n_k) on the population scale is described by the equation

$$d\mathbf{n}_k/dt = G(\mathbf{n}_k, \bar{\varphi}_k). \quad \text{Eq. 21}$$

Using Eq. (21) and initial conditions, we can determine $\mathbf{n}_k(t, \bar{\varphi}_k)$.

An individual-scale model is modeled as a Markov process with transition rates derived from the population-scale model, Eqs. (9) – (16). Here we define $\mathbf{x}_k(t)$ as an individual's probability density over the life-history state space with a vaccination strategy, φ_k , at time t ($k=1, 2$). Therefore, assuming that the population has reached the endemic steady state distributions, $\mathbf{n}_k^*$, the state of an individual is described by

$$d\mathbf{x}_k/dt = Q_k(\mathbf{n}_k, \varphi_k) \mathbf{x}_k \quad \text{Eq. 22}$$

Here Q_k is the transition-rate matrix of the life-history process in behavioral group k , which is defined as

$$Q_k(\mathbf{n}_k^*, \varphi_k) = \begin{bmatrix} -\lambda - \mu & 0 & 0 & 0 \\ \lambda & -\gamma - \mu & 0 & 0 \\ 0 & \gamma & -\mu & 0 \\ 0 & 0 & 0 & -\mu \end{bmatrix}, \quad \text{Eq. 23}$$

where $\lambda = \beta(i_1^* + i_2^*)$. All individuals enter the population as either susceptible or immunized newborns, depending on their parents' vaccination strategy (φ_k), so the initial state of an individual in behavioral group k is given by:

$$\mathbf{x}_k(0) = [1 - \varphi_k, 0, 0, \varphi_k]^T. \quad \text{Eq. 24}$$

Since transition-rate matrix (Q_k) is determined by $\mathbf{n}_k(t, \bar{\varphi}_k)$, the individual's probability density over the life-history state in Eq. (22) is dependent on both the individual's measles

vaccination strategy, ϕ_k , and the average vaccination strategy of behavioral group k , $\bar{\phi}_k$, by way of its impact on disease incidence.

The instantaneous payoff gains for a Markov process can be represented in terms of a vector (f) of gains per unit of time for residents of each state and a vector (F) of instantaneous payoff gains associated with each transition. Using these definitions, it follows that

$$f_k = [0, -c_{I,k}, 0, 0]^T, \quad \text{Eq. 25}$$

$$F_k = [0, 0, 0, -C_{V,k}]^T \quad \text{Eq. 26}$$

By applying the Bellman equation for a continuous-time Markov process (Bellman, 1957), we calculate the expected present values of each state, conditional on the measles vaccination strategy. The expected present value is calculated based on the probabilities of all future events and discounted future costs relative to immediate costs. Thus, the expected payoff is

$$U_k = F_k x_k(0) + \int_0^\infty e^{-\delta t} f_k^T x_k(t) dt, \quad \text{Eq. 27}$$

where δ is a positive discount rate ($\delta=0.03/\text{yr}$). As the time horizon of the payoff calculation becomes infinitely long ($t_f \rightarrow \infty$), the expected payoff has the closed form,

$$U_k = [F_k^T + f_k^T (\delta I - Q_k^*)^{-1}] x_k(0). \quad \text{Eq. 28}$$

Using Eqs. (23) and (24), one can reduce Eq. (28) to

$$U_k = -\phi_k C_{V,k} - (1 - \phi_k) c_{I,k} \left(\frac{\lambda^*}{\delta + \lambda^* + \mu} \right) \left(\frac{1}{\delta + \gamma + \mu} \right) \quad \text{Eq. 29}$$

where $\lambda = \beta(i_1^* + i_2^*)$, as determined by the non-uniform endemic steady state distribution, Eq. (20). Unless otherwise specified, we used the following as a baseline parameter set for simulations: $q_I=0.3$, $q_2=0.7$, $\beta=2.14/\text{day}$, $1/\gamma=7$ days, $1/\mu=12410$ days, $C_{V,1}/c_{I,1}=4.8$, and $C_{V,2}/c_{I,2}=2.4$ (Tables 1 and 2).

Calculation of Optimal Measles Vaccination Strategy Driven by Self-interest—

In order to determine the Nash strategy for the population game, we first define a region of reachable stationary incidence of measles (i_1^* , i_2^*) in Eq. (20) by varying resident strategies, $\bar{\phi}_k$ ($k=1, 2$) (Fig 1) (Reluga, 2009). For each point in the reachable region of incidence, the force of infection exerted on the individuals in a behavioral group can be uniquely determined. The endemic disease incidence of measles (i_1^* , i_2^*) decreases with an increase in the resident vaccination strategies, $\bar{\phi}_k$. We use this monotonicity of the endemic stationary solution to plot the incidence of measles in behavioral groups 1 and 2 at the endemic equilibrium, Eq. (20). Specifically, using Eqs. (17) and (18), we can derive

$$\frac{\partial i_1^*}{\partial \bar{\varphi}_1} = -q_1 \left\{ \frac{\mu}{\gamma+\mu} - \frac{\mu}{\beta(1-q_1\bar{\varphi}_1-q_2\bar{\varphi}_2)} \right\} - q_1(1-\bar{\varphi}_1) \left\{ \frac{\mu q_1}{\beta(1-q_1\bar{\varphi}_1-q_2\bar{\varphi}_2)^2} \right\} \quad \text{Eq. 30}$$

and

$$\frac{\partial i_1^*}{\partial \bar{\varphi}_2} = -q_1(1-\bar{\varphi}_1) \left\{ \frac{\mu q_2}{\beta(1-q_1\bar{\varphi}_1-q_2\bar{\varphi}_2)^2} \right\} \quad \text{Eq. 31}$$

Thus, $\frac{\partial i_1^*}{\partial \bar{\varphi}_1} \leq 0$ and $\frac{\partial i_1^*}{\partial \bar{\varphi}_2} \leq 0$ when $\bar{\varphi}_1 \in [0,1)$ and $\bar{\varphi}_2 \in [0,1)$, provided that $R_c > 1$. Note that if no one in behavioral group 1 is vaccinated against measles, i.e. $\bar{\varphi}_1=0$, Eq. (17) becomes

$$\beta(i_1+i_2)(q_1-i_1-\frac{\gamma}{\mu}i_1)=(\gamma+\mu)i_1. \quad \text{Eq. 32}$$

Similarly, if the measles vaccine coverage in behavioral group 2 is zero, i.e. $\bar{\varphi}_2=0$, Eq. (18) becomes

$$\beta(i_1+i_2)(q_2-i_2-\frac{\gamma}{\mu}i_2)=(\gamma+\mu)i_2. \quad \text{Eq. 33}$$

The feasible domain of endemic equilibria can be drawn based on Eqs. (32) and (33). The right boundary of the reachable region corresponds to $\phi_I=0$, whereas the top boundary of the reachable region corresponds to $\phi_2=0$.

In a game-theoretic context, individuals are strategists who strive to maximize their expected payoff. Thus, the Nash strategy for a population game described by Eqs. (9)-(16) is the best response that maximizes the expected payoff, Eq (29). Differentiating U_k with respect to φ_k , we find that the Nash strategy is given by

$$\operatorname{argmax}_{\varphi_k} U_k(\varphi_k, \bar{\varphi}_1, \bar{\varphi}_2) = \begin{cases} 0 & \text{if } \lambda < \lambda_k^+ \equiv \frac{C_{V,k}(\delta+\mu)(\delta+\gamma+\mu)}{c_{I,k}-C_{V,k}(\delta+\gamma+\mu)}, \\ [0, 1] & \text{if } \lambda = \lambda_k^+, \\ 1 & \text{if } \lambda > \lambda_k^+, \end{cases} \quad \text{Eq. 34}$$

The Nash strategies (Eq. 34) are step functions, as shown in the individual payoff, Eq. (29). The Nash strategy for the population game (Eqs. 9–16) can be determined by examining the threshold forces of infection (λ_k^+) over the reachable region (Fig 1). Specifically, if the force of infection is below the threshold λ_k^+ in behavioral group k , the Nash strategy is to refuse vaccination ($\varphi_k^*=0$), as shown in Eq. (34). For a special case, if the disease incidence at endemic steady states in the absence of vaccination is below both threshold forces of infection—that is, $\lambda(\bar{\varphi}_1=\bar{\varphi}_2=0) < \lambda_1^+$ and $\lambda(\bar{\varphi}_1=\bar{\varphi}_2=0) < \lambda_2^+$ —then the resulting Nash strategy for both sub-populations will be to refuse vaccination ($\varphi_1^*=\varphi_2^*=0$).

On the other hand, individuals accept vaccination ($\varphi_k^*=1$) if the force of infection is above the threshold value λ_k^+ (see Eq. 34); for instance, if the threshold forces of infection are negative ($\lambda_1^+ < 0$ and $\lambda_2^+ < 0$)—that is, $c_{I,k}/C_{V,k} - (\delta+\gamma+\mu) < 0$ ($k=1,2$)—then the Nash strategy is complete vaccine coverage ($\varphi_1^*=\varphi_2^*=1$) for both behavioral groups. Finally, if the force

of infection is exactly the threshold value, the individual payoff will be the same for all vaccination strategies. Therefore, the Nash strategy $(\varphi_1^*, \varphi_2^*)$ can be obtained by solving for vaccination strategies (φ_k^*) at the intersection of $\lambda = \lambda_1^+$ and $\lambda = \lambda_2^+$ within the reachable region. In this case, one or both behavioral groups may prefer some intermediate vaccination level. Specifically, if λ_k^+ is non-zero but sufficiently low, there is a unique Nash equilibrium with some level of vaccination propensity among vaccine believers and less-than-complete vaccination among vaccine skeptics.

Vaccine skeptics have a higher threshold than vaccine believers $(\lambda_1^+ > \lambda_2^+)$ because of the

inequality, $\delta + \gamma + \mu < \frac{c_{I,1}}{C_{V,1}} < \frac{c_{I,2}}{C_{V,2}}$ if $C_{V,k} = 0$ for $k=1, 2$. Note that, from Eq. (34), thresholds $\lambda = \lambda_1^+$ and $\lambda = \lambda_2^+$ do not cross, so no incidence of measles in the feasible region of incidence imposes forces of infection at threshold levels for both behavioral groups simultaneously.

2.4 Calculation of optimal vaccination strategy driven by group interest

The average payoff for the population is defined as the total societal cost per individual, and the utilitarian strategy is calculated by maximizing the expected average payoff (Bauch and Earn, 2004). Because the utilitarian strategy is the normatively optimal solution (often determined at a policy level), the best estimate of the parameters of infection and vaccination cost is used as a baseline parameter. Using endemic non-uniform steady state distributions, we can further calculate the average payoff:

$$\Omega = -\varphi \cdot C_V \frac{(1-\varphi) \cdot \Delta \cdot c_I}{(\Delta + \mu + \delta)(\gamma + \mu + \delta)} = -\varphi \cdot C_V - \frac{(1-\varphi)\mu \cdot c_I}{\gamma + \mu + \delta} \left\{ \frac{(1-\varphi)\beta - (\gamma + \mu)}{(1-\varphi)\beta\mu + \delta + (\gamma + \mu)} \right\}$$

where $A = \beta\mu \left(\frac{1-\varphi}{\gamma + \mu} - \frac{1}{\beta} \right)$. Note that $\frac{\partial \Omega}{\partial \varphi} = 0$ if and only if

$$\begin{aligned} \varphi_{\pm} &= \frac{\{\delta(\gamma + \mu) + \beta\mu\}\{c_I - C_V(\gamma + \mu + \delta)\} \pm (\gamma + \mu) \sqrt{c_I \delta(\mu + \delta)\{c_I - C_V(\gamma + \mu + \delta)\}}}{\{c_I - C_V(\gamma + \mu + \delta)\}\beta\mu} \\ &= 1 + \frac{\delta(\gamma + \mu)}{\beta\mu} \pm \frac{(\gamma + \mu) \sqrt{c_I \delta(\mu + \delta)}}{\beta\mu \sqrt{c_I - C_V(\gamma + \mu + \delta)}}. \end{aligned}$$

It follows that $\frac{\partial^2 \Omega}{\partial \varphi^2} \Big|_{\varphi=\varphi_+} = \frac{2\beta\mu\{c_I - C_V(\gamma + \mu + \delta)\}^2}{(\gamma + \mu + \delta)(\gamma + \mu) \sqrt{c_I \delta(\mu + \delta)\{c_I - C_V(\gamma + \mu + \delta)\}}}$ and

$$\frac{\partial^2 \Omega}{\partial \varphi^2} \Big|_{\varphi=\varphi_-} = \frac{-2\beta\mu\{c_I - C_V(\gamma + \mu + \delta)\}^2}{(\gamma + \mu + \delta)(\gamma + \mu) \sqrt{c_I \delta(\mu + \delta)\{c_I - C_V(\gamma + \mu + \delta)\}}}.$$

Thus we conclude that the optimal measles vaccine coverage for the population is achieved

at $\varphi_- = 1 + \frac{\delta(\gamma + \mu)}{\beta\mu} - \frac{(\gamma + \mu) \sqrt{c_I \delta(\mu + \delta)}}{\beta\mu \sqrt{c_I - C_V(\gamma + \mu + \delta)}}$, provided that $\varphi_- \in [0, 1]$, which is satisfied with the parameter sets selected for our simulations and sensitivity analysis.

Results

We examined how the Nash vaccination levels would change as the relative sizes of vaccine skeptics and vaccine believers varied. Specifically, if the population is mostly made up of vaccine believers ($q_1=0.1$ and $q_2=0.9$), the Nash vaccination level among vaccine believers is less than complete, while the Nash strategy for vaccine skeptics is to reject measles vaccine, i.e. $\phi_1 = 0$ and $\phi_2 \in (0,1)$ (marked as a dot A in Fig 1). Thus, when both behavioral groups are vaccinated according to the Nash strategy, the resulting measles vaccine coverage in the population is 86% at baseline parameters, which is not sufficient to eradicate measles. Nevertheless, vaccine skeptics are expected to refuse measles vaccine due to their misperception on vaccine safety and/or underestimated benefits of measles vaccine. This strategy of refusing measles vaccine among vaccine skeptics was found to be consistent over the range of transmissibility of measles for a basic reproductive ratio examined ($R_0=13-17$), as long as a proportion of vaccine skeptics is less than 30% (Fig 2A).

On the other hand, when the proportion of vaccine skeptics increases to 30% of the population ($q_1=0.3$ and $q_2=0.7$), complete vaccine coverage ($\phi_2 = 1$) is expected to be achieved among vaccine believers when vaccination is dictated by the Nash strategy. However, complete vaccine coverage among vaccine believers alone is insufficient to reduce the force of infection to their threshold (λ_2^+), although it is sufficient to reduce the force of infection below the threshold of vaccine skeptics (λ_1^+). As a result, the Nash strategy for vaccine skeptics is to reject the measles vaccine ($\phi_1 = 0$) (marked as a dot B in Fig 1), while they are partially protected from infection due to vaccination of vaccine believers. In this case, the average measles vaccine coverage in the population is 70%, which is insufficient to achieve herd immunity (Figs 2B and 2C), as indicated in previous studies (Anderson and May, 1991; Berger and Omer, 2010). Therefore, an outbreak of measles is likely to occur with 70% coverage of measles vaccine, the resulting incidence of measles is estimated at 132 cases per million, and the expected probability of infection among the unvaccinated is 63% (Figs 2C and 2D).

When the proportion of vaccine skeptics increases to 40% ($q_1=0.4$), an outbreak of measles is inevitable for a range of basic reproductive ratio examined ($R_0=13-17$) (Fig 2C). In this case, the Nash vaccination strategy for vaccine believers will be to accept measles vaccination fully ($\phi_2 = 1$), while the Nash strategy of vaccine skeptics will result in less than complete vaccine coverage (as marked as a dot C in Fig 1). In other words, the Nash strategy of vaccine skeptics may lead to incomplete coverage, i.e., $\phi_1 \in (0,1)$, or refusal of measles vaccination, depending on the extent to which they overestimate the risk of the vaccine (Fig. A.1). For instance, if vaccine skeptics perceive that the cost of vaccination is twice as large as the normative cost of vaccination, their demand for measles vaccine is estimated at 9% coverage when vaccination adheres to the Nash strategy. The resulting overall measles vaccine coverage in the population would be 64% under this scenario (Figs 2A and 2B), which is much less than what is required to achieve herd immunity. Therefore, the resulting incidence of measles is estimated at 168 cases per million individuals, and the probability of infection among the unvaccinated is 63% (Figs 2C and 2D).

In general, our results indicate that the Nash vaccination level among vaccine believers is likely to increase as the proportion of vaccine skeptics increases. This is because the overall vaccine coverage in the population will decrease with the increasing proportion of vaccine skeptics, resulting in a heightened risk of infection. Similarly, the demand for measles vaccine among vaccine skeptics is expected to increase slightly when more people become vaccine skeptics. This is because the free-riding effect diminishes once vaccine coverage in the population falls below the threshold level to achieve herd immunity. When both behavioral groups are vaccinated according to the Nash strategy, the probability of infection

among vaccine skeptics increases initially as the number of vaccine skeptics increases, but it decreases once the vaccine skeptics begin receiving the vaccination (Figs 2A and 2D). This inflection occurs because the decline in herd immunity that resulted from the falling level of vaccination by vaccine skeptics generates a rebound in vaccine demand.

Nash vaccination of vaccine skeptics reveals the tradeoff between the risk of infection and vaccine cost (a function of perceived severity and probability of all potential costs and risks) (Fig 3A). At low vaccine costs, even vaccine skeptics are likely to seek vaccination. However, at higher vaccine costs, the demand for vaccination among vaccine skeptics drops dramatically, resulting in increased incidence of measles (Figs 3B). The threshold cost of vaccination at which the demand for vaccine starts to drop increases with a basic reproductive ratio (Fig 3A); that is, the more transmissible a disease becomes, the lower the barrier to vaccination becomes among vaccine skeptics.

In order to examine the impact of heterogeneity in risk perception on vaccine uptake, the Nash vaccination was simulated as the perceived cost of vaccination was varied relative to the cost of infection (Fig 4). Specifically, the vaccine risk perception of two behavioral groups ($C_{V,1}/c_{I,1}$ and $C_{V,2}/c_{I,2}$) was varied while the average vaccine risk perception in

population ($q_1 \cdot \frac{C_{V,1}}{c_{I,1}} + q_2 \cdot \frac{C_{V,2}}{c_{I,2}}$) was kept constant. Here, remained constant at its baseline values ($q_1 = 0.3$ and $q_2 = 0.7$), and the simulation was initiated with the case where both behavioral groups had the same risk perception ($C_{V,1}/c_{I,1} = C_{V,2}/c_{I,2} = 3.4$), resulting in a relatively high overall vaccine coverage. Then the risk perception ($C_{V,1}/c_{I,1}$) for vaccine skeptics was increased, whereas $C_{V,2}/c_{I,2}$ was decreased accordingly so that the average vaccine risk perception remained constant. This was achieved by weighting the risk perception according to the sizes of two behavioral groups (q_i). Finally, the risk perception among vaccine skeptics ($C_{V,1}/c_{I,1}$) was increased until the baseline scenario was recovered, i.e. ($C_{V,1}/c_{I,1} = 4.8$) and $C_{V,2}/c_{I,2} = 2.4$. Fig 4 indicates that, generally speaking, the resulting overall vaccine coverage is higher with increasing heterogeneity in risk perception, qualitatively consistent with previous findings (Cojocaru et al., 2007). Furthermore, it is shown that vaccine coverage is higher in a population where there is a minority group that overestimates the risk of vaccines (Cojocaru et al., 2007).

When both behavioral groups are vaccinated according to the utilitarian strategy, levels of measles incidence are significantly lower than they are when vaccination adheres to the Nash strategy (Figs 3 and 5). For the current vaccine cost (value of 2.4 on the x axis of Figs 3B and 5B), the incidence of measles was estimated to be 40 lower per million individuals if vaccination adheres to the utilitarian strategy than if vaccination is guided by the Nash strategy (Figs 3B and 5B). The gap between the incidence of measles under the Nash and utilitarian vaccination strategies becomes wider as the perceived cost of vaccination increases among vaccine skeptics (Figs 5A and A.2). This is because utilitarian vaccination is less elastic to increasing vaccine cost than the Nash vaccination over the wide range of R_0 examined (Figs 3A, 5A, and A.2). For instance, if the vaccine were perceived twice as risky/costly, it is predicted that vaccine skeptics would refuse measles vaccine, leading to a incidence level of 132 cases per million individuals, compared to a prediction of 22 cases per million with the utilitarian vaccination strategy.

Discussion

Using our proposed model, we identified discrepancies between vaccination strategies driven by self-interest among vaccine skeptics and vaccine believers. As such, we evaluated an expected coverage of measles vaccine for vaccine skeptics, that is, individuals who may overestimate the risk of vaccines and/or underestimate the risk of infection. We also

compared the Nash and utilitarian strategies for measles vaccination implementation and the potential public health repercussions of imperfect adherence.

Our results show that the pursuit of self-interest is likely to lead to sub-optimal implementations of vaccination policies and increased risk of measles outbreak, especially in the presence of vaccine skeptics. The vaccine coverage level governed by utilitarian strategy is 95% with baseline parameters ($R_0=15$) (Figs 5A). In comparison to the utilitarian vaccination strategy, the vaccine coverage determined by the Nash strategy is generally lower, and Fig 2C indicates that the discrepancy between the Nash strategy and the utilitarian strategy increases with an increasing proportion of vaccine skeptics. Furthermore, perceived cost of vaccination among vaccine skeptics (e.g. perceived barriers to vaccination such as overestimated risk of measles vaccines) may also lower their vaccine uptake, widening the gap between the Nash strategy and the utilitarian strategy (Figs A2). Nevertheless, the discrepancy between the Nash strategy and the utilitarian strategy was found to be more sensitive to a proportion of vaccine skeptics than to the extent to which vaccine skeptics overestimate the risk of vaccines (Figs 2C, 5A and A2).

Measles vaccines have stopped the wide spread of measles in the US, so the memory of measles has faded from the public consciousness. Without the memory of the damage the disease can do, the perceived risks of vaccination in some parents' minds have begun to outweigh their perceptions of the benefits of vaccination (Omer et al., 2009). According to a survey of fellows of the American Academy of Pediatrics (AAP) on immunization-administration practices, MMR vaccine was listed as the most frequently refused vaccine, followed by varicella vaccine, pneumococcal conjugate vaccine, hepatitis B vaccine, and diphtheria and tetanus toxoids and pertussis vaccines (Diekema). As a result, measles vaccine refusal triggered the largest measles outbreak in ten years in the US in 2008, infecting at least 127 individuals in 15 states. Parents who choose not to vaccinate their own children increase the risk of infection not only for their children, but also for the whole community, including vulnerable newborns too young to have received vaccines (Omer et al., 2009).

Major reasons for vaccine refusal were found to be a low level of concern about the risk of infection, parental perceptions of effectiveness of vaccine, and concerns about vaccine safety (Omer et al., 2009), all of which may reduce the perceived benefits of vaccination. Media messages about even a single adverse vaccine event can quickly change behavior, leading to major declines in vaccine coverage. Furthermore, when there is high vaccine coverage in a population, there is little individual incentive to vaccinate, since unvaccinated individuals derive protection through herd immunity. Therefore, if the perceived risk of vaccination increases sufficiently, vaccine coverage levels could drop because of the temptation to free-ride.

A limitation of the model is that it does not account for quality-of-life impacts due to morbidity from the disease or vaccine adverse events, although most adverse reactions after receipt of MMR vaccine are generally mild (Zhou et al., 2004). Minor reactions to MMR vaccine include local pain, rash, fever, and vomiting (Zhou et al., 2004). Although our model does not explicitly include the cost associated with vaccine adverse events, we varied the perceived cost of vaccination for sensitivity analysis in order to incorporate a range of misperception on vaccine side effects. Such misperception might include, for instance, perceived morbidity of autism, as shown during MMR vaccine scare in the UK (Jansen et al., 2003). Another limitation of our model is that we assume homogeneous mixing for the transmission of measles. If heterogeneity in contact patterns was assumed instead (using assortative mixing, for instance), the gap between Nash vaccination levels among vaccine believers and vaccine skeptics would have been much reduced, although the resulting Nash

vaccination level would have been still higher for vaccine believers than for vaccine skeptics. This is because the indirect protection through a high level of vaccine uptake among vaccine believers would not be shared as much with vaccine skeptics, if contacts **between** two behavioral groups are significantly reduced.

There has been an increasing interest in the application of mathematical models in addressing questions of behavioral determinants of health outcomes. These studies have integrated an understanding of how individuals behave and respond to recommended intervention strategies into computational models of disease epidemiology (Bauch and Earn, 2004; Bauch et al., 2003; Bauch et al., 2010; Chen, 2006; Cojocaru et al., 2007; Cornforth et al.; Fine and Clarkson, 1986; Francis, 2004; Galvani et al., 2007; Reluga, 2009; Reluga et al., 2006; Shim et al., 2009; Shim et al., 2010a; Shim et al., 2010b). The game-theoretic epidemiological model we propose can yield insights into the interplay between anti-vaccine behavior, vaccine coverage, and disease dynamics. An individual's vaccination decision depends on the perception of the benefits of vaccination, and these decisions affect the degree of population-level immunity and the force of infection in the population. Our study demonstrates that if the enormous benefits to society from measles vaccination are to be maintained, the public will need to be educated about those benefits in order to increase public confidence as we monitor and ensure vaccine safety (Omer et al., 2009). In future studies, we will examine the sensitivity of this analysis to the underlying assumptions of game theory. In particular, we will investigate the effects of relaxing the assumptions of homogeneous behavior among vaccine skeptics and vaccine believers, and the assumption of perfect rationality as well as the access to perfect population-level information. Furthermore, perceptions on benefits of vaccine can vary over time, based on observed complications and observed measles cases; thus in future studies, we will explore the impact of varying perceptions over time on the relative proportion of vaccine skeptics and vaccine believers.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- We proposed a game-theoretic model of measles transmission.
- The impact of perceived vaccine risks on the vaccine uptake was examined.
- The vaccination levels driven by self-interest may be suboptimal for a population.
- Measles vaccine uptake is highly dependent on the number of vaccine skeptics.
- Education about the vaccine safety is required to maintain herd immunity.

Figure 1.

Plots of the reachable region of disease incidence (i_1, i_2) and the threshold forces of infection under various resident strategies, $(\bar{\varphi}_1, \bar{\varphi}_2)$. Each plot corresponds to the relative proportion of vaccine skeptics ($q_I=0.1, 0.3$ and 0.4). The right boundary of the reachable region corresponds to $\bar{\varphi}_1 = 0$, and the top boundary of the reachable region corresponds to $\bar{\varphi}_2 = 0$. The threshold forces of infection are plotted as lines over the reachable regions of disease incidence. Specifically, dotted and solid lines indicate the threshold force of infection of behavioral groups 1 ($i_1^* + i_2^* = \lambda_1^+ / \beta$) and 2 ($i_1^* + i_2^* = \lambda_2^+ / \beta$), respectively. Depending on the relative size of behavioral groups and the balance between the cost of vaccination and the cost of infection, there may be various types of Nash strategies (marked by dots) for the population game, Eqs. (9)-(16). If the proportion of vaccine skeptics is relatively small ($q_I=0.1, q_Z=0.9$), then the resulting Nash strategy is $\bar{\varphi}_1=0$ and $\bar{\varphi}_2 \in (0,1)$, marked as a dot A. If the proportion of vaccine skeptics is 30% of the population ($q_I=0.3, q_Z=0.7$), then the resulting Nash strategy is $\bar{\varphi}_1=0$ and $\bar{\varphi}_2=1$, marked as a dot B. Finally, if the proportion of vaccine skeptics is 40% of the population ($q_I=0.4, q_Z=0.6$), the resulting Nash equilibrium is $\bar{\varphi}_1 \in (0,1)$ and $\bar{\varphi}_2=1$ (marked as a dot C).

Figure 2.

The effects of the proportion of vaccine skeptics on the demand for measles vaccine and on the resulting measles incidence, when both behavioral groups are assumed to vaccinate according to the Nash strategy. (A) Coverage of measles vaccine among vaccine skeptics increases with the proportion of vaccine skeptics and with a basic reproductive ratio. (B) Overall measles vaccine coverage in the population, combining both vaccine skeptics and vaccine believers, decreases with the proportion of vaccine skeptics. (C) The incidence of measles when vaccination levels are at the Nash equilibrium increases with the proportion of vaccine skeptics. (D) The probability of infection among the unvaccinated increases initially as the number of vaccine skeptics increases, but it decreases once vaccine skeptics starts to

accept vaccination due to heightened risk of infection. In this case, the vaccine believers always vaccinate with baseline parameters, so all unvaccinated individuals are vaccine skeptics.

Figure 3.

Sensitivity analysis of the vaccination decision among vaccine skeptics when the cost of vaccination relative to the daily cost of infection ($C_{V,1}/c_{I,1}$) varies. A basic reproductive ratio is varied from 13 to 17, and it is assumed that $q_I=0.3$ for illustration purpose. (A) The Nash strategy dictates whether to get a vaccination or not, depending on the relative cost of vaccination. With an increasing cost of vaccination, vaccine skeptics are less likely to vaccinate. (B) The incidence of measles under the Nash vaccination strategy increases with the relative cost of vaccination. (C) When the level of vaccination adheres to the Nash strategy, the probability of infection among the unvaccinated increases with the relative cost of vaccination.

Figure 4.

The impact of heterogeneity in risk perception on vaccine uptake. The Nash vaccination for both behavioral groups is examined as the relative (perceived) cost of vaccination, i.e., $C_{V,i}/c_{I,i}$ is varied. Here, q_i was kept constant at its baseline values ($q_1 = 0.3$ and $q_2 = 0.7$), and

the average vaccine risk perception in population ($q_1 \cdot \frac{C_{V,1}}{c_{I,1}} + q_2 \cdot \frac{C_{V,2}}{c_{I,2}}$) was fixed at 3.4. The risk perception ($C_{V,1}/c_{I,1}$) for vaccine skeptics was increased while $C_{V,2}/c_{I,2}$ is decreased accordingly so that the average vaccine risk perception is kept constant. The resulting overall vaccine coverage increases when heterogeneity in risk perception is introduced into the model.

Figure 5.

Utilitarian measles vaccination strategy and its impact on the incidence of measles. (A) The measles vaccine coverage level dictated by the utilitarian strategy decreases as the cost of vaccination rises and the basic reproductive ratio falls. (B) Measles is likely to become epidemic when the relative cost of vaccination compared to that of infection (C_V/c_I) is over 3.5, at the range of basic reproductive ratios considered (i.e., 13–17).

Table 1**Cost of Measles Vaccination**

Variable	Value	Weighted average *	Reference
Price of MMR vaccine (per dose)	\$18.64 (public) \$50.16 (private)	\$42.60	(CDC, 2011)
Administrative cost (per dose)	\$7.03 (public) ** \$25.06 (private) **	\$20.73	(Zhou et al., 2005)
Travel cost for a round trip	\$4.70		(Zhou et al., 2004)
Two hours of time-off from work to take the child for vaccination	\$22.85 **		(Zhou et al., 2005)
Total vaccination cost for two doses		\$181.76	

* We assumed that 76% of children obtain their measles vaccines from private health care providers, and 24% from public providers (Zhou et al., 2005).

** 2001 costs were inflated to 2011 costs

Table 2

Disease costs

Disease Costs	Average direct cost per case	Reference
Uncomplicated (85%) *	\$150	(Miller et al., 1998)
Hospitalized (15%) *	\$2,659	(Miller et al., 1998)
Weighted average	\$526	
Average cost per day of infection	\$75	

* Inflated from 1997 to 2011 costs