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Prevention of treatable infectious diseases: A game-theoretic approach

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ABSTRACT

We model outcomes of voluntary prevention using an imperfect vaccine, which confers protection only to a fraction of vaccinees for a limited duration. Our mathematical model combines a single-player game for the individual-level decision to get vaccinated, and a compartmental model for the epidemic dynamics. Mathematical analysis yields a characterization for the effective vaccination coverage, as a function of the relative cost of prevention versus treatment; note that cost may involve monetary as well as non-monetary aspects. Three behaviors are possible. First, the relative cost may be too high, so individuals do not get vaccinated. Second, the relative cost may be moderate, such that some individuals get vaccinated and voluntary vaccination alleviates the epidemic. In this case, the vaccination coverage grows steadily with decreasing relative cost of vaccination versus treatment. Unlike previous studies, we find a third case where relative cost is sufficiently low so epidemics may be averted through the use of prevention, even for an imperfect vaccine. However, we also found that disease elimination is only temporary—as no equilibrium exists for the individual strategy in this third case—and, with increasing perceived cost of vaccination versus treatment, the situation may be reversed toward the epidemic edge, where the effective reproductive number is 1. Thus, maintaining relative cost sufficiently low will be the main challenge to maintain disease elimination. Furthermore, our model offers insight on vaccine parameters, which are otherwise difficult to estimate. We apply our findings to the epidemiology of measles.
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1. Introduction

The 20th century has witnessed tremendous achievements in infectious disease prevention, especially with the development of effective preventive vaccines [1], often far less costly than treatment [2]. Still, the preference between prevention and treatment remains a dilemma. Some studies found no preference [3–5], others a preference for prevention [6,7], or a preference for treatment [8,9], or that preference for prevention versus treatment depends on the circumstances [10,11].

The prevention of treatable infectious diseases still poses challenges for public health authorities [12]. Faced with infection risk, individuals may decide to use prevention, or else get treated if they acquired infection. Whereas treatment is generally well accepted by infected individuals, prevention may have a wide range of acceptability profiles for the susceptible. Individual-level perceptions of risk, as well as weighing pros and cons of prevention versus treatment, may differ from the recommendations of the public health authority [13], for a variety of reasons [14,15].

The decision to use voluntary vaccination and its impact on disease transmission has been theoretically studied using mathematical models with two components: one describing the population-level epidemiology and another describing the strategy by which an individual makes his choice of whether or not to get vaccinated [16–39]. Both compartmental models [16–18,28,33–39] and social networks [19–22] have been used as the population-level model component. For the individual-level component, imitation dynamics [22,23,39], "wait and see" strategies [38], social distancing strategies [24,25], maximization of the utility of prevention [16,26–31] and inductive reasoning [33–36] have been studied. The role of altruism for the individual-level strategy has also been considered [32]. Several modeling studies discuss the impact of public misperceptions about vaccination programs on vaccination uptake [16,23,27,28,22].

The main research direction of the modeling work has been individual and group behavior in the dilemma of whether or not to get vaccinated [16–20,22–32,37–39]. Another direction has been vaccination subsidies and incentives [21,33–36]. A review of recent literature can be found in Ref. [40].

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The purpose of the current work is to assess the performance of a voluntary prevention program, utilizing an imperfect vaccine, which confers protection only to a fraction of vaccinees for a limited duration. We show that voluntary vaccination with an imperfect vaccine may temporarily eliminate epidemics. We apply our findings to the measles epidemiology.

2. Model

We propose a mathematical model describing the interplay between voluntary vaccination and treatment during the course of an epidemic. In particular, our model addresses the setup where vaccination is available as a prevention method against childhood infectious diseases. However, we assume that the vaccine is imperfect [41,42]. We consider two aspects of vaccine failure and introduce appropriate parameters. First, the vaccine may not take for all vaccinees; the fraction of vaccinees for which the vaccine yields an immune response is called *vaccine efficacy*. This has been largely used to model voluntary vaccination [27–29,32,38,39]. In this case, the key epidemiological concept is the *effective vaccination coverage* [43,44], the fraction of the population that acquires immunity due to vaccination. Second, even if the vaccinee acquires an immune response, this may not result in lifelong immunity. That is, the vaccinee acquires a limited *duration of immunity*, a feature much less studied in the modeling of voluntary vaccination [20].

We describe epidemic dynamics using an *SEIR*-type system of ordinary differential equations. Recovery may be reached naturally or through treatment, which may be either symptomatic or therapeutic. Furthermore, we involve an individual-level model of decision-making about whether or not to get vaccinated. We assume that individuals make their decisions by judging pros and cons for vaccination versus treatment, and have a sense of the imminence of getting infected and then treated. According to game theory, such a decision-making process may be modeled as a *non-cooperative game*, where individuals act in their own interest to maximize the utility of vaccination versus treatment. However, an individual's decision is indirectly influenced by those of others: the sum of all individuals' decisions determines the proportion of the population that gets vaccinated, which, in turn, affects the epidemic progression and the probability of acquiring infection. The game model is intertwined with the model of epidemic dynamics. Model analyses assume that the resolution of the dilemma of vaccination versus treatment yields stable disease epidemiology.

2.1. The compartmental model

We make further assumptions for our deterministic *SEIR*-type model. The vaccination program is constantly in place, regardless of whether or not there is an epidemic. Treatment is available in unlimited supply, and no decision-making is involved about when to start treatment. Complete recovery is possible, with the benefit of lifelong immunity. These assumptions lead to the following ordinary differential equations of *SEIR* type:

$$\begin{aligned}
\tfrac{dV}{dt} &= \epsilon p\,\pi - (\rho+\mu)V,\\
\tfrac{dS}{dt} &= (1-\epsilon p)\,\pi + \rho V - \tfrac{\beta I}{N} S - \mu S,\\
\tfrac{dE}{dt} &= \tfrac{\beta I}{N} S - (\nu+\mu)E,\\
\tfrac{dI}{dt} &= \nu E - (\sigma+\gamma+\mu)I,\\
\tfrac{dR}{dt} &= (1-\xi)\,\sigma I + \gamma I - \mu R,\\
\tfrac{dT}{dt} &= \xi\,\sigma I - \mu T.
\end{aligned} \tag{1}$$

Newborns can remain susceptible (S) or acquire vaccine-induced immunity (V), in which case they may become susceptible thereafter, as vaccine-induced immunity wanes. Recently infected individuals (E) pass through a latent stage of infection. Then, they become infectious (I) and can recover either naturally (R) or through treatment (T). The total population size is given by $N = V + S + E + I + R + T$.

The probability of getting vaccinated is denoted by p and the vaccine parameters are ϵ, the vaccine efficacy, and ρ, the rate of waning of vaccine-induced immunity. The parameter π stands for the inflow of newborns, μ is the disease-unrelated death rate, β stands for the disease transmissibility, ν for the progression through the latency stage, σ is the rate at which individuals start treatment, ξ represents the treatment efficacy and γ is the natural recovery rate. All variables and parameters are positively defined.

The model has two equilibria: a disease-free state (DFS) where

$$V_{\mathrm{DFS}} = \frac{\epsilon p \pi}{\rho+\mu}, \quad S_{\mathrm{DFS}} = \frac{\rho \epsilon p \pi}{\mu(\rho+\mu)} + \frac{(1-\epsilon p)\pi}{\mu}, \tag{2}$$

and $E_{\mathrm{DFS}} = I_{\mathrm{DFS}} = R_{\mathrm{DFS}} = T_{\mathrm{DFS}} = 0$, and an endemic state (ES) where all the equilibrium components are non-zero

$$\begin{aligned}
&V_{\mathrm{ES}} = \frac{\epsilon p \pi}{\rho+\mu}, \quad S_{\mathrm{ES}} = \frac{\pi}{\mu R_0}, \quad I_{\mathrm{ES}} = \frac{\pi}{\beta}(R^*-1),\\
&E_{\mathrm{ES}} = \frac{\sigma+\gamma+\mu}{\nu} I_{\mathrm{ES}}, \quad R_{\mathrm{ES}} = \frac{(1-\xi)\sigma+\gamma}{\mu} I_{\mathrm{ES}}, \quad T_{\mathrm{ES}} = \frac{\xi\sigma}{\mu} I_{\mathrm{ES}},
\end{aligned} \tag{3}$$

where

$$R^* = \left(1 - \frac{\epsilon p \mu}{\rho+\mu}\right) R_0, \tag{4}$$

and

$$R_0 = \frac{\beta \nu}{(\nu+\mu)(\sigma+\gamma+\mu)}. \tag{5}$$

R^* is called the *effective reproduction number*, representing the expected number of secondary cases produced by a single infectious individual within a disease-naive population. It is important to note that, in a population undergoing disease prevention, R^* depends on the level of disease susceptibility. In our case, R^* is a function of p, the probability of getting vaccinated. The *SEIR*-type model (1) undergoes a transcritical bifurcation [45] at $R^* = 1$. If $R^* > 1$, then ES will be reached; otherwise, $R^* \leqslant 1$ and DFS will be reached. R_0 is the *basic reproduction number* [46,47,45], obtained from the model in the absence of prevention (i.e., $p = 0$). To quantify the impact of vaccination on epidemics, we analyze $R^*(p)$ given that there is an epidemic in absence of vaccination; i.e., $R_0 > 1$.

Using Eqs. (2) and (3), the *endemic prevalence* of the infectious disease can be written as

$$\Pi(p) = \begin{cases} \Pi_{\mathrm{DFS}}(p), & \text{if } R^* \leqslant 1,\\ \Pi_{\mathrm{ES}}(p), & \text{if } R^* > 1; \end{cases} \tag{6}$$

where

$$\Pi_{\mathrm{DFS}}(p) = \frac{I_{\mathrm{DFS}} + E_{\mathrm{DFS}}}{N_{\mathrm{DFS}}} = 0, \tag{7}$$

and

$$\Pi_{\mathrm{ES}}(p) = \frac{I_{\mathrm{ES}} + E_{\mathrm{ES}}}{N_{\mathrm{ES}}} = \frac{\mu}{\beta}\left(1 + \frac{\sigma+\gamma+\mu}{\nu}\right)(R^*(p) - 1). \tag{8}$$

A critical vaccination coverage, p_c, may be defined using $R^*(p_c) = 1$ or, equivalently, $\Pi_{\mathrm{ES}}(p_c) = 0$, and verifies

$$\epsilon p_c = \left(1 + \frac{\rho}{\mu}\right)\left(1 - \frac{1}{R_0}\right). \tag{9}$$

A similar formula is provided in Ref. [41, Eq. (8)]. In the case of a perfect vaccine (i.e., $\rho = 0$ and $\epsilon = 1$), Eq. (9) recovers a well-known result; see Refs. [46, p. 87] and [47, ch. 6].

A diagram of disease prevalence at the equilibria of the *SEIR*-type model (1), as a function of p, is shown in Fig. 1. ES is always

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