The Bioethics of Infecions

A Modeler Perspective

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Abstract

Bioethics should take into account conflicts between individuals and the community such as the conflict arisen by vaccination against infectious diseases. The aim of this paper is to present a modeler perspective of the ethical issues raised by the conflicts arisen by the attempt to control infectious diseases through vaccination. We aim to propose that mathematical models can help in the design of vaccination strategies that minimizes adverse effects and the harm imposed by the infection at the same time. We apply the concepts of game theory, with a particular emphasis on Nash equilibria of population games related to the decision of the persons to accept the vaccine preemptly offered in mass vaccination campaigns, versus the decision of be vaccinated only in case of outbreaks. We argue that the use of mathematical models for designing immunization strategies should be an ethical priority since they help minimize the conflict between the interests of individuals and those of society at large.

Keywords

Bioethics; Infectious Diseases; Vaccination; Mathematical Models; Smallpox; Yellow Fever; Poliomyelitis

Introduction

Much of the work of early bioethics consisted in the discussion of dilemma-cases (Battin et al., 2009). The core initial areas of concern of bioethics were experimentation with human subjects, genetics, organ transplantation and artificial organs, the ethics of death and dying, and reproductive ethics (Jonsen, 1998). In contrast, for almost all of bioethics' history, infectious diseases have simply been left out. The reasons for the virtual neglect of infectious diseases by the bioethics community have been extensively discussed in the recent literature. Here we quoted the work by Selgelid (2005), who suggested why ethical issues associated with infectious diseases have not been more prominent in bioethics literature basing on six arguments: 1) bioethics was born at a time of important advances of medical technology and thus has largely focused on these; 2) the birth and initial development of medical ethics occurred at a time when it was believed that infectious diseases was almost completely conquered by medicine (this lead the Surgeon General of the United States to the limit of hubris in his (in)famous pronouncement of 1967: "The book of infectious diseases must be closed..."); 3) the biased point of view that infectious diseases are problems of 'others'; 4) the difficulty in carrying out research on infectious diseases in the developing world due to fact that they are so empirical and interdisciplinary; 5) the ethical questions posed by infectious diseases do not appear to pose the kind of 'deep' philosophical questions that academic ethicists of the developed world are interested in; and 6) debate in bioethics has, to a large extend, been hijacked by religion.

According to Battin et al (2009), canonical accounts of principles in bioethics (Beichamp and Childless, 1979), autonomy, nonmaleficence, beneficence and justice were also no tested by infectious diseases examples.

Bioethics has focused on protecting individuals but infectious diseases challenges bioethics to develop new ways of understanding autonomy and related concepts[1] since it is difficult to strike a balance between the utilitarian aim of promoting public health, on one hand, and the libertarian aims of protecting privacy and freedom of movement, on the other (Selgelid, 2005).

Infectious diseases deeply involve issues of justice[3] and at the same time, raise difficult philosophical and ethical questions of their own. The measures required for their control, required to protect individuals and society involve surveillance and notification of authorities (against privacy), mandatory testing, vaccination or treatment (against autonomy), isolation

of individuals, quarantine of regions or restriction to travel (against liberty of movements).

The aim of this paper is to present a modeler perspective of the ethical issues raised by the attempt to control infectious diseases through vaccination. We aim to propose that mathematical models can help in the design of vaccination strategies that minimizes adverse affects and the harm imposed by the infection at the same time. We apply the concepts of game theory (von Neumann and Morgenstern, 1944), with a particular emphasis on Nash equilibria of population games related to the decision of the persons to accept the vaccine preemptly offered in mass vaccination campaigns, versus the decision of be vaccinated only in case of outbreaks. Our model relies heavily on previously published works related to smallpox (Bauch, Galvani and Earn, 2003) and yellow fever (Massad et al., 2005). We argue that the use of mathematical models for designing immunization strategies should be an ethical priority since they help minimize the conflict between the interests of individuals and those of society at large.

Ethical Dilemmas in Public Health

With the increasing emergence and resurgence of infectious diseases around the world and the consequent implementation of public health actions to control them, conflicts between the perceptions of rights (individual versus collective) are bound to grow (Velimirovic, 1987). This kind of conflict is as old as the first effective public health actions, such as inoculation against smallpox. In 1760, the great Swiss mathematician Daniel Bernoulli set out to calculate the increase in average life expectancy that would result from inoculation against smallpox and came up with a figure of two years (Dietz and Heesterbek, 2002). Those who resisted inoculation questioned whether most people were actually prepared to run the significant risk of immediate death, one in a hundred, in order to gain only two years of life (Valleron, 2000).

Another emblematic instance is that involving the U.S. Supreme Court case of *Jacobson v. Massachusetts.* One hundred years ago, this case established a four-part test for evaluating claims of individuals that government public health authorities were infringing on their liberty by imposing compulsory vaccination (Fabro and Jacobson, 1970; Parmet et al., 2005; Blum and Talib, 2006).

No remedial intervention of any sort is absolutely risk-free. Even the commonest drug may carry some degree of risk to a fairly large number of users, and a possibly life threatening risk to an exceedingly small number of persons who are hypersensitive to it. Any public health or medical judgment must be made on the basis of balancing the values and the problems of one procedure against those of another procedure and against the risk of doing nothing at all (Melnick, 1978). Vaccination, a deliberate attempt to protect humans and animals against diseases is not different.

Since the time of Edward Jenner, vaccination has controlled ten major human diseases, at least in some parts of the world (Plotkin, 1994): smallpox, rabies, diphtheria, tetanus, yellow fever, pertussis, poliomyelitis, measles, mumps, and rubella.

Unfortunately, the development of resistance against antibiotics and the environmental disruption and political turmoil of last century determined a growing difficulty to control old pathogens and the emergence of new ones. In addition, serious side-effects of old and new vaccines started to be reported in the last few years. The reversal of vaccine to wild type of attenuated virus vaccines like the Sabin vaccine against poliomyelitis and the deaths associated with yellow fever and smallpox vaccines are causing great concern among public health (and more recently, military) authorities.

Voluntary vaccination policies for childhood diseases present parents with a subtle challenge: if a sufficient proportion of the population is already immune, either naturally or by vaccination, then even the slightest risk associated with vaccination will outweigh the risk from infection. As a result, individual self-interest might preclude complete eradication of a vaccine-preventable disease. We show that a formal game theoretical analysis of this problem leads to new insights that help to explain human decision-making with respect to vaccination. Increases in perceived vaccine risk will tend to induce larger declines in vaccine uptake for pathogens that cause more secondary infections (such as measles and pertussis). After a vaccine scare, even if perceived vaccine risk is greatly reduced, it will be relatively difficult to restore prescare vaccine coverage levels (Bauch and Earn, 2004).

Non-innocent Vaccines

As mentioned above, there is no public health intervention totally devoid of inconveniences. In the case of vaccines, side-effects vary from the nuisance of going to the vaccination post, to the pain of injection, fever, mild local hypersensitivity reactions, serious

general reactions, to the end of the spectrum with death.

From the herd immunity point of view, the best strategy for the individual would not be vaccinated , whilst all other members of the community were vaccinated. The individual would avoid all the inconveniences/risks related to the vaccine and would be indirectly protected at the same time. This strategy was at frontal conflict with the interests of the community, which would optimize its protection by vaccinating the maximum number of individuals, if possible all.

In this work, we present the case of three specific, non-innocent vaccines, namely, smallpox, poliomyelitis and yellow fever, and propose an optimal strategy based on game-theory, which is aimed to minimize the number of individuals presenting side-effects and infection at the same time.

Smallpox has reemerged recently as a public health issue. Because of the lack of information on smallpox transmission in contemporary populations, mathematical modeling has an especially important role to play in policy development. Suggestions for vaccination policy have ranged from preemptive mass vaccination (Kaplan, Craft and Wein, 2002) to post-outbreak ring vaccination (Halloran et al., 2002). The most serious adverse effects of smallpox vaccination are encephalopathy and encephalomyelitis, with death probability estimated in around 16 per million doses (Henderson and Moss, 1999).

Yellow fever (YF) was one of the most feared lethal diseases before the development of an effective vaccine (Monath, 2001). Even today, about 200,000 new cases are reported every year in tropical regions of Africa and South America. The main reservoirs for the yellow fever virus are some species of monkeys, and transmission occurs through the bites of infected mosquitos. In the sylvatic cycle , the main vectors are mosquitoes from the genera *Haemagogus* and *Sabethes*, whilst the urban cycle involves men and mosquitos of the genus *Aedes*, in particular *Aedes aegypti* and *Aedes albopictus*. The bridge between the sylvatic and the urban cycles depends on humans that go to the sylvatic areas for leisure or work, eventually returning to the urban areas carrying the YF virus.

The disease can be prevented by a live attenuated vaccine prepared from the 17D strain of YF virus, that induces seroconversion in more than 95% of recipients and provides immunity for 30 years or longer (Polland et l., 1981). YF vaccine has been incorporated into routine vaccination programs in South America, but in Africa, coverages rates are low (Martin et al., 2001). Vaccination policies has ranged from preemptive mass vaccination to post-outbreak ring vaccination.

Unfortunately, in recent years, a growing number of death associated with the YF vaccine has been reported in the literature (Martin et al., 2001; Vasconcelos et al., 2001; Chan et al., 2001; CDC, 2002). The risk of fatal adverse events associated with the 17DD yellow fever vaccine used in Brazil was estimated by Struchiner et. al. (2004). Their estimation varied from 0.017 to 12.071 fatalities per million doses administered.

Inactivated (Salk) poliovirus vaccine referred to as IPV has been in use since 1955. Live attenuated (Sabin) trivalent poliovirus vaccine or OPV has been the vaccine of choice in most countries since 1963. Mass immunization has been most successful, and wild-type poliovirus transmission has been eradicated from North America and most industrialized countries in the Western hemisphere in 1991(WHO, 2003; CDC, 2003). Global eradication of poliomyelitis is within reach and is likely to be attained within the next decade (WHO, 2003).

The risk of oral polio vaccine-associated poliomyelitis has been estimated by the World Health Organization between 0.5 and 3.4 cases per million doses in susceptible children [who],and this has re-established a role for the use of the inactivated vaccine and a new strategy for immunization with IPV in the USA and elsewhere (CDC, 2003).

Nash Equilibrium

In order to solve the conflict between individual self-interests and the population interests related to vaccination, Bauch et al. (2003, 2004) devised a vaccination game that takes account of the risk associated to the vaccine and that related to the disease, that is, people not vaccinated by self-interest can catch the infection in the case of an outbreak and suffer the consequences. The game seeks an optimum strategy that minimizes the total number of deaths both by the vaccine and the disease. We present those authors results for smallpox, the results for yellow fever from Massad et al. (2005) and present a new analysis for poliomyelitis vaccine.

The most commonly solution concept in game theory is that of Nash equilibrium (Osborne and Bubistein, 1994). This notion captures a steady state of the play of a strategic game in which each player holds the correct

expectation about the other players' behavior and acts rationally. It does not attempt to examine the process by which a steady state is reached.

The concept of Nash equilibrium is so named after for the mathematician, economist and Nobel Prize winner John Nash, whose work in the late 1940s and early 1950s established this solution method for non-cooperative games (Dixit and Skeat, 1999). At Nash equilibrium, each player must be satisfied with the strategy choice she has made, given what other players have chosen.

Bauch and Earn's (2004) vaccination game is a population game, meaning that the payoff to an individual choosing a particular strategy depends on the average behavior of the population. The two basic strategies are "vaccinator" (obtain preemptive vaccination) and "delayer" (decline preemptive vaccination but seek vaccination in the event of an attack). For any strategy, the payoff to an individual is measured in terms of a cost function for the risks of death due to vaccination and/or the disease.

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

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

$$E_{vac} = -d_v \tag{1}$$

where d_v is the probability of adverse effect from the vaccine.

The payoff to an individual choosing the delayer strategy is

$$E_{del}(p) = -r\left[\varphi_s(p)d_s + \varphi_v(p)d_v\right] \tag{2}$$

If

$$E_{vac} > E_{del}(0) \tag{3}$$

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

$$E_{vac} = E_{del}(p_{ind}) \tag{4}$$

If

$$E_{vac} \le E_{del}(0) \tag{5}$$

then the pure delayer strategy ($p_{ind} = 0$) is the unique Nash equilibrium.

Now, if p is the proportion of the population that is preemptively vaccinated in campaigns before outbreaks, we can express the expected cost $C(p)$ due to vaccination and potential outbreaks as

$$C(p) = pd_v + r(1-p)\left[\left(d_s - d_v\right)\varphi_s(p) + d_v\right] \tag{6}$$

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

Smallpox

The smallpox model (Bauch and Earn, 2004) tracks the time evolution of the densities of individuals who are susceptible (S), infected but not yet infectious (E), infectious (I), removed (dead/immune) due to smallpox infection (D), and removed (dead/immune) due to vaccination (V) (the *SEIDV* model). The model equations are:

$$\begin{aligned}
\frac{dS}{dt} &= -\beta SI - f(S,t)\\
\frac{dE}{dt} &= \beta SI - \sigma E\\
\frac{dI}{dt} &= \sigma E - \gamma I\\
\frac{dD}{dt} &= \gamma I\\
\frac{dV}{dt} &= f(S,t)
\end{aligned} \tag{7}$$

where is the β means transmission rate, $1/\sigma$ is the mean latent period, and $1/\gamma$ is the mean infectious period (here defined as the time between the onset of infectiousness and the isolation of the symptomatic patient). The effect of pos-attack intervention by health

authorities is expressed through the function $f(S,t)$, which is the rate of mass vaccination of susceptible individuals. We assume that mass vaccination is initiated t_{res} days after the initial smallpox exposure (the "response time") and that susceptible individuals are vaccinated at a constant rate v until all have been vaccinated; hence

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

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

The result by Bauch and Earn (2004) is summarized in figure 1 in which the optimum coverage is displayed as a function of the Basic Reproduction Ratio.

As can be seen, the group optimum vaccine coverage is always greater than the individual equilibrium.

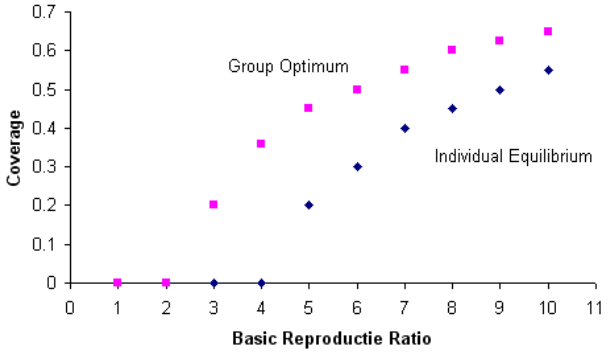


FIGURE 1 RESULTS OF THE GAME FOR SMALLPOX. OPTIMUM VACCINE COVERAGE AS A FUNCTION OF THE BASIC REPRODUCION RATIO (FROM BAUCH AND EARN, 2004)

Yellow Fever

The yellow fever game (Massad et l., 2005) proposed has the structure of the one proposed for smallpox, that is, a proportion p of susceptibles is preemptively vaccinated and its complement $(1-p)$ decides to wait until an outbreak is established.

In order to calculate the proportion of cases and deaths after a YF outbreak, as well as the proportion of people vaccinated during the outbreak, we modeled the epidemic with a dynamical system, described by the following system of differential equations:

$$\begin{aligned}
\frac{dM_s}{dt} &= -caM_sH_i / N_h + \mu_M M_s \\
\frac{dM_i}{dt} &= ca\exp(-\mu_M\tau)M_s(t-\tau)H_i(t-\tau) / N_h(t-\tau) \\
&\quad -(\alpha_M + \mu_M)M_s \\
\frac{dH's}{dt} &= -baM_iH_s / H_h - (\nu_h + \mu_h)H_s \\
\frac{dH"s}{dt} &= -(\mu_v + \mu_h)H"_s \\
\frac{dH_i}{dt} &= baM_iH's / N_h - (\gamma_h + \mu_h + \alpha_h)H_i \\
\frac{dH_v}{dt} &= \nu_h H's - (\mu_h + \mu_v)H_v \\
\frac{dH_r}{dt} &= \gamma_h H_i - \mu_h H_r
\end{aligned} \quad (9)$$

We now briefly describe some features of the system. Consider first the mosquito population, described by the first two equations of system (9). When a susceptible (without the infection) mosquito bites an infected person it may became (with a certain probability) infected. If it survives for a period of time τ (the extrinsic incubation period) it will become infective, that is, if it bites a human it may transmit (with a certain probability) the infection. We are not interested in infected but not yet infective mosquitoes, but rather we consider only susceptible mosquitoes, M_s, and infective mosquitoes, M_i. The first two equations of the system bellow describe the dynamics of those two populations. Consider the first equation. We call a the biting rate of the mosquitoes. So aM_s is the number of bites the susceptible mosquitoes inflict per unit of time in humans. Of those, only a proportion H_i / N_h will be on infected humans and of those, only a proportion c will result in infected mosquitoes. Susceptible mosquitoes are assumed to die with a rate μ_M. The first term of the second equation describes the number of mosquitoes that became infected τ units of time earlier, survived a time interval τ and now became infective. The infective mosquitoes are assumed to die with a rate $\alpha_M + \mu_M$.

Let's now consider the human population. Humans are divided into those who were preemptively vaccinated, denoted $H_s^{''}$, and those who did not receive the vaccine and are, therefore, truly susceptible, denoted $H_s^{'}$. The latter acquired the infection from infective mosquitoes through the bites $aM_iH_s^{'} / N_h$, a fraction of which, b, are actually infective. They may be vaccinated during an outbreak, with a rate ν_h, or dye by natural causes, with a rate μ_h. The individuals preemptively vaccinated, $H_s^{''}$, dye with rates μ_v (by the effect of the vaccine) and

μ_h, the natural mortality rate of humans. Once infected, H_i, individuals can either recover from the infection, with rate γ_h, or dye with rates α_h (the mortality rate of yellow fever) or μ_h, the natural mortality rate of humans. Individuals vaccinated during the outbreaks, H_v, can die by natural causes, or by the vaccine, with rates μ_h, and μ_v, respectively. Those recovered from the infection, H_r, dye only by natural causes.

From the system (9), it is possible to calculate the threshold for the establishment of an epidemic, resulting in

$$T = \frac{N_m}{N_h} \frac{a^2 bce^{-\mu_m \tau}}{(\gamma + \mu_h + \alpha_h)(\mu_m + \alpha_m)} \qquad (10)$$

Expression (10) is the basic reproduction number as defined by Macdonald (1952, see also Massad et al., 1994). Its numerical value can also be estimated through the analysis of the doubling time of the initial phase of an epidemic (Anderson and May, 1991).

The values of T of dengue were calculated for 17 cities of the State of São Paulo, through the doubling time of the initial phase of the epidemic, as described by (Anderson and May, 1991; Massad et al., 2001; 2003; Fine, 2010). Then, we calculate T of YF. Next, we calculated the size of the mosquito population for each city analyzed, by the relation:

$$N_m = \frac{N_h}{T_{yf}} \frac{(\gamma + \mu_h + \alpha_h)(\mu_m + \alpha_m)}{a^2 bce^{-\mu_m \tau}} \qquad (11)$$

since N_h was known and other parameters were assumed to be the same for all the cities analyzed because they were all in the same microclimatic region of the State of São Paulo.

We numerically solved the system (9) in order to obtain the quantities necessary to estimate the optimum proportion to vaccinate, p_{gr}, that minimizes the total number of deaths:

$$\begin{aligned}
\pi_{yf}(p) &= \frac{\int_0^\infty baM_i H's / N_h dt}{(1-p)N_h} \\
d_{yf}(p) &= \frac{\int_0^\infty (\mu_h + \alpha_h) H_i dt}{(1-p)N_h} \\
\pi_v(p) &= \frac{\int_0^\infty \nu_h H's dt}{(1-p)N_h} \\
d'_v(p) &= \frac{\int_0^\infty \mu_v H_v dt}{(1-p)N_h}
\end{aligned} \qquad (12)$$

where p is the proportion of the population preemptively vaccinated, as described in the main text.

Our main result can be summarized by figure 2. It can be seen that for low risk of outbreaks, the optimum equilibrium is no vaccination. As the risk increases, however, there is a minimum in the mortality due to both vaccination and natural mortality. Note also that after a critical level, vaccination always worsens the death toll.

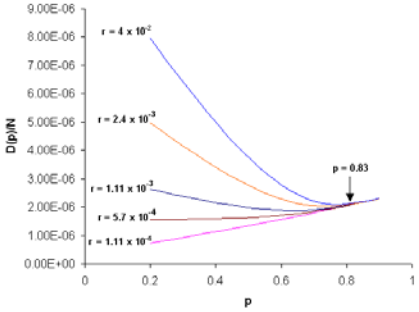


FIGURE 2 OPTIMUM VACCINATION COVERAGE THAT MINIMIZES THE TOTAL MORTALITY. DIFFERENT LINES DENOTE DIFFERENT RISKS OF OUTBREAKS (FROM[7])

Poliomyelitis

The poliomyelitis model considers the same game structure as the other previous models, namely, a fraction p of the population is preemptively vaccinated in campaigns and a complement $(1-p)$ is vaccinated only in the course of an outbreak.

The model in its generalized form considers also two competing polio vaccines, the inactivated vaccine, also known as Salk after Jonas Salk its inventor, and an attenuated vaccine, also known as Sabin, after Albert Sabin, its inventor. However, in spite of presenting the full model, we consider here only the case of attenuated Sabin vaccine because of its reversal to virulent strain phenomenon, which is causing major concern among public health authorities of developed countries.

The full model is described by the following system of equations:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - pS\beta_1 E_{NI} I - qS\beta_2 E_{VAC} V_{SAB} \\
&\quad - b\nu_{SAB} - (1-b)\nu_{SALK} S \\
&\quad + \gamma R + \tau_{SAB} V_{SAB} + \tau_{SALK} V_{SALK} - \mu S \\
\frac{dI}{dt} &= pS\beta_1 E_{NI} I + \sigma V_{SAB} - (\delta + \mu + \alpha) I \\
\frac{dV_{SAB}}{dt} &= qS\beta_2 E_{VAC} V_{SAB} S + b\nu_{SAB} S \\
&\quad - (\tau_{SAB} + \mu + \sigma) V_{SAB} \\
\frac{dV_{SALK}}{dt} &= (1-b)\nu_{SALK} S - (\tau_{SALK} + \mu) V_{SALK} \\
\frac{dR}{dt} &= \delta I - (\gamma + \mu) R
\end{aligned} \qquad (13)$$

where S stands for susceptible children, I for infected, V_{SAB} are the children vaccinated with the attenuated polio vaccine, V_{SALK} are the children vaccinated with the death virus vaccine, and R are the children who recovered from the infection and who will eventually lost the immune protection conferred by natural infection.

The parameters that determine the system dynamics are described in the following table:

Λ = Number of children born per year
β_1 = Contact rate with the wild virus contaminated environment - E_{NI}
β_2 = Contact rate with the Sabin virus contaminated environment - E_{VAC}
p = Probability of being infected with environment - E_{NI}
q = Probability of being infected with environment - E_{VAC}
b = Ratio Sabin/Salk
ν_{SAB} = Sabin vaccination rate
ν_{SALK} = Salk vaccination rate
τ_{SAB} = Loss of immunity of the Sabin vaccine
τ_{SALK} = Loss of immunity of the Salk vaccine
σ = Revertion to virulence of the Sabin virus
α = Additional mortality rate of poliomyelitis
δ = Rate of developing flaccid paralysis
μ = Natural mortality rate of the population
γ = Recovery rate of paralysis

This model allowed us to test another game, which is central in the discussion of polio vaccines, namely, the substitution of the attenuated virus Sabin by the death virus Salk vaccine. In countries where the wild virus circulation is reduced to close to zero, the risk of vaccinal paralysis due to the Sabin vaccine, the substitution of this vaccine by the Salk one is already in course.. We simulated the game of Sabin versus Salk vaccine, in order to estimate the Nash equilibrium that would minimize the number of flaccid paralysis both by the wild strain of the polio virus and the attenuated vaccination Sabin strain.

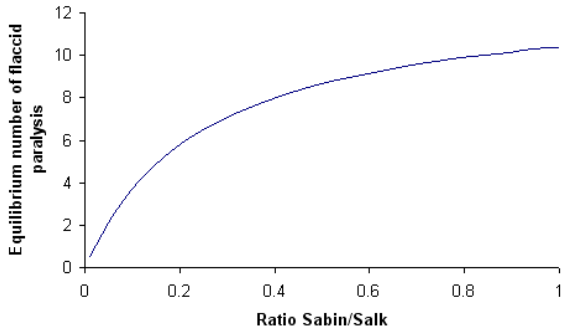


FIGURE 3 EQUILIBRIUM NUMBER OF FLACID PARALYSIS AS A FUNCTION OF THE RATIO SABIN/SALK VACCINES. NOTE THAT THE NUMBER OF PARALYSIS IS MINIMIZED BY THE SUBSTITUTION OF THE LIVE BY THE ATTENUATED VACCINE

The preliminary results pointed to the Nash equilibrium with zero proportion of children being vaccinated with the Sabin vaccine and all children being vaccinated with the Salk vaccine. This was obtained even considering a small risk of the wild type outbreak and with an efficacy attributed to the Sabin twice as much as that of the Salk. Figure 3 summarizes our results.

It can be seen that the number of flaccid paralysis at equilibrium is minimized by the pure strategy vaccination with Salk only.

Discussion

Vaccines for infectious diseases have been effective in nearly eradication of several diseases from the developed world. These vaccines are effective not only to the individual recipients, but also create herd immunity, reducing the incidence of those infections in whole communities. This dual effect has raised ethical issues when several individuals, families, religious groups, or homeopathy followers assert rights to refuse vaccination and as a result increase the risk of the remaining population to infection (Battin et al., 2009).

The current study examines what is probably the most common conflict of interest in vaccination, namely the interest of individuals (not to be vaccinated provided that everyone else is vaccinated) against the interest of the community (everybody should be vaccinated). This conflict arises because of the well-defined potential risks of vaccines causing serious and sometimes even fatal illness in the recipient of the vaccine or the spreading live-viruses vaccine to immune compromised patients at high risk of developing serious complications. More specifically we dealt with the application of mathematical models to minimize the conflict of interest in vaccination. As mentioned by Fine (2010), the more complex a phenomenon is, the more difficult and expensive it is to study, the greater the ethical implications of carrying out research, then the greater is the motive to explore mathematical models. Therefore, immunization with non-innocent vaccines is an obvious subject to modeling due to the ethical issues involved in its application.

This study found that it is possible to minimize the conflicts between the individual and the social interests involved in vaccination, provided the right tools are applied. In addition, the models presented are probably the only available alternatives to decision-making in public health dilemmas such as the substitution of live attenuated polio vaccine by the inactivated vaccine. It will be ethically impossible to

carry out a case-control study in order to estimate the strategy that will minimize the cases of flaccid paralysis. Hence the obvious choices are the models of the type presented in this work.

As mentioned above, vaccination policies for some infectious diseases present individuals with a conflict: if a sufficient proportion of the population is already immune, either naturally or by vaccination, then even the slightest inconvenience associated with vaccination will outweigh the risk from infection. As a result, individual self-interest might preclude complete eradication of a vaccine-preventable disease. In this paper we show that a formal game theoretical analysis of this problem leads to new insights that help to explain human decision-making with respect to vaccination. We show that the Nash equilibrium, whenever possible to be estimated, provides the optimum strategy in conflict situation. So, both in the cases of smallpox and yellow fever, two vaccines with a non negligible death rate associated with them, if the risk of outbreaks by the wild virus is too small, it may be better not to vaccinate. In the case of the attenuated oral polio vaccine with the Sabin strain, the conflict is the one currently in course in developed nations that do not present any case of wild virus paralysis for several years. In those places , a substantial number of paralysis cases induced by the attenuated vaccine is causing major concerns among public health authorities. Our model tested several mixed strategies with both the Sabin and Salk vaccine combinations and concluded that the Nash equilibrium that minimizes the number of flaccid paralysis is obtained by the pure Salk vaccination.

Finally, bioethics should take into account conflicts between individuals and the community such as the conflict arisen by vaccination against infectious diseases. In the presence of such an efficacious tool as mathematical models, which have demonstrated their potential as optimizer of public health strategies, it would be unethical not to apply them as an auxiliary technique in decision making to mitigate potential conflicts.

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