Mathematical Biosciences 263 (2015) 180–197

Contents lists available at ScienceDirect

Mathematical Biosciences

journal homepage: www.elsevier.com/locate/mbs

Global optimal vaccination in the SIR model: Properties of the value function and application to cost-effectiveness analysis ☆

Laetitia Laguzet [a], Gabriel Turinici [b,*]

[a] CEREMADE, Université Paris Dauphine, France
[b] Institut Universitaire de France

ARTICLE INFO

Article history:
Received 29 September 2014
Revised 26 February 2015
Accepted 3 March 2015
Available online 12 March 2015

Keywords:
Optimal vaccination
SIR model
Vaccination region
Herd immunity and cost-effectiveness

ABSTRACT

This work focuses on optimal vaccination policies for an Susceptible–Infected–Recovered (SIR) model; the impact of the disease is minimized with respect to the vaccination strategy. The problem is formulated as an optimal control problem and we show that the value function is the unique viscosity solution of an Hamilton–Jacobi–Bellman (HJB) equation. This allows to find the best vaccination policy. At odds with existing literature, it is seen that the value function is not always smooth (sometimes only Lipschitz) and the optimal vaccination policies are not unique. Moreover we rigorously analyze the situation when vaccination can be modeled as instantaneous (with respect to the time evolution of the epidemic) and identify the global optimum solutions. Numerical applications illustrate the theoretical results. In addition the pertussis vaccination in adults is considered from two perspectives: first the maximization of DALY averted in presence of vaccine side-effects; then the impact of the herd immunity on the cost-effectiveness analysis is discussed on a concrete example.

1. Outline of the paper

1.1. Background on vaccination strategies

The mathematical modeling of the spread of an infection disease allows to propose control strategies to decrease the cost of the epidemic. Among such control strategies we focus in this work on the vaccination. A vaccination policy indicates when and how many people should be vaccinated in order to minimize the overall impact of the epidemic. We consider here a cost that sums the cost of the infected individuals and the cost to vaccinate the individuals (see formula (3) below for the mathematical definition). We also apply the same methodology to cost-effectiveness analysis in the context of a constrained public health budget.

1.2. State of the art and motivation

The mathematical analysis of the cost, as a function of the vaccination policy, allows to obtain an optimal vaccination strategy. Consider the epidemic in Fig. 1 (see caption for the detail of the parameters) where the abscissa represents the number of the susceptible in the population, and the ordinate the proportion of infected people. In the literature several proposals for the best vaccination strategy are presented (see for example [1–4]); however previous works operated under specific assumptions on the value function (see below) and consequently did not always selected the best vaccination policy.

For instance, as we illustrate in Fig. 1 the solution available in the literature is, in some cases, not optimal. The two curves represent two scenarios for an epidemic starting for an initial point X_0. The solid curve represents the epidemic evolution when there is no vaccination (the state of the art solution for this set of parameters) and the dashed curve plots the epidemic evolution when there is some partial vaccination. The partial vaccination is seen to outperform the no vaccination policy.

For further information see the literature review in Section 2.4.

1.3. Methodology and results

Prompted by this remark we look in this work into the details of the calculation of the best vaccination strategy (using the technique of the "viscosity solutions") and note that all previous works used a specific assumption which is not always true; we explain precisely when the assumption is correct (and thus the previous works identified correctly the optimal vaccination policy) and when it is not (and in this case we describe the best vaccination policy).

☆ This work was supported by a grant from "Fondation Sciences Mathématiques de Paris" and "Région Ile de France".

* Corresponding author. Tel.: + 33 1 44 05 48 58; fax: + 33 1 44 05 45 99.
E-mail address: Gabriel.Turinici@dauphine.fr (G. Turinici).

http://dx.doi.org/10.1016/j.mbs.2015.03.002
0025-5564/

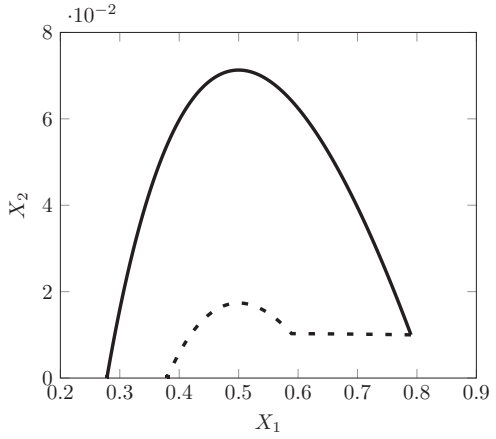

Fig. 1. Two trajectories of an epidemic evolution (corresponding to the SIR model in Eqs. (1)) are presented. The epidemic starts from $X_0 = (0.79, 0.0053)$. The parameters used are $\beta = 73$, $\gamma = 36.5$, $u_{\max} = 100$, $r_I = 1$ and $r_V = 1.5$ (see formula (3) for the meaning of the parameters r_I and r_V and Section 2.2 for $u_{\max}$). The solid curve represents the epidemic evolution when there is no vaccination (which is the state of the art solution, see [1,3,4]) and the dashed curve plots the epidemic evolution when there is some partial vaccination. The cost for the first trajectory is 0.51 and for the second is 0.49.

1.4. Structure of the paper

The paper is organized as follows: in the next section we describe the mathematical model (Section 2.1), the admissible vaccination policies (Section 2.2), introduce some notations in Section 2.3 and give an overview of the contributions from the literature in Section 2.4; finally we present some technical obstacles in Section 2.5.

In Section 3 several applications of the theoretical results (proved in Appendixes D and E) are presented. A summary of the numerical procedure to find the best vaccination strategy is the object of Section 4.

Then in Section 5 we consider two applications to the optimal pertussis vaccination in adults. Finally, conclusions are the object of Section 6.

2. Model, notations and first remarks

2.1. The model

In order to model the evolution of an epidemic, we use an SIR (Susceptible–Infected–Recovered) compartment model (cf., [5–7] for additional details).

We seek to optimize the cost of the vaccination policy; to this end denote by $V(t)$ the proportion of people vaccinated by the time t (of course $\lim_{t\to\infty} V(t) \le 1$); we consider vaccines that confer lifetime immunity so that V is an increasing function. The evolution of the disease is described by the following equations:

$$\begin{cases} dX_1(t) = -\beta X_1(t)X_2(t)dt - dV(t), & X_1(0) = X_{10}, \\ dX_2(t) = (\beta X_1(t)X_2(t) - \gamma X_2(t))dt, & X_2(0) = X_{20}, \\ dX_3(t) = \gamma X_2(t)dt, & X_3(0) = X_{30}, \\ X_4(t) = \int_0^t dV, & X_4(0) = 0. \end{cases} \tag{1}$$

Here X_1, X_2, X_3, X_4 are the proportion of people in the "susceptible" respectively "infectious", "recovered" and "vaccinated" classes. Initially $X_1(0) + X_2(0) + X_3(0) = 1$ and $X_4(0) = 0$ (but X_4 need not be continuous in 0). See Fig. 2 for a graphical view of system (1). Note that (1) implies $X_1(t) + X_2(t) + X_3(t) + X_4(t) = 1$, $\forall t \ge 0$.

Here β is the transmission rate of the disease, V is the control to be optimized and γ is the recovery rate.

We denote r_V the unitary cost associated with vaccination including the cost of the vaccine and all possible side-effects and r_I the unitary cost incurred by infected persons. To simplify the presentation we suppose that costs are expressed in money and postpone to Section 5 the more realistic and interesting situations when costs are expressed as medical conditions.

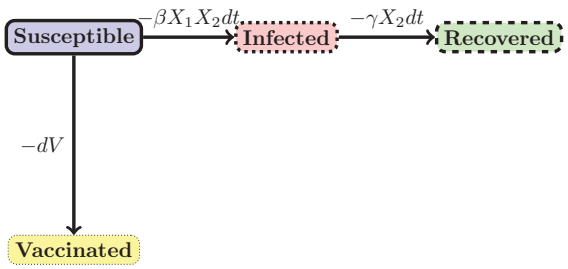

Fig. 2. Graphical illustration of the SIR-V model.

The cost of the disease is independent of the classes X_3 and X_4 (but dependent on the control $V(t)$), so we can restrict ourselves to the evolution of X_1 and X_2. From now on a vector X will only be supposed to have two coordinates X_1 and X_2. Denoting:

$$\Omega = \{X = (X_1, X_2) \in \mathbb{R}^2 \mid X_1, X_2 > 0, X_1 + X_2 < 1\}, \tag{2}$$

we will work under the constraints $X \in \overline{\Omega}$.

We introduce $\Phi^{Y,dV}(t) = (\Phi_1^{Y,dV}(t), \Phi_2^{Y,dV}(t))$ to denote, at time $t \ge 0$, the solution of the system (1) starting at point $X(0) = Y$ and with control dV; in addition $Z = \Phi^{Y,dV(\cdot)}(-t)$ means $Y = \Phi^{Z,dV(t-\cdot)}(t)$ (the reverse system has a well defined mathematical meaning). To ease notations, when the measure dV is absolutely continuous with respect to the canonical Lebesgue measure dt on $[0, \infty[$ i.e., when dV can be written $dV = u(t)dt$ we will also write $\Phi^{Y,u(t)}(t)$ instead of $\Phi^{Y,u(t)dt}(t)$ (and the same for the components $\Phi_1^{Y,u(t)dt}(t)$ and $\Phi_2^{Y,u(t)dt}(t)$).

Remark 1. Here and in all that follows we consider the interval $[0, \infty[$ open at infinity. This simply means that ∞ is not an admissible value and no strategy can vaccinate at $t = \infty$; on the contrary instantaneous vaccination at $t = 0$ is possible.

The cost of the disease is:

$$J(Y, dV) = \int_0^\infty r_I \beta \Phi_1^{Y,dV}(t)\Phi_2^{Y,dV}(t)dt + \int_0^\infty r_V dV(t). \tag{3}$$

Moreover we will use the following notation $J_0(Y) = J(Y, 0)$; note that $J_0(Y)$ is a cost proportional with the number of people infected in absence of vaccination. This number will be denoted $\zeta(Y)$ thus $J_0(Y) = r_I \zeta(Y)$ (see Appendix A for the properties of ζ).

Remark 2. Equation (1) implies

$$\begin{aligned} \Phi_2^{X,dV}(\infty) &= \Phi_2^{X,dV}(0) + \int_0^\infty d\Phi_2^{X,dV}(t) \\ &= \Phi_2^{X,dV}(0) + \int_0^\infty (\beta \Phi_1^{X,dV}(t)\Phi_2^{X,dV}(t) - \gamma \Phi_2^{X,dV}(t))dt. \end{aligned} \tag{4}$$

Thus, since $\Phi_2^{X,dV}(\infty) = 0$:

$$\int_0^\infty r_I \beta \Phi_1^{X,dV}(t)\Phi_2^{X,dV}(t)dt = \int_0^\infty r_I \gamma \Phi_2^{X,dV}(t)dt - \Phi_2^{X,dV}(0). \tag{5}$$

This allows to conclude that the cost functional

$$J^d(Y, dV) = \int_0^\infty r_I^d \Phi_2^{Y,dV}(t)dt + \int_0^\infty r_V dV(t) \tag{6}$$

with $r_I^d = r_I \gamma$ satisfies

$$J^d(Y, dV) = J(Y, dV) + Y_2. \tag{7}$$

Both J^d and J will thus have same optimal strategies (because their difference is independent of the strategy dV). Here r_I^d can be seen as the unitary cost of infection per unit time.