Prevention of Infectious Diseases in the Context of Efficient Treatment : a game-theoretic approach

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1. Introduction

The preference for prevention over treatment remains a subject of debate due to limited resources allocation in public health. It remains a key objective to know whether and how the voluntary use of prevention by individuals impacts an epidemic.

Game Theory is a mathematical discipline that allows, among other things, to model rational individual's decision-making and strategies. Currently, it is widely used in areas such as Economics, Biology and Politics [1].

Some history

- **1713** First known discussion about strategies of a two-person cards game.
- **1913** First mathematical formulation for the chess game made by the logician Zermelo.
- **1944** First designation of Game Theory as a research field with applications in Economics, after the book *Theory of Games and Economic Behavior* by von Neumann and Morgenstern was published.
- **1950s** Extensive development of the field among mathematicians.
- **1970s** Development of applications in Biology and Evolution.
- **11** game-theorists have won the Nobel Prize in Economics to date.

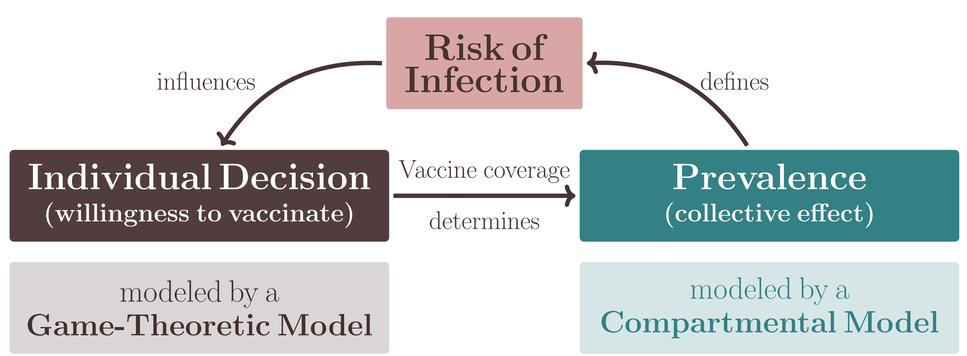
Game theory has been recently applied to evaluate the impact of voluntary vaccination on treatable childhood infectious disease transmission [2, 3].

The aim of this project is **to combine game theory with an infectious disease transmission model** in order to determine the acceptance of prevention in a context where efficient treatment exists and to determine if prevention could be sufficient to avert the epidemic.

Here, we reassess the impact of voluntary vaccination on a treatable childhood disease transmission. Next, we will apply this methodology to the issue of prevention versus treatment in the context of the HIV epidemic.

2. Conceptual framework

2.1. We build a paradigm model combining a utility game for the individual's decision-making and a compartmental model for the epidemic's dynamic.



Every individual's decision is indirectly influenced by those of others: the sum of all individuals' decisions will determine the level of prevention coverage, which will affect the epidemic's progression and thus the prevalence of the disease [3, 2].

2.2. We apply this coupled system to a setup where vaccination becomes available as a prevention method for a treatable childhood disease with complete natural recovery [3].

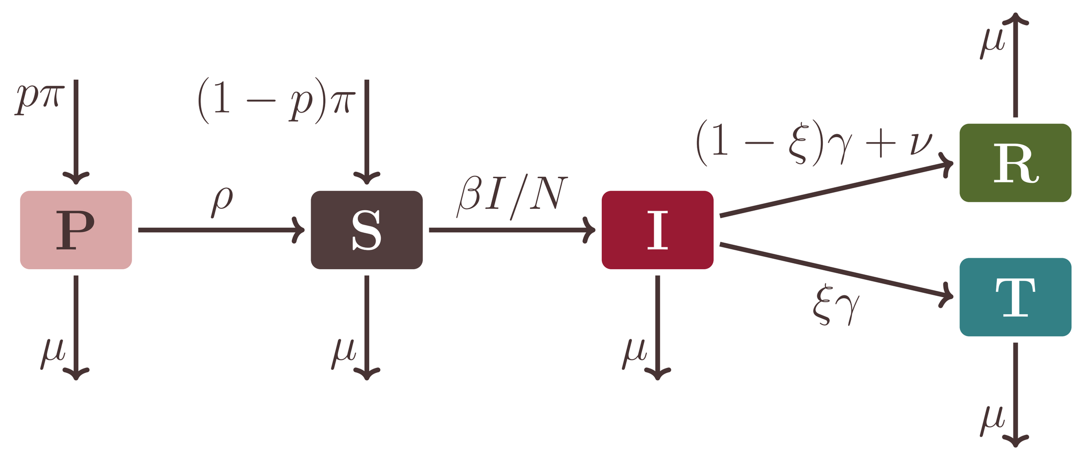
2.3. We assume treatment is mandatory while vaccination is voluntary.

2.4. We assume that individuals decide to enroll in vaccination programs not only when an epidemic occurs, but also due to other reasons such as epidemic threat, recommendations from health authorities, peer pressure, social altruism, etc. This assumption differs from that made in previous studies [2], where it was assumed that individuals vaccinate only when an epidemic occurs, yielding an impossibility of averting an epidemic through prevention.

3. Compartmental model of childhood disease transmission

Newborns can get vaccinated (P) or remain susceptible (S). Then, if they become infected (I), they can naturally recover (R) or get on treatment (T). The total population is defined by $N = P + S + I + R + T$.

The parameter π stands for the inflow of newborns, p stands for vaccine coverage, μ for the disease-unrelated death rate, β for disease transmissibility, ν for the natural recovery rate and γ for the treatment rate. Treatment efficacy is represented by ξ and ρ represents the rate of waning vaccine-induced immunity.



The flowchart above can be represented by the following system of ordinary differential equations:

$$
(1)\quad \begin{cases} dP/dt = p\pi - (\rho + \mu)\, P, \\ dS/dt = (1-p)\pi + \rho P - \beta IS/N - \mu S, \\ dI/dt = \beta IS/N - (\gamma + \nu + \mu) I, \\ dR/dt = (1-\xi)\gamma I + \nu I - \mu R, \\ dT/dt = \xi \gamma I - \mu T. \end{cases}
$$

The basic reproduction number (R_0) is a standard threshold signaling whether transmission of an infectious disease is self-sustained and maintains an epidemic. If $R_0 > 1$, transmission is self-sustained; if $R_0 < 1$ transmission is not self-sustained [4, 5].

Calculating the basic reproduction number [6] for the system (1) before vaccine is introduced, i.e. when $p = 0$ and $P \equiv 0$, we get

$$R_0 = \beta/(\mu + \nu + \gamma).$$

The basic reproduction number for system (1), i.e. including vaccination, is calculated as

$$R_0^p = \big(1 - p\mu/(\mu + \rho)\big) R_0.$$

4. Game theory: the decision-making model

We assume that individuals make the decision of whether or not to get vaccinated by weighing the benefits and inconveniences of the vaccine versus those of the treatment.

The decision-making process can be mathematically modeled by maximizing a *utility function* defined as follows:

$$
U(p, r) = \begin{cases} p\,(-r) - (1-p)\,\Pi, & \text{if } R_0 > 1, \\ 0, & \text{if } R_0 \le 1, \end{cases}
$$

where

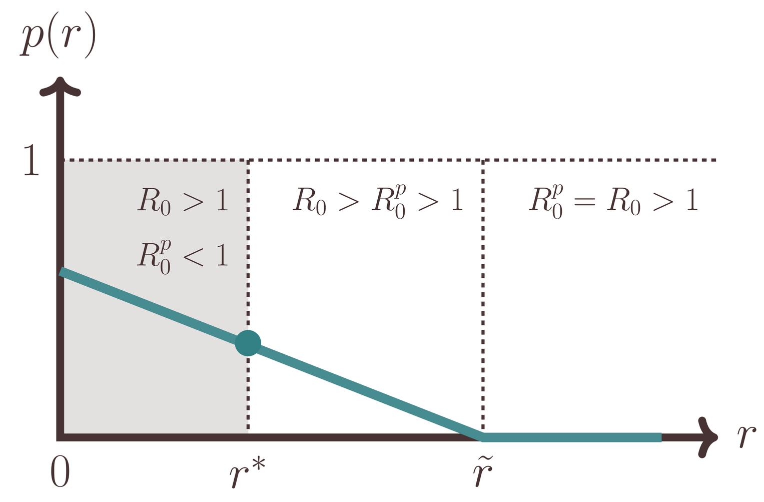
- p is the vaccine coverage,
- Π is the endemic prevalence of the system (1), and
- $r = c_p/c_t$ is the relative cost, with c_p standing for the cost of prevention and c_t for the cost of treatment.

Prevalence is interpreted by the individual as the probability of getting infected.

Cost represents the individual's perception of the inconveniences associated with vaccine or treatment: it may involve monetary and/or non-monetary aspects such as secondary effects, time spent for the procedure, etc.

5. Results & Conclusion

We derived an expression for the prevention coverage $p(r)$ by maximizing the utility function U.



We obtained the thresholds for r that lead to attenuate and avert the epidemic. Notably, **we obtained that if the relative cost r is sufficiently low and the vaccine-induced immunity is sufficiently long-lasting, epidemic may be averted through the use of prevention alone**.

Mathematically, we found the necessary and sufficient conditions so that R_0^p verifies $R_0^p < 1$. Indeed, we found that the gray region of the figure above exists if and only if

$$\frac{\rho}{\mu} \le \frac{1}{R_0 - 1}.$$

Interpretation. If the parameterization of the problem yields $\rho/\mu > 1/(R_0 - 1)$, the gray region would not exist. This means that, even for zero cost ($r = 0$), the prevention program would not eliminate the epidemic because the vaccine-induced immunity would not last long enough; i.e. ρ would be too large.

Conclusion. **Vaccination programs successfully avert epidemics if they are delivered at low cost and the immunity induced by them is long-lasting**. This is the case with the Measles–Mumps–Rubella vaccine; most other vaccines require a booster.

6. Perspectives

Applications to the HIV epidemic

Pre-exposure prophylaxis (PrEP) is a new prevention method that has shown an efficacy of 86% (95% CI: [40–99]) along the IPERGAY clinical trial, which was conducted in France and Canada among men who have sex with men (MSM) at very high risk of HIV infection [7].

As part of my doctoral thesis, we will apply this coupled model to the context of HIV epidemic among MSM in Île-de-France, in order to assess the impact of the rollout of PrEP.

Objective. We want to find out whether and under what conditions PrEP could avert the HIV epidemic.

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