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OPTIMAL INDIVIDUAL STRATEGIES FOR INFLUENZA VACCINES WITH IMPERFECT EFFICACY AND DURABILITY OF PROTECTION

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Abstract. We analyze a model of agent based vaccination campaign against influenza with imperfect vaccine efficacy and durability of protection. We prove the existence of a Nash equilibrium by Kakutani's fixed point theorem in the context of non-persistent immunity. Subsequently, we propose and test a novel numerical method to find the equilibrium. Various issues of the model are then discussed, such as the dependence of the optimal policy with respect to the imperfections of the vaccine, as well as the best vaccination timing. The numerical results show that, under specific circumstances, some counter-intuitive behaviors are optimal, such as, for example, an increase of the fraction of vaccinated individuals when the efficacy of the vaccine is decreasing up to a threshold. The possibility of finding optimal strategies at the individual level can help public health decision makers in designing efficient vaccination campaigns and policies.

1. **Introduction.** Vaccination is a widely used epidemic control tool which may (and should) be analyzed from several perspectives, such as the design of fabrication techniques, the study of its action mechanisms, the analysis – at the individual level – of the medical issues of the vaccine, including its side effects, and the global impact on the epidemic spread of some carefully designed vaccination protocols.

Obviously, these different viewpoints are strictly interconnected: for example, the action mechanism of a vaccine determines its features and its protection effect against the target illness, and the public health strategies are a consequence of the former two aspects.

When looking at vaccination policies, two approaches are possible.

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The first one supposes that a health authority can decide of a vaccination plan, which is then implemented. The plan optimizes the vaccination strategy as a function of the severity of the epidemic, its medical risks and the (economic and medical) costs associated to the vaccine.

This framework, that is suitable for compulsory vaccination or when the individuals fully adhere to the recommendations of the health authority, has been the first one considered in the literature (see [39, 1, 52, 59, 23, 4, 46]).

However, this kind of studies is oriented to the best possible strategy for the population as a whole, and it does not take into account the individual viewpoints. Indeed, when the vaccination is a choice – on a voluntary basis – or when there are debates on the risks or costs of the vaccine, the previous approach is not valid anymore and the situation is better described by models that take into account the individual decision level.

In this second group of models, the agents decide for themselves whether the vaccination is suitable or not, but they cannot individually influence the epidemic propagation, which is given by the collective choice of the population as a whole.

The study of the collective behavior of large populations of non-cooperative interacting individuals – such as the problem considered in the present article – is a complicated problem, but it recently received a firm mathematical ground thanks to the *Mean Field Game* (MFG) theory, introduced in the literature by the pioneering works of Lasry and Lions [49, 48, 50] and of Huang, Malhamé and Caines [41, 40]. From the point of view of modeling, mean field game theory combines mean field theories, which are widely used in Physics and Mechanics, together with the notion of Nash equilibria in game theory.

One of the main goals of MFG is the study of the existence of equilibria for the whole population, namely a stable collection of individual strategies such that nobody has any incentive to change his own strategy.

Before the development of the MFG theory, some earlier works were already looking into this direction. We quote, for example, [30, 12, 35] which study the question of disease eradication, market equilibrium and externalities regarding vaccination. More recent contributions (see [7, 6, 60, 31, 58, 47]) study the question of Nash equilibria for a large number of individuals dealing with an epidemic. They investigated many aspects, such as the impact of the subjective perceptions and individual behaviors on the equilibrium (see, for example, [19, 18, 57]), the presence of several groups having distinct epidemic characteristics (see [34, 20, 16]), particular vaccination strategies or specific models about the available information at the individual level (see [13, 8, 27, 25, 26, 33, 69, 11, 24]).

In this article, we introduce and analyze a model for a non-compulsory vaccination campaign against influenza viruses, with imperfect vaccine efficacy and limited durability of protection (sometimes also called persistence as a shorthand for *persistence of antibodies*). Our main purpose is the computation of the optimal individual strategy (which allows to deduce the fraction of the population which chooses to be vaccinated in absence of a specific obligation), with the purpose of helping decision makers in designing efficient public health policies. Since compulsory vaccination is the source of some ethical issues on informed consent and individual freedom, knowledge of the optimal individual strategy is an essential step before deciding that a given vaccine is mandatory. On the other hand, advertisement campaigns for non-compulsory vaccination are effective only if their goal is compatible with the optimal individual strategy.

As the features of the target infectious disease heavily influence the dynamics of the epidemic spread, our model cannot be immediately generalized to the vaccination against other diseases. However, the global strategy can be easily modified, *mutatis mutandis*, for obtaining models adapted to other situations with a similar behavior (i.e. the vaccine is imperfect and the immunity is not permanent).

We focus our attention on countries with temperate climates, which experience a marked seasonal influenza peak during the winter months [66]. Hence our time horizon will be annual.

Since influenza is a contagious disease, the major available tool against the spread of the illness is given by vaccination.

However, vaccination has no permanent effect. Indeed, as pointed out in [21], the protection against a virus, provided by the corresponding vaccine to an individual, persists after some years and it is still effective in case of slight genetic mutations. But, because of the antigenic drift [15], sufficient changes can accumulate in the virus to allow influenza to reinfect the same host. The protection given by a previous vaccine can hence become useless. In order to overcome this phenomenon, the influenza vaccine formula is annually reviewed. Note that vaccine mismatch is not taken into account in our study, because it would lead to introduce different questions, oriented to the modeling of the vaccine itself, rather than to the vaccination policies (which suppose, of course, that the annual release of the vaccine has a good efficacy).

We moreover suppose that the immunity provided by the vaccine is time-dependent. Indeed, as pointed out in several studies, the estimated protection against infection, based on hemagglutination-inhibiting (HAI) antibody titers has a maximum 2-4 weeks after the vaccination, and it subsequently strictly decreases afterwards [71, 54]. In particular, [54] estimates that there is a marked decline of the immunity some months after the vaccination. This behavior is taken into account in our analysis because it can be practically observed before reaching the time horizon of the problem.

The aforementioned features of the illness will be considered, in this article, as given data. Two main attributes of the vaccine are considered:

- the durability of protection, that can span from several months up to several years – see [21, 17, 5] and the literature therein;
- the vaccine efficacy (noted VE, an input in our model), which is the theoretical success rate (to be distinguished from the vaccine efficiency, which is the practical observed success and is the output of the model – see [70] for a presentation of the differences between the two). The VE can range from several percents to almost perfect efficacy – see the meta-analysis in [56] and also [55]; other references include [51] and [67]. The VE can have effects on susceptibility, infectiousness, disease progression, and so on; we only consider here the impact on susceptibility, thus our VE is more specifically, with notations in [38, Section 2.2], of VE_S kind.

Hence, our model is suitable for studying imperfect vaccines and takes into account not only the individual decision about the vaccination, but also the best timing of the vaccination if the individual decides to be vaccinated.

Since the choice of the best timing problem of a vaccination campaign is very actual and it is carefully studied by the health authorities, we hope that our model can give a contribution to a better understanding of the vaccination dynamics in order to suggest efficient policies. In particular, our model forecasts that, in the

non-cooperative setting, when the protection given by the vaccine is not optimal, the individual behaviors are only partially in agreement with the suggestions of the World Health Organization (WHO), which encourages vaccination as soon as the vaccine of the corresponding seasonal influenza is available [22]: the agents could tend to delay the vaccination in order to arrive at the peak of the epidemic with the best possible protection (see [62, Section "Vaccination Before October"] and also [3, 29, 44, 9, 61] for recent references to intra-season waning of the vaccine-induced immunity and its impact on vaccination timing).

Because of the relatively short time horizon of the model, we do not consider any population dynamics, or any reinfection, since we suppose that antigenic drift is not very important on such small time scales [15].

From the mathematical point of view, in this article we work in a discrete setting and our model is described in terms of Markov chains. As far as the time horizon of seasonal influenza has the order of magnitude of one year, this choice allows us to model the coarse graining of the real situation and makes this model more suitable for the applications.

Firstly, we prove that the individual vaccine model proposed here admits an equilibrium. However, up to our knowledge, the equilibrium is not explicitly known. Far from being a disadvantage, this situation prompted us into proposing a general numerical method to find the equilibrium; this is a second contribution of this work (see also [65] for some alternatives coming from the physics community for general Mean Field Games). The numerical method is adapted from general works in game theory (see Section 3) and is expected to give accurate results in any situation when an individual chooses the right timing to perform some action (here vaccination) with time-dependent costs. This procedure has been extensively tested in our model and performs in a satisfactory way.

The structure of the paper is the following: the model is presented in Section 2 and the theoretical result guaranteeing the existence of an equilibrium in Section 2.3. The numerical algorithm for finding the equilibrium is presented in Section 3 and the numerical results in Section 4.

First of all, the numerical simulations describe a standard situation for seasonal influenza dynamics. Subsequently, we test our model on two extreme cases (the duration of the immunity is of one or six months only, see also [29]), which show some striking behaviors of the population and which may help to understand the strategic policies of the population.

Section 5 collects some considerations on the pertinence and validity of our approach.

2. **The model.** The model studies the dynamics of an epidemic in a population. In what follows we will suppose that

- the infection does not cause the death of the patient (as it is well known, the mortality associated to influenza does not induce significant modifications in the population structure [28]); moreover, by considering a time horizon of twelve months, we suppose that births and deaths, as well as age shifts, are non relevant;
- after the disease, the individuals who have been infected acquire permanent immunity (throughout the time horizon of our model): this means that we will suppose the existence of a predominant virus strain, instead of considering a mixing of viruses and therefore reinfection is a rare phenomenon;
- the incubation period is short when compared to the time scale of the model;

- the individuals can be vaccinated. If the vaccine is successful, the protection of the vaccine is maximal (but possibly not total) after a time delay, it remains high during some period and then it decreases (see [54]);
- the vaccine is imperfect and the imperfections can be of two kinds (see [63, 38, 64] for further discussions): *i)* a *all-or-none* effect, where a fixed fraction f of the vaccinated individuals is not at all protected (vaccination failure) and the remainder fraction $1-f$ is effectively immunized, and *ii)* a *leaky* (or incomplete) protection – which means that a vaccinated individual with effective immunization can still be infected (but not as much as a non-vaccinated individual or a failed-vaccinated invidual). This *leaky* protection evolves in time;
- the evolution of the epidemic can be influenced by seasonal effects, as is it the case of influenza in temperate regions.

In what follows, we describe the model in pure mathematical terms, the quantification of the different parameters will be then discussed in Section 4.

We suppose that the time horizon T is finite, and that it can be discretized in $(N+1)$ $(N \in \mathbb{N})$ time instants $t_0 = 0$, $t_1 = \Delta T$, $t_2 = 2\Delta T, \ldots, t_n = n\Delta T, \ldots, t_N = T$. The population is composed of

- *susceptible individuals:* S_n is the proportion of individuals in this class at time t_n;
- *infected individuals:* I_n^ω is the proportion of individuals in this class at time t_n, who have been infected at time $t_{n-\omega}$; moreover we denote by I_n the sum of all I_n^ω;
- *recovered individuals*, is the proportion of individuals once they recover from illness (after leaving the class of infected individuals);
- *vaccinated individuals:* V_n^θ is the proportion of individuals who have vaccinated at time $t_{n-\theta}$ and have not been infected yet;
- *failed vaccinated individuals:* F_n is the proportion of individuals that vaccinated at $t \leq t_n$, whose vaccination failed and have not been infected yet.

The quantities ω and θ are counters. The first one measures the time interval between the infection instant and the current instant, $\omega = 0,\ 1, \ldots,\ \Omega \in \mathbb{N}$, whereas the second one measures the time lapse between the vaccination and the current instant, $\theta = 0,\ 1, \ldots,\ \Theta \in \mathbb{N}$.

The upper bound Θ indicates the maximal duration of the (possibly partial) immunity given by the vaccine. In the case of seasonal influenza Θ is, in principle, greater than the time horizon of the problem. However, in order to make our model applicable also to other situations, we decide to take into account the theoretical possibility to manage vaccines with very short persistency. For this reason, we consider also the class V^Θ, which describes the vaccinated individuals that lost the immunity given by the vaccine. Since we suppose that they do not vaccinate twice, we need a specific class for describing them.

Similarly, Ω is the maximum time before recovery, and it depends on the properties of the illness itself.

The equations of the model, which conserves the total number of individuals, have the following form:

$$S_{n+1} = (S_n - U_n) - \beta_{\Delta T}^n I_n (S_n - U_n) \tag{1}$$

$$I^0_{n+1} = \beta^n_{\Delta T}\left[F_n + S_n + \sum_{\theta=0}^{N-1}\alpha_\theta V^\theta_n\right] I_n \tag{2}$$

$$I^{\omega+1}_{n+1} = (1-\gamma^\omega_{\Delta T})I^\omega_n \qquad \omega = 0,\dots,\Omega-1 \tag{3}$$

$$V^0_{n+1} = (1-f)\,(1-\beta^n_{\Delta T}I_n)\,U_n \tag{4}$$

$$V^{\theta+1}_{n+1} = (1-\beta^n_{\Delta T}\alpha_\theta I_n)\,V^\theta_n, \qquad \theta = 0,\dots,\Theta-2 \tag{5}$$

$$V^\Theta_{n+1} = (1-\beta^n_{\Delta T}\alpha_{\Theta-1}I_n)\,V^{\Theta-1}_n + (1-\beta^n_{\Delta T}I_n)\,V^\Theta_n \tag{6}$$

$$F_{n+1} = f\,(1-\beta^n_{\Delta T}I_n)\,U_n + F_n\,(1-\beta^n_{\Delta T}I_n) \tag{7}$$

with initial conditions

$$S_0 = S_{0^-}, \quad I^\omega_0 = I^\omega_{0^-}, \quad V^\theta_0 = 0, \quad \forall\theta\geq 0,\ F_0 = 0, \tag{8}$$

where

- U describes the vaccination: $U_n = u_n S_n$, where u_n is the proportion of individuals vaccinated after time t_n and before t_{n+1}; the admissible strategies correspond to $u_n \in [0,1]$;
- the vector $\gamma = (\gamma^0,\dots,\gamma^\Omega) \in (\mathbb{R}_+)^{\Omega+1}$ describes how fast an infected individual recovers and depends on the duration of the illness itself. In particular, when $\gamma^\omega = 0$, the individual will not recover in the next time instant; on the contrary, when $\gamma^\omega = 1$, the individual will recover with certainty in the next time instant.
- The function $\beta(t)$ quantifies how infectious is a contact between an infected individual and susceptible one at time t. To take into account the length of the time interval ΔT, we work with $\beta^n_{\Delta T} := \beta(t_n)\Delta T$ and $\gamma^\omega_{\Delta T} := \gamma^\omega \Delta T$. In order to take into account the possible seasonality $\beta(\cdot)$ is taken time-dependent, see Section 4 for an example.
- The vector α_θ describes the time instants of a function $A(\cdot)$ ($\alpha_\theta = A(\theta\Delta T)$) with values in $[0,1]$. This vector quantifies the protection given by the vaccine in terms of the probability of infection if an individual is vaccinated. It is known that this protection is not instantaneous, the immunity conferred by the vaccine being maximal after a latency period. As explained in the introduction, in the case of influenza vaccine, the protection is not complete, and the effects of the vaccine decrease with time.

  In what follows, we suppose that there exists a maximal time $\Theta > 0$ of the vaccine protection (which can be, however, greater than the time horizon of the model). In particular $\alpha_\Theta = 1$. Some possible candidates for the function A are shown in Figure 1.

2.1. **The societal cost and individual cost.** Let r_I and r_V be the individual cost for the illness and the vaccination respectively. These costs are intended to be *global costs*. For example, they can be the monetary cost of the illness and of the vaccine, but they can also express the medical side-effects of the vaccine and the possible side-effects of the illness (see, for example, [53]).

We work under the meaningful assumption that $r_I > r_V$ (although the alternative $r_I \leq r_V$ may also give non-trivial problems in particular situations, see [46]).

The total societal cost associated to the vaccination strategy U is:

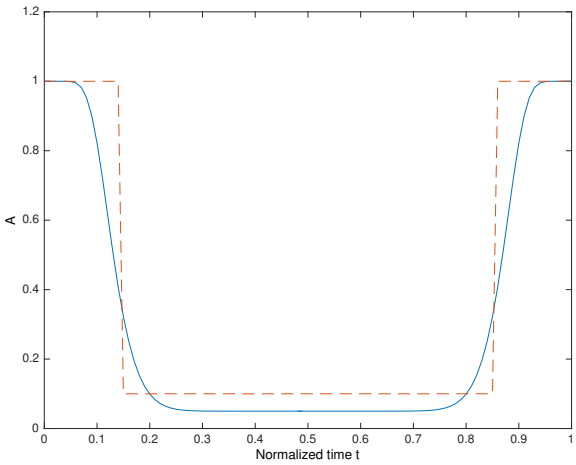

FIGURE 1. Two possible forms for the function A.

$$J(S_0, I_0, U) = r_I \sum_{n=0}^{N} I_n + r_V \sum_{n=0}^{N-1} U_n, \tag{9}$$

which has to be minimized (see [39, 1, 52, 59, 23, 46]) within the set of all admissible vaccination strategies U.

However this is not the strategy followed by individuals. They rather optimize an individual cost function. In order to define it, we have to consider the individual dynamics (see Figure 2 for an illustration). It takes the form of a controlled Markov chain with several states, *susceptible (S)*, *failed vaccination (F)*, *recovered (R)*, *infected* (indexed by the time counter ω: $I^0, \dots, I^\Omega$), and, finally, *vaccinated* states (indexed by the time counter θ: $V^0, \dots, V^\Theta$).

The Markov chain of the individual, denoted M_n, is described in terms of passage probabilities:

$$\begin{aligned}
&\mathbb{P}(M_{n+1} = S | M_n = S) && = (1-\lambda_n)\,(1-\beta^n_{\Delta T} I_n) && \\
&\mathbb{P}(M_{n+1} = I^0 | M_n = S) && = \beta^n_{\Delta T} I_n && \\
&\mathbb{P}(M_{n+1} = V^0 | M_n = S) && = (1-f)\lambda_n\,(1-\beta^n_{\Delta T} I_n) && \\
&\mathbb{P}(M_{n+1} = F | M_n = S) && = f\lambda_n\,(1-\beta^n_{\Delta T} I_n) && \\
&\mathbb{P}(M_{n+1} = R | M_n = I^\Omega) && = 1 && \\
&\mathbb{P}(M_{n+1} = R | M_n = I^\omega) && = \gamma^\omega_{\Delta T}, && \omega = 0, \dots, \Omega-1 \\
&\mathbb{P}(M_{n+1} = I^{\omega+1} | M_n = I^\omega) && = 1-\gamma^\omega_{\Delta T}, && \omega = 0, \dots, \Omega-1 \\
&\mathbb{P}(M_{n+1} = I^0 | M_n = V^\theta) && = \alpha_\theta \beta^n_{\Delta T} I_n, && \theta = 0, \dots, \Theta-1 \\
&\mathbb{P}(M_{n+1} = V^{\theta+1} | M_n = V^\theta) && = 1-\alpha_\theta \beta^n_{\Delta T} I_n, && \theta = 0, \dots, \Theta-1 \\
&\mathbb{P}(M_{n+1} = I^0 | M_n = V^\Theta) && = \beta^n_{\Delta T} I_n &&
\end{aligned} \tag{10}$$

$$\mathbb{P}(M_{n+1} = V^{\Theta} | M_n = V^{\Theta}) = 1 - \beta^n_{\Delta T} I_n,$$

$$\mathbb{P}(M_{n+1} = I^0 | M_n = F) = \beta^n_{\Delta T} I_n,$$

$$\mathbb{P}(M_{n+1} = F | M_n = F) = 1 - \beta^n_{\Delta T} I_n.$$

The conditions $\beta^n_{\Delta T} \leq 1$, $\gamma^{\omega}_{\Delta T} \leq 1$, $\lambda_n \geq 0$, $\lambda_n \leq 1$ ensure the well-posedness of this definition.

The conditional rates λ_n are derived from a probability density ξ defined on $\{t_0, \ldots, t_{N-1}\} \cup \{\infty\}$; the value ξ_n is the probability that the individual vaccinates at time t_n (if it was not infected before t_n). In practice, the agent chooses the probability distribution ξ before the dynamics starts. Then, he selects a random number n distributed with the aforementioned probability ξ, which means that before the beginning of the epidemic he knows the time t_n at which he will vaccinate (unless he is already infected by that time).

There is a mapping between $\lambda = (\lambda_n)_{n=0}^{N-1}$ and ξ defined by:

$$\xi_{\infty} = \prod_{n=0}^{N-1} (1 - \lambda_n), \qquad \xi_n = \lambda_n \prod_{k=0}^{n-1} (1 - \lambda_k), \qquad n \leq N-1 \tag{11}$$

$$\forall n \leq N-1 : \ \lambda_n = \begin{cases} \dfrac{\xi_n}{\xi_n + \cdots + \xi_{\infty}}, & \text{if } \xi_n + \cdots + \xi_{\infty} > 0 \\ 0, & \text{otherwise.} \end{cases} \tag{12}$$

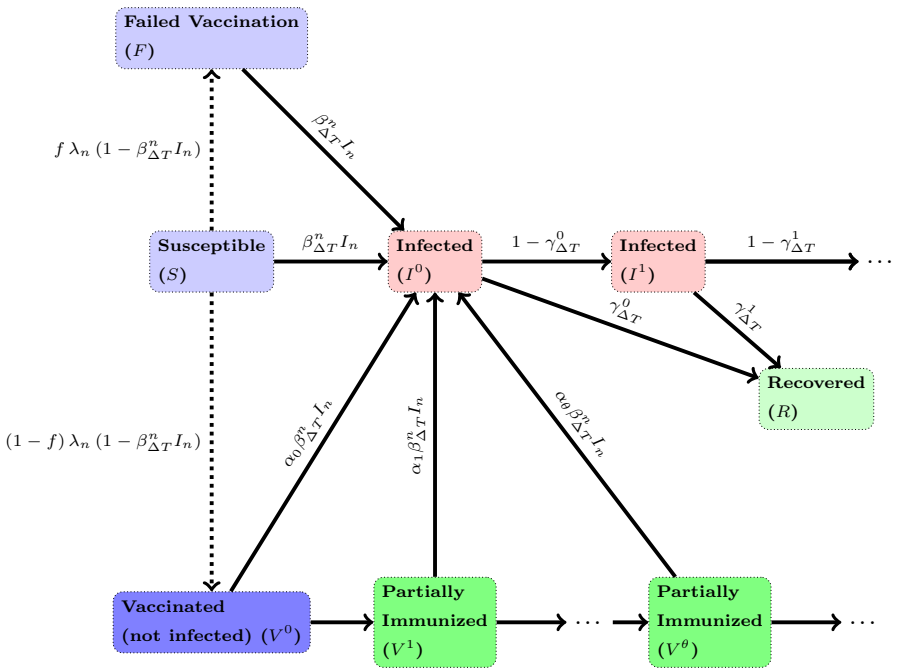

FIGURE 2. Individual model.

The cost of a vaccination strategy depends on ξ (see [47] for a similar situation). The individual bears the cost r_I when he enters class I^0 and then he bears the cost r_V when he enters class V^0. The cost for an individual will have three components:

- the cost r_I of being infected before vaccination;
- the cost r_V of vaccination plus a possible cost of being infected while immunity is still building or after the end of the protection period;
- the cost r_V of failed vaccination plus a possible cost of being infected.

Note that an individual may incur both costs if he vaccinates and, moreover, if he is infected. For an individual starting at $M_0 = S$, the total cost is:

$$\begin{aligned} J_{indi}(\xi;U) &= r_V \mathbb{P}\left(\cup_{n<N}\{M_{n+1}=V^0, M_n \neq V^0\}\Big| M_0 = S\right) \\ &+ r_V \mathbb{P}\left(\cup_{n<N}\{M_{n+1}=F, M_n \neq F\}\Big| M_0 = S\right) \\ &+ r_I \mathbb{P}\left(\cup_{n<N}\{M_{n+1}=I^0, M_n \neq I^0\}\Big| M_0 = S\right). \end{aligned} \tag{13}$$

This form for $J_{indi}(\xi;U)$ is impractical and has to be made more explicit. One possibility is to sum over the first passages from S to I^0, V^0 of F. The following quantities are useful for general n:

- the probability $\psi_n^{V,I}$ of infection (at time t_{n+1} or later) of an individual that vaccinated in the interval $[t_n, t_{n+1}]$, given by the formula:

$$\psi_n^{V,I} = 1 - \prod_{k=n}^{\Theta} \left(1 - \beta_{\Delta T}^k \alpha_{k-n-1} I_k\right), \tag{14}$$

  where we introduce the coefficient $\alpha_{-1} = 1$;

- the conditional probability of being infected (strictly) before t_{n+1} (of a person that did not vaccinate)

$$\varphi_n^I = \mathbb{P}\left[\cup_{k=0}^n \{M_k = I\} | M_0 = S, M_k \neq V^0, M_k \neq F, k \leq n\right],$$

  given by the formula:

$$\varphi_n^I = 1 - \prod_{k=0}^{n} \left(1 - \beta_{\Delta T}^k I_k\right), \forall n < N-1. \tag{15}$$

Note that the probability of being infected after the time $n < N-1$ is

$$1 - \frac{1-\varphi_\infty^I}{1-\varphi_n^I} = \frac{\varphi_\infty^I - \varphi_n^I}{1-\varphi_n^I},$$

where

$$\varphi_\infty^I = 1 - \prod_{k=0}^{N-1} \left(1 - \beta_{\Delta T}^k I_k\right).$$

Then, after elementary computations:

$$J_{indi}(\xi;U) = r_I \varphi_\infty^I \xi_\infty + \sum_{n=0}^{N-1} \left[r_I \varphi_n^I + (1-\varphi_n^I)(r_V + (1-f) r_I \psi_n^{V,I}) + r_I f(\varphi_\infty^I - \varphi_n^I)\right] \xi_n. \tag{16}$$

The individual cannot change U_n neither S_n, I_n^ω nor V_n^θ. He can only choose his vaccination strategy ξ. Denote

$$g_n^U = \begin{cases} r_I\varphi_n^I + (1-\varphi_n^I)(r_V + (1-f)r_I\psi_n^{V,I}) + r_I f(\varphi_\infty^I - \varphi_n^I), \text{ for } n \le N-1 \\ \\ r_I\varphi_\infty^I \text{ for } n = N. \end{cases} \tag{17}$$

If we denote the Euclidean scalar product between two vectors $X, Y \in \mathbb{R}^{N+1}$ by

$$\langle X, Y\rangle := \sum_{k=1}^{N+1} X_k Y_k, \tag{18}$$

then $J_{indi}(\xi; U) = \langle \xi, g^U\rangle$, where g^U and ξ are seen as vectors in $\mathbb{R}^{N+1}$. It has to be minimized under the constraint $\xi_0 + \cdots + \xi_{N-1} + \xi_\infty = 1$. Then any probability distribution ξ with support in $\{n \,|\, g_n^U \le g_k^U, k = 0, \ldots, N\}$ attains the minimum.

Now, for a given individual policy ξ one can ask whether the equations (1)-(8) are obtained when *all* individuals follow this vaccination policy, and in this case what is the compatibility relationship between ξ and U. Supposing identical initial conditions S_{0^-} and I_{0^-}, the compatibility relation between the two dynamics is:

$$U_n = \lambda_n S_n, \tag{19}$$

i.e. $\lambda_n = u_n$, see the discussion after formula (8).

2.2. **Failed vaccination.** A simplified model can be proposed to tackle the possibility of vaccination failure. Note that, for $n \le N-1$,

$$g_n^U = r_I f\varphi_\infty^I + (1-f)[r_I\varphi_n^I + (1-\varphi_n^I)(r_V/(1-f) + r_I\psi_n^{V,I})].$$

Therefore, since the term $r_I f\varphi_\infty^I$ does not depend on n and $(1-f)$ is an overall factor, the cost has exactly the same minimum as the one of a model without the class F when we replace r_V by $r_V/(1-f)$. Therefore, when the efficacy $1-f$ of the vaccine is not 100%, this can be treated by considering that the cost of the vaccine is multiplied by $(1-f)^{-1}$. See Section 4 for some numerical illustrations.

Note however that this is a first order approximation as, in practice, the quantities $\psi_n^{V,I}$ depend on the precise values of I_n^ω and a different model with different classes will change those values.

2.3. **Equilibrium.** Consider now the following mapping: for any given probability law η on $\{t_0, \ldots, t_{N-1}\} \cup \{\infty\}$ define λ by (12) (using η_n instead of ξ_n), U_n, S_n, I_n recursively by the relations (1)-(5) and (19). Denote $\mathcal{C}_\eta = g^U$.

Let $\mathcal{J}(\eta)$ be the ensemble containing all optimal individual strategies ξ that minimize the cost $\langle \xi, \mathcal{C}_\eta\rangle$.

The goal of this subsection is to deduce the existence of an equilibrium of the system, i.e. a common strategy which is a Nash equilibrium when it is used by all agents of the population. The following result holds.

Theorem 2.1. *There exists at least one law η such that $\eta \in \mathcal{J}(\eta)$ (i.e., an equilibrium).*

Proof. We use Kakutani's fixed point theorem (see [43, page 457]) for the function $\mathcal{J}(\cdot)$ defined on the simplex

$$\Sigma_{N+1} = \{(x_0, \ldots, x_N) \in \mathbb{R}^{N+1} | x_k \ge 0,\ x_0 + \cdots + x_N = 1\}. \tag{20}$$

Recall that the assumptions of the theorem are the following:

1. for any $\eta \in \Sigma_{N+1}$, the set $\mathcal{J}(\eta)$ is non-void, closed and convex; this property is trivially verified in our setting.
2. the mapping $\mathcal{J}(\cdot)$ is upper semi-continuous, or, stated otherwise, it has the closed graph property.

The only hypothesis to check is the closed graph property of $\mathcal{J}(\cdot)$. Let η^ℓ be a sequence of points in Σ_{N+1} (i.e., probability laws on $\{t_0, \dots, t_{N-1}\} \cup \{\infty\}$) converging to η and $\xi^\ell \in \mathcal{J}(\eta^\ell)$ converging to ξ. We have to prove that $\xi \in \mathcal{J}(\eta)$.

We denote by S^ℓ, U^ℓ, I^ℓ, g^{U^ℓ} (respectively S, U, I, g^U) the dynamics corresponding to η^ℓ (respectively η).

Let Z be the first index such that $\eta_Z + \dots + \eta_\infty = 0$. We consider the non-trivial case when $Z > 1$.

Consider λ^ℓ (respectively λ) the rates associated to η^ℓ (respectively η) by the formula (12). In particular $\eta_{Z-1} > 0$ and $\lambda^\ell_{Z-1} = 1$.

Although $\eta^\ell \to \eta$ as $\ell \to \infty$ we do not have that $\lambda^\ell \to \lambda$, but we have instead that $\lambda^\ell_n \to \lambda_n$ for all $n < Z$. In particular $\lambda^\ell_n S^\ell_n \to \lambda_n S_n$ for all $n < Z$. On the other hand, since $\lambda_{Z-1} = 1$ we have $S_Z = S_{Z-1}(1 - \lambda_{Z-1})(1 - \beta^n_{\Delta T} I_{Z-1}) = 0$ and $\lambda^\ell_{Z-1} \to 1$ implies $S^\ell_Z \to 0$; furthermore, S^ℓ being monotonically decreasing we also have $S^\ell_n \to 0$ for any $n \geq Z$.

Since all rates λ^ℓ are bounded by 1 we obtain thus that $\lambda^\ell_n S^\ell_n \to 0 = \lambda_n S_n$ for all $n \geq Z$ and thus ultimately $\lambda^\ell_n S^\ell_n \to \lambda_n S_n$ for all $n \leq N$. This, combined with the formulas (1)-(8) and (19) show that $U^\ell \to U$, $S^\ell \to S$, $I^\ell \to I$ as $\ell \to \infty$. Thus we also have $\mathcal{C}_{\eta^\ell} \to \mathcal{C}_\eta$; therefore the limit of any converging sequence of minimas of $\mathcal{C}_{\eta^\ell}$ is also a minima of $\mathcal{C}_\eta$ which, given its definition, proves the closed graph property of $\mathcal{J}(\cdot)$. □

Remark 1. The theorem reduces the existence of the equilibrium to the study of the mapping $\eta \mapsto \mathcal{C}_\eta$. This mapping has a well-defined meaning for a large class of vaccination games because the variable ξ is nothing else than the (mixed) individual strategy and the vector $\mathcal{C}_\xi$ collects the cost of pure strategies of the individual (given the overall epidemic propagation dynamics). We expect that this methodology can be generalized to other situations.

Remark 2. The result does not give any information about the uniqueness of the fixed point. In the Mean Field Game framework, uniqueness results usually from convexity considerations (see e.g., [49, 48, 41]) and it is not guaranteed, see [45] for a situation where there is no uniqueness. Although this setting is not convex, in all numerical simulations we pursued, a unique solution has always been found.

3. **Finding the equilibrium.** The result of the Section 2.3 guarantees the existence of at least one equilibrium. But, it does not prescribe a constructive method to find it.

For arbitrary strategy ξ, introduce the quantity $E(\xi)$ defined as follows: consider a situation when all individuals use the strategy ξ. If the individual follows himself the strategy ξ the expected cost is the average, with respect to the probability distribution ξ, of costs $\mathcal{C}_\xi$. By using the Euclidian scalar product (18) the cost can be written as $\langle \xi, \mathcal{C}_\xi \rangle$. But the individual can also choose some other strategies to minimize his cost. For instance if $\mathcal{C}_\xi$ reaches its minimum at the k-th component, the best cost is obtained with a strategy that vaccinates at time t_k with certainty. When the minimum is not unique, the general value of the lowest cost that the individual can reach is $\min_{\eta \in \Sigma_{N+1}} \langle \eta, \mathcal{C}_\xi \rangle$ where Σ_{N+1} is the space of all possible

strategies. The mismatch between the cost of "following the others" and the "lowest possible cost" is denoted with $E(\xi)$. It represents the maximum gain obtained by an individual if he changes unilaterally his strategy (and everybody else remaining with the strategy ξ). In mathematical terms:

$$E(\xi) = \langle \xi, \mathcal{C}_\xi \rangle - \min_{\eta \in \Sigma_{N+1}} \langle \eta, \mathcal{C}_\xi \rangle. \tag{21}$$

Note that $E(\cdot) \geq 0$ and that an equilibrium corresponds to a ξ such that $\langle \xi, \mathcal{C}_\xi \rangle \leq \langle \eta, \mathcal{C}_\xi \rangle$ for any other strategy $\eta \in \Sigma_{N+1}$, which means $E(\xi) = 0$. The equilibrium can be rephrased as finding a strategy ξ such that the mapping $\xi \mapsto E(\xi)$ is minimized.

A natural idea is then to try to minimize $E(\cdot)$ over Σ_{N+1}. But, this intuitive approach is not always the best one because, in order to be efficient, the minimization of $E(\cdot)$ requires to compute, for instance, some gradient of $\mathcal{C}_\xi$ with respect to ξ, which could make the computations complicated.

Another idea is simpler and intuitively more appealing: the equilibrium will be found by successive approximations in a way that mimics a real-life repeated game (see also [32] for additional considerations). Consider a strategy candidate ξ_k obtained at the iteration k and construct the cost $\mathcal{C}_{\xi_k}$ obtained if everybody uses the strategy ξ_k. An individual of this population will test whether ξ_k is optimal, i.e. if it is a minimum of $E(\cdot)$. If this is the case then the equilibrium is ξ_k; otherwise the individual will adjust its strategy ξ_k by exploring a strategy ξ_{k+1}, which is not too far from ξ_k but that goes towards the lowest possible cost $\min_{\eta \in \Sigma_{N+1}} \langle \eta, \mathcal{C}_{\xi_k} \rangle$. In practice (with ideas close to the general framework of gradient flows, see [42] for an entry point to this literature), one can choose ξ_{k+1} to be a minimizer of a weighted sum containing both *desiderata*, which can be expressed in mathematical terms:

$$\xi_{k+1} \text{ is a minimizer over } \Sigma_{N+1} \text{ of } \eta \mapsto \frac{dist(\eta, \xi_k)^2}{2\tau} + \langle \eta, \mathcal{C}_{\xi_k} \rangle, \tag{22}$$

where $dist(\cdot, \cdot)$ is some suitable distance in Σ_{N+1}. Then the procedure is iterated till convergence. This idea is similar to the paradigms of "Best Reply" (see [10]), "fictitious play" (see [14]) or "equilibrium flows" for which some proofs of convergence exist under specific hypotheses. In particular the results in (see [68, Theorem 2, item 2]) show that convergence is attained when the mapping $\eta \mapsto \mathcal{C}_\eta$ in Remark 1 is continuous, which is proved in Theorem 2.1.

The term $1/2\tau$ weights the relative importance of staying close to ξ_k with respect to optimizing the cost. In particular τ can be interpreted as a pseudo-time counting the number of infinitesimal adjustments required to converge to the equilibrium. Note also that, when $\tau \to 0$, the distance $dist$ is the Euclidian distance and Σ_{N+1} is the whole $\mathbb{R}^{N+1}$, the strategy ξ can be seen as the time-indexed solution of the differential equation

$$\frac{d}{d\tau}\xi(\tau) = \mathcal{C}_{\xi(\tau)}.$$

In order to keep the presentation as simple as possible, we used as distance in (22) the standard euclidian distance on $\mathbb{R}^{N+1}$ although in principle other distances (such as the 2-Wasserstein distance) may give better performances.

In practice, the algorithm applied is the following:

Step 1. Choose a step $\tau > 0$ and a starting distribution ξ_1.

Set iteration count $k = 1$.

Step 2. Compute ξ_{k+1} as in formula (22).

Step 3. If $E(\xi_{k+1})$ is smaller than a given tolerance then stop and

`exit, otherwise set` $k \to k+1$ `and go back to Step 1.`

In practice Step 2 is computed with a quadratic programming routine (`quadprog` in `Matlab/Gnu Octave`) that can accommodate linear constraints.

Remark 3. The procedure proposed above can be extended in a straightforward manner to any 'rational individual' vaccination model, by replacing the vector $\mathcal{C}_\xi$ by a time-dependent function $c(\cdot)$, where $c(t)$ is the cost of the pure strategy consisting in vaccinating at the time t under the assumption that everybody follows the strategy ξ.

4. Numerical results.

In order to test the model, we simulated the situation of an epidemic with several sets of parameters, such as long or short durability of protection, as indicated below.

4.1. Preliminary tests.

We first tested the procedure for a situation when the analytic result is known (see [31, 47]): we used the parameters in [47, Figure 5] and obtained that the optimum individual strategy is a mixed strategy with $\xi_0 = 33\%$ probability of vaccination at $t = 0$ and $\xi_\infty = 67\%$ probability of no vaccination; its cost is 0.5067; this result is in a good agreement with the analytic result, i.e. a mixed strategy with $\xi_0 = 34\%$, $\xi_\infty = 66\%$ and a cost 0.5.

4.2. Equilibrium with decreasing immunity and imperfect efficacy.

The numerical values used in this simulations are the following: total simulation time $T = 1$ (one year), number of time instants: $N = 365\times 3$ (three times a day); recovery rate $\gamma^\omega = \gamma = 365/3.2$ (mean recovery time 3.2 days, $\Omega = 20$), high season basic reproduction number $R_0 = 1.35$, thus $\beta = \gamma R_0$; recall that the basic reproduction number is the average number of secondary infections generated by an infected individual in a susceptible population and in absence of any vaccination, for details see [2, Section 2.2 and beyond] and also [36, Section 3]. The initial proportion of susceptibles is $S_0 = 0.94$ and the initial proportion of infected individuals is $I_0 = 2.0 \times 10^{-6}$; the relative costs are $r_I = 1$ and $r_V = 0.005$. To take into account the seasonality of $\beta(t)$, we set $\beta_{min} = \gamma/S_0$ and $\beta(t) = \beta$ for $t \le t_2^\beta := 1/2$ (6 months) and then $\beta(t) = \beta_{min}$ for $t > t_2^\beta = 1/2$; these parameters model an epidemic lasting 6 months.

We set the vaccine efficacy to $f = 50\%$; the durability of protection of the vaccine is related to the decrease of the immunity. Although very few studies on decreasing immunity dynamics are available, it is generally accepted that the immunity is rising and reaches a peak after some weeks (here we took 3 weeks). Then it slowly declines in a timescale of the order of months (see also [17, 29, 44, 9]). For instance, the study in [54] found a significant decay (20% to 50%) over a period of 9 months. As we will see, even if the immunity is not completely lost by the end of the season, this decay influences the equilibrium. The main ingredient of the time-dependence $t \mapsto A(t)$ is an exponential decay term (see e.g., [37, page 458]); however in the exponential model the immunity is acquired instantaneously upon vaccination. In order to take into account the gradual gain in immunity, we included a multiplicative polynomial term, which becomes negligible for large times; see also section 4.3.1 for a different choice of $A(t)$. With our notations, the function $A(t)$ is

$$A(t) = 1 - c_1 t^{c_2} e^{-c_3 t}, \tag{23}$$

with constants c_1, c_2, c_3 set such that the minimum value (zero) is reached in $t = 3/52$ while 9 months after, i.e., at $t = 3/52 + 9/12$ the value is either $\mathcal{M}_1 =$

1/10 (which corresponds to 9/10 immunity still active 9 months after the peak) or $\mathcal{M}_2 = 1/3$ (which corresponds to 2/3 immunity still active 9 months after the peak).

We considered first the 'ideal' case of instantaneous and non-decaying immunity. The corresponding equilibrium is a policy when people vaccinate at $t = 0$ (10% of them). Intuitively, it means that, when the persistence is greater than the time horizon of the problem, individuals choose to be vaccinated as soon as possible.

Then the equilibrium for $\mathcal{M}_1$ was computed. The results are shown in Figure 3. Note that the vaccination peak is delayed by one month, even if the decay in the immunity is relatively moderate (immunity is still at 90% after 9 months).

Finally, a different situation when immunity falls to 66% is presented in Figure 4; here the vaccination is delayed with approximately two months.

The differences between these three situations, both in the vaccination timing and in the fraction of vaccinated individuals, are a consequence of the optimal criterion of the agents, of the durability of protection of the vaccine and of the nonlinearity of the contagion process. Due to the partial loss of immunity before the end of the season, the agents tend to delay the vaccination in order to have the best possible protection during the peak of epidemics. On the other hand, the reduction of the efficiency of the vaccine motivates more individuals to be vaccinated in order to increase group immunity and hence to reduce the contagion.

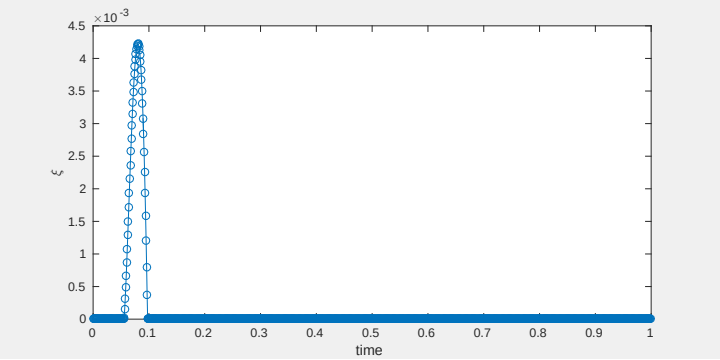

FIGURE 3. The optimal converged strategy ξ^{MFG} at times $\{t_0, ..., t_{N-1}\}$ for subsection 4.2, case $\mathcal{M}_1$. The weight of the non-vaccinating pure strategy (i.e., corresponding to time $t = \infty$) is 88%; this means that 12% of the population vaccinates.

4.3. **Relationships between freedom of choice, durability of protection and efficacy of the vaccine.** We investigate in this subsection the robustness of the numerical results with respect to various choices of parameters, in particular the durability of protection and efficacy, as detailed below. The results of these tests show that the freedom of choice to obtain the best individual result could lead to more expensive individual costs than those obtained in a regulated setting, where public health authorities prescribe individual policies (this phenomenon is the so-called *cost of anarchy*, see Subsection 4.3.1). On the other hand, we show that imperfect vaccines (i.e., with short durability of protection and limited efficacy)

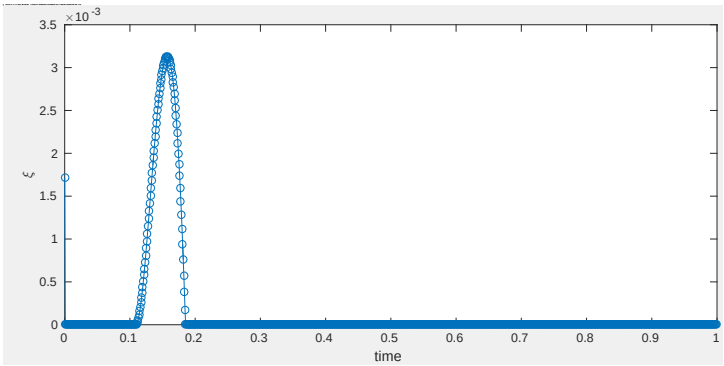

FIGURE 4. The optimal converged strategy ξ^{MFG} at times $\{t_0, ..., t_{N-1}\}$ for subsection 4.2, case $\mathcal{M}_2$. Here 15% of the population vaccinates.

may be also acceptable, for a fraction of the population, as a tool for reducing the contagion process, even if the vaccination is not compulsory.

4.3.1. *Short durability of protection, large efficacy.* To define the durability of protection of the vaccine we set $t_1 = 5/365$, $t_2 = 1/12$ (one month, $\Theta = 93$) and $A(t) = 1 - \mathbb{1}_{[t_1,t_2]}$. The vaccine efficacy is set to 100%, i.e., we suppose a failure rate $f = 0$. The step is $\tau = 0.1$ and we performed 1000 iterations.

The results are displayed in Figures 5, 6 and 7. A good quality equilibrium is found, that is, the incentive to change the strategy $E(\xi)$ is smaller than 10^{-3} (two orders of magnitude lower at the solution than at the initial guess). The cost of the solution $\langle \xi^{MFG}, \mathcal{C}_{\xi^{MFG}} \rangle$ is 0.0237.

The solution is a strategy ξ^{MFG} supported at several time instants between 0.25 and 0.43 and also having 68% of the mass at the non-vaccinating time $t = \infty$. Note that the cost is adapted accordingly, reaching its minimum at all points in the support of the solution ξ^{MFG}. Generally the vaccination occurs when I_n has large values, except at the end of the epidemic (time 0.5) when people expect the epidemic to end and estimate that their infection probability is low; the individuals have a strategic behavior, in coherence with the model. This can be compared with the model in [8] where the vaccination rate is supposed proportional with the number of people infected. The two models agree in a majority of time instants except the end of the epidemic. This behavior has been observed across a wide range of protection periods and initial conditions (the results are not shown here). It is remarkably to see that a simple model such as in [8] has such a considerable applicability.

It should be mentioned that the solution ξ^{MFG}, with cost 0.0237, is *not* the solution that minimizes the average cost across individuals (see also equation (9)) which is $M(\xi) = \langle \xi, \mathcal{C}_\xi \rangle$: for instance the strategy ξ^{min} that vaccinates with certainty at time $t = 0.0$ (unless infected by that time) has $M(\xi^{min}) = 0.005$. This result is not surprising and often appears in such contexts (see [47]). When $M(\xi^{MFG}) > M(\xi^{min})$ the game is said to have a positive *cost of anarchy*. It can be intuitively explained as follows: suppose that everybody uses the strategy ξ^{min}. The cost of an individual with strategy η will be $\langle \eta, \mathcal{C}_{\xi^{min}} \rangle$ and it turns out that

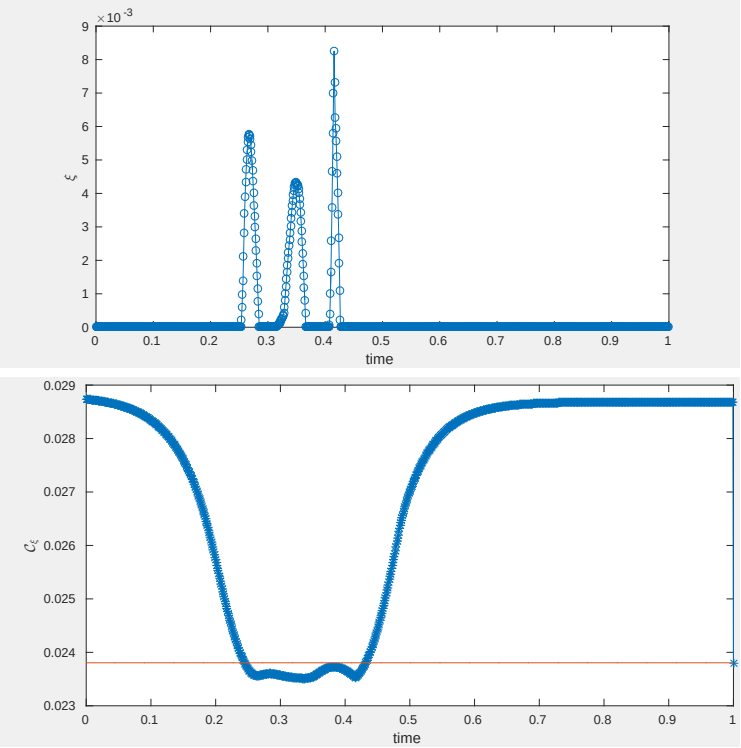

FIGURE 5. Results for Subsection 4.3.1. Top: the optimal converged strategy ξ^{MFG} at times $\{t_0, ..., t_{N-1}\}$. The weight of the non-vaccinating pure strategy (i.e., corresponding to time $t = \infty$) is 68%. Bottom: the corresponding cost $\mathcal{C}_{\xi^{MFG}}$. The red line corresponds to the cost of the non-vaccinating pure strategy $(\mathcal{C}_{\xi^{MFG}})_{N+1}$.

there exists some η_1 with $\langle \eta_1, \mathcal{C}_{\xi^{min}} \rangle < \langle \xi^{min}, \mathcal{C}_{\xi^{min}} \rangle$. For instance here η_1 can be a pure non-vaccinator strategy whose cost is very low 8.0×10^{-6}. Therefore any individual with current strategy ξ^{min} has an incentive to change his strategy (and use η_1) by hoping that everybody else remains with the strategy ξ^{min}. This does not happen and everybody slides towards η_1 and so on until the Nash equilibrium ξ^{MFG} is found. In the process the cost of *everybody* will increase and this is the price to pay for equilibrium.

4.3.2. *Long durability of protection,* 100% *efficacy.* The parameters are identical as in Subsection 4.3.1, except the durability of protection of the vaccine time t_2 which is set now to 6 months $t_2 = 1/2$ ($\Theta = 549$). The convergence is quickly attained (100 iterations) and the results are displayed in Figure 8. Although fewer people vaccinate (only 9% here, to compare with 32% in Subsection 4.3.1), the higher durability of protection of the vaccine improves the outcome. The equilibrium cost becomes 5.18×10^{-3}, almost one order of magnitude lower than in the previous test.

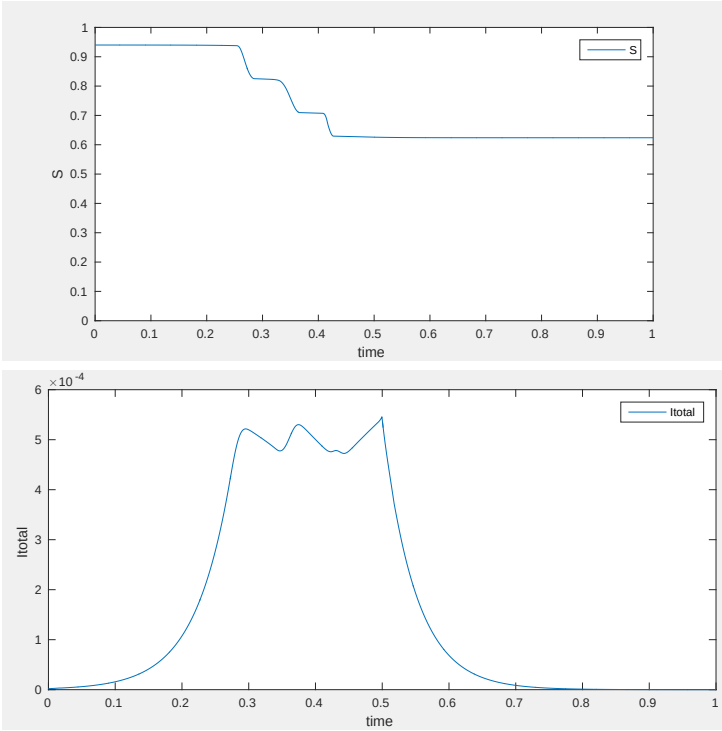

FIGURE 6. Results of Subsection 4.3.1. Top: the evolution of the susceptible class S_n; bottom: the (total) infected class I_n.

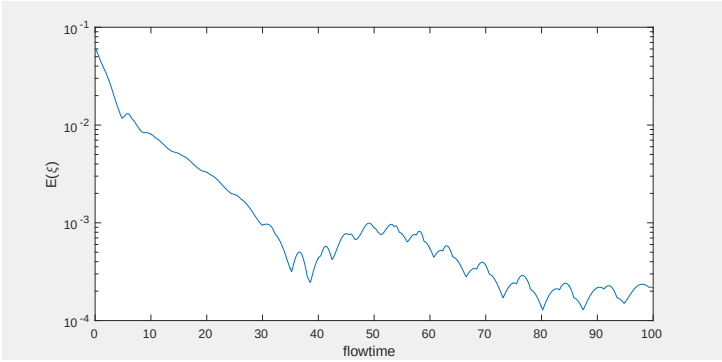

FIGURE 7. The decrease of the incentive to change strategy $E(\xi_k)$. Note that $E(\xi_k)$ does not decrease monotonically. In fact, there is no reason to expect such a behavior, since we are not minimizing $E(\cdot)$ in a monotonic fashion.

4.3.3. *Long durability of protection, smaller efficacy.* In this Subsection, we test a situation when the vaccine efficacy is only 50%. All other inputs are as in Subsection 4.3.2. The result, not shown here because very similar to those described in the previous tests, has however several differences:

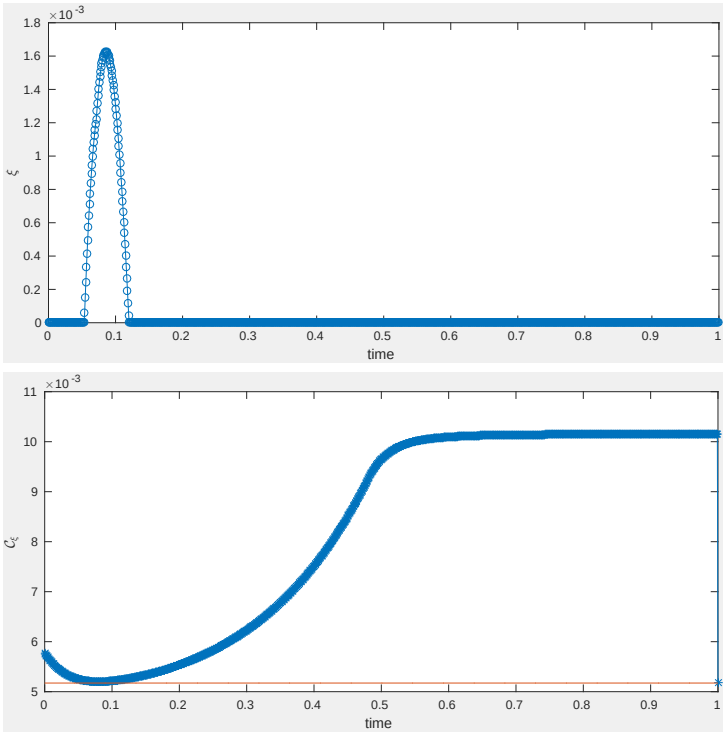

FIGURE 8. Results of Subsection 4.3.2. Top: the optimal converged strategy ξ^{MFG}. The weight of the non-vaccinating pure strategy (i.e., corresponding to time $t = \infty$) is 91%. Bottom: the corresponding cost $\mathcal{C}_{\xi^{MFG}}$. The thin horizontal line corresponds to the cost of the non-vaccinating pure strategy $(\mathcal{C}_{\xi^{MFG}})_{N+1}$.

- the probability of the non-vaccinating strategy is now 86% (i.e. 14% of people vaccinate);
- the cost of the optimal strategy is 0.0101.

Therefore the equilibrium shifts towards a bigger fraction of the population that vaccinate (in order to compensate lower vaccine efficacy). However, the overall number of protected people is lower (50% of 14% being smaller than 100% of 9%) which results in a larger overall equilibrium cost (about twice larger). We tested other settings and these conclusions were consistently obtained: the introduction of imperfect vaccines (here lower efficacy) generates overall lower coverage rates and larger costs.

We also compared the previous result with the output of the model obtained by setting the cost $r_V \to r_V/(1-f) = 0.01$, $f \to 0$. In this case the cost is 0.0103 and the fraction of vaccinated individuals is 6.6%. This result confirms the qualitative analysis of Subsection 2.2.

4.4. **Effects of the failed vaccination rate on the vaccination strategy.** We analyze in this subsection the effects of the failed vaccination rate on the overall vaccination policy. The numerical value of the vaccination cost is $r_V = 0.025$,

whereas the other parameters are the same as in Subsection 4.3.3. The results are presented in Table 1.

Failed vaccination rate f	Vaccination rate $1-\xi_\infty$
0.00	5.04%
0.25	5.94%
0.50	7.02%
0.55	7.20%
0.60	7.29%
0.65	7.23%
0.75	5.74%
0.80	2.93%
0.85	0.00%

TABLE 1. Results for the Subsection 4.4. Individual vaccination policy with respect to the failed vaccination rate of the vaccine.

When the failure rate f is small, the vaccination rate $(1-\xi_\infty)$ is increasing with f. However, when the failure rate f is larger than a given value (in our numerical simulations, when $f \geq 0.60$), the vaccination rate decreases as f increases.

When the failure rate is small, individuals tend to vaccinate more to compensate the decrease in efficacy and therefore to contribute to the group protection and to profit from it. However, after a given threshold, the construction of a group protection is too expensive, and consequently the individuals are reluctant to vaccination (if $f = 0.85$, the vaccination rate $(1-\xi_\infty)$ is zero; in this case, the probability of being infected is 14.38%).

5. **Discussion.** We analyzed in this work the vaccination equilibrium in a context of rational individual vaccination choices; the situation is modeled as a Nash equilibrium with an infinity of players. In our work, a special attention is given to the presence of imperfect vaccines. We presented a theoretical approach (existence of an equilibrium via the Kakutani fixed point theorem) and a numerical algorithm (similar to a gradient flow). Both approaches have the advantage to use rather weak assumptions on the structure of the model. For this reason, we hope that our study will be useful even in more general situations, as those listed later on in this section, which take into account more complicated individual and collective behaviors.

In the simulations dealing with an influenza epidemic, we remark that the long-term behavior of the vaccine-induced immunity influences the best timing for the individuals to vaccinate. Indeed, when the protection of the vaccine against influenza does not decrease within the time horizon of the problem, the individuals vaccinate as soon as possible (in agreement with the recommendation given by WHO [22]). However, if the vaccine efficacy decreases, the behavior of the population changes and delays the vaccination for optimizing the vaccine protection around the peak of the epidemic.

In addition, the previous simulations show that the imperfections of the vaccine increase the overall cost. But the obtained equilibrium is such that the increased vaccination rate does not compensate for the lower efficacy (or durability of protection) of the vaccine.

When the failure rate is below a given threshold, the cost for building a group protection is advantageous with respect to the infection cost. In this case, a higher

vaccination rate can be optimal to compensate for an increase in the failure rate. However, this individual policy is far from the societal level optimal strategy, which would consist in a global optimization of the vaccination policy.

Several assumptions in this work may motivate further studies:

- a general question is whether the individuals choose their vaccination strategies beforehand; for instance, Fine and Clarkson (see [30]) argue that the individuals will rather respond to the prevalence; see also [8] where the vaccination rate is dependent on the number of people infected. However the "learning" of an equilibrium is a topic in itself in game theory (we refer to the monograph [32] for general considerations). In our specific setting, an encouraging factor is that the "game" is played several times (once each season, although with possible different vaccine efficacies), in such a way that a learning mechanism could be recognized. Moreover, individuals have appropriate feedbacks (through general news for instance) on both the history of the epidemic and the vaccination dynamics, as well as – more importantly – projections for the upcoming season (for example, data on the potential severity of the epidemic and the expected dynamics of vaccination). Other factors can also influence the decision, such as the number of reported cases and public health campaigns. But, of course, the setting presented here remains ideal and the interpretability of the results is dependent on our hypotheses. A model that can detect to which extent the individuals adhere to this assumption would be more versatile.
- the individuals are supposed perfectly aware of the past, present and future epidemic dynamics: a model with limited information may be more realistic. Such models can be at the mid-way between the MFG and the *feedback* (also known as *information-based*) vaccination models, see [26, 25, 13];
- the individuals are identical. In particular the cost of the illness is exactly the same, irrespective of age: considering several age groups may give interesting results, especially if their strategies are different;
- the geographical heterogeneity in the propagation of the epidemic is neglected: travels and intra/inter-community contacts may be important for the epidemic propagation.

Some of the previous limitations can be overcome. For example, the geographical heterogeneity in the propagation of the epidemic can be taken into account by converting our model to a PDE-based description, and then by coupling it with a population dynamics model. On the other hand, the stratification by age could be handled by writing a more general model with a supplementary age variable. We aim to take into account some of these perspectives in future studies.

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