ORIGINAL PAPER



Communication strategies to contrast anti-vax action: a differential game approach

Alessandra Buratto¹ · Rudy Cesaretto¹ · Maddalena Muttoni¹

Accepted: 20 April 2024 © The Author(s) 2024

Abstract

Vaccination is one of the greatest discoveries of modern medicine, capable of defeating many diseases. However, misleading information on the effectiveness of vaccines has caused a decline in vaccination coverage in some countries, leading to the reappearance of related diseases. Therefore, a proper and well-planned pro-vax communication campaign may be effective in convincing people to get vaccinated. We formulate and solve a differential game with an infinite horizon played à la Nash. The players involved in the game are the national healthcare system and a pharmaceutical firm that produces and sells a certain type of vaccine. The former aims to minimize the healthcare costs that unvaccinated people would entail. In turn, the pharmaceutical firm wants to minimize the missed profits from unsold vaccines. The two players run suitable vaccination advertising campaigns to diminish the *à-régime* number of unvaccinated. The Hamilton-Jacobi-Bellman approach is used to determine a Markovian-Nash equilibrium, studying how communication strategies can be effective in reducing the strength of anti-vax word of mouth.

Keywords Differential games · Stationary Markovian nash equilibrium · Vaccine communication policy · Advertising

Mathematics Subject Classification 49N90 · 90B60 · 49N10

Rudy Cesaretto and Maddalena Muttoni have contributed equally to this work.

Alessandra Buratto alessandra.buratto@unipd.it

> Rudy Cesaretto rudy.cesaretto@gmail.com

Maddalena Muttoni maddalena.muttoni@studenti.unipd.it

¹ Department of Mathematics "Tullio Levi-Civita", Università degli Studi di Padova, Via Trieste, 63, 35121 Padova, Italy

1 Introduction

Vaccination is one of the greatest discoveries of modern medicine. Thanks to vaccines, diseases such as poliomyelitis, tetanus, smallpox, diphtheria, and rubella have been eradicated in many countries. Furthermore, vaccination has recently been shown to reduce the incidence of some other diseases, for example, human papillomavirus (HPV) infection (Takla et al. 2018), meningitis (Buonomo et al. 2022), and some forms of cancer. The public health benefits brought by such discoveries are so important that several countries have even devised mandatory childhood vaccination policies^{1,2} .Committees on Vaccination have been constituted in many countries to plan communication campaigns in favor of vaccination, such as the (STIKO) in Germany by Robert Koch-Institut³ and the European Centre for Disease Prevention and Control⁴ have done.

However, people often do not perceive the importance of vaccines, either because some of the diseases that were eradicated are no longer visible or because their effects may show up only after long periods. In case a given vaccination is not mandatory, without memory of the damage the related disease can cause, the perceived risks of vaccination among some people have begun to outweigh their perceived benefits (Omer et al. 2009; Buonomo et al. 2013). Some people focus only on the risk of side effects, which for them appears to be extremely high compared to the risk associated with contracting the disease, (Salmon et al. 2006). Furthermore, vaccine efficacy has recently been debated by skeptics who try to spread the idea that vaccines are ineffective and even dangerous (see, e.g., Shim et al. (2013), Carrillo and Lopalco (2012), and Hotez (2017)).

In turn, media, such as magazines, television, the Internet, and social networks, often present news related to vaccines without submitting them to strict verification by scientific and health authorities. Sometimes, they spread alarming news without any foundation, in the worst cases even claiming an association between vaccines and serious diseases. Just to mention, even though Andrew Wakefield's claim about a causal relation between vaccines and autism was refuted by the scientific community; see Taylor et al. (2014), such a conjecture has caused a decline in vaccination coverage, especially in certain countries.

Due to these fake news, some diseases were taken too lightly and gave rise to the vaccine hesitancy effect; see, e.g., Bozzola et al. (2018) and White et al. (2023). Shim et al., Shim et al. (2013), assert that if the great benefits to society of measles vaccination are to be maintained, the public must be educated about these benefits in order to increase public confidence. When organizing vaccine administration, national health systems must consider many aspects, and in the last decade the issue of correct communication about the vaccination campaign has become crucial. The authors observe that the effectiveness of vaccination programs can be jeopardized

¹ https://www.immunize.org/laws, retrieved on 2023/06/19.

² https://ijponline.biomedcentral.com, retrieved on 2023/06/19.

³ https://www.rki.de/EN/Content/infections, retrieved on 2023/06/19.

⁴ https://www.ecdc.europa.eu/en, retrieved on 2023/06/19.

by public misperceptions of vaccine risk. They illustrate "the importance of public education on vaccine safety and infection risk to achieve vaccination levels that are sufficient to maintain herd immunity."

In this paper, we study the effect of a vaccination advertising campaign in supporting countries to increase the coverage of measles, rubella, and other vaccines. The idea arises from a recent report by the World Health Organization (WHO), which underscores the impact of the COVID-19 pandemic on surveillance and immunization efforts. The report highlights that the suspension of immunization services has decreased the estimates of immunization coverage for many infectious diseases. In fact, during the last three years, the COVID-19 pandemic stopped surveillance and immunization efforts, putting many children at risk for preventable diseases. "Approximately 25 million infants missed at least one dose of the measles vaccine through routine immunization in 2021."⁵ Globally low immunization rates increased the chances of outbreaks and endanger unvaccinated children. The World Health Organization just decided to work towards regional measles elimination by strengthening immunization programs (e.g., Measles and rubella strategic framework: 2021-2030) and implementing effective surveillance systems.

Perceiving the same need for a focused public educational system, this paper aims to formalize in a mathematical context the problem of planning a pro-vax communication campaign to convince people to get vaccinated. In what follows, we assume that the vaccination we are dealing with is not mandatory.

Our research questions are as follows.

- How does negative word of mouth affect the evolution toward herd immunity?
- How can the pro-vax communication campaigns of the national health-care system and of pharmaceutical firms speed up such an achievement?
- How can a proper pro-vaccination campaign sustain the vaccination efficiency of the national health-care system?

The remainder of the paper is organized as follows. In Sect. 2 we briefly review the literature and position our contribution. In Sect. 3 we introduce our model for a controlled evolution of the unvaccinated population, together with the cost functionals associated with such an attempt. We formalize the problem in a differential game framework. In Sect. 4 we determine the optimal communication strategies that constitute the associated steady-state feedback Nash equilibrium. Section 5 presents some sensitivity analysis of the solution together with interpretations of the results. Section 6 concludes.

⁵ https://www.who.int/news-room/, retrieved on 2023-06-19.

2 Brief literature background

A consistent stream of literature tackles the issue of controlling infectious diseases based on epidemic models, in particular, on behavioral Susceptible-Infected-Recovered (SIR) models. In the book Manfredi and d'Onofrio (2013) a vast literature on vaccination and other influences of human behavior on the spread of infectious diseases is presented. A detailed report reviewing models that account for behavioral feedback and / or the spatial / social structure of the population can be found in Wang et al. (2016). More recent publications among the same stream of literature are e.g. d'Onofrio and Manfredi (2020) and Buonomo et al. (2022). An interesting approach to the vaccination problem in the context of game theory is tackled in Shim et al. (2013), where a game-theoretic model of disease transmission and vaccination is formalized as a population game. Here, the game-theoretic epidemiological analysis performed can yield insights into the interplay between anti-vaccine behavior, vaccine coverage, and disease dynamics. More recently in Matusik and Nowakowski (2022) a game-theoretical approach has been used to model the control of COVID-19 transmission, always in the context of SIR dynamics.

The so-called word-of-mouth effect plays a crucial role in the spread of antivax beliefs. Bauch in Bauch (2005) studies the strategic interaction between individuals when they decide whether or not to vaccinate, using an imitation dynamic game. The role of word of mouth in voluntary vaccination planning is presented in Bhattacharyya et al. (2015), where the synergetic feedback between word of mouth and the epidemic dynamics controlled by voluntary vaccination is analyzed. The authors present an epidemiological model with a social learning component that incorporates the reciprocal influence of population groups, as well as the feedback that can occur from the incidence of diseases. They model this social interaction through a game-theoretical framework using the concept of payoff, adapted from applications of Game Theory to Economics.

Just because anti-vax behavior is often associated with word of mouth, rather than with scientific data and information, it seems interesting to tackle the problem not necessarily from an epidemiological point of view but from a sociological point of view. Therefore, the communication approach derived from the theory of dynamic advertising models, described in Huang et al. (2012), suggests a correct communication policy to defeat the spread of the anti-vax movement. In a communication framework, El Ouardighi et al. in El Ouardighi et al. (2016) consider two different types of word of mouth: negative (or adverse) and positive (or favorable) according to the different reactions of satisfied and dissatisfied customers. The authors stress how negative word of mouth is more influential than positive, especially for brands with which potential customers are not familiar, and this could be the case for the vaccine issue.

Within the literature stream based on dynamic advertising models, Grosset and Viscolani (2021) formulate and solve an optimal control problem to determine a provaccination communication campaign that contrasts the effect of antivaccination word of mouth, with the objective of minimizing the care cost induced by unvaccinated people and the cost resulting from the communication campaign. The authors propose an upper bound to the final number of unvaccinated people to guarantee herd immunity. In such a model the programming interval is fixed, while in Grosset and Viscolani (2020) the authors study a variable-final-time optimal control problem to stress the importance of reaching the given herd immunity threshold, rather than reducing costs in a fixed-length programming period.

In Buratto et al. (2020), a model for the aforementioned national health problem is proposed using a linear-quadratic differential game in a finite time horizon. The model aspires to understand how an optimal interaction between the communication campaigns of the healthcare system and of a pharmaceutical firm that produces a given vaccine can help increase vaccination coverage. The healthcare system wants to minimize the number of unvaccinated people at a minimum cost. The pharmaceutical firm aims to maximize its profits while reducing the number of unvaccinated people.

This paper belongs to the last group of models presented above, named *Communication models*, where the focus is on the communicative approach and considers the "educational plan to vaccination" as a possible communication strategy that can be planned by both the national healthcare system and pharmaceutical firms. References cited above Grosset and Viscolani (2020, 2021), and Buratto et al. (2020)) ssume that the unvaccinated population, affected by negative word of mouth, diverges to infinity if it is not supported by a pro-vaccine campaign. Here, we adopt a more realistic dynamics where the \hat{a} -régime number of unvaccinated people is increased by the adverse action of anti-vax negative word of mouth and converges to a finite value, which can be deduced from the annual report published by the World Health Organization (WHO).⁶

Moreover, the literature cited above considers only finite-time horizon optimal control problems, while in this paper, being interested in a long-term plan for the provaccination campaign, we consider the plan over an infinite horizon.

We study the interaction between the communication campaigns of the healthcare system and of a pharmaceutical firm that produces a vaccine for a given disease, formulating a differential game played à la Nash. We use the Hamilton-Jacobi-Bellman approach to determine a Markovian-Nash equilibrium. In recent years, with the introduction of big data solutions, healthcare management can rely on accurate and up-to-date reports. Mobile contact track & trace apps, recently urged by the Covid-19 emergency, provide constant information on the number of vaccinated (and consequently of unvaccinated) individuals.⁷ Therefore, feedback strategies based on the number of unvaccinated are not only credible but also more reliable than Open-Loop ones, as the former are time-consistent. It is commonly known, as reported also in

⁶ To be precise, WHO reports annually the report on global vaccination coverage for each infectious disease in https://www.who.int/news-room. The number of unvaccinated people for a given disease can be deduced by subtracting the WHO declaration from the size of the population interested in the related vaccination.

⁷ see e.g. https://thevaccineapp.com/, retrieved on 2023/06/19.

Della-Marca and d'Onofrio (2021), that in health economics, it is preferable, whenever possible, to control a system by means of a feedback-based strategy, which aims to minimize the economic and human burden of some health-related phenomena. On the basis of these considerations, we look for communication strategies that constitute a Markovian Nash equilibrium.

3 The model

We assume that the population to which vaccination is devoted is stationary. The dynamics we analyze describes the evolution of the unvaccinated population, as is done in the related literature cited above (see Grosset and Viscolani (2020, 2021), and Buratto et al. (2020)).

For this purpose, let x(t) be the number of unvaccinated individuals at time t, and let x_0 be its value at the initial time.

The World Health Organization annually publishes data related to global trends and the total number of reported cases of vaccine-preventable diseases (VPD).⁸ In an idealistic vaccination system, the number of unvaccinated should decrease and tend to zero (neglecting people who cannot be vaccinated due to more serious immunodeficences). However, it can be observed from WHO's data that there is always a significantly high average number of unvaccinated. This residual number of unvaccinated can be attributed to the presence of antivax action. On the other hand, in each time unit, a fixed percentage of the unvaccinated population voluntary gets the vaccine, convinced by peers and networks, or even by the spread of the disease. We can formalize this type of scenario with the following dynamics of the unvaccinated people

$$\dot{x}(t) = w - rx(t). \tag{1}$$

The term w > 0 represents the constant number of people that at a given time may be considered as new-unvaccinated, because they've just entered into the subset of population ought to be vaccinated and did not get the vaccine. The reasons for such a decision can be varied, including the negative information about vaccines and vaccination that *no-vax* movement spreads throughout a word-of-mouth mechanism. For simplicity, in what follows we will call the parameter *w* a word-of-mouth parameter.

The parameter r > 0 represents the instantaneous vaccination rate. It measures the intensity of vaccination and in some way it describes the efficiency of the national vaccination system: the faster the national healthcare system in the vaccination issue, the higher r. From the dynamics we can observe that the number of unvaccinated increases with w, however, it decreases due to the effect of spontaneous vaccinations. Unlike in Grosset and Viscolani (2021), where the number of unvaccinated tends to explode in the absence of a communication action, due to negative word of mouth, here we assume, in a more realistic formalization,

⁸ https://www.who.int/news-room/fact-sheets/detail/immunization-coverage, retrieved on 2023/06/19.

that the unvaccinated group converges to a finite positive value. Indeed, as t goes to infinity in dynamics (1), the number of unvaccinated tends to the following \hat{a} -régime level

$$\widehat{x}_{SS} = \frac{w}{r}.$$
(2)

This value, which increases in w and decreases in r, is in any case finite, and it corresponds to the nonnegative residual of unvaccinated people that can be deduced by the annual World Health Organization report.

However, as Wang et al. stress in Wang et al. (2016), there are scenarios in which voluntary vaccination is not sufficient to provide herd immunity. If word of mouth w is too high or the effectiveness of vaccination r is too low, then \hat{x}_{SS} may be too large; far from the level requested for herd immunity. This issue may become too expensive for the national healthcare system to sustain; therefore, a pro-vaccination communication campaign is needed.

In this paper, we formulate a dynamic model assuming to be exactly in the situation in which the negative word of mouth is so high that a pro-vaccination campaign is necessary. Since we are interested in the scenario where communication is necessary, in what follows we will assume that the parameter w is greater than a given threshold, which guarantees nontrivial equilibrium strategies. The value of such a threshold will be specified later in the next section.

We assume that both the national healthcare system (S) and the pharmaceutical firm (F) are independently planning their own communication campaign to promote vaccination. Let $\phi_S(t) \in U_S$ and $\phi_F(t) \in U_F$ be the pro-vax advertising efforts of the national healthcare system and the pharmaceutical company, respectively. We assume that feasible communication strategies are non-negative and reasonably bounded. In what follows, we assume that the upper bounds for such strategy functions are sufficiently high. This will permit us to concentrate on the characteristics of non-trivial inner solutions. Let δ_S , $\delta_F > 0$ be the effectiveness of the two communication intensities, as in Buratto et al. (2020). The evolution of the unvaccinated is affected by these controls according to the following dynamics

$$\begin{cases} \dot{x}(t) = w - rx(t) - \delta_S \phi_S(t) - \delta_F \phi_F(t), \\ x(0) = x_0. \end{cases}$$
(3)

At first glance, we can observe that if the number of unvaccinated x is zero at a given time, then a positive communication effort may drive the state function below zero, and this would not be meaningful. However, it will be proved that under optimal conditions, given our assumption of a significantly high value for the variable w, the positivity of the state function is ensured.

After describing the dynamics, let us focus on the payoff functions of the two players. The national healthcare system and the pharmaceutical firm both seek to minimize their respective costs associated with the number of unvaccinated individuals, along with reducing their communication costs. For any $t \ge 0$, we assume the following cost flows for the two players respectively

$$C_{S}(t) = \frac{\beta}{2}x^{2}(t) + \frac{\kappa_{S}}{2}\phi_{S}^{2}(t), \qquad C_{F}(t) = \theta x(t) + \frac{\kappa_{F}}{2}\phi_{F}^{2}(t)$$
(4)

For what concerns the costs due to the number of unvaccinated individuals, from the national healthcare system point of view, the number of unvaccinated individuals affects national healthcare costs because a relevant percentage of them need medications and sometimes even hospitalization. While in Grosset and Viscolani (2020, 2021) these costs are assumed to be proportional to the number of unvaccinated people and therefore linear in the variable *x*, in our model we assume that national healthcare costs are quadratic and convex, formalized by the term $\frac{\beta}{2}x^2(t)$ (with $\beta > 0$), to underscore the significant expenses associated with hospital therapy. Furthermore, this assumption highlights the crucial point that vaccine refusal not only puts those who decline vaccination at risk but also increases the chances of disease transmission for people who interact with unvaccinated individuals. A similar quadratic assumption for national health system costs due to the number of unvaccinated has also been considered in Buratto et al. (2020), where a linear-quadratic differential game is formulated and solved, although in a finite time horizon.

From the pharmaceutical firm point of view, the number of unvaccinated affects the revenue of the pharmaceutical firm, although in a different way. Assuming $\theta > 0$ to be the unit profit of a given vaccine, the consequent missed revenue for each unsold vaccine is here formalized as the linear cost $\theta x(t)$.

Finally, both players sustain the communication costs associated to their pro-vax advertising efforts, here assumed to have the following quadratic and convex formulation $\frac{k_s}{2}\phi_S^2(t)$ and $\frac{k_F}{2}\phi_F^2(t)$ (with $k_S > 0$ and $k_F > 0$) for the healthcare system and the firm respectively.

All the models cited above neglect the cost of vaccination, as we also do; nevertheless, few papers in the related literature evaluate vaccination costs; among them, we mention the real option approach used in Favato et al. (2013).

We consider the problem over an infinite horizon. In such a setting, taking into account the dynamics (3), and discounting the costs $C_S(t)$ and $C_F(t)$ in (4), we formulate the following differential game played à la Nash⁹

healthcare System (S)	pharmaceutical Firm (F)			
$\min_{\phi_S \in U_S} \int_0^{+\infty} e^{-\rho t} \left(\frac{\beta}{2} x^2(t) + \frac{\kappa_S}{2} \phi_S^2(t) \right) dt$	$\min_{\phi_F \in U_F} \int_0^{+\infty} e^{-\rho t} \left(\theta x(t) + \frac{\kappa_F}{2} \phi_F^2(t) \right) dt$			

$$\begin{cases} \dot{x}(t) = w - rx(t) - \delta_S \phi_S(t) - \delta_F \phi_F(t), \\ x(0) = x_0. \end{cases}$$
(5)

The table below collects the meaning of the parameters:

⁹ Observe that in this formulation in infinite horizon we are discounting the costs that appear in Buratto et al. (2020), obviously neglecting the "residual value functions".

Communication strategies to contrast anti-vax action: a...

ρ	discount rate ($\rho > 0$)
β	health care and social cost ($\beta > 0$)
θ	missed profit due to each unsold vaccine ($\theta > 0$)
κ_S, κ_F	communication cost parameters ($\kappa_S, \kappa_F > 0$)
w	word-of-mouth coefficient ($w > 0$)
r	instantaneous constant vaccination rate,
δ_S, δ_F	pro-vax communication effectiveness ($\delta_S, \delta_F > 0$)

It is interesting to observe the asymmetry of the game due to the different types of costs associated with the unvaccinated group. This asymmetry will emerge in the different forms of the value functions of the two players and, consequently, in the equilibrium strategies of (S) and (F), respectively. The problem above is formulated over an infinite horizon and is autonomous (because there is no other explicit time dependence in its formulation, apart from the discount factors). Therefore, we are interested in looking for a stationary solution. Stationarity means that each player's strategy is determined as a function of the state variable only: $\phi_j^*(x) \ j \in \{S, F\}$ as stated in Dockner et al. (2000), p.210.

4 The solution (Markovian nash equilibrium)

We are interested in feedback advertising strategies based on the number of unvaccinated individuals, so we look for a Markovian Nash equilibrium that, being the game autonomous, turns out to be subgame perfect (Dockner et al. 2000, p.105).

Proposition 1 The Markovian Nash Equilibrium Feedback strategies that represent the pro-vax communication strategies are

$$\phi_{S}^{*}(x) = \frac{1}{\delta_{S}}(\eta - (\rho + r)) \left[x + \left(w - \frac{\delta_{F}^{2} \theta}{\kappa_{F} \eta} \right) / \eta \right], \tag{6}$$

$$\phi_F^*(x) = \frac{\delta_F \theta}{\kappa_F \eta},\tag{7}$$

where

$$\eta = \sqrt{\left[\frac{\rho}{2} + r\right]^2 + \beta \frac{\delta_s^2}{\kappa_s}} + \frac{\rho}{2}.$$
(8)

Proof See Appendix 1.

It can be immediately observed that $\phi_F^*(\cdot)$ is strictly positive (being δ_F , θ , $k_F > 0$, and $\eta > \rho + r > \rho > 0$). Furthermore, $\phi_F^*(\cdot)$ does not depend on *x*, therefore it constitutes a degenerate feedback strategy. It represents the constant positive communication contribution of the pharmaceutical firm to contrast the antivax action.¹⁰ From now on, we will denote it by ϕ_F^* . As an economic interpretation, since the firm is interested in minimizing its missed profits due to unvaccinated, its optimal communication strategy is adopted at a positive constant rate, independently of the number of unvaccinated individuals.

Remark 1 For what concerns the communication strategy of the national healthcare system $\phi_S^*(\cdot)$, it is easy to prove that $\phi_S^*(x) > 0$ for all feasible x, since $\eta > \rho + r > 0$. Observing that if $w > \frac{\delta_F^2 \theta}{\kappa_F \eta}$, then $\phi_S^*(x) > 0$ for all $x \ge 0$, we can conclude that if the negative word of mouth is so high that it compromises herd immunity, as assumed in the problem formulation, then the national healthcare system needs to support the firm's pro-vaccination campaign.

4.1 Steady state

These kinds of problems are known in the literature as "Discounted Autonomous Infinite Horizon Models" (DAM), (Grass et al. 2008, p.159). The main computational effort to solve optimal control models of this type is calculating the stable manifolds of the occurring saddles. Let us substitute the optimal strategies (6) and (7) in the dynamics of the unvaccinated individuals, then we obtain

$$\dot{x}(t) = w - rx(t) - \delta_S \phi_S^*(x) - \delta_F \phi_F^* = -(\eta - \rho)x(t) + \frac{(\rho + r)}{\eta} \left(w - \frac{\delta_F^2 \theta}{\kappa_F \eta} \right).$$
(9)

Proposition 2 *The steady-state number of unvaccinated people, while adopting the optimal pro-vax communications turns out to be*

$$x_{SS} = \frac{(\rho + r) \left(w - \frac{\delta_F^2 \theta}{\kappa_F \eta} \right)}{\eta(\eta - \rho)}.$$
 (10)

Proof Differentiating the dynamics in (9), we obtain the optimal state trajectory

$$x^{*}(t) = x_{SS} + (x_0 - x_{SS})e^{-(\eta - \rho)t} = x_{SS}(1 - e^{-(\eta - \rho)t}) + x_0e^{-(\eta - \rho)t}.$$
 (11)

It is easy to verify that $x^*(t) \ge 0$ for any starting point $x_0 \ge 0$ and, since $\eta > \rho$, the state converges to the stable positive steady state x_{SS} in (10).

¹⁰ Mathematically, such a constant structure could be predicted from the linear form of the value function of player F.

Table 1Sensitivity analysiswith respect to main parameters		η	ϕ^*_S	$\pmb{\phi}_F^*$	x _{SS}	Cost _S	Cost _F
	w	_	7	_	7	7	7
	θ	_	\mathbf{Y}	7	\mathbf{Y}	\mathbf{Y}	7
	δ_F	_	\mathbf{Y}	7	\mathbf{Y}	\mathbf{Y}	\mathbf{N}
	κ_F	_	1	\mathbf{Y}	1	7	7

As expected, the steady-state level of unvaccinated individuals under the actions of pro-vax communication campaigns of the two involved players increases with negative word of mouth w, and it is lower than the *à-régime* unvaccinated level observed in (2) without pro-vax communications. In fact, for any set of values of the problem parameters, it holds

$$x_{SS} \le \hat{x}_{SS} = \frac{w}{r}.$$
 (12)

As a result, in case the word of mouth is too high, then the joint effects of the provax communication campaigns (6) and (7) may contribute to lower the number of unvaccinated and to bring it down to the stationary level (10). This will help to reach herd immunity.

5 Sensitivity analysis and simulations

In the previous section, we obtained the analytical form for the strategies that constitute the stationary Markovian Nash equilibrium of the pro-vax communication game and the associated steady-state level of unvaccinated people. The simple dependence of the solution on some of the parameters that characterize the problem allows us to perform a sensitivity analysis.

In Table 1, we report the existing monotonicity properties, when analytically computable, of the equilibrium strategies at the steady state, of the steady state level of the unvaccinated, and of the optimal costs for the two players. For the reader's convenience, since the optimal solution contains the constant η , in the first column of the table, the dependencies of the constant η on all the analyzed parameters are also included. The arrows indicate either increasing monotonicity (\nearrow) or decreasing monotonicity (\searrow), while the lines "–" mean constant behavior.

Impact of Word-of-Mouth Effectiveness w (Table 1)

Parameter *w* takes into account the word-of-mouth effects on the evolution of the unvaccinated people. Here we assume, as stated in the previous section, that the negative word of mouth is so high that it requires nonzero pro-vax communications, more precisely $w > \frac{\delta_F^2 \theta}{\kappa_F \eta}$.

The effect of the negative word of mouth w drives the national healthcare system to increase its pro-vax communication strategy (ϕ_s^*), with increased associated costs. Moreover, as expected, the steady state number of unvaccinated

Table 2 Sensitivity analysis with respect to δ_S and κ_S		η	ϕ^*_S	ϕ_F^*
	δ_S	7	no	\mathbf{k}
	κ_S	\searrow	\searrow	7
Table 3 Sensitivity analysis with respect to β and r		η	$\phi^*_{\scriptscriptstyle S}$	ϕ_F^*
	β	7	7	\mathbf{N}
	r	7	no	\mathbf{Y}

 (x_{SS}) increases in w. These results are in line with the ones obtained in Buratto et al. (2020), where the final level of unvaccinated people x(T) is increasing in the word-of-mouth parameter. Another expected result is that both players have increased costs as anti-vax word of mouth increases. However, it becomes interesting to note that the optimal pharmaceutical strategy ϕ_F^* is not dependent on w; the firm conducts its communication campaign independently of word of mouth because its cost is not an effective loss, but a missed income.

Impact of vaccine unit profit θ (Table 1)

Parameter θ represents the unit profit of a vaccine and is considered as the virtual cost of each unsold vaccine. From Table 1 we can observe that the higher the unit profit, the higher the strategy communication of the firm (ϕ_F^*) and consequently its cost. With a higher pro-vax campaign, the steady state level of unvaccinated individuals (x_{SS}) decreases. At the same time, the national healthcare system can count on the firm's action, so, as strategic substitutes do, it can reduce its communication campaign (ϕ_s^*) and, therefore, its total cost.

Impact of communication effectiveness and marginal costs (δ_F, κ_F) of the firm (Table 1)

It is straightforward to prove that ϕ_F^* increases in δ_F and decreases in κ_F : The more effective (or less costly) the firm pro-vax campaign, the more intensive it will be. This result is typical for dynamic advertising models Huang et al. (2012): each optimal communication strategy increases in its corresponding communication efficacy and decreases in its corresponding marginal cost. Moreover, since both strategies act jointly to decrease the number of unvaccinated people, they are strategic substitutes, so that each optimal communication strategy decreases with the communication efficacy of the other player and increases with the communication marginal cost of the other player. In particular, ϕ_S^* is decreasing in δ_F : The more effective the firm's pro-vax campaign, the less the national healthcare system needs to implement its own pro-vax communication. Finally, the steady state (x_{SS}) computed in (10) decreases in δ_F , while it increases in the marginal cost κ_F .



Fig. 1 Steady state x_{SS} w.r.t. δ_S ($w = 0.1, \theta = 0.1, \kappa_S = 4, \delta_F = 0.6, \kappa_F = 0.8, \rho = 0.05, \beta = 0.3, r = 0.1$)



Fig. 2 Steady state x_{SS} w.r.t. κ_S ($w = 0.1, \theta = 0.1, \delta_S = 0.6, \delta_F = 0.6, \kappa_F = 0.8, \rho = 0.05, \beta = 0.3, r = 0.1$)

Impact of communication strategies to communication effectiveness and marginal costs (δ_{s}, κ_{s}) of national health-care system (Table 2)

Let us observe in Table (2) that η is increasing in δ_S and decreasing in κ_S , therefore ϕ_F^* , which is decreasing in η (see (7)), turns out to be decreasing in δ_S and increasing in κ_S . Furthermore, ϕ_S^* turns out to be decreasing in κ_S , while no kind of monotonicity nor regularity can be verified with respect to δ_S , (a "no" appears in the corresponding cell of Table 2).

Sensitivity of communication strategies to social cost β and vaccination rate *r* (Table 3)

The parameter β represents the social cost for the national healthcare system. Analytical results in Table 3 highlight how a severe social cost motivates the healthcare system to increase its pro-vaccination campaign, thus allowing the pharmaceutical firm to reduce its own.

The parameter r represents the vaccination rate, in other words the efficiency of the national vaccination system. Analytical results highlight how an increase in the efficiency of vaccination in the national healthcare system allows the pharmaceutical firm to lighten its own communication campaign. On the other hand, no kind of monotonicity can be analytically proved in the national health-care system communication effort with respect to r.



Fig. 3 Steady state x_{SS} w.r.t. β ($w = 0.1, \theta = 0.1, \delta_S = 0.6, \kappa_S = 4, \delta_F = 0.6, \kappa_F = 0.8, \rho = 0.05, r = 0.1$)



Fig. 4 Steady state x_{SS} w.r.t. r ($w = 0.1, \theta = 0.1, \delta_S = 0.6, \kappa_S = 4, \delta_F = 0.6, \kappa_F = 0.8, \rho = 0.05, \beta = 0.3$)

Numerical analysis of the steady state

The dependence of the steady state x_{SS} with respect to the parameters δ_S , k_S , β , and *r* cannot be proved analytically, therefore, we performed some numerical simulations fixing, for each analysis, n - 1 parameters and letting one parameter vary within its feasible values (such as to guarantee non-zero advertising strategies).¹¹ In the following Figs. 1, 2, 3, 4, it is evident, as analytically proven in (12), that in the long run, the steady-state number of unvaccinated people while adopting pro-vaccination communication (x_{SS} - solid lines) is smaller compared to the values \hat{a} -régime without such communication policies (\hat{x}_{SS} - dotdashed lines).

All the simulations conducted demonstrate a consistent pattern, specifically a quasi-concave shape characterized by an initial convex-concave increase followed by a subsequent decrease. We can interpret these results by noting the presence of a *threshold effect*: Only sufficiently high values of the parameter with respect to which the analysis is carried out make it possible for the national health-care system to reduce the number of unvaccinated individuals to the extent necessary to achieve herd immunity.

It should be noted in Fig. 4 that the dotdashed line, representing the à-régime unvaccinated level \hat{x}_{SS} without the pro-vax communications, is not constant (as the

¹¹ Most of parameter values come from Buratto et al. (2020), as a reference.

corresponding dotdashed lines in the previous figures) because \hat{x}_{SS} , defined in (2), decreases in *r*. Furthermore, the gap between the two lines is large in correspondence to small values of *r*. This permits to conclude that if the national healthcare system is characterized by a low vaccination rate, then investing in effective and targeted communication strategies becomes crucial in order to significantly slow down the number of unvaccinated individuals and mitigate the potential consequences.

6 Conclusion

Vaccination can reduce the incidence of many diseases, but unfortunately, a negative word of mouth based on fake news recently caused a decline in vaccination coverage in many countries. This phenomenon has increased the residual level of unvaccinated people reported each year by the World Health Organisation. In this paper, we tackle the problem of planning a pro-vaccination communication campaign to convince hesitant individuals to get vaccinated, so as to reduce the residual level of unvaccinated people.

We formulate and solve an asymmetric differential game model over an infinite horizon. Two players are involved in the provaccination communication campaign: the national healthcare system and a pharmaceutical firm. The Hamilton-Jacobi-Bellman approach is used to determine the optimal communication strategies that constitute a Markovian-Nash equilibrium for the game. The two players act as strategic substitutes; the smaller the healthcare system campaign, the higher the firm's one. Sensitivity analyzes are performed with respect to the parameters of the problem to study their impact on the equilibrium strategies and steady-state solutions.

Let us answer the research questions declared in the Introduction: Our model confirms that the national healthcare system needs to increase its investment in vaccine communication to contrast the effect of negative antivax word of mouth and to aim at herd immunity. On the other hand, the firm's pro-vaccine communication campaign is not affected by negative word of mouth.

The proposed model also includes the vaccination rate as an index that characterizes the efficiency of the national healthcare system. As far as we are aware, such a parameter is not taken into account in the related literature. Our results show that immunization can be obtained either by increasing vaccination efficiency, i.e., vaccinating at a high rate, or implementing a well-planned pro-vaccination communication campaign. These results emphasize the importance of the "Immunization Agenda 2030 Measles & Rubella Partnership" (M&RP)¹² led by the American Red Cross, United Nations Foundation, Centers for Disease Control and Prevention (CDC), Gavi, the Vaccines Alliance, the Bill and Melinda French Gates Foundation, UNICEF and WHO, to achieve the IA2030 measles and rubella specific goals.

These results also confirm the importance of national healthcare management in maintaining a sufficiently high vaccination rate or, at least, in designing an efficient provaccination campaign.

¹² https://measlesrubellainitiative.org/learn/about-us, retrieved on 2023/07/06.

Different extensions of this work can be envisioned. The first considers the game played à la Stackelberg, where the leader may be the national healthcare system and the follower the pharmaceutical company. A specific analysis of the cases where the optimal communication strategy can turn out to be zero is an idea that deserves investigation in order to take into account the various types of costs that the national healthcare system must bear.

The important role that parameter r plays in the results may suggest considering the vaccination rate as a decision variable to be optimally set by the national healthcare system together with the communication campaign for vaccination.

It can be interesting to analyze the stochastic evolution of the number of unvaccinated people. This goal could be obtained by introducing a stochastic effect in communication campaigns and changing the ordinary differential equation (3) into a stochastic one (see Wang et al. 2016).

Appendix A:Proof of Proposition 1

Let $V_S(x)$ and $V_F(x)$ be the stationary value functions associated with the healthcare system and the pharmaceutical firm, respectively. Let us assume that these functions are differentiable, and let us denote by $V'_S(x)$ and $V'_F(x)$ their derivatives w.r.t. x. They must solve the following Hamilton Jacobi Bellman equations associated to the problems of the two players

$$\rho V_S(x) = \max_{\phi_S \ge 0} \left\{ \left[w - rx - \delta_F \phi_F(x) - \delta_S \phi_S \right] V'_S(x) - \left[\frac{\beta}{2} x^2 + \frac{\kappa_S}{2} \phi_S^2 \right] \right\}$$
(A1)

$$\rho V_F(x) = \max_{\phi_F \ge 0} \left\{ \left[w - px - \delta_F \phi_F - \delta_S \phi_S(x) \right] V'_F(x) - \left[\theta x + \frac{\kappa_F}{2} \phi_F^2 \right] \right\}$$
(A2)

Maximising the r.h.s. of (A1) and (A2) with respect to ϕ_S and ϕ_F respectively, we obtain

$$\phi_S(x) = \max\left\{0, -\frac{\delta_S}{\kappa_S}V'_S(x)\right\}, \qquad \phi_F(x) = \max\left\{0, -\frac{\delta_F}{\kappa_F}V'_F(x)\right\}.$$
(A3)

Being interested in a non-trivial Nash equilibrium, we look for the best response strategies in the region $\{x \in \mathbb{R} : V'_S(x), V'_F(x) \le 0\}$, in such a case

$$\phi_i(x) = -\frac{\delta_i}{\kappa_i} V_i'(x), \quad i \in \{S, F\}.$$
(A4)

After substituting (A4) in (A1) and (A2), the HJB equations for the two players can be rewritten as the following system

٢

$$\begin{cases} \rho V_{S}(x) = \left[w - rx + \frac{\delta_{F}^{2}}{\kappa_{F}} V_{F}'(x) \right] V_{S}'(x) - \frac{\beta}{2} x^{2} + \frac{\delta_{S}^{2}}{2\kappa_{S}} (V_{S}'(x))^{2}, \\ \rho V_{F}(x) = \left[w - rx + \frac{\delta_{S}^{2}}{\kappa_{S}} V_{S}'(x) \right] V_{F}'(x) - \theta x + \frac{\delta_{F}^{2}}{2\kappa_{F}} (V_{F}'(x))^{2}. \end{cases}$$
(A5)

Notice the asymmetry in the resulting equations with respect to the state variable *x*: This entails the corresponding value functions featuring the same asymmetry; therefore, we assume the following forms for V_S and V_F :

$$V_S(x) = \frac{1}{2}Ax^2 + Bx + C, \qquad V_F(x) = D x + E,$$
 (A6)

where the coefficients A, B, C, D, and E are assumed constant, as we focus on stationary strategies.

After substituting the value functions (A6) into the HJB equations (A5) and comparing the coefficients of the resulting polynomials in the variable x, the real coefficients A, B, C, D, and E satisfy the following system of algebraic equations (known as algebraic Riccati equations)

$$\begin{cases} \frac{\delta_s^2}{2\kappa_s} A^2 - \left[\frac{\rho}{2} + r\right] A - \frac{\beta}{2} = 0\\ \left[\rho + r - \frac{\delta_s^2}{\kappa_s} A\right] D + \theta = 0\\ \left[\rho + r - \frac{\delta_s^2}{\kappa_s} A\right] B - \left(w + \frac{\delta_F^2}{\kappa_F} D\right) A = 0\\ \rho E - \left[w + \left(\frac{\delta_s^2}{\kappa_s} B + \frac{\delta_F^2}{2\kappa_F} D\right)\right] D = 0\\ \rho C - \left[w + \left(\frac{\delta_F^2}{\kappa_F} D + \frac{\delta_s^2}{2\kappa_s} B\right)\right] B = 0 \end{cases}$$
(A7)

From the first equation we get the two solutions

$$A_{\pm} = \frac{\kappa_S}{\delta_S^2} \Biggl\{ \Biggl[\frac{\rho}{2} + r \Biggr] \pm \sqrt{\Biggl[\frac{\rho}{2} + r \Biggr]^2 + \beta \frac{\delta_S^2}{\kappa_S}} \Biggr\},$$

where $A_+ > 0$ and $A_- < 0$. We discard the positive root because once substituted into the second equation in (A7) to obtain the coefficient *D*, it would be incompatible with assumption $V'_F(x) \le 0$. From now on, let us denote $A = A_- < 0$. Observe that if we define

$$\eta = \left[\rho + r - \frac{\delta_s^2}{\kappa_s} A\right] = \sqrt{\left[\frac{\rho}{2} + r\right]^2 + \beta \frac{\delta_s^2}{\kappa_s}} + \frac{\rho}{2},\tag{A8}$$

it is easy to prove that $\eta > \rho + r > \rho > 0$, and that the system (A7) admits the following unique solution

$$\begin{cases}
A = \frac{\kappa_s}{\delta_s^2} \{\rho + r - \eta\} < 0, \\
B = \left(w + \frac{\delta_r^2}{\kappa_F} D\right) A/\eta = \left(w - \frac{\delta_r^2 \theta}{\kappa_F \eta}\right) A/\eta, \\
C = \left(w + \frac{\delta_r^2}{\kappa_F} D + \frac{\delta_s^2}{2\kappa_S} B\right) B/\rho, \\
D = -\theta/\eta < 0, \\
E = \left(w + \frac{\delta_r^2}{2\kappa_F} D - \frac{\delta_s^2}{\kappa_S} B\right) D/\rho.
\end{cases}$$
(A9)

Substituting these values into (A6) we obtain the continuously differentiable value functions, whose derivatives are

$$V'_{S}(x) = Ax + B = A\left[x + \frac{1}{\eta}\left(w - \frac{\delta_{F}^{2}\theta}{\kappa_{F}\eta}\right)\right], \qquad V'_{F}(x) = D < 0.$$
(A10)

Observe that indeed the constant *A* is negative; moreover, from the second equation, we can infer that if the word-of-mouth level *w* is high, $\left(w > \frac{\delta_F^2 \theta}{\kappa_F \eta}\right)$, then the positivity of the term inside the round brackets also guarantees the negativity of the constant *B*. This implies that if we restrict the domain to nonnegative values of *x*, which are those that have a physical meaning, then $V'_S(x) < 0$ for all $x \in \mathbb{R}^+$.

The Markovian Nash equilibrium strategies representing the optimal pro-vax communication efforts can be obtained in feedback form by substituting coefficients (A9) into (A10), and in turn into (A4), obtaining

$$\phi_S^*(x) = -\frac{\delta_S}{\kappa_S}(A \ x + B) \qquad \phi_F^*(x) = -\frac{\delta_F}{\kappa_F}D.$$

Once substitutes the values of parameters A, B, C, and D, we obtain (6) and (7).

Funding Open access funding provided by Università degli Studi di Padova within the CRUI-CARE Agreement.

Declarations

Conflict of interest We confirm that the manuscript is the authors' original work and the manuscript has not received prior publication and is not under consideration for publication elsewhere. All authors have contributed to this paper, reviewed and approved the current form of the manuscript to be submitted. We confirm that all authors of the manuscript have no conflict of interest to declare.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

References

- Bauch C (2005) Imitation dynamics predict vaccinating behaviour. Proc R Soc B Biol Sci 272(1573):1669–1675. https://doi.org/10.1098/rspb.2005.3153
- Bhattacharyya Samit, Bauch Chris T, Breban Romulus (2015) Role of word-of-mouth for programs of voluntary vaccination: a game-theoretic approach. Math Biosci 269:130–134 https://doi.org/10. 1016/j.mbs.2015.08.023
- Bozzola E, Spina G, Russo R, Bozzola M, Corsello G, Villani A (2018) Mandatory vaccinations in European countries, undocumented information, false news and the impact on vaccination uptake: the position of the Italian pediatric society. Italian J Pediatrics 44(1):67. https://doi.org/10.1186/ s13052-018-0504-y
- Buonomo B, d'Onofrio A, Kassa SM, Workineh YH (2022) Modeling the effects of information-dependent vaccination behavior on meningitis transmission. Math Methods Appl Sci 45(2):732–748. https://doi.org/10.1002/mma.7808
- Buonomo B, d'Onofrio A, Lacitignola D (2013) The geometric approach to global stability in behavioral epidemiology. Modeling the interplay between human behavior and the spread of infectious diseases, pp 289–308
- Buratto A, Grosset L, Viscolani B (2020) In: Pineau P-O, Sigué S, Taboubi S (eds) A LQ vaccine communication game, pp 353–367. Springer, Cham
- Carrillo Santisteve P, Lopalco PL (2012) Measles still spreads in Europe: Who is responsible for the failure to vaccinate? Clin Microbiol Infection 18:50–56
- Della-Marca R, d'Onofrio A (2021) Volatile opinions and optimal control of vaccine awareness campaigns: chaotic behaviour of the forward-backward sweep algorithm vs. heuristic direct optimization. Commun Nonlinear Sci Numer Simul 98:105768
- Dockner E, Jørgensen S, Van Long N, Sorger G (2000) Differential games in economics and management science. Cambridge Univ. Press, Cambridge
- d'Onofrio A, Manfredi P (2020) The interplay between voluntary vaccination and reduction of risky behavior: a general behavior-implicit. Current Trends Dyn Syst Biol Nat Sci 21:185
- El Ouardighi F, Feichtinger G, Grass D, Hartl RF, Kort PM (2016) Advertising and quality-dependent word-of-mouth in a contagion sales model. J Opt Theory Appl 170(1):323–342. https://doi.org/10. 1007/s10957-015-0855-0
- Favato G, Baio G, Capone A, Marcellusi A, Saverio Mennini F (2013) A novel method to value real options in health care: the case of a multicohort human papillomavirus vaccination strategy. Clin Therapeut 35(7):904–914
- Grass D, Caulkins JP, Feichtinger G, Tragler G, Behrens DA (2008) Optimal control of nonlinear processes. Springer, Berlin
- Grosset L, Viscolani B (2021) A dynamic advertising model in a vaccination campaign. Central Eur J Oper Res 29(2):737–751. https://doi.org/10.1007/s10100-020-00675-9
- Grosset L, Viscolani B (2020) Advertising in a vaccination campaign: a variable time control problem. J Interdiscip Math 23(6):1197–1211. https://doi.org/10.1080/09720502.2020.1759208
- Hotez PJ (2017) How the anti-vaxxers are winning. https://www.nytimes.com/2017/02/08/opinion/how-the-anti-vaxxers-are-winning.html. Accessed: 2022-04-11
- Huang J, Leng M, Liang L (2012) Recent developments in dynamic advertising research. Eur J Oper Res 220:591–609 https://doi.org/10.1016/j.ejor.2012.02.031
- Manfredi P, d'Onofrio A (2013) Modeling the interplay between human behavior and the spread of infectious diseases. New York, NY: Springer. https://doi.org/10.1007/978-1-4614-5474-8
- Matusik R, Nowakowski A (2022) Control of covid-19 transmission dynamics, a game theoretical approach. Nonlinear Dyn 110:857–877
- Omer SB, Salmon DA, Orenstein WA, deHart MP, Halsey N (2009) Vaccine refusal, mandatory immunization, and the risks of vaccine-preventable diseases. New Engl J Med 360(19):1981–1988. https:// doi.org/10.1056/NEJMsa0806477. (PMID: 19420367)
- Salmon D, Teret S, MacIntyre C, Salisbury D, Burgess M, Halsey N (2006) Compulsory vaccination and conscientious or philosophical exemptions: past, present, and future. Lancet 367(9508):436–442. https://doi.org/10.1016/S0140-6736(06)68144-0
- Shim E, Grefenstette JJ, Albert SM, Cakouros BE, Bohn L, Burke DS (2013) In: Manfredi, P., d'Onofrio, A. (eds.) Impact of vaccine behavior on the resurgence of measles, pp 255–266. Springer, New York, NY

- Takla A, Wiese-Posselt M, Harder T, Meerpohl JJ, Röbl-Mathieu M, Terhardt M, Sande M, Wichmann O, Zepp F, Klug SJ (2018) Background paper for the recommendation of hpv vaccination for boys in germany. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 61(9):1170–1186
- Taylor L, Swerdfeger A, Eslick G (2014) Vaccines are not associated with autism: an evidence-based meta-analysis of case-control and cohort studies. Vaccine 32(29):3623–3629. https://doi.org/10. 1016/j.vaccine.2014.04.085
- Wang Z, Bauch CT, Bhattacharyya S, d'Onofrio A, Manfredi P, Perc M, Perra N, Salathé M, Zhao D (2016) Statistical physics of vaccination. Phys Rep 664, 1–113 https://doi.org/10.1016/j.physrep. 2016.10.006arXiv:1608.09010 [physics.soc-ph]
- White JL, Grabowski MK, Rositch AF, Gravitt PE, Quinn TC, Tobian AAR, Patel EU (2023) Trends in adolescent human papillomavirus vaccination and parental hesitancy in the United States. J Infectious Dis https://doi.org/10.1093/infdis/jiad055 https://academic.oup.com/jid/advance-article-pdf/ doi/10.1093/infdis/jiad055/49415369/jiad055.pdf. jiad055

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.