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GAME-THEORETICAL MODEL OF COVID-19 VACCINATION IN THE ENDEMIC EQUILIBRIUM

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An outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), epicentred in Hubei Province of the People's Republic of China, quickly spread worldwide and caused COVID-19 pandemic. It infected hundreds of millions of people and caused millions of deaths. In this paper, we develop a compartmental ODE model of COVID-19 transmission. We consider a possibility of breakthrough infections after the vaccination and account for both symptomatic and asymptomatic infections and transmissions. We also incorporate game theory to study the optimal vaccination decisions from the individuals' perspective. We show that vaccination alone is unlikely to eliminate COVID-19. To achieve herd immunity, the individuals would have to receive a dose of a vaccine more frequently than once every 3 months. It is therefore crucial to adhere to various guidelines, such as quarantine, isolate and wear a mask if tested positive for COVID-19.

Keywords: COVID-19; Vaccination; Nash Equilibrium; Game Theory.

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1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was discovered in Wuhan, Hubei province, the People's Republic of China in January 2020.[1] The virus epidemic eventually became a pandemic and was named COVID-19 (the coronavirus disease 2019). By November 2022, there have been over 629 millions confirmed cases of COVID-19 worldwide (or about 8% of the worldwide population), including over 6.5 millions deaths (0.08% of the population), reported to WHO.[2] In Guam, by the same period, there were over 49 thousands confirmed cases of COVID-19 with 404 deaths which amounts to 28.8% and 0.237% of the population of Guam.

Early in the pandemic, the USS Theodore Roosevelt, an aircraft carrier with 4779 crew, was sent to its base in Guam after three crew members tested positive for SARS-CoV-2.[3,4] During the outbreak on this ship, a total of 1271 (26.6%) crew members tested positive and another 60 were suspected cases.[5] Notably, 76.9% of the positive cases had no symptoms at the time of testing and 45% never developed any symptoms.[4]

SARS CoV-2 is airborne and transmitted through aerosols carrying infectious viruses.[6] COVID-19 can be prevented by vaccination, including boosters,[7] and by following an evolving set of guidelines which includes isolating, quarantining and masking.[8] By November 2022, a total of almost 13 billion vaccine doses had been administered worldwide (1.66 doses per person on average) and just over 368 thousands vaccine doses were administered in Guam (2.16 doses per person on average).

In exposed individuals, symptoms like fever, cough, shortness of breath, body aches, new loss of taste or smell, sore throat, congestion, and many others may appear 2–14 days after exposure to the virus.[9] Different virus variants can present with different symptoms and the symptoms can vary depending on vaccination status.[9]

Mathematical modelling is crucial for understanding the control and possible elimination of diseases.[10,11] There are now thousands of different models of COVID-19 epidemics.[12–17] When the models incorporate human behavior, they can provide even better predictions.[18–20] It is thus not surprising that game theory has been applied to modeling COVID-19.[21–31] as well as many other diseases.[32–43]

There are several approaches to incorporate individual decisions into epidemiological models. One approach is to consider the decision process as an active and continuous process. The decisions depend on the present epidemic situation and the outcomes of individual decisions in turn influence epidemiological evolution. The game-theoretical foundations to these models have been laid out by Ref. 44. These imitation dynamic models have been applied to understand the human behavior element in a repeated behavior, such as social distancing during COVID-19 epidemics[21] as well as to model the use of insecticide treated nets to prevent malaria[45] or practice facial cleanliness to prevent trachoma.[46] The analyses of these models can be quite complex because the decision dynamics and the epidemiological

dynamics are coupled. It is often not clear what is the long-time behavior of the system and whether or not the equilibria of the system are stable or exist.

The second and more static approach was popularized by Ref. 47 and applied to situations where individuals typically decide just once whether to vaccinate or not. However, it was also applied to influenza[48] and COVID-19[49] where the vaccination decisions are repeated. These models decouple the decision process from the underlying epidemiology and consider a population game played in the endemic equilibrium.

In this paper, we construct a model of COVID-19 transmission based on Refs. 21 and 22. We consider a possibility of breakthrough infections after the vaccination and account for both symptomatic and asymptomatic infections and transmissions. Our goal is to determine the vaccine coverage needed for herd immunity. We also incorporate game theory to study the optimal vaccination decisions in the endemic equilibrium from the individuals' perspective.

2. Mathematical Model

We extend the basic susceptible–vaccinated–exposed–infected–recovered (SVEIR) model by (a) allowing asymptomatic infections (A) and (b) separating breakthrough infections of vaccinated individuals from the infections of individuals without any current vaccine immunity. Thus, the population is split into the following; susceptible (S), vaccinated (V), exposed with or without vaccine protection (E_V and E_S), asymptomatic infectious with or without vaccine (A_V and A_S), symptomatic infectious with or without vaccine (I_V and I_S), and recovered (R).

Susceptible individuals vaccinate at rate ν, i.e., on average an individual will get a dose of a vaccine every ν^{-1} days. The vaccine wanes at rate w, i.e., does not offer any protection after w^{-1} days on average, and the vaccinated individuals become susceptible again. In general, as common in compartmental models,[50] we will assume that the rate of progression from one compartment to another is the inverse of the average observed duration of such a change.

Susceptible individuals become exposed upon contact with infectious individuals. The force of infection is given by

$$\lambda = \beta(I_S + t_{A_S} A_S + t_{I_V} I_V + t_{A_V} A_V), \tag{2.1}$$

where β is the COVID-19 transmission rate and t_{A_S}, t_{A_V}, and t_{I_V} are the modification parameters representing reduced infectiousness of cases in A_S, A_V, and I_V compartments.

The vaccine is not 100% effective and even the vaccinated individuals can become exposed. We assume that the force of infection for vaccinated individuals is simply expressed by $(1 - e)\lambda$ where e is the efficiency of the vaccine.

The incubation period lasts σ^{-1} days after which the exposed individuals become either asymptomatic (with probability q_S) or symptomatic (with probability $1 - q_S$). Similarly, the individuals in E_V, exposed after vaccination, stay in

E_V for σ^{-1} and they become asymptomatic with probability q_V and symptomatic with probability $1 - q_V$.

Asymptomatic and symptomatic individuals recover (i.e., stop being infectious) at rate γ_S and γ_V, respectively. The recovered individuals are temporarily immune against reinfections, but they lose their immunity and become susceptible again at rate φ.

As in Ref. 21, we are more concerned with short term dynamics and thus ignore birth and natural mortality. Additionally, as the treatment options progress, we ignore the COVID-19 related mortality. As shown in Table 1, the duration of vaccine protection is the longest time interval considered in our model and it is still under a year. We therefore consider the population closed and treat compartment sizes as proportions of the entire population. While this assumption is not completely realistic, no model can be 100% accurate.[61,62]

Table 1. Model parameters. The times are in days, rates are per capita per day. The range show is used in uncertainty and sensitivity analysis.

Symbol	Meaning	Value	Range	Reference
ν	Vaccination rate	Variable	$[0, 0.02]$	
ω^{-1}	Duration of vaccine protection	180	$[120, 360]$	Nordström *et al.*[51]
e	Vaccine efficiency	0.85	$[0.6, 0.95]$	Harder *et al.*[52]
λ	Force of infection	(2.1)		
β	Transmission rate	0.6	$[0.4, 0.8]$	Estimated based on Alimohamadi *et al.*[53]
t_{A_S}	Modification parameter, reduction of infectiousness in A_S	0.2	$[0.1, 0.3]$	Yanes–Lane[54]
t_{A_V}	Modification parameter, reduction of infectiousness in A_V	0.2	$[0.1, 0.3]$	Assumed
t_{I_V}	Modification parameter, reduction of infectiousness in I_V	0.2	$[0.1, 0.3]$	Assumed
σ^{-1}	Incubation period	6	$[2, 12]$	Elias *et al.*[55] and Zaki and Mohamed[56]
q_S	Probability of becoming asymptomatic when not vaccinated	0.25	$[0.16, 0.38]$	Alene *et al.*[57]
q_V	Probability of becoming asymptomatic after being vaccinated	0.3	$[0.2, 0.4]$	CDV *et al.*[58]
γ_S^{-1}	Duration of infections period if unvaccinated	7	$[5, 11]$	Alvarado *et al.*[59]
γ_V^{-1}	Duration of infections period if vaccinated	7	$[5, 11]$	Alvarado *et al.*[59]
φ^{-1}	Duration of natural immunity	180	$[150, 210]$	Ripperger *et al.*[60]
C_V	Cost of vaccination	1	—	Assumed
C_{I_S}	Cost of symptomatic infection if unvaccinated (relative to C_V)	10	$[1, 20]$	Assumed
C_{I_V}	Cost of symptomatic infection if vaccinated (relative to C_V)	1	$[1, 2]$	Assumed

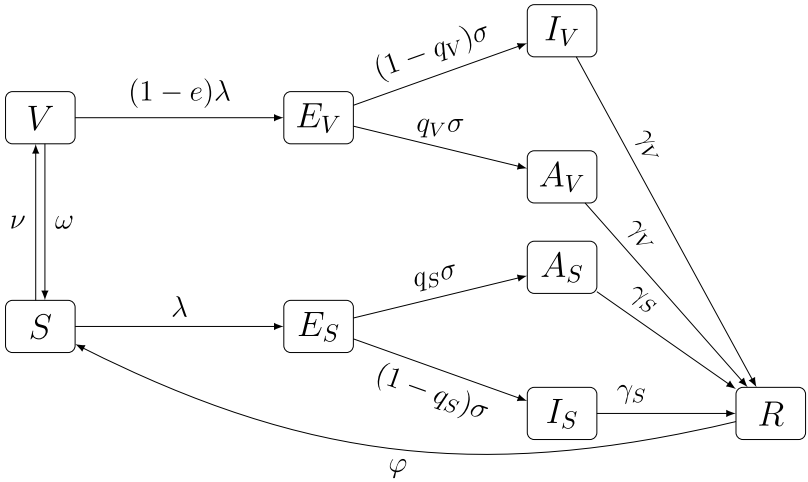

Fig. 1. Scheme of the compartmental ODE model for COVID-19 transmission. The compartments represent susceptible (S), vaccinated (V), exposed with or without vaccine protection (E_V and E_S), asymptomatic infectious with or without vaccine (A_V and A_S), symptomatic infectious with or without vaccine (I_V and I_S), and recovered (R). Solid arrows represent the transitions between compartments. The letters next to the arrows specify the per capita rates of the transitions. The force of infection λ is given by (2.1). The parameters are summarized in Table 1.

The model diagram is shown in Fig. 1. The parameters are summarized in Table 1. The model yields the following system of ordinary differential equations.

$$\frac{dS}{dt} = \varphi R + \omega V - \nu S - \lambda S, \tag{2.2}$$

$$\frac{dV}{dt} = \nu S - \omega V - (1-e)\lambda V, \tag{2.3}$$

$$\frac{dE_S}{dt} = \lambda S - \sigma E_S, \tag{2.4}$$

$$\frac{dE_V}{dt} = (1-e)\lambda V - \sigma E_V, \tag{2.5}$$

$$\frac{dA_S}{dt} = \sigma q_S E_S - \gamma_S A_S, \tag{2.6}$$

$$\frac{dI_S}{dt} = \sigma(1-q_S)E_S - \gamma_S I_S, \tag{2.7}$$

$$\frac{dA_V}{dt} = \sigma q_V E_V - \gamma_V A_V, \tag{2.8}$$

$$\frac{dI_V}{dt} = \sigma(1-q_V)E_V - \gamma_V I_V, \tag{2.9}$$

$$\frac{dR}{dt} = \gamma_S(A_S + I_S) + \gamma_V(A_V + I_V) - \varphi R. \tag{2.10}$$

3. Analysis of the ODE System

The detailed calculations accompanying this section are shown in Appendix A.

For any parameter values, there are at most two equilibria, i.e., two steady states of the system (2.2)–(2.10). The disease-free equilibrium $\mathcal{E}^0 = (S^0, V^0, E_S^0, E_V^0, A_S^0, I_S^0, A_V^0, I_V^0, R^0)$ is given by

$$\mathcal{E}^0 = \left(\frac{\omega}{\omega+\nu}, \frac{\nu}{\omega+\nu}, 0, 0, 0, 0, 0, 0, 0\right). \tag{3.1}$$

The endemic equilibrium $\mathcal{E}^* = (S^*, V^*, E_S^*, E_V^*, A_S^*, I_S^*, A_V^*, I_V^*, R^*)$ (with some infected individuals in the population) exists only if the disease-free equilibrium is unstable.

The local stability of the disease-free equilibrium is determined by the effective reproduction number

$$\mathcal{R} = \left(\frac{\beta}{\gamma_S \gamma_V}\right)\left(\frac{\omega r_S \gamma_V + \nu(1-e) r_V \gamma_S}{\omega+\nu}\right), \tag{3.2}$$

where

$$r_S = 1 - q_S + q_S t_{A_S}, \tag{3.3}$$

$$r_V = t_{I_V} - q_V t_{I_V} + q_V t_{A_V}. \tag{3.4}$$

As in Ref. 63, the disease-free equilibrium is locally asymptotically stable if $\mathcal{R} < 1$ and it is not stable if $\mathcal{R} > 1$.

It follows that there is a unique vaccination rate ν_{HI} defined by

$$\nu_{\mathrm{HI}} = \begin{cases} 0 & \text{if } \dfrac{\beta}{\gamma_S} r_S \le 1, \\ \omega \dfrac{\frac{\beta}{\gamma_S} r_S - 1}{1 - (1-e)\frac{\beta}{\gamma_V} r_V} & \text{if } \dfrac{\beta}{\gamma_S} r_S > 1 \quad \text{and} \quad (1-e)\dfrac{\beta}{\gamma_V} r_V < 1, \\ \infty & \text{if } \dfrac{\beta}{\gamma_S} r_S > 1 \quad \text{and} \quad \dfrac{\beta}{\gamma_V}(1-e) r_V \ge 1, \end{cases} \tag{3.5}$$

such that the disease-free equilibrium is locally asymptotically stable if and only if $\nu \ge \nu_{\mathrm{HI}}$.

We can interpret the formula (3.5) as follows. The auxiliary variable r_S describes the infectiousness of the infected population (symptomatic with probability $1 - q_S$ and asymptomatic with probability q_S and reduced infectiousness t_{A_S}). The meaning of the auxiliary variable r_V is analogous. The term $\beta r_S/\gamma_S$ is thus a relatively standard formula for reproduction number;[64] the term $(1-e)\beta r_V/\gamma_V$ is analogous as one can see the vaccination to reduce the transmission rate by a factor $(1-e)$. If, in the absence of vaccination, the reproduction number is below 1 (as in the first option of (3.5)), then there is no need to vaccinate as the population should reach disease-free equilibrium. On the other hand, if even at full vaccination, the

reproduction number is larger than 1 (the last option in (3.5)), then the vaccination cannot eliminate COVID-19. This would be possible if the vaccine was not very effective (small e, large t_{I_V}, and large aAV). Only when the vaccine is effective enough and, without the vaccine, the reproduction number is above 1 (the second option of (3.5)), then there is a minimal vaccination rate, ν_{HI}, needed to reach herd immunity. We can see that the rate ν_{HI} is increasing with vaccine waning rate ω, the "reproduction number" in susceptible only population, $\beta r_S/\gamma_S$, and the "reproduction number" in fully vaccinated population, $(1-e)\beta r_V/\gamma_V$.

4. Game Theory — Optimal Individual Decisions

To study the optimal vaccination decisions from the individuals' perspective, we add the game-theoretic component on top of the epidemiological model.

The vaccination game is a population game that is played by susceptible individuals who decide whether to (re-)vaccinate.[48] As in Refs. 47 and 48, all individuals are assumed to be rational, have complete information about the epidemic, and act in their own interest. They evaluate costs of their own actions and select the action that minimizes their own costs.

The risks of the infection depend on many factors, including the time and the current COVID-19 levels. However, for simplicity, we adopt the Nash equilibrium approach used by Ref. 47 as well as later by many others.[48] We assume that all individuals select their strategy — the frequency to vaccinate — once and independently of each other. The optimal strategy, or the Nash equilibrium, is such a strategy that, if adopted by everyone in the population, nobody has an incentive to deviate from it.[65] To evaluate the payoffs and eventually the potential incentive to deviate from the common strategy, we assume, as in Refs. 47 and 48, that enough time lapsed and the population reached the steady state of the disease dynamics. This will allow us to properly quantify the risks of contracting COVID-19 in such a situation.

To proceed with the Nash equilibrium analysis we assume that, with the exception of a single focal individual, all susceptible individuals vaccinate at rate ν. We now focus on that one focal individual and try to determine whether or not the vaccination is beneficial.

The population is large enough and so the vaccination decision of the focal individual does not have an impact on the steady state of the dynamics. Moreover, we assume that the population is at or near the steady state, i.e., the endemic equilibrium. Hence force of infection is, as in (2.1), given by

$$\lambda^*(\nu) = \begin{cases} 0 & \text{if } \mathcal{R} \leq 1, \\ \beta(I_S^* + t_{A_S} A_S^* + t_{A_V} A_V^* + t_{I_V} I_V^*) & \text{if } \mathcal{R} > 1, \end{cases} \tag{4.1}$$

where I_S^*, A_S^*, A_V^*, and I_V^* are endemic equilibrium proportions of infectious individuals. The proportions and the force of infection can be evaluated numerically.

If, at time t, an individual decides to get vaccinated, they will pay the cost C_V for the vaccination. The vaccine provides only a partial immunity and only for an expected time ω^{-1}. When we are interested in the probability a vaccinated individual becomes exposed, we consider $\frac{dV}{dt} = -(1-e)\lambda V$ with a solution (when λ is constant) given by $V(\tau) = V(0)\exp(-(1-e)\lambda\tau)$. Similarly, the probability of a breakthrough infection between time t and $t+\omega^{-1}$ is given by

$$\begin{aligned}\pi_{V\to E_V} &= 1 - \exp\left(-\int_t^{t+\omega^{-1}} (1-e)\lambda^*(\nu)d\tau\right)\\ &= 1 - \exp\left(-(1-e)\frac{\lambda^*(\nu)}{\omega}\right).\end{aligned} \tag{4.2}$$

The symptomatic infection will result only in $1-q_V$ cases. The remaining proportion will be asymptomatic and will not incur any costs. The total cost of vaccination is thus given by

$$C_V + (1-q_V)\pi_{V\to E_V} C_{I_V}. \tag{4.3}$$

Similarly, the probability that a susceptible individual becomes exposed between a time t and $t+\omega^{-1}$ is given by

$$\pi_{S\to E_S} = 1 - \exp\left(-\frac{\lambda^*(\nu)}{\omega}\right) \tag{4.4}$$

and only the fraction $(1-q_S)$ of the individuals will experience symptomatic infection and pay the cost C_{I_S}.

The incentive to vaccinate, i.e., the cost of not vaccinating minus the cost of vaccinating, is given by

$$\begin{aligned}h(\nu) = (1-q_S)\left(1-\exp\left(-\frac{\lambda^*(\nu)}{\omega}\right)\right)C_{I_S}\\ - C_V - (1-q_V)\left(1-\exp\left(-(1-e)\frac{\lambda^*(\nu)}{\omega}\right)\right)C_{I_V}.\end{aligned} \tag{4.5}$$

The Nash equilibrium is generally obtained by solving $h(\nu)=0$ as for that rate the payoffs for vaccinating or not vaccinating are the same. There is also a possibility that it is not beneficial to vaccinate even if nobody vaccinates (if $h(0)<0$) or that it is always beneficial to vaccinate no matter what everybody else is doing ($h(\nu)>0$ for all ν). Hence, the Nash equilibrium ν_{NE} is given by

$$\nu_{\mathrm{NE}} = \begin{cases} 0 & \text{if } h(0)<0,\\ \nu & \text{for which } h(\nu)=0,\\ \text{does not exist} & \text{if } h(\nu)>0 \text{ for all } \nu.\end{cases} \tag{4.6}$$

The Nash equilibrium can be obtained numerically by solving (4.6).

5. Model Calibration

In this section, we describe how the parameter values and ranges were chosen.

The protection from vaccines can last over seven months but can be lost as fast as in as fast as four months for some vaccines.[51] We will thus consider $\omega^{-1} = 6$ months with a range of [4, 12] months.

Vaccine efficacy varies greatly based on the specific vaccine[66] and based on the most prevalent COVID-19 variant.[67] The review in Ref. 52 shows that in most cases the efficacy is about 80–90%; we will thus assume $e = 0.85$. At the same time, the efficacy can vary depending on the vaccine and the virus variant. We will thus assume the range [0.6, 0.95].

Reference 55 reviewed 99 studies about incubation period and gives the pooled estimate of the mean across the studies as 6.38 days, with 95% CI (5.79; 6.97). Also, Ref. 56 reviews the articles from early 2020 and gives the mean incubation period as 7.8 days, which falls into the ranges proposed by the WHO (0–14 days) and the ECDC (2–12 days). We will thus assume the incubation period is $\sigma^{-1} = 6$ days with the range [2, 12]. We note, however, that other studies reported much shorter periods, for example Ref. 12 considered periods that were about 50% less than what we consider here. Moreover, new findings, such as those presented in Ref. 68 show that viral shedding starts relatively soon and peaks 7 days after exposure, possibly indicating that the incubation period is shorter.

After the infection, neutralizing and spike-specific antibody production persists for at least 5–7 months.[60] We will thus assume that the natural immunity acquired after the infection lasts 6 months with the range [5, 7] months.

The proportion of asymptomatic infections varies greatly from study to study.[54] The review of Ref. 57 for the unvaccinated cases shows the range from 1.4% to 78.3% with the weighted pooled proportion of asymptomatic COVID-19 cases throughout the course of infection was 25% (95%CI: 16–38). We will thus consider $q_S = 0.25$ with the range [0.16, 0.38].

Reference 54 notes that among five transmission studies, 18 of 96 (18.8%) close contacts exposed to asymptomatic index patients were COVID-19 positive. We will thus assume $t_{A_S} \approx 0.2$ with the range [0.1, 0.3]. We will assume that t_{A_V} and t_{I_V} are about the same and with the same range.

The proportion of asymptomatic infections is larger for vaccinated cases.[69] On the other hand, meta-analysis in Ref. 70 shows no significant differences between vaccinated and unvaccinated infections. In a large study 10,262 SARS-CoV-2 vaccine breakthrough infections,[58] 2725 vaccine breakthrough infections were asymptomatic and not hospitalized. Additionally, 289 were asymptomatic or hospitalized for a reason unrelated to COVID-19. This gives $q_V \approx 0.30$. We will assume the range to be [0.2, 0.4].

A median symptom duration is 7 days with range 5–11 days.[59] This agrees with the recommendation to isolate and/or to wear the mask for 10 days since the

beginning of the symptoms.[8] We will thus assume $\gamma_S^{-1} = \gamma_V^{-1} = 7$ days with the range [5, 11].

To estimate the transmission rate β, we use the formula for the reproduction number without vaccination, $\mathcal{R}_0 = \frac{\beta}{\gamma_S}(1 - q_S + q_S t_{A_S})$ which yields $\beta = \mathcal{R}_0 \frac{\gamma_S}{1-q_S+q_S t_{A_S}}$. Since the pooled estimate for $\mathcal{R}_0$ for COVID-19 was estimated as 3.32 with 95% confidence interval between 2.81 and 3.82,[53] we get that $\beta \approx 0.6$. We will assume the range between [0.4, 0.8].

For the case of COVID-19, we will assume that the cost associated with vaccination and actual disease is mostly perceived and stems from potential vaccine side-effects as well as from the necessity to isolate during the infection. To keep the costs relative to the cost of vaccination, we will keep $C_V = 1$. We will also assume $C_{I_S} = 10$ and $C_{I_V} = 1$. While we are strictly assuming those values, we note that the performed uncertainty and sensitivity analysis demonstrates how the model outcomes do not significantly depend on C_{I_V}. The optimal vaccination rate is quite sensitive to $C_{I_S} = 10$. Should the true cost be higher, the optimal rate would be higher as well; on the other hand, should the true cost be lower, the rate would be lower too.

6. Results

For the parameters as described in Table 1, the basic reproduction number without vaccination ($\nu = 0$) is $\mathcal{R} \approx 3.36$. $\mathcal{R}$ is decreasing in ν as shown in Fig. 2(a); and $\mathcal{R} = 1$ for $\nu_{\text{HI}} \approx 0.015$. Figure 2(b) shows sensitivity of $\mathcal{R}$ on model parameters. It is most sensitive to vaccination rate ν and the duration of vaccine protection ω^{-1} (any increase in these two will cause $\mathcal{R}$ to decrease). $\mathcal{R}$ is also quite sensitive on transmission rate, β, and the duration of infectious period of unvaccinated cases, γ_S^{-1} (any increase in those will cause $\mathcal{R}$ to increase). Figure 2(c) shows the uncertainty of $\mathcal{R}$. For the majority of the parameter values, $\mathcal{R}$ is between 1 and 5 and it is below 1 mostly only when $\nu > \nu_{\text{HI}}$.

As already demonstrated above, our model suggests that the vaccination rate needed for herd immunity is $\nu = 0.015$ per day. This means that the whole population needs to be vaccinated in $\nu_{\text{HI}}^{-1} \approx 66$ days. Figure 3(a) shows uncertainty analysis of ν_{HI} for the parameters with ranges as in Table 1. Note that for the majority of parameter values, $\nu_{\text{HI}} > 0.01$, i.e., the individuals need to be (re)-vaccinated every 100 days (or more often). To better understand the vaccination rates, Fig. 3(b) shows the times between vaccinations that are needed to achieve the herd immunity. Again, we see that for the vast majority of the parameters, the time has to be much less than 5 months. Figure 3(c) shows the sensitivity analysis of ν_{HI} on various parameters. It is most sensitive on transmission rate, β, and the duration of infectious period of unvaccinated individuals, γ_S^{-1}; increase of any of these two will cause ν_{HI} to increase. It is also sensitive to the duration of vaccine

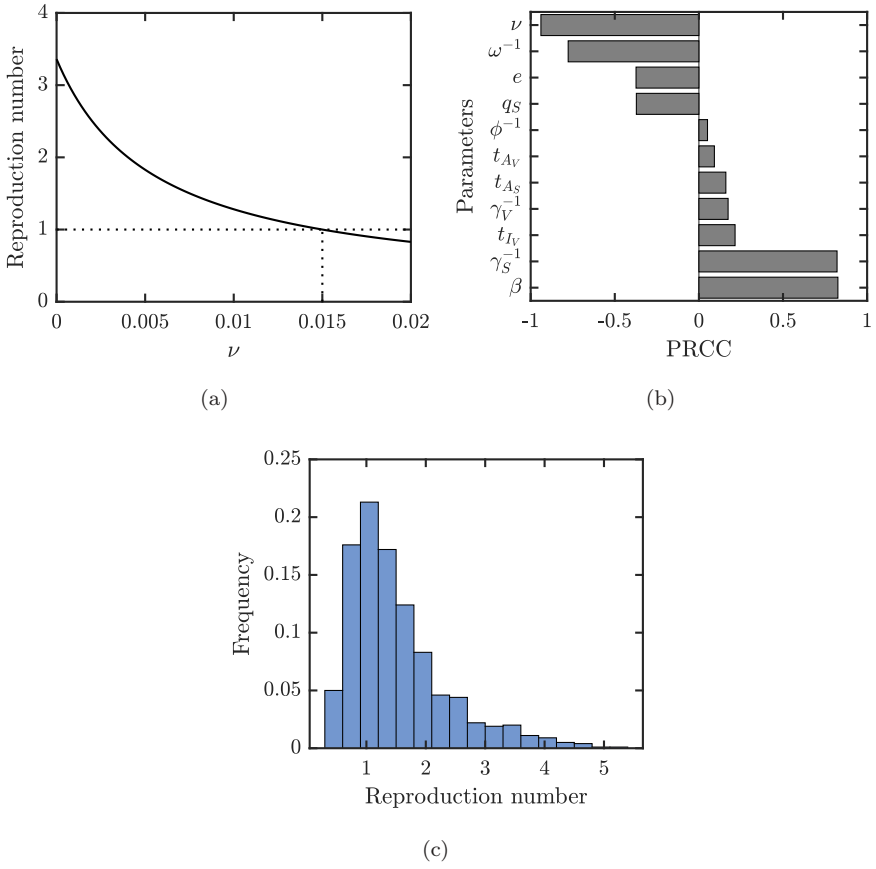

Fig. 2. (a) The dependence of the reproduction number $\mathcal{R}$ on the vaccination rate ν. Other parameters as in Table 1. (b) Sensitivity analysis of the reproduction number. (c) Uncertainty of the reproduction number. The uncertainty and sensitivity analysis was done using the Latin hyper-cube sampling with partial rank correlation coefficient (LHS-PRCC) scheme.[71–73] Parameter ranges as specified in Table 1.

protection, ω^{-1}, and vaccine efficacy, e; an increase of any of these two parameters will cause ν_{HI} to decrease.

The Nash equilibrium value of the vaccination rate is about $\nu_{\mathrm{NE}} \approx 0.0136$, i.e., it is in the individual's best interest to (re-)vaccinate every 73 days. Figure 4 shows sensitivity and uncertainty analysis of ν_{NE}. It follows that it is most sensitive on transmission rate, β, and the duration of infectious period of unvaccinated individuals, γ_S^{-1} and the cost of infection C_{I_S}; increase of any of these three parameters will cause ν_{NE} to increase. It is also sensitive to the duration of vaccine protection, ω^{-1}, and the probability of getting asymptomatic when vaccinated, q_S; an increase of any of these two parameters will cause ν_{NE} to decrease.

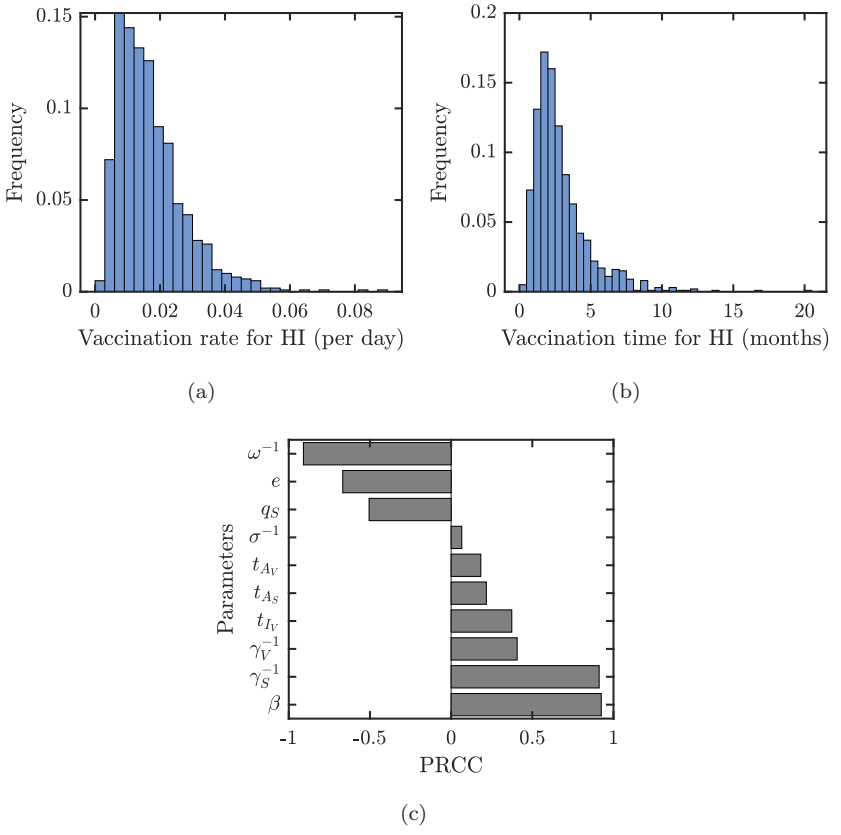

Fig. 3. (a) Uncertainty of the vaccination rate needed to achieve herd immunity, ν_{HI}. (b) Uncertainty analysis of the frequency at which the whole population needs to be vaccinated to achieve herd immunity, ν_{HI}^{-1}. (c) The sensitivity analysis of ν_{HI}. Parameter ranges as specified in Table 1.

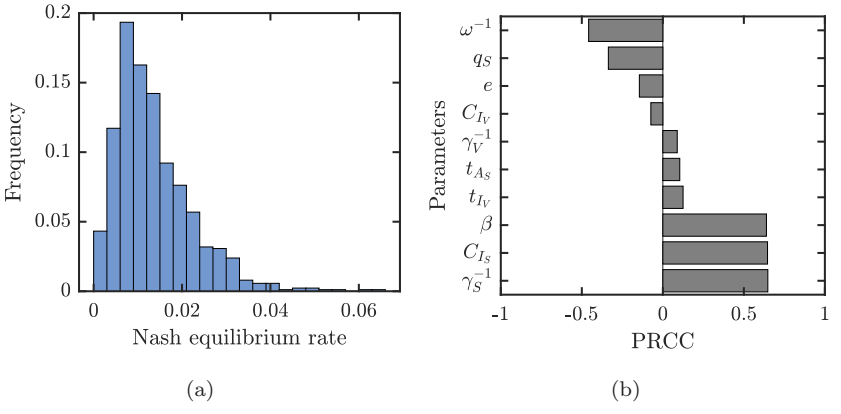

Fig. 4. (a) Uncertainty of the optimal vaccination rate ν_{NE}. (b) The sensitivity analysis of ν_{NE}. Parameter ranges as specified in Table 1.

7. Conclusions and Discussion

We created a compartmental ODE model for COVID-19 transmission that considers asymptomatic infections. We added a game theory component on top of the epidemiological model to account for an individual's vaccination behavior at the endemic equilibrium.

We have seen that vaccination alone is unlikely to eliminate COVID-19. To achieve herd immunity, the individuals would have to receive a dose of a vaccine every 66 days. From the individual's perspective, the optimal frequency is to vaccinate every 73 days. If the vaccine was 100% effective, the frequency for herd immunity could be a little lower at about once every 76 days and the optimal individual frequency would be about once every 84 days. All of these frequencies are unrealistically high since the current recommendations are to re-vaccinate about once every 6 months.

Our model is similar in many aspects to the model of Ref. 49 who also considered breakthrough infections. In our model, we can explicitly fine-tune parameters to make the breakthrough cases less (or more) likely to be asymptomatic and less (or more) infectious while Ref. 49 assumed all parameters to be the same. The sensitivity analysis we performed shows that the difference between the infections do not play any significant role in the outcomes, i.e., they do not significantly affect the vaccination rates needed to achieve the herd immunity nor the optimal Nash equilibrium vaccination rates. We also considered only a short term model and ignored any natural births and deaths explicitly incorporated in Ref. 49 but these modifications did not seem to play any crucial role in the outcomes either.

It has been shown in Ref. 74 that insufficient COVID-19 vaccine coverage can make the pandemic worse. The re-vaccination rates could be lower if either (a) the vaccine protection lasted longer or (b) the transmission rate was not so high. There is not much individuals can do about vaccine waning. It is therefore crucial to adhere to various guidelines, such as quarantine, isolate and wear a mask if tested positive for COVID-19.[8]

As with any mathematical model, our model has a number of limitations. For our game theoretical model, we assumed that all individuals are rational, have complete information about the epidemic, and act in their own interest by selecting the action that minimizes their own costs. Empirical studies[75] as well as theoretical studies[34,40] demonstrate rational behavior and that the actual level of vaccination depends on the perceived cost of the protection. However, individuals may have incomplete[76] or incorrect[77] information. The evidence from a growing body of literature on disease transmission and misinformation suggests that misinformation can prevent the suppression of epidemics.[78–81]

We performed the analysis as if COVID-19 already reached the endemic state. While this is a likely outcome, we may not be there yet.[82,83] The vaccination adoption behaviour can allow for co-evolution[84] and the coupling of game and epidemic models can lead to oscillations in vaccine uptake over time.[85] The vaccine-generated protection can lower COVID-19 infection risk which would cause individuals to

cease vaccinating which in turn causes uptick in disease incidence.[86] To better understand the coupled dynamics between vaccination behavior and disease transmission, one can adopt the imitation dynamic approach for the vaccination game theory[44] as done, for example, in Ref. 31.

Conflict of Interest

There is no conflict of interest.

Author Contributions

Conceptualization, H. O., J. R. and D. T.; Methodology, V. C., H. O., J. R. and D. T.; Software, J. R. and D. T.; Formal Analysis, R. M., M. M., J. S., K. Y., V. C., H. O., J. R., D. T.; Investigation, R. M., M. M., J. S., K. Y., V. C., H. O., J. R., D. T.; Resources, V. C. and H. O.; Writing Original Draft Preparation, R. M., M. M., J. S., K. Y., V. C., H. O., J. R., D. T.; Writing Review & Editing, H. O., J. R. and D. T.; Visualization, J. R. and D. T.; Supervision, V. C., H. O., J. R., D. T.; Project Administration, H. O.; Funding Acquisition, H. O. and D. T.

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Appendix A. Calculations

The equilibria of the dynamics (2.2)–(2.10) are obtained as solutions of the following system of algebraic equations:

$$0 = \varphi R + \omega V - \nu S - \lambda S, \tag{A.1}$$

$$0 = \nu S - \omega V - (1-e)\lambda V, \tag{A.2}$$

$$0 = \lambda S - \sigma E_S, \tag{A.3}$$

$$0 = (1-e)\lambda V - \sigma E_V, \tag{A.4}$$

$$0 = \sigma q_S E_S - \gamma_S A_S, \tag{A.5}$$

$$0 = \sigma(1-q_S)E_S - \gamma_S I_S, \tag{A.6}$$

$$0 = \sigma q_V E_V - \gamma_V A_V, \tag{A.7}$$

$$0 = \sigma(1-q_V)E_V - \gamma_V I_V, \tag{A.8}$$

$$0 = \gamma_S(A_S + I_S) + \gamma_V(A_V + I_V) - \varphi R, \tag{A.9}$$

subject to the constraint

$$1 = S + V + E_S + E_V + A_S + I_S + A_V + I_V + R. \tag{A.10}$$

A.1. *Disease-free equilibrium*

The disease-free equilibrium (with no infections and thus with $\lambda = 0$) is given by solution of

$$0 = \omega V - \nu S, \tag{A.11}$$

$$1 = S + V. \tag{A.12}$$

Thus, $S^0 = \frac{\omega}{\omega+\nu}$ and $V^0 = \frac{\nu}{\omega+\nu}$.

A.2. *Reproduction number*

To assess the local stability of the disease-free equilibrium, we calculate the effective reproduction number following the next-generation matrix method.[63] We order the compartments with infection as $E_S, A_S, I_S, E_V, A_V, I_V$. This gives the vector corresponding to the rates of new infections as

$$\mathcal{F} = (\lambda S,\ 0,\ 0,\ (1-e)\lambda V,\ 0,\ 0)^T \tag{A.13}$$

and the vector corresponding to the transfers between compartments as

$$\mathcal{V} = \begin{pmatrix} \sigma E_S \\ -\sigma q_S E_S + \gamma_S A_S \\ -\sigma(1-q_S)E_S + \gamma_S I_S \\ \sigma E_V \\ -\sigma q_V E_V + \gamma_V A_V \\ -\sigma(1-q_V)E_V + \gamma_V I_V \end{pmatrix}. \tag{A.14}$$

Thus, the derivatives evaluated at the disease-free equilibrium are given by

$$\mathbf{F} = D\mathcal{F} = \begin{pmatrix} 0 & \beta t_{A_S} S^0 & \beta S^0 & 0 & \beta t_{A_V} S^0 & \beta t_{I_V} S^0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & (1-e)\beta t_{A_S} V^0 & (1-e)\beta V^0 & 0 & (1-e)\beta t_{A_V} V^0 & (1-e)\beta t_{I_V} V^0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \tag{A.15}$$

$$\mathbf{V} = D\mathcal{V} = \begin{pmatrix} \sigma & 0 & 0 & 0 & 0 & 0 \\ -\sigma q_S & \gamma_S & 0 & 0 & 0 & 0 \\ -\sigma(1-q_S) & 0 & \gamma_S & 0 & 0 & 0 \\ 0 & 0 & 0 & \sigma & 0 & 0 \\ 0 & 0 & 0 & -\sigma q_V & \gamma_V & 0 \\ 0 & 0 & 0 & -\sigma(1-q_V) & 0 & \gamma_V \end{pmatrix}. \tag{A.16}$$

This yields

$$\mathbf{V}^{-1} = \begin{pmatrix} \sigma^{-1} & 0 & 0 & 0 & 0 & 0 \\ q_S\gamma_S^{-1} & \gamma_S^{-1} & 0 & 0 & 0 & 0 \\ (1-q_S)\gamma_S^{-1} & 0 & \gamma_S^{-1} & 0 & 0 & 0 \\ 0 & 0 & 0 & \sigma^{-1} & 0 & 0 \\ 0 & 0 & 0 & q_V\gamma_V^{-1} & \gamma_V^{-1} & 0 \\ 0 & 0 & 0 & (1-q_V)\gamma_V^{-1} & 0 & \gamma_V^{-1} \end{pmatrix}, \tag{A.17}$$

$$\mathbf{FV}^{-1} = \beta \begin{pmatrix} \frac{S^0 r_S}{\gamma_S} & \frac{S^0 t_{A_S}}{\gamma_S} & \frac{S^0}{\gamma_S} & \frac{S^0 r_V}{\gamma_V} & \frac{S^0 t_{A_V}}{\gamma_V} & \frac{S^0 t_{I_V}}{\gamma_V} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{V^0(1-e) r_S}{\gamma_S} & \frac{V^0(1-e) t_{A_S}}{\gamma_S} & \frac{V^0(1-e)}{\gamma_S} & \frac{V^0(1-e) r_V}{\gamma_V} & \frac{V^0(1-e) t_{A_V}}{\gamma_V} & \frac{V^0(1-e) t_{I_V}}{\gamma_V} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \tag{A.18}$$

where

$$r_S = 1 - q_S + q_S t_{A_S}, \tag{A.19}$$

$$r_V = t_{I_V} - q_V t_{I_V} + q_V t_{A_V}. \tag{A.20}$$

There is only one nonzero eigenvalue of $\mathbf{FV}^{-1}$ given by

$$\mathcal{R} = \left(\frac{\beta}{\gamma_S \gamma_V}\right)\left(\frac{\omega r_S \gamma_V + \nu(1-e) r_V \gamma_S}{\omega + \nu}\right). \tag{A.21}$$

As in Ref. 63, the disease-free equilibrium is locally asymptotically stable if $\mathcal{R} < 1$ and it is not stable if $\mathcal{R} > 1$.

A.3. *Vaccination rate needed to achieve herd immunity*

We have

$$\frac{\partial \mathcal{R}}{\partial \nu} = -\left(\frac{\beta\omega}{\gamma_S\gamma_V(\omega+\nu)^2}\right)(r_S\gamma_V - (1-e)r_V\gamma_S). \tag{A.22}$$

For realistic values of parameters $q_S < q_V$, $r_S > r_V$ and $\gamma_V \geq \gamma_S$. Consequently, as a function of ν, $\mathcal{R}$ is decreasing; see Fig. 2(a). If $\mathcal{R} < 1$ when $\nu = 0$, then there is a herd immunity even with no vaccination. If, on the other hand, $\mathcal{R} > 1$ even as $\nu \to \infty$, then the herd immunity can never be achieved. Thus, there is a unique vaccination rate ν_{HI} defined by

$$\nu_{\mathrm{HI}} = \begin{cases} 0 & \text{if } \dfrac{\beta}{\gamma_S} r_S \leq 1, \\ \omega \dfrac{\frac{\beta}{\gamma_S} r_S - 1}{1-(1-e)\frac{\beta}{\gamma_V} r_V} & \text{if } \dfrac{\beta}{\gamma_S} r_S > 1 \quad \text{and} \quad (1-e)\dfrac{\beta}{\gamma_V} r_V < 1, \\ \infty & \text{if } \dfrac{\beta}{\gamma_S} r_S > 1 \quad \text{and} \quad \dfrac{\beta}{\gamma_V}(1-e) r_V \geq 1, \end{cases} \tag{A.23}$$

such that the disease-free equilibrium is locally asymptotically stable if and only if $\nu \geq \nu_{\mathrm{HI}}$.

A.4. *Endemic equilibrium and stability*

The endemic equilibrium (with positive I_S and thus positive force of infection λ) can be obtained by numerically solving the system of equations (A.1)–(A.10). Numerical experiments with different parameter values showed that there is always at most one biologically relevant (with non-negative values) solution of the system that is not disease-free equilibrium. We therefore conjecture that, for the parameter values as in Table 1, the dynamics (2.2)–(2.10) has at most two steady states: (1) the disease-free equilibrium which is globally asymptotically stable if and only if $\mathcal{R} \leq 1$, and (2) the endemic equilibrium which exists and is globally asymptotically stable if and only if $\mathcal{R} > 1$. We believe this conjecture could be proved by Lyapunov approach as done, for example, in the mpox case in Ref. 87; however, we have not succeeded with the proof.