



Research article

Effects of co-infection on vaccination behavior and disease propagation

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Abstract: Coinfection is the process of an infection of a single host with two or more pathogen variants or with two or more distinct pathogen species, which often threatens public health and the stability of economies. In this paper, we propose a novel two-strain epidemic model characterizing the co-evolution of coinfection and voluntary vaccination strategies. In the framework of evolutionary vaccination, we design two game rules, the individual-based risk assessment (IB-RA) updated rule, and the strategy-based risk assessment (SB-RA) updated rule, to update the vaccination policy. Through detailed numerical analysis, we find that increasing the vaccine effectiveness and decreasing the transmission rate effectively suppress the disease prevalence, and moreover, the outcome of the SB-RA updated rule is more encouraging than those results of the IB-RA rule for curbing the disease transmission. Coinfection complicates the effects of the transmission rate of each strain on the final epidemic sizes.

Keywords: evolutionary game theory; co-infection; imperfect vaccination

1. Introduction

Many infectious diseases, such as novel coronavirus pneumonia (COVID-19), Ebola and monkeypox, are caused by pathogen variants that can be spread among people and which endanger human life and threaten national security. With the increase of the convenience of modern logistics, some extinct diseases recur, and some re-surgings epidemics emerge. Therefore, how to effectively curtail the disease spread has been a major concern of the whole modern society.

Vaccines can boost the production of competent antibodies by stimulating the immune system and lower the morbidity and mortality rates. Hence, vaccination plays a crucial role in preventing and controlling outbreaks of the diseases. Specific immunity induced by vaccination effectively fights against the invasion of viruses, bacteria and other pathogens. With the advancement of science and technology, more and more vaccines have been developed to effectively resist infectious diseases and radically eradicate the diseases, such as smallpox, diphtheria, varicella, etc.

Facing an emerging disease, it is sometimes possible to take a voluntary vaccination strategy to curb its prevalence. In this case, everyone is inclined to either get vaccinated or not. Therefore, the onset of an epidemic depends not only on the transmission mechanisms of an infectious disease, but also on the choices of potential vaccine recipients. For a bounded rationality, they will evaluate the payoff from vaccination, including the side effects of vaccines and the potential risk if they do not take the vaccine, to decide to get vaccinated or not [1]. A myriad of studies has shown that voluntary vaccination policies cannot radically eliminate the outbreak of an epidemic because of the behavior-disease-vaccination interactions, which may form a feedback loop [2–5]. When a disease breaks out and causes lots of deaths, most people would like to receive a vaccination for preventing the disease infection. Once the vaccination coverage reaches a certain level and produces herd immunity, the disease will be effectively controlled. As a consequence, the non-vaccinated have no motivation to get vaccinated and lead to the resurgence of the epidemic.

To further study how individuals' behaviors influence infectious diseases, researchers have employed the evolutionary game theory to set up co-evolutionary models of infectious diseases and human behaviors [6–14]. Indeed, such models provide useful tools to understand the effects of human behaviors on the development of an epidemic. For instance, Kuge and Tanimoto simultaneously proposed a susceptible-infected-recovered (SIR) epidemic model to consider the effects of innate immunity from the treatment and specific immunity from vaccination [15]. Alam et al. adopted an SIR epidemic model to find that imperfect immunization attenuates the rate of virus transmission and gives a second protection to the vaccinated even though they do not receive perfect vaccine protection [16]. Later, Alam coupled the vaccination evolutionary game and an SEIR/V model to study the effects of two control strategies: isolation and quarantine. It was found that the effects of isolation are better than those of quarantine [17]. Arefin et al, based on evolutionary game theory, proposed a two-strain model to evaluate the trade-off of the evolutionary mutation [18]. Kabir et al. combined the SIR model with unawareness and awareness to study the effect of information dissemination on preventing the transmission of infectious diseases [19]. Huang et al. proposed a mathematical model based on complex networks to investigate the co-evolution of epidemic transmission and individuals' behaviors [20].

Most infectious diseases are caused by a single pathogenic strain, but in reality, the disease may be caused by different variants of the pathogen, such as the variants of COVID-19 represented by more than 5 serotypes: alpha, beta, gamma, delta and omicron [21]. Influenza can be categorized by three serotypes: A, B and C. Such multi-strains interact with each other, and some trade-off mechanisms have been identified that result in the coexistence of pathogens in epidemic models. Coinfection is one such trade-off mechanism, and it is defined as a process of the single host infected by two or more pathogenic strains. Evidences has shown that coinfection is common in HIV (human immunodeficiency virus) infection, with combined infections with TB, hepatitis and malaria. Most importantly, co-infection by variants of a pathogen often leads to more mortality and brings a huge

challenge to public health. Therefore, it is necessary to create appropriate approaches to evaluate the effects of coinfection. Many researchers have used infectious disease models to analyze the impacts of coinfection on epidemic spread. Gao et al. showed that coinfection leads to the coexistence of multi-strain mechanisms [22]. In [23], Elaiw et al. proposed a single-host SARS-CoV-2/HIV co-infection model, and they showed that weak CD4+ T cell immunity in co-infected patients can cause severe SARS-CoV-2 infections from a cellular perspective. Hezam et al. proposed the co-infection phenomenon between COVID-19 and cholera to evaluate the combinations of the best policies for curbing such two diseases [24]. Newman and Ferrario studied a co-infection model on a contact network and showed that the results on scale-free networks are in agreement with those results on large wired networks [25]. Osman and Makinde built a listeriosis and anthrax coinfection model, and they studied the effects on each strain and coinfecting strain by varying exposure rates [26]. Martcheva and Pilyugin used an age-structured epidemic model to characterize the coinfection phenomena [27]. Through detailed analysis, they showed that coinfection produces rich dynamics, including backward bifurcation and Hopf bifurcation. Li et al. proposed a multiscale system taking into account for interplays of within and between systems [28]. On an intra-host scale, the two strains compete with each other, and the one with a larger basic reproduction number dominates. On a population scale, co-infection results in the coexistence of the two strains. Sanz et al. proposed a two-strain epidemic model with coinfection on complex networks [29].

In most of the reviewed existing epidemic models with coinfection, they have neglected the effects of individual vaccination behaviors on the evolution of the epidemic infection. In this paper, we couple the evolutionary vaccination behaviors and epidemic models to examine the effect of the co-infection mechanism on the development of an epidemic. The aim of this paper is to explore the co-evolution of flu infection and uptaking vaccination strategies of individuals.

This paper is organized as follows: In Section 2, we design a game theoretical-compartmental epidemic model with coinfection. In Section 3, we study the dynamics of the model through a detailed analysis. Finally, in Section 4, we end with a brief discussion.

2. The model formulation

We assume that an outbreak of an epidemic happens at two distinct time scales. One is the local time scale (t_{local}), and the other is the global time scale (t_{global}). On the first time scale, the period goes through the onset to the end of the epidemic. On the last time scale, individuals taking vaccines dynamically evolves along with periodical outbreaks of the epidemic.

2.1. The epidemic model

Similar to [18], we classify the total population into eight categories: $S(t_{local})$ is the proportion of susceptible individuals at time t , $V(t_{local})$ is the proportion of vaccinated individuals at time t_{local} , $I_{1S}(t_{local})$ is the proportion of susceptible individuals infected by strain one at time t_{local} , $I_{1V}(t_{local})$ is the proportion of vaccinated individuals infected by strain one at time t_{local} , $I_{2S}(t_{local})$ is the proportion of susceptible individuals infected by strain two at time t_{local} , $I_{2V}(t_{local})$ is the proportion of vaccinated individuals infected by strain two at time t_{local} , $J(t_{local})$ is the proportion of individuals infected by strain one and strain two at time t_{local} , and $R(t_{local})$ is the proportion of recovered individuals at time t_{local} .

We assume that individuals initially infected by strain 1 can be re-infected by strain 2, and they

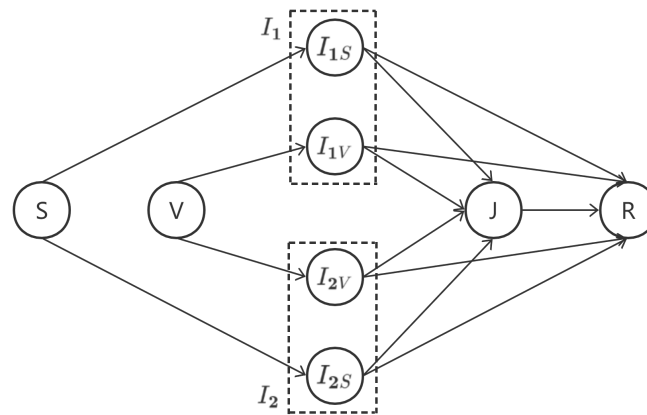


Figure 1. Schematic diagram of the $S VI_1 I_2 JR$ (susceptible-vaccinated-infected with strain 1-infected with strain 2-coinfected-recovered) epidemic model.

move to the co-infection class ($J(t_{local})$). Similarly, individuals initially infected by strain 2 can be re-infected by strain 1, and they move to the co-infection class ($J(t_{local})$). Since the vaccine is not fully effective, we assume that its efficacy values for strain 1 and strain 2 are the coefficients e_1 and e_2 . Susceptibles ($S(t_{local})$), vaccinated individuals ($V(t_{local})$), susceptibles infected by strain 2 ($I_{2S}(t_{local})$) and vaccinated individuals infected by strain 2 ($I_{2V}(t_{local})$) can become individuals infected by strain 1 at transmission rate β_1 . Susceptibles ($S(t_{local})$), vaccinated individuals ($V(t_{local})$), susceptibles infected by strain 1 ($I_{1S}(t_{local})$) and vaccinated individuals infected by strain 1 ($I_{1V}(t_{local})$) can become ones infected by strain 2 at a transmission rate β_2 . Individuals infected by strain 1 ($I_{1S}(t_{local}), I_{1V}(t_{local})$) recover at rate γ_1 , and then they move to the recovery class ($R(t_{local})$). Individuals infected by strain 2 ($I_{2S}(t_{local}), I_{2V}(t_{local})$) recover at a rate of γ_2 , and then they move to the recovery class ($R(t_{local})$). It is assumed that co-infected individuals ($J(t_{local})$) take a longer time to recover than individuals infected by one of the strains alone ($\gamma_3 < \min\{\gamma_1, \gamma_2\}$). A schematic diagram of our model is presented in Figure 1. The framework of a two-strain epidemic model with coinfection takes the following form.

$$\begin{aligned}
 \frac{dS(t_{local})}{dt} &= -\beta_1 S(t_{local})(I_1(t_{local}) + J(t_{local})) - \beta_2 S(t_{local})(I_2(t_{local}) + J(t_{local})), \\
 \frac{dV(t_{local})}{dt} &= -\beta_1 (V(t_{local}) - e_1 V(0))(I_1(t_{local}) + J(t_{local})) \\
 &\quad - \beta_2 (V(t_{local}) - e_2 V(0))(I_2(t_{local}) + J(t_{local})), \\
 \frac{dI_{1S}(t_{local})}{dt} &= \beta_1 S(t_{local})(I_1(t_{local}) + J(t_{local})) - \beta_2 I_{1S}(t_{local})(I_2(t_{local}) + J(t_{local})) - \gamma_1 I_{1S}(t_{local}), \\
 \frac{dI_{1V}(t_{local})}{dt} &= \beta_1 (V(t_{local}) - e_1 V(0))(I_1(t_{local}) + J(t_{local})) \\
 &\quad - \beta_2 I_{1V}(t_{local})(I_2(t_{local}) + J(t_{local})) - \gamma_1 I_{1V}(t_{local}), \\
 \frac{dI_{2S}(t_{local})}{dt} &= \beta_2 S(t_{local})(I_2(t_{local}) + J(t_{local})) - \beta_1 I_{2S}(t_{local})(I_1(t_{local}) + J(t_{local})) - \gamma_2 I_{2S}(t_{local}), \quad (2.1) \\
 \frac{dI_{2V}(t_{local})}{dt} &= \beta_2 (V(t_{local}) - e_2 V(0))(I_2(t_{local}) + J(t_{local}))
 \end{aligned}$$

$$\begin{aligned}
& -\beta_1 I_{2V}(t_{local})(I_1(t_{local}) + J(t_{local})) - \gamma_2 I_{2V}(t_{local}), \\
\frac{dJ(t_{local})}{dt} & = \beta_2 I_{1S}(t_{local})(I_2(t_{local}) + J(t_{local})) + \beta_2 I_{1V}(t_{local})(I_2(t_{local}) + J(t_{local})) \\
& + \beta_1 I_{2S}(t_{local})(I_1(t_{local}) + J(t_{local})) + \beta_1 I_{2V}(t_{local})(I_1(t_{local}) + J(t_{local})) - \gamma_3 J(t_{local}), \\
\frac{dR(t_{local})}{dt} & = \gamma_1 I_{1S}(t_{local}) + \gamma_1 I_{1V}(t_{local}) + \gamma_2 I_{2S}(t_{local}) + \gamma_2 I_{2V}(t_{local}) + \gamma_3 J(t_{local}).
\end{aligned}$$

Define

$$I_1(t_{local}) = I_{1S}(t_{local}) + I_{1V}(t_{local}), I_2(t_{local}) = I_{2S}(t_{local}) + I_{2V}(t_{local}).$$

To satisfy the biological significance, all parameters are positive, and they are chosen from Table 1. The total population is given by

$$S(t_{local}) + V(t_{local}) + I_1(t_{local}) + I_2(t_{local}) + J(t_{local}) + R(t_{local}) = 1.$$

The initial values satisfy

$$S(0) = 1 - x > 0, V(0) = x \geq 0, I_1(0) = 0, I_2(0) = 0, J(0) = 0, R(0) = 0.$$

Table 1. Summary of the parameters of model (2.1).

Parameters	Description	Value	Source
β_1	The transmission rate for strain 1	0.5 day ⁻¹	Assumed
β_2	The transmission rate for strain 2	0.7 day ⁻¹	Assumed
γ_1	Recovery rate after infection by strain 1	1/11 day ⁻¹	[30]
γ_2	Recovery rate after infection by strain 2	1/9 day ⁻¹	[30]
γ_3	Recovery rate after infection by strain 1 and strain 2	1/14 day ⁻¹	Assumed
e_1	Effectiveness of vaccination at protecting against strain 1	0.61	[31]
e_2	Effectiveness of vaccination at protecting against strain 2	0.33	[31]

In fact, in model 2.1, strain 1 can be considered as influenza A (H1N1) virus, and strain 2 is associated with influenza A (H3N2) virus. As we know, an influenza quadrivalent vaccine can protect against four different influenza viruses. In addition, all people over 6 months of age need to get an annual flu shot for slowing down influenza transmission.

2.1.1. The final epidemic size

The final epidemic size is the proportion of the population that is infected at the end of the epidemic. Since all the infected individuals finally become the recovered ones at the end of the disease, the proportion of recovered individuals at the final stage of the epidemic ($(t_{local} = \infty)$) is the final size of the epidemic, denoted by $R(\infty)$. Similarly, we have the following.

- HV is a collective term referring to individuals who choose to get vaccinated before the outbreak, but they are not infected by any strain during the epidemic, represented by $HV(\infty)$.
- I_1V is a collective term referring to individuals who choose to get vaccinated before the outbreak, and they are infected by strain 1 during the epidemic, represented by $I_1V(\infty)$.

- I_2V is a collective term referring to individuals who choose to get vaccinated before the outbreak, and they are infected by strain 2 during the epidemic, represented by $I_2V(\infty)$.
- IV is another collective term referring to individuals who choose to get vaccinated before the outbreak, and they are co-infected by strains 1 and 2 during the epidemic, represented by $IV(\infty)$.
- SFR is a collective term referring to individuals who are not vaccinated before the outbreak, and they are not infected by any strain during the epidemic, represented by $SFR(\infty)$.
- FFR_1 is a collective term referring to individuals who are not vaccinated before the outbreak, but they are infected by strain 1 during the epidemic, represented by $FFR_1(\infty)$.
- FFR_2 is a collective term referring to individuals who are not vaccinated before the outbreak, but they are infected by strain 2 during the epidemic, represented by $FFR_2(\infty)$.
- FFR is a collective term referring to individuals who are not vaccinated before the outbreak, but they are infected by both strain 1 and strain 2 during the epidemic, represented by $FFR(\infty)$.

2.1.2. The reproduction number

Based on the next generation matrix [32], the reproduction number associated with each strain is defined by

$$R_i = \frac{\beta_i(1 - e_i x)}{\gamma_i}, i = 1, 2.$$

Hence, the basic reproduction number is

$$R_0 = \max \{R_1, R_2\}.$$

When $R_0 < 1$, system (2.1) has only a disease-free equilibrium (DFE), which means that neither strain colonizes the host, and the disease becomes extinct. When $R_1 > 1, R_2 < 1$, it follows from the competitive exclusion principle that strain 1 is dominant, and strain 2 is eliminated. Similarly, when $R_2 > 1, R_1 < 1$, strain 2 is dominant, and strain 1 is eradicated. When $R_1 > 1, R_2 > 1$, the two strains coexist, and the two strains both invade the host.

2.2. The decision-making stage

Although the extermination of smallpox served as a perfect example of completely eliminating a disease by vaccines, there are still many diseases that cannot be radically eradicated in a region. There is a paradox in immuno-epidemiology: While vaccination leads to herd immunity, individuals who have not been vaccinated are indirectly protected against the disease with no incentive to take vaccines, and they don't pay any costs. These are called free riders. From a personal payment perspective, free riders are not required to pay any costs associated with the epidemic.

Next, we analyze the payoffs of different types of people. The cost of the vaccinated from direct costs and side-effects is denoted by C_V . The payoff of potential infection from the risk of death and suffering is denoted by C_I . Thus, the relative payoff of vaccination is $C_r = C_V/C_I$. We assume that the payoff of the vaccinated is less than the that of the non-vaccinated, and $0 < C_r \leq 1$. Here, we divide the relative payoffs of the population into eight categories (see Table 2). We can obtain the average social payoff π , the average vaccinated payoff $\langle \pi_V \rangle$, and the average unvaccinated payoff $\langle \pi_{NV} \rangle$.

$$\begin{aligned} \pi = & -C_r HV(\infty) - (C_r + 1)(I_1V(\infty) + I_2V(\infty)) - (C_r + 2)IV(\infty) \\ & - (FFR_1(\infty) + FFR_2(\infty) + 2FFR(\infty)), \end{aligned} \quad (2.2)$$

$$\langle \pi_V \rangle = - (C_r HV(\infty) + (C_r + 1)(I_1V(\infty) + I_2V(\infty)) + (C_r + 2)IV(\infty)) / x, \quad (2.3)$$

$$\langle \pi_{NV} \rangle = - (FFR_1(\infty) + FFR_2(\infty) + 2FFR(\infty)) / (1 - x). \quad (2.4)$$

Table 2. Fractions of four types of individuals existing in a population at equilibrium.

State/Strategy	Healthy	Infected with strain 1	Infected with strain 2	Coinfected with strain 1 and strain 2
Vaccination (V)	$\pi_{HV} = -C_r$	$\pi_{I_1V} = -C_r - 1$	$\pi_{I_2V} = -C_r - 1$	$\pi_{IV} = -C_r - 2$
Non-vaccination (NV)	$\pi_{SFR} = 0$	$\pi_{FFR_1} = -1$	$\pi_{FFR_2} = -1$	$\pi_{FFR} = -2$

2.2.1. Strategy adaptation

Unlike adopting static game-theoretic strategies, we assume that the information about the epidemic is limited, which implies that at the end of each cycle of the epidemic, individuals update their strategies for the next period depending on their neighbors' payoffs. For the sake of convenience, we employ the individual-based risk assessment (IB-RA) strategy proposed by Fu et al. [33] and the strategy-based risk assessment (SB-RA) strategy proposed by Fukuda et al. [34] to derive the evolutionary game-theoretical model.

1) Individual-based risk assessment (IB-RA) model

To explore the role played by individual imitative behavior and group structure in vaccination, Fu et al. [33] proposed an evolutionary game approach. Individual i randomly selects one of his or her neighbours j to imitate, and he or her would like to imitate one who acquired higher benefits in the previous epidemic course. The probability of individual i adopting the strategy of individual j is assumed to be given in the Fermi type [26-29], which takes the form of

$$P(S_i \leftarrow S_j) = \frac{1}{1 + \exp[-(\pi_j - \pi_i)/\kappa]}, \quad (2.5)$$

where S_i denotes the strategy adopted by individual i . π_i denotes the payoff by individual i during the previous epidemic. κ denotes selection intensity. The larger the value of κ , the more likely the individual is to switch his behaviors. For example, the probability that a healthy vaccinator (HV) will imitate a successful free-rider (SFR) is formulated by

$$P(HV \leftarrow SFR) = \frac{1}{1 + \exp[-(0 - (-C_r))/\kappa]}.$$

Other cases are shown in the appendix.

2) Strategy-based risk assessment (SB-RA) model

Fukuda et al. modified the uptaken IB-RA rule from the payoff of an individual to an average one. The transfer probability for individual i is taken in the form of

$$P(S_i \leftarrow S_j) = \frac{1}{1 + \exp[-(\langle \pi_j \rangle - \pi_i)/\kappa]}, \quad (2.6)$$

where $\langle \pi_j \rangle$ denotes the average payoff for individuals who adopt strategy S_j . For example, the probability that a healthy vaccinator (HV) imitates non-vaccinators is

$$P(HV \leftarrow NV) = \frac{1}{1 + \exp[-(\langle \pi_{NV} \rangle - (-C_r))/\kappa]}.$$

Similarly, other cases are shown in the appendix.

2.3. Evolutionary dynamics

The vaccination dynamics corresponding to different imitative behaviors can be derived from the imitation probabilities mentioned above. The global dynamics of an individual behavior in the IB-RA framework at the global time scale (t_{global}) is given by

$$\begin{aligned} \frac{dx}{dt_{global}} = & HV(\infty) \cdot SFR(\infty) \cdot (P(SFR \leftarrow HV) - P(HV \leftarrow SFR)) \\ & + HV(\infty) \cdot FFR_1(\infty) \cdot (P(FFR_1 \leftarrow HV) - P(HV \leftarrow FFR_1)) \\ & + HV(\infty) \cdot FFR_2(\infty) \cdot (P(FFR_2 \leftarrow HV) - P(HV \leftarrow FFR_2)) \\ & + HV(\infty) \cdot FFR(\infty) \cdot (P(FFR \leftarrow HV) - P(HV \leftarrow FFR)) \\ & + I_1V(\infty) \cdot SFR(\infty) \cdot (P(SFR \leftarrow I_1V) - P(I_1V \leftarrow SFR)) \\ & + I_1V(\infty) \cdot FFR_1(\infty) \cdot (P(FFR_1 \leftarrow I_1V) - P(I_1V \leftarrow FFR_1)) \\ & + I_1V(\infty) \cdot FFR_2(\infty) \cdot (P(FFR_2 \leftarrow I_1V) - P(I_1V \leftarrow FFR_2)) \\ & + I_1V(\infty) \cdot FFR(\infty) \cdot (P(FFR \leftarrow I_1V) - P(I_1V \leftarrow FFR)) \\ & + I_2V(\infty) \cdot SFR(\infty) \cdot (P(SFR \leftarrow I_2V) - P(I_2V \leftarrow SFR)) \\ & + I_2V(\infty) \cdot FFR_1(\infty) \cdot (P(FFR_1 \leftarrow I_2V) - P(I_2V \leftarrow FFR_1)) \\ & + I_2V(\infty) \cdot FFR_2(\infty) \cdot (P(FFR_2 \leftarrow I_2V) - P(I_2V \leftarrow FFR_2)) \\ & + I_2V(\infty) \cdot FFR(\infty) \cdot (P(FFR \leftarrow I_2V) - P(I_2V \leftarrow FFR)) \\ & + IV(\infty) \cdot SFR(\infty) \cdot (P(SFR \leftarrow IV) - P(IV \leftarrow SFR)) \\ & + IV(\infty) \cdot FFR_1(\infty) \cdot (P(FFR_1 \leftarrow IV) - P(IV \leftarrow FFR_1)) \\ & + IV(\infty) \cdot FFR_2(\infty) \cdot (P(FFR_2 \leftarrow IV) - P(IV \leftarrow FFR_2)) \\ & + IV(\infty) \cdot FFR(\infty) \cdot (P(FFR \leftarrow IV) - P(IV \leftarrow FFR)). \end{aligned} \quad (2.7)$$

The global dynamics of individual behavior in the SB-RA framework at the global time scale (t_{global}) is taken in the form of

$$\begin{aligned} \frac{dx}{dt_{global}} = & SFR(\infty) \cdot V(\infty) \cdot P(SFR \leftarrow V) + FFR_1(\infty) \cdot V(\infty) \cdot P(FFR_1 \leftarrow V) \\ & + FFR_2(\infty) \cdot V(\infty) \cdot P(FFR_2 \leftarrow V) + FFR(\infty) \cdot V(\infty) \cdot P(FFR \leftarrow V) \\ & - HV(\infty) \cdot NV(\infty) \cdot P(HV \leftarrow NV) - I_1V(\infty) \cdot NV(\infty) \cdot P(I_1V \leftarrow NV) \\ & - I_2V(\infty) \cdot NV(\infty) \cdot P(I_2V \leftarrow NV) - IV(\infty) \cdot NV(\infty) \cdot P(IV \leftarrow NV). \end{aligned} \quad (2.8)$$

3. Diagram analyses

Due to the complexity of the system, we have conducted numerical simulations to show the dynamics of the model. We focus on how the parameters affect the dynamics. Similar to [18], we first investigated the influence of vaccine effectiveness on the game-theoretic epidemic system in the frameworks of the IB-RA and SB-RA rules. Meanwhile, we investigated the effects of the transmission rate of each strain on the evolutionary game system by adopting such two rules.

3.1. The effects of vaccine effectiveness values e_1 and e_2

The top and bottom panels of Figure 2 respectively show the influence of e_1 and e_2 on the reproduction number of Strain 1 (R_1), the reproduction number of Strain 2 (R_2), final epidemic size (FES), vaccination coverage (VC) and social average payment (ASP) in the frameworks of the IB-RA and SB-RA rules. In Figure 2, the horizontal coordinate represents the effectiveness of the vaccine against Strain 1 and the vertical coordinate indicates the effectiveness of the vaccine against Strain 2. First, we have noted that there exists a triangular region in the lower left corners of subplots of Figure 2. In such regions, the efficacy of vaccines is not high enough to curtail the two strains, a large number of people will be infected, and fewer people will take vaccines. As a consequence, it will cause a huge socioeconomic burden. With the increase of the vaccine effectiveness against Strain 1, the reproduction number associated with strain 1 is monotonically decreasing. Similarly, the reproduction number with respect to strain 2 monotonically decreases as e_2 increases (see Figure 2b-*). This phenomenon suggests that improving the efficacy of immunity from vaccines is in favor of controlling the disease spread. From Figure 2c-*, 2d-* and 2e-*, we have concluded that the efficacies of vaccines associated with the two strains are equal and high, and this leads to the best response for curbing the disease transmission. Comparing the results by adopting the IB-RA and SB-RA strategies, we found that the SB-RA strategy is more effective in preventing the disease.

3.2. The effects of transmission rates β_1 and β_2

The top and bottom panels of Figure 3 show the effects of β_1 and β_2 on the reproduction number of strain 1 (R_1), the reproduction number of strain 2 (R_2), final size (FES), vaccine coverage (VC), and social average payment (ASP) corresponding to the IB-RA and SB-RA rules, respectively. In Figure 3, the horizontal coordinate represents the transmission rate of strain 1, and the vertical coordinate represents the transmission rate of strain 2.

In Figure 3a-*, the reproduction number associated with strain 1 monotonically increases as the rate of transmission of strain 1 increases. A familiar trend was observed for the reproduction number with respect to strain 2 in Figure 3b-*. Furthermore, the reproduction number associated with strain 2 is not only dependent on β_2 , but it is influenced by β_1 . Figure 3c-* displays the regions of disease-free equilibrium (DFE), the dominance of strain 1, the dominance of strain 2 and the coexistence area (see Figure 3c-*), which is substantially different when compared with the results of [18]. Comparing the results of the IB-RA and SB-RA updated rules, we have seen that that the epidemic, by adopting the SB-RA strategy, has a larger final size, a less vaccine coverage, and a greater economic burden on society.

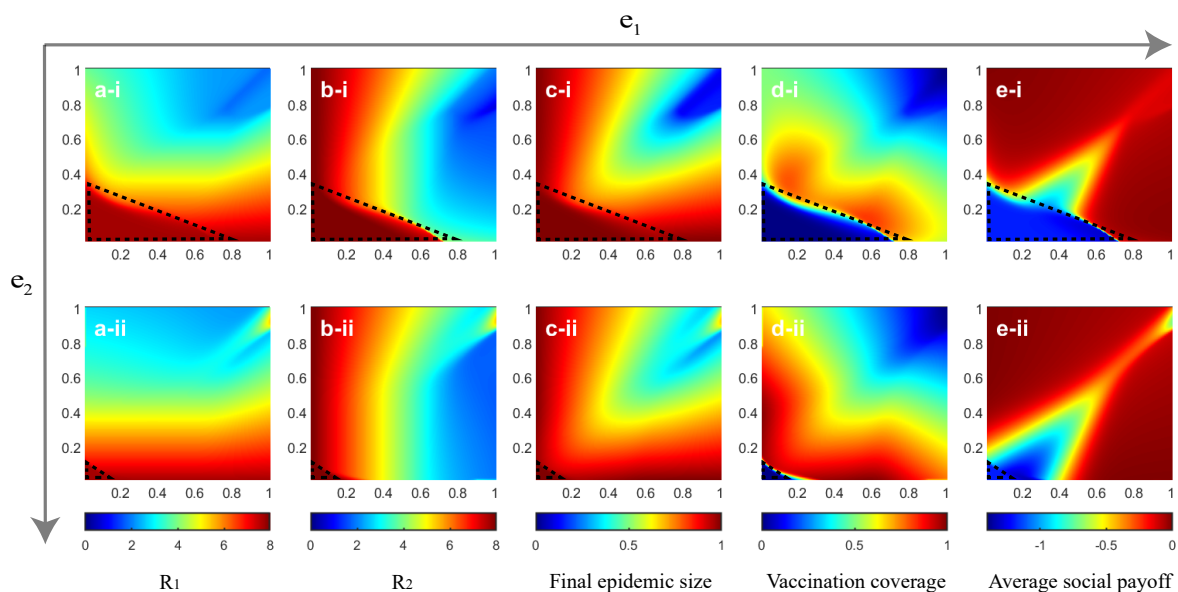


Figure 2. The effects of the efficacy of vaccines (e_1, e_2) on the reproduction number with respect to each strain (a-*,b-*), the final epidemic size (c-*), the vaccination coverage (d-*) and social average payoff (e-*) in the IB-RA and SB-RA updated rules.

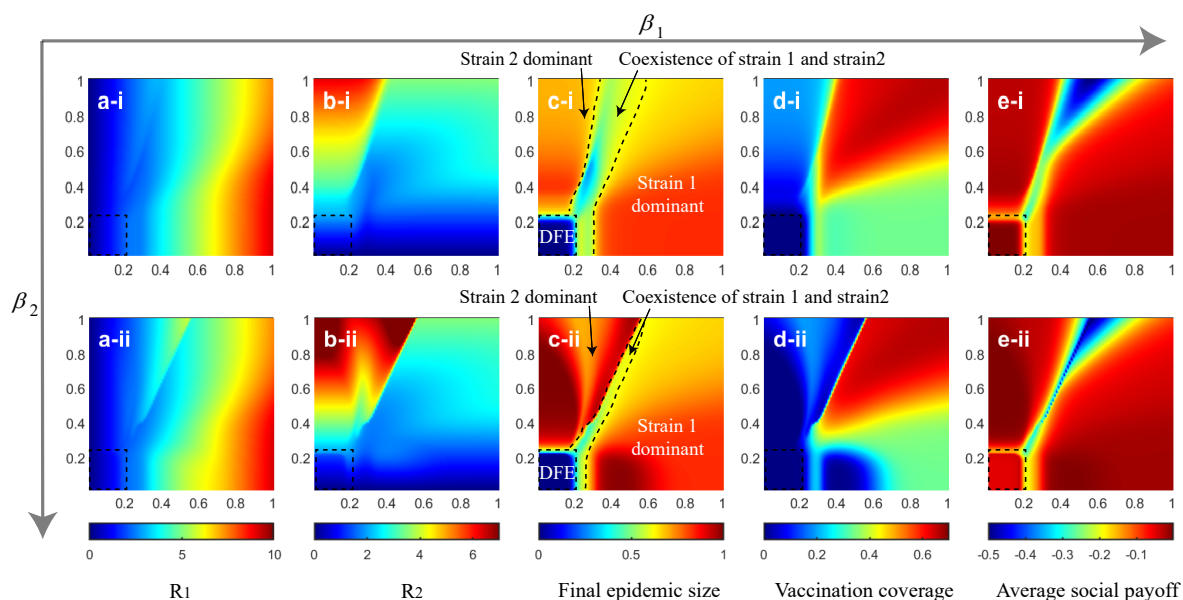


Figure 3. The effects of transmission rates (β_1, β_2) on the reproduction number associated with each strain (a-*,b-*), the final epidemic size (c-*), the vaccination coverage (d-*) and social average payoff (e-*) in IB-RA and SB-RA updated rules.

4. Conclusions and discussion

This work aims to study the co-evolution of a two-strain epidemic with coinfection and the evolution of game-theoretical vaccination behaviors. We adopted the IB-RA and the SB-RA updated rules to uptake the individuals' vaccination strategies. Through numerical analysis, we have found that coinfection deeply aggravates the spread of disease, and the basic reproduction number is closely related with both β_1 and β_2 . Similarly, those biomass, such as the epidemic final size, the average social payoff, etc. strongly depend on the efficacy of each strain $\epsilon_j (j = 1, 2)$. This is substantially different from those outcomes of traditional epidemic models with only a single strain. We have shown that higher vaccine effectiveness and lower transmission rate are encouraged in curbing infectious diseases under the IB-RA and SB-RA updated rules, which are consistent with those results in [18]. Comparing with those results, adopting SB-RA updated rules has a better effect on reducing the epidemic final size and lowering the payoff of society.

Due to the introduction of the coinfection mechanism, there exists four scenarios: the region of the eradication of the disease, the region of strain 1 dominating, the area of strain 2 dominating and the area of the coexistence. The closer the transmission rates of the two strains are, the heavier the social burden will be, even if a huge proportion of people would like to get vaccinated. All these findings are significant guidance for the control of epidemics with coinfection by two strains.

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Conflict of interest

All authors declare no conflicts of interest in this paper.

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Appendix

1. Transition probabilities for IB-RA update rule

$$\begin{aligned}
 P(HV \leftarrow SFR) &= \frac{1}{1 + \exp[-(0 - (-C_r)) / \kappa]}, & P(SFR \leftarrow HV) &= \frac{1}{1 + \exp[-(-C_r - 0) / \kappa]}, \\
 P(HV \leftarrow FFR_1) &= \frac{1}{1 + \exp[-(-1 - (-C_r)) / \kappa]}, & P(SFR \leftarrow I_1V) &= \frac{1}{1 + \exp[-(-C_r - 1 - 0) / \kappa]}, \\
 P(HV \leftarrow FFR_2) &= \frac{1}{1 + \exp[-(-1 - (-C_r)) / \kappa]}, & P(SFR \leftarrow I_2V) &= \frac{1}{1 + \exp[-(-C_r - 1 - 0) / \kappa]}, \\
 P(HV \leftarrow FFR) &= \frac{1}{1 + \exp[-(-2 - (-C_r)) / \kappa]}, & P(SFR \leftarrow IV) &= \frac{1}{1 + \exp[-(-C_r - 2 - 0) / \kappa]}, \\
 P(I_1V \leftarrow SFR) &= \frac{1}{1 + \exp[-(0 - (-C_r - 1)) / \kappa]}, & P(FFR_1 \leftarrow HV) &= \frac{1}{1 + \exp[-(-C_r - (-1)) / \kappa]}, \\
 P(I_1V \leftarrow FFR_1) &= \frac{1}{1 + \exp[-(-1 - (-C_r - 1)) / \kappa]}, & P(FFR_1 \leftarrow I_1V) &= \frac{1}{1 + \exp[-(-C_r - 1 - (-1)) / \kappa]}, \\
 P(I_1V \leftarrow FFR_2) &= \frac{1}{1 + \exp[-(-1 - (-C_r - 1)) / \kappa]}, & P(FFR_1 \leftarrow I_2V) &= \frac{1}{1 + \exp[-(-C_r - 1 - (-1)) / \kappa]}, \\
 P(I_1V \leftarrow FFR) &= \frac{1}{1 + \exp[-(-2 - (-C_r - 1)) / \kappa]}, & P(FFR_1 \leftarrow IV) &= \frac{1}{1 + \exp[-(-C_r - 2 - (-1)) / \kappa]}, \\
 P(I_2V \leftarrow SFR) &= \frac{1}{1 + \exp[-(0 - (-C_r - 1)) / \kappa]}, & P(FFR_2 \leftarrow HV) &= \frac{1}{1 + \exp[-(-C_r - (-1)) / \kappa]}, \\
 P(I_2V \leftarrow FFR_1) &= \frac{1}{1 + \exp[-(-1 - (-C_r - 1)) / \kappa]}, & P(FFR_2 \leftarrow I_1V) &= \frac{1}{1 + \exp[-(-C_r - 1 - (-1)) / \kappa]}, \\
 P(I_2V \leftarrow FFR_2) &= \frac{1}{1 + \exp[-(-1 - (-C_r - 1)) / \kappa]}, & P(FFR_2 \leftarrow I_2V) &= \frac{1}{1 + \exp[-(-C_r - 1 - (-1)) / \kappa]}, \\
 P(I_2V \leftarrow FFR) &= \frac{1}{1 + \exp[-(-2 - (-C_r - 1)) / \kappa]}, & P(FFR_2 \leftarrow IV) &= \frac{1}{1 + \exp[-(-C_r - 2 - (-1)) / \kappa]}, \\
 P(IV \leftarrow SFR) &= \frac{1}{1 + \exp[-(0 - (-C_r - 2)) / \kappa]}, & P(FFR \leftarrow HV) &= \frac{1}{1 + \exp[-(-C_r - (-2)) / \kappa]}, \\
 P(IV \leftarrow FFR_1) &= \frac{1}{1 + \exp[-(-1 - (-C_r - 2)) / \kappa]}, & P(FFR \leftarrow I_1V) &= \frac{1}{1 + \exp[-(-C_r - 1 - (-2)) / \kappa]}, \\
 P(IV \leftarrow FFR_2) &= \frac{1}{1 + \exp[-(-1 - (-C_r - 2)) / \kappa]}, & P(FFR \leftarrow I_2V) &= \frac{1}{1 + \exp[-(-C_r - 1 - (-2)) / \kappa]}, \\
 P(IV \leftarrow FFR) &= \frac{1}{1 + \exp[-(-2 - (-C_r - 2)) / \kappa]}, & P(FFR \leftarrow IV) &= \frac{1}{1 + \exp[-(-C_r - 2 - (-2)) / \kappa]}.
 \end{aligned}$$

2. Transition probabilities for SB-RA update rule

$$\begin{aligned}
 P(HV \leftarrow NV) &= \frac{1}{1 + \exp[-(\langle\pi_{NV}\rangle - (-C_r)) / \kappa]}, & P(SFR \leftarrow V) &= \frac{1}{1 + \exp[-(\langle\pi_V\rangle - (0)) / \kappa]}, \\
 P(I_1V \leftarrow NV) &= \frac{1}{1 + \exp[-(\langle\pi_{NV}\rangle - (-C_r - 1)) / \kappa]}, & P(FFR_1 \leftarrow V) &= \frac{1}{1 + \exp[-(\langle\pi_V\rangle - (-1)) / \kappa]}, \\
 P(I_2V \leftarrow NV) &= \frac{1}{1 + \exp[-(\langle\pi_{NV}\rangle - (-C_r - 1)) / \kappa]}, & P(FFR_2 \leftarrow V) &= \frac{1}{1 + \exp[-(\langle\pi_V\rangle - (-1)) / \kappa]}, \\
 P(IV \leftarrow NV) &= \frac{1}{1 + \exp[-(\langle\pi_{NV}\rangle - (-C_r - 2)) / \kappa]}, & P(FFR \leftarrow V) &= \frac{1}{1 + \exp[-(\langle\pi_V\rangle - (-2)) / \kappa]}.
 \end{aligned}$$



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