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A Game-Theoretic Modeling Approach to Comprehend the Advantage of Dynamic Health Interventions in Limiting the Transmission of Multi-Strain Epidemics

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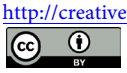

Abstract

In the situation of inadequate vaccines and rapid mutation of virulent strains, alternative health interventions play a crucial role in the containment of emerging epidemics. This study elucidates the critical aspects of health interventions to control epidemic resurgence. Besides, human behavioral response to epidemics plays an instrumental role in bringing the success of control efforts. The appearance of multi-strain epidemics has become a global health concern that requires special attention. Here, we introduce a novel mean-field epidemic game approach to predict the evolutionary dynamics of flu-like epidemics having multiple disease strains. Our model illustrates the importance of multiple provisions alongside their timely execution for better disease attenuation. In addition to vaccination, we introduce self-protection as a potential alternative that yields safeguard against either strain. Both these imperfect provisions render better efficacy against primary (resident) strain than secondary (mutant) to contain epidemic transmission. The simulation-backed model analysis further sheds some light on the crucial impacts of control interventions to limit the invasion of virulent strains from qualitative and quantitative viewpoints. It explicates how vaccination and self-protection complement each other as per situation demands. Our full-fledged theoretical approach further illustrates the dynamic trade-off between the cost and efficacy of a certain intervention. We confirm that the disease dies out when the basic reproduction number of individual strains is less than one and becomes en-

demic if it is greater than one. Finally, the model addresses the evolutionary consequences when mutation takes place from primary to secondary strain. Some impressive facts while employing dual provisions have been reinforced using a game-theoretic framework.

Keywords

Vaccine Efficacy, Evolutionary Dynamics, Strategy Imitation, Social Dilemma, Intermediate Defense Measure, Multiple Strains, Social Payoff

1. Introduction

Epidemic prevalence continues to have adverse impacts on public health, imposing substantial burdens over the years. The endemic of emerging infectious diseases has become a global threat to human existence. Every single country is consistently being exposed to the potential emergence of these diseases. Several factors, such as drastic changes in ecology, climate, and human demographics, play essential roles in a complex mechanism contributing to the multiple occurrences of infectious diseases. A few crucial aspects of controlling the outbreaks are surveillance, preparedness, and early response. Pre-emptive vaccination, in this context, undoubtedly, is considered one of the most economical and effective public health interventions in terms of preventing the transmission of infectious diseases and reducing the morbidity and mortality of immunized individuals [1] [2] [3] [4] [5]. Infectious diseases like measles, mumps, HIV, pertussis, influenza, and many more have been threatening mankind for centuries, while new emerging infectious diseases, e.g., Ebola, Zika virus, SARS, and MERSE are still bubbling up from animal populations and make a jump to human populations, or sometimes deliberately transmitting to human societies due to climate change and diverse anthropogenic disturbances [6]. In the modern era of globalization, the outbreaks of such diseases can spread rapidly due to the booming international travel and trade taking place around the world. However, with the significant improvement of modern transportation systems, human contact has been multiplied, which is undoubtedly one of the prime sources responsible for the faster spreading of a pathogen from epidemic areas to take the shape of a global epidemic [7] [8]. Either the disease outbreaks can be of three types: endemic, epidemic, or pandemic, depending on the intensity of the pathogen, its mode of transmission, herd immunity, and prevalence and incidence of illness. Therefore, understanding and restricting disease transmission is treated as a contemporary issue for human societies. Infectious diseases will continue to emerge and re-emerge, leading to unpredictable epidemics and unwanted challenges to public health issues as these diseases are fully responsible for bringing devastating negative impacts and inflicting a substantial financial burden on our societies. It is now high time to propose more effective intervention techniques to control the epidemic breakout of infectious diseases. Computational epidemiology, backed

by mathematical modeling, offers multiple sets of modeling tools for estimating the spread of epidemic diseases alongside the efficacy of various public-health interventions, e.g., vaccination, self-protection, and social awareness.

Among the numerous attempts taken globally, vaccination is treated as the most successful means of disease prevention and attenuation. Although it incurs a partial cost to each vaccinee under a voluntary vaccination scheme, committing vaccines is solely driven by human decision-making or behavioral responses to inhibiting the epidemic prevalence. It reflects how people weigh the infection risk and the cost of vaccination against the spreading of vaccine-preventable diseases [9]. Individuals committing vaccines in large numbers not only help themselves become partially or fully immune but also reduce the chance of getting infected for non-vaccinees living adjacent to them. This invokes a social dilemma, as it allows an agent to rely entirely on the so-called "herd immunity" to protect him from infection other than getting vaccinated. Consequently, a substantial incentive amid people comes up for free riding which helps to increase the number of "free riders" who pay none of the costs, e.g., vaccination cost, infection cost, potential risk of by-effects and psychological negative-costs brought about by vaccination or any other alternative provision but eventually get benefited from the "herd immunity" as a fruit of public goods. Thus, an obvious conflict remains between individuals' and social benefits. Entailing epidemiology with evolutionary game theory (EGT) could thus be a promising approach to resolving this existing conflict. Here, vaccination or other pre-emptive provisions may consider as a "game" on a complex social network. This specific structure of social dilemma is known as the "vaccination dilemma", caused by these complex interrelations, and has successfully been modeled in the well-known framework of "vaccination game" [10] [11]. This framework is best suitable to work on the intrinsic natures of human behavioral responses, thereby would be a challenging field of future research [12] [13].

Recently, considerable attention has been paid to justifying the role of social factors in epidemic modeling. Game-theoretic analysis has thus been widely used in modeling the behavioral dynamics in response to infectious diseases. On top of that, epidemic modeling triggered by vaccination game ([1] [14]-[23]) has been playing a crucial role to examine the impact of vaccination on various infectious diseases. This idea incorporates individuals' vaccinating behavior analyzing the perceived risks and benefits of committing vaccines. Several previous studies have shown the positive effects of intermediate defense measure (IDM), [1] [18] [24] as an alternative pre-emptive provision besides vaccination, as well as the impacts of information spreading and awareness effects [22] [25] [26] in the human decision-making process to oppress the disease spreading severity. Some studies dealing with vaccination game considered vaccination as a perfect intervention that ensures perfect immunity to vaccinator, which sounds idealized. However, a majority of vaccines used for infectious diseases such as influenza, malaria, and HIV are imperfect. Vaccines rarely provide absolute protection from disease. Statistics reveal that the intrinsic, unavoidable, primary

vaccine failure rates have been found to range from 2 to 50 percent for licensed vaccines under ideal circumstances in clinical trials [27]. Based on varying disease-types and the working efficacy of each vaccine, vaccine-induced immunity may be short-lived or life-long. Moreover, individuals may sometimes require to take repeated vaccination to improve their immunity level, as reported by the authors of [28]. One of the most difficult challenges of a vaccination campaign is to protect form the disease having a relatively poor natural immunity rate. On the other hand, imperfect vaccination can trigger pathogenic virulence, which eventually makes the situation even worse. Nonetheless, the vaccine provides indirect protection to unvaccinated individuals. It thereby facilitates them with the added incentives of not undergoing the perceived risks associated with vaccination, e.g., vaccine complications and other adverse side effects, thus saving them from the expenditure of preventive measures once the herd immunity establishes. This imperfect behavior of vaccines intrigued modern researchers to incorporate the idea of "effectiveness of vaccination" to make the epidemic disease modeling being more realistic [20]. Though imperfect vaccines do not protect infection purely, yet, it can minimize the infection chance or lessen the impact of getting infected [29]. In practice, we have diverse alternative precautions against infectious diseases other than vaccination, e.g., wearing masks, gargling, taking energy drinks, self-isolation, washing hands frequently, etc., which in general, is termed as "intermediate defense measure (IDM)". Although the cost of such protective measures is reasonably cheaper than that of vaccination, it cannot hinder the intrusion of infections absolutely. Incorporating these intermediate effects, an imperfect vaccination, as well as self-defense against contagion, necessitates a mathematical model considering the stochastic effects. The authors of [20] have uncovered a new game-theoretic framework in an infinite and well-mixed population, revising the standard SIR epidemic model to represent two different scenarios, namely imperfect vaccination (effectiveness model) and defense against contagion (efficiency model). They incorporated these two models into a single mathematical framework that carried out impressive facts on vaccination behaviors, which evolve with time governed by the epidemic dynamics. Prominently, contagion protection is critically substandard to imperfect vaccination.

A bunch of antecedent studies of epidemiological models coupled with the EGT has already been inscribed over the preceding years. Fu *et al.* conduct one such pioneering study, presenting the template of the vaccination game by adding the imitation dynamics to predict individuals' vaccinating behavior based on payoffs received at the immediate time step using multi-agent simulation (MAS) approach [30]. Inspired by them, afterward, the authors of [2] introduced a novel strategy-updating scheme. They later analyzed what would appear if an epidemic transmission topology is incompatible with network topology [16], if obstinate vaccinees as well as non-vaccinees exist in the network [17]. In the recent past, Kuga *et al.* developed a mean-field approximation (MFA) technique [20] besides the MAS approach integrating two imperfect provisions, namely pre-emptive

vaccination and intermediate defense measure (IDM). They adopted the imitation dynamics proposed initially by Fu *et al*. and favorably revived a similar approach in the MFA framework. Later on, they examined the identical situation assuming a heterogeneous structured population [21]. A few recent investigations suggested models for defense against contagion, presuming a lower disease transmittance rate [31] [32]. Furthermore, Iwamura *et al*. estimated a coarser infection risk in their vaccination game model, considering spatial populations [24]. One interesting study suggested that when a population is occupied with many self-interested individuals, there exists an overshooting of vaccine uptake levels as the vaccine efficacy increases [33]. Some other relevant studies incorporating imperfect vaccination in the framework of vaccination games can also be observed in Ref. [32] [34] [35] [36] [37]. It is worth mentioning that all these studies are dedicated to reviewing the consequences of pre-emptive vaccination and other precautionary measures employed on a single strain (infection) epidemic modeling.

One of the biggest challenges in limiting the spread of infectious diseases is to deal with the genetic alterations of pathogens. Several pathogens are stewarded by more than one antigenically different variant of the causative agent [38]. The existence of multiple alternatives of a pathogen is commonly due to counter immune attacks of the host or persuaded by treatment with antibodies or antiviral drugs [39]. Such variants are referred to as different strains of a microorganism, which eventually leads to the persistence of infection in a host. Pathogen mutation contributes to the presence of multi-variants. Therefore, more than one pathogen strains launch many diseases like influenza, dengue fever, HIV-AIDS, and notably, a few of them are sexually transmitted. The evolution of some highly mutating viruses, such as influenza, HCV (hepatitis C virus), of which more than 100 strains of the virus have been identified so far, are frequently generating multiple strains. However, the presence of numerous variants of the pathogen has a significant negative impact on the vaccination campaigns as it increases the possibility of the emergence of vaccine-resistant strains of the disease. Such campaigns create unique opportunities for new strains to evolve within a vaccinated population [40]. Sometimes vaccination does not work efficiently or even gives meager protection against highly mutable viruses. Moreover, vaccines against highly mutable diseases such as HIV and HCV are currently unavailable. Securing adequate immunity against influenza has become a challenging job nowadays. As the virus continuously mutates and generates new strains, any safeguard equipped by a vaccine or by infection is short-lived, and in the next flu season, the same host encounters a new set of strains. One good example illustrates that an antigenic drift of influenza type A virus produces new virus strains to which the host has only partial immunity or no immunity at all, leaving the host vulnerable to reinfection with the disease itself. In these circumstances, IDM can play a vital role in controlling the mutable epidemic spreading. That is why the researchers have paid considerable attention to developing more realistic epidemic dynamics of pathogen-host interactions having multiple strains. So far,

numerous studies have been dedicated to analyzing the two-strain epidemic model with a single vaccination scheme. Due to the severity of the flu endemic, extensive and intensive research has been performed, concentrating on surmising the transmission mechanism and control strategies. Castillo-Chavez *et al.* [41] proposed the original template of a two-strain epidemic model with single vaccination incorporating cross-immunity, proportionate mixing, and age structure while formulating the infectious disease dynamics. Afterwards, the authors of [42] examined the effect of a single-strain vaccine on the dynamics of a two-strain epidemic flu model. Their investigation also carried out the impact of vaccination for one strain (primary) on the spread of newer strain (secondary) using a mathematical model. Several other studies (see Ref. [42]-[48]) also focused on various aspects of multi-strain interactions, including mutation, competitive exclusion as well as coexistence and vaccine-induced pathogen strain replacement when a single vaccination is employed for all strains. Notably, all these remarkable efforts did not incorporate human vaccinating behaviors and other alternative pre-emptive provisions alongside vaccination, which might still be a promising arena for future researchers. As of now, only a few studies have been dedicated to exploring the impact of human vaccinating behavior on two-strain epidemic modeling. Being a focal concern, the study [49] justified how adaptive social behavior can influence differing pathogen virulence in a coupled behavior-disease differential equation model. Additionally, their model allows individuals to enhance their usage of practices (for example, social distancing and handwashing) when the perceived severity of infection prevalence increases, thereby reduce transmission rates and boost up population-level immunity. Yet, they delicately avoid long-term evolutionary processes with repeated rounds of mutation and selection. Contrary to that, Bauch *et al.* [35] [37] relied on EGT with imitation dynamics to illustrate the salient features of evolutionary behavior and its interplay with the epidemics. Some contemporary efforts to incorporate human behavior into disease models have also reviewed [50]. They ended up showing the gaps in conjecturing the reciprocation between infectious disease dynamics and human behavior.

To this end, motivated by the abovementioned precursor studies, we aim to incorporate an evolutionary game-theoretic framework considering repeated epidemic seasons to discern a holistic outline of the development and evolution of a disease governed by two strains. Adding an alternative pre-emptive provision to vaccination, namely IDM, we plan to investigate the coordinated effects of single vaccination and IDM on a two-strain epidemic model based on the MFA technique presuming an infinite and well-mixed homogeneous population. Here, we mainly follow the game scheme improved by Kuga *et al.* [20] for MFA concerning the efficacy and cost of vaccination. In line with that, we introduce the effectiveness of vaccination and efficiency of IDM, alongside their provisional cost values. Keeping in mind all relevant factors contributing to the efficacy of a vaccine against disease strains mentioned in Ref [39] [51], we include the idea of imperfect vaccination as well as imperfect IDM in epidemic dynamics, where

both vaccination and IDM offer better effectiveness against the resident strain (primary strain) than the new or mutant strain (secondary strain). Meanwhile, we split our entire study into two-fold: the presence and absence of mutation. No mutation refers to the indirect connection between strains, yet, mutual competition is there via susceptible agents. On the other hand, the presence of mutation confers to the genetic changes, which furnish a competitive advantage to the mutant strain, as reported in [39]. Our theoretical model, unlike preceding studies, incorporates dual pre-emptive provisions into a two-strain epidemic model fostering imitation dynamics under the framework of EGT.

Overall, the manuscript is organized as follows: In Section 2, we first formulate a two-strain epidemic model with rigorous mathematical formulation using a game-theoretic approach. To validate our proposed model, an in-depth theoretical analysis supported by a series of numerical simulation have been presented in Section 3, and finally, Section 4 illustrates a holistic summary of the proposed model with sufficient discussions on some of the novel findings of this study.

2. Model Description with Methods

Entailing the conventional vaccination game structure with an epidemiological model provides insight into possible mechanisms for various pre-emptive provisions in disease dynamics. In this study, we presume the seasonality of infectious diseases as the protective efficacy of most vaccines lasts less than a year due to waning antibodies and year-to-year changes of the circulating virus. Therefore, we can split the evolutionary dynamics into two stages: vaccination campaign dovetailed with self-protection strategy (stage-I) and epidemic season (stage-II). Here, a disease spreading takes place within a local time scale, and evolutionary human decision-making process is evaluated at a global time scale (depicted in **Figure 1**). Generally, an epidemic season sustains until a single infected person is present in the population. At the closing of an epidemic season, we can stratify nine fractions of individuals depending upon their health condition and strategy adoption. As our model deals influenza-like epidemic diseases, the number of vaccinators, self-protectors as well as other fractions remains the same throughout an epidemic season. Only at the beginning of stage-I, individuals can make their decisions of picking either of the pre-emptive provisions weighing the payoffs among other neighboring groups of individuals (illustrated in **Table 1**) received in the last epidemic season. The underlying payoff of each individual is estimated with the help of imitation dynamics generated by Pair-wise Fermi functions. Subsequently, the fraction of vaccinators and self-protectors is refreshed using the evolutionary dynamics. The whole process gets repeated for multiple seasons until it reaches to some social equilibrium (steady-state situation). Henceforth, striking epidemic behaviors can be explained using a non-linear deterministic $SVMI_PI_SR$ model, proposed to estimate the transmission dynamics coupled with vaccination and IDM (self-protection) policies.

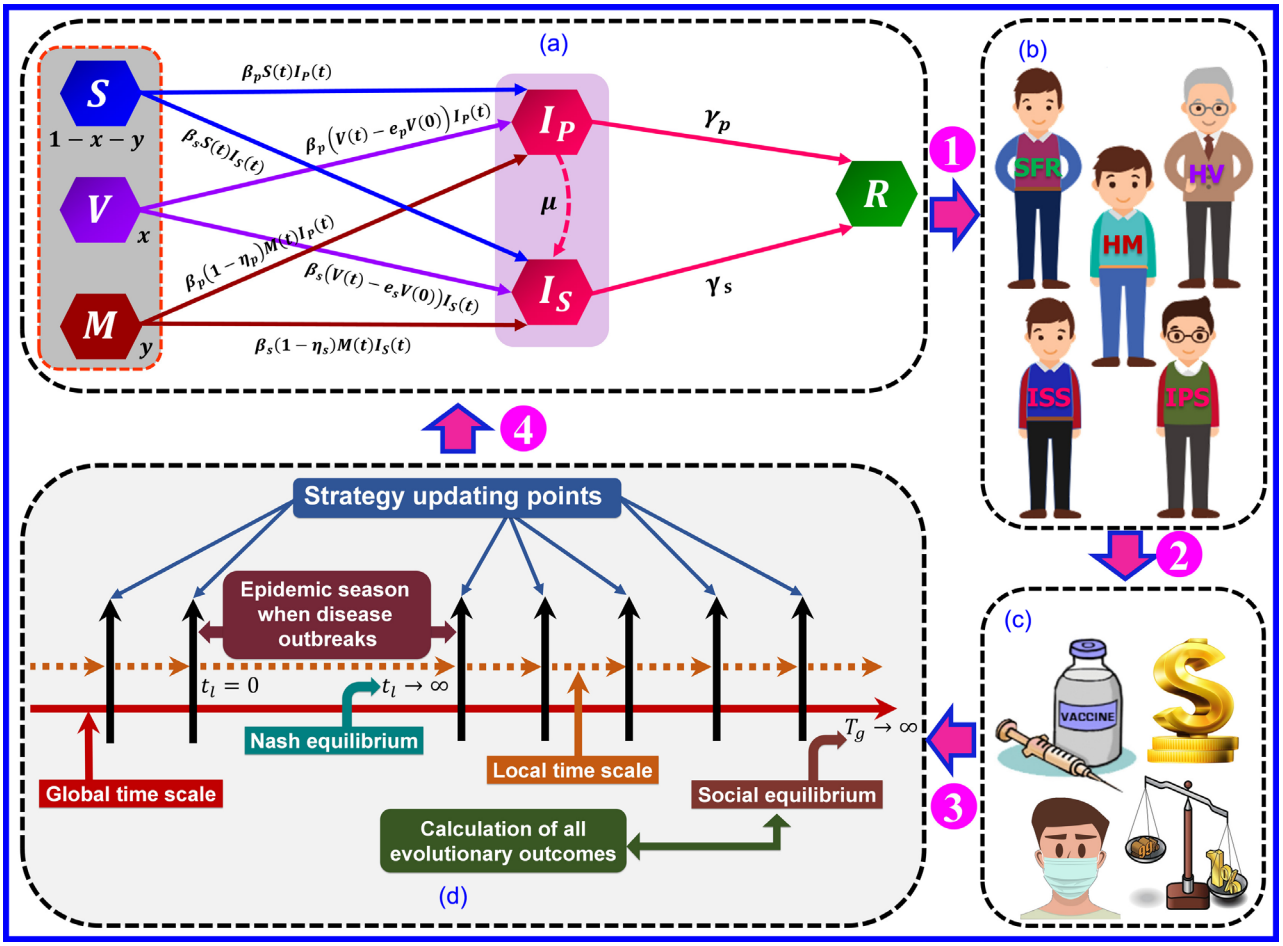

Figure 1. Schematic diagram of the proposed model: the entire process can be distinguished into four segments shown in a clockwise direction directed by arrows. Epidemic outbreaks at the local time scale marked with t_l which follows a two-strain SIR-type epidemic model equipped with two pre-emptive provisions, namely vaccination (V) and intermediated defense measure (M). In the epidemic spreading phase, the red dashed arrow directed from I_P to I_S indicates a mutation taking place from primary strain to secondary strain with a mutation rate μ. During the seasonal outbreak when it reaches to some Nash equilibrium (denoted with local time scale, t_l) we determine the fractions of individuals classified as healthy vaccinators, healthy self-protectors, successful free-rider, infected with primary strain, and infected with secondary strain. For convenience, we use two parameters $e_p\left(0 \le e_p \le 1\right)$ and $e_s\left(0 \le e_s \le e_p\right)$ to represent the effectiveness of vaccination against the primary and secondary strains, respectively. Henceforth, $V(t) - e_u V(0)$, for $u = \{p, s\}$ illustrates the fraction of vaccinators who are susceptible to strain u (where, $V(0)$ represents the fraction of vaccinators at the outset of an epidemic season and $V(t)$ defines the fraction of vaccinator at any given time t). Similarly, another set of parameters η_p and $\eta_s\left(\eta_s \le \eta_p\right)$ is introduced to represent the efficiency of IDM against primary and secondary disease strains, respectively. Intuitively, the proportion of individuals remaining in the S, V, and M compartments at the end of a local time scale (precisely at Nash Equilibrium point) are categorized respectively as "successful free riders", "healthy vaccinators", and "healthy self-protectors". Then we estimate the payoff structure for individuals who took either interventions in the last epidemic season. Based on that, individuals take decisions on a suitable pre-emptive provision for the upcoming epidemic season (taken at a global time scale T_g). The entire process revolves for a couple of times until the system reaches to some stead-state situation evaluated on the global scale. (a) Disease spreading dynamics; (b) Strategy fractions; (c) Payoff estimation; (d) Strategy updating for next epidemic season.

2.1. Formulation of the Two-Strain Epidemic Dynamical Model

Traditional mathematical models used in epidemiology rely on the compart-

mentalization of agents living in the sweeping epidemic society depending upon their current health status. The initial step of our dynamical setup is based on the evolution of the epidemic model capturing influenza-type infections. Here, we extend a widely accepted Susceptible-Infected-Recovered (SIR) model to propose a new predictive protocol, including two new compartments, namely vaccinated and self-protected by IDM, to implement a comprehensive game-theoretic framework assuming imperfect vaccination and self-protection as two distinct pre-emptive interventions. The dynamics of our proposed two-strain epidemic model assumes the population size is infinite and ideally well-mixed without considering any spatial structure. Moreover, we suppose that no individuals would simultaneously be infected with both strains, which means there is no coinfection. However, the primary disease strain (PDS) can mutate into secondary disease strain (SDS) at a rate μ. For simplicity, we split the entire population into the following six compartments: susceptible (S), vaccinated (V), self-protected by IDM (M), infected with the primary (original) strain (I_P), infected with secondary (induced or new) strain (I_S), and recovered (R). A susceptible person is a non-infected person who might be infected through active contacts with infected persons. When an utterly susceptible individual gets in touch with an infected individual who is supposed to be a carrier of PDS, then the susceptible or vulnerable individual also becomes infected with PDS at a rate β_p. Likewise, if the infected individual is the bearer of SDS, it prompts the susceptible individual to be affected with secondary strain at a rate β_s. A vaccinated person is one who commits vaccination, whereas a self-protected individual relies on IDM. Both these two groups of individuals vaccinated and self-protected encounter infected individuals and later can also be infected due to the imperfectness of their adopted provisions. An infected person is symptomatic and infectious to others, who already got infected with the one of the disease strains. Subsequently, he recovers at a constant recovery rate and obtains perfect immunity that is only valid for the focal season.

Our proposed model contains the following set of parameters: β_p, β_s representing the transmission rate of infection from primary and secondary disease strains, respectively; μ stands the mutation rate from primary to secondary strain; γ_p, γ_s stand for the infection recovery rate of individuals infected with PDS and SDS, respectively. Commonly there are three mechanisms by which virus strains experience evolutionary changes, primarily mutation (antigenic drift), reassortment (antigenic shift), and sometimes recombination [52]. Precisely speaking, antigenic drift is the gradual evolution of viral strains due to frequent mutations. Our model solely considers mutation that leads a PDS to be converted into a newly emerged SDS within the host via an antigenic drift. Such evolution yields through a mutation that can influence the host specificity and pathogenicity of these viruses. Habitually, a mutant strain has more potent virulence to transmit disease; therefore, a vaccinated individual inevitably has more plausibility of being infected after having close contact with an individual infected with SDS. Antigenic drifts are the leading causes of new variants and gen-

erate annual outbreaks. Although such mutations may not lead to pandemics, its repetition for a while can make the induced strain considerably different from the original one. Thus, the consequence of antigenic drift on vaccine efficacy differs between seasons. Although an antigenically drifted strain can result in reduced vaccine effectiveness, not all drifted strains elude vaccine-induced immunity in the society. In such a situation, taking IDM can sometimes be a more reliable alternative to vaccination as it offers better efficacy against multiple strains. Supported by the findings of [53], we assume vaccination as well as IDM that yield better protective efficacy against the PDS (original strain) than that of the SDS (newer strain). For simplicity, we deliberately skip superinfection and coinfection phenomena in our current model. That means that an individual cannot be infected with both strains at the same time and, once infected with one of the strains, would never be infected with the remaining other strain within a single epidemic episode. This model subdivides the susceptible population into three groups of individuals, namely, vaccinated, self-protected by IDM, and non-vaccinated as well as non-self-protected, because we presume one of the two provisions can be taken, not allowing both simultaneously. Since pre-emptive vaccination is assumed to be imperfect, therefore, we would like to mention two important aspects of vaccine failures. Firstly, the vaccine may not work uniformly to all vaccinees, which gives rise to the concept of "effectiveness of vaccination", intuitively meaning the fraction of vaccinators who receives an immune response from it. Secondly, acquiring an immune response does not necessarily guarantee life-long immunity, which pushes vaccinators very much towards the risks of being re-infected with the same disease due to its waning immunity. Likewise, self-protection adopting IDM, does not render absolute protective efficacy against disease strains. Henceforth, we introduce the "efficiency of IDM" to estimate how effective taking an IDM could be as an alternative provision while tackling a two-strain epidemic disease. All vaccinators living in the society can be distinguished into two subclasses: immune individuals and non-immune individuals. Immune individuals get absolute immunity from the disease, whereas non-immune individuals happen to be susceptible to either strain, inescapably. Understandably we can take two different effectiveness parameters, e_p and e_s $\left(0 \le e_p, e_s \le 1\right)$ representing vaccine efficacy (effectiveness) against the primary and secondary strains, respectively, but of course maintaining a strict condition, $e_p \ge e_s$. Similarly, we presume an analogous setting for self-protection, taking into account two different efficiency parameters, η_p and η_s $\left(0 \le \eta_p, \eta_s \le 1\right)$, standing respectively for the protective efficacy (efficiency) of IDM against primary and secondary strains, indeed with the analogous strict relation $\left(\eta_p \ge \eta_s\right)$. At any time, t, throughout the time domain within our proposed dynamical setup, all individuals are partitioned into six fractions leveled with $S(t), V(t), M(t), I_P(t), I_S(t)$ and $R(t)$. For simpler assumption, let us take $V(0) = V_{int}$, as the initial fraction of vaccinators at the beginning of an epidemic season. Then, the product $e_u V_{int}$ expresses the fraction of vaccinators securing immunity from strain u (u = primary, secondary), yet the proportion

$\left(V(t)-e_uV_{int}\right)$ still remains susceptible to strain *u*, where $V(t)$ is the fraction of vaccinators existing in the vaccinated compartment at any time *t*. Similarly, consider $M(0)=M_{int}$, as the initial fraction of self-protectors before the commencement of an epidemic season. Consequently, the product η_uM_{int} would be representing the fraction of self-protectors obtaining immunity from strain *u*. Nevertheless, the proportion $(1-\eta_u)M(t)$ outlasts as susceptible to strain *u*, hither $M(t)$ is the fraction depicting self-protectors remaining in the self-protected compartment at any given time *t*. The dynamics of epidemic paradigm combined with dual pre-emptive interventions, namely imperfect vaccination, and self-protection triggered by IDM can be stipulated by the following set of non-linear ordinary differential Equations (1)-(6). To this end, a holistic preview of our proposed SI_PI_SR/VM epidemic model along with its brief game theoretic mechanism is thus portrayed in **Figure 1**.

$$\dot{S}(t)=\left(\beta_pI_P(t)+\beta_sI_S(t)\right)S(t), \tag{1}$$

$$\dot{V}(t)=-\left(\beta_p\left(V(t)-e_pV(0)\right)I_P(t)+\beta_s\left(V(t)-e_sV(0)\right)I_S(t)\right), \tag{2}$$

$$\dot{M}(t)=-\left(\beta_p(1-\eta_p)I_P(t)+\beta_s(1-\eta_s)I_S(t)\right)M(t), \tag{3}$$

$$\dot{I}_P(t)=\beta_p\left(\left(S(t)+V(t)-e_pV(0)\right)+(1-\eta_p)M(t)\right)I_P(t)-\left(\gamma_p+\mu\right)I_P(t), \tag{4}$$

$$\dot{I}_S(t)=\beta_s\left(\left(S(t)+V(t)-e_sV(0)\right)+(1-\eta_s)M(t)\right)I_S(t)-(\gamma_s-\mu)I_S(t), \tag{5}$$

$$\dot{R}(t)=\gamma_pI_P(t)+\gamma_sI_S(t). \tag{6}$$

Subsequently, the initial conditions of the governing differential Equations (1)-(6) takes the form:

$$\begin{aligned}&S(x,y,0)=1-x-y\geq 0, V(x,y,0)=x\geq 0, M(x,y,0)=y\geq 0,\\ &I_P(x,y,0)\geq 0, I_S(x,y,0)\geq 0, R(x,y,0)\geq 0.\end{aligned} \tag{7}$$

where, *x*, *y*, and $1-x-y$ respectively assign the fractions of vaccinators, self-protectors, and susceptible persons at the outset of an epidemic season. The compartment-based state variables used in our model do not consider any specific size of the given population; instead, it takes the fraction of the total population belonging to any state at any given time, *t*. For convenience, while applying MFA scheme, we assume the overall size of the population be unity. It justifies the fact that the entire population is comprised of several compartment whose sum at any given time is kept as a fixed value, say, for example,
$S(t)+V(t)+I_P(t)+I_S(t)+R(t)=1$. Indeed, all acquired solutions of the proposed dynamical system of Equations (1)-(6) implemented with the initial conditions (7) at equilibrium are bounded on $[0,\infty)$ and remain strictly positive for all $t\geq 0$. Each of the parameters $\beta_p,\beta_s,\gamma_p,\gamma_s,e_p,e_s,\eta_p,\eta_s$ and μ used in the above set of dynamical equations are non-negative constants. Here, the parameter μ represents the mutation rate from primary strain (original) to secondary strain (newly emerged). Intuitively, $\mu=0$ means the absence of mutation. Henceforth a non-zero value of μ illustrates the rate at which mutation takes place from primary to secondary strain.

Based on the prevailing health status and financial cost burden, our game-theoretic framework classifies individuals into nine assortments: 1) a healthy vaccinator (*HV*), who just pays the vaccination cost and remains healthy during an epidemic season, 2) an infected vaccinator who can either be affected with the primary strain (IV_P) or 3) by the secondary strain (IV_S); individuals classified in (2) and (3) are vaccinators, yet, they become infected; therefore, supposed to bear vaccination cost as well as infection cost, 4) a healthy self-protector (*HM*) solely pays the IDM cost and survives as healthy throughout the epidemic season. Similarly, 5) an infected self-protector is someone who might either be infected with the primary strain (IM_P) or 6) by the secondary strain (IM_S), individuals existing in both these groups are obliged to pay the infection cost alongside the IDM cost itself, 7) a successful free rider (*SFR*) who exerts neither safety provision but luckily stays healthy, thereby does not bear any sort of cost burden, 8) a failed-free rider gets infected respectively with primary strain FFR_P and 9) secondary strain FFR_S utterly relies on herd immunity rather taking either protective provision, which ultimately put him at risk of being infected. This situation inevitably drives him to carry the infection cost itself. Due to analytical complexity in solving the mathematical model, governed by the set of Equations (1)-(6), we cannot solve it adopting the so-called analytical approach. Yet, we can evaluate diverse fractions of individuals living in one of the compartments using the concept of flux "$\varphi_{P\to Q}$", meaning the cumulative fraction of individuals transferring through state P to state Q. Our present study includes a total of six flux terms, given by $\varphi_{V\to I_P}, \varphi_{V\to I_S}, \varphi_{M\to I_P}, \varphi_{M\to I_S}, \varphi_{S\to I_P}$ and $\varphi_{S\to I_S}$, showing respectively the transferring flux from vaccinated to infected with primary strain, vaccinated to infected with secondary strain, self-protected to infected with primary strain, self-protected to infected with secondary strain, susceptible (non-provisioned) to infected with primary strain, and susceptible (non-provisioned) to infected with secondary strain at a social equilibrium point. Meanwhile, the fraction of healthy vaccinators (*HV*), healthy self-protectors (*HM*), and successful-free-rider (*SFR*) at the social equilibrium point ($t\to\infty$) can also be estimated respectively by $V(x,y,\infty), M(x,y,\infty)$, $S(x,y,\infty)$. For convenience, we compile all corresponding fractions of individuals belonging to each of the nine classes constituting the entire population, as depicted in Table 1. These nine fractions of individuals can be represented mathematically by the following Equations (8)-(16): (Table 1)

$$HV(x,y,\infty)=V(x,y,\infty); \tag{8}$$

$$HM(x,y,\infty)=M(x,y,\infty); \tag{9}$$

$$SFR(x,y,\infty)=S(x,y,\infty); \tag{10}$$

$$IV_P(x,y,\infty)=\int_{t=0}^{\infty}\varphi_{V\to I_P}(x,y,t)\,\mathrm{d}t; \tag{11}$$

$$IV_S(x,y,\infty)=\int_{t=0}^{\infty}\varphi_{V\to I_S}(x,y,t)\,\mathrm{d}t; \tag{12}$$

Table 1. The fraction of nine varieties of individuals enduring in the steady-state situation (social equilibrium point).

Strategy \ State	Healthy	Infected	
Vaccinated (V)	$HV(x,y,\infty)$	Vaccinated yet infected with either strain	
		$IV_P(x,y,\infty)$	$IV_S(x,y,\infty)$
Self-protected (M)	$HM(x,y,\infty)$	Self-protected yet infected with either strain	
		$IM_P(x,y,\infty)$	$IM_S(x,y,\infty)$
Non-provisioned (free-rider, F)	$SFR(x,y,\infty)$	Failed-free-rider as infected with either strain	
		$FFR_P(x,y,\infty)$	$FFR_S(x,y,\infty)$

Table 2. Glossary of terms used in the proposed model.

Name	Description
Antigen	A foreign substance that elicits an immune response.
Co-infection	Simultaneous infection of a host by multiple strains.
Cross immunity	A partial immune protection against a strain. If two parallel strains of a virus are circulating in a population, then individuals who have already been infected by one strain may have partial immunity or lessened susceptibility to the other strain.
Herd immunity	Resistance of the entire population to the spread of an infectious disease due to the immunity of a high proportion of that population.
Super infection	The process of a strain taking over a host already infected by a different strain. In general, it refers to those affected with one of the strains that cannot be infected with others.
Perfect vaccine	A vaccine uniformly and completely effective against all strains of a pathogen. It further signifies vaccines that can be treated as a complete safeguard against the targeted strains.
IDM	Intermediate defense measure
PDS	Primary disease strain
SDS	Secondary disease strain
EGT	Evolutionary Game Theory
DFE	Disease Free Equilibrium
EE	Endemic Equilibrium

$$IM_P(x,y,\infty)=\int_{t=0}^{\infty}\varphi_{M\to I_P}(x,y,t)\,\mathrm{d}t; \tag{13}$$

$$IM_S(x,y,\infty)=\int_{t=0}^{\infty}\varphi_{M\to I_S}(x,y,t)\,\mathrm{d}t; \tag{14}$$

$$FFR_P(x,y,\infty)=\int_{t=0}^{\infty}\varphi_{S\to I_P}(x,y,t)\,\mathrm{d}t; \tag{15}$$

$$FFR_S(x,y,\infty)=\int_{t=0}^{\infty}\varphi_{S\to I_S}(x,y,t)\,\mathrm{d}t. \tag{16}$$

2.2. Formulation of Basic Reproduction Number

A unique characteristic feature of any infectious disease is its capability to invade a population quite naturally. Several epidemiological paradigms own a disease-free equilibrium (*DFE*) at which the absence of disease intrusion among the people is recognized. Usually, these models possess a threshold parameter known as the basic reproduction number (*BRN*), R_0, representing the expected number of secondary cases generated within a fully susceptible population by typical infective individuals. On a different note, this *BRN* can be viewed as a threshold quantity that determines when infection penetrates and persists in a new host population. If $R<1$, the *DFE* is locally asymptotically stable, thereby the disease cannot invade the population. Yet, under the condition of $R>1$, the *DFE* converts to an unstable equilibrium; therefore, the plausibility of disease incursion becomes inevitable [54] [55]. Following the detailed procedures of [56], after having a rigorous mathematical calculation we can derive the basic reproduction number corresponding to primary and secondary strains on the basis of two distinct pre-emptive provisions as follows.

$$R_0^p=\frac{\beta_p}{\gamma_p+\mu}\left(S(0)+(1-e_p)V(0)+(1-\eta_p)M(0)\right); \tag{17}$$

$$R_0^s=\frac{\beta_s}{\gamma_s-\mu}\left(S(0)+(1-e_s)V(0)+(1-\eta_s)M(0)\right). \tag{18}$$

It is worthwhile to mention that if $R_0^p<1$ and $R_0^s<1$, then, both these strains die out immediately, thereby a stable *DFE* establishes. Furthermore, while either or both *BRN* (*BRNs*) is (are) greater than one, the DFE converts to an unstable equilibrium that allows the strains to start evading into the human population again. For the case of $R_0^p>1$ and $R_0^s>1$ having a condition $R_0^p>R_0^s$ (or a logically opposite situation, $R_0^p<R_0^s$), primary (secondary) strain dominates secondary (primary) strain. As a result, the relatively stronger strain outperforms the weaker ones, and eventually, the relatively weaker strain fades out completely. On the other hand, when both *BRNs* are equal but, of course, greater than unity, it supports both (primary as well as secondary) strains to coexist in the human population. In line with that, we will sanctify a further investigation regarding the effects of pre-emptive provision-based *BRN* under the framework of evolutionary game theory entailed with a two-strain infection model (**Table 2**).

2.3. Evolutionary Game Payoff Structure

Individuals dwelling in the diverse population groups are often affected by epidemics. Here, we apply evolutionary game theory to illustrate the decision-making

of individuals who usually devote a couple of intervention techniques, such as pre-emptive vaccination and self-protection (adopting IDM), to avoid an epidemic outbreak. Once the *SIR*/*VM* dynamics die out, it is believed that the outbreak period has finished. Before the ensuing epidemic dynamics begins, individuals independently decide whether to utilize a pre-emptive provision for the upcoming season. To this end, evolutionary dynamics take place by consigning a payoff to each of the individuals depending solely on their experience accumulated during the last epidemic propagation. Generally, preventable epidemic diseases have societal and economic costs besides morbidity and premature deaths resulting from these diseases. These societal expenses occur mostly due to the loss of fecundity and workdays; absenteeism resulting from the requirement to take care of family members, hospitalization, frequent physician office visits, etc. are also responsible for increasing the expenses. A typical epidemic season comes to an end when all susceptible and infected individuals move to the recovery state (*R*). Subsequently, individuals can improve or alter their current prudent strategy for the next epidemic season by analyzing their payoff attained from the prior season. An individual's destiny during an epidemic season quantifies his perceived expenses, and at the same time, it also secures his ultimate profit or loss in the form of social payoff. To fix each individual's game payoff, without out the loss of generality, we consider the relative cost of vaccination, $C_v = V_C / I_C$ who takes vaccine and relative cost of IDM, $C_m = M_C / I_C$ $(0 \le V_C, M_C \le 1)$ for those who prefer self-protection, where V_C, M_C and I_C stand for the cost of vaccination, cost of IDM, and cost of infection, respectively. As a general premise, we assume the cost for infection being −1. Thus, at the end of each epidemic season, we can classify each class of individual, as shown in Table 1, depending on their strategy selection (whether preferring vaccination, self-protection, or free-riding) and final health condition (whether being healthy or infected) at a social equilibrium point (estimated in the local time scale depicted in Figure 1). Thus, by the end of each epidemic season, we can classify each class of individual (as conferred in Table 3) in terms of their strategy selection (whether preferring vaccination, self-protection, or free-riding) and final health condition (whether being healthy or infected) at a social equilibrium point (estimated in the local time scale portrayed in Figure 1). To make things more transparent, we

Table 3. Payoff composition of nine distinct fractions of individuals as estimated at the end of each epidemic season.

Strategy \ State	Healthy	Infected	
		with primary strain	with secondary strain
Vaccinated (V)	$-C_v$	$-C_v - 1$	$-C_v - 1$
Self-protected (M)	$-C_m$	$-C_m - 1$	$-C_m - 1$
Non-provisioned (free-rider, F)	0	−1	−1

formulate all expected payoffs employing the average social payoff, $\hat{\pi}$, the average payoff for committing vaccination, $\hat{\pi}_V$ (vaccinators), the average payoff for taking IDM, $\hat{\pi}_M$ (self-protectors), and the average payoff for not using any pre-emptive provision, $\hat{\pi}_F$ (free-riders or defectors), presented by the following equations:

$$\begin{aligned}\hat{\pi} = &-C_v HV(x,y,\infty) - (C_v+1)\left(IV_P(x,y,\infty) + IV_S(x,y,\infty)\right)\\ &- C_m HM(x,y,\infty) - (C_m+1)\left(IM_P(x,y,\infty) + IM_S(x,y,\infty)\right)\\ &- \left(FFR_P(x,y,\infty) + FFR_S(x,y,\infty)\right),\end{aligned} \tag{19}$$

$$\hat{\pi}_V = \left(-C_v HV(x,y,\infty) - (C_v+1)\left(IV_P(x,y,\infty) + IV_S(x,y,\infty)\right)\right)\Big/x, \tag{20}$$

$$\hat{\pi}_M = \left(-C_m HM(x,y,\infty) - (C_m+1)\left(IM_P(x,y,\infty) + IM_S(x,y,\infty)\right)\right)\Big/y, \tag{21}$$

$$\hat{\pi}_F = \left(-\left(FFR_P(x,y,\infty) + FFR_S(x,y,\infty)\right)\Big/(1-x-y)\right). \tag{22}$$

2.4. Strategy Updating Protocol

The type of preventive provisions as reflected on intervention decision-making is a multi-dimensional genre that incorporates frequency of the game (whether repeating or non-repeating), mechanism of evaluating utilities that includes the coupling mechanism between the epidemic model and the game-theoretic framework which may include self-learning for each game player based on the induction by knowledge and experience or imitating relatively successful players, and imitation-based strategy adoption. Pre-emptive provisions enable individuals to adopt a suitable strategy before an epidemic outbreak occurs. As mentioned earlier, the decision-making process is fully modeled under a game-theoretic framework which evaluates utilities of different strategies while presuming that a vast majority of the given population consists of rational decision-makers. However, the decision to exercise either protective provisions is purely voluntary, in addition, individuals have their freedom to choose none of the preventive clauses according to their way of thinking. As strategy updating takes place before an epidemic season initiates, individuals usually adjust or alter their strategy by analyzing their estimated payoff attained in the last epidemic season. Mostly there are two different strategy updating protocols, namely individual-based risk assessment update rule, and strategy-based risk assessment update rule frequently used in the human decision-making process, proposed respectively by Fu *et al.* [30] and Fukuda *et al.* [2] while using a game-theoretic framework. Even though these two updating rules have initially been designed for agent-based modeling, our present study does not contemplate any networked population having a spatial structure. Instead, we confine our model to relying on the MFA technique where the population is ideally well-mixed, and all individuals falling to each state exactly follow the same strategy. Here, we thoroughly follow these two well-established update protocols, namely individual-based risk assessment as well as strategy-based risk assessment update rules to capture the holistic evolutionary phenomena taking place in a two-strain epidemic model entailed with multiple

pre-emptive provisions.

2.4.1. Individual-Based Risk Assessment (IB-RA) Update Rule [30]

Individual-based risk assessment (IB-RA) is analogous to the pair-wise Fermi rule, which plays a crucially important role in the evolutionary game-theoretic analysis. Although Fu *et al.* formerly adopted this pair-wise Fermi function for a structured population, in the following work, Fukuda *et al.* [2] defined this rule as individual-based risk assessment as the interplay takes place between individuals is one to one. More precisely, the course of this strategy adaptation can be interpreted as a circumstance where everyone judges both the risks of maintaining his own strategy and imitating that of his opponent, thereby finally picks the one with smaller risk. Here, an individual (say, for example, *i*) randomly selects one of his neighbors (say, *j*) and decides whether to imitate his chosen neighbor's strategy by comparing their payoffs π_i and π_j, respectively. That means if an agent "*i*" (currently holding strategy S_i) imitates his neighbor "*j*" (having strategy S_j) for strategy updating, then its probability can be evaluated by the following Fermi function:

$$P\left(S_i \leftarrow S_j\right) = \frac{1}{1+\exp\left(-\left(\pi_j - \pi_i\right)/\kappa\right)} \tag{23}$$

where the parameter $\kappa > 0$ characterizes the selection strength, more precisely, it justifies the sensitivity of individuals to their payoff difference (selection pressure); a smaller κ symbolizes more sensitivity to their payoff difference. In our current study, we set the baseline value for κ is 0.1, which has been employed as an archetypal selection in many previous literatures (e.g., [1] [14] [19] [20] [51] [57] [58]). Relying on the work, reported by the authors of [20], we follow their protocol in our mean-field game approach, where every single fraction (depicted in **Table 1**) estimates its payoff with that of other relevant fractions in accordance with the formula given by Equation (9) rather than taking agent to agent interaction. Therefore, the total number of transition probabilities would be fifty-four if we consider all interactions (one to one) between the nine fractions encapsulated in **Table 1**. For illustration, when healthy vaccinators (*HV*) analyze their payoff with that of healthy self-protectors (*HM*), this phenomenon can be estimated by the following probability equation:

$$P\left(HV \leftarrow HM\right) = \frac{1}{1+\exp\left(-\left(-C_m - \left(-C_v\right)\right)/\kappa\right)},$$

$$P\left(HV \leftarrow SFR\right) = \frac{1}{1+\exp\left(-\left(0 - \left(-C_v\right)\right)/\kappa\right)}.$$

Likewise, the remaining transition probabilities can be calculated using **Table 3**.

2.4.2. Strategy-Based Risk Assessment (SB-RA) Update Rule [2]

The aforementioned strategy updating protocol is suggested by Fukuda *et al.* [2],

who employed this precept while investigating human decision-making in agent-based modeling. The novel mechanism of this protocol yields a focal agent to confront his game payoff with the socially averaged payoff generated by all his neighboring agents holding the same strategy, but of course, their strategy would be different from that of the focal agent. The most unique character of this rule, unlike what IB-RA assumes, is that it enables an individual to cross-check his strategy with the strategy adopted by most of his neighboring people living in the society rather than comparing it with a single individual around him. Moreover, if statements regarding the consequences of using a distinct strategy are exposed to the society where everyone has access to those consequences, then individuals no longer rely profoundly on the payoff of a single neighbor. Rather, while adapting their strategy, they mean to assess the risk based on a socially averaged payoff that occurs from using that precise strategy. To ponder the above situation, the modified imitation probability can be expressed as follows:

$$P\left(S_i \leftarrow S_j\right) = \frac{1}{1+\exp\left(-\left(\hat{\pi}_j - \pi_i\right)/\kappa\right)} \tag{24}$$

where, $\hat{\pi}_j$ denotes the average payoff, which is obtained by averaging the payoffs of those fellow neighbors taking the same strategy S_j, of a randomly picked up neighbor "*j*" of the focal player "*i*" whose current strategy being S_i. Meanwhile, we can apply this strategy updating rule in our proposed mean-field game model by resembling a particular fraction's payoff (let us say, HV-which belongs to the group of vaccinators) with the average payoff of other fractions pertaining to a separate or mutually exclusive groups (say, HM-refers to the group of self-protectors). To make things simpler, if HV-fraction compares its payoff $\left(-C_v\right)$ with the average payoff of the group consists of free-riders, FR (whose payoff is $\hat{\pi}_F$, given by Equation (23)), then using the definition of SB-RA strategy updating rule, the imitation probability function can be written as:

$$P\left(HV \leftarrow F\right) = \frac{1}{1+\exp\left(-\left(\hat{\pi}_F - \left(-C_v\right)\right)/\kappa\right)}$$

Subsequently, all other fractions belonging to a certain group compare their payoff with the average payoff generated by the group which is mutually exclusive to them for strategy updating. All relevant transition probabilities employing IB-RA and SB-RA strategy updating protocols can be derived using the master equation mentioned above.

2.5. Evolutionary Dynamics

Evolutionary dynamics facilitate the framework to execute the dynamic evolution of strategies. As mentioned earlier, the individuals can update or alter their current strategies under the framework of evolutionary game theory before a new epidemic season commences. Thus, the system of global dynamical equations can approximate the quantitative rate of change of different strategy frac-

tions at any given time for the next epidemic season. For either strategy updating rule, manipulating all possible transition probabilities into the governing dynamical equation, we can evaluate the rate of change of vaccinators and that of self-protectors for recurrent epidemic seasons. Therefore, the temporal evolution of the fractions of two different types of pre-emptive provisions, *i.e.*, the rate of change of the fractions of vaccinators and self-protectors, are briefly illustrated by the following set of ordinary differential equations.

Case-I: Implementing IB-RA strategy updating rule

$$\begin{aligned}\frac{\mathrm{d}x}{\mathrm{d}t} &= HV(x,y,\infty)\cdot HM(x,y,\infty)\cdot\left(P(HM\leftarrow HV)-P(HV\leftarrow HM)\right)\\ &+HV(x,y,\infty)\cdot IM_P(x,y,\infty)\cdot\left(P(IM_P\leftarrow HV)-P(HV\leftarrow IM_P)\right)\\ &+HV(x,y,\infty)\cdot IM_S(x,y,\infty)\cdot\left(P(IM_S\leftarrow HV)-P(HV\leftarrow IM_S)\right)\\ &+HV(x,y,\infty)\cdot SFR(x,y,\infty)\cdot\left(P(SFR\leftarrow HV)-P(HV\leftarrow SFR)\right)\\ &+HV(x,y,\infty)\cdot FFR_P(x,y,\infty)\cdot\left(P(FFR_P\leftarrow HV)-P(HV\leftarrow FFR_P)\right)\\ &+HV(x,y,\infty)\cdot FFR_S(x,y,\infty)\cdot\left(P(FFR_S\leftarrow HV)-P(HV\leftarrow FFR_S)\right)\\ &+IV_P(x,y,\infty)\cdot HM(x,y,\infty)\cdot\left(P(HM\leftarrow IV_P)-P(IV_P\leftarrow HM)\right)\\ &+IV_P(x,y,\infty)\cdot IM_P(x,y,\infty)\cdot\left(P(IM_P\leftarrow IV_P)-P(IV_P\leftarrow IM_P)\right)\\ &+IV_P(x,y,\infty)\cdot IM_S(x,y,\infty)\cdot\left(P(IM_S\leftarrow IV_P)-P(IV_P\leftarrow IM_S)\right)\\ &+IV_P(x,y,\infty)\cdot SFR(x,y,\infty)\cdot\left(P(SFR\leftarrow IV_P)-P(IV_P\leftarrow SFR)\right)\\ &+IV_P(x,y,\infty)\cdot FFR_P(x,y,\infty)\cdot\left(P(FFR_P\leftarrow IV_P)-P(IV_P\leftarrow FFR_P)\right)\\ &+IV_P(x,y,\infty)\cdot FFR_S(x,y,\infty)\cdot\left(P(FFR_S\leftarrow IV_P)-P(IV_P\leftarrow FFR_S)\right)\\ &+IV_S(x,y,\infty)\cdot HM(x,y,\infty)\cdot\left(P(HM\leftarrow IV_S)-P(IV_S\leftarrow HM)\right)\\ &+IV_S(x,y,\infty)\cdot IM_P(x,y,\infty)\cdot\left(P(IM_P\leftarrow IV_S)-P(IV_S\leftarrow IM_P)\right)\\ &+IV_S(x,y,\infty)\cdot IM_S(x,y,\infty)\cdot\left(P(IM_S\leftarrow IV_S)-P(IV_S\leftarrow IM_S)\right)\\ &+IV_S(x,y,\infty)\cdot SFR(x,y,\infty)\cdot\left(P(SFR\leftarrow IV_S)-P(IV_S\leftarrow SFR)\right)\\ &+IV_S(x,y,\infty)\cdot FFR_P(x,y,\infty)\cdot\left(P(FFR_P\leftarrow IV_S)-P(IV_S\leftarrow FFR_P)\right)\\ &+IV_S(x,y,\infty)\cdot FFR_S(x,y,\infty)\cdot\left(P(FFR_S\leftarrow IV_S)-P(IV_S\leftarrow FFR_S)\right);\end{aligned}\quad(25)$$

$$\begin{aligned}\frac{\mathrm{d}y}{\mathrm{d}t} &= HM(x,y,\infty)\cdot HV(x,y,\infty).\left(P(HV\leftarrow HM)-P(HM\leftarrow HV)\right)\\ &+HM(x,y,\infty)\cdot IV_P(x,y,\infty)\cdot\left(P(IV_P\leftarrow HM)-P(HM\leftarrow IV_P)\right)\\ &+HM(x,y,\infty)\cdot IV_S(x,y,\infty)\cdot\left(P(IV_S\leftarrow HM)-P(HM\leftarrow IV_S)\right)\\ &+HM(x,y,\infty)\cdot SFR(x,y,\infty)\cdot\left(P(SFR\leftarrow HM)-P(HM\leftarrow SFR)\right)\\ &+HM(x,y,\infty)\cdot FFR_P(x,y,\infty)\cdot\left(P(FFR_P\leftarrow HM)-P(HM\leftarrow FFR_P)\right)\\ &+HM(x,y,\infty)\cdot FFR_S(x,y,\infty)\cdot\left(P(FFR_S\leftarrow HM)-P(HM\leftarrow FFR_S)\right)\\ &+IM_P(x,y,\infty)\cdot HV(x,y,\infty)\cdot\left(P(HV\leftarrow IM_P)-P(IM_P\leftarrow HV)\right)\\ &+IM_P(x,y,\infty)\cdot IV_P(x,y,\infty)\cdot\left(P(IV_P\leftarrow IM_P)-P(IM_P\leftarrow IV_P)\right)\\ &+IM_P(x,y,\infty)\cdot IV_S(x,y,\infty)\cdot\left(P(IV_S\leftarrow IM_P)-P(IM_P\leftarrow IV_S)\right)\\ &+IM_P(x,y,\infty)\cdot SFR(x,y,\infty)\cdot\left(P(SFR\leftarrow IM_P)-P(IM_P\leftarrow SFR)\right)\end{aligned}$$

$$
\begin{aligned}
&+IM_P(x,y,\infty)\cdot FFR_P(x,y,\infty)\cdot\left(P(FFR_P\leftarrow IM_P)-P(IM_P\leftarrow FFR_P)\right)\\
&+IM_P(x,y,\infty)\cdot FFR_S(x,y,\infty)\cdot\left(P(FFR_S\leftarrow IM_P)-P(IM_P\leftarrow FFR_S)\right)\\
&+IM_S(x,y,\infty)\cdot HV(x,y,\infty)\cdot\left(P(HV\leftarrow IM_S)-P(IM_S\leftarrow HV)\right)\\
&+IM_S(x,y,\infty)\cdot IV_P(x,y,\infty)\cdot\left(P(IV_P\leftarrow IM_S)-P(IM_S\leftarrow IV_P)\right)\\
&+IM_S(x,y,\infty)\cdot IV_S(x,y,\infty)\cdot\left(P(IV_S\leftarrow IM_S)-P(IM_S\leftarrow IV_S)\right)\\
&+IM_S(x,y,\infty)\cdot SFR(x,y,\infty)\cdot\left(P(SFR\leftarrow IM_S)-P(IM_S\leftarrow SFR)\right)\\
&+IM_S(x,y,\infty)\cdot FFR_P(x,y,\infty)\cdot\left(P(FFR_P\leftarrow IM_S)-P(IM_S\leftarrow FFR_P)\right)\\
&+IM_S(x,y,\infty)\cdot FFR_S(x,y,\infty)\cdot\left(P(FFR_S\leftarrow IM_S)-P(IM_S\leftarrow FFR_S)\right).
\end{aligned}
\tag{26}
$$

***Case-II*: Implementing SB-RA strategy updating rule**

$$
\begin{aligned}
\frac{\mathrm{d}x}{\mathrm{d}t}&=HM(x,y,\infty)\cdot V(x,y,\infty)\cdot P(HM\leftarrow V)\\
&+IM_P(x,y,\infty)\cdot V(x,y,\infty)\cdot P(IM_P\leftarrow V)\\
&+IM_S(x,y,\infty)\cdot V(x,y,\infty)\cdot P(IM_S\leftarrow V)\\
&+SFR(x,y,\infty)\cdot V(x,y,\infty)\cdot P(SFR\leftarrow V)\\
&+FFR_P(x,y,\infty)\cdot V(x,y,\infty)\cdot P(FFR_P\leftarrow V)\\
&+FFR_S(x,y,\infty)\cdot V(x,y,\infty)\cdot P(FFR_S\leftarrow V)\\
&-HV(x,y,\infty)\cdot M(x,y,\infty)\cdot P(HV\leftarrow M)\\
&-IV_P(x,y,\infty)\cdot M(x,y,\infty)\cdot P(IV_P\leftarrow M)\\
&-IV_S(x,y,\infty)\cdot M(x,y,\infty)\cdot P(IV_S\leftarrow M)\\
&-HV(x,y,\infty)\cdot F(x,y,\infty)\cdot P(HV\leftarrow F)\\
&-IV_P(x,y,\infty)\cdot F(x,y,\infty)\cdot P(IV_P\leftarrow F)\\
&-IV_S(x,y,\infty)\cdot F(x,y,\infty)\cdot P(IV_S\leftarrow F);
\end{aligned}
\tag{27}
$$

$$
\begin{aligned}
\frac{\mathrm{d}y}{\mathrm{d}t}&=HV(x,y,\infty)\cdot M(x,y,\infty)\cdot P(HV\leftarrow M)\\
&+IV_P(x,y,\infty)\cdot M(x,y,\infty)\cdot P(IV_P\leftarrow M)\\
&+IV_S(x,y,\infty)\cdot M(x,y,\infty)\cdot P(IV_S\leftarrow M)\\
&+SFR(x,y,\infty)\cdot M(x,y,\infty)\cdot P(SFR\leftarrow M)\\
&+FFR_P(x,y,\infty)\cdot M(x,y,\infty)\cdot P(FFR_P\leftarrow M)\\
&+FFR_S(x,y,\infty)\cdot M(x,y,\infty)\cdot P(FFR_S\leftarrow M)\\
&-HM(x,y,\infty)\cdot V(x,y,\infty)\cdot P(HM\leftarrow V)\\
&-IM_P(x,y,\infty)\cdot V(x,y,\infty)\cdot P(IM_P\leftarrow V)\\
&-IM_S(x,y,\infty)\cdot V(x,y,\infty)\cdot P(IM_S\leftarrow V)\\
&-HM(x,y,\infty)\cdot F(x,y,\infty)\cdot P(HM\leftarrow F)\\
&-IM_P(x,y,\infty)\cdot F(x,y,\infty)\cdot P(IM_P\leftarrow F)\\
&-IM_S(x,y,\infty)\cdot F(x,y,\infty)\cdot P(IM_S\leftarrow F).
\end{aligned}
\tag{28}
$$

We can classify all the terms used in the global dynamical equations into two categories: the terms with positive (+) signs symbolize an inflow into a state while the remaining terms with negative (−) signs indicate an outflow from that

state. Solving the set of non-linear differential Equations (26)-(29) using a suitable numerical technique lets the system converge to a steady state as $t \to \infty$ (Table 1).

3. Result and Discussion

In this article, we study the growth and evolution of a disease drawn by two strains. Moreover, we build a mathematical model for single infection (immunity of infected individuals to the other strain) that includes vaccination and self-protection as two well-defined pre-emptive provisions using a mean-field game approach. Our model classifies the susceptible population into two subgroups depending upon whether vaccination or IDM provides primary protection against one of the strains (say, primary strain) but only partial protection against the other (say, secondary strain), which might be a plausible assumption. However, the primary strain can mutate into a secondary strain, controlled by a specific mutation rate. The ubiquity of mutation composes the entire mechanism to be more intricate. Thus, the existing dilemma can be split into two elements namely, the absence of mutation and the presence of mutation. To obtain further insight into how human decision-making on vaccination or any other alternative pre-emptive provisions directly influences the invasion of more virulent strain, we turn our attention to numerical simulation triggered by a generation of time series as well as parameter-based phase plane analysis.

Table 4. Baseline parameter values for the entire epidemiological setup. Here, the primary strain (PS) is recognized as more virulent mutant strain, whereas the secondary strain (SS) can be treated as less destructive resident strain.

Notation	Definition	Value
β_p	disease transmission rate for primary strain	0.75 per day per person (assumed)
β_s	disease transmission rate for secondary strain	0.50 per day per person (assumed)
γ_p	recovery rate for primary strain	0.30 per day (assumed)
γ_s	recovery rate for secondary strain	0.20 per day (assumed)
μ	mutation rate from primary to secondary strain (when considered)	0.05 (5%) (assumed)
e_p	effectiveness of vaccination against primary strain	$[0,1]$ (assumed)
e_s	effectiveness of vaccination against secondary strain	$[0,e_p]$ (assumed)
η_p	efficiency of self-protection (IDM) against primary strain	$[0,1]$ (assumed)
η_s	efficiency of self-protection (IDM) against secondary strain	$[0,\eta_p]$ (assumed)
κ	selection parameter	0.1 [1] [59]

3.1. Single Season Time Series Analysis

At the outset of this section, we limit our discussion to using a set of line graphs generated by time-series evolution within a single episode of epidemic emergence. There are mainly two types of efficacy parameters controlling an individual's level of reliability on vaccination and self-protection schemes. **Figure 2**, depicts the evolutionary fractions of susceptible, vaccinated, and self-protected individuals in line with disease progression within a single epidemic season. Since we use two-different mechanisms for effectiveness and efficiency models, respectively covering the strategies of taking vaccination and IDM backed self-protection. **Figure 2** illustrates a symmetric situation resulting from the variation of effectiveness and efficiency controlling parameters e and η. For simplicity, we presume the efficacy level of both provisions is identical irrespective of primary and secondary strains. At a glance, **Figure 2** exposes the superiority and

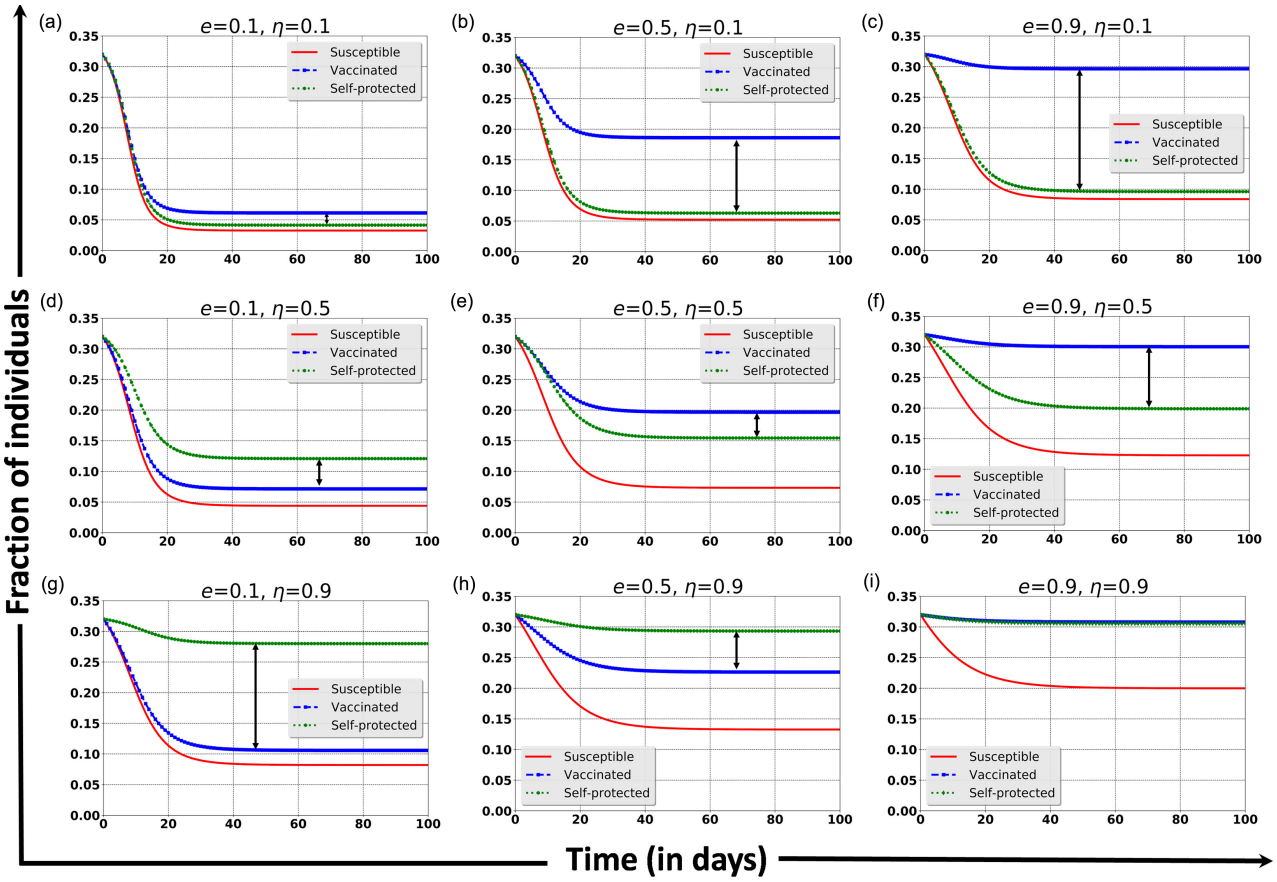

Figure 2. Time series analysis of three types of individuals: these line graphs illustrate the fraction of susceptible $S(t)$, vaccinated $V(t)$, and self-protected $M(t)$ individuals at any given time for three different efficacy levels (namely, meager, average, and extreme) of vaccination as well as self-protection. We set the value of $e=\eta=0.1$ as a meager efficacy level, whereas 0.5 and 0.9 respectively stand for average and extreme efficacy levels for the respective provisions. For simplicity, we assume the effectiveness of vaccination $\left(e_p=e_s=e\right)$ and efficiency of IDM-driven self-protection $\left(\eta_p=\eta_s=\eta\right)$ against primary and secondary strains work equally. Altering the values of e (in row-wise direction) and η (in column-wise direction), we manifest a total of nine panels ((a)-(i)) to investigate what kind of symmetricity exists within the model in terms of two efficacy parameters.

inferiority lies between vaccination and self-protection schemes, while three-different efficacy levels, namely meager (0.1), average (0.5), and satisfactory (0.9), are considered for both provisions. Our theoretical study reveals that when both e and η seem meager (e.g., 0.1), an individual's prime choice for strategy selection always goes with vaccination instead of taking self-protection (IDM), and it prevails until $e \geq \eta$. In such a situation, vaccination is treated as more trustworthy than other provisions. Consequently, if the efficacy levels being equal for both provisions, individuals' first choice always sticks to vaccination (see panels a, e, and i of **Figure 2**), thereby the fraction of vaccinators remains higher than the remaining other two fractions (susceptible and self-protected individuals) at a social equilibrium point. Yet, if we consider panels b and d having set with a symmetric manner in terms of e and η, the fraction of self-protectors drops down more frequently (see panel (d)) compared to its counterpart fraction of vaccinators (panel (b)). Parametric setting, represented by panel (d), allows more defectors (free-riders) than cooperators (sum of vaccinators and self-protectors) to survive in the population. Understandably, the strategy selection between vaccination and self-protection cannot be a definite alternative to each other even if the efficacy level is purely altered. Hence, employing the same altered efficacy settings, we end up with the faction of vaccinators being a bit higher than its counterpart fraction of self-protectors. Therefore, a relatively higher IDM efficacy (say, panel (d)) cannot even bring a significant difference between existing strategy fractions (shown by two-directional arrows), unlike what vaccination does (see panel (b)). Almost similar conclusions can be drawn while comparing panels f and h of **Figure 2**. On the other hand, if the difference between the two efficacy levels is considerably high (say, for example, panels (c) and (g)), the corresponding strategy fractions for respective provisions can somehow be comparable to each other, keeping the difference between the strategy fractions analogous.

Let us now briefly explain the relative disease propagation dynamics set off by primary and secondary strains under different circumstances (illustrated in **Figure 3**). The infection uptake considering varying transmission rate $\left(\beta_p = 0.75, \beta_s = 0.50\right)$, recovery time $\left(\gamma_p = 0.3, \gamma_s = 0.2\right)$, and initial infected proportion for respective disease strains is depicted employing none of the game aspect. The initial vaccination coverage and self-protection coverage for both strains are assumed to be approximately 33%, *i.e.*, $V(0) = M(0) = 0.33333$. For all cases, (**Figure 3**, panels (a)-(d)) the basic reproduction number for each strain has been kept at a fixed constant value $\left(R_0^P = R_0^S = 2.5\right)$. For highlighting the contribution from IDM in restricting the epidemic growth, the efficacy of committing vaccine is considered to be 50% for both strains, *i.e.*, $e = 0.5$. Our investigation confirms that a relatively higher IDM efficiency of a particular disease strain can restrict the epidemic growth of that targeted strain. That is, for a fixed vaccine efficacy, IDM efficiency can still improve the situation by controlling the transmission of a particular disease strain. Yet, the strain having higher transmission rate $\left(\beta_p > \beta_s\right)$ is found to be dominant irrespective to the initial

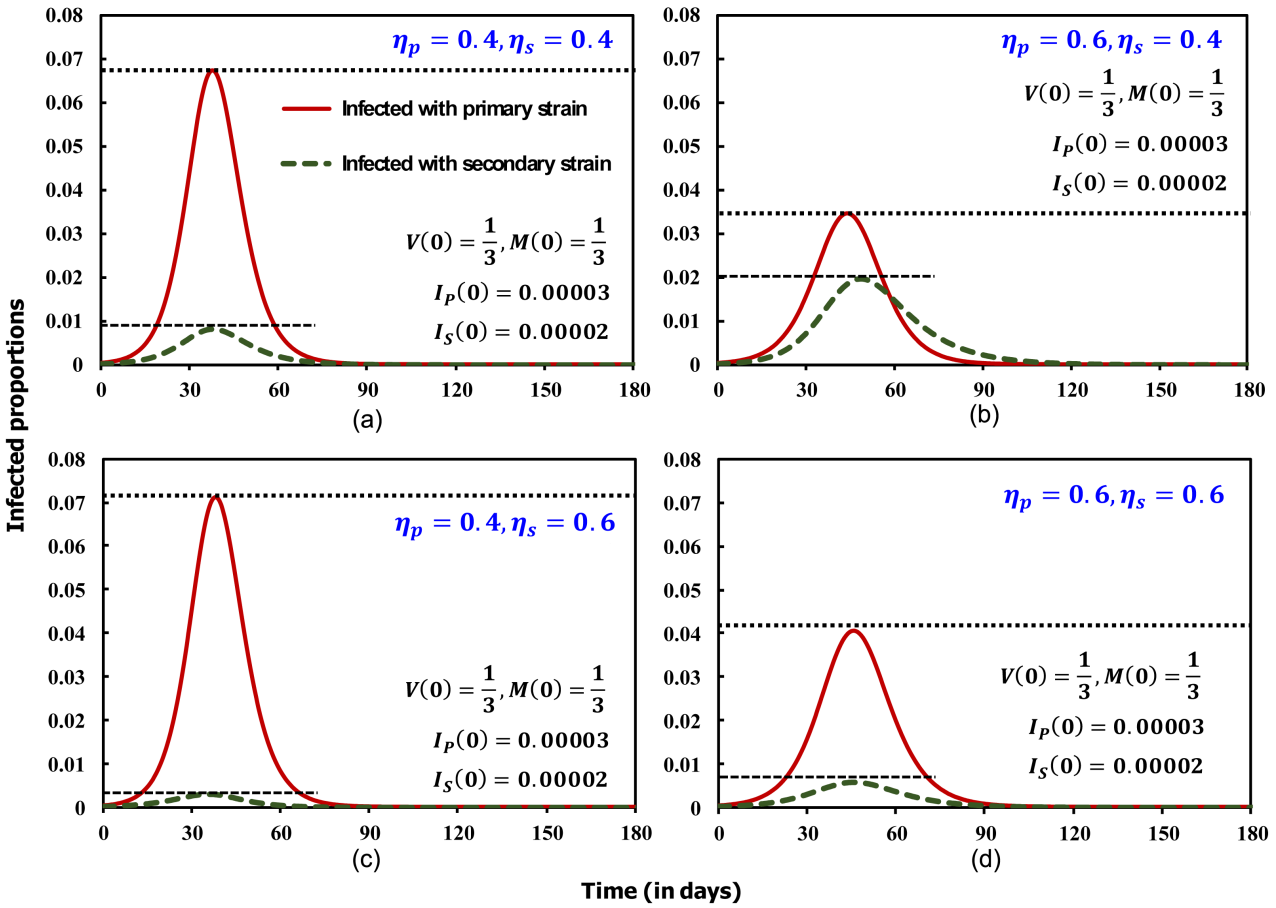

Figure 3. Time series analysis of fractions of infection by two strains for different IDM efficiency rates without considering game approach: A relatively higher IDM efficiency of a particular disease strain can restrict the epidemic growth of that targeted strain. That is, at a fixed vaccine effectiveness, IDM efficiency can still improve the situation by controlling the transmission of a particular disease strain. The vaccination coverage and self-protection coverage for both strains are assumed to be approximately 33%. For all cases (panels a-d) the basic reproduction number for each strain has been considered as a fixed constant value $\left(R_0^P = R_0^S = 2.5\right)$ and the effectiveness of vaccination for both strains is $e = 0.6$.

infection proportions. Thus, the sensitivity coming from initial infected fractions seems insignificant in comparison to the transmission rates, *i.e.*, strains having higher spreading tendency can be more impactful on virus dominance (Table 4).

3.2. Repeating Season Epidemic Growth Analysis

This section deliberately estimates the epidemic growth using a couple of line graphs, illustrating the FES as a function effectiveness of vaccination (e). In Figure 4, we portray critical lines of FES at varying price for vaccination to justify the impact of vaccine efficacy in controlling the unprecedented growth of an epidemic under a perceived cost and efficiency of IDM (e.g., $C_m = 0.4$ and $\eta = 40\%$). For simplicity, we assume the effectiveness of vaccination (e) and the efficiency of IDM (η) remain identical for either strains while IB-RA strategy updating rule is implemented. A reasonably lower provisional price makes the combined strategy (taking both vaccine and IDM) more tractable for individuals,

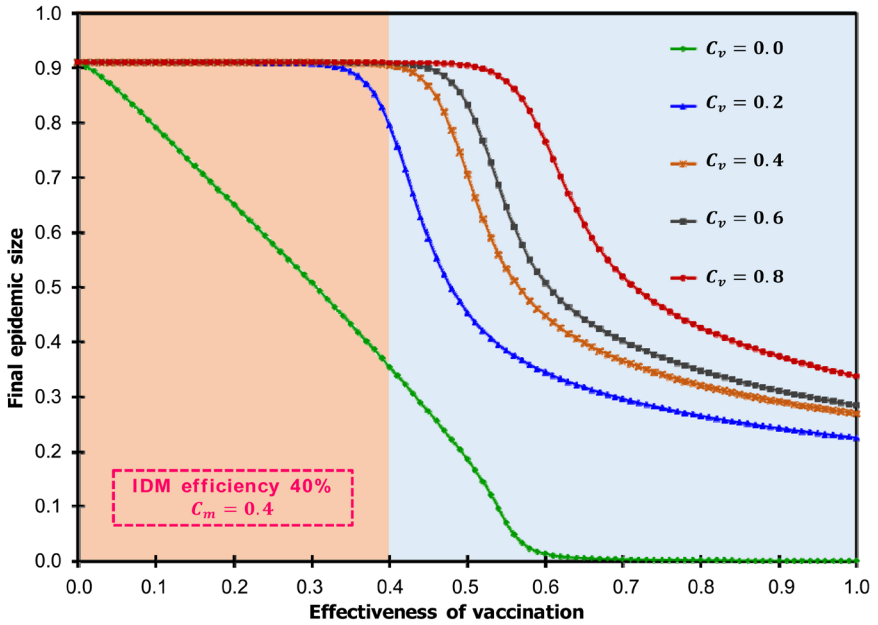

Figure 4. Impact of provisional efficacy in controlling the epidemic growth: here, we choose five different vaccination cost (C_v) values for investigating the effect of vaccination cost in disease attenuation. Other model parameters used for this simulation are $C_m = 0.4$ and $\eta = 40\%$.

which in turn, ensures much better protection from disease strains. Based on different vaccine price, we depict five FES lines to illustrate the epidemic prevalence under different circumstances. As a general tendency, FES gradually decreases with the increase of vaccine efficacy. More precisely, the epidemic size is somewhat controllable if vaccination is more that 40% effective (*i.e.*, $e > 0.4$), as suggested by **Figure 4**. Intuitively, when the vaccine efficacy is marginally high, the added contribution from self-protection reduce the epidemic size quite significantly. One novel finding of this study reveals that a slightly increased vaccine price slightly extends the FES thresholds as long as $e \le 0.4$. Contrarily, a sufficiently higher vaccine efficacy $(e \ge 0.5)$ can single-handedly lessen the epidemic dominance. Although we relied on IB-RA strategy updating protocol for the time being, it is expected that disease can be better attenuated if SB-RA imitation dynamics would have been adopted.

3.3. A Comprehensive Phase Plane Analysis Using Two-Dimensional Heat Maps

To help capture the holistic outline of epidemic evolution under the framework of EGT, we generate an adequate number of two-dimensional heat maps taking human decision making into consideration for repeated epidemic seasons. Visuals that portraying the final epidemic size (FES) for respective strains, self-protection coverage (MC), vaccination coverage (VC), fraction of free-riders (FF), and the average social payoff (ASP) are handy stuff in predicting the threatening scourge existing in human society. A specific thumb rule for monotonic color

transition is strictly followed while generating the heat maps or phase diagrams) for each of the evolutionary outcomes throughout this study. The color transmuting from deep blue to deep red illustrates a society being shifted from better to worse state in terms of the evolutionary consequences, and vice-versa. As a next step, we present a rigorous phase-plane analysis varying the vaccine efficacies in controlling the primary (secondary) disease strain along the *x*-axis (*y*-axis) direction. Meanwhile, the portrayal of e_s versus e_p heat maps for respective evolutionary outcomes considers three discrete provisional cost values (e.g., 0.0, 0.4, and 0.8) for vaccination as well as self-protection shown in two different directions (vaccine cost in row-wise direction and IDM cost in column-wise direction). Besides, our theoretical model has two-fold: without mutation and with mutation (e.g., 5%) from primary to secondary strain. The concept of mutation used here reflects the piling up of infection, transferring from primary to secondary strain. Thus, each of the heat maps contains a set of nine panels (marked with (a-*)) designating without mutation case and another set of nine panels (marked with (b-*)) illustrating a 5% mutation. These two cases are thus separated by a green vertical bar. Intuitively, all these heat maps are upper triangular-shaped to meet up with the assumed condition of $e_p \geq e_s$. Throughout the study, we employ two-different strategy updating rules to reveal the evolutionary consequences at a wide variety of parameter setting.

Arguably **Figures 5-11** illustrate all evolutionary fractions implementing IB-RA strategy updating rule. Let us start with **Figure 5** and **Figure 6**, depicting the final size of infection posed by respective disease strains at distinct costs while varying e_s and e_p in two directions. These discrete cost values: C_v and C_m have sequentially been placed in row-wise and column-wise directions. Intuitively, we can characterize the provisional expenses into three classes based on their relative cost values: completely free of cost (when $C_v = C_m = 0.0$), requires an average price (if $C_v = C_m = 0.4$), and a reasonably expensive price is requisite to owning it (if $C_v = C_m = 0.0$). For simulation purpose, IDM efficiency for primary and secondary strains is kept at fixed rates $\left(\eta_p = 0.6, \eta_s = 0.5\right)$, which is quite conceivable set-up for repeated epidemic seasons under a game-theoretic framework. Following **Figure 5**, it is persuasive to say that infection spreading prompted by primary strain is readily controllable if either provisional expense is free of cost regardless of cases having a 5% mutation or not (see first row and first column of **Figure 5** for $\mu = 0.0$ and $\mu = 0.05$). As we know, the FES or the total infection size imposed by a certain disease-strain is deeply related to the provisional cost of an adopted provision and its level of protective efficacy against that strain. Therefore, with the increase of vaccination and self-protection costs, individuals are less like to take any preventive provision that allows infection to spread up quite naturally, especially at the parametric regions where both effectiveness are pretty low. Meanwhile, disease posed by primary strain can significantly be eliminated only if effectiveness of vaccine against either strain is above a certain threshold level, say, for example, $e_p, e_s > 0.4$. At a

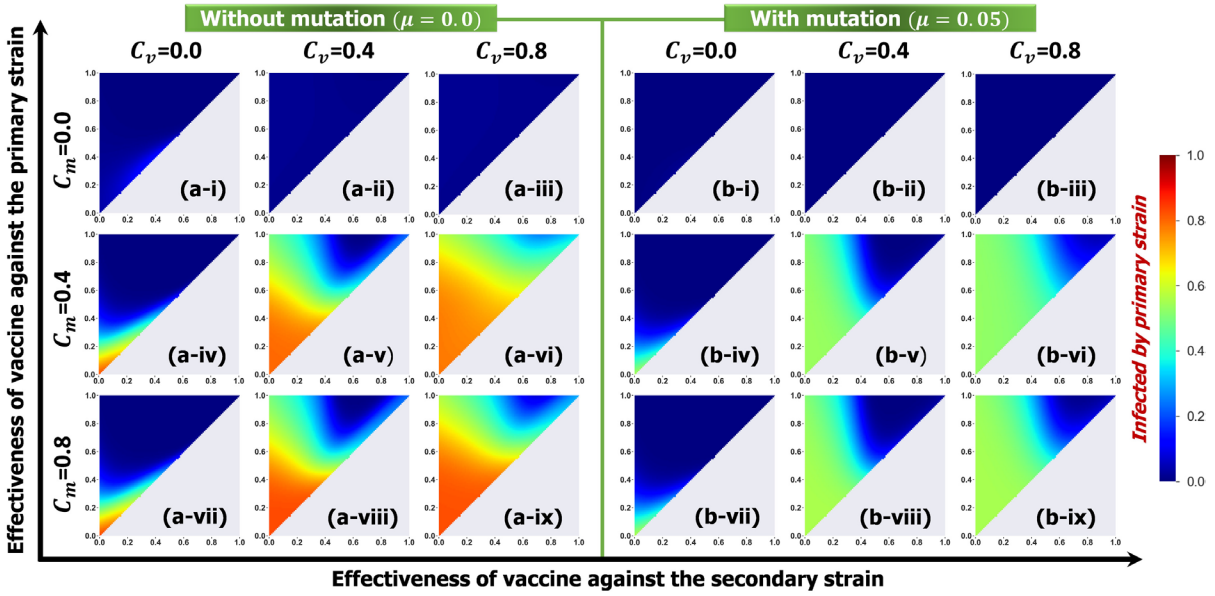

Figure 5. The final size of infection brought by primary disease strain using IB-RA: these two-dimensional e_s versus e_p heat maps illustrate the FES generated by primary strain under a certain pair of intervention cost values. Here, we consider two types of costs, namely vaccination cost C_v in row-wise direction and IDM cost C_m in column-wise direction. Both these costs are presumed to be 0.0, 0.4, and 0.8. This figure has two-fold: without mutation and with mutation cases (precisely, a 5% mutation takes place from primary to secondary strain controlled by the parameter, μ). The left panels (a-*) present the outcomes without pondering any mutation from primary to secondary strain, meanwhile, the right panels (b-*) depict the evolutionary outcomes under the same set of parametric conditions considering 5% mutation. *A solid green-colored vertical line has separated both these phenomena while IB-RA updating rule is employed. Primary disease strain essentially survives when vaccine efficacies are relatively low.* Other simulation parameters used here are: $\eta_p = 0.6$, $\eta_s = 0.5$.

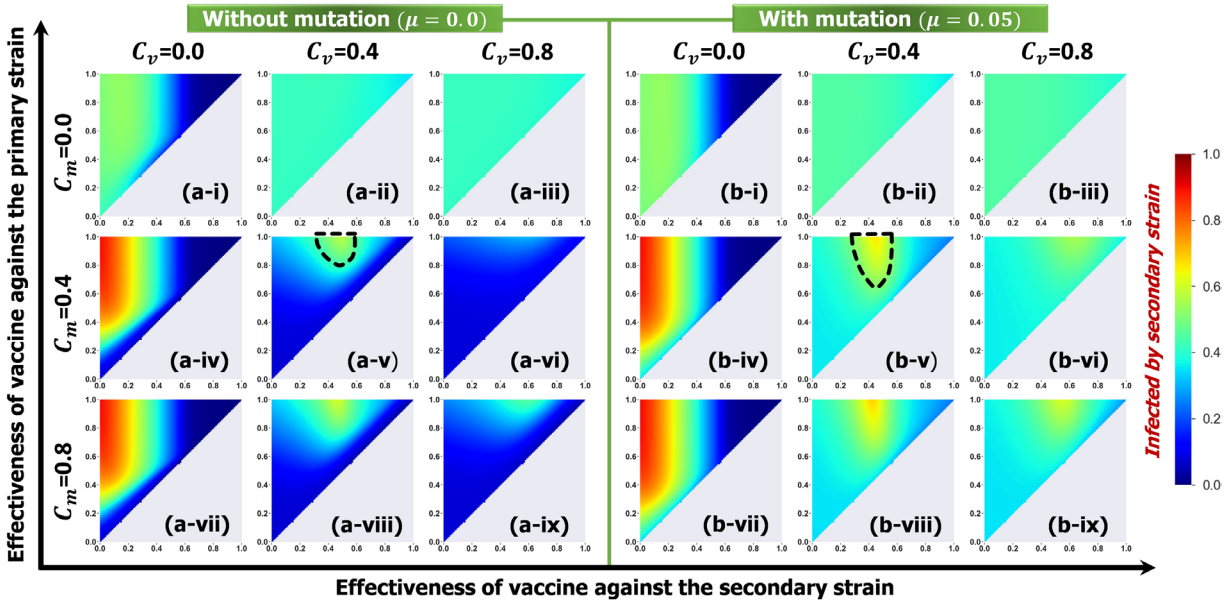

Figure 6. The final size of infection brought by secondary disease strain using IB-RA: these two-dimensional e_s versus e_p heat maps illustrate the FES generated by secondary strain under a certain pair of provisional cost values. The entire parametric setup is kept similar to what we presumed in **Figure 5**. *This secondary strain borne disease sustains until the vaccine efficacy against secondary strain is meager.*

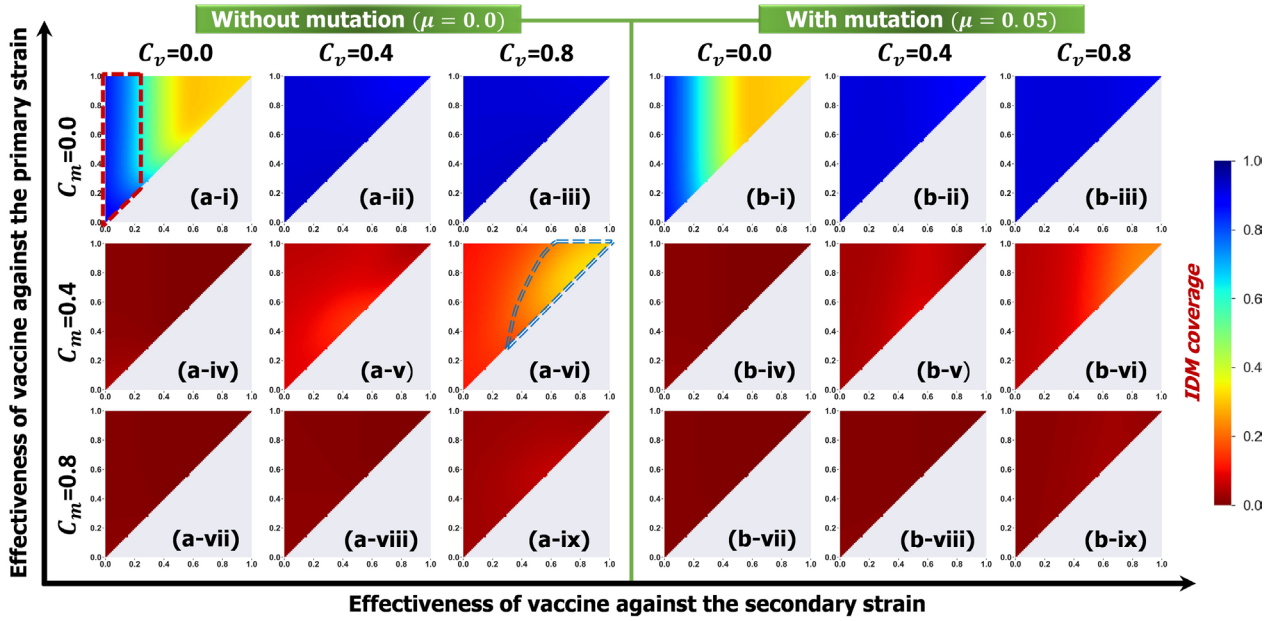

Figure 7. The self-protection coverage (MC) brought by IDM using IB-RA: these two-dimensional e_s versus e_p heat maps illustrate the IDM uptake for either strain under a certain pair of provisional cost values. Under the same parametric setting, IDM is strongly favored when it is available to free of cost.

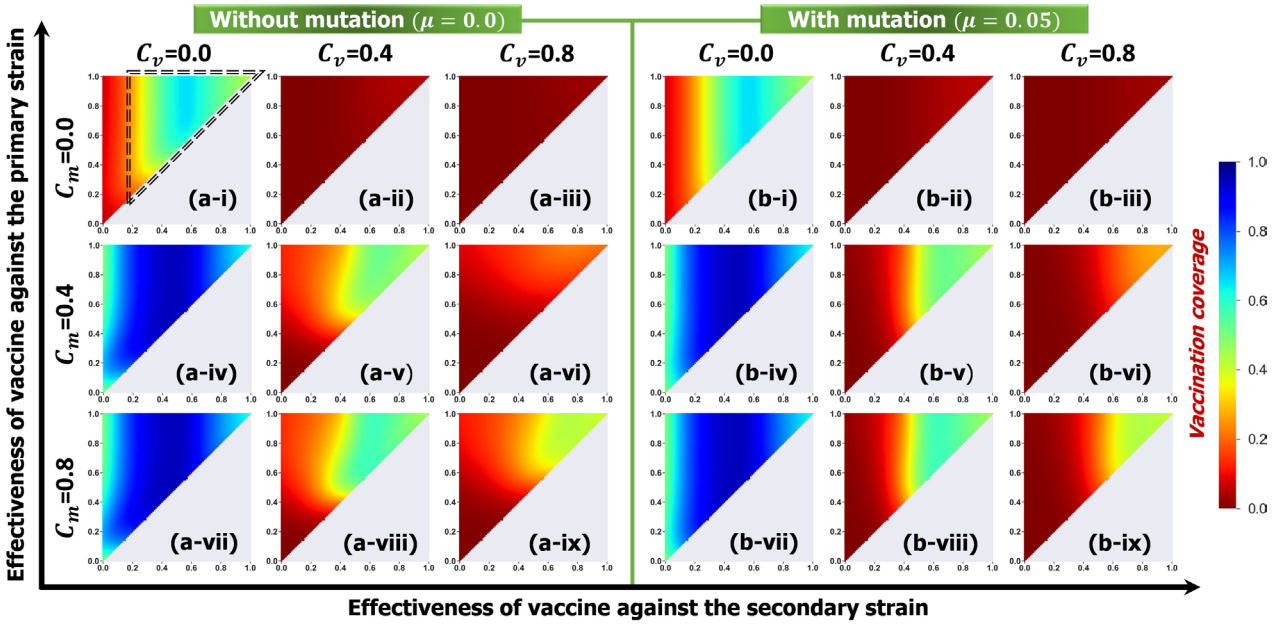

Figure 8. The vaccination coverage (VC) brought by vaccine using IB-RA: these two-dimensional e_s versus e_p heat maps exhibit the contribution coming from vaccine irrespective to strains under a certain pair of provisional cost values. *VC is sufficiently higher when vaccine efficacies being moderately high.*

glance, the monotonic change in color gradient indicates a better disease attenuation towards a reasonably higher vaccine efficacy level (see panels (a-v), and (a-viii) depicted in Figure 5). One appealing feature that could observe from the panels (b-*) of Figure 5 is the severity of the primary strain gradually weakened

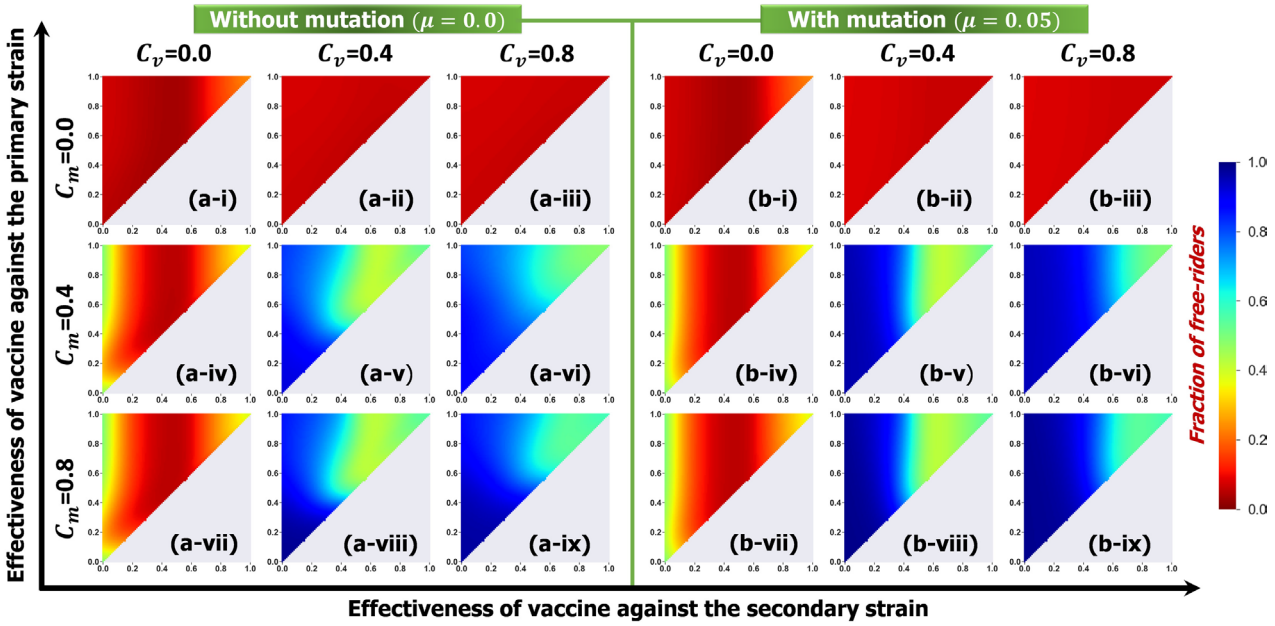

Figure 9. The fraction of free-riders (FF) triggered by free riding tendency observed in non-provisional individuals using IB-RA: these two-dimensional e_s versus e_p heat maps justify the adverse contribution coming from free-riders under a certain pair of provisional costs. For consistency, we follow the same parametric setting while showing FF.

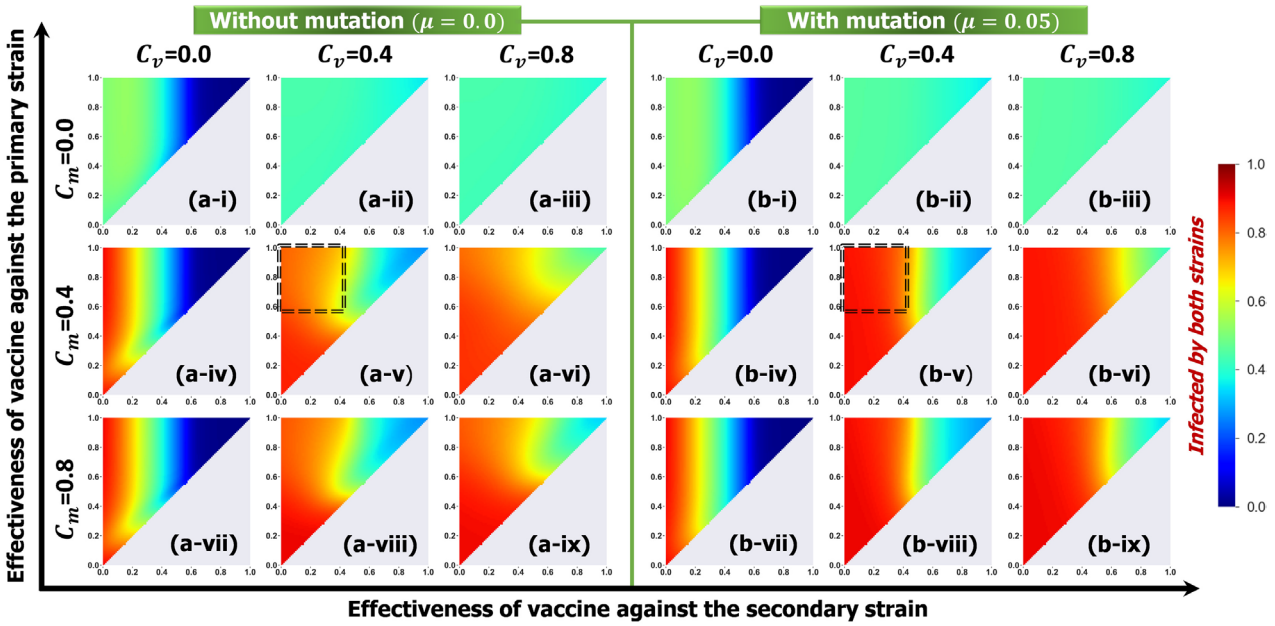

Figure 10. The total size of infection generated by both strains using IB-RA: these two-dimensional e_s versus e_p heat maps show the prevalence of FES under a certain pair of provisional costs. DFE is attainable only if vaccination is free and its efficacies being very high.

with the increase of mutation rate (μ). An increased rate of mutation paves the way to extensive conversion of a primary disease strain to that of secondary. Thus, the efficacy of the primary vaccine becomes less sensitive to oppress primary strain, and this fact can be validated if we move vertically along the direction

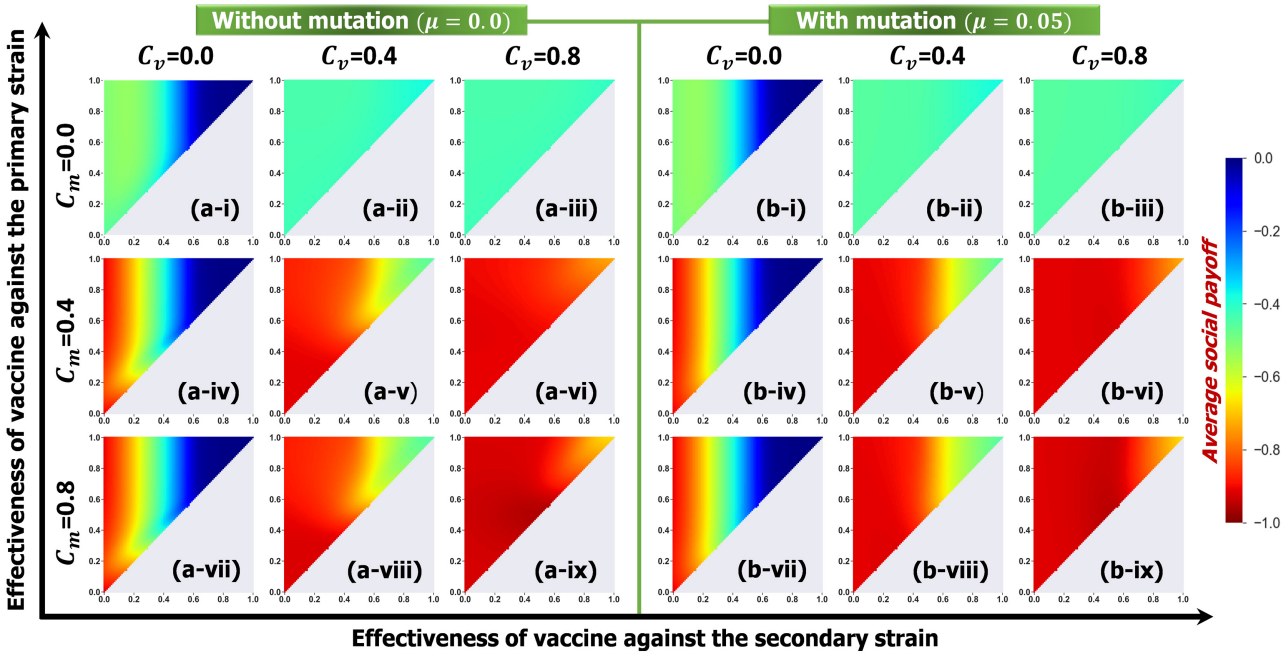

Figure 11. The average payoff attained by individuals living in an epidemic prevailing population using IB-RA: these two-dimension e_s versus e_p heat maps illustrate the ASP, relying on a particular provision under a certain pair of provisional cost values.

of e_p. Again, Figure 6 presents a fair indication of how the secondary infection gets over the 2D parametric space under a given intervention cost pair (C_v, C_m). Albeit one of the provisions is free of cost, there are still many free-riders who intentionally deny taking either pre-emptive provision, which causes the emergence of secondary infection quite often. Irrespective of non-mutation and mutation cases, the first column of Figure 6 stand for free vaccination cases (see panels (a-i), (a-iv), (a-vii) for non-mutation cases and panels (b-i), (b-iv), (b-vii) for mutation cases), illustrating the existence of secondary infection being quite high, especially around the regions where e_p is reasonably higher. The presence of too many free riders makes it much more challenging to oppress the secondary strain-borne infection even though the vaccination is free of cost as well as the vaccine efficacy against primary strain is somewhat higher. Meager vaccine effectiveness against the secondary strain around that particular parametric regions, depicted in the phase plane, cannot fight alone in attenuating the secondary infection entirely from a population. From the first row of Figure 6, we could see the infection size resulting from secondary strain remains non-monotonic when self-protection is offered to free of cost (justified by panels (a-ii), (a-iii), (b-ii), (b-iii)). For non-mutation case, the remaining panels of Figure 6 (e.g., (a-v), (a-vi), (a-viii), and (a-ix)) suggest that the infection generated by secondary strain could be well controlled even if the vaccine efficacy for either strain is lower. Few exceptions can also be observed in the middle course region of e_s (specifically between 0.4 to 0.6) where individuals are somehow attracted to free-riding (take a look at panel (a-v) of Figure 9 for justification), thereby the permanence of secondary infection is still surviving like an island

city (marked with a black dotted line in panel (a-v) of Figure 6) around the neighborhood where e_p is sufficiently large $\left(e_p > 0.6\right)$. Unlike what we observe in FES for primary strain (depicted in panels (b-*) of Figure 5 taking mutation into account), the severity of secondary infection gets stronger with the increase of mutation rate. Phase diagrams manifesting each provision's coverage demonstrates how people think while adopting a particular pre-emptive measure. For instance, Figure 7 and Figure 8 expose the contributions respectively coming from self-protection and vaccination schemes to oppress disease transmission induced by either strain. We consider IDM as a supplement of vaccine that helps restraining the transmission of the epidemic having multiple strains. Accordingly, these two protective measures complement each other to retain the FES controllable. Examining panels (a-i) of Figure 7 and Figure 8 makes things conceivable to predict how these control provisions work together at varying vaccine efficacies. For simplicity, we trace the existence of self-protectors by a red dotted line (panel (a-i) of Figure 7) and that of the vaccinators by a black dashed triangle (panel (a-i) of Figure 8) when both provisions are free of cost. If both costs are very cheap or even free, most individuals prefer to take IDM when e_s is lower, and less than 40% individuals choose IDM when both e_p and e_s are reasonably higher. An utterly opposing tendency is noticed among individuals interested in taking the vaccination as long as costs for provisions remain identical. Increasing vaccine efficacies, a little bit, especially when both $e_p, e_s > 0.2$, individuals seem more confident to vaccination, and approximately more than 40% of people prefer to commit vaccines instead of merely relying on IDM. Roughly 100 % individuals take IDM as a rational selection when it costs nothing (panels (a-ii), (a-iii) of Figure 7), and so is vaccination when being offered to free of cost (panels (a-iv), (a-vii) of Figure 8). Some 30% of individuals skillfully take IDM when its cost is half that of vaccination, and both e_p and e_s being relatively high as well (see panel (a-vi) of Figure 7 marked with blue-dashed line). While vaccine price is a bit cheaper, or let us say identical with IDM cost, individuals accept vaccination as the most entrusted provision as long as its efficacy against either strain is reasonably high (panels (a-v), (a-viii), (a-ix) of Figure 8). Notably, we could see an extended appearance of greedy free-riders who mostly rely on the herd immunity until either one or both vaccine efficacy being relatively meager (see panels (a-v) and (a-vi) and (a-viii) and (a-ix) of Figure 9). It seems pretty clear for mutation cases that IDM is no longer an effective means of protection as mutation allows the secondary strain to get even stronger than before. So, individuals only choose IDM when it is free. Essentially there is no such reliable provision other than vaccination. People intend to choose provision if it is free of cost or its efficacy to protect themselves being infected is marginally higher ($e_p, e_s > 0.2$). Unequivocally, such a situation promotes more free riders to survive in the entire parametric space. We can readily explain this obvious fact, simply relying on the panels (b-*) of Figures 7-9. Disease prevalence shifts from primary to secondary strain when a mutation ensues. Thus, presuming higher η_s value could render better performance in terms of infection mi-

tigation or disease oppression. For example, if the mutation rate is too high, e.g., $\mu = 0.1$ or let us say 10%, it yields a substantial transferring path from primary to secondary strain. Hence, primary disease strain becomes weaker and can sufficiently be oppressed with minimum efforts as infection shifts to secondary strain. Such a situation essentially brings a social dilemma to the common people who rely on either pre-emptive provision. The reason responsible for that possibly comes from the fundamental premise of the model, *i.e.*, strictly assuming a relatively lower efficacy value for either provision against the secondary strain. From the technical viewpoint, whenever two different mutually exclusive strains exist within a population, it becomes challenging to ensure an equal level of protection against both strains by committing a single vaccine, which is initially designed for the primary disease strain. To some extent, it confers partial protection against the secondary strain, yet, most of the time, it becomes arduous to control secondary infection if the protective efficacies against secondary disease strain are relatively meager in spite of the provisional costs remain very cheap. To proffer a precise evolutionary outline of emerging epidemics over recurrent seasons, we present the total size of infection generated by both strains along the 2D parametric plane in **Figure 10**. This figure provides a snapshot of how the epidemic evolves over seasons within a well-accepted framework of evolutionary game theory (EGT). Besides, it signifies a disease-free equilibrium (DFE) when vaccines are free, and its efficacy level against either strain is higher than 0.4. It also confirms that an endemic equilibrium (EE) would be existing if none of the provisions is free of cost, and vaccine efficacies are strictly less than 0.4. An increasing mutation rate pushes the epidemic to become more severe than the mutation-free condition. Albeit we presume a 5% mutation throughout the study, it makes the situation troublesome for individuals to control the FES following multiple pre-emptive provisions (for example, see panels (a-v) and (b-v) marked with a black-dashed square in **Figure 10**). To this end, we reveal the societal payoff obtained by participating in a specific protective scheme in **Figure 11**. Game-theory commonly explicates the interplay between the cost and benefit (return) of selecting a particular strategy. Thereby, heat maps showing the ASP is thus an essential outcome for us to prophesy what type of rational responses would be expected from individuals to overcome the epidemic burden. In sum, a better ASP is directly proportional to the success rate of disease eradication and inversely proportional to the sum of expenses employed to exercising pre-emptive provisions. At a glance, the obtained ASP seems quite analogous regardless of mutation and non-mutation cases.

Now we will be focusing on **Figures 12-18**, which explore an identical set of evolutionary consequences following the SB-RA strategy updating rule. It is acceptable, as illustrated in **Figure 12**, that the disease prevalence aided by PDS can thoroughly be suppressed if the self-protection scheme is cost-free regardless of cases having a mutation or not (see the first row of **Figure 12**). Individual's unwillingness to participate in free vaccination policy around their meager efficacy regions yields the primary infection probably ended up being endemic

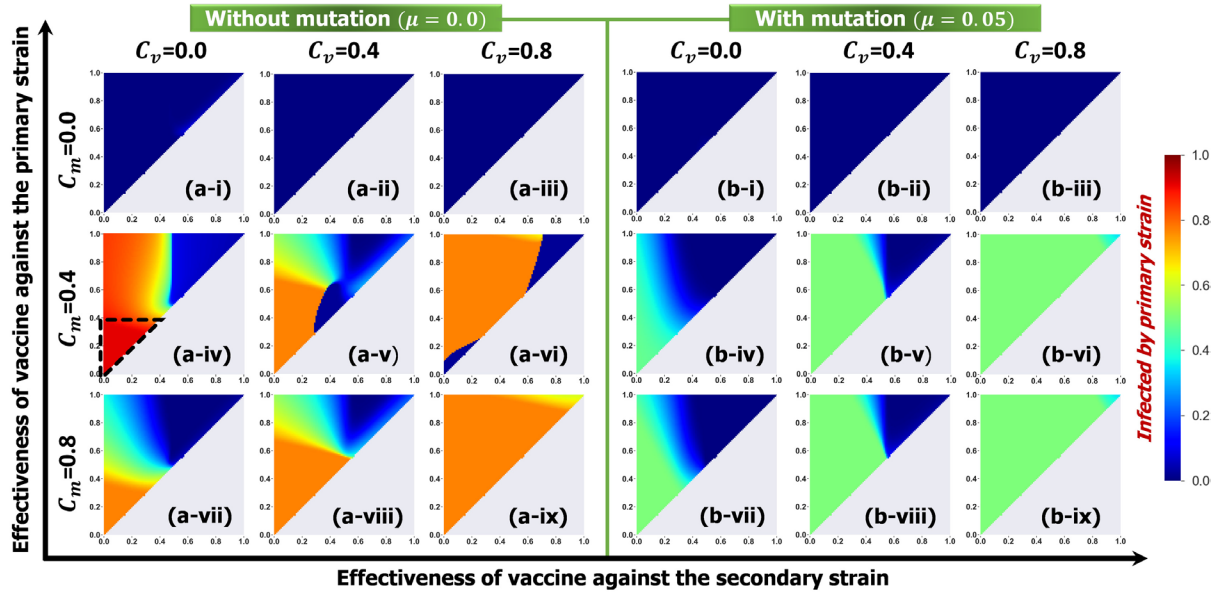

Figure 12. The final size of infection brought by primary disease strain using SB-RA: these two-dimensional e_s versus e_p heat maps illustrate the FES generated by primary strain under a certain pair of provisional cost values. Here, we consider two types of costs, namely vaccination cost C_v in row-wise direction and IDM cost C_m in column-wise direction. Both these costs are presumed to be 0.0, 0.4, and 0.8. This figure has two-fold: without mutation and with mutation cases (precisely, a 5% mutation takes place from primary to secondary strain controlled by the parameter, μ). The left panels (a-*) present the outcomes without pondering any mutation from primary to secondary strain, meanwhile, the right panels (b-*) depict the evolutionary outcomes under the same set of parametric conditions considering 5% mutation. *A solid green-colored vertical line has separated both these phenomena while IB-RA updating rule is employed. Primary disease strain essentially survives when vaccine efficacies are relatively low.* Other simulation parameters used here are: $\eta_p = 0.6, \eta_s = 0.5$.

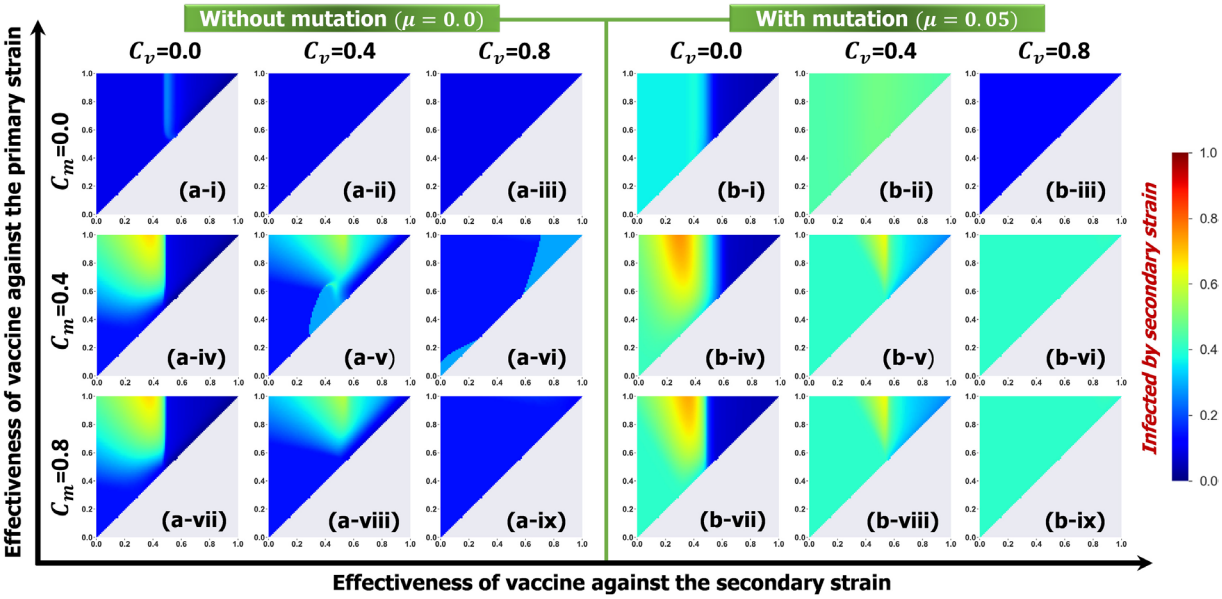

Figure 13. The final size of infection brought by secondary strain using SB-RA: these two-dimensional e_s versus e_p heat maps represent the FES generated by secondary strain under a certain pair of provisional cost values. The entire parametric setup is kept analogous to what we presumed in Figure 12. The SDS can be fully eliminated when vaccine efficacies against either strain is significantly high.

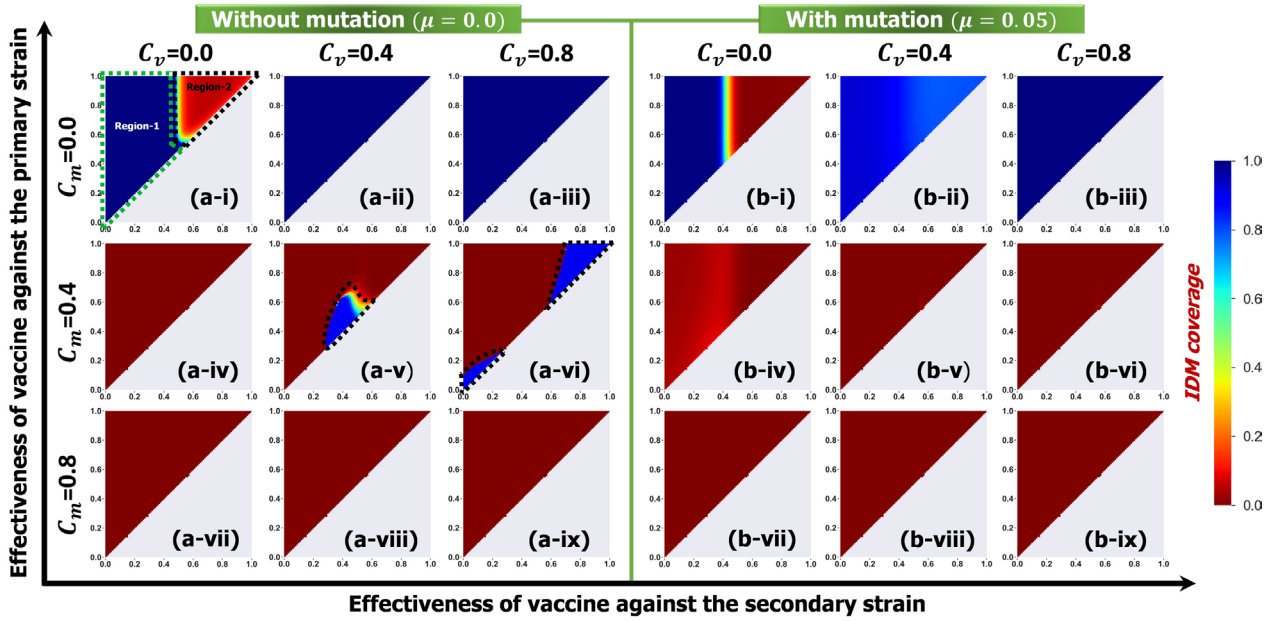

Figure 14. The self-protection coverage (MC) brought by IDM using SB-RA: these two-dimensional e_s versus e_p heat maps illustrate the IDM uptake for either strain under a certain pair of provisional cost values. Under the same parametric setting, IDM is strongly favored when it is available to free of cost as well as vaccine efficacies remain meager.

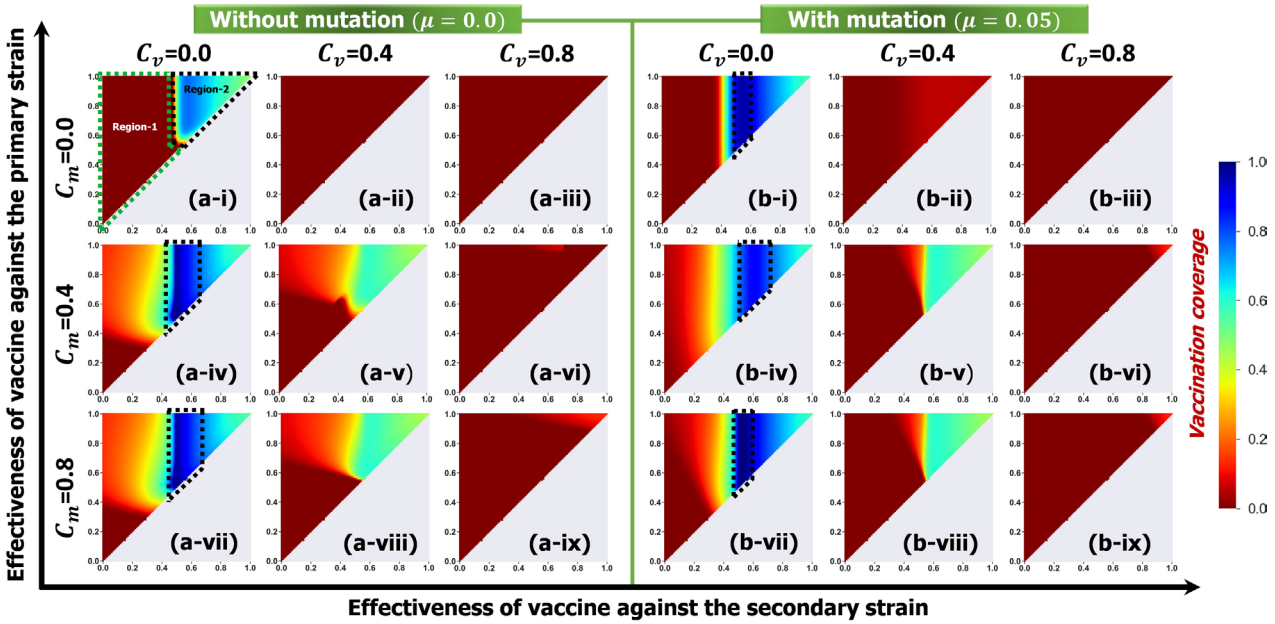

Figure 15. The vaccination coverage (VC) brought by vaccine using SB-RA: these two-dimensional e_s versus e_p heat maps exhibit the contribution coming from vaccine irrespective to strains under a certain pair of provisional costs. *VC is sufficiently higher when vaccine efficacies being moderately high.*

(panel (a-iv) of Figure 12). Apparently, the SB-RA strategy updating rule triggers individuals to respond more rationally while picking up strategies. The biggest reason for that is the inherent mechanism of this protocol itself. Under this updating rule, imitation process takes place by comparing an individual's payoff

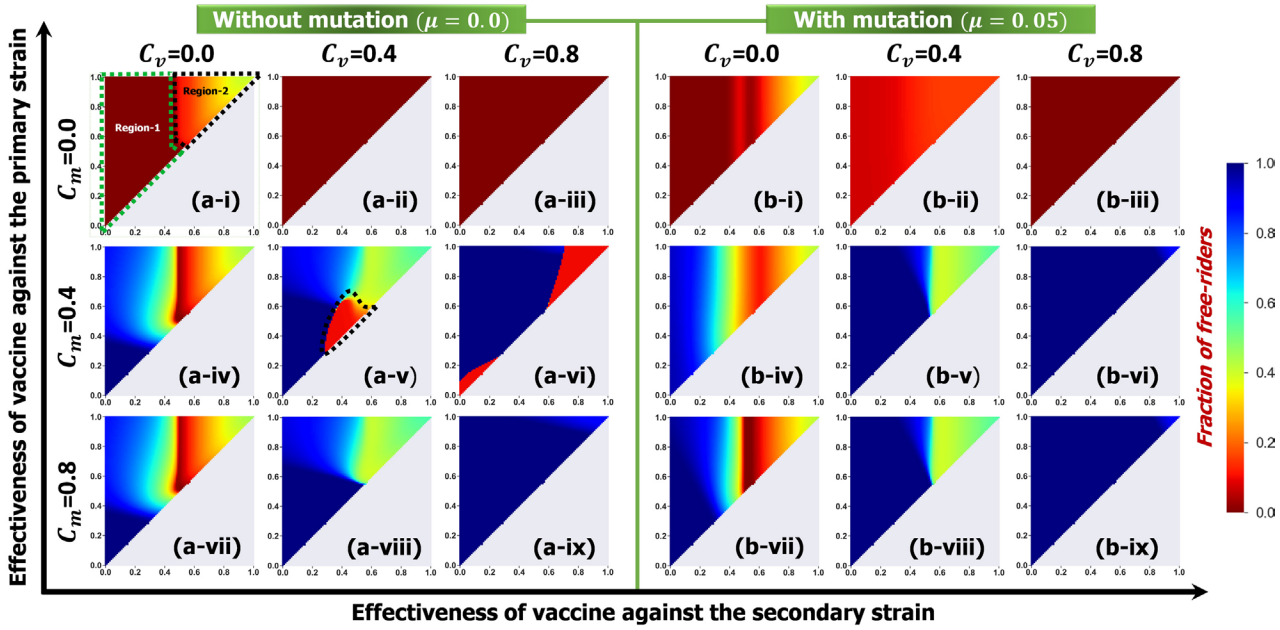

Figure 16. The fraction of free-riders (FF) triggered by free riding tendency observed in non-provisional individuals using SB-RA: these two-dimensional e_s versus e_p heat maps justify the adverse contribution coming from free-riders under a certain pair of provisional cost values. FF increases abruptly when vaccine efficacies and provisional costs are presumed to be mid-level values. For consistency, we follow the same parametric setting while showing FF.

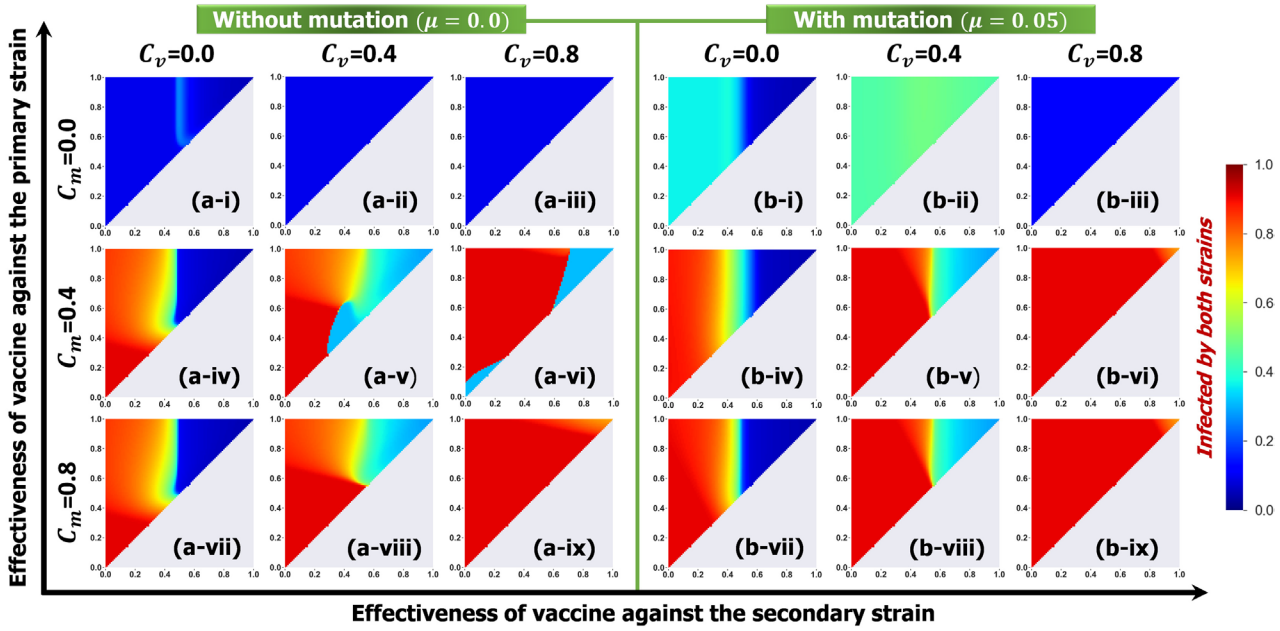

Figure 17. The total size of infection generated by both strains using SB-RA: these two-dimensional e_s versus e_p heat maps show the prevalence of FES prevails under a certain pair of provisional costs. DFE is attainable only if vaccination is free and its efficacies being very high.

with the average payoff of the strategy group to which his game opponent belongs. In other words, it compares an individual's payoff with the average payoff of another strategy group where all individuals belonging to that group follow

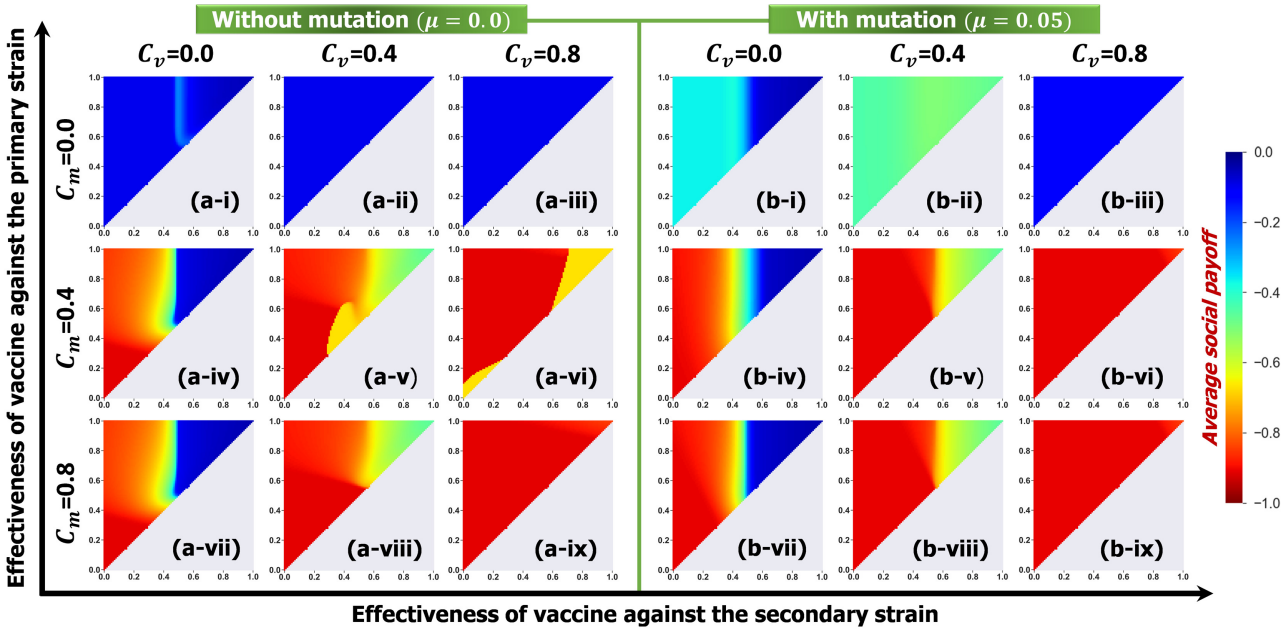

Figure 18. The average payoff attained by individuals living in an epidemic prevailing population using SB-RA: these two-dimensional e_s versus e_p heat maps illustrate the ASP, relying on a particular provision under a certain pair of provisional cost values.

the same strategy. In sum, SB-RA is an individual versus group payoff comparison tool, while IB-RA examines one to one payoff comparison. Hence, SB-RA always reflects the averaged situation of an individual's game opponent. That is why free vaccination does not motivate people frantically to adopting that strategy (see panels (a-iv) of **Figure 12** and **Figure 15**); instead, it makes them more concerned whether its efficacy level is reliable or not ($e_p, e_s \geq 0.5$). Meanwhile, if both costs are equally reasonable, let us say, 0.4, a mutual contribution from vaccinators and self-protectors comes into play to restrain the epidemic prevalence inflicted by primary strain (see panels (a-v) of **Figure 12** and **Figure 14** and **Figure 15**). Likewise, IB-RA, the overall situation of infection prevalence caused by primary strain improves very much (panels (b-*) of **Figure 12**) for the case of a 5% mutation. From **Figure 6** and **Figure 13**, representing identical evolutionary outcomes, we end up saying SB-RA outperforms IB-RA in terms of infection remission caused by secondary strain. It is true for most of the cost pair (C_v, C_m) regardless of cases tackling non-mutation and mutation. Employing SB-RA strategy updating rule, the FES induced by primary strain gets weaker, and the FES generated by secondary strain becomes more severe when mutation is considered. That is quite analogous to what we observe when using the IB-RA updating rule. Now, let us investigate the neighborhoods and selection conditions under which self-protectors, vaccinators, and free-riders exist in the parametric phase plane. **Figures 14-16**, respectively showing self-protection coverage (MC), vaccination coverage (VC), and the fraction of free-riders (FF), render a brief idea of how people think while sticking to a particular provision following SB-RA. This time we confine our discussion solely to some interesting points

that emerged in these figures. First off, vaccination and self-protection complement if these provisions are free of cost (take a look panel (a-i) of Figure 14 and Figure 15). Under this circumstance, we can distinguish the entire parametric plane into two distinct regions: region-1 and region-2, labeled with green and black dotted polygons, respectively. Region-1 $\left(0 \le e_p \le 1, e_s < 0.5\right)$ is fully occupied with self-protectors, whereas vaccinators mostly persist in region-2 $\left(e_p, e_s > 0.5\right)$. Notably, free riders are partially existing in the later region too. If IDM is free and paying for vaccination is the only alternative, then individuals' sensible choice for strategy selection sticks to self-protection (panels (a-ii), (a-iii) of Figure 15). Examining the opposite situation in terms of provision's cost does not bring an identical evolutionary scenario. Despite free vaccination, the SB-RA updating rule does not recommend individuals to commit vaccines without considering other aspects passionately. Instead, it pushes them to pay more attention to the average level of vaccination efficacy than its price. Therefore, we could see the maximum VC appears somewhere within region-2 (precisely, when $e_p > 0.5$ and $0.4 < e_s < 0.7$, depicted with black dotted lines in panel (a-iv) of Figure 15). Meanwhile, the remaining region-1 is partially occupied with free-riders (see the corresponding panel (a-iv) of Figure 16). We end up with the same conclusion even though panel (a-vii) of Figure 15 and Figure 16 is concerned. Someone can perceive the most striking result employing the SB-RA updating rule depicted in panel (a-v) of Figure 14, where costs for both provisions are identical as well as reasonably higher. Unlike IB-RA, we find self-protectors existing like an island city around the neighborhood marked with black dotted lines when the vaccine efficacies against either strain maintain an average trustworthy level. The presence of too many self-protectors kicks out the free-riders triumphantly and thereby secures a more relaxed condition in terms of disease prevalence. Sometimes individuals may go through several tricky situations that probably enjoin them to respond smartly. Say, for example, if the cost of vaccination is precisely the double that of IDM, what should they do? Game theory can answer this question in a more rational way of how human decision-making occurs while updating its strategy for the next epidemic season. Result suggests that instead of spending extra cost for a single vaccine shoot, some individuals would intuitively go for self-protection strategy at two different conditions, namely when vaccines' reliability against either strain is too low or too high. That brave decision essentially allows them to oppress the primary disease strain significantly, thereby contributing to upholding the ASP and kicking out free-riders from the epidemic stricken society (justified by the panel (a-vi) of each of the Figures 12-18). Mutation brings about a weird situation when the vaccination cost is too high $\left(C_v = 0.8\right)$, and IDM is absolutely free (illustrated in panel (b-iii) of each of the Figures 12-18). Indeed, it needs to be figured out how we can cope up with this tricky situation. Backed by Figure 14 (look at the panel (b-iii)), all individuals under this circumstance would unquestionably be relying on IDM regardless of the vaccine's reliability against either strain. Holding up

this strategy undertakes a remarkable disease attenuation and ensures an increased social payoff; nonetheless, it works exceptionally well against secondary strain. From the discussion so far, one point is evident that each of the preemptive provisions works exceedingly well regardless of strains when its average efficacy level is presumed. Moreover, when human decision-making comes into play, SB-RA provides us with more averaged information regarding the game opponents and the ASP obtained following a particular strategy at recurrent epidemic seasons. Combining these two ideas, this time, we will be focusing on the same set of evolutionary outcomes but, of course, keeping in mind the effectiveness of vaccination and efficiency of IDM being equal for either strain. To keep things simpler, we limit our discussion only to the non-mutation case. The new parametric setup considers the effectiveness of vaccination $\left(e_p = e_s = e\right)$ along the horizontal axis (*x*-axis) and the efficiency of IDM $\left(\eta_p = \eta_s = \eta\right)$ along the vertical axis (*y*-axis). While depicting heat maps, we presume three types of cost values, namely very cheap $\left(C_v = C_m = 0.1\right)$, average $\left(C_v = C_m = 0.5\right)$, and very expensive $\left(C_v = C_m = 0.9\right)$, for both these provisions. Also, we choose the disease spreading rates and recovery rates to be identical for either strain *i.e.*, $\beta_p = \beta_s = \beta = 0.75$ and $\gamma_p = \gamma_s = \beta = 0.3$. Varying the costs in two different directions (C_v in a row-wise direction and C_m in a column-wise direction), we design **Figures 19-21** to capture a more general idea about the evolutionary outcomes. Precisely speaking, this $\left(3\times 3\right)$ panel setting in terms of cost elucidates the threshold level of η, highlighting the working efficacy of self-protection as well the threshold level of e, which designates the success rate of vaccination. An in-depth analysis using **Figure 20**, we end up with the following information about the threshold level for η as well as e. First, we show the threshold level of η at the following conditions: 1) at a very cheap IDM price, self-protectors exist if $0.4 \le \eta \le 0.8$; 2) for an average IDM cost, self-protectors exist when $\eta > 0.6$; 3) if the price for IDM is very expensive, self-protectors do not exist for $0 \le \eta \le 1$. Likewise, we can determine the threshold level of e as below: 1) at a very cheap vaccine price, vaccinators exist as long as $e > 0.4$; for an average C_v, vaccinators survive when $e > 0.5$; 2) if C_v is quite expensive, vaccinators do not exist for $0 \le e \le 1$. The above classification suggests that an expensive intervention cost (e.g., $C_v = C_m = 0.9$) is not affordable for anybody living in the society; thus, no one takes either provision with that price. Our simulation results reveal that the transmission of primary disease stain can be better attenuated than secondary strain if the reliability of vaccine and IDM remains identical against each of the strains. **Figure 19** justify the extent of PDS is always lower than SDS. Thus, the SDS is principally accountable for epidemic emergence. Now, let us get back to the most averaged situation in terms of costs (see the central panel (a-5) of **Figures 19-21**) to capture the controllable epidemic regions triggered by multiple provisions marked with dotted boxes. The black dotted box illustrates the contribution coming from the self-protection strategy, while the red one represents the benefaction to the vaccination scheme in overall disease attenuation.

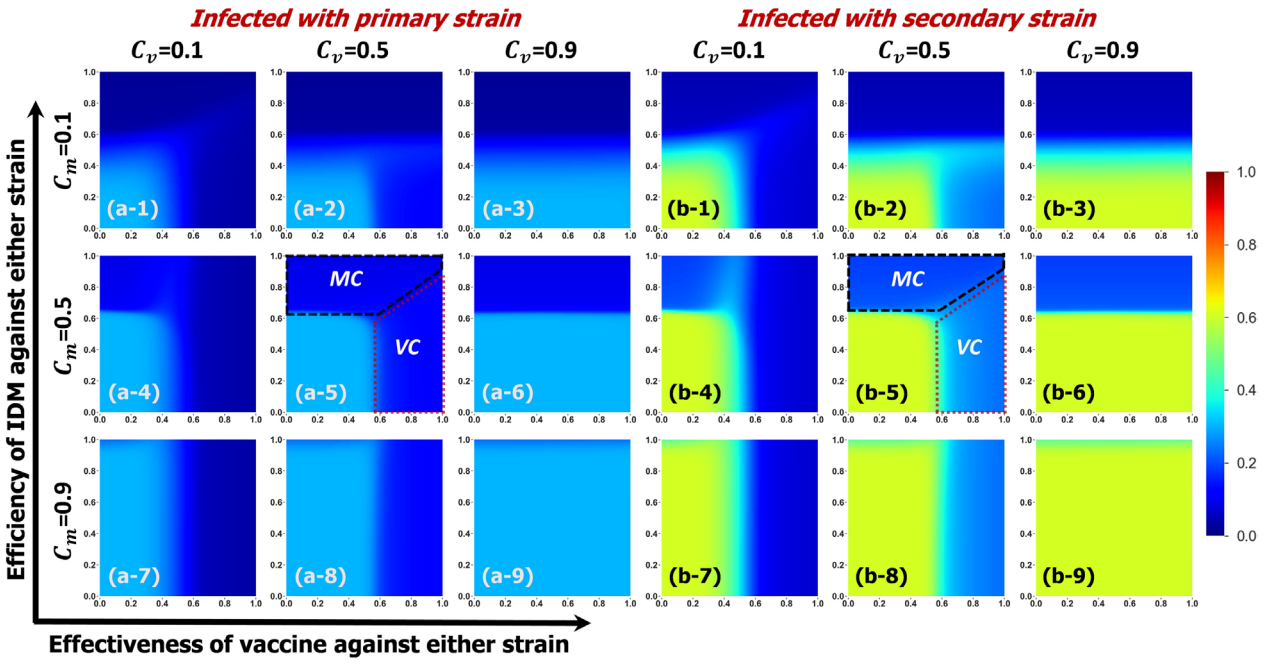

Figure 19. FES for primary disease strain (panels (a-*)) and secondary disease strain (panels (b-*)) presuming equal provisional efficacies: these two dimensional effectiveness of vaccine $\left(e_p = e_s = e\right)$ versus efficiency of IDM $\left(\eta_p = \eta_s = \eta\right)$ heat maps have been depicted assuming the disease spreading rates for primary and secondary strains being equal $\left(\beta_p = \beta_s = \beta = 0.75\right)$. Likewise, the recovery rates for both strains are kept as uniform $\gamma_p = \gamma_s = \gamma = 0.30$. Then, we vary the provisional costs for vaccination as well as IDM by putting them into three different categories as follows: (i) very cheap $\left(C_v = C_m = 0.1\right)$, (ii) average $\left(C_v = C_m = 0.5\right)$, and (iii) very expensive $\left(C_v = C_m = 0.9\right)$. For convenience, we take three different C_v in row-wise direction and C_m in column-wise direction employing SB-RA strategy updating rule.

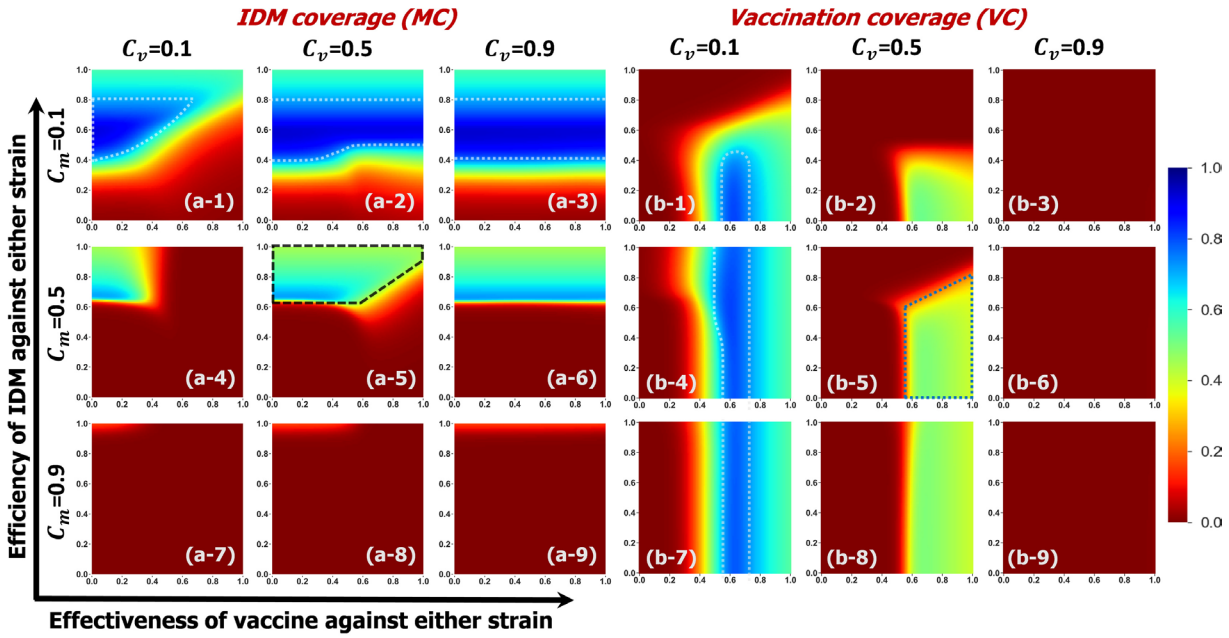

Figure 20. Self-protection coverage (panels (a-*)) and vaccination coverage (panels (b-*)) presuming equal provisional efficacies. An identical parametric setting has been considered as presumed in Figure 19.

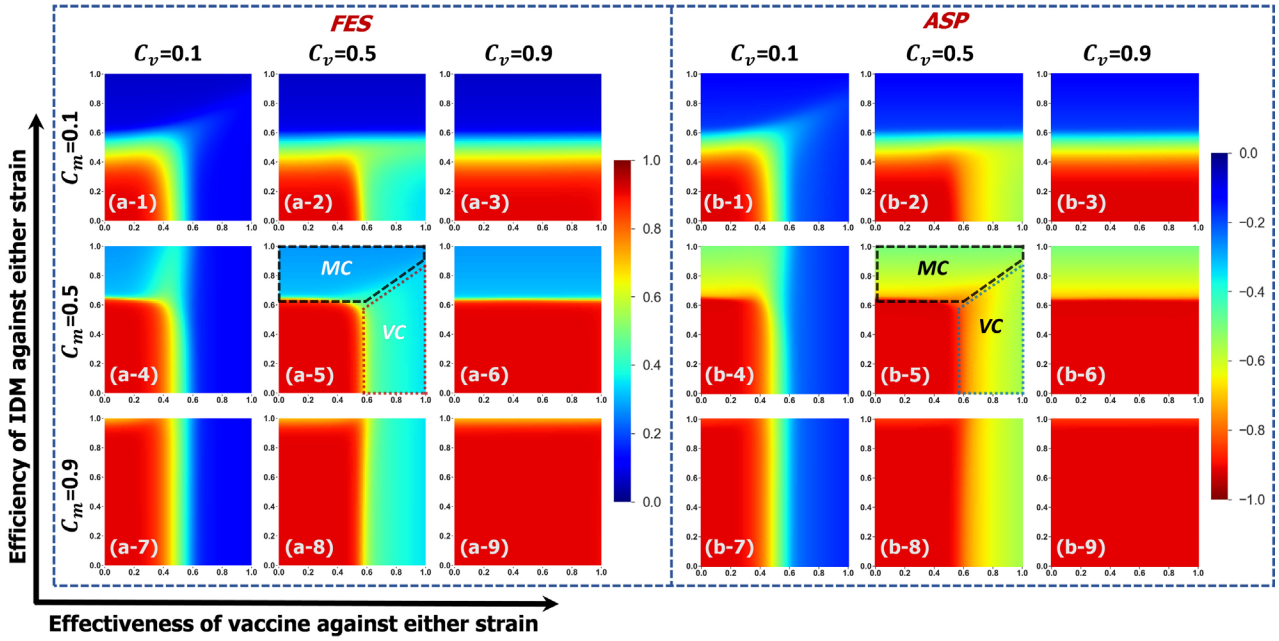

Figure 21. FES for both strains (panels (a-*)) and ASP (panels (b-*)) assuming equal provisional efficacies. An identical parametric setting has been considered as presumed in Figure 19.

Meanwhile, the remaining uncontrollable zone, which might also be termed as an endemic regime, is fully occupied with free-riders. The best performing zone for IDM at a lower price is represented by white dotted lines, whereas a mid-level contribution at an average price is marked with a black dotted box (see panels (a-1), (a-2), (a-3), and (a-5) of Figure 20). Similarly, the best working zone for vaccination at a cheaper price is labeled with white dotted lines, while the mid-level protection from the same strategy is depicted with blued dotted lines (panels (b-1), (b-4), (b-5), and (b-7) of Figure 20). Inevitably, Figure 21 draws one of the crucial findings of this study as it promptly justifies the reason why we firmly ask for dual health interventions in response to multi-strain epidemics. Considering an averaged parametric condition depicted in panel (a-5) of Figure 21, we probably get to know why taking dual provisions is essential in controlling the severity of epidemic spreading. In other words, it elucidates the necessity of introducing IDM besides vaccination to control the epidemic emergence triggered by multiple disease strains more effectively. Based on the total epidemic size, one could readily imagine the attained average social payoff for adopting an available provision at varying cost values (illustrated by Figure 21). Under this specific type of parametric setting, vaccination and self-protection can be treated as suitable pre-emptive provisions that combat equally against either strain in diminishing the severity of the epidemic at a considerably high level of satisfaction.

As the next step of further investigation, we will show how sensitive these efficacy parameters are at varying cost values to predict the evolutionary consequences. Now, we can have a clear image regarding the best-performing zone

triggered by a suitable efficacy parameter set-up that ensures a considerable oppression of the epidemic. In most cases, the range lies between 0.4 to 0.6. Here, we presume the effectiveness of vaccination, and the efficiency of IDM performs equally against either strain. At the same time, we focus on how much it varies depending upon human decision-making protocol. Setting 0.5 as the baseline average value for the two critically important system parameters e and η, our primary concern is to show how much impact does it bring when the efficacy level deviates slightly from its average value. Thus, we try with three different combinations of efficacy pair (e,η) to manifest all evolutionary outcomes using two distinct strategy updating rules. Figure 22 and Figure 23 illustrate the consequences when using IB-RA and SB-RA strategy updating rules, respectively. Irrespective of Figure 22 and Figure 23, first row (see panels (*-i)) stands for the efficacy pair (0.4, 0.6) that illustrates a situation when e drops down, and η increases a little bit from their standard level. Meanwhile, the second row (see

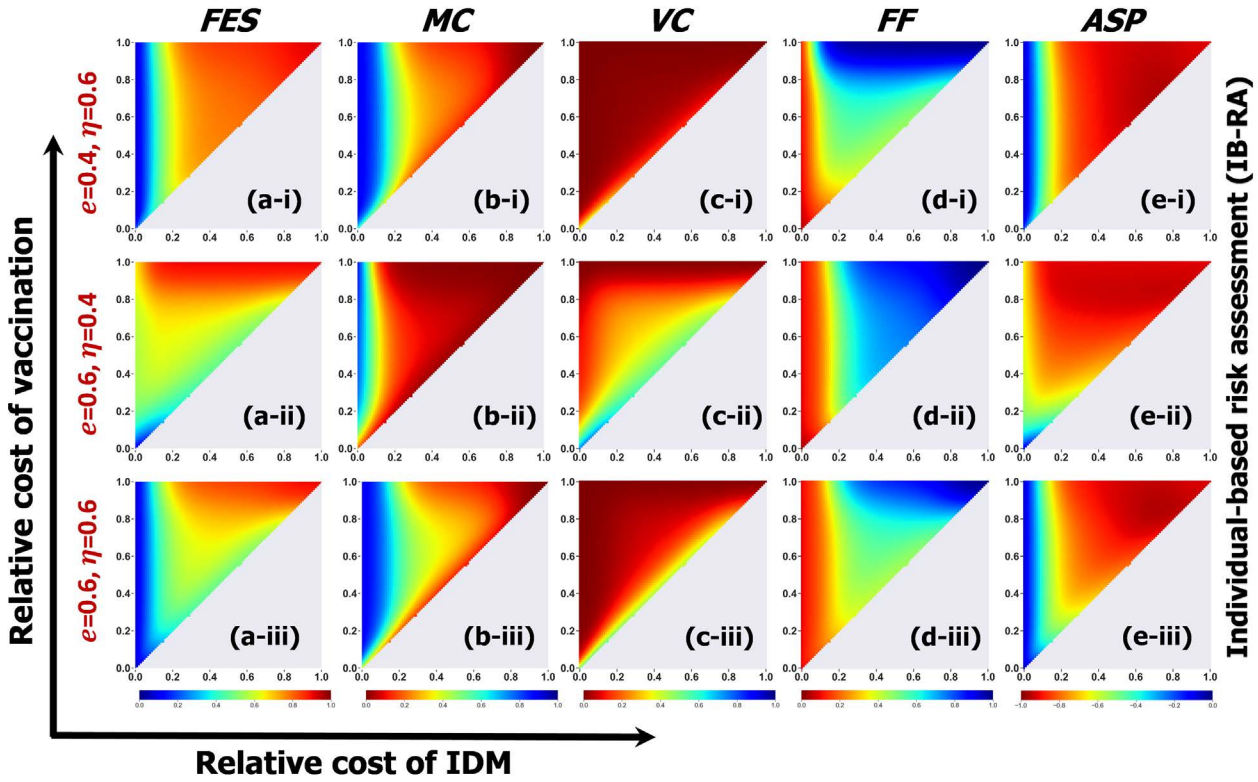

Figure 22. Summary of all evolutionary outcomes at a suitable pair of efficacy values (e,η) using IB-RA strategy updating rule: these C_m versus C_v heat maps depict a holistic evolutionary consequences within a single figure. Here, we present three crucially significant combinations of e and η values as follows: (i) first row (panels (*-i)) shows results where $e=0.4$ is below the average and $e=0.6$ is slightly higher than the average value, (ii) second row (panels (*-ii)) presents completely alternating situation of first row in terms of e and η values selection, and finally, (iii) third row (panels (*-iii)) is designed in such a way that both e and η can take values $(e=\eta=0.6)$ which is slightly above the average value (=0.5). For evolutionary process the values of the corresponding parameters are fixed as: $\beta_p=0.75, \beta_s=0.50, \eta_p=0.30, \eta_s=0.20$. Evolutionary outcomes like FES (depicted in panels (a-*)), MC (panels (b-*)), VC (panels (c-*)), FF (panels (d-*)), and ASP (panels (e-*)) have been displayed in a column-wise direction.

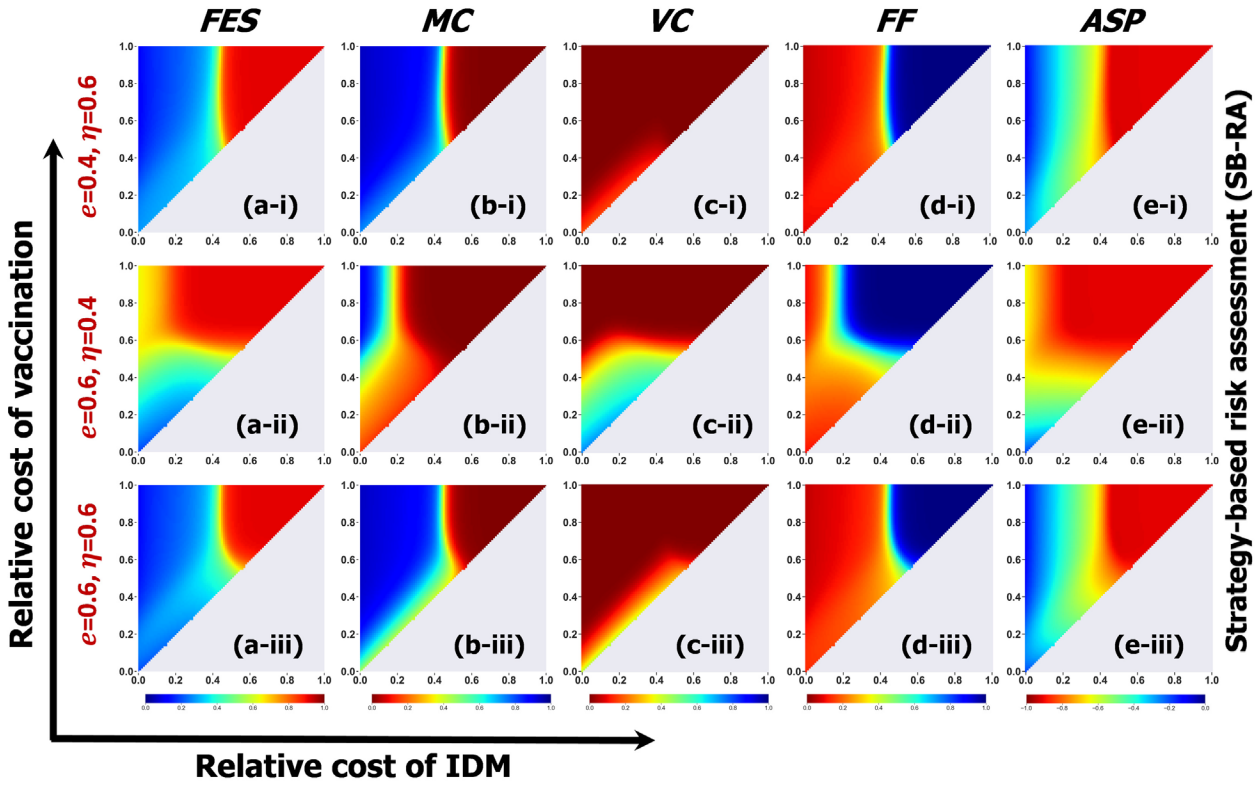

Figure 23. Representation of all evolutionary outcomes at a suitable pair of efficacy values (e,η) using SB-RA strategy updating rule: these C_m versus C_v heat maps expose precisely the same set of evolutionary consequences as **Figure 22** does but following a different imitation rule.

panels (*-ii)), that is designed for efficacy pair (0.6, 0.4), presents precisely the opposite scenario shown in the first row. Finally, the third row holds for the efficacy pair (0.6, 0.6), which explains the case when both the efficacy parameters increase a little (given in panels (*-iii)). When individuals rely on the IB-RA strategy updating rule (see **Figure 22**), the first row of self-protection cost versus vaccination cost heat maps shows a better contribution from IDM coverage than that of vaccination in controlling the FES. The ASP becomes higher at a meager IDM cost as both these provisions successfully kill out free-riders from that region. Analyzing the second row, we end up with an average level of disease attenuation due to the reduction of self-protectors. Although VC increases a bit, yet, too many free-riders make it challenging to control the spreading of disease. Thus, the ASP reduces down quite conceivably. Finally, the third row represents an almost analogous situation that we observe in the first row itself. Hence, boosting up IDM efficacy turns out to a better option than upgrading vaccine efficacy in restraining the FES. In other words, enhancing the reliability level of both provisions provides almost an equivalent protection against the epidemic outbreak, which can easily be secured by a sole improvement in IDM efficacy. As a whole, the parameter η seems to play a more sensitive role in oppressing the disease prevalence than the parameter e. We can confirm the points mentioned

above more prominently with the help of Figure 23, when the SB-RA strategy updating rule is implemented. Say, for example, a small deterioration in η value from its standard baseline value can significantly increase the FES (for illustration, see panels (a-ii) and (a-iii) in Figure 23). Similarly, from the second row of the same figure, we could see a notable raise of vaccinators (see panel (c-ii)) and free-riders (panel (d-ii)) compared to the first row. Since the MC reduces down so much (in panel (b-ii)), therefore, the system fails to ensure a better ASP (see panel (E-ii)) in comparison to the case mentioned in the first row of Figure 23.

Finally, we devote our efforts to investigating the epidemic threshold in terms of the basic reproduction number (BRN) corresponding to each disease strain. In Figure 24, we draw β_p versus β_s phase diagrams, fixing up the efficacies of vaccination and self-protection schemes against either strain. As suggested by the simulation results, DFE can be attained as long as the disease transmission rate of either strain remains relatively smaller. Besides that, the phase diagrams for the FES generated by both strains (a-*), BRN for respective strains (panels (b-*) and (c-*)), MC (d-*), and VC (e-*) simply provide us with a holistic idea of how and under which conditions the disease spreading can be fully oppressed, or the epidemic emergence can be eradicated from the population. Here, the DFE is marked with a white dotted rectangle (see panel (a-*)), and it is possible only when the BRN for both strains being strictly less than 1. Therefore, this parametric region can be paraphrased as no provision required (NPR) zone (shown in

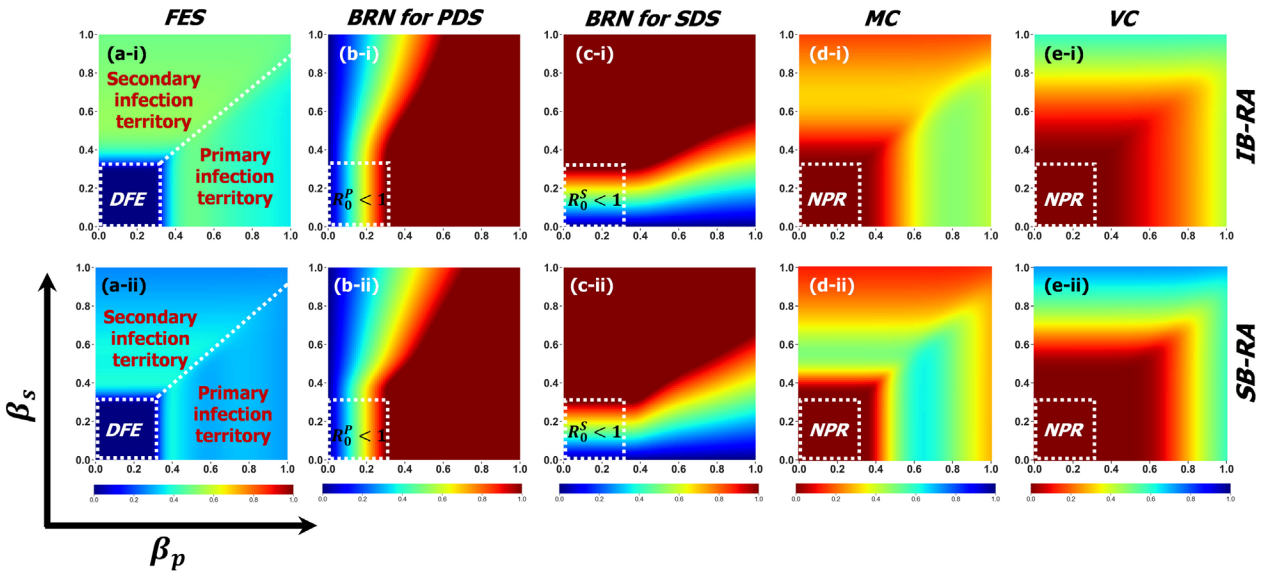

Figure 24. Exhibition of the epidemic threshold in terms of BRN corresponding to each strain relying on IB-RA (panels (*-i)) and SB-RA (panels (*-ii)) strategy updating rules: these β_p versus β_s heat maps confirms a DFE if transmission rate pair (β_p, β_s) remains relatively smaller (see panels (a-*)). The DFE (enclosed by white dotted box) emerges where the corresponding BRN for primary (b-*) and secondary (c-*) strains are strictly less than unity. Besides, disease prevalence posed by primary and secondary strains has been depicted in panels (a-*). Here, panels (d-*) render IDM coverage, meanwhile panels (e-*) show vaccination coverage. A white dotted box indicates the precinct where no pre-emptive provision is required (marked with NPR). Model parameters used here are: $e_p = 0.75, e_s = 0.50, \eta_p = 0.30, \eta_s = 0.20, C_v = 0.4, C_m = 0.3$.

panels (d-*), (e-*)). With the increase of disease spreading rate, responsible for either strain, DFE starts converting into an endemic equilibrium. That means only a partial remission of disease from that region is possible, which inevitably divides it into two infection territories depending upon the strain existing in that particular section. For convenience, we separate these two infection territories by a white dotted line depicted in **Figure 24(a-*)**.

4. Conclusion

In this study, we have implemented dual intervention techniques to oppress a two-strain epidemic model employing evolutionary game aspects. Our proposed scheme for single infection (immunity of infected individuals to the other strain) model included vaccination and self-protection as two distinct precautionary measures when a disease spreads by two independent strains considering an infinite and well-mixed population. We found that in a homogeneously well-mixed population, the infection risk for individuals depends mostly on the proportions of vaccinators and self-protectors due to the effect of herd immunity. Incorporating EGT into epidemiology, our theoretical analysis further investigated the complex interaction between the cost and efficacy of a particular provision and thereby label it as a reliable protective measure in terms of its capabilities to disease eradication. Under a wide variety of parametric settings, our model facilitates us with a comprehensive knowledge of picking the best suitable policy up amid a couple of alternatives from quantitative and qualitative viewpoints under given circumstances. Unless either provision being free of cost, primary strain remains more severe than a secondary strain as most of the individuals do not take any intervention. The presence of too many free riders makes the situation worse; therefore, a relatively higher efficacy for vaccination as well as IDM is requisite to bring back the reliability of these provisions among individuals. In other words, the situation may get even worse if the number of free riders increases considerably. Meanwhile, we also considered a specific rate of mutation taking place from primary to secondary strain. In such a situation, some fraction of individuals infected with primary strain converts to a secondary strain infected, which inevitably makes the primary strain somehow weaker than the secondary strain. Hence, the secondary strain is now believed to be the principal contributor to epidemic ubiquity. Coupling mean-field approximation with two different strategy updating rules, our model successfully addresses the necessity of dual provisional safety in terms of public health issues, which has never been used for a two-strain epidemic model employing a game-theoretic framework. Quantitatively and qualitatively, the same general tendency has been observed when the SB-RA rule has been implemented instead of IB-RA. Other than having a few discrepancies that were inherently coming from the substantial difference between these strategy updating protocols originating from the construction pattern of each protocol governed by pair-wise Fermi probability functions. Some of our previous works also drew a similar conclusion regarding the evolu-

tionary outcomes followed by either updating protocols [1] [23]. As far as average efficacy and cost values for each provision are concerned, vaccination outperforms self-protection as a strategy when IB-RA strategy updating rule is used and vice-versa while the strategy updating rule is SB-RA. In sum, our findings suggest that any disease-control policy should be handled with extreme care as its success mostly depends on the complex interplay among the intrinsic mathematical rules of epidemic spreading, regulatory schemes, and, more importantly, individuals' behavioral responses. Indeed, infectious diseases are likely to have been with humans for our entire existence. Although various strategies to prevent flu-like diseases have been developed, there is still a long way to go in order to eradicate these diseases completely from human societies. Unlike some previous works, our model does not consider any structured population; rather, it relies on a mean-field approximation, which seems somewhat idealized. Nevertheless, in reality, individuals living in society are connected through several types of social networks, each having a different structure. Those previous studies heavily relied on a multi-agent simulation (MAS) approach, while our study is conducted through the theoretical approach. Henceforth, it would be fascinating to explore our proposed model under a structured population. Besides that, addressing some other realistic features like superinfection, cross-immunity, forced control policies (quarantine or isolation) [60], late vaccination, mandatory or subsidized vaccination policy as a middle course control provision would help our model being a comprehensive mechanism for disease anticipation.

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Conflicts of Interest

We declare that we have no competing interests.

Authors' Contribution

M. A. developed the model, carried out the numerical simulations to validate the proposed model, analyzed the model outcomes, drafted the original manuscript, and critically revised the manuscript. J. T. helped organizing the study, coordinated the study, and guided reviewing the manuscript. Both authors gave final approval for publication and agree to be held accountable for the work performed herein.

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