Stability analysis of an epidemic model with two competing variants and cross-infections

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Stability analysis of an epidemic model with two competing variants and cross-infections

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Abstract:	The competition between pathogens is an essential issue in epidemiology. As the COVID-19 pandemic persists, new variants mutate resulting in further waves of infections. In this work, we propose a simple two-variant susceptible-infected-removed-susceptible (SIRS) model for studying the competitive epidemic processes. We obtain the global basic reproduction number of our proposed model and show that whether the epidemic persists or diminishes depends on the more contagious of the two variants. Furthermore, by studying the stability of the endemic equilibria, given a specific choice of parameters, we can predict whether either variant will eventually dominate the competitive epidemic process, or if both variants will persist. Numerical results show that periodic solutions become viable if the two variants' cross-infectivities are unequal, i.e., recovery from one variant offers unequal protection against the other. In other words, reducing the infectivity of a variant via non-pharmaceutical interventions

	may trigger periodic or even chaotic behavior and paradoxically cause healthcare demand to increase. Note that our model is sufficiently general so as to be used for studying competitive behavior in other areas of science.
Response to Reviewers:	Response to Reviewers' Comments Manuscript Number: NODY-D-23-00815 Original Title: A competitive epidemic model of two variants Revised Title: Stability analysis of an epidemic model with two competing variants and cross-infections Dear Editor, We hereby submit a revised version of the above-mentioned manuscript previously submitted to Nonlinear Dynamics. The changes in the revised manuscript are highlighted. We would like to express our thanks to the reviewers for their efforts to provide thorough and helpful reviews. According to the reviewers' comments, we have substantially changed the revised paper. In. particular, we found sufficient conditions where two variants coexist. In addition to sufficient conditions in the original manuscript for the existence and stability in which only the new variant remains, we now have a more complete theoretical result in the revised manuscript. Furthermore, we reduce the redundant results and make the manuscript more focused on the stability analysis. The periodical solutions in numerical experiments show more unrevealed mysteries in such systems. We will continue our study to analyze those interesting phenomena in our future work. In the following, we address each of the reviewers' comments and provide detailed responses. The originality of this paper is evident and significant. Therefore, our paper has immense potential in the field of epidemiology. We hope you find the revised manuscript worthy of publication in Nonlinear Dynamics. Best regards, Eric W. M. Wong for all authors Reviewers' comments: Reviewer #1: 1.The article deals with the mathematical modeling of the spread of two virus variants. The topic is relevant. The authors proved stability of equilibrium points. The authors did numerical simulations and studied different scenarios. The presentation must be improved. Response: We greatly appreciate your acknowledgment of our manuscript. We have thoroughly reviewed and implemented all of the suggestions you provided in order to improve the quality of our work. Thank you for your valuable input and we hope that you will find the revised manuscript to be satisfactory. 2.The introduction needs to be improved. There are some references to works that study the two variants scenarios that have not included. More detailed results about two variants would help the readers to grasp the novelty of this work. Response: We appreciate your diligent scrutiny of our manuscript. As per your suggestions, we have incorporated additional related works in the introductory section and have presented a more comprehensive analysis in Section 3. We hope that these revisions have addressed any concerns you may have had and have enhanced the overall quality of our work. Thank you for taking the time to review our paper. The main changes are as follows: 1.In the introduction, we included a paragraph to introduce other works that are based on two variant models. "There have been many research publications on the competition dynamics between two or more disease variants. An early example of such work is [24] (published in 1991), which proposed a simple two-variant SI model with cell division and deaths, but no recovery. Reference [25] presented a convergence and equilibria analysis of two

viruses spreading across the same populations with different network structures. In the case of homogeneous parameters, cases were presented with both a finite number of equilibria and an infinite number of equilibria along a line. In [26], a two-layer network model was proposed in which each layer represented the spreading dynamics of the corresponding virus, such that the two layers share the same nodes (representing individuals) but may have different edges and/or edge weights (representing transmission rates between individuals). Generic infection rates were also considered in [26], i.e., the generic model includes the linear model and ones with nonlinear infection rates. An analysis of competitive spreading via directed infection graphs in the SIS model is presented in [27], along with an analysis of equilibria under different infection rate parameter conditions. References [28] and [29] considered a competitive epidemic process in a two-layer network to find the optimal allocation of control resources, yielding necessary and sufficient conditions for the mean-field approximation of a selected epidemic process to be stabilized to extinction exponentially."
"[24] Nowak, M.: The evolution of viruses. competition between horizontal and vertical transmission of mobile genes. Journal of theoretical biology 150(3), 339–347 (1991)
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[28] Watkins, N.J., Nowzari, C., Preciado, V.M., Pappas, G.J.: Optimal resource allocation for competing epidemics over arbitrary networks. In: 2015 American Control Conference (ACC), pp. 1381–1386 (2015). IEEE
[29] Watkins, N.J., Nowzari, C., Preciado, V.M., Pappas, G.J.: Optimal resource allocation for competitive spreading processes on bilayer networks. IEEE Transactions on Control of Network Systems 5(1), 298–307 (2016)"
2.We have made some updates to our document. Firstly, on page 13, we have included additional information to Theorem 2 to provide a stable condition for Variant-1-only EE. Additionally, we have included Section 3.3, which analyzes the coexisting EE for both variants and presents Theorem 3 to summarize the overall result.
3.The novelty of this work is discussed on page 5."…… we consider the effect of mutation, whereby infections of the first variant transform into infections of the second variant at a given (usually low) rate. As a result, infections of the second variant may emerge in our model even if the initial state contains only infections of the first variant. The ability of the new variant to infect individuals recovered from the first variant is known as immune escape and is a key mechanism in the development of new disease strains."
"In particular, we find a set of sufficient conditions for the existence and stability of the EE in which only the new variant remains and the one where two variants coexist."

3.The model needs further explanation. For instance, there is waning of immunity for R1 and R2, but not for people in P. Notice that people from R1 can go to S and from there can get variant 1 or 2.
Response:
I appreciate your helpful suggestions. Just to clarify, in Figure 1, the arrow points from P to S, indicating a decrease in P immunity.

4.It seems from Theorem 1 that only one endemic equilibrium point exists. From Fig 2 it is clear that there is co-existence. The results needs much better explanation. Can variant 2 disappear and variant 1 become endemic? No theorem for this situation?
Response:
We have taken your valuable feedback into consideration and have made significant modifications to address your concerns. In Section 3, we have included detailed analyses to offer a thorough comprehension of the subject matter. Specifically, on page 12, we have supplemented Theorem 2 to provide a stable condition for Variant-1-only EE. Additionally, we have added Section 3.3 to analyze the coexisting EE for both variants and have presented Theorem 3 to summarize the outcome. As per Theorem 2, Variant 2 can vanish, and Variant 1 can become endemic. We hope that these

revisions meet your expectations, and we appreciate your time and efforts in reviewing our work.

5.The discussion needs improvements. Discuss better, when periodic solutions are obtained. When chaos may occur. A summary Table would be very helpful.
Response:
Thank you for your helpful suggestions. We have made revisions to the discussion section and included a summary table of our findings. The key modifications are outlined below.
1.We have added the following contents to page 24, “In Section 3, we investigated the stability of the model's disease-free equilibrium (DFE), generated sufficient conditions under which a single Variant endemic equilibrium (EE) is locally asymptotically stable, and gave the sufficient conditions under which both variants endemic equilibrium (EE) is globally asymptotically stable.”
2.More content has been added to page 25, “Notably, the existence of periodic or chaotic behavior in our epidemic model means that a decrease in active cases does not necessarily signal the end of an epidemic. Additionally, reducing the infectivity of a variant by implementing non-pharmaceutical interventions can potentially cause such periodic or even chaotic behavior to emerge, paradoxically increasing healthcare demand. Therefore, governments and other policymakers must be careful when introducing epidemic prevention policies.”
3.We have included a summary table on page 9 that outlines our main findings.
“In this section, we prove that conditions can be found where neither, either, or both variants exist in a stable equilibrium. These equilibria and their conditions are summarized in Table 2 and described in detail below.”

6.Mention limitations of this study. For instance, no vaccination included.
Response:
We appreciate the reviewer's kind comments and have made the necessary revisions to the introduction. The main changes can be found on page 25.
“Our work also has some limitations, most notably, the lack of investigations of the impact of vaccination and the data study on COVID-19 or other infectious diseases. Furthermore, theoretical analysis of periodical results is not included due to the difficulty and space limitations. Regarding the model, it is only capable of handling scenarios involving two viruses, rather than multiple viruses. This forms part of our future work.”
Reviewer #3:
The results listed in the paper in the form of formulas, figures, and analysis seems true and correct. The paper is well written and it is written in a truly sporty manner. English is generally good, I think it needs to be polished further and some typos need to be revised. Further punctuation marks should be checking through the paper, especially after the equations and at the end of the statements.

* Remark, comments, and questions:

Title of paper is not clear. Try to clear meaning of the title. The abstract is a little thin and does not quite convey the vibrancy of the findings and the depth of the main conclusions. The authors should please extend this somewhat for a better first impression. The manuscript lacks motivation. Author needs to include the motivation of the study. Authors should write keywords in professional way.

Response:
Thank you for taking the time to process the submission of our original paper. We have made accordingly amendments to the paper.
1.We have changed the title to, “Stability analysis of an epidemic model with two competing variants and cross-infections”
2.We have made the following modification in the abstract, “The competition between pathogens is an essential issue in epidemiology. As the COVID-19 pandemic persists, new variants mutate resulting in further waves of infections. In this work, we propose a simple two-variant susceptible-infected-removed-susceptible (SIRS) model for studying the competitive epidemic processes. We obtain the global basic reproduction number of our proposed model and show that whether the epidemic persists or diminishes depends on the more contagious of the two variants. Furthermore, by studying the stability of the endemic equilibria, given a specific choice of parameters, we can predict

whether either variant will eventually dominate the competitive epidemic process, or if both variants will persist. Numerical results show that periodic solutions become viable when the two variants' cross-infectivities are unequal, i.e., recovery from one variant offers unequal protection against the other. In other words, reducing the infectivity of a variant via non-pharmaceutical interventions may trigger periodic or even chaotic behavior and paradoxically cause healthcare demand to increase. Note that our model is sufficiently general so as to be used for studying competitive behavior in other areas of science."
3.We have emphasized the motivation on page 4, "The current situation of coexisting Omicron subvariants, without a single dominant COVID-19 strain, requires new models and methodologies to capture the behavior of multiple competing viral strains."

There is already an abundance of modeling studies on COVID-19, vaccinations, and the months or years to come. However, apart from Ferguson's (now classic) work, Moore and Giordano, very little is said about similar modeling works. This is an issue for three reasons. First, the intended audience for such pieces is made of policy-makers and the general public: they are already facing an abundance of (occasionally conflicting) findings from models. If there is no attempt to contextualize the findings from this piece among others, then we're more likely to be adding noise to a crowded space, instead of providing valuable guidance. Second, several of the modeling assumptions made here may be in line with other pieces (which may provide some strength to the methods) or may be rather unique (which may need more discussion). Finally, as a piece of scientific literature, the contributions should be situated based on what already exists. In sum, the authors should explain how each of their assumptions and modeling choices compares to the literature; how their findings compare to the literature; and hence what is their specific contribution. Related models include, but are not limited to:
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--arXiv:2005.06286v2

--https://urldefense.com/v3/__https://www.researchsquare.com/article/rs-872671/v1__;!!KjDnqvtInNPT!h-wDV22Y0qyU7lX1YXxJh0p-dRqdwd5rGDhPDEg8NrQbIFtB8_6dnhTZHSPW45asH9xFdZaCOQyP9AdsNcuh$

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dRqdwd5rGDhPDEg8NrQbIFtB8_6dnhTZHSPW45asH9xFdZaCOQyP9GlARl6n$
Response:
Thank you for your thoughtful suggestions. We have incorporated more relevant works into the introduction of our paper. Additionally, we would like to clarify that our paper addresses not only COVID-19 but also provides a comprehensive solution for managing competitive epidemic processes. Please find below the main changes that have been made:
“The COVID-19 pandemic has resulted in a massive increase in epidemiological research publications and preprints, with an early 2022 study finding nearly 10 thousand published COVID-19 papers solely within first-quartile General and Internal Medicine journals, according to ClarvariateTM [17– 20].”
“[17] Cosentino, N., Marenzi, G., Chiesa, M.: The impact of COVID-19 pandemic on scientific research: an upcoming new wave? Journal of General Internal Medicine 37(10), 2553–2555 (2022). https://doi.org/10.1007/ s11606-022-07647-6
[18] Khajanchi, S., Sarkar, K.: Forecasting the daily and cumulative number of cases for the covid-19 pandemic in india. Chaos: An interdisciplinary journal of nonlinear science 30(7) (2020)
[19] Samui, P., Mondal, J., Khajanchi, S.: A mathematical model for covid-19 transmission dynamics with a case study of india. Chaos, Solitons & Fractals 140, 110173 (2020)
[20] Mondal, J., Khajanchi, S.: Mathematical modeling and optimal intervention strategies of the covid-19 outbreak. Nonlinear Dynamics 109(1), 177–202 (2022)”
Some other questions:

1.Is there any experimental data to validate the mathematical model? The authors at least describe the basic reproduction number R_0 and its impact on covid-19 pandemic. The basic reproduction number R_0 is one of the most crucial quantities in infectious diseases, as R_0 measures how contagious a disease is. In this context the authors include the reference "Mathematical analysis of the global dynamics of a HTLV-I infection model, considering the role of cytotoxic T-lymphocytes, Math. Comput. Simul. 180(2021) 354-378", "Dynamics of an HTLV-I infection model with delayed CTLs immune response, Appl Math Comput 2022"
Response:
Thank you for taking the time to carefully read our manuscript. In Section 4, we conducted a significant number of numerical experiments and validated the theoretical results presented in Section 3. However, we plan to extend our research in future work and include studies on real data analysis. The main changes we have made are as follows:
We made some updates to our report on page 12. Specifically, we added information about the stable condition for Variant-1-only EE in Theorem 2. Additionally, we included a new section, 3.3, which analyzes the coexisting EE for both variants and presents a summary of the findings in Theorem 3.

2.Authors should insert all figures in appropriate places.
Response:
Thank you for your valuable suggestions. We have made the necessary changes to the figures as per your recommendations.

3.Conclusion should be written in a more clear way. So try to short it and write in a professional way.
Response:
Thank you for your suggestions. We have taken them into consideration and made some adjustments to the conclusion. The main changes are as follows:
“This paper studied a competitive epidemic process with two variants based on the susceptible-infected-removed-susceptible (SIRS) model. The global basic reproduction number R_0 was derived, demonstrating that the more contagious variant of the two determined the threshold of whether the epidemic would persist or fade. Furthermore, by studying the stability of the endemic equilibrium, we obtain the conditions under which the newly introduced variant may completely replace the original variant. Based on theoretical and numerical results, we can predict which variant (or both) will survive the long-term evolution of the epidemic. We also performed numerical analysis on the effect of different first- and cross-exposure infectivities on the evolution of the epidemic model and demonstrated that periodic or chaotic behavior can emerge in some cases, especially when the cross-exposure infectivities of the two variants are unequal.

	Finally, note that our proposed model is general enough to be applied to fields beyond infectious disease epidemiology in future work." 4.Analysis is missing in paper so add it. Response: We appreciate the reviewer's kind remarks and have included additional analysis in Section 3. 5.Authors should improve the English of paper. Response: We appreciate your kind suggestions and we have amended the manuscript accordingly. 6.Authors should correct grammatical error at few stage of paper. Response: Thank you for your thoughtful suggestions. We have made the necessary changes to the manuscript based on your input. 7.Presentation of paper should be improved. Response: We greatly appreciate your valuable suggestions. After carefully reviewing the manuscript, we have implemented some adjustments based on your feedback. We have streamlined certain sections and refined the discussion portion accordingly. Thank you again for your insightful comments. The key modifications are outlined below. 4.We have added the following contents to page 24, "In Section 3, we investigated the stability of the model's disease-free equilibrium (DFE), generated sufficient conditions under which a single Variant endemic equilibrium (EE) is locally asymptotically stable, and gave the sufficient conditions under which both variants endemic equilibrium (EE) is globally asymptotically stable." 5.More content has been added to page 25, "Notably, the existence of periodic or chaotic behavior in our epidemic model means that a decrease in active cases does not necessarily signal the end of an epidemic. Additionally, reducing the infectivity of a variant by implementing non-pharmaceutical interventions can potentially cause such periodic or even chaotic behavior to emerge, paradoxically increasing healthcare demand. Therefore, governments and other policymakers must be careful when introducing epidemic prevention policies." 6.We have included a summary table on page 9 that outlines our main findings. "In this section, we prove that conditions can be found where neither, either, or both variants exist in a stable equilibrium. These equilibria and their conditions are summarized in Table 2 and described in detail below." 8.Try to reduce similarity of work. Response: Thank you for your helpful suggestions. We have taken them into consideration and removed some similar search results accordingly. 9.References list are not appropriate. Respond: We appreciate your kind suggestions and we have updated the references as required. "[18] Khajanchi, S., Sarkar, K.: Forecasting the daily and cumulative number of cases for. the covid-19 pandemic in india. Chaos: An interdisciplinary journal of nonlinear science 30(7) (2020) [19] Samui, P., Mondal, J., Khajanchi, S.: A mathematical model for covid-19 transmission. dynamics with a case study of india. Chaos, Solitons & Fractals 140, 110173 (2020) [20] Mondal, J., Khajanchi, S.: Mathematical modeling and optimal intervention strategies. of the covid-19 outbreak. Nonlinear Dynamics 109(1), 177–202 (2022)"
Order of Authors (with Contributor Roles):	Ruiwu Niu (Conceptualization: Lead; Formal analysis: Lead; Methodology: Lead; Software: Lead; Visualization: Lead; Writing – original draft: Lead)
	Yin-Chi Chan (Visualization: Supporting; Writing – original draft: Supporting; Writing – review & editing: Supporting)

	Simin Liu (Formal analysis: Supporting; Writing – original draft: Supporting; Writing – review & editing: Supporting)
	Eric W. M. Wong (Supervision: Lead; Writing – review & editing: Supporting)
	Michael Antonie van Wyk (Conceptualization: Supporting; Formal analysis: Supporting; Methodology: Supporting; Supervision: Supporting; Writing – review & editing: Supporting)

Stability analysis of an epidemic model with two competing variants and cross-infections

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Abstract

The competition between pathogens is an essential issue in epidemiology. As the COVID-19 pandemic persists, new variants mutate resulting in further waves of infections. In this work, we propose a simple two-variant susceptible-infected-removed-susceptible (SIRS) model for studying the competitive epidemic processes. We obtain the global basic reproduction number of our proposed model and show that whether the epidemic persists or diminishes depends on the more contagious of the two variants. Furthermore, by studying the stability of the endemic equilibria, given a specific choice of parameters, we can predict whether either variant will eventually dominate the competitive epidemic process, or if both variants will persist. Numerical results show that periodic solutions become viable if the two variants' cross-infectivities are unequal, i.e., recovery from one variant offers unequal protection against the other. In other words, reducing the infectivity of a variant via non-pharmaceutical interventions may trigger periodic or even chaotic behavior and paradoxically cause healthcare demand to increase. Note that our model is sufficiently general so as to be used for studying competitive behavior in other areas of science.

Keywords: competitive epidemic process, compartmental model, epidemiology, COVID-19

1 Introduction

After three years since the start of the COVID-19 pandemic, caused by the SARS-CoV-2 virus, the disease is widely expected to become endemic [1, 2]. New variants of the virus have become less pathogenic, while the proportion of asymptomatic cases has increased [1]. In particular, the Omicron variant of SARS-CoV-2 is associated with higher infectivity but lower disease severity compared to the Delta variant, with a lower in-hospital mortality rate despite high-risk groups, e.g., the elderly, forming a higher proportion of admissions [3].

However, the risk of new COVID-19 variants with increased lethality remains, due to continuing viral mutation. Therefore, the epidemiological study of such competing disease variants is essential to predict the future evolutionary behavior of COVID-19 and potential future epidemics. Furthermore, a general model of competitive evolution may have additional potential applications within and beyond epidemiology, e.g., the spreading of information/disinformation [4, 5], sentiment, and malware [6].

1.1 Early studies

Ross [7] first developed the concept of thresholds for disease transmission based on mathematical models of malaria transmission between humans and mosquitoes. The methodology was further developed in [8–10] in collaboration with Hudson. Subsequently, Kermack and McKendrick [11] developed the susceptible-infected-removed (SIR) compartmental model, forming the foundation for modern models of infectious diseases. In the SIR model, it is assumed that recovered individuals obtain permanent immunity from re-infection; later, the SIS and SIRS models were proposed for the cases where recovery provides no immunity and time-limited immunity, respectively. Another related

model is the susceptible-exposed-infected-recovered (SEIR) model [12], where exposed individuals undergo a latent period before becoming infectious.

Associated with epidemiological models is the concept of the *basic reproduction number* R_0, representing the expected number of secondary infections caused by an infectious individual in a fully susceptible population. This concept was formally introduced and coined by MacDonald in [13] where it was recognized that an R_0 value below one indicates a disappearing disease whereas a value above one indicates a persisting disease. Hethcote [12] later proved that for an SIRS model with a basic reproduction number greater than one, the proportion of individuals in each compartment eventually reaches an equilibrium.

Notably, R_0 is a function of the disease and of human behavior, and can therefore be reduced via (for example) social distancing measures [14]. Surveys on the taxonomy and stability analysis of compartmental epidemiological models include [12, 15].

1.2 Related work

The COVID-19 pandemic has resulted in a massive increase in epidemiological research publications and preprints, with an early 2022 study finding nearly 10 thousand published COVID-19 papers solely within first-quartile General and Internal Medicine journals, according to Clarvariate™ [16–19]. One compartmental model developed for the study of COVID-19 is a susceptible-exposed-infected-hospitalized-removed (SEIHR) model [20]. This SEIHR model was shown to accurately model the third wave of the COVID-19 outbreak in Hong Kong and other regions. A stochastic version of the SEIHR model was subsequently proposed, while the effect of vaccination

was incorporated into the model, yielding a susceptible-vaccinated-exposed-infected-hospitalized-removed (SVEIHR) model [21]. As of the beginning of August 2023, the most prevalent variants of COVID-19 in the United States are EG.5 and XBB.1.16, with no variant exceeding 25 % of all sequenced cases [22]. The current situation of coexisting Omicron subvariants, without a single dominant COVID-19 strain, requires new models and methodologies to capture the behavior of multiple competing viral strains.

There have been many research publications on the competition dynamics between two or more disease variants. An early example of such work is [23] (published in 1991), which proposed a simple two-variant SI model with cell division and deaths, but no recovery. Reference [24] presented a convergence and equilibria analysis of two viruses spreading across the same populations with different network structures. In the case of homogeneous parameters, cases were presented with both a finite number of equilibria and an infinite number of equilibria along a line. In [25], a two-layer network model was proposed in which each layer represented the spreading dynamics of the corresponding virus, such that the two layers share the same nodes (representing individuals) but may have different edges and/or edge weights (representing transmission rates between individuals). Generic infection rates were also considered in [25], i.e., the generic model includes the linear model and ones with nonlinear infection rates. An analysis of competitive spreading via directed infection graphs in the SIS model is presented in [26], along with an analysis of equilibria under different infection rate parameter conditions. References [27] and [28] considered a competitive epidemic process in a two-layer network to find the optimal allocation of control resources, yielding necessary and sufficient conditions for the mean-field approximation of a selected epidemic process to be stabilized to extinction exponentially.

1.3 Contributions of this study

This paper considers a version of the SIRS model with two competing variants. We assume that individuals can be only infected by one variant of the disease at a time; however, individuals having recovered from one disease variant remain susceptible to the other variant. Unlike existing compartmental models with two variants [23–26], we consider the effect of mutation, whereby infections of the first variant transform into infections of the second variant at a given (usually low) rate. As a result, infections of the second variant may emerge in our model even if the initial state contains only infections of the first variant. The ability of the new variant to infect individuals recovered from the first variant is known as *immune escape* and is a key mechanism in the development of new disease strains.

Next, we analyze the stability of disease-free (DFE) and endemic (EE) equilibria of our proposed model and derive an expression for the global basic reproduction number. In particular, we find a set of sufficient conditions for the existence and stability of EEs in which only the new variant remains and ones where two variants coexist. This enables us to predict, for a given set of model parameters, whether both variants of the disease will die out, only the new variant will persist, or both variants will coexist.

Subsequently, we present a number of numerical analyses of our proposed model under various conditions. Of particular interest is the effect of first-exposure versus cross-exposure infectivity on the competitive epidemic process. Numerical results demonstrate that under certain conditions, the proportion of each variant among the active cases of the epidemic may exhibit oscillatory behavior. It has previously been shown that under certain conditions, competition between two viral strains can lead to oscillatory behavior [29, 30]. The

ability to predict such oscillatory behavior will allow hospitals to prepare for the resultant surges in healthcare demand.

2 Model Formulation

To study the competitive epidemic process of two variants, we assume that each variant alone follows the evolutionary rules of the standard SIRS model. This assumption will simplify the formulation of our combined model. Consider an open system with a natural birth rate of b and a per-capita natural death rate of d. We shall assume that the birth rate is constant and thus independent of the population size. Let Variant 1 be the original variant in the system. During the epidemic process, infections of Variant 1 will mutate into infections of a new variant, namely Variant 2, with rate m. Subsequently, both variants will compete with each other in the epidemic process.

We define "**first**" infections to mean infections in fully susceptible individuals with no immunity to either variant of the disease, i.e. either they were never previously infected or any immunity gained previously has been lost. Additionally, we shall use the term **cross**-infections to denote the case where an individual with immunity to one disease variant is infected by the other variant. Our model thus contains the following compartments:

- Fully susceptible (S)
- First-exposure infected by Variant i (I_i), $i \in \{1, 2\}$
- Recovered with temporary immunity against Variant i (R_i), $i \in \{1, 2\}$
- Recovered with temporary immunity against Variant j, then cross-infected by Variant i (I_i^*), $i \in \{1, 2\}$, $i \neq j$
- Recovered with temporary immunity against both variants (P)

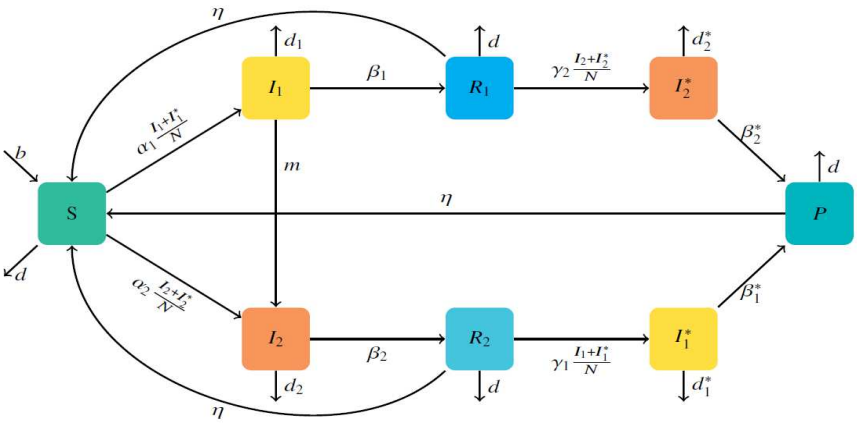


Fig. 1: Flowchart of the competitive epidemic model with two variants.

Table 1: Definition of parameters in the competitive epidemic model shown in Figure 1. All rates are per-capita except for b.

Parameter	Definition
b	Natural birth rate
d	Natural death rate
m	Mutation rate from Variant 1 to Variant 2
α_i	First-exposure infection rate of Variant i for fully susceptible individuals, $i \in \{1, 2\}$
γ_i	Cross-exposure infection rate of Variant i for individuals recovered from the other variant, $i \in \{1, 2\}$
β_i	Recovery rate for individuals infected by Variant i (first-exposure), $i \in \{1, 2\}$
β_i^*	Recovery rate for individuals infected by Variant i (cross-exposure), $i \in \{1, 2\}$
d_i	Mortality rate for individuals infected by Variant i (first-exposure), $i \in \{1, 2\}$
d_i^*	Mortality rate for individuals infected by Variant i (cross-exposure), $i \in \{1, 2\}$
η	Rate at which recovery-based immunity is lost

The state of super-infection (simultaneous infection by both variants) has been deliberately excluded from the model to keep its complexity low while still being able to capture the key dynamical aspects of interest.

Figure 1 shows the flowchart of the competitive epidemic model, while Table 1 lists the definitions of the model parameters. At time $t = 0$, only Variant 1 exists. Individuals in compartment S have no immunity to any variant and are infected by Variant 1 at rate $\alpha_1 \frac{I_1+I_1^*}{N}$ and thus move to compartment I_1. In compartment I_1, infections of Variant 1 have a chance to mutate and become infections of Variant 2, thus entering compartment I_2, with a rate of m. Usually, m is a very small value. At the same time, individuals in compartment I_1 recover and move to compartment R_1 at rate β_1, or become deceased and leave the system at rate d_1. In compartment R_1, individuals lose immunity with rate η and return to compartment S, or become infected with Variant 2 at rate $\gamma_2 \frac{I_2+I_2^*}{N}$ and enter compartment I_2^*, or die at rate d. Individuals in compartment I_2^* recover at rate β_2^* and enter compartment P, or die at rate d_2^*. Individuals in compartment P lose immunity at rate η and return to compartment S, or die at rate d. Finally, the list of possible transitions involving Variant 2 (bottom half of Fig. 1) as the initial infection is similar to that involving Variant 1 as the initial infection (top half).

The transitions $S \to I_1$ and $S \to I_2$ are associated with **first-exposure** infections, while the transitions $R_1 \to I_2^*$ and $R_2 \to I_1^*$ are associated with **cross-infections**. We define cross-protective immunity or **cross-immunity** as the protection against a given variant gained via past exposure to its rival variant. We will consider positive, zero, and negative cross-immunity in this paper, where recovery from one variant leads to decreased, unchanged, or increased susceptibility to the other variant, respectively.

Let

$$\rho_i(t) = \frac{I_i(t) + I_i^*(t)}{N(t)}.$$

Table 2: Summary table for our findings.

Phenonemon	Proof of existence
Locally asymptotically stable equilibrium for Variant 2	Theorem 1
Locally asymptotically stable equilibrium for Variant 1	Theorem 2
Globally asymptotically stable equilibrium for both variants	Theorem 3
Periodic solutions and possible chaos	N/A (numeric support only)

The dynamics of the proposed model is described by the following system of differential equations:

$$\dot{S}(t) = -[\alpha_1\rho_1(t) + \alpha_2\rho_2(t) + d]S(t) + \eta[R_1(t) + R_2(t) + P(t)] + b \tag{1a}$$

$$\dot{I}_1(t) = \alpha_1\rho_1(t)S(t) - [\beta_1 + m + d_1]I_1(t) \tag{1b}$$

$$\dot{I}_2(t) = mI_1(t) + \alpha_2\rho_2(t)S(t) - [\beta_2 + d_2]I_2(t) \tag{1c}$$

$$\dot{I}_1^*(t) = \gamma_1\rho_1(t)R_2(t) - [\beta_1^* + d_1^*]I_1^*(t) \tag{1d}$$

$$\dot{I}_2^*(t) = \gamma_2\rho_2(t)R_1(t) - [\beta_2^* + d_2^*]I_2^*(t) \tag{1e}$$

$$\dot{R}_1(t) = \beta_1 I_1(t) - [\gamma_2\rho_2(t) + \eta + d]R_1(t) \tag{1f}$$

$$\dot{R}_2(t) = \beta_2 I_2(t) - [\gamma_1\rho_1(t) + \eta + d]R_2(t) \tag{1g}$$

$$\dot{P}(t) = \beta_1^* I_1^*(t) + \beta_2^* I_2^*(t) - [\eta + d]P(t) \tag{1h}$$

We shall use the notation $X(t) = (S(t), I_1(t), I_2(t), I_1^*(t), I_2^*(t), R_1(t), R_2(t), P(t))^T$ to denote the state of the population at time t.

3 Stability Analysis

In this section, we prove that conditions can be found where neither, either, or both variants exist in a stable equilibrium. These equilibria and their conditions are summarized in Table 2 and described in detail below.

3.1 Disease-free equilibrium and global basic reproduction number

For system (1), there is a disease-free equilibrium (DFE), namely $E_0 = (N, 0, 0, 0, 0, 0, 0, 0)^T$. This can be verified by observing that all eight derivatives in system (1) evaluate to zero at point E_0.

It is important to find the critical condition for asymptotic stability of the DFE, as this defines the boundary between a disease vanishing or persisting within the population. Associated with this critical condition is a global basic reproduction number R_0 reflecting the spreading rate of the epidemic. Note that while multiple methods of evaluating R_0 exist, which may be inconsistent with each other [31], all methods have the epidemic threshold of $R_0 = 1$.

To find a set of sufficient conditions such that $R_0 < 1$, we apply the next-generation matrix method [32]. Note that due to linearization of the model about E_2, the I_1^* and I_2^* infectious states can be ignored, leaving only I_1 and I_2 as the infectious states of the linearized model. This gives:

$$\mathcal{F} = \begin{bmatrix} \alpha_1 & \rho_1 S \\ \alpha_2 & \rho_2 S \end{bmatrix} \text{ and } \mathcal{V} = \begin{bmatrix} \beta_1 I_1 + m I_1 + d_1 I_1 \\ \beta_2 I_2 - m I_1 + d_2 I_2 \end{bmatrix},$$

where $\mathcal{F}$ represents the rate of new infections into compartments I_1 and I_2 and $\mathcal{V}$ represents the net outflow (outflow minus inflow) of individuals from these two compartments by other means (including mutation from I_1 to I_2).

Computing the Jacobian matrices of $\mathcal{F}$ and $\mathcal{V}$ at E_0, we obtain:

$$F = \begin{bmatrix} \alpha_1 & 0 \\ 0 & \alpha_2 \end{bmatrix}, \qquad V = \begin{bmatrix} \beta_1 + m + d_1 & 0 \\ -m & \beta_2 + d_2 \end{bmatrix}$$

and

$$FV^{-1} = \begin{bmatrix} \dfrac{\alpha_1}{\beta_1 + m + d_1} & 0 \\ \dfrac{m\alpha_2}{(\beta_1 + m + d_1)(\beta_2 + d_2)} & \dfrac{\alpha_2}{\beta_2 + d_2} \end{bmatrix}.$$

The basic reproduction number R_0 of the epidemic model equals the spectral radius of FV^{-1}. As FV^{-1} is triangular and non-negative, this is equivalent to its maximum diagonal element, i.e.,

$$R_0 = \max\{R_0^{(1)}, R_0^{(2)}\}, \tag{2}$$

where $R_0^{(i)} = \alpha_i/(\beta_i + d_i + m\chi_{\{i=1\}})$ is the basic reproduction number for Variant i, $i \in \{1, 2\}$. Here, χ denotes the indicator function.

3.2 Existence condition for a single-variant endemic equilibrium

In system (1), if $R_0^{(2)} = \alpha_2/(\beta_2 + d_2) > 1$, then there exists an endemic equilibrium. By substituting E_2 into (1), we can prove the existence of E_2 when $R_0^{(2)} > 1$ and compute the population of each non-zero compartment:

$$\hat{S} = \frac{\beta_2 + d_2}{\alpha_2} N, \qquad \hat{I}_2 = \frac{1 - \frac{\beta_2 + d_2}{\alpha_2}}{1 + \frac{\beta_2}{\eta + d}} N, \qquad \hat{R}_2 = \frac{\beta_2}{\eta + d} \hat{I}_2,$$

where

$$N = \frac{b\alpha_2 \left(\eta + \beta_2 + d\right)}{\alpha_2 \left(d_2\eta + d\beta_2 + dd_2\right) - \left(d_2 - d\right)\left(\beta_2 + d_2\right)\left(\eta + d\right)}.$$

Analyzing the Jacobian matrix of system (1) at E_2 and applying the Routh-Hurwitz stability criterion [33, 34], we obtain the following thresholds for

stability:

$$\tilde{R}_1 = \frac{\alpha_2(\beta_2 + d + \gamma_2 + \eta)}{(\beta_2 + \delta_2)\gamma_2} \tag{3}$$

$$\tilde{R}_2 = \frac{\alpha_2(\beta_1 + d_1 + m)(\beta_2 + d + \eta)(\beta_1^* + d_1^*) + \beta_2\gamma_1(\beta_1 + d_1 + m)(\beta_2 + d_2)}{\alpha_2\beta_2\gamma_1(\beta_1 + d_1 + m) + \alpha_1(\beta_1 + d_2)(\beta_2 + d + \eta)(\beta_1^* + d_1^*)} \tag{4}$$

$$\tilde{R}_3 = \frac{\alpha_2(\beta_1 + d_1 + m)(\beta_2 + d + \eta) + (\beta_2 + d + \eta)(\beta_1^* + d_1^*) + \beta_2\gamma_1(\beta_2 + d_2)}{\alpha_1(\beta_2 + d_2)(\beta_2 + d + \eta) + \alpha_2\beta_2\gamma_1} \tag{5}$$

$$\tilde{R}_4 = \frac{\left[\beta_2\eta + \alpha_2(d + \eta)\right](\beta_2 + d_2)}{\alpha_2\beta_2\eta + (d + \eta)(\beta_2 + d_2)^2}. \tag{6}$$

A sufficient condition for the stability of E_2 is as follows:

Theorem 1 *For system (1), if $\tilde{R}_i > 1$ for all $i \in \{1, 2, 3, 4\}$, then the endemic equilibrium $E_2 = (\hat{S}, 0, \hat{I}_2, 0, 0, 0, \hat{R}_2, 0)^T$ is locally asymptotically stable.*

The proof of Theorem 1 is presented in Appendix A. Notably, because of the near symmetry of our model, we can obtain the characteristic polynomial of the endemic equilibrium $E_1 = (\hat{S}, \hat{I}_1, 0, 0, 0, \hat{R}_1, 0, 0)^T$ by replacing (A1) with its corresponding Jacobian matrix for point E_1. Proceeding in a similar manner as in Appendix A gives the following stability threshold for E_1:

$$\bar{R}_1 = \frac{\alpha_1(\beta_1 + d + \gamma_1 + \eta)}{(\beta_1 + \delta_1)\gamma_1} \tag{7}$$

$$\bar{R}_2 = \frac{\alpha_1(\beta_2 + d_2)(\beta_1 + d + \eta)(\beta_2^* + d_2^*) + \beta_1\gamma_2(\beta_2 + d_2)(\beta_1 + d_1 + m)}{\alpha_1\beta_1\gamma_2(\beta_2 + d_2) + \alpha_2(\beta_2 + d_1)(\beta_1 + d + \eta)(\beta_2^* + d_2^*)} \tag{8}$$

$$\bar{R}_3 = \frac{\alpha_1(\beta_2 + d_2)(\beta_1 + d + \eta) + (\beta_1 + d + \eta)(\beta_2^* + d_2^*) + \beta_1\gamma_2(\beta_1 + d_1)}{\alpha_2(\beta_1 + d_1 + m)(\beta_1 + d + \eta) + \alpha_1\beta_1\gamma_2} \tag{9}$$

$$\bar{R}_4 = \frac{\left[\beta_1\eta + \alpha_1(d + \eta)\right](\beta_1 + d_1)}{\alpha_1\beta_1\eta + (d + \eta)(\beta_1 + d_1 + m)^2}. \tag{10}$$

Therefore, a sufficient condition for the stability of E_1 is as follows:

Theorem 2 *For system (1), if $\bar{R}_i > 1$ for all $i \in \{1,2,3,4\}$, then the endemic equilibrium $E_1 = (\hat{S}, \hat{I}_1, 0, 0, 0, \hat{R}_1, 0, 0)^T$ is locally asymptotically stable.*

Note that in addition to the two cases described in this subsection, in which either variant becomes the sole variant among the population, it is also possible for two-variant equilibria to exist. Such cases are described in Section 3.3.

3.3 Existence condition for two-variants endemic equilibrium.

In system (1), in order to investigate the endemic equilibrium for both two variants, $E_{co} = (\hat{S}, \hat{I}_1, \hat{I}_2, \hat{I}_1^*, \hat{I}_2^*, \hat{R}_1, \hat{R}_2, \hat{P})^T$, we firstly find the existence of such a equilibrium. As shown in Appendix B, an unique endemic equilibrium exists if following conditions are satisfied:

$$\frac{R_0^{(1)} R_0^{(2)} B_1 B_2 \hat{S}^2}{(1 - R_0^{(1)} \tilde{R}_0^{(1)} \hat{S})(1 - R_0^{(2)} \tilde{R}_0^{(2)} \hat{S})} > 1,$$

$$R_0^{(1)} \hat{S} < 1, \qquad R_0^{(2)} \hat{S} < 1,$$

where

$$R_0^{(1)} = \frac{\alpha_1}{\beta_1 + m + d_1}, \qquad \tilde{R}_0^{(1)} = \frac{\gamma_1}{\beta_1^* + d_1^*},$$

$$R_0^{(2)} = \frac{\alpha_2}{\beta_2 + d_2}, \qquad \tilde{R}_0^{(2)} = \frac{\gamma_2}{\beta_2^* + d_2^*},$$

$$B_1 = \frac{\beta_1}{\beta_1^* + d_1^*}, \qquad B_2 = \frac{\beta_2}{\beta_2^* + d_2^*}.$$

$R_0^{(i)}$ is the basic reproduction number for Variant i, $\tilde{R}_0^{(i)}$ represents the ability of cross-infection.

The next step is to prove the global asymptotic stability of the whole system (1). For simplicity, we will only consider the case where $d_1 = d_2 = d$, $\beta_1 = \beta_1^*$, and $\beta_2 = \beta_2^*$. A sufficient condition for the stability of E_{co} is as follows:

Theorem 3 *For system (1), if a coexisting endemic equilibrium* $E_{co} = (\hat{S}, \hat{I}_1, \hat{I}_2, \hat{I}_1^*, \hat{I}_2^*, \hat{R}_1, \hat{R}_2, \hat{P})^T$ *exists, then the coexisting endemic equilibrium is globally asymptotically stable.*

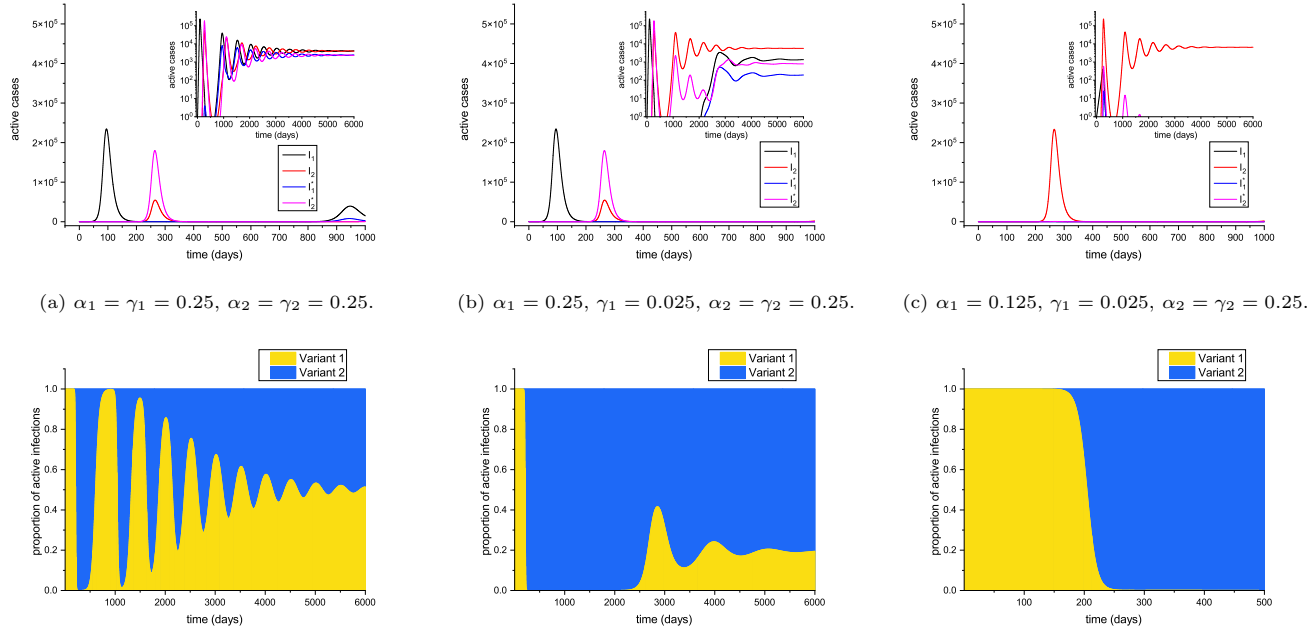
The proof of Theorem 3 and the value of E_{co} (in terms of the model parameters) are presented in Appendix B.

4 Competitive epidemic processes of two variants

This section and the following one present a series of numerical results based on system (1). Unless specified, the initial state of the population is $X(0) = (10^6 - 1, 1, 0, 0, 0, 0, 0, 0)^T$. The objective is to understand how the infectivity of the variants influences the dynamic process. We set our model parameters as follows: $m = 10^{-12}$, $\beta_1 = \beta_2 = \beta_1^* = \beta_2^* = 0.1$, $\eta = 10^{-3}$, $d = d_1 = d_2 = d_1^* = d_2^* = 10^{-4}$, and $b = 100$, with α_1, α_2, γ_1, and γ_2 specified for each scenario. A consequence of our chosen parameters is that the total population N remains constant and equal to 10^6 in all our scenarios.

4.1 Examples

Figure 2 shows examples of the competitive epidemic process with two variants as defined in system (1). Panels (a–c) illustrate the temporal trajectories of the active cases, while panels (d–f) show the proportion of each variant among the infected individuals over time. As specified by our model parameters, Variant 1 starts to spread the system at time $t = 0$ and causes an epidemic. This results in a large number of infections, some of which mutate to Variant 2, causing a new epidemic wave. Note that if Variants 1 and 2 share the same infectivity (panels (a) and (d)), they will converge to a state where both variants are equally



(a) $\alpha_1 = \gamma_1 = 0.25$, $\alpha_2 = \gamma_2 = 0.25$.

(b) $\alpha_1 = 0.25$, $\gamma_1 = 0.025$, $\alpha_2 = \gamma_2 = 0.25$.

(c) $\alpha_1 = 0.125$, $\gamma_1 = 0.025$, $\alpha_2 = \gamma_2 = 0.25$.

(d) $\alpha_1 = \gamma_1 = 0.25$, $\alpha_2 = \gamma_2 = 0.25$.

(e) $\alpha_1 = 0.25$, $\gamma_1 = 0.025$, $\alpha_2 = \gamma_2 = 0.25$.

(f) $\alpha_1 = 0.125$, $\gamma_1 = 0.025$, $\alpha_2 = \gamma_2 = 0.25$.

Fig. 2: Examples of the competitive epidemic process.

prevalent in the population. On the other hand, reducing Variant 1's cross-exposure infectivity below that of Variant 2 causes Variant 1 to comprise a smaller proportion of total infections in the endemic equilibrium. Furthermore, if both the first- and cross-infectivity of Variant 1 is low (panels (c) and (f)), Variant 1 will become extinct during the epidemic process, leaving Variant 2 as the sole remaining strain. Notably, the trajectories of the epidemic processes may show damped oscillations before converging to the endemic equilibrium as $t \to \infty$.

4.2 Effect of first-exposure infectivity

Figures 3 and 4 shows the proportion of each variant among the infected population at time $t = 6000$ days, with respect to the first-exposure infectivity rates α_1 and α_2. In particular, Figure 3 considers the case where the cross-exposure infectivities of the two variants are equal, while Figure 4 considers the case where they are unequal. In each figure, the left set of panels show the theoretical bounds of the Variant-2-only region as defined by the threshold set in Theorem 1. In accordance with Theorem 1, we plot the minimum value of $\tilde{R}_i$, $i \in \{1, 2, 3, 4\}$, and mark the contour where this minimum is equal to the threshold of 1.

The middle panels show the proportion of Variant 2 infections among all infected individuals in the population at $t = 6000$ days. Finally, the right panels show the absolute number of Variant 2 infections, also for $t = 6000$. The results demonstrate consistency with Theorem 1, showing that almost all infections are of Variant 2 if the threshold condition of Theorem 1 is met.

4.2.1 Equal cross-immunity

If the cross-exposure infectivities of the two variants are equal, then the parameter space of the two variants' first-exposure infectivities can be partitioned

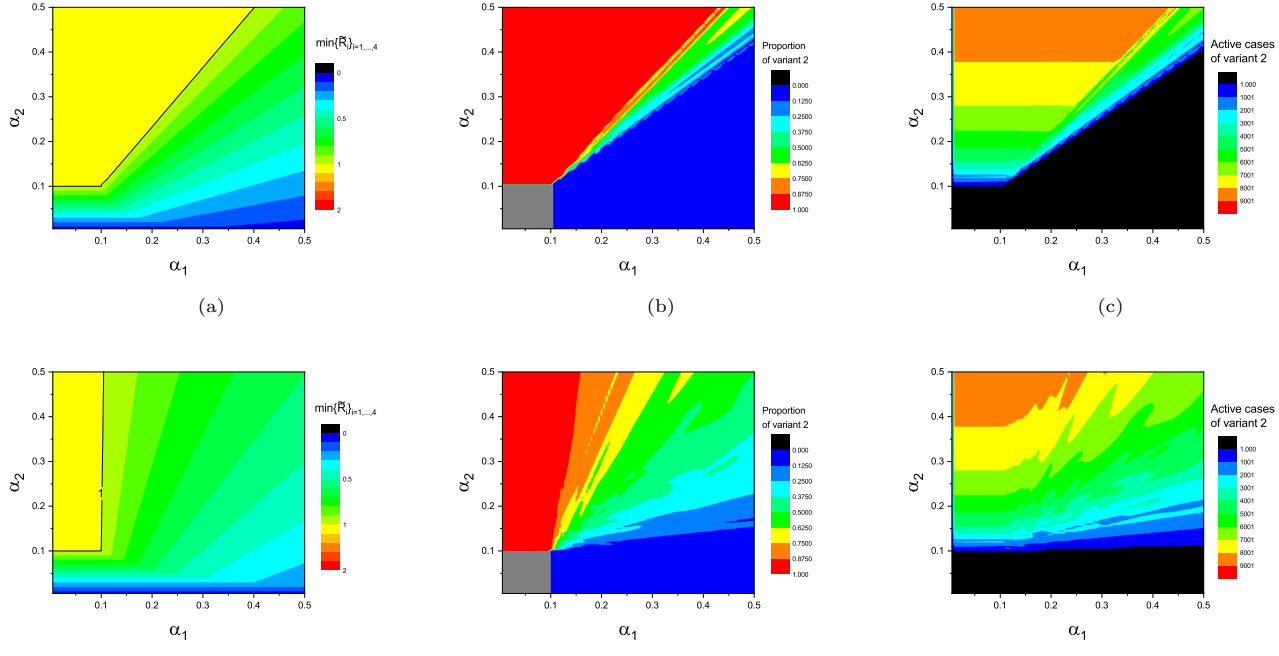


Fig. 3: Trade-off between first-exposure infectivities if the cross-exposure infectivities are equal. The left panels show the theoretical bounds of the Variant-2-only region as deduced from Theorem 1, the middle panels show the proportion of Variant 2 infections among the infected population on at $t = 6000$ days, and the right panels show the number of Variant 2 infections at $t = 6000$. **(a–c)**: $\gamma_1 = \gamma_2 = 0.025$; **(d–f)**: $\gamma_1 = \gamma_2 = 0.1$; **(g–i)**: $\gamma_1 = \gamma_2 = 0.5$.

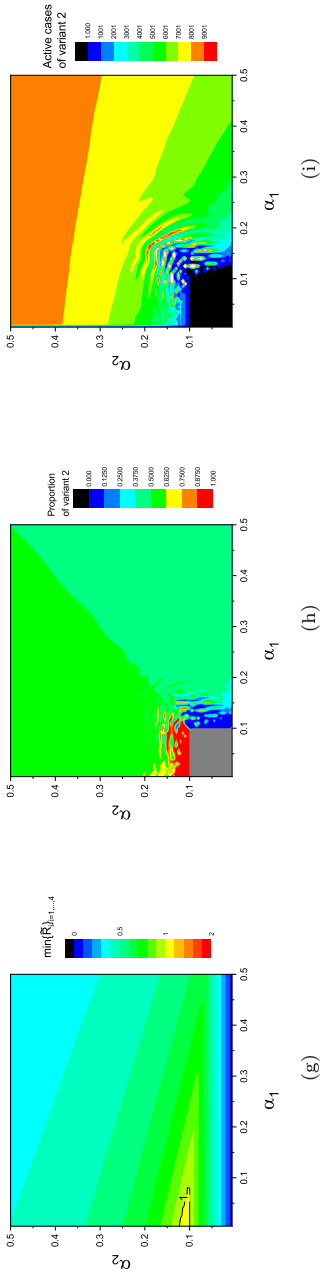


Fig. 3: (Continued)

into four regions, as shown in Fig. 3(b, e, h), based on the asymptotic behavior of the system. These four parts are the disease-free region (gray), the Variant-1-only region (blue), the Variant-2-only region (red), and the coexistence region. Note that the two single-variant regions appear to be nearly symmetrical about the line $\alpha_1 = \alpha_2$, with Variant 2 more likely to become the dominant strain if $\alpha_2 > \alpha_1$ (and vice versa).

If the cross-exposure infectivities are low, as shown in Fig. 3(a–c) where $\gamma_1 = \gamma_2 = 0.025$, then the Variant-2-only region occupies a large area. As $\gamma_1 = \gamma_2$ increases, the single-variant regions shrink in size, while the coexistence region expands. In other words, high cross-infectivity makes it more difficult for either variant to become or remain dominant over time, regardless of whether either variant has a competitive advantage for first-exposure infections, as recovered cases of one variant more easily become infected cases of the other. Finally, there are some ripples in the coexistence regions, implying the possibility of periodic or chaotic solutions with multiple endemic equilibria.

4.2.2 Unequal cross-immunity

If the cross-exposure infectivities of the two variants are unequal, the parameter space of the two variants is also divided into multiple parts, as shown in Fig. 4(b, e, h). However, unlike in Section 4.2.1, the coexistence region is clearly divided into two distinct parts – a smooth region and an unstable region with many rapid fluctuations in the epidemic behavior. Interestingly, the sizes of the Variant-2-only regions are unaffected by the changes in cross-immunity and are similar to that in Fig. 4(a, d, g). This is despite the appearance of γ_1 and γ_2 terms in the conditions underlying Theorem 1. Furthermore, the unstable region mostly exists below the $\alpha_1 = \alpha_2$ diagonal (i.e., in the $\alpha_1 > \alpha_2$ region) if $\gamma_1 < \gamma_2$, and above the diagonal if $\gamma_1 > \gamma_2$. In other words, instability is

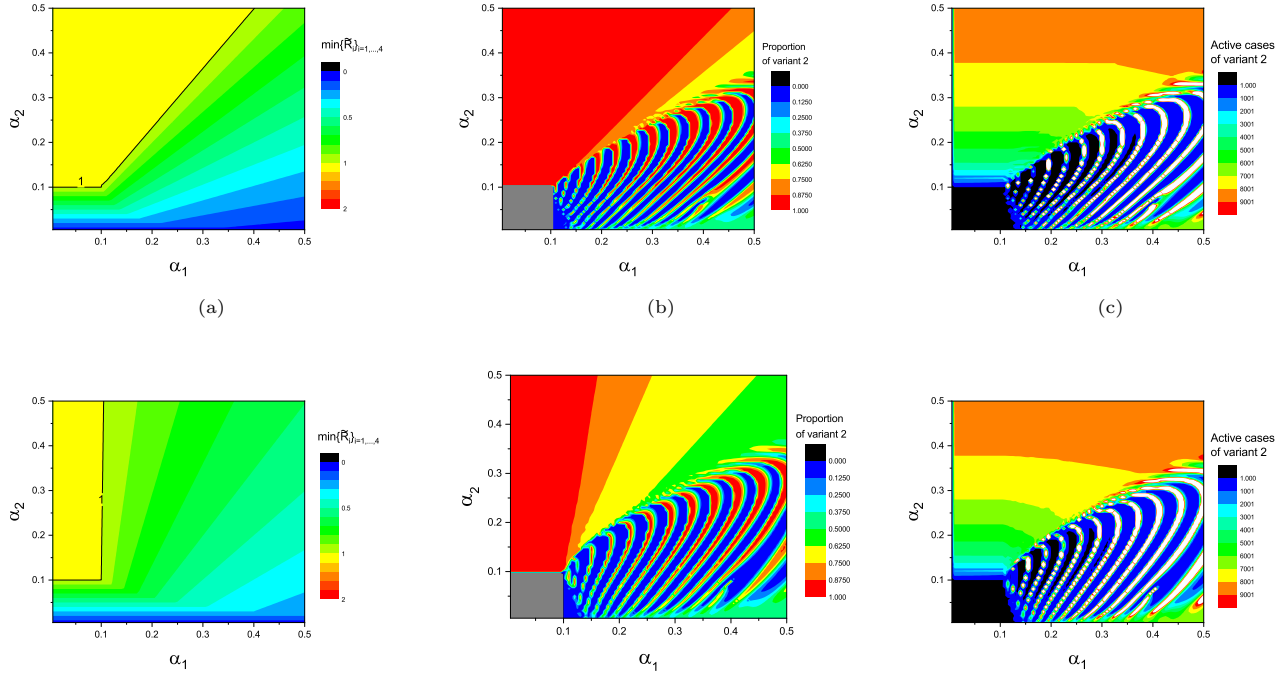


Fig. 4: Trade-off between first-exposure infectivities if the cross-exposure infectivities are unequal. The left panels show the theoretical bounds of the Variant-2-only region as deduced from Theorem 1, the middle panels show the proportion of Variant 2 infections among the infected population on at $t = 6000$ days, and the right panels show the number of Variant 2 infections at $t = 6000$. **(a–c)**: $\gamma_1 0.025$, $\gamma_2 = 0.5$; **(d–f)**: $\gamma_1 = 0.1$, $\gamma_2 = 0.5$; **(g–i)**: $\gamma_1 = 0.5$, $\gamma_2 = 0.1$.

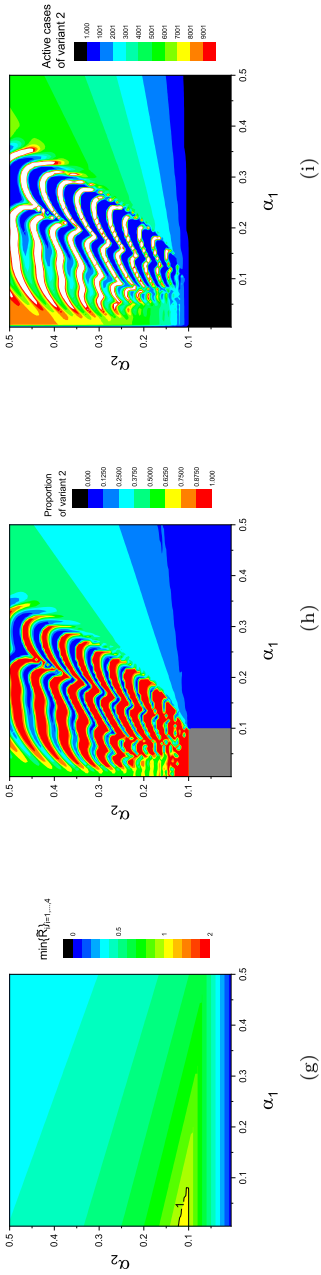


Fig. 4: (Continued)

most likely to occur if the competitive advantages/disadvantages of Variant 2 for first- and cross-exposure infections lie in opposite directions.

4.3 Analysis of sample epidemic trajectories

To better understand the behavior of the epidemic model in the single-variant, smooth coexistence, and unstable regions, we sample some parameter settings from Fig. 4(e) and plot the trajectory of the epidemic over time for four different points on the parameter plane, as shown in Fig. 5. In particular, we select one point from the Variant-2-only region of Fig. 4(e)'s parameter space, one point from the smooth part of the coexistence region, and two points from an unstable region in which the day-6000 proportion of Variant 2 cases shows rapid fluctuations. The dynamical properties of the epidemic for each parameter setting is represented as a phase graph in three dimensions, based on projecting the state of the full model (1) to the 3-vector $(S, V_1, V_2)^T$ where $V_i = I_i + I_i^*$.

Point A ($\alpha_1 = \alpha_2 = 0.3$) is located in the smooth part of the coexistence region, and its trajectory converges to a single endemic equilibrium, namely $E_{\text{co}} = (\hat{S}, \hat{V}_1, \hat{V}_2)^T$. In contrast, point D ($\alpha_1 = 0.05$, $\alpha_2 = 0.3$) is located in the Variant-2-only region, and its trajectory converges towards the endemic equilibrium $E_2 = (\hat{S}, 0, \hat{V}_2)^T$. Finally, points B ($\alpha_1 = 0.3$, $\alpha_2 = 0.1$) and C ($\alpha_1 = 0.4$, $\alpha_2 = 0.25$) lie within the unstable region, and their trajectories appear to exhibit periodic properties, with two sets of loops near the $V_1 = 0$ and $V_2 = 0$ planes, respectively. Additional numerical investigations of the unstable region further suggest that the number/proportion of active cases of the two variants exhibits periodic oscillations in this region. The emergence of such periodic behavior suggests that our competitive epidemic model is sufficient to show complex evolutionary behavior despite its simple formulation,

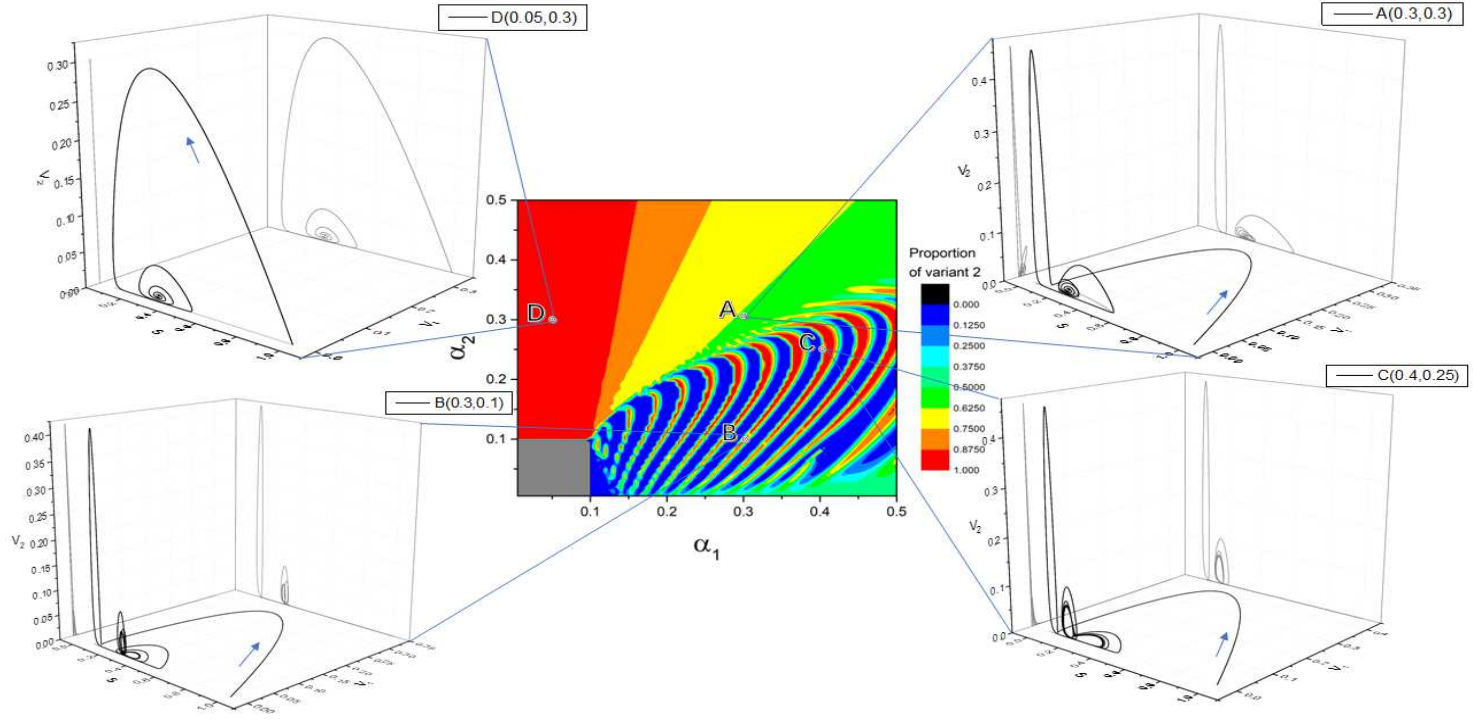


Fig. 5: Epidemic trajectories for four different points in the parameter space of Fig. 4(e).

and motivates the need to further explore such periodic (and possibly chaotic) behaviors in future work.

5 Discussion

The SARS-CoV-2 virus that causes COVID-19 is still spreading and mutating and will keep doing so for the foreseeable future. The virus's high ability to achieve immune escape makes it impossible to eliminate from human society. Additionally, many other viruses circulating in humans, e.g., influenza, also have multiple strains. It is therefore essential to investigate the competitive processes of such virus strains. As an extension of existing compartmental epidemic models in the literature, we have proposed a simple dual-SIRS model to describe the competitive process of two disease variants.

In Section 3, we investigated the stability of the model's disease-free equilibrium (DFE), generated sufficient conditions under which a single Variant endemic equilibrium (EE) is locally asymptotically stable, and gave the sufficient conditions under which both variants endemic equilibrium (EE) is globally asymptotically stable. From the DFE, the competitive epidemic process' basic reproduction number, R_0, can be obtained. The derivation of R_0 shows that the rate of disease spread (including both variants) depends solely on the more contagious of the two variants. In the numerical results in Sections 4, our analysis allows us to predict which variant (if any) will dominate the competitive epidemic process. Although our work is limited to the study of two disease variants, it forms a good starting point for analyzing more complex epidemic models in future work.

In Sections 4, we used numerical analysis to study how first-exposure and cross-exposure infectivity affects the long-term evolution of the competitive epidemic process. While the numerical results verify our theoretical results

regarding the stability of the Variant-2-only EE if $\tilde{R}_i > 1$ for all $i \in \{1, 2, 3, 4\}$, it also shows the variety of results that can occur outside of this region, including periodic or chaotic behavior. The ability to predict such behavior may help hospitals and other healthcare organizations to prepare the necessary medical resources before a surge in caseload occurs.

Notably, the existence of periodic or chaotic behavior in our epidemic model means that a decrease in active cases does not necessarily signal the end of an epidemic. Additionally, reducing the infectivity of a variant by implementing non-pharmaceutical interventions can potentially cause such periodic or even possibly chaotic behavior to emerge, paradoxically increasing healthcare demand. Therefore, governments and other policymakers must be careful when introducing epidemic prevention policies.

Our work also has some limitations, most notably, the lack of investigations of the impact of vaccination and the data study on COVID-19 or other infectious diseases. Furthermore, theoretical analysis of periodical results is not included due to the difficulty and space limitations. Regarding the model, it is only capable of handling scenarios involving two viruses, rather than multiple viruses. This forms part of our future work.

Finally, note that our proposed model is general enough to be applied to fields beyond infectious disease epidemiology. As noted in the Introduction, additional potential applications include modeling the spreading of information/disinformation [4, 5] and malware [6].

6 Concluding Remarks

This paper studied a competitive epidemic process with two variants based on the susceptible-infected-removed-susceptible (SIRS) model. The global basic reproduction number R_0 was derived, demonstrating that the more contagious

variant of the two determined the threshold of whether the epidemic would persist or fade. Furthermore, by studying the stability of the endemic equilibrium, we obtain the conditions under which the newly introduced variant may completely replace the original variant. Based on theoretical and numerical results, we can predict which variant (or both) will survive the long-term evolution of the epidemic. We also performed numerical analysis on the effect of different first- and cross-exposure infectivities on the evolution of the epidemic model and demonstrated that periodic or chaotic behavior can emerge in some cases, especially when the cross-exposure infectivities of the two variants are unequal. Finally, note that our proposed model is sufficiently general to be applied to various fields beyond infectious disease epidemiology in future work.

Declarations

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Authors' contributions. **R. Niu**: Conceptualization, Methodology, Software, Formal Analysis, Writing — Original Draft, Visualization. **Y.-C. Chan**: Writing – Original Draft, Writing – Review & Editing, Validation. **S. Liu**: Formal Analysis, Writing – Original Draft, Writing – Review & Editing. **E. W. M. Wong**: Supervision, Writing – Review & Editing. **M. A. van Wyk**: Conceptualization, Methodology, Formal Analysis, Writing – Review & Editing, Supervision.

Data Availability. This manuscript has no associated data.

Appendix A Proof of Theorem 1

Consider the Jacobian matrix of system (1) at point $E_2 = (\hat{S}, 0, \hat{I}_2, 0, 0, 0, \hat{R}_2, 0)^T$, namely

$$J = [J_L \mid J_R] \tag{A1}$$

where

$$J_L = \begin{bmatrix} -\alpha_2\frac{\hat{I}_2}{N} - d & -\alpha_1\frac{\hat{S}}{N} & -\alpha_2\frac{\hat{S}}{N} & -\alpha_1\frac{\hat{S}}{N} \\ 0 & \alpha_2\frac{\hat{I}_2}{N} - \beta_1 - m - d_1 & 0 & \alpha_1\frac{\hat{S}}{N} \\ \alpha_2\frac{\hat{I}_2}{N} & m & \alpha_2\frac{\hat{S}}{N} - \beta_2 - d_2 & 0 \\ 0 & \gamma_1\frac{\hat{R}_2}{N} & 0 & \gamma_1\frac{\hat{R}_2}{N} - \beta_1^* - d_1^* \\ 0 & 0 & 0 & 0 \\ 0 & \beta_1 & 0 & 0 \\ 0 & -\gamma_1\frac{\hat{R}_2}{N} & \beta_2 & -\gamma_1\frac{\hat{R}_2}{N} \\ 0 & 0 & 0 & \beta_1^* \end{bmatrix}$$

$$J_R = \begin{bmatrix} -\alpha_2\frac{\hat{S}}{N} & \eta & \eta & \eta \\ 0 & 0 & 0 & 0 \\ \alpha_2\frac{\hat{S}}{N} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ -\beta_2^* - d_2^* & \gamma_2\frac{\hat{I}_2}{N} & 0 & 0 \\ 0 & -\gamma_2\frac{\hat{I}_2}{N} - \eta - d & 0 & 0 \\ 0 & 0 & -\eta - d & 0 \\ \beta_2^* & 0 & 0 & -\eta - d \end{bmatrix}.$$

The characteristic polynomial of matrix J is

$$\begin{aligned} P(x) &= \det(x\mathbf{I} - J) \\ &= -a_2^{-7} q_2^{-6} k_4(x) k_5(x) \\ &\quad \times \alpha_2^2 q_2^2 k_1(x)[k_3(x)k_2(x) + q_1] \\ &\quad \times \Big(\alpha_2\beta_2\eta q_2(d+\eta)[k_3(x) - \alpha_2 + \beta_2] + h(x)k_4(x)\Big) \end{aligned} \tag{A2}$$

where

$$\begin{aligned} k_1(x) &= -\alpha_1\beta_2 d - \alpha_2 d^2 - \alpha_2\beta_2\eta - 2\alpha_2 d\eta - \alpha_2\eta^2 - \alpha_2 d\gamma_2 + \beta_2 d\gamma_2 \\ &\quad + dd_2\gamma_2 - \alpha_2\eta\gamma_2 + \beta_2\eta\gamma_2 + d_2\eta\gamma_2 - \alpha_2 q_2 x \\ k_2(x) &= -\alpha_2\beta_1^*\beta_2 - \alpha_2\beta_1^* d - \alpha_2\beta_2 d_1^* - \alpha_2 dd_1 - \alpha_2\beta_1^*\eta - \alpha_2 d_1^*\eta \\ &\quad + \alpha_2\beta_2\gamma_1 - \beta_2^2\gamma_1 - \beta_2 d_2\gamma_1 - \alpha_2 q_2 x \\ k_3(x) &= \alpha_2[\alpha_1(\beta_2 + d_2) - \alpha_2(\beta_1 + d_1 + m + x)] \\ k_4(x) &= d + \eta + x \\ k_5(x) &= \beta_2 + d_2 + x \\ h(x) &= \alpha_2 q_3(\beta_2 + d_2)(d+\eta)q_2 + \alpha_2 q_2 x[\alpha_2 d + d^2 - dd_2 + (q_3 + d)\eta + q_2 x] \\ q_1 &= -\alpha_1\alpha_2\beta_2 q_3(\beta_2 + d_2)\gamma_1 \\ q_2 &= \beta_2 + d + \eta \\ q_3 &= \alpha_2 - \beta_2 - d_2 \end{aligned}$$

Note that the $k_i(x)$'s are all degree-1 in x and $h(x)$ is degree-2 in x; thus $P(x)$ is has a degree of 8 in x. Theorem 1 thus reduces to the following:

Proposition 1 *The Routh-Hurwitz criterion [33, 34] is satisfied, i.e., the real parts of the roots of* (A2) *are all negative, if* $\tilde{R}_i > 1$ *for all* $i \in \{1, \ldots, 7\}$*, where* $\tilde{R}_1$ *to* $\tilde{R}_4$ *are defined as in* (3)–(6) *and:*

$$\tilde{R}_5 = \frac{\alpha_2 X_4 + X_5 X_1}{X_4^2 + X_3}$$

$$\tilde{R}_6 = \frac{X_1 (X_2 + X_5)}{X_3}$$

$$\tilde{R}_7 = \frac{(X_1 X_2 + X_5)(\alpha_2 X_4 + X_5 X_1) + X_3 \left(X_4^2 + X_3\right) + X_2 \left(\alpha_2 \beta_2 \eta + X_1 X_4^2\right)}{(X_1 X_2 + X_5)\left(X_4^2 + X_3\right) + X_3 (\alpha_2 X_4 + X_1 X_5) + X_2 (\beta_2 \eta + \alpha_2 X_1) X_4},$$

where

$$X_1 = d + \eta$$

$$X_2 = \beta_2 + d + \eta$$

$$X_3 = d_2 \eta + d d_2 + \beta_2 \eta$$

$$X_4 = \beta_2 + d_2$$

$$X_5 = \alpha_2 + d.$$

Proof By considering each factor of P(x) and requiring each element of the first column of their Routh arrays to be positive (therefore resulting in zero sign changes), then rearranging each inequality to contain 1 on the right-hand side, we obtain the thresholds $\tilde{R}_i$, $i \in 1, 2, \ldots, 7$ as listed above. □

Proposition 2 $\tilde{R}_i > 1$ *for all* $i \in \{5, 6, 7\}$ *whenever whenever* E_2 *exists and* $\tilde{R}_i > 1$ *for all* $i \in \{1, \ldots, 4\}$*.*

Proof Note that $\frac{\alpha_2}{\beta_2 + d_2} > 1$ whenever E_2 exists, i.e. $R_0^{(2)}$ as defined in Section 3.1 is greater than 1. From this we obtain:

$$\tilde{R}_5 = \frac{\alpha_2 X_4 + X_1 X_5}{X_4^2 + X_3}$$

$$
\begin{aligned}
&> \frac{X_4^2 + (\beta_2 + d_2 + d)X_1}{X_4^2 + X_3} \\
&= 1 + \frac{d\beta_2 + d^2 + d\eta}{X_4^2 + X_3} > 1
\end{aligned}
$$

$$
\begin{aligned}
\tilde{R}_6 &= \frac{X_1(\beta_2 + 2d + \eta + \alpha_2)}{X_3} \\
&> \frac{\alpha_2 X_1}{X_3} \\
&> \frac{X_1 X_4}{X_3} \\
&= 1 + \frac{d\beta_2}{X_3} > 1
\end{aligned}
$$

$$
\tilde{R}_7 = \frac{(X_1X_2 + X_5)(\alpha_2X_4 + X_1X_5) + X_3(X_4^2 + X_3) + X_2(\alpha_2\beta_2\eta + X_1X_4^2)}{(X_1X_2 + X_5)(X_4^2 + X_3) + X_3(\alpha_2X_4 + X_1X_5) + X_2X_4(\beta_2\eta + \alpha_2X_1)}.
$$

The numerator of $\tilde{R}_7$ can be rewritten as

$$
\begin{aligned}
&(X_1X_2 + X_5 - X_3)(\alpha_2X_4 + X_1X_5) + X_3(\alpha_2X_4 + X_1X_5) \\
&- (X_1X_2 + X_5 - X_3)(X_4^2 + X_3) + (X_1X_2 + X_5)(X_4^2 + X_3) \\
&+ X_2(\alpha_2\beta_2\eta + X_1X_4^2 - (\beta_2\eta X_4 + \alpha_2X_1X_4)) + X_2X_4(\beta_2\eta + \alpha_2X_1) \\
=&(X_1X_2 + X_5 - X_3)(\alpha_2X_4 + X_1X_5 - (X_4^2 + X_3)) + X_3(\alpha_2X_4 + X_1X_5) \\
&+ (X_1X_2 + X_5)(X_4^2 + X_3) + X_2(\alpha_2\beta_2\eta + X_1X_4^2 - (\beta_2\eta X_4 + \alpha_2X_1X_4)) \\
&+ X_2X_4(\beta_2\eta + \alpha_2X_1) \\
=&(X_1X_2 + X_5)(X_4^2 + X_3) + X_3(\alpha_2X_4 + X_1X_5) + X_2X_4(\beta_2\eta + \alpha_2X_1) \\
&+ (X_1X_2 + X_5 - X_3)(\varphi X_4 + \varphi\eta + \beta_2 d + \varphi d + d(d + \eta)) \\
&- \varphi(dd_2 + \beta_2 d + \eta d_2)X_2.
\end{aligned}
$$

where $\varphi = \alpha_2 - \beta_2 - d_2$. Note that all parameters in our model (lowercase greek and latin characters) are positive. Let

$$
f = (X_1X_2 + X_5 - X_3)(\varphi X_4 + \varphi\eta + \beta_2 d + \varphi d + d(d + \eta))
$$

$$- \varphi(dd_2 + \beta_2 d + \eta d_2)X_2.$$

we have

$$X_5 - X_3 = \alpha_2 + d - d_2\eta - dd_2 - \beta_2\eta > \varphi + d - d > 0.$$

Therefore,

$$\begin{aligned} f >& X_1X_2(\varphi X_4 + \varphi\eta + \beta_2 d + \varphi d + d(d+\eta)) - \varphi(dd_2 + \beta_2 d + \eta d_2)X_2 \\ >& X_2\varphi(X_4 + \eta + d - dd_2 - \beta_2 d - \eta d_2) \\ >& X_2\varphi(X_4 + \eta + d - d_2 - \beta_2 - \eta) > d > 0. \end{aligned}$$

Hence,

$$\begin{aligned} \tilde{R}_7 &= \frac{(X_1X_2 + X_5)(X_4^2 + X_3) + X_3(\alpha_2X_4 + X_1X_5) + X_2X_4(\beta_2\eta + \alpha_2X_1) + f}{(X_1X_2 + X_5)(X_4^2 + X_3) + X_3(\alpha_2X_4 + X_1X_5) + X_2X_4(\beta_2\eta + \alpha_2X_1)} \\ &= 1 + \frac{f}{(X_1X_2 + X_5)(X_4^2 + X_3) + X_3(\alpha_2X_4 + X_1X_5) + X_2X_4(\beta_2\eta + \alpha_2X_1)} > 1. \end{aligned}$$

Combining Propositions 1 and 2 completes the proof of Theorem 1. □

Appendix B Proof of Theorem 3

Proposition 3 *In system 1, an unique endemic equilibrium* $E_{co} = (\hat{S}, \hat{I}_1, \hat{I}_2, \hat{I}_1^*, \hat{I}_2^*, \hat{R}_1, \hat{R}_2, \hat{P})^T$ *exists if following conditions are satisfied,*

$$\frac{R_0^{(1)}R_0^{(2)}B_1B_2\hat{S}^2}{(1 - R_0^{(1)}\tilde{R}_0^{(1)}\hat{S})(1 - R_0^{(2)}\tilde{R}_0^{(2)}\hat{S})} > 1,$$
$$R_0^{(1)}\hat{S} < 1, \qquad R_0^{(2)}\hat{S} < 1.$$

Proof By substituting E_{co} into the normalized (1), we can get

$$[\alpha_1\hat{\rho}_1 + \alpha_2\hat{\rho}_2 + d]\hat{S} - \eta[\hat{R}_1 + \hat{R}_2 + \hat{P}] + b = 0 \tag{B3a}$$

$$\alpha_1\hat{\rho}_1\hat{S} - [\beta_1 + m + d_1]\hat{I}_1 = 0 \tag{B3b}$$

$$m\hat{I}_1 + \alpha_2\hat{\rho}_2\hat{S} - [\beta_2 + d_2]\hat{I}_2 = 0 \tag{B3c}$$

$$\gamma_1\hat{\rho}_1\hat{R}_2 - [\beta_1^* + d_1^*]\hat{I}_1^* = 0 \tag{B3d}$$

$$\gamma_2\hat{\rho}_2\hat{R}_1 - [\beta_2^* + d_2^*]\hat{I}_2^* = 0 \tag{B3e}$$

$$\beta_1\hat{I}_1 - [\gamma_2\hat{\rho}_2 + \eta + d]\hat{R}_1 = 0 \tag{B3f}$$

$$\beta_2\hat{I}_2 - [\gamma_1\hat{\rho}_1 + \eta + d]\hat{R}_2 = 0 \tag{B3g}$$

$$\beta_1^*\hat{I}_1^* + \beta_2^*\hat{I}_2^* - [\eta + d]\hat{P} = 0 \tag{B3h}$$

Hence, we can get the following equations that reveal the relationships between parameters.

$$\hat{I}_1 = \frac{\alpha_1\hat{\rho}_1\hat{S}}{\beta_1 + m + d_1} \tag{B4a}$$

$$\hat{I}_2 = \frac{m\hat{I}_1}{\beta_2 + d_2} + \frac{\alpha_2\hat{\rho}_2\hat{S}}{\beta_2 + d_2} \tag{B4b}$$

$$\hat{I}_1^* = \frac{\gamma_1\hat{\rho}_1\hat{R}_2}{\beta_1^* + d_1^*} \tag{B4c}$$

$$\hat{I}_2^* = \frac{\gamma_2\hat{\rho}_2\hat{R}_1}{\beta_2^* + d_2^*} \tag{B4d}$$

$$\hat{I}_1 = \frac{[\gamma_2\hat{\rho}_2 + \eta + d]\hat{R}_1}{\beta_1} \tag{B4e}$$

$$\hat{I}_2 = \frac{[\gamma_1\hat{\rho}_1 + \eta + d]\hat{R}_2}{\beta_2} \tag{B4f}$$

For sufficiently small m, combining (B4a) and (B4b), we get

$$\frac{\alpha_1\hat{S}}{\beta_1 + m + d_1} + \frac{\gamma_1\hat{R}_2}{\beta_1^* + d_1^*} = 1$$

Similarly, by combining (B4a) and (B4c), we have

$$\frac{\alpha_1\hat{S}}{\beta_1 + d_1} + \frac{\gamma_1\hat{R}_2}{\beta_1^* + d_1^*} = 1$$

Then,

$$\hat{R}_1 = \frac{\beta_2^* + d_2^*}{\gamma_2}\left(1 - \frac{\alpha_2\hat{S}}{\beta_2 + d_2}\right) \tag{B5a}$$

$$\hat{R}_2 = \frac{\beta_1^* + d_1^*}{\gamma_1}\left(1 - \frac{\alpha_1\hat{S}}{\beta_1 + m + d_1}\right) \tag{B5b}$$

are obtained. Then, since $\hat{R}_1$ and $\hat{R}_2$ need to be larger than 0, we have

$$\frac{\alpha_2 \hat{S}}{\beta_2 + d_2} < 1 \tag{B6a}$$

$$\frac{\alpha_1 \hat{S}}{\beta_1 + m + d_1} < 1 \tag{B6b}$$

Next, we use functions of $\hat{S}$ to represent the rest of the other parameters $\hat{\rho}_i$, $i = 1, 2$. From (B4a) and (B4e),

$$\frac{\alpha_1 \hat{\rho}_1 \hat{S}}{\beta_1 + m + d_1} = \frac{[\gamma_2 \hat{\rho}_2 + \eta + d]\hat{R}_1}{\beta_1}$$

and (B4b) and (B4f) show that

$$\frac{\alpha_2 \hat{\rho}_2 \hat{S}}{\beta_2 + d_2} = \frac{[\gamma_1 \hat{\rho}_1 + \eta + d]\hat{R}_2}{\beta_2}$$

Then,

$$\hat{\rho}_1 = \frac{[\gamma_2 \hat{\rho}_2 + \eta + d]\hat{R}_1}{\beta_1} \times \frac{\beta_1 + m + d_1}{\alpha_1 \hat{S}} \tag{B7a}$$

$$\hat{\rho}_2 = \frac{[\gamma_1 \hat{\rho}_1 + \eta + d]\hat{R}_2}{\beta_2} \times \frac{\beta_2 + d_2}{\alpha_2 \hat{S}} \tag{B7b}$$

Substituting (B7a) into (B7b), have

$$\frac{\alpha_2 \hat{\rho}_2 \hat{S}}{\beta_2 + d_2} = [\gamma_1 \frac{[\gamma_2 \hat{\rho}_2 + \eta + d]\hat{R}_1}{\beta_1} \times \frac{\beta_1 + m + d_1}{\alpha_1 \hat{S}} + \eta + d]\hat{R}_2/\beta_2$$

such that

$$\hat{\rho}_2 = \frac{(\eta + d)[\gamma_1 \hat{R}_1 \hat{R}_2 \frac{(\beta_2 + d_2)(\beta_1 + m + d_1)}{\alpha_1 \beta_1 \hat{S}} + 1]}{\alpha_2 \beta_2 \hat{S} - \gamma_1 \gamma_2 \hat{R}_1 \hat{R}_2 \times \frac{(\beta_2 + d_2)(\beta_1 + m + d_1)}{\alpha_1 \beta_1 \hat{S}}} \tag{B8}$$

Similarly,

$$\hat{\rho}_1 = \frac{(\eta + d)[\gamma_2 \hat{R}_1 \hat{R}_2 \frac{(\beta_2 + d_2)(\beta_1 + m + d_1)}{\alpha_2 \beta_2 \hat{S}} + 1]}{\alpha_1 \beta_1 \hat{S} - \gamma_1 \gamma_2 \hat{R}_1 \hat{R}_2 \times \frac{(\beta_2 + d_2)(\beta_1 + m + d_1)}{\alpha_2 \beta_2 \hat{S}}} \tag{B9}$$

To make sure $\hat{\rho}_i$ and $i = 1, 2$ have their practical meaning, their denominator must be larger than 0, which indicates that

$$\frac{\alpha_1 \alpha_2 \beta_1 \beta_2 \hat{S}^2}{\gamma_1 \gamma_2 \hat{R}_1 \hat{R}_2 (\beta_2 + d_2)(\beta_1 + m + d_1)} > 1$$

Then, combing (B5a) and (B5b), the following equation exists:

$$\frac{\alpha_1\alpha_2\beta_1\beta_2\hat{S}^2}{[(\beta_1+m+d_1)(\beta_1^*+d_1^*)-\alpha_1\gamma_1\hat{S}][(\beta_2+d_2)(\beta_2^*+d_2^*)-\alpha_2\gamma_2\hat{S}]}>1 \tag{B10}$$

Let

$$R_0^{(1)}=\frac{\alpha_1}{\beta_1+m+d_1},\qquad \tilde{R}_0^{(1)}=\frac{\gamma_1}{\beta_1^*+d_1^*},$$
$$R_0^{(2)}=\frac{\alpha_2}{\beta_2+d_2},\qquad \tilde{R}_0^{(2)}=\frac{\gamma_2}{\beta_2^*+d_2^*},$$
$$B_1=\frac{\beta_1}{\beta_1^*+d_1^*},\qquad B_2=\frac{\beta_2}{\beta_2^*+d_2^*}$$

where $R_0^{(1)},\tilde{R}_0^{(1)},R_0^{(2)},\tilde{R}_0^{(2)}$ can properly represent the basic reproduction number of first-exposure and cross-exposure of variant 1 and 2 accordingly. We can finally give the existence condition that the endemic equilibrium of the co-existence of the two variants as follows:

$$\frac{R_0^{(1)}R_0^{(2)}B_1B_2\hat{S}^2}{(1-R_0^{(1)}\tilde{R}_0^{(1)}\hat{S})(1-R_0^{(2)}\tilde{R}_0^{(2)}\hat{S})}>1,$$
$$R_0^{(1)}\hat{S}<1,\qquad R_0^{(2)}\hat{S}<1.$$

□

Proposition 4 *For system (1), if the coexisting endemic equilibrium* $E_{co}=(\hat{S},\hat{I}_1,\hat{I}_2,\hat{I}_1^*,\hat{I}_2^*,\hat{R}_1,\hat{R}_2,\hat{P})^T$ *exists, then the coexisting endemic equilibrium is globally asymptotically stable.*

Proof Under the assumption of $d_1=d_2=d$, $\beta_1=\beta_1^*$, and $\beta_2=\beta_2^*$, the normalized (1) can be written into the following equations:

$$\frac{\mathrm{d}S}{\mathrm{d}t}=-(\alpha_1\rho_1+\alpha_2\rho_2+d)S+\eta R+b \tag{B11a}$$
$$\frac{\mathrm{d}\rho_1}{\mathrm{d}t}=\alpha_1\rho_1S+\gamma_1\rho_1R_2-(\beta_1+d)\rho_1-mI_1 \tag{B11b}$$
$$\frac{\mathrm{d}\rho_2}{\mathrm{d}t}=\alpha_2\rho_2S+\gamma_2\rho_2R_1-(\beta_2+d)\rho_2+mI_1 \tag{B11c}$$
$$\frac{\mathrm{d}R}{\mathrm{d}t}=\beta_1\rho_1+\beta_2\rho_2-\gamma_1\rho_1R_2-\gamma_2\rho_2R_1-(\eta+d)R \tag{B11d}$$

where $R = R_1 + R_2 + P$. Sum up the above equations, we have

$$\frac{\mathrm{d}}{\mathrm{d}t}(S + \rho_1 + \rho_2 + R) = b - dS - d\rho_1 - d\rho_2 - dR \tag{B12}$$

At the co-existing endemic equilibrium, according to the above equation, we have $b = d(\hat{S} + \hat{\rho}_1 + \hat{\rho}_2 + \hat{R})$. Substituting b into (B12), we have

$$\frac{\mathrm{d}}{\mathrm{d}t}(S + \rho_1 + \rho_2 + R) = -d(S - \hat{S} + \rho_1 - \hat{\rho}_1 + \rho_2 - \hat{\rho}_2 + R - \hat{R}) \tag{B13}$$

Let us consider a possible Lyapunov function

$$V = \frac{1}{2}(S - \hat{S} + \rho_1 - \hat{\rho}_1 + \rho_2 - \hat{\rho}_2 + R - \hat{R})^2 \tag{B14}$$

Note that as S, ρ_1, ρ_2, and R approach infinity, the function V also approaches infinity, indicating that V is radially unbounded. Its derivative along the trajectories of (B11) is

$$\begin{aligned} V' &= (S - \hat{S} + \rho_1 - \hat{\rho}_1 + \rho_2 - \hat{\rho}_2 + R - \hat{R})\frac{\mathrm{d}}{\mathrm{d}t}(S + \rho_1 + \rho_2 + R) \\ &= -d(S - \hat{S} + \rho_1 - \hat{\rho}_1 + \rho_2 - \hat{\rho}_2 + R - \hat{R})^2. \end{aligned}$$

Clearly, $V' < 0$ always holds except at the equilibrium. By the Lyapunov asymptotic stability theorem, the co-existing endemic equilibrium is globally asymptotically stable in the positive quadrant when it exists [35].

Combining Propositions 3 and 4 completes the proof of Theorem 3. □

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