

Effects of vaccination on the two-strain transmission dynamics of COVID-19: Dougherty County, Georgia, USA, as a case study

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The emergence of multiple strains of SARS-CoV-2 has made it complicated to predict and control the COVID-19 pandemic. Although some vaccines have been effective in reducing the severity of the disease, these vaccines are designed for a specific strain of the virus and are usually less effective for other strains. In addition, the waning of vaccine-induced immunity, reinfection of recovered people, and incomplete vaccination are challenging to the vaccination program. In this study, we developed a detailed model to describe the multi-strain transmission dynamics of COVID-19 under vaccination. We implemented our model to examine the impact of inter-strain transmission competition under vaccination on the critical outbreak indicators: hospitalized cases, undiagnosed cases, basic reproduction numbers, and the overtaking-time by a new strain to the existing strain. In particular, our results on the dependence of the overtaking-time on vaccination rates, progression-to-infectious rate, and relative transmission rates provide helpful information for managing a pandemic with circulating two strains. Furthermore, our results suggest that a reduction in the relative transmission rates and a decrease in vaccination dropout rates or an increase in vaccination rates help keep the reproduction number of both strains below unity and keep the number of hospitalized cases and undiagnosed cases at their lowest levels. Moreover, our analysis shows that the second and booster-dose vaccinations are useful for further reducing the reproduction number.

Keywords: COVID-19; vaccination; booster dose; multi-strain.

1. Introduction

Caused by Severe Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), Coronavirus Disease (COVID-19) is an ongoing pandemic that has infected and killed millions of people and impacted social, economic, and political systems around the world (CDC, COVID-19, 2021; Worldmeter, 2020; Arruda *et al.*, 2021; Bubar *et al.*, 2021; CDC, COVID-19 Vaccinations, 2021a). As of 26 October 2022, almost 644 million cases and more than 6.58 million deaths worldwide have been reported (Worldmeter, 2020).

Several vaccines have been developed and known to prevent the severe illness of the disease, but the efficacy of these vaccines varies according to the vaccine type, circulating virus strain, and completion status of vaccine doses (CDC, COVID-19 Vaccinations, 2021a; News, 2021; Pantha *et al.*, 2021; Giordano *et al.*, 2021; Moore *et al.*, 2021a,b; Mumtaz *et al.*, 2021; Polack *et al.*, 2021). The waning of vaccine-induced immunity, the emergence of new strains, and people's hesitance toward vaccines are some challenges public health administrations face in controlling the spread of disease (Arruda *et al.*, 2021; CDC, COVID-19 Vaccinations, 2021a). To boost the waning immunity, a booster shot has been recommended by various agencies recently (CDC, COVID-19 Vaccinations, 2021a). On the other hand, disease symptoms, infection severity, transmission rates, hospitalization rates, death rates, and vaccine effectiveness can differ for different variants of SARS-CoV-2 (Coronavirus: COVID-19 Symptoms and Variants, 2022; , New COVID-19 Vaccine Effectiveness Data Showcase Protection Gained by 3rd and 4th Doses). For example, the Omicron strain was predominant in the later phase of the pandemic and is found to be more infectious but less severe than the Delta strain (CDC, COVID-19 Vaccinations, 2021b). Thus, studies focusing on multiple virus variants, their transmissibility, and the overtake-time from one variant to the other are essential to design strain-specific policies, including vaccination programs.

Several SEIR-based mathematical models have been developed and used to study the dynamics of the COVID-19 spread, and a few of them have considered multiple strains (Arruda *et al.*, 2021; Polack *et al.*, 2021; Tchoumi *et al.*, 2021; Betti *et al.*, 2021; Gotz *et al.*, 2021; Patel *et al.*, 2021). Arruda *et al.* (2021) developed an SEIR type multi-strain virus model and considered the possibility of re-infection due to the waning of immunity in the recovered individuals and used non-pharmaceutical intervention strategies. Their results show that relaxation in mitigating strategies causes the rapid spread of the infection. Tchoumi *et al.* (2021) developed a multi-strain SVIR type model containing two infected compartments corresponding to strains 1 and 2 with vaccination targeted to the first strain. The study evaluated the strain-wise basic reproduction number and endemic equilibria. Under the vaccination for strain 1, strain 2 will dominate if $R_1 < 1, R_2 > 1$ or $R_2 > 2R_1$. But if both $R_1 = R_2 > 1$, strain 2 can eventually die out and strain 1 persists. They also focused on the need for non-pharmaceutical intervention strategies to control the spread. Betti *et al.* (2021) developed a two-strain ODE model with the total cases, known cases, mild cases, and severe cases for both wild-type and mutant viral strains. Their work used location-specific data to estimate parameters and studied the outbreak for several scenarios. Their result suggest that both vaccination and non-pharmaceutical intervention strategies should be continued to contain the spread of both strains. Gotz *et al.* (2021) considered a two-stain SIR model to explain the spread of variants in Germany. They estimated the time that strain 2 overcomes strain 1 in Germany. However, none of these studies have focused on the timing for a new strain to overtake the existing one or the vaccination impact on the overtake-time.

In this study, we extend our previous COVID-19 transmission model under vaccination to a complex two-strain model, consisting of all three doses (first, second, and booster shot) of vaccination, dropping out from vaccination, and re-infection of infected individuals by a different strain. We formulate the basic reproduction number using our model. We performed parameter sensitivity analyses of four critical epidemic indicators: hospitalized cases, undiagnosed cases, basic reproduction numbers, and the overtake-time by a new strain to the existing strain. We used the model with parameters estimated from the infection data in Dougherty County of Georgia, USA, to compute these critical epidemic indicators. We also examined how these indicators vary according to the combinations of relative transmission rates and vaccination programs. Although our research primarily centers around data from COVID-19 infections, our models possess the potential for application to other infectious diseases characterized by the presence of two circulating strains.

2. Mathematical model

2.1 Model formulation

We extend our previous COVID-19 transmission model to develop a new two-strain compartmental SVEIR (Susceptible, Vaccinated, Exposed, Infected and Recovered) model (Pantha *et al.*). In this complex model, we include five compartments of vaccinated group: vaccinated with first dose (V_1 and V_{10}), vaccinated with 2 doses (V_2 and V_{20}) and vaccinated with two doses plus an additional booster dose (V_B). Note that people in compartment V_{10} drop out from vaccination after the first dose (never second dose) and V_{20} dropout after the second dose (never booster). Also, the exposed class for new and existing strains has two compartments: $E_V^{(i)}$, exposed people who get at least one dose of vaccination and, $E_S^{(i)}$, exposed people who never get any vaccines. Here, the superscript $i = 1$ denotes compartment infected or exposed with existing strain (strain 1) and superscript $i = 2$ denotes compartments exposed or infected with new strain (strain 2). The people in the Infected compartment are divided into three sub compartments for each strain $i = 1, 2$: hospitalized ($I_H^{(i)}$), diagnosed and isolated ($I_D^{(i)}$), and undiagnosed ($I_U^{(i)}$). The recovered compartments from existing and new strains are denoted by $R^{(1)}$ and $R^{(2)}$, respectively. Our model consists of 18 variables in total. The flow diagram of the interactions between the compartments are presented in Figure 1.

Individuals in all compartments die with natural death rate μ . The susceptible individuals are recruited with rate Λ , get vaccinated with first dose at rate v_1 , and exposed with COVID-19 upon interaction with undiagnosed individual infected with existing or new strains at rates β_1, β_2 , respectively. The vaccinated individuals with first dose (V_1) get second dose with rate v_2 but θ_1 fraction of V_1 dropout from further vaccination (never get second dose of the vaccines). Similarly, vaccinated individuals with second dose get the booster dose at the rate v_3 but θ_2 fraction of V_2 dropout from further vaccination (never get the booster dose). As the vaccines are not 100% protective, we assume that α_1, α_2 , and α_3 be the fraction of the vaccinated individuals in V_1, V_2, V_B , respectively, that are not protected from the virus of existing strain (strain 1) and α_4, α_5 , and α_6 be the fraction of the vaccinated individuals that are still not protected from new strain (strain 2) in compartments V_1, V_2 , and V_B , respectively. Previous studies (Cromer *et al.*, 2022) on the efficacy of vaccines in various strains of concern have shown similar results on all strains. We assumed the new strain to be more infectious than the existing strain to mimic the Omicron-Delta scenario and considered the vaccine effects for the new strain to be lower than the existing strain for the potential escape of this new variant from the old vaccine.

The exposed individuals ($E_S^{(1)}, E_V^{(1)}$) to the strain 1 leave the compartment with rate κ_1 and the other exposed groups ($E_S^{(2)}, E_V^{(2)}$) from strain 2 leave the compartment with rates κ_2 , respectively. Among the individuals who are exposed with strain 1, $\eta_i^{(1)}$ fraction are diagnosed and isolated, $\gamma_i^{(1)}$ fraction are undiagnosed and the remaining fraction $1 - \eta_i^{(1)} - \gamma_i^{(1)}$ are hospitalized, where the subscripts $i = 1, 2$ represent the fraction that are coming from $E_S^{(1)}$ (exposed who are never vaccinated) and $E_V^{(1)}$ (exposed who have at least one dose of vaccine), respectively. Similarly, among the individuals who are exposed with strain 2, a fraction $\eta_j^{(2)}$ are diagnosed and isolated, a fraction $\gamma_j^{(2)}$ are undiagnosed and the remaining fraction $1 - \eta_j^{(2)} - \gamma_j^{(2)}$ are hospitalized, where $j = 3, 4$ represent the fraction that are coming from $E_S^{(2)}$ and $E_V^{(2)}$, respectively. Also, all infected individuals (diagnosed/isolated, undiagnosed hospitalized) with strains 1 and 2 recover with rates λ_1 and λ_2 , respectively. Similarly, diagnosed/isolated and undiagnosed people with strains 1 and 2 die due to the disease with rates δ_1 and δ_2 , respectively, and the hospitalized people from strain 1 and 2 die at rates $\delta_{11} (> \delta_1)$ and $\delta_{21} (> \delta_2)$, respectively. The individuals that are

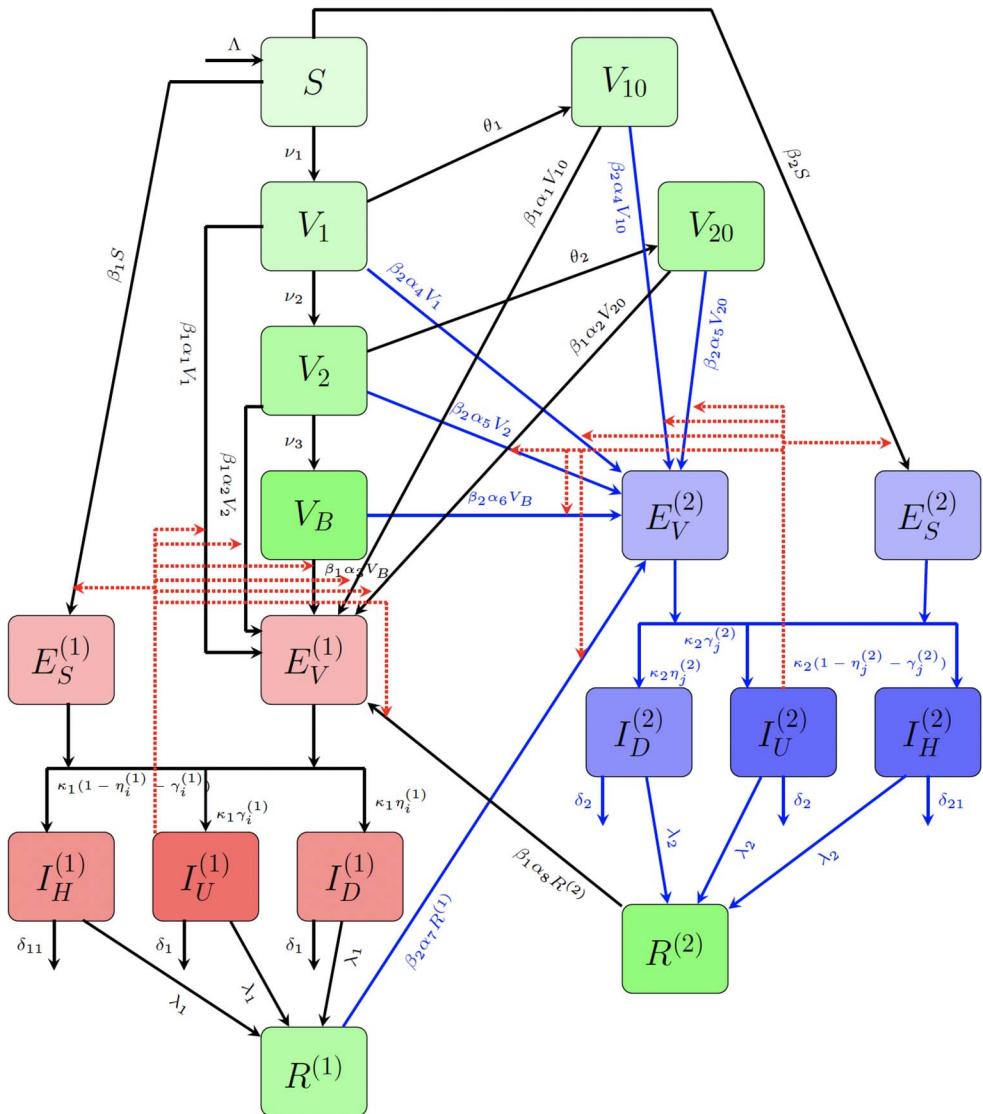


FIG. 1. **Schematic diagram of the two strain Covid-19 transmission model.** The bold pointed solid lines represent transfer of individuals to another compartment due to infection or progression. The pointed dotted red lines represent the interaction with different compartments that lead to new infections. The black solid lines represent infection or transfer due to first strain and blue solid lines represent infection or transfer due to second strain. For clarity of the diagram, the natural deaths are not included in the flow diagram.

recovered from strain 1 may get exposed with strain 2 at rate α_7 and the individuals that are recovered from strain 2 may get exposed to strain 1 at rate α_8 .

In our model, we also make the following assumptions: (i) since only a few cases of co-infection by multiple strains are reported, we do not consider a potential co-infection; (ii) since diagnosed people

usually get isolated or hospitalized and have limited contact with other people, we ignore a potential transmission from diagnosed and hospitalized people; (iii) since recovered people from one virus variant can get re-infection from a different variant as early as 90 days and reinfection from the same virus variant is less likely for at least in a short period of time (Ducharme, 2022; Padmanabhan *et al.*, 2022), we assume that there is no immediate re-infection by the same virus variant; (iv) we do not consider move-in and move-out of people in the city; and (v) we do not consider waning of vaccines efficacies during our study period.

Based on the description above, the rate of change of people in each compartment can be expressed as the following system of equations 1:

$$\begin{aligned}
 \frac{dS}{dt} &= \Lambda - \beta_1 SI_U^{(1)} - \beta_2 SI_U^{(2)} - (\nu_1 + \mu)S \\
 \frac{dV_1}{dt} &= \nu_1 S - \beta_1 \alpha_1 V_1 I_U^{(1)} - \beta_2 \alpha_4 V_1 I_U^{(2)} - (\nu_2 + \theta_1 + \mu)V_1 \\
 \frac{dV_{10}}{dt} &= \theta_1 V_1 - \beta_1 \alpha_1 V_{10} I_U^{(1)} - \beta_2 \alpha_4 V_{10} I_U^{(2)} - \mu V_{10} \\
 \frac{dV_2}{dt} &= \nu_2 V_1 - \beta_1 \alpha_2 V_2 I_U^{(1)} - \beta_2 \alpha_5 V_2 I_U^{(2)} - (\nu_3 + \theta_2 + \mu)V_2 \\
 \frac{dV_{20}}{dt} &= \theta_2 V_2 - \beta_1 \alpha_2 V_{20} I_U^{(1)} - \beta_2 \alpha_5 V_{20} I_U^{(2)} - \mu V_{20} \\
 \frac{dV_B}{dt} &= \nu_3 V_2 - \beta_1 \alpha_3 V_B I_U^{(1)} - \beta_2 \alpha_6 V_B I_U^{(2)} - \mu V_B \\
 \frac{dE_S^{(1)}}{dt} &= \beta_1 SI_U^{(1)} - (\kappa_1 + \mu)E_S^{(1)} \\
 \frac{dE_V^{(1)}}{dt} &= \beta_1 \alpha_1 (V_1 + V_{10}) I_U^{(1)} + \beta_1 \alpha_2 (V_2 + V_{20}) I_U^{(1)} + \beta_1 \alpha_3 V_B I_U^{(1)} + \beta_1 \alpha_8 R^{(2)} I_U^{(1)} - (\kappa_1 + \mu)E_V^{(1)} \\
 \frac{dI_H^{(1)}}{dt} &= \kappa_1 (1 - \gamma_1^{(1)} - \eta_1^{(1)}) E_S^{(1)} + \kappa_1 (1 - \gamma_2^{(1)} - \eta_2^{(1)}) E_V^{(1)} - (\lambda_{11} + \delta_{11} + \mu) I_H^{(1)} \\
 \frac{dI_U^{(1)}}{dt} &= \kappa_1 \gamma_1^{(1)} E_S^{(1)} + \kappa_1 \gamma_2^{(1)} E_V^{(1)} - (\lambda_1 + \delta_1 + \mu) I_U^{(1)} \\
 \frac{dI_D^{(1)}}{dt} &= \kappa_1 \eta_1^{(1)} E_S^{(1)} + \kappa_1 \eta_2^{(1)} E_V^{(1)} - (\lambda_1 + \delta_1 + \mu) I_D^{(1)} \\
 \frac{dR^{(1)}}{dt} &= \lambda_1 (I_U^{(1)} + I_D^{(1)}) + \lambda_{11} I_H^{(1)} - \beta_2 \alpha_7 R^{(1)} I_U^{(2)} - \mu R^{(1)} \\
 \frac{dE_S^{(2)}}{dt} &= \beta_2 SI_U^{(2)} - (\kappa_2 + \mu)E_S^{(2)} \\
 \frac{dE_V^{(2)}}{dt} &= \beta_2 \alpha_4 (V_1 + V_{10}) I_U^{(2)} + \beta_2 \alpha_5 (V_2 + V_{20}) I_U^{(2)} + \beta_2 \alpha_6 V_B I_U^{(2)} + \beta_2 \alpha_7 R^{(1)} I_U^{(2)} - (\kappa_2 + \mu)E_V^{(2)}
 \end{aligned} \tag{1}$$

$$\begin{aligned}
\frac{dI_H^{(2)}}{dt} &= \kappa_2(1 - \gamma_3^{(2)} - \eta_3^{(2)})E_S^{(2)} + \kappa_2(1 - \gamma_4^{(2)} - \eta_4^{(2)})E_V^{(2)} - (\lambda_{21} + \delta_{21} + \mu)I_H^{(2)} \\
\frac{dI_U^{(2)}}{dt} &= \kappa_2\gamma_3^{(2)}E_S^{(2)} + \kappa_2\gamma_4^{(2)}E_V^{(2)} - (\lambda_2 + \delta_2 + \mu)I_U^{(2)} \\
\frac{dI_D^{(2)}}{dt} &= \kappa_2\eta_3^{(2)}E_S^{(2)} + \kappa_2\eta_4^{(2)}E_V^{(2)} - (\lambda_2 + \delta_2 + \mu)I_D^{(2)} \\
\frac{dR^{(2)}}{dt} &= \lambda_2(I_U^{(2)} + I_D^{(2)}) + \lambda_{21}I_H^{(2)} - \beta_1\alpha_8R^{(2)}I_U^{(1)} - \mu R^{(2)}
\end{aligned}$$

A description of the model variables and related parameters is presented in Table 1.

TABLE 1 *Description of the variables and parameters of the model (1)*

Variable	Description
S	Susceptible
V_1	Vaccinated with first dose
V_{10}	Vaccinated with first dose but no more vaccines
V_2	Vaccinated with first and doses
V_{20}	Vaccinated with first and second doses but no booster shots
V_B	Vaccinated with booster dose
$E_S^{(1)}$	Exposed in strain 1 who are never vaccinated
$E_V^{(1)}$	Exposed in strain 1 who got at least one dose of vaccine
$E_S^{(2)}$	Exposed in strain 2 who are never vaccinated
$E_V^{(2)}$	Exposed in strain 2 who got at least one dose of vaccine
$I_H^{(i)}, I_U^{(i)}, I_D^{(i)}$	Infected: hospitalized, undiagnosed, and diagnosed/isolated from strains $i = 1, 2$
$R^{(1)}, R^{(2)}$	Recovered from strains $i = 1, 2$
Parameter	Description
Λ	Recruitment rate
μ	Natural death rate
β_1, β_2	Transmission probability per contact for susceptible humans for strain $i = 1, 2$
ν_1, ν_2, ν_3	Rate at which people get first, second and booster doses
θ_1, θ_2	Fraction of vaccinated (with 1 st and 2 nd doses) drop out from further vaccination
$\alpha_1, \alpha_2, \alpha_3$	Fraction of vaccinated (with 1 st , 2 nd and booster doses) that are not protected against strain 1
$\alpha_4, \alpha_5, \alpha_6$	Fraction of vaccinated (with 1 st , 2 nd and booster doses) that are not protected against strain 2
α_7, α_8	Fraction of recovered that are not protected against strain 1 and 2, respectively
κ_1, κ_2	Rate at which the exposed individuals with strain 1 and 2 leave the compartment
$\eta_1^{(1)}, \eta_2^{(1)}$	Fraction of the exposed individual ($E_S^{(1)}, E_V^{(1)}$) diagnosed with the COVID with strain 1
$\gamma_1^{(1)}, \gamma_2^{(1)}$	Fraction of the exposed individual ($E_S^{(1)}, E_V^{(1)}$) (strain 1) progressed to undiagnosed class
$\eta_3^{(2)}, \eta_4^{(2)}$	Fraction of the exposed individual ($E_S^{(2)}, E_V^{(2)}$) diagnosed with the COVID with strain 2
$\gamma_3^{(2)}, \gamma_4^{(2)}$	Fraction of the exposed individual ($E_S^{(2)}, E_V^{(2)}$) (strain 2) progressed to undiagnosed class
λ_1, λ_2	Recovery rate of infected individuals from strain 1 and 2, respectively
δ_1, δ_2	Death rate of (diagnosed/undiagnosed) individuals from strain 1 and 2, respectively
δ_{11}, δ_{21}	Death rate of (hospitalized) individuals of strains 1 and 2, respectively

2.2 Formulation of the basic reproduction number

The basic reproduction number (\mathcal{R}_0) is the average number of secondary infections produced by a typical case of an infection in a population where everyone is susceptible. Let S^* , V_1^* , V_{10}^* , V_2^* , V_{20}^* and V_B^* be defined by

$$\begin{aligned}
S^* &= \frac{\Lambda}{\nu_1 + \mu}, \quad V_1^* = \frac{\nu_1 \Lambda}{(\nu_1 + \mu)(\nu_2 + \theta_1 + \mu)}, \quad V_{10}^* = \frac{\theta_1 \nu_1 \Lambda}{\mu(\nu_1 + \mu)(\nu_2 + \theta_1 + \mu)}, \\
V_2^* &= \frac{\nu_1 \nu_2 \Lambda}{(\nu_1 + \mu)(\nu_2 + \theta_1 + \mu)(\nu_3 + \theta_2 + \mu)}, \quad V_{20}^* = \frac{\theta_2 \nu_1 \nu_2 \Lambda}{\mu(\nu_1 + \mu)(\nu_2 + \theta_1 + \mu)(\nu_3 + \theta_2 + \mu)}, \text{ and} \\
V_B^* &= \frac{\nu_3 \nu_1 \nu_2 \Lambda}{\mu(\nu_1 + \mu)(\nu_2 + \theta_1 + \mu)(\nu_3 + \theta_2 + \mu)}.
\end{aligned}$$

The disease free equilibrium \mathcal{E}_0 of our model is given by

Using the next generation matrix approach (Van den Driessche & Watmough, 2002), the basic reproduction number, \mathcal{R}_0 , of the model 1, is the dominant eigenvalue or spectral radius of the next generation matrix $\mathcal{F}\mathcal{V}^{-1}$, where

$$\mathcal{F} = \begin{pmatrix} 0 & \beta_1 S^* & 0 & 0 & 0 & 0 \\ 0 & \beta_1 \alpha_1 (V_1^* + V_{10}^*) + \beta_1 \alpha_2 (V_2^* + V_{20}^*) + \beta_1 \alpha_3 V_B^* & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \beta_2 S^* & 0 \\ 0 & 0 & 0 & 0 & \beta_2 \alpha_4 (V_1^* + V_{10}^*) + \beta_2 \alpha_5 (V_2^* + V_{20}^*) + \beta_2 \alpha_6 V_B^* & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$\mathcal{V} = \begin{pmatrix} \kappa_1 + \mu & 0 & 0 & 0 & 0 & 0 \\ 0 & \kappa_1 + \mu & 0 & 0 & 0 & 0 \\ -\kappa_1 \gamma_1^{(1)} & -\kappa_1 \gamma_2^{(1)} & \lambda_1 + \delta_1 + \mu & 0 & 0 & 0 \\ 0 & 0 & 0 & \kappa_2 + \mu & 0 & 0 \\ 0 & 0 & 0 & 0 & \kappa_2 + \mu & 0 \\ 0 & 0 & 0 & -\kappa_2 \gamma_3^{(2)} & -\kappa_2 \gamma_4^{(2)} & \lambda_2 + \delta_2 + \mu \end{pmatrix}.$$

Therefore, the basic reproduction number, \mathcal{R}_0 , for our model is

$$\mathcal{R}_0 \equiv \max\{\mathcal{R}_{0+}, \mathcal{R}_{0-}\}, \quad (2)$$

where

$$\mathcal{R}_{0_1} = \frac{\kappa_1 \beta_1 \left[\alpha_1 \gamma_2^{(1)} (V_1^* + V_{10}^*) + \alpha_2 \gamma_2^{(1)} (V_2^* + V_{20}^*) + \alpha_3 \gamma_2^{(1)} V_B^* + \gamma_1^{(1)} S^* \right]}{(\kappa_1 + \mu)(\lambda_1 + \delta_1 + \mu)},$$

$$\mathcal{R}_{0_2} = \frac{\kappa_2 \beta_2 \left[\alpha_4 \gamma_4^{(2)} (V_1^* + V_{10}^*) + \alpha_5 \gamma_4^{(2)} (V_2^* + V_{20}^*) + \alpha_6 \gamma_4^{(2)} V_B^* + \gamma_3^{(2)} S^* \right]}{(\kappa_2 + \mu)(\lambda_2 + \delta_2 + \mu)}.$$

The local stability results follow from Theorem 2 of [Van den Driessche & Watmough \(2002\)](#).

THEOREM 1 Consider the model (1). Then, the disease-free equilibrium (\mathcal{E}_0) is locally-asymptotically stable if $\mathcal{R}_0 < 1$, and unstable if $\mathcal{R}_0 > 1$.

3. Model parameters

3.1 Initial values

We used data from Dougherty County Georgia, USA ([CDC, COVID-19 Vaccinations, 2021c; USAfacts, 2021](#); [WPReview, 2020](#)). Located in south west of the state of Georgia, Daughtry County has about 87,000 population. To mimic the situation when the Omicron variant is prevailing the most part of the world, we assume that compartments with subscript 1 are associated with the Omicron variant (strain 1) ([CDC, COVID-19 Vaccinations, 2021b](#)). Based on the data available in [covidactnow.org](#) ([Covid ActNow](#)), about 48,720 (56% of the total) people got at least one dose of COVID-19 vaccine until 11 February 2022. As about 48,198 people (55.4%) got at least first dose of vaccines before 22 January, only 522 new people got the first dose of vaccine between 22 January to 12 February. Then the number of people who got first dose of vaccine in this time period is $V_1(0) = 552$. Also, by 12 February 2022, about 38,280 people were never vaccinated ($S(0) = 38,280$) and 6,699 people who got first dose did not get the second dose of vaccine within the required time window ($V_{10}(0) = 6,699$). We assume that $V_{20}(0) = 0$. Also, by 12 February 2022, about 41,499 received second dose of the vaccine (47.7%) and 14,355 (16.5%) people received booster dose ($V_B(0) = 14,355$). Therefore, the number of people who got second dose but did not get booster shot is 27,231 ($V_2(0) = 27,231$).

About 130 people were hospitalized, 46 people were diagnosed on 10 February, i.e., $I_D^{(1)}(0) = 46$ and $I_H^{(1)}(0) = 130$. Assume that about five times more infected people are undiagnosed i.e., $I_U^{(1)} = 200$. The Omicron variant of COVID-19 started in GA on 5 December 2021 and since then there were 4,749 reported cases, assume that about 1,500 people were recovered by 10 February, i.e., $R^{(1)}(0) = 1,500$. Also, the initial values for exposed, diagnosed, undiagnosed, hospitalized, and recovered from strain 2 are assumed to be $E_S^{(2)} = 1, E_V^{(2)} = 1, I_H^{(2)} = 0, I_U^{(2)} = 0, I_D^{(2)} = 0, R^{(2)} = 0$. The initial values of all variables are presented in Table 2.

3.2 Parameters related to transmission and progression

The average life expectancy of the people in Dougherty county is 75.05 years ([Healthdata, 2021](#)). Thus, the natural death rate is $\mu = \frac{1}{75.05 \times 365}$ per day. Assuming the steady state level before the start of the epidemics, we set $\Lambda - \mu S_0 = 0$, where S_0 is the total population before the start of the epidemic. Thus, the recruitment rate is $\Lambda = \frac{1}{75.05 \times 365} S_0$ per day. Since the median incubation period of Omicron

TABLE 2 *Initial values of variables (11 February 2022)*

Variable	Values	Sources	Variable	Values	Sources
$S(0)$	38,280	USAfacts (2021); WPReview (2020)	$I_U^{(1)}(0)$	200	Assumption
$V_1(0)$	552	(Covid ActNow)	$I_D^{(1)}(0)$	46	(Covid ActNow)
$V_{10}(0)$	6,699	(Covid ActNow)	$R^{(1)}(0)$	1500	Assumption
$V_2(0)$	27,231	(Covid ActNow)	$E_S^{(2)}(0)$	1	Assumption
$V_{20}(0)$	0	Assumption	$E_V^{(2)}(0)$	1	Assumption
$V_B(0)$	14,355	(Covid ActNow)	$I_H^{(2)}(0)$	0	Assumption
$E_S^{(1)}(0)$	200	Assumption	$I_U^{(2)}(0)$	0	Assumption
$E_V^{(1)}(0)$	300	(Covid ActNow)	$I_D^{(2)}(0)$	0	Assumption
$I_H^{(1)}(0)$	130	(Covid ActNow)	$R^{(2)}(0)$	0	Assumption

variant of COVID-19 is 3 days ([CDC, COVID-19 Vaccinations, 2021d](#)), we take $k_1 = \frac{1}{3}$ per day. For the second strain, we assume the base value for progression rate from exposed to infected is $k_2 = \frac{1}{3}$. The infected individuals either die or recover and since there were only 32 reported deaths out of 4,749 infections between 11 December 2021 and 12 February 2022 ([USAfacts, 2021](#)), the probability that a diagnosed patient dies with the first strain can be approximated as 0.0067. Also, an infected individual can be infectious up to 10 days ([CDC, COVID-19 Vaccinations, 2021a](#)). Assuming the same death rate for both diagnosed and undiagnosed individuals, we obtain $\delta_1 = 0.0067 \times \frac{1}{10} = 0.00067$, which implies the recovery rate for strain 1 to be $\lambda_1 = (1 - 0.067) \times \frac{1}{10} = 0.099$ per day.

We assume that hospitalized patients have 5 times higher death rates than non hospitalized patients in both strains i.e., $\delta_{11} = 5 \times \delta_1, \delta_{21} = 5 \times \delta_2$. We assume that the recovery rate of the strain 2 is half times slower than the strain 1 implying $\lambda_2 = 0.0495$. For the transmission rates (β_1) for strain 1, we used the estimated value from our previous work ([Pantha et al.](#)) $\beta_1 = 4.613 \times 10^{-6}$ and for the strain 2, we assume $\beta_2 = 5 \times \beta_1$ and about one third of individuals exposed with either of strain 1 or strain 2 are tested positive and isolated. Also, we assume that about three fifth fraction of individuals remain undiagnosed. This implies $\eta_i \sim 0.3, \gamma_i \sim 0.6$, for $i = 1, 2, 3, 4$.

3.3 Parameters related to vaccination

Based on the currently implemented two-dose vaccines, Pfizer and Moderna, we consider 25 days apart on average (Pfizer 21 days, Moderna 28 days) between the first and the second dose of the vaccines ([CDC, COVID-19 Vaccinations, 2021a](#)). For the base case computation, we assume that 60% of the susceptible population get the first dose vaccine within 5 months. Also, 85% of the first-dose vaccinated population get the second dose within 25 days of their first dose and it takes an additional 14 days for the vaccines to be fully effective. Note that the solution of $\frac{dS}{dt} = -\nu_1 S$ provides $\nu_1 = -\frac{\ln(S(t)/S_0)}{t}$. With this formulation, for 60% population to be vaccinated within 5 months (150 days), we require the vaccination rate of $\nu_1 = 0.006$. Similarly, to fully protect 85% of the first-dose vaccinated population in 39 days, we require the second dose vaccination rate to be $\nu_2 = \frac{0.85}{39} = 0.022$.

Since the vaccination trend shows a slower rate of booster dose vaccination, we assume the booster dose vaccination rate as half as the second dose vaccination rate, i.e., $\nu_3 = 0.011$. The efficacy of the Pfizer mRNA vaccine has been found to be between 52.4% and 68.5% with its first dose, and 92% after

TABLE 3 *Parameters of the model (1) and their base values*

Parameter	Base value	Source	Parameter	Base value	Source
Λ	3.176	Calculated	δ_{11}	0.00335	Assumption
μ	3.65×10^{-5}	Healthdata (2021)	δ_2	0.0013	Assumption
β_1	4.613×10^{-6}	(Pantha <i>et al.</i>)	δ_{21}	0.0067	Assumption
β_2	2.3065×10^{-5}	Assumption	v_1	0.006	Calculated
α_1	0.35	Polack <i>et al.</i> (2021)	v_2	0.022	Calculated
α_2	0.08	Polack <i>et al.</i> (2021)	v_3	0.011	Calculated
α_3	0.04	Polack <i>et al.</i> (2021)	α_4	1.75	Assumption
θ_1	0.0035	Assumption	α_5	0.4	Assumption
θ_2	0.002	Assumption	α_6	0.2	Assumption
κ_1, κ_2	$\frac{1}{3}, \frac{1}{3}$	CDC, COVID-19 Vaccinations (2021d)	α_7	0.1	Assumption
$\eta_1^{(1)}$	0.3	Assumption	α_8	0.02	Assumption
$\eta_2^{(1)}$	0.3	Assumption	$\eta_3^{(2)}$	0.33	Assumption
$\gamma_1^{(1)}$	0.6	Assumption	$\eta_4^{(2)}$	0.33	Assumption
$\gamma_2^{(1)}$	0.65	Assumption	$\gamma_3^{(2)}$	0.62	Assumption
λ_1	0.099	Calculated	$\gamma_4^{(2)}$	0.64	Assumption
δ_1	0.00067	Calculated	λ_2	0.0495	Assumption

completing the second dose (Polack *et al.*, 2021). Therefore, we assume that the first dose of the vaccine provides 65% protection, implying $\alpha_1 = 0.35$, and the both doses of the vaccination provide 92% of the protection, implying $\alpha_2 = 0.08$. Also, we assume a booster dose in addition to two doses provides 96% of the protection, implying $\alpha_3 = 0.04$. We also assume that 10% of the first dose vaccinated population do not get the second dose in the first month, implying $\theta_1 = 0.0035$ and 30% of the second dose vaccinated population do not get the booster dose in the next 6 months, implying $\theta_2 = 0.002$. The parameter values are given in Table 3.

4. Results and discussions

4.1 Computation of the basic reproduction number, \mathcal{R}_0

We use the expression for the basic reproduction number from Section 3 and the parameter values from Tables 2 and 3 to evaluate the value of \mathcal{R}_0 . We obtained the basic reproduction number of the strain 1 to be $\mathcal{R}_1 = 0.24$ and of the strain 2 to be $\mathcal{R}_2 = 11.43$, implying $\mathcal{R}_0 = \max\{\mathcal{R}_1, \mathcal{R}_2\} = 11.43$. This suggests that the strain 2 is on the rise while the strain 1 is on the declining phase. In Figure 2, we plot \mathcal{R}_0 for various values of transmission rates β_1 (strain 1) and β_2 (strain 2) keeping other parameters in their baseline values. In $\beta_1\beta_2$ -parameter space (Figure 2a), we presented subregions corresponding to the dominating strains (the strain 1 or strain 2). Corresponding three dimensional plot is presented in Figure 2b, in which we observe that the strain 2 transmission rate (β_2) more sensitively contribute to the value of \mathcal{R}_0 than the strain 1 transmission rate (β_1). Also, the value of \mathcal{R}_0 remains less than 1 when the values of $\beta_1 < 1.9 \times 10^{-5}$ and $\beta_2 < 2 \times 10^{-6}$ simultaneously (Figure 2b). Therefore, a higher effort should be put in controlling the strain 2 than the strain 1 for the overall control of the disease.

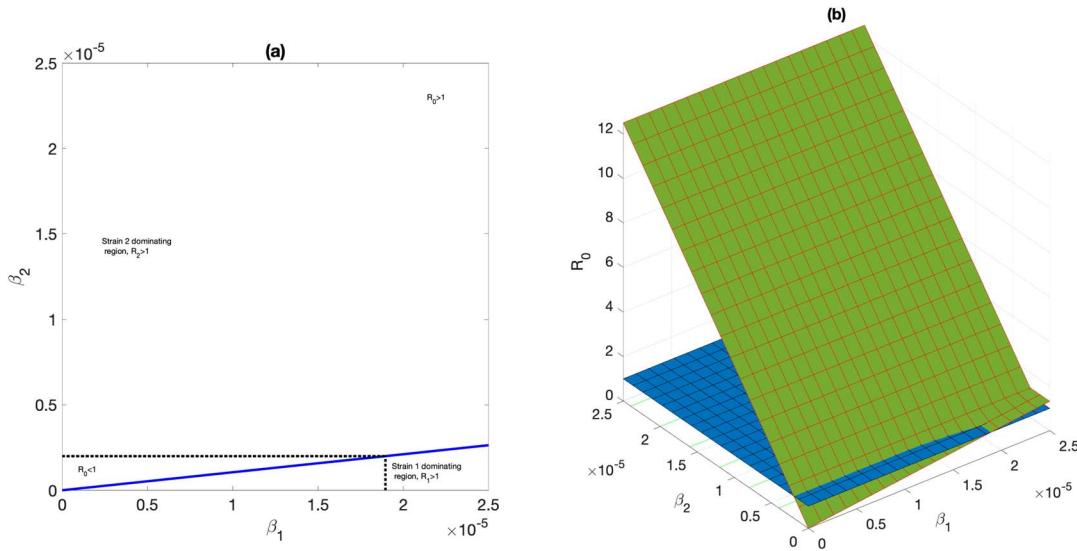


FIG. 2. (a) Contour plot (b) 3-D plot to show the dependence of basic reproduction number \mathcal{R}_0 on the transmission rates β_1 (for strain 1) and β_2 (for strain 2).

In Figure 3, we plot the basic reproduction number \mathcal{R}_0 for various combination of relative transmission rates $\frac{\beta_2}{\beta_1}$ and other vaccination and progression related parameters. Here, we denote $\frac{\beta_2}{\beta_1} = K$, indicating the new strain (strain 2) has K times more transmissibility than existing strain (strain 1), i.e., $\beta_2 = K\beta_1$. We observe that \mathcal{R}_0 increases rapidly with increasing value of relative transmission rates K and vaccine dropout rates $\theta_i, i = 1, 2$, and decreases for decreasing values of vaccination rates (second dose, v_2 , and booster, v_3). For example, when the new strain (strain 2) is taken to have 30% higher transmission rate than the existing strain (strain 1), i.e., $K = 0.3$, and $\beta_1 = 4.613 \times 10^{-6}$, the value of \mathcal{R}_0 is 1.59 for the low level of second dose vaccination rate ($v_2 = 0.012$). Increasing the second dose vaccination rate to $v_2 = 0.048$, the value of \mathcal{R}_0 decreases to 0.93, causing the decline in the disease spread (Figure 3b). With the increased value of relative transmission, \mathcal{R}_0 can reach as high as 10.07 when $\beta_2 = 3 \times \beta_1$, which can again be lowered to almost half by increasing v_2 ($\mathcal{R}_0 = 5.36, v_2 = 0.05, \beta_2 = 3 \times \beta_1$). Hence, increasing the second dose vaccination rate helps to reduce the spread significantly. On the other hand, increasing the vaccine dropout rates or relative transmission rates increases \mathcal{R}_0 . For example, when the relative transmission rate $K = 0.2$ and $\theta_1 = 0.011$ (low vaccine dropout rate), the basic reproduction number $\mathcal{R}_0 = 0.75 < 1$ (Figure 3e) but increasing the dropout rate $\theta_1 = 0.2$ results in $\mathcal{R}_0 = 1.58 > 1$. Furthermore, for $K = 3$ and $\theta_1 = 0.011$, the reproduction number becomes $\mathcal{R}_0 = 12.06$, which can further dramatically increase ($\mathcal{R}_0 = 25.4$) with the a higher dropout rate of $\theta_1 = 0.2$.

4.2 Overtake-time by the new strain

In this subsection, we present the overtake-time by new strain (strain 2) over existing strain (strain 1) for combination of relative transmission rates and other vaccinations or vaccine dropout parameters. In Figure 4, we observe that the time to overtake by new strain is shortened rapidly with increase in the relative transmission rate $\frac{\beta_2}{\beta_1}$ and increase in the first dose vaccination rate, v_1 . For example, when

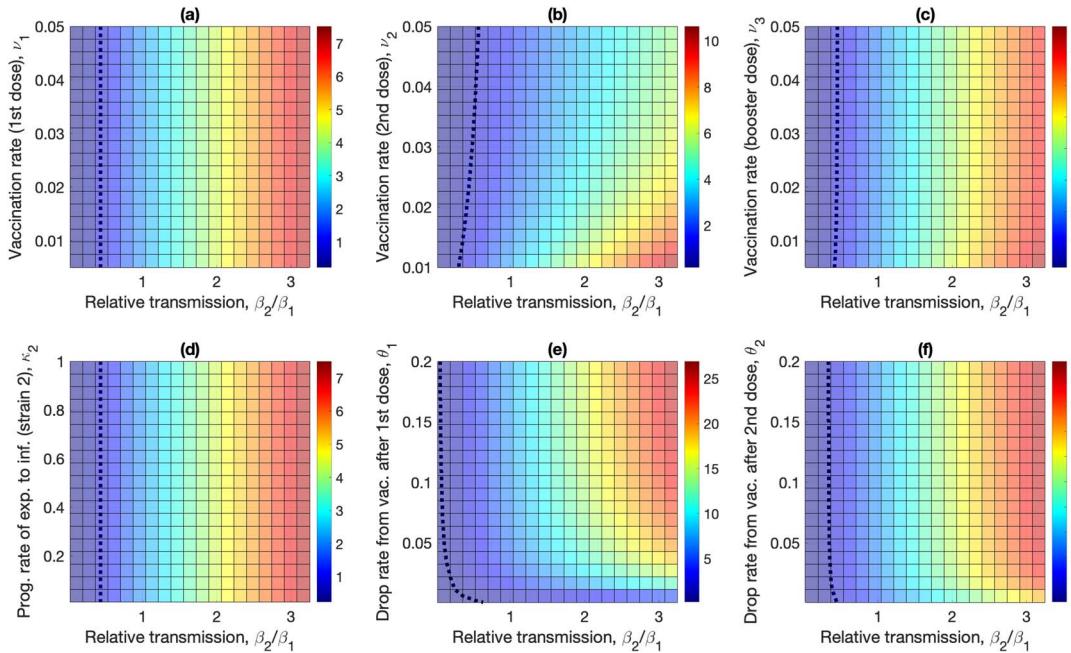


FIG. 3. Reproduction numbers for various (a) relative transmission rates and first dose vaccination rates, (b) relative transmission rates and second dose vaccination rates, (c) relative transmission rates and second dose vaccination rates, (d) relative transmission rates and progression rates from exposed to infected, (e) relative transmission rates and vaccine dropout rates after first dose and (f) relative transmission rates and vaccine dropout rates after second dose. The bold dotted line denotes $\mathcal{R}_0 = 1$.

$\frac{\beta_2}{\beta_1} = 1.19$ and first dose vaccination rate is $v_1 = 0.0036$, the time to overtake by new strain is about 65 days but this time reduces to just 27 days with the same $v_1 = 0.0036$ and higher relative transmission rates $\frac{\beta_2}{\beta_1} = 3.13$ (Figure 4a). On the other hand, when the first dose vaccination rate, v_1 , is increased to 0.047, the time to overtake by new strain decreases to 47 days for the lower level of the relative transmission rate $\frac{\beta_2}{\beta_1} = 1.19$. This is because vaccination does not stop or lower the transmission against strain 2, it just lowers the severity of the disease. As shown in Figure 4(b,c,e,f), increasing vaccination rates with second and booster dose, as well as the vaccine dropout rates, throughout their range delay the time to overtake (by new strain) by merely two days. Also, as expected, increasing the progression rate of new strain from exposed to infected can significantly shorten the time to overtake by the new strain (Figure 4d).

4.3 Number of hospitalized and undiagnosed

Here, we present the number of undiagnosed cases and number of hospitalized cases for the combination of relative transmission with other vaccination and progression related parameters for 180 days (first 6 months). From Figure 5, we observe that increasing the relative transmission rates, $\frac{\beta_2}{\beta_1}$, increases the number of hospitalized cases, while increasing the vaccination rates decreases the number of hospitalized cases. For example, as shown in Figure 5a, the number of hospitalized cases for $\frac{\beta_2}{\beta_1} = 1.19$ and $v_1 = 0.0035$ is 1452 but increasing the first dose vaccination $v_1 = 0.047$ decreases the number of hospitalization by 62% to 547. This result underscores the importance of first dose vaccination. The

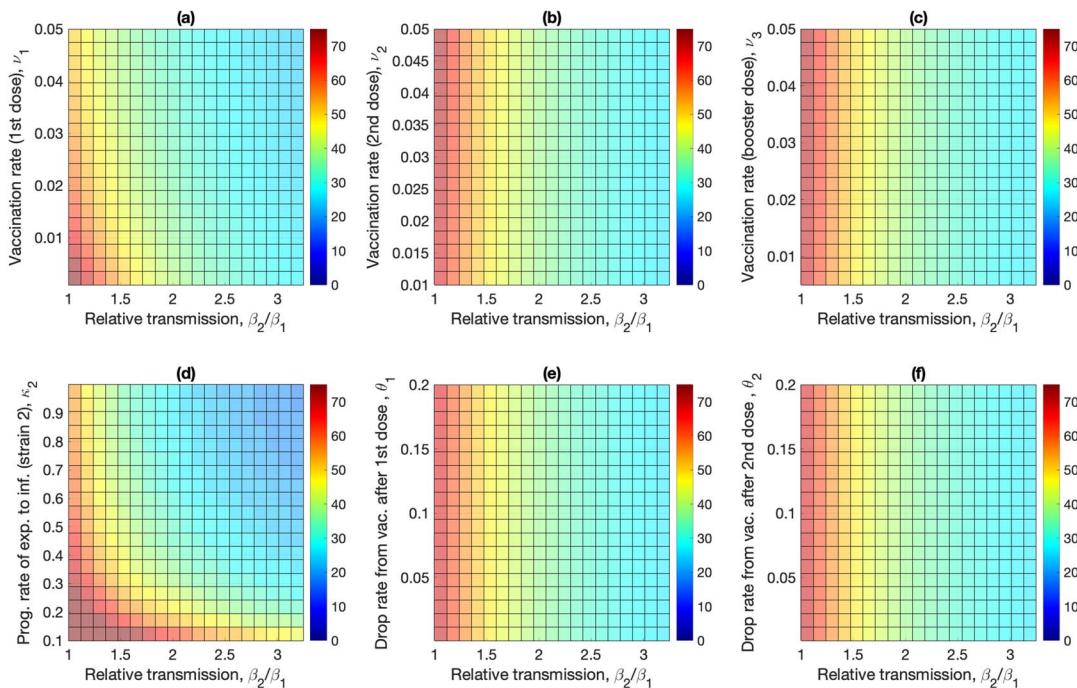


FIG. 4. The time at which the new strain (strain 2) overtakes the existing strain (strain 1) for various (a) relative transmission rate and first dose vaccination rate, (b) relative transmission rate and second dose vaccination rate, (c) relative transmission rate and booster dose vaccination rate, (d) relative transmission rate and progression rate from exposed to infected, (e) relative transmission rate and vaccine dropout rate after first dose and (f) relative transmission rate and vaccine dropout rate after second dose.

increase in the second dose vaccination rate does not decrease the hospitalized cases significantly (1296 versus 1259 when ν_2 goes from 0.012 to 0.047 and $\frac{\beta_2}{\beta_1} = 1.19$, Figure 5b). A similar result is obtained for the booster dose (Figure 5c). An increase in the progression rate, κ_2 , from exposed to infected (new strain) or the dropout rate increases the number of hospitalized cases (Figure 5d, e, f).

Next, in Figure 6, we present that increasing the relative transmission rate, $\frac{\beta_2}{\beta_1}$, increases the number of undiagnosed cases, which is, however, less affected by the vaccination rate. This is because the vaccines considered here reduce the severity of disease, hospitalization, and symptomatic infection but are not fully protective against new infection or spread. For example, in Figure 6a, the number of undiagnosed cases in the first 6 months for $\frac{\beta_2}{\beta_1} = 1.119$ and $\nu_1 = 0.0035$ is 44,980 but increasing the first dose vaccination to $\nu_1 = 0.047$ decreases the number of undiagnosed by just 1000 (merely a 2.2% decrease). On the other hand, if the relative transmission rate, $\frac{\beta_2}{\beta_1}$, is increased to 3.13, the number of undiagnosed cases becomes 53,230 (about 18.34% higher) for $\nu_1 = 0.0035$. Similar outcomes are observed for second and booster dose vaccination rate and relative transmission rate (Figure 6(b,c)).

An increase in the progression rates, κ_2 , from exposed to infected (new strain) or vaccine dropout rates, $\theta_i, i = 1, 2$, increases the number of undiagnosed cases (Figure 5d, e, f). Hence, relative transmission have greater impact in number of undiagnosed cases compared to the vaccination related parameters (vaccination rates and dropout rates). This suggests that the vaccination plan should be

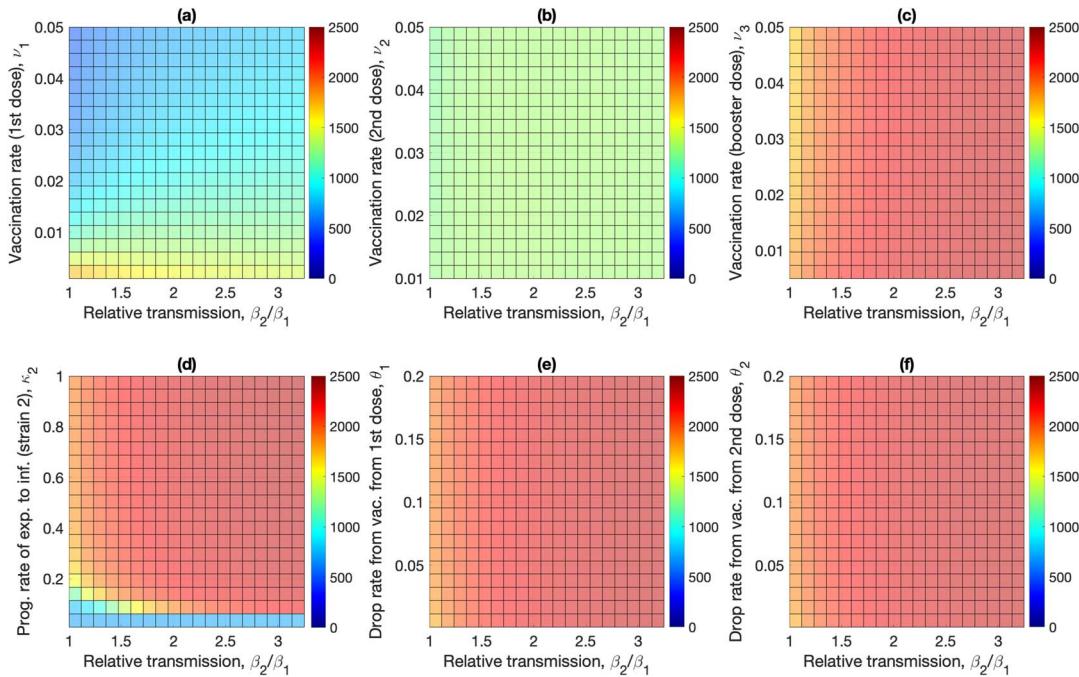


FIG. 5. Number of hospitalized patients for various (a) relative transmission rate and first dose vaccination rate, (b) relative transmission rate and second dose vaccination rate, (c) relative transmission rate and second dose vaccination rate, (d) relative transmission rate and progression rate from exposed to infected, (e) relative transmission rate and vaccine dropout rate after first dose and (f) relative transmission rate and vaccine dropout rate after second dose.

accompanied with other strategies that reduce the transmission, such as masking, social distancing, and washing hands to control the spread.

4.4 Sensitivity of parameters

To find out parameters that has greater impact in the disease spread, we performed a sensitivity analysis using LHS-PRCC package in Matlab ([MATLAB, M](#)). Latin Hypercube Sampling (LHS) technique generates N sample values for each of K parameters with given range around the baseline values from Table 3 (we considered the range of $\pm 20\%$ around the baseline values). We assumed uniform distribution for each sample parameter value. The parameter space constructed in such a way is an $N \times K$ matrix where N is the number of possible values for each parameter and K is the total parameters involved in the analysis. In our case $K = 33$, and we chose $N=1000$. Each row of the matrix represent a set of parameters. For each set of parameter, differential equation solver *ODE45* was run and the value of output (response) variables were recorded.

For our model, we consider four output variables: the basic reproduction number (\mathcal{R}_0), the overtaking-time by strain 2, the total number of undiagnosed cases $\left[\int_0^{180} \kappa_1 \gamma_1^{(1)} E_S^{(1)} + \kappa_1 \gamma_2^{(1)} E_V^{(1)} + \kappa_2 \gamma_3^{(2)} E_S^{(2)} + \kappa_2 \gamma_4^{(2)} E_V^{(2)} dt \right]$ and the total number of hospitalized cases $\left[\int_0^{180} \kappa_1 (1 - \gamma_1^{(1)} - \eta_1^{(1)}) E_S^{(1)} + \kappa_1 (1 - \gamma_2^{(1)} - \eta_2^{(1)}) E_V^{(1)} + \kappa_2 (1 - \gamma_3^{(2)} - \eta_3^{(2)}) E_S^{(2)} + \kappa_2 (1 - \gamma_4^{(2)} - \eta_4^{(2)}) E_V^{(2)} dt \right]$ during the first 180 days. A parameter

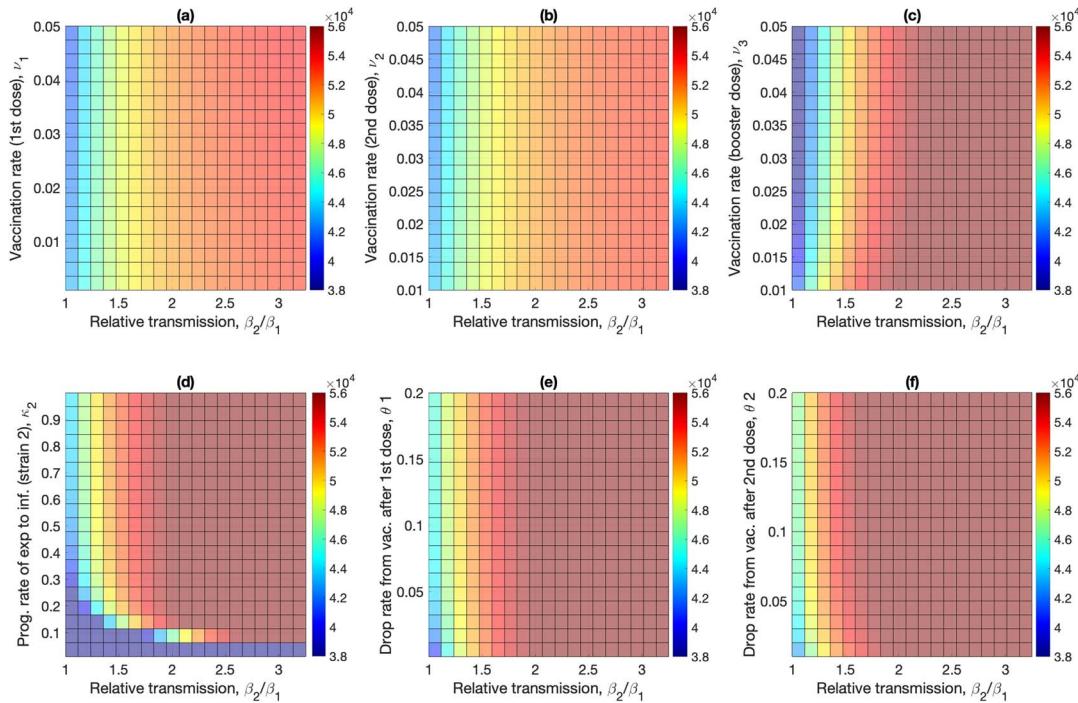


FIG. 6. Number of undiagnosed patients for various transmission rate of new strain of COVID-19. (a) relative transmission rate and first dose vaccination rate, (b) relative transmission rate and second dose vaccination rate, (c) relative transmission rate and second dose vaccination rate, (d) relative transmission rate and progression rate from exposed to infected, (e) relative transmission rate and vaccine dropout rate after first dose and (f) relative transmission rate and vaccine dropout rate after second dose.

with a PRCC value greater than 0.5 in magnitude (and correspondingly small p-value (< 0.05)) indicates that the chosen output (response) variable is highly sensitive to the parameter. A PRCC value closer to +1 or -1 indicates a stronger influence, with the negative sign indicating that the parameter is inversely proportional to the response variable.

The partial rank correlation coefficient is evaluated and their significance test was performed for the parameter space of each variable and values of each for output variable. From the sensitivity analysis (Figures 7 (a-d)), we observed that the basic reproduction number is sensitive to the parameters $\gamma_4^{(2)}, \beta_2, \Lambda, \theta_1$, and α_4 with corresponding p-value less than 0.05. The parameters $\gamma_4^{(2)}, \beta_2, \Lambda, \theta_1$, and α_4 are proportional to \mathcal{R}_0 and the parameters $\lambda_2, \mu, \nu_2, \nu_3$ are inversely proportional to \mathcal{R}_0 . Similarly, the parameters $k_2, \gamma_3^{(2)}, \gamma_4^{(2)}, \beta_2, \lambda_1^{(1)}, \alpha_4$ are proportional to the overtake-time by strain 2 and the parameter β_1 is inversely proportional to the overtake-time by strain 2 with corresponding p-value less than 0.05. The number of hospitalized cases for the first 180 days is sensitive to the parameters $\eta_3, \eta_4, \gamma_3^{(2)}, \gamma_4^{(2)}$ with p-value less than 0.05. These parameters are inversely proportional to the number of hospitalized cases. Similarly, the parameters $\gamma_3^{(2)}, \gamma_4^{(2)}, \beta_2, \lambda_2$, and α_5 are sensitive to the total number of undiagnosed cases while the parameter λ_2 is inversely proportional to the number of undiagnosed cases.

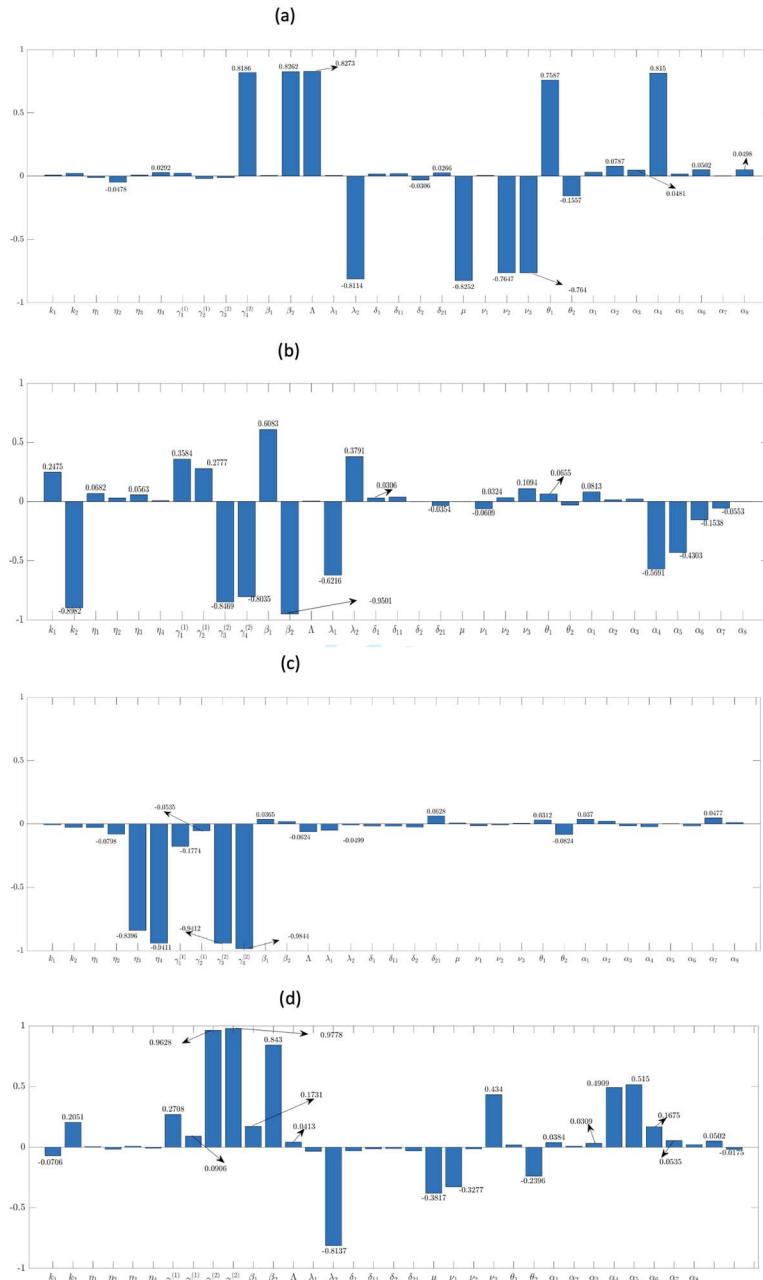


FIG. 7. The partial rank correlation coefficients (PRCC) for output (response) variables: (a) Basic reproduction number, (b) overtaking time by strain 2, (c) number of hospitalized in the interval [0,180] days, and (d) number of undiagnosed in the interval [0,180] days.

5. Conclusions

COVID-19 pandemic is an ongoing threat to the public health in almost all nations in the world. Although effective vaccines are developed and are in use, the emergence of new and highly transmissible virus strains with severe symptoms have made it very challenging to contain the spread. Waning of the vaccines immunity and infection of vaccinated or recovered people by variant strains pose an additional complication to the control of the disease. In this work, we developed a mathematical models to study the COVID-19 transmission dynamics of two strains of SARS-CoV-2. We illustrated our numerical results using the data from Daugherty County of Georgia, USA.

We derived the basic reproduction number for two strain COVID-19 dynamics, \mathcal{R}_0 , which is equal to the maximum of individual strain's reproduction numbers, \mathcal{R}_1 and \mathcal{R}_2 . Assuming the strain 2 is five fold more transmissible than strain 1, our analysis shows the basic reproduction number in Daugherty County can reach as high as 11.43 indicating a severe outbreak of the disease. Our study suggests that the reproduction number can be kept below 1 by lowering transmission rates and vaccine dropout rates. The two doses of vaccines are more effective in reducing the value of \mathcal{R}_0 . Increasing the vaccination dropout rates can quickly increase the reproduction number beyond unity. In case of high transmission scenarios, only vaccination is not enough to reduce the \mathcal{R}_0 and should be accompanied by other measures, such as sanitizing, practicing personal hygiene, masking and lowering activities, that help reduce the public interactions.

Using our model, we generated values of outbreak indicator variables: basic reproduction numbers, the total number of hospitalized cases and undiagnosed cases in the first 180 days. We also evaluated the overtaking-time by a new strain. Our study suggests that increasing the relative transmission rate β_2/β_1 increases the outbreak indicator variables but decreases the overtaking-time by strain 2. Similarly, an increased level of first dose vaccination rate decreases overtaking-time by strain 2 when the relative transmission rate β_2/β_1 is in the low level. The number of hospitalized cases decreases significantly with an increased vaccination rates, a lowered progression rates or a lowered dropout rate.

Some limitations of our study include a lack of detailed information about a new strain and parameters associated to it. Many parameters related to the strain 2 were assumed at some reasonable level for the purpose of computation. Estimating parameters with the new strain data would help obtain more accurate results of our simulations. Our study have limited analytical results due to the complexity of the model. We did not consider the reinfection from the same strain or the co-infection by multiple strains at the same time.

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