Modeling COVID-19 Breakthrough Infections in a Vaccinated Population

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Abstract: - The consequences of the COVID-19 pandemic that originated in Wuhan, China in 2019 are still being felt globally. At the onset of the pandemic, countries had several measures in place to prevent the spread of the virus. The development and availability of COVID-19 vaccines turned out to be one of the most effective tools for containing the pandemic, especially in developed countries. This paper considers a model of COVID-19 breakthrough infections, which are cases where individuals become infected with COVID-19 despite being fully vaccinated. The model proposed is a type of the SIR model with a compartment accounting for vaccinated individuals and is governed by a system of differential equations. We compute the basic reproduction number of the model and use it to analyze the equilibria for both local and global stability. Further, we use numerical simulations of the model to understand the factors that contribute to breakthrough infections such as vaccination rates, vaccine efficacy, and virus transmission dynamics.

Key-Words: - COVID-19, SARS-CoV-2, Mathematical model, Vaccinations, Basic reproduction number

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1 Introduction

The COVID-19 pandemic has affected millions of people globally, causing unprecedented loss of life and disrupting economies and social systems. Vaccination emerged as one of the key tools in the fight against the pandemic. Vaccines have been developed and administered to people worldwide to provide immunity against the virus, and they have been shown to be highly effective, [1], [2]. However, there is still a risk of breakthrough infections, where fully vaccinated individuals contract the virus. Breakthrough infections occur when an individual contracts COVID-19 after being fully vaccinated, [3], [4]. These infections can occur for several reasons, including vaccine efficacy, virus variants, and individual immunity. While vaccines are highly effective in preventing severe illness and death, they are not 100% effective, [5]. This means that even fully vaccinated individuals can still contract the virus.

Virus variants, such as the Delta variant and omicron variant, can also increase the risk of breakthrough infections, [6]. These variants have mutations that make them more transmissible and resistant to antibodies, potentially reducing vaccine efficacy, [7], [8]. Furthermore, individual immunity can also play a role in breakthrough infections. Factors such as age, underlying health conditions,

and medications can affect an individual's immune response to the vaccine, [9]. Despite the risk of breakthrough infections, vaccination remains critical in the fight against COVID-19. Vaccines have been shown to reduce the severity of illness and the risk of hospitalization and death in breakthrough infections, [10]. They also help to reduce the transmission of the virus by providing herd immunity, making it harder for the virus to spread and mutate, [11], [12], [13].

Mathematical models have played significant roles in epidemiological research and have been widely used in the fight against COVID-19 since the beginning of the pandemic, [14], [15], [16], [17], [18], [19]. These models are computer simulations that use mathematical equations to predict the spread of the virus, the impact of interventions, and the potential outcomes of different scenarios. One of the key benefits of mathematical models is their ability to provide early warning signals of potential outbreaks, [20]. By analyzing data on the spread of the virus, mathematical models can predict the future trajectory of the pandemic, [21]. Mathematical models can also be used to evaluate the effectiveness of different interventions, [22]. For example, models can be used to compare the impact of different vaccination strategies, such as

prioritizing certain age groups or populations, to identify the most effective approach, [23].

Several investigators have developed targeted mathematical models for the transmission dynamics of COVID-19 to facilitate further understanding of the virus' characteristics and impact on humans, [24], [25], [26], [27], [28]. In this study, we present a mathematical model with breakthrough infections in vaccinated populations by COVID-19 or its variants. We considered a SIR-type model of the form SVIRD, where "V" and "D" represents the vaccinated and death compartments, respectively. The transitions between the compartments are governed by a set of differential equations that describe how the disease spreads over time. The equations are based on the assumption that the rate of transmission of the disease depends on the number of susceptible individuals, the number of infectious individuals, and the efficacy of the vaccine. The model further assumes that vaccinated populations are not immune from being infected by the virus or its variants. Using the quantitative results of the model, we will analyze the impact of COVID-19 on a given population.

2 Mathematical Model

An SVIRD model is a mathematical model used to simulate the spread of an infectious disease in a population. It is an extension of the classic SIR model, which stands for the Susceptible-Infectious-Recovered model. The SVIRD model adds two additional compartments to the SIR model: the Vaccinated and Deaths compartments. The compartments in the SVIRD model are defined as follows: susceptible (S) are individuals who are susceptible to getting infected by the disease; vaccinated (V) are individuals who have received a vaccine against the disease and are thus protected from getting infected; infectious (I) are individuals who have been infected with the disease and are capable of transmitting it to others; recovered (R) are individuals who have recovered from the disease and are no longer infectious; and deaths (D) are individuals who have died from the disease.

We assume that the total human population at any time t denoted by $N(t)$ is:

$$N(t) = S(t) + V(t) + I(t) + R(t) + D(t).$$

The transition rates between compartments together with their descriptions are given in Table 1, and a schematic diagram of the SVIRD model is given in Figure 1.
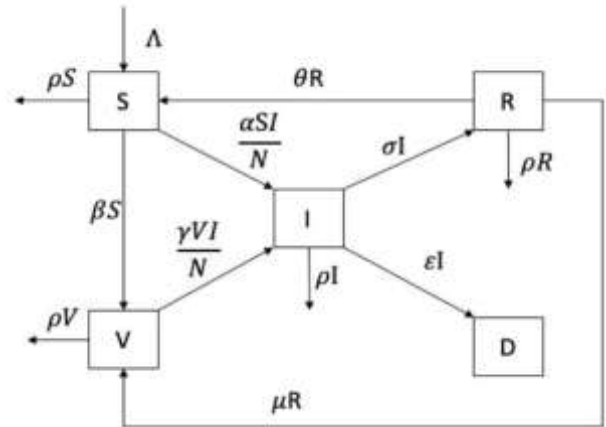

Fig. 1: Schematic diagram of the SVIRD model.

The solid lines represent population movement from one compartment to another. The transition from S to I or V to I is a result of interaction between individuals in the two compartments.

The system of differential equations that governs the model is as follows:

Table 1. Description of variables and parameters in the model, [1]

Symbols	Description
Λ	Recruitment rate into the population
ρ	Natural death rate of human individuals
α	The transmission rate to susceptibles
σ	The recovery rate from infection
θ	The transition rate from recovered to
γ	The transmission rate to vaccinated class
β	The vaccination rate of susceptible
μ	The vaccination rate of recovered
ϵ	The death rate from infection

$$\frac{dS}{dt} = \Lambda - \alpha S \frac{I}{N} - \beta S + \theta R - \rho S \tag{1}$$

$$\frac{dV}{dt} = -\gamma V \frac{I}{N} + \beta S + \mu R - \rho V \tag{2}$$

$$\frac{dI}{dt} = \alpha S \frac{I}{N} + \gamma V \frac{I}{N} - \sigma I - \epsilon I - \rho I \tag{3}$$

$$\frac{dR}{dt} = \sigma I - \mu R - \theta R - \rho R \tag{4}$$

$$\frac{dD}{dt} = \epsilon I \tag{5}$$

where it is assumed that all the parameters are positive and the initial conditions

$S(0) = S_0$, $V(0) = V_0$, $I(0) = I_0, R(0) = R_0$ and $D(0) = D_0$, are all nonnegative.

Before proceeding, we note here that the fifth equation is decoupled from the rest of the system and thus will be neglected from subsequent analysis. We also observe that if $\Lambda = 0$ and $\rho = 0$, then the model does not possess any vital dynamics. Further, it is not difficult to establish that the right-hand side of the system is locally Lipschitz continuous, thus a solution $(S(t), V(t), I(t), R(t))$ with the prescribed initial conditions exists and is unique. It can also be easily shown that the model presented only admits positive solutions since

$S(t) = S_0 \exp \int_0^t \left(-\beta - \rho - \alpha \frac{I(\eta)}{N(\eta)} + \frac{\Lambda + \theta R(\eta)}{S(\eta)} \right) d\eta$,

$V(t) = V_0 \exp \int_0^t \left(-\rho - \gamma \frac{I(\eta)}{N(\eta)} + \frac{\beta S(\eta) + \mu R(\eta)}{V(\eta)} \right) d\eta$,

$I(t) = I_0 \exp \int_0^t \left(-\sigma - \epsilon - \rho + \alpha \frac{S(\eta)}{N(\eta)} + \gamma \frac{V(\eta)}{N(\eta)} \right) d\eta$,

and

$R(t) = R_0 \exp \int_0^t \left(-\mu - \theta - \rho + \sigma \frac{I(\eta)}{R(\eta)} \right) d\eta$,

are always positive.

3 Analysis of the Model

In this section, we state the disease-free equilibrium (DFE) and the basic reproduction number of the model. The DFE is defined as a steady-state solution of the model in which the number of infected individuals is zero. The basic reproduction number, often denote as R_0, is a threshold parameter used to describe the potential of a contagious disease to spread within a population. It is defined as the average number of secondary infections that result from a single infected individual in a susceptible population. We use R_0 to show that the DFE is locally and globally stable. Further, we establish the existence of an endemic equilibrium (EE), a state where the disease is present at a relatively stable level, if $R_0 > 1$.

To compute the equilibria of the model, we set the derivatives in the first four equations, [1], to zero and solve for the steady states (S^*, V^*, I^*, R^*) in the following equations where for simplicity we let $N = N^*$

$$0 = \Lambda - \alpha S^* \frac{I^*}{N} - \beta S^* + \theta R^* - \rho S^* \quad (6)$$

$$0 = -\gamma V^* \frac{I^*}{N} + \beta S^* + \mu R^* - \rho V^* \quad (7)$$

$$0 = \alpha S^* \frac{I^*}{N} + \gamma V^* \frac{I^*}{N} - \sigma I^* - \epsilon I^* - \rho I^* \quad (8)$$

$$0 = \sigma I^* - \mu R^* - \theta R^* - \rho R^*. \quad (9)$$

From above, by factoring I^* in equation (8), it is obvious that the DFE of the model is

$$(S^*, V^*, I^*, R^*) := \left(\frac{\Lambda}{(\beta + \rho)}, \frac{\beta \Lambda}{(\beta + \rho)\rho}, 0, 0 \right).$$

Next, computing the reproduction number R_0 as the spectral radius of the next-generation matrix was evaluated at the DFE, we obtained,

$$R_0 = \frac{\alpha \rho \Lambda + \gamma \beta \Lambda}{N \rho (\beta + \rho)(\sigma + \epsilon + \rho)}.$$

Remark 3.1. The value of R_0 stated above can be interpreted as a product of the sum of the transmissibilities to susceptiles $\left(\frac{\alpha \Lambda}{N(\beta + \rho)} \right)$ and vaccinated $\left(\frac{\gamma \beta \Lambda}{N \rho (\beta + \rho)} \right)$, and the mean duration of infectiousness $\frac{1}{\sigma + \epsilon + \rho}$. If we assume that the population is constant by setting the recruitment rate $\Lambda = \rho N$, then we get $R_0 = \frac{\alpha \rho + \gamma \beta}{(\beta + \rho)(\sigma + \epsilon + \rho)}$.

We now move on to establish the existence of an endemic equilibrium that is biologically relevant, that is, a positive equilibrium since the model does not admit negative solutions. To achieve this objective, we revisit equations (6), (8), and (9), and observe that if $I^* \neq 0$ then we get

$R^* = A_1 I^*, S^* = \frac{N(\Lambda + \theta A_1 I^*)}{\alpha I^* + N(\beta + \rho)}$ and

$V^* = N \left(A_2 - \frac{\alpha}{\gamma} \frac{N(\Lambda + \theta A_1 I^*)}{\alpha I^* + N(\beta + \rho)} \right)$, where

$A_1 = \sigma / (\theta + \mu + \rho)$ and $A_2 = (\sigma + \epsilon + \rho)/\gamma$. Substituting for S^*, V^* and R^* in equation (7) we obtain the following quadratic equation in the variable I^* :

$$B_2 I^{*2} + B_1 I^* + B_0 = 0,$$

where

$B_0 = \rho(\beta + \rho)A_2 N^2 (R_0 - 1)$

$B_1 = \gamma(\beta + \rho)A_2 N(R_0 - 1) + A_1 N[\beta\theta + \mu(\beta + \rho) + \alpha\theta\rho/\gamma] - \gamma\Lambda/\rho - \alpha\rho A_2 N$

$B_2 = -\alpha(\epsilon + \rho + \rho A_1)$.

The following result guarantees that the model will always contain at least one positive endemic equilibrium.

Theorem 3.1. *If $R_0 > 1$, then the model presented possesses at least one positive endemic equilibrium.*

Proof. Let $f(I^*)$ be a polynomial given by the left-hand side of equation (10), that is,

$$f(I^*) = B_2 I^{*2} + B_1 I^* + B_0.$$

Observe that $B_2 < 0$ from above. For $I^* = 0$ we get that $f(0) = B_0 > 0$ if $R_0 > 1$. Next, we see that $f \to -\infty$ as $I^* \to \infty$. Thus, by the intermediate value theorem, the function f has a positive root on the interval $[0, \infty)$ yields an endemic equilibrium.

We now consider the stability of the DFE. The following result provides a condition under which the DFE is locally stable. ■

Theorem 3.2. *The disease-free equilibrium of the model is locally asymptotically stable if the reproduction number $R_o < 1$, otherwise, it is unstable.*

Proof. Evaluating the Jacobian matrix of the model at the DFE gives

$$\begin{bmatrix} -\beta - \rho & 0 & -\dfrac{\alpha\Lambda}{N(\beta+\rho)} & \theta \\ \beta & -\rho & -\dfrac{\gamma\beta\Lambda}{N\rho(\beta+\rho)} & \mu \\ 0 & 0 & (\sigma+\epsilon+\rho)(R_0-1) & 0 \\ 0 & 0 & \sigma & -\mu-\theta-\rho \end{bmatrix}$$

whose eigenvalues are $-\beta - \rho, -\rho, (\sigma + \epsilon + \rho)(R_0 - 1)$ and $-\mu - \theta - \rho$. Clearly, if $R_0 < 1$, then the eigenvalues are all negative, thus rendering the DFE to be locally asymptotically stable. If $R_0 > 1$, then one of the eigenvalues is positive therefore rendering the DFE unstable.

We will require the following lemma to show that the DFE is globally stable.

Lemma 3.1. *Suppose that $S(0) \leq \dfrac{\Lambda}{\beta+\rho}$ and $V(0) \leq \dfrac{\beta\Lambda}{\rho(\beta+\rho)}$, then respectively, $S(t) \leq \dfrac{\Lambda}{\beta+\rho}$ and $V(t) \leq \dfrac{\beta\Lambda}{\rho(\beta+\rho)}$.*

Proof. From the differential equation 1, we obtain the differential inequality.

$$\frac{dS}{dt} \leq \Lambda - \beta S + \theta R - \rho S$$

whose solution is given as

$$S(t) \leq \frac{\Lambda}{\beta+\rho} - \left(\frac{\Lambda}{\beta+\rho} - S(0)\right) \times$$

$$\exp - (\beta + \rho)\int_0^t \left(1 + \frac{\theta R(\eta)}{\Lambda - (\beta+\rho)S(\eta)}\right) d\eta.$$

Clearly, $S(t) \leq \frac{\Lambda}{\beta+\rho}$ if $S(0) \leq \frac{\Lambda}{\beta+\rho}$. To establish the second inequality, we use the differential inequality

$$\frac{dV}{dt} \leq \beta S + \mu R - \rho V$$

which is a consequence of the differential equation (2). On substituting for $S(t) \leq \frac{\Lambda}{\beta+\rho}$ in the above inequality, we get

$$\frac{dV}{dt} \leq \frac{\beta\Lambda}{\beta+\rho} + \mu R - \rho V$$

whose solution satisfies

$$V(t) \leq \frac{\beta\Lambda}{\rho(\beta+\rho)} - \left(\frac{\beta\Lambda}{\rho(\beta+\rho)} - V(0)\right) \times$$

$$\exp - \rho \int_0^t \left(1 + \frac{\mu R(\eta)}{\beta\Lambda/(\beta+\rho) - \rho V(\eta)}\right) d\eta.$$

It follows that $V(t) \leq \frac{\beta\Lambda}{\rho(\beta+\rho)}$ if $V(0) \leq \frac{\beta\Lambda}{\rho(\beta+\rho)}$. ■

The next result which is stronger than the previous theorem establishes the global stability of the DFE by using a Lyapunov function and LaSalle's invariance theorem, [29].

Theorem 3.3. *Suppose that $S(t) \leq \dfrac{\Lambda}{\beta+\rho}$ and $V(t) \leq \dfrac{\beta\Lambda}{\beta+\rho}$ according to Lemma 3.1. Then the disease-free equilibrium of the model is globally asymptotically stable if the basic reproduction number $R_0 < 1$.*

Proof. We consider the Lyapunov function candidate

$$L(t) = \frac{1}{2}I^2.$$

Differentiating with respect to t gives

$$\begin{aligned} \frac{dL}{dt} &= I\frac{dI}{dt} \\ &= I\left(\alpha S\frac{I}{N} + \gamma V\frac{I}{N} - \sigma I - \epsilon I - \rho I\right) \\ &= \left(\alpha\frac{S}{N} + \gamma\frac{V}{N} - \sigma - \epsilon - \rho\right)I^2 \\ &\leq \left(\frac{\alpha\Lambda}{N(\beta+\rho)} + \frac{\beta\gamma\Lambda}{N\rho(\beta+\rho)} - \sigma - \epsilon - \rho\right)I^2. \end{aligned}$$

Clearly, if $R_0 < 1$ then we have that

$$\frac{dL}{dt} \leq (\sigma + \epsilon + \rho)(R_0 - 1) < 0.$$

Therefore by LaSalle's invariance principle, the DFE is globally asymptotically stable. ∎

4 Numerical Results and Discussion

In this section, we present numerical simulations of the model for different scenarios. The values of the parameters used in the simulations were estimated based on values from the published literature for COVID-19, [30], [31], [32], [33], [34], and other parameter values were assumed to demonstrate the predictions of the model. All populations were normalized to the total population N. We also assume that the recruitment rate $\Lambda = \rho N$ so that the population remains constant. The simulations reported in this paper were carried out using the initial conditions $S(0) = 0.99999, V(0) = 0$, $I(0) = 0.00001, R(0) = 0$ and $D(0) = 0$. We remark here that several simulations were carried out with small perturbations or different sets of initial conditions and the long-term behavior of the model's predictions were unchanged.
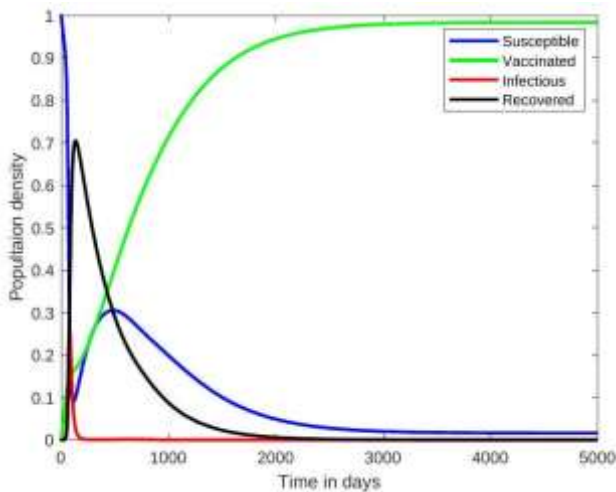

Fig. 2: Model simulations demonstrating a disease-free equilibrium for parameter values $\alpha = 0.25, \beta = 0.0024, \theta = 0.025, \gamma = 0.0025, \rho = 1/(365 \times 70), \mu = 1.5 \times 10^{-4}, \epsilon = 10^{-5}$, and $\sigma = 1/14$.

We start by confirming numerically the analytic results established in the previous section. The simulations in Figure 2 demonstrate numerically both the existence and global stability of the disease-free equilibrium. The introduction of an infected individual leads to a wave of COVID-19 propagating within the population until it reaches a peaking. After cresting, the wave continues to die out till there are no more infectious individuals left in the population.
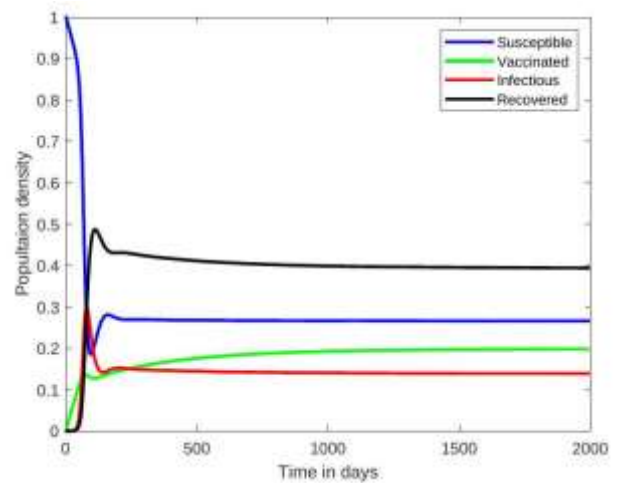

Fig. 3: Model simulations demonstrating an endemic equilibrium. The parameter values are the same as in Figure 2 with the exception that $\gamma = 0.025$.

This result appears to reflect a pattern so far observed in COVID-19. That is the emergence of a variant that eventually dies out or is displaced by a more competitive variant. Recall that we only established the existence of an endemic equilibrium in the previous section without discussing its stability. The result in Figure 3 represents an endemic equilibrium for the chosen parameter values. The results demonstrate COVID-19 persisting in the population after a wave has crested, however, at a stable level.
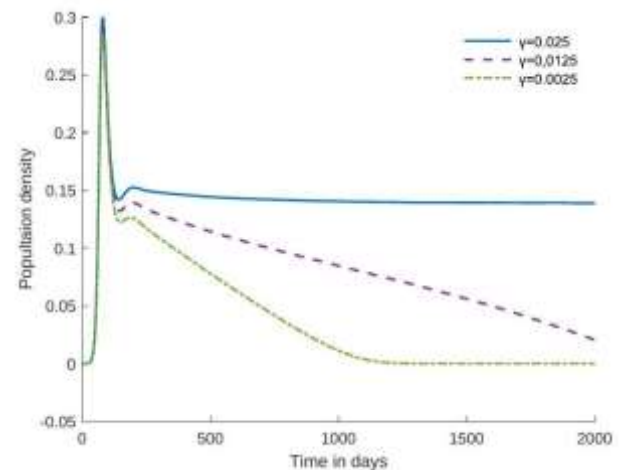

Fig. 4: Model simulations of COVID-19 infections demonstrating the efficacy of a vaccine.

Here we simulate the number of cases by varying the transmission rate γ to vaccinated individuals. All other parameter values are as stated in Figure 2.
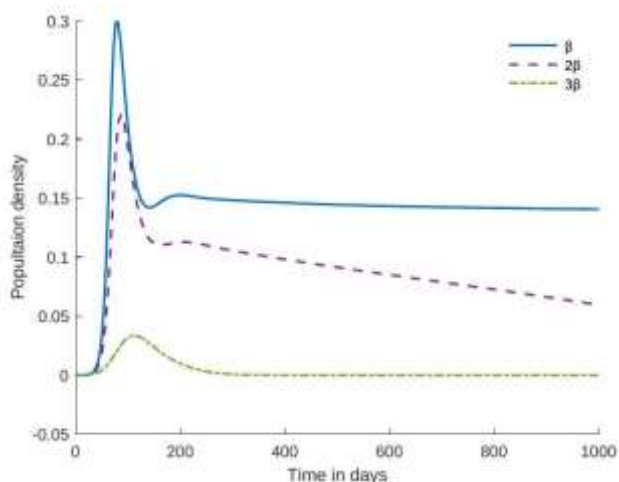
Fig. 5: Model simulations of COVID-19 infections demonstrating the effect of the vaccination rate β on the trajectory of COVID-19. Here we vary β, set $\gamma = 0.025$ and all other parameter values are as stated in Figure 2.

Next, we turn our attention to simulating the efficacy of COVID-19 vaccines. We do so by comparing the number of COVID-19 infections for vaccinations having different degrees of effectiveness. We assume that a vaccine is more effective if the transmissibility rate to vaccinated individuals γ approaches zero, and that 100% effectiveness is achieved if $\gamma = 0$. The results presented in Figure 4 show the number of COVID-19 cases for each vaccination regiment. A vaccine having a high transmissibility rate $\gamma = 0.025$ will lead to COVID-19 being endemic while one with a much lower transmission rate $\gamma = 0.0025$ will eventually lead to the eradication of the virus. It is important to observe that in the simulations provided, it takes a while before a disease-free equilibrium is attained. This underscores the necessity of public health officials to recommend additional measures needed to combat the pandemic. A mildly effective vaccine is better than none. Though an effective vaccine is crucial in reducing the overall incidence of COVID-19, the results in Figure 5 do show that the behavior of the population plays an important role. No matter how effective a vaccine is, if only a small proportion of the population is getting vaccinated, then COVID-19 will persist in the population. However, a higher vaccination rate will shift an endemic state to a disease-free state. Put together, the simulations in Figures 4 and 5 demonstrate that to move the population towards herd immunity, the vaccine has to be very effective and the rate of vaccine uptake should also be very high.
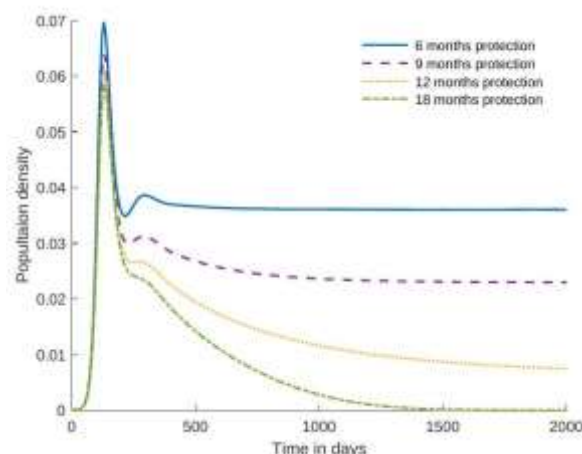

Fig. 6: Model simulations of COVID-19 infections demonstrating the longevity of immunity provided by the vaccine.

Here, we set $\gamma = 0.025$ and vary the vaccine waning rate ψ. We consider the effect on the number of cases ranging from $6 - 18$ months of protection. All other parameter values are as stated in Figure 2.

The efficacy of a vaccine is also dependent on the longevity of the immunity it provides. To investigate this, we slightly modify the first two equations of the model by subtracting a vaccine waning term ψV from the vaccination compartment and adding it to the susceptible compartment. With this modification, the DFE of the model is $\left(\frac{(\rho+\psi)\Lambda}{\rho(\beta+\rho+\psi)}, \frac{\beta\Lambda}{\rho(\beta+\rho+\psi)}, 0, 0 \right)$. A corresponding basic reproduction number is $R_0 = \frac{\alpha(\rho+\psi)+\gamma\beta}{\rho(\beta+\rho+\psi)(\sigma+\epsilon+\rho)}$, where we have set $\Lambda = \rho N$ (see Remark 3.1). Clearly, if $\psi = 0$ we recover the previous DFE and R_0. Here, we take ψ to be the rate at which the COVID-19 vaccine is waning. The results given in Figure 6 consider different cases where the protection granted by COVID-19 ranges from $6 - 18$ months. We can see that, the shorter the duration of afforded protection, the more the number of COVID-19 cases, thus necessitating the need for more frequent vaccination or boasting.
Finally, the mean duration of infectiousness, that is, how long it takes infectious people to recover and stop being a threat to others plays an important role in determining the trajectory of each COVID-19 or its variants. The results in Figure 7 simulate the trajectory of COVID-19 for infectiousness periods of 7 and 14 days for vaccination and non-vaccination regiments. The results indicate that COVID-19 or a variant that has an infectiousness period of up to 14 days is likely to remain endemic

even in a vaccinated population. On the other hand, a variant with a shorter infectiousness period when combined with vaccination will be quickly eradicated.
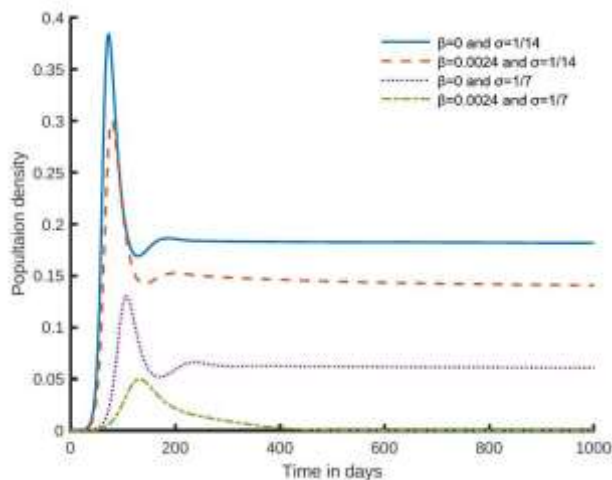

Fig. 7: Model simulations of COVID-19 infections by comparing different vaccinations status β and recovery rates σ.

We let $\beta = 0$ represent no vaccine uptake and $\beta = 0.0024$ for vaccine uptake. The recovery rates σ are set at $1/7$ and $1/14$, indicating an infectiousness period of 7 and 14 days, respectively.

5 Conclusion

In this paper, we have developed an SVIRD model for COVID-19 and used it to study breakthrough infections in a vaccinated population. The model is based on the assumption that COVID-19 vaccinations do not provide full immunity to vaccinated individuals. The model is formulated as a system of differential equations and the existence of a disease-free equilibrium that is globally stable when the basic reproduction number is less than one is established. The existence of an endemic equilibrium is also ascertaining if the basic reproduction number is greater than one and numerical simulations do show that it is globally stable. We used simulations of the model to study different vaccination strategies and the predictions do provide early warning signals of potential outbreaks. A key prediction of the model is that an effective vaccine will reduce the number of infections in a short amount of time as long as there is a high vaccination rate. Considered alone, a very effective vaccine, or one that protects for more than a year, combined with low vaccine uptake may eventually eradicate the disease, however, only after a very long time. The model also predicts that given

any vaccine that affords some immunity, if there is a high vaccination turnout, then the virus will still be eradicated in a shorter amount of time. Further predictions of the model suggest that knowing the infectious period of COVID-19 or its variants is very important. Variants with shorter duration of infectiousness are easily eradicated while those with long durations are likely to become endemic within a population. The predictions made in this study are mostly limited to the assumptions made and the values of the parameters used. The model does not account for all the factors that can influence the spread of the virus, such as human behavior and social dynamics. In conclusion, while breakthrough infections do occur, vaccination remains an essential tool in the fight against COVID-19. Vaccines are highly effective in preventing severe illness and death, and they can help to reduce the spread of the virus. Additional measures, such as booster shots, masks, and social distancing, can also help to reduce the risk of breakthrough infections and protect individuals who are not yet vaccinated. Individuals must continue to follow public health guidelines and get vaccinated to help bring an end to the pandemic.

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The authors equally contributed in the present research, at all stages from the formulation of the problem to the final findings and solution.

Conflict of Interest
The authors have no conflict of interest to declare.