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Mathematical Modeling of Post-Exposure Prophylaxis of SARS-CoV-2

Makayla Preston

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Makayla Preston
Department of Mathematics
Faculty Mentor: Eric Numfor, Ph.D., Department of Mathematics

ABSTRACT
The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in December 2019, and as of August 29, 2022, this virus was responsible for about 6 million confirmed deaths and about 450 million confirmed cases of COVID-19 globally. In this project, we used mathematical modeling to investigate the impact of post-exposure prophylaxis in preventing the spread of SARS-CoV-2. The disease-free equilibrium of our model is derived, and the basic reproduction number is computed, using the next generation matrix approach. We studied the elasticity indices of the reproduction number with respect to each parameter and identified parameters that are most sensitive in increasing the reproduction number and those that are most sensitive in decreasing the reproduction number. Numerical simulations suggest that an increase in the modification parameter for the transmission rate of breakthrough cases results in more infectiousness for those not on prophylaxis when compared to individuals on prophylaxis. The outcomes of our contour plot suggest the possibility of eradicating the virus from the population under different combinations of the proportion of individuals who recently came in contact with an infectious individual and have been administered an antiviral drug such as REGEN-CoV. Results of numerical simulations and contour plots highlight the importance of post-exposure prophylaxis on the transmission of SARS-CoV-2 in the population.

Keywords: SARS-CoV-2, COVID-19, coronavirus, mathematical modeling, post-exposure prophylaxis

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Correspondence: Makayla Preston, Augusta University, 1120 15th St. Augusta, GA 30912, MPRESTON@augusta.edu
INTRODUCTION

The coronavirus disease pandemic of December 2019 (COVID-19) is considered a zoonotic disease that originated from viral particles in bats, and is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As of August 29, 2022, this virus was responsible for about 6.4 million confirmed deaths and 597 million confirmed cases globally. In the United States alone, there has been over 94 million confirmed cases of COVID-19, and about one million confirmed deaths. SARS-CoV-2 can be transmitted through person-to-person contact, airborne routes, and environmental contamination. Person-to-person contact occurs through respiratory droplets when an infected person coughs, sneezes, or talks. On the other hand, the airborne route occurs when someone inhales infected SARS-CoV-2 particles. Finally, environmental contamination occurs when a susceptible person touches viruses present on surfaces and transfer infectious particles to their eyes, mouth, or nose. Common symptoms of COVID-19 include fever or chills, cough, shortness of breath, fatigue, muscle or body aches, headache, sore throat, diarrhea and congestion or runny nose. These symptoms typically appear within 2 - 14 days of exposure to the virus (Centers for Disease Control and Prevention 2019, 2021a, 2021b).

Several non-pharmaceutical and pharmaceutical mitigating efforts against the pandemic have been implemented. Non-pharmaceutical interventions include social distancing, community lockdown, contact tracing, quarantine of suspected cases, isolation of confirmed cases and the use of face masks in public (CDC, 2019). Social distancing involves avoiding congregating into groups and maintaining six feet distance from others. Contact tracing on the other hand is the practice of identifying, notifying, and monitoring individuals who may have been in close contact with a person having a confirmed or possible case of an infectious disease as a means of controlling the spread of infection (Merriam-Webster, n.d.). Contact tracing includes notifying people who may have come into close contact with someone with a confirmed COVID-19 test. Face masks are used to help block large-particle droplets that contain germs from reaching your mouth and nose (Center for Devices and Radiological Health, 2021). Pharmaceutical interventions include vaccination and treatment (CDC, 2019).

Vaccination remains a highly effective way to prevent SARS-CoV-2 infection. Despite widespread availability of COVID-19 vaccines, a number of individuals who have been exposed to an individual infected with SARS-CoV-2 or who are at high risk of exposure to an individual infected with SARS-CoV-2 due to occurrence of SARS-CoV-2 infection in other individuals in the same institutional setting (such as nursing
homes, prisons, or healthcare facilities) are either not fully vaccinated or are fully vaccinated but have immune systems that cannot produce enough antibodies to fight against the virus. For such individuals, post-exposure prophylaxis (PEP) is an important approach in reducing the spread of the COVID-19 epidemic.

Post-exposure prophylaxis is a well-established strategy for the prevention of infectious diseases, in which recently exposed humans take a short course of medication to prevent infection. In the United States, REGEN-COV is an approved medication for PEP in adults and pediatric individuals (12 years of age and older weighing at least 40 kg).

We collected data on the number of infectious individuals in nursing homes in the United States, and Figure 1 depicts an analysis of the data (CDC, 2022). Figure 1 shows that there are spikes and declines in COVID-19 cases in nursing homes with devastating effects in individuals with comorbidities. Therefore, it is important to study the effects of post-exposure prophylaxis in high-exposure settings such as nursing homes and prisons.

Figure 1: COVID-19 cases taken from nursing homes across the United States at the end of each week from September 19, 2021 - September 11, 2022.
Objectives

In this thesis, we will use mathematical modeling to investigate the impact of PEP in preventing the spread of SARS-CoV-2. This is done by formulating a susceptible-exposed-infectious-recovered (SEIR) model for post-exposure prophylaxis against SARS-CoV-2 in settings such as nursing homes, prisons, and health care facilities. Thus, the objectives of our project are to:

i. Formulate and analyze a mathematical model for post-exposure prophylaxis against SARS-CoV-2 in settings such as nursing homes, prisons, and health care facilities.
ii. Investigate the impact of post-exposure prophylaxis on the spread of SARS-CoV-2.

LITERATURE REVIEW

Several studies have been conducted on the pre-exposure prophylaxis of infectious diseases, but there are limited number of studies on the post-exposure prophylaxis of infectious diseases (Conway, Konrad, & Coombs, 2013; McCaw & McVernon, 2007). McCaw and McVernon (2007) investigated the effect of prophylaxis and treatment on influenza in order to determine whether prophylaxis or treatment is better in the control of the spread of influenza. In our work, we will formulate and analyze a model of SARS-CoV-2 that incorporates post-exposure prophylaxis.

The remainder of the work in this thesis is organized as follows: In Section 1, we formulate a mathematical model with post-exposure prophylaxis (see 1.1). In Section 1.2, we compute the control reproduction number of the model. In Section 1.3, we focus on the prophylaxis-only sub-model and derive the steady states of the model. Section 1.4 is devoted to numerical simulations of the prophylaxis-only sub-model using MATLAB. In section 2, we analyze the elasticity indices and carry out numerical simulations of the complete model. We estimate the parameters for the complete model in Section 2.1 and evaluate the elasticity indices in Section 2.2. The stability of the disease-free equilibrium of the complete model is investigated in Section 2.3, and numerical simulations are carried out in Section 2.4. Concluding remarks of our work are presented in Section 3, followed by a glossary.

SECTION 1. MODEL WITH POST-EXPOSURE PROPHYLAXIS

Section 1.1 Model Formulation

We formulate an SEIR-type model with multiple exposed and infectious classes,
consisting of individuals on prophylaxis \((E_p \text{ and } I_p)\) and those who are not on prophylaxis \((E_{np} \text{ and } I_{np})\), with total population

\[
N(t) = S(t) + E_p(t) + E_{np}(t) + I_p(t) + I_{np}(t) + R(t),
\]

where \(S(t)\) and \(R(t)\) are susceptible and recovered individuals at time \(t\), respectively. It is assumed that susceptibility to infection is reduced by the provision of prophylaxis and protection is not perfect, so that some individuals on prophylaxis will still progress to the exposed class (breakthrough cases), but at a reduced level of infection. We assume that \(\varepsilon\) is the proportion of susceptible individuals who recently came in contact with an infectious individual and have been administered an antiviral drug. When susceptible humans come in contact with infectious humans who are not on prophylaxis, they become exposed at rate \(\beta\), and at rate \(\theta \beta\) for individuals on prophylaxis, where \(\theta \in (0, 1)\) is a modification parameter for the transmission rate of breakthrough cases, so that \(\theta \beta < \beta\). Thus, the force of infection for breakthrough cases and individuals not on prophylaxis are,

\[
\lambda_p = \theta \beta I_p \text{ and } \lambda_{np} = \beta I_{np},
\]

respectively. The number of exposed individuals on prophylaxis and exposed individuals not on prophylaxis are

\[
\theta \beta \varepsilon SI_p \text{ and } \beta (1 - \varepsilon) SI_{np},
\]

respectively, where \(\varepsilon S\) is the number of susceptible humans who come in contact with infectious individuals on prophylaxis and \((1-\varepsilon)S\) is the number of susceptible humans who come in contact with infectious individuals not on prophylaxis. Exposed humans on prophylaxis progress to infectious humans on prophylaxis at rate \(\sigma_p\), and exposed humans not on prophylaxis progress to infectious humans not on prophylaxis at rate \(\sigma_{np}\). All infected individuals on prophylaxis and those not on prophylaxis recover at rate \(\gamma_p\) and \(\gamma_{np}\), respectively, and all individuals in the population are assumed to die at a natural death rate \(\mu\). Different interactions in the population are depicted in Figure 2.
From the schematic diagram in Figure 2, we obtain the following system of differential equations:

\[
\frac{dS}{dt} = \Lambda - \theta \beta \epsilon IpS - \beta (1 - \epsilon)InpS - \mu S, \quad (1)
\]

\[
\frac{dEp}{dt} = \theta \beta \epsilon IpS - \sigma Ep - \mu Ep, \quad (2)
\]

\[
\frac{dEnp}{dt} = \beta (1 - \epsilon)InpS - \sigma npEnp - \mu Enp, \quad (3)
\]

\[
\frac{dIp}{dt} = \sigma Ep - \gamma Ip - \mu Ip, \quad (4)
\]

\[
\frac{dInp}{dt} = \sigma npEnp - \gamma npInp - \mu Inp, \quad (5)
\]

\[
\frac{dR}{dt} = \gamma Ip + \gamma npInp - \mu R. \quad (6)
\]

The parameters of the model are represented in Table 1. In the next section, we determine the control reproduction number of system (1) - (6).
<table>
<thead>
<tr>
<th>Params.</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \Lambda )</td>
<td>Recruitment rate</td>
</tr>
<tr>
<td>( \theta )</td>
<td>Modification parameter for the transmission rate of breakthrough cases</td>
</tr>
<tr>
<td>( \varepsilon )</td>
<td>The proportion of susceptible individuals who recently came in contact with an infectious individual and have been administered an antiviral drug such as REGEN-CoV</td>
</tr>
<tr>
<td>( \sigma_p )</td>
<td>Rate at which exposed people on prophylaxis become infected</td>
</tr>
<tr>
<td>( \sigma_{np} )</td>
<td>Rate at which exposed people not on prophylaxis become infected</td>
</tr>
<tr>
<td>( \gamma_p )</td>
<td>Rate that people on prophylaxis recover from infection</td>
</tr>
<tr>
<td>( \Upsilon_{np} )</td>
<td>Rate at which people not on prophylaxis recover from infection</td>
</tr>
<tr>
<td>( \mu )</td>
<td>Death rate</td>
</tr>
</tbody>
</table>

Table 1: Description of parameters of system (1) - (6).

**Section 1.2. Basic Reproduction Number**

The basic reproduction number, denoted by \( R_0 \), is the number of secondary infections that result from the introduction of a single infectious individual into a completely susceptible population during the individual’s entire period of infectiousness (Driessche, 2017; Feng, 2019; Watmough & Driessche, 2002). If the reproduction number is less than one (i.e., \( R_0 < 1 \)), then an infectious individual produces less than one new infected individual over the course of its infectious period, and the infection cannot spread. If \( R_0 > 1 \), then each infected individual produces, on the average, more than one new infection, and the disease can multiply throughout the population (Feng, 2019) When \( R_0 = 1 \), bifurcation (change in qualitative behavior) occurs, the disease will alternate between transmission and no transmission. In the presence of any form of control, we call the basic reproduction number, \( R_0 \), the control reproduction number, denoted by \( R_C \). One way of calculating the reproduction number is by the next generation matrix approach (Feng, 2019).

**Section 1.2.1. Next Generation Matrix Method**

The next generation matrix method is demonstrated by the process where exposed individuals are not immediately infected (Center for Devices and Radiological Health,
During this time, the exposed individual is not yet capable of transmission of the disease. The first step of the next generation matrix method is to divide the population into two groups or compartments: infected and non-infected. A compartment is infected if the individuals in that compartment are infected or infectious, while a non-infected compartment holds those that are healthy or not infected. For this model, let \( n \) represent the infected compartments, comprising the exposed and infectious classes, and \( m \) represent the noninfected compartments consisting of the susceptible and recovered classes. Therefore, the ordinary differential equation (ODE) for the model has \( m + n \) dependent variables. If \( x \) represents the vector of dependent variables in the infected compartments, and \( y \) represents the vector of dependent variables in the non-infected compartments, the ODE system can be written as:

\[
\begin{align*}
\dot{x}_i &= f_i(x, y), \quad i = 1, \ldots, n, \\
\dot{y}_j &= g_j(x, y), \quad j = 1, \ldots, m.
\end{align*}
\]

Next, we partition the infected compartment as follows:

\[ x_i = \mathcal{F}_i(x, y) - \mathcal{V}_i(x, y), \quad i = 1, \ldots, n \]

In this modified system, we introduced the vectors \( \mathcal{F}(k) \) and \( \mathcal{V}(k) \), where \( \mathcal{F} \) is the rate of appearance of new infections. \( \mathcal{V} \) can be written as \( \mathcal{V}(k) = \mathcal{V}(k^-) - \mathcal{V}(k^+) \), where \( \mathcal{V}^- \) is the rate of transfer of individuals out of a compartment, and \( \mathcal{V}^+ \) is the rate of transfer of individuals into a compartment by all other means (other than transmission).

Next, we determine matrices \( \mathcal{F} \) and \( \mathcal{V} \), where

\[
\mathcal{F} = \begin{bmatrix} \frac{\partial F(\mathcal{E}_0)}{\partial X_j} \end{bmatrix}, \quad \text{and} \quad \mathcal{V} = \begin{bmatrix} \frac{\partial \mathcal{V}(\mathcal{E}_0)}{\partial X_j} \end{bmatrix}.
\]

Here, \( \mathcal{E}_0 \) is the disease-free equilibrium of the model, \( X_j \) represents the infected classes and \( \partial \) denotes partial derivatives. Finally, the next generation matrix is defined by \( \mathcal{F}\mathcal{V}^{-1} \), and the control reproduction number is the largest eigenvalue of \( \mathcal{F}\mathcal{V}^{-1} \), written as \( R_c = \rho(\mathcal{F}\mathcal{V}^{-1}) \), where \( \rho(A) \) represents the spectral radius of \( A \). For our epidemiological model with post-exposure prophylaxis, we begin by setting the infected classes to zero, and the rate of change of variables in the non-infected classes to zero. This leads to the subsystem:
\[ \frac{dS}{dt} = \Lambda - \mu S \]
\[ \frac{dR}{dt} = -\mu R \]

Setting \( \frac{dS}{dt} = \frac{dR}{dt} = 0 \), we obtain the disease-free equilibrium

\[ E_0 : (S^*, E^*_{np}, I^*_{np}, R^*) = (\frac{\Lambda}{\mu}, 0, 0, 0, 0) \]

Now, let \( k \) be a vector of the two disease compartments, \( E \) and \( I \). Then, we can write equations for the infected compartment, \( E \) and \( I \), in the following form:

\[ \frac{dk}{dt} = F(k) - \nu(k) \]

**Section 1.2.2. Computation of Reproduction Number, \( R_c \)**

Using the method described in subsection 1.2.1, we compute the control reproduction number of our model. From the schematic diagram in Figure 2, we obtain the following:

\[ \frac{dk}{dt} = \begin{bmatrix} E_p \\ E_{np} \\ I_p \\ I_{np} \end{bmatrix} = \mathcal{F}(k) - \left( \mathcal{V}^-(k) - \mathcal{V}^+(k) \right) \]

\[ = \begin{bmatrix} \frac{\theta \beta S}{\beta (1 - \epsilon) I_{np} S} \\ 0 \\ 0 \end{bmatrix} - \begin{bmatrix} \frac{(\sigma_p + \mu) E_p}{(\sigma_{np} + \mu) E_{np}} \\ \frac{(\gamma_p + \mu) I_p}{(\gamma_{np} + \mu) I_{np}} \end{bmatrix} \]

\[ = \begin{bmatrix} \frac{\theta \beta S}{\beta (1 - \epsilon) I_{np} S} \\ 0 \\ 0 \end{bmatrix} \begin{bmatrix} \frac{(\sigma_p + \mu) E_p}{(\sigma_{np} + \mu) E_{np}} \\ \frac{(\gamma_p + \mu) I_p - \sigma_p E_p}{(\gamma_{np} + \mu) I_{np} - \sigma_{np} E_{np}} \end{bmatrix} \]
From the system of equations above, we define the vectors $F$ and $V$ as follows:

$$
F = \begin{bmatrix}
\theta \beta e I_p S \\
\beta (1 - e) I_{np} S \\
0 \\
0
\end{bmatrix}, \quad \text{and} \quad V = \begin{bmatrix}
(\sigma_p + \mu) E_p \\
(\sigma_{np} + \mu) E_{np} \\
(\gamma_p + \mu) I_p - \sigma_p E_p \\
(\gamma_{np} + \mu) I_{np} - \sigma_{np} E_{np}
\end{bmatrix}.
$$

In order to derive the next generation matrix, we find matrices $F$ and $V$ by finding partial derivatives of $F$ and $V$, evaluated at the disease-free equilibrium, $E_0$. That is,

$$
F = \left[ \frac{\partial F(E_0)}{\partial X_j} \right], \quad \text{and} \quad V = \left[ \frac{\partial V(E_0)}{\partial X_j} \right],
$$

where $X_j = (E_p, E_{np}, I_p, I_{np})$. Therefore, the matrices $F$ and $V$ are

$$
F = \begin{bmatrix}
0 & 0 & \frac{\theta \beta e \Lambda}{\mu} & 0 \\
0 & 0 & 0 & \frac{\beta (1 - e) \Lambda}{\mu} \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0
\end{bmatrix} \quad \text{and} \quad V = \begin{bmatrix}
\sigma_p + \mu & 0 & 0 & 0 \\
0 & \sigma_{np} + \mu & 0 & 0 \\
-\sigma_p & 0 & \gamma_p + \mu & 0 \\
0 & -\sigma_{np} & 0 & \gamma_{np} + \mu
\end{bmatrix}.
$$

Using the Symbolic Toolbox in MATLAB, we find the inverse of $V$. This gives

$$
V^{-1} = \begin{bmatrix}
\frac{1}{(\mu + \sigma_p)} & 0 & 0 & 0 \\
0 & \frac{1}{(\mu + \sigma_{np})} & 0 & 0 \\
\sigma_p & 0 & \frac{1}{(\gamma_p + \mu)} & 0 \\
0 & \sigma_{np} & 0 & \frac{1}{(\gamma_{np} + \mu)}
\end{bmatrix}.
$$

Entry $(1, 1)$ of $V^{-1}$ is the average length of time exposed individuals on prophylaxis spend
in compartment $E_p$ during their lifetime assuming that the population remains near the disease-free equilibrium and with no reinfection. Similarly, entry $(4,4)$ is the average length of time infectious individuals not on prophylaxis spend in compartment $I_{np}$ during their lifetime assuming that the population remains near the disease-free equilibrium and with no reinfection.

The next generation matrix is obtained as the product of $F$ and the inverse of $V$, which is the matrix of secondary infections. Thus, the next generation matrix is

$$FV^{-1} = \begin{bmatrix}
\frac{\beta\varepsilon\Lambda\sigma_p\theta}{\mu(\gamma_p+\mu)(\mu+\sigma_p)} & 0 & \frac{\beta\varepsilon\Lambda\theta}{\mu(\gamma_p+\mu)} & 0 \\
0 & -\frac{\beta\Lambda\sigma_{np}(\varepsilon-1)}{\mu(\gamma_{np}+\mu)(\mu+\sigma_{np})} & 0 & -\frac{\beta\Lambda(\varepsilon-1)}{\mu(\gamma_{np}+\mu)} \\
0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0
\end{bmatrix}.$$  

The next generation matrix indicates that $\frac{\beta\varepsilon\Lambda\sigma_p\theta}{\mu(\gamma_p+\mu)(\mu+\sigma_p)}$ in entry $(1,1)$ of $FV^{-1}$ is the number of secondary infections produced by individuals in compartment $E_p$ by an infected individual initially in $E_p$. Also $\frac{\beta\varepsilon\Lambda\theta}{\mu(\gamma_p+\mu)}$ in entry $(1,3)$ is the number of secondary infections produced by individuals in compartment $I_p$ who were originally in $E_p$. Using the built-in function $\text{eig}(.)$, we obtain the eigenvalues of the next generation matrix:

$$\lambda = 0, \quad 0, \quad \frac{\beta\Lambda\sigma_{np}(1-\varepsilon)}{\mu(\gamma_{np}+\mu)(\mu+\sigma_{np})}, \quad \frac{\beta\varepsilon\Lambda\sigma_p\theta}{\mu(\gamma_p+\mu)(\mu+\sigma_p)}.$$  

Since the basic reproduction number is $R_c = \rho(FV^{-1})$, where $\rho(A)$ is the largest eigenvalue of $A$, we obtain the reproduction number of our model as

$$R_c = \max\{R_{01}, R_{02}\},$$  

where

$$R_{01} = \frac{\beta(1-\varepsilon)\Lambda\sigma_{np}}{\mu(\gamma_{np}+\mu)(\mu+\sigma_{np})} \quad \text{and} \quad R_{02} = \frac{\beta\varepsilon\Lambda\sigma_p\theta}{\mu(\gamma_p+\mu)(\mu+\sigma_p)}. \quad (9)$$
In equation (9), $R_{01}$ is the reproduction number for individuals not on prophylaxis and $R_{02}$ is the reproduction for individuals on prophylaxis. Therefore, the reproduction number of the population is the bigger of the two reproductions.

**Section 1.2.3. Interpretation of $R_c$**

In order to interpret the reproduction number in the population, we rewrite $R_{01}$ and $R_{02}$ as:

$$R_{01} = \frac{\beta(1-\varepsilon)\Lambda}{\mu} \times \frac{\sigma_{np}}{\mu + \sigma_{np}} \times \frac{1}{\gamma_{np} + \mu} \quad \text{and} \quad R_{02} = \frac{\theta\beta\varepsilon\Lambda}{\mu} \times \frac{\sigma_{p}}{\mu + \sigma_{p}} \times \frac{1}{\gamma_{p} + \mu}.$$

Starting with $R_{01}$, $\frac{\beta(1-\varepsilon)\Lambda}{\mu}$ is the average number of contacts by susceptible individuals not on prophylaxis, where $\frac{\Lambda}{\mu}$ is the number of susceptible humans at the DFE. The term $\frac{\sigma_{np}}{\mu + \sigma_{np}}$ is the proportion of exposed individuals not on prophylaxis who survived the exposed class, and $\frac{1}{\gamma_{np} + \mu}$ is the average length of time infectious individuals not on prophylaxis spend in infectious compartment.

**Section 1.3. Prophylaxis-only Sub-model**

**Section 1.3.1. Model Formulation**

The formulation of the prophylaxis-only sub-model follows from the formulation of the complete model in Section 2. Focusing on infected individuals on prophylaxis, the total population of individuals in the presence of prophylaxis can be represented as:

$$N(t) = S(t) + E_p(t) + I_p(t) + R(t).$$

A schematic diagram representing this scenario is given in Figure 3.

Figure 3: A schematic diagram of the prophylaxis-only sub-model.
From Figure 3, we obtain the following prophylaxis-only sub-model of system (1) - (6):

\[
\begin{align*}
\frac{dS}{dt} &= \Lambda - \theta \beta \epsilon I_p S - \mu S \\
\frac{dE_p}{dt} &= \theta \beta \epsilon I_p S - (\sigma_p + \mu) E_p \\
\frac{dI_p}{dt} &= \sigma_p E_p - (\gamma_p + \mu) I_p \\
\frac{dR}{dt} &= \gamma_p I_p - \mu R.
\end{align*}
\]  

\(10\)  

\(11\)  

\(12\)  

\(13\)

Section 1.3.2. Prophylaxis-dependent Reproduction Number, \(R_p\)

In Figure 3, the proportion of individuals who are on the prophylaxis drug is represented by the parameter \(\epsilon\). This parameter is no longer significant in the absence of prophylaxis. Thus, when \(\epsilon = 0\), our model reduces to the standard \(SEIR\) model in epidemiology. From equation (9), \(R_{02}\) is the reproduction number of the prophylaxis only sub-model, denoted by \(R_p\) and written as

\[
R_p = \frac{\theta \beta \epsilon \Lambda \sigma_p}{\mu (\gamma_p + \mu) (\mu + \sigma_p)}.  
\]  

\(14\)

In order to interpret the reproduction number, we rewrite \(R_p\) as

\[
R_p = \frac{\theta \epsilon \beta \Lambda}{\mu} \times \frac{\sigma_p}{\mu + \sigma_p} \times \frac{1}{\gamma_p + \mu}.  
\]

The quantity \(\frac{\Lambda}{\mu}\) is the number of susceptible humans at the DFE. Thus, \(\frac{\theta \beta \epsilon \Lambda}{\mu}\) is the average number of contacts by susceptible humans. On the other hand, the term \(\frac{\sigma_p}{\mu + \sigma_p}\) is the fraction of exposed \(E\) progressing to \(I\), and the term \(\frac{1}{\gamma_p + \mu}\) represents the mean time spent in the \(I\)
compartment. Thus, $R_p$ is the average number of breakthrough cases in the population.

Section 1.3.3. Steady States and Stability Analysis

In the absence of the disease in the population, we compute the disease-free equilibrium by setting $E_p = I_p = 0$ and equate the time derivatives of the remaining subsystem to zero. This gives the disease-free equilibrium

$$E_0 : (S^*, E^*_p, I^*_p, R^*) = \left( \frac{\Lambda}{\mu}, 0, 0, 0, \right).$$

In order to find the endemic equilibrium, we set each right-hand side of system (10) - (13) to zero and solve for the dependent variables. Setting the right-hand side of system (10) - (13) to zero, we obtain

$$S^* = \frac{\Lambda}{\theta \beta I^*_p + \mu},$$

$$E^*_p = \frac{\theta \beta I^*_p S^*}{\sigma_p + \mu},$$

$$I^*_p = \frac{\sigma_p E^*_p}{\gamma_p + \mu},$$

$$R^* = \frac{\gamma_p I^*_p}{\mu}.$$

We substitute $I^*_p$ in equation (17) into $E^*_p$ to have

$$E^*_p = \frac{\theta \beta I^*_p S^*}{\sigma_p + \mu} = \frac{\theta \beta \sigma_p E^*_p S^*}{(\sigma_p + \mu)(\gamma_p + \mu)} \iff 1 = \frac{\theta \beta \sigma_p S^*}{(\sigma_p + \mu)(\gamma_p + \mu)}.$$

Solving for $S^*$, we obtain

$$S^* = \frac{\sigma_p + \mu)(\gamma_p + \mu)}{\theta \beta \sigma_p}.$$
Next, substituting the expression of $S^*$ into $S^*$ in equation (15), we have

$$S^* = \frac{\Lambda}{\theta \varepsilon \beta I_p^* + \mu} \iff \frac{(\sigma_p + \mu)(\gamma_p + \mu)}{\theta \varepsilon \beta \sigma_p} = \frac{\Lambda}{\beta I_p^* + \mu}.$$  

Solving for $I_p^*$, we obtain

$$I_p^* = \frac{\sigma_p \Lambda}{(\sigma_p + \mu)(\gamma_p + \mu)} - \frac{\mu}{\theta \varepsilon \beta}.$$  

Substituting $I_p^*$ into $R^*$ in equation (18), we have

$$R^* = \frac{\gamma_p I_p^*}{\mu} = \frac{\gamma_p}{\mu} \left( \frac{\sigma_p \Lambda}{(\sigma_p + \mu)(\gamma_p + \mu)} - \frac{\mu}{\theta \varepsilon \beta} \right) = \frac{\gamma_p \sigma_p \Lambda}{\mu (\sigma_p + \mu)(\gamma_p + \mu)} - \frac{\gamma_p}{\theta \varepsilon \beta}.$$  

Here, we obtain

$$R^* = \frac{\gamma_p \sigma_p \Lambda}{\mu (\sigma_p + \mu)(\gamma_p + \mu)} - \frac{\gamma_p}{\theta \varepsilon \beta}.$$  

Lastly, substituting $I_p^*$ into $I_p^*$ in equation (17), we have

$$I_p^* = \frac{\sigma_p E_p^*}{\gamma_p + \mu} \iff \frac{\sigma_p \Lambda}{(\sigma_p + \mu)(\gamma_p + \mu)} - \frac{\mu}{\theta \varepsilon \beta} = \frac{\sigma_p E_p^*}{\gamma_p + \mu} \iff E_p = \left( \frac{\gamma_p + \mu}{\sigma_p} \right) \left( \frac{\sigma_p \Lambda}{(\sigma_p + \mu)(\gamma_p + \mu)} - \frac{\mu}{\theta \varepsilon \beta} \right).$$
This gives

\[ E_p^* = \frac{\Lambda}{\sigma_p + \mu} - \frac{(\gamma_p + \mu)\mu}{\theta \varepsilon \beta \sigma_p}. \]

Thus, the endemic equilibrium of the prophylaxis-only submodel is

\[ E_1 : (S^*, E_p^*, I_p^*, R^*), \]

where

\[ S^* = \frac{(\sigma_p + \mu)(\gamma_p + \mu)}{\theta \varepsilon \beta \sigma_p}, \]
\[ E_p^* = \frac{\Lambda}{\sigma_p + \mu} - \frac{(\gamma_p + \mu)\mu}{\theta \varepsilon \beta \sigma_p}, \]
\[ I_p^* = \frac{\sigma_p \Lambda}{(\sigma_p + \mu)(\gamma_p + \mu)} - \frac{\mu}{\theta \varepsilon \beta}, \]
\[ R^* = \frac{\gamma_p \sigma_p \Lambda}{\mu(\sigma_p + \mu)(\gamma_p + \mu)} - \frac{\gamma_p}{\theta \varepsilon \beta}. \]

In order to interpret the endemic equilibrium biologically, we rewrite \( E_1 \) in terms of the prophylaxis-dependent reproduction number \( R_p \) in equation (14). Substituting the expression for \( R_p \) in equation (14) into \( S^*, E_p^*, I_p^*, R^* \), we have

\[ E_1 : (S^*, E_p^*, I_p^*, R^*) = \left( \frac{\Lambda}{\mu R_p}, \frac{\mu(\gamma_p + \mu)(R_p - 1)}{\theta \varepsilon \beta \sigma_p}, \frac{\mu(R_p - 1)}{\theta \varepsilon \beta}, \frac{\gamma_p n_p(R_p - 1)}{\beta} \right). \] (19)

We observe from equation (19) that the endemic equilibrium exists biologically if \( R_p > 1 \) and it reduces to the disease-free equilibrium if \( R_p = 1 \). When \( R_p < 1 \), the endemic equilibrium is biologically unrealistic since \( E_p^* < 0, I_p^* < 0 \) and \( R^* < 0 \).
Theorem 2.1. The disease-free equilibrium $E_0 : (S^*, E^*_p, I^*_p, R^*) = (\frac{\Lambda}{\mu}, 0, 0, 0,)$ is locally asymptotically stable if $R_p < 1$ and unstable if $R_p > 1.$

Proof. We prove the local stability of the disease-free equilibrium by showing that all eigenvalues of the Jacobian matrix of prophylaxis-free subsystem (10) - (13) are negative or complex numbers with negative real parts. The Jacobian matrix of prophylaxis-free subsystem is

$$J(S^*, E^*_p, I^*_p, R^*) = \begin{bmatrix}
\frac{\partial f_1}{\partial S} & \frac{\partial f_1}{\partial E_p} & \frac{\partial f_1}{\partial I_p} & \frac{\partial f_1}{\partial R} \\
\frac{\partial f_2}{\partial S} & \frac{\partial f_2}{\partial E_p} & \frac{\partial f_2}{\partial I_p} & \frac{\partial f_2}{\partial R} \\
\frac{\partial f_3}{\partial S} & \frac{\partial f_3}{\partial E_p} & \frac{\partial f_3}{\partial I_p} & \frac{\partial f_3}{\partial R} \\
\frac{\partial f_4}{\partial S} & \frac{\partial f_4}{\partial E_p} & \frac{\partial f_4}{\partial I_p} & \frac{\partial f_4}{\partial R}
\end{bmatrix}_{E_0},$$

where $f_1, f_2, f_3$ and $f_4$ are the respective right-hand sides of the differential equations in $S, E_p, I_p,$ and $R$ given in system (10) - (13). The eigenvalues of $J$ are obtained by solving the characteristic equation $\det(J - \lambda I) = 0$. Therefore,

$$\begin{vmatrix}
-\mu - \lambda & 0 & -\frac{\theta e^\beta \Lambda}{\mu} & 0 \\
0 & -(\sigma_p + \mu) - \lambda & \frac{\theta e^\beta \Lambda}{\mu} & 0 \\
0 & \sigma_p & -(\gamma_p + \mu) - \lambda & 0 \\
0 & 0 & \gamma_p & -\mu - \lambda
\end{vmatrix} = 0.$$

This gives

$$\begin{vmatrix}
-\mu - \lambda & -(\sigma_p + \mu) - \lambda & \frac{\theta e^\beta \Lambda}{\mu} & 0 \\
\sigma_p & -(\gamma_p + \mu) - \lambda & 0 & 0 \\
0 & \gamma_p & -\mu - \lambda
\end{vmatrix} = 0$$

$$\iff (\mu - \lambda)^2 \begin{vmatrix}
-\sigma_p & -(\sigma_p + \mu) - \lambda & \frac{\theta e^\beta \Lambda}{\mu} & 0 \\
0 & -(\gamma_p + \mu) - \lambda & 0 & 0 \\
0 & \gamma_p & -\mu - \lambda
\end{vmatrix} = 0.$$
This leads to

\[(\mu + \lambda)^2[(\sigma_p + \mu + \lambda)(\gamma_p + \mu + \lambda) - \frac{\theta \epsilon \beta \Lambda}{\mu} \sigma_p] = 0\]

Thus, \(\lambda = -\mu\) of multiplicity two, and the other roots are obtained from the equation

\[\lambda^2 + (\sigma_p + 2\mu + \gamma_p)\lambda + (\sigma_p + \mu)(\gamma_p + \mu) - \frac{\theta \epsilon \beta \Lambda \sigma_p}{\mu} = 0.\]

This equation is equivalent to

\[\lambda^2 + A\lambda + B = 0,\]

where the coefficients \(A\) and \(B\) are given by

\[A = \sigma_p + \gamma_p + 2\mu,\]

\[B = (\gamma_p + \mu)(\sigma_p + \mu) - \frac{\theta \epsilon \beta \Lambda \sigma_p}{\mu} = \frac{\theta \epsilon \beta \Lambda \sigma_p}{\mu} \left(1 - \mathcal{R}_p\right).\]

The coefficient \(A > 0\), and \(B > 0\) if \(\mathcal{R}_p < 1\). Thus, there is no sign change in the coefficients of the polynomial \(p(\lambda)\), where \(p(\lambda) = \lambda^2 + A\lambda + B\). Hence, the polynomial equation \(p(\lambda) = 0\) has no positive root by Descarte’s rule of signs. Replacing \(\lambda\) with \(-\lambda\), we have

\[(-\lambda)^2 + A(-\lambda) + B = 0 \iff \lambda^2 - A\lambda + B = 0,\]

with two sign changes. Therefore, \(p(\lambda) = 0\) has two negative roots by Descarte’s rule of signs. Hence, the disease-free equilibrium is locally asymptotically stable when \(\mathcal{R}_p < 1\). On the other hand, \(A > 0\) and \(B < 0\) when \(\mathcal{R}_p > 1\). Therefore, there is one sign change in the coefficients of polynomial \(p(\lambda)\). Hence, \(p(\lambda) = 0\) has one positive root by Descarte’s rule of signs. Therefore, \(p(\lambda) = 0\) has one negative root and one positive root. This means the disease-free equilibrium is unstable if \(\mathcal{R}_p > 1\).

Section 1.3.4. Parameter Estimation

The Centers for Disease Control and Prevention (CDC) suggests that once an individual contracts SARS-CoV-2, they are required to quarantine for at least 5 days followed by 5 days of wearing a mask in public (CDC, 2021). Thus, we set the rate at which individuals not on prophylaxis recover, \(\gamma np\), to \(\frac{1}{10}\) per day (Ngonghala et al., 2020).
A study published in the Annals of Internal Medicine estimated the incubation period of SARS-CoV-2 to be between 2-14 days and sometimes 5-6 days (Lauer et al., 2020), with the median incubation period estimated as 5.1 days. Since $\sigma_{np}$ is the rate at which exposed people not on prophylaxis become infected, we set $\sigma_p$ to $\frac{1}{15}$ per day (Ngonghala et al., 2020). We summarize the parameter values of the prophylaxis-only sub-model in Table 2.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Parameter Values</th>
<th>Source(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Lambda$</td>
<td>2</td>
<td>Assumed</td>
</tr>
<tr>
<td>$\beta$</td>
<td>0.55</td>
<td>Agusto et al., 2022</td>
</tr>
<tr>
<td>$\mu$</td>
<td>0.01</td>
<td>Estimated</td>
</tr>
<tr>
<td>$\theta$</td>
<td>0.01</td>
<td>Assumed</td>
</tr>
<tr>
<td>$\varepsilon$</td>
<td>0 – 1</td>
<td>Vary</td>
</tr>
<tr>
<td>$\sigma_p$</td>
<td>$\frac{1}{5.1}$</td>
<td>Ngonghala et al., 2020; Lauer et al., 2020</td>
</tr>
<tr>
<td>$\gamma_p$</td>
<td>$\frac{1}{10}$</td>
<td>CDC, 2021; Preston, Carter, &amp; Numfor, 2022</td>
</tr>
</tbody>
</table>

Table 2: Parameter values of the prophylaxis-only submodel

Section 1.3.5. Elasticity Indices

The elasticity index (or normalized sensitivity index) is the measure of the relative changes of the reproduction number to changes in different parameters of the reproduction number. This is commonly denoted as $E_{q, p}^{R, p}$, and defined as

$$E_{q, p}^{R, p} = \frac{\partial R_p}{\partial q} \times \frac{q}{R_p}.$$  

Elasticity indices can be used to determine the most effective means of control for a disease. If the elasticity of a parameter is negative, an increase in that parameter would lead to a decrease in the reproduction number, and if the elasticity of a parameter is positive, an increase in that parameter results in an increase of the reproduction number. In particular, the elasticity of $\mu$ is

$$E_{\mu, p}^{R, p} = \frac{\partial R_p}{\partial \mu} \times \frac{\mu}{R_p} = -\left(1 + \frac{\mu}{(\sigma_p + \mu)} + \frac{\mu}{(\gamma_p + \mu)}\right) = -1.139,$$

where we have used the parameter values in Table 2. The elasticity of $\mu$ suggests that a 10% increase in $\mu$ results in 11.39% decrease in $R_p$. Similarly, the elasticity indices of parameters in $R_p$ are computed and summarized in Table 3.
Table 3: Elasticity indices of the prophylaxis-dependent reproduction number $R_p$ of the prophylaxis-only submodel

The elasticity indices of the prophylaxis-dependent reproduction number $R_p$ are represented in Figure 4.

![Elasticity indices of $R_p$](image)

The elasticity indices of the reproduction number, $R_p$, depicted in Figure 4 suggests that $\mu$ and $\gamma_p$ have inverse relationships with $R_p$ while $\beta$, $\Lambda$, $\theta$ and $\varepsilon$ have direct relationships with $R_p$. 
Section 1.4. Numerical Simulations

We use the built-in function ode45 in MATLAB and the parameter values in Table 2 to carry out simulations of the prophylaxis-only sub-model for different parameter regimes.

Section 1.4.1. Effects of Progression to Infectiousness ($\sigma_p$)

In this subsection, we numerically investigate the effect of progression to infectiousness on prevalence by considering different values of $\sigma_p$. Results of simulations are represented in Figure 5. Figure 5 suggests that as the progression to infectious by individuals on prophylaxis increases, there is an increase in the infectiousness for about 25 days, but then decreases afterwards.

As seen in Figure 5, a two-fold increase in the value of $\sigma_p$ results in a 33.3% increase in the peak of prevalence of those on prophylaxis, and a 10-fold increase in $\sigma_p$ results in an 47.8% increase in the peak of prevalence. As more individuals are on prophylaxis, the progression to infection decreases as shown in the exposed population.
Section 1.4.2. Effects of Modification Parameter (θ) on Prevalence

We investigate the effect of the modification parameter for the transmission rate of breakthrough cases on prevalence by considering different values of θ. Results of our simulations are depicted in Figure 6. Figure 6 represents simulations for the effect of the modification parameter θ for the transmission rate of breakthrough cases on prevalence. Small values of θ indicate how effective the drug is in reducing the number of infectious cases as shown in Figure 6. This results in more susceptible cases in the population and fewer individuals progress from exposed to infectious.

Figure 6: Numerical simulations of the prophylaxis-only sub-model with different values of θ.

Figure 7 (i) is a contour plot of the prophylaxis-dependent reproduction number as a function of the proportion of susceptible individuals on prophylaxis (ε) and the rate of reduction in infectiousness (θ). The numbers within the contour plot are the values of the reproduction number $R_p$. The contour with the number one tells us that if the proportion of susceptible individuals on prophylaxis is less than 0.076 and the rate of reduction in
infectiousness is more than $3.7 \times 10^{-3}$, then all the values of the reproduction number are less than one. Thus, under this condition, the disease can be controlled. Figure 7 (ii) represents simulations for the reproduction number as a function of the modification parameter for the transmission rate of breakthrough cases ($\theta$). As number of individuals on prophylaxis increases, the rate of reduction in infectiousness increases, which agrees with the results in Figure 6.
SECTION 2. ANALYSIS OF THE COMPLETE MODEL

We return to the complete model and investigate the elasticity of the control reproduction number and stability of the disease-free equilibrium.

Section 2.1. Parameter Estimation

The parameter estimation in this section follows from the parameter estimation in Section 1.3.4. We summarize the parameter values of the complete model in Table 4. Table 4 contains the parameter values for the complete SEIR model. These parameter values will be used in calculating the elasticity indices of the control reproduction number of the complete model given in equation (9).
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Parameter Values</th>
<th>Source(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \Lambda )</td>
<td>2</td>
<td>Assumed</td>
</tr>
<tr>
<td>( \beta )</td>
<td>0.55</td>
<td>Agusto et al., 2022</td>
</tr>
<tr>
<td>( \theta )</td>
<td>0.01</td>
<td>Assumed</td>
</tr>
<tr>
<td>( \varepsilon )</td>
<td>0 – –1</td>
<td>Vary</td>
</tr>
<tr>
<td>( \mu )</td>
<td>0.01</td>
<td>Estimated</td>
</tr>
<tr>
<td>( \sigma_{np} )</td>
<td>( \frac{1}{5.1} )</td>
<td>Ngonghala et al., 2020; Lauer et al., 2020</td>
</tr>
<tr>
<td>( \sigma_p )</td>
<td>( \frac{1}{5.1} )</td>
<td>Ngonghala et al., 2020; Lauer et al., 2020</td>
</tr>
<tr>
<td>( \gamma_{np} )</td>
<td>( \frac{1}{10} )</td>
<td>CDC, 2021; Preston, Carter, &amp; Numfor, 2022</td>
</tr>
<tr>
<td>( \gamma_p )</td>
<td>( \frac{1}{10} )</td>
<td>CDC, 2021; Preston, Carter, &amp; Numfor, 2022</td>
</tr>
</tbody>
</table>

Table 4: Parameter values of the complete model

**Section 2.2. Elasticity Indices of the Reproduction Number, \( R_c \)**

As in Section 1.3.5., we compute the elasticity indices of the control reproduction number of model (1) – (6). The elasticity index of the control reproduction number \( R_c \) is denoted as \( E_{q}^{R_c} \), and defined as

\[
E_{q}^{R_c} = \frac{\partial R_c}{\partial q} \times \frac{q}{R_c},
\]

where the control reproduction number \( R_c \) is given in (9). For example, the elasticity of \( \sigma_p \) is

\[
E_{\sigma_p}^{R_c} = \frac{\partial R_c}{\partial \sigma_p} \times \frac{\sigma_p}{R_c} = 0.0476,
\]

where we have used the parameter values in Table 4. The elasticity of \( \sigma_p \) suggests that a 10% increase in \( \sigma_p \) results in a 0.476% increase in the reproduction number. Similarly, the elasticity indices of parameters in \( R_c \) are computed and summarized in Table 5.
Table 5: Elasticity indices of the control reproduction number $R_c$.

The elasticity indices of the reproduction number of the complete model are represented in Figure 8. Figure 8 suggests that the recovery and mortality rates of both individuals on and not on prophylaxis have an inverse relationship with elasticity of the reproduction number, and $\beta$, $\Lambda$, $\theta$ and $\varepsilon$ are directly related to $R_c$. 
Figure 8: Elasticity indices of the reproduction number $\mathcal{R}_c$ of the complete model.

Section 2.3. Stability Analysis

Theorem 3.1. The disease-free equilibrium $\varepsilon_0: (S^*, E^*_p, I^*_p, \mathcal{R}^*) = (\frac{\Lambda}{\mu}, 0, 0, 0)$ is locally asymptotically stable if $\mathcal{R}_c < 1$ and unstable if $\mathcal{R}_c > 1$.

Proof. To prove the stability of the disease-free equilibrium of the complete model, one must show that all the eigenvalues of the Jacobian matrix of (1) – (6) are negative or complex numbers with negative real parts. Since $\mathcal{R}_c$ is not contained in any of the equations in $S$, $E_{np}$, $E_p$, $I_{np}$, and $I_p$, we eliminate $\mathcal{R}$ by setting $\mathcal{R} = N - S - E_p - E_{np} - I_p - I_{np}$. Thus, the Jacobian matrix of the reduced subsystem of system (1) – (6) at the DFE is

$$J(S^*, E^*_p, E^*_{np}, I^*_p, I^*_{np}) = egin{bmatrix}
\frac{\partial f_1}{\partial S} & \frac{\partial f_1}{\partial E_p} & \frac{\partial f_1}{\partial E_{np}} & \frac{\partial f_1}{\partial I_p} & \frac{\partial f_1}{\partial I_{np}} \\
\frac{\partial f_2}{\partial S} & \frac{\partial f_2}{\partial E_p} & \frac{\partial f_2}{\partial E_{np}} & \frac{\partial f_2}{\partial I_p} & \frac{\partial f_2}{\partial I_{np}} \\
\frac{\partial f_3}{\partial S} & \frac{\partial f_3}{\partial E_p} & \frac{\partial f_3}{\partial E_{np}} & \frac{\partial f_3}{\partial I_p} & \frac{\partial f_3}{\partial I_{np}} \\
\frac{\partial f_4}{\partial S} & \frac{\partial f_4}{\partial E_p} & \frac{\partial f_4}{\partial E_{np}} & \frac{\partial f_4}{\partial I_p} & \frac{\partial f_4}{\partial I_{np}} \\
\frac{\partial f_5}{\partial S} & \frac{\partial f_5}{\partial E_p} & \frac{\partial f_5}{\partial E_{np}} & \frac{\partial f_5}{\partial I_p} & \frac{\partial f_5}{\partial I_{np}}
\end{bmatrix} \varepsilon_0$$
where \( f_1, f_2, \ldots, f_5 \) are the right-hand sides of system (1) – (5). Thus, the Jacobian matrix of the reduced system evaluated at the DFE is:

\[
J(S^*, E_p^*, E_{np}^*, I_p^*, I_{np}^*) = \begin{bmatrix}
-\mu & 0 & 0 & -\frac{\theta \beta \epsilon \Lambda}{\mu} & -\frac{\beta \Lambda (1-\epsilon)}{\mu} \\
0 & -(\sigma_p + \mu) & 0 & \frac{\theta \beta \epsilon \Lambda}{\mu} & 0 \\
0 & 0 & -(\sigma_{np} + \mu) & 0 & \frac{\beta \Lambda (1-\epsilon)}{\mu} \\
0 & \sigma_p & 0 & -\gamma_p - \mu & 0 \\
0 & 0 & \sigma_{np} & 0 & -\gamma_{np} - \mu
\end{bmatrix}.
\]

The eigenvalues of \( J \) are obtained by solving the characteristic equation \( \det(J - \lambda I) = 0 \). This is equivalent to:

\[
\begin{vmatrix}
-\mu - \lambda & 0 & 0 & \frac{\theta \beta \epsilon \Lambda}{\mu} & -\frac{\beta \Lambda (1-\epsilon)}{\mu} \\
0 & -(\sigma_p + \mu) - \lambda & 0 & 0 & \frac{\beta \Lambda (1-\epsilon)}{\mu} \\
0 & 0 & -(\sigma_{np} + \mu) - \lambda & 0 & 0 \\
0 & \sigma_p & 0 & -\gamma_p - \mu - \lambda & 0 \\
0 & 0 & \sigma_{np} & 0 & -\gamma_{np} - \mu - \lambda
\end{vmatrix} = 0
\]

\[
\iff
\begin{vmatrix}
-(\sigma_p + \mu) - \lambda & 0 & \frac{\theta \beta \epsilon \Lambda}{\mu} & 0 & \frac{\beta \Lambda (1-\epsilon)}{\mu} \\
0 & -(\sigma_{np} + \mu) - \lambda & 0 & \frac{\beta \Lambda (1-\epsilon)}{\mu} & 0 \\
\sigma_p & 0 & -\gamma_p - \mu - \lambda & 0 & 0 \\
0 & \sigma_{np} & 0 & -\gamma_{np} - \mu - \lambda
\end{vmatrix} = 0.
\]
One of the eigenvalues is \( \lambda = -\mu < 0 \), and the others are obtained by solving

\[
0 = -(\sigma_p + \mu + \lambda) \left[ \begin{array}{cccc}
-(\sigma_{np} + \mu) - \lambda & 0 & \frac{\beta \Lambda (1-\varepsilon)}{\mu} \\
0 & -(\gamma_p + \mu) - \lambda & 0 \\
0 & 0 & -(\gamma_{np} + \mu) - \lambda \\
\end{array} \right] \\
+ \sigma_p \left[ \begin{array}{cccc}
0 & \frac{\theta \beta \varepsilon \Lambda}{\mu} & 0 \\
0 & \frac{\beta \Lambda (1-\varepsilon)}{\mu} & 0 \\
0 & 0 & \frac{\beta \Lambda (1-\varepsilon)}{\mu} \\
\end{array} \right]
\]

\[
= (\sigma_p + \mu + \lambda)(\gamma_p + \mu + \lambda) \left[ \begin{array}{cccc}
-(\sigma_{np} + \mu + \lambda) & \frac{\beta \Lambda (1-\varepsilon)}{\mu} \\
0 & -(\gamma_{np} + \mu + \lambda) \\
\end{array} \right] \\
- \left( \frac{\sigma_p \theta \beta \varepsilon \Lambda}{\mu} \right) \left[ \begin{array}{cccc}
-(\sigma_{np} + \mu + \lambda) & \frac{\beta \Lambda (1-\varepsilon)}{\mu} \\
0 & -(\gamma_{np} + \mu + \lambda) \\
\end{array} \right]
\]

\[
= \left( \lambda^2 + (\sigma_p + \gamma_p + 2\mu)\lambda + (\sigma_p + \mu)(\gamma_p + \mu) - \left( \frac{\sigma_p \theta \beta \varepsilon \Lambda}{\mu} \right) \right) \times \\
\left( (\sigma_{np} + \mu + \lambda)(\gamma_{np} + \mu + \lambda) - \frac{\sigma_{np} \beta \Lambda (1-\varepsilon)}{\mu} \right)
\]

\[
= (\lambda^2 + (\sigma_p + \gamma_p + 2\mu)\lambda + (\sigma_p + \mu)(\gamma_p + \mu) - (\mu + \sigma_p)(\mu + \gamma_p)R_{02}) \times \\
(\lambda^2 + (\sigma_{np} + \gamma_{np} + 2\mu)\lambda + (\sigma_{np} + \mu)(\gamma_{np} + \mu) - (\mu + \sigma_{np})(\mu + \gamma_{np})R_{01})
\]

\[
= (\lambda^2 + (\sigma_p + \gamma_p + 2\mu)\lambda + (\sigma_p + \mu)(\gamma_p + \mu)(1 - R_{02})) \times \\
(\lambda^2 + (\sigma_{np} + \gamma_{np} + 2\mu)\lambda + (\sigma_{np} + \mu)(\gamma_{np} + \mu)(1 - R_{01}))
\]

\[
P_1(\lambda)P_2(\lambda),
\]

where

\[
P_1(\lambda) = (\lambda^2 + (\sigma_p + \gamma_p + 2\mu)\lambda + (\sigma_p + \mu)(\gamma_p + \mu)(1 - R_{02}))
\]

\[
P_2(\lambda) = (\lambda^2 + (\sigma_{np} + \gamma_{np} + 2\mu)\lambda + (\sigma_{np} + \mu)(\gamma_{np} + \mu)(1 - R_{01})).
\]
All the coefficients of $P_1(\lambda)$ and $P_2(\lambda)$ are positive if $R_c < 1$, since $R_c = \max\{R_{01}, R_{02}\}$. Thus, there is no change in the coefficients of the polynomials $P_1$ and $P_2$. Thus, $P_1(\lambda) = 0$ and $P_2(\lambda) = 0$ have no positive roots by Decarte’s rule of signs. Hence, the disease-free equilibrium is locally asymptotically stable if $R_c < 1$ and unstable if $R_c > 1$.

Section 2.4. Numerical Simulations

In this section, we use the built-in function, ode45 in MATLAB, to carry out numerical simulations for the complete model. Here, we will analyze the effects of post-exposure prophylaxis on prevalence.

Section 2.4.1. Effects of the modification parameter ($\theta$) on prevalence

As in subsection 1.4.2, we explore the effect of varying the modification parameter, $\theta$, for the transmission rate of breakthrough cases on prevalence.

Figure 9: Numerical simulations of the complete model with different modification parameters.

Figure 9 is a numerical simulation for prevalence for different values of the modification parameter ($\theta$) for the transmission rate of breakthrough cases. An increase in of this parameter displays higher infectiousness in individuals not on prophylaxis when
compared to individuals on prophylaxis. Thus, higher values of \( \theta \) result in an increase in the number of breakthrough cases. In comparison with individuals not on prophylaxis, there is approximately a 95% decrease in the number of individuals on prophylaxis progressing to infectious compared to those who are not on prophylaxis. This suggests that prophylaxis directly correlates to a reduction in infections for those who work in a high-exposure environment.

**CONCLUSION**

The coronavirus disease pandemic of 2019 is considered a zoonotic disease, and its origin is derived from viral particles in bats. We formulated a SEIR-type model with two exposed and infectious classes comprising individuals who are on prophylaxis and those who are not on prophylaxis. We derived the disease-free equilibrium of our model and calculated the control reproduction number, \( R_c \), using the next generation matrix approach.

We considered the prophylaxis-only sub-model and determined the disease-free and endemic equilibria and the prophylaxis-dependent reproduction number, \( R_p \), of the reduced model. We showed that the disease-free equilibrium of the prophylaxis-only sub-model is locally asymptotically stable when \( R_p < 1 \) and unstable whenever \( R_p > 1 \). In order to ascertain parameters that are most sensitive in reducing \( R_p \), we studied the elasticity indices of \( R_p \). We observed that the parameters \( \mu \) and \( \gamma_p \) are significant in reducing \( R_p \), and the parameters \( \beta, \theta \) and \( \epsilon \) are significant in increasing \( R_p \). Using the built-in function ode45 in MATLAB, we carried out numerical simulation. Simulations suggest that the smaller the values of the modification parameter \( \theta \), the more effective the drug is in reducing the number of infectious cases as shown in Figure 6. This results in more susceptible cases in the population and fewer individuals progress from exposed to infectious. Results of contour plots show that if the proportion of susceptible individuals on prophylaxis is less than 0.076, and the rate of reduction in infectiousness is more than \( 3.7 \times 10^{-3} \), then the reproduction number is below one and the disease can be controlled.

We considered the complete model and derived the disease-free equilibrium of the complete model and proved that the disease-free equilibrium. We showed that the DFE is locally asymptotically stable whenever \( R_c < 1 \) and is unstable if \( R_c > 1 \). Numerical simulations of the complete model suggests that there is approximately a 95% decrease in the number of individuals on prophylaxis progressing to infectious compared to those not on prophylaxis. This suggests that post-exposure prophylaxis directly correlates to a reduction in infectiousness for those who work in high-exposure environments such as nursing homes and prisons.
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I would like to express my deepest appreciation to Dr. Eric Numfor from the Department of Mathematics at Augusta University who was instrumental in the completion of my thesis. His continued advice, assistance, and patience during my undergraduate years provided me with the ability to complete mathematical epidemiology research. I would like to extend my sincere thanks to Dr. Hannah Bennett and Dr. Olusegun Otunuga for being a part of my thesis panel and for their unwavering guidance. This research would not have been possible without the Augusta University Honors Program and the Center for Undergraduate Research and Scholarship, and for that, I am grateful.

REFERENCES


**GLOSSARY**

*Antibody:* A blood protein produced in response to counteracting a specific antigen.

*Asymptotic Stability:* Solutions that start close enough not only remain close enough but also eventually converge to the equilibrium

*Breakthrough Cases:* Individuals on prophylaxis who eventually progressed from exposed to infectious

*Contact Tracing:* The process of quickly identifying, assessing, and managing people who have been exposed to a disease to prevent additional transmission
**Disease-free Equilibrium:** The point at which no disease is present in the population

**Eigenvalue:** An eigenvalue of an $n \times n$ matrix $A$ is a number $\lambda \in \mathbb{C}$ such that $Ax = \lambda x$, where $x \in \mathbb{C}^n$.

**Elasticity Index:** The change in a variable as a percentage of the original amount of the variable

**Endemic Equilibrium:** Point where the disease persists in the population

**Epidemiology:** The study and analysis of the distribution, patterns and determinants of health and disease conditions in defined populations

**Equilibrium:** A state of adjustment between opposing or divergent influences or elements

**Exposed Individuals:** Individuals in contact with an infectious individual and who are infected

**Force of Infection:** Rate at which susceptible individuals in a population acquire an infectious disease in that population per unit time

**Infectious Individuals:** People who are transmitting or capable of transmitting infections; containing pathogenic agents which may be transmitted

**Jacobian Matrix:** A matrix of partial derivatives

**Nucleotide Identity:** Measure of nucleotide-level genomic similarity between the coding regions of two genomes

**Prevalence:** The number of new infections in a population

**Prophylaxis:** A process of guarding against the development of a specific disease by a treatment or action

**Recovered Individuals:** People who are no longer infected with the virus

**Reproduction Number:** The average number of secondary infectious produced by a single infectious individual in a completely susceptible population during an individual’s entire period of infectiousness

**Schematic:** A picture that represents the components of a process, population, or other object using
abstract, often standardized symbols and lines

**Social Distancing**: Putting space between yourself and other people at all times

**Spectral Radius**: The maximum of the absolute values of the eigenvalues of a matrix

**Susceptible Individuals**: Healthy individuals who are not yet infected but can become infected upon contact with an infected individual

**Stability**: Condition in which a slight disturbance in a system does not produce too disrupting an effect on that system

**Zoonotic Disease**: Any of a group of diseases that can be transmitted to humans by nonhuman vertebrate animals