Mathematical Modeling of Two-Dose Vaccines

Project Seminar

Guided By:

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Mathematical Modeling, Simulation and Optimization

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August 31, 2023

Declaration

We hereby solemnly declare that the project seminar report titled "Mathematical Modeling of Two-Dose Vaccines" represents our original and genuine work. This report has been completed under the meticulous guidance of Prof. Dr. Thomas Götz. The ideas, concepts, and expressions presented within this report are the outcome of our own intellectual efforts. Whenever we have incorporated concepts or text from external sources, proper citations and references have been diligently provided to acknowledge the origin of such material. This report is submitted to fulfil the academic requirements of our project seminar and is a true reflection of our dedication, understanding, and commitment to the subject matter.

Date: 31 August 2023

Acknowledgment

We are delighted to share this report concerning the SIVR model of two-dose vaccines. Initially and most importantly, we express gratitude to God Almighty for the blessings received during our seminar work. We sincerely appreciate the invaluable direction, exceptional mentorship, and consistent motivation provided by our respected mentor, Prof. Dr. Thomas Götz throughout the entire duration of our efforts. Lastly, we extend our thanks to our families, friends, and all those who supported and encouraged us during the project seminar.

Abstract

This study examines the dynamics of two-dose vaccines, particularly for infectious diseases, aiming to identify scenarios necessitating multiple doses for effective disease control. The research modifies the classic SIR model by incorporating a new class of vaccinated individuals and explores the viability of single-dose vaccines. Key analyses include disease-free equilibrium, endemic equilibrium, and the basic reproduction number. Results reveal that an effective single-dose vaccination program requires minimal waning immunity, otherwise, a two-dose approach is necessary. This research enhances our understanding of vaccination strategies and their impact on disease spread.

Contents

Chapter 1

Introduction

Throughout the human history, infectious illness management has been a serious concern. Infectious illnesses have resulted in enormous sickness, fatalities, and societal destruction, from dreadful pandemics to neighbourhood outbreaks. However, the creation and use of vaccinations have completely changed disease prevention methods, providing a potent weapon to defend people and communities against the dangers presented by viruses. To prevent infections, advance public health, and increase disease resistance, vaccinations must stimulate the immune system and build resistance to diseases. Nevertheless, vaccine immunity plays an important role during the vaccination. This study examines the dynamics of multi-dose vaccines, specifically the susceptible, infected, vaccinated, and recovered (SIVR) model, to address questions surrounding infectious diseases, their vaccination strategies, and the potential for single-dose solutions [1].

Chapter 2

SIVR model

The Kermack and McKendrick-developed SIR epidemiology model serves as the basis for the SIVR model employed in this investigation [1]. This model divides the population into three separate subgroups: Susceptible (S), Infected (I), and Recovered (R), while assuming constant birth and death rates. People who are susceptible (S) are at risk of infection but have not yet developed the illness. Recovered people (R) have already contracted the disease but have made a full recovery. Those who are infected (I) have the illness and run the risk of passing it on to other people. The diagram below illustrates the flow of the SIR model.

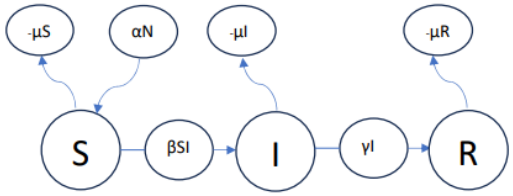

Figure 2.1: SIR Flow Diagram

The subsequent set of differential equations defines the fundamental SIR model.

$$\begin{aligned} \dot{S} &= \frac{dS}{dt} = \alpha N - \beta SI - \mu S \\ \dot{I} &= \frac{dI}{dt} = \beta SI - \mu I - \gamma I \\ \dot{R} &= \frac{dR}{dt} = \gamma I - \mu R \end{aligned} \tag{2.1}$$

Our aim is to analyze the dynamics of a SIR model expanded with a vaccinated class, representing those who've received the initial dose for partial immunity. This enhancement leads to the SIVR model, built upon the original SIR framework. The extended SIVR model incorporates a "V" class for vaccinated individuals, allowing analysis of vaccination dynamics alongside the traditional SIR model. The model is assumed to have the conditions of constant population size. The following figure shows a flow diagram of the SIVR model.

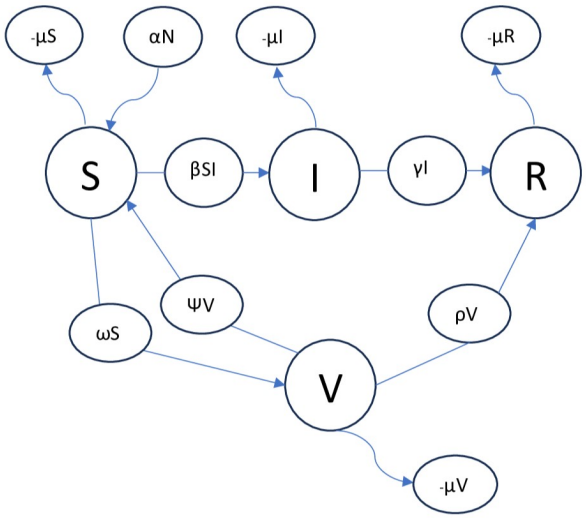

Figure 2.2: SIVR Flow Diagram

The number of infected individuals in the population increases when individuals from the infected class come into contact with those from the susceptible class at rate βSI. Simultaneously, infected individuals recover from the infected class at a rate represented by γI. The size of the recovered class is influenced by two factors: individuals recovering from the infected class at a rate denoted by γI, and individuals receiving a vaccine dose to recover at a rate represented by ρV. All sub-classes experience a reduction in population size due to the natural death rate represented by μ. An increase in population occurs as individuals from the susceptible class receive a vaccine dose at a rate denoted by ωS. A decrease in population occurs as individuals in the vaccination class experience waning immunity for the first dose of the vaccine at a rate represented by ψV.

Below are the differential equations that define the SIVR model.

$$\begin{aligned}
\dot{S} &= \frac{dS}{dt} = \alpha N - \beta SI - \mu S - \omega S + \psi V \\
\dot{V} &= \frac{dV}{dt} = \omega S - \mu V - \psi V - \rho V \\
\dot{I} &= \frac{dI}{dt} = \beta SI - \mu I - \gamma I \\
\dot{R} &= \frac{dR}{dt} = \gamma I - \mu R + \rho V
\end{aligned} \tag{2.2}$$

Since we have assumed a constant population size it can be noticed that N = S + I + V + R.

Parameter	Interpretation
α	Birth Rate
β	Infection Rate
ω	Rate of first Dose of Vaccination
ψ	First dose wane in immunity
ρ	Time between First and Second Dose
γ	Recover Rate
μ	Death Rate

Table 2.1: Parameter of the Model

Chapter 3

Model Analysis

In this model, there are two critical states that the system can reach: the **Disease-Free Equilibrium Point(DFEP)** and the **Endemic Equilibrium Point(EEP)**. Two equilibrium points may be found by setting the infection rate to zero. I = 0 and $S^* = \frac{\mu+\gamma}{\beta}$.

3.1 Disease-Free Equilibrium Point(DFEP)

When there are no active cases of the disease in the community, this condition exists. In a sense, the infection has been effectively contained, and there are now no longer any affected people. When the disease is not actively spreading and the population is in good health, the system stabilizes.

In this section, we implement I = 0 into our system, we obtain a new equation.

$$\begin{aligned} \dot{S} &= \alpha N - \mu S - \omega S + \psi V \\ \dot{V} &= \omega S - \mu V - \psi V - \rho V \\ \dot{R} &= -\mu R + \rho V \end{aligned} \tag{3.1}$$

To find disease-free equilibrium points we have to set $\dot{S}$, $\dot{V}$ and $\dot{R}$ as equal to zero. Mathematically, when we solve three equations, we obtain

$$\begin{aligned} V &= \frac{\omega\alpha N}{[(\mu+\psi+\rho)(\mu+\omega)-(\omega\psi)]} \\ S &= \frac{\mu N(\mu+\psi+\rho)(\mu+\omega)}{(\mu+\omega)[(\mu+\psi+\rho)(\mu+\omega)-\omega\psi]} \\ R &= \frac{\rho\omega N}{(\mu+\psi+\rho)(\mu+\omega)-\omega\psi} \end{aligned} \tag{3.2}$$

3.2 Endemic Equilibrium Point(EEP)

When a disease is continually present in a community without needing to be reintroduced from outside, it is said to be in an equilibrium known as an endemic condition.

In this section, we obtain the endemic equilibrium point, taking $S^* = \frac{\mu+\gamma}{\beta}$, we set $\dot{S}$, $\dot{I}$, $\dot{V}$, $\dot{R}$ as equal to zero and When we solve equations, we obtain

$$V^* = \frac{\omega(\mu+\gamma)}{\beta(\mu+\psi+\rho)}$$

$$I^* = \frac{\mu N}{\mu+\gamma} + \frac{\psi\omega}{\beta(\mu+\psi+\rho)} - \frac{\mu+\omega}{\beta} \tag{3.3}$$

$$R^* = \frac{\gamma(\frac{\mu N}{\mu+\gamma} + \frac{\psi\omega}{\beta(\mu+\psi+\rho)} - \frac{\mu+\omega}{\beta}) + \rho(\frac{\omega(\mu+\gamma)}{\beta(\mu+\psi+\rho)})}{\mu}$$

3.3 Basic reproduction Number

Understanding the dynamics of a disease requires an understanding of the fundamental reproduction number R_0. It indicates the total number of secondary infections that result from infected individual. We can predict whether a disease will eventually dissipate or spread throughout a community by evaluating the value of R_0 [2].

If $R_0 > 1$, the disease is still present, and if $R_0 \leq 1$, the infection has stopped spreading. Remarkably, the Disease-Free Equilibrium is unstable when $R_0 > 1$, which results in the disease's persistence. In contrast, the Disease-Free Equilibrium stays steady when R0 is lower than or equal to 1, which causes the infection to disappear.

We consider only the equation involving "I" as the one responsible for handling infected individuals, while the "V" class has no involvement in contributing to infections. As a result, we establish $\mathscr{F}$ to represent the rate at which new infections appear within the compartment, and $\mathscr{V}$ to represent the rate at which infected individuals move in and out of the compartment.

In the SIVR model, $\mathscr{F} = \beta IS$ and $\mathscr{V} = I(\mu + \gamma)$. By calculating the derivative with respect to I, we simplify $F = \beta S$ and $V = \mu + \gamma$. Additionally, we deduce that $V^{-1} = \frac{1}{\mu+\gamma}$ To determine the value of R_0, we compute the spectral radius of the product of F and V^{-1}, which can be represented as $R_0 = FV^{-1}$ [2].

Applying this to the model in our project, we have found that, $R_o = \frac{\beta S}{\mu+\gamma}$

3.4 Stability

In this study, we have identified two equilibrium points: one representing a disease-free equilibrium point and the other an endemic equilibrium point. To assess their stability, we employ the Jacobian matrix derived from our SIVR model's system of partial differential equations. The Jacobian matrix is defined as follows:

$$J = \begin{bmatrix} -\mu - \omega - \beta I & -\beta S & 0 & \psi \\ \beta I & -\mu + \beta S - \gamma & 0 & 0 \\ 0 & \gamma & -\mu & \rho \\ \omega & 0 & 0 & -\mu - \omega - \rho \end{bmatrix}$$

The subsequent step involves evaluating the Jacobian matrix at the equilibrium point determined in the preceding section. To ascertain the stability of this equilibrium, we proceed by finding the eigenvalues of the Jacobian matrix, denoted as J, through the process of solving the characteristic equation det(J - λ * Id) = 0 for λ. It's important to note that in our case, we will obtain four eigenvalues since our Jacobian matrix is of size 4x4.

When the basic reproduction number R_0 is less than or equal to 1, our study adopts parameter values $\alpha = 0.003$, $\beta = 0.00001$, $\omega = 0.002$, $\gamma = 0.02$, $\rho = 0.0033$, $\psi = 0.005$, and $\mu = 0.003$. By substituting these values into the Jacobian matrix, we compute the eigenvalues as follows:$\lambda 1$ = -0.003, $\lambda 2$ = -0.00368, $\lambda 3$ = -0.0126, and $\lambda 4$ = -0.0157. Notably, all eigenvalues possess negative real parts, leading us to conclude that the system is stable at the disease-free equilibrium point. Conversely, for the same parameter values, we observe the eigenvalues at the endemic equilibrium point: $\lambda 1$ = -0.003, $\lambda 2$ = 0.01028617, $\lambda 3$ = -0.00869558, and $\lambda 4$ = -0.01330998. Evidently, one eigenvalue becomes positive at the endemic equilibrium. Thus, when R_0 is less than or equal to 1, we deduce that the disease-free equilibrium is stable, whereas the endemic equilibrium is unstable.

When the basic reproduction number R_0 is greater than 1, our study utilizes the following parameter values: α = 0.003, β= 0.00004, ω= 0.002,γ = 0.02, ρ = 0.0033, ψ = 0.005, and μ = 0.003. Upon inserting these values into the Jacobian matrix, we calculate the eigenvalues as follows: $\lambda 1$ = -0.003, $\lambda 2$ = -0.00368654, $\lambda 3$ = -0.01261346, and $\lambda 4$ = 0.00616129. Remarkably, one of the eigenvalues exhibits a positive real part, leading us to conclude that the system is unstable at the disease-free equilibrium point.Conversely, when considering the same parameter values, we examine the eigenvalues at the endemic equilibrium point: $\lambda 1$ = -0.003 + 0j, $\lambda 2$ = -0.00245707 + 0.0041115j, $\lambda 3$ = -0.00245707 - 0.0041115j, and $\lambda 4$ = -0.0124882 + 0j. Significantly, all eigenvalues exhibit negative real parts at the endemic equilibrium. Thus, when R_0 is greater than 1, we conclude that the disease-free equilibrium is unstable, while the endemic equilibrium is stable.

Chapter 4

Simulation

When basic reproduction number $R_0 \leq 1$. In this project, simulations are generated for a better understanding of two-dose vaccination model. We choose initial conditions in which Susceptible is 980, Infected is 20, Vaccinated and Recovered are zero as well as we use other parameters like $\alpha = 0.003$, $\beta = 0.00001$, $\omega = 0.002$, $\gamma = 0.02$, $\rho = 0.0033$, $\psi = 0.005$, $\mu = 0.003$, and $n = 400$. (X-axis is represent time(n) in days and Y-axis is represent population(N))

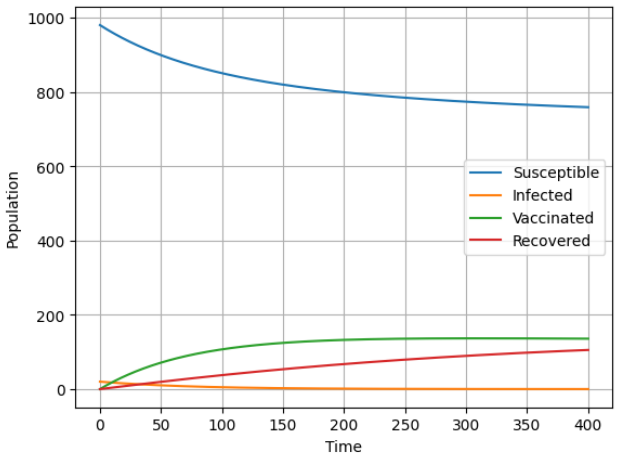

Figure 4.1: For $R_0 \leq 1$

In Figure 4.1, the basic reproduction number $R_0 \leq 1$ then there is no need to vaccinate anyone. This makes sense, because if $R_0 \leq 1$ then the disease will never spread and the SIVR model converges to the Disease-Free Equilibrium.

Now we consider three scenarios where the basic reproduction number is greater than one.

Case 1. Two-dose vaccination program.

Case 2. Single dose vaccination program.

Case 3. Single dose vaccination program with a small value of ψ.

4.1 Case 1. Two-dose vaccination program

When basic reproduction number $R_0 > 1$. In this case $R_0 = 1.7$. We choose initial conditions in which Susceptible is 980, Infected is 20, and Vaccinated and Recovered are zero. Additionally, we used other parameters such as $\alpha = 0.003$, $\beta = 0.00004$, $\omega = 0.002$, $\gamma = 0.02$, $\rho = 0.0033$, $\psi = 0.005$, $\mu = 0.003$, and $n = 1000$. (X-axis is represent time(n) in days and Y-axis is represent population(N))

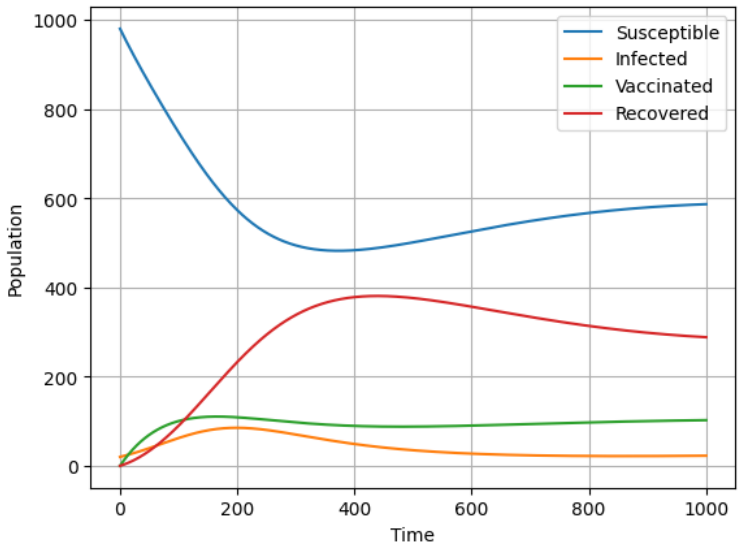

Figure 4.2: Analysis of Two-dose vaccination program

In Figure 4.2, the basic reproduction number is $R_0 > 1$ and the system converges to endemic an equilibrium point. However, it's important to note that this outcome may not apply to all cases with $R_0 > 1$ because it depends on the critical vaccination rate [3].

4.2 Case 2. Single dose vaccination program.

In this case, we are analysing a single-dose vaccination program and trying to find the answer to whether it is better to have a single-dose vaccination program. Is there any way to create a single vaccination program to reduce the financial burden? For a single-dose vaccination program, ρ(time between first and second dose) is equal to zero. In this case, where psi is equal to 0.005, it indicates that the first vaccination dose confers immunity for a period of approximately 200 days.

We choose initial conditions in which Susceptible is 980, Infected is 20, and Vaccinated and Recovered are zero. Additionally, we used other parameters such as $\alpha = 0.003$, $\beta = 0.00004$, $\omega = 0.002$, $\gamma = 0.02$, $\rho = 0$, $\psi = 0.005$, $\mu = 0.003$, and $n = 5000$. (X-axis is represent time(n) in days and Y-axis is represent population(N))

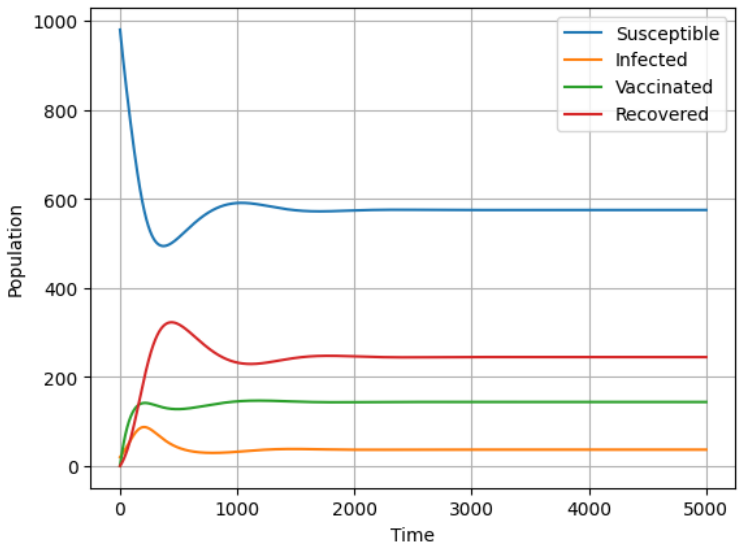

Figure 4.3: Analysis of Single dose vaccination program

It can be noticed that the two-dose vaccination program produces fewer infected individuals than the single-dose vaccination program. We will get a better idea from Figure 4.3.

4.3 Case 3. Single dose vaccination program with a small value of ψ

The question is raised, Is it possible to achieve the results of a two-dose vaccination program using just a single dose? Let us consider a situation where we have $\rho = 0$ and ψ is small enough. In this scenario, with ψ equal to 0.0025, it indicates that the first vaccination dose confers immunity for approximately 400 days. When comparing with case 2, we can observe that in this instance, the vaccine provides immunity for approximately twice the duration.

We choose initial conditions in which Susceptible is 980, Infected is 20, and Vaccinated and Recovered are zero. Additionally, we used other parameters such as $\alpha = 0.003$, $\beta = 0.00004$, $\omega = 0.002$, $\gamma = 0.02$, $\rho = 0$, $\psi = 0.0025$, $\mu = 0.003$, and $n = 5000$. (X-axis is represent time(n) in days and Y-axis is represent population(N))

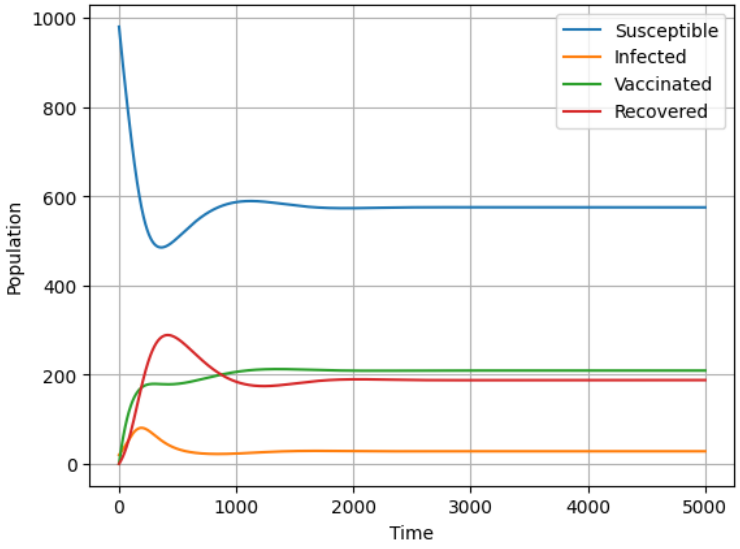

Figure 4.4: Analysis of Single dose vaccination program with a small value of ψ

It can be noticed that it may be possible to administrate a single-dose vaccination, and from simulation results, we can conclude that it yields better results when compared to Single-dose vaccination.

4.4 Comparative analysis

Now, we are going to perform a comparative analysis of the susceptible, recovered, infected, and vaccinated populations for all three cases. This will enhance visualization and improve understanding.

First, we will focus on the number of infected individuals from all three cases and compare them collectively.

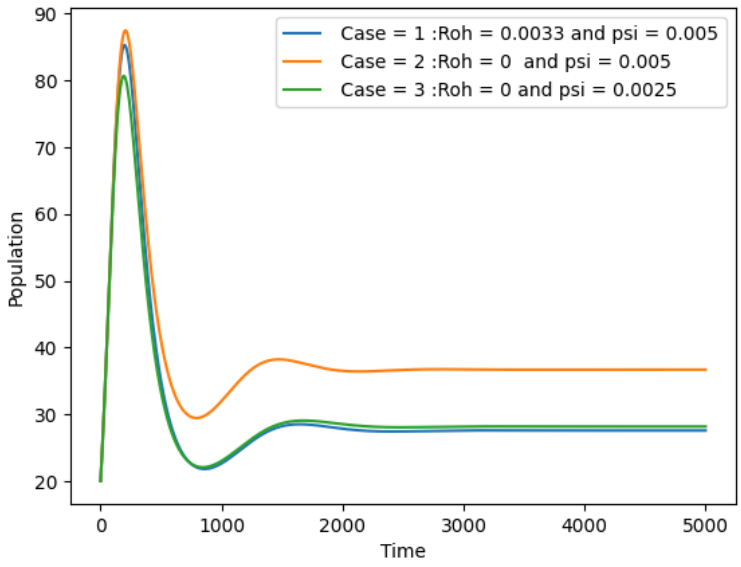

Figure 4.5: Comparative analysis of infected individuals

After reaching equilibrium, it becomes evident that in case 1, we achieved a lower percentage of infected individuals, specifically 2.755%. In case 2, we observed a higher percentage, at 3.668% of infected individuals, and in case 3, we recorded 2.816% of infected individuals, a result close to that of case 1. By analyzing all three cases, we can conclude that in case 1, the infection rate is lower compared to the other two cases, which involve single-dose vaccination

Now, we will shift our attention to vaccinated individuals from both single and multi-dose vaccination scenarios and compare them collectively.

After equilibrium, we can analyse Figure 4.6 reveals that in case 3, which employs a single-dose vaccination program with a small ψ, approximately 20.90% of the population is vaccinated. In contrast, case 2, also a single-dose vaccination program, sees 14.375% of the population vaccinated. Notably, case 2 demonstrates more favourable outcomes compared to case 3. In case 1, around 10.17% of individuals are vaccinated post-pandemic, marking a significantly better outcome than both case 1 and case 2.

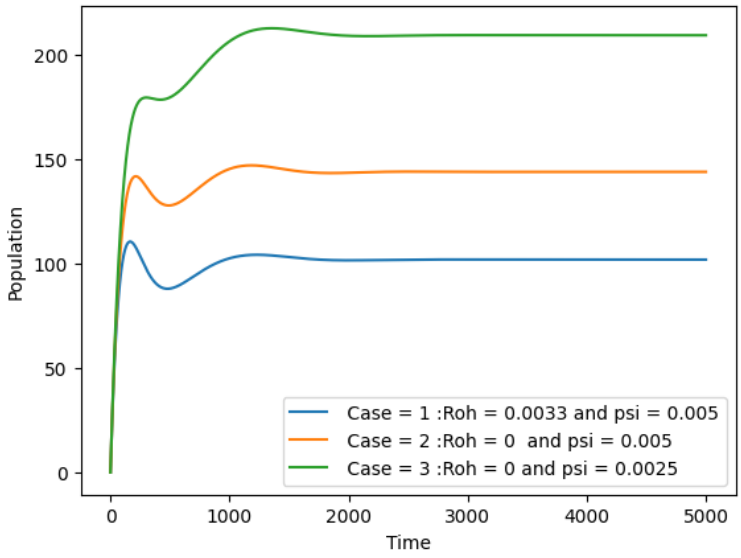

Figure 4.6: Comparative analysis of vaccinated individuals

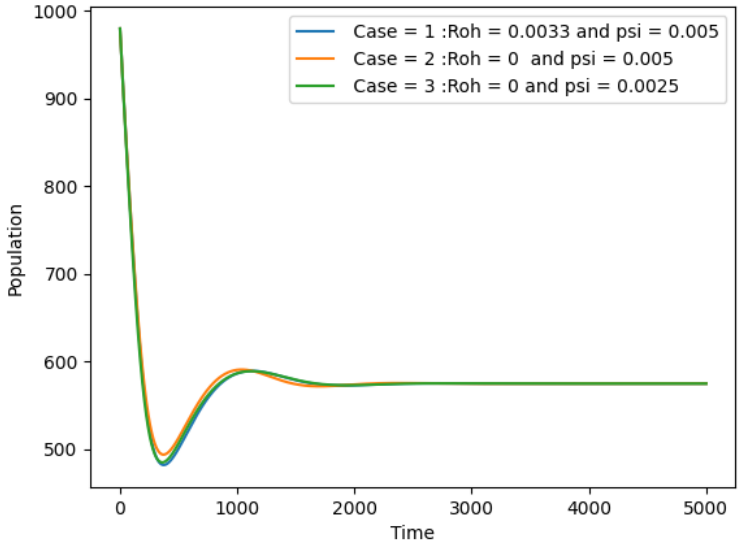

Figure 4.7: Comparative analysis of susceptible individuals

From the information presented in Figure 4.7 above, after reaching equilibrium, it becomes evident that in all three cases, 57% of the population remains susceptible.

Finally, we will examine the number of recovered individuals from all three cases and make a collective comparison.

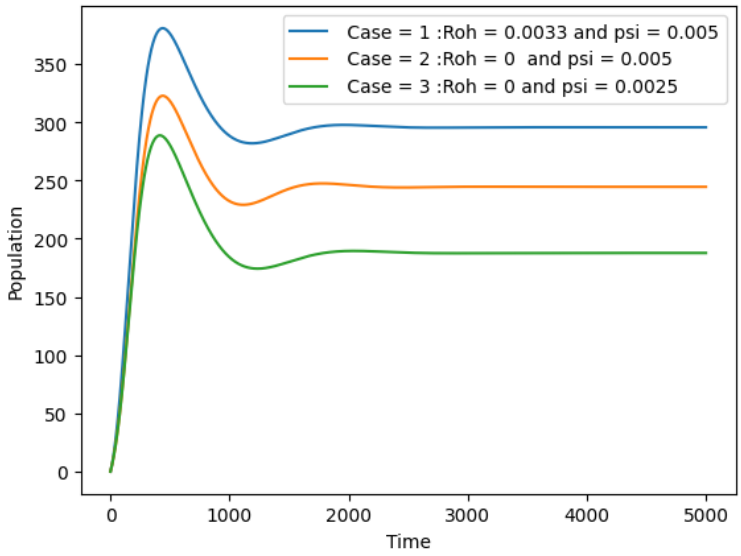

Figure 4.8: Comparative analysis of recovered individuals

After reaching equilibrium, as depicted in the Figure above, we can analyze that in the two-dose vaccination program, 29.56% of the population has recovered. In the single-dose vaccination program, 24.45% of the population has recovered, and in case 3, 18.77% of the population has recovered after the pandemic. Therefore, in this context, we can conclude that in case 1, more people have recovered compared to both case 2 and case 3.

Chapter 5

Conclusion

Analyzing all the comparison graphs, we can conclude that the two-dose vaccination program results in fewer infected individuals and a higher number of recoveries compared to the single-dose vaccination program. Hence, it is evident that implementing a two-dose vaccination program is the more favourable approach. While considering a single-dose vaccination program might be feasible when ψ is exceptionally small, this assumes the development of an extraordinarily potent vaccine with long-lasting immunity a practically improbable endeavour.

Chapter 6

Reference

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