A MATHEMATICAL MODEL ON REINFECTION AND VACCINATION ON THE DYNAMICS OF COVID-19

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A RESEARCH THESIS SUBMITTED TO SCHOOL OF PURE AND APPLIED SCIENCES IN FULFILLMENT FOR THE AWARD OF THE DEGREE OF MASTERS OF SCIENCE IN APPLIED MATHEMATICS OF MAASAI MARA UNIVERSITY

2024

DECLARATION

This research thesis is my original work with the support of the sources named and has not been presented by anyone for any degree award.

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ACKNOWLEDGMENTS

To God be the glory for making me reach this far to accomplish the work. To my supervisors, Dr Harun Makwata, Dr. Muthiga Samuel and Dr. Edward Njuguna, I deeply appreciate for all the support and guidance throughout the entire period of research. In addition, thanks to you Prof. Adu Wasike for the priceless insights and suggestions. Finally I am grateful to all the members of faculty and the department of mathematical and physical sciences.

DEDICATION

This work is dedicated to my family and all faculty members in mathematics and physical sciences department. You have been a great inspiration in my life.

ABSTRACT

In this study a mathematical model that investigates reinfection and vaccination on the dynamics of COVID-19 was considered. The model particularly takes into account the waning rate of immunity after vaccination as well as administration of booster vaccine. Positivity and boundedness of solutions of the model was proved as well as both the basic and effective reproduction numbers of the model determined by use of the next generation matrix. Further, using the effective reproduction number, the minimum critical value of individuals to be vaccinated for containment of the disease was determined. It was found that the value is less for a perfect vaccine compared to an imperfect vaccine. Sensitivity and elasticity of the effective reproduction number was also carried out and it was observed that the effective reproduction number is mostly affected by the recovery rate of individuals and least affected by natural death. Both disease free equilibrium and endemic equilibrium were determined as well as their stability analyzed using Routh Hurwitz stability criteria and Lyapunov stability. Numerical simulation was performed and we established that re-infection and waning rate of immunity contribute a lot in the disease staying in the population. In addition, results from numerical simulations show that booster vaccination increases the period of protection against the disease. Administration of booster vaccines is thus recommended for management of Corona Virus disease. The results show that reinfection, the waning rate of immunity after vaccination and the waning of immunity after infection contributes much on the diseases staying in the population.

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Notations and Symbols

COVOD-19: Coronavirus disease 2019

WHO: World Health Organization

DFE: Disease Free Equilibrium

EE: Endemic Equilibrium

NGM: Next Generation Matrix

α: Alpha

β: Beta

η: Eta

ϵ: Epsilon

$\Gamma(\gamma)$: Gamma (gamma)

$\Lambda(\lambda)$: Lambda (lambda)

μ: Mu

$\Omega(\omega)$: Omega(omega)

ρ: Rho

σ: Sigma

τ: Tau

θ: Theta

CHAPTER ONE

INTRODUCTION

In this chapter, section 1.1 describes the background information about COVID-19 as well as mathematical background related to our study, section 1.2 describes the statement of the problem while section 1.3 takes care of objectives of the study and methods used in the study. We conclude the chapter with justification of the study in section 1.4

1.1 Background of the Study

1.1.1 Background information about COVID-19

Coronavirus disease 2019 (COVID-19) is a novel corona virus that was first identified in December 2019 in China ("WHO coronavirus(COVID-19) Dashboard", 2024). It is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Baloch et al., 2020). COVID-19 is likened to the severe acute respiratory syndrome(SARS) which occurred in 2003 (Wilder-Smith et al., 2020). However COVID-19 is more contagious than SARS of 2003 as within 3 months of outbreak there were more than 100,000 confirmed cases and more than 3000 death cases (Wilder-Smith et al., 2020). In addition, in February 2020, it was found that, the reproduction number for COVID-19 was about 3.28, which is higher as compared to 2.79 for (SARS) (Wilder-Smith et al., 2020). As much as the virus is a threat to everyone, symptoms vary from person to person. Most individuals experience fever, coughing and shortness of breath, while others may face severe symptoms such as damage to the lungs, acute respiratory failure (Baloch et al., 2020) or others end up dying. Other symptoms include, fatigue, muscle aches, headache, loss of taste, sore throat, nausea and runny nose. The virus has since spread to over 100 countries resulting in approximately 775 million confirmed cases and 7

million deaths world wide ("WHO coronavirus(COVID-19) Dashboard", 2024). The latest cases as from 5th July, 2024 to 5th August, 2024 are about 200,000 confirmed cases and 3000 death cases("WHO coronavirus(COVID-19) Dashboard", 2024). The earlier outbreak caused widespread panic and disruption across the globe with many countries implementing strict travel restrictions and lockdown measures in an attempt to contain the virus. The virus has a long incubation period and is highly contagious. The incubation period as in (Del Rio & Malani, 2020) and (Baloch et al., 2020) is about 2-14 days. One thing to note about the virus is that it can spread through asymptomatic carriers which makes it difficult to identify and isolate infected individuals. More cases from the disease and more so for patients requiring a lot of health care, for example those who are diabetic may result in potentially healthy systems being overwhelmed (Baloch et al., 2020).

Several interventions were put into place in order to reduce the spread of the disease. One potential solution that was proposed is the implementation of non-pharmaceutical measures which include; wearing face mask, public event bans, school and workplace closure, keeping social distance, public transport shutdowns, restrictions on internal movement, international travel controls and stay at home requirements (Wilder-Smith et al., 2020). Implementation of these measures have shown to be effective in containing the spread of other viruses, such as SARS-Cov (Chen et al., 2005). And hence these measures can also be used to contain the spread of COVID-19 since they fall in the same group. However, implementation of these measures can negatively affect the economy and other health outcomes, including mental health and chronic conditions (Adams et al., 2020) . Vaccination is the common method that is relied on apart from the measures above. Vaccination not only provides protection for the individual it also provides it for the community at large since it keeps the effective reproduction rate below the level which would allow an epidemic to start, hence the so called 'herd immunity' (Murray, 2002). As virus constantly change, including the one that causes COVID-19, there is need for people to get vaccinated since the changes can lead to emergence

of variants that can increase the risk of reinfection (Hall et al., 2022). The emergence of new variants for the disease is discussed in more details in (Kumar et al., 2024). This explains why COVID-19 remains a global health concern.

Studies show that after vaccination or infection the body produces protective immune responses as antibodies increase in concentration for weeks and months (Hall et al., 2022). By three months people gain a robust antibody response. By six months, antibodies start declining leading to reduction in immunity. This means people will be susceptible to the disease again due to 'waning immunity'. In Hall et al. (2011) a recent study from the U.K. Health Security Agency showed that protection against infection from two doses of vaccine may last for up to six months. That means the effectiveness of the vaccine decreased by about seven months. This may be due to the emergence of new strains of the virus. The study in Hall et al. (2011) indicates that the protective immunity acquired from the combination of a COVID-19 infection followed by vaccination is very potent and is effective for more than a year. This urges people to be vaccinated more so those who had a prior infection. With the evidence from Hall et al. (2011) that protective immunity changes with time after vaccination or an infection, we include in our study a parameter that represent the waning rate of immunity.

1.1.2 Mathematical Background

In this section we describe the basic mathematical concepts related to our study

Definition 1.1.1 (Invariant set) *A set Ω is said to be invariant if any solution with initial condition in the set remains in the set for all time $t \geq 0$*

Definition 1.1.2 (Spectral radius) *The spectral radius of a matrix T is the largest of the absolute values of the eigenvalues of T*

Definition 1.1.3 *A matrix T is said to be a non-singular M-matrix if it has a Z-sign pattern and it is invertible. Here the Z-sign pattern means the off diagonal elements are non-positive*

Definition 1.1.4 *The basic reproduction number, usually denoted by R_o, is the average number of secondary cases produced by one infected individual introduced into a population of susceptible individuals without any interventions in place. If interventions like vaccination are put in place then we determine effective reproduction number analogous to R_o, which we denote as R_e*

To determine reproduction number we use the Next Generation Matrix method which is described below

1.1.3 The Next Generation Matrix Method

This is a method used in determination of R_o and it is based on dividing the compartments under study into two;

(i) Disease compartment- This is the compartment in which individuals are infected

(ii) Non-disease compartment- Individuals here are disease free.

Following (Brauer et al., 2012) we assume that there are n disease compartments and m non-disease compartments. We also assume that there are x and y subpopulations in each of the compartments n and m respectively. That is, $x \in \mathbb{R}^n$ and

$y \in \mathbb{R}^m$. We then denote the rate at which new infections increase the i^{th} infected compartment by F_i while V_i denote the rate of decrease in the i^{th} compartment by disease progression, death and recovery. The general compartmental model thus take the form;

$$\begin{aligned} x_i &= F_i(x,y) - V_i(x,y), i = 1,2,...,n \\ y_j &= g_j(x,y),\ j = 1,2,...,m \end{aligned} \tag{1.1}$$

Next we put some conditions on F_i and V_i;

$F_i(x,y) \geq 0$ for all $x \geq 0$, $y \geq 0$ and $i = 1,2,...,n$. Since F represent new infections it is non-negative

$V_i(x,y) \leq 0$ provided $x_i = 0$ for $i = 1,2,...,n$. V_i is the net outflow from compartment i hence it must be negative whenever the compartment is empty

$\sum_{i=1}^{n} V_i(x,y) \geq 0$ for all $x \geq 0$, $y \geq 0$. This represent the total outflow from all infected compartments. For determination of the basic reproduction number using this method we only consider the infected compartments. Moreover, determining R_o involves the linearization of the ODEs in the infected compartments about the disease free equilibrium(DFE). The disease free equilibrium for the above general model will be $(0, y_o)$. After linearization about the DFE, we obtain two matrices F and V given by

$$F = \frac{\partial F_i(0,y_o)}{\partial x_i}, \quad V = \frac{\partial V_i(0,y_o)}{\partial x_i}$$

The matrix given by FV^{-1} is known as the next generation matrix. The spectral radius of this matrix is what we refer as the basic reproduction number.

1.2 Statement of the problem

Many mathematical models have described the transmission dynamics of COVID-19. However, most of the models do not incorporate the possibility of reinfection despite evidence that COVID-19 reinfection is possible. In this study we bring in the reinfection mechanism in the model. While some models include vaccination, they never consider the waning rate of immunity post-vaccination and after infection. We therefore in this study look at how the waning rate of immunity can change the dynamics of the disease. In addition most existing model have not taken into account the booster vaccination program. This study examines the impact of booster vaccination on the disease dynamics.

1.3 Objectives

1.3.1 Main Objective

The main objective of the study is to develop a mathematical COVID-19 model with vaccination and reinfection.

1.3.2 Specific Objectives

(i) To investigate how the waning rate of immunity affects the dynamics of COVID-19

(ii) To determine how administration of booster vaccine will impact the dynamic spread of the disease

1.4 Methods used in the Study

The following methods are used in this study

(i) Deterministic compartmental model of ordinary differential equations.

(ii) Next Generation Matrix method in finding the basic reproduction number

(iii) Stability analysis of equilibrium points

(iv) Numerical simulation using MATLAB software

1.5 Justification of the study

The study provides a mathematical model that investigates the immunity after vaccination against COVID-19. The model was used to simulate the spread of the virus and the effectiveness of vaccination in controlling it. From the analysis the threshold level of individuals to be vaccinated in order to contain the disease is determined. In addition , as much as effectiveness of vaccines is concerned, resurgence of some infections such as measles is a major concern to public health and COVID-19 is no exception. One of the reasons for such resurgence is incomplete protection from imperfect vaccines as well as the reduction of vaccine-induced immunity. To address such scenario, there is need for a booster vaccination program. The model therefore helps public health to determine the threshold to be vaccinated when the booster vaccination is incorporated. Moreover, the hybrid immunity, which is acquired from both COVID-19 infection and vaccination as in (Hall et al., 2022) is very strong lasting for almost more than a year after infection. Individuals are therefore asked to be vaccinated whether they had been infected or not. More so those who had a prior infection are urged to be vaccinated as they will acquire hybrid-induced immunity.

CHAPTER TWO

LITERATURE REVIEW

This chapter deals with the following; section 2.1 captures a brief introduction about COVID-19, section 2.2 introduces the the basic model on any infectious disease, while section 2.3 ends the chapter by reviewing some of the models that have been developed by researchers on the spread of COVID-19 as well as capturing the gaps in each model with respect to our study.

2.1 Introduction

The potential benefits of non-pharmaceutical measures in containing the spread of COVID-19 has been in spotlight . These measures have shown to be effective in containing the spread of other viruses, such as SARS-CoV (Chen et al., 2005). In addition, vaccination is the common method of reducing individuals who are susceptible to a certain disease, there by reducing the basic reproduction number. This has been successful in eradicating small pox (Murray, 2002). Since the start of COVID-19 there have been many mathematical models to provide understanding on the spread of the disease and suggest to the public health on what should be done in order to reduce the spread of the disease. Mathematical modeling in epidemiology provides understanding of the underlying mechanisms that influence the spread of diseases, and in the process it suggests control strategies (Murray, 2002).

2.2 The Basic Model on Infectious Diseases

In most infectious disease, the population under study is divided into three compartments; S(t), this represents individuals who are susceptible to the disease under study, I(t), which represent infected individuals and R(t) representing the

recovered individuals. From the three compartments we have the famous SIR model by Kermack-Mckendrick (Brauer et al., 2012) who were among the first to come up with mathematical models to describe the transmission of infectious diseases as given in equation (2.1)

$$\begin{aligned} \dot{S} &= -\beta SI, \\ \dot{I} &= \beta SI - \gamma I, \\ \dot{R} &= \gamma I \end{aligned} \tag{2.1}$$

Where β and γ are the transmission rate of infection and recovery rate respectively. Since for COVID-19 there is a latent period before individuals become infectious, there is need to incorporate the exposed class,E, in the SIR model above. We thus review mathematical COVID-19 models incorporating the exposed class.

2.3 Review of Mathematical models on COVID-19

A lot of models have been used to describe the dynamics of COVID-19. We start by looking at the model considered in (Moussaoui & Auger, 2020). They incorporated the exposed class and came up with two scenarios ; the first scenario was a model with no control measures put into place while in the second one, at a certain date T, drastic control measures were taken. In the first scenario they considered an SEIR model in which S(t) denote the fraction of individuals who are susceptible to the disease but not yet infected, E(t) denote the fraction of exposed or latent individuals, that is, who are infected but not yet infectious , I(t) denote the fraction of infected individuals assumed infectious and able to spread the disease by contact with susceptible, R(t) denotes the fraction of cumulative number of known cases (infectious but confined at home, hospitals,recover or die from the disease). The system of differential equations used to describe the model

were;

$$\begin{aligned}
\frac{dS}{dt} &= -\beta SI, \\
\frac{dE}{dt} &= \beta SI - kE, \\
\frac{dI}{dt} &= kE - \alpha I, \\
\frac{dR}{dt} &= \alpha I
\end{aligned} \tag{2.2}$$

with $S + E + I + R = 1$

Where β is the transmission rate per infectious individual, k is the infection rate,$\frac{1}{\alpha}$ is the average time in compartment I before isolation. Using the next generation matrix they computed the basic reproduction number to be $R_o = \frac{\beta}{\alpha}$

They modified the model above in the second scenario by dividing the compartments S, E, I into two states each,the first state corresponding to total protection in which an individual can not be infected while in the second state an individual is unprotected. The main output of the model was the function v of its time that an average individual spends in fully protected state 1 and the compliment u=1-v in state 2 without any protection. Since S, E and I are divided into two sub-populations each they let $S = S_1 + S_2$, $E = E_1 + E_2$, $I = I_1 + I_2$. Individuals in S_1,E_1 and I_1 can change states daily at a rate m_2 by returning to a risk-free activity while the rate of returning to a risky activity is m_1. The model now

becomes

$$\begin{aligned}
\frac{dS_1}{d\tau} &= m_2 S_2 - m_1 S_1, \\
\frac{dS_2}{d\tau} &= m_1 S_1 - m_2 S_2 - \epsilon(\beta S_2 I_2), \\
\frac{dE_1}{d\tau} &= m_2 E_2 - m_1 E_1 - \epsilon(k E_1), \\
\frac{dE_2}{d\tau} &= m_1 E_1 - m_2 E_2 + \epsilon(\beta S_2 I_2 - k E_2), \\
\frac{dI_1}{d\tau} &= m_2 I_2 - m_1 I_1 + \epsilon(k E_1 - \alpha I_1), \\
\frac{dI_2}{d\tau} &= m_1 I_1 - m_2 I_2 + \epsilon(k E_2 - \alpha I_2), \\
\frac{dR}{d\tau} &= \epsilon(\alpha I_1 + \alpha I_2)
\end{aligned} \tag{2.3}$$

where τ is the fast time, $t = \epsilon\tau$ is the slow time and $\epsilon << 1$ is small dimensionless parameter. They used aggregation of variables method to obtain a reduced model thus

$$\begin{aligned}
\frac{dS}{dt} &= -\beta_1 S I, \\
\frac{dE}{dt} &= \beta_1 S I - k E, \\
\frac{dI}{dt} &= k E - \alpha I, \\
\frac{dR}{dt} &= \alpha I
\end{aligned} \tag{2.4}$$

where $\beta_1 = u^2\beta$. The model was used to determine a threshold for the release of confinement making it possible to avoid a second epidemic peak.The threshold was found to be $u^* = \frac{1}{\sqrt{R_o S(T^*)}}$ where T* is a time of release of confinement of the third phase. The model in Moussaoui and Auger (2020) never included reinfection which is something to note about the transmission of COVID-19.

In Wangari et al. (2021) they included re-infection and they let S be susceptible individuals, E exposed individuals, I_a infectious asymptomatic individuals, I_m infectious symptomatic with mild symptoms, I_s infectious symptomatic with severe

symptoms, I_d infectious asymptomatic isolated from general population via contact tracing, H hospitalized individuals, $R_I$recovered individuals with protective COVID-19 immunity and R_L recovered individuals with weak or no COVID-19 protective immunity. The model thus becomes

$$\begin{aligned}
\frac{dS}{dt} &= -\lambda S, \\
\frac{dE}{dt} &= \lambda S + \theta\lambda R_L - \sigma E, \\
\frac{dI_a}{dt} &= f\sigma E - (\alpha + \epsilon + d_a + \gamma_1) I_a, \\
\frac{dI_m}{dt} &= (1-f)\sigma E + \epsilon I_a - (\nu + \eta_1 + d_m + \gamma_2) I_m, \\
\frac{dI_s}{dt} &= \nu I_m - (d_s + \eta_2) I_s, \\
\frac{dH}{dt} &= \eta_1 I_m + \eta_2 I_s - (\gamma_3 + d_h) H, \\
\frac{dI_d}{dt} &= \alpha I_a - (d_c + \gamma_4) I_d, \\
\frac{dR_I}{dt} &= \gamma_1 I_a + \gamma_2 I_m + \gamma_3 H + \gamma_4 I_d - \rho R_I \\
\frac{dR_L}{dt} &= \rho R_I - \theta\lambda R_L
\end{aligned} \tag{2.5}$$

Where λ is the force of infection, $\frac{1}{\sigma}$ is the intrinsic incubation period for individuals exposed to COVID-19, f is the proportion of exposed individuals who progress to infectious asymptomatic class, α is the rate at which asymptomatic individuals are detected via contact tracing and then isolated, ϵ is the rate at which asymptomatic individuals develop COVID-19 mild symptoms γ_i i=1,2,3,4 is the recovery rates of I_a, I_m, H and I_d respectively, η_1 is the rate at which individuals with mild symptoms are hospitalized, η_2 is the rate at which individuals with severe COVID-19 are hospitalized, ν is the rate at which infectious humans with mild symptoms develop severe symptoms, $\frac{1}{\rho}$ is the duration of COVID-19 protective immunity d_a, d_m, d_s, d_d and d_h respectively represent COVID-19 induced mortality rate in compartments I_a, I_m, I_s, I_d and H and θ is the reduction rate of infectiousness. Sensitivity and uncertainty analysis was conducted on the basic reproduction number and findings suggest that non-pharmaceutical measures

are effective in curbing the spread of COVID-19 as supported by a high negative PRCC values. With just wearing face masks and maintaining social distance, COVID-19 peak infections was significantly delayed. Further their findings suggest that increase of reinfection with COVID-19 can lead to a surge of cumulative cases. In particular there will be a large pool of asymptotic individuals which lead to prolonged COVID-19 outbreak. The model in (Wangari et al., 2021) although included reinfection but never considered vaccination of individuals.

In Faria (2021) they first considered an SEIR model with no vaccine and then incorporated a vaccine compartment. The vaccine considered was imperfect meaning individuals who are vaccinated can still contract the virus but at a reduced rate. The system of differential equations to describe the model was as follows

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \eta S - \beta_1 SE - \beta_2 SI - \mu S, \\
\frac{dV}{dt} &= \eta S - (1-\epsilon_v)\beta_1 VE - (1-\epsilon_v)\beta_2 VI - \mu V, \\
\frac{dE}{dt} &= \beta_1 SE + \beta_2 SI + (1-\epsilon_v)\beta_1 VE + (1-\epsilon_v)\beta_2 VI - \gamma E - \sigma E - \mu E, \\
\frac{dI}{dt} &= \gamma E - \kappa I - \delta I - \mu I, \\
\frac{dR}{dt} &= \sigma E + \kappa I - \mu R
\end{aligned} \tag{2.6}$$

Where Λ is the recruitment rate, β_1 is the rate of contraction of susceptible from exposed, β_2 is the rate of contraction of susceptible from infectious, γ is the rate at which exposed individual becomes infectious, σ the rate at which an exposed individual recovers, κ the rate at which an infectious individual recovers, δ is the disease induced death rate, μ is natural death rate, ϵ_v is the efficacy of the vaccine and η is the vaccination rate.

The analysis was done and the disease free equilibrium(DFE) for the model without the vaccination compartment compared with the model with vaccinated compartment suggest that the susceptible individuals are reduced when a vaccine compartment is incorporated. That is, the DFE with no vaccine compartment

was $S^o = \frac{\Lambda}{\mu}$ while with the vaccine compartment was $S_v^o = \frac{\Lambda}{\eta+\mu}$. It is clear that $S_v^o < S^o$

The basic reproduction number for both models was also determined and it was found that the one for the model with the vaccine compartment was smaller than the model with no vaccine. They included vaccination of individuals but never the waning of immunity after vaccination.

All the models that we have come across for COVID-19, most of them do not include administration of booster vaccine. Moreover, most of the mathematical models that have been studied do not include reinfection mechanism and waning of immunity after both vaccination and prior infection. In this study we consider a model with reinfection and vaccine compartments in which after vaccination, individuals start loosing immunity over time. We also introduce the rate of administration of booster vaccine to previously vaccinated individuals.

CHAPTER THREE

FORMULATION OF THE MODEL

In this chapter, section 3.1 focuses on stating the assumptions behind the model as well as describing the parameters of the model. We end the chapter by formulating the model.

3.1 Assumptions

The population under study is divided into the following compartments S(t) which denote individuals who are susceptible to COVID-19 but not yet infected at time t, E(t) are exposed individuals who are infected but not yet infectious at time t, $I(t)$ are infective individuals, R(t) are vaccinated and recovered individuals, and V(t) are vaccinated individuals. For notational convenience we define the following variables;

$S(t) = S$, $E(t) = E$, $V(t) = V$, $I(t) = I$ and $R(t) = R$

We make the following assumptions for the model

(i) Individuals in each compartment are uniformly mixed.

(ii) Immunity induced by vaccination wanes and vaccines are imperfect, thus we introduce booster vaccination.

(iii) Infectivity rate of exposed individuals is less compared to infectivity of infected individuals.

(iv) Individuals in compartment V can be infected if they make contact with individuals in compartments E and I as the vaccines are imperfect.

(v) There is death due to COVID-19 in compartment I.

(v) Individuals in compartment R who were administered a booster vaccine are considered to have protective immunity at a longer period of time .

(vi) The total population size in consideration is a constant N.

The following parameters are used in the model

(i) β is the transmission rate of the disease, it describes the number of new cases that arise from each existing case.

(ii) λ_E is the infection rate of exposed individuals

(iii) η is the rate at which individuals are vaccinated while ρ is the efficacy of the vaccine

(iv) γ is the rate at which exposed members become infectious

(v) r_E and r_I are the rates at which exposed and infective members recover respectively, d is COVID-19 mortality rate, μ is the natural death rate in each compartment, b is rate of administering booster vaccine and ω is the rate at which individuals in R become susceptible to the disease again.

3.2 The Model

The schematic diagram for the model is as shown below. The arrows indicate individuals progressing from one compartment to another

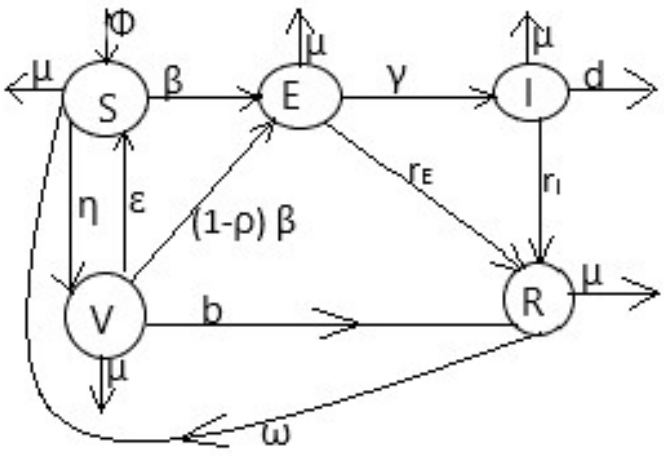

Figure 3.1: Schematic diagram showing the progression from one state to another

From the schematic diagram above, we first describe the evolution in each compartment then write down a system of differential equations which describes the model.

In S the gain is due to recruitment rate ϕ as well as from individuals who are re-infected and due to waning immunity from vaccinated individuals, hence they will contribute positively to the rate of change in S. The loss is due to individuals being exposed, vaccinated and also due to natural death. In the schematic diagram we are assuming that individuals are first exposed before being infectious. The evolution in V is described by adding individuals into the compartment through vaccination while individuals leave the compartment through exposure to the disease, being administered booster vaccine and also natural death. In E, the gain is from the loss from both S and V to exposed while the loss is due to individuals becoming infectious, recovery and natural death. In I, the exposed individuals

who become infectious add to the compartment while the loss is due to recovery, death induced by COVID-19 and natural death. In R, the gain is as a result of individuals who recover, that is from compartments E and I and also due to individuals being administered a booster vaccine. The loss is due to individuals being reinfected and natural death. In each compartment the gain and loss will be represented by a positive sign and a negative sign respectively. Using this information and also with the above assumptions and parameters, the system of differential equations describing the model becomes

$$\begin{aligned}
\frac{dS}{dt} &= \phi - \beta S(\lambda_E E + I) - (\eta + \mu)S + \varepsilon V + \omega R, \\
\frac{dV}{dt} &= \eta S - (1-\rho)\beta V[\lambda_E E + I] - (b + \mu + \varepsilon)V, \\
\frac{dE}{dt} &= \beta S(\lambda_E E + I) + (1-\rho)\beta V[\lambda_E E + I)] - (\gamma + r_E + \mu)E, \\
\frac{dI}{dt} &= \gamma E - (r_I + d + \mu)I, \\
\frac{dR}{dt} &= r_E E + r_I I - (\omega + \mu)R + bV
\end{aligned} \tag{3.1}$$

Equation (3.1) is subject to the initial condition $S(0) \geq 0$, $V(0) \geq 0$, $E(0) \geq 0$, $I(0) \geq 0$, and $R(0) \geq 0$. We have formulated our model and hence the system of differential equations describing it. We now analyze the system, first starting with its basic properties, positivity and boundedness of solutions, which we describe in the next chapter

CHAPTER FOUR

ANALYSIS OF THE MODEL

This chapter focuses on the analysis of our model. Section 4.1 deals with the positivity and boundedness of the solutions. Section 4.2 describes the basic reproduction number as well as sensitivity analysis of it. In addition we determine the threshold value of individuals needed to be vaccinated in order to contain the disease. Section 4.3 deals with determination of equilibrium points and their stability to understand the long term behaviour of the solutions. We end the chapter by performing numerical simulation.

4.1 Positivity and Boundedness of Solutions

Since we are dealing with human population, the solutions set {S(t),V(t),E(t),I(t),R(t)} must be positive and bounded. We therefore state and prove the following theorems with respect to our model.

Theorem 4.1.1 *The solutions set {S(t),V(t),E(t),I(t),R(t)} for system* (3.1) *is positive with the initial conditions* $\{S(0) \geq 0,\ V(0) \geq 0,\ E(0) \geq 0,\ I(0) \geq 0,\ R(0) \geq 0\}$ *for all* $t > 0$ *and all nonnegative parameters.*

Proof

For $\frac{dS}{dt}$ we have

$$\begin{aligned} \frac{dS}{dt} &= \phi - \beta S(\lambda_E E + I) - (\eta + \mu)S + \varepsilon V + \omega R \\ &= \phi + \varepsilon V + \omega R - \beta S(\lambda_E E + I) - (\eta + \mu)S \\ &\geq -S(\beta\lambda_E E + \beta I + \eta + \mu) \end{aligned}$$

Letting $\psi(t) = \beta\lambda_E E + \beta I + \eta + \mu$ we have

$$\frac{dS}{dt} \geq -S\psi(t)$$

Just like a separable differential equation, the inequality is separable. We thus use separation of variables technique to solve the inequality. That is,

$$\int \frac{dS}{S} \geq \int -\psi(t)dt$$

We integrate from 0 to t to obtain

$$[lnS]_o^t \geq -\int_0^t \psi(\tau)d\tau$$

$\Longrightarrow$

$$S(t) \geq S(0)exp\left(-\int_0^t \psi(\tau)d\tau\right)$$

Since $S(0) \geq 0$ and an exponential function is always positive we have that $S(t) \geq 0$

In a similar manner, we can prove that V(t),E(t),I(t) and R(t) are all nonnegative.

Theorem 4.1.2 *The solution set of system* (3.1) *is bounded within the invariant region* $\Omega \in \mathbb{R}^5_+$. *Where* $\Omega = \left\{(S, V, E, I, R) : N \leq \frac{\phi}{\mu}\right\}$

Proof

Adding the differential equations in system (3.1), we have

$$N' = S' + V' + E' + I' + R'$$

Where $\prime; = \frac{d}{dt}$. From system (3.1) we have

$$\begin{aligned} N' &= \phi - \mu S - \mu V - \mu E - (d+\mu)I - \mu R \\ &= \phi - \mu(S+V+E+I+R) - dI \\ &= \phi - \mu N - dI \end{aligned}$$

If there is an infection in the population $I(t) > 0$. And since $I \leq N \implies dI \leq dN$. Thus,

$$\begin{aligned} N' &\geq \phi - \mu N - dN = \phi - (\mu + d)N \\ N' &\geq \phi - (\mu + d)N \end{aligned} \tag{4.1}$$

If there is no infection, then I(t)=0. Thus,

$$N' \leq \phi - \mu N \tag{4.2}$$

From (4.1) and (4.2) we obtain

$$\phi - (\mu + d)N \leq N' \leq \phi - \mu N$$

By the variation of constant formulae and taking the limits of integration from 0 to t we have

$$e^{-(\mu+d)t}\left[N(0) + \int_0^t \phi e^{(\mu+d)\tau} d\tau\right] \leq N \leq e^{-\mu t}\left[N(0) + \int_0^t \phi e^{\mu\tau} d\tau\right] \tag{4.3}$$

Upon integration we obtain

$$e^{-(\mu+d)t}\left[N(0) + \frac{\phi}{\mu+d}\left(e^{(\mu+d)t} - 1\right)\right] \leq N \leq e^{-\mu t}\left[N(0) + \frac{\phi}{\mu}\left(e^{\mu t} - 1\right)\right] \tag{4.4}$$

After simplifying we have

$$\frac{\phi}{\mu+d}+e^{-(\mu+d)t}\left(N(0)-\frac{\phi}{\mu+d}\right)\leq N\leq\frac{\phi}{\mu}+e^{-\mu t}\left(N(0)-\frac{\phi}{\mu}\right) \tag{4.5}$$

As t approaches ∞ we have

$$\frac{\phi}{\mu+d} \;\leq\; N\leq\frac{\phi}{\mu} \tag{4.6}$$

Therefore from (4.6) we conclude that the solution sets for system (3.1) are bounded within the invariant region Ω. Thus from positivity and boundedness of solutions we can clearly conclude that the model is valid since population is always positive and the population in each compartment should not exceed the total population N

4.2 The Basic Reproduction Number

Both R_o and R_e help us know how many individuals one infected person can infect which in turn help us know if an epidemic will occur or not. For instance if $R_0>1$ or $R_e>1$ there will be an epidemic, that is, there will be a widespread occurrence of the disease in the population for some period. However if $R_o<1$ or $R_e<1$ then the disease will die out. To compute the basic reproduction number, we use the next generation matrix method which we discussed in section 1.1. With that knowledge on the next generation matrix, we compute the effective reproduction number but first starting with determination of the disease free equilibrium(DFE) since we will need it for determination of F and V as we saw in section 1.1. The DFE is determined by equating each of the equations in (3.1) to 0 and taking E,I,R to be equal to 0 since there is no disease in the population. After these simple steps we only remain with two equations thus

$$\begin{aligned}\phi-(\eta+\mu)S_o+\varepsilon V_o&=0\\ \eta S_o-(b+\mu+\varepsilon)V_o&=0\end{aligned} \tag{4.7}$$

Solving system (4.7) for S_o and V_o we obtain

$$\begin{aligned} S_o &= \frac{\phi(b+\mu+\varepsilon)}{(b+\mu)(\eta+\mu)+\mu\varepsilon} \\ V_o &= \frac{\phi\eta}{(b+\mu)(\eta+\mu)+\mu\varepsilon} \end{aligned}$$

With S_o and V_o as given above the DFE becomes $(S_o, V_o, 0, 0, 0)$. For our model in (3.1) the disease compartments are E and I. Therefore we will only focus on the differential equations;

$$\begin{aligned} \frac{dE}{dt} &= \beta S(\lambda_E E + I) + (1-\rho(t))\beta V[\lambda_E E + I)] - (\gamma + r_E + \mu)E, \\ \frac{dI}{dt} &= \gamma E - (r_I + d + \mu)I \end{aligned} \tag{4.8}$$

From (4.8) we form F_i and V_i which will help us determine F and V. Since we only have two disease compartments, $i = 1, 2$. Therefore we have for F_i

$$\begin{aligned} F_1 &= \beta S(\lambda_E E + I) + (1-\rho)\beta V[\lambda_E E + I)], \\ F_2 &= 0 \end{aligned} \tag{4.9}$$

$F_2 = 0$ in equation (4.9) is due to the fact that there are no new infections in compartment I . For V_i we have

$$\begin{aligned} V_1 &= (\gamma + r_E + \mu)E \\ V_2 &= (r_I + \mu + d)I - \gamma E \end{aligned} \tag{4.10}$$

Letting $\gamma + r_E + \mu = c_1$, $r_I + \mu + d = c_2$ and linearizing systems (4.9) and (4.10) about the DFE $(S_o, V_o, 0, 0, 0)$ we obtain matrices F and V. That is;

$$\text{F}=\begin{pmatrix} \beta\lambda_E[S_o + (1-\rho)V_o] & \beta[S_o + (1-\rho)V_o] \\ 0 & 0 \end{pmatrix}$$

$$\text{V}=\begin{pmatrix} c_1 & 0 \\ -\gamma & c_2 \end{pmatrix}$$

To determine the basic reproduction number we have to find FV^{-1}. First, we determine V^{-1}. We first determine if determinant of V, $|V|$, exists and $|V| \neq 0$ so that V^{-1} exists. We easily compute $|V|$ as follows

$|V| = \begin{vmatrix} c_1 & 0 \\ -\gamma & c_2 \end{vmatrix} = c_1 c_2 \neq 0$. Thus V^{-1} exists and it is given by

$$V^{-1} = \frac{1}{c_1 c_2} \begin{pmatrix} c_2 & 0 \\ \gamma & c_1 \end{pmatrix}$$

With F and V^{-1} we compute the next generation matrix FV^{-1}. That is;

$$\begin{aligned} FV^{-1} &= \frac{1}{c_1 c_2} \begin{pmatrix} \beta\lambda_E[S_o + (1-\rho)V_o] & \beta[S_o + (1-\rho)V_o] \\ 0 & 0 \end{pmatrix} \begin{pmatrix} c_2 & 0 \\ \gamma & c_1 \end{pmatrix} \\ &= \frac{1}{c_1 c_2} \begin{pmatrix} c_2\beta\lambda_E[S_o(1-\rho)V_o] + \gamma\beta[S_o + (1-\rho)V_o] & c_1\beta[S_o + (1-\rho)V_o] \\ 0 & 0 \end{pmatrix} \end{aligned}$$

The effective reproduction number, R_e, is the dominant eigenvalue of the matrix FV^{-1}. Thus we have

$$\begin{aligned} R_e &= \frac{1}{c_1 c_2} \{c_2\beta\lambda_E[S_o(1-\rho)V_o] + \gamma\beta[S_o + (1-\rho)V_o]\} \\ &= \frac{1}{c_1}\beta\lambda_E S_o + \frac{\gamma}{c_1}\frac{1}{c_2}\beta S_o + \frac{1}{c_1}\beta\lambda_E(1-\rho)V_o + \frac{\gamma}{c_1}\frac{1}{c_2}\beta(1-\rho)V_o \quad (4.11) \end{aligned}$$

We can clearly see that the effective reproduction number is as a result of susceptible individuals who are not vaccinated and vaccinated individuals. Thus we can express it as

$$R_e = R_o^{S_o} + R_o^{V_o} \quad (4.12)$$

Where

$$\begin{aligned} R_o^{S_o} &= \frac{1}{c_1}\beta\lambda_E S_o + \frac{\gamma}{c_1}\frac{1}{c_2}\beta S_o \ \ and \\ R_o^{V_o} &= \frac{1}{c_1}\beta\lambda_E(1-\rho)V_o + \frac{\gamma}{c_1}\frac{1}{c_2}\beta(1-\rho)V_o \end{aligned}$$

After substituting c_1 and c_2 as we had let earlier we get

$$R_o^{S_o} = \frac{1}{\gamma + r_E + \mu}\beta\lambda_E S_o + \frac{\gamma}{\gamma + r_E + \mu}\frac{1}{r_I + \mu + d}\beta S_o \tag{4.13}$$

$$R_o^{V_o} = \frac{1}{\gamma + r_E + \mu}\beta\lambda_E(1-\rho)V_o + \frac{\gamma}{\gamma + r_E + \mu}\frac{1}{r_I + \mu + d}\beta(1-\rho)V_o \tag{4.14}$$

With no interventions, from the effective reproduction number we obtain the basic reproduction number as

$$R_o = \frac{1}{\gamma + r_E + \mu}\beta\lambda_E S_o + \frac{\gamma}{\gamma + r_E + \mu}\frac{1}{r_I + \mu + d}\beta S_o \tag{4.15}$$

Where $S_o = \frac{\phi}{\mu} = 1$. What this means is that before the disease invasion, the total population is equal to the susceptible population. Next we express the effective reproduction number in terms of R_o for ease of determination of the minimum critical value to be vaccinated to contain the disease. Note that from now in our analysis we are going to assume that the rates of recovery of exposed individuals and infected individuals are equal, thus we take $r_E = r_I = r$. In addition we take $1 - \rho = \psi$. After substituting $S_o = \frac{\phi}{\mu} = 1$ in the equation for R_o we obtain

$$R_o = \frac{\beta\lambda_E}{(\gamma + r + \mu)} + \frac{\gamma\beta}{(\gamma + r + \mu)(r + \mu + d)} \tag{4.16}$$

We now express R_e in terms of R_o starting with$R_o^{S_o}$

$$R_o^{S_o} = \frac{\beta\lambda_E\phi(b + \mu + \varepsilon)}{(\gamma + r + \mu)\left[(b + \mu)(\eta + \mu) + \mu\varepsilon\right]} + \frac{\gamma\beta\phi(b + \mu + \varepsilon)}{(\gamma + r + \mu)(r + \mu + d)\left[(b + \mu)(\eta + \mu) + \mu\varepsilon\right]}$$

Simplifying we obtain

$$R_o^{S_o} = \frac{(b+\mu+\varepsilon)\phi}{(b+\mu)(\eta+\mu)+\mu\varepsilon}\left[\frac{\beta\lambda_E}{(\gamma+r+\mu)} + \frac{\gamma\beta}{(\gamma+r+\mu)(r+\mu+d)}\right]$$

Which after using R_o simplifies to

$$R_o^{S_o} = \frac{(b+\mu+\varepsilon)\phi}{(b+\mu)(\eta+\mu)+\mu\varepsilon}\,(R_o)$$

In a similar manner we obtain $R_o^{V_o}$ as

$$R_o^{V_o} = \frac{\phi\psi\eta}{(b+\mu)(\eta+\mu)+\mu\varepsilon}\,(R_o)$$

. Thus

$$\begin{aligned} R_e &= \frac{\phi R_o}{(b+\mu)(\eta+\mu)+\mu\varepsilon}\,[b+\mu+\varepsilon+\eta\psi] \\ &= (S_o+\psi V_o)R_o \end{aligned} \tag{4.17}$$

For the minimum value to contain the disease as seen in (Keeling & Rohani, 2011), $R_e = 1$. Therefore

$$\frac{\phi R_o}{(b+\mu)(\eta+\mu)+\mu\varepsilon}\,[b+\mu+\varepsilon+\eta\psi] = 1$$

$\Longrightarrow$

$$\phi R_o(b+\mu+\varepsilon+\eta\psi) = (b+\mu)(\eta+\mu)+\mu\varepsilon \tag{4.18}$$

Our aim is determining the critical value η_c which is easily archived by making η the subject in equation (4.18). After some simple algebra we obtain

$$\eta_c = \frac{\phi(b+\mu+\varepsilon)(R_o-1)}{b+\mu-\phi\psi R_o} \tag{4.19}$$

This is the minimum critical value that need to be vaccinated in order to contain the disease. If there is no booster vaccination we have

$$\eta_{c_1} = \frac{(\mu+\varepsilon)(R_o-1)}{1-\psi R_o} \tag{4.20}$$

For a perfect vaccine and there is no booster vaccination, that is, for $1-\rho=\psi=0$ and b=0 we have

$$\eta_{c_2} = (\mu+\varepsilon)(R_o-1) \tag{4.21}$$

For a perfect vaccine we expect the critical value to be vaccinated to be less compared to when the vaccine is imperfect. Thus, it should be clear that the expression for η_c in equation (4.20) should be greater than the expression for η_c in equation (4.21). In deed this is true. Let's prove this by contradiction. Let's assume that

$$(\mu+\varepsilon)(R_o-1) > \frac{(\mu+\varepsilon)(R_o-1)}{1-\psi R_o}$$

$$\Longrightarrow$$

$$1 > \frac{1}{1-\psi R_o}$$

$$\Longrightarrow$$

$$1-\psi R_o > 1$$

$$\Longrightarrow$$

$$\psi R_0 < 0$$

We know that ψ and R_o are nonnegative thus $\psi R_0 < 0$ is false, hence our assumption is false. Therefore

$$(\mu+\varepsilon)(R_o-1) < \frac{(\mu+\varepsilon)(R_o-1)}{1-\psi R_o}$$

If there is no waning of immunity, there is no need of booster vaccination thus from equation (4.19) we obtain

$$\eta_{c_3} = \frac{\phi(R_o - 1)}{1 - \psi R_o} \tag{4.22}$$

It is also clear that $\eta_{c_1} > \eta_{c_3}$. Having determined the effective reproduction number we carry out sensitivity and elasticity analysis to know how parameters affect the effective reproduction number.

4.2.1 Sensitivity and Elasticity Analysis of R_e

Sensitivity is used to predict which parameters have a great impact on R_e (Van den Driessche, 2017). We define the sensitivity index of R_e with respect to a parameter β as $\frac{\partial R_e}{\partial \beta}$. Elasticity index measures the relative change of R_e with respect to a parameter (Van den Driessche, 2017). The elasticity index of a parameter β is defined as $Y_\beta^{R_e} = \frac{\partial R_e}{\partial \beta} \times \frac{\beta}{R_e}$. If the elasticity index is positive then R_e increases with increase in the parameter while if it is negative R_e decreases with increase in the parameter. The magnitude of the elasticity index determines the relative importance of the parameter. With this knowledge on sensitivity and elasticity we determine elasticity indices for both of our parameters in the model equation (3.1). Remember R_e is given in equation (4.12)

Starting with β we have

$$\begin{aligned} Y_\beta^{R_e} &= \frac{\partial R_e}{\partial \beta} \times \frac{\beta}{R_e} \\ &= \left[\frac{\lambda_E S_o}{\gamma + r + \mu} + \frac{\gamma S_o}{(\gamma + r + \mu)(r + \mu + d)} + \frac{\lambda_E \psi V_o}{\gamma + r + \mu} + \frac{\gamma \psi V_o}{(\gamma + r + \mu)(r + \mu + d)} \right] \frac{\beta}{R_e} \end{aligned}$$

Simplifying by opening the brackets with β we obtain $Y_\beta^{R_e} = \frac{R_e}{R_e} = 1$. Analogous to determining $Y_\beta^{R_e}$ above, we find the sensitivity index for each of the other

parameters thus

$$
\begin{aligned}
Y_{\lambda_E}^{R_e} &= \frac{\lambda_E \beta}{R_e(\gamma + r + \mu)} \left[S_o + \psi V_o\right] \\
Y_{d}^{R_e} &= \frac{-d}{R_e(r + \mu + d)^3} \left[S_o + \psi V_o\right] \\
Y_{r}^{R_e} &= \frac{-r}{R_e(\gamma + r + \mu)} \left[R_e + \frac{\gamma\beta}{(r + \mu + d)^2} \left(S_o + \psi V_o\right)\right] \\
Y_{\mu}^{R_e} &= \frac{-\mu}{R_e(\gamma + r + \mu)} \left[R_e + \frac{\gamma\beta}{(r + \mu + d)^2} \left(S_o + \psi V_o\right)\right] \\
Y_{\gamma}^{R_e} &= \frac{1}{R_e(\gamma + r + \mu)} \left[-\gamma R_e + \frac{\gamma\beta S_o}{r + \mu + d} + \frac{\gamma\beta\psi V_o}{r + \mu + d}\right] \\
Y_{\psi}^{R_e} &= \frac{\psi V_o R_o}{R_e} \\
Y_{\eta}^{R_e} &= \frac{R_o \eta}{((b + \mu)(\eta + \mu) + \mu\varepsilon)R_e} \left(\frac{\mu\psi V_o(b + \mu + \varepsilon)}{\eta} - S_o(b + \mu)\right) \\
Y_{b}^{R_e} &= \frac{-R_o b}{((b + \mu)(\eta + \mu) + \mu\varepsilon)R_e} \left(\frac{\eta\varepsilon S_o}{b + \mu + \varepsilon} + \psi V_o(\eta + \mu)\right) \\
Y_{\varepsilon}^{R_e} &= \frac{R_o \varepsilon}{((b + \mu)(\eta + \mu) + \mu\varepsilon)R_e} \left(\frac{\eta S_o(b + \mu)}{b + \mu + \varepsilon} - \mu\psi V_o\right) \\
Y_{\phi}^{R_e} &= 1
\end{aligned}
$$

Clearly without the exact values of the parameters, we can say that R_e increases with increase in β, ϕ λ_E and ψ since their elasticity indices are all positive. It is also clear that R_e decreases with increase in d, r μ and b since their elasticity indices are negative. For other parameters we will know how exactly they affect R_e after carrying out numerical simulations. We have computed the basic and effective reproduction numbers and used them in different analysis but we haven't described the long term behaviour of our dynamical system in equation (3.1). To achieve this we carry out stability analysis of the system.

4.3 Stability Analysis

To carry out stability analysis of the system we must have the equilibrium points, that is where the system isn't changing with respect to time. There are two types of equilibrium points; the disease free equilibrium (DFE) where there is no dis-

ease in the population and the endemic equilibrium where the disease persist in the population. After determining the equilibrium points, we linearize the system under study to obtain the Jacobian matrix of the system at the equilibrium points , from which we find the eigenvalues to help us determine if the equilibrium point is stable or unstable. If the real part of the eigenvalues of the matrix are all negative then the equilibrium point is said to be stable. If at least one eigenvalue is positive then the equilibrium point is unstable. In case at least one eigenvalue is zero then we can't use linearization to determine the stability of the steady state. For stability we determine local stability and global stability. Local stability of an equilibrium point considers points close to that equilibrium point while global stability considers all points not only those with initial values close to the equilibrium point. As seen earlier we already computed the DFE and so we proceed in determining it's stability first starting with local stability.

4.3.1 Local Stability of the DFE

For the DFE we determine its stability using the theorem below

Theorem 4.3.1 *The DFE is locally asymptotically stable if* $R_e < 1$ *but unstable if* $R_e > 1$

We prove this theorem with respect to our system **Proof**

Recall that the DFE is given by

$$(S_o, V_o, E_o, I_o, R_o) = \left(\frac{\phi(b+\mu+\varepsilon)}{(b+\mu)(\eta+\mu)+\mu}, \frac{\phi\eta}{(b+\mu)(\eta+\mu)+\mu\varepsilon}, 0, 0, 0 \right)$$

We will denote it by $\epsilon_o = (S_o, V_o, E_o, I_o, R_o)$. To determine the stability of the DFE we find the Jacobian matrix of system (3.1) evaluated at the DFE. Let's denote this Jacobian matrix by A. Defining the equations in (3.1) by f_1,f_2,f_3,f_4 and f_5 respectively, A is given by

$$A = \begin{pmatrix} (f_1)_S & (f_1)_V & (f_1)_E & (f_1)_I & (f_1)_R \\ (f_2)_S & (f_2)_V & (f_2)_E & (f_2)_I & (f_2)_R \\ (f_3)_S & (f_3)_V & (f_3)_E & (f_3)_I & (f_3)_R \\ (f_4)_S & (f_4)_V & (f_4)_E & (f_4)_I & (f_4)_R \\ (f_5)_S & (f_5)_V & (f_5)_E & (f_5)_I & (f_5)_R \end{pmatrix}$$

Where subscripts denote partial derivatives with respect to S,V,E,I and R. Thus

$$A = \begin{pmatrix} -\beta(\lambda_E E + I) - k_1 & \varepsilon & -\beta\lambda_E S & -\beta S & \omega \\ \eta & -\psi\beta(\lambda_E E + I) - c & -\psi\beta\lambda_E V & -\psi\beta V & 0 \\ \beta(\lambda_E E + I) & \psi\beta(\lambda_E E + I) & \beta\lambda_E(S + \psi V) - k & \beta(S + \psi V) & 0 \\ 0 & 0 & \gamma & -(r + d + \mu) & 0 \\ 0 & b & r & r & -(\omega + \mu) \end{pmatrix}$$

Where we have let $c = (b + \mu + \varepsilon)$, $k = (\gamma + r + \mu)$, $k_1 = \eta + \mu$

Evaluating A at the DFE and letting $k_2 = \beta\lambda_E S_o$, $k_3 = \beta S_o$, $k_4 = b + \mu + \varepsilon$, $k_5 = \psi\beta\lambda_E V_o$, $k_6 = \psi\beta V_o$, $k_7 = \beta\lambda_E(S + \psi V) - (\gamma + r + \mu)$, $k_8 = \beta(S_o + \psi V_o)$,

$k_9 = r + d + \mu$, $k_{10} = \omega + \mu$ we obtain;

$$A(\epsilon_o) = \begin{pmatrix} -k_1 & \varepsilon & -k_2 & -k_3 & \omega \\ \eta & -k_4 & -k_5 & -k_6 & 0 \\ 0 & 0 & k_7 & k_8 & 0 \\ 0 & 0 & \gamma & -k_9 & 0 \\ 0 & b & r & r & -k_{10} \end{pmatrix}$$

We determine the stability of ϵ_o by finding the eigenvalues of the matrix $A(\epsilon_o)$. That is, we solve

$$\begin{vmatrix} \lambda + k_1 & \varepsilon & -k_2 & -k_3 & \omega \\ \eta & \lambda + k_4 & -k_5 & -k_6 & 0 \\ 0 & 0 & \lambda - k_7 & k_8 & 0 \\ 0 & 0 & \gamma & \lambda + k_9 & 0 \\ 0 & b & r & r & \lambda + k_{10} \end{vmatrix} = 0$$

$$(\lambda + k_1) \begin{vmatrix} \lambda + k_4 & -k_5 & -k_6 & 0 \\ 0 & \lambda - k_7 & k_8 & 0 \\ 0 & \gamma & \lambda + k_9 & 0 \\ b & r & r & \lambda + k_{10} \end{vmatrix} - \eta \begin{vmatrix} \varepsilon & -k_2 & -k_3 & \omega \\ 0 & \lambda - k_7 & k_8 & 0 \\ 0 & \gamma & \lambda + k_9 & 0 \\ b & r & r & \lambda + k_{10} \end{vmatrix} = 0$$

$$(\lambda + k_1)(\lambda + k_{10}) \begin{vmatrix} \lambda + k_4 & -k_5 & -k_6 \\ 0 & \lambda - k_7 & k_8 \\ 0 & \gamma & \lambda + k_9 \end{vmatrix} - \eta(\varepsilon(\lambda + k_{10}) - b\omega) \begin{vmatrix} \lambda - k_7 & k_8 \\ \gamma & \lambda + k_9 \end{vmatrix} = 0$$

$$(\lambda + k_1)(\lambda + k_{10})(\lambda + k_4) \begin{vmatrix} \lambda - k_7 & k_8 \\ \gamma & \lambda + k_9 \end{vmatrix} - \eta(\varepsilon(\lambda + k_{10}) - b\omega) \begin{vmatrix} \lambda - k_7 & k_8 \\ \gamma & \lambda + k_9 \end{vmatrix} = 0$$

$$\lambda - k_7)(\lambda + k_9) - \gamma k_8 \left[(\lambda + k_1)(\lambda + k_{10})(\lambda + k_4) - \eta(\varepsilon(\lambda + k_{10}) - b\omega)\right] = 0$$

$\Longrightarrow$

$$(\lambda - k_7)(\lambda + k_9) - \gamma k_8 = 0 \quad (4.23)$$

$$(\lambda + k_1)(\lambda + k_{10})(\lambda + k_4) - \eta(\varepsilon(\lambda + k_{10}) - b\omega) = 0 \quad (4.24)$$

From equations (4.23) and (4.24) we respectively obtain

$$\lambda^2 + (k_9 - k_7)\lambda - (k_7 k_9 + k_8\gamma) = 0$$

$$\lambda^3 + (k_1 + k_4 + k_{10})\lambda^2 + (k_1 k_4 + k_1 k_{10} + k_4 k_{10} - \eta\varepsilon)\lambda + k_1 k_4 k_{10} + \eta b\omega - \eta\varepsilon k_{10} = 0$$

We check the signs of the roots of the two latter equations using the Routh-Hurwitz stability criterion which we refer in (Bodson, 2019; Murray, 2002). Just to summarize it: If the first column of the Routh-Hurwitz array contains non-zero elements for a given polynomial p(x) then

(i) the number of positive roots of p(x)is equal to the number of sign changes in the first column of the array

(ii) the roots of p(x) are all negative if all the elements in the first row have the same sign

(iii) there can be no root of p(x) on the imaginary axis unless the first column has a zero element

We now make use of the criterion
For

$$\lambda^2 + (k_9 - k_7)\lambda - (k_7 k_9 + k_8\gamma) = 0 \quad (4.25)$$

the coefficients in the polynomial will make the first column of the Routh-Hurrwitz array and we can easily see that they are all non-zero. That is the first column will take the elements 1,$(k_9 - k_7)$ and $-(k_7 k_9 + k_8\gamma)$. All we need to check are the signs of these elements.

Obviously $1 > 0$. We check $(k_9 - k_7)$. Let's assume $(k_9 - k_7) < 0 \implies k_9 < k_7$ Recalling k_7 and k_9 we have

$$r + d + \mu < \beta\lambda_E(S_o + \psi V_o) - (\gamma + r + \mu)$$

Which can be written as

$$\frac{r + d + \mu}{\gamma + r + \mu} < \frac{\beta\lambda_E S_o}{\gamma + r + \mu} + \frac{\beta\lambda_E \psi V_o}{\gamma + r + \mu} - 1$$

Which we can easily express the right hand side(RHS) in terms of R_e by adding

$$\frac{\gamma\beta S_o}{(\gamma + r + \mu)(r + \mu + d)} + \frac{\gamma\beta\psi V_o}{(\gamma + r + \mu)(r + \mu + d)}$$

of which the inequality still holds and we obtain $\frac{r+d+\mu}{\gamma+r+\mu} < R_e - 1$. The left hand side(LHS) is division of positive numbers which the quotient will be positive, thus for the inequality to hold $R_e > 1$ which implies that $k_9 - k_7 < 0$ if $R_e > 1$. This further implies $k_9 - k_7 > 0$ if $R_e < 1$. For $-(k_7k_9 + k_8)$ let's assume $-(k_7k_9 + k_8) > 0$ $\implies k_7k_9 + k_8 < 0$

Which also implies $k_7k_9 < -k_8$. Recalling k_7, k_9 and k_8 we have

$$\left[\beta\lambda_E(S + \psi V) - (\gamma + r + \mu)\right](r + d + \mu) < -\beta(S_o + \psi V_o)$$

$\implies$

$$\beta\lambda_E(S + \psi V) - (\gamma + r + \mu) < -\frac{\beta S_o}{(r + d + \mu)} - \frac{\psi V_o}{(r + d + \mu)}$$

Dividing through by $\gamma + r + \mu$ and rearranging terms we obtain

$$R_e - 1 < 0$$

$\implies -(k_7k_9 + k_8) > 0$ if $R_e < 1$ and $-(k_7k_9 + k_8) < 0$ if $R_e > 1$. We thus see that for $R_e < 1$ the elements are all positive but for $R_e > 1$ there is change in signs.

What this means is that for $R_e < 1$ all the two eigenvalues will be negative while for $R_e > 1$ at least one of the eigenvalues will be positive. We now check for

$$\lambda^3 + (k_1 + k_4 + k_{10})\lambda^2 + (k_1k_4 + k_1k_{10} + k_4k_{10} - \eta\varepsilon)\lambda + k_1k_4k_{10} + \eta b\omega - \eta\varepsilon k_{10} \;=\; 0$$

The Routh-Hurrwitz array of this polynomial is

λ^3	1	$k_1k_4 + k_1k_{10} + k_4k_{10} - \eta\varepsilon$
λ^2	$k_1 + k_4 + k_{10}$	$k_1k_4k_{10} + \eta b\omega - \eta\varepsilon k_{10}$
λ^1	K	
λ^0	$k_1k_4k_{10} + \eta b\omega - \eta\varepsilon k_{10}$	

Where

$$K = \frac{k_1k_4 + k_1k_{10} + k_4k_{10} - \eta\varepsilon - (k_1 + k_4 + k_{10})(\eta b\omega - \eta\varepsilon k_{10})}{k_1 + k_4 + k_{10}}$$

We see that all the elements in the first column are non-zero. All we need to do is check the sign of each element, 1 is trivial. We go to $k_1 + k_4 + k_{10}$ which is easily seen as $k_1 + k_4 + k_{10} > 0$ because k_1, k_2 and k_{10} are all positive. For K let's assume it's also positive that's

$$\frac{k_1k_4 + k_1k_{10} + k_4k_{10} - \eta\varepsilon - (k_1 + k_4 + k_{10})(\eta b\omega - \eta\varepsilon k_{10})}{k_1 + k_4 + k_{10}} > 0$$

Implying that

$$(k_1 + k_4 + k_{10})(k_1k_4 + k_1k_{10} + k_4k_{10} - \eta\varepsilon) - (\eta b\omega - \eta\varepsilon k_{10}) > 0$$

We observe that $\eta\varepsilon$ term is contained in (k_1k_2) with a positive sign hence they will cancel out. Also $\eta b\omega$ term is contained in $(k_1k_4k_{10})$ with a positive sign and they will cancel out. Thus we remain with positive constants which implies our

assumption is correct. That is

$$\frac{k_1k_4 + k_1k_{10} + k_4k_{10} - \eta\varepsilon - (k_1 + k_4 + k_{10})(\eta b\omega - \eta\varepsilon k_{10})}{k_1 + k_4 + k_{10}} > 0$$

$\implies K > 0$. Finally we check $k_1k_4k_{10} + \eta b\omega - \eta\varepsilon k_{10}$. Since $\eta\varepsilon k_{10}$ is contained in $(k_1k_4k_{10})$ as positive they will cancel out thus obtaining $k_1k_4k_{10} + \eta b\omega - \eta\varepsilon k_{10} > 0$. All these results imply that the first column of the Routh-Hurrwitz array contains elements with same sign. Thus all the roots of the polynomial are negative. We see that for $R_e < 1$ all the eigenvalues are negative, thus the DFE is locally asymptotically stable.However, for $R_e > 1$ at least one eigenvalue is positive hence the DFE is unstable to small perturbations.

4.3.2 Global Stability of DFE

We now turn our attention to global stability of the DFE. First we outline some information that will help us determine the global stability of the DFE. Let's for a moment recall the Next Generation Matrix method we used in determining the effective reproduction number. That is we assume that there are n disease compartments and m non-disease compartments. We also assume that there are x and y subpopulations in each of the compartments n and m respectively. That is, $x \in \mathbb{R}^n$ and $y \in \mathbb{R}^m$. We then denote the rate at which new infections increase the i^{th} infected compartment by F_i while V_i denote the rate of decrease in the i^{th} compartment by disease progression, death and recovery. The general compartmental model thus take the form;

$$\begin{aligned} \dot{x_i} &= F_i(x, y) - V_i(x, y), i = 1, 2, ..., n \\ \dot{y_j} &= g_j(x, y),\ j = 1, 2, ..., m \end{aligned} \tag{4.26}$$

Next we put some conditions on F_i and V_i;

$F_i(x, y) \geq 0$ for all $x \geq 0$, $y \geq 0$ and $i = 1, 2, ..., n$. Since F represent new infections and therefore it is nonnegative

$V_i(x, y) \leq 0$ provided $x_i = 0$ for $i = 1, 2, ..., n$. V_i is the net outflow from compartment i hence it must be negative whenever the compartment is empty
$\sum_{i=1}^{n} V_i(x, y) \geq 0$ for all $x \geq 0$, $y \geq 0$. This represent the total outflow from all infected compartments. Also recall that matrices F and V can be determined as

$$F = \frac{\partial F_i(0, y_o)}{\partial x_i} \quad V = \frac{\partial V_i(0, y_o)}{\partial x_i}$$

Following (Brauer et al., 2012) system (4.26) can be written as

$$\begin{aligned} \dot{x_i} &= (F - V)x - f(x, y) i = 1, 2, ..., n \\ \dot{y_j} &= g_j(x, y), \ j = 1, 2, ..., m \end{aligned} \tag{4.27}$$

Where $f(x, y) = (F - V)x - F_i + V_i$. Taking $F - V = -T$ equation (4.27) becomes

$$\begin{aligned} \dot{x_i} &= -Tx - f(x, y) \\ \dot{y_j} &= g_j(x, y) \end{aligned} \tag{4.28}$$

We now state the theorem that will help us determine the global stability of the DFE of the general system in (4.28) and thus our system.

Theorem 4.3.2 (Castillo-Chavez, Feng and Huang) *If -T is a nonsingular M-matrix, $f(x,y) \geq 0$, $F \geq 0$ and if $R_o < 1$ then the DFE is globally asymptotically stable.*

The proof of this theorem can be found in (Brauer et al., 2012). All we need to check is if the conditions in Theorem 4.3.2 above are satisfied so that we make use of the theorem to determine the global stability of the DFE of our system. Recall that for our system in (3.1)

$$F = \begin{pmatrix} \beta\lambda_E(S_o + \psi V_o) & \beta(S_o + \psi V_o) \\ 0 & 0 \end{pmatrix}$$

$$\text{V} = \begin{pmatrix} c_1 & 0 \\ -\gamma & c_2 \end{pmatrix}$$

Where $c_1 = \gamma + \mu + r$, $c_2 = r + \mu + d$

$$-T = -(F - V) = -\begin{pmatrix} \beta\lambda_E(S_o + \psi V_o) - c_1 & \beta(S_o + \psi V_o) \\ \gamma & -c_2 \end{pmatrix}$$

$$\implies -T = \begin{pmatrix} c_1 - \beta\lambda_E(S_o + \psi V_o) & -\beta(S_o + \psi V_o) \\ -\gamma & c_2 \end{pmatrix}$$

Since the off-diagonal elements of -T are negative it implies -T is a nonsingular M-matrix. It is also clear that $F \geq 0$ and all that remains to be checked is if $f(x,y) \geq 0$. Recall that $f(x,y) = (F - V)x - F_i + V_i$. Since x represents the disease compartments, $x = \begin{pmatrix} E \\ I \end{pmatrix}$ Thus

$$\begin{aligned} (F - V)x &= \begin{pmatrix} \beta\lambda_E(S_o + \psi V_o) - c_1 & \beta(S_o + \psi V_o) \\ \gamma & -c_2 \end{pmatrix} \begin{pmatrix} E \\ I \end{pmatrix} \\ &= \begin{pmatrix} E\beta\lambda_E(S_o + \psi V_o) - c_1 E + \beta I(S_o + \psi V_o) & \gamma E - c_2 I \end{pmatrix} \end{aligned} \quad (4.29)$$

Also from the definitions of F_i and V_i we have

$$-(F_i - V_i) = -\begin{pmatrix} \beta S(\lambda_E E + I) + \psi\beta V(\lambda_E E + I) - c_1 E & -c_2 I + \gamma I \end{pmatrix} \quad (4.30)$$

From equations (4.29) and (4.30) we have

$$\begin{aligned} f(x,y) &= \begin{pmatrix} \beta\lambda_E E(S_o+\psi V_o)+\beta I(S_o+\psi V_o)-\beta S(\lambda_E E+I)-\psi\beta V(\lambda_E E+I) & 0 \end{pmatrix} \\ &= \begin{pmatrix} (\beta I+\beta\lambda_E E)(S_o-S)+(\beta\psi\lambda_E E+\beta\psi I)(V_o-V) & 0 \end{pmatrix} \end{aligned}$$

Clearly $f(x,y) \geq 0$ since $S_o \geq S$ and $V_o \geq V$. Since all the conditions of Theorem 4.3.2 are satisfied, it implies that the DFE of our system is globally asymptotically stable. This implies that even if the disease is present in the population and $R_e < 1$ then the disease will be wiped out of the population since all the solutions will approach the DFE.

4.3.3 Stability of the Endemic Equilibrium

The endemic equilibrium(EE) means that the disease persists in the population. Thus it makes sense to know if the disease will stay in the population forever or it dies out. We start by determining the EE and then it's stability. We will assume that after vaccination and booster vaccination program are imposed, individuals stay for a long period of time in the recovery before being susceptible to the disease again thus we take $\omega << 1$ for the determination and further stability analysis of the EE. In fact from the expression of R_e, there is no dependence of R_e on the parameter ω. Therefore recalling system (3.1) and noting that R does not appear in the first four equations, we equate each of the differential equation to 0 and thus obtain a reduced system

$$\begin{aligned} 0 &= \phi-\beta S^*(\lambda_E E^*+I^*)-(\eta+\mu)S^*+\varepsilon V^* \\ 0 &= \eta S^*-\psi\beta V^*(\lambda_E E^*+I^*)-(b+\mu+\varepsilon)V^* \\ 0 &= \beta S^*(\lambda_E E^*+I^*)+\psi\beta V^*(\lambda_E E^*+I^*)-(\gamma+r+\mu)E^* \\ 0 &= \gamma E^*-(r+d+\mu)I^* \end{aligned} \tag{4.31}$$

Where (S^*, V^*, E^*, I^*) represent the endemic equilibrium values

From the last equation in (4.31) we obtain

$$I^* = \left(\frac{\gamma}{r+d+\mu}\right) E^* = k_1 E^* \tag{4.32}$$

Using (4.32) in the other three equations of (4.31) and letting $k_2 = \frac{\lambda_E(r+d+\mu)+\gamma}{r+d+\mu}$ we obtain

$$\begin{aligned} 0 &= \phi - \beta k_2 S^* E^* - (\eta+\mu)S^* + \varepsilon V^* \\ 0 &= \eta S^* - \psi\beta k_2 V^* E^* - (b+\mu+\varepsilon)V^* \\ 0 &= \beta k_2 S^* E^* + \psi\beta k_2 V^* E^* - (\gamma+r+\mu)E^* \end{aligned} \tag{4.33}$$

The last equation of (4.33) gives

$$\left(\beta k_2 S^* + \psi\beta k_2 V^* - (\gamma+r+\mu)\right) E^* = 0$$

$E^* = 0$ will give us the DFE, we thus take

$$\beta k_2 S^* + \psi\beta k_2 V^* - (\gamma+r+\mu) = 0$$

$\implies S^* = k_3 - \psi V$ where

$$k_3 = \frac{\gamma+r+\mu}{\beta k_2} = \frac{(\gamma+r+\mu)(r+d+\mu)}{\beta\lambda_E(r+d+\mu)+\beta\gamma}$$

Adding the the last two equations of (4.33) to the first equation and using $S^* = k_3 - \psi V$ we obtain

$$\phi - (b+\mu)V^* - (\gamma+r+\mu)E^* - \mu(k_3 - \psi V^*) = 0 \tag{4.34}$$

From equation (4.34) we get

$$\begin{aligned} V^* &= \frac{\phi(1-k_3)}{\mu(1-\psi)+b} - \left(\frac{\gamma+r+\mu}{\mu(1-\psi)+b}\right) E^* \\ V^* &= k_4 - k_5 E^* \end{aligned} \tag{4.35}$$

Thus

$$S^* = k_3 - \psi k_4 + \psi k_5 E^*$$

That is

$$S^* = k_6 + \psi k_5 E^* \tag{4.36}$$

We now use equations (4.35) and (4.36) into the second equation of (4.33) to get

$$\psi\beta k_2 k_5 E^{*2} + (\eta\psi k_5 + (b+\mu+\varepsilon)k_5 - \psi\beta k_2 k_4)E^* - ((b+\mu+\varepsilon)k_4 - \eta k_6) = 0$$

Which can be written as

$$a_1 E^{*2} + a_2 E^* - a_3 = 0 \tag{4.37}$$

Where $a_1 = \psi\beta k_2 k_5$, $a_2 = (\eta\psi k_5 + (b+\mu+\varepsilon)k_5 - \psi\beta k_2 k_4)$ and $a_3 = ((b+\mu+\varepsilon)k_4 - \eta k_6)$
We note that $a_1 = \psi\beta k_2 k_5 > 0$ since $k_2 = \frac{\lambda_E(r+d+\mu)+\gamma}{r+d+\mu} > 0$ and
$k_5 = \left(\frac{\gamma+r+\mu}{\mu(1-\psi)+b}\right) > 0$.
Also using $R_o = \frac{\beta\lambda_E}{(\gamma+r+\mu)} + \frac{\gamma\beta}{(\gamma+r+\mu)(r+\mu+d)}$ we have $k_3 = \frac{(\gamma+r+\mu)(r+d+\mu)}{\beta\lambda_E(r+d+\mu)+\beta\gamma} = \frac{1}{R_o}$. We thus obtain

$$((b+\mu+\varepsilon)k_4 - \eta k_6) = \frac{1}{R_o}\left[\frac{\phi(\eta\psi+b+\mu+\varepsilon)}{\mu(1-\psi)+b}(R_o-1) - \eta\right] > 0$$

if $R_o > 1$. Thus $a_3 > 0$ if $R_o > 1$. With the fact that $a_1 > 0$ and $a_3 > 0$ for $R_o > 1$, equation (4.37) will have two distinct roots, one positive and the other

negative, that is

$$E_{\pm}^{*} = \frac{-a_2 \pm \sqrt{a_2^2 + 4a_1a_3}}{2a_1} \tag{4.38}$$

For the endemic equilibrium to be biologically relevant we take

$$E_{+}^{*} = \frac{-a_2 + \sqrt{a_2^2 + 4a_1a_3}}{2a_1} \tag{4.39}$$

We use equation (4.39) in equations (4.31), (4.35) and (4.36) to obtain the expressions I^*, V^* and S^* respectively. That is

$$\begin{aligned} I^* &= k_1 E_{+}^{*} \\ V^* &= k_4 - k_5 E_{+}^{*} \\ S^* &= k_6 + \psi k_5 E_{+}^{*} \end{aligned} \tag{4.40}$$

Equation (4.39) and system (4.40) give us the endemic equilibrium
We are done with finding the endemic equilibrium and thus we proceed to determine it's stability. We are going to make use of Lyapunov function to help us determine the stability. Thus it will make sense if we proceed as follows;

Consider a system of differential equations given by

$$\dot{x_i} = f_i(x_1, x_2, ..., x_n) \tag{4.41}$$

Where $\dot{} = \frac{d}{dt}$ and $x_i = x_i(t)$. Let x_i^* be an equilibrium point of equation (4.41). A function L is said to be a Lyponov function of equation (4.41) if it satisfies the following

(i) $L(x_i^*) = 0$

(ii) $L(x_i) > 0$ for $x_i \neq x_i^*$

(iii) $\frac{dL}{dt} \leq 0$ over the solutions of equation (4.41)

As in (Bate, 2015; Joseph & Solomon, 1961) we state the following principle which together with a suitable Lypunov function help in determination of the stability of the EE.

Lasalle Invariance Principle

Assume that L(x) is a Lyapunov function of equation (4.41) on a subset $G \subset R^n$, $n \geq 1$. Define a set $S = \{x \in G : \dot{L}(x) = 0\}$. Let M be the largest invariant set contained in S. Then for $t \geq 0$, every bounded trajectory of equation (4.41) that remains in G approaches the set M as $t \to \infty$

We need to make use of this principle to show the stability of the endemic equilibrium. Following (Shuai & van den Driessche, 2013) we let

$$\begin{aligned} L_1 &= S - S^* - S^* ln\frac{S}{S^*} \\ L_2 &= V - V^* - V^* ln\frac{V}{V^*} \\ L_3 &= E - E^* - E^* ln\frac{E}{E^*} \\ L_4 &= I - I^* - I^* ln\frac{I}{I^*} \end{aligned}$$

To use the principle above, we have to show that L given by $L = L_1 + L_2 + L_3 + L_4$ is a Lyapunov function for the system in equation (3.1)

Let $P^* = (S^*, V^*, E^*, I^*)$ denote the endemic equilibrium. Clearly $L(P^*) = 0$. To show the remaining conditions for a Lypunov function we use the inequality $1 - x + lnx \leq 0$ for $x > 0$ and the equality only holds if $x = 1$.

We can write L_1 as

$$\begin{aligned} L_1 &= S^* \left(\frac{S}{S^*} - 1 - ln\frac{S}{S^*} \right) \\ &= -S^* \left(1 - \frac{S}{S^*} + ln\frac{S}{S^*} \right) > 0 \end{aligned}$$

$$since \;\; 1 - \frac{S}{S^*} + ln\frac{S}{S^*} < 0$$

Similarly $L_2 > 0$, $L_3 > 0$, $L_4 > 0$ for $P^* \neq (S, V, E, I)$. Thus $L > 0$ for $P^* \neq (S, V, E, I)$. We now determine the derivative of the Lyapunov function over

the solutions of equation (3.1).

Differentiating each of $L_i, \quad i = 1, 2, 3, 4$ and using equation (3.1) we have

$$\begin{aligned}
\dot{L}_1 &= \left(1 - \frac{S^*}{S}\right)\Big[\phi - \beta S(\lambda_E E + I) - (\eta + \mu)S + \varepsilon V + \omega R\Big] \\
\dot{L}_2 &= \left(1 - \frac{V^*}{V}\right)\Big[\eta S - \psi\beta V(\lambda_E E + I) - (b + \mu + \varepsilon)V\Big] \\
\dot{L}_3 &= \left(1 - \frac{E^*}{E}\right)\Big[\beta S\lambda_E E + \psi\beta V(\lambda_E E) - (r + \mu)E\Big] \\
\dot{L}_4 &= \left(1 - \frac{I^*}{I}\right)\Big[\beta S I + \beta V I - (r + d + \mu)I\Big]
\end{aligned}$$

Using $\phi = \beta S^*(\lambda_E E^* + I^*) + (\eta + \mu)S^* - \varepsilon V^*$, $\dot{L}_1$ becomes

$$\begin{aligned}
\dot{L}_1 &= \left(1 - \frac{S^*}{S}\right)\Big[\beta S^*(\lambda_E E^* + I^*) + (\eta + \mu)S^* - \varepsilon V^* - \beta S(\lambda_E E + I) - (\eta + \mu)S + \varepsilon V\Big] \\
&= -\mu\frac{(S - S^*)^2}{S} + \left(1 - \frac{S^*}{S}\right)\Big[\beta S^*(\lambda_E E^* + I^*) - \varepsilon V^* + \eta S^* - \eta S - \beta S(\lambda_E E + I) + \varepsilon V\Big] \\
&\leq \beta\lambda_E S^* E^*\left(1 - \frac{S^*}{S}\right)\left(1 - \frac{SE}{S^*E^*}\right) + \beta S^* I^*\left(1 - \frac{S^*}{S}\right)\left(1 - \frac{SI}{S^*I^*}\right) \\
&+ \varepsilon V^*\left(1 - \frac{S^*}{S}\right)\left(\frac{V}{V^*} - 1\right) + \eta S^*\left(1 - \frac{S^*}{S}\right)\left(1 - \frac{S}{S^*}\right) \\
&\leq \beta\lambda_E S^* E^*\left(1 - \frac{SE}{S^*E^*} - \frac{S^*}{S} + \frac{E}{E^*}\right) + \beta S^* I^*\left(1 - \frac{SI}{S^*I^*} - \frac{S^*}{S} + \frac{I}{I^*}\right) \\
&+ \varepsilon V^*\left(\frac{V}{V^*} - 1 - \frac{VS^*}{SV^*} + \frac{S^*}{S}\right) + \eta S^*\left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right)
\end{aligned}$$

Let's assume that individuals who are vaccinated are equal to the individuals whose immunity wanes and become susceptible again. Then expressing each of the terms in brackets in terms of the inequality $1 - x + lnx \leq 0$ for any $x > 0$ then using the inequality we obtain

$$\begin{aligned}
\dot{L}_1 &\leq \beta\lambda_E S^* E^*\left(\frac{E}{E^*} - ln\frac{E}{E^*} + ln\frac{SE}{S^*E^*} - \frac{SE}{S^*E^*}\right) + \beta S^* I^*\left(\frac{I}{I^*} - ln\frac{I}{I^*} + ln\frac{SI}{S^*I^*} - \frac{SI}{S^*I^*}\right) \\
&+ \eta S^*\left(ln\frac{S}{S^*} - \frac{S}{S^*} + \frac{V}{V^*} - ln\frac{V}{V^*}\right)
\end{aligned}$$

Similarly using the inequality $1 - x + lnx \leq 0$ $\dot{L}_2$, becomes

$$\begin{aligned}
\dot{L}_2 &\leq \psi\beta\lambda_E V^* E^* \left(\frac{E}{E^*} - ln\frac{E}{E^*} + ln\frac{VE}{V^*E^*} - \frac{VE}{V^*E^*}\right) \\
&+ \psi\beta V^* I^* \left(\frac{I}{I^*} - ln\frac{I}{I^*} + ln\frac{VI}{V^*I^*} - \frac{VI}{V^*I^*}\right) \\
&+ \eta S^* \left(\frac{S}{S^*} - ln\frac{S}{S^*} + \frac{V}{V^*} - ln\frac{V}{V^*}\right)
\end{aligned}$$

For $\dot{L}_3$ we have

$$\begin{aligned}
\dot{L}_3 &\leq \beta\lambda_E S^* E^* \left(ln\frac{E}{E^*} - \frac{E}{E^*} + \frac{SE}{S^*E^*} - ln\frac{SE}{S^*E^*}\right) \\
&+ \psi\beta\lambda_E V^* E^* \left(ln\frac{E}{E^*} - \frac{E}{E^*} + \frac{VE}{V^*E^*} - ln\frac{VE}{V^*E^*}\right)
\end{aligned}$$

Finally $\dot{L}_4$ satisfies

$$\begin{aligned}
\dot{L}_4 &\leq \beta S^* I^* \left(ln\frac{I}{I^*} - \frac{I}{I^*} + \frac{SI}{S^*I^*} + ln\frac{SI}{S^*I^*}\right) \\
&+ \psi\beta V^* I^* \left(ln\frac{I}{I^*} - \frac{I}{I^*} + \frac{VI}{V^*I^*} - ln\frac{VI}{V^*I^*}\right)
\end{aligned}$$

Recalling the term $-\mu\frac{(S-S^*)^2}{S}$ in $\dot{L}_1$ and using the inequalities we have obtained for $\dot{L}_1, \dot{L}_2, \dot{L}_3$ *and* $\dot{L}_4$ we have

$$\frac{dL}{dt} \leq -\mu\frac{(S-S^*)^2}{S} \leq 0 \tag{4.42}$$

Clearly from equation (4.42) we see that the equality only holds at the EE. Therefore by the Lasalle's Invariance Principle above, the EE is the largest invariance subset of the system in equation (3.1). Thus all trajectories approach the EE, hence it is globally asymptotically stable. Biologically this means that as long as $R_e > 1$ then it is difficult to wipe the disease completely out of the population since all solutions will approach the endemic equilibrium which describes the presence of the disease in the population

4.4 Numerical Simulations

In this section we carry out numerical simulation of the model in equation (3.1). The simulation is done specifically to achieve the two specific objectives of our study. We describe parameter values that will help us carry out numerical simulations.

We estimate some parameters from COVID-19 data available and some from literature. The table below shows the values of the parameters used in simulation

Table 4.1: Parameter Values

Parameter	Value	Source
ϕ	0.00005	(Niohuru, 2023)
β	0.5	(Wangari et al., 2021)
λ_E	0.314	(Wangari et al., 2021)
η	0.0005	Assumed
μ	0.00005	("World Population Review", 2023)
ω	0.0033	(Edridge et al., n.d.)
ε	0.0042	(Hall et al., 2022)
ψ	0.2	Assumed
b	0.0001	Assumed
γ	0.1667	(Lauer et al., 2020)
r	0.1	(Baloch et al., 2020)
d	0.0016	(Wangari et al., 2021)

With the parameters above R_o and R_e are 3.6625 and 2.7860 respectively. Also we can determine the numeric value for η_c, that is

$$\eta_c = \frac{\phi(b+\mu+\varepsilon)(R_o-1)}{b+\mu-\phi\psi R_o} = 0.0051$$

Without booster vaccine, that is for b=0, we have

$$\eta_c = 0.0423$$

We can clearly see that when booster vaccination is included, the critical value to be vaccinated to achieve elimination of the disease is less compared to when there is no booster vaccination. We can also compute the values for the DFE before

and after vaccination is incorporated.

$$\begin{aligned} S_o &= \frac{\phi(b+\mu+\varepsilon)}{(b+\mu)(\eta+\mu)+\mu\varepsilon} \\ V_o &= \frac{\phi\eta}{(b+\mu)(\eta+\mu)+\mu\varepsilon} \end{aligned}$$

For sensitivity and elasticity analysis of R_e, using the values of R_o,R_e and recalling the expressions for elasticity indices for each parameter we obtain the elasticity index values as shown in the table below.

Table 4.2: Numerical values for elasticity indices

Parameter	Elasticity index
ϕ	1
β	1
λ_E	0.1667
η	-0.2730
μ	-6.0028×10^{-4}
ε	0.2566
ψ	0.0611
b	-0.2098
γ	0.2144
r	-1.2006
d	-0.4159

The Figures below show how R_e varies with our parameters of interest, that is, the rate of vaccination, the rate of administering booster vaccine and the waning rate of immunity after vaccination.

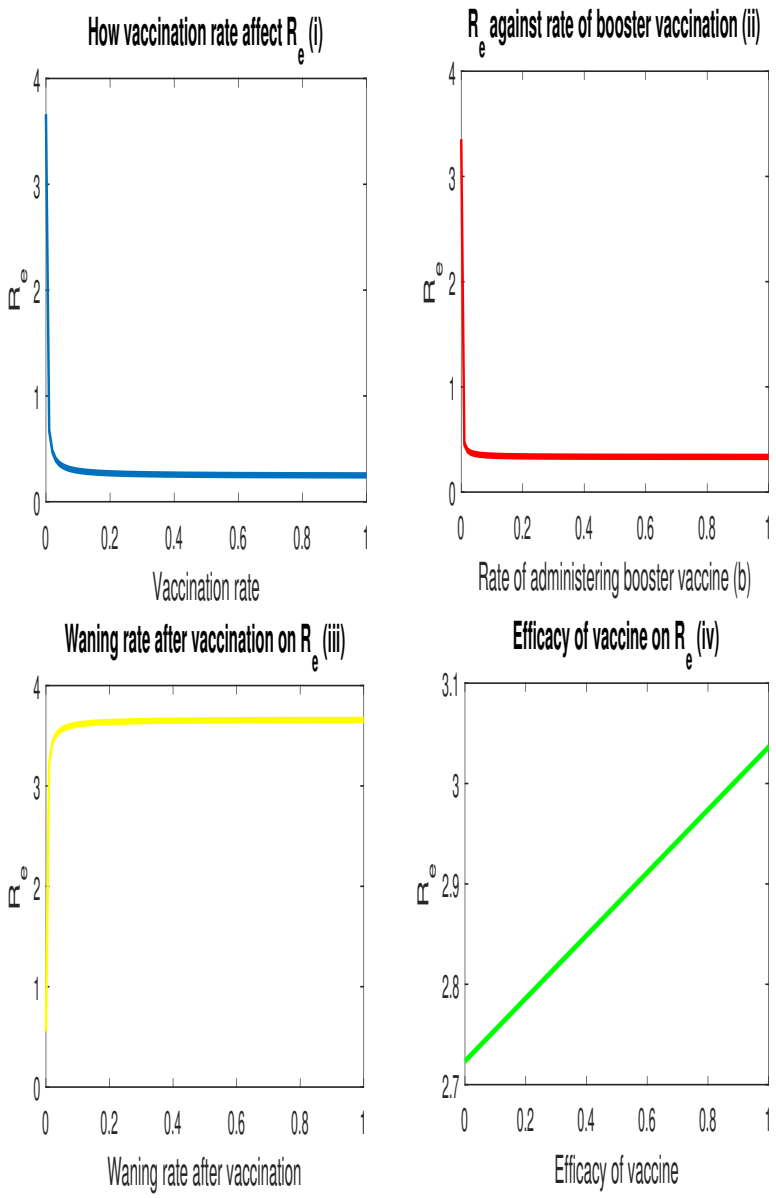

Figure 4.1: How the effective reproduction number, R_e, varies with different parameters

We can clearly see that from Figure 4.1 (i) and (ii), R_e decreases as η and b increases. For the vaccination rate we observe that for $\eta \geq 0.0051$, $R_e \leq 1$. Thus there will be no epidemic. Similarly for booster vaccination we can see that when $b \geq 0.0101$, $R_e \leq 1$ and therefore no epidemic. Thus increasing the rates η and b higher than 0.0051 and 0.0101 respectively will reduce R_e and in turn prevent an epidemic to occur. On the waning rate after vaccination, Figure 4.1 (iii), we observe that R_e increases as the waning rate (ε) increases. Therefore, if the immunity after vaccination wanes at a higher rate the disease will remain in the population. Lastly, for Figure 4.1 (iv), when the vaccine is perfect($\psi = 0$)

$R_e = 2.725 > 1$. Thus there will be an epidemic even if the vaccine is perfect. This is due to the waning rate of immunity after vaccination which makes individuals exposed to the infection. We can also see that as the efficacy of the vaccine reduces ($\psi > 0$), R_e increases.

We now turn our attention to the dynamics of the disease described by the solution curves of equation (3.10). Since our model includes a vaccine compartment we take initial data as from the day vaccines were first administered. That is as from 5^{th} March, 2021. As of 2021, the total population of Kenya was about 53,005,614 ("World Population Review", 2023). According to the data given by WHO, we averagely take the initial infectives to be 1000 individuals. As our compartments represent fractions the initial data will thus be;

$S(0) = 0.99998113, V(0) = 0, E(0) = 0, I(0) = 0.00001887, R(0) = 0.$

Using the initial data and the parameter values in Table 4.1 we obtain the following simulations

Figures 4.2 and 4.3 describe the dynamics of COVID-19 when there is no vaccine but 4.3 only describes how the disease compartments evolve with time. Similarly, Figures 4.4 and 4.5 describe the dynamics of the disease but only when the vaccine compartment is included.

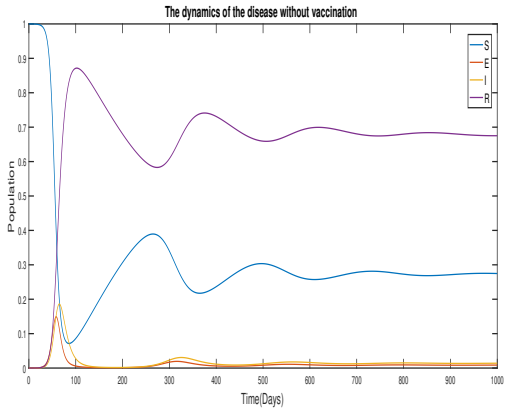

Figure 4.2: Before vaccination

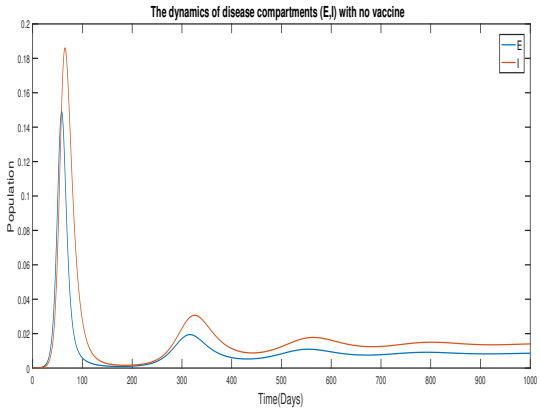

Figure 4.3: E and I

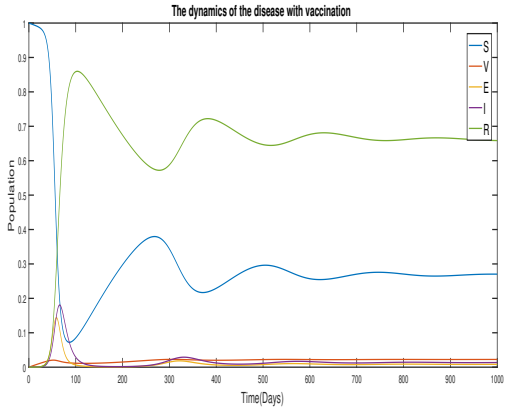

Figure 4.4: After Vaccination

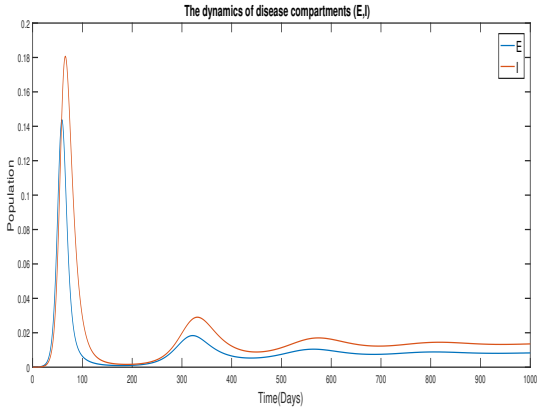

Figure 4.5: E and I

We can see that from Figures 4.2 and 4.3 the disease spreads into the the population with the infective individuals increasing up to a peak of 0.1857 after about 65 days and the spread reduces to almost being depleted and then start increasing then decreasing to a level which the disease stays in the population. The increase up to the peak is due to the rapid spread of the disease caused by a high transmission rate($\beta = 0.5$) and $R_e > 1$ which causes a single infected individual to produce more than one secondary infections. The reduction is due to most individuals gaining protective immunity from the infection. The immunity is temporary and thus the increase and the disease staying in the population is mostly caused by the re-infection of individuals, the rate of administering booster vaccination is low

and the rate at which individuals lose vaccine induced immunity is high (about 6 months), which contributes much on individuals becoming susceptible again even after vaccination.

From Figure 4.5, we see that the peak is reduced to 0.18 after about 65 days. The curves look similar to the one in Figure 4.3 because of low vaccination coverage($\eta = 0.005$). Moreover, the rate of administering booster vaccination is low and the rate at which individuals lose vaccine induced immunity is high (about 6 months), which contributes much on individuals becoming susceptible again even after vaccination. Thus there is need to increase vaccination coverage and decrease the waning rate of immunity after vaccination. In fact if the rate of vaccination is at the critical value $\eta_c = 0.0051$ we obtain

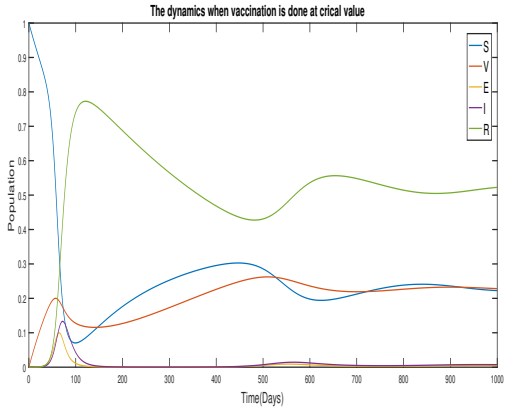

Figure 4.6: Vaccination at η_c

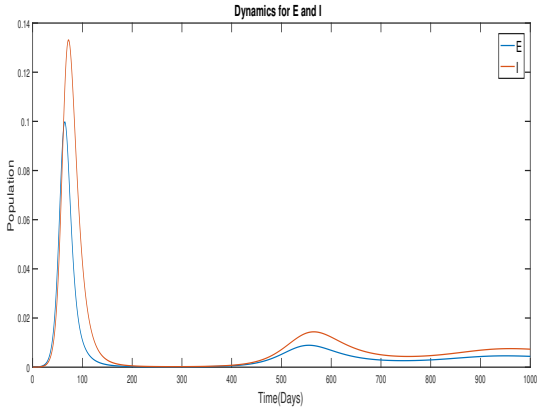

Figure 4.7: E and I

We observe that the number of individuals who stay in the population as vaccinated is much higher in Figure 4.6 than in Figure 4.4. Also comparing Figure 4.7 and Figure 4.4 we clearly see that the peak of infection is low (0.13) and delayed for about 15 days in Figure 4.7. In addition the number of infectives who stay in the population is low in Figure 4.7 since a lot of people are vaccinated and gain protective immunity for some time before the immunity start waning. We can see that even if the rate of vaccination is done at critical value $\eta_c = 0.0051$ the disease will not be completely eradicated from the population but the severity of

the disease is reduced since we will have a small number of infected individuals staying in the population.

If there is no re-infection of individuals then the solution curves for E and I are as shown below.

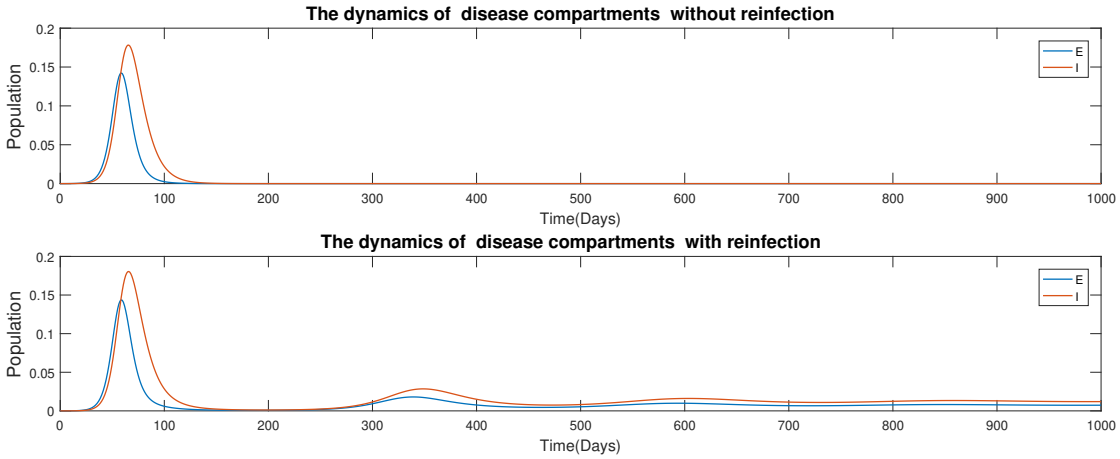

Figure 4.8: Evolution for E and I with no re-infection

We can easily observe that the disease will be wiped out completely as long as there is no re-infection. As re-infection is evident for COVID-19, it really plays a big role in the disease staying in the population even if vaccination program is in place just as seen in the bottom figure of Figure 4.8.

For waning of immunity after vaccination we have

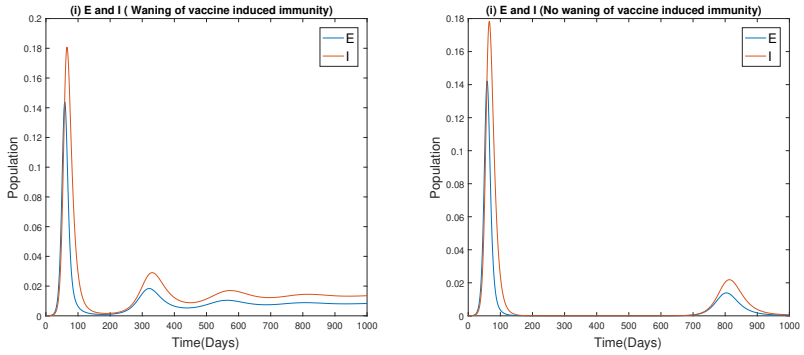

Figure 4.9: The Effect of waning immunity after vaccination

We easily observe in Figure 4.9 (i) that the disease is kept low in the population for some period of time in case the immunity induced by vaccine does not wane. But this is not enough to eradicate the disease completely out of the population. For booster vaccination we have the following figure

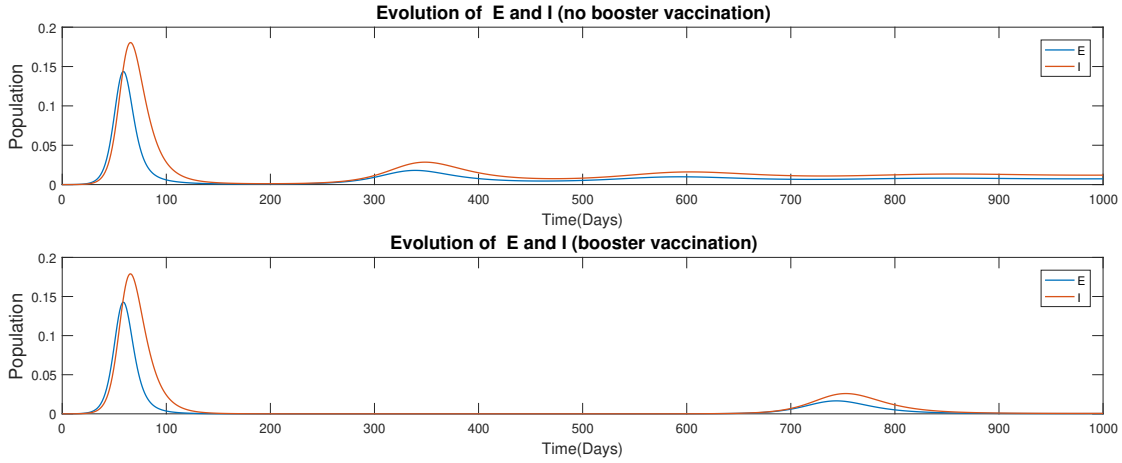

Figure 4.10: Evolution for E and I with and without booster vaccination

We observe that when booster vaccination is included, the infection is kept low in the population for some period of time before it starts increasing to a new peak. This shows that booster vaccination increases the protection period against the disease

CHAPTER FIVE

DISCUSSION, CONCLUSION AND RECOMMENDATION

5.1 Discussion

We saw that using the parameters, $R_o = 3.6625$(before vaccination) and $R_e = 2.7860$(after vaccination). $R_o > 1$ which means the endemic equilibrium is stable. This is evident in Figure 4.2. Also even after vaccination $R_e > 1$, which means that the disease stay in the population. This is evident in figure 4.4. Showing that the endemic equilibrium is stable. In both cases all the compartments are positive and stabilizes in the population. We recall that for DFE,

$$S_o = \frac{\phi(b+\mu+\varepsilon)}{(b+\mu)(\eta+\mu)+\mu\varepsilon}, \tag{5.1}$$

With no vaccine we will have

$$S_o = \frac{\phi}{\mu} \tag{5.2}$$

Comparing the two expressions from equations (5.1) and (5.2) we have

$$\frac{\phi}{\mu} - \frac{\phi(b+\mu+\varepsilon)}{(b+\mu)(\eta+\mu)+\mu\varepsilon} = \frac{\phi\eta(b+\mu)}{\mu(b+\mu)(\eta+\mu)+\mu\varepsilon)} > 0 \tag{5.3}$$

The inequality in (5.3) shows that the susceptible individuals are reduced after vaccination is incorporated. From numerical simulation we have that before vaccination $S_0 = 1$ and after vaccination $S_o = 0.3023$. Clearly the value after vaccination is less compared to the value before vaccination which is in line with analytic results. From figure 4.10, as expected from the literature, when booster vaccination is included the period of protection against the disease is longer as compared to when there is no booster vaccination.

5.2 Conclusion

The infection still persists even when vaccination program is in place. This is due to low vaccination coverage and temporary immunity gained from the vaccine. Higher vaccination coverage tends to eliminate the disease from the population but re-infection as well as waning rate of immunity after vaccination and infection play a major role for the infection to start increasing again. Booster vaccination reduces the critical value needed to be vaccinated in order to contain the disease. Moreover, booster vaccination increases the period of protection against the disease. The disease staying in the population is due to waning rate of immunity after vaccination and infection, re-infection of individuals and low vaccination coverage.

5.3 Recommendation

Going for booster vaccination will increase the period of protection of individuals against the disease, individuals are therefore urged to go for booster vaccination. Further development of vaccines that improve the protection against the disease for a longer period is highly recommended. The study has not considered the risk level of infection in different geographical locations. Moreover time dependent waning immunity is more practical. A model considering these two aspects is recommended for future studies.

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