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TITLE: **MODELING INTERVENTION STRATEGIES IN EPIDEMIC DISEASE OUTBREAKS**

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MODELING INTERVENTION STRATEGIES IN EPIDEMIC DISEASE OUTBREAKS

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ABSTRACT

Modeling Intervention Strategies in Epidemic Disease Outbreaks

By

Israel Tellez

Mathematical modeling is an essential tool in epidemiology. Models are constructed to describe the spread of an infectious disease in a population. This thesis focuses on deterministic compartmental models in which population is divided into distinct compartments depending on the state of infection of an individual throughout the course of an outbreak. The most basic model uses three compartments: Susceptible (S), Infected (I), and Recovered (R) as building blocks. We study improved SIR-type models involving more compartments to accommodate different states of infection, enabling response strategies to control the spread of a specific disease.

Epidemics depend heavily on transmissibility of the disease, which can be measured by the *basic reproduction number*. We derive the basic reproduction number for each SIR-type model and use it to analyze the epidemic behavior. Response strategies to the spread of an infectious disease in a population often focus on containment and isolation of infected individuals as well as different types of vaccination programs. We use mathematical models and numerical simulations to predict the effect of vaccination and quarantine strategies on the spread of a disease in a homogeneous population. We conclude that a combination of intervention steps with highest priority on *mass vaccination* generate the best outcome in reducing and shortening the outbreak.

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Introduction

The threat of infectious diseases has been a global concern throughout history. Thousands of people, especially those in areas with scarce resources, die every year from a wide variety of diseases. For this reason, it is important to study disease dynamics and management methods such as interventions and treatment. This is one of the main motivations in the effort to construct mathematical models which describe disease dynamics. Such models allow scientists to conduct theoretical experiments that simulate real world situations. A mathematical model is constructed based on certain hypotheses about how a particular disease spreads; these hypotheses are drawn from historical records of specific disease epidemics. The work of Daniel Bernoulli in 1790 is one of the earliest accounts of the development of a mathematical model for a disease epidemic [3]. Later in 1927, O.W. Kermack and A.G. McKendrick formulated a compartmental model which successfully predicted disease behavior. The contributions of Bernoulli, Kermack and McKendrick served as a catalyst for the advancement of modern epidemiology.

Mathematical modeling is an essential tool in understanding the transmission of infectious diseases and assessing the effects of different interventions such as vaccination, quarantine and behavioral changes of the population [2, 7, 10, 17, 21]. Modeling intervention strategies is particularly useful when there is a limited amount

of resources available, so that priority can be given to the most effective one. Smallpox is one such disease that motivates the modeling of intervention strategies due to its short latent period and high transmission rate. The World Health Organization (WHO) has declared the eradication of smallpox in 1980 following its global immunization campaign. However, after the 9/11 terrorist attack, the possibility of using biological agents such as smallpox as a weapon for bio-terrorist attack cannot be considered negligible [7, 10, 13, 16, 18, 22]. In this paper we study general mathematical models focusing primarily on intervention strategies and their effect on the spread of an infectious disease.

This thesis is organized as follows. In Chapter 2 we discuss the development of basic SIR (Susceptible, Infected, Recovered) and SEIR (Susceptible, Exposed, Infected, Recovered) models. We employ the Next Generation Method (NGM) technique developed by Diekmann et al. [11] to calculate the basic reproduction number $\mathcal{R}_0$ of the model when finitely many different categories of individuals are recognized. The basic reproduction number provides a way to measure of disease transmissibility. We further analyze the threshold value that determines the occurrence of the epidemic in the basic SIR-type model. Chapter 3 will detail the construction of intervention models which include quarantine and two types of vaccination programs, namely mass and ring vaccinations, and their qualitative behavior. In Chapter 4, we numerically solve the models using the Fourth-Order Runge-Kutta method and the built-in MATLAB ODE solver, ode45. The detailed discussion and derivation of the Fourth-Order Runge-Kutta method is given in Appendix A. We analyze our simulation results and conduct sensitivity analysis of model parameters. Lastly, in

Chapter 5 we test the model against specific epidemic data of a smallpox outbreak and obtain a good qualitative agreement, indicating the predictive potential of the model for disease dynamics and the implementation of intervention strategies.

CHAPTER 2

Basic Epidemic Models

In compartmental models, we group the individuals in a population into distinct classes according to their disease stage at a given time. The basic model consists of three classes: *Susceptible* (S), *Infected* (I) and *Recovered* (R). This model from now on is referred to as the SIR model. In this and the next chapter, we study the basic SIR model and several improvements which include the *Exposed* (E), *Vaccinated* (V) and *Quarantined* (Q) compartments. The choice of these different compartments depends on the characteristics of the particular disease being modeled. For each of the models that we study, we also calculate their *basic reproduction number*, commonly denoted by $\mathcal{R}_0$. The basic reproduction number is the average number of secondary infections caused by a single infected individual in an entirely susceptible population [24]. These secondary infections are often regarded in a demographic sense as new generations of infectious individuals, purely for the analogy of seeing new infections as "births". For this reason the basic reproduction number can be used to measure the transmissibility of the infection and to further predict the final size of the epidemic.

2.1 SIR Model

In the SIR model, $S(t)$ represents the number of individuals who are susceptible to the disease at time t. An individual who is susceptible has not yet been infected by the disease. We denote those who have been infected at time t by $I(t)$. The

infected class is capable of spreading the disease to the susceptible class. Typically, individuals who are in the susceptible class progress into the infected class as they come in contact with the disease, and then onto the recovered class. Those who have recovered at a time t or died due to the disease are then represented by $R(t)$. For this reason, it should be noted that the recovered class should be considered as those who have been "removed" and thus no longer susceptible. The values of $S(t), I(t)$ and $R(t)$ are fractions of respective classes in the total population.

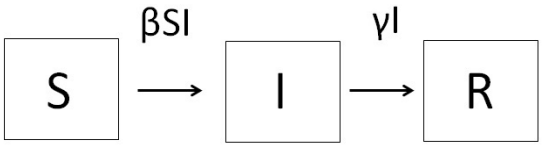

Figure 2.1: SIR flow dynamics with infection and recovery rates.

Figure 2.1 shows the flow of individuals from one class to the next. The flow in this SIR model is in one direction and hence the recovered individuals are assumed to be immune and can no longer get infected.

We now state several assumptions that are used in the basic SIR model:

(1) The disease spreads in a closed population in the sense that there is no emigration or immigration and the course of the disease is short enough to disregard births and disease-unrelated deaths. The population therefore remains constant, so that $S(t) + I(t) + R(t) = N$, where $N = 1$ is the total population.

(2) There is homogeneous mixing among individuals in the population, which means all individuals are identical with respect to their susceptibility, infectiousness, and immunity.

(3) Disease spreads through human-to-human contacts only, which is also assumed to be uniform among individuals in the population.

Based on the above assumptions, we construct the following system of ordinary differential equations (ODEs) to model the rate of change of each population compartment:

$$\frac{dS}{dt} = -\beta SI \tag{2.1}$$

$$\frac{dI}{dt} = \beta SI - \gamma I \tag{2.2}$$

$$\frac{dR}{dt} = \gamma I \tag{2.3}$$

In the above model, the infection rate β is the per capita rate at which two individuals (an infected and a susceptible) come into effective contact that is sufficient to lead to infection. Thus, during the time interval Δt, the number of newly infected individuals $\Delta I(t)$ is given by

$$\Delta I(t) = I(t + \Delta t) - I(t) = \beta SI\Delta t.$$

Taking the limit as $\Delta t \to 0$, we obtain the term βSI in (2.2) and $-\beta SI$ in (2.1). In this basic SIR model, we assume β to be constant. However, in a more realistic setting, β may depend on several factors, such as age, time at which the outbreak takes place, environmental conditions, and behaviors of individuals in the population [24].

The recovery rate γ is also assumed to be uniform and constant. The term

$\gamma I \Delta t$ gives the number of individuals who recover from or die because of the disease during the time interval Δt. Using the fact that the rate at which an event occurs is given by the inverse of the duration of the event, we note that the average duration of infection is given by $\frac{1}{\gamma}$. Knowing the duration of infectiousness we can quickly calculate the recovery rate and vice versa.

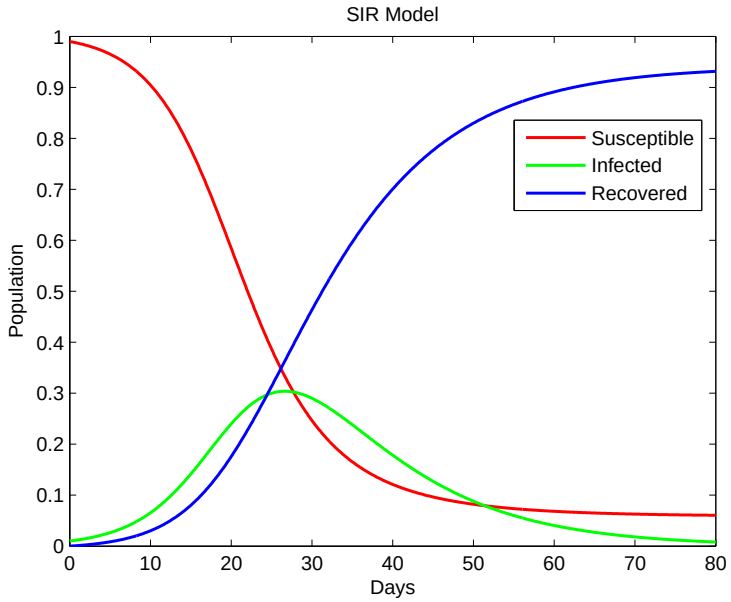

Figure 2.2: SIR Model, equations (2.1)-(2.3) with $S(0) = 0.99, I(0) = 0.01, R(0) = 0, \beta = 0.3, \gamma = 0.1$.

The rates β and γ are positive constants in the SIR model. Since $\frac{dS}{dt} < 0$ in (2.1) and $\frac{dR}{dt} > 0$ in (2.3), the number of susceptible individuals will decrease and the number of recovered individuals will increase over time. We numerically solve the system (2.1)-(2.3) using different values for β. Figure 2.2 shows the plots for S, I, and R versus time t with $\beta = 0.3, \gamma = 0.1$. The initial values are $S(0) = 0.99, I(0) = 0.01$ and $R(0) = 0$ indicating that initially almost the entire population is susceptible and only 1% are infected. The average duration of infection is $\frac{1}{\gamma} = \frac{1}{0.1} = 10$ days.

In Figure 2.2 we can see that the susceptible population quickly decreases to zero, while the infected population increases, reaching the maximum value of approximately 0.3038 at around 26.8 days, and decreases back to zero. This scenario shows the occurrence of the epidemic. We again solve the system (2.1)-(2.3) taking $\beta = 0.08$

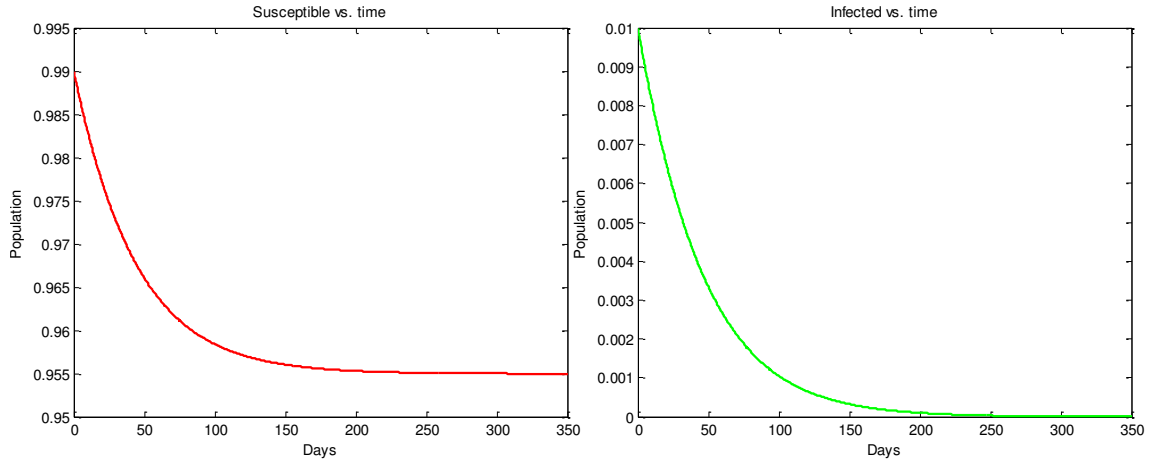

Figure 2.3: SIR model with β=0.08.

and keeping the other parameter and initial values the same. Figure 2.3 shows the solution curves for the susceptible and infected populations separately; for this reason it is advisable to pay particular attention to the scale of each individual plot. We notice that the number of susceptibles slightly decreases and the number of infected individuals decreases to 0 and never increases. In this case, the disease fails to invade the population.

2.1.1 Threshold Value and Basic Reproduction Number

One goal in epidemic modeling is to know what can be done to control an outbreak. Note that, intuitively, an epidemic will occur if the number of infected persons increases and is high relative to the overall number of persons in the population. Since the input for I comes from the S compartment (Figure 2.1), we are interested in dis-

covering the threshold value in the susceptible population that allows the epidemic to occur.

From equation (2.2), we observe the following

$$\begin{aligned}\frac{dI}{dt} &= \beta SI - \gamma I > 0 \\ &\Leftrightarrow I(\beta S - \gamma) > 0 \\ &\Leftrightarrow S > \frac{\gamma}{\beta}.\end{aligned}$$

Similarly, $\frac{dI}{dt} < 0$ whenever $S < \frac{\gamma}{\beta}$. This implies that for the epidemic to occur the fraction of susceptibles in the population needs to be greater than γ/β. We call $S^* = \frac{\gamma}{\beta}$ the threshold value for the susceptible population in the SIR model.

The calculation of the basic reproduction number $\mathcal{R}_0$ for the SIR model is rather straight forward. Recall that by definition, $\mathcal{R}_0$ is the number of secondary infections caused by one infectious individual when introduced to a totally susceptible population, that is, $S(0) \approx 1$. Since we assume that all rates are constant, we see that the duration of infection is simply given by γ^{-1} and that

$$\mathcal{R}_0 = (\beta S)\left(\frac{1}{\gamma}\right) \approx \frac{\beta}{\gamma} \tag{2.4}$$

We rewrite equation (2.2) with $S \approx 1$ as follows

$$\begin{aligned}\frac{dI}{dt} &= (\beta - \gamma)I \\ &= (\frac{\beta}{\gamma} - 1)\gamma I \\ &= (\mathcal{R}_0 - 1)\gamma I.\end{aligned}$$

Then it is easy to see that if $\mathcal{R}_0 < 1$ then $\frac{dI}{dt} < 0$. Conversely, if $\mathcal{R}_0 > 1$ then $\frac{dI}{dt} > 0$. This result tells us that if one infected can only replace itself with no more than one infected, then $I(t)$ decreases and there is no epidemic. However, if one infected can infect more than one susceptible, then $I(t)$ increases and an epidemic occurs. For this reason, $\mathcal{R}_0$ is often called the *contact number* or *replacement number* when the disease invasion begins [17].

The threshold value in the susceptible population, expressed as

$$S^* = \frac{\gamma}{\beta} = \frac{1}{\mathcal{R}_0},$$

indicates that the number of susceptibles must be kept at less than $1/\mathcal{R}_0$ to prevent the epidemic from occuring. In other words, the number of immune individuals must be greater than $1 - (1/\mathcal{R}_0)$ to acquire the herd immunity. As a consequence, diseases with smaller $\mathcal{R}_0$ can be eradicated more easily than diseases with higher $\mathcal{R}_0$. As an example, basic reproduction numbers for measles and smallpox are 16 and 6, respectively [24]. The herd immunity threshold for measles is about 94% and 83% for smallpox. Since it is easier to achieve a herd immunity of 83% than on of 94%,

this explains the fact that measles still persists to this day, while smallpox has been eradicated in 1970s.

2.1.2 Phase Plane Analysis

Under the assumption that the population is closed, we can write $R(t) = 1-S(t)-I(t)$ and further analyze the behavior of the epidemic from the SI-plane. Note that

$$\frac{\frac{dI}{dt}}{\frac{dS}{dt}} = \frac{dI}{dS} = \frac{\beta SI - \gamma I}{-\beta SI} = -1 + \frac{\gamma}{\beta S}. \tag{2.5}$$

By separation of variables we get

$$\begin{aligned} dI &= \left(-1 + \frac{\gamma}{\beta S}\right) dS \\ \implies \int dI &= \int \left(-1 + \frac{\gamma}{\beta S}\right) dS \\ \implies I(S) &= -S + \frac{\gamma}{\beta} \ln(S) + c, \end{aligned}$$

where c is an integration constant. Using the initial values $I(0) = I_0$ and $S(0) = S_0$, we obtain

$$\begin{aligned} I_0 &= -S_0 + \frac{\gamma}{\beta} \ln(S_0) + c \\ \Rightarrow c &= I_0 + S_0 - \frac{\gamma}{\beta} \ln(S_0) \end{aligned}$$

and hence the solution curve is given by

$$I(S) = I_0 + (S_0 - S) + \frac{\gamma}{\beta} \ln\left(\frac{S}{S_0}\right). \tag{2.6}$$

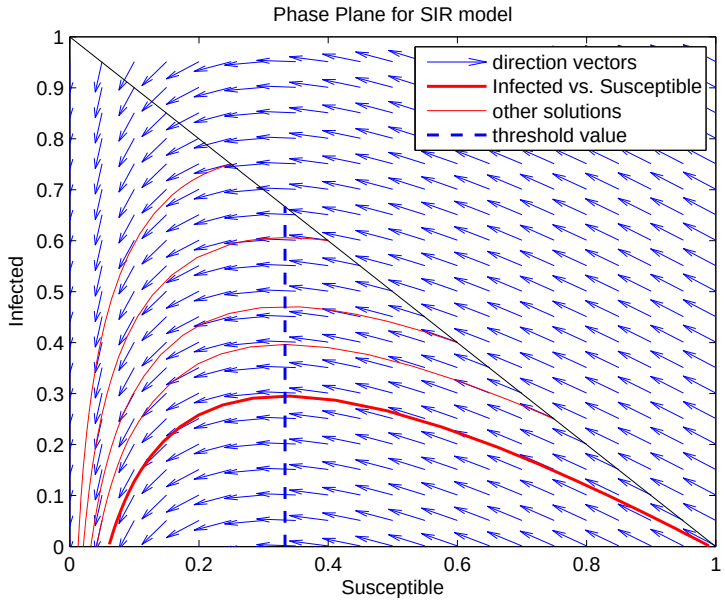

Figure 2.4: Phase portrait for the SIR Model with $\beta = 0.3, \gamma = 0.1$.

Figures 2.4 and 2.5 show the SI phase portraits and solution curves given by (2.6) with average infection period $1/\gamma = 10$ days, and infection rate $\beta = 0.3$ and $\beta = 0.08$, respectively. By looking at these solution curves we can predict the size of the epidemic $I_{\max}$ (the maximum number of infection cases) and the final size of the susceptible population S_∞ (the fraction of susceptible population that does not get infected) for various combinations of initial values S_0 and I_0. In Figure 2.4, the threshold value $S^* = \frac{\gamma}{\beta} = 0.1/0.3 = 1/3$ is shown by the vertical line and the vectors in the phase plane at this value are horizontal. If $S_0 > S^*$, then I increases for all $t \geq 0$, and decreases otherwise. The particular solution for which $S_0 = 0.99$ and $I_0 = 0.01$ is shown in bold in Figure 2.4. Other solution curves with different initial conditions but same the parameter values are shown in thin lines.

The values $I_{\max}$ and S_∞ can also be computed analytically given the initial

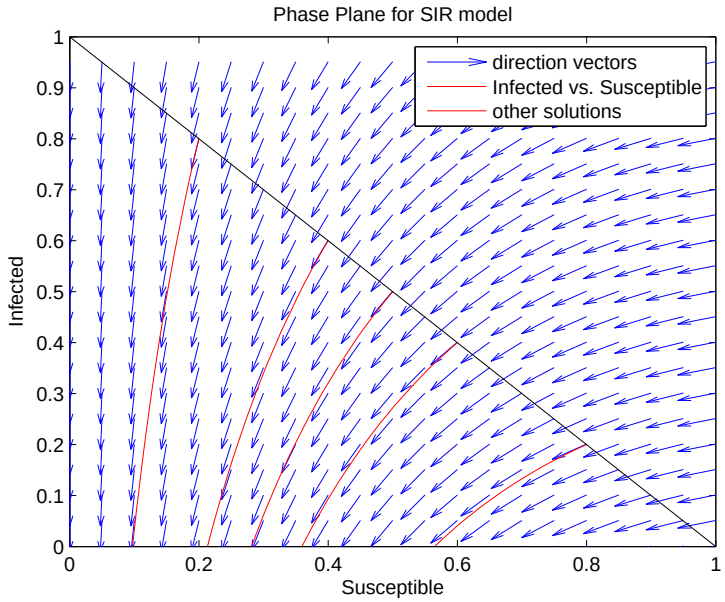

Figure 2.5: Phase portrait for the SIR Model with $\beta = 0.08, \gamma = 0.1$.

values S_0 and I_0 as well as some estimates of β and γ. From (2.6)

$$\begin{aligned} I_{\max} &= I(S^*) \\ &= I(\gamma/\beta) \\ &= I_0 + (S_0 - \gamma/\beta) + (\gamma/\beta)\ln\left(\frac{\gamma/\beta}{S_0}\right). \end{aligned}$$

The final size of susceptible population can be obtained from (2.6) by setting $I(S_\infty) = 0$, that is, S_∞ will be the root of the equation

$$I_0 + (S_0 - S_\infty) + (\gamma/\beta)\ln\left(\frac{S_\infty}{S_0}\right) = 0.$$

The root is unique on the interval $(0, S^*)$ as shown in Figure 2.4.

2.2 SEIR Model

In the basic SEIR Model, the population is divided into four compartments: *Susceptible* (S), *Exposed* (E), *Infected* (I) and *Recovered* (R). In contrast to the SIR model, individuals first progress into an "exposed" class E before becoming infected; that is, individuals in the exposed class have come in contact with an infected individual but are not yet infectious themselves. The exposed state encompasses two different periods of infection. The *latent period*, the time from infection to the time that an individual is able to transmit the disease, is one such period. The other is the *incubation period*, defined as the time from infection to the onset of symptoms that would classify the individual as clinically infected. Incubation period is easier to observe and predict, however, some diseases may spread even though the infected individuals have not shown any symptoms. The "Exposed" compartment in the SEIR model technically represents the number of individuals who are in the latent period, but the SEIR model can still be generally applied to diseases with different latent and incubation periods such as HIV, smallpox, measles, mumps, and rubella [14, 16, 22]. We let β denote the infection rate, σ is the rate at which exposed individuals become infectious and γ is the recovery rate. We once again assume that the population remains constant, that is, $S(t) + E(t) + I(t) + R(t) = N = 1$.

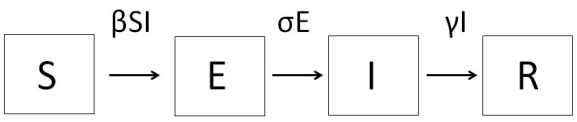

Figure 2.6: SEIR flow dynamics with infection and recovery rates.

Under the same assumption as before that the time scale of the disease is small enough to allow us to disregard birth and disease-unrelated death rates, we have the following system of ODEs:

$$\frac{dS}{dt} = -\beta SI \tag{2.7}$$
$$\frac{dE}{dt} = \beta SI - \sigma E \tag{2.8}$$
$$\frac{dI}{dt} = \sigma E - \gamma I \tag{2.9}$$
$$\frac{dR}{dt} = \gamma I \tag{2.10}$$

2.2.1 Reproduction Number

Recall that the reproduction number, $\mathcal{R}_0$, is defined as the expected number of secondary cases of infections that arise from a single infected individual. The calculation of $\mathcal{R}_0$ is not as straight-forward here as in the SIR model, and we will use the *Next Generation Matrix (NGM)* approach as described in [11] to calculate it. The terms "Next Generation" serve as an analogy to the demographic idea of a generation. Epidemiologically, new infections caused by disease transmission are seen as "births", therefore contributing to a new consecutive generation of infected individuals.

We begin by considering those equations in the system (2.7)-(2.10) which describe new infections and the changes in states of infected individuals. The disease-carrying equations in the SEIR model are Equations (2.8) and (2.9). Evaluating this sub-system at the infection-free steady state ($S = 1$) allows us to observe the poten-

tial for initial spread of infection when a disease is introduced into a fully susceptible population. Linearizing the infected sub-system in this way, with small E and I, we arrive at the system

$$\frac{dE}{dt} = \beta I - \sigma E \tag{2.11}$$

$$\frac{dI}{dt} = \sigma E - \gamma I \tag{2.12}$$

We call these equations the *infected sub-system* of the SEIR equations, which can be written in the form $\dot{\mathbf{x}} = (T - \Sigma)\mathbf{x}$ where $\mathbf{x} = \begin{pmatrix} E \\ I \end{pmatrix}$. The matrix T corresponds to transmissions in the epidemiological sense and it consists of elements that leads to the production of new infections. The matrix Σ corresponds to transitions and it consists of elements describing changes in state of infected individuals. The term βI in (2.11) describes the production of new infections and hence belongs to matrix T, while all other terms in (2.11)-(2.12) belong to matrix Σ. We rewrite the above sub-system as follows

$$\begin{pmatrix} \dot{E} \\ \dot{I} \end{pmatrix} = \Big[\underbrace{\begin{pmatrix} 0 & \beta \\ 0 & 0 \end{pmatrix}}_{T} - \underbrace{\begin{pmatrix} \sigma & 0 \\ -\sigma & \gamma \end{pmatrix}}_{\Sigma} \Big] \begin{pmatrix} E \\ I \end{pmatrix}. \tag{2.13}$$

The element $T_{i,j}$ describes the rate at which new infections in state i occur due to contacts with the infectives in state j. Intuitively then, $T_{i,j} = 0$ tells us that no new cases in state i can arise from individuals in state j. To illustrate this, let $i, j = 1$ correspond to the E (Exposed) state and $i, j = 2$ to the I (Infected) state. Then the element $T_{1,1}$ is the number of new cases in the E (Exposed) state caused by individuals

in the E (Exposed) state. Since new infections can only be caused by contacts with an infected individual in state I, we have $T_{1,1} = 0$. Similarly, the element $T_{2,1}$ is the number of new cases in the I (Infected) state produced by individuals in the E (Exposed) state. Again $T_{2,1} = 0$ as an individual in the E (Exposed) state is not yet infectious and thus cannot spread the disease.

The next generation matrix (NGM) is defined as $G = T\Sigma^{-1}$ and $\mathcal{R}_0$ can be shown to be the dominant eigenvalue of G. From (2.13), we construct the matrix

$$\Sigma^{-1} = \frac{1}{\sigma\gamma}\begin{pmatrix} \gamma & 0 \\ \sigma & \sigma \end{pmatrix}$$

and therefore

$$T\Sigma^{-1} = \begin{pmatrix} 0 & \beta \\ 0 & 0 \end{pmatrix}\begin{pmatrix} 1/\sigma & 0 \\ 1/\gamma & 1/\gamma \end{pmatrix} = \begin{pmatrix} \frac{\beta}{\gamma} & \frac{\beta}{\gamma} \\ 0 & 0 \end{pmatrix}.$$

Since $T\Sigma^{-1}$ is an upper triangular matrix, the eigenvalues are the entries in the main diagonal, and the dominant eigenvalue is $\mathcal{R}_0 = \frac{\beta}{\gamma}$.

It is worth mentioning that calculating Σ^{-1} can be computationally expensive for large systems. However, understanding the epidemiological interpretation of the elements in Σ^{-1} can make the calculation of its entries much easier. The entry $\Sigma^{-1}_{i,j}$ is the expected time that an individual in state j will spend in state i for the entire remaining course of infection. For the matrix above we see that individuals who are presently in the exposed state will stay exposed for $1/\sigma$ days, this value corresponds to the entry $\Sigma^{-1}_{1,1}$. Furthermore, individuals who are presently infected cannot return to the exposed state and so $\Sigma^{-1}_{1,2} = 0$. Lastly, those in exposed and infected states

will spend $1/\gamma$ days in infected state, yielding $\Sigma_{2,1}^{-1} = \Sigma_{2,2}^{-1} = 1/\gamma$. Thus, we have fully defined Σ^{-1} using the purely epidemiological approach.

We notice that the values of $\mathcal{R}_0$ for the SIR and SEIR models are the same. The same analysis also holds true for the reproduction number of the SEIR model. That is, if $\mathcal{R}_0 > 1$ then the spread of the disease causes an epidemic, whereas if $\mathcal{R}_0 < 1$ then the disease dies out and no epidemic occurs.

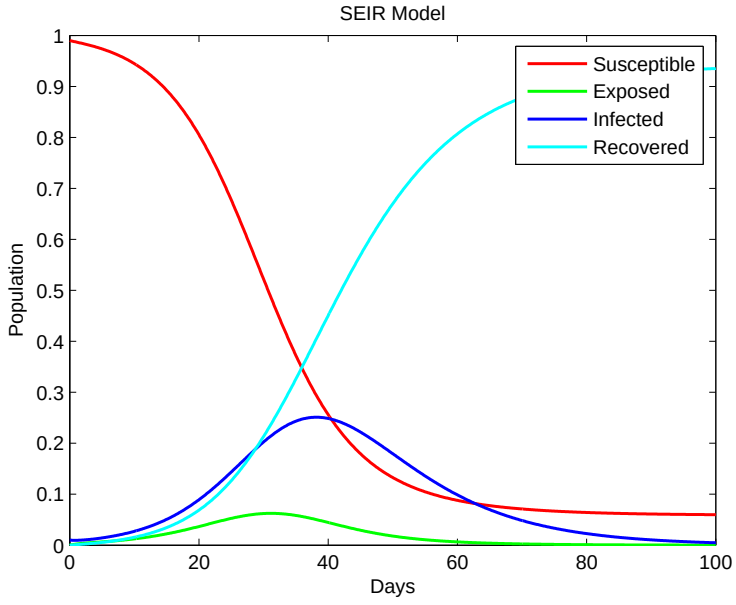

Figure 2.7: SEIR model with $\beta = 0.3, \sigma = 0.5$ and $\gamma = 0.1$.

We solve the SEIR model (equations (2.7)-(2.10)) numerically using the same initial and parameter values as in the SIR model: $S(0) = 0.99, I(0) = 0.01, E(0) = R(0) = 0, \gamma = 0.1$. We take the latent period to be $1/\sigma = 2$ days. Figure 2.7 shows the simulation result for $\beta = 0.3$, that is, $\mathcal{R}_0 = 3 > 1$. Here we see similar behavior to that of the SIR model (Fig. 2.2) in which the number of susceptible individuals drops, while the number of recovered individuals rises as time goes on. The number of exposed and infected individuals will initially rise and then drop towards zero. The

course of outbreak takes longer (100 days) in SEIR model than in the SIR model (80 days). However, $I_{\max}$ in the SEIR model is slightly smaller than in the SIR model.

Likewise, for $\beta = 0.08$ and $\mathcal{R}_0 = 0.8 < 1$, the number of infected individuals never increases. Also, the numbers of exposed and recovered individuals slightly increase, then decrease towards 0 or plateau at a maximum value, respectively. See Figure 2.8, where we have omitted the Susceptible curve for display purposes.

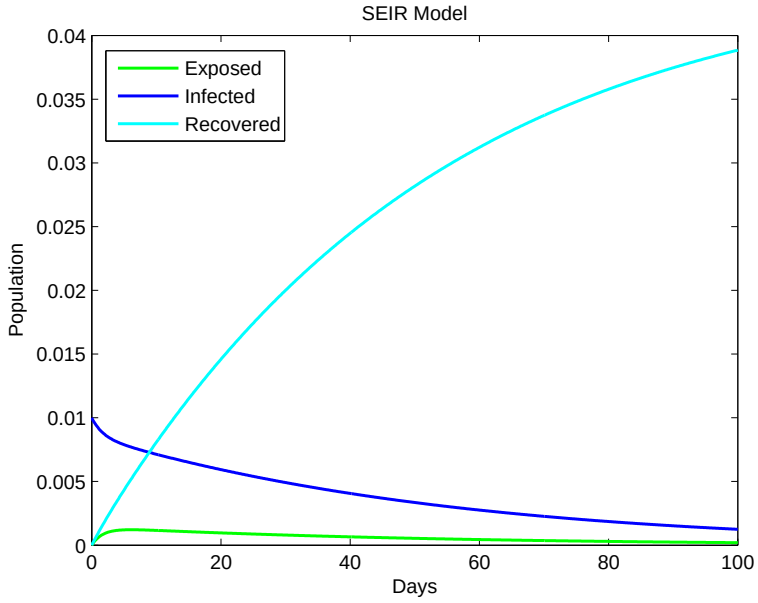

Figure 2.8: SEIR model with $\beta = 0.08, \sigma = 0.5$ and $\gamma = 0.1$.

CHAPTER 3

Modeling Interventions on Disease Transmission

The construction of a mathematical model is done to meet certain objectives that will help in understanding the dynamics of an infectious disease. For the simple models, those objectives are often to describe the spread of the disease through a susceptible population, calculate new and accumulated cases of infection, and predict the final size of the epidemic[22]. The modeling of infectious diseases, however, is in no way limited to these aforementioned objectives. In order to obtain more realistic results, crude models such as the SIR and SEIR models are improved to better describe the behavioral characteristics of individuals in human-to-human disease transmission, as well as the intervention strategies for controlling an outbreak. The model constructed by Gonçalves et al. [14] considers both the different stages of the smallpox disease and the mobility of infected persons. Ferguson et al. [13] illustrate the complexities of mathematical models by considering different types of model structures as well as the effects of various control methods. In addition, the form in which an infectious disease is introduced and where it is introduced will adversely affect the spread of that disease, as detailed by Bozzette et al. [4]. In this chapter we will discuss extensions of the SEIR model discussed in Chapter 2 which include some intervention strategies, such as vaccination and quarantine of infected individuals.

3.1 SEIRV Vaccination Model

A vaccination program is an effective tool for preventing infection and is often a much better strategy for disease control as compared to treating symptoms of already infected persons. This argument agrees with the analysis of the threshold value of the susceptible population of the SIR model in Section 2.1.1 of Chapter 2 which indicates that the epidemic can be prevented if the fraction of susceptibles in the population is below γ/β. One way to achieve this is by vaccinating enough susceptible population. For diseases with latent period (SEIR model), vaccinating those who have been exposed to the disease but are not yet infectious can also prevent the epidemic. To understand the impact of vaccination on the dynamics of the system, we add the *Vaccinated* compartment $V(t)$ into the model. Individuals who are susceptible to the disease and those who have been exposed but are not yet infectious can be vaccinated and moved into the V compartment. Under the same assumption of the homogeneous mixing of the population, we let ν_1 and ν_2 be the rates at which individuals in the S and E compartments, respectively, are vaccinated as a preventive measure.

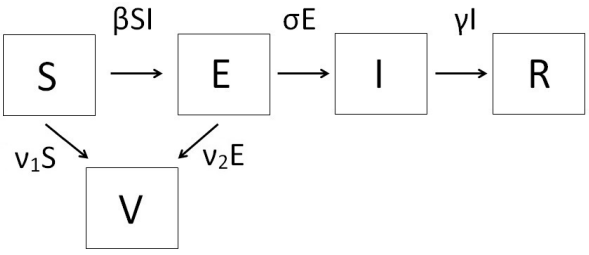

Figure 3.1: SEIRV flow dynamics.

We obtain the following system:

$$\frac{dS}{dt} = -\beta SI - \nu_1 S \tag{3.1}$$

$$\frac{dE}{dt} = \beta SI - (\sigma + \nu_2)E \tag{3.2}$$

$$\frac{dI}{dt} = \sigma E - \gamma I \tag{3.3}$$

$$\frac{dR}{dt} = \gamma I \tag{3.4}$$

$$\frac{dV}{dt} = \nu_1 S + \nu_2 E \tag{3.5}$$

3.1.1 Reproduction Number

We calculate the reproduction number for the SEIRV model using the NGM approach as before. The infected sub-system consists of the equations (3.2)-(3.3). Evaluating the system at the disease-free steady state, we can write the sub-system as follows:

$$\begin{pmatrix} \dot{E} \\ \dot{I} \end{pmatrix} = \Big[\underbrace{\begin{pmatrix} 0 & \beta \\ 0 & 0 \end{pmatrix}}_{T} - \underbrace{\begin{pmatrix} \sigma + \nu_2 & 0 \\ -\sigma & \gamma \end{pmatrix}}_{\Sigma} \Big] \begin{pmatrix} E \\ I \end{pmatrix} \tag{3.6}$$

Lastly, multiplying the matrices T and Σ^{-1} gives us the NGM matrix

$$G = T\Sigma^{-1} = \begin{pmatrix} 0 & \beta \\ 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{\sigma+\nu_2} & 0 \\ \frac{\sigma}{\gamma(\sigma+\nu_2)} & \frac{1}{\gamma} \end{pmatrix} = \begin{pmatrix} \frac{\sigma\beta}{\gamma(\sigma+\nu_2)} & \frac{\beta}{\gamma} \\ 0 & 0 \end{pmatrix}$$

with dominant eigenvalue $\mathcal{R}_0 = \frac{\sigma\beta}{\gamma(\sigma+\nu_2)}$. Again we have that if $\mathcal{R}_0 > 1$ then an epidemic occurs and the disease dies out otherwise (see Appendix A in [11]).

3.1.2 Ring Vaccination vs. Mass Vaccination

In the event of a disease outbreak it would be necessary to verify the suspected cases, as well as investigate the source of infection and anybody who they may have come into contact with and exposed to the disease. This information would allow scientists and public health organizations to determine the scope of the outbreak and thus make decisions about whether to formulate focused or large-scale vaccination strategies. Localized confirmed cases could indicate that vaccination could be focused on a smaller number of persons; while multiple cases across different cities could specify the need of a mass vaccination of the entire population to combat the intentional introduction of the virus. Mass vaccination would require a large enough stockpile of vaccines to be readily available.

The *ring vaccination* strategy is one such method that in the past has proven to be the most successful in stopping certain outbreaks such as smallpox. This strategy involves tracing people who have come into close contact with an infected person (and therefore have been exposed to the virus) and vaccinating them as well as their own (secondary) close contacts. Doing so would create a "ring" of individuals around an infected person who have been vaccinated, thus halting further transmission of the disease. This strategy maximizes the effectiveness of the vaccination by focusing mainly on those who are at highest risk of becoming infected. Ring vaccination also requires a close monitoring of the primary and secondary contacts as well as the immediate isolation of infected persons [20]. This method was proven to be notably effective in the case of smallpox eradication in the 1970's.

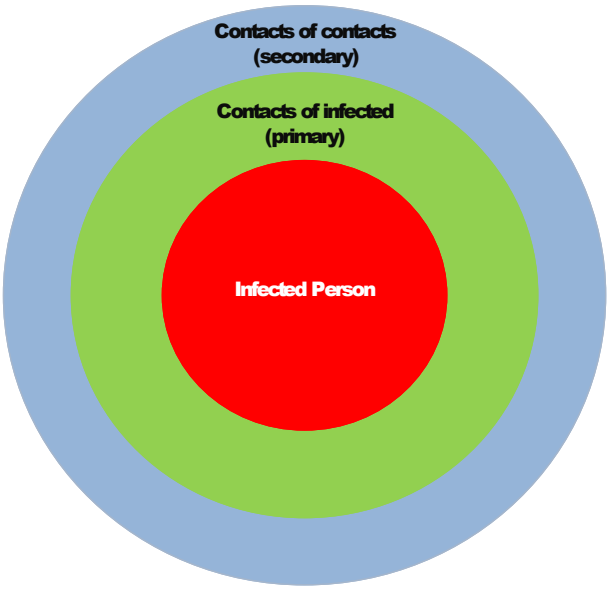

Figure 3.2: Ring vaccination schematic.

In contrast to the previous strategy, the *mass vaccination* strategy involves vaccinating large groups of persons who have not yet been exposed to the disease. While this strategy helped protect people from the virus, it was not infallible and presented certain notable risks. Some of these risks were that once vaccinated, persons who were not previously exposed to the disease still became infected after later exposure due to vaccine failure or waning immunity. Also, people refusing to get vaccinated and those who were difficult to reach in order to vaccinate could still spread the disease. Most notably, adverse effects of vaccinations in the form of life-threatening complications often could lead to vaccine-related deaths [19]. The strength of mass vaccination in the simulations comes from particular assumptions which set up a best-case scenario. These assumptions are that vaccination grants absolute immunity for the duration of the outbreak, there are no vaccine-related deaths, and that vaccination is not refused by anyone in the susceptible population.

The difference between ring and mass vaccinations from a modeling perspective lies in the parameter values ν_1 and ν_2. In ring vaccination, we vaccinate the individuals who have had primary or secondary contact with an infectious individuals. In other words, they have been exposed to the disease and are in the E compartment. Hence, in the diagram shown in Figure 3.1, we set the rates $\nu_1 = 0, \nu_2 > 0$ to model a ring vaccination policy. On the other hand, mass vaccination is given to those individuals who are still susceptible and have not yet been exposed to the disease. Thus, $\nu_1 > 0$ and $\nu_2 = 0$ in mass vaccination.

We run simulations to compare the effectiveness of each strategy. In all simulations shown below, the parameter and initial values are as follows:

Parameter/initial condition	Value
β	0.3
σ	0.5
γ	0.1
$S(0)$	0.99
$E(0)$	0
$I(0)$	0.01
$R(0)$	0
$V(0)$	0

Table 3.1: Parameter and initial values for SEIRV simulation.

We simulate the following five scenarios for vaccination policy:

(1) Mass vaccination only (MV)

(2) Ring vaccination only (RV)

(3) Combined mass and ring vaccinations with higher mass vaccination rate ($\nu_1 > \nu_2$)

(4) Combined mass and ring vaccinations with higher ring vaccination rate ($\nu_1 < \nu_2$)

(5) Combined mass and ring vaccinations with equal rates ($\nu_1 = \nu_2$)

with parameter values for the rates ν_1 and ν_2 shown in Table 3.2.

	ν_1 (mass vacc. rate)	ν_2 (ring vacc. rate)
MV	0.03	0
RV	0	0.03
MV,RV	0.02	0.01
MV,RV	0.01	0.02
MV,RV	0.015	0.015

Table 3.2: Vaccination rates for five different policies.

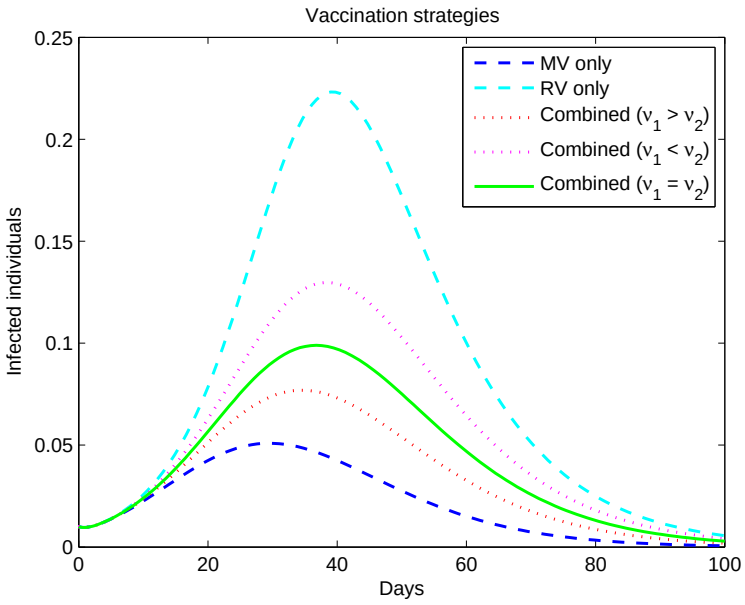

Figure 3.3: Infected (I) curves for five scenarios of vaccination policies.

In Figure 3.3 we look at the peak of infection curve $I(t)$ and the time when it is attained. Moreover, due to the fact that the recovered population R is made of individuals who got the disease and have recovered from it as well as those who died from the disease, one can look at the size of the recovered population at the end of the outbreak to measure the severity of the epidemic (Figure 3.4). We observe that in all cases, the total number of infected individuals is less than that in the case of no interventions (SEIR Model, Figure 2.7). Further, we see that employing RV on its own is the least effective strategy due to the fact that it targets mainly

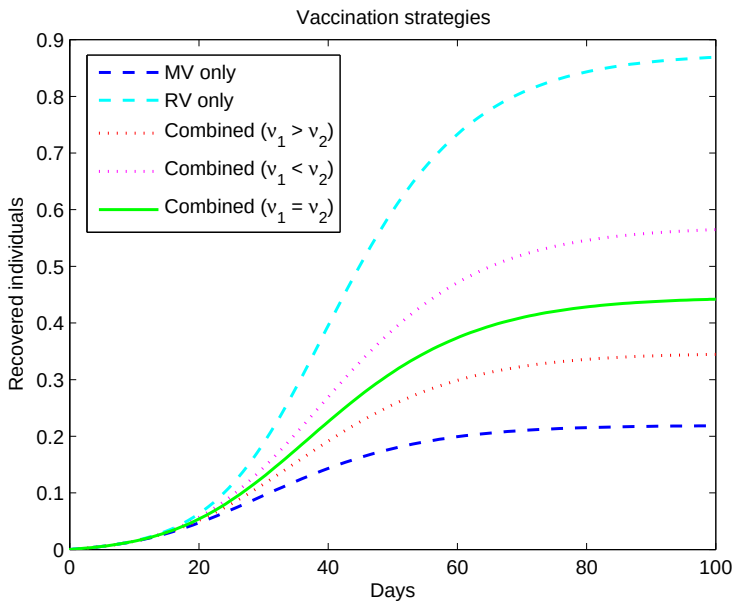

Figure 3.4: Recovered (R) curves for five scenarios of vaccination policies.

those in the exposed state (E), failing to minimize the interactions between infected and susceptible individuals. Similarly, combined interventions showed that the most effective policy was that in which the MV rate was higher. Lastly, Figure 3.3 shows that employing MV on its own has the greatest positive effect on the number of infected individuals; surely, the model prediction for this scenario is less realistic because of the factors described previously. We will discuss this in greater details in Chapter 5.

These results might lead one to believe that an effective vaccination program is sufficient to reduce the spread of an infectious disease below the threshold needed for an epidemic to occur. This of course has been disproved in many literary works published on this topic [2, 21]. It is important to point out that in the above construction, we assume that there is no failed vaccination (best case scenario). However, it is often likely that vaccine efficacy along with a high number of initially infected persons can

still lead to an epidemic; moreover, a partially effective vaccination program can still allow an epidemic to occur as well [21]. One should also take into consideration that the aggressiveness in coverage, success rate and vaccine efficacy must all be relatively high to make a significant positive impact on an outbreak.

Lastly, it is worth mentioning a possible improvement to the vaccination model. Note that the populations receiving mass vaccination (susceptibles) and those receiving ring vaccination (exposed) are very different in terms of size. Then if there are a fixed number of vaccinations, X, that can be administered during the time period Δt, it would be more realistic to weigh the vaccination rates by their target population size at time t, so that $X = \nu_1 S(t) + \nu_2 E(t)$. This would be done so that the vaccination rates can be varied as the population sizes change over time. As a consequence, this model with variable vaccination rates would allow for ν_1 and ν_2 to increase or decrease as time goes on in order to administer the desired X amount of vaccinations.

3.2 SEIRQ Quarantine Model

Another method of intervention commonly employed for infectious diseases with latent periods is quarantine. Quarantine involves isolating infected individuals from the population, as an attempt to reduce the number of encounters between susceptible and infected persons. Once an individual has gone through the disease's incubation period and entered the infected state I they are considered to be a confirmed case of that disease, displaying all clinical symptoms of the disease and having been identified by some health organization. This organization, employing a quarantine protocol, then orders that the infected individual be isolated to confined quarters

either at home, at a hospital, or designated location depending on the severity of the symptoms. Once in quarantine the individual will remain there until they are fully recovered and no longer infectious, namely $1/\gamma$ days. Thus, those in the quarantined state enter the recovered state R at the rate γ. To simulate the effects of quarantine on disease transmission, we allow individuals in the infected class I to be placed into a *Quarantined* class, $Q(t)$, at a rate κ.

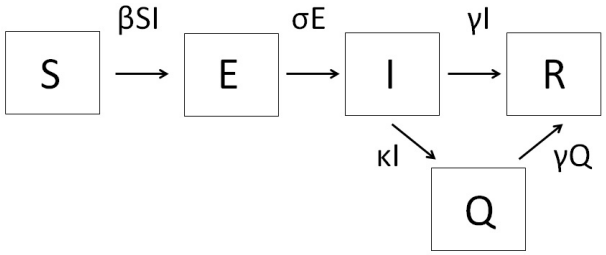

Figure 3.5: SEIRQ flow dynamics.

With the assumptions of homogeneous mixing and constant population we obtain the system

$$\frac{dS}{dt} = -\beta SI \tag{3.7}$$

$$\frac{dE}{dt} = \beta SI - \sigma E \tag{3.8}$$

$$\frac{dI}{dt} = \sigma E - (\gamma + \kappa)I \tag{3.9}$$

$$\frac{dR}{dt} = \gamma(I + Q) \tag{3.10}$$

$$\frac{dQ}{dt} = \kappa I - \gamma Q \tag{3.11}$$

The solution curves are shown in Figure 3.6 with the same initial and parameter values as shown in Table 3.1 along with the quarantine rate $\kappa = 0.03$ and $Q(0) = 0$.

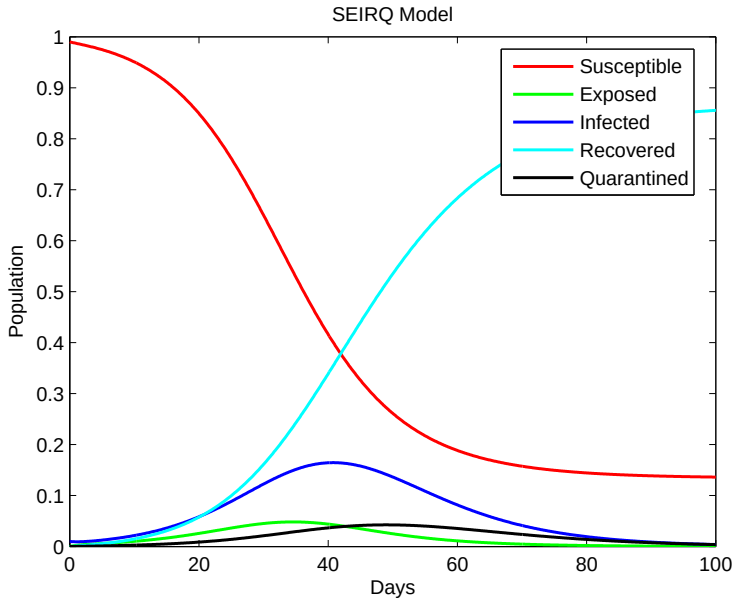

Figure 3.6: SEIRQ model with $\beta = 0.3, \sigma = 0.5, \gamma = 0.1, \kappa = 0.03$.

3.2.1 Reproduction Number

We use the NGM approach as before to calculate the reproduction number $\mathcal{R}_0$ for the SEIRQ model. However, note that we now have another infectious state Q to account for since those in quarantine still can become infectious even if no new cases arise from them. For this reason our NGM will be a 3×3 matrix. The infected sub-system consists of the equations (3.8), (3.9) and (3.11). Evaluating the system at the disease-free steady state ($S = 1$), we can write the sub-system as follows:

$$\begin{pmatrix} \dot{E} \\ \dot{I} \\ \dot{Q} \end{pmatrix} = \Bigg[\underbrace{\begin{pmatrix} 0 & \beta & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}}_{T} - \underbrace{\begin{pmatrix} \sigma & 0 & 0 \\ -\sigma & \gamma + \kappa & 0 \\ 0 & -\kappa & \gamma \end{pmatrix}}_{\Sigma} \Bigg] \begin{pmatrix} E \\ I \\ Q \end{pmatrix}$$

To avoid actually computing the inverse of Σ we derive it using purely the epidemiological interpretation. The (i, j)-th entry of Σ^{-1} matrix corresponds to the

amount of time that an individual in state j will spend in state i. The index values $i, j = 1, 2, 3$ refer to the exposed, infected and quarantined classes, respectively. Thus, the entry $\Sigma_{1,1}^{-1}$ corresponds to the time an individual currently in the exposed state E will spend in exposed state E, so that

$$\Sigma_{1,1}^{-1} = \frac{1}{\sigma}.$$

Similarly, we have that

$$\Sigma_{1,2}^{-1} = \Sigma_{1,3}^{-1} = \Sigma_{2,3}^{-1} = 0$$

since infected and quarantined persons cannot go back to the exposed state, and quarantined individuals cannot go back to the infected state, respectively. The entries $\Sigma_{2,1}^{-1}$ and $\Sigma_{2,2}^{-1}$ describe the time an exposed or infected individual will spend in infected state for the remainder of the outbreak, respectively. In other words, the rate at which an infected person leaves the infected state is $\gamma + \kappa$ so that the amount of time spent in infected state is given by

$$\Sigma_{2,1}^{-1} = \frac{1}{\gamma + \kappa} = \Sigma_{2,2}^{-1}.$$

Now, $\Sigma_{3,1}^{-1}$ and $\Sigma_{3,2}^{-1}$ describe the amount of time an exposed or infected person will spend in quarantine for the remainder of the outbreak. Note that in this case, a person in state E needs to first make it to state I, then goes to state Q. The probability that an individual in E goes to I is 1, while the probability that an individual in I will proceed to Q is $\kappa/(\kappa + \gamma)$. Upon reaching Q, this individual will spend $1/\gamma$ days in

that state. Hence, the amount of time an exposed individual will spend in quarantine is given by

$$\Sigma_{3,1}^{-1} = \frac{\kappa}{\kappa+\gamma} \cdot \frac{1}{\gamma} = \frac{\kappa}{\gamma(\kappa+\gamma)}.$$

Also,

$$\Sigma_{3,2}^{-1} = \frac{\kappa}{\gamma(\kappa+\gamma)}$$

by similar reasoning. Finally,

$$\Sigma_{3,3}^{-1} = \frac{1}{\gamma}$$

since this entry describes the amount of time a quarantined person will spend in quarantined state for the remainder of the outbreak. Putting this together, we have the lower triangular matrix

$$\Sigma^{-1} = \begin{pmatrix} \frac{1}{\sigma} & 0 & 0 \\ \frac{1}{\gamma+\kappa} & \frac{1}{\gamma+\kappa} & 0 \\ \frac{\kappa}{\gamma(\gamma+\kappa)} & \frac{\kappa}{\gamma(\gamma+\kappa)} & \frac{1}{\gamma} \end{pmatrix}.$$

Lastly, multiplying the matrices T and Σ^{-1} gives us the next-generation matrix

$$G = T\Sigma^{-1} = \begin{pmatrix} 0 & \beta & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{\sigma} & 0 & 0 \\ \frac{1}{\gamma+\kappa} & \frac{1}{\gamma+\kappa} & 0 \\ \frac{\kappa}{\gamma(\gamma+\kappa)} & \frac{\kappa}{\gamma(\gamma+\kappa)} & \frac{1}{\gamma} \end{pmatrix} = \begin{pmatrix} \frac{\beta}{\gamma+\kappa} & \frac{\beta}{\gamma+\kappa} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$$

with a dominant eigenvalue of

$$\mathcal{R}_0 = \frac{\beta}{\gamma+\kappa}.$$

The effectiveness of this intervention is due to the protocols implemented. In other words, the fact that the flow into the quarantined class Q comes directly from the infected class I means that there are fewer infectious individuals making effective

contact with susceptible individuals. Regardless, by referring to the infected curve in Figures 3.3 and 3.6 it can still be seen that the quarantine intervention only beats RV in reducing the maximum number of infected persons, while all other combinations of vaccination strategies remain more effective in reducing the maximum number of infected persons than quarantine. It can be inferred then that quarantine could best be used as a means of enhancing other strategies such as vaccination.

3.3 SEIRVQ Combined Intervention Model

We have seen two intervention strategies commonly used to control an epidemic. The methods of ring vaccination, mass vaccination and quarantine all proved to make a notable impact on the spread of an infectious disease in a population. In most cases, however, the impact of the strategies alone were not enough to drastically reduce the size of the epidemic. Naturally, the next step is to analyze a combination of all three strategies. The model is constructed by combining the SEIRV and SEIRQ models.

For this model, we assume that a combination of MV, RV and quarantine interventions are employed. The reason for this follows from the results in the vaccination model (SEIRV), which tell us that a (closer to) realistic program should include a combination of interventions for which MV has a higher vaccination rate.

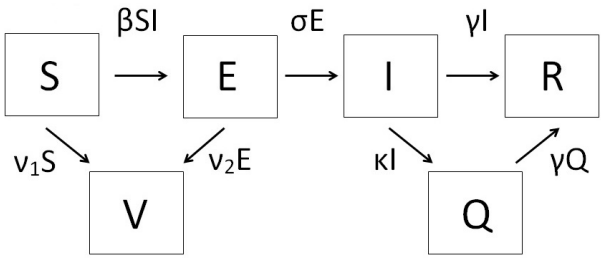

Figure 3.7: SEIRVQ flow dynamics.

These details are discussed further in the next chapter. The system describing the model is given by:

$$\frac{dS}{dt} = -\beta SI - \nu_1 S \tag{3.12}$$

$$\frac{dE}{dt} = \beta SI - (\sigma + \nu_2)E \tag{3.13}$$

$$\frac{dI}{dt} = \sigma E - (\gamma + \kappa)I \tag{3.14}$$

$$\frac{dR}{dt} = \gamma(I + Q) \tag{3.15}$$

$$\frac{dV}{dt} = \nu_1 S + \nu_2 E \tag{3.16}$$

$$\frac{dQ}{dt} = \kappa I - \gamma Q \tag{3.17}$$

We simulate the model using the initial and parameter values given in Table 3.1 along with $Q(0) = 0, \nu_1 = 0.02, \nu_2 = 0.01$ and $\kappa = 0.03$. The solution curves are shown in Figure 3.8.

Upon comparison to the SEIR model simulation (Figure 2.7), we see that the size of the epidemic is significantly reduced when a combination of ring/mass vaccination and quarantine interventions are employed.

3.3.1 Reproduction Number

To further illustrate the effect of multiple intervention strategies for controlling an epidemic we calculate $\mathcal{R}_0$ for the SEIRVQ model. As before we use the NGM approach. This time the infected sub-system consists of the equations (3.13), (3.14) and (3.17). Evaluating the system at the disease-free steady state ($S = 1$), we can write

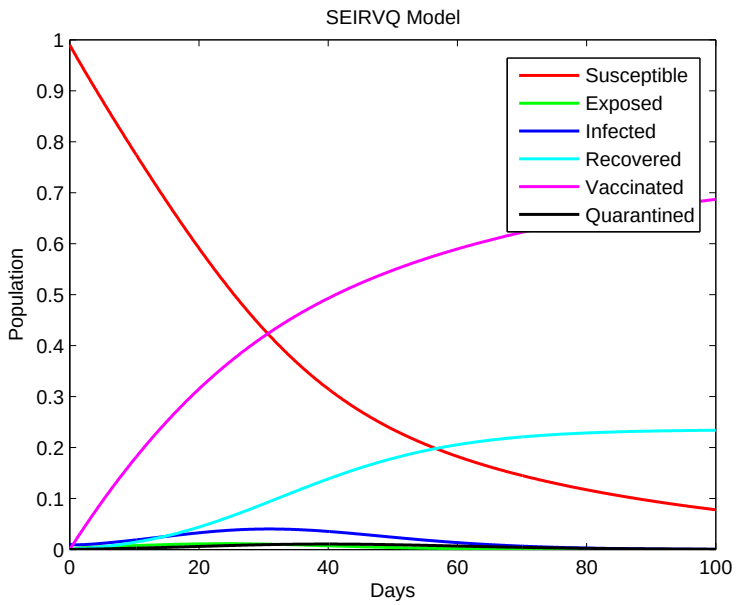

Figure 3.8: SEIRVQ model; $\beta = 0.3, \sigma = 0.5, \gamma = 0.1, \nu_1 = 0.02, \nu_2 = 0.01, \kappa = 0.03$.

the sub-system as follows:

$$\begin{pmatrix} \dot{E} \\ \dot{I} \\ \dot{Q} \end{pmatrix} = \Bigg[\underbrace{\begin{pmatrix} 0 & \beta & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}}_{T} - \underbrace{\begin{pmatrix} \nu_2 + \sigma & 0 & 0 \\ -\sigma & \gamma + \kappa & 0 \\ 0 & -\kappa & \gamma \end{pmatrix}}_{\Sigma} \Bigg] \begin{pmatrix} E \\ I \\ Q \end{pmatrix}$$

Again we calculate Σ^{-1} using purely epidemiological interpretation. The entry $\Sigma^{-1}_{1,1}$ corresponds to the time an individual currently in exposed state E will spend in exposed state E. Since such an individual now can leave with combined rate of $\sigma + \nu_2$ to either state I or V, the amount of time he/she spends in E will be equal to

$$\Sigma^{-1}_{1,1} = \frac{1}{\sigma + \nu_2}.$$

Similarly, the entry $\Sigma^{-1}_{2,2}$ describes the time an infected person stays in the infectious state I and is given by

$$\Sigma^{-1}_{2,2} = \frac{1}{\gamma + \kappa}.$$

The entries

$$\Sigma^{-1}_{1,2} = \Sigma^{-1}_{1,3} = \Sigma^{-1}_{2,3} = 0$$

since infected and quarantined persons cannot go back to the exposed state, and quarantined individuals cannot go back to infected state, respectively. The entry $\Sigma^{-1}_{2,1}$ represents the time an exposed individual will spend in infected state for the remainder of the outbreak, that is,

$$\Sigma^{-1}_{2,1} = \left(\frac{\sigma}{\sigma + \nu_2}\right) \cdot \left(\frac{1}{\gamma + \kappa}\right) = \frac{\sigma}{(\sigma + \nu_2)(\gamma + \kappa)}.$$

The first factor $\sigma/(\sigma + \nu_2)$ is the probability that an exposed individual will not be vaccinated, while the second factor $1/(\gamma + \kappa)$ is the duration of infectiousness of that person upon becoming infectious. Further, $\Sigma^{-1}_{3,1}$ describes the amount of time an exposed individual will spend in quarantine for the remainder of the outbreak. As before, a person in state E goes to state I with probability $\sigma/(\sigma + \nu_2)$, then gets quarantined with probability $\kappa/(\kappa + \gamma)$ and spends $1/\gamma$ in quarantine state. Hence,

$$\Sigma^{-1}_{3,1} = \left(\frac{\sigma}{\sigma + \nu_2}\right) \cdot \left(\frac{\kappa}{\kappa + \gamma}\right) \cdot \frac{1}{\gamma} = \frac{\sigma\kappa}{\gamma(\sigma + \nu_2)(\kappa + \gamma)}.$$

With similar reasoning, the amount of time an infected person spends in quarantine is given by

$$\Sigma_{3,2}^{-1} = \left(\frac{\kappa}{\kappa+\gamma}\right) \cdot \frac{1}{\gamma} = \frac{\kappa}{\gamma(\kappa+\gamma)}.$$

Finally,

$$\Sigma_{3,3}^{-1} = \frac{1}{\gamma}$$

since this entry describes the amount of time a quarantined person will spend in quarantined state for the remainder of the outbreak.

Multiplying the matrices T and Σ^{-1} gives the NGM

$$\begin{aligned} G = T\Sigma^{-1} &= \begin{pmatrix} 0 & \beta & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{\sigma+\nu_2} & 0 & 0 \\ \frac{\sigma}{(\sigma+\nu_2)(\gamma+\kappa)} & \frac{1}{\gamma+\kappa} & 0 \\ \frac{\sigma\kappa}{\gamma(\sigma+\nu_2)(\gamma+\kappa)} & \frac{\kappa}{\gamma(\kappa+\gamma)} & \frac{1}{\gamma} \end{pmatrix} \\ &= \begin{pmatrix} \frac{\beta\sigma}{(\sigma+\nu_2)(\gamma+\kappa)} & \frac{\beta}{\gamma+\kappa} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \end{aligned}$$

with dominant eigenvalue

$$\mathcal{R}_0 = \frac{\beta\sigma}{(\sigma+\nu_2)(\gamma+\kappa)}.$$

From the expression for $\mathcal{R}_0$ above, one can further observe that

$$\begin{aligned} \frac{\beta\sigma}{(\sigma+\nu_2)(\gamma+\kappa)} &= \frac{\beta\sigma}{\sigma(1+\frac{\nu_2}{\sigma})\gamma(1+\frac{\kappa}{\gamma})} \\ &= \frac{\beta}{\gamma}\frac{1}{(1+\frac{\nu_2}{\sigma})(1+\frac{\kappa}{\gamma})} \\ &< \frac{\beta}{\gamma}. \end{aligned}$$

The basic reproduction number for the SEIR model is β/γ. Using the same parameter values chosen earlier, the $\mathcal{R}_0$ for the SEIR model without interventions is $\beta/\gamma = 0.3/0.1 = 3$, while the SEIRVQ model has the basic reproduction number $\mathcal{R}_0 = \frac{(0.3)(0.5)}{(0.5+0.01)(0.1+0.03)} \approx 2.26$. This implies that for the same infection rate β and recovery rate γ, any control strategies can theoretically reduce the spread of the disease. The vaccination strategies would reduce the number of susceptibles, while the quarantine would reduce the number of infectives. As a consequence, the effective contacts between susceptible and infected persons would be reduced.

CHAPTER 4

Simulation Results

We have considered the intervention strategies of mass and ring vaccination (MV and RV) as well as quarantine for epidemic disease outbreaks. Each strategy was modeled and simulated on its own and in combination with other strategies. All simulations assume there are 1% initially infectious individuals (I(0)=0.01) in a fully susceptible population. The infection, incubation, and recovery rates remain the same for all simulations to maintain consistency, that is, $\beta = 0.3, \sigma = 0.5$ and $\gamma = 0.1$ respectively. For the vaccination strategies, we compare the combination of MV and RV in which $\nu_1 > \nu_2$ and $\nu_1 = \nu_2$ since they had the most significant effects on the epidemic. Figure 4.1 shows the number of infected individuals over time corresponding to each intervention strategy. It can be seen that the number is higher when no intervention is implemented, and that cumulative number is decreased as interventions are employed individually and in combination.

We simulate the mass and ring vaccination strategies in combination with each other, to illustrate their effectiveness when one program has higher vaccination rate than the other. For these strategies, we see that MV has the greatest effect on the total number of infected individuals. This is mainly due to the term $\nu_1 S$ in equation (2.7). It can be seen that this term reduces the overall "flow" of susceptible individuals to the exposed state, and in turn lowers the number of individuals that transition from

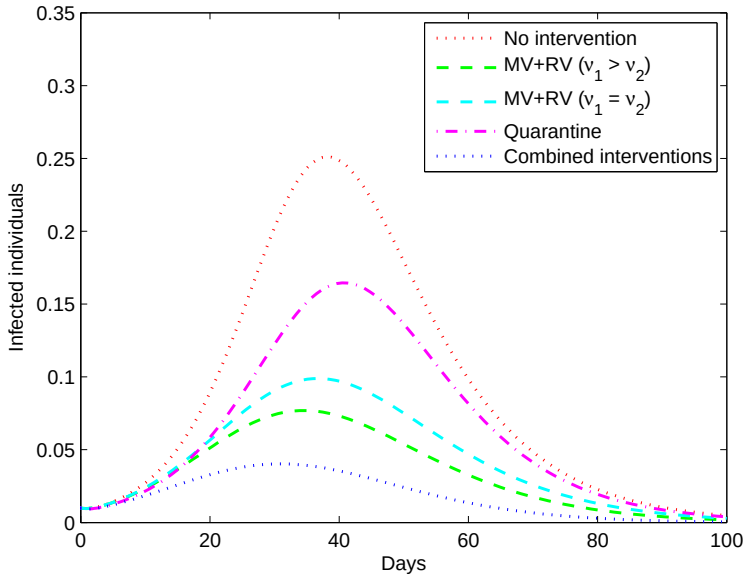

Figure 4.1: Number of infected individuals for various intervention strategies.

exposed to infected state. Conversely, RV focuses its efforts on tracing the contacts of infected persons who are thus considered to be in the exposed state. However, RV has little effect on the number of susceptible persons still coming into effective contact with an infectious person. That is, the term βSI in equation (3.3) is ungoverned by the intervention; since this term comes directly from interactions between susceptible and infected persons, the overall "flow" of individuals from susceptible (S) to exposed (E) state remains relatively unhindered, telling us that the number of infected individuals will remain relatively high. In fact, the total number of infected individuals remains higher than that of the mass vaccination strategy.

The quarantine intervention strategy is also simulated as before. Here we have that the term βSI is affected by the intervention, therefore reducing the number of effective contacts that occur between susceptible and infected individuals. However, the results show that even though this strategy directly targets individuals in the

infected state (I), the maximum number of individuals that still become infected remains higher than that of all combinations of vaccination strategies. This is mainly due to the rate at which persons are quarantined. Surely one could argue that a higher quarantine rate could have a more significant effect on I. Yet realistically one must also consider the capacity, the availability of resources and the effectiveness of the facilities being used for quarantine.

For each of the interventions the basic reproduction number, $\mathcal{R}_0$, is calculated. This is done to establish the validity of our argument that the value of $\mathcal{R}_0$ decreases as intervention strategies are implemented and combined. The $\mathcal{R}_0$ values for each different strategy are shown in Table 4.2 along with the peak of infected population I_{max}, the total number of infected individuals R_∞ and the total number of days until the end of the epidemic (days until $I(t) < 0.01$). Note that R_∞ is found by the relation $1 - S_\infty - V_\infty \approx R_\infty$ where $V_\infty = 0$ for the case of no intervention and quarantine only. For these models, no distinction is made between disease-related deaths and those who recovered successfully from the disease; both cases are grouped in the recovered compartment R.

Parameter	Value	Initial Values
β	0.3	$S(0) = 0.99$
σ	0.5	$E(0) = 0$
γ	0.1	$I(0) = 0.01$
ν_1	0.02 or 0.015	$R(0) = 0$
ν_2	0.01 or 0.015	$V(0) = 0$
κ	0.03	$Q(0) = 0$

Table 4.1: Combined intervention simulation values.

Table 4.1 shows the values of the parameters and initial conditions for the combined intervention model where ν_1 and ν_2 vary depending on the intervention

Intervention	$\mathcal{R}_0$	I_{max}	R_∞	Length of outbreak (days)
None	3	0.251	0.9351	91.3
Combined vacc. $(\nu_1 > \nu_2)$	2.94	0.0768	0.3447	78.2
Combined vacc. $(\nu_1 = \nu_2)$	2.91	0.0989	0.442	83.9
Quarantine	2.31	0.1645	0.8556	88.7
Combined $(\nu_1 > \nu_2)$	2.26	0.0402	0.234	64.6

Table 4.2: Numerical simulation results for intervention strategies.

combinations. It is important to mention that even though combined vaccinations with $\nu_1 > \nu_2$ was more effective than when $\nu_1 = \nu_2$ in reducing the total number of infected individuals, the value for $\mathcal{R}_0$ is larger in the case of high MV rate than in the case of equal rates. This is due to the expression for $\mathcal{R}_0$ in the vaccination strategies, $\mathcal{R}_0 = \frac{\sigma\beta}{\gamma(\sigma+\nu_2)}$. Both MV and RV strategies were simulated together and the overall vaccination rate $(\nu_1 + \nu_2)$ remained fixed for all vaccination scenarios. For this reason, we have that when MV has a higher rate $(\nu_1 > \nu_2)$ the expression for $\mathcal{R}_0$ has a smaller denominator versus when the rates are equal $(\nu_1 = \nu_2)$. The smaller denominator in the case of a high MV rate makes the value of $\mathcal{R}_0$ larger, whereas a larger denominator in the case of equal rates makes the value for $\mathcal{R}_0$ slightly smaller.

To further illustrate the results from our numerical simulations, we can consider looking at the cumulative number of individuals in the recovered state R as before. Figure 4.2 shows the number of recovered persons for each intervention strategy. As before, when no intervention is used, the total number of infected persons will be high and in turn so will the number of recovered persons. Similarly, quarantine

Intervention	$\mathcal{R}_0$	Value
None	β/γ	3
Vacc. $(\nu_1 > \nu_2)$	$\beta\sigma/\left(\gamma(\sigma+\nu_2)\right)$	2.94
Vacc. $(\nu_1 = \nu_2)$	$\beta\sigma/\left(\gamma(\sigma+\nu_2)\right)$	2.91
Quarantine	$\beta/\left(\gamma+\kappa\right)$	2.31
Combined $(\nu_1 > \nu_2)$	$\beta\sigma/\left((\gamma+\nu_2)(\gamma+\kappa)\right)$	2.26

Table 4.3: Expressions and values of $\mathcal{R}_0$ for intervention strategies.

has less of an effect on the epidemic and the number of recovered individuals remains high. Lastly, MV, RV and a combination of all strategies have the least amount of recovered individuals, indicating that the cumulative number of infected persons was low.

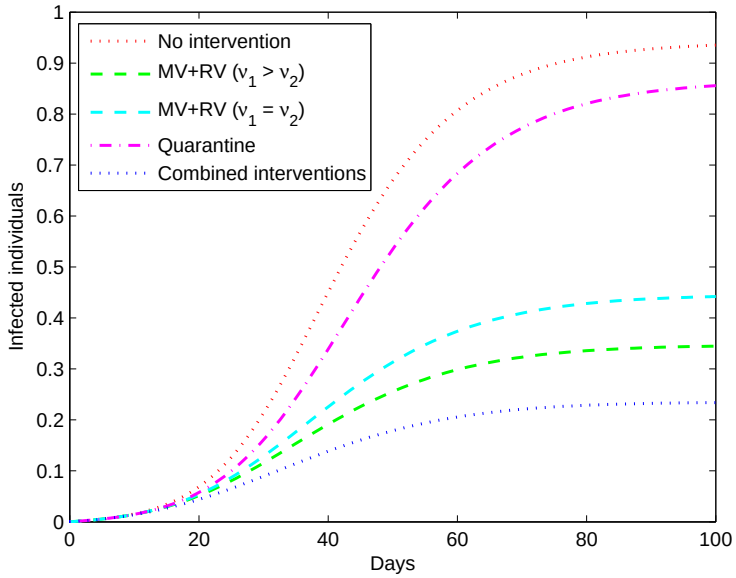

Figure 4.2: Number of recovered individuals for various intervention strategies.

4.1 Sensitivity Analysis

Because the parameters used in these models and simulations were rough estimates from epidemiological data, there is a degree of flexibility and uncertainty in their values which remains to be explored. The goal is to determine which parameter affects the result the most. Also in the case of having limited resources, sensitivity analysis can help deduce which intervention should be implemented with highest priority. Varying the values of the parameters showed that the all of the models discussed were sensitive to changes in the parameters as well as initial values.

The basic reproduction number $\mathcal{R}_0$ describes the average number of secondary cases of infection arising from one infectious individual. It was seen in the previous section that the implementation of intervention strategies in most cases reduces the value of $\mathcal{R}_0$, this is due to the changes made to its expression according to each strategy. In particular, as combinations of interventions are made, the expression for $\mathcal{R}_0$ describes a growing denominator value which of course leads to $\mathcal{R}_0$ decreasing in overall value since all rates are positive.

The number of initially infected individuals has a profound impact on an epidemic. Considering the basic SIR model we can refer to Figure 2.4 in which the different solution curves shown correspond to varying initially infected individuals. Increasing the number of initial cases while keeping all parameters fixed reduces the duration of the epidemic but also tends to increase the peak of the epidemic curve. For example we consider the initial values I(0)=0.4 so that S(0)=0.6. For this simulation we have that the number of infected persons reaches a max of I(4.3)$\approx$ 0.4707, and the epidemic dies out by day 40. Conversely, when I(0) = 0.99 and S(0)=0.01 a max of I(26)$\approx$ 0.3038 is reached and the epidemic dies out by day 77.

The infection rate β is a major governing parameter not only for $\mathcal{R}_0$ but for the epidemic overall. As we increased the value of β (while keeping all other parameters fixed) we saw a significant rise in the number of infected individuals as well as higher values for $\mathcal{R}_0$ in all models including those with intervention strategies. For example, in the SEIR model with $\beta = 0.4$ we have that $\mathcal{R}_0 = 4$ and I(29) $\approx$ 0.33. Conversely, when $\beta = 0.2$ we have a smaller reproduction number, $\mathcal{R}_0 = 2$, and an infected max of I(57)$\approx$ 0.13. The incubation rate was increased to illustrate the effect of diseases with

longer incubation/latent periods while all other parameters remained fixed. This had the effect of not only reducing the maximum number of infected but also prolonging the duration of the epidemic, namely I(76)$\approx$ 0.13 when $\sigma = 0.08$ as opposed to I(38)$\approx$ 0.25 when $\sigma = 0.5$ for the SEIR model.

Vaccination rates were varied by $\pm$5% and $\pm$10% while all other parameters remained fixed. The baseline reference simulation shows the effect when 100% of the current vaccination rates are used for each individual strategy. Vaccination rate simulations were run to show the effect of variations in use and availability of resources, and we can deduce from the results shown in Table 4.4 that the models are sensitive to changes in ν_1.

Scenario	value of ν_1	I_{max}	% of population infected
90%	0.018	0.0857	38.4 %
95%	0.019	0.08117	36.38 %
100%	0.02	0.0768	34.47 %
105%	0.021	0.07296	32.67 %
110%	0.022	0.0693	30.98 %

Table 4.4: Sensitivity of mass vaccination rate ν_1.

Similarly, we vary the vaccination rate ν_2 by $\pm$5% and $\pm$10% while keeping all other parameters fixed. The results in Table 4.5 show that the models are only slightly sensitive to changes in the values of ν_2.

Percentage used	value of ν_2	I_{max}	% of population infected
90%	0.018	0.1311	56.9 %
95%	0.019	0.1304	56.69 %
100%	0.02	0.1298	56.49 %
105%	0.021	0.1291	56.28 %
110%	0.022	0.1284	56.08 %

Table 4.5: Sensitivity of ring vaccination rate ν_2.

Quarantine rate κ was also varied in the same way as ν_1 and ν_2. From the results shown in Table 4.6 we see that the models are only slightly sensitive to changes in

the quarantine rate as well. The conclusion can be made that in the case of a limited amount of resources, priority should be given to the mass vaccination strategy and resources should be allocated accordingly.

Percentage used	value of κ	I_{max}	% of population infected
90%	0.027	0.1719	86.5 %
95%	0.0285	0.1682	86.04 %
100%	0.03	0.1645	85.56 %
105%	0.0315	0.1609	85.08 %
110%	0.033	0.1574	84.6 %

Table 4.6: Sensitivity of quarantine rate κ.

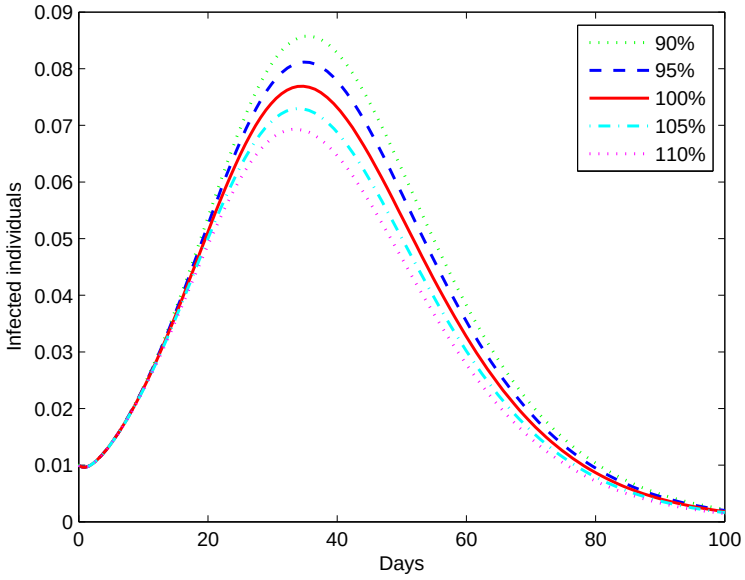

Figure 4.3: Sensitivity plot for ν_1.

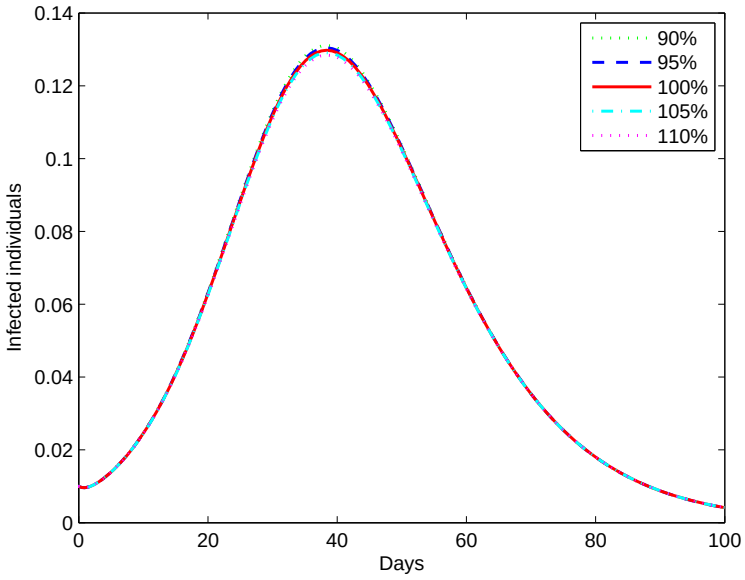

Figure 4.4: Sensitivity plot for ν_2.

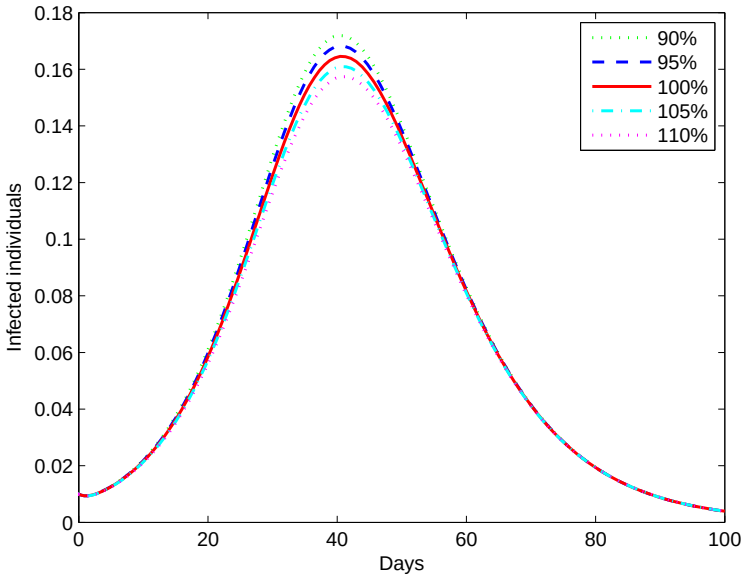

Figure 4.5: Sensitivity plot for κ.

CHAPTER 5

Comparing the Models to Case Studies

In order to test the intervention models we compare the output of the model to a case study using historical data published by the World Health Organization (WHO). It is necessary to test the models to determine how capable they are in predicting epidemics. Due to limited availability of detailed historical data on these epidemics, we consider a case study for which the susceptible population is relatively small and found in less developed areas. The method for testing the model against data collected from a case report of a smallpox outbreak in Nigeria is described below.

We begin by defining values such as total population size, average pre-infectious days (incubation period), average duration of infectiousness, $\mathcal{R}_0$, and the initial number of infected individuals. These values are estimated directly from [8, 23] as well as [12]. The incubation period for smallpox has been historically reported as lasting from 10-14 days; for this reason we take the incubation period to be 12 days. The duration of infectiousness for smallpox varies, depending on factors such as prior vaccination, so we estimate this time to be roughly 20 days. The value of $\mathcal{R}_0$ for smallpox also varies with the literature [7, 8, 10, 12], and so for this reason we take the value of $\mathcal{R}_0 = 6.87$ calculated in [12] specifically for this case report. Using these values, the contact rate β, infectious rate σ and recovery rate γ are estimated and the model is

run. The expressions used to estimate each parameter are defined in [24] as follows:

$$\beta = \frac{\mathcal{R}_0}{(\text{duration of infectiousness})(\text{total susceptible population})}$$

$$\sigma = \frac{1}{\text{average pre-infectious period}}$$

$$\gamma = \frac{1}{\text{duration of infectiousness}}$$

The reasoning behind these expressions can be shown with our previous understanding of the definition for $\mathcal{R}_0$ and the biological interpretations of each parameter.

We begin with β, which is defined as the rate at which two specific individuals come into effective contact per unit time. Here, "effective contact" is defined as a contact between a susceptible and infected individual sufficient enough to lead to the infection of the susceptible person. Let $D = 1/\gamma$ be the duration of infection, then $\frac{\mathcal{R}_0}{D}$ is the number of effective contacts made by each person per unit time. From this it follows that $\frac{\frac{\mathcal{R}_0}{D}}{N}$ is the number of per capita effective contacts made by an individual per unit time. That is, $\frac{\frac{\mathcal{R}_0}{D}}{N} = \frac{\mathcal{R}_0}{ND} = \beta$. Similarly, we know that σ is defined as the average rate of onset of infectiousness per unit time and γ is the average recovery rate per unit time, just as they are defined above.

5.1 Abakaliki, Nigeria: A Smallpox Epidemic Case Study

In the last weeks of May of 1967 a case of smallpox was reported in Abakaliki, an urban trading town in Nigeria. Abakaliki was the site of a mass vaccination program which successfully vaccinated at least 88.5% of the entire population in February of that same year. The striking occurrence of a case of smallpox was elucidated by

the fact that it occurred among a religious group, Faith Tabernacle, a group which steadfastly refuses any preventative or curative health services [23]. Thirty of the thirty-two cases reported during the twelve week period occurred among members of the Faith Tabernacle group. Because of their religious beliefs, the group members remained somewhat isolated from the rest of the community with which they resided.

The origins of this outbreak were traced back to a ten-year-old girl who was brought from a nearby village where a severe smallpox outbreak had occurred just months before; when she reached Abakaliki she was showing symptoms of a fever. Over the course of the next two to three weeks she developed the pustular rashes which are the clinical signs of a case of smallpox. Approximately two weeks later, an individual living in the same housing compound developed similar symptoms and rashes. The disease first spread among family members, those in close contact with infected individuals, and then progressed to secondary contacts at church meetings or during interactions in the town market. Over the course of roughly twelve weeks the outbreak spread to nine other housing compounds in Abakaliki and 32 confirmed cases were reported overall.

Week:	1	2	3	4	5	6	7	8	9	10	11	12
Cases reported:	1	0	1	2	5	1	5	3	6	4	3	1

Table 5.1: Weekly reported cases of smallpox in 1967 in Abakaliki, Nigeria.

To fit the intervention models to the recorded data from this outbreak we consider a delayed intervention approach in three stages. In accordance with the case report, the quarantine intervention did not begin until the 11^{th} case was discovered and vaccination did not begin until the 21^{st} case. We consider that a small percentage

of infected individuals initially remained isolated in their households during the first stage and so we begin the model with a low quarantine rate κ. We use the data generated by the model as initial values for the second stage model with high κ, indicating when the WHO discovered the 11^{th} case and implemented a strict quarantine intervention. Similarly, the output data from the second stage model is used as initial values for the combined intervention model (third stage) in which vaccination is implemented along with quarantine. The values $\beta \approx 0.011565657$, $\sigma \approx 0.0833333333$, and $\gamma \approx 0.05$ remain the same for all three stages. In Stage two, we have that $Q(0) \approx 21.24$ (90% of infected persons at day 38). Similarly, in Stage three we have that $V(0) \approx 158.4$ (90% of 176 susceptible non-Faith Tabernacle Church members living in compounds with church members) as specified in the case report.

The case data is shown as a cumulative number of cases and is displayed as a bar graph in Figure 5.1 along with the model predictions. We see that the models predict the recorded data closely; see Table 5.3 for case study data. The discrepancies in the recorded data and model prediction arise from several factors. One of these is the non-homogeneity in the population due to the fact that Faith-Tabernacle Church members lived together in clusters and only encountered non-members in marketplaces and other public places. Furthermore, the fact that some of the first people to become infected recovered by day 50 explains the gap between the second stage model prediction and the recorded data.

Some important things to note about this case are the spread of the disease and its behavior in regards to intervention strategies. As individuals became infected they were advised to remain in their homes. This, however, was simply advice and

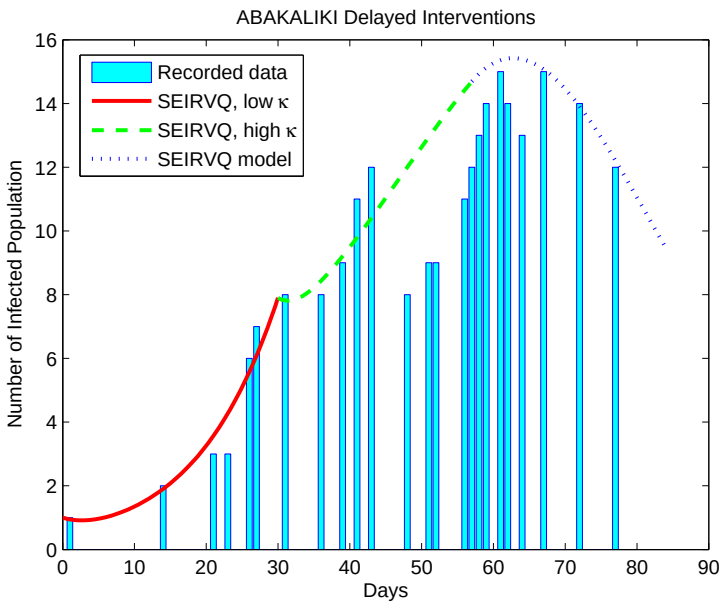

Figure 5.1: Abakaliki Smallpox outbreak.

was not enforced by any health organization. Furthermore, infectious persons who remained at home still posed a threat to those who resided in the household and compound. It was not until the WHO began intervening that newly infected persons were strictly isolated in hospitals. This was the only intervention to which Faith Tabernacle Church members conceded. Though a few individuals living in the compounds in which smallpox cases occurred were previously vaccinated, the frequency of close contact with those infected still lead them to become infected themselves. This suggests that transmission could still occur in a population where the overall number of vaccinated individuals is high, given that there is a small group of poorly-protected individuals among them. For this reason, it is not advisable to accept any percentage of vaccination coverage of a population as being high enough to stop the spread of smallpox when there is non-homogenous mixing within the population [23].

	Parameter values	Initial values
Stage 1	$\nu_1 = 0$ $\nu_2 = 0$ $\kappa = 0.02$	$S(0) = 297$ $E(0) = 0$ $I(0) = 1$ $R(0) = 0$ $V(0) = 0$ $Q(0) = 0$
Stage 2	$\nu_1 = 0$ $\nu_2 = 0$ $\kappa = 0.125$	$S(0) \approx 269.35$ $E(0) \approx 14.83$ $I(0) \approx 7.90$ $R(0) \approx 4.78$ $V(0) = 0$ $Q(0) \approx 21.24$
Stage 3	$\nu_1 = 0.025$ $\nu_2 = 0.015$ $\kappa = 0.125$	$S(0) \approx 193$ $E(0) \approx 34.04$ $I(0) \approx 14.69$ $R(0) \approx 49.82$ $V(0) \approx 158.4$ $Q(0) \approx 26.96$

Table 5.2: Case study simulation values.

Date	Cases Reported	Total Infected	Intervention
Apr 5	1	1	Low Quarantine
Apr 18	1	2	.
Apr 25	1	3	.
Apr 27	1	3	.
Apr 30	3	6	.
May 1	1	7	.
May 5	1	8	.
May 10	1	8	.
May 13	1	9	High Quarantine
May 15	2	11	.
May 17	2	12	.
May 22	1	8	.
May 25	1	9	.
May 26	1	9	.
May 30	2	11	.
May 31	2	12	Vaccination/Quarantine
Jun 1	1	13	.
Jun 2	1	14	.
Jun 4	2	15	.
Jun 5	1	14	.
Jun 7	1	13	.
Jun 10	2	15	.
Jun 15	1	14	.
Jun 20	1	12	.

Table 5.3: Case study data.

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APPENDIX A

Numerical Solution to Ordinary Differential Equations

In this appendix we discuss some well-known numerical methods for solving a system of ordinary differential equations (ODEs) with some initial values, also known as *initial value problems* (IVP). It is important to note that the numerical methods used to solve IVPs do not yield a continuous solution but rather approximations to the solution are found at certain equally spaced points.

A.1 Euler's Method

Euler's method is the most elementary approximation technique for solving an IVP [5]. We will take advantage of the simplicity of its derivation as a basis for discussing more advanced methods.

The main goal of Euler's method is to obtain numerical approximations to the IVP

$$\frac{dy}{dt} = f(t, y), \qquad a \leq t \leq b, \qquad y(a) = \alpha \tag{A.1}$$

As stated before, the approximations will be obtained at specific equally spaced points in the interval $[a, b]$ on which our function is being considered. We define each specific point by

$$t_i = a + h, \qquad \text{for all } i = 0, 1, 2, \ldots, N \tag{A.2}$$

where h is the **step size**, or distance between each points, defined by $h = (b-a)/N$. Denote the solution to (A.1) by $y(t)$ and suppose that $y(t)$ has continuous second derivatives on the interval $[a, b]$. Then by Taylor's Theorem we have that

$$y(t_{i+h}) = y(t_i) + (t_{i+h} - t_i)y'(t_i) + \frac{(t_{i+h} - t_i)^2}{2!}y''(\xi_i), \qquad \xi_i \in (t_i, t_{i+1}).$$

Furthermore,

$$y(t_{i+1}) = y(t_i) + hf(t_i, y(t_i)) + \frac{h^2}{2}y''(\xi_i) \tag{A.3}$$

since $y(t)$ is the solution to (A.1).

Now, let ω_i be an approximate solution at t_i, that is

$$\omega_i \approx y(t_i), \text{ for all } i = 0, 1, 2, \ldots, N. \tag{A.4}$$

Assuming that h is small, we omit the remainder term $\frac{h^2}{2}y''(\xi_i)$ and obtain Euler's method:

$$\begin{aligned} \omega_0 &= \alpha, \\ \omega_{i+1} &= \omega_i + hf(t_i, w_i) \qquad \text{for all } i = 0, 1, \ldots, N-1. \end{aligned} \tag{A.5}$$

The remainder term $\tau = \frac{h^2}{2}y''(\xi_i)$ is also known as the *local truncation error*. In other words, τ is the error committed at each step and it is proportional to h^2. Recall that the number of steps is determined by $\frac{t-t_0}{h}$, which is proportional to $1/h$. Then we

have that the *global truncation error* is proportional to $\frac{h^2}{h} = h$. This tells us that the truncation error grows linearly and so we say that Euler's method has order $\mathcal{O}(h)$. By retaining more terms in the Taylor series expansion of the solution $y(t)$ to an IVP we can derive methods that have a higher order of accuracy.

A.2 Runge-Kutta Methods

One of the goals in using numerical methods for solving IVPs is to obtain accurate solutions that are computationally inexpensive. Runge-Kutta methods are among the best known methods for solving IVP due to the fact that they do not require the computation and evaluation of derivatives of the function $f(t, y)$, as opposed to Taylor methods [5]. Runge-Kutta methods were first studied by Carle Runga and Martin Kutta around the year 1901, with more modern developments brought about by John Butcher in the 1960's [6].

A.2.1 Second Order Runge-Kutta Method

Consider a system of ODEs

$$\mathbf{y}'(t) = \mathbf{f}(t, \mathbf{y}(t)). \tag{A.6}$$

As before, we begin with the Taylor expansion

$$\mathbf{y}(t+h) = \mathbf{y}(t) + h\mathbf{y}'(t) + \frac{h^2}{2}\mathbf{y}''(t) + \mathcal{O}(h^3). \tag{A.7}$$

Differentiating (A.6) and using substitution we have

$$\begin{aligned}\mathbf{y}''(t) &= \mathbf{f}_t(t,\mathbf{y}) + \mathbf{f}_\mathbf{y}(t,\mathbf{y})\mathbf{y}'(t) \\ &= \mathbf{f}_t(t,\mathbf{y}) + \mathbf{f}_\mathbf{y}(t,\mathbf{y})\mathbf{f}(t,\mathbf{y})\end{aligned}$$

where $\mathbf{f}_\mathbf{y}$ is the partial derivative of $\mathbf{f}$ with respect to $\mathbf{y}$. We then obtain

$$\begin{aligned}\mathbf{y}(t+h) &= \mathbf{y}(t) + h\mathbf{f}(t,\mathbf{y}) + \frac{h^2}{2}[\mathbf{f}_t(t,\mathbf{y}) + \mathbf{f}_\mathbf{y}(t,\mathbf{y})\mathbf{f}(t,\mathbf{y})] + \mathcal{O}(h^3) \\ &= \mathbf{y}(t) + \frac{h}{2}\mathbf{f}(t,\mathbf{y}) + \frac{h}{2}[\mathbf{f}(t,\mathbf{y}) + h\mathbf{f}_t(t,\mathbf{y}) + h\mathbf{f}_\mathbf{y}(t,\mathbf{y})\mathbf{f}(t,\mathbf{y})] + \mathcal{O}(h^3) \qquad \text{(A.8)}\end{aligned}$$

Now, considering the multi-variable Taylor expansion

$$\mathbf{f}(t+h,\mathbf{y}+k) = \mathbf{f}(t,\mathbf{y}) + h\mathbf{f}_t(t,\mathbf{y}) + k\mathbf{f}_\mathbf{y}(t,\mathbf{y}) + \frac{1}{2}[h^2\mathbf{f}_{tt}(t,\mathbf{y}) + 2hk\mathbf{f}_{t\mathbf{y}}(t,\mathbf{y}) + k^2\mathbf{f}_{\mathbf{yy}}(t,\mathbf{y})] + \ldots$$

we can rewrite (A.6) as

$$\mathbf{f}(t+h,\mathbf{y}+h\mathbf{f}(t,\mathbf{y})) = \mathbf{f}(t,\mathbf{y}) + h\mathbf{f}_t(t,\mathbf{y}) + h\mathbf{f}_\mathbf{y}(t,\mathbf{y})\mathbf{f}(t,\mathbf{y}) + \mathcal{O}(h^2)$$

and therefore

$$\mathbf{y}(t+h) = \mathbf{y}(t) + \frac{h}{2}\mathbf{f}(t,\mathbf{y}) + \frac{h}{2}\mathbf{f}(t+h,\mathbf{y}+h\mathbf{f}(t,\mathbf{y})) + \mathcal{O}(h^3)$$

or more simply

$$\mathbf{y}_{n+1} = \mathbf{y}_n + \frac{h}{2}(k_1 + k_2) \tag{A.9}$$

where

$$k_1 = \mathbf{f}(t_n, \mathbf{y}_n)$$

$$k_2 = \mathbf{f}(t_{n+1}, \mathbf{y}_n + hk_1).$$

The numerical method (A.9) is known as the classical second-order Runge-Kutta method.

A.2.2 Fourth-Order Runge-Kutta Method

The fourth-order Runge-Kutta method (RK4) can be derived using the same approach as the second-order method. This time, however, we define

$$\mathbf{y}_{n+1} = \mathbf{y}_n + h\left[\frac{k_1}{6} + \frac{k_2}{3} + \frac{k_3}{3} + \frac{k_4}{6}\right] \tag{A.10}$$

where

$$
\begin{aligned}
k_1 &= \mathbf{f}(t_n, \mathbf{y}_n) \\
k_2 &= \mathbf{f}\left(t_n + \frac{h}{2}, \mathbf{y}_n + k_1\frac{h}{2}\right) \\
k_3 &= \mathbf{f}\left(t_n + \frac{h}{2}, \mathbf{y}_n + k_2\frac{h}{2}\right) \\
k_4 &= \mathbf{f}(t_{n+1}, \mathbf{y}_n + k_3 h).
\end{aligned}
$$

The global error for RK4 is $\mathcal{O}(h^4)$. Since the goal of many numerical methods is to obtain a desired accuracy to the solution of an IVP with the fewest number of computations, it makes sense that RK4 is a more desirable method in contrast to Euler's method. This is further reinforced by the fact that RK4 allows the use of a larger step size h that still satisfies accuracy conditions but results in fewer computations, even though RK4 requires more function evaluations per step.

APPENDIX B

MATLAB Code

```
%%%%%%%%%%%%%%%%%%%%%%% sir.m %%%%%%%%%%%%%%%%%%%%%%%
function sir = sir(t,y)
% infection rate
     beta = 0.3;
%      beta = 0.08;
% recovery rate
     gamma = .1;
%dS/dt
    sir(1) = -beta*y(1)*y(2);
%dI/dt
    sir(2) = beta*y(1)*y(2)-gamma*y(2);
%dR/dt
    sir(3) = gamma*y(2);
    sir = [sir(1), sir(2), sir(3)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%%% SIRmodel.m %%%%%%%%%%%%%%%%%%%%%%%
clear all;
format long;
% INITIAL [Susceptible, Infected, Recovered]
yo = [0.99,0.01,0];
%%%%%%%%%%%%%%%%%%%    4th Order Runge-Kutta     %%%%%%%%%%%%%%%%%%%
    [t, w] = RK4E(0,80,1000,yo);
    plot(t,w(1,:),'r','LineWidth',1.5);
    hold on
    plot(t,w(2,:),'g','LineWidth',1.5);
    plot(t,w(3,:),'b','LineWidth',1.5);
%%%%%%%%%%%%%%%%%%%            Plots             %%%%%%%%%%%%%%%%%%%
title('SIR Model')
xlabel('Days')
ylabel('Population')
legend ('Susceptible','Infected','Recovered' )
```

```
%%%%%%%%%%%%%%%%%%%%%%% pplaneSIR.m %%%%%%%%%%%%%%%%%%%%%%%
figure;
%%%% Vector field %%%%
[x,z]=meshgrid(0:.05:1,0.001:.05:1);
dx = -(0.3).*x.*z;
dz = (0.3).*x.*z - (0.1).*z;
```

```
dxn = dx./sqrt(dx.^2 + dz.^2);
dzn = dz./sqrt(dx.^2 + dz.^2);
q = quiver(x,z,dxn,dzn);
xlabel('Susceptible')
ylabel('Infected')
title('Phase Plane for SIR model')
xlim([0 1]);
ylim([0 1]);
%%%% Solution Curves %%%%
hold on
to = 0;
tf = 100;
%%% Initial Values
        %%% Ro > 1
    yo = [.99, .001, .2];
    vo = [.4, .6, 0];
    wo = [.75, .25, 0];
    so = [.25, .75 , 0];
    uo = [.6, .4, 0];
        %%% Ro < 1
%     uo=[0.2, 0.8, 0];
%     vo=[0.4, 0.6, 0];
%     wo=[0.6, 0.4, 0];
%     so=[0.8, 0.2, 0];
%     yo=[0.5, 0.5, 0];
%%% Different initial values, same infection and recovery rates
[t, s] = ode45('sir', [to, tf], so);
[t, u] = ode45('sir', [to, tf], uo);
[t, v] = ode45('sir', [to, tf], vo);
[t, w] = ode45('sir', [to, tf], wo);
[t, y] = ode45('sir', [to, tf], yo);
%%% Plots
p = plot(y(:,1),y(:,2),'r','LineWidth',1.5);
m = plot(u(:,1),u(:,2),'r');
n = plot(v(:,1),v(:,2),'r');
l = plot(w(:,1),w(:,2),'r');
j = plot(s(:,1),s(:,2),'r');
k = plot([1 0],[0 1],'k');
%%% Threshold value line
 r = plot([.3333 .3333],[0 .6670],'b--', 'LineWidth',1.5);
legend([q,p,m,r],'direction vectors','Infected vs. ...
    Susceptible','other solutions','threshold value')
% legend([q,p,m],'direction vectors','Infected vs. ...
    Susceptible','other solutions')
```

```
%%%%%%%%%%%%%%%%%%%%%%% seir.m %%%%%%%%%%%%%%%%%%%%%%%
function seir = seir(t,u)
%infection rate
beta = 0.3;
%incubation rate
sigma = 0.5;
%recovery rate
```

```
gamma = 0.1;
%initial population size
N = 1;
%dS/dt
seir(1) = - beta*((u(1)*u(3))/N);
%dE/dt
seir(2) = beta*(u(1)*u(3))/N - sigma*u(2);
%dI/dt
seir(3) = sigma*u(2) - gamma*u(3);
%dR/dt
seir(4) = gamma*u(3);

seir = [seir(1), seir(2), seir(3), seir(4)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%%% SEIRmodel.m %%%%%%%%%%%%%%%%%%%%%%%
clear all;
format long;
% INITIAL [Susceptible, Exposed, Infected, Recovered]
yo = [0.99, 0, 0.01, 0];
%%%%%%%%%%%%%%%%%%%%    4th Order Runge-Kutta     %%%%%%%%%%%%%%%%%%%%
    [t, w] = RK4E(0,100,1000,yo);
    plot(t,w(1,:),'r','LineWidth',1.5);
%     hold on;
    plot(t,w(2,:),'g','LineWidth',1.5);
    hold on
    plot(t,w(3,:),'b','LineWidth',1.5);
    plot(t,w(4,:),'c','LineWidth',1.5);
%%%%%%%%%%%%%%%%%%%%                                  %%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%%%%%            Plots                 %%%%%%%%%%%%%%%%%%%%
title('SEIR Model')
xlabel('Days')
ylabel('Population')
% legend ('Susceptible','Exposed','Infected','Recovered')
legend ('Exposed','Infected','Recovered')
```

```
%%%%%%%%%%%%%%%%%%%%%%% SEIRVmodel.m %%%%%%%%%%%%%%%%%%%%%%%
clear all;
format long;
to = 0;
tf = 100;
% INITIAL [Susceptible, Exposed, Infected, Recovered, Vaccinated]
yo = [0.99, 0, 0.01, 0, 0];
%%%%%%%%%%%%%%%%%%%%            ODE45                 %%%%%%%%%%%%%%%%%%%%
    [t, y] = ode45('massvacc', [to, tf], yo);
%     [t, y] = ode45('ringvacc', [to, tf], yo);
    plot(t,y(:,1),'r','LineWidth',1.5);
    hold on;
    plot(t,y(:,2),'g','LineWidth',1.5);
    plot(t,y(:,3),'b','LineWidth',1.5);
    plot(t,y(:,4),'c','LineWidth',1.5);
```

```
    plot(t,y(:,5),'m','LineWidth',1.5);
%%%%%%%%%%%%%%%%%%%            Plots              %%%%%%%%%%%%%%%%%%%
title('SEIRV Model')
xlabel('Days')
ylabel('Population')
legend ('Susceptible','Exposed','Infected','Recovered', 'Vaccinated')
```

```
%%%%%%%%%%%%%%%%%%%%%% equalvacc.m %%%%%%%%%%%%%%%%%%%%%%
function equalvacc = equalvacc(t,a)
%infection rate
beta = 0.3;
%rate E becomes I
sigma = 0.5;
%recovery rate
gamma = 0.1;
%vaccination rates (equal)
nu1 = 0.015;
nu2 = 0.015;
%initial population size
N = 1;
%dS/dt
equalvacc(1) = - beta*((a(1)*a(3))/N) - nu1*(a(1));
%dE/dt
equalvacc(2) = beta*((a(1)*a(3))/N) - a(2)*(sigma + nu2);
%dI/dt
equalvacc(3) = sigma*a(2) - gamma*a(3);
%dR/dt
equalvacc(4) = gamma*a(3);
%dV/dt
equalvacc(5) = nu1*a(1) + nu2*a(2);

equalvacc = [equalvacc(1), equalvacc(2), equalvacc(3), ...
    equalvacc(4), equalvacc(5)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%% massvacc.m %%%%%%%%%%%%%%%%%%%%%%
function massvacc = massvacc(t,b)
%infection rate
beta = 0.3;
%rate E becomes I
sigma = 0.5;
%recovery rate
gamma = 0.1;
%vaccination rates (higher mass vaccination)
nu1 = 0.02;
nu2 = 0.01;
%initial population size
N = 1;
%dS/dt
massvacc(1) = - beta*((b(1)*b(3))/N) - nu1*(b(1));
%dE/dt
```

```
massvacc(2) = beta*((b(1)*b(3))/N) - b(2)*(sigma + nu2);
%dI/dt
massvacc(3) = sigma*b(2) - gamma*b(3);
%dR/dt
massvacc(4) = gamma*b(3);
%dV/dt
massvacc(5) = nu1*b(1) + nu2*b(2);

massvacc = [massvacc(1), massvacc(2), massvacc(3), massvacc(4), ...
    massvacc(5)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%% Massonly.m %%%%%%%%%%%%%%%%%%%%%%
function Massonly = Massonly(t,d)
%infection rate
beta = 0.3;
%rate E becomes I
sigma = 0.5;
%recovery rate
gamma = 0.1;
%vaccination rates (mass vacc only)
nu1 = 0.03;
nu2 = 0;
%initial population size
N = 1;
%dS/dt
Massonly(1) = - beta*((d(1)*d(3))/N) - nu1*(d(1));
%dE/dt
Massonly(2) = beta*((d(1)*d(3))/N) - d(2)*(sigma + nu2);
%dI/dt
Massonly(3) = sigma*d(2) - gamma*d(3);
%dR/dt
Massonly(4) = gamma*d(3);
%dV/dt
Massonly(5) = nu1*d(1) + nu2*d(2);

Massonly = [Massonly(1), Massonly(2), Massonly(3), Massonly(4), ...
    Massonly(5)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%% ringvacc.m %%%%%%%%%%%%%%%%%%%%%%
function ringvacc = ringvacc(t,c)
%infection rate
beta = 0.3;
%rate E becomes I
sigma = 0.5;
%recovery rate
gamma = 0.1;
%vaccination rates (higher ring vaccination)
nu2 = 0.02;
nu1 = 0.01;
```

```
%initial population size
N = 1;
%dS/dt
ringvacc(1) = - beta*((c(1)*c(3))/N) - nu1*(c(1));
%dE/dt
ringvacc(2) = beta*((c(1)*c(3))/N) - c(2)*(sigma + nu2);
%dI/dt
ringvacc(3) = sigma*c(2) - gamma*c(3);
%dR/dt
ringvacc(4) = gamma*c(3);
%dV/dt
ringvacc(5) = nu1*c(1) + nu2*c(2);

ringvacc = [ringvacc(1), ringvacc(2), ringvacc(3), ringvacc(4), ...
    ringvacc(5)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%% Ringonly.m %%%%%%%%%%%%%%%%%%%%%%
function Ringonly = Ringonly(t,e)
%infection rate
beta = 0.3;
%rate E becomes I
sigma = 0.5;
%recovery rate
gamma = 0.1;
%vaccination rates (ring vacc only)
nu1 = 0;
nu2 = 0.03;
%initial population size
N = 1;
%dS/dt
Ringonly(1) = - beta*((e(1)*e(3))/N) - nu1*(e(1));
%dE/dt
Ringonly(2) = beta*((e(1)*e(3))/N) - e(2)*(sigma + nu2);
%dI/dt
Ringonly(3) = sigma*e(2) - gamma*e(3);
%dR/dt
Ringonly(4) = gamma*e(3);
%dV/dt
Ringonly(5) = nu1*e(1) + nu2*e(2);

Ringonly = [Ringonly(1), Ringonly(2), Ringonly(3), Ringonly(4), ...
    Ringonly(5)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%% Vaccs.m %%%%%%%%%%%%%%%%%%%%%%
clear all;
format long;
to = 0;
tf = 100;
%initial conditions
```

```
bo = [0.99, 0, 0.01, 0, 0];

[t, d] = ode45('Massonly', [to, tf], bo);
plot(t,d(:,4),'--b','LineWidth',1.5);
hold on;
[t, e] = ode45('Ringonly', [to, tf], bo);
plot(t,e(:,4),'--c','LineWidth',1.5);
[t, b] = ode45('massvacc', [to, tf], bo);
plot(t,b(:,4),':r','LineWidth',1.5);
[t, c] = ode45('ringvacc', [to, tf], bo);
plot(t,c(:,4),':m','LineWidth',1.5);
[t, a] = ode45('equalvacc', [to, tf], bo);
plot(t,a(:,4),'g','LineWidth',1.5);

title('Vaccination strategies')
xlabel('Days')
ylabel('Recovered individuals')
legend ('MV only','RV only','Combined (\nu_1 > \nu_2)','Combined ...
    (\nu_1 < \nu_2)','Combined (\nu_1 = \nu_2)')
```

```
%%%%%%%%%%%%%%%%%%%%%% seirq.m %%%%%%%%%%%%%%%%%%%%%%
function seirq = seirq(t,x)
%infection rate
beta = 0.3;
% beta = 0.0011565657; % Abakaliki
%rate at which exposed becomes infected
sigma = 0.5;
% sigma = 0.0833333333; % Abakaliki
%recovery rate
gamma = 0.1;
% gamma = 0.05; % Abakaliki
%quarantine rate
kappa = 0.03;
% kappa = 0.4; % Abakaliki
%initial population size
N = 1;
%dS/dt
seirq(1) = - beta*((x(1)*x(3))/N);
%dE/dt
seirq(2) = beta*((x(1)*x(3))/N) - sigma*x(2);
%dI/dt
seirq(3) = sigma*x(2) - (gamma + kappa)*x(3);
%dR/dt
seirq(4) = gamma*(x(3) + x(5));
%dQ/dt
seirq(5) = kappa*x(3) - gamma*x(5);
seirq = [seirq(1), seirq(2), seirq(3), seirq(4), seirq(5)]';
end
```

```
clear all;
format long;
```

```
% INITIAL [Susceptible, Exposed, Infected, Recovered, Quarantined]
yo = [0.99, 0, 0.01, 0, 0];
%%%%%%%%%%%%%%%%%%%    4th Order Runge-Kutta     %%%%%%%%%%%%%%%%%%%
     [t, w] = RK4E(0, 100, 1000, yo);
    plot(t,w(1,:),'r','LineWidth',1.5);
    hold on;
    plot(t,w(2,:),'g','LineWidth',1.5);
    plot(t,w(3,:),'b','LineWidth',1.5);
    plot(t,w(4,:),'c','LineWidth',1.5);
    plot(t,w(5,:),'k','LineWidth',1.5);
%%%%%%%%%%%%%%%%%%%            Plots             %%%%%%%%%%%%%%%%%%%
title('SEIRQ Model')
xlabel('Days')
ylabel('Population')
legend ('Susceptible','Exposed','Infected','Recovered', ...
    'Quarantined')
```

```
%%%%%%%%%%%%%%%%%%%%%%% seirvq.m %%%%%%%%%%%%%%%%%%%%%%%
function seirvq = seirvq(t,z)
%infection rate
beta = 0.3;
% beta = 0.0011565657; % Abakaliki
%rate at which E becomes I
sigma = 0.5;
% sigma = 0.0833333333; % Abakaliki
%recovery rate
gamma = 0.1;
% gamma = 0.05; % Abakaliki
%vaccination rates
nu1 = 0.02;
nu2 = 0.01;
% nu1 = 0.4; % Abakaliki
% nu2 = 0.25; % Abakaliki
%quarantine rate
kappa = 0.03;
% kappa = 0.3; % Abakaliki
%initial population size
N = 1;
%dS/dt
seirvq(1) = - beta*((z(1)*z(3))/N) - z(1)*nu1;
%dE/dt
seirvq(2) = beta*((z(1)*z(3))/N) - z(2)*(sigma + nu2);
%dI/dt
seirvq(3) = sigma*z(2) - (gamma + kappa)*z(3);
%dR/dt
seirvq(4) = gamma*(z(3) + z(6));
%dV/dt
seirvq(5) = nu1*z(1) + nu2*z(2);
%dQ/dt
seirvq(6) = kappa*z(3) - gamma*z(6);

```

```
seirvq = [seirvq(1), seirvq(2), seirvq(3), seirvq(4), seirvq(5), ...
    seirvq(6)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%% SEIRVQmodel.m %%%%%%%%%%%%%%%%%%%%%%
clear all;
format long;
% INITIAL [Susceptible, Exposed, Infected, Recovered, Vaccinated, ...
    Quarantined]
yo = [0.99, 0, 0.01, 0, 0, 0];
%%%%%%%%%%%%%%%%%%    4th Order Runge-Kutta     %%%%%%%%%%%%%%%%%%
    [t, w] = RK4E(0, 100, 1000, yo);
    plot(t,w(1,:),'r','LineWidth',1.5);
    hold on;
    plot(t,w(2,:),'g','LineWidth',1.5);
    plot(t,w(3,:),'b','LineWidth',1.5);
    plot(t,w(4,:),'c','LineWidth',1.5);
    plot(t,w(5,:),'m','LineWidth',1.5);
    plot(t,w(6,:),'k','LineWidth',1.5);
%%%%%%%%%%%%%%%%%%            Plots             %%%%%%%%%%%%%%%%%%
title('SEIRVQ Model')
xlabel('Days')
ylabel('Population')
legend ...
    ('Susceptible','Exposed','Infected','Recovered','Vaccinated','Quarantined')
```

```
%%%%%%%%%%%%%%%%%%%%%% Interventions.m %%%%%%%%%%%%%%%%%%%%%%
clear all;
format long;
to = 0;
tf = 100;
% Initial Conditions
ao = [0.99, 0, 0.01, 0];
bo = [0.99, 0, 0.01, 0, 0];
do = [0.99, 0, 0.01, 0, 0, 0];
% Solve each model
[t, a] = ode45('seir', [to, tf], ao);
plot(t,a(:,4),':r','LineWidth',1.5);
hold on;
[t, b] = ode45('massvacc', [to, tf], bo);
plot(t,b(:,4),'--g','LineWidth',1.5);
[t, c] = ode45('equalvacc', [to, tf], bo);
plot(t,c(:,4),'--c','LineWidth',1.5);
[t, d] = ode45('seirq', [to, tf], bo);
plot(t,d(:,4),'-.m','LineWidth',1.5);
[t, e] = ode45('seirvq', [to, tf], do);
plot(t,e(:,4),':b','LineWidth',1.5);

xlabel('Days')
ylabel('Infected individuals')
```

```
legend ('No intervention','MV+RV (\nu_1 > \nu_2)','MV+RV (\nu_1 = ... \nu_2)','Quarantine','Combined interventions')
```

```
%%%%%%%%%%%%%%%%%%%%%% Sensitivity.m %%%%%%%%%%%%%%%%%%%%%%
clear all;
format long;
to = 0;
tf = 100;
%initial conditions
bo = [0.99, 0, 0.01, 0, 0];
% [t, a] = ode45('mv1', [to, tf], bo);
[t, u] = ode45('q1', [to, tf], bo);
plot(t,u(:,3),':g','LineWidth',1.5);
hold on;

% [t, c] = ode45('mv2', [to, tf], bo);
[t, v] = ode45('q2', [to, tf], bo);
plot(t,v(:,3),'--b','LineWidth',1.5);

% [t, b] = ode45('ringvacc', [to, tf], bo);
[t, x] = ode45('seirq', [to, tf], bo);
plot(t,x(:,3),'r','LineWidth',1.5);

% [t, d] = ode45('mv3', [to, tf], bo);
[t, w] = ode45('q3', [to, tf], bo);
plot(t,w(:,3),'-.c','LineWidth',1.5);

% [t, e] = ode45('mv4', [to, tf], bo);
[t, y] = ode45('q4', [to, tf], bo);
plot(t,y(:,3),':m','LineWidth',1.5);

xlabel('Days')
ylabel('Infected individuals')
legend ('90%','95%','100%','105%','110%')
```

```
%%%%%%%%%%%%%%%%%%%%%% mv1.m %%%%%%%%%%%%%%%%%%%%%%
function mv1 = mv1(t,a)
%infection rate
beta = 0.3;
%rate E becomes I
sigma = 0.5;
%recovery rate
gamma = 0.1;
%vaccination rates (higher mass vaccination)
nu2 = 0.018;
nu1 = 0.01;
%initial population size
N = 1;
%dS/dt
mv1(1) = - beta*((a(1)*a(3))/N) - nu1*(a(1));
%dE/dt
```

```
mv1(2) = beta*((a(1)*a(3))/N) - a(2)*(sigma + nu2);
%dI/dt
mv1(3) = sigma*a(2) - gamma*a(3);
%dR/dt
mv1(4) = gamma*a(3);
%dV/dt
mv1(5) = nu1*a(1) + nu2*a(2);

mv1 = [mv1(1), mv1(2), mv1(3), mv1(4), mv1(5)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%% mv2.m %%%%%%%%%%%%%%%%%%%%%%
function mv2 = mv2(t,c)
%infection rate
beta = 0.3;
%rate E becomes I
sigma = 0.5;
%recovery rate
gamma = 0.1;
%vaccination rates (higher mass vaccination)
nu2 = 0.019;
nu1 = 0.01;
%initial population size
N = 1;
%dS/dt
mv2(1) = - beta*((c(1)*c(3))/N) - nu1*(c(1));
%dE/dt
mv2(2) = beta*((c(1)*c(3))/N) - c(2)*(sigma + nu2);
%dI/dt
mv2(3) = sigma*c(2) - gamma*c(3);
%dR/dt
mv2(4) = gamma*c(3);
%dV/dt
mv2(5) = nu1*c(1) + nu2*c(2);

mv2 = [mv2(1), mv2(2), mv2(3), mv2(4), mv2(5)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%% mv3.m %%%%%%%%%%%%%%%%%%%%%%
function mv3 = mv3(t,d)
%infection rate
beta = 0.3;
%rate E becomes I
sigma = 0.5;
%recovery rate
gamma = 0.1;
%vaccination rates (higher mass vaccination)
nu2 = 0.021;
nu1 = 0.01;
%initial population size
N = 1;
```

```
%dS/dt
mv3(1) = - beta*((d(1)*d(3))/N) - nu1*(d(1));
%dE/dt
mv3(2) = beta*((d(1)*d(3))/N) - d(2)*(sigma + nu2);
%dI/dt
mv3(3) = sigma*d(2) - gamma*d(3);
%dR/dt
mv3(4) = gamma*d(3);
%dV/dt
mv3(5) = nu1*d(1) + nu2*d(2);

mv3 = [mv3(1), mv3(2), mv3(3), mv3(4), mv3(5)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%%% mv4.m %%%%%%%%%%%%%%%%%%%%%%%
function mv4 = mv4(t,e)
%infection rate
beta = 0.3;
%rate E becomes I
sigma = 0.5;
%recovery rate
gamma = 0.1;
%vaccination rates (higher mass vaccination)
nu2 = 0.022;
nu1 = 0.01;
%initial population size
N = 1;
%dS/dt
mv4(1) = - beta*((e(1)*e(3))/N) - nu1*(e(1));
%dE/dt
mv4(2) = beta*((e(1)*e(3))/N) - e(2)*(sigma + nu2);
%dI/dt
mv4(3) = sigma*e(2) - gamma*e(3);
%dR/dt
mv4(4) = gamma*e(3);
%dV/dt
mv4(5) = nu1*e(1) + nu2*e(2);

mv4 = [mv4(1), mv4(2), mv4(3), mv4(4), mv4(5)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%%% q1.m %%%%%%%%%%%%%%%%%%%%%%%
function q1 = q1(t,x)
%infection rate
beta = 0.3;
%rate at which exposed becomes infected
sigma = 0.5;
%recovery rate
gamma = 0.1;
%quarantine rate
kappa = 0.027;
```

```
%initial population size
N = 1;
%dS/dt
q1(1) = - beta*((x(1)*x(3))/N);
%dE/dt
q1(2) = beta*((x(1)*x(3))/N) - sigma*x(2);
%dI/dt
q1(3) = sigma*x(2) - (gamma + kappa)*x(3);
%dR/dt
q1(4) = gamma*(x(3) + x(5));
%dQ/dt
q1(5) = kappa*x(3) - gamma*x(5);

q1 = [q1(1), q1(2), q1(3), q1(4), q1(5)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%% q2.m %%%%%%%%%%%%%%%%%%%%%%
function q2 = q2(t,x)
%infection rate
beta = 0.3;
%rate at which exposed becomes infected
sigma = 0.5;
%recovery rate
gamma = 0.1;
%quarantine rate
kappa = 0.0285;
%initial population size
N = 1;
%dS/dt
q2(1) = - beta*((x(1)*x(3))/N);
%dE/dt
q2(2) = beta*((x(1)*x(3))/N) - sigma*x(2);
%dI/dt
q2(3) = sigma*x(2) - (gamma + kappa)*x(3);
%dR/dt
q2(4) = gamma*(x(3) + x(5));
%dQ/dt
q2(5) = kappa*x(3) - gamma*x(5);

q2 = [q2(1), q2(2), q2(3), q2(4), q2(5)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%% q3.m %%%%%%%%%%%%%%%%%%%%%%
function q3 = q3(t,x)
%infection rate
beta = 0.3;
%rate at which exposed becomes infected
sigma = 0.5;
%recovery rate
gamma = 0.1;
%quarantine rate
```

```
kappa = 0.0315;
%initial population size
N = 1;
%dS/dt
q3(1) = - beta*((x(1)*x(3))/N);
%dE/dt
q3(2) = beta*((x(1)*x(3))/N) - sigma*x(2);
%dI/dt
q3(3) = sigma*x(2) - (gamma + kappa)*x(3);
%dR/dt
q3(4) = gamma*(x(3) + x(5));
%dQ/dt
q3(5) = kappa*x(3) - gamma*x(5);

q3 = [q3(1), q3(2), q3(3), q3(4), q3(5)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%% q4.m %%%%%%%%%%%%%%%%%%%%%%
function q4 = q4(t,x)
%infection rate
beta = 0.3;
%rate at which exposed becomes infected
sigma = 0.5;
%recovery rate
gamma = 0.1;
%quarantine rate
kappa = 0.033;
%initial population size
N = 1;
%dS/dt
q4(1) = - beta*((x(1)*x(3))/N);
%dE/dt
q4(2) = beta*((x(1)*x(3))/N) - sigma*x(2);
%dI/dt
q4(3) = sigma*x(2) - (gamma + kappa)*x(3);
%dR/dt
q4(4) = gamma*(x(3) + x(5));
%dQ/dt
q4(5) = kappa*x(3) - gamma*x(5);

q4 = [q4(1), q4(2), q4(3), q4(4), q4(5)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%% CaseStudy.m %%%%%%%%%%%%%%%%%%%%%%
clear all;
format long;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
load cases3.dat;
[n,p] = size(cases3);
t=1:n;
bar(t,cases3,'c','EdgeColor','b')
```

```
hold on;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
    % time points
to=0;
tisol=30; % WHO quarantine program
tvacc=57; % WHO vaccination program
tf=84;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
    % Initial values for SEIRQ model
    % [So, Eo, Io, Ro, Vo, Qo]
xo = [297, 0, 1, 0, 0, 0];
    % solve SEIRVQ system with ode45
[t,x] = ode45('seirvq3',[to,tisol],xo);   %SEIRVQ with low ...
    quarantine rate
    % plot infected solution curve
plot(t,x(:,3),'r','LineWidth',2)
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
    % Initial values for SEIRVQ2 model. These are the final values
    % computed in the SEIRVQ3 model
yo = [x(65,1),x(65,2),x(65,3),x(65,4), 0, 21.24]; % Qo=90% of inf ...
    @ day 38
[t,y] = ode45('seirvq2',[tisol,tvacc],yo);  %SEIRVQ with high ...
    quarantine
plot(t,y(:,3),'--g','LineWidth',2)
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
    % Initial values for SEIRV model. These are the final values
    % computed in the SEIRQ2 model
zo = [y(45,1),y(45,2),y(45,3),y(45,4),158.4,y(45,5)]; % Vo= 90% ...
    of non FTC
[t,z] = ode45('seirvq',[tvacc,tf],zo); % Vaccination implemented
plot(t,z(:,3),':b','LineWidth',2)
hold off;
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
    % figure
title('ABAKALIKI Delayed Interventions')
xlabel('Days')
ylabel('Number of Infected Population')
legend('Recorded data','SEIRVQ, low \kappa','SEIRVQ, high ...
    \kappa','SEIRVQ model')
```

```
%%%%%%%%%%%%%%%%%%%%%%% seirvq2.m %%%%%%%%%%%%%%%%%%%%%%%
function seirvq2 = seirvq2(t,z)
%infection rate
beta = 0.0011565657; % Abakaliki
%rate at which E becomes I
sigma = 0.0833333333; % Abakaliki
%recovery rate
gamma = 0.05; % Abakaliki
%vaccination rates
nu1 = 0;
nu2 = 0;
%quarantine rate
```

```
kappa = 0.125; % Abakaliki
%initial population size
N = 1;
%dS/dt
seirvq2(1) = - beta*((z(1)*z(3))/N) - z(1)*nu1;
%dE/dt
seirvq2(2) = beta*((z(1)*z(3))/N) - z(2)*(sigma + nu2);
%dI/dt
seirvq2(3) = sigma*z(2) - (gamma + kappa)*z(3);
%dR/dt
seirvq2(4) = gamma*(z(3) + z(6));
%dV/dt
seirvq2(5) = nu1*z(1) + nu2*z(2);
%dQ/dt
seirvq2(6) = kappa*z(3) - gamma*z(6);

seirvq2 = [seirvq2(1), seirvq2(2), seirvq2(3), seirvq2(4), ...
    seirvq2(5), seirvq2(6)]';
end
```

```
%%%%%%%%%%%%%%%%%%%%%% serivq3.m %%%%%%%%%%%%%%%%%%%%%%
function seirvq3 = seirvq3(t,z)
%infection rate
beta = 0.0011565657; % Abakaliki
%rate at which E becomes I
sigma = 0.0833333333; % Abakaliki
%recovery rate
gamma = 0.05; % Abakaliki
%vaccination rates
nu1 = 0;
nu2 = 0;
%quarantine rate
kappa = 0.02; % Abakaliki
%initial population size
N = 1;
%dS/dt
seirvq3(1) = - beta*((z(1)*z(3))/N) - z(1)*nu1;
%dE/dt
seirvq3(2) = beta*((z(1)*z(3))/N) - z(2)*(sigma + nu2);
%dI/dt
seirvq3(3) = sigma*z(2) - (gamma + kappa)*z(3);
%dR/dt
seirvq3(4) = gamma*(z(3) + z(6));
%dV/dt
seirvq3(5) = nu1*z(1) + nu2*z(2);
%dQ/dt
seirvq3(6) = kappa*z(3) - gamma*z(6);

seirvq3 = [seirvq3(1), seirvq3(2), seirvq3(3), seirvq3(4), ...
    seirvq3(5), seirvq3(6)]';
end
```

```
%%% Classical 4th Order Runge-Kutta Method for SEIR/SIR Epidemic ...
    Models %%%
function [t,w] = RK4E(a,b,n,alpha)
%%%%%%%% initialize w vector
    % SIR
%         w = zeros(3,n+1);
    % SEIR
        w = zeros(4,n+1);
    % SEIRV/Q
%         w = zeros(5,n+1);
    % SEIRVQ
%        w = zeros(6,n+1);
%%%%%%%% initialize t vector
    t = zeros(1,n+1);
%%%%%%%% h is stepsize for method
    h = (b-a)/n;
%%%%%%%% initial conditions vector
    w(:,1) = alpha;
%%%%%%%% t vector loop
    for i=1:n+1
        t(i)=a+(i-1)*h;
    end
%%%%%%%% method loop
    for i = 2:(n+1)
       k1 = h*f(t(i-1), w(:,i-1));
       k2 = h*f(t(i-1) + h/2, w(:,i-1) + k1/2);
       k3 = h*f(t(i-1) + h/2, w(:,i-1) + k2/2);
       k4 = h*f(t(i) + h, w(:,i-1) + k3);
       w(:,i) = w(:,i-1) + (k1 + 2*k2 + 2*k3 + k4)/6;
    end
end
%%%%%%%%%%%%%%%%%%%%%%       ODE Systems        %%%%%%%%%%%%%%%%%%%%%%

%%%%%%%%%%%%%%%%%  SIR  %%%%%%%%%%%%%%%%%%%%%%
% function sir = f(t,y)
% % infection rate
% % epidemic
% %     beta =0.3;
% % no epidemic
%      beta = 0.08;
% % recovery rate
%     gamma = .1;
% %dS/dt
%     sir(1) = -beta*y(1)*y(2);
% %dI/dt
%     sir(2) = beta*y(1)*y(2)-gamma*y(2);
% %dR/dt
%     sir(3) = gamma*y(2);
%     sir = [sir(1), sir(2), sir(3)]';
% end

%%%%%%%%%%%%%%%%%  SEIR  %%%%%%%%%%%%%%%%%%%%%%
function seir = f(t,y)
```

```
%infection rate
%     beta = 0.3;
    beta = 0.08;
%rate at which exposed becomes infected
    sigma = 0.5;
%recovery rate
    gamma = 0.1;
%initial population size
    N = 1;
%dS/dt
    seir(1) = - beta*((y(1)*y(3)))/N;
%dE/dt
    seir(2) = beta*(y(1)*y(3))/N - sigma*y(2);
%dI/dt
    seir(3) = sigma*y(2) - gamma*y(3);
%dR/dt
    seir(4) = gamma*y(3);
    seir = [seir(1), seir(2), seir(3), seir(4)]';
end

% %%%%%%%%%%%%%%%%  SEIRV  %%%%%%%%%%%%%%%%%%%%%
% function seirv = f(t,y)
% %infection rate
% beta = 0.3;
% %rate E becomes I
% sigma = 0.5;
% %recovery rate
% gamma = 0.1;
% %vaccination rates
% nu1 = 0.019;
% nu2 = 0.011;
% % nu1 = 0.03;
% % nu2 = 0.03;
% %initial population size
% N = 1;
% %dS/dt
% seirv(1) = - beta*((y(1)*y(3))/N) - nu1*(y(1));
% %dE/dt
% seirv(2) = beta*((y(1)*y(3))/N) - y(2)*(sigma + nu2);
% %dI/dt
% seirv(3) = sigma*y(2) - gamma*y(3);
% %dR/dt
% seirv(4) = gamma*y(3);
% %dV/dt
% seirv(5) = nu1*y(1) + nu2*y(2);
% seirv = [seirv(1), seirv(2), seirv(3), seirv(4), seirv(5)]';
% end

%%%%%%%%%%%%%%%%  SEIRQ  %%%%%%%%%%%%%%%%%%%%%
% function seirq = f(t,y)
% %infection rate
% beta = 0.3;
% %rate at which exposed becomes infected
% sigma = 0.5;
```

```
% %recovery rate
% gamma = 0.1;
% %quarantine rate
% kappa = 0.03;
% %initial population size
% N = 1;
% %dS/dt
% seirq(1) = - beta*((y(1)*y(3))/N);
% %dE/dt
% seirq(2) = beta*((y(1)*y(3))/N) - y(2)*sigma;
% %dI/dt
% seirq(3) = sigma*y(2) - y(3)*(gamma + kappa);
% %dR/dt
% seirq(4) = gamma*(y(3)+y(5));
% %dQ/dt
% seirq(5) = kappa*y(3)- gamma*y(5);
% seirq = [seirq(1), seirq(2), seirq(3), seirq(4), seirq(5)]';
% end

%%%%%%%%%%%%%%%%  SEIRVQ  %%%%%%%%%%%%%%%%%%%%%
% function seirvq = f(t,y)
% %infection rate
% beta = 0.3;
% %rate at which E becomes I
% sigma = 0.5;
% %recovery rate
% gamma = 0.1;
% %vaccination rates
% nu1 = 0.02;
% nu2 = 0.01;
% %quarantine rate
% kappa = 0.03;
% %initial population size
% N = 1;
% %dS/dt
% seirvq(1) = - beta*((y(1)*y(3))/N) - y(1)*nu1;
% %dE/dt
% seirvq(2) = beta*((y(1)*y(3))/N) - y(2)*(sigma + nu2);
% %dI/dt
% seirvq(3) = sigma*y(2) - (gamma + kappa)*y(3);
% %dR/dt
% seirvq(4) = gamma*(y(3) + y(6));
% %dV/dt
% seirvq(5) = nu1*y(1) + nu2*y(2);
% %dQ/dt
% seirvq(6) = kappa*y(3) - gamma*y(6);
% seirvq = [seirvq(1), seirvq(2), seirvq(3), seirvq(4), ...
    seirvq(5), seirvq(6)]';
% end
```