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Analysis and Control of an SEIQR Epidemic Model with Application to Ebola Disease Vaccination

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ABSTRACT

Introduction: A modified Susceptible - Exposed - Infected - Quarantined - Recovered (SEIQR) epidemic model with vaccination is considered to understand the transmission dynamics of Ebola disease. **Methods:** The impact of vaccination as a control strategy is investigated in two cases: vaccination is a constant function of time and time - dependent vaccination. For the first case, the reproduction number $\mathcal{R}_0$ is derived and mathematical analysis reveals that the existence of equilibrium points and the qualitative properties of solutions of the resulting autonomous model are completely determined by $\mathcal{R}_0$. For the second case, we conduct an analysis that is based on optimal control theory to determine optimal application of vaccination control. **Results:** It is shown that the disease - free equilibrium is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$. When $\mathcal{R}_0 > 1$, the disease - free equilibrium loses its stability and an endemic equilibrium point that is locally asymptotically stable emerges as also verified by demonstrating the existence of forward bifurcation at $\mathcal{R}_0 = 1$ using the method by Castillo - Chavez and Song. Optimal control analysis shows that that vaccination effort is affected by the cost associated with it. Vaccination control of Ebola can be carried out at maximum rate from the onset of the outbreak if it is not costly. **Conclusion:** Vaccination is an important intervention strategy in controlling Ebola outbreaks.

Citation:

INTRODUCTION

The Ebola Virus Disease (EVD), also known as Ebola haemorrhagic fever, has captured the attention of the general public constantly causing fear due to its high infectivity as well as fatality rate ranging between 50% to 90% [1-4]. It is caused by Ebola virus which is a single - stranded RNA virus belonging to the order Mononegalevirales, family Filoviridae and genus Ebolavirus [5-6]. There are five different strains of Ebolavirus: the Zaire Ebola virus, Tai Forest Ebola virus, Sudan Ebola virus, Bundibugyo Ebola virus and Reston Ebola virus [5-8]. The strains Zaire Ebola virus, Sudan Ebola virus and Bundibugyo Ebola virus are responsible for several outbreaks in different parts of the African continent with the Zaire Ebola virus being the most virulent one [6, 8-9].

Because of its occasional occurrences in the African region, the Ebola virus disease (EVD) is one of the diseases that has also become a subject of recent modelling studies. A number of mathematical models integrating various intervention strategies have been formulated and analyzed in order to understand the transmission dynamics and control of the disease which has already claimed numerous lives since its discovery in 1976. In the last seven years, the world has witnessed a very destructive outbreak of Ebola virus disease in West Africa and even if a recent outbreak of the disease in Democratic Republic of Congo had been successfully contained, the emergence of another dreadful outbreak remains a major concern including in previously uninfected areas [10].

During the previous EVD outbreaks, there have been no licensed vaccines available for use. It is only until the recent outbreak in Democratic Republic of Congo that an experimental vaccine became available and administered to, at least, control the outbreak. When cases of Ebola disease emerged during May and June 2018 in Democratic Republic of Congo, a vaccination strategy involving the recombinant, replication - competent, vesicular stomatitis virus - based vaccine expressing the glycoprotein of a Zaire Ebolavirus (rVSV - ZEBOV) was implemented and more than 3,000 individuals were vaccinated using this vaccine as a part of the WHO response to EVD outbreaks [11-12]. Although not yet licensed at that time, this vaccine is proven to be safe and highly protective against Ebola virus based on the data from clinical trials conducted in Africa, Europe and US in 2015. Last December 19, 2019, the US Food and Drug Administration have finally announced in its website the approval of Ervebo (brand name of rVSV-ZEBOV), the first FDA - approved

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vaccine that prevents EVD for 18 years of age and older [13]. Ervebo remains to be the only vaccine available against the disease to date. Another promising vaccine candidate that is on its advanced stage of development is an adenovirus type 26 - vectored vaccine encoding Ebola virus glycoprotein (Ad26.ZEBOV) boosted by a modified vaccinia Ankara - vectored vaccine encoding glycoproteins from Ebola, Sudan and Marburg viruses as well as the nucleoprotein of Tai Forest virus (MVA - BN - Filo) [14]. Initial report shows that the combination of Ad26.ZEBOV and MVA - BN - Filo confers immunity for at least 360 days and is well tolerated with good safety profile [15].

With the recently approved vaccine for EVD, Ervebo, an additional intervention strategy in the form of vaccination is available in dealing with future outbreaks of the disease. However, most of the countries in Africa that are being hit by EVD are developing countries where there can be few resources in battling such public health threat. Given the limitations on resources, strategic administration of the vaccine to control the disease is always the primary goal which we will be exploring via mathematical modelling in this work.

The main objective of this study is to investigate the dynamics of Ebola disease in the population with vaccination as the main intervention strategy. The basic SIR model by Kermack and McKendrick was used by Rachah and Torres in [16] to understand the dynamics of Liberian population infected by EVD in 2014. The model has been extended by adding a vaccination term to study the effect of vaccination on the spread of the disease. Our model extends this model by accounting for the role of exposed individuals in disease transmission, adding quarantined class and allowing demographic process to take place during the outbreak. The present model also enriches the recent model due to Li et al. in [17] by incorporating a vaccination term and by using the standard incidence.

MATERIALS AND METHODS

Model Formulation

To formulate the model, we make the following assumptions. First, we assume that there is vital dynamics as outbreaks of the disease can last for more than two years where the change in the population in that period of time is no longer negligible. Secondly, we assume that there is no vertical transmission of the disease, i.e., newborns are born susceptible. We further assume that exposed individuals are capable of transmitting the disease and dead bodies of individuals dying from the disease are properly disposed of and they do not contribute to the transmission of disease. Finally, we suppose that there is homogeneous mixing, i.e., all susceptible individuals have equal chances of becoming infected by exposed asymptomatic and infectious individuals.

With the assumptions enumerated, we develop an SEIQR model with vaccination to describe the spread of Ebola disease within a population. The model consists of five classes that are functions of time t: the susceptible class $S(t)$, the exposed class $E(t)$, the infected class $I(t)$, the quarantined class $Q(t)$, and the recovered class $R(t)$. The equations that represent the change in each class at any time t are constructed as follows.

The susceptible class is increased by a constant recruitment of individuals at rate Λ. Susceptible class is reduced when there is an adequate contact of a susceptible with an exposed or infected individual. The susceptible individuals acquire the infection from exposed and infected individuals at rates $\beta_1 \frac{S}{N}$ and $\beta_2 \frac{S}{N}$, respectively. Therefore, transfers of susceptible individuals to the exposed class occur at rates $\beta_1 \frac{ES}{N}$ and $\beta_2 \frac{IS}{N}$. We adopt the incidence terms $\beta_1 \frac{ES}{N}$ and $\beta_2 \frac{IS}{N}$ because contact rates in rural areas are constant. This is based on the observation in [18] which states that contact rate is in proportion with population density, which is constant in rural areas as they tend to expand as population increases to maintain a constant population density. The susceptible class is further reduced by vaccination at per capita rate ξ and by deaths due to natural causes at per capita rate μ. Thus, the rate of change of the population for the susceptible class is given by

$$\frac{dS(t)}{dt} = \Lambda - \beta_1 \frac{ES}{N} - \beta_2 \frac{IS}{N} - (\mu + \xi)S.$$

As a result of contact (sufficient for transmission of infection) between susceptibles and individuals in either the exposed or infected class, the exposed population is increased by $\beta_1 \frac{ES}{N}$ and $\beta_2 \frac{IS}{N}$. It is decreased by death due to natural causes at per capita rate μ and by transfer of exposed individuals at per capita rate ϵ to infected class. These lead to the equation

$$\frac{dE(t)}{dt} = \beta_1 \frac{ES}{N} + \beta_2 \frac{IS}{N} - (\mu + \epsilon)E.$$

The transfer of individuals from the exposed class to the infected class occurs when exposed individuals start to show symptoms and become more infectious. The infected class size is increased by E and it is diminished by quarantine (hospitalization) at rate ν for appropriate treatment measures, death due to the disease at rate α_1 before the infected are brought to treatment sites, or death due to natural causes at rate μ. Therefore, the change in infected class is described by the equation

$$\frac{dI(t)}{dt} = \epsilon E - (\mu + \nu + \alpha_1)I.$$

In this study, we emphasize that the quarantine is equivalent to hospitalization. The quarantined class is generated at rate ν, decreases due to recovery from disease at rate γ, from death due to the disease at rate α_2, or death due to natural causes at rate μ so that

$$\frac{dQ(t)}{dt} = \nu I - (\mu + \gamma + \alpha_2)Q.$$

Finally, the size of recovered class is increased by vaccination at rate ξ and by recovery at rate γ and decreased by death due to natural causes at rate μ. The equation that describes the rate of change of population for the recovered class is given by

$$\frac{dR(t)}{dt} = \xi S + \gamma Q - \mu R.$$

These processes are outlined in the following schematic diagram:

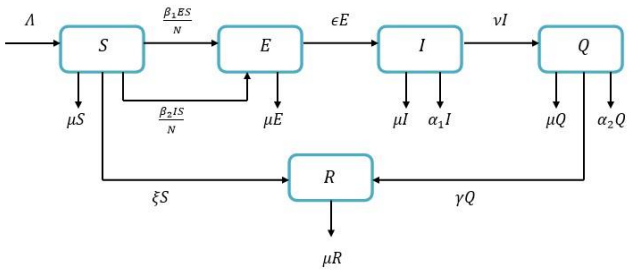

Fig. 1. Schematic diagram for the EVD model.

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Thus the model which describes the spread of the Ebola disease within a community in the presence of vaccination is given by the following system of nonlinear ordinary differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda - \beta_1 \frac{ES}{N} - \beta_2 \frac{IS}{N} - (\mu + \xi)S \\
\frac{dE}{dt} &= \beta_1 \frac{ES}{N} + \beta_2 \frac{IS}{N} - (\mu + \epsilon)E \\
\frac{dI}{dt} &= \epsilon E - (\mu + \nu + \alpha_1)I \\
\frac{dQ}{dt} &= \nu I - (\mu + \gamma + \alpha_2)Q \\
\frac{dR}{dt} &= \xi S + \gamma Q - \mu R
\end{aligned} \tag{1}$$

together with the following initial conditions $S(0) > 0$, $E(0) \geq 0$, $I(0) \geq 0$, $Q(0) \geq 0$, and $R(0) \geq 0$. (2)

Well - Posedness of the Model

In this section, we demonstrate the well - posedness of model system (1). We proceed by showing the existence and uniqueness of solutions, positivity and boundedness.

Existence and Uniqueness of Solutions

Theorem 1: Consider system (1) with nonnegative initial conditions (2). Solutions to the initial value problem (1, 2) exist and are unique for all $t \geq 0$.

Proof. If we introduce the transformations $S = x_1$, $E = x_2$, $I = x_3$, $Q = x_4$, $R = x_5$ and let $x = (x_1, x_2, x_3, x_4, x_5)^T$ then system (1) can be written in the form

$$x' = f(x),$$

where $f = (f_1, f_2, f_3, f_4, f_5)^T$ with

$$\begin{aligned}
f_1 &= \Lambda - \beta_1 \frac{x_1 x_2}{x_1 + x_2 + x_3 + x_4 + x_5} - \beta_2 \frac{x_1 x_3}{x_1 + x_2 + x_3 + x_4 + x_5} - (\mu + \xi)x_1 \\
f_2 &= \beta_1 \frac{x_1 x_2}{x_1 + x_2 + x_3 + x_4 + x_5} + \beta_2 \frac{x_1 x_3}{x_1 + x_2 + x_3 + x_4 + x_5} - (\mu + \epsilon)x_2 \\
f_3 &= \epsilon x_2 - (\mu + \nu + \alpha_1)x_3 \\
f_4 &= \nu x_3 - (\mu + \gamma + \alpha_2)x_4 \\
f_5 &= \xi x_1 + \gamma x_4 - \mu x_5
\end{aligned}$$

Because f_is are composed of sums of continuous functions, f_is are continuous functions on $\mathbb{R}^5$ and the partial derivatives $\frac{\partial f_i}{\partial x_1}, \frac{\partial f_i}{\partial x_2}, \frac{\partial f_i}{\partial x_3}, \frac{\partial f_i}{\partial x_4}$ and $\frac{\partial f_i}{\partial x_5}$ exist and are continuous. Therefore, a unique solution exists to the initial value problem (1, 2).

Positivity of Solutions

Since the model system (1) tracks the changes in human population, it is important to show that the solutions of system (1) with nonnegative initial conditions will remain nonnegative for all $t > 0$.

Theorem 2: Given that the initial conditions of system (1) are such that $S(0) \geq 0$, $E(0) \geq 0$, $I(0) \geq 0$, $Q(0) \geq 0$ and $R(0) \geq 0$. Then solutions $S(t)$, $E(t)$, $I(t)$, $Q(t)$ and $R(t)$ of model (1), with nonnegative initial conditions, will remain nonnegative for all $t > 0$.

Proof. Assume that $S(0) \geq 0$, $E(0) \geq 0$, $I(0) \geq 0$, $Q(0) \geq 0$ and $R(0) \geq 0$. From the first equation of system (1), we have

$$\frac{dS}{dt} = \Lambda - \beta_1 \frac{ES}{N} - \beta_2 \frac{IS}{N} - (\mu + \xi)S. \tag{3}$$

With the integrating factor $e^{\left[(\mu+\xi)t + \beta_1 \int_0^t \frac{E(\eta)}{N(\eta)} d\eta + \beta_2 \int_0^t \frac{I(\eta)}{N(\eta)} d\eta\right]}$ we can write (3) as

$$\frac{d}{dt}\left\{S(t) e^{\left[(\mu+\xi)t + \beta_1 \int_0^t \frac{E(\eta)}{N(\eta)} d\eta + \beta_2 \int_0^e \frac{I(\eta)}{N(\eta)} d\eta\right]}\right\} = \Lambda e^{\left[(\mu+\xi)t + \beta_1 \int_0^t \frac{E(\eta)}{N(\eta)} d\eta + \beta_2 \int_0^t \frac{I(\eta)}{N(\eta)} d\eta\right]}. \tag{4}$$

Integrating both sides of (4) gives

$$S(t) e^{\left[(\mu+\xi)t + \beta_1 \int_0^t \frac{E(\eta)}{N(\eta)} d\eta + \beta_2 \int_0^t \frac{I(\eta)}{N(\eta)} d\eta\right]} = \int_0^t \Lambda e^{\left[(\mu+\xi)\tau + \beta_1 \int_0^\tau \frac{E(\eta)}{N(\eta)} d\eta + \beta_2 \int_0^\tau \frac{I(\eta)}{N(\eta)} d\eta\right]} d\tau + S(0)$$

where $S(0)$ is the constant of integration. Hence,

$$\begin{aligned}
S(t) = S(0) e^{-\left[(\mu+\xi)t + \beta_1 \int_0^t \frac{E(\eta)}{N(\eta)} d\eta + \beta_2 \int_0^t \frac{H(\eta)}{N(\eta)} d\eta\right]} + e^{-\left[(\mu+\xi)t + \beta_1 \int_0^t \frac{E(\eta)}{N(\eta)} d\eta + \beta_2 \int_0^t \frac{I(\eta)}{N(\eta)} d\eta\right]} \\
\times \left[\int_0^t \Lambda e^{\left[(\mu+\xi)\tau + \beta_1 \int_0^\tau \frac{E(\eta)}{N(\eta)} d\eta + \beta_2 \int_0^\tau \frac{I(\eta)}{N(\eta)} d\eta\right]} d\tau\right] \geq 0.
\end{aligned}$$

Using similar argument on the four remaining variables, we obtain the following:

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$$\frac{dE}{dt} \geq -(\mu+\epsilon)E \Longrightarrow E(t) \geq E(0)e^{-(\mu+\varepsilon)t} \geq 0$$
$$\frac{dI}{dt} \geq -(\mu+\nu+\alpha_1)I \Longrightarrow I(t) \geq I(0)e^{-(\mu+\nu+\alpha_1)t} \geq 0$$
$$\frac{dQ}{dt} \geq -(\mu+\gamma+\alpha_2)Q \Longrightarrow Q(t) \geq Q(0)e^{-(\mu+\gamma+\alpha_2)t} \geq 0$$
$$\frac{dR}{dt} \geq -\mu R \Longrightarrow R(t) \geq R(0)e^{-\mu t} \geq 0.$$

Therefore, all solutions of (1) with nonnegative initial conditions will remain nonnegative for all time $t > 0$.

Boundedness

Theorem 3: The closed set

$$\Omega = \left\{(S,E,I,Q,R) \in \mathbb{R}_+^5 : 0 \leq N \leq \frac{\Lambda}{\mu}\right\}$$

is positively invariant and attracting with respect to model (1).

Proof. Let $S(t)$, $E(t)$, $I(t)$, $Q(t)$ and $R(t)$ be any solution of system (1) with nonnegative initial conditions. Adding all the equations in (1) yields the inequality

$$\frac{dN}{dt} = \Lambda - \mu N - \alpha_1 I - \alpha_2 Q \leq \Lambda - \mu N.$$

By using Gronwall's inequality, we have

$$N(t) \leq \frac{\Lambda}{\mu} + \left(N(0) - \frac{\Lambda}{\mu}\right)e^{-\mu t} \tag{5}$$

where $N(0)$ represents the initial population. It follows from (5) that $N(t) \to \frac{\Lambda}{\mu}$ as $t \to \infty$. In particular, $N(t) \leq \frac{\Lambda}{\mu}$ if $N(0) \leq \frac{\Lambda}{\mu}$. Thus, under the flow induced by (1), the region Ω is positively invariant. On the other hand, if $N(0) > \frac{\Lambda}{\mu}$, then either the solution enters Ω in finite time or asymptotically approaches $\frac{\Lambda}{\mu}$ as $t \to \infty$. Hence, in the region Ω, model (1) is said to be mathematically and epidemiologically well - posed and the dynamics of the model will be considered in Ω.

Local Stability Analysis

In mathematical modelling's point of view, the primary goal of having vaccination as a main public health intervention strategy during Ebola outbreaks can be interpreted as establishing conditions so that model system (1) can be brought to a situation wherein the disease - free equilibrium is stable and there is no stable positive equilibrium point. These considerations serve as a motivation to study the asymptotic properties of the equilibrium solutions of model system (1).

Existence of Equilibrium Points

The equilibrium points of model system (1) are the points where the derivative of S, E, I, Q, and R is zero, that is, $\frac{dS}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dQ}{dt} = \frac{dR}{dt} = 0$ which can be found by solving the system

$$\begin{aligned}
\Lambda - \beta_1\frac{ES}{N} - \beta_2\frac{IS}{N} - (\mu+\xi)S &= 0\\
\beta_1\frac{ES}{N} + \beta_2\frac{IS}{N} - (\mu+\epsilon)E &= 0\\
\epsilon E - (\mu+\nu+\alpha_1)I &= 0\\
\nu I - (\mu+\gamma+\alpha_2)Q &= 0\\
\xi S + \gamma Q - \mu R &= 0
\end{aligned} \tag{6}$$

for S, E, I, Q and R. Because of the involvement of the variable N in the first and second equations of system (6), we include the equation $\frac{dN}{dt} = 0$ in the computation of equilibrium points. Thus, we instead solve the system:

$$\begin{aligned}
\Lambda - \beta_1\frac{ES}{N} - \beta_2\frac{IS}{N} - (\mu+\xi)S &= 0\\
\beta_1\frac{ES}{N} + \beta_2\frac{IS}{N} - (\mu+\epsilon)E &= 0\\
\epsilon E - (\mu+\nu+\alpha_1)I &= 0.\\
\nu I - (\mu+\gamma+\alpha_2)Q &= 0\\
\xi S + \gamma Q - \mu R &= 0\\
\Lambda - \mu N - \alpha_1 I - \alpha_2 Q &= 0
\end{aligned} \tag{7}$$

The third and fourth equations in (7), respectively, lead to

$$E = \frac{\mu+\nu+\alpha_1}{\epsilon}I \tag{8}$$

and

$$Q = \frac{\nu}{\mu+\gamma+\alpha_1}. \tag{9}$$

From the sixth equation in (7), together with (9), we will have

$$N = \frac{\Lambda}{\mu} - \frac{1}{\mu}\left(\alpha_1 + \frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)I. \tag{10}$$

Using equations (8) - (10), then the first equation in (7) yields

$$S = \frac{\Lambda N}{\beta_1 E + \beta_2 I + (\mu+\xi)N} = \frac{\frac{\Lambda}{\mu}\left[\Lambda - \left(\alpha_1 + \frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)I\right]}{\frac{(\mu+\xi)\Lambda}{\mu} + \left[\left(\beta_1\frac{\mu+\nu+\alpha_1}{\epsilon} + \beta_2\right) - \frac{\mu+\xi}{\mu}\left(\alpha_1 + \frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)\right]I} \tag{11}$$

Using (9) and (11), then we can also have

$$R = \frac{1}{\mu}\left\{\xi\left[\frac{\frac{\Lambda}{\mu}\left[\Lambda - \left(\alpha_1 + \frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)I\right]}{\frac{(\mu+\xi)\Lambda}{\mu} + \left[\left(\beta_1\frac{\mu+\nu+\alpha_1}{\epsilon} + \beta_2\right) - \frac{\mu+\xi}{\mu}\left(\alpha_1 + \frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)\right]I}\right] + \frac{\gamma\nu}{\mu+\gamma+\alpha_2}I\right\} \tag{12}$$

The second equation in (7), gives the equilibrium condition

$$(\beta_1 E + \beta_2 I)\frac{S}{N} = (\mu+\epsilon)E$$

where, after substituting (8)-(11), we obtain

$$(\mu+\epsilon)\frac{\mu+\nu+\alpha_1}{\epsilon}\left[\left(\beta_1\frac{\mu+\nu+\alpha_1}{\epsilon} + \beta_2\right) - \frac{\mu+\xi}{\mu}\left(\alpha_1 + \frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)\right]I^2 - \left[\Lambda\left(\beta_1\frac{\mu+\nu+\alpha_1}{\epsilon} + \beta_2\right) - \frac{(\mu+\epsilon)(\mu+\nu+\alpha_1)(\mu+\xi)\Lambda}{\mu\epsilon}\right]I = 0$$

which has two solutions. One solution is $I_0 = 0$ where we obtain the following from equations (8), (9) , (11) and (12), respectively:

$$E_0 = 0, \quad Q_0 = 0, \quad S_0 = \frac{\Lambda}{\mu+\xi}, \text{ and } \quad R_0 = \frac{\Lambda}{\mu(\mu+\xi)}.$$

Hence, the solution $I_0 = 0$ corresponds to the disease - free equilibrium which we denote as P_0. The other solution is given by:

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$$I_1 = \frac{\Lambda\left(\beta_1\frac{\mu+\nu+\alpha_1}{\epsilon}+\beta_2\right)-\frac{(\mu+e)(\mu+\nu+\alpha_1)(\mu+\xi)\Lambda}{\mu e}}{(\mu+\epsilon)\frac{\mu+\nu+\alpha_1}{c}\left[\left(\beta_1\frac{\mu+\nu+\alpha_1}{\epsilon}+\beta_2\right)-\frac{\mu+\xi}{\mu}\left(\alpha_1+\frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)\right]}$$

$$= \frac{\frac{(\mu+e)(\mu+\nu+\alpha_1)(\mu+\xi)\Lambda}{\mu\epsilon}(\mathcal{R}_0-1)}{(\mu+\epsilon)\frac{\mu+\nu+\alpha_1}{\epsilon}\left[\left(\beta_1\frac{\mu+\nu+\alpha_1}{\epsilon}+\beta_2\right)-\frac{\mu+\xi}{\mu}\left(\alpha_1+\frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)\right]}$$

$$I_1 = \frac{(\mu+\xi)\Lambda(\mathcal{R}_0-1)}{\mu\left[\left(\beta_1\frac{\mu+\nu+\alpha_1}{\epsilon}+\beta_2\right)-\frac{\mu+\xi}{\mu}\left(\alpha_1+\frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)\right]}$$

which corresponds to the endemic equilibrium, denoted as P_1, and this exists uniquely in the interior of Ω provided

$$\mathcal{R}_0 = \frac{\mu[\beta_1(\mu+\nu+\alpha_1)+\epsilon\beta_2]}{(\mu+\epsilon)(\mu+\nu+\alpha_1)(\mu+\xi)} > 1.$$

The quantity $\mathcal{R}_0$ is the basic reproduction number of our model which we will derive in the succeeding section. We state the following theorem on existence of equilibrium points of the model.

Theorem 4: If $\mathcal{R}_0 \leq 1$, then model system (1) has only the disease - free equilibrium $P_0 = (S_0, 0,0,0, R_0) = \left(\frac{\Lambda}{\mu+\xi}, 0,0,0, \frac{\xi\Lambda}{\mu(\mu+\xi)}\right)$ with $N_0 = \frac{\Lambda}{\mu}$ in Ω. If $\mathcal{R}_0$, then model system (1) has two equilibrium points: the disease - free equilibrium P_0 and a unique endemic equilibrium $P_1 = (S_1, E_1, I_1, Q_1, R_1)$, where

$$S_1 = \frac{\frac{\Lambda}{\mu}\left[\Lambda-\left(\alpha_1+\frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)I_1\right]}{\frac{(\mu+\xi)\Lambda}{\mu}+\left[\left(\beta_1\frac{\mu+\nu+\alpha_1}{e}+\beta_2\right)-\frac{\mu+\xi}{\mu}\left(\alpha_1+\frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)\right]I_1}$$

$$E_1 = \frac{\mu+\nu+\alpha_1}{\epsilon}I_1$$

$$I_1 = \frac{(\mu+\xi)\Lambda(\mathcal{R}_0-1)}{\mu\left[\left(\beta_1\frac{\mu+\nu+\alpha_1}{e}+\beta_2\right)-\frac{\mu+\xi}{\mu}\left(\alpha_1+\frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)\right]}$$

$$Q_1 = \frac{\nu}{\mu+\gamma+\alpha_2}I_1$$

$$R_1 = \frac{1}{\mu}\left\{\xi\left[\frac{\frac{\Lambda}{\mu}\left[\Lambda-\left(\alpha_1+\frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)I_1\right]}{\frac{(\mu+\xi)\Lambda}{\mu}+\left[\left(\beta_1\frac{\mu+\nu+\alpha_1}{\epsilon}+\beta_2\right)-\frac{\mu+\xi}{\mu}\left(\alpha_1+\frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)\right]I_1}\right]+\frac{\gamma\nu}{\mu+\gamma+\alpha_2}I_1\right\}$$

with

$$N_1 = \frac{\Lambda}{\mu}-\frac{1}{\mu}\left(\alpha_1+\frac{\alpha_2\nu}{\mu+\gamma+\alpha_2}\right)I_1.$$

The Basic Reproduction Number

In this section, we derive the basic reproduction number $\mathcal{R}_0$ which is interpreted as the average number of secondary infections generated by a single infectious individual when introduced to a wholly susceptible population [19-20]. Theorem 4 shows that a disease - free equilibrium always exists for model system (1) and is given by $P_0 = (S_0, 0,0,0, R_0) = \left(\frac{\Lambda}{\mu+\xi}, 0,0,0, \frac{\xi\Lambda}{\mu(\mu+\xi)}\right)$. The infected compartments of model system (1) are E,I and Q and the noninfected compartments are S and R. We let $X = (E, I, Q, S, R)^T$, i.e. infected compartments first, and follow the general procedure developed by van den Driessche and Watmough in [20]. We will take $X_0 = (S_0, 0,0,0, R_0) = \left(\frac{\Lambda}{\mu+\xi}, 0,0,0, \frac{\xi\Lambda}{\mu(\mu+\xi)}\right)$ to be the equivalent formulation for the disease - free equilibrium. Then we can write model system (1) in the form

$$\frac{dX}{dt} = \mathcal{F}(X) - \mathcal{V}(X), \qquad (13)$$

where

$$\mathcal{F}(X) = \begin{bmatrix} \beta_1\frac{ES}{N}+\beta_2\frac{IS}{N} \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix}$$

and

$$\mathcal{V}(X) = \begin{bmatrix} (\mu+\epsilon)E \\ (\mu+\nu+\alpha_1)I-\epsilon E \\ (\mu+\gamma+\alpha_2)Q-\nu I \\ \beta_1\frac{ES}{N}+\beta_2\frac{IS}{N}+(\mu+\xi)S-\Lambda \\ \mu R-\xi S-\gamma Q \end{bmatrix}.$$

Closely following [32], because there are m = 3 infected compartments, F and V are 3 × 3 matrices of the form:

$$F = \left[\frac{\partial\mathcal{F}_i}{\partial x_j}(X_0)\right] \quad \text{and} \quad V = \left[\frac{\partial\mathcal{V}_i}{\partial x_j}(X_0)\right]$$

with $1 \leq i, j \leq 3$. Matrices F and V are found to be

$$F = \begin{bmatrix} \beta_1\frac{S_0}{N_0} & \beta_2\frac{S_0}{N_0} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}, \quad V = \begin{bmatrix} \mu+\epsilon & 0 & 0 \\ -\epsilon & \mu+\nu+\alpha_1 & 0 \\ 0 & -\nu & \mu+\gamma+\alpha_2 \end{bmatrix}.$$

Hence, the next generation matrix is given by

$$FV^{-1} = \begin{bmatrix} \frac{\beta_1\frac{S_0}{N_0}}{\mu+\epsilon}+\frac{\epsilon\beta_2\frac{S_0}{N_0}}{(\mu+\epsilon)(\mu+\nu+\alpha_1)} & \frac{\beta_2\frac{S_0}{N_0}}{\mu+\nu+\alpha_1} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}.$$

The basic reproduction number denoted by $\mathcal{R}_0$ is defined to be the spectral radius of the next generation matrix FV^{-1}. Therefore,

$$\mathcal{R}_0 = \rho(FV^{-1}) = \frac{\mu[\beta_1(\mu+\nu+\alpha_1)+\epsilon\beta_2]}{(\mu+\epsilon)(\mu+\nu+\alpha_1)(\mu+\xi)}.$$

Stability of Equilibrium Points

As established in Theorem 4, under the condition that $\mathcal{R}_0 \leq 1$, our model has only one biologically feasible equilibrium point which is given by the disease - free equilibrium (DFE) that represents a community that is free of

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the disease. When $\mathcal{R}_0 > 1$, then in addition to the DFE, there is an endemic equilibrium (EE) which represents a community where there is disease prevalence. In this section, we study the stability of these equilibrium points. We present the following result.

Theorem 5: The disease - free equilibrium point $P_0 = (S_0, 0,0,0, R_0) = \left(\frac{\Lambda}{\mu+\xi}, 0,0,0, \frac{\xi\Lambda}{\mu(\mu+\xi)}\right)$ is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.

Proof. The local stability of DFE is governed by the eigenvalues of the Jacobian matrix. To ensure local stability of the DFE, the requirement is that the eigenvalues of the Jacobian matrix of model system (1) evaluated at that point must have negative real part. The Jacobian of (1) evaluated at the DFE P_0 is

$$J(P_0) = \begin{bmatrix} -(\mu+\xi) & -\beta_1\frac{S_0}{N_0} & -\beta_2\frac{S_0}{N_0} & 0 & 0 \\ 0 & \beta_1\frac{S_0}{N_0} - (\mu+\epsilon) & \beta_2\frac{S_0}{N_0} & 0 & 0 \\ 0 & \epsilon & -(\mu+\nu+\alpha_1) & 0 & 0 \\ 0 & 0 & \nu & -(\mu+\gamma+\alpha_2) & 0 \\ \xi & 0 & 0 & \gamma & -\mu \end{bmatrix}$$

(14)

with characteristic equation

$$(-\mu-\lambda)[-(\mu+\xi)-\lambda][-(\mu+\gamma+\alpha_2)-\lambda](\lambda^2 + a_1\lambda + a_2) = 0,$$

where

$$a_1 = 2\mu + \nu + \alpha_1 + \epsilon - \frac{\beta_1\mu}{\mu+\xi},$$

$$a_2 = (\mu+\nu+\alpha_1)(\mu+\epsilon) - \frac{\mu[\beta_1(\mu+\nu+\alpha_1)+\epsilon\beta_2]}{\mu+\xi}.$$

The eigenvalues of (14) are precisely the roots of equation (15). Clearly, there exist three roots $\lambda_1 = -\mu$, $\lambda_2 = -(\mu+\gamma+\alpha_2)$ and $\lambda_3 = -(\mu+\xi)$ which are always negative. The local stability of P_0 now depends on the two roots coming from the equation $\lambda^2 + a_1\lambda + a_2 = 0$. From the condition $\mathcal{R}_0 < 1$, we can derive the following inequalities:

$$\mu + \epsilon > \frac{\beta_1\mu}{\mu+\xi} + \frac{\epsilon\beta_2\mu}{(\mu+\xi)(\mu+\nu+\alpha_1)}$$

(16)

and

$$(\mu+\nu+\alpha_1)(\mu+\epsilon) > \frac{\mu[\beta_1(\mu+\nu+\alpha_1)+\epsilon\beta_2]}{\mu+\xi}.$$

(17)

From the inequality in (16), we obtain

$$a_1 > \mu + \nu + \alpha_1 + \frac{\epsilon\beta_2\mu}{(\mu+\xi)(\mu+\nu+\alpha_1)} > 0$$

and from (17), we have $a_2 > 0$.

Since a_1 and a_2 are positive, the product a_1a_2 is also positive. According to Routh - Hurwitz criterion, these roots have negative real parts. We note that if $\mathcal{R}_0 > 1$ then $a_2 < 0$ so that at least one of the roots is positive. Thus, the disease free equilibrium P_0 is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.

Now, to show the local stability of the endemic equilibrium point, we examine if all the eigenvalues of the Jacobian matrix of model system (1) evaluated at $P_1 = (S_1, E_1, I_1, Q_1, R_1)$ with $N_1 = S_1 + E_1 + I_1 + Q_1 + R_1$ have negative real parts. The Jacobian matrix of (1) at EE P_1 is given by

$$J(P_1) = \begin{bmatrix} -g_1 + g_2 - (\mu+\xi) & -\beta_1\frac{S_1}{N_1} + g_2 & -\beta_2\frac{S_1}{N_1} + g_2 & g_2 & g_2 \\ g_1 - g_2 & g_3 - g_2 & \beta_2\frac{S_1}{N_1} - g_2 & -g_2 & -g_2 \\ 0 & \epsilon & -(\mu+\nu+\alpha_1) & 0 & 0 \\ 0 & 0 & \nu & -(\mu+\gamma+\alpha_2) & 0 \\ \xi & 0 & 0 & \gamma & -\mu \end{bmatrix},$$

(18)

where

$g_1 = \beta_1\frac{E_1}{N_1} + \beta_2\frac{I_1}{N_1}$, $g_2 = \beta_1\frac{E_1S_1}{N_1^2} + \beta_2\frac{I_1S_1}{N_1^2}$ and $g_3 = \beta_1\frac{S_1}{N_1} - (\mu+\epsilon)$.

The characteristic equation of (18) is obtained as

$$\lambda^5 + b_1\lambda^4 + b_2\lambda^3 + b_3\lambda^2 + b_4\lambda + b_5 = 0,$$

(19)

where

$b_1 = 2\mu + \gamma + \alpha_2 + k_1$

$b_2 = \xi g_2 + k_2 + (2\mu+\gamma+\alpha_2)k_1 + \mu(\mu+\gamma+\alpha_2)$

$b_3 = (3\mu+\gamma+\alpha_2+\nu+\alpha_1+\epsilon)\xi g_2 + \epsilon\nu g_2 + k_3 + (2\mu+\gamma+\alpha_2)k_2 + \mu(\mu+\gamma+\alpha_2)k_1$

$b_4 = [(\mu+\gamma+\alpha_1)(\mu+\nu+\alpha_1) + (\mu+\gamma+\alpha_1)(\mu+\epsilon) + (\mu+\epsilon)(\mu+\nu+\alpha_1)]\xi g_2 + \mu\epsilon\nu g_2 + (\mu+\xi)\epsilon\nu g_2 + (2\mu+\gamma+\alpha_2)k_3 + \mu(\mu+\gamma+\alpha_2)k_2$

$b_5 = (\mu+\epsilon)(\mu+\nu+\alpha_1)(\mu+\gamma+\alpha_2) + \mu(\mu+\xi)\epsilon\nu g_2 + \mu(\mu+\gamma+\alpha_2)k_3$

with

$k_1 = 2\mu + \xi + \nu + \alpha_1 + g_1 - g_3$

$k_2 = (\mu+\nu+\alpha_1)(g_1+\mu+\xi-g_3) - \epsilon\left(\beta_2\frac{S_1}{N_1} - g_2\right) - (g_3-g_2)(g_1-g_2+\mu+\xi) - (g_1-g_2)\left(-\beta_1\frac{S_1}{N_1} + g_2\right)$

$k_3 = (\mu+\nu+\alpha_1)(g_2-g_3)(g_1-g_2+\mu+\xi) - (\mu+\nu+\alpha_1)(g_1-g_2)\left(-\beta_1\frac{S_1}{N_1} + g_2\right) - \epsilon\left(-\beta_2\frac{S_1}{N_1} + g_2\right)(g_1-g_2) - \epsilon\left(\beta_2\frac{S_1}{N_1} - g_2\right)(g_1-g_2+\mu+\xi)$

Algebraic manipulations on k_2 and k_3 and the use of the identity

$$\beta_2\frac{S_1}{N_1} + g_3(\mu+\nu+\alpha_1) = 0$$

lead to the following simplified forms:

$k_2 = (\mu+\nu+\alpha_1)(g_1+\mu+\xi) + (\mu+\xi)(g_2-g_3) + \epsilon g_2 + (\mu+\epsilon)(g_1-g_2)$

$k_3 = (\mu+\nu+\alpha_1)(\mu+\xi)g_2 + (\mu+\epsilon)(\mu+\nu+\alpha_1)(g_1-g_2) + \epsilon(\mu+\xi)g_2.$

By the Routh - Hurwitz criterion, all roots of (19) will have negative real parts if the following conditions are satisfied: $b_1 > 0$; $b_1b_2 - b_3 > 0$; $b_1b_2b_3 - b_1^2b_4 - b_3^2 + b_1b_5 > 0$; $b_2(b_3b_4 - b_2b_5) - (b_1b_4 - b_5)^2 > 0$; and $b_1b_4b_5(b_2b_3 - b_1b_4) - b_1b_2^2b_5^2 + b_1b_4b_5^2 - b_4b_5(b_3^2 - b_1b_5) + b_2b_3b_5^2 - b_5^2 > 0$. Because

$$g_3 = \beta_1\frac{S_1}{N_1} - (\mu+\epsilon) = -\frac{\epsilon(\mu+\epsilon)\beta_2}{\beta_1(\mu+\nu+\alpha_1) + \epsilon\beta_2} < 0$$

and

$$g_1 - g_2 = \left(\beta_1\frac{E_1}{N_1} + \beta_2\frac{I_1}{N_1}\right)\left(1 - \frac{S_1}{N_1}\right) \geq 0$$

since $S_1 \leq N_1$ and $\frac{S_1}{N_1} \leq 1$, it follows that $k_1 > 0$, $k_2 > 0$ and $k_3 > 0$. Hence, b_1 is positive. As a matter of fact, all the coefficients of the characteristic equation (19) are positive, i.e., $b_i > 0$ for $i = 1,2,3,4,5$. Now, we determine an expression for $b_1b_2 - b_3 > 0$:

$$b_1b_2 - b_3 = (2\mu+\xi+g_1)\xi g_2 + \left(k_1k_2 - k_3 - \epsilon\nu g_2 - \xi\beta_1\frac{S_1}{N_1}g_2\right) + (2\mu+\gamma+\alpha_2)k_1^2 + (2\mu+\gamma+\alpha_2)^2k_1 + \mu(2\mu+\gamma+\alpha_2)(\mu+\gamma+\alpha_2)$$

Since the expression $k_1k_2 - k_3 - \epsilon\nu g_2 - \xi\beta_1\frac{S_1}{N_1}g_2$ is positive, it follows that $b_1b_2 - b_3$ is also positive. Thus we can state the following theorem.

Theorem 6: The endemic equilibrium point P_1 is locally asymptotically stable if the following conditions are satisfied: $b_2(b_3b_4 - b_2b_5) - (b_1b_4 - b_5)^2 > 0$; $b_2(b_3b_4 - b_2b_5) - (b_1b_4 - b_5)^2 > 0$; and $b_1b_4b_5(b_2b_3 - b_1b_4) - b_1b_2^2b_5^2 + b_1b_4b_5^2 - b_4b_5(b_3^2 - b_1b_5) + b_2b_3b_5^2 - b_5^2 > 0$.

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Bifurcation Analysis

As defined by Strogatz [21], bifurcation is the qualitative change in the dynamics of the system as a parameter in the system is varied. In this study, we carry out bifurcation analysis to further investigate the local stability of EE. To do this, we study the bifurcation of model system (1) at $\mathcal{R}_0 = 1$ using approach established by Castillo- Chavez and Song that is stated as Theorem 4.1 in paper by Castillo-Chavez and Song [22]. This approach is based on Center Manifold Theory and is used widely to examine the existence of a forward or backward bifurcation. When the bifurcation is forward, the disease - free equilibrium is locally asymptotically stable for $R_0 < 1$ which implies the gradual disappearance of the disease in the community whereas when $R_0 > 1$ the endemic equilibrium point is locally asymptotically stable which implies that the disease can invade the population. In order to apply the theorem, we need to introduce the following transformations: $S = x_1,\ E = x_2,\ I = x_3,\ Q = x_4,\ R = x_5$. Letting $x = (x_1, x_2, x_3, x_4, x_5)^T$ then system (1) can be written as

$\frac{dx}{dt} = f(x)$,

where $f = (f_1, f_2, f_3, f_4, f_5)^T$. Hence we have

$$\begin{aligned}
\frac{dx_1}{dt} &= \Lambda - \beta_1 \frac{x_1 x_2}{x_1 + x_2 + x_3 + x_4 + x_5} - \beta_2 \frac{x_1 x_3}{x_1 + x_2 + x_3 + x_4 + x_5} - (\mu + \xi) x_1 =: f_1 \\
\frac{dx_2}{dt} &= \beta_1 \frac{x_1 x_2}{x_1 + x_2 + x_3 + x_4 + x_5} + \beta_2 \frac{x_1 x_3}{x_1 + x_2 + x_3 + x_4 + x_5} - (\mu + \epsilon) x_2 =: f_2 \\
\frac{dx_3}{dt} &= \epsilon x_2 - (\mu + \nu + \alpha_1) x_3 =: f_3 \\
\frac{dx_4}{dt} &= \nu x_3 - (\mu + \gamma + \alpha_2) x_4 =: f_4 \\
\frac{dx_5}{dt} &= \xi x_1 + \gamma x_4 - \mu x_5 =: f_5
\end{aligned} \tag{20}$$

We pick β_2 as our bifurcation parameter. Setting $\mathcal{R}_0 = 1$ and solving for $\beta_2 = \beta_2^*$ gives

$$\beta_2^* = \frac{N_0(\mu + \nu + \alpha_1)\left(\mu + \epsilon - \beta_1 \frac{S_0}{N_0}\right)}{\epsilon S_0}.$$

Here, the DFE is the equilibrium of interest, i.e. $x_0 = P_0$. The Jacobian matrix of the transformed system (20) evaluated at the disease - free equilibrium point P_0 and with $\beta_2 = \beta_2^*$ is

$$J(P_0, \beta_2^*) = \begin{pmatrix} -(\mu + \xi) & -\beta_1 \frac{S_0}{N_0} & -\beta_2^* \frac{S_0}{N_0} & 0 & 0 \\ 0 & \beta_1 \frac{S_0}{N_0} - (\mu + \epsilon) & \beta_2^* \frac{S_0}{N_0} & 0 & 0 \\ 0 & \epsilon & -(\mu + \nu + \alpha_1) & 0 & 0 \\ 0 & 0 & \nu & -(\mu + \gamma + \alpha_2) & 0 \\ \xi & 0 & 0 & \gamma & -\mu \end{pmatrix}$$

The matrix $J(P_0, \beta_2^*)$ has a simple zero eigenvalue, say, $\lambda_5 = 0$, and all other eigenvalues are negative or have negative real parts. We let $v = (v_1, v_2, v_3, v_4, v_5)^T$ be the right eigenvector associated with the eigenvalue $\lambda_5 = 0$ so it satisfies

$$J(P_0, \beta_2^*)v = \lambda_5 v \Longrightarrow J(P_0, \beta_2^*)v = 0.$$

thus,

$$\begin{pmatrix} -(\mu + \xi) & -\beta_1 \frac{S_0}{N_0} & -\beta_2^* \frac{S_0}{N_0} & 0 & 0 \\ 0 & \beta_1 \frac{S_0}{N_0} - (\mu + \epsilon) & \beta_2^* \frac{S_0}{N_0} & 0 & 0 \\ 0 & \epsilon & -(\mu + \nu + \alpha_1) & 0 & 0 \\ 0 & 0 & \nu & -(\mu + \gamma + \alpha_2) & 0 \\ \xi & 0 & 0 & \gamma & -\mu \end{pmatrix} \begin{pmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

from which we get the system

$$\begin{aligned}
-(\mu + \xi)v_1 - \beta_1 \frac{S_0}{N_0} v_2 - \beta_2^* \frac{S_0}{N_0} v_3 &= 0 \\
\left(\beta_1 \frac{S_0}{N_0} - (\mu + \epsilon)\right) v_2 + \beta_2^* \frac{S_0}{N_0} v_3 &= 0 \\
\epsilon v_2 - (\mu + \nu + \alpha_1) v_3 &= 0. \\
\nu v_3 - (\mu + \gamma + \alpha_1) v_4 &= 0 \\
\xi v_1 + \gamma v_4 - \mu v_5 &= 0
\end{aligned} \tag{21}$$

Solving system (21), we get

$$v := \left(-\frac{(\mu+\epsilon)(\mu+\nu+\alpha_1)}{\epsilon(\mu+\xi)},\ \frac{\mu+\nu+\alpha_1}{\epsilon},\ 1,\ \frac{\nu}{\mu+\gamma+\alpha_1},\ \frac{\epsilon\gamma\nu(\mu+\xi)-\xi(\mu+\epsilon)(\mu+\nu+\alpha_1)(\mu+\gamma+\alpha_2)}{\mu\epsilon(\mu+\xi)(\mu+\gamma+\alpha_2)}\right)^T \tag{22}$$

Since P_0 is a nonnegative equilibrium of the model, S_0 and R_0 (the first and the fifth components of P_0) are both positive. Hence, v_1 and v_5 do not need to be positive based on a remark in [7].

We further let $w = (w_1, w_2, w_3, w_4, w_5)^T$ be the left eigenvector associated with the eigenvalue $\lambda_5 = 0$ so it satisfies

$$wJ(P_0, \beta_2^*) = 0$$

which gives the system

$$\begin{aligned}
-(\mu + \xi)w_1 + \xi w_5 &= 0 \\
-\beta_1 \frac{S_0}{N_0} w_1 + \left(\beta_1 \frac{S_0}{N_0} - (\mu + \epsilon)\right) w_2 + \epsilon w_3 &= 0 \\
-\beta_2^* \frac{S_0}{N_0} w_1 + \beta_2^* \frac{S_0}{N_0} w_2 - (\mu + \nu + \alpha_1) w_3 + \nu w_4 &= 0 \\
-(\mu + \gamma + \alpha_2) w_4 + \gamma w_5 &= 0 \\
-\mu w_5 &= 0
\end{aligned} \tag{23}$$

We solve system (23) with

$$\frac{\mu + \nu + \alpha_1}{\epsilon} w_2 + w_3 = 1$$

to achieve the property $wv = 1$. We thus obtain

$$w := \left(0, \frac{\epsilon}{2\mu + \epsilon - \beta_1 \frac{S_0}{N_0} + \nu + \alpha_1}, \quad \frac{\mu + \epsilon - \beta_1 \frac{S_0}{N_0}}{2\mu + \epsilon - \beta_1 \frac{S_0}{N_0} + \nu + \alpha_1}, 0, 0\right)$$

The sign of a is associated with the following non - zero partial derivatives of f evaluated at (P_0, β_2^*):

$$\frac{\partial^2 f_1}{\partial x_1 \partial x_2} = \frac{\partial^2 f_1}{\partial x_2 \partial x_1} = -\beta_1 \frac{S_0}{N_0^2}, \frac{\partial^2 f_1}{\partial x_1 \partial x_3} = \frac{\partial^2 f_1}{\partial x_3 \partial x_1} = -\beta_2^* \frac{S_0}{N_0^2}, \frac{\partial^2 f_1}{\partial x_2 \partial x_3} = \frac{\partial^2 f_1}{\partial x_3 \partial x_2} = \beta_1 \frac{S_0}{N_0^2} + \beta_2^* \frac{S_0}{N_0^2}$$

$$\frac{\partial^2 f_2}{\partial x_1 \partial x_2} = \frac{\partial^2 f_2}{\partial x_2 \partial x_1} = \beta_1 \frac{S_0}{N_0^2}, \frac{\partial^2 f_2}{\partial x_1 \partial x_3} = \frac{\partial^2 f_2}{\partial x_3 \partial x_1} = \beta_2^* \frac{S_0}{N_0^2}, \frac{\partial^2 f_2}{\partial x_2 \partial x_3} = \frac{\partial^2 f_2}{\partial x_3 \partial x_2} = -\beta_1 \frac{S_0}{N_0^2} - \beta_2^* \frac{S_0}{N_0^2}$$

$$\frac{\partial^2 f_1}{\partial x_2^2} = 2\beta_1 \frac{S_0}{N_0^2}, \frac{\partial^2 f_1}{\partial x_3^2} = 2\beta_2^* \frac{S_0}{N_0^2}, \frac{\partial^2 f_2}{\partial x_2^2} = -2\beta_1 \frac{S_0}{N_0^2}, \frac{\partial^2 f_2}{\partial x_3^2} = -2\beta_2^* \frac{S_0}{N_0^2}$$

while the sign of b is associated with the following non - zero partial derivatives of f evaluated at (P_0, β_2^*):

$$\frac{\partial^2 f_1}{\partial x_3 \partial \beta_2} = \frac{\partial^2 f_1}{\partial \beta_2 \partial x_3} = -\frac{S_0}{N_0}, \quad \frac{\partial^2 f_2}{\partial x_3 \partial \beta_2} = \frac{\partial^2 f_2}{\partial \beta_2 \partial x_3} = \frac{S_0}{N_0}$$

The bifurcation coefficients a and b are evaluated as follows:

$$\begin{aligned}
a &= \sum_{k,i,j=1}^{5} w_k v_i v_j \frac{\partial^2 f_k}{\partial x_i \partial x_j}(P_0, \beta_2^*) \\
&= w_2 v_1 v_2 \frac{\partial^2 f_2}{\partial x_1 \partial x_2}(P_0, \beta_2^*) + w_2 v_1 v_3 \frac{\partial^2 f_2}{\partial x_1 \partial x_3}(P_0, \beta_2^*) + w_2 v_2 v_1 \frac{\partial^2 f_2}{\partial x_2 \partial x_1}(P_0, \beta_2^*) \\
&\quad + w_2 v_2 v_2 \frac{\partial^2 f_2}{\partial x_2^2}(P_0, \beta_2^*) + w_2 v_2 v_3 \frac{\partial^2 f_2}{\partial x_2 \partial x_3}(P_0, \beta_2^*) + w_2 v_3 v_1 \frac{\partial^2 f_2}{\partial x_3 \partial x_1}(P_0, \beta_2^*) \\
&\quad + w_2 v_3 v_2 \frac{\partial^2 f_2}{\partial x_3 \partial x_2}(P_0, \beta_2^*) + w_2 v_3 v_3 \frac{\partial^2 f_2}{\partial x_3^2}(P_0, \beta_2^*) \\
&\quad + w_2 v_2^2 \left(-2\beta_1 \frac{S_0}{N_0^2}\right) + w_2 v_3^2 \left(-2\beta_2^* \frac{S_0}{N_0^2}\right)
\end{aligned}$$

and

$$b = \sum_{k,i=1}^{5} w_k v_i \frac{\partial^2 f_k}{\partial x_i \partial \beta_2}(P_0, \beta_2^*) = w_2 v_3 \frac{\partial^2 f_2}{\partial x_3 \partial \beta_2}(P_0, \beta_2^*).$$

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Using (22) and (24), it follows that

$$a = -\frac{2\beta_1 S_0(\mu+\epsilon)(\mu+\nu+\alpha_1)^2}{\epsilon\left(2\mu+\epsilon-\beta_1\frac{S_0}{N_0}+\nu+\alpha_1\right)(\mu+\xi)N_0^2} - \frac{2\beta_2^* S_0(\mu+\epsilon)(\mu+\nu+\alpha_1)^2}{\left(2\mu+\epsilon-\beta_1\frac{S_0}{N_0}+\nu+\alpha_1\right)(\mu+\xi)N_0^2} - \frac{2(\beta_1+\beta_2^*)S_0(\mu+\nu+\alpha_1)^2}{\left(2\mu+\epsilon-\beta_1\frac{S_0}{N_0}+\nu+\alpha_1\right)(\mu+\xi)N_0^2} - \frac{2\beta_1 S_0(\mu+\nu+\alpha_1)^2}{\epsilon\left(2\mu+\epsilon-\beta_1\frac{S_0}{N_0}+\nu+\alpha_1\right)N_0^2} - \frac{2\epsilon\beta_2^* S_0}{\left(2\mu+\epsilon-\beta_1\frac{S_0}{N_0}+\nu+\alpha_1\right)(\mu+\xi)N_0^2}$$

and

$$b = \frac{\epsilon S_0}{\left(2\mu+\epsilon-\beta_1\frac{S_0}{N_0}+\nu+\alpha_1\right)N_0}$$

Because $\left(2\mu+\epsilon-\beta_1\frac{S_0}{N_0}+\nu+\alpha_1\right)>0$, we have that $a<0$ and $b>0$. Based on item (iv) of the theorem, we conclude that when $\beta_2-\beta_2^*$ changes from negative to positive, P_0 changes its stability from stable to unstable. Correspondingly, a negative unstable equilibrium becomes positive and locally asymptotically stable and a forward bifurcation appears [20].

Theorem 7: Model system (1) with constant vaccination control exhibits a forward bifurcation at $\mathcal{R}_0=1$.

Because the direction of the bifurcation of system (1) is forward, existence of another equilibrium point (the EE) bifurcating from the nonhyperbolic equilibrium point (the DFE) is guaranteed when $\mathcal{R}_0>1$ and this point is locally asymptotically stable. Moreover, Theorem 7 also shows that a backward bifurcation scenario is impossible for model system (1) which has an epidemiological implication that reducing the basic reproduction number to below one is sufficient to wipe out the disease.

Optimal Control Analysis: Formulation of the Problem

Optimal control theory has always been of great help to many social planners to arrive at optimal strategies that will minimize the number of infected individuals and the cost associated with implementing the intervention measures [23]. Determining how to effectively administer vaccination during EVD outbreak to minimize the number of cases and associated cost is an interesting problem that is helpful in designing public health policy when resolved. To gain introductory insights into this complicated and broad problem, we reconsider the model system (1) with vaccination rate that is time - dependent, that is, we change the parameter ξ to $\xi(t)$ so that model system (1) becomes

$$\begin{aligned}
\frac{dS}{dt} &= \Lambda-\beta_1\frac{ES}{N}-\beta_2\frac{IS}{N}-(\mu+\xi(t))S\\
\frac{dE}{dt} &= \beta_1\frac{ES}{N}+\beta_2\frac{IS}{N}-(\mu+\epsilon)E\\
\frac{dI}{dt} &= \epsilon E-(\mu+\nu+\alpha_1)I.\\
\frac{dQ}{dt} &= \nu I-(\mu+\gamma+\alpha_2)Q\\
\frac{dR}{dt} &= \xi(t)S+\gamma Q-\mu R
\end{aligned} \tag{25}$$

The control $\xi(t)$ is used to control the infection by vaccinating susceptible individuals which means that we have more recovered individuals who cannot catch the disease within a certain period of time. Our goal of minimizing the number of infected individuals and the cost associated with the vaccination control on $[0,t_f]$ where t_f is the time to be controlled, can be viewed mathematically as finding a control $\xi^*(t)$ and associated state variables S^*, E^*, I^*, Q^* and R^* that minimize the objective functional given by

$$\mathcal{J}(\xi(t)) = \int_0^{t_f}\left[I(t)+\frac{c}{2}\xi^2(t)\right]dt. \tag{26}$$

In the objective functional (26), the quantity c represents the weight parameter for the vaccination control. The cost associated with the vaccination program is described by the term $\frac{c}{2}\xi^2(t)$. This choice for the representation of the cost in implementing the vaccination control is due to nonlinear costs that can arise potentially from high intervention levels [24- 25]. Such choice of representation for the cost regardless of control strategies being implemented is used widely in the literature. The cost for vaccination control can include the cost of the vaccine, cost of syringes, shipment - related costs and other incidental expenses [26]. The cost per vaccine according to the estimate that was given in [26] is $ 135.90. If we set $\xi^*(t)$ as the optimal vaccination control, then our problem is summarized as

$$(\xi^*(t)) = min\{\mathcal{J}(\xi(t)) \mid \xi(t)\in\Xi\}$$

subject to system (25) with initial conditions $S(0)>0,\quad E(0)\geq 0,\quad I(0)\geq 0,\quad Q(0)\geq 0,\quad R(0)\geq 0$ (27) with

$$\Xi = \{\xi(t) \mid \xi(t)\ is\ measurable\ and\ 0\leq\xi(t)\leq\xi max<1\ for\ t\in[0,tf]\}$$

where ξ_{max} is a constraint that stands for the limitations on vaccination effort, that is, there is a maximum rate at which susceptible individuals may be vaccinated in a given period of time.

Characterization of the Optimal Control

To find the optimal solution, our next step will be to define the Hamiltonian for the problem and then use the Pontryagin's Maximum Principle to obtain the characterization for the optimal control. In view of these, we begin defining the Hamiltonian

$$H = I(t)+\frac{c}{2}\xi^2(t)+\lambda_S\left[\Lambda-\beta_1\frac{ES}{N}-\beta_2\frac{IS}{N}-(\mu+\xi(t))S\right]+\lambda_E\left[\beta_1\frac{ES}{N}+\beta_2\frac{IS}{N}-(\mu+\epsilon)E\right]+\lambda_I[\epsilon E-(\mu+\nu+\alpha_1)I]+\lambda_Q[\nu I-(\mu+\gamma+\alpha_2)Q]+\lambda_R(\xi(t)S+\gamma Q-\mu R)$$

where λ_S, λ_E, λ_I, λ_Q, and λ_R are the adjoint variables corresponding to states S,E,I,Q and R, respectively. We state and prove the following theorem.

Theorem 8: Given an optimal control ξ^* and corresponding state solutions S^*, E^*, I^*, Q^* and R^* of the state system (25), there exist adjoint variables λ_S, λ_E, λ_I, λ_Q, and λ_R that satisfy the system:

$$\begin{aligned}
\frac{d\lambda_S}{dt} &= (\lambda_S-\lambda_E)\left(\frac{\beta_1E^*+\beta_2I^*}{N^*}\right)\left(1-\frac{S^*}{N^*}\right)+(\lambda_S-\lambda_R)\xi^*(t)+\mu\lambda_S\\
\frac{d\lambda_E}{dt} &= (\lambda_S-\lambda_E)\beta_1\frac{S^*}{N^*}\left(1-\frac{E^*}{N^*}\right)-(\lambda_S-\lambda_E)\beta_2\frac{I^*S^*}{(N^*)^2}+(\lambda_E-\lambda_I)\epsilon+\mu\lambda_E\\
\frac{d\lambda_I}{dt} &= -1-(\lambda_S-\lambda_E)\beta_1\frac{E^*S^*}{(N^*)^2}+(\lambda_S-\lambda_E)\beta_2\frac{S^*}{N^*}\left(1-\frac{I^*}{N^*}\right)+(\lambda_I-\lambda_Q)\nu+(\mu+\alpha_1)\lambda_I.\\
\frac{d\lambda_Q}{dt} &= (\lambda_E-\lambda_S)\left(\frac{\beta_1E^*S^*+\beta_2I^*S^*}{(N^*)^2}\right)+(\lambda_Q-\lambda_R)\gamma+(\mu+\alpha_2)\lambda_Q\\
\frac{d\lambda_R}{dt} &= (\lambda_E-\lambda_S)\left(\frac{\beta_1E^*S^*+\beta_2I^*S^*}{(N^*)^2}\right)+\mu\lambda_R
\end{aligned} \tag{28}$$

with transversality conditions

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$$\lambda_S(t_f) = \lambda_E(t_f) = \lambda_I(t_f) = \lambda_Q(t_f) = \lambda_R(t_f) = 0, \quad (29)$$

where $N^* = S^* + E^* + I^* + Q^* + R^*$. Furthermore, the optimal control ξ^* is given by

$$\xi^*(t) = max\left(0, min\left(\frac{(\lambda_S - \lambda_R)S^*}{c}, \xi_{max}\right)\right)$$

Proof. Differentiating the Hamiltonian H with respect to the states and putting

$$\xi(t) = \xi^*(t), S(t) = S^*(t), E(t) = E^*(t), I(t) = I^*(t), Q(t) = Q^*(t), R(t) = R^*(t)$$

with $N^* = S^* + E^* + I^* + Q^* + R^*$ give the following

$$\frac{\partial H}{\partial S} = -(\lambda_S - \lambda_E)\left(\frac{\beta_1 E^* + \beta_2 I^*}{N^*}\right)\left(1 - \frac{S^*}{N^*}\right) - (\lambda_S - \lambda_R)\xi^*(t) - \mu\lambda_S$$
$$\frac{\partial H}{\partial E} = -(\lambda_S - \lambda_E)\beta_1\frac{S^*}{N^*}\left(1 - \frac{E^*}{N^*}\right) + (\lambda_S - \lambda_E)\beta_2\frac{I^*S^*}{(N^*)^2} - (\lambda_E - \lambda_I)\epsilon - \mu\lambda_E$$
$$\frac{\partial H}{\partial I} = 1 + (\lambda_S - \lambda_E)\beta_1\frac{E^*S^*}{(N^*)^2} - (\lambda_S - \lambda_E)\beta_2\frac{S^*}{N^*}\left(1 - \frac{I^*}{N^*}\right) - (\lambda_I - \lambda_Q)\nu - (\mu + \alpha_1)\lambda_I$$
$$\frac{\partial H}{\partial Q} = -(\lambda_E - \lambda_S)\left(\frac{\beta_1 E^*S^* + \beta_2 I^*S^*}{(N^*)^2}\right) - (\lambda_Q - \lambda_R)\gamma - (\mu + \alpha_2)\lambda_Q$$
$$\frac{\partial H}{\partial R} = -(\lambda_E - \lambda_S)\left(\frac{\beta_1 E^*S^* + \beta_2 I^*S^*}{(N^*)^2}\right) - \mu\lambda_R \quad (30)$$

According to Pontryagin's Maximum Principle, the adjoint system is given by

$$\frac{d\lambda_S}{dt} = -\frac{\partial H}{\partial S}, \frac{d\lambda_E}{dt} = -\frac{\partial H}{\partial E}, \frac{d\lambda_I}{dt} = -\frac{\partial H}{\partial I}$$
$$\frac{d\lambda_Q}{dt} = -\frac{\partial H}{\partial Q}, \frac{d\lambda_R}{dt} = -\frac{\partial H}{\partial R}$$

To find the characterization of the optimal control $\xi^*(t)$ we consider the following cases concerning the bounds of the control:

i. On the set $\{t \mid 0 < \xi^*(t) < \xi_{max}\}$, we have

$$\frac{\partial H}{\partial \xi}\Big|_{\xi^*} = 0 \Longrightarrow 0 = c\xi^*(t) - \lambda_S S^* + \lambda_R S^*.$$

Solving for $\xi^*(t)$ yields

$$\xi^*(t) = \frac{(\lambda_S - \lambda_R)S^*}{c}.$$

ii. On the set $\{t \mid \xi^*(t) = 0\}$,we have

$$\frac{\partial H}{\partial \xi}\Big|_{\xi^*} \geq 0 \Longrightarrow 0 = c\xi^*(t) - \lambda_S S^* + \lambda_R S^* \geq 0.$$

and obtain

$$\frac{(\lambda_S - \lambda_R)S^*}{c} \leq \xi^*(t) = 0.$$

iii. On the set $\{t \mid \xi^*(t) = \xi_{max}\}$ we have

$$\frac{\partial H}{\partial \xi}\Big|_{\xi^*} \leq 0 \Longrightarrow 0 = c\xi^*(t) - \lambda_S S^* + \lambda_R S^* \leq 0$$

and obtain

$$\frac{(\lambda_S - \lambda_R)S^*}{c} \geq \xi^*(t) = \xi_{max}$$

Combining the three cases above, we found the characterization of $\xi^*(t)$ to be

$$\xi^*(t) = max\left(0, min\left(\frac{(\lambda_S - \lambda_R)S^*}{c}, \xi_{max}\right)\right).$$

RESULTS

Numerical Simulations

In this section, we carry out numerical simulations for the proposed SEIQR model with constant and time - dependent vaccination rate using data on the 2014 Ebola outbreak in Guinea. During the said outbreak, no licensed vaccine was used to protect the susceptible individuals but the WHO had raised awareness about the disease in order to reduce risk of transmission and encouraged hospitalization for the infected [27]. We perform numerical simulations by letting the vaccine related parameter ξ be variable. Furthermore, as exposed individuals are not easily avoided because they do not exhibit symptoms of the disease, we choose a value for β_1 such that $\beta_1 > \beta_2$ in our simulations. Based on [17], the initial values for the 2014 Outbreak in Guinea are: $S(0) = 11{,}744{,}951$, $E(0) = 37$, $I(0) = 49$, $Q(0) = 20$, and $R(0) = 0$. Table 1 displays the values for parameters of the model which are taken from recent works on Ebola modelling in Guinea that are based on actual data.

Table 1. Numerical values for parameters of the model.

Parameter	Description	Value	Source
Λ	recruitment rate	1159	[17, 28-29]
μ	natural death rate	2.6578×10^{-5}	[17, 29]
β_1	transmission rate of exposed individuals	0.18	-
β_2	transmission rate of infectious individuals	0.14	[30]
ξ	vaccination rate	-	-
ϵ	rate at which exposed individuals become infected	$\frac{1}{9.7}$	[31, 32]
ν	quarantine rate	0.5000	[31]
α_1	disease - related death rate of infected unquarantined individuals	0.2950	[31]
α_2	disease - related death rate of quarantined individuals	0.0149	[31]
γ	recovery rate	0.0011	[31]

As shown in Fig. 2, our simulation results using the parameter values in Table 1 and, in the meantime, assumed the absence of vaccination, i.e. $\xi = 0$, which was the case during the 2014 outbreak in Guinea. In the absence of vaccination, our value for the reproduction number can be as high as 1.9216. One can see from the simulations the sharp decline in the number of susceptible individuals in about 70 days. This is because of the movement of the members of this susceptible class to other classes due to the disease. Also, Fig. 2 also depicts an increase in the number of exposed, infected and quarantined individuals which reaches a peak at about 132 days, 134 days and 160 days, respectively, and before declining to positive steady states. At the peak, 16.32% of the total population will be exposed, 2.11 % will be infected and 29.97% will be quarantined. It is only after about 60 days that

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the number of recovered individuals begins to increase due to recovery from disease by drug or support treatment.

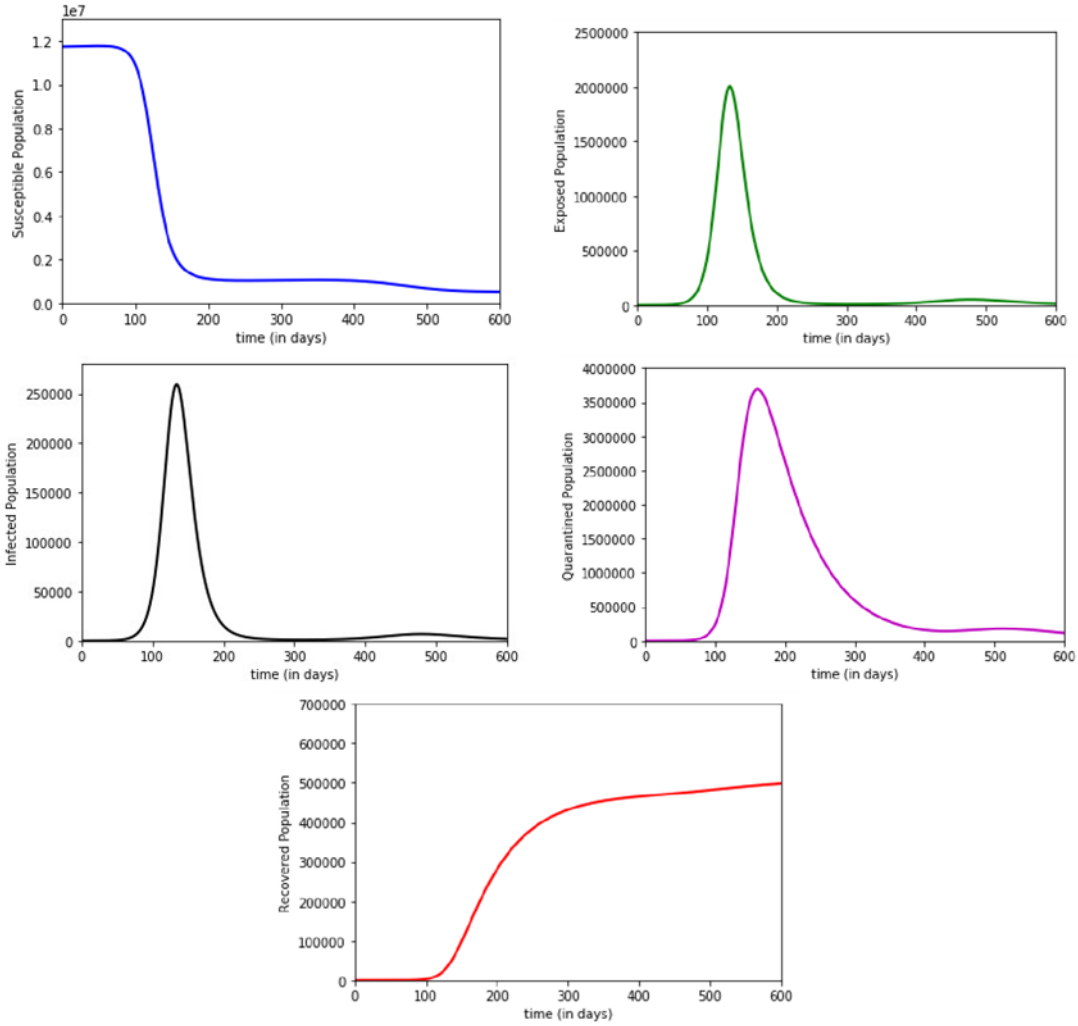

Fig. 2. Simulation results using parameter values in Table 1 assuming the absence of vaccination

The effect of having a vaccination campaign for Ebola disease is demonstrated in Fig. 3. In the simulation, we assume that the vaccination rate ξ is 0.2530. In the figure, we can see a steady decline in the number of susceptible individuals before stabilizing to a positive value. This is because of the movement of the members of susceptible compartment to the recovered compartment due to vaccination resulting in the observed steady increase in the number of recovered individuals before it also stabilizes to a positive value. The figure also shows a steady decline in the number of infected individuals going to zero while the number of exposed and quarantine individuals both reach a peak at about 3 days and 18 days, respectively, before finally settling down to zero.

In about 60 days, there will be no more infected individuals which indicates Ebola disease elimination from the population because of the presence of vaccination. This must be the case because of the reduced value of the reproduction number. Due to the vaccination rate $\xi = 0.2530$, the value of the reproduction number greatly decreased to approximately 0.0002 which is less than unity.

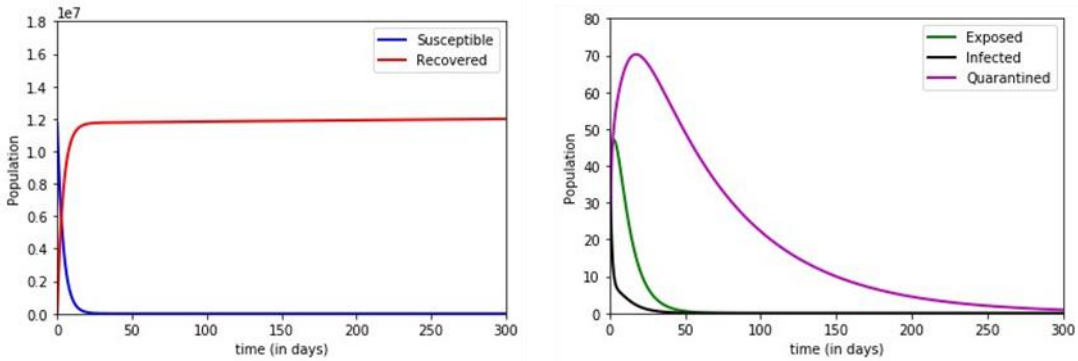

Fig. 3. Simulation results using parameter values in Table 1 and with vaccination rate $\xi = 0.2530$.

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From the definition of the basic reproduction number of the model, we can derive a quantity known as the critical vaccination rate for susceptible individuals. To obtain the critical vaccination rate, we set $\mathcal{R}_0 = 1$ and solve for ξ which gives

$$\xi_{crit} = \mu\widetilde{\mathcal{R}_0}\left(1 - \frac{1}{\widetilde{\mathcal{R}_0}}\right)$$

where $\widetilde{\mathcal{R}_0}$ is the reproduction number in the absence of vaccination. We note that the critical vaccination rate is positive only when $\widetilde{\mathcal{R}_0} > 1$. If $\widetilde{\mathcal{R}_0} \leq 1$, then any initial vaccination rate is capable of putting the situation under control. The condition $\mathcal{R}_0 < 1$ holds when $\xi > \xi_{crit}$. Thus, a vaccination rate that is maintained at $\xi > \xi_{crit}$ may succeed in controlling the disease in the long run. A vaccination response that falls below the critical vaccination rate may not be helpful in dealing with the disease and reduced vaccination effort may only lead to disease persistence as $\xi < \xi_{crit}$ is equivalent to $\mathcal{R}_0 > 1$ which is the condition for the emergence of an endemic equilibrium that is locally asymptotically stable.

We now turn our attention to the numerical study of the time - dependent vaccination as a control strategy in the course of Ebola epidemics. Systems (25) and (28) together with the initial conditions (27) and transversality conditions (29), respectively, form part of what is known as the optimality system. The optimality system which is composed of ten differential equations is solved numerically using the Forward - Backward Sweep Method that was discussed in full detail in [33]. In the simulation, we set the time period for the control at $t_f = 120$ days and the upper bound for the vaccination control at $\xi_{max} = 0.90$ while the weight on the cost of vaccination program is arbitrarily chosen for illustration purposes.

Simulation results showing the impact of optimal vaccination strategy on the exposed, infected and quarantined groups are presented in Fig. 4. Rapid decrease on the number of infected individuals is seen if optimal vaccination is employed. Though initially there will be a slight increase in the number of exposed and quarantined individuals, this only lasts for several days and is followed by a continuous fall that leads to Ebola – free stage.

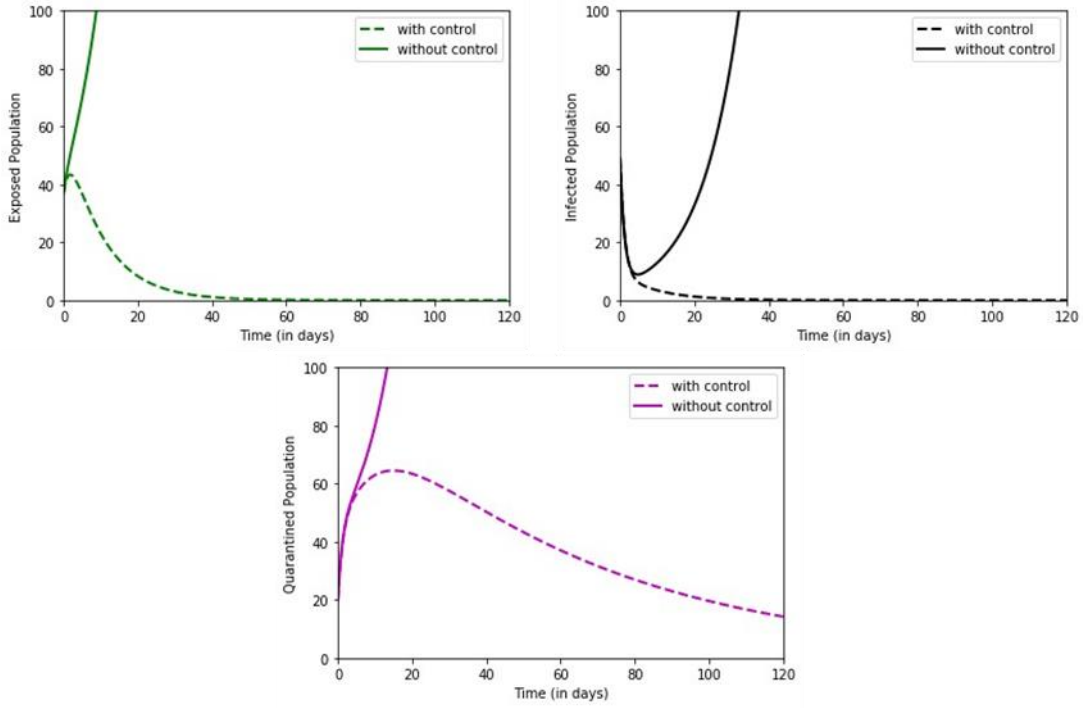

Fig. 4. Dynamics of the exposed, infected and quarantined individuals with optimal vaccination and without vaccination for $c = 10$.

As depicted in Fig.5, the evolution of the control profile over time. It shows that if $c = 10$, then it is optimal to start vaccination at the maximum rate but for the first two days only after cases are detected and decrease it in time. If we can exert this required effort on vaccination then we can have a community that is free from the disease.

With the controlled model, we notice that vaccination, depending on the cost associated with it, cannot always be carried out at maximum rate. As an example, when $c = 100$, the optimal way is to administer vaccination at the beginning starting with the 55% rate only and gradually decrease it in time as shown in Fig. 5 right panel. Thus, as the cost of vaccination control becomes expensive, it will not be optimal to start the vaccination strategy at the maximum rate. This finding agrees with the result that is given earlier in [34] using a simpler model.

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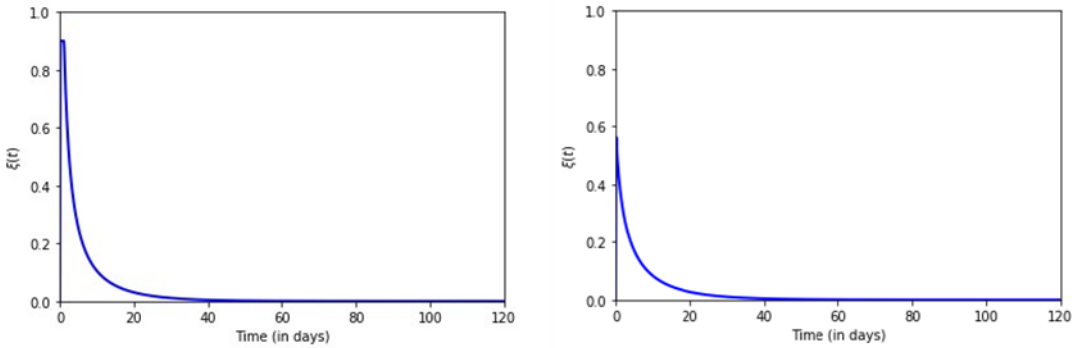

Fig. 5. Graphical representation of vaccination strategies for $c = 10$ (left panel) and for $c = 100$ (right panel).

DISCUSSION

This study mainly explores the importance of vaccination as an immediate response in mitigating the spread of EVD. Because EVD possesses a considerable incubation period and because we want to reflect in the model the effect of quarantine (or hospitalization) measure which played a major role in containing past outbreaks of the disease, our model is more realistic for our objective than SIS - type models. For the model with constant vaccination, we derive the basic reproduction number $\mathcal{R}_0$ using the next generation matrix. It is shown that the existence of equilibrium points and the qualitative properties of solutions of the model with constant vaccination are completely determined by the basic reproduction number $\mathcal{R}_0$. We prove using Routh - Hurwitz criterion the local stability of the equilibrium points. We see that the disease- free equilibrium of the system is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$. If $\mathcal{R}_0 > 1$ then a unique endemic equilibrium point exists and it is locally asymptotically stable which means that the infection will remain in the community. The existence of a forward bifurcation at $\mathcal{R}_0 = 1$ is demonstrated using the approach by Castillo - Chavez and Song. The result on the existence of a forward bifurcation suggests that maintaining the reproduction number $\mathcal{R}_0$ to below unity by using vaccination measure is sufficient for disease eradication and its existence precludes the occurrence of backward bifurcation scenario wherein disease persistence is still possible even if we are successful at reducing $\mathcal{R}_0$ to below unity. In the simulation stage, we use a set of parameter values from various literature that considered Ebola disease to illustrate possible scenarios to expect when there is a vaccination campaign for the disease. Our simulations show that if $\mathcal{R}_0 < 1$, then the solutions tend to the disease - free equilibrium whereas if $\mathcal{R}_0 > 1$, then there will be disease persistence which matched our theoretical results. From the expression of the basic reproduction number of the model, we compute the critical vaccination rate which can serve as a basis for determining what vaccination rate is capable of controlling the epidemic.

For the model where we allowed the vaccination to vary with time, we conduct a study based on optimal control theory acknowledging the fact that in situations where our ultimate objective is to stop the spread of a disease through implementation of available control strategies, there will always be limitations on resources which are unavoidable. The optimal control study helps us determine an optimal vaccination strategy which has the potential to minimize the number of infected individuals and thus the outbreak size. The characterization of the optimal vaccination control is derived with the aid of Pontryagin's Maximum Principle. In our simulations we use the same set of parameter values used in the simulation of the model with constant rate of vaccination. Simulations reveal that if we apply optimal vaccination, then disease eradication is more pronounced and is achievable in a short period of time as compared to the situations with no vaccination at all, that is, we only rely on quarantine (or hospitalization) as a control measure. The simulation results enable us to address public health - related questions whether we start vaccination control as soon as possible or delay it for some time and if we should start vaccinating at maximum rate or not.

For future considerations, the authors suggest that a sensitivity analysis using the method due to Chitnis et al. in [35] be performed to identify other control measures that may be implemented along with vaccination to achieve better results in controlling the disease. The authors also recommend looking into the dynamics of the disease when vaccination and quarantine controls are both time dependent.

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CONFLICT OF INTEREST

The author declares that she has no conflict of interest.

REFERENCES

1. Iván, A, Losada, J, Ndaïrou F, Nieto JJ, Tcheutia, DD. Mathematical modeling of 2014 Ebola outbreak. Mathematical Methods in the Applied Sciences. 2015; 40(17):6114 – 6122. doi: 10.1002/mma.3794.
2. Baştuğ A, Bodur, H. Ebola viral disease: What should be done to combat the epidemic in 2014? Turk J Med Sci. 2015; 45(1):1–5. doi: 10.3906/sag-1411-37.
3. Boujakjian H. Modeling the spread of Ebola with SEIR and optimal control. SIAM Undergraduate Research Online. 2016; 9:299–310. doi:10.1137/16S015061.

[Downloaded from vacres.pasteur.ac.ir on 2026-11-16]

[DOI: 10.52547/vacres.8.1.23]

4. Bukreyev AA, Chandran K, Dolnik O, Dye JM, Ebihara H, Leroy EM, et al. Discussions and decisions of the 2012-2014 International Committee on Taxonomy of Viruses (ICTV) Filoviridae Study Group, January 2012-June 2013. Arch Virol. 2014; 159(4):821–830. doi:10.1007/s00705-013-1846-9.
5. Buonomo B, Lacitignola D, and Vargas-De-Léon C. Qualitative analysis and optimal control of an epidemic model with vaccination and treatment. Mathematics and Computers in Simulation. 2014; 100:88–102. doi.10.1016/j.matcom.2013.11.005.
6. Castillo-Chavez, C and Song B. Dynamical models of tuberculosis and their applications. Mathematical Biosciences & Engineering. 2004; 1(2):361-404. doi:10.3934/mbe.2004.1.361.
7. Cenciarelli O, Pietropaoli S, Malizia A, Carestia M, D'Amico F, Sassolini A, et al. Ebola virus disease 2013-2014 outbreak in West Africa: An analysis of the epidemic spread and response. Int J Microbiol. 2015. doi: 10.1155/2015/769121.
8. Changula K, Kajihara M, Mweene AS, Takada A. Ebola and Marburg virus diseases in Africa: Increased risk of outbreaks in previously unaffected areas? Microbiol Immunol. 2014; 58(9):483–491. doi:10.1111/1348-0421.12181.
9. Chitnis N, Hyman JM, Cushing JM. Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model. Bull Math Biol. 2008. doi: 10.1007/s11538-008-9299-0.
10. Chowell G, Hengartner NW, Castillo-Chavez C, Fenimore PW, Hyman JM. The basic reproductive number of Ebola and the effects of public health measures: the cases of Congo and Uganda. J Theor Biol. 2004; 229(1):119–126. doi: 10.1016/j.jtbi.2004.03.006.
11. Diaz P, Constantine P, Kalmbach K, Jones E, Pankavich S. A modified SEIR model for the spread of Ebola in Western Africa and metrics for resource allocation. Applied Mathematics and Computation. 2018; 324:141–155. doi.10.1016/j.amc.2017.11.039.
12. Diekmann O, Heesterbeek JAP, Metz JA. On the definition and the computation of the basic reproduction ratio R_0 in models for infectious diseases in heterogeneous populations. J Math Biol. 1990; 28(4): 365–382. doi.10.1007/BF00178324.
13. République Démocratique du Congo Ministére de la Santé. Echos Ebola RDC 2018. https: //mailchi.mp/4bc30620b518/ebola_rdc_17juin?e=892a63cca2 (2018). Accessed June 27, 2020.
14. Wikipedia The Free Encyclopedia. List of sovereign states and dependent territories by birth rate. https://en.wikipedia.org/wiki/List_of_sovereign_states_and_dependent_ territories_by_birth_rate (2020). Accessed June 27, 2020.
15. The World Factbook. Guinea. https://www.cia.gov/library/publications/ the-world-factbook/geos/gv.html (2020). Accessed June 27, 2020.
16. Feldmann H, Klenk H. Marburg and Ebola viruses. Adv Virus Res. 1996; 47: 1–52. doi: 10.1016/s0065-3527(08)60733-2.
17. US Food and Drug Adminstration. https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/ebola-preparedness-and-response-updates-fda (2019). Accessed June 27, 2020.
18. Kucharski AJ, Edmunds WJ. Case fatality rate for Ebola virus disease in West Africa. The Lancet. 2014. doi:10.1016/S0140-6736(14)61706-2.
19. Lefebvre A, Fiet C, Belpois-Duchamp C, Tiv M, Astruc K, Aho Glélé LS. Case fatality rates of Ebola virus diseases: A meta-analysis of World Health Organization data. Medecine et maladies infectieuses. 2014; 44(9):412–416. doi: 10.1016/j.medmal.2014.08.005.
20. Lenhart S, Workman JT. Optimal control applied to biological models. CRC press; 2007.
21. Lévy Y, Lane C, Piot P, Beavogui AH, Kieh M, Leigh B, et al. Prevention of Ebola virus disease through vaccination: where we are in 2018. The Lancet. 2018; 392(10149):787–790. doi: 10.1016/S0140-6736(18)31710-0.
22. Li Z, Teng Z, Feng X, Li Y, Zhang H. Dynamical analysis of an SEIT epidemic model with application to Ebola virus transmission in Guinea. Computational and Mathematical Methods in Medicine. 2015. doi: 10.1155/2015/582625.
23. Milligan ID, Gibani MM, Sewell R, Clutterbuck EA, Campbell D, Plested E, et al. Safety and immunogenicity of novel adenovirus type 26– and modified vaccinia ankara–vectored ebola vaccines: a randomized clinical trial. JAMA. 2016; 315(15):1610-23. doi: 10.1001/jama.2016.4218.
24. Muyembe-Tamfum JJ, Kemp A, Kayembe JM, Masumu J, Paweska JT, Mulangu S. Ebola virus outbreaks in Africa: past and present. Onderstepoort Journal of Veterinary Research. 2012; 79(2):1–8. doi: 10.4102/ojvr.v79i2.451.
25. Ndanguza D, Tchuenche JM, Haario H. Statistical data analysis of the 1995 Ebola outbreak in the Democratic Republic of Congo. Afrika Matematika. 2013; 24(1):55–68. doi:10.1007/s13370-011-0039-5.
26. Miller Neilan RL, Schaefer E, Gaff H, Fister KR, Lenhart S. Modeling optimal intervention strategies for Cholera. Bull Math Biol. 2010;72(8):2004–2018. doi: 10.1007/s11538-010-9521-8.
27. World Health Organization. Ebola: Information for the general public. https://www.who.int/ csr/disease/ebola/what-you-need-to-know/en/ (2015). Accessed June 27, 2020.
28. World Health Organization. Cost estimate for vaccine deployment. https://www.who.int/csr/resources/publications/ebola/GEVIT_guidance_AppendixK.pdf?ua=1 (2016). Accessed June 27, 2020.
29. Posny D, Wang J, Mukandavire Z, Modnak C. Analyzing transmission dynamics of Cholera with public health interventions. Mathematical biosciences. 2015;264:38–53. doi: 10.1016/j.mbs.2015.03.006.
30. Rachah A, Torres D FM. Mathematical modelling, simulation, and optimal control of the 2014 Ebola outbreak in West Africa. Discrete Dynamics in Nature and Society. 2015. doi:10.1155/2015/842792.
31. Strogatz SH. Nonlinear Dynamics and Chaos with Applications to Physics, Biology, Chemistry, and Engineering. CRC press; 2018.
32. Van den Driessche P, Watmough J. Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission. Mathematical Biosciences, 2002; 180:29–48. doi: 10.1016/s0025-5564(02)00108-6.
33. Winslow RL, Milligan ID, Voysey M, Luhn K, Shukarev G, Douoguih M, Snape MD. Immune responses to novel adenovirus type 26 and modified vaccinia virus ankara–vectored ebola vaccines at 1 year. JAMA. 2017; 317(10):1075–1077. doi: 10.1001/jama.2016.20644.
34. Wong ZSY, Bui CM, Chughtai AA, Macintyre CR. A systematic review of early modelling studies of Ebola virus disease in West Africa. Epidemiology & Infection. 2017; 145(6):1069–1094. doi: 10.1017/S0950268817000164.
35. Li MY. An introduction to mathematical modeling of infectious diseases. Springer; 2018.

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