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Determining Important Parameters in Ebola Epidemics

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Abstract

The dynamics of Ebola can best be understood using a mathematical model that determines its dynamics in the community. The model designed in this study explicitly incorporates the latency period, the different transmission compartments, and immigration and emigration effects. The steady states of the system are analysed for existence of equilibria and their stability investigated. From qualitative analysis of the model, it is established that a disease-free equilibrium exists and is stable when $\mathcal{R}_0 < 1$. When $\mathcal{R}_0 > 1$, an endemic equilibrium state exists and is stable. Results show further that the model undergoes a hopf bifurcation at the endemic equilibrium and exhibits periodic oscillations. Sensitivity analysis shows that the most effective control measures are increasing hospitalization and reducing transmission rates. The numerical simulations performed demonstrated the theoretical results.

Keywords: Ebola; Hopf bifurcation; Sensitivity indices; Basic reproductive number; Prevalence.

1. Introduction

Ebola Hemorrhagic Fever (EHF) is a highly infectious and deadly disease in humans and non-human primates such as monkeys, gorillas and chimpanzees [1]. It is caused by infection with Ebola virus [2, 3]. The virus is a family of ribonucleic acid (RNA) viruses called the [4, 5].

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Its natural reservoirs may include fruit bats [6]. When bats drop partially eaten fruits and pulp, terrestrial mammals such as gorillas, chimpanzees and duikers feed on these fallen fruits. This chain of events forms a possible indirect means of transmission from the natural host to animal populations. Fruit production, animal behaviours, viral shedding in saliva of bats, and other factors vary at different times and places, which may trigger outbreaks among animal populations [7]. Transmission between natural reservoirs and humans are rare, and an outbreak is usually traceable to a single index case where an individual has handled the carcass of a gorilla, chimpanzee or duiker [8]. The virus then spreads from human to human through direct contact with the blood, bodily secretions, tissues or semen of the infected living. It is also transmitted by dead humans, especially within families, hospitals or during some mortuary rituals where contact among individuals becomes more common [9]. Individuals exposed to the virus become infectious from 1 - 21 days [10].

EHF has been recognised as an emerging and a re-emerging disease and is a serious problem for international public health, especially in Africa [11]. The affected countries include DRC, Republic of Southern Sudan, Uganda, Ivory Coast and Gabon. Between 1976 and 2003, over 1850 cases of Ebola infections with 1200 deaths were reported to the World Health Organisation [12]. In 2000 and 2001 the largest human epidemic with 425 cases and 224 deaths was reported in Gulu, Mbarara and Masindi districts of Uganda [13]. Specifically, the area in which the epidemic was mainly concentrated was Gulu district, a savannah area located in the north of Uganda (393 cases and 203 deaths) with Case Fatality Ratio (CFR) of 51.7% . The most recent Ebola outbreak in Uganda was in Kibaale district from July 2012 to August with about 53 reported cases and 22 deaths [14]. Clinically, there are four identified known strains of Ebola virus: Ebola-Zaire, Ebola-Sudan, Ebola-Ivory Coast and Ebola-Reston [15]. Of these, Ebola-Zaire and Ebola-Sudan are the most common and have caused outbreaks in DRC, Republic of Southern Sudan and Uganda respectively. The symptoms associated with their infections include high fever, prostration, myalgia, headache and pharyngitis. These symptoms progress to vomiting, diarrhoea, rash, impaired kidney and liver functions, and internal and external bleeding. Infected individuals receive limited care as no specific treatment or vaccine is proven and therefore most infected individuals die due to hypovolemic shock or organ failure within 6 - 10 days of their infections [16]. Individuals who recovered from illness may experience severe loss of strength, hearing and eyesight. Recovery usually occurs within 14 - 60 days after the onset of symptoms.

The threat of infectious diseases to humans and animals is not only a major cause of death and misery but also has the potential to result in a major societal and economic impact [17]. The economic impact of EHF in human and non-human primates is severe. For example, the Ebola outbreak in 2000 reduced Uganda tourism industry and resulted in loss of revenues [18]. Moreover many health workers died because of infections by their patients in hospitals. In an attempt to control epidemic diseases, mathematical models are essential tools in studying a diverse range of diseases [19, 20, 21, 22].

The models allow us to simulate the spread of diseases through the different compartments and explore different kinds of interventions. Models developed by epidemiologists are invaluable and can be used to guide national health policies concerning vaccination and sensitization strategies for diseases such as Hepatitis B and Ebola, and can be used to forewarn of impending epidemics by using data already collected to model the future behaviour of the spread of diseases such as Hepatitis E [23]. They are also useful in helping researchers to

understand the underlying mechanisms that influence the spread of disease and, in the process, suggest control strategies [24].

Numerous mathematical models have been proposed, based on the flow patterns between compartments, to analyse the dynamics of Ebola epidemics. Studies such as in [25], [26], [27], and [18], and the references therein, have all modelled Ebola with interesting results. In this study, a deterministic mathematical model that takes into account immigration and emigration is formulated. It is analysed for the basic reproductive number $\mathcal{R}_0$ and solutions of the model determined. The effects of variation of transmission rates and the impact of interventions are demonstrated through numerical simulations.

2. Materials and Methods

The model developed is based on prior studies as in [18], but allow variability of the population. This is done by including immigration and emigration as described in Fig. 1 of the compartmentalised diagram. The variables are defined as follows: $\boldsymbol{S(t)}$, the number of susceptible individuals; $\boldsymbol{E(t)}$, the number of exposed individuals who have been infected by Ebola virus but are not yet infectious or symptomatic; $\boldsymbol{I(t)}$, the number of symptomatic and infectious individuals in the community; $\boldsymbol{H(t)}$, the number of hospitalised Ebola case individuals who are infectious; $\boldsymbol{F(t)}$, the number of dead Ebola case individuals who may transmit virus during funerals and $\boldsymbol{R(t)}$, the number of individuals removed from the chain of transmission, all at time $\boldsymbol{t}$. Similarly, the parameters are defined as follows: $\boldsymbol{\Lambda}$ is the rate of immigration into the susceptible population; $\boldsymbol{e}$ is the rate of emigration; $\boldsymbol{\beta_I}$ is the rate of transmission of infection in the community before interventions and $\boldsymbol{\beta_H}$ is the rate of transmission of infection at hospitals. We further define $\boldsymbol{\beta_F}$ as the rate of transmission of infection during traditional funerals; $\boldsymbol{K}$ as the rate at which the exposed individuals progress to infectious class $\boldsymbol{I}$; $\boldsymbol{\gamma}$ as the per capita rate at which the infectious and symptomatic individuals in the community are hospitalised; $\boldsymbol{\rho}$ as the fraction of the infectious and symptomatic individuals in the community who are hospitalised; $\boldsymbol{1-\rho}$ is the fraction of the infectious and symptomatic individuals in the community who are not hospitalised; $\boldsymbol{\varepsilon}$ as the fraction of the infectious and symptomatic individuals in the community who die implying that $\boldsymbol{1-\varepsilon}$ recover/survive. The hospitalised Ebola case individuals are removed at a per capita rate $\boldsymbol{\delta}$. A fraction $\boldsymbol{q}$ of these die and are buried/cremated at per capita rate $\boldsymbol{\phi}$, while $\boldsymbol{1-q}$ recover/survive. Those who recover gain permanent immunity to Ebola.

In the model, the per-capita natural births and deaths are ignored since the epidemic takes a short time (3 - 4 months) [26]. Since the $R-$ class consists of individuals cured or dead and buried, they do not contribute to further spread of the disease. As such, the total at-risk-population at time t is $N(t) = S(t) + E(t) + I(t) + H(t) + F(t)$.Moreover, infectious and symptomatic individuals are bed-ridden and thus do not immigrate or emigrate. The above definitions and assumptions give rise to the following system of equations:

$$\frac{dS}{dt} = \Lambda - \frac{1}{N}(\beta_I SI + \beta_H SH + \beta_F SF) - eS,$$

$$\frac{dE}{dt} = \frac{1}{N}(\beta_I SI + \beta_H SH + \beta_F SF) - (K + e)E,$$

$$\frac{dI}{dt} = KE - \gamma I, \qquad (1)$$

$$\frac{dH}{dt} = \rho\gamma I - \delta H,$$

$$\frac{dF}{dt} = q\delta H + \gamma(1-\rho)\varepsilon I - \phi F,$$

$$\frac{dR}{dt} = \phi F + \delta(1-q)H + \gamma(1-\rho)(1-\varepsilon)I.$$

3. Results

To solve for equilibrium points, the left-hand side of Eq. (1) is equated to zero. Note that due to the immigration term $\boldsymbol{\Lambda}$ into the susceptible group, the population would never go to extinction. This implies that there is no trivial equilibrium point i.e. $(\boldsymbol{S}^*, \boldsymbol{E}^*, \boldsymbol{I}^*, \boldsymbol{H}^*, \boldsymbol{F}^*) \neq (\mathbf{0}, \mathbf{0}, \mathbf{0}, \mathbf{0}, \mathbf{0})$. Without disease in the population, there is a disease-free equilibrium state (DFE) at the point $\boldsymbol{E}^* = \boldsymbol{I}^* = \boldsymbol{H}^* = \boldsymbol{F}^* = \mathbf{0}$, at which $\boldsymbol{S}^* = \boldsymbol{\Lambda}/\boldsymbol{e}$. This is the asymptotic carrying capacity of the total population. In other words the population size $\boldsymbol{S} \to \infty$ as $\boldsymbol{t} \to \infty$. Stability of the system is determined by linearising and using the Routh-Hurwitz criterion. The basic reproductive number $\boldsymbol{\mathcal{R}_0}$ is derived as shown in Appendix 1. The basic reproductive number $\boldsymbol{\mathcal{R}_0}$ is defined as the number of secondary infections produced by a single infectious individual during his/her entire lifetime as an infective when introduced in a susceptible population [28, 29]. Therefore,

$$\boldsymbol{\mathcal{R}_0} = \left(\frac{\boldsymbol{\beta_I}}{\boldsymbol{\gamma}} + \frac{\boldsymbol{\beta_H \rho}}{\boldsymbol{\delta}} + \frac{\boldsymbol{\beta_F q \rho}}{\boldsymbol{\phi}} + \frac{\boldsymbol{\beta_F(1-\rho)\varepsilon}}{\boldsymbol{\phi}}\right)\left(\frac{\boldsymbol{K}}{\boldsymbol{K+e}}\right). \qquad (2)$$

To contain the EHF incidence, the population sizes of the exposed, infected in the community, hospitalised and the unburied dead Ebola cases should decrease. This is realized when

$\boldsymbol{\frac{dE}{dt} < 0, \frac{dI}{dt} < 0}$, $\boldsymbol{\frac{dH}{dt} < 0}$ and $\boldsymbol{\frac{dF}{dt} < 0}$.

Using these conditions, that the necessary condition on the susceptible population for the containment of EHF is (steps omitted),

$$\boldsymbol{\frac{S}{N} < \frac{1}{\mathcal{R}_0}}. \qquad (3)$$

It is concluded therefore that to contain EHF incidence in a population, the proportion of susceptible population should be strictly less than the reciprocal of the basic reproductive number $\mathcal{R}_0$. This means that a proportion of susceptible $\geq 1 - 1/\mathcal{R}_0$ ($\equiv 80.59\%$) should be sensitized**.** But, since, then $1 < 1/\mathcal{R}_0$ or $\mathcal{R}_0 < 1$. This agrees with the earlier result that the DFE is stable if $\mathcal{R}_0 < 1$. In addition, there is no global asymptotically stability due to possibility of hopf bifurcation when $\mathcal{R}_0 > 1$ as described by the endemic equilibrium in Eq. (4) below. The EE gives the point when $S \neq 0, E \neq 0, I \neq 0, H \neq 0$ and $F \neq 0$. To obtain this state, the derivatives of S, E, I, H and F are equated to zero and the resulting system solved. This gives (steps omitted),

$$(S^*, E^*, I^*, H^*, F^*) =$$

$$\left(\frac{\{\delta\phi\gamma + \gamma\delta Kq\rho + K\delta\phi + K\rho\gamma\phi + \gamma\delta K\varepsilon(1-\rho)\}\Lambda}{(\beta_I\delta\phi + \beta_H\rho\gamma\phi + \gamma\delta\beta_F q\rho + \gamma\delta\beta_F\varepsilon(1-\rho) + e\delta\phi + e\rho\gamma\phi + \gamma\delta eq\rho + \gamma\delta e\varepsilon(1-\rho) - \delta\phi\gamma)K}\right.,$$

$$\frac{\{\gamma\delta\beta_F q\rho K + \gamma\delta\beta_F\varepsilon K + \beta_I\delta\phi K + \beta_H\rho\gamma\phi K - \delta\phi\gamma K - \delta\phi\gamma e - \gamma\delta\beta_F\varepsilon\rho K\}\Lambda}{(K+e)(\beta_I\delta\phi + \beta_H\rho\gamma\phi + \gamma\delta\beta_F q\rho + \gamma\delta\beta_F\varepsilon(1-\rho) + e\delta\phi + e\rho\gamma\phi + \gamma\delta eq\rho + \gamma\delta e\varepsilon(1-\rho) - \delta\phi\gamma)K},$$

$$\frac{\rho\{\gamma\delta\beta_F q\rho K + \gamma\delta\beta_F\varepsilon K + \beta_I\delta\phi K + \beta_H\rho\gamma\phi K - \delta\phi\gamma K - \delta\phi\gamma e - \gamma\delta\beta_F\varepsilon\rho K\}\Lambda}{(K+e)(\beta_I\delta\phi + \beta_H\rho\gamma\phi + \gamma\delta\beta_F q\rho + \gamma\delta\beta_F\varepsilon(1-\rho) + e\delta\phi + e\rho\gamma\phi + \gamma\delta eq\rho + \gamma\delta e\varepsilon(1-\rho) - \delta\phi\gamma)\delta},$$

$$\frac{\{\gamma\delta\beta_F q\rho K + \gamma\delta\beta_F\varepsilon K + \beta_I\delta\phi K + \beta_H\rho\gamma\phi K - \delta\phi\gamma K - \delta\phi\gamma e - \gamma\delta\beta_F\varepsilon\rho K\}\Lambda}{(K+e)(\beta_I\delta\phi + \beta_H\rho\gamma\phi + \gamma\delta\beta_F q\rho + \gamma\delta\beta_F\varepsilon(1-\rho) + e\delta\phi + e\rho\gamma\phi + \gamma\delta eq\rho + \gamma\delta e\varepsilon(1-\rho) - \delta\phi\gamma)\gamma},$$

$$\left.\frac{(\gamma\delta\beta_F q\rho K + \gamma\delta\beta_F\varepsilon K + \beta_I\delta\phi K + \beta_H\rho\gamma\phi K - \delta\phi\gamma K - \delta\phi\gamma e - \gamma\delta\beta_F\varepsilon\rho K)(q\rho + \varepsilon - \rho\varepsilon)\Lambda}{(K+e)(\beta_I\delta\phi + \beta_H\rho\gamma\phi + \gamma\delta\beta_F q\rho + \gamma\delta\beta_F\varepsilon(1-\rho) + e\delta\phi + e\rho\gamma\phi + \gamma\delta eq\rho + \gamma\delta e\varepsilon(1-\rho) - \delta\phi\gamma)\phi}\right).$$

For endemic Equilibrium point to exist $E^*, I^*, H^*, F^* > 0$. Thus

$$\beta_I\delta\phi K + \beta_H\rho\gamma\phi K + \gamma\delta\beta_F q\rho K + \gamma\delta\beta_F\varepsilon(1-\rho)K - \delta\phi\gamma(K+e) > 0$$

implies

$\beta_I\delta\phi K + \beta_H\rho\gamma\phi K + \gamma\delta\beta_F q\rho K + \gamma\delta\beta_F\varepsilon(1-\rho)K > \delta\phi\gamma(K+e)$ or $\mathcal{R}_0 > 1$, where $\mathcal{R}_0$ is as defined in Eq. (2). In terms of $\mathcal{R}_0$, the expressions for S^*, E^*, I^*, H^* and F^* are given by

$$(S^*, E^*, I^*, H^*, F^*) = \left(\frac{a_1 S_0}{b_1\mathcal{R}_0 + b_2}, \frac{\mathcal{R}_0 - 1}{a_2(b\mathcal{R}_0 + c)}, \frac{\mathcal{R}_0 - 1}{a_3(b\mathcal{R}_0 + c)}, \frac{\mathcal{R}_0 - 1}{a_4(b\mathcal{R}_0 + c)}, \frac{\mathcal{R}_0 - 1}{a_5(b\mathcal{R}_0 + c)}\right) \quad (4)$$

The derivation of this point is achieved by dividing both numerator and denominator for expression of $S^*$by $(K+e)\delta\gamma\phi e$ and expressions of E^*, I^*, H^*, F^* by $(K+e)\delta\gamma\phi$, where $a_1, a_2, a_3, a_4, a_5, b, b_1, b_2, c$ are all constants. Using the parameter values in Table 1 and the endemic equilibrium expressed in terms of $\mathcal{R}_0$, numerical results (not shown), confirm a hopf bifurcation and periodic solutions. Thus, a persistent Ebola infection with some interventions can be established for the model. The periodic solutions are due to the number of contacts between susceptibles and infectives influenced by the quarantined class. Therefore, it is concluded that the strategies to reduce $\mathcal{R}_0$ to below unity can successfully control EHF. Hence, to contain Ebola Hemorrhagic Fever, the strategies should be aimed at reducing $\mathcal{R}_0$ sufficiently close to zero [30] i.e. $\gamma > 1.1$.

Figure 1 shows the schematic compartmental diagram for the SEIHFR Ebola model. The parameters and dynamics are described previously within this section.

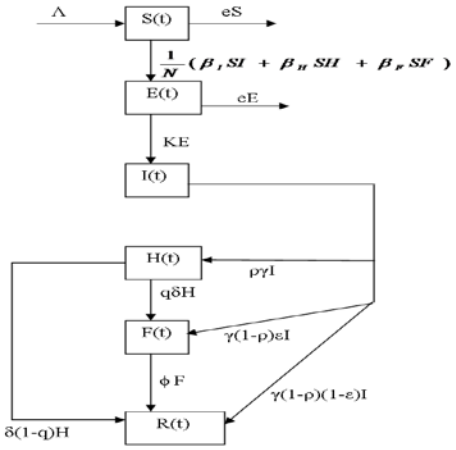

Figure 1: A schematic compartmental diagram for the SEIHFR Ebola model

4. Sensitivity Analysis

In order to identify possible interventions and control strategies for EHF epidemic, it is necessary to quantify the relative contribution of the different factors responsible for its transmission and prevalence. Prevalence refers to the proportion of persons in a population who have the disease in a given period of time. The rate at which initial disease transmission occurs is proportional to the basic reproductive number $\mathcal{R}_0$ whereas disease prevalence is proportional to the EE. This section presents the relative amount and type of change inherent in the model as captured by the terms which define $\mathcal{R}_0$. The sensitivity indices of the model parameters are computed using the approach in [31] as follows.

Suppose we let λ represent any of the non-negative parameters $\beta_I, \beta_H, \beta_F, K, e, \gamma, \delta, \rho, q, \varepsilon$ and ϕ that define the basic reproductive number in Eq. (2). If a small perturbation $\partial\lambda$ is made to the parameter λ, a corresponding change will occur in $\mathcal{R}_0$ as $\partial\mathcal{R}_0$, where

$$\partial\mathcal{R}_0 = \mathcal{R}_0(\lambda + \partial\lambda) - \mathcal{R}_0(\lambda) \approx \partial\lambda \frac{\partial\mathcal{R}_0}{\partial\lambda}. \quad (5)$$

The normalized sensitivity index Φ_λ is the ratio of the corresponding normalized changes and is defined as

$$\Phi_\lambda := \frac{\frac{\partial\mathcal{R}_0}{\mathcal{R}_0}}{\frac{\partial\lambda}{\lambda}} = \frac{\lambda}{\mathcal{R}_0}\frac{\partial\mathcal{R}_0}{\partial\lambda}. \quad (6)$$

The perturbed value of $\mathcal{R}_0$ in terms of Φ_λ is determined as follows:

From equation (5), we have

$$\mathcal{R}_0(\lambda + \partial\lambda) \approx \mathcal{R}_0(\lambda) + \partial\lambda \frac{\partial \mathcal{R}_0}{\partial \lambda}. \quad (7)$$

From eq. (6) we get

$$\frac{\partial \mathcal{R}_0}{\partial \lambda} = \frac{\mathcal{R}_0}{\lambda} \Phi_\lambda. \quad (8)$$

Substituting for $\frac{\partial \mathcal{R}_0}{\partial \lambda}$ in eq. (7) and simplifying gives

$$\mathcal{R}_0(\lambda + \partial\lambda) \approx \left(1 + \frac{\partial\lambda}{\lambda} \Phi_\lambda\right) \mathcal{R}_0 \quad (9)$$

Making $\frac{\partial\lambda}{\lambda}$ the subject from eqn. (9) implies

$$\frac{\partial\lambda}{\lambda} = -\left(\frac{\mathcal{R}_0(\lambda) - \mathcal{R}_0(\lambda+\partial\lambda)}{\mathcal{R}_0(\lambda)}\right) \frac{1}{\Phi_\lambda}. \quad (10)$$

Equation (10) is applied to each of the parameters λ and the respective indices obtained as shown in Table 1. For the values of the parameters used in this model, the sensitivity indices Φ_{β_I}, $\Phi_{\beta_F}, \Phi_{\beta_H}, \Phi_\rho$, Φ_K, Φ_q and Φ_ε are positive and Φ_e, Φ_δ, Φ_ϕ and Φ_γ are negative. Furthermore, since all of the indices are functions of the parameters, the sensitivity indices will change as the parameter values change. For the specific case of parameter values in Table 2, the results are summarized for the sensitivity indices and the associated percentage changes needed to effect a 1% decrease in $\mathcal{R}_0$ in Table 1. The parameters are arranged from the most sensitive to the least sensitive. The positive sign of the index shows that when the value of the parameter is increased, the value of $\mathcal{R}_0$ increases and when the value of the parameter is reduced, the value of $\mathcal{R}_0$ decreases. The negative sign of the index shows that when the value of the parameter is increased, the value of $\mathcal{R}_0$ reduces and when the value of the parameter is reduced, the value of $\mathcal{R}_0$ increases. The magnitudes of the indices are used to compare and determine the sensitive parameters of the model. From Table 1, it can be seen that the most effective way to reduce $\mathcal{R}_0$ is to decrease the transmission rate in community β_I, and increase the hospitalization rate γ. $\Phi_{\beta_I} = 0.72309$ means that a 1.38% decrease in β_I, that is from $\beta_I = 0.50457$ to $\beta_I = 0.49761$, results in a 1% decrease in $\mathcal{R}_0$, whereas the value $\gamma = 0.2381$ means that the mean time to hospitalise an infected individual in the community is approximately 4.2 days. $\Phi_\gamma = -0.72309$ means that a 1.38% increase in hospitalization rate γ, results in a 1% decrease in $\mathcal{R}_0$. However, since bounds exist on how much a given parameter can change in practice, achieving control $\mathcal{R}_0 < 1$) can require changing parameter values including those with lower or least sensitivity indices. For example, other feasible intervention strategies include reducing transmission rate during funeral activities β_F, reducing transmission rate at hospital, H, increasing the burial rate ϕ and the per-capita survival rate at hospital δ. The least sensitive in the initial disease spread is to reduce the case fatality ratios q and ε. The value $\Phi_q = 0.06882$ means that a 14.53% decrease in q results in a 1% decrease in R_0 and the value $\Phi_\varepsilon = 0.03706$ means that a 26.98% decrease in ε results in a 1% decrease in $\mathcal{R}_0$. Clearly, it can be concluded that reducing q and $\in$ are not important factors in the initial disease transmission since they are probabilities in which we have no control. In the calculation of indices, it can be concluded further that the sensitivity indices of $\mathcal{R}_0$ depend on other parameters that define $\mathcal{R}_0$.

Table 1: Parameter estimates for the Ebola virus model

Symbol	Biological meaning	Value	Reference
ϕ	Per-capita burial rate	0.5	[26]
δ	Per-capita survival rate at hospital	0.1471	[39]
K	Progression rate to infectious stage	0.09091	[7]
β_I	Transmission rate in community	0.50457	[26]
β_H	Transmission rate at hospital	0.11343	[26]
β_F	Transmission rate during burial	0.3001	[26]
ε	Case fatality ratio in community	0.517	[34]
q	Case fatality ratio at hospital	0.517	[34]
ρ	Proportion of cases hospitalised	0.65	[26]
γ	Per-capita hospitalization rate	0.2381	[26]
Λ	Immigration rate	76	[Estimated]
e	Per-capita emigration rate	0.076	[Estimated]

5. Parameter Estimates

The main reason for research in mathematical epidemiology is to estimate parameters. Accurate parameter estimate enables an investigator to make inferences about the world we live in [32]. In this research, some parameter values have been obtained while others derived from epidemiological and demographic literature of [18,10,33,13,34].

Table 2: Sensitivity indices

Parameter	Sensitivity index	% change for a 1% decrease in $\mathcal{R}_0$
Ψ_{β_I}	0.72309	-1.38
Ψ_{γ}	-0.72309	1.38
Ψ_{K}	0.45534	-2.20
Ψ_{e}	-0.45534	2.20
Ψ_{β_H}	0.17103	-5.85
Ψ_{δ}	-0.17103	5.85
Ψ_{ρ}	0.17103	-5.85
Ψ_{β_F}	0.10588	-9.44
Ψ_{ϕ}	-0.10588	9.44
Ψ_{q}	0.06882	-14.53
Ψ_{ε}	0.03706	-26.98

Table 3: Parameter values for the Ebola virus model before and after interventions

Symbol	Biological meaning	Value before	Value after
ϕ	Per-capita burial rate	0.5	4
δ	Per-capita survival rate at hospital	0.1471	0.1471
K	Progression rate to infectious stage	0.09091	0.09091
β_I	Transmission rate in community	0.53914	0.05757
β_H	Transmission rate at hospital	0.91814	0
β_F	Transmission rate during burial	3.03671	0
ε	Case fatality ratio in community	0.517	0.517
q	Case fatality ratio at hospital	0.517	0.517
ρ	Proportion of cases hospitalised	0.65	0.65
γ	Per-capita hospitalization rate	0.2381	1
Λ	Immigration rate	76	76
e	Per-capita emigration rate	0.076	0.076

The per-capita burial rate ϕ is assumed to be inversely proportional to the period for which Ebola dead case patients are infectious. In the work of Legrand [18], the average infectious period is 2 days after their deaths, implying $\phi = 1/2 = 0.5$. Similarly, per-capita survival rate δ varies from strain to strain and from country to country. [18] argued that per-capita survival rate δ is estimated from $1/(1/\gamma_i - 1/\gamma)$, where $1/\gamma_i = 11$ days is the mean duration of the infectious period for patients who survived to their illness and $1/\gamma = 4.2$ days is the mean duration between onset of symptoms and hospitalisation. Therefore, δ is computed to be 0.17241. According to Bray [10], individuals exposed to the virus become infectious between 1-21 days. The average incubation period is $1/K$ =11 days. Therefore, for this study it is taken that K=0.09091 day^{-1}. β_I, the rate at which the susceptibles are getting infected in community before interventions, β_H, the rate at which the susceptibles are getting infected at hospitals and β_F, the rate at which the susceptibles are getting infected during traditional burials are set to match the expected number of infections produced in $1/\gamma$, $1/\delta$ and $1/\phi$ days, respectively. The mean effective infectious periods $1/\gamma$, $1/\delta$ and $1/\phi$ are more than the periods of time during which the individual is potentially infectious. This is because transmission increases with duration of the disease and direct contact with infected individuals during late stages of illness [17]. After interventions, no transmission occurred at hospital or during burial and transmission in the community decreased [18]. It is therefore taken that $\beta_I = 0.50457\ (0.05757 - 0.53914)$ day^{-1}, $\beta_H = 0.11343\ (0 - 0.91814)$ day^{-1} and $\beta_I = 0.50457\ (0.05757 - 0.53914)$ day^{-1}, $\beta_F = 0.3001\ (0 - 3.03671)$ day^{-1}. According to Oyok [13], 393 cases of Ebola with 203 deaths occurred in Gulu. Case fatality ratio, $CFR = (\text{Number of cases})/(\text{Total number of cases}) = 203/393 = 0.517$. For the purpose of this research, it is considered that $\varepsilon = q = 0.517$ since the difference between cases and deaths at hospital and in community before interventions is negligible. This is because there is no specific treatment proven and thus, case fatality ratio at hospital = CFR in community. Proportion of cases hospitalised is 80% but the effective proportion of cases hospitalised is

$\rho = 0.65$ [18]. Legrand [18] further stated that the average period from onset to hospitalisation is $1/\gamma = (1 - 4.2)$ days. Therefore, the value $\gamma = 0.23810\ (0.23810 - 1)\ \text{day}^{-1}$ is adopted. According to the Uganda Bureau of Statistics in [34], the total arrivals of residents and non-residents increased from 524,000 in 2002 to 770,000 in 2006 in Uganda through the twenty entry/exit points. Immigrants per entry point per day is: $\Lambda = (\text{Total arrivals in Gulu District})/(\text{Number of days in a year}) = 26200/365 = 71.78082192$. In this research, it is assumed that $\Lambda = 76\ \text{immigrants day}^{-1}$ instead of $\Lambda = 72\ \text{immigrants day}^{-1}$ to account for unrecorded immigration. Emigration is the process of individuals leaving their habitat for another one. Immigration rate Λ and emigration rate e control the total population sizes because the asymptomatic carrying capacity is Λ/e. It is determined by the observed population growth. This is set at $\Lambda/e \cong 1000$ [33], implying that $e = 76/1000 = 0.076\ \text{day}^{-1}$. The parameter values are summarised as in Tables 1 and 3.

6. Conclusions

Infectious disease models are important for both the building and testing of theories [28]. They are used in comparing, planning, implementing and evaluating various detection, prevention and control programme [28]. Indeed, one of the most important issues in epidemiology is the controlled eradication of a disease. Sensitivity analysis of the model shows that the most important parameters are transmission rate in community β_I (50.457% per day) and hospitalization rate γ (23.81% per day), which plays a leading role in the initial spread of the disease.

Simulations have played an important role in explaining the dynamics of the disease through investigating the variations in the effects of basic reproductive number $\mathcal{R}_0$. Both the qualitative and numerical results agree that the disease goes to extinction when $\mathcal{R}_0 < 1$ and persists when $\mathcal{R}_0 > 1$. The calculated $\mathcal{R}_0$ ranged from 0.03135635193 to 5.153260765. This makes sense since it shows that Ebola patients were infected more before interventions due to misdiagnosis and misunderstanding about the Ebola virus. However, from the value of $\mathcal{R}_0 = 1.596235632$ obtained, it can be concluded that the system is not globally asymptotically stable and it agrees with the result in Section 3, which states that there exists a bifurcation in the model.

Simulation results further demonstrate that the dynamics of EHF is influenced by $\mathcal{R}_0$. Intuitively, this means that the dynamics of EHF changes with the following factors: hospitalisation rate, transmission rates, case fatality ratios, burial rate, emigration rate, progression rate from latent to infective class, survival rate at hospital and proportion of cases hospitalised. Basing on the observations of the changes in the trend of EHF incidence level due to variations in the above parameters (Tables 1 and 3), it can be concluded that the measures to eradicate EHF should target hospitalisation rate, transmission rates, survival rate at hospital and burial rate.

The study established that a reduction in the basic reproductive number can be done through reducing transmission rates, case fatality ratios, progression rate and increasing hospitalisation rate, burial rate, survival rate and emigration rate. These findings concur with the intervention measures investigated by [35], which comprised: social mobilization, health education and training, case management, laboratory confirmation,

active surveillance, resource or logistics mobilization and improved communication. These control interventions therefore, aim at minimizing transmission in the health care setting and in the community, reducing the case fatality ratios, strengthening coordination for the response and building capacity for surveillance and control.

7. Recommendations for Further Studies

The study is only based on deterministic model in humans. This model can be developed further by formulating a mathematical model in both animals and humans. This could provide better results once the Ebola virus is zoonotic.

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Appendix 1: Deriving Basic Reproductive Number $\mathcal{R}_0$

The basic reproductive number $\mathcal{R}_0$ defined as the number of secondary infections produced by a single infectious individual during his/her entire lifetime as an infective, when introduced in a susceptible population [28, 29]. In this derivation, the method of van den Driessche and Watmough [29] introduced by Diekmann et al. [20] is used. The compartments of the model are recorded so that the first four infective classes (E, I, H, followed by F) come first. Then the terms in each equation of the system (1) are categorized into terms describing newly exposed individuals, stored in a matrix, $(\hat{\mathcal{F}}_i)$ ($\hat{\mathcal{F}}_i$ is used to represent terms describing newly exposed individuals instead of $\mathcal{F}_\mathrm{i}$ to avoid confusion with infective class, F) and the transition terms, stored in a matrix, $(\mathcal{V}_\mathrm{i})$.

Therefore

$$\frac{dE}{dt} = \frac{1}{N}(\beta_I SI + \beta_H SH + \beta_F SF) - (K + e)E,$$

$$\frac{dI}{dt} = KE - \gamma I,$$

$$\frac{dH}{dt} = \rho\gamma I - \delta H,$$

$$\frac{dF}{dt} = q\delta H + \gamma(1 - \rho)\varepsilon I - \phi F,$$

$$\frac{dS}{dt} = \Lambda - \frac{1}{N}(\beta_I SI + \beta_H SH + \beta_F SF) - eS,$$

$$\hat{\mathcal{F}}_i = \begin{pmatrix} \frac{1}{N}(\beta_I SI + \beta_H SH + \beta_F SF) \\ 0 \\ 0 \\ 0 \end{pmatrix} \text{ and } \mathcal{V}_i = \begin{pmatrix} (K+e)E \\ \gamma I - KE \\ \delta H - \rho\gamma I \\ \phi F - q\delta H - \gamma(1-\rho)\varepsilon I \end{pmatrix}.$$

Thus,

$$\hat{\mathrm{F}}_i = \begin{pmatrix} \frac{\partial \hat{\mathcal{F}}_1}{\partial E} & \frac{\partial \hat{\mathcal{F}}_1}{\partial I} & \frac{\partial \hat{\mathcal{F}}_1}{\partial H} & \frac{\partial \hat{\mathcal{F}}_1}{\partial F} \\ \frac{\partial \hat{\mathcal{F}}_2}{\partial E} & \frac{\partial \hat{\mathcal{F}}_2}{\partial I} & \frac{\partial \hat{\mathcal{F}}_2}{\partial H} & \frac{\partial \hat{\mathcal{F}}_2}{\partial F} \\ \frac{\partial \hat{\mathcal{F}}_3}{\partial E} & \frac{\partial \hat{\mathcal{F}}_3}{\partial I} & \frac{\partial \hat{\mathcal{F}}_3}{\partial H} & \frac{\partial \hat{\mathcal{F}}_3}{\partial F} \\ \frac{\partial \hat{\mathcal{F}}_4}{\partial E} & \frac{\partial \hat{\mathcal{F}}_4}{\partial I} & \frac{\partial \hat{\mathcal{F}}_4}{\partial H} & \frac{\partial \hat{\mathcal{F}}_4}{\partial F} \end{pmatrix} = \begin{pmatrix} -\frac{1}{N^2}(\beta_I SI + \beta_H SH + \beta_F SF) & \frac{\beta_I SN - \beta_I SI}{N^2} & \frac{\beta_H SN - \beta_H SH}{N^2} & \frac{\beta_F SN - \beta_F SF}{N^2} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$\mathrm{V}_i = \begin{pmatrix} \frac{\partial \mathcal{V}_1}{\partial E} & \frac{\partial \mathcal{V}_1}{\partial I} & \frac{\partial \mathcal{V}_1}{\partial H} & \frac{\partial \mathcal{V}_1}{\partial F} \\ \frac{\partial \mathcal{V}_2}{\partial E} & \frac{\partial \mathcal{V}_2}{\partial I} & \frac{\partial \mathcal{V}_2}{\partial H} & \frac{\partial \mathcal{V}_2}{\partial F} \\ \frac{\partial \mathcal{V}_3}{\partial E} & \frac{\partial \mathcal{V}_3}{\partial I} & \frac{\partial \mathcal{V}_3}{\partial H} & \frac{\partial \mathcal{V}_3}{\partial F} \\ \frac{\partial \mathcal{V}_4}{\partial E} & \frac{\partial \mathcal{V}_4}{\partial I} & \frac{\partial \mathcal{V}_4}{\partial H} & \frac{\partial \mathcal{V}_4}{\partial F} \end{pmatrix} = \begin{pmatrix} K+e & 0 & 0 & 0 \\ -K & \gamma & 0 & 0 \\ 0 & -\rho\gamma & \delta & 0 \\ 0 & -\gamma(1-\rho)\varepsilon & -q\delta & \phi \end{pmatrix}.$$

At $P_0 = \left(\frac{\Lambda}{e}, 0, 0, 0, 0\right)$

$$\hat{\mathrm{F}}_i = \begin{pmatrix} 0 & \beta_I & \beta_H & \beta_F \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \text{ and}$$

$$\mathrm{V}_i = \begin{pmatrix} K+e & 0 & 0 & 0 \\ -K & \gamma & 0 & 0 \\ 0 & -\rho\gamma & \delta & 0 \\ 0 & -\gamma(1-\rho)\varepsilon & -q\delta & \phi \end{pmatrix}.$$

Using maple 13, the inverse of V_i is given by

$$\mathrm{V}_i^{-1} = \begin{pmatrix} \frac{1}{K+e} & 0 & 0 & 0 \\ \frac{K}{\gamma(K+e)} & \frac{1}{\gamma} & 0 & 0 \\ \frac{K\rho}{\delta(K+e)} & \frac{\rho}{\gamma} & \frac{1}{\delta} & 0 \\ \frac{K\rho q}{\phi(K+e)} + \frac{K(1-\rho)\varepsilon}{\phi(K+e)} & \frac{q\rho+(1-\rho)\varepsilon}{\phi} & \frac{q}{\phi} & \frac{1}{\phi} \end{pmatrix}$$

and $\hat{F}_i V_i^{-1} = \begin{pmatrix} 0 & \beta_I & \beta_H & \beta_F \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{K+e} & 0 & 0 & 0 \\ \frac{K}{\gamma(K+e)} & \frac{1}{\gamma} & 0 & 0 \\ \frac{K\rho}{\delta(K+e)} & \frac{\rho}{\gamma} & \frac{1}{\delta} & 0 \\ \frac{K\rho q}{\phi(K+e)} + \frac{K(1-\rho)\varepsilon}{\phi(K+e)} & \frac{q\rho+(1-\rho)\varepsilon}{\phi} & \frac{q}{\phi} & \frac{1}{\phi} \end{pmatrix}$

$$\hat{F}_i V_i^{-1} = \begin{pmatrix} \frac{\beta_I \boldsymbol{K}}{\gamma(K+e)} + \frac{\beta_H \rho K}{\delta(K+e)} + \frac{\beta_F K q \rho}{\phi(K+e)} + \frac{\beta_F(1-\rho)\varepsilon K}{\phi(K+e)} & \frac{\beta_I}{\gamma} + \frac{\rho\beta_H}{\delta} + \frac{\beta_F(q\rho+(1-\rho)\varepsilon)}{\phi} & \frac{\beta_H}{\delta} + \frac{\beta_H q}{\phi} & \frac{\beta_F}{\phi} \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}.$$

The eigenvalues of the matrix $\hat{F}_i V_i^{-1}$ are given by

$$\lambda_1 = \frac{\beta_I \boldsymbol{K}}{\gamma(K+e)} + \frac{\beta_H \rho K}{\delta(K+e)} + \frac{\beta_F K q \rho}{\phi(K+e)} + \frac{\beta_F(1-\rho)\varepsilon K}{\phi(K+e)}, \lambda_2 = \lambda_3 = \lambda_4.$$

Hence,

$$\mathcal{R}_0 = \max\{|\lambda_1|, |\lambda_2|, |\lambda_3|, |\lambda_4|\} = \frac{\beta_I \boldsymbol{K}}{\gamma(K+e)} + \frac{\beta_H \rho K}{\delta(K+e)} + \frac{\beta_F K q \rho}{\phi(K+e)} + \frac{\beta_F(1-\rho)\varepsilon K}{\phi(K+e)},$$

which is

$$\mathcal{R}_0 = \left(\frac{\boldsymbol{\beta_I}}{\boldsymbol{\gamma}} + \frac{\boldsymbol{\beta_H \rho}}{\boldsymbol{\delta}} + \frac{\boldsymbol{\beta_F q \rho}}{\boldsymbol{\phi}} + \frac{\boldsymbol{\beta_F(1-\rho)\varepsilon}}{\boldsymbol{\phi}}\right)\left(\frac{K}{K+e}\right). \quad (11)$$