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Existence and Uniqueness of Solution of Ebola Virus Disease Model with Contact Tracing and Quarantine as Controls

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Abstract

In this paper, we begin the study of the transmission dynamics of a model of Ebola Virus disease (EVD) incorporating contact tracing and quarantine as control measures. Furthermore, we present the proof of the existence and uniqueness of the solution of the model.

1. Introduction

Ebola virus disease is a serious and deadly disease that has become a global concern, especially in Sub-Saharan Africa where it is endemic. It belongs to the family of non-segmented, negative-sense single stranded ribonucleic acid (RNA) viruses called the filoviruses (King *et al.,* 2014). The Ebola virus was first discovered in 1976 in North Western Democratic Republic of Congo (DRC) formerly Zaire (Lamunu *et al.,* 2004; ECDC, 2014a). There are more than 25 epidemics of Ebola since the discovery of the virus in 1976 with the 2014 epidemics in West African being the most severe. The 2014 epidemics began in Guinea in December 2013 and then spread to Liberia, Sierra Leone, Nigeria and Senegal where the highest mortality in history was recorded with about 28,608 cases and 11,305 deaths (WHO, 2016). The Ebola virus has an incubation period that varies from 2 to 21 days. The virus is spread through close contact with the blood, secretions, organs or other bodily fluids of infected animals or infected person found ill or

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dead in the population (WHO, 2014a; Hauora, 2014). The signs and symptoms associated with the Ebola virus are usually mistaken for other diseases such as malaria, typhoid fever, influenza, or various other bacterial infections (WHO, 2014b).

Currently, there is no medication or vaccine for Ebola patients rather treatment is intensive supportive therapy (ECDC, 2014b). Non-pharmaceutical interventions such as contact tracing and quarantine are used to control the spread of disease, especially when there is no vaccine or antiviral drug to halt the spread of disease. Contact tracing is defined as the process of identifying, assessing and managing people who have been in contact with an infected person in order to prevent transmission to others (CDC, 2014). It is used to detect new EVD infected persons early before they start showing symptoms and as such prevents secondary transmission of the Ebola virus in the community. Quarantine, on the other hand, is the restriction of movement of those exposed to a communicable disease for a period of time equivalent to its incubation period. It is aimed at preventing disease transmission during the incubation period if infection should occur (CORE Public Health Functions for BC, 2010).

Several mathematical models have been developed to analyse mathematically the spread of Ebola virus disease. For example, Arreola *et al.* (1999) studied the effect of quarantine in the spread of Ebola epidemic by using a deterministic SIR model and Legrand *et. al.* (2007) used modified SEIR model to study the dynamics of epidemics by subdividing infected individuals into hospitalized, funeral, and infectious and symptomatic cases. The study is motivated by the work of Legrand *et al.* (2007) who used the mathematical model to study the dynamics of Ebola epidemics for Democratic Republic of Congo in 1995 and Uganda in 2000. Here, we intend to formulate a mathematical model of Ebola virus disease with contact tracing and quarantine as control measures using the model by Legrand *et al.* (2007) as a guide. The existence and uniqueness of solution of the model will be established and proved.

2. Model Formulation

2.1. **The Existing Model.** In the model by Legrand *et. al.* (2007), the total population size at time t denoted by $N(t)$ is divided into six sub-populations. These are the susceptible individuals, $S(t)$, at time t who can be infected by Ebola virus following a contact with infective individuals; Exposed individuals, $E(t)$, at time t who are infected by the virus but are not yet infectious; Infected individuals, $I(t)$, at time t who are infected with virus in the community and are capable of spreading the disease to susceptible individuals; Hospitalized individuals, $H(t)$, at time t who are infected and hospitalized in the hospitals, and are receiving treatment; Funeral individuals, $F(t)$, at time t who are infected and hospitalized individuals who died of the disease but not yet buried and may

transmit the disease during funerals, while removed individuals, $R(t)$, at time t are those who recovered from the disease or died of the disease, are buried and thus removed from the chain of transmission.

The following are the assumptions of the existing model

(i) The infected, hospitalized, and funeral individuals are assumed to be infectious and can transmit the Ebola virus.
(ii) All observed cases (except index case) were assumed to be related to human- to- human transmission.
(iii) There are no vital dynamics such as birth and death in the population. The total population remain a constant (N) for all time t, that is

$$S(t) + E(t) + I(t) + H(t) + F(t) + R(t) = N.$$

(iv) Infected and hospitalized individuals either recover or die and the dead remain infectious until buried.
(v) The infected individuals are hospitalized in the hospital.

Table 1. Existing model parameters

Parameter	Parameter description
β_I	Transmission rate in the community
β_H	Transmission rate in the hospital
β_F	Transmission rate during funerals
α	Rate at which exposed individuals progress to infectious and symptomaticclass
γ_H	Rate at which infectious and symptomatic class become hospitalized
γ_D	Rate at which infectious and symptomatic individuals die but not yet buried
γ_F	Rate at which the dead are buried and moved to remove class
γ_I	Rate at which infectious and symptomatic individuals recovered by treatment
γ_{IH}	Rate at which hospitalized individuals recovered by treatment
γ_{DH}	Rate at which hospitalized individuals died but not yet buried
δ_2	Proportion of hospitalized individuals who died but not yet buried
τ	Proportion of infectious and symptomatic individuals hospitalized
$(1-\delta_2)$	Proportion of hospitalized individuals who recovered by treatment
$\delta_1(1-\tau)$	Proportion of infectious and symptomatic individuals who die but not yet buried

Figure 1: A flow diagram for the existing model

Using the above flow diagram, variables, parameters and assumptions with $\lambda =$

$\frac{(\beta_I SI+\beta_H SH+\beta_F SF)}{N}$, Legrand *et al.* (2007) derived the following system of differential equations:

$$\begin{aligned}
\frac{dS}{dt} &= -\frac{(\beta_I SI + \beta_H SH + \beta_F SF)}{N} \\
\frac{dE}{dt} &= \frac{(\beta_I SI + \beta_H SH + \beta_F SF)}{N} - \alpha E \\
\frac{dI}{dt} &= \alpha E - (\gamma_H t + \gamma_I (1-t)(1-\delta_1) + \gamma_D (1-t)\delta_1) I \\
\frac{dH}{dt} &= \gamma_H t I - (\gamma_{DH}\delta_2 + \gamma_{IH}(1-\delta_2)) H \\
\frac{dF}{dt} &= \gamma_D (1-t)\delta_1 I + \gamma_{DH}\delta_2 H - \gamma_F F \\
\frac{dR}{dt} &= \gamma_I (1-t)(1-\delta_1) I + \gamma_{IH}(1-\delta_2) H + \gamma_F F
\end{aligned}$$

2.2. **The New Model.** The new model considers the deterministic model of EVD with contact tracing and quarantine. The model examines the dynamics of four classes of individuals in the population namely: Susceptible, $S(t)$, Quarantined, $Q(t)$, Infected, $I(t)$, and Treated, $T(t)$, individuals at time t. The susceptible individuals, $S(t)$ can be infected by Ebola virus following a contact with infective individuals, infected individuals, $I(t)$, are infected with virus in the community and are capable of spreading the disease to susceptible individuals. The Quarantined individuals, $Q(t)$, consist of two groups: immigrants with EVD who enter the unaffected population and some susceptible individuals identified through active contact tracing. Treated individuals, $T(t)$, are those who receive treatment in hospitals. The total population size denoted by $N(t)$ at time t is given by $N(t) = S(t) + Q(t) + I(t) + T(t)$.

The new model is based on the following assumptions:
(i.) The population is homogeneous;
(ii.) Immigrants from EVD affected population are quarantined for a period of time equivalent to the incubation period of the virus;
(iii.) Treated individuals may become susceptible again when they recover since EVD is not known to confer immunity (Atangana and Goufo, 2014; Kalu *et. al.,* 2016);
(iv.) Individuals who died of the disease are immediately buried, preventing transmission after death (Leward *et al.*, 2014);
(v.) Exposed class of individuals is ignored since the incubation period of the disease is short; and
(vi.) A natural death rate is assumed in all classes of the model except the quarantined class in which the death rate is assumed a smaller value since quarantined individuals have short stay in the quarantine that is twenty-one days.

Table 2. Model parameters and variables

Parameter	Description
β	Disease transmission rate
$C(T,I)$	Contact tracing rate for infected individuals
$C(S,I)$	Contact tracing rate for susceptible that are exposed individuals
d_1	Ebola induced death rate for infected class
Λ	Human recruitment rate
σ	Transfer rate from quarantined class to susceptible class after incubation period without developing symptoms
ϕ	Rate at which treated individuals recover and become susceptible again
ε	Immigration rate from Ebola affected area
μ	Natural death rate for susceptible, infected and treated classes
μ_1	Death rate for quarantined class
φ	Treatment rate of quarantined persons
α	Treatment rate of individuals other than the quarantined persons

Figure 2: A flow diagram for the new model.
In view of the assumptions of the new model stated above and the flow diagram in Figure 2, the new model equations are derived as follows:

$$
\begin{array}{ll}
\frac{dS}{dt} = \Lambda - \frac{\beta SI}{N} + \sigma Q + \phi T - \mu S - C(S,T) & , S(0) = S_0 \\
\frac{dQ}{dt} = \varepsilon + C(S,T) - \sigma Q - \varphi Q - \mu_1 Q & , Q(0) = Q_0 \\
\frac{dI}{dt} = \frac{\beta SI}{N} - (\mu + \alpha + d_1) I - C(I,T) & , I(0) = I_0 \\
\frac{dT}{dt} = \alpha I + \varphi Q + C(I,T) - \mu T - \phi T & , T(0) = T_0
\end{array} \tag{1}
$$

where, S_0, Q_0 , I_0 , and T_0 are assumed to be non-negative.
The functions $C(S,T)$ and $C(I,T)$ are as given in Hsieh *et al.* (2005) and Mubayi *et al.* (2009). These are best represented as $C(S,T) = c_1 S$ and $C(I,T) = c_2 I$, where c_1 = the rate at which susceptible individuals that are exposed are traced and c_2 = the rate at which infected individuals are traced. Thus, the system (1) can be rewritten as

$$
\begin{array}{l}
\frac{dS}{dt} = \Lambda - \frac{\beta SI}{N} + \sigma Q + \phi T - \mu S - c_1 S \\
\frac{dQ}{dt} = \varepsilon + c_1 S - \sigma Q - \varphi Q - \mu_1 Q \\
\frac{dI}{dt} = \frac{\beta SI}{N} - (\mu + \alpha + d_1) I - c_2 I \\
\frac{dT}{dt} = \alpha I + \varphi Q + c_2 I - \mu T - \phi T
\end{array} \tag{2}
$$

3. Invariant region

In this section, the invariant region of the model is studied to show that every solution of the model with initial conditions in $\mathbb{R}^4_+$ remains or enters the region Ω at all time t. We state the following lemma.

Lemma 1 The model (2) has solution which are contained in the feasible region $\Omega = \left\{ (\mathrm{S}, \mathrm{Q}, \mathrm{I}, \mathrm{T}) \in \mathbb{R}^4_+ : \mathrm{N} \leq \frac{\varepsilon + \Lambda}{\mu} \right\}$.

Proof. The proof is provided in two steps.

Step 1: We show that the solution set $(S(t), Q(t), I(t), T(t)) \in \mathbb{R}^4_+$ of the model (2) corresponding to initial conditions $S(0) > 0$, $Q(0) \geq 0$, $I(0) \geq 0$, $T(0) \geq 0$ are non-negative.

Consider the first equation of the model (2)

$$\frac{dS}{dt} = \Lambda - \frac{\beta IS}{N} + \sigma Q + \phi T - \mu S - c_1 S.$$

This implies that

$$\frac{dS}{dt} \geq -\left(\frac{\beta I}{N} + \mu + c_1 \right) S. \tag{3}$$

Now, $\frac{\beta I}{N} < \beta$ since $\frac{I}{N} \leq 1$, therefore (3) can be written as

$$\frac{dS}{dt} \geq -(\beta + \mu + c_1) S \tag{4}$$

Integrating (4) by separation of variables and applying the initial condition $S(0) = S_0$ yields

$$S(t) \geq S_0 e^{-(\beta + \mu + c_1)t} \text{ for } t > 0 \tag{5}$$

From the second equation of model (2), we have

$$\frac{dQ}{dt} = \varepsilon + c_1 S - \sigma Q - \varphi Q - \mu_1 Q.$$

This means that

$$\frac{dQ}{dt} \geq -(\sigma + \varphi + \mu_1) Q. \tag{6}$$

Integrating (6) by separation of variables and applying the initial condition $Q(0) = Q_0$ yields

$$Q(t) \geq Q_0 e^{-(\sigma + \varphi + \mu_1)t} \text{ for } t > 0 \tag{7}$$

We also get the following from the third equation of (2)

$$\frac{dI}{dt} = \frac{\beta IS}{N} - (\mu + \alpha + d_1 + c_2) I.$$

This implies that

$$\frac{dI}{dt} \geq -(d_1 + \mu + \alpha + c_2) I. \tag{8}$$

Integrating (8) by separation of variables and applying the initial condition $I(0) = I_0$ yields

$$I(t) \geq I(0) e^{-(d_1 + \mu + \alpha + c_2)t} \text{ for } t > 0 \tag{9}$$

From the fourth equation of (2), we have

$$\frac{dT}{dt} \geq -(\mu+\phi)\,T. \tag{10}$$

Integrating (10) by separation of variables and applying the initial condition $T(0) = T_0$ yields

$$T(t) \geq T(0)\,e^{-(\phi+\mu)t} \text{ for } t > 0 \tag{11}$$

Therefore, from (5), (7), (9) and (11) the solution set $(\mathrm{S}(t), \mathrm{Q}(t), \mathrm{I}(t), \mathrm{T}(t))$ of the model (2) is positive for all $t > 0$ since exponential functions are positive functions.

Step 2: We prove that the total population of humans at time t, $N(t)$ satisfies the inequality $N(t) \leq \frac{\varepsilon+\Lambda}{\mu}$. Adding the right hand sides of (2), we get

$$\frac{dN}{dt} = \varepsilon + \Lambda - \mu(S+I+T) - \mu_1 Q - d_1 I,$$

and this gives

$$\frac{dN}{dt} \leq \varepsilon + \Lambda - \mu(S+I+T) - \mu_1 Q. \tag{12}$$

Since $\mu_1 \geq \mu$, (12) can be rewrite as

$$\frac{dN}{dt} + \mu N \leq \varepsilon + \Lambda. \tag{13}$$

Using the method of integrating factor to solve (13) and applying the initial condition $N(0) = N_0$, we get

$$N(t) \leq \frac{\varepsilon+\Lambda}{\mu} + \left[N_0 - \frac{\varepsilon+\Lambda}{\mu}\right] e^{-\mu t}. \tag{14}$$

The population size, $N(t) \to \frac{\varepsilon+\Lambda}{\mu}$, as $t \to \infty$ in (14), which implies that $0 \leq N(t) \leq \frac{\varepsilon+\Lambda}{\mu}$. If $N_0 < \frac{\varepsilon+\Lambda}{\mu}$ then as $t \to \infty$, the trajectories approach $\frac{\varepsilon+\Lambda}{\mu}$; If $N_0 > \frac{\varepsilon+\Lambda}{\mu}$, the solution $N(t)$ decrease to $\frac{\varepsilon+\Lambda}{\mu}$ as $t \to \infty$. In either case the solution approaches $N(t) = \frac{\varepsilon+\Lambda}{\mu}$ as $t \to \infty$. Hence, the feasible solution set of the model (2) enters the region $\Omega = \left\{(\mathrm{S},\mathrm{Q},\mathrm{I},\mathrm{T}) \in \mathbb{R}^4_+ : \mathrm{N} \leq \frac{\varepsilon+\Lambda}{\mu}\right\}$, which is a positively invariant set. According to Hethcote (2000), the model (2) is biologically meaningful and epidemiologically well posed in the region Ω.

4. Existence and Uniqueness of Solution

Consider the system of ordinary differential equations below

$$\boldsymbol{x}' = \boldsymbol{f}(t, \boldsymbol{x}), \quad \boldsymbol{x}(t_0) = \boldsymbol{x}_0 \tag{15}$$

where $\boldsymbol{x} \in D \subset \mathbb{R}^n$ is an unknown function of the independent variable $t \in I \subset \mathbb{R}$, $\boldsymbol{f}$ is continuous and real valued on a set $U \subset \mathbb{R}\times\mathbb{R}^n$, with $(t_0, x_0) \in U$.

Definition 1: (Hu and Li, 2005): A function $f(t, \boldsymbol{x})$ is said to satisfy a Lipschitz condition in the vector $\boldsymbol{x}$ on a set $D \subset \mathbb{R}^{n+1}$ if a constant $L > 0$ exists with

$$\|\boldsymbol{f}(t, \boldsymbol{x}) - \boldsymbol{f}(t, \boldsymbol{y})\| \leq L \|\boldsymbol{x} - \boldsymbol{y}\|, \tag{16}$$

whenever $(t, \boldsymbol{x}) \in D$. The constant L is called a Lipschitz constant for $\boldsymbol{f}$.

Theorem 1. (Derrick and Grossman, 1976): Suppose that

$$D = \{(t, \boldsymbol{x}) \, | a \leq t \leq b, \quad |x_i| < \infty, \ 1 \leq i \leq n\}$$

and that $\boldsymbol{f}(t, \boldsymbol{x})$ is continuous on D. If $\boldsymbol{f}$ satisfies a Lipschitz condition on D in the variable $\boldsymbol{x}$, then, the system (15) has a unique solution $\boldsymbol{x(t)}$ for $a \leq t \leq b$

To show that a unique solution of the model (2) exists within a region Ω that is biologically meaningful, let $\boldsymbol{x} = (S, Q, I, T) \in \Omega$, $\boldsymbol{y} = (S_1, Q_{\mathbf{1}}, I_{\mathbf{1}}, T_{\mathbf{1}}) \in \Omega$, $\boldsymbol{f} = (f_1, f_2, f_3, f_4)$, $N = S + Q + I + T$, and $N_1 = S_1 + Q_1 + I_1 + T_1$. Then, the model (2) with the initial condition $\boldsymbol{x_0} = (S_0, Q_0, I_0, T_0)$ can be rewritten as follows

$$\begin{aligned} f_1 &= \Lambda - \tfrac{\beta SI}{N} + \sigma Q + \phi T - \mu S - c_1 S \\ f_2 &= \varepsilon + c_1 S - \sigma Q - \varphi Q - \mu_1 Q \\ f_3 &= \tfrac{\beta SI}{N} - (\mu + d_1 + \alpha + c_2) I \\ f_4 &= (\alpha + c_2) I + \varphi Q - \mu T - \phi T \end{aligned} \tag{17}$$

Using definition 1 and theorem 1, we state and prove the following uniqueness and existence theorem for the model (2).

Theorem 2. Let $\Omega = \{\boldsymbol{x}(t) : |a \leq t \leq b, |\boldsymbol{x}| < \infty\}$. The model (2) has a unique solution if $\boldsymbol{f}(t, \boldsymbol{x})$ is continuous and satisfies a Lipschitz condition on Ω.
Proof: We shall apply theorem 1, and show that the model (2) is continuous and satisfies a Lipschitz condition using the definition of uniform continuity on Ω. We have from (15) that

$$\begin{aligned} &\|\boldsymbol{f}(t, \boldsymbol{x}) - \boldsymbol{f}(t, \boldsymbol{y})\| \\ &= |f_1(t, \boldsymbol{x}) - f_1(t, \boldsymbol{y})| + |f_2(t, \boldsymbol{x}) - f_2(t, \boldsymbol{y})| \\ &+ |f_3(t, \boldsymbol{x}) - f_3(t, \boldsymbol{y})| + |f_4(t, \boldsymbol{x}) - f_4(t, \boldsymbol{y})| \end{aligned} \tag{18}$$

Using (17), we get

$$
\begin{aligned}
&\|\boldsymbol{f}(t,\boldsymbol{x})-\boldsymbol{f}(t,\boldsymbol{y})\| \\
&=\left|-\tfrac{\beta}{NN_1}(SIN_1-S_1I_1N)-\mu(S-S_1)\right. \\
&+\phi(T-T_1)+\sigma(Q-Q_1)-c_1(S-S_1) \\
&\left.+|c_1(S-S_1)-(\sigma+\mu_1+\varphi)(Q-Q_1)|\right. \\
&+\left|\tfrac{\beta}{NN_1}(SIN_1-S_1I_1N)-(\mu+\alpha+d_1+c_2)(I-I_1)\right| \\
&+|-(\mu+\phi)(T-T_1)+\varphi(Q-\ Q_1)+(c_2+\alpha)(I-I_1)| \\
&\leq\left|\mu+2c_1+\tfrac{2\beta I_1}{NN_1}(Q_1+T_1+I)\right||S-S_1| \\
&+\left|2\sigma+2\varphi+\mu_1+\tfrac{2\beta I_1S_1}{NN_1}\right||Q-Q_1| \\
&+\left|\mu+2(\alpha+c_2)+d_1+\tfrac{2\beta S}{NN_1}(S_1+T_1+Q)\right||I-I_1| \\
&+\left|2\phi+\mu+\tfrac{2\beta I_1S_1}{NN_1}\right||T-T_1|
\end{aligned}
\tag{19}
$$

$$
\tag{20}
$$

Since $|N|\ ,\ |N_1|<\infty$, let

$$
\begin{aligned}
A=max\Bigg\{&\left|\mu+2c_1+\frac{2\beta I_1}{NN_1}(Q_1+T_1+I)\right|,\left|2\sigma+2\varphi+\mu_1+\frac{2\beta I_1S_1}{NN_1}\right|,\\
&\left|\mu+2(\alpha+c_2)+d_1+\frac{2\beta S}{NN_1}(S_1+T_1+Q)\right|,\left|2\phi+\mu+\frac{2\beta I_1S_1}{NN_1}\right|.
\end{aligned}
$$

Therefore

$$
\|\boldsymbol{f}(t,\boldsymbol{x})-\boldsymbol{f}(t,\boldsymbol{y})\|\leq A\left[|S-S_1|+|Q-Q_1|+|I-I_1|+|T-T_1|\right]\ , \tag{21}
$$

and this gives

$$
\|\boldsymbol{f}(t,\boldsymbol{x})-\boldsymbol{f}(t,\boldsymbol{y})\|\leq A\|\boldsymbol{x}-\boldsymbol{y}\|. \tag{22}
$$

Hence, $\boldsymbol{f}$ satisfies a Lipschtiz condition for all $(t,\boldsymbol{x})\in\Omega$. Choose $\varepsilon>0$. Let $\delta=\frac{\varepsilon}{A}$. Given $\|\boldsymbol{x}-\boldsymbol{y}\|<\delta$, then $\|\boldsymbol{f}(t,\boldsymbol{x})-\boldsymbol{f}(t,\boldsymbol{y})\|<\varepsilon$. Therefore, $\boldsymbol{f}(t,\boldsymbol{x})$ is uniformly continuous and then continuous in Ω. Hence, the model (2) has a unique solution $\boldsymbol{x}$.

5. Discussion and Conclusion

In this study, a deterministic model for the dynamics of EVD is formulated. The model incorporates contact tracing and quarantine as control measures. A feasible region Ω where the model is epidemiologically and mathematically well posed is constructed. Finally, it is proved that a unique solution of the model exists in Ω.

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