Sensitivity Analysis of the Dynamical Spread of Ebola Virus Disease

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Abstract— *The deterministic epidemiological model of (S, E, I_u, I_d, R) were studied to gain insight into the dynamical spread of Ebola virus disease. Local and global stability of the model are explored for disease-free and endemic equilibria. Sensitivity analysis is performed on basic reproduction number to check the importance of each parameter on the transmission of Ebola disease. Positivity solution is analyzed for mathematical and epidemiological posedness of the model. Numerical simulation was analyzed by MAPLE 18 software using embedded Runge-Kutta method of order (4) which shows the parameter that has high impact in the spread of the disease spread of Ebola virus disease.*

Keywords— *Ebola Virus Disease, Infected undetected, Infected detected, Reproduction number, Stability, Sensitivity, Critical points.*

I. INTRODUCTION

Ebola virus disease (EVD) (formerly known as Ebola haemorrhagic fever), named after the river in Democratic Republic of Congo (DRC, formerly Zaire) where it was initially discovered in 1976, is a lethal virus for humans [12] and a virulent filovirus that is known to affect humans and primates. The virus is most commonly spread via personal contact, and it has an incubation period of two to twenty – one days [9]. It takes approximately eight hours for the virus to replicate, and can occur several times before the onset of symptoms. "Hundreds to thousands of new virus particles are then released during periods of hours to a few days, before the cell dies." [1]. The death rate of Ebola is somewhere between 50% to 90%. Until now, there is no specific cure or vaccine for Ebola but, efforts are on-going to find a viable treatment [9]. Symptoms that occur within a few days after transmission include, high fever, headache, muscle aches, stomach pain, fatigue, diarrhea sore throat, hiccups, rash, red and itchy eyes, vomiting blood, bloody diarrhea [2].

The first known occurrence of Ebola was in 1976 in almost simultaneous outbreaks in the Democratic Republic of the Congo (DRC) and Sudan, each escorted by fatality rate beyond 50%. The disease then disappeared after 1979 and did not re-appear again until 1994 [3]. As of October 8, 2014, the World Health Organization (WHO) reported 4656 cases of Ebola virus deaths, with most cases occurring in Liberia [10]. The extremely rapid increase of the disease and the high mortality rate make this virus a major problem for public health [11]. Since, outbreaks have been occurring with increasing frequency, the most horrible outbreak of Ebola till date is currently occurring in West Africa, and it's been a long affair that has infected well over 24000[9].

The present outbreak of EVD in West Africa happens to be the most severe in recorded history; hence, the need to explore the dynamics of the disease through mathematical modeling, in order to control further outbreak of the disease in Nigeria [9]. A great many mathematicians have developed mathematical models to better improve our understanding of the dynamics and spread of EVD in order to curb its prevalence and stem the incessant outbreaks of the virus[4] - [8].The research aims to analyze the availability of isolation centers, rate of public enlightenment and improved personal hygiene.

II. MATHEMATICAL MODEL

We considered four (5) compartmental deterministic mathematical model using the S, L, I_u, I_d, R to have better understanding of efficacy and compliance of condom on Gonorrhea disease. The population size $N(t)$ is sub–divided into sub–classes of individuals who are Susceptible $S(t)$, Latent L(t), Infected undetected $I_u(t)$, Infected detected $I_d(t)$, and Recovered $R(t)$, where

$$N(t) = S(t) + L(t) + I_u(t) + I_d(t) + R(t)$$

$$(1)$$

Susceptible (S): Susceptible individual is a member of a population who is at risk of becoming infected by a disease. The population of susceptible individuals increases by the recruitment of sexually-active individuals at a rate π. The population decreased by natural death at a rate μ also, by force of infection of infected detected λ.

Latent (E): Latent individual is a member of a population who is infected but not infectious. The population of latent individuals increases through the product of slow progressor and infection of susceptible and are assumed to show no disease symptoms initially. The population of latent class diminished by the progression rate of infected individual to infectious class I_d, disease induced death and natural death at a rate μ.

Infected detected (I$_d$): Infected detected individual is a member of a population who is infected and capable of transmitting the disease. The population of infected detected individuals increases through the infection of susceptible, detection rate and the progression rate of infected individual to infectious class I_d that is latent. The population is decreased by recovery rate of infectious, natural death,

disease induced death and endogenous reactivation with progression rate (τ_2),

(μ), (δ) and ($\alpha\tau_1$) respectively

Infected undetected (I$_u$): Infected undetected individual is a member of a population who is infected and capable of transmitting the disease. The population of infected detected individuals increases through the endogenous reactivation with progression rate. The population is decreased by recovery rate of infected, natural death, disease induced death and detection rate (τ_3), (μ),

(δ) and (r) respectively.

Recovered (R): Recovered individual is a member of a population who recovered from the disease. The population of recovered individual is increased by the treatment of infectious individual at a rate (τ_2) and treatment of infected individual at a rate (τ_3), this population later decreased by natural death at the rate (μ).

Hence, we have the following non linear system of differential equations:

$$\left.\begin{aligned}
\frac{dS}{dt} &= \pi - \lambda S(t) - \mu S(t) \\
\frac{dL}{dt} &= \varepsilon \lambda S(t) - (\tau_1 + \delta_L + \mu) L(t) \\
\frac{dI_d}{dt} &= (1-\varepsilon) \lambda S(t) - (\tau_2 + \delta_{I_d} + \mu) I_d(t) + r I_u(t) + (1-\alpha) \tau_1 L(t) \\
\frac{dI_u}{dt} &= \alpha \tau_1 L(t) - (r + \tau_3 + \delta_{I_U} + \mu) I_u(t) \\
\frac{dR}{dt} &= \tau_2 I_d(t) + \tau_3 I_u(t) - \mu R(t)
\end{aligned}\right\} \tag{2}$$

Table 1. Description of Variables

Variables	Definitions
S	Susceptible individuals
L	Exposed individual
I_u	Infected individual undetected
I_d	Infected individual detected
R	Recovered individual

Table 2. Description of Parameters

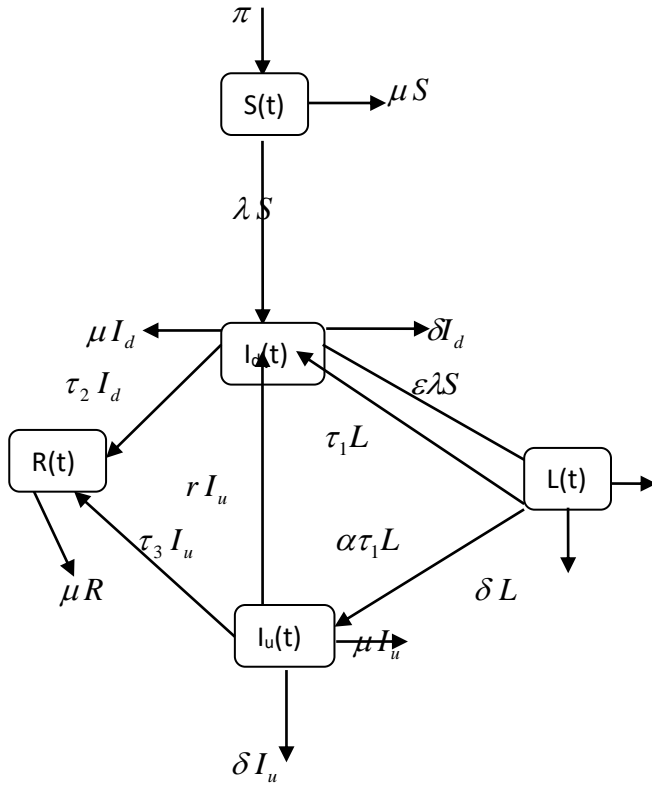| Parameters	Definitions
τ_1	Progression rate of infected individual to infectious individual
τ_2	Recovery rate of infected detected individual due to treatment
τ_3	Recovery rate of infected undetected individual due to treatment
r	Detection rate of infected undetected individual

ϕ	Rate of public enlightenment
π	Recruitment rate
μ	Natural death rate
α	Endogenous reactivation rate
ι	Surveillance coverage
δ	Induced mortality rate
β	Effective contact rate
N	Total population
λ	Force of infection
ε	
q	Slow progressor
v	Number of quarantined individuals
k	Availability of isolation centers
	Enhanced personal hygiene due to public enlightenment

Fig.1: Flow Chat

Positivity of Solution

Lemma 1

The closed set $D = \{(S + L + I_u + I_d + R) \in R^5_+ : N \leq \pi/\mu \}$

is positively-invariant and attracting with respect to the model in (2)

Proof: Consider the biologically-feasible region D, defined above. The rate of change of the total population, obtained by adding all equations of the model in (2), is given by

$$\frac{dN}{dt} = \pi - \mu N - \delta \tag{3}$$

It follows that $\dfrac{dN}{dt} < 0$ whenever $N > \dfrac{\pi}{\mu}$. Furthermore,

Since $\dfrac{dN}{dt} \leq \pi - \mu N$, it is clear that $N(t) \leq \dfrac{\pi}{\mu}$ if $N(0) \leq \dfrac{\pi}{\mu}$.

Therefore, all solutions of the model with initial conditions in D remain in D for all $t > 0$ (i.e., the ω-limits sets of the system in (2) are contained in D). Thus, D is positively-invariant and attracting. In this region, the model can be considered as been epidemiologically and mathematically well posed

Disease Free Equilibrium (DFE)

For disease free equilibrium, we set;

$$\frac{dS}{dt} = \frac{dL}{dt} = \frac{dI_u}{dt} = \frac{dI_d}{dt} = \frac{dR}{dt} = 0 \tag{4}$$

At disease free equilibrium, we assumed there is no infection in the population.

Let E_0 denotes the disease free equilibrium. Thus;

The model in (2) has disease free equilibrium given by

$$E_0 = (S, L, I_u, I_d, R) = \left(\frac{\pi}{\mu}, 0, 0, 0, 0 \right) \tag{5}$$

Endemic Equilibrium

The endemic equilibrium of the model (2) is given below;

$$\left. \begin{array}{l} S^* = \dfrac{\pi}{\lambda + \mu} \\[2ex] L^* = \dfrac{\varepsilon \lambda \pi}{K_1 (\lambda + \mu)} \\[2ex] I_u^* = \dfrac{\alpha \tau_1 \varepsilon \lambda \pi}{K_1 K_2 (\lambda + \mu)} \\[2ex] I_d^* = \dfrac{\pi \lambda ((K_1 - \alpha \varepsilon \tau_1 - \varepsilon \mu) K_4 - \varepsilon \mu K_5 - \varepsilon \delta_L K_6 + \mu K_7)}{K_1 K_2 K_3 (\lambda + \mu)} \\[2ex] R^* = \dfrac{\pi \lambda (\alpha \varepsilon \tau_1 K_8 K_9 - \alpha \mu \tau_2 (K_2 + \delta_L) - \tau_2 K_6 K_{10} + \mu \tau_2 (K_4 + K_7))}{K_1 K_2 K_3 (\lambda + \mu)} \end{array} \right\} \tag{6}$$

Where

$$K_1 = \tau_1 + \delta_L + \mu \qquad\qquad K_2 = r + \tau_3 + \delta_{I_u} + \mu \qquad\qquad K_3 = \tau_2 + \delta_{I_d} + \mu$$

$$K_4 = \tau_3 + \delta_{I_u} + \mu \qquad\qquad K_5 = r + \delta_L \qquad\qquad K_6 = \tau_3 + \delta_{I_u} + r$$

$$K_7 = \tau_1 + \delta_L + r \qquad\qquad K_8 = \mu + \delta_{I_u} \qquad\qquad K_9 = \tau_3 - \tau_2$$

$$K_{10} = \varepsilon \delta_L - \delta_L - \tau_1 \qquad\qquad \lambda = \frac{\beta (1 - q \iota v)(1 - k \phi) I_d}{N}$$

Basic Reproduction Number (R_0)

Using next generation matrix [10], the non-negative matrix F (new infection terms) and non-singular matrix V (other transferring terms) of the model are given, respectively by;

$$F = \begin{pmatrix} \dfrac{\beta (1 - q \iota v)(1 - K\phi) I_d S}{N} \\ 0 \\ 0 \\ 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} (\tau_1 + \delta_L + \mu) L \\ (\tau_2 + \delta_{I_d} + \mu) I_d - r I_u - (1 - \alpha) \tau_1 L \\ -\alpha \tau_1 L + (r + \tau_3 + \mu + \delta_{I_u}) I_u \\ -\tau_2 I_d - \tau_3 I_u - \mu R \end{pmatrix} \tag{7}$$

After taking partial derivatives of F and V, we have:

$$F = \begin{pmatrix} 0 & \dfrac{\beta(1-q\iota v)(1-K\phi)\pi}{\mu} & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \qquad (8)$$

$$V = \begin{pmatrix} K_1 & 0 & 0 & 0 \\ -(1-\alpha)\tau_1 & K_3 & -r & 0 \\ -\alpha\tau_1 & 0 & K_2 & 0 \\ 0 & -\tau_2 & -\tau_3 & -\mu \end{pmatrix} \qquad (9)$$

Thus;

$$R_0 = \frac{\pi\beta\tau_1(\alpha r - \alpha K_2 + K_2)((\iota q v - 1)(K\phi - 1))}{K_1 K_2 K_3 \mu} \qquad (10)$$

The threshold quantity R_0 is the basic reproduction number of the normalized model system (2) for Ebola infection. It is the average number of new secondary infections generated by a single infected individual in his or her infectious period. [1].

Local Stability

Theorem 1: The disease free equilibrium of the modeled in equation (2) is locally asymptotically stable (LAS) if $R_0 < 1$ and unstable if $R_0 > 1$.

Proof: To determine the local stability of E_0, the following Jacobian matrix is computed corresponding to equilibrium point E_0.

Considering the stability of the disease free equilibrium at the critical point $\left(\dfrac{\pi}{\mu}, 0, 0, 0, 0\right)$. We have

$$J_G = \begin{pmatrix} -\mu-\lambda & 0 & \dfrac{\beta(1-q\iota v)(1-K\phi)\pi}{\mu} & 0 & 0 \\ 0 & -K_1-\lambda & \dfrac{\varepsilon\beta(1-q\iota v)(1-K\phi)\pi}{\mu} & 0 & 0 \\ 0 & (1-\alpha)\tau_1 & \dfrac{(1-\varepsilon)\beta(1-q\iota v)(1-K\phi)\pi}{\mu}-K_3-\lambda & r & 0 \\ 0 & \alpha\tau_1 & 0 & K_2-\lambda & 0 \\ 0 & 0 & \tau_2 & \tau_3 & \mu-\lambda \end{pmatrix}$$

The characteristics polynomial of (10) is given by

$$B_5\lambda^5 + B_4\lambda^4 + B_3\lambda^3 + B_2\lambda^2 + B_1\lambda + B_0 = 0 \qquad (11)$$

And

$$B_0 = \pi\beta\tau_1(\alpha r - \alpha K_2 + K_2)((\iota q v - 1)(K\phi - 1)) - K_1 K_2 K_3 \mu$$

Thus by Routh – Hurwitz criteria, E$_o$ is locally asymptoticly stable as it can be seen for

$$B_1 > 0, B_2 > 0, B_3 > 0, B_4 > 0, B_1 B_3 - B_3 > 0 \ and \ B_1 B_2 B_3 - B_3^2 - B_1^2 B_4 > 0 \tag{13}$$

Thus, using $B_0 > 0$

$$B_0 = \frac{\pi \beta \tau_1 (\alpha r - \alpha K_2 + K_2)((\iota q v - 1)(K \phi - 1))}{K_1 K_2 K_3 \mu} < 1$$

Hence

$$R_0 < 1$$

The result from Routh Hurwitz criterion shows that, all eigen values of the polynomial are negative which shows that the disease free equilibrium is locally asymptotically stable.

Global Stability

Theorem 2: The disease free-equilibrium of the system in (2) is globally asymptotically stable (GAS) whenever $R_0 < 1$ and unstable if $R_0 > 1$.

Proof: It follows that $S = N^* - L - I_u - I_d - R$ at steady state. The proof is based on using the comparison theorem [18]. The rate of change of the variables representing the infected component of the system can be written as follows.

$$\left.\begin{aligned}
\frac{dL}{dt} &= \varepsilon \lambda (N^* - L - I_u - I_d - R) - (\tau_1 + \delta_L + \mu) L \\
\frac{dI_d}{dt} &= (1 - \varepsilon) \lambda (N^* - L - I_u - I_d - R) - (\tau_2 + \delta_{I_d} + \mu) I_d + r I_u + (1 - \alpha) \tau_1 L) \\
\frac{dI_u}{dt} &= \alpha \tau_1 L(t) - (r + \tau_3 + \delta_{I_U} + \mu) I_u(t) \\
\frac{dR}{dt} &= \tau_2 I_d(t) + \tau_3 I_u(t) - \mu R(t)
\end{aligned}\right\} \tag{13}$$

For the model in (2), the associated reproduction number is denoted by R_0,

where

$$R_0 = \frac{\pi \beta \tau_1 (\alpha r - \alpha K_2 + K_2)((\iota q v - 1)(K \phi - 1))}{K_1 K_2 K_3 \mu}$$

The DFE of the model (2) is GAS in D^* if $R_0 < 1$.

Using comparison method, we have,

$$\begin{pmatrix} \frac{dL}{dt} \\ \frac{dI_d}{dt} \\ \frac{dI_u}{dt} \\ \frac{dR}{dt} \end{pmatrix} = (F - V) \begin{pmatrix} L \\ I_d \\ I_u \\ R \end{pmatrix} - Fi \begin{pmatrix} L \\ I_d \\ I_u \\ R \end{pmatrix} \tag{14}$$

Then

$$\begin{pmatrix} \dfrac{dL}{dt} \\[2mm] \dfrac{dI_d}{dt} \\[2mm] \dfrac{dI_u}{dt} \\[2mm] \dfrac{dR}{dt} \end{pmatrix} \leq (F - V) \begin{pmatrix} L \\ I_d \\ I_u \\ R \end{pmatrix} \qquad (15)$$

According to [10], all eigenvalues of the matrix $F - V$ have negative real parts. It follows that the linearized differential inequality above is stable whenever $R_0 < 1$. Consequently $S = (L = I_d = I_u = R = 0) \to (0,\,0,\,0,0)\ at\ t \to \infty$. Substituting

$L = I_d = I_u = R = 0$ in (R_0) gives

$S(t) \to S(0)\ as\ t \to \infty$.

Hence, we have established that the disease free equilibrium is globally asymptotically stable whenever $R_0 < 1$.

Sensitivity Analysis

Sensitivity analysis is a crucial analysis that shows importance of each parameter to disease transmission. The sensitivity index of parameters with respect to the basic reproduction number was calculated, to know how crucial each parameter is to the disease transmission; intervention control strategies that target such parameter should be employed in the control/prevention of Ebola disease.

Definition 1. The normalized forward sensitivity index of a variable ω that depends differentiable on a parameter p is defined as:

$$X_P^\omega = \frac{\partial \omega}{\partial P} \times \frac{P}{\omega}. \qquad (16)$$

As we have explicit formula for R_o, we derive an analytical expression for the sensitivity of R_o as

$$X_P^{R_o} = \frac{dR_o}{dP} \times \frac{P}{R_o}$$

The signs of the sensitivity index of R_0 are as shown in the table 3.

Table.3: Signs of Sensitivity Index of R_0

Parameter	Value [9]	Sensitivity Index
ε	0.7	Negative
τ_1	0.088	Positive
	0.045	Negative
τ_2	0.2	Positive
r	0.15	Positive
τ_3	0.9	Positive
	0.75	Negative
β	0.65	Negative
q	0.3	Negative
v	0.9	Negative
K	0.75	Negative
ϕ		
ι		

Numerical Simulation

Numerical simulation was carried out by MAPLE 18 software using Runge-Kutta method of order four with the set of parameter values given in table 3. Dynamic spread of Ebola is checked simultaneously on Susceptible, Latent,

Infected undetected and detected individuals since the spread of Ebola is a function of time. $S(0)=300, I_d(0)=0.02, I_u(0)=150, R(0)=100, L(0)=100$

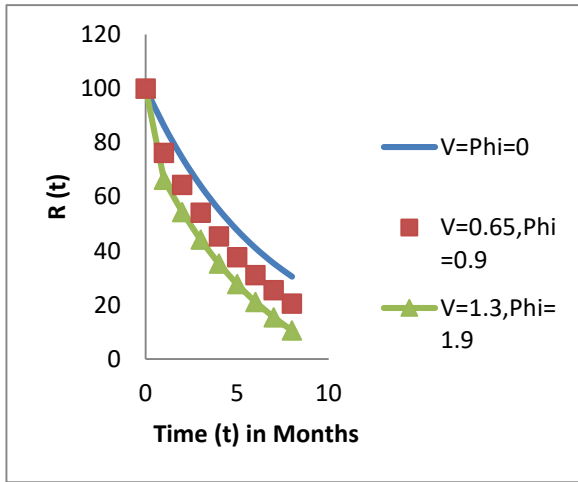Figures 1-4 below are the results obtained from numerical simulation of the Ebola model with the dynamic spread.

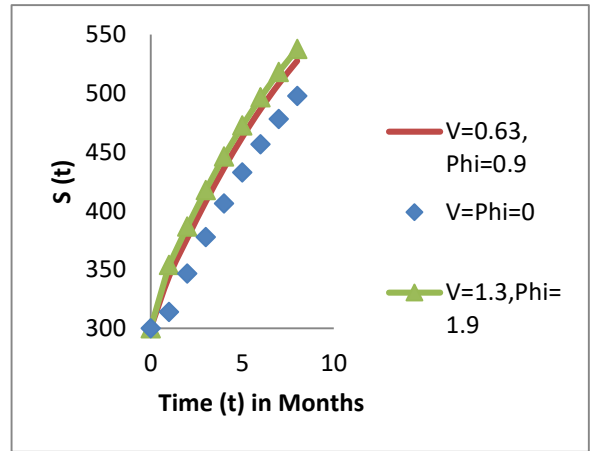*Fig.1: Graph of Recovered individuals for various values of isolation centers and public enlightenment*

Fig.2:Graph of Latent individuals for various values of isolation centers and public enlightenment

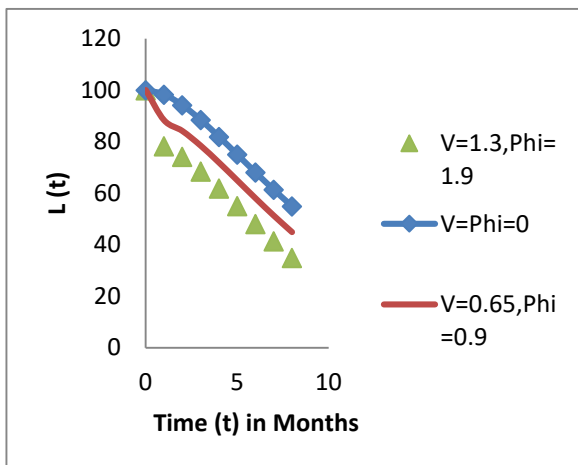*Fig.3: Graph of Susceptible individuals for various values of isolation centers and public enlightenment*
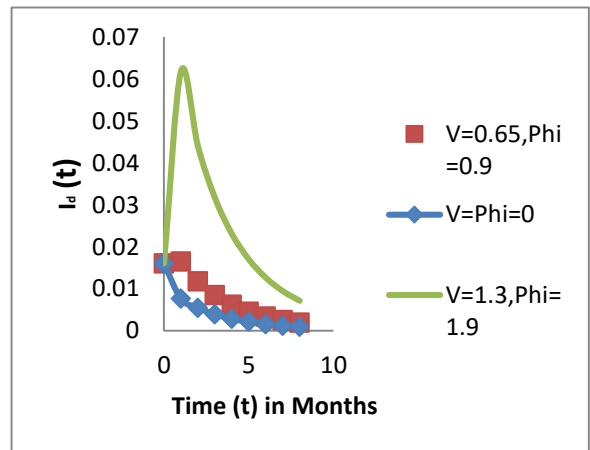

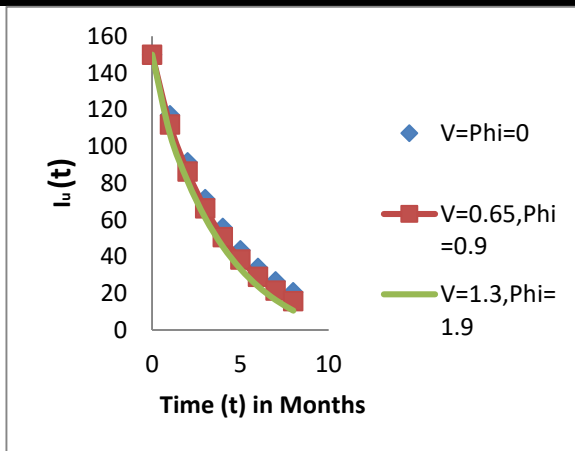*Fig.4: Graph of Infected detected individuals for various values of isolation centers and public enlightenment.*

Fig.5 Graph of Infected undetected individuals for various values of isolation centers and public enlightenment

III.   RESULTS AND DISCUSSIONS

In In this study, Five (5) deterministic epidemiological model of (S, L, I_u, I_d, R) are presented to gain insight into the the dynamical spread of Ebola virus disease. Positivity of solution shows that, the model presented is mathematically and epidemiologically well posed. Local and global stability of the model shows that, disease-free equilibrium is asymptotically stable whenever the threshold quantity 'R_0' is less than unity and otherwise endemic when it is greater than unity. Sensitivity analysis of the model shows that increase or

decrease in the value of each parameter with negative sign in basic reproduction number 'R_0' can increase or decrease 'R_0'. **Figures 1-5** of numerical simulation showed that, increasing the rate of spread of Ebola reduces the latent and infected individuals.

In conclusion, the rate of public enlightenment and availability of isolation centers can reduce the spread of Ebola virus disease. Increment in the values of public enlightenment and isolation centers reduced the basic reproduction number 'R_0' since the spread of disease is dependent on the value of 'R_0'. Therefore effort that targets the use of condom as a control measure should be encouraged.

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