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On Mathematical Model of Transmission of Ebola Virus: Impact of Control Intervention

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Abstract: *In this paper, we proposed and formulated using ordinary differential equations a set of 4-Dimensional nonlinear mathematical dynamic Ebola model, which accounted for the impact and effectiveness of control intervention strategies for the prevention of transmission of Ebola virus. The model was presented as a SIER epidemics flow-chart with derived model transformed and analyzed using finite difference scheme. Analysis showed that control interventions are classified into four main categories. In-built Runge-Kutter of order of precision 4 in a Mathcad surface was utilized in the numerical simulations of derived model. Result of numerical computations indicated rapid contamination of susceptible population within 12 days of Ebola onset infection. Moreso, the interplay of primary through secondary control interventions led to significant control of infection epidemic within 10 days. The study therefore, suggests rapid implementation of intermediary and secondary intervention strategies at local medical centers and community grouping. Furthermore, optimization control strategy that could lead to maximization of control intervention sources will offer more insight to the benefits of control application.*

Keyword: *Nosocomial; Vulnerable; Epidemic-Outbreak; Symptomatic; Epidemiological; Surveillance;*

1. INTRODUCTION

The Ebola Virus Disease (EVD), otherwise known as Ebola hemorrhagic Fever, named after River Ebola in Democratic Republic of Congo, was first identified in 1976 [1]. The causative Ebola strain is the two most deadly Ebola strains known as Ebola-Zaire and Ebola-Sudan which were identified in those parts of the countries [2-4]. Since then, the virus has become a focus of much concern; following it largest outbreak in 2014, particularly in the West Africa regions with fatality nearing 5,000 and recently, a total of 7,178, reported cases including 3,338 deaths as at October 1, 2014, [5, 6].

The diverse nature of the recent 2014 Ebola outbreak have been adjudged the largest most severe and complex epidemics in nearly 40 years history of the disease with a widespread transmission affecting multiple countries of West Africa (Guinea, Liberia, Sierra Leone) and previously seeded reported outbreaks in Nigeria, Senegal, Spain, United States and Mali [7-9].

Like few other infectious diseases, Ebola is a unique member of the ribonucleic acid virus family with no known natural reservoir, making it somewhat obscure and the fastest killing disease in the planet. The incubation period of Ebola is 2 -21 days and the infectious period is 4 -10 days [10, 11].The spread of Ebola virus is basically by direct (or physical) contact of families and friends with body fluids, secretions, tissues or semen from infected individuals [2, 12]. Other means of transmission is known as Nosocomial transmission, a process that involves patients within hospital settings been treated by unprepared hospital personnel and which requires the observation of barrier nursing techniques [1, 10].

The onset of Ebola is characterized by early gastrointestinal symptoms, high fever, severe headache, malaise, which rapidly progress to vomiting, diarrhea, rash, severe bleeding (both internal and external) and shock, leading to death [13].

Infected individuals are exposed to limited medical care due to non-existence of well-established medical treatment or vaccine, leaving them with a greater option of death within 10 days of initial infection. The mortality rate of Ebola is anywhere around 50% - 90% with most vulnerable population as the Children of less than 5 years of age, the elderly and the pregnant women among others [13-15].

At this point, it is enormous to say that, in the absence of cogent medical care and the lack of instant intervention due to fear of the death-defying nature of the disease, mathematical modeling have become the fastest possible means of not only accessing the dimension of the spread of the disease but most importantly, the means to which we can safely evaluate the dynamics of the spread and access the impact of

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available control interventions. Modeling the transmission of infectious disease provides a means to access the effectiveness of control interventions and allow the development of more efficient means to reign in the spread of disease in the future [5]. Comprehensive modeling of the spread and control of viral hemorrhagic fever including Ebola, in the reality of African countries are still schematic in approach.

Nevertheless, notable mathematical models in this direction includes: [16], which employed SEIR model with the time-dependency on the reproduction number to capture the effect of the control interventions; the model [17] analyzes each of the affected countries specific data independently, while the model [18] explicitly accounted for the risk of international spread and the basic reproduction number. A model designed by Yaneer Bar-Yam (2006), shows that Ebola could rapidly spread and in a worst case scenario even caused an extension event, if enough infected people make it through an international airport [8]. Notably also, are the structured transmission model, which studied Ebola epidemics with contributions to the force of infection from the community, funerals, and healthcare settings [19] and the 2014 Ebola virus disease outbreak in West Africa [20].

In the context of 2014 Ebola outbreak in West Africa, this present model is motivated by [1]. That model studied the cause of Ebola outbreak in Congo and Uganda using SEIR epidemic model that included a smooth transmission rate with control interventions taken into account. A flow-chart of the model is shown in Figure 1 below. Of note, these aforementioned noble scientific literatures on Ebola transmission dynamics neither accounted nor evaluated impacts of Ebola prevention interventions. Thus, in this present model, we formulate a set of 4-Dimensional non-linear differential equations, which not only account for the effectiveness of the control measures of Ebola transmission epidemics, but also, to study the various impacts of the parameters of Ebola transmission at a given period of time. Therefore, the novelty of this present work is the development of an enhanced SEIR flow-chart, which not only allow the interactions of susceptible population and the exposed group but that which enhances the investigation of Ebola intervention strategies under the classification – zero, primary, intermediaries and secondary interventions.

Explicitly, the present investigation is structured into six sections with section 1 devoted to the introductory aspects. Section 2 focuses on materials and methods for Ebola intervention impacts model, which accounts for the mathematical formulation of the model differential equations. The transformation of the derived model equations to non-dimensional form and method of analysis, which explores finite difference of scheme, are presented in section3. In section 4, numerical simulations and result analysis were conducted to validate the investigation. We discuss the outcome of simulated model in section 5. Finally, incisive and succinct conclusion and remarks forms the last section 6 of the study. It is hope that the present model will throw more insight into the effectiveness of the control measures with possible improved recommendations.

2. MATREIAL AND METHODS FOR EBOLA INTERVENTION MODEL

We present in this section the schematic SIER flow-chart, which leads to the formulation of the system model equations. Here, we introduce the SEIR flow-chart by [1] as seen in Figure1 below. Using the below SIER model, we construct an epidemic flow-chart for the control of Ebola virus infection in a heterogeneous population. A non-linear ordinary differential equation is derived, which are then transformed into proportions. This is followed by computer simulations of the transformed equations. A finite difference scheme is used in performing a number of numerical experiments from which analysis of the effect of some parameters on each of the population components are conducted.

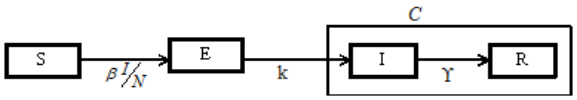

Figure 1 The SEIR model flow-chart for the basic reproductive number of Ebola virus [1]

2.1 Formulation of Differential Equations for Ebola Model

From the SEIR model approach of the Ebola epidemic outbreak, the functions (parameters) prescribing the model is defined as follows: $S_i(t)$ - Number of susceptible class of individuals at time t; $E_i(t)$ - Number of exposed class of individuals to virus at time t; $I_i(t)$ - Number of infectious class of individuals at time t; $R_i(t)$ - Number of recover or dead (removed) population at time t; N_i - Total effective population size at time t; where, $N_i = S_i(t) + E_i(t) + I_i(t) + R_i(t)$. Other parameters includes: β - Probability of transmission by the infectious per day $\beta \geq 0$; B_c - Per-capita rate of susceptible being exposed to virus and becoming infectious; λ - Per-capita rate at which infectious recovers (or die), at time t, $\lambda \geq 0$; k - Rate at which exposed individuals move to symptomatic and infectious class at time t, $k \geq 0$; b - Natural birth rate,

ISSN: 2456 - 3935
International Journal of Advances in Computer and Electronics Engineering
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$b > 0; q$ - Rate at which recovered infectious individuals are recruited, $q \geq 0; \mu$ - Natural death rate, $\mu > 0; \alpha$ - Ebola infected-related death rate, $\alpha \geq 0; \nu$ - Average number of contacts by the susceptible with exposed individuals per time; and $C(t)$ - Cumulative number of Ebola cases from the time of outset of symptoms. The assumptions considered in this model are population of the epidemiological state such as: susceptible (at the risk of contracting the disease) S ; exposed (infected but not yet infectious) E ; infective (capable of transmitting the disease) I ;removed (those who recover or die from the disease) R .Others include: uniform mixing of the population; exposed individuals are symptomatic at the period of incubation (having or showing no symptoms of disease);there is no Nosocomial transmission (transmission from patient within hospitalsettings); the population is recruited at birth rate b , and rate of recovering q ; and the days from onset to removeperiod is cumulative.

Base on the above defined parameters and prescribed assumptions, an enhanced epidemic flow-chat for the transmission dynamics of Ebola virus infection on the constituted population is as shown in Figure 2 below:

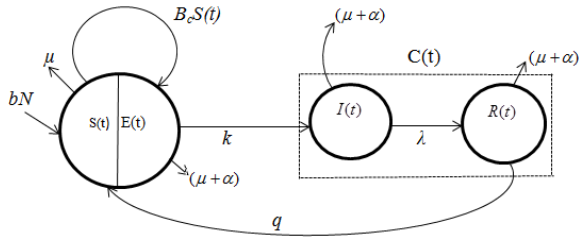

Figure 2 Epidemic flow-chart for the transmission dynamics of Ebola virus infection

From Figure 2 above, the model equations are governed by the following mathematical equations:

$$S_i' = bN + qR_i - B_cS_i - \mu S_i \quad (2.1)$$

$$E_i' = B_cS_i - (\mu + \alpha + k)E_i \quad (2.2)$$

$$I_i' = kE_i - (\mu + \alpha + \lambda)I_i \quad (2.3)$$

$$R_i' = \lambda I_i - (\mu + \alpha + q)R_i \quad (2.4)$$

$$N = S_i + E_i + I_i + R_i \quad (2.5)$$

$$B_c = v\beta\frac{I_i}{N} \quad (2.6)$$

$$C(t) = kE_i - (I_i + R_i) \quad (2.7)$$

Note that Equation (2.7) is not an epidemiological case, rather, a reservoir for cumulative number of Ebola cases.

3. TRANSFORMATION OF MODEL EQUATIONS INTO NON-DIMENSIONAL FORM

In this section, we shall transform the derived model equations into proportions. It is worth mentioning that the transformation is essential as:

i. it simplify the number of equations in the model for easy manipulations;
ii. the proportion of infected individuals have biological meaning as they define prevalence of infection; and
iii. serves as a means of evaluating the impacts of the various intervention strategic components in relation to parameter indicators at time t .

Let,

$$s_i = \frac{S_i}{N} \quad (2.8)$$

$$e_i = \frac{E_i}{N} \quad (2.9)$$

$$y_i = \frac{I_i}{N} \quad (2.10)$$

$$r_i = \frac{R_i}{N} \quad (2.11)$$

Clearly, from equations (2.8)-(2.11) we have in terms of proportion,

$$m(t) = \frac{N_i(t)}{N} = s_i + e_i + y_i + r_i = 1 \quad (2.12)$$

Therefore, substituting equation (2.12) into equation (2.6) we obtain

$$B_C = v\beta\frac{y_i}{m(t)} \quad (2.13)$$

Now, from equations (2.1)-(2.4), the transformations for the infection process are as derived below:

$$s_i' = bm(t) + qr_i - B_cs_i - \mu s_i \quad (2.14)$$

$$e_i' = B_cs_i - (\mu + \alpha + k)e_i \quad (2.15)$$

$$y_i' = ke_i - (\mu + \alpha + \lambda)y_i \quad (2.16)$$

$$r_i' = \lambda yi - (\mu + \alpha + q)r_i \quad (2.17)$$

Thus, the various changes in each of the population class can be simulated and analyzed in terms of equations (2.14)-(2.17) as summarized in the Table 1, below:

ISSN: 2456 - 3935
International Journal of Advances in Computer and Electronics Engineering
Volume 2, Issue 8, August 2017, pp. 8–14

TABLE 1 PROPORTION OF THE DYNAMICS OF HIV TRANSMISSION

Class	Derivatives	Eqn. no.
S_i	$s_i^{'} = bm(t) + qr_i - B_c s_i - \mu s_i$	(2.14)
E_i	$e_i^{'} = B_c s_i - (\mu + \alpha + k)e_i$	(2.15)
I_i	$y_i^{'} = ke_i - (\mu + \alpha + \lambda)y_i$	(2.16)
R_i	$r_i^{'} = \lambda yi - (\mu + \alpha + q)r_i$	(2.17)

4. NUMERICAL SIMULATIONS AND ANALYSIS

Of note, the model represents a set of 4-Dimensional nonlinear ordinary differential equations involving 4 class of the population (s_i, e_i, y_i, r_i). In simulating the model equations, we use the model parameters with established data from known studies [1,10, 11] as in Table 2 below, noting from the innovative study by [22] that the highlighted parameters defines predominant indicators under investigation.

To enable the discussion and assimilation of the impact of the core control interventions strategies, which includes – surveillance, contact tracing, random screening, quarantine of suspected cases, barrier nursing techniques and rapid cremation of death bodies, we classify these indicators into four major components in relation to their corresponding parameter indicators (i.e. zero, primary, intermediary and secondary interventions).

Zero intervention investigates the situation where no intervention occurs. Primary intervention isthe identification vulnerable populationviasurveillance, contact tracing and random screening which are closely associated to theparameters k, β, α. Intermediary intervention is the immediate quarantining of suspected infected individuals, which is closely studied by activities of those parameters β, λ, k. Lastly, secondary intervention strategy includes barrier nursing techniques and rapid cremation of the dead bodies. The parameter indicators associated to these are β, k, q. We summarize the above as seen in Table 3 below: We now vector the initial parameters for compatibility with the Mathcad program, by letting

$$(s_i, e_i, y_i, r_i) = \{H_i\}_{i-1}^{4} \Rightarrow \sum_{i=1}^{4} H_i .$$

Therefore, the differential equation in its vector form can be written as:

$$\begin{cases} \dfrac{dH}{dt} = f(H), t \in [0,T] \\ H(0) = H_0 \end{cases} \quad (2.18)$$

Here, we recommended the use of Mathcad program due its in-built rkfixed Runge-Kutter method of accuracy of order 4. The efficacies of the control and intervention measures are determined by the indicators $k, .\lambda, q, \beta, \alpha$, which represent the treatment factors. Other parameters are as well accorded importance in the investigation process.

TABLE 2 VALUES OF PARAMETER INDICATORS FOR EBOLA INFECTIONCONTROL INTERVENTIONS

Variant	b	μ	α	k	λ	q	v	β	$s_i(0)$	$e_i(0)$	$y_i(0)$	$r_i(0)$
1	0.02	0.1	0.1	**0.2**	0	0	5	0.2	0.7	0.1	0.1	0.1
2	0.02	0.1	0.05	**0.1**	0.1	0.04	5	0.15	0.7	0.1	0.1	0.1
3	0.02	0.1	0.02	**0.05**	0.15	0.1	5	0.1	0.7	0.1	0.1	0.1
4	0.02	0.1	0	**0**	0.2	0.15	5	0	0.7	0.1	0.1	0.1

TABLE 3 CONTROL INTERVENTION STRATEGIES

Stage	Intervention stage	Intervention mode	Indicators
1	Zero intervention	No control measures	λ, q
2	Primary intervention	surveillance, contact tracing, random screening	k, β, α
3	Intermediary intervention	Suspects quarantined	β, λ, k
4	Secondary intervention	Barrier nursing techniques, rapid cremation	β, k, q

Graphically, we let $U^{\langle 1 \rangle}$ represent time (in days) and $U^{\langle 2-5 \rangle}$ represent our variables (s_i, e_i, y_i, r_i) respectively. Then from Table 2, applying equation (2.18), we obtain the simulations of the model as in Figures (3-6) below.

From figure 3 below, we studied the case of no intervention strategy with indicators $\lambda = 0, q = 0$

ISSN: 2456 - 3935
International Journal of Advances in Computer and Electronics Engineering
Volume 2, Issue 8, August 2017, pp. 8–14

and $k = 0.2.\beta = 0.2, \alpha = 0.1$; while allowing other parameters as in Table 2. It is observed that within 12 days, the susceptible had been exposed to infection and remains infectious within 30 days. In this interval, extinction of the infected population is experience in a span of 12 days. Numerically, we expressed the changes in proportion as $s_i \le 12, e_i \le 20, y_i \le 30, r_i \le 12, A_i \le 30$.

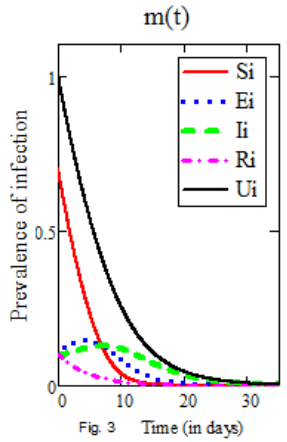

Figure 3 Graphical simulations of s_i, e_i, y_i, r_i from model (2.14) – (2.17) against time with $U^{<i>}$ -the sum of proportions of various group populationswith no intervention strategy. Parameter values are in variants1 - Table 2

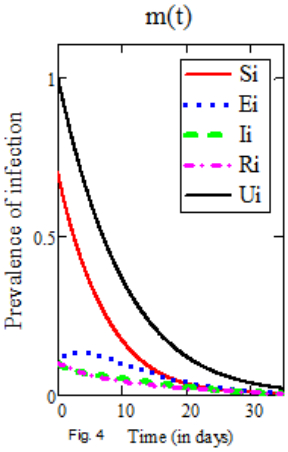

Figure4 Graphical simulations of s_i, e_i, y_i, r_i from model (2.14) – (2.17) against time with $U^{<i>}$ -the sum of proportions of various group populations with primaryinterventions. Parameter values are in variants2 – Table 2

The implication is that the entire population A_i, is been wiped by Ebola virus infection within 30 days (days are cumulative – see assumption), if no intervention is extended.With figure 4 above, we investigate the primary intervention stage accompanied by slight increase in $\lambda = 0.1, q = 0.04$, with reduced $k = 0.1, \beta = 0.15, \alpha = 0.05$. Here the result indicates survival of the susceptible with prolong number of days (25 days), before becoming exposure to infection, as compared to the situation when no intervention was applied (as in figure 3). Furthermore, we observed that the rate at which the exposed becomes infectious is seen to gradually reduced, which translate to more recovery been recruited to s_i. Thus, leading to more survival of lives after 35 days. Generally, $s_i \le 25, e_i \le 30, y_i \le 25, r_i \le 30, A_i \ge 30$.

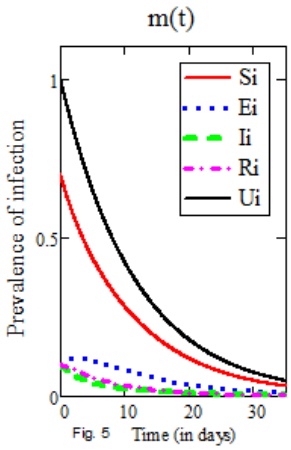

Figure 5Graphical simulations of s_i, e_i, y_i, r_i from model (2.14) – (2.17) against time with $U^{<i>}$ - the sum of proportions of various group populations with intermediary intervention strategy. Parameter values are invariants3- Table 2

In figure 5 above, increase in $\lambda = 0.15, q = 0.1, k = 0.15$ with reduced $\beta = 0.1, \alpha = 0.02$, which defines intermediary intervention strategy leads to significant improvement. The observed proportional changes are given by $s_i > 35, e_i \le 32, y_i \le 20, r_i \le 20, A_i > 35$. Theimplication is a tremendous control of spread of the infection, as expose class was not infectious even after 32 days. Moreover, the infectious were identified and quarantined, leading to rapid recovery within 20 days. The situation is affirmed by the visible increase in susceptible population and which surpasses the 3 – weeks of incubation period and quarantine stage.

Finally, from Figure 6 below, we further intensified our investigation by considering thesecondary stage of control intervention which basically include barrier nursing techniques and cremation of disease bodies. We see that with these factors complementing primary and secondary factors, the indicators k, β, α were positively under control leading to increase in λ, q. This shows that $s_i > 35, e_i \le 20, y_i \le 10, r_i \le 15, A_i > 35$.

ISSN: 2456 - 3935
International Journal of Advances in Computer and Electronics Engineering
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Clearly, the exposed population are completely identified in less than 20 days while infectious are been quarantine and taking care within 10 days with cumulative 15 days of recovery and possibly recruited into the susceptible class. The recruitment of the recovery is established by the considerable survival of the infectious into the susceptible which defined the entire population after 35 days. Thus, our analysis have shown that we evaluated the effectiveness of intervention strategies in terms of k, λ, q, β and α. This present result is in comparative with the result by [1], in which the effect of intervention strategies was studied using the disease reproduction number R_0, whereas the study [21] evaluated intervention measures using stochastic model.

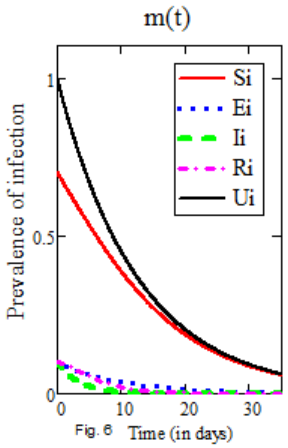

Fig. 6

Figure6 Graphical simulations of s_i, e_i, y_i, r_i from model (2.14) – (2.17) against time with $U^{<i>}$ - the sum of proportions of various group populations withsecondary intervention. Parameter values are invariants 4- Table 2

5. DISCUSSION

We formulate a mathematical model that cohesively studied the impact of control interventions strategiesin the eradication of the spread of Ebola virus infection under four major components (as in Table 3). To assimilate these impacts, we carefully analyzed each of the components in relation to the performance of some vital parameter indicators which predominantly includes $k, \lambda, q, \beta, \alpha$. The model was implemented using non-linear differential equations leading to 4-Dimensional systems of equations. Computation and analysis was conducted using Mathcad program on a set of well-established data [1, 10, 11] as in Table 2 above.

From the numerical analysis, we arrive at: For a zero intervention strategy, the investigation shows that the susceptible were rapidly exposed to infection resulting to contamination of the population with Ebola virus (infectious class) and subsequently leading to removal stage within 27 days from the incubation period. The infectious class clearly defined the epidemic level of the entire population – Figure 3.

Initiating primary intervention strategies saw a gradual reduction in the spread of the Ebola virus due to early contact tracing, random screening and surveillance. Infectious class could only survive within 25 days. The depleting susceptible population, which defined the entire existing population as, was marginally increased by the countable lives from the remove class – Figure 4.

Investigation further revealed that, enhancing the primary intervention strategy with the implementation of the intermediary intervention (quarantining suspected cases), further reduces the chances of the spread of the virus as infectious were contained within 20 days leading to significant recovery and subsequent recruitment into the susceptible group, which is seen to comfortably surpass the incubation period of 21 days. Clearly, infection was gradually under control – Figure 5.

Following cases of incessant contraction of Ebola infection at hospital settings and during dispose of death bodies arising from infection, recommended by medical experts, were the secondary intervention strategy. This stage further strengthens primary and intermediary strategies. We see that the expose class declined sharply to a negligible proportion after 20 days and cases of infectious were under control within 10 days. In 15 days of medical care, recovered were said to be recruited into the susceptible population. This is obvious as the proportion of the susceptible significantly increased compared to that of Figures (3-5) and more interestingly, submerging with the entire population after 30 days – Figure 6.

Exposed by this study were a number of limitations, which bordered around: Lack of cogent and comprehensive barrier nursing techniques by health medical authorities; Inconsistent contact tracing method; and Lack of instant cremation of infected dead corpse by relative of victims.

6. CONCLUSION

In this paper, we explored the sensitivity of the various forms of control interventions, studied under four major components as related to five major parameter indicators. From the result of the analysis, it was observed that at zero intervention, the entire susceptible population was contaminated with Ebola virus infection within 12 days of onset. A partial control intervention (primary intervention), insignificantly ameliorated the spread of Ebola virus. However, only the interplay of the last three stages of the control intervention strategies led to a significant control of the epidemic within 10 days (figure 6, with $y_i \leq 10$). Furthermore, increased and rapid implementation of control measures such as intermediary and secondary

ISSN: 2456 - 3935
International Journal of Advances in Computer and Electronics Engineering
Volume 2, Issue 8, August 2017, pp. 8–14

intervention strategies at both local medical care centres and community grouping should be considered as critical components in all contingency plans towards the eradication of future Ebola outbreaks. The model therefore, recommends consistent, effective and cogent implementation of the studied intervention measures towards achieving the much expected zero Ebola society.

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