

An Optimal Control for Ebola Virus Disease with a Convex Incidence Rate: Imputing from the Outbreak in Uganda.

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Abstract

Ebola Virus disease (EVD) is an emerging and re-emerging zoonotic disease which mostly occur in Africa. Both prediction of the next EVD and controlling an ongoing outbreak remain challenging to disease prone countries. Depending on previous experiences to curb an outbreak is subjective and often inadequate as temporal socioeconomic advances are dynamic and complex at each disease. We hypothesize that a scientific model would predict EVD disease outbreak control. In this work, a mathematical model with a convex incidence rate for an optimal control model of Ebola Virus Disease is formulated and analyzed. An optimal control strategy which aims at reducing the number of infected individuals in the population and increasing the number of recovered through treatment is evaluated. Three control measures: tracing of contacts, lock-down and treatment have been considered. A qualitative analysis and numerical experiments are performed on the model and the findings reveal that the most expensive strategy involved imposing lock-down and contact tracing of the infected while the cheapest alternative was lock-down and treatment of the infected. Hence, policy makers should concentrate on treatment and lock down to combat the disease.

Keywords: Ebola Virus disease; optimal control strategy; Convex incidence rate; Zoonotic diseases, cost effectiveness

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1 Introduction

Ebola Virus disease (EVD) is severe and often fatal infectious disease that is epidemiologically characterized as an emerging and re-emerging zoonosis affecting humans and non-human primates [1]. Since it was first discovered in Africa was in 1976 [2]. EVD has increased in frequency, geographical scope and health morbidity and mortality burden in the most prone West and East African sub regions of Sub-Saharan Africa. The 2014-2016 EVD outbreak epidemic in West Africa affected Guinea, Sierra Leone, Liberia and Nigeria was the largest since the virus was first discovered [3]. It resulted in 28,616 cases, 11,310 deaths([4]), and economic cost of \$ 2.8 billion (\$ 600 million for Guinea, \$ 300 million for Liberia, and \$ 1.9 billion for Sierra Leone) [5]. On 25th June, 2020, World Health Organization (WHO) announced the world's second largest Ebola outbreak in Northern Kivu/Ituri, DRC in which over 3481 cases were recorded with 2299 fatalities. [6].

Chronology of previous EVD outbreaks include 18 countries since the first outbreak with the 2021 (Guinea and DRC) ongoing, over 8 and 7 outbreaks in DRC and Uganda respectively of Zaire and Sudan ebolavirus species [7]. Uganda has experienced EVD outbreaks caused by Sudan ebolavirus (four outbreaks) and Zaire ebolavirus (three outbreaks). On the 26th October 2022, the World Health Organization (WHO), declared an Ebola outbreak caused by Sudan EbolaVirus (SUVD) in Uganda [8].

By 18th November 2022, 114 cases EBV has reportedly been The outbreak of EBV is attributed to the transmission from humans, animals, on objects or surfaces contaminated by body fluids of an infected person for example clothing of or bedding of a sick person that have not been cleaned [10]. The EBV is a very contagious disease with signs and symptoms including severe fever, headache, muscle pain, weakness, fatigue, vomiting, diarrhea, stomach pain, and bleeding from all body openings. The incubation period for Ebola can be anywhere from 2 to 21 days. An infected person becomes infectious and can infect others when he/she develops the symptoms and the infection spreads mainly in hospitals between outpatients, in patients, caretakers, medical personnel, schools, churches, interaction with family members and friends at social gatherings like funerals, wedding and birthday parties, workplaces, and people in the household with close contact with the infected person (see Figure 1 below showing the pathways of Ebola Virus Disease transmission).

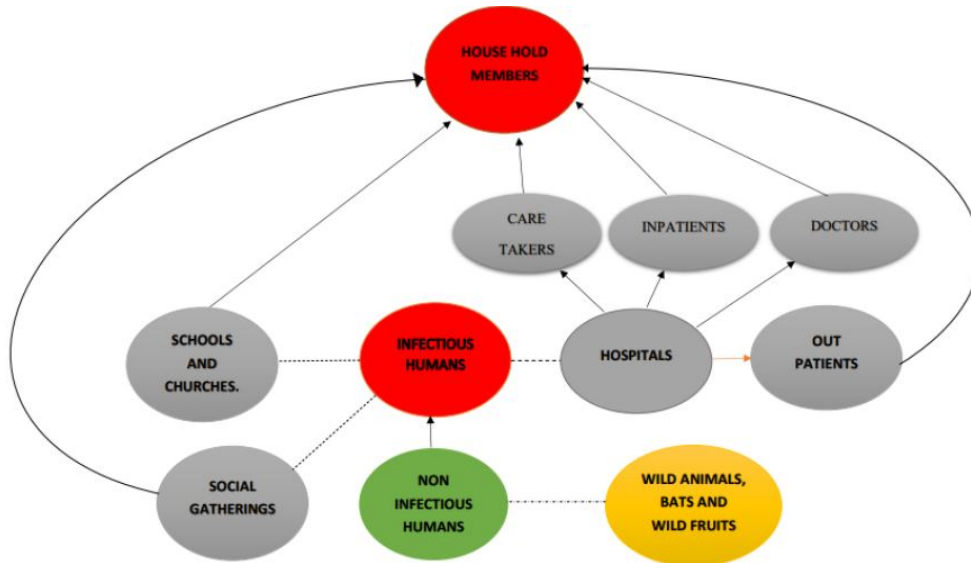


Figure 1: Transmission Means of Ebola Virus Disease between Humans

It's believed that men who have recovered from Ebola transmit the virus (up to 90 days after recovery) to their partner through semen. Breastfeeding is also a risk factor as babies may acquire the virus through breast milk of infected mothers [11, 12]. The epidemiology of the disease is complicated with spill overs even when the area has been declared ebola-free. This makes implementing control measures somewhat difficult. Previous EVD outbreak experiences have been relied on to build a country's response and resilience capacity. However, an outbreak that comes back-to-back with COVID-19 poses challenges on its control. Lessons from COVID-19 lockdown in disease outbreak control have been implemented for the control of the current EVD outbreak in Uganda, but their impact have not been well described. The national temporal socioeconomic advances are dynamic and complex with each disease outbreak. Hypothesise driven scientific modelling of control measures for EVD are timely and may pave a way for ease of future disease outbreak control. Applying a combination of intervention measures, specifically case management, infection prevention and control practices, surveillance and contact tracing, a good laboratory service, safe and dignified burials and social mobilization are important, but models that appraise these interventions are even more critical.

Mathematical models have been used by scholars to help in directing policy makers to set standard control measures to mitigate the spread of infectious diseases in communities. Most existing mathematical models use the traditional bilinear and non-linear incidence rates ([13]-[18]). However, such incidence rates are helpful during the initial stages of the disease outbreak and not useful as the disease progresses in the population in the long run. Therefore, adapting to a new incidence rate for example the convex incidence rate gives a better understanding of the disease progression in communities especially where individuals are doubly exposed to the infection which increases the risk of transmission. Convex incidence rate has been used in describing the dynamics of Hepatitis B virus diseases by [19] and [20] used a convex incidence rate in modelling infectious diseases like Hepatitis

B Virus disease.

Optimal control theory has proved to be an effective tool in understanding ways to curtail the spread of infectious diseases in susceptible populations by instituting optimal intervention measures that help decision makers devise better policies to control infectious diseases [21]. Mathematical models of Ebola Virus disease with optimal control for reducing the spread in populations have been studied for example ([22]- [26]). However, literature on EBV models incorporating a convex incidence rate are limited. This study, aims at using a convex incidence rate in a Susceptible-Exposed-Infected-Treated-Recovered-Death (SEITRD) EBV model to determine the effect of the control strategies instituted to reduce the spread of the deadly disease in the population.

1.1 Organization of the manuscript

Section 1 has discussed the introduction and Section 2, an (S-E-I-T-R-D) model with a convex incidence is designed, variables and parameters defined, description of the model is given and finally ordinary differential equations are generated. Section 3, gives a]the computation of reproduction number and its importance to disease spread in the community. Section 4, gives the modification of S-E-I-R-T-D model into an optimal control system, a qualitative analysis and numerical experiments are carried out. In section 5, cost effectiveness analysis is carried out and a general discussion of the findings, concluding remarks and future research directions are outlined.

2 The Susceptible-Exposed-Infected-Treated-Recovered-Dead (S-E-I-T-R-D) EBV Model Design

In this section, we design a mathematical model for the dynamics EBV incorporating a convex incidence rate based on the propagation of the virus transmission in the human population. The human population is represented by $N(t)$ which is partitioned into six sub-populations namely: susceptible persons $S(t)$ showing persons that can contract the virus if in direct contact with infected humans, exposed sub-population $E(t)$ referring to persons that have been exposed to the virus but have not developed signs; infected persons $I(t)$ representing individuals with signs of EBV and can spread the virus if there is a direct contact with a susceptible person; treated persons $T(t)$ representing screened persons that are undergoing medication; recovered sub-population $R(t)$ showing persons responding to treatment and recovering from EBV infection and the dead sub population $D(t)$, individuals who die both a natural death and EVD induced death. In all sub populations we assume individuals to die a natural death, μ . Further, we assume that the convex incidence rate $f(S, I, T, D)$ satisfies the following;

H1: $f(S, I, T, D)$ is a continuous differentiable function $\forall S, I, T, D > 0$.

H2: $f(S, I, T, D) > \forall S, I, T, D > 0$ and $f(0, I, T, D) = f(S, 0, T, D) = f(S, I, 0, D) = f(S, I, T, 0) = 0 \forall S, I, T, D > 0$ and non negative $\forall S \geq 0, I \geq 0, T \geq 0, D \geq 0$.

H3: The partial derivatives $f'_S = \frac{\partial f(S, I, T, D)}{\partial S}$, $f'_I = \frac{\partial f(S, I, T, D)}{\partial I}$, $f'_T = \frac{\partial f(S, I, T, D)}{\partial T}$ and $f'_D = \frac{\partial f(S, I, T, D)}{\partial D}$ are positive $\forall S \geq 0, I \geq 0, T \geq 0, D \geq 0$

All parameters considered in this model are positive. In the initial stages of the disease spread the transmission rates are represented with βSI , $\beta_0 ST$ and $\beta_1 SD$ and in the long run new infections due to double exposure are represented with βSI^2 , $\beta_0 ST^2$ and $\beta_1 SD^2$. Other parameter values are described in Table 1 below.

Table 1: **Description of EVD Model Parameters**

Parameter	Description	Base Value	Ref
β	Disease transmission rate through the infected	0.2244	[27]
β_0	Disease transmission rate through persons on treatment	0.1122	[27]
β_1	Disease transmission rate through the dead body	0.1683	[27]
γ	Rate of recovered humans to become Susceptible	0.5366/day	[28]
λ	Recruitment rate of susceptible persons	variable	Assumed
ζ_0	Total deaths rate from the infected class	0.5500	[29]
δ_0	Ebola induced death rate for the infected	0.5499	computed
δ_1	Ebola induced death rate for the treated	0.1600	[30]
μ	Natural death rate	0.00005/day	[31]
ω	Transfer rate from the infected class to the treatment class	28 days	assumed
ϕ	Progress rate from the exposed class to the infected class	0.0833	[32]
h	Rate at which the treated persons respond to medication	0.0608	[33]
c_1	Control effort based on lock down of all the susceptible population	[0 1]	Assumed
c_2	Control effort through contact tracing of the exposed persons	[0 1]	Assumed
c_3	Control effort based on treatment of all the infected persons	[0 1]	Assumed
τ	Contact tracing rate for persons with a history of exposure with the infectious persons	0.06	[34]
s	Cremation/burial rate of Ebola-deceased persons	0.5000/day	[35]
α_0	Weight factor for infection from infected to susceptible population	0.0006	[36]
α_2	Weight factor for infection from the dead to susceptible population	0.0006	[36]
α_1	Weight factor for contact rate between susceptible and treatment population	[0 1]	[25]

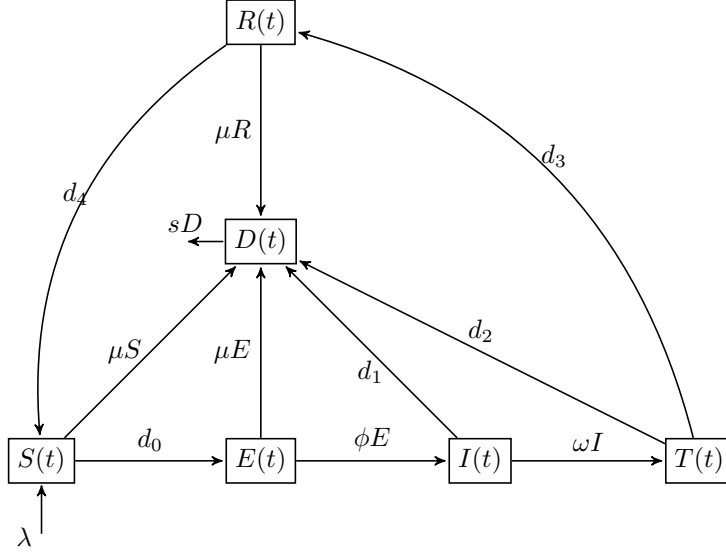


Figure 2: A schematic diagram for SEITRD Model

with $Q(t) = S(t) + E(t) + I(t) + T(t) + R(t)$, $d_0 = f(S, I, T, D) = S(\beta I(1 + \alpha_0 I) + \beta_0 T(1 + \alpha_1 T) + \beta_1 D(1 + \alpha_2 D))$, $d_1 = (\mu + \delta_0)I$, $d_2 = (\mu + \delta_1)T$, $d_3 = hT$, $d_4 = \gamma R$.

The system of equations governing the dynamics of EVD is:

$$\begin{aligned}
 \dot{S}(t) &= \lambda + \gamma R - f(S, I, T, D) - \mu S, \\
 \dot{E}(t) &= f(S, I, T, D) - a_0 E, \\
 \dot{I}(t) &= \phi E - a_1 I, \\
 \dot{T}(t) &= \omega I - a_2 T, \\
 \dot{R}(t) &= hT - a_3 R, \\
 \dot{D}(t) &= \delta_0 I + \delta_1 T + \mu Q - sD.
 \end{aligned} \tag{2.1}$$

where $a_0 = (\phi + \mu)$; $a_1 = (\omega + d_1)$; $a_2 = (d_2 + h)$ and $a_3 = (\gamma + \mu)$;
 $d_0 = f(S, I, T, D) = S(\beta I(1 + \alpha_0 I) + \beta_0 T(1 + \alpha_1 T) + \beta_1 D(1 + \alpha_2 D))$.

Expanding Eq.(2.1)

$$\begin{aligned}
 \dot{S}(t) &= \lambda + \gamma R - S[\beta I(1 + \alpha_0 I) + \beta_0 T(1 + \alpha_1 T) + \beta_1 D(1 + \alpha_2 D)] - \mu S^*, \\
 \dot{E}(t) &= S^*[\beta I(1 + \alpha_0 I) + \beta_0 T(1 + \alpha_1 T) + \beta_1 D(1 + \alpha_2 D)] - (\phi + \mu)E, \\
 \dot{I}(t) &= \phi E - (\omega + \mu + \delta_0)I, \\
 \dot{T}(t) &= \omega I - (\mu + \delta_1 + h)T, \\
 \dot{R}(t) &= hT - (\gamma + \mu)R, \\
 \dot{D}(t) &= \delta_0 I + \delta_1 T + \mu Q - sD.
 \end{aligned} \tag{2.2}$$

where $Q(t) = S(t) + E(t) + I(t) + T(t) + R(t)$ is a total number of live individuals in the

human population. Summing up equations in system (2.2) we get

$$\frac{dN(t)}{dt} = \lambda - sD(t), \quad (2.3)$$

Subject to $N(0) = N_0$.

In this work, an assumption that the overall death rate ($\mu + \delta_0 + \delta_1$) is greater than or equal to the cremation/burial rate (s) is made. If this condition is not met, it implies that the deceased individuals totally disappear from the community and the class of D in the model is inappropriate.

2.1 The Equilibria and Reproduction Number

2.1.1 Disease Free Equilibrium (DFE)

This is a point attained when there is no disease propagation in the population. We assume there are no infected $I(t)$, no exposed $E(t)$, no treated $T(t)$, no recovered $R(t)$ and therefore no death related to disease $D(t)$ that is $E(t) = I(t) = T(t) = R(t) = D(t) = 0$. Setting the right hand side (RHS) of Eq.(2.2) to zero and substituting for $E(t) = I(t) = T(t) = R(t) = D(t) = 0$, the DFE, $E_0 = (S_0, E_0, I_0, T_0, R_0, D_0) = \{\frac{\lambda}{\mu}, 0, 0, 0, 0, 0\}$.

2.1.2 Reproduction Number, R_0 without control

The transmission of an infection in a human population can well be explained by the reproductive number, R_0 defined as a measure of the mean number of EBV cases caused by a single Ebola-infected person (living or dead) introduced into a wholly-susceptible human population. In assessing the effect of introducing an infectious individual in a population free of the disease the reproductive number is computed using the next generation approach. Let $Y = (E, I, T, D)$ be a composition of compartments with infected individuals. $\frac{dY}{dt} = F - V$ where F and V represent new infection and transition matrices at disease free equilibrium respectively. Therefore, we have the following

$$\begin{aligned} F &= \begin{pmatrix} 0 & S_0\beta & S_0\beta_0 & S_0\beta_1 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}, \\ V &= \begin{pmatrix} (\phi + \mu) & 0 & 0 & 0 \\ -\phi & (\omega + \mu + \delta_0) & 0 & 0 \\ 0 & -\omega & (\mu + \delta_1 + h) & 0 \\ \mu & (\mu - \delta_0) & (\mu - \delta_1) & s \end{pmatrix}, \\ V^{-1} &= \begin{pmatrix} v_0 & 0 & 0 & 0 \\ \phi v_0 v_1 & v_1 & 0 & 0 \\ \phi v_0 v_1 v_2 \omega & v_1 v_2 \omega & v_2 & 0 \\ v_3 & v_4 & v_5 & v_6 \end{pmatrix}. \end{aligned} \quad (2.4)$$

with

$$\begin{aligned}
v_0 &= \frac{1}{\phi + \mu}, \\
v_1 &= \frac{1}{\omega + \mu + \delta_0}, \\
v_2 &= \frac{1}{\omega + \mu + \delta_1}, \\
v_3 &= \frac{\phi\omega(\delta_1 - \mu) + \phi(\delta_0 - \mu)(\mu + \delta_1 + h)}{s(\phi + \mu)(\omega + \mu + \delta_0)(\mu + \delta_1 + h)}, \\
v_4 &= \frac{\omega(\delta_1 - \mu) + (\delta_0 - \mu)(\mu + \delta_1 + h)}{s(\omega + \mu + \delta_0)(\mu + \delta_1 + h)}, \\
v_5 &= \frac{(\delta_1 - \mu)}{s(\mu + \delta_1 + h)}, \\
v_6 &= \frac{1}{s}.
\end{aligned}$$

The effective reproduction number of EVD is given by the dominant eigenvalues ($\rho(F \times V^{-1})$). Therefore,

$$R_0 = \frac{s\phi S_0(\beta_0\omega + \beta(\mu + \delta_1 + h)) - S_0\beta_1\{\phi\omega(\mu - \delta_1) + (\mu + \delta_1 + h)[\mu(\omega + \mu + \delta_0) + \phi(\mu - \delta_0)]\}}{s(\phi + \mu)(\omega + \mu + \delta_0)(\mu + \delta_1 + h)}. \quad (2.5)$$

$R_0 = R_I + R_T + R_D$ in which

$$\begin{aligned}
R_I &= \frac{\phi\beta_0\omega S_0}{(\phi + \mu)(\omega + \mu + \delta_0)(\mu + \delta_1 + h)}, \\
R_T &= \frac{\phi\beta S_0}{(\phi + \mu)(\omega + \mu + \delta_0)}, \\
R_D &= \frac{\beta_1 S_0\{\phi\omega(\delta_1 - \mu) - (\mu + \delta_1 + h)[\mu(\omega + \mu + \delta_0) + \phi(\mu - \delta_0)]\}}{s(\phi + \mu)(\omega + \mu + \delta_0)(\mu + \delta_1 + h)},
\end{aligned}$$

where R_I = contribution of new infections of EVD disease from infectious individuals $I(t)$; R_T = contribution of new infections due to EVD disease resulting from contact with individuals on EVD treatment $T(t)$ and R_D = contribution of new infections resulting from contact with the dead due to EVD, $D(t)$. Using the initial values given in Table 1, the reproductive number for EVD is found to be 1.5904 before interventions. Since $R_0 > 1$, this means that the EVD may continue to spread in the population and eventually wipes it out if no control measures are put in place.

2.1.3 The endemic Equilibrium (EE)

The endemic equilibrium (E_2) for EVD is a point for which the human population (atleast $(S^*, E^*, I^*, T^*, R^*, D^* > 0)$). Equating the RHS of Eq. (2.2), we obtain

$$\begin{aligned}
\lambda + \gamma R^* - S^*[\beta I^*(1 + \alpha_0 I^*) + \beta_0 T^*(1 + \alpha_1 T^*) + \beta_1 D^*(1 + \alpha_2 D^*)] - \mu S &= 0, \\
S[\beta I^*(1 + \alpha_0 I^*) + \beta_0 T^*(1 + \alpha_1 T^*) + \beta_1 D^*(1 + \alpha_2 D^*)] - (\phi + \mu)E^* &= 0, \\
\phi E^* - (\omega + \mu + \delta_0)I^* &= 0, \\
\omega I^* - (\mu + \delta_1 + h)T^* &= 0, \quad (2.6) \\
hT^* - (\gamma + \mu)R^* &= 0, \\
\delta_0 I^* + \delta_1 T^* + \mu Q^* - sD^* &= 0.
\end{aligned}$$

Where $Q^* = S^* + E^* + I^* + T^* + R^*$. Rearranging equations in system (3.1) to get solutions of $(S^*, E^*, I^*, T^*, R^*, D^*)$ in terms of I^* . Adding equations (1) and (2) of system (3.2) we get $S^* = \frac{p_0(\lambda - p_1 I^*) + p_2 I^*}{\mu \phi p_0}$ and rearranging equations of system (3.1) we obtain

$$\begin{aligned}
S^* &= \frac{p_0(\lambda \phi - p_1 I^*) + p_2 I^*}{\mu \phi p_0}, \\
E^* &= \frac{(\omega + \mu + \delta_0)I^*}{\phi}, \\
T^* &= \frac{\omega I^*}{(\mu + \delta_1 + h)}, \quad (2.7)
\end{aligned}$$

$$\begin{aligned}
R^* &= \frac{h\omega I^*}{(\gamma + \mu)(\mu + \delta_1 + h)}, \\
D^* &= d_0 + d_1 I^* \quad (2.8)
\end{aligned}$$

where

$$\begin{aligned}
p_0 &= (\gamma + \mu)(\mu + \delta_1 + h), \quad p_1 = (\phi + \mu)(\omega + \mu + \delta_0), \quad p_2 = \mu \phi \gamma \omega h \quad d_0 = \frac{\delta_0(\mu + \delta_1 + h) + \delta_1 \omega}{s \mu \phi ((\mu + \delta_1 + h))}, \\
d_1 &= \frac{k_0 + k_1(k_2 + k_3 + k_4 + k_5)}{k_6}, \quad k_0 = \delta_0(\mu + \delta_1 + h) + \delta_1 \omega, \quad k_1 = \mu(\mu + \delta_1 + h), \\
k_2 &= \frac{\gamma \omega h}{\mu(\gamma + \mu)(\mu + \delta_1 + h)} + \frac{(\phi + \mu)(\omega + \mu + \delta_0)}{\mu \phi}, \quad k_3 = \frac{h\omega}{(\gamma + \mu)(\mu + \delta_1 + h)}, \quad k_4 = \frac{\omega + \mu + \delta_0}{\phi}, \\
k_5 &= \frac{\omega}{\mu + \delta_1 + h}, \quad k_6 = s(\mu + \delta_1 + h).
\end{aligned}$$

3 Optimal Control

The main objective of optimal control theory applied in control of infectious diseases is to identify a control set that minimizes the number of exposed, infected individuals in a stipulated time interval. On the other hand in the process of undertaking control measures the cost of vaccination, tracing contacts, implementing lockdown and curfew, treatment, awareness to public through social media and public education have to be maintained at low costs by all means. Modifying model system 3.2 with control efforts through lock down and curfew of populations (c_1), contact tracing of the exposed persons (c_2) and treating the infected persons (c_3) we get an optimal control system as follows

Expanded Equation

$$\begin{aligned}
\dot{S}(t) &= \lambda + \gamma R - (1 - c_1)S[\beta I(1 + \alpha_0 I) + \beta_0 T(1 + \alpha_1 T)] - S\beta_1 D(1 + \alpha_2 D) - \mu S, \\
\dot{E}(t) &= (1 - c_1)S[\beta I(1 + \alpha_0 I) + \beta_0 T(1 + \alpha_1 T)] + S\beta_1 D(1 + \alpha_2 D) - (\phi + \mu + c_2\tau)E, \\
\dot{I}(t) &= (\phi + c_2\tau)E - (\omega + \mu + \delta_0)I, \\
\dot{T}(t) &= \omega I - (\mu + \delta_1 + (1 + c_3)h)T, \\
\dot{R}(t) &= (1 + c_3)hT - (\gamma + \mu)R, \\
\dot{D}(t) &= \delta_0 I + \delta_1 T + \mu N(t) - sD.
\end{aligned} \tag{3.1}$$

that reduces to

$$\begin{aligned}
\dot{S}(t) &= \lambda + \gamma R - g(S, I, T, D) - \mu S, \\
\dot{E}(t) &= g(S, I, T, D) - b_0 E, \\
\dot{I}(t) &= b_1 E - b_2 I, \\
\dot{T}(t) &= \omega I - (b_3 + b_4)T, \\
\dot{R}(t) &= (1 + c_3)hT - a_3 R, \\
\dot{D}(t) &= \delta_0 I + \delta_1 T + \mu N(t) - sD.
\end{aligned} \tag{3.2}$$

with initial conditions $S(0) = S_0 \geq 0; E(0) = E_0 \geq 0; I(0) = I_0 \geq 0;$
 $T(0) \geq T_0; R(0) = R_0 \geq 0; D(0) = D_0 = 0.$

Where $g(S, I, T, D) = (1 - c_1)[S(\beta I(1 + \alpha_0 I) + \beta_0 T(1 + \alpha_1 T))] + \beta_1 S D(1 + \alpha_2 D); b_0 =$
 $(\mu + \phi + c_2\tau); b_1 = (\phi + c_2\tau); b_2 = (\omega + \mu + \delta_0); b_3 = (1 + c_3)h; b_4 = (\mu + \delta_1)$

Referring to the above optimal control system we get the objective function as follows.

$$f(c_1, c_2, c_3) = \int_0^T \left(b_0 E + b_1 I + b_2 T + \frac{1}{2} \sum_{i=1}^3 (k_i c_i^2) \right) dt \tag{3.3}$$

with $T =$ Time when interventions are implemented, b_0, b_1, b_2 are coefficients balancing the controls, $k_i/i = 0, 1, 2$ are weight constants on the benefit and cost, $\frac{1}{2}k_i c_i/i=1,2,3$ are cost of tracing contacts, implementing lock down and curfew and treatment costs.

Hypothesis: Let C be a measurable control set, the control functions c_i are bounded and lebesgue measurable functions such that $\{c_i(t) \in C : 0 \leq c_i(t) \leq 1\}, t \in [0, T], i = 1, 2, 3.$ Hence the optimal control is given as

$$f(c_1^*, c_2^*, c_3^*) = \min_C f(c_1, c_2, c_3) \tag{3.4}$$

It is worth noting that a quadratic objective functional is preferred because control strategies are assumed to be nonlinear [37].

3.1 Existence of an optimal control

3.2 Characterization of the Optimal Control

The Pontryagin's Maximum Principle is used to derive the necessary conditions for the optimal control function. The principle transforms the model system of Eq 3.2 and Eq 3.3 into a Hamiltonian minimization problem H with regard to the control variables $c_1, c_2, c_3.$

Suppose $L = b_oE + b_1I + b_2T + \frac{1}{2} \sum_{i=1}^3 (k_i c_i^2)$ be the Lagrangian function. Then the Hamiltonian function H for the control problem is as follows

$$H = L + e_1 \frac{dS}{dt} + e_2 \frac{dE}{dt} + e_3 \frac{dI}{dt} + e_4 \frac{dT}{dt} + e_5 \frac{dR}{dt} + e_6 \frac{dD}{dt}. \quad (3.5)$$

With $e_i, i = 1, 2, \dots, 6$ representing adjoint variables related to that state variables $\{S, E, I, T, R, D\}$. Substituting quantities of Eq.3.2 into Eq. 3.5 we obtain the Hamiltonian function H as

$$\begin{aligned} H = & b_oE + b_1I + b_2T + \frac{1}{2} [k_1c_1^2 + k_2c_2^2 + k_3c_3^2] \\ & + e_1 (\lambda + \gamma R - (1 - c_1)S[\beta I(1 + \alpha_0I) + \beta_0T(1 + \alpha_1T)] - S\beta_1D(1 + \alpha_2D) - \mu S) \\ & + e_2 ((1 - c_1)S[\beta I(1 + \alpha_0I) + \beta_0T(1 + \alpha_1T)] + S\beta_1D(1 + \alpha_2D) - (\phi + \mu + c_2\tau)E) \\ & + e_3 ((\phi + c_2\tau)E - (\omega + \mu + \delta_0)I) \\ & + e_4 (\omega I - (\mu + \delta_1 + (1 + c_3)h)T) \\ & + e_5 ((1 + c_3)hT - (\gamma + \mu)R) \\ & + e_6 (\delta_0I + \delta_1T + \mu N(t) - sD). \end{aligned} \quad (3.6)$$

Performing derivative operations of Eq. 3.6 with respect to state variables $\{S, E, I, T, R, D\} \in Z$ and using $\frac{de_i}{dt} = -\frac{\partial H}{\partial Z_i}$

$$\begin{aligned} \frac{de_1}{dt} &= (e_1 - e_2) ((1 - c_1)[\beta I(1 + \alpha_0I) + \beta_0T(1 + \alpha_1T)]) - e_1\mu, \\ \frac{de_2}{dt} &= (e_2 - e_3)(\phi + c_2\tau) + e_2\mu, \\ \frac{de_3}{dt} &= (e_1 - e_2)(1 - c_1)S[\beta(1 + 2\alpha_0I) + \omega(e_3 - e_4) + e_3(\mu + \delta_0)], \\ \frac{de_4}{dt} &= (e_1 - e_2)(1 - c_1)S[\beta_0(1 + 2\alpha_1T)] + (e_4 - e_5)(1 + c_3)h + e_4(\mu + \delta_1), \quad (3.7) \\ \frac{de_5}{dt} &= e_5\mu, \\ \frac{de_6}{dt} &= (e_1 - e_2)(S\beta_1(1 + 2\alpha_2D) + se_6). \end{aligned}$$

Finding the Optimal control functions Taking derivatives of the Hamiltonian function H with respect to controls $\frac{\partial H}{\partial c_i}$ we obtain the following system

$$\begin{aligned} \frac{\partial H}{\partial c_1} &= k_1c_1 + (e_1 - e_2)S[\beta I(1 + \alpha_0I) + \beta_0T(1 + \alpha_1T)] = 0, \\ \frac{\partial H}{\partial c_2} &= k_2c_2 + (e_3 - e_2)\tau E = 0, \\ \frac{\partial H}{\partial c_3} &= k_3c_3 + (e_5 - e_4)hT = 0. \end{aligned} \quad (3.8)$$

From Eq. 3.8 we solve for c_1, c_2, c_3 to get

$$\begin{aligned} c_1 &= \frac{(e_1 - e_2)S[\beta I(1 + \alpha_0 I) + \beta_0 T(1 + \alpha_1 T)]}{k_1}, \\ c_2 &= \frac{(e_3 - e_2)\tau E}{k_2}, \\ c_3 &= \frac{(e_5 - e_4)hT}{k_3}. \end{aligned} \quad (3.9)$$

Using bounds we can obtain the optimal control strategies c_1^*, c_2^*, c_3^* as

$$\begin{aligned} c_1^* &= \max\{0, \min(1, \frac{(e_1 - e_2)S[\beta I(1 + \alpha_0 I) + \beta_0 T(1 + \alpha_1 T)]}{k_1})\}, \\ c_2^* &= \max\{0, \min(1, \frac{(e_3 - e_2)\tau E}{k_2})\}, \\ c_3^* &= \max\{0, \min(1, \frac{(e_5 - e_4)hT}{k_3})\}. \end{aligned} \quad (3.10)$$

4 Numerical Simulations

The method described in [39] was used for the numerical solution of the optimal control problem using the parameter values in Table 1.

In determining the impact of each control strategy on eradicating Ebola, we employ the following control strategies; Lockdown, Contact tracing, combination of Lockdown and contact tracing, combination of Contact tracing and treatment of infected population as well as combination of Lock down and treatment of infected population.

4.1 Strategy I: Control with Lockdown ($c_1 > 0, c_2 = c_3 = 0$)

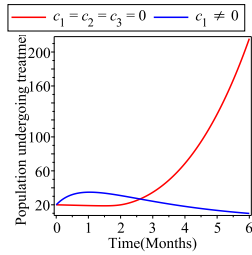


Figure 3: Population under treatment.

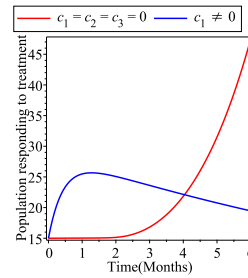


Figure 4: Population responding positively to treatment.

Incorporating an optimal control measure as lockdown, the population undergoing treatment and those responding positively to treatment reduced drastically as shown in Figure 3 and

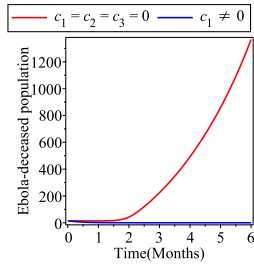


Figure 5: Ebola deceased population with controls

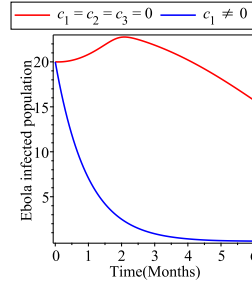


Figure 6: Ebola infected population with controls

Figure 4 respectively. It is evident that lockdown as a control measure has an effect on the susceptible population as far as the spread of Ebola infection is concerned.

The population infected with the Ebola virus increases with time. As the lock-down was introduced as a control measure, the population reduces with time. The implication is that no additional infection was recorded as a result of the lockdown as an optimal control measure as indicated in Figure 5 and Figure 6. Death recordings as a result of Ebola reduced exponentially with time as a result of lockdown as a control measure as shown in Figure 5.

4.2 Strategy II: Control with tracing contacts ($c_2 > 0, c_1 = c_3 = 0$)

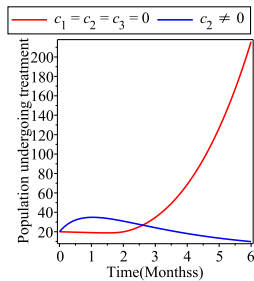


Figure 7: Population undergoing treatment

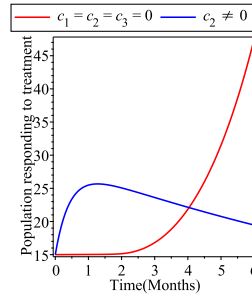


Figure 8: Population responding positively to treatment

Suspected cases of Ebola are usually traced and monitored. This control measure ensures that no new cases are recorded and also infected cases are treated in isolation. Contact tracing as an optimal control measure has an effect on the population under treatment and those responding positively to treatment as shown in Figure 7 and Figure 8.

The dynamics of Ebola deceased population and infected population are observed in Figure 9 and Figure 10. Both the deceased and infected populations decreased as a result of contact tracing. The implication is that both death and infected populations are under control as a result of contact tracing.

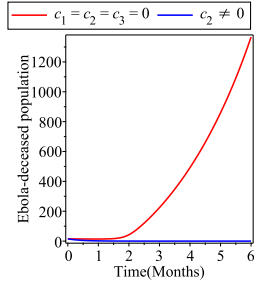


Figure 9: Ebola deceased population with controls.

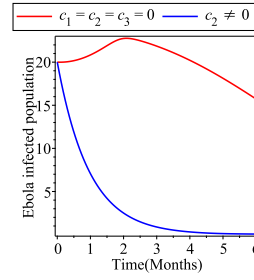


Figure 10: Ebola infected population with controls.

4.3 Strategy III: Combination of tracing contacts ($c_2 > 0$) and treatment of the infected ($c_3 > 0$, $c_1 = 0$)

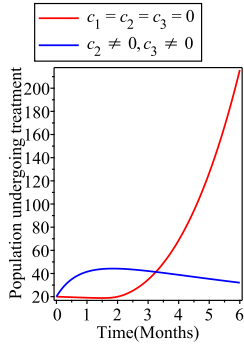


Figure 11: Population under treatment with controls.

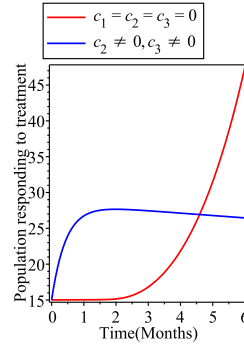


Figure 12: Population responding positively to treatment with controls.

The combination of contact tracing and treatment to the population under treatment and those responding positively to treatment has yielded positive results. This control measure has caused a reduction in the population under treatment. This is an indication more people are not tested positive to Ebola infection as shown in Figure 11 and Figure 12.

It can be observed that Ebola deceased population and Ebola infected population increase steadily with time in the absence of any control measure. When a contact tracing and treatment were instituted, there has been a reduction in Ebola infected and deceased populations. This control strategy impacted positively as indicated in Figure 13 and Figure 14.

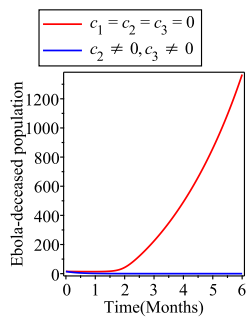


Figure 13: Ebola deceased population with controls.

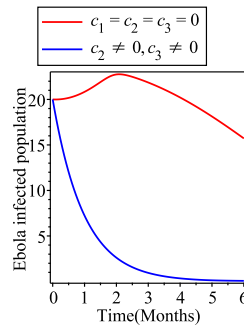


Figure 14: Ebola infected population with controls.

4.3.1 Strategy IV: Combination of Lock down ($c_1 > 0$) and treatment of the infected ($c_3 > 0$), $c_2 = 0$

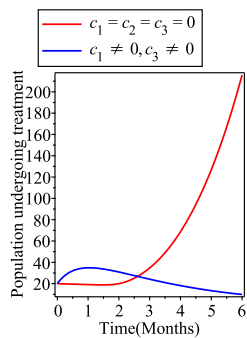


Figure 15: Poulation under treatment with controls.

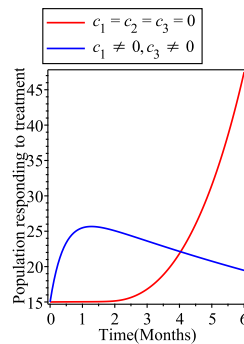


Figure 16: Population responding positively to treatment with controls.

The combination of lockdown and treatment of Ebola population have resulted in the reduction of population responding positively to treatment as shown in Figure 15 and Figure 16. The biological implication is that combination of lockdown and curfew plus treatment of infected population can be an effective control measure in combating Ebola.

Combining lockdown and treating the population infected with Ebola can be an effective control strategy in fighting the infection. It can be observed in Figure 17 and Figure 18 that this strategy has resulted in decreasing both Ebola deceased and infected population as indicated in 17 and 18 respectively.

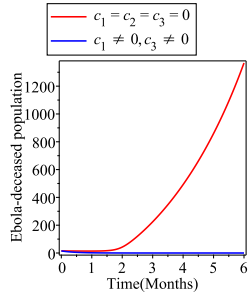


Figure 17: Ebola deceased population with controls.

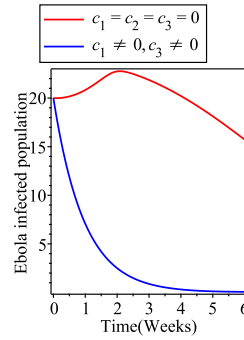


Figure 18: Ebola infected population with controls.

4.4 Strategy V: Combination of Lockdown ($c_1 > 0$) and tracing contacts ($c_2 > 0$) .

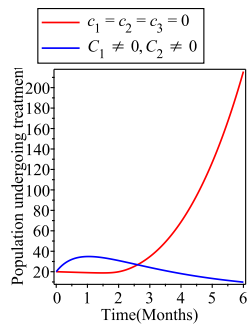


Figure 19: Population under treatment with controls.

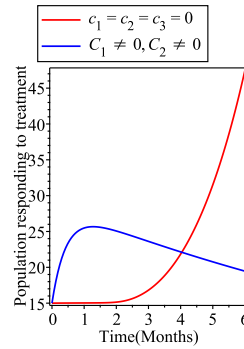


Figure 20: Population responding positively to treatment with controls.

The population under treatment and the population responding positively to treatment experienced changes in population dynamics. This is as a result of the combination of contact tracing, lockdown and curfew as control measures. Figure 21 and Figure 22 shows the population dynamics of the population responding positively to treatment and those under treatment.

The combination of contact tracing and lockdown as a control measure is one of the most effective control measures in combating the infection as evident in Figure 19 and Figure 20. There is a sharp reduction in the population infected and deceased with the virus as indicated in Figure 19 and Figure 20.

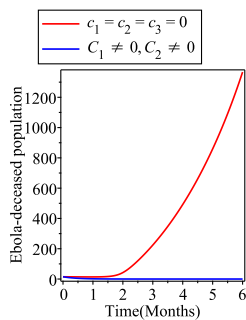


Figure 21: with controls.

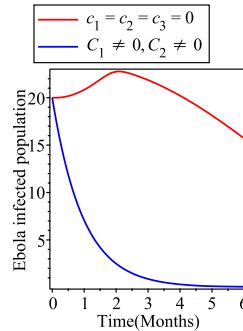


Figure 22: with controls.

5 Cost-effectiveness analysis

Applying health intervention strategies can be both cost and labour intensive. Hence the need to identify and consider the best intervention strategy that comes with less cost. This therefore calls for cost effectiveness analysis. Authors in [38], employed the Incremental Cost-Effectiveness Ratio (ICER) to compare the costs and infections averted (outcomes) of two alternative interventions strategies. This approach is usually done by computing total infection averted by each of the strategies and its corresponding costs.

The ICER between strategies **A** and **B** is the ratio of differences in cost to differences in infection averted (outcomes). This is given by the relation;

$$ICER(A) = \frac{\text{Cost of strategy A} - \text{Cost of strategy B}}{\text{Total infection averted by strategy A} - \text{Total infection averted by strategy B}} \quad (5.1)$$

The analysis of Incremental Cost-Effectiveness Ratio (ICER) assumes that costs of various interventions are proportional to the number of controls employed. All strategies are compared incrementally by comparing one strategy to the next less effective alternative.

When only one intervention is applied, it can be effective in combating a disease dynamic system or population. Hence, the emphasis is on the analysis of strategies that involves more than one intervention. The total cost for the implementation of various strategies are computed from the cost;

$$\frac{k_1 c_1^2}{2}, \frac{k_2 c_2^2}{2} \text{ and } \frac{k_3 c_3^2}{2}.$$

Generally, Incremental Cost-Effectiveness Ratio (ICER) is first applied by putting all strategies in order of increasing infection averted as shown in Table 2.

Table 2: **Total infection averted and total cost**

Strategies	Description	Total infection averted	Total cost
III	Contact tracing and treatment	22	31,355.00
V	Lock down and contact tracing	23	35,255.00
IV	Lock down and treatment	25	32,452.00

Depending on infection averted, all control strategies are ranked in increasing order of effectiveness. Considering Strategy (III) as the base line, we compare Strategy (III) and Strategy (V).

$$ICER(III) = \frac{31,355}{22}$$

ICER (III) = 1,425.2273
and

$$ICER(V) = \frac{35,255 - 31,355}{23 - 22}$$

ICER (V) = 3,900.0000

Comparing Strategy (III) and Strategy (V), we reject Strategy (V) as it is very expensive to implement as compared to Strategy (III).

Now comparing Strategy (III) and Strategy (IV).

ICER (III) = 1,425.2273
and

$$ICER(IV) = \frac{32,452 - 31,355}{25 - 22}$$

ICER (IV) = 365.6667

Comparing Strategy (III) and Strategy (IV), we reject Strategy (III) as it is very expensive to implement as compared to Strategy (IV). Hence, the best intervention strategy to be implemented is Strategy (IV). This is the most cost effective intervention strategy that comes with less cost. However, the most expensive intervention strategy to be implemented is Strategy (V). This strategy should be avoided by policy or decision makers.

Figure 23 shows the plots for all intervention strategies. The most expensive intervention strategy is Lock down and contact tracing. However, the cheapest intervention strategy to be implemented is lock down and treatment of infected population.

Using all the intervention strategies would not be advisable considering the cost implications as shown in Figure 23. Moreover, the use of only one intervention strategy should never be considered since it is not effective in disease eradication.

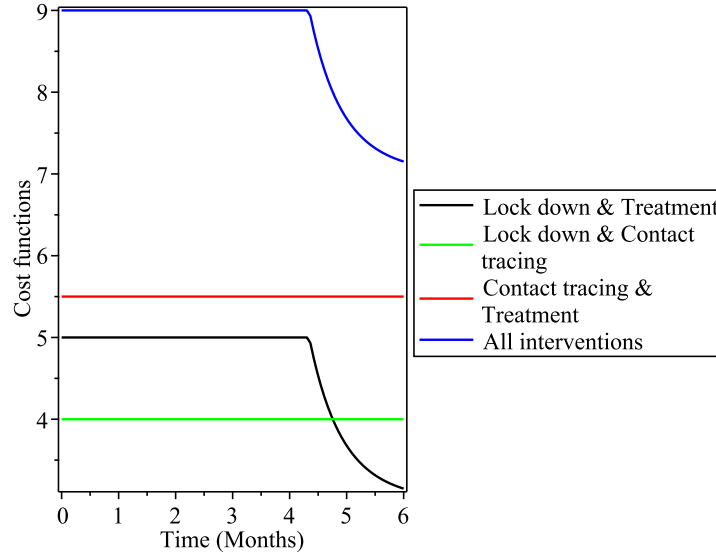


Figure 23: Cost function for the intervention strategies for a period of six months.

6 Discussion and Conclusion

In this study, we formulated and analyzed a deterministic nonlinear model for the transmission dynamics of Ebola virus disease premised on the 4-month 2022 Ebola outbreak in Uganda in which a total of 141 cases were recorded with 55 fatalities representing a case fatality rate of 39%. The WHO officially announced an end to the outbreak on 11th January 2023. The model incorporates a convex incidence term in the force of infection to account for a possible double exposure to infection by the susceptible population. Using the next generation matrix approach, we derived the expression for the basic reproduction number R_0 which is a measure of the severity of the outbreak. We estimated the basic reproduction number for the 2022 Ebola outbreak in Uganda to be $R_0 = 1.5904$. This value is comparable with the 2000 Uganda outbreak ($R_0 = 1.34$ as well as the 2014 Ebola outbreak in West Africa $R_0 = 1.757$ for Liberia, $R_0 = 1.492$ for Sierra Leone as well as $R_0 = 1.83$ and $R_0 = 1.59$ for the 1995 and 2000 Ebola outbreaks in DR Congo. For ease of analysis, the expression for R_0 was split into expressions represents contributions from individual infectious classes and we found out that $R_0 = R_I + R_T + R_D$ representing the infectious, treated and deceased classes.

An optimal control framework was designed based on the Pontryagin's Maximum principle to illustrate the effect of the following controls ranged against Ebola: imposing lockdown and curfew to limit interactions between populations; contact tracing of exposed and infected and treatment of the infected persons. These control measures are widely employed in fighting an outbreak of Ebola virus and are aimed at minimizing the number of exposed as well as infected and deceased persons while maximizing the number of treated and recovered individuals at minimal costs in terms of resources.

A number of strategies to combat the outbreak were designed by applying these control measures either singly or in combination. The first strategy involved enforcing lock-down and curfew singly and it's effect is well illustrated in Figures 3-6. For the 2022, Ebola

outbreak in Uganda, partial lock-down together with a dusk-to-dawn curfew were imposed in the districts where an outbreak had been confirmed. The second strategy involved carrying out contact tracing of the exposed and infected individuals and its effect is shown in Figures 7-10.

Contact tracing is a very laborious but rewarding exercise and involves even tracing contacts of contacts which can be time consuming and tedious. Without contact tracing, the number of both infected and deceased keeps on increasing. In the early stages of an Ebola outbreak, its crucial to get the population on board through sensitization and mobilization to help in identifying contacts either voluntarily and/or otherwise.

Another strategy involved carrying out contact tracing and treatment of the infected in combination and the effect is well captured in Figures 11-14. Yet another strategy involved a combination of lock-down and curfew together with treatment of the infected persons. As shown in Figures 15-18, this strategy ensures that the number of infected and deceased persons falls to zero within six months while the number under treatment and recovery increase sharply hitting the peak value in about half the time. This is a desirable outcome. Lastly, a combination of lock-down and curfew together with contact tracing was simulated and Figures 19-22 illustrate their effect. To consider the best intervention strategy to employ in combating an outbreak of Ebola in a locality, a cost effective analysis was conducted via the incremental cost-effective ratio (ICER) that compares the costs involved and the infections averted.

From our analysis, we found that the most expensive strategy involved imposing lock-down and curfew together with contact tracing of the infected while the cheapest alternative was lock-down and curfew together with treatment of the infected. As shown in Figure 23, implementation of all the three controls is more expensive than any of the strategies that employ only any two of the three controls.

However, given the seriousness of Ebola in terms of its case fatality rate, very fast progress and the disruption and mayhem to the economy and society at large, it's imperative that no costs should be spared in combating its outbreak in a locality. All resources should be mobilized and availed to bring an end to an outbreak as soon as possible. This in part entails prompt action, sensitization of the masses and availing all necessary resources.

Data availability

Data supporting this model are found in this manuscript.

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Conflict of interest

The authors declare that there is no conflict of interests pertaining to the publication of this work.

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