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Numerical Study and Sensitivity Analysis of Ebola Model with Multi-Intervention Strategies in a Heterogeneous Population

Reuben Iortyer Gweryina[1*], Anande Richard Kimbir[1] and Terhemen Aboiyar[1]

[1]Department of Mathematics and Statistics and Computer Science, Federal University of Agriculture, Makurdi, Benue, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Author RIG designed the study, performed the numerical and sensitivity analysis, wrote the protocol, and the first draft of the manuscript. Authors ARK and TA managed the analyses of the study. All authors read and approved the manuscript.

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Abstract

We perform numerical simulation and sensitivity analysis on a mathematical model of Ebola transmission to determine the biological significance of key model parameters in relation to disease transmissions and prevalence. The indices from the forward sensitivity of R_{eff} affirm that average contacts and transmission rates championed the disease outbreaks. Similarly, a model with multi-intervention strategies has proved to effectively reduce the contact and prevalence of Ebola virus disease than the models with one intervention at a time. This suggests that strategies targeting contact reduction (such as education and isolation) and those that focus on recovery rates (such as prompt treatment of the infected persons) can be successful in curtailing the Ebola epidemic.

Keywords: Numerical simulation; forward sensitivity index; Ebola virus disease; quarantine; education and treatment.

**Corresponding author: E-mail: reub.ior.gweryina@gmail.com, reub.ior.gweyina@gmail.com;*

ABBREVIATIONS

CDC : Centers for Disease Control and Prevention
CFSPH : Center for Food Security and Public Health
WHO : World Health Organization

1 Introduction

The Ebola virus is one of the most deadly etiological agents of viral infections that causes Ebola hemorrhagic fever in both humans and non-human primates. The virus whose natural reservoir remains elusive till date had more than 25 human sporadic outbreaks in Africa (the dark continent-popularly perceived as the hotbed of diseases) since its discovery in Zaire [1]. In 2014, nearly 20,206 people became newly infected with the Ebola virus and 7905 deaths recorded around the world. So far, this remains the largest outbreak ever in history [2]. Globally, the number of Ebola cases continues to grow from 602 people in 1976 to 28,646 cases in 2016 [3,4].

Transmission of the disease from human-to-human is purely by physical contact with infected blood, bodily secretions (including semen, urine, sweat, tears, faeces, breast milk and saliva), organs or body fluids of infected humans (dead or alive) [2,5]. Indeed, mother to child transmission can occur during childbirth or breastfeeding [5,6]. However, accidental needle injuries, unprotected sex, touching of the deceased body and eating of some bush meats (fruit bats in particular) are other agents of transmission [7,8]. So far, there has been no case of Ebola being transmitted by air, birds, reptiles, amphibians and arthropods [9].

After being infected with the virus, symptoms can manifest 2 to 21 days later (incubation period) and the infectious period can last from 4-10 days [10]. When the virus gets into the human body, infecting a cell, a secreted Ebola virus glycoprotein (sGP) uses a combination of host and a virally coded enzyme called Niemann Pick C1 to convert its negative sense RNA to the positive strand to replicate it using the cell's machinery. The virus, without delay, attacks and destroys the innate immune system of the host making monocytes, macrophages and dendritic cells (DCs) as its primary targets [11]. The inability of the infected DCs to mature promotes poor immune response (including antigen and cytokines) by natural killer (NK), T and B cells which consequently appreciate the uncontrolled spread and growth of the virus [12,13].

Even though there are no licensed antivirals or human vaccines against Ebola virus infection [14], Ebola can be controlled by quarantine/isolation of suspected/symptomatic individuals and adopting early supportive therapy (for the infected patients) [15,16]. More so, increasing the awareness of Ebola infection among the risk population is a prerequisite to expanding access to Ebola prevention, treatment and care [17].

Studies have provided evidence that those who survive the infection develop antibodies that may last for at least 10 years [14]. No case of reinfection has been reported about the disease at the moment.

A number of mathematical modelling studies have been developed to shade more light on the transmission dynamics of the disease, for example, Khan et al. [18] estimated the basic reproduction ratios of 2014 Ebola outbreaks in Guinea and Sierra Leone. Their model though considers the exposed class and hospital effects on disease transmission, it lacks parameter for the average number of contacts as well as heterogeneities of the infected people. Berge et al. [19] formulated a simple SIR mathematical model for Ebola in Africa, in which direct and indirect routes of transmission were included. Despite the fact that the disease can be controlled in the absence of recruitment of Ebola viruses as well as in the absence of shedding of the infected individuals, the model suggests further extension in the area of incorporating human behaviour through educational campaigns and media broadcasting. Modelling the Ebola epidemic with at most two control measures can be found in [20,21]. Meanwhile, single intervention strategies alone has been proved to be inadequate in eliminating the disease particularly, hospital-based techniques such as isolation [22], treatment [23] and media broadcasting [20]. However, more educated people have shown to acquire fewer cases of Ebola infection than the uneducated [24].

Based on the information provided above, Gweryina et al. [25,26] derived motivation from the work of Khan et al. [18] to develop a mathematical model of Ebola with multi-intervention strategies namely, quarantine, educational campaign and treatment in a heterogeneous population. The model has already been studied for mathematical and epidemiological well-posedness, and stability analysis both locally and globally.The present study intends to conduct a numerical simulation and sensitivity analysis of the model by Gweryina et al. [26] as recommended.

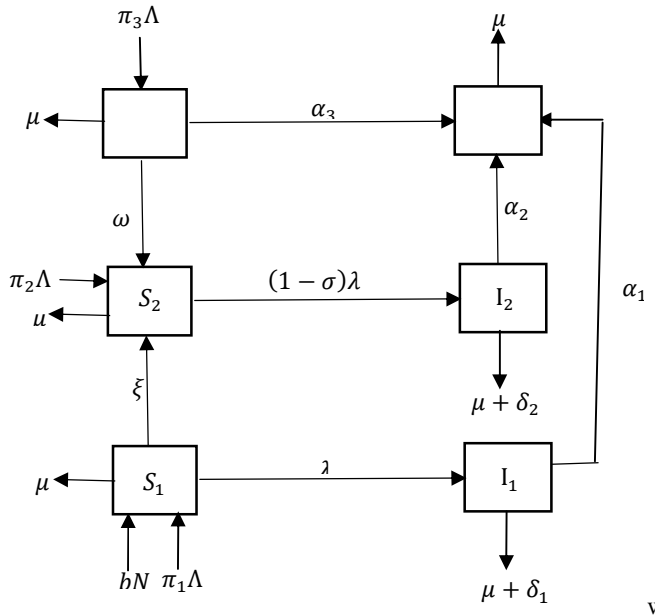
The rest of the paper is arranged as follows: In section 2, we recast the model framework of Gweryina et al. [26]. Simulation results and sensitivities are discussed in sections 3 and concluding remarks is then provided in section 4.

2 Materials and Methods

2.1 Mathematical model and analysis

The Ebola model [25] with state variables (Table 1) and parameters (Table 2) is governed by

$$\left.\begin{aligned}
\frac{dS_1}{dt} &= \pi_1\Lambda + \mathrm{bN} - \phi\left(\frac{\beta_1 \mathrm{I}_1+\beta_2 \mathrm{I}_2}{N}\right)S_1 - (\mu+\xi)S_1\\
\frac{dI_1}{dt} &= \phi\left(\frac{\beta_1 \mathrm{I}_1+\beta_2 \mathrm{I}_2}{N}\right)S_1 - (\mu+\alpha_1+\delta_1)\mathrm{I}_1\\
\frac{dS_2}{dt} &= \pi_2\Lambda + \xi S_1 + \omega Q - (1-\sigma)\phi\left(\frac{\beta_1 \mathrm{I}_1+\beta_2 \mathrm{I}_2}{N}\right)S_2 - \mu S_2\\
\frac{dI_2}{dt} &= (1-\sigma)\phi\left(\frac{\beta_1 \mathrm{I}_1+\beta_2 \mathrm{I}_2}{N}\right)S_2 - (\mu+\alpha_2+\delta_2)\mathrm{I}_2\\
\frac{dQ}{dt} &= \pi_3\Lambda - (\mu+\alpha_3+\omega)Q\\
\frac{dT}{dt} &= \alpha_1\mathrm{I}_1 + \alpha_2\mathrm{I}_2 + \alpha_3 Q - \mu T\\
\frac{dN}{dt} &= \Lambda + (b-\mu)N - (\delta_1\mathrm{I}_1 + \delta_2\mathrm{I}_2)
\end{aligned}\right\}, \tag{2.1}$$



where $\mathrm{N} = \mathrm{S}_1 + \mathrm{I}_1 + \mathrm{S}_2 + \mathrm{I}_2 + \mathrm{Q} + \mathrm{T}$.

Fig. 1. Schematic diagram of the model (2.1)

Table 1. The variables for the original model (2.1) and the scaled model (2.2)

Variables	Definition
$S_1(t)$	Number of uneducated susceptible individuals at time t
$S_2(t)$	Number of educated susceptible individuals at time t
$I_1(t)$	Number of uneducated infected individuals at time t
$I_2(t)$	Number of educated infected individuals at time t
$Q(t)$	Number of quarantined individuals at time t
$T(t)$	Number of treated individuals at time t
$s_1(t)$	Proportion of uneducated susceptible individuals
$s_2(t)$	Proportion of educated susceptible individuals at time t
$i_1(t)$	Proportion of uneducated infected individuals at time t
$i_2(t)$	Proportion of educated infected individuals at time t
$q(t)$	Proportion of quarantined individuals at time t
$r(t)$	Proportion of treated individuals at time t

We converted the model into proportions to obtain the governing equations [25]

$$\left.\begin{aligned}
\frac{ds_1}{dt} &= \boldsymbol{\pi_1}a + b - \phi(\beta_1 i_1 + \beta_2 i_2)s_1 - (b + \xi + a)s_1 + (\delta_1 i_1 + \delta_2 i_2)s_1 \\
\frac{di_1}{dt} &= \phi(\beta_1 i_1 + \beta_2 i_2)s_1 - (b + a + \alpha_1 + \delta_1)i_1 + (\delta_1 i_1 + \delta_2 i_2)i_1 \\
\frac{ds_2}{dt} &= \pi_2 a + \xi s_1 + \omega q - \phi(1-\sigma)(\beta_1 i_1 + \beta_2 i_2)s_2 - (b + a)s_2 + \dots \\
&\quad (\delta_1 i_1 + \delta_2 i_2)s_2 \\
\frac{di_2}{dt} &= \phi(1-\sigma)(\beta_1 i_1 + \beta_2 i_2)s_2 - (b + a + \alpha_2 + \delta_2)i_2 + (\delta_1 i_1 + \delta_2 i_2)i_2 \\
\frac{dq}{dt} &= \pi_3 a - (b + a + \alpha_3 + \omega)q + (\delta_1 i_1 + \delta_2 i_2)q
\end{aligned}\right\}, \qquad (2.2)$$

where the new state variables maintain their initial meaning as given in Table 1.

Table 2. Parameters of model (2.1)

Parameters	Definition
Λ	Influx of Susceptible population
π_3	Proportion of quarantined susceptible immigrants that come from the affected and infected zones.
π_2	Proportion of unquarantined susceptible immigrants that come from the Ebola-free zones who are aware of the virus
π_1	Proportion of unquarantined susceptible immigrants that come from the Ebola-free zones who are unaware of the virus
σ	Efficacy of public health education in preventing infection $(0 \leq \sigma \leq 1)$
Φ	The average number of contacts made per unit time
λ	The force of infection
ξ	Rate of educating uneducated susceptible individuals
ω	Rate at which quarantined individuals (free from Ebola) join the educated susceptible individuals
a	The arrival rate of immigrants per person per time
$\beta_i (i = 1,2)$	The rate of infection by the uneducated and educated infectives respectively
$\alpha_i (i = 1,2)$	Treatment rates for the uneducated and educated infectives respectively
α_3	Treatment rate of the infected quarantined individuals
μ	Natural death rate

$\delta_i(i = 1,2)$	Disease-induced death rate of the uneducated and educated infectives respectively

The reduced model (2.2) is proved to be mathematically and epidemiologically well-posed in the positive invariant region

$$\Gamma = \{(s_1, i_1, s_2, i_2, q\ ) \in \mathbb{R}^5{}_+ : s_1 + i_1 + s_2 + i_2 + q \leq 1\},$$

and has a unique solution that remains attractive in that domain for all $t \geq 0$ [25].

The equilibrium states of the model (2.2) and its associated effective reproduction number, R_{eff} have been investigated in Gweryina et al. [26] as stated

$$R_{\text{eff}} = R^1_{\text{eff}} + R^2_{\text{eff}}, \tag{2.3}$$

where

$$R^1_{\text{eff}} = \phi \frac{\beta_1(b + \pi_1 a)}{(b + \xi + a)(b + a + \alpha_1 + \delta_1)} \text{ and } R^2_{\text{eff}} = \phi(1 - \sigma)\beta_2(Z_1 + Z_2 + Z_3),$$

with

$$Z_1 = \frac{\xi(b + \pi_1 a)}{(b + a)(b + \xi + a)(b + a + \alpha_2 + \delta_2)}, Z_2 = \frac{\pi_2 a}{(b + a)(b + a + \alpha_2 + \delta_2)}$$

and $Z_3 = \dfrac{\omega\pi_3 a}{(b + a)(b + a + \alpha_3 + \omega)(b + a + \alpha_2 + \delta_2)}$

Details on the global stability and bifurcation analysis of the model (2.2) can be found in Gweryina et al. [26]. So based on their recommendation, we restrict this paper on two subjects: numerical simulation and sensitivity analysis (for the model parameters in (2.3)) which are examined in the next section.

2.2 Sensitivity analysis

In order to draw a conclusion on the best way to reduce death and morbidity due to infection in question, it is necessary to study the relative importance of different factors responsible for its transmission and prevalence [27]. In view of this, we compute the sensitivity indices of the effective reproduction number with respect to some of the model parameters. The sensitivity analysis allows us to measure the relative change in a state variable when a parameter changes. It unfolds parameter(s) that deserve the most numerical attention. Following the approach of Chnitis et al. [27], we adopt the normalized forward sensitivity index (NFSI) which is the backbone of almost all other sensitivity analysis techniques. Contour map illustrations were also done. Because the effective reproduction number, R_{eff} is a differentiable function of the model parameters, the NFSI may be defined using partial derivatives as represented

$$X_u^{R_{\text{eff}}} = \left(\frac{\partial R_{\text{eff}}}{\partial u}\right) \times \left(\frac{\text{u}}{R_{\text{eff}}}\right), \tag{2.4}$$

where u is any arbitrary parameter on which R_{eff} depends. In particular, u stands for some selected important parameters such as $\phi, \beta_1, \beta_2, \xi, \sigma, a, \alpha_j, j = 1, 2, 3.$

Below are algebraic expressions of the sensitivity index of R_{eff} to the parameter u.

$$X_\phi^{R_{\text{eff}}} = \left(\frac{\partial R_{\text{eff}}}{\partial \phi}\right) \times \left(\frac{\phi}{R_{\text{eff}}}\right) = +1 \tag{2.5}$$

$$X_{\beta_1}^{R_{\text{eff}}} = \left(\frac{\partial R_{\text{eff}}}{\partial \beta_1}\right) \times \left(\frac{\beta_1}{R_{\text{eff}}}\right) = \frac{\Omega_1}{\Omega_1 + \Omega_2}, \tag{2.6}$$

With

$$\Omega_1 = \frac{\beta_1(b+\pi_1 a)}{(b+\xi+a)(b+a+\alpha_1+\delta_1)}$$

and

$$\Omega_2 = \frac{(1-\sigma)\beta_2}{(b+a)(b+a+\alpha_2+\delta_2)}\left(\frac{\xi(b+\pi_1 a)}{(b+\xi+a)} + \pi_2 a + \frac{\omega\pi_3 a}{(b+a+\alpha_3+\omega)}\right)$$

$$X_{\beta_2}^{R_{\text{eff}}} = \left(\frac{\partial R_{\text{eff}}}{\partial \beta_2}\right) \times \left(\frac{\beta_2}{R_{\text{eff}}}\right) = \frac{\Omega_2}{\Omega_1+\Omega_2} \tag{2.7}$$

$$X_{\xi}^{R_{\text{eff}}} = \left(\frac{\partial R_{\text{eff}}}{\partial \xi}\right) \times \left(\frac{\xi}{R_{\text{eff}}}\right) = \frac{\frac{\xi(b+\pi_1 a)}{(b+\xi+a)^2}\left(\frac{(1-\sigma)\beta_2}{b+a+\alpha_2+\delta_2} - \frac{\beta_1}{b+a+\alpha_1+\delta_1}\right) + \Omega_3,'}{\Omega_1+\Omega_2} \tag{2.8}$$

where

$$\Omega_3 = \frac{\xi(1-\sigma)\beta_2\pi_3 a(b+a+\alpha_3)}{(b+a)(b+a+\alpha_2+\delta_2)(b+a+\alpha_3+\omega)^2}.$$

$$X_{\sigma}^{R_{\text{eff}}} = \left(\frac{\partial R_{\text{eff}}}{\partial \sigma}\right) \times \left(\frac{\sigma}{R_{\text{eff}}}\right) = -\left(\frac{\sigma}{1-\sigma}\right)\left(\frac{\Omega_1}{\Omega_1+\Omega_2}\right) \tag{2.9}$$

$$X_{\boldsymbol{\alpha_1}}^{R_{\text{eff}}} = \left(\frac{\partial R_{\text{eff}}}{\partial \boldsymbol{\alpha_1}}\right) \times \left(\frac{\boldsymbol{\alpha_1}}{R_{\text{eff}}}\right) = -\beta_1\left(\frac{b+\pi_1 a}{(\pi_3)(b+a+\alpha_1+\delta_1)^2}\right)\left(\frac{\alpha_1}{\Omega_1+\Omega_2}\right) \tag{2.10}$$

$$X_{\boldsymbol{\pi_3}}^{R_{\text{eff}}} = \left(\frac{\partial R_{\text{eff}}}{\partial \boldsymbol{\pi_3}}\right) \times \left(\frac{\boldsymbol{\pi_3}}{R_{\text{eff}}}\right) = (1-\sigma)\beta_2\left(\frac{\omega\pi_3 a}{(b+a)(b+a+\alpha_2+\delta_2)(b+a+\alpha_3+\omega)}\right)\left(\frac{1}{\Omega_1+\Omega_2}\right) \tag{2.11}$$

$$\begin{aligned} X_{\boldsymbol{a}}^{R_{\text{eff}}} &= \left(\frac{\partial R_{\text{eff}}}{\partial \boldsymbol{a}}\right) \times \left(\frac{\boldsymbol{a}}{R_{\text{eff}}}\right) \\ &= \frac{a}{\Omega_1+\Omega_2}\left(\Omega_1\left(\frac{\pi_1}{a\Pi_1+b} - \frac{1}{b+a+\xi} - \frac{1}{b+a+\alpha_2+\delta_2}\right)\right. \\ &+ \frac{(1-\sigma)\beta_2}{(b+a+\alpha_2+\delta_2)(b+a)}\left(\frac{\xi\pi_1}{b+a+\xi} - \frac{\xi(a\pi_1+b)}{(b+a+\xi)^2} + \pi_2 + \frac{(\omega+\xi)\pi_3}{b+a+\alpha_3+\omega}\right. \\ &\left.\left. - \frac{\omega\pi_3 a}{(b+a+\alpha_3+\omega)^2}\right) - \Omega_2\left(\frac{1}{b+a} + \frac{1}{b+a+\alpha_2+\delta_2}\right)\right) \end{aligned} \tag{2.12}$$

The above parameters serve as a health managing tool and guide towards which the elimination of Ebola epidemic can be achieved. By inspection, we saw from equations (2.5)-(2.12) that an average number of contact ϕ increases R_{eff} which expedites the disease transmission and prevalence. The maximum absolute value of the sensitivity index of R_{eff} to the parameter is 1 which has been attributed to the parameter ϕ, and the smallest absolute value occurs for the parameter α_3. The sensitivity of other parameters R_{eff} is over the

range $(-1,1)$. The specific values for the sensitivity indices for all the parameters are depicted in Table 4 according to the decreasing order of their sensitivities.

3 Results and Discussion

3.1 Numerical simulations of the model (2.2)

In this sub-section, we carried out a numerical simulation of the scaled equations using the set of reasonable parameter values given in Table 3 and under figures.

Table 3. Parameter values for numerical simulations and sensitivity analysis

Parameter	Range	Value	Ref.
b		0.0001041day^{-1}	Estimated
π_3		0.4	Assumed
π_2		0.2	Assumed
π_1		0.4	Assumed
σ	$[0,1]$	0.01	Assumed
ϕ	$[1,1500]\text{day}^{-1}$	5	[20]
ξ	$[0,1]\text{day}^{-1}$	0.3day^{-1}	[20]
ω		$\frac{1}{21}\text{day}^{-1}$	Estimated
a		0.35	Assumed
β_1	$[0.2,1]$	0.7	Estimated
β_2	$[0.2,1]$	0.3	Estimated
α_1	$\left[0.1,\frac{1}{4}\right]\text{day}^{-1}$	0.1day^{-1}	Estimated
α_2	$\left[0.1,\frac{1}{4}\right]\text{day}^{-1}$	0.25day^{-1}	Estimated
α_3		0.3day^{-1}	[33]
δ_1	$[0.2,0.9]\text{day}^{-1}$	0.25day^{-1}	[20]
δ_2	$[0.2,0.9]\text{day}^{-1}$	0.2day^{-1}	[20]

The following scenarios are considered

3.1.1 Evaluating the impact of non-intervention/intervention models

Here, we present numerically a situation where there is no intervention (with $\sigma = \xi = \omega = \alpha_1 = \alpha_2 = \alpha_3 = \pi_2 = \pi_3 = 0$) and compare with the intervention model with the worst scenario (see Table 3 for the parameter values). We also demonstrate graphically the trends of some of the variables of the scaled model for easy comparison between the educated and uneducated classes in the categories of the susceptibles and the infected. Furthermore, we will investigate the effect of effective intervention recipes with $\xi = \sigma = \pi_3 = \alpha_1 = \alpha_2 = \alpha_3 = 1$ on the infected populations.

Numerical results depicted in Fig. 2 indicate that with low educational campaigns ($\xi = 0.01$ and $\sigma = 0.3$) and ineffective treatment, the number of Ebola cases increase rapidly, however, not as much as the worst-case situation (without control). This means that the ineffective educational campaigns (described with low efficacy) alongside treatment and quarantine may not have the capacity of eradicating the disease since after receiving knowledge on early treatment as a key of survival for Ebola victims, risky behaviour amongst the people become difficult to be controlled. In this case, there is a need for effective educational campaigns (with high efficacy) and treatment as well as proper quarantining of suspected individuals. In this scenario, $R_{\text{eff}} = 2.266350759$ and $R_0 = 2.333969080$.

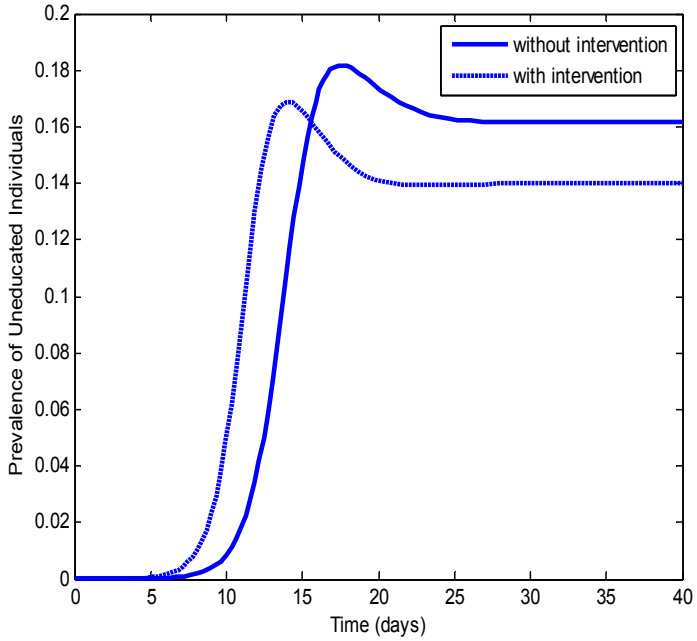


Fig. 2. The time variation of uneducated infectives for the model (2.2) with and without intervention strategies

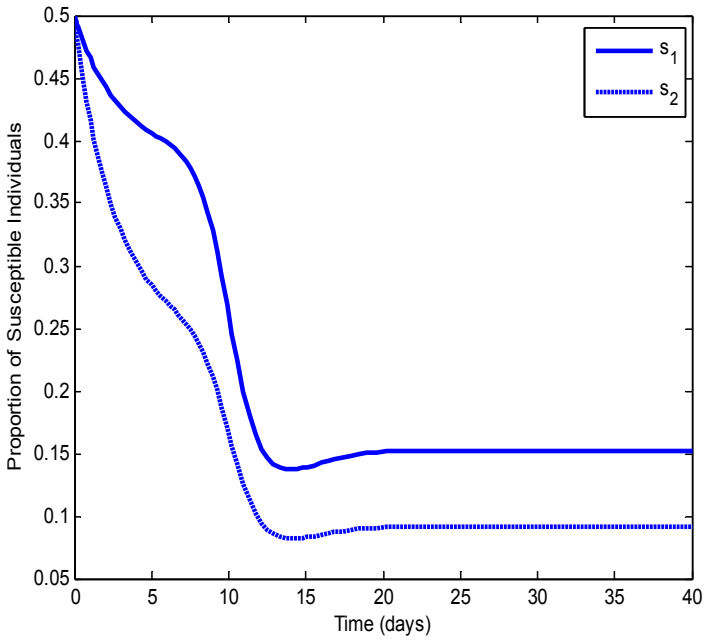


Fig. 3. The time variation of educated and uneducated susceptible individuals

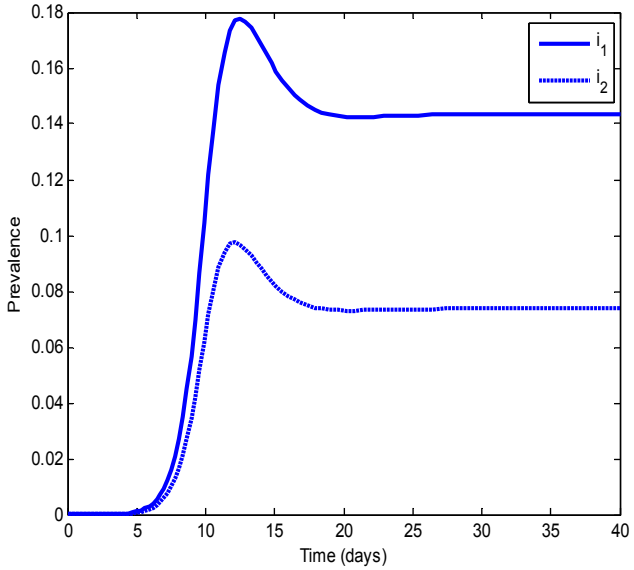


Fig. 4. The time variation of educated and uneducated infectives

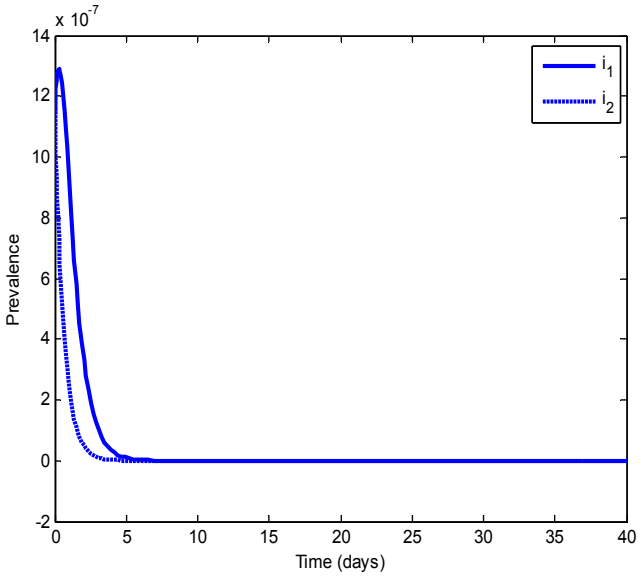


Fig. 5. The time variation of educated and uneducated infectives with $\xi = \sigma = \pi_3 = \alpha_1 = \alpha_2 = \alpha_3 = 1$

We observed from Fig. 3 that with interventions, the susceptible populations, s_1 and s_2 both declined significantly. However, the fraction of uneducated susceptible individuals decreases with a delay before increasing to its carrying capacity. We also note that the graph of susceptible educated individuals is below that of the uneducated susceptible individuals. This is due to the fact that there is reduced susceptibility among the educated individuals as observed in the two plots. The graph of the uneducated susceptibles is slightly higher implying that the most of the uneducated people get exposed to the Ebola pathogen in greater number than the educated ones. Both populations do not diminish to zero because not all susceptibles are involved in risky behaviour.

In a similar manner, Fig. 4 shows that even with low intervention, uneducated infectives get more people infected than the educated ones since the educated take precautionary measures on risk factors. Meanwhile when both educated and uneducated infected have been subjected to high interventions (with $\xi = \sigma = 1, \alpha_1 = \alpha_2 = \alpha_3 = 1$), Fig. 5 reveals that the proportion of educated infectives decays faster than that of uneducated people (those who initially show some level of resistance). This is so because educated individuals ad-head to control regimens without being forced which is not the case with the uneducated. Nevertheless, the proportion of both infectives reach zero within a finite time with $R_{\text{eff}} = 0.2269882595$.

3.1.2 The effect of intervention strategies on the infected populations

We consider under this sub-section the following cases:

Case (a): The effect of education coverage and efficacy on the infected population

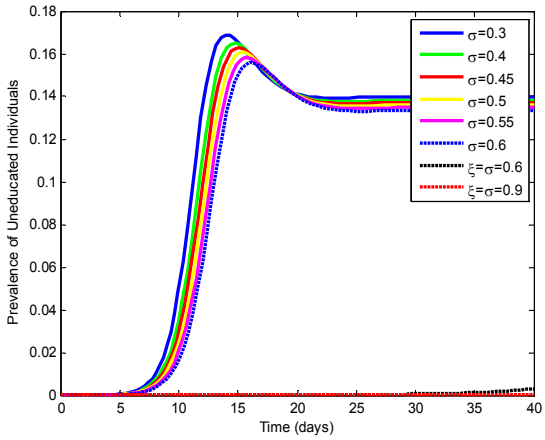


Fig. 6a. The effect of education coverage level and efficacy on the uneducated infectives with $\sigma = 0.3, 0.4, 0.45, 0.5, 0.55, 0.6$ and $\xi = \sigma = 0.6, 0.9$

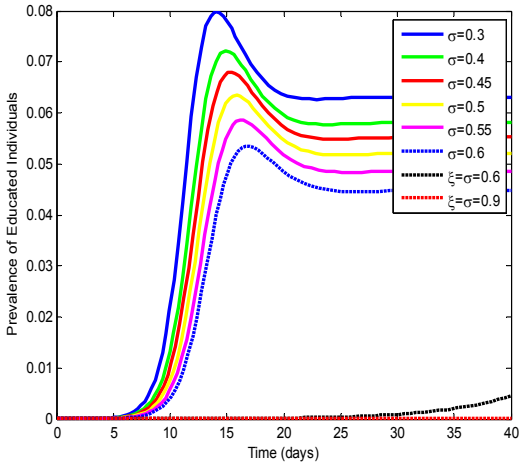


Fig. 6b. The effect of education coverage level and efficacy on the educated infectives ($\sigma = 0.3, 0.4, 0.45, 0.5, 0.55, 0.6$ and $\xi = \sigma = 0.6, 0.9$)

In Fig. 6, we investigated the impact of education coverage level and its efficacy on Ebola dynamics. An increase in these parameters tends to a decline in the effective reproduction number and consequently a decrease in the number of infection, which is a potential indicator of disease burden reduction. Both Figs. (6a & 6b) indicate that educational campaigns with coverage at 60% each will not meet the control standard of the disease irrespective of the educational status of the people. This is because when $\xi = \sigma = 0.6$ we have $R_{\text{eff}} = 1.226572108 > 1$ which is still a sign of disease persistence. On the contrary, an increase of coverage rate and education effectiveness to 90% each will drag the disease to extinction with $R_{\text{eff}} = 0.696292205 < 1$. This is consistent with the result of Njankou [20] on Ebola dynamics which stipulates that the media campaign against Ebola should be spaced out (on a large coverage) for it to be more efficacious. We notice, from the two graphs that both infectives increase, however, with high prevalence on the side of the uneducated. The two infected started to be infectious on the 4th day which agrees with the literature on the infectious period of the disease.

Case (b): The effect of varying treatment rates on the infected population

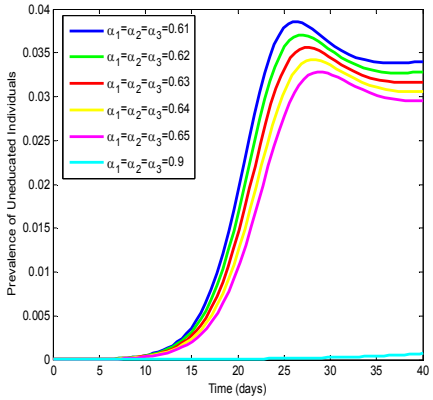


Fig. 7a. The Effect of Treatment rates on the Uneducated Infectives with $(\alpha_1 = \alpha_2 = \alpha_3 = 0.61, 0.62, 0.63, 0.64, 0.65, 0.9)$

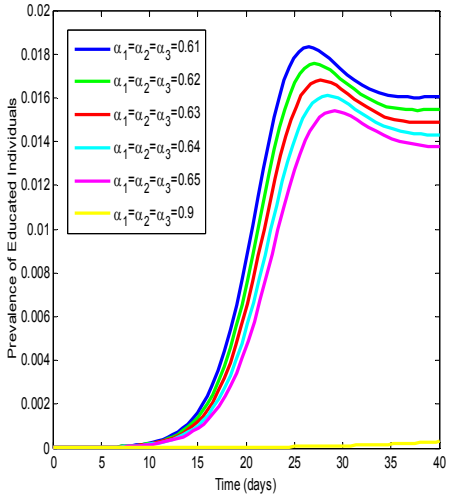


Fig. 7b. The effect of treatment rates on the educated infectives $(\alpha_1 = \alpha_2 = \alpha_3 = 0.61, 0.62, 0.63, 0.64, 0.65, 0.9)$

Increasing the rates of treatment yields a corresponding decrease in the fraction of infectives for both the uneducated and educated as illustrated in the Figs. 7a and 7b respectively. It is observed that given treatment rates (each) at 90% while keeping other parameters constant will fail to eradicate the disease since $R_{\text{eff}} = 1.00513058$. That means for complete Ebola elimination, we needed to combine other control measures like educational campaigns to meet 100% Ebola free society target.

Case (c): The effect of quarantine rate on the infected populations

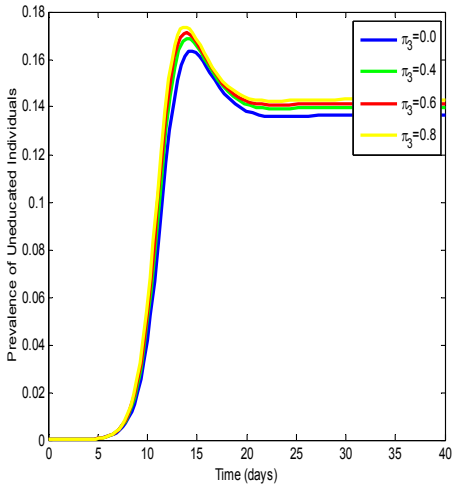


Fig. 8a. The effect of mass quarantine rate on the uneducated infectives $(\pi_3 = 0.0, 0.4, 0.6, 0.8)$

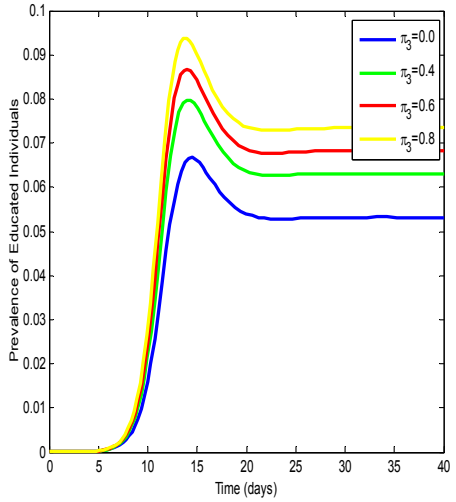


Fig. 8b. The effect of mass quarantine rate on the educated infectives. $(\pi_3 = 0.0, 0.4, 0.6, 0.8)$

In the Figs. 8a and 8b, we have shown that the proportion of the infectives (uneducated and educated) increases with increase in π_3. This implies that the mass recruitment of immigrants into the quarantine zone without proper screening can also contribute to the spread of the disease. This result agrees with Giubilini et al. [28] which say that quarantine is ethnically problematic in terms of exposing more susceptible people to Ebola virus and thus, increasing their chances of infection. However, the proportion of infected individuals

differs from the uneducated to educated. It is seen that the uneducated suffers more from the epidemic. Others experiments also agree to this summation

Case (d): The effect of combining different strategies on the force of infection

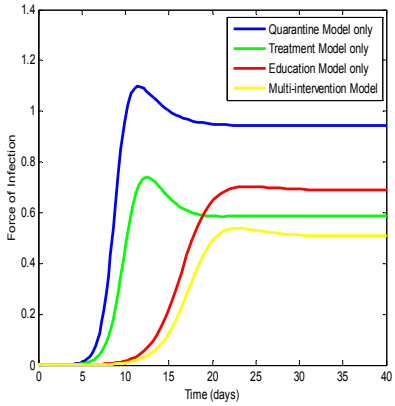


Fig. 9. The combined effect of intervention strategies on the force of infection dynamics with $\xi = \sigma = 0.3$

In Fig. 9, we studied the dynamics of the force of infection with respect to the control measures so as to gain insight on the transmission pattern of the disease within the population over a period of time. The graphs in Fig. 9 maintain that the force of infection increases for all the four scenarios, but declines to the least value for the hybrid of quarantine, education and treatment. This indicates that both strategies if administrated concurrently will minimize the spread of the disease.

Case (e): The effect of the average number of contacts on the infected populations

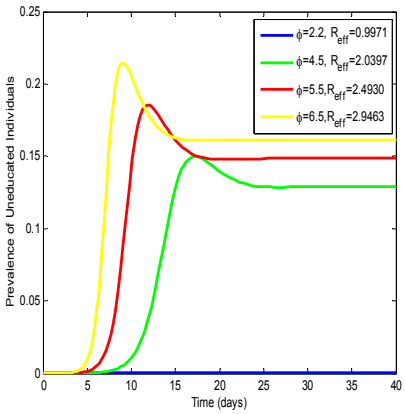


Fig. 10. The effect of average number of contacts on the uneducated Infectives in relationship with the effective reproduction number, R_{eff}

In Fig. 10, we observed that increasing the average number of contacts increases the spread of the disease. As indicated in the study, any average contact greater than 2.2 paves a way for an epidemic to set in since $R_{\text{eff}} > 1$. Therefore, interventions meant for reducing contact between the infected and the susceptibles should be advocated.

3.2 Sensitivity results on effective reproduction number

In view of the sensitivity analysis done in sub-section 2.3 above, we have the following results

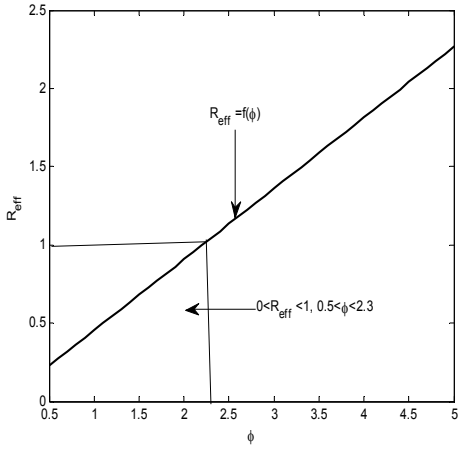


Fig. 11a. Linear relationship between R_{eff} and ϕ

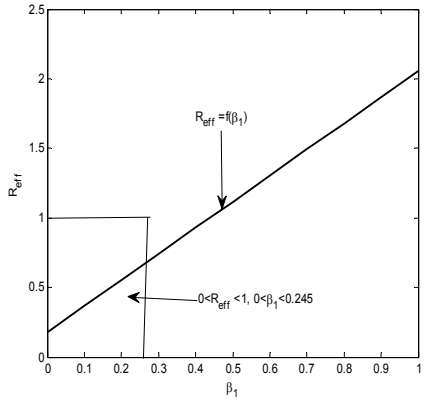


Fig. 11b. Linear relationship between R_{eff} and β_1

Table 4. Sensitivity indices (S. I) of R_{eff}

S/N	Parameter	Sensitivity index	Sign
1	Φ	1.00000000	+
2	β_1	0.85822483	+
3	β_2	0.14177517	+
4	π_3	0.01956482	+
5	a	0.48348424	-
6	α_1	0.06076079	-
7	σ	0.04429898	-
8	α_2	0.01459121	-
9	ξ	0.00826562	-
10	α_3	0.06076079	-

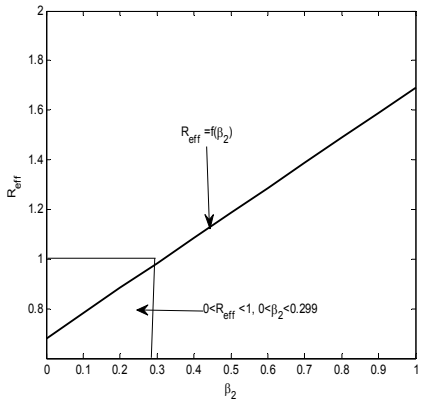


Fig. 11c. Linear relationship between R_{eff} and β_2

Table 4 remarkably provides the sensitivity indices of the effective reproduction number to some approximate values of the parameters of the model. We observe that apart from, whose index is constant, changes initiated in the rest of the parameters have an impact on the global change in the value of R_{eff}. The parameters such as $\phi, \beta_1, \beta_2,$ and π_3 with a positive sign will each increase the value of R_{eff} when each of them is varied and subsequently appreciates the endemicity of the disease while those with negative indices will decrease the value of R_{eff} when increased, and in turn decline the level of persistence of Ebola virus. Specifically speaking, β_1, β_2 shows a positive linear relationship with respect to R_{eff} as demonstrated in the Figs. 11b and 11c respectively. To stop further spread of Ebola within a few numbers of contacts on average $(\phi = 5)$, the inequalities $\beta_1 < 0.245$ and $\beta_2 < 0.299$ must be maintained in order to keep R_{eff}<1. Cutting off the disease from the people requires the combined efforts of $\sigma, \xi, \alpha_j (j = 1, 2, 3)$ since each parameter reduce R_{eff} significantly to a value below unity if $\sigma = \xi > 0.6$ and $\alpha_j > 0.9$ is implemented in the population. Therefore, for the complete elimination of Ebola burden, susceptible individuals have to exhibit zero tolerance to risky behavioural practices that could accelerate the disease transmission, and present themselves early enough when infected for treatment since it reduces the number of Ebola-related deaths and of course, new infection cases.

It is evident from Fig. 11a that with high transmission rates, a global control of the disease burden can be achieved within the region $\phi \in [0.5, 2.3)$, outside which the epidemic sets in. Therefore, interventions focusing on contact reduction and positive risky behavioural change for enhancing infection-free community should be targeted.

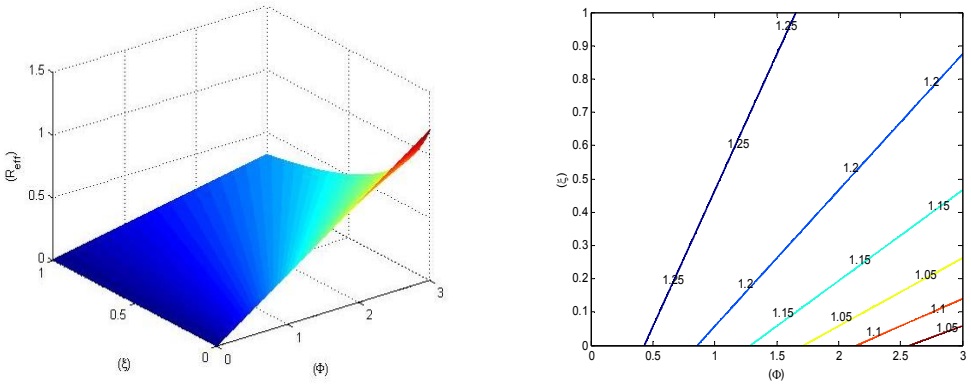
3.2.1 Contour plots

Contour plot gives us the opportunity to check the effect of two parameters on R_{eff} at a time. To that effect, we carry out contour plots of R_{eff} as a function of ξ and α_1, ξ and π_3, and α_1 and π_3 in MATLAB using values in Table 3 and the results depicted as thus.

The impact of changing ξ and ϕ on R_{eff} with $\sigma = 1$ was examined. Fig. 12 indicates that increasing the coverage level of awareness alongside the average number of contacts generated between susceptible and the infected may not have the full potential to eliminate the disease since $R_{\text{eff}} > 1$. That means even with educational campaigns, reduction of risky behaviour is key for Ebola control. However, any contact created within the range $0 \leq \phi \leq 2.3$ will not result in new infections in the presence of effective education. This is because it reduces R_{eff} below 1.

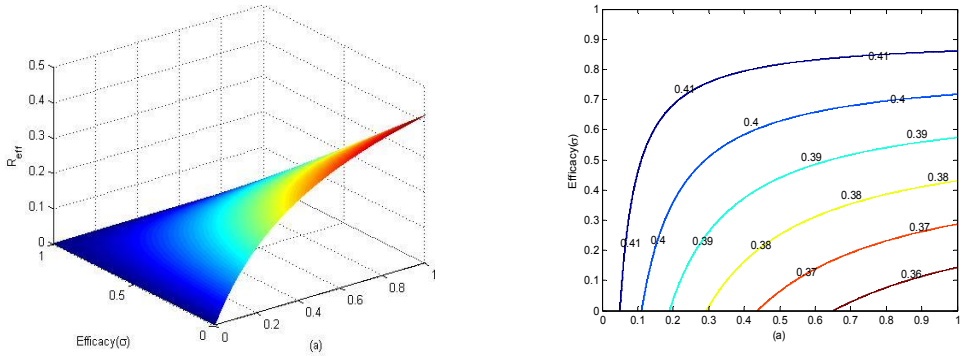
Fig. 13 shows that the continuous inflow of immigrants into the population (native) has a limited effect on the dynamics of Ebola model with multi-interventions. This is contrary to the literature [29] that migrants are

the principal drivers of epidemics. Therefore, by this result, we agree with the decision of WHO as reported in Ross et al. [30] that ban on international travel is not necessary during the epidemic, but rather travellers from the affected regions be subjected to screening.



12a **12b**

Fig. 12. Plot showing the combined effect of ξ and ϕ



13a **13b**

Fig. 13. Plot showing the combined effect of σ and a on R_{eff}

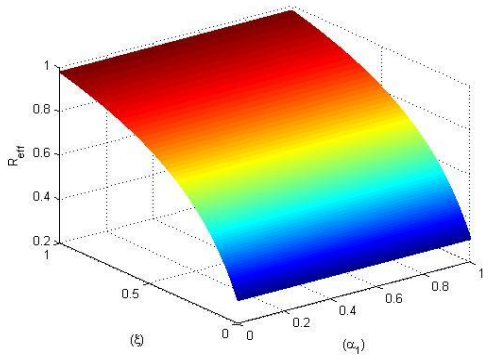


Fig. 14. Plot showing the combined effect of ξ and α_1 on R_{eff}

In Fig. 14, we observed that with a high level of education coverage ξ alongside the treatment rate α_1 of the uneducated individuals, the disease will be eradicated since their impacts on R_{eff} yields a positive result ($R_{\text{eff}} < 1$). That means the collaboration of the two recipes on Ebola reduction is critical and if implemented efficiently will save the (native) population from the pandemic. Thus, the behavioural change of any population on Ebola risky factors will help limit the spread of the disease and quickly respond to early treatment when infected. This outcome is consistent with the work of Lara-Cabrera et al. [31] which concludes that pre-treatment and peer co-led education can improve patient activation in community mental health care setting.

4 Conclusion

We carried out numerical simulations and forward sensitivity analysis on a non-linear mathematical model of Ebola dynamics with quarantine, public health education campaign and treatment in a heterogeneous population that was developed, transformed into proportions and analyzed for stability by Gweryina et al. [26]. In this paper, we did the comparison of the transformed equations with intervention and without intervention. In like manner, we compared numerically the behaviour of the educated and uneducated populations in the categories of susceptibles and infections. Results have indicated that the uneducated are more vulnerable to infection and the educated infections are fewer in number and respond faster to treatment than the uneducated. Meanwhile, recruitment of immigrants into the quarantine class gave rise to the increase of both infections which is contrarily to the popular belief that quarantine lowers infection level. The study also highlights the risk of increasing the average number of contacts on the spread of the disease and the corresponding changes to the effective reproduction number. Some of the sensitivity indices obtained agreed with the intuitive expectations. However, we noted that R_{eff} was most sensitive to the average number of contacts followed by the transmission rates.

Simulation and contour plots all gave evidence that the hybrid strategy of quarantine of suspected individuals, educating of the susceptible individuals and treatment of the infected population will alleviate the disease burden faster than either of the single strategies. Mass quarantine on its own is the least effective control strategy. This is because it combines both the susceptible and infected populations together, thereby appreciating infection in the process. Treatment, on the other hand, is better than education since it protects the individual and the community. Education campaign has no doubt contributed to the elimination of the disease but attitudinal change among the risk population is difficult and that has posed a greater challenge for complete compliance. The best results would come from implementing both strategies at the same time. In real life, resources and funds are often limited especially in developing countries. So it will be more appealing to focus resources on treatment and education based on the fact that some literature [29,32] admitted that mass quarantine has limitations. However, our results have shown that the hybrid of these strategies has more than additive impact.

Competing Interests

Authors have declared that no competing interests exist.

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