

A mathematical model for Ebola epidemic with self-protection measures

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A mathematical model presented in Ref. 7 for the transmission dynamics of Ebola virus is extended to incorporate vaccination and change of behavior for self-protection of susceptible individuals. In the new setting, it is shown that the disease-free equilibrium is globally asymptotically stable when the basic reproduction number \mathcal{R}_0 is less than or equal to unity and unstable when $\mathcal{R}_0 > 1$. In the latter case, the model system admits at least one endemic equilibrium point, which is locally asymptotically stable. Using the parameters relevant to the transmission dynamics of the Ebola virus disease, we give sensitivity analysis of the model. We show that the number of infectious individuals is much smaller than that obtained in the absence of any intervention. In the case of the mass action formulation with vaccination and education, we establish that the number of infectious individuals decreases as the intervention efforts increase. In the new formulation, apart from supporting the theory, numerical simulations of a nonstandard finite difference scheme that we have constructed suggests that the results on the decrease of the number of infectious individuals is valid.

Keywords: Ebola virus disease; dynamical systems; behaviour change; sensitivity analysis; nonstandard finite difference method.

1. Introduction

The Ebola virus disease (EVD) is named so after the Ebola River valley in Zaire (now Democratic Republic of Congo) where it appeared for the first time in 1976 (Ref. 35). Since then, other outbreaks have been identified in parts of Central Africa, see for example Refs. 1, 7, 8, 13, 35. The most devastating outbreak was observed recently (2014) in some West African countries: Guinea, Liberia, Nigeria, Senegal and Sierra Leone. In almost all the outbreaks, the initial infection is due to contacts with infected animals (hunted for food), such as fruit bats and primates (ape, monkey, chimpanzee) (Refs. 7, 22, 23). This highlights the importance of considering the indirect contacts with the surrounding environment as a transmission route of the virus.

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Of course, the direct transmission of EVD cannot be underestimated. Typically, the direct transmission involves contact with blood or body fluid and with objects that have been contaminated with Ebola viruses. A detailed literature review on direct and indirect transmission of EVD is given in Ref. 7 and the references therein.

The model investigated in Ref. 7 enriched the few existing models by incorporating the indirect transmission route in the following specific manner:

- (i) Infection through the contaminated environment resulting from African practices, hospitality and poor hygienic conditions;
- (ii) Provision or recruitment source of Ebola virus linked to the consumption of bats, hunted meat and fruits from the rain-forest.

The findings in Ref. 7 with regard to the control strategy of EVD included educating the population against the practices contained in items (i) and (ii) above. In the present paper, we broaden the education of the population in two additional ways outlined below.

- (iii) *We add a vaccinated compartment.* This addition is motivated by a recent study that suggested a ring vaccination of all susceptible individuals in a prescribed area around an outbreak of an EVD (Refs.14, 19). This is used, for example, in the control strategy of Smallpox eradication program which could help also to reduce Ebola transmission. As a matter of fact, in March 2015, the ministry of Health in Guinea started a ring vaccination trial, and interim trial results suggested that the vaccine could have a high level of efficacy in humans (Ref. 19). Other viable Ebola vaccine candidates are mentioned in Ref. 13.
- (iv) *We take into consideration the awareness of the population and their behavioral change for self-protection by adding a compartment of trained individuals.* Some public health educational interventions, including the creation of Ebola response teams in local communities and preparedness at household level to minimize the transmission of EVD, are suggested in Ref. 1.

The model is carefully analysed to get insight on the impact of all these sets of educational interventions. Under these interventions, we observe that the number of infectious individuals is much smaller than that obtained in Ref. 7. It was already observed in Ref. 7 that the use of standard numerical methods could produce unreasonable discrete solutions such as negative ones. On the contrary, the nonstandard finite difference (NSFD) method has the potential to replicate the dynamics of the continuous model (Refs. 4, 5, 27, 28, 31). Using the Mickens' rules (Refs. 7, 26), we have constructed a NSFD scheme, which is dynamically consistent with EVD model.

The rest of the paper is organized as follows. The model is formulated in Section 2. In Section 3, the quantitative and qualitative analysis of the model is given. The sensitivity analysis of the model is presented in Section 4. In Section 5, we propose a nonstandard finite difference scheme for the continuous model. Numerical simulations and concluding remarks are given in Sections 6 and 7, respectively.

2. Model formulation

In this section, we extend the model for the EVD in Ref. 7 by incorporating vaccination and behavioral change of susceptible individuals. The following assumptions are made. The population under consideration is grouped into disjoint classes or compartments. Individuals who are susceptible to EVD are grouped in the S class. Ebola infected individuals are placed in class I . The R class contains individuals recovered from EVD. Individuals who receive public health training on how to prevent themselves from contracting Ebola and vaccinated individuals are categorised as the classes T and V , respectively. The class of EVD deceased individuals is represented by D , while P denotes the Ebola virus concentration in the environment due to shedding by infectious and Ebola deceased individuals. The flow diagram of the transmission dynamics of the EVD is given in Fig. 1.

The corresponding system of nonlinear differential equations is

$$\begin{aligned}
 \frac{dS}{dt} &= \Pi - (\epsilon e + \lambda + \nu + \mu)S, \\
 \frac{dI}{dt} &= \lambda S - (\gamma + \delta + \mu)I + (1 - \theta)\lambda T, \\
 \frac{dR}{dt} &= \gamma I - \mu R, \\
 \frac{dT}{dt} &= \epsilon e S - (1 - \theta)\lambda T - \mu T, \\
 \frac{dV}{dt} &= \nu S - \mu V, \\
 \frac{dD}{dt} &= (\delta + \mu)I - bD, \\
 \frac{dP}{dt} &= \xi I + \alpha D - \eta P,
 \end{aligned} \tag{2.1}$$

where

$$N(t) = S(t) + I(t) + R(t) + T(t) + V(t)$$

is the total population at time $t \geq 0$. All parameters are nonnegative and they are described in Table 1. The force of infection λ , the behavioral change function e and the governing equation for the evolution of the virus concentration in the environment deserve more specific descriptions and comments as outlined below. Susceptible individuals S may acquire infection after effective contacts with infectious individuals I , EVD deceased human bodies D and contaminated environment P at the rates β_1 , β_2 and β_3 , respectively. While the first source of infection of susceptible is typically formulated by standard incidence (Ref. 15), a couple of options are available in the literature regarding the other two sources. For instance, in Ref. 36, indirect transmission through environment occurs in a saturated manner and takes the form

$$\frac{\beta_3 SP}{K + P},$$

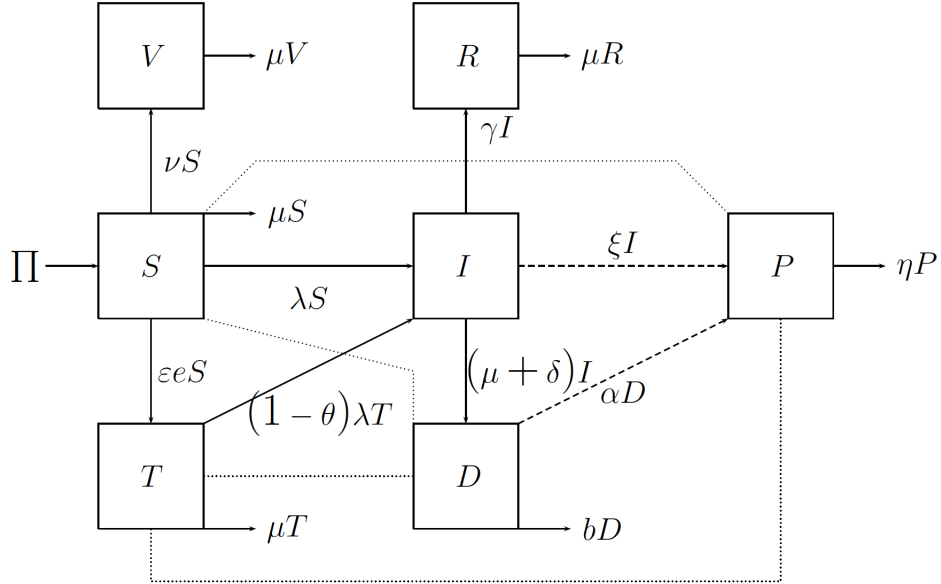


Fig. 1. Schematic diagram of EVD transmission dynamics.

where K is the concentration of the disease pathogen in the environment which increases 50% chance of triggering the disease transmission.

In the present work, we follow Ref. 32 and formulate the force of infection as

$$\lambda = \frac{\beta_1 I}{N} + \beta_2 D + \beta_3 P, \quad (2.3)$$

with mass action incidence for the last two terms. Thus, (2.3) extends the formulation in Ref. 7 where the mass action principle is used for the three sources of infection.

As noted in Ref. 18, human learning behavior does not keep on increasing for ever. After a sharp increase, the rate of increase in the awareness function e slows down and settles to some value asymptotically. Therefore, we define the awareness function $e(\lambda)$ by the Hill-type function in terms of the force of infection

$$e(\lambda) = \frac{\lambda^n}{\lambda_0^n + \lambda^n}, \quad (2.4)$$

where λ_0 is the value of the force of infection corresponding to the threshold infectivity in which the individuals start reacting swiftly. At the beginning of an EVD outbreak, individuals understand very little about it; there could be no reaction and this can be related to the situation at the disease-free equilibrium such that

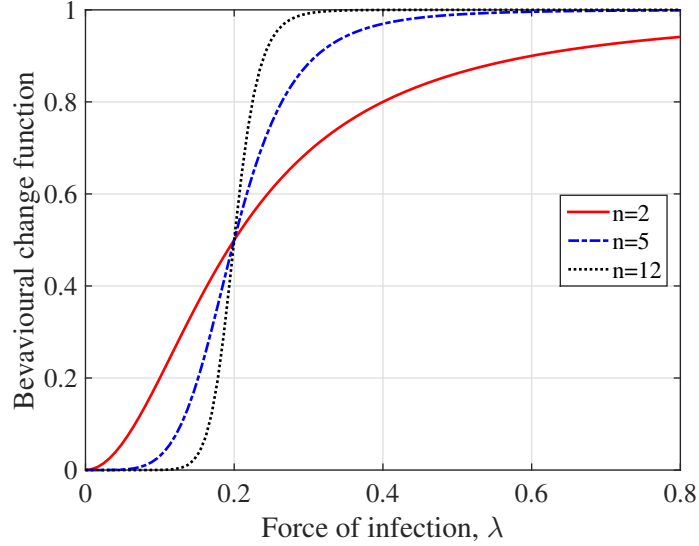


Fig. 2. Change of behavior with respect to the force of infection for $\lambda_0 = 0.2$.

$e(\lambda) = e(0) = 0$. However, as the risk of the disease increases, individuals start to think of the type of measures to take in order to avoid all means of contracting the disease. These protection measures, if perfect, account for an increase in the values of e to unity. The order n of the function $e(\lambda)$ is a Hill coefficient that portrays the rate of reaction by the population. See Fig. 2 for the relation between e and the force of infection λ .

It is possible to add in the last equation of (2.1) a recruitment rate function σ of the disease pathogens in the environment. The recruitment σ could be a logistic growth function, specifically in the case of free-living pathogens such as bacteria (Refs. 5,6). It could also be a positive constant, implying then that the disease will persist (Ref. 7). In this paper, we assume that $\sigma = 0$, resulting in the existence of a disease-free equilibrium, the stability analysis of which will be considered in the next section.

The system (2.1) is appended with the following nonnegative initial conditions:

$$S(0) = S_0, I(0) = I_0, R(0) = R_0, T(0) = T_0, V(0) = V_0, D(0) = D_0 \text{ and } P(0) = P_0.$$

3. Quantitative and qualitative analysis

We start with the well-posedness result which is stated as follows.

Theorem 3.1 *The Ebola model (2.1) is a dynamical system on the biologically*

Parameter	Description
Π	Recruitment rate of susceptible individuals
γ	Rate of recovery
μ	Natural death rate
δ	Ebola-induced death rate
ϵ	Rate of dissemination of information about the disease in the population
ν	Rate of vaccination
$\frac{1}{b}$	Mean caring duration of Ebola deceased human individuals
α	Shedding rate of Ebola deceased individuals to the environment
ξ	Shedding rate of infectious individuals to the environment
θ	Average effectiveness of existing self-preventive measures
η	Decay rate of Ebola virus in the environment
β_1	Contact rate to the I class
β_2	Contact rate to the D class
β_3	Contact rate to the P class

Table 1. Description of parameters of the model (2.1).

feasible region

$$\Omega = \left\{ (S, I, R, T, V, D, P) \in \mathbb{R}_+^7 : 0 \leq S(t) + I(t) + R(t) + T(t) + V(t) = N(t) \leq \frac{\Pi}{\mu}, \right. \\ \left. D(t) \leq \frac{(\mu + \delta)\Pi}{b\mu} \text{ and } P(t) \leq \frac{1}{\eta} \left(\frac{\xi\Pi}{\mu} + \frac{\alpha(\mu + \delta)\Pi}{b\mu} \right) \right\}.$$

The proof of Theorem 3.1, based on the method mentioned in Ref. 9 to show positivity and Theorem 2.1.5 in Ref. 34, is given in Appendix A.

Next, we determine the equilibrium solutions of the system (2.1). We set the right-hand side of (2.1) equal to zero:

$$\begin{aligned} \Pi - (\epsilon e + \lambda + \nu + \mu)S &= 0, \\ \lambda S - (\gamma + \delta + \mu)I + (1 - \theta)\lambda T &= 0, \\ \gamma I - \mu R &= 0, \\ \epsilon e S - (1 - \theta)\lambda T - \mu T &= 0, \\ \nu S - \mu V &= 0, \\ (\mu + \delta)I - bD &= 0, \\ \xi I + \alpha D - \eta P &= 0. \end{aligned} \tag{3.1}$$

Then, the disease-free equilibrium (DFE) is

$$E_0 = (S, I, R, T, V, D, P) = \left(\frac{\Pi}{\mu + \nu}, 0, 0, 0, \frac{\nu\Pi}{\mu(\mu + \nu)}, 0, 0 \right). \tag{3.2}$$

At the disease-free equilibrium, the behavioral change function $e(\lambda) = e(0) = 0$.

The basic reproduction number, which is very important for the qualitative analysis of the model, is determined by using the method of the next generation matrix in Refs. 12, 38.

For the model under consideration, using the notation $X = (I, D, P)$, we have the vector functions

$$\mathcal{F}(X) = \begin{pmatrix} \lambda S + (1 - \theta)\lambda T \\ 0 \\ 0 \end{pmatrix} \quad \text{and} \quad \mathcal{U}(X) = \begin{pmatrix} (\mu + \delta + \gamma)I \\ -(\mu + \delta)I + bD \\ -\xi I - \alpha D + \eta P \end{pmatrix}$$

representing the rates at which disease compartments increase and decrease in size due to the disease, respectively. The next generation matrix is given by

$$\mathcal{B} = J_{\mathcal{F}} J_{\mathcal{U}}^{-1}, \quad (3.3)$$

where

$$J_{\mathcal{F}} = \begin{pmatrix} \frac{\mu\beta_1}{\mu + \nu} & \frac{\beta_2\Pi}{\mu + \nu} & \frac{\beta_3\Pi}{\mu + \nu} \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix} \quad \text{and} \quad J_{\mathcal{U}} = \begin{pmatrix} \mu + \delta + \gamma & 0 & 0 \\ -(\mu + \delta) & b & 0 \\ -\xi & -\alpha & \eta \end{pmatrix}$$

are the Jacobian matrices of \mathcal{F} and \mathcal{U} at E_0 , respectively.

The basic reproduction number, denoted by \mathcal{R}_0 , is defined as the average number of secondary cases produced in a completely susceptible population by a typical Ebola virus infected individual (i.e., alive or deceased but not buried) during its entire period of being infectious (Ref. 38). Mathematically, \mathcal{R}_0 is the spectral radius of \mathcal{B} in (3.3), which is explicitly found to be

$$\mathcal{R}_0 = \frac{\mu\beta_1}{(\nu + \mu)(\gamma + \delta + \mu)} + \frac{(\delta + \mu)\beta_2\Pi}{(\nu + \mu)b(\gamma + \delta + \mu)} + \frac{(b\xi + \alpha(\delta + \mu))\beta_3\Pi}{b\eta(\nu + \mu)(\gamma + \delta + \mu)}. \quad (3.5)$$

Remark 3.1 *A few comments are in order with regard to (3.5). The basic reproduction number in (3.5) consists of the three contributions of the infectious class I, the deceased class D and the Ebola virus concentration in the environment compartment P, respectively. It is clear that increasing the vaccination rate ν , increasing the decay rate η of Ebola in the environment and decreasing the shedding rates ξ and α from the infectious and deceased compartments will decrease the value of \mathcal{R}_0 .*

In Ref. 7, where the mass action incidence formulation, i.e.,

$$\lambda = \beta_1 I + \beta_2 D + \beta_3 P$$

is used, the basic reproduction number is

$$\mathcal{R}_0^{MA} = \frac{\beta_1\Pi}{\mu(\gamma + \delta + \mu)} + \frac{(\delta + \mu)\beta_2\Pi}{b\mu(\gamma + \delta + \mu)} + \frac{(b\xi + \alpha(\delta + \mu))\beta_3\Pi}{b\mu\eta(\gamma + \delta + \mu)}.$$

By adding self-protection interventions (e.g vaccination) to the setting of Ref. 7, the threshold quantity \mathcal{R}_0^{MA} is improved to

$$\mathcal{R}_0^{MAV} = \frac{\beta_1\Pi}{(\nu + \mu)(\gamma + \delta + \mu)} + \frac{(\delta + \mu)\beta_2\Pi}{(\nu + \mu)b(\gamma + \delta + \mu)} + \frac{(b\xi + \alpha(\delta + \mu))\beta_3\Pi}{(\nu + \mu)b\eta(\gamma + \delta + \mu)}$$

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in the sense that $\mathcal{R}_0^{MAV} \leq \mathcal{R}_0^{MA}$. Furthermore, the advantage of self-protection interventions is captured by the fact that the contribution of the deceased class D and the Ebola virus class P to \mathcal{R}_0 in (3.5) is much less than their counterparts in \mathcal{R}_0^{MA} .

Theorem 3.2 *The disease-free equilibrium point E_0 given in (3.2) is locally asymptotically stable (LAS) if $\mathcal{R}_0 < 1$ and unstable when $\mathcal{R}_0 > 1$.*

The proof of Theorem 3.2 is given in Appendix A. Furthermore, based on Kamgang-Sallet Stability Theorem (Ref. 17), we have proved the next result which improves Theorem 3.2.

Theorem 3.3 *The disease-free equilibrium E_0 is globally asymptotically stable (GAS) if $\mathcal{R}_0 \leq 1$.*

To determine the endemic equilibria of (2.1), let

$$E^* = (S^*, I^*, R^*, T^*, V^*, D^*, P^*),$$

denote an equilibrium point. Then from (3.1), we obtain the relations

$$\begin{aligned} S^* &= \frac{\Pi}{\epsilon e^* + \lambda^* + \nu + \mu}, & T^* &= \frac{\epsilon e^*}{(1-\theta)\lambda^* + \mu} S^*, & V^* &= \frac{\nu}{\mu} S^*, \\ I^* &= \frac{\lambda^*}{\gamma + \delta + \mu} \left(1 + \frac{(1-\theta)\epsilon e^*}{(1-\theta)\lambda^* + \mu} \right) \frac{\Pi}{\epsilon e^* + \lambda^* + \nu + \mu}, \\ R^* &= \frac{\gamma I^*}{\mu}, & D^* &= \frac{\mu + \delta}{b} I^*, & P^* &= \frac{1}{b\eta} [b\xi + \alpha(\mu + \delta)] I^*, \\ N^* &= \frac{1}{\mu} [\Pi - \delta I^*], \end{aligned} \tag{3.9}$$

where

$$e^* = \frac{(\lambda^*)^n}{\lambda_0^n + (\lambda^*)^n} \quad \text{and} \quad \lambda^* = \frac{\beta_1 I^*}{N^*} + \beta_2 D^* + \beta_3 P^*. \tag{3.10}$$

By incorporating (3.9) into (3.10) and doing some algebraic manipulations, we derive the $(2n + 5)$ degree polynomial in λ^*

$$Q(\lambda^*) = \Pi \lambda^* H(\lambda^*), \tag{3.11}$$

where

$$\begin{aligned} H(\lambda^*) &= (\lambda^*)^{2n} [A_4(\lambda^*)^4 + A_3(\lambda^*)^3 + A_2(\lambda^*)^2 + A_1\lambda^* + A_0] \\ &\quad + (\lambda^*)^n [B_4(\lambda^*)^4 + B_3(\lambda^*)^3 + B_2(\lambda^*)^2 + B_1\lambda^* + B_0] \\ &\quad + (\lambda^*)^{2n} [C_4(\lambda^*)^4 + C_3(\lambda^*)^3 + C_2(\lambda^*)^2 + C_1\lambda^* + C_0], \end{aligned} \tag{3.12}$$

with coefficients

$$\begin{aligned}
A_4 &= k_5(1-\theta)^2(\mu+\gamma) > 0, \\
A_3 &= k_5(1-\theta) [((1-\theta)(2\epsilon+k_6)+2\mu)(\mu+\gamma) + k_5k_6(1-\theta)(1-\mathcal{R}_0)], \\
&\quad + \delta k_3 \Pi (1-\theta)^2, \\
A_2 &= 2\delta k_3(1-\theta) [\mu + (1-\theta)\epsilon] \Pi + k_5^2 [(1-\theta)(\epsilon+k_6)((1-\theta)(\epsilon+k_6)+4\mu) + \mu^2] \\
&\quad - k_5 [(1-\theta)(\delta(\mu+(1-\theta)\epsilon)(\epsilon+k_6) + \mu k_4)] \\
&\quad - k_5 [((1-\theta)k_4 + \mu\delta)((1-\theta)(2\epsilon+k_6) + \mu)], \\
A_1 &= \delta k_3 \Pi ((1-\theta)\epsilon + \mu)^2 + k_5^2 [2\mu(\epsilon+k_6)((1-\theta)(\epsilon+k_6) + \mu)] \\
&\quad - k_5 [(\epsilon+k_6)((1-\theta)k_4 + \mu\delta)(\mu + (1-\theta)\epsilon) + \mu k_4 ((1-\theta)(2\epsilon+k_6) + \mu)], \\
A_0 &= k_5^2 \mu(\epsilon+k_6) [\mu(\nu+\mu)(1-\mathcal{R}_0) + \epsilon\mu - \epsilon(1-\theta)(\nu+\mu)\mathcal{R}_0], \\
B_4 &= 2k_5\lambda_0^n(1-\theta)^2(\mu+\gamma) > 0, \\
B_3 &= 2\lambda_0^n \delta k_3 \Pi (1-\theta)^2 + 2\lambda_0^n k_5(1-\theta) [(1-\theta)(\epsilon+2k_6) + 2\mu] \\
&\quad - 2\lambda_0^n k_5(1-\theta) [\delta((1-\theta)(\epsilon+k_6) + 2\mu) + (1-\theta)k_4], \\
B_2 &= 2\delta k_3(1-\theta)\lambda_0^n \Pi [2\mu + (1-\theta)\epsilon] + 2\lambda_0^n k_5^2(1-\theta) [k_6(1-\theta)(\epsilon+k_6) + 2\mu(\epsilon+2k_6)] \\
&\quad - k_5\lambda_0^n [(1-\theta) [\delta[\mu(\epsilon+k_6) + (\mu+(1-\theta)\epsilon)k_6] + 2\mu k_4]] \\
&\quad - k_5\lambda_0^n [2((1-\theta)k_4 + \mu\delta)((1-\theta)(\epsilon+k_6) + \mu)], \\
B_1 &= 2\mu\delta k_3 \lambda_0^n \Pi (\mu + (1-\theta)\epsilon) + 2\mu k_5^2 \lambda_0^n [2(1-\theta)(\epsilon+k_6)k_6 + \mu(\epsilon+2k_6)] \\
&\quad - k_5\lambda_0^n [((1-\theta)k_4 + \mu\delta)(\mu(\epsilon+k_6) + (\mu+(1-\theta)\epsilon)k_6) +] \\
&\quad - 2k_5\lambda_0^n \mu k_4 ((1-\theta)(\epsilon+k_6) + \mu), \\
B_0 &= 2\mu^2 k_5^2 k_6 \lambda_0^n (\epsilon+k_6) - \mu k_4 k_5 \lambda_0^n [\mu(\epsilon+k_6) + (\mu+(1-\theta)\epsilon)k_6], \\
C_4 &= k_5(1-\theta)^2(\mu+\gamma) > 0, \\
C_3 &= \delta k_3 \Pi (1-\theta)^2 + 2k_5^2(1-\theta) [(1-\theta)k_6 + \mu] \\
&\quad - k_5(1-\theta) [\delta[(1-\theta)k_6 + \mu] + [(1-\theta)k_4 + \mu\delta]], \\
C_2 &= 2\mu\delta k_3 \Pi (1-\theta) + k_5^2 [(1-\theta)^2 k_6 + \mu^2 + 4\mu(1-\theta)k_6] \\
&\quad - k_5 [(1-\theta)\mu(k_4 + \delta k_6) + [(1-\theta)k_4 + \mu\delta][(1-\theta)k_4 + \mu]], \\
C_1 &= \delta\mu^2 k_3 \Pi + 2\mu k_5^2 k_6 [(1-\theta)k_6 + \mu] - \mu k_5 [k_6[(1-\theta)k_4 + \mu\delta] + k_4[(1-\theta)k_6 + \mu]], \\
C_0 &= \mu^2 k_5^2 k_6^2 (1-\mathcal{R}_0),
\end{aligned}$$

and

$$k_4 = k_5 k_6 \mathcal{R}_0, \quad k_5 = \gamma + \delta + \mu \quad \text{and} \quad k_6 = \nu + \mu.$$

Thus, λ^* is a non-negative real root of $Q(\lambda^*)$ and $\lambda^* = 0$ gives the disease-free equilibrium. When $\mathcal{R}_0 > 1$, we have $C_0 < 0$. Since $H(\lambda^*)$ is a polynomial of even degree $(2n+4)$ with leading $(A_4 > 0)$ and constant $(C_0 < 0)$ terms of opposite signs, there is always an odd number of sign changes on its non-zero coefficients. In line with Descartes' rule of signs, the existence of at least one positive root is guaranteed. Thus, the existence part of the following theorem, its stability part being proved by the Center Manifold Theory (Ref. 10) in Appendix A.

Theorem 3.4 *When $\mathcal{R}_0 > 1$, the Ebola model (2.1) has at least one endemic equilibrium point, which is locally asymptotically stable.*

Theorem 3.3 already implies that there is no LAS endemic equilibria when $\mathcal{R}_0 < 1$ and we will use the Center Manifold Theory (Ref. 10) in Appendix A to confirm the following result.

Theorem 3.5 *The model (2.1) does not undergo a backward bifurcation at $\mathcal{R}_0 = 1$.*

Let us now address the severity of the disease when $\mathcal{R}_0 > 1$.

Theorem 3.6 *Let $I^*(\nu, \epsilon)$ denote the infectious component of the endemic equilibrium point corresponding to the parameters ν and ϵ . Then $I^*(\nu, \epsilon) < I^*(0, 0)$.*

Proof. At the endemic equilibrium point $E^* = (S^*, I^*, R^*, T^*, V^*, D^*, P^*)$, the conservation law in Eq. (A.1) becomes

$$\Pi - \mu N^* - \delta I^* = 0 \quad \text{where} \quad N^* = S^* + I^* + R^* + T^* + V^*.$$

Hence,

$$I^*(\nu, \epsilon) = \frac{\Pi - \mu(S^* + R^* + T^* + V^*)}{\delta + \mu} < \frac{\Pi - \mu(S^* + R^*)}{\delta + \mu} = I^*(0, 0).$$

This completes the proof. \square

4. Sensitivity analysis

The basic reproduction number \mathcal{R}_0 is an important quantity that depends on the parameters involved in the system of differential equations (2.1). In this section, we would like to know how \mathcal{R}_0 responds to the changes in the parameters. The change in the value of \mathcal{R}_0 with respect to changes in the values of the parameters is measured by the derivative of this quantity with respect to that parameter. Mathematically, the sensitivity of \mathcal{R}_0 with respect to a parameter p is given by Ref. 25,

$$\gamma_p^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial p}. \quad (4.1)$$

A much more powerful tool is the normalized sensitivity index of \mathcal{R}_0 , which measures the change in the value of \mathcal{R}_0 with respect to the change in the parameter p . It is given by

$$\mathcal{E}_p^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial p} \frac{p}{\mathcal{R}_0} = \frac{\Delta \mathcal{R}_0 \%}{\Delta p \%}. \quad (4.2)$$

Hence, if p changes by $y\%$, then \mathcal{R}_0 will change by $\mathcal{E}_p^{\mathcal{R}_0} y\%$. The sensitivity index of \mathcal{R}_0 with respect to the parameter p is positive if \mathcal{R}_0 is increasing with respect to p and negative if \mathcal{R}_0 is decreasing with respect to p . The calculation of sensitivity indices of \mathcal{R}_0 at the baseline parameter values of the model is given in Table 2.

By using the reproduction number \mathcal{R}_0 as the response function, Table 2 can be used to propose effective control strategies to avoid direct and indirect contacts

Parameter	Baseline Value	Sensitivity index	Source
β_1	0.6	0.0013	Ref. 11
β_2	0.12	0.0099	Ref. 37
β_3	0.01	0.9888	Assumed
α	0.04	0.5493	Assumed
ξ	0.04	0.4395	Assumed
Π	30	0.9987	Assumed
b	0.4	-0.5592	Ref. 21
η	0.003	-0.9888	Ref. 8
δ	0.48	-0.3203	Ref. 2
ν	0.005	-0.2000	Assumed
μ	0.02	-0.8021	Ref. 29
γ	0.06	-0.1071	Ref. 11

Table 2. Table for the sensitivity index of \mathcal{R}_0 with respect to each parameter in (3.5).

with the potential Ebola virus sources. It is evident, from Table 2, that η is the most sensitive parameter in the control of EVD. This will be discussed further in the numerical simulations.

5. NSFD scheme

Given the rich dynamics of the model (2.1) and the well-documented shortcomings of standard numerical methods to correctly replicate these dynamics (Refs. 4, 5, 27, 28, 31), we design in this section a NSFD scheme. This is done by using Mickens' rules on complex denominator function of discrete derivative and nonlocal approximation of nonlinear terms (Refs. 4, 26).

Let $Y_k = (S_k, I_k, R_k, T_k, V_k, D_k, P_k)$ denote an approximation of $Y(t_k)$ at the discrete time $t_k = k\Delta t$ where $k \in \mathbb{N}$ and $h = \Delta t > 0$ is the step size. We propose the NSFD scheme

$$\begin{aligned}
\frac{S_{k+1} - S_k}{\phi} &= \Pi - (\epsilon e_k + \lambda_k + \nu + \mu)S_{k+1}, \\
\frac{I_{k+1} - I_k}{\phi} &= \lambda_k S_{k+1} - (\gamma + \delta + \mu)I_{k+1} + (1 - \theta)\lambda_k T_{k+1}, \\
\frac{R_{k+1} - R_k}{\phi} &= \gamma I_{k+1} - \mu R_{k+1}, \\
\frac{T_{k+1} - T_k}{\phi} &= \epsilon e_k S_{k+1} - ((1 - \theta)\lambda_k + \mu)T_{k+1}, \\
\frac{V_{k+1} - V_k}{\phi} &= \nu S_{k+1} - \mu V_{k+1}, \\
\frac{D_{k+1} - D_k}{\phi} &= (\mu + \delta)I_{k+1} - bD_{k+1}, \\
\frac{P_{k+1} - P_k}{\phi} &= \xi I_k + \alpha D_k - \eta P_{k+1},
\end{aligned} \tag{5.1}$$

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where the complex denominator function

$$\phi = \phi(h) = \frac{1 - e^{-(\gamma+\delta+\mu)h}}{\gamma + \delta + \mu},$$

satisfies the asymptotic property

$$\phi(h) = h + \mathcal{O}(h^2).$$

The nonlocal approximation of nonlinear terms is reinforced by observing that

$$\lambda_k = \frac{\beta_1 I_k}{N_k} + \beta_2 D_k + \beta_3 P_k \quad \text{and} \quad e_k = e(\lambda_k) = \frac{\lambda_k^n}{\lambda_0^n + \lambda_k^n}.$$

The NSFD scheme (5.1) is an extension of the one in Ref. 7, through the form of λ_k and the presence of e_k , V_k and T_k .

By rearranging (5.1), we obtain

$$\begin{aligned} S_{k+1} &= \frac{\Pi\phi + S_k}{1 + (\epsilon e_k + \lambda_k + \nu + \mu)\phi}, \\ I_{k+1} &= \frac{\lambda_k \phi(S_{k+1} + (1 - \theta)T_{k+1}) + I_k}{1 + (\gamma + \delta + \mu)\phi}, \\ R_{k+1} &= \frac{\gamma \phi I_{k+1} + R_k}{1 + \mu\phi}, \\ T_{k+1} &= \frac{\phi \epsilon e_k S_{k+1} + T_k}{1 + ((1 - \theta)\lambda_k + \mu)\phi}, \\ V_{k+1} &= \frac{\nu \phi S_{k+1} + V_k}{1 + \mu\phi}, \\ D_{k+1} &= \frac{(\delta + \mu)\phi I_{k+1} + D_k}{1 + b\phi}, \\ P_{k+1} &= \frac{(\xi I_k + \alpha D_k)\phi + P_k}{1 + \eta\phi}. \end{aligned} \tag{5.5}$$

The equivalent form (5.5) has a Gauss-Seidel structure for the computation of the terms one after the other.

By following the ideas in Refs. 4,26, as it is done in Ref. 7, the following results can be proved:

Theorem 5.1 *Irrespective of the value of the step size Δt , the NSFD scheme (5.1) replicates the dynamics of the model (2.1) as stated in Theorems 3.1-3.6.*

6. Numerical simulations

In this section, numerical simulations for the proposed NSFD scheme (5.1) or (5.5) are given. Parameter values to be used are in Table 2 while $\theta = 0.5$, $\epsilon = 0.9$ and $n = 2$.

The global and local asymptotic stability of the disease-free and endemic equilibrium points guaranteed by Theorems 3.3-3.4 are illustrated in Fig. 3 for $\mathcal{R}_0 = 0.68$ and $\mathcal{R}_0 = 8.7$, respectively. The numerical solutions of the proposed model under different protection interventions are presented to highlight their contribution on the reduction of the severity and the endemicity of the disease.

For instance, in Fig. 4 (a), it is observed how interventions reduce the number of infectious individuals on the long run. In accordance with Theorem 3.6, the implementation

of all interventions stabilises the trajectories at the endemic equilibrium $I^* = 14$ whereas in the absence of interventions $I^* = 17$. This represents a 17.6% reduction in the number of infectious individuals. Additional information about the contribution of education and vaccination interventions on the reduction of infectious individuals is presented in Fig. 4 (b). These findings are made more precise in Fig. 5. Fig. 5(a) illustrates that the endemic equilibrium I^* decreases as the vaccination rate (ν) and decay rate of Ebola virus in the environment (η) increase while Fig. 5(b) shows that the endemic equilibrium I^* increases as the contact rates (β_1 , β_2 and β_3) increase. In particular, the contact rate with the environment (β_3), contributes to a significant increase in I^* compared to the other contact rates. By considering the mass action principle with self protection interventions, the endemic equilibrium I^* is less than that of the mass action principle without interventions, as illustrated in Fig. 6(a). This is in line with Remark 3.1. Finally, in Fig. 6(b), we observe the inverse relationship between the number of infective individuals and the self-preventive measure parameter θ .

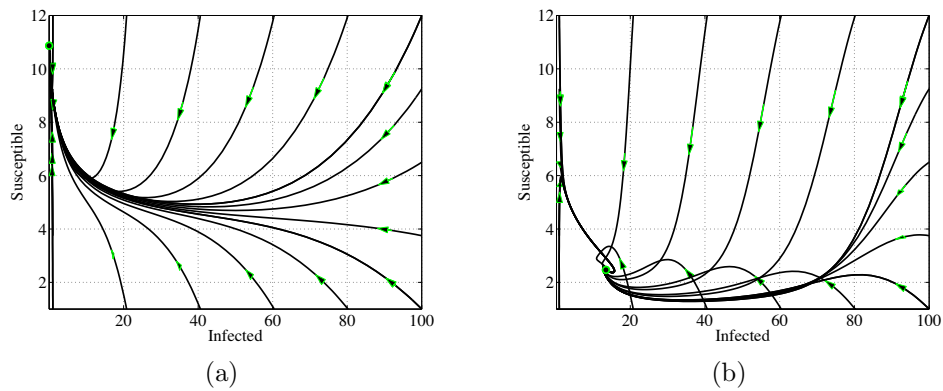


Fig. 3. a) GAS of the disease-free equilibrium. b) LAS of the endemic equilibrium point.

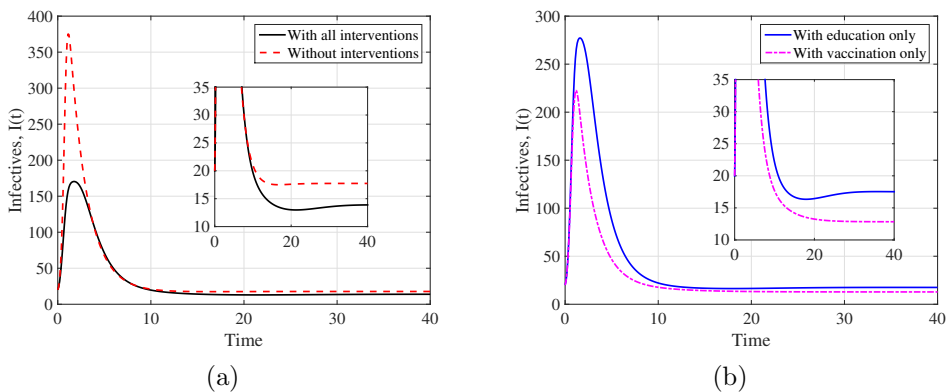


Fig. 4. (a) Number of infectious with and without interventions (b) Number of infectious with education and vaccination interventions.

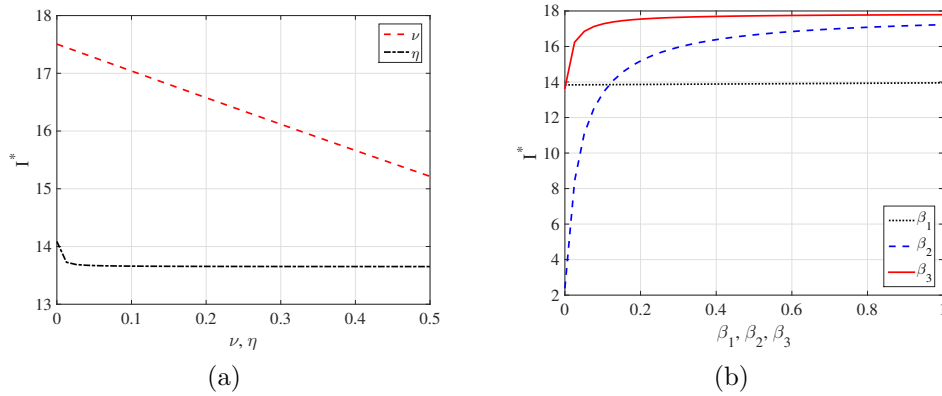


Fig. 5. (a): Sensitivity analysis with respect to ν and η . (b): Sensitivity analysis with respect to β_1 , β_2 and β_3 .

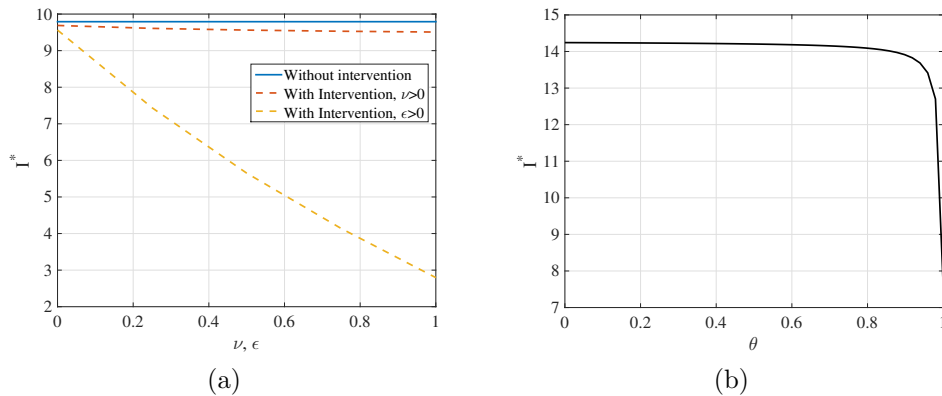


Fig. 6. (a) Mass action with and without self protection interventions. (b) The relation between I^* and self-preventive measure θ .

7. Conclusion

The transmission dynamics of the Ebola outbreak in the Central and Western Africa has been studied in Refs. 1, 2, 16, 21, 29 by using the mass action formulation but without the environment class and the vital dynamics of the population. A mathematical model proposed in Ref. 7 incorporated the vital dynamics and the contribution of the environment in the transmission dynamics of the EVD. Here, we have enriched the work in Ref. 7 by widening the educational interventions on the population and by combining the standard incidence and the mass action principle in the formulation of the force of infection. This resulted in the formulation of model (2.1). In the analysis of the model, we proved the global asymptotic stability of the disease-free equilibrium point when $\mathcal{R}_0 \leq 1$. The existence and the local asymptotic stability of the endemic equilibrium point are guaranteed for $\mathcal{R}_0 >$

1. The contribution of vaccination and training of susceptible individuals in the control strategy of the EVD are shown analytically and illustrated graphically. More precisely, applying both type of interventions is very important to have less number of infectious individuals which minimize the severity of EVD in the population. Our findings in this study strengthen the recommendations given in Ref. 7 to eradicate the EVD.

The sensitivity indexes of \mathcal{R}_0 with respect to the parameters involved in the model are computed and the more influential parameters on \mathcal{R}_0 are identified. For instance, when the contact rate β_3 increases, the basic reproduction number \mathcal{R}_0 will increase correspondingly. On the other hand, increasing b, η or ν decreases the value of \mathcal{R}_0 . Hence, this study recommends to the health policy makers to take into account the following points in their policies in order to have less damage of Ebola virus outbreak in the population:

- (i) avoiding contacts with Ebola virus infectious individuals, Ebola deceased bodies and Ebola contaminated environment,
- (ii) minimizing the mean caring duration of deceased human bodies due to EVD,
- (iii) increasing the decay rate of Ebola virus in the environment and vaccination rate of individuals who are living in Ebola outbreak areas.

These recommendations can be achieved by using successive training in the population.

From the numerical simulations point of view, our NSFD scheme helps to observe the properties of the continuous model.

Although the above recommendations in (i)-(iii) (if strictly implemented) can be effective to eradicate the disease, it has been observed for the fast outbreaks that additional control measures are needed. As a consequence, possible extension of this work includes:

- (1) the incorporation of contact tracing as additional control measure (Refs. 24,30),
- (2) the multi-species setting to account for the extreme case where a region is attacked by more than one Ebola virus species,
- (3) the incorporation of patches to account for the circulation of the disease in many countries,
- (4) the use of the theory of optimal control to determine when and to what extent we can control the most influential parameters in the transmission dynamics of the EVD,
- (5) the investigation of the uniqueness of the endemic equilibrium and its global asymptotic stability.

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Appendix A.

Proof of Theorem 3.1. We want to show that for nonnegative initial data, the system (2.1) possesses at all time $t \geq 0$ a unique nonnegative solution which lies in region Ω . The proof will follow two steps.

Following the approach in Ref. 9, it can be shown that any solution of (2.1) corresponding to nonnegative initial conditions is nonnegative.

In a second step, we have that any solution satisfies some a priori estimates. By adding

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the first five equations of (2.1), we obtain

$$\frac{dN}{dt} = \Pi - \mu N - \delta I. \quad (\text{A.1})$$

Thus

$$\Pi - (\delta + \mu)N \leq \frac{dN}{dt} = \Pi - \mu N - \delta I \leq \Pi - \mu N, \quad (\text{A.2})$$

which by applying Gronwall inequality implies

$$0 \leq N(t) \leq \frac{\Pi}{\mu} \quad \text{for} \quad 0 \leq N_0 \leq \frac{\Pi}{\mu}. \quad (\text{A.3})$$

Since the last two equations of (2.1) imply that

$$\frac{dD}{dt} \leq (\delta + \mu)\frac{\Pi}{\mu} - bD \quad \text{and} \quad \frac{dP}{dt} \leq \frac{\xi\Pi}{\mu} + \frac{\alpha(\delta + \mu)\Pi}{b\mu} - \eta P,$$

another application of Gronwall inequality leads to

$$0 \leq D(t) \leq \frac{(\delta + \mu)\Pi}{b\mu} \quad \text{for} \quad 0 \leq D_0 \leq \frac{(\delta + \mu)\Pi}{b\mu}$$

and

$$0 \leq P(t) \leq \frac{1}{\eta} \left(\frac{\xi\Pi}{\mu} + \frac{\alpha(\delta + \mu)\Pi}{b\mu} \right) \quad \text{for} \quad 0 \leq P_0 \leq \frac{1}{\eta} \left(\frac{\xi\Pi}{\mu} + \frac{\alpha(\delta + \mu)\Pi}{b\mu} \right).$$

Combining the above two steps and using the well-known result (see Theorem 2.1.5 in Ref. 34), we conclude that (2.1) defines a dynamical system on Ω . \square

Proof of Theorem 3.2. To show that E_0 is locally asymptotically stable, we use the Jacobian matrix of the functions at the right-hand side of (2.1) at E_0 . We exclude the equation related to the variable R since the analysis is not affected by this equation. Thus

$$J_6(E_0) = \begin{pmatrix} -(\nu + \mu) & \frac{\mu\beta_1}{\nu + \mu} & 0 & 0 & -\frac{\beta_2\Pi}{\nu + \mu} - \frac{\beta_3\Pi}{\nu + \mu} \\ 0 & \frac{\mu\beta_1}{\nu + \mu} - (\gamma + \delta + \mu) & 0 & 0 & \frac{\beta_2\Pi}{\nu + \mu} & \frac{\beta_3\Pi}{\nu + \mu} \\ 0 & 0 & -\mu & 0 & 0 & 0 \\ \nu & 0 & 0 & -\mu & 0 & 0 \\ 0 & \delta + \mu & 0 & 0 & -b & 0 \\ 0 & \xi & 0 & 0 & \alpha & -\eta \end{pmatrix}.$$

Expanding the determinant in the characteristic equation $|\lambda I_6 - J_6| = 0$ by the third and fourth columns, where I_6 is 6×6 identity matrix, we obtain two eigenvalues $\lambda_1 = -\mu$ and $\lambda_2 = -\mu$. The remaining four eigenvalues are those of the matrix

$$J_4 = \begin{pmatrix} -(\nu + \mu) & \frac{\mu\beta_1}{\nu + \mu} & -\frac{\beta_2\Pi}{\nu + \mu} - \frac{\beta_3\Pi}{\nu + \mu} \\ 0 & \frac{\mu\beta_1}{\nu + \mu} - (\gamma + \delta + \mu) & \frac{\beta_2\Pi}{\nu + \mu} & \frac{\beta_3\Pi}{\nu + \mu} \\ 0 & \delta + \mu & -b & 0 \\ 0 & \xi & \alpha & -\eta \end{pmatrix}.$$

The characteristic equation takes the form $|\lambda I_4 - J_4| = 0$ and the expansion along the first column gives a third eigenvalue $\lambda_3 = -(\nu + \mu)$. Then the remaining eigenvalues are those of the matrix

$$J_3 = \begin{pmatrix} \frac{\mu\beta_1}{\nu+\mu} - (\gamma + \delta + \mu) & \frac{\beta_2\Pi}{\nu+\mu} & \frac{\beta_3\Pi}{\nu+\mu} \\ \delta + \mu & -b & 0 \\ \xi & \alpha & -\eta \end{pmatrix}.$$

The corresponding characteristic equation $|\lambda I_3 - J_3| = 0$ gives the following polynomial in λ :

$$Q(\lambda) := \lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0,$$

where

$$a_1 = \eta + b + (\gamma + \delta + \mu)[1 - \mathcal{R}_0] + \frac{\beta_2(\delta + \mu)\Pi}{(\nu + \mu)} + \frac{\beta_3\Pi [b\xi + \alpha(\delta + \mu)]}{b\eta(\nu + \mu)},$$

$$a_2 = \eta b + (\eta + b)(\gamma + \delta + \mu) \times \left[1 - \mathcal{R}_0 + \frac{\eta\beta_2(\delta + \mu)\Pi}{b(\eta + b)(\nu + \mu)(\gamma + \delta + \mu)} + \frac{\beta_3\Pi [\alpha(\delta + \mu)(\eta + b) + b^2\xi]}{b\eta(\eta + b)(\nu + \mu)(\gamma + \delta + \mu)} \right],$$

$$a_3 = -\eta b(\gamma + \delta + \mu)(\mathcal{R}_0 - 1).$$

For $\mathcal{R}_0 < 1$, we have $a_1 > 0$, $a_2 > 0$ and $a_3 > 0$. It is also direct to show that $a_1 a_2 > a_3$. Hence, by the Routh-Hurwitz criterion, the real parts of the remaining three eigenvalues are negative. Thus, the disease free equilibrium is locally asymptotically stable for $\mathcal{R}_0 < 1$. When $\mathcal{R}_0 > 1$, the criterion is violated and thus the DFE is unstable. \square

Proof of Theorem 3.3. We use Kamgang-Sallet Stability Theorem in Ref. 17. Let $X = (X_1, X_2)$, $X_1 = (S, R, T, V) \in \mathbb{R}^4$ and $X_2 = (I, D, P) \in \mathbb{R}^3$. Then the system (2.1) can be written as

$$\dot{X}_1 = A_1(X)(X_1 - X_1^*) + A_{12}(X)X_2, \quad (\text{A.6})$$

$$\dot{X}_2 = A_2(X)X_2, \quad (\text{A.7})$$

where $X_1^* = \left(\frac{\Pi}{\nu+\mu}, 0, 0, \frac{\nu\Pi}{\mu(\nu+\mu)} \right)$,

$$A_1(X) = \begin{pmatrix} -(\nu + \mu) & 0 & 0 & 0 \\ 0 & -\mu & 0 & 0 \\ 0 & 0 & -\mu & 0 \\ \nu & 0 & 0 & -\mu \end{pmatrix},$$

$A_{12}(X)$ is

$$\begin{pmatrix} \left(-1 - \epsilon \frac{\lambda^{n-1}}{\lambda_0^n + \lambda^n} \right) \frac{\beta_1 S}{N} & \left(-1 - \epsilon \frac{\lambda^{n-1}}{\lambda_0^n + \lambda^n} \right) \beta_2 S & \left(-1 - \epsilon \frac{\lambda^{n-1}}{\lambda_0^n + \lambda^n} \right) \beta_3 S \\ \gamma & 0 & 0 \\ \left(\frac{\epsilon \lambda^{n-1}}{\lambda_0^n + \lambda^n} S - (1 - \theta)T \right) \frac{\beta_1}{N} & \left(\frac{\epsilon \lambda^{n-1}}{\lambda_0^n + \lambda^n} S - (1 - \theta)T \right) \beta_2 & \left(\frac{\epsilon \lambda^{n-1}}{\lambda_0^n + \lambda^n} S - (1 - \theta)T \right) \beta_3 \\ 0 & 0 & 0 \end{pmatrix},$$

and $A_2(X)$ is

$$\begin{pmatrix} \frac{\beta_1}{N} [S + (1 - \theta)T] - (\gamma + \delta + \mu) & \beta_2 [S + (1 - \theta)T] & \beta_3 [S + (1 - \theta)T] \\ \mu + \delta & -b & 0 \\ \xi & \alpha & -\eta \end{pmatrix}.$$

We show that the five sufficient conditions of Kamgang-Sallet Theorem are satisfied as follows.

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- (1) The system (2.1) is a dynamical system on Ω . This is proved in Theorem 3.1.
- (2) The equilibrium X_1^* is GAS for the subsystem $\dot{X}_1 = A_1(X_1, 0)(X_1 - X_1^*)$. This is obvious from the structure of the involved matrix.
- (3) The matrix $A_2(X)$ is Metzler (i.e., all the off-diagonal elements are nonnegative) and irreducible for any given $X \in \Omega$. This is also obvious.
- (4) There exists an upper-bound matrix \bar{A}_2 for the set

$$\mathcal{M} = \{A_2(X) : X \in \Omega\}.$$

Indeed, since $\frac{S+(1-\theta)T}{N} \leq 1$,

$$\bar{A}_2 = \begin{pmatrix} \beta_1 - (\gamma + \delta + \mu) & \beta_2 & \frac{\Pi\beta_3}{\mu} \\ \mu + \delta & -b & 0 \\ \xi & \alpha & -\eta \end{pmatrix}$$

is an upper-bound of \mathcal{M} .

- (5) For $\mathcal{R}_0 \leq 1$ in (3.5)

$$\alpha(\bar{A}_2) = \max \{Re(\lambda) : \lambda \text{ eigenvalue of } \bar{A}_2\} \leq 0.$$

Hence, by the Kamgang-Sallet Stability Theorem, the disease-free equilibrium is globally asymptotically stable for $\mathcal{R}_0 \leq 1$. \square

Proof of Theorem 3.5. We check the local stability of the endemic equilibrium of the system (2.1) at $\mathcal{R}_0 = 1$. To this end, in the setting of Theorem 4.1 in Ref. 10 where the sign of the numbers a and b below are crucial. We introduce variables $x = (x_1, x_2, x_3, x_4, x_5, x_6, x_7)$ where,

$$x_1 = \frac{\Pi}{\mu + \nu} - S, \quad x_2 = I, \quad x_3 = R, \quad x_4 = T, \quad x_5 = V - \frac{\nu\Pi}{\mu(\mu + \nu)}, \quad x_6 = D \quad \text{and} \quad x_7 = P.$$

Let $\phi = b\eta\mu\beta_1 + b\eta\Pi(\mu + \delta)\beta_2 + \beta_3\Pi(b\xi + \alpha(\mu + \delta))$ be the bifurcation parameter so that $\mathcal{R}_0 = \frac{\phi}{b\eta(\nu + \mu)(\gamma + \delta + \mu)}$. Thus $\mathcal{R}_0 = 1$ if and only if $\phi = \phi^* = b\eta(\nu + \mu)(\gamma + \delta + \mu)$ and $\mathcal{R}_0 < 1$ if and only if $\phi < \phi^*$. Using the above variables, the system (2.1) becomes

$$\begin{aligned} \frac{dx_1}{dt} &= (\epsilon e + \lambda_1) \left(\frac{\Pi}{\mu + \nu} - x_1 \right) - (\nu + \mu)x_1 =: f_1, \\ \frac{dx_2}{dt} &= \lambda_1 \left(\frac{\Pi}{\mu + \nu} - x_1 \right) - (\gamma + \delta + \mu)x_2 + (1 - \theta)\lambda_1 x_4 =: f_2, \\ \frac{dx_3}{dt} &= \gamma x_2 - \mu x_3 =: f_3, \\ \frac{dx_4}{dt} &= \epsilon e \left(\frac{\Pi}{\mu + \nu} - x_1 \right) - (1 - \theta)\lambda_1 x_4 - \mu x_4 =: f_4, \\ \frac{dx_5}{dt} &= -\nu x_1 - \mu x_5 =: f_5, \\ \frac{dx_6}{dt} &= (\mu + \delta)x_2 - b x_6 =: f_6, \\ \frac{dx_7}{dt} &= \xi x_2 + \alpha x_6 - \eta x_7 =: f_7, \end{aligned} \tag{A.8}$$

where $N = \frac{\Pi}{\mu} - x_1 + x_2 + x_3 + x_4 + x_5$ and $\lambda_1 = \frac{\beta_1 x_2}{N} + \beta_2 x_6 + \beta_3 x_7$. The disease-free equilibrium of (A.8) which corresponds to E_0 is $x^* = (0, 0, 0, 0, 0, 0, 0)$. The Jacobian matrix J of the right-side of the system (A.8) at x^* denoted by $J(x^*)$ is

$$J(x^*) = \begin{pmatrix} -(\mu + \nu) & \frac{\beta_1 \mu}{\mu + \nu} & 0 & 0 & 0 & \frac{\beta_2 \Pi}{\mu + \nu} & \frac{\beta_3 \Pi}{\mu + \nu} \\ 0 & \frac{\beta_1 \mu}{\mu + \nu} - (\gamma + \delta + \mu) & 0 & 0 & 0 & \frac{\beta_2 \Pi}{\mu + \nu} & \frac{\beta_3 \Pi}{\mu + \nu} \\ 0 & \gamma & -\mu & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\mu & 0 & 0 & 0 \\ -\nu & 0 & 0 & 0 & -\mu & 0 & 0 \\ 0 & \mu + \delta & 0 & 0 & 0 & -b & 0 \\ 0 & \xi & 0 & 0 & 0 & \alpha & -\eta \end{pmatrix}.$$

When $\mathcal{R}_0 = 1$, $J(x^*)$ has a simple zero eigenvalue and all the other eigenvalues have negative real part. This is the setting of Theorem 4.1 in Ref. 10. The right-eigenvector $w = (w_1, w_2, w_3, w_4, w_5, w_6, w_7)$ and the left-eigenvector $v = (v_1, v_2, v_3, v_4, v_5, v_6, v_7)$ associated with the zero eigenvalue such that $w \cdot v = 1$ are determined the systems

$$J(x^*)w = 0. \quad \text{and} \quad vJ(x^*) = 0. \quad (\text{A.9})$$

Simplification of (A.9) gives

$$\begin{aligned} w_1 &= \frac{b\beta_1\mu}{(\mu + \nu)(\mu + \delta)} + \frac{\beta_2\Pi}{\mu + \nu} + \frac{\beta_3\Pi}{(\mu + \nu)\eta(\mu + \delta)}(b\xi + \alpha(\mu + \delta)), \\ w_2 &= \frac{b(\mu + \nu)}{\mu + \delta}, \quad w_3 = \frac{b\gamma(\mu + \nu)}{\mu(\mu + \delta)}, \quad w_4 = 0, \\ w_5 &= \frac{-\nu}{\mu} \left[\frac{b\beta_1\mu}{(\mu + \nu)(\mu + \delta)} + \frac{\beta_2\Pi}{\mu + \nu} + \frac{\beta_3\Pi}{(\mu + \nu)\eta(\mu + \delta)}(b\xi + \alpha(\mu + \delta)) \right], \\ w_6 &= \mu + \nu \quad \text{and} \quad w_7 = \frac{(\mu + \nu)(b\xi + \alpha(\mu + \delta))}{\eta(\mu + \delta)}. \end{aligned}$$

$$(v_1, v_2, v_3, v_4, v_5, v_6, v_7) = \left(0, \frac{1}{q}, 0, 0, 0, \frac{\Pi}{bq(\mu + \nu)} \left(\beta_2 + \frac{\alpha\beta_3}{\eta} \right), \frac{\beta_3\Pi}{\eta(\mu + \nu)q} \right),$$

where $q = (\mu + \nu)^2 \left[\frac{b(\mu + \nu)}{\mu + \delta} + \frac{\beta_2}{b} + \frac{\beta_3\Pi}{\eta} \left(\frac{\alpha}{b} + \alpha + \frac{b\xi}{\mu + \delta} \right) \right]$. The bifurcation coefficients a and b are

$$\begin{aligned} a &= \sum_{k,i,j=1}^7 v_k w_i w_j \frac{\partial^2 f_k(x^*, \phi^*)}{\partial x_i \partial x_j} \\ &= \sum_{i,j=1}^7 \left[v_2 w_i w_j \frac{\partial^2 f_2(x^*, \phi^*)}{\partial x_i \partial x_j} + v_6 w_i w_j \frac{\partial^2 f_6(x^*, \phi^*)}{\partial x_i \partial x_j} + v_7 w_i w_j \frac{\partial^2 f_7(x^*, \phi^*)}{\partial x_i \partial x_j} \right] \\ &= v_2 \sum_{i,j=1}^7 w_i w_j \frac{\partial^2 f_2(x^*, \phi^*)}{\partial x_i \partial x_j}, \quad \text{the other terms equal to zero} \\ &= -2w_1 v_2 (\beta_1 w_2 + \beta_2 w_6 + \beta_3 w_7) \\ &< 0 \end{aligned}$$

and

$$\begin{aligned} b &= \sum_{k,j=1}^7 v_k w_j \frac{\partial^2 f_k(x^*, \phi^*)}{\partial x_j \partial \phi} \\ &= \sum_{j=1}^7 \left[v_2 w_j \frac{\partial^2 f_2(x^*, \phi^*)}{\partial x_j \partial \phi} + v_6 w_j \frac{\partial^2 f_6(x^*, \phi^*)}{\partial x_j \partial \phi} + v_7 w_j \frac{\partial^2 f_7(x^*, \phi^*)}{\partial x_j \partial \phi} \right]. \end{aligned}$$

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Further simplification yields

$$b = \frac{v_6}{\eta\beta_2 + \alpha\beta_3} > 0.$$

Since $a < 0$ and $b > 0$, the following conclusion holds. When ϕ passes through the point $\phi = \phi^*$ (or equivalently \mathcal{R}_0 crosses 1) from left to right, the stability of E_0 changes from globally asymptotic stable (see Theorem 3.2 and 3.3) to unstable and there exists at least one endemic equilibrium which is locally asymptotically stable for $\mathcal{R}_0 > 1$. \square