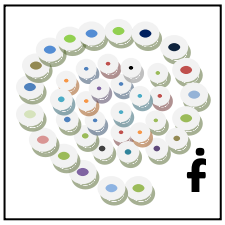

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Effects of quarantine and delay on transmission dynamics of cholera model with Holling Type - II incidence function

Ahmed Nakaka*and Adamu Shitu Hassan†

Abstract

A delay cholera model with Holling Type - II saturated incidence function and quarantine measure as intervention is formulated and dynamically analyzed with the aim of investigating the effects of time delay and quarantine measure. Basic properties of the model are investigated, and two equilibria are found to be locally and globally asymptotically stable whenever the control reproduction number is below and above unity, respectively. Quarantine intervention is found to reduce the infectivity of cholera when fully implemented. Although time delay does not alter the qualitative dynamics of the model, however it decreases the burden of cholera when the delay is beyond a critical value. Numerical simulations are conducted to illustrate all our results.

Keywords: Cholera; Holling Type -II; Delay; Quarantine; Global Stabilities.

1 Introduction

Cholera is an acute, water-borne, infectious diarrhoeal disease caused by bacterium known as *Vibrio Cholerae* serogroup $O1$ and $O139$. Only toxigenic strain of serogroup $O1$ and $O139$ have caused widespread epidemics and are reported to the World Health Organization (WHO). Humans are one of the reservoirs for pathogenic form of *Vibrio Cholerae* $O1$ and $O139$. The disease causes much havoc, especially to underdeveloped countries and massive threat to their economic development. Without prompt treatment, an infected individual may die of dehydration within hours especially in severe cases [5]. The incubation period of cholera range between few hours to 5 days [21, 26]. Some of the control and intervention measures for cholera include antibiotics, rehydration therapy, effective sanitation, proper waste management, personal hygiene and vaccination [4, 38]. After several years of steady increase, from 2007 the number of cholera reported cases to WHO indicate a considerable decrease [33]. The disease is still a threat to many countries. For instance in 2012 alone, a cumulative total of $245,393$ cases, including $3,034$ deaths with a case fatality of 1.2% were reported to WHO from all countries [1]. The disease still remains a major public health problem, affecting primarily developing world populations lacking access to adequate water and sanitation. The most recent is the September, 2018 cholera outbreak in Yobe state, North-east Nigeria which was declared by the state's ministry of Health. Two weeks after, the same outbreak was declared in the neighbouring Borno state. The cumulative number of recorded cases in the two states as of Thursday, 20 September, 2018 stands at $3,126$ including 97 deaths. This represents a cumulative case fatality rate of 7.8% [29].

*Department of Mathematical Sciences, Faculty of Physical Sciences, Bayero University, Kano, Nigeria
†Department of Mathematical Sciences, Faculty of Physical Sciences, Bayero University, Kano, Nigeria; hashitu.mth@buk.edu.ng

Mathematical models have been proposed to investigate the complex epidemic and endemic behavior of cholera using time delay as incubation period [16, 24, 32, 34] and some without delay [5, 23]. In 2001, Codeço [5] formulated a pioneer mathematical model of cholera that incorporated an environmental reservoir of *Vibrio cholerae* with the objective of exploring the role of aquatic reservoir on the persistence of endemic cholera and to define minimum conditions for the development of epidemic and endemic cholera. In [1], Berge, *et al* studied a two-patch model for the transmission of cholera using the environmental reservoir in [5] as pathogen compartment. In their model, they categorized the mode of transmission into two, namely; fast (human-human transmission) and slow (human-environment transmission) as reported in [5, 12]. The main aim of the study was to investigate the impact of human population movements between two cities (patches) in the transmission of cholera. They obtained the basic reproduction number R_0, which defends on the rate of human movement, in addition to other model parameters. Nirwani *et al* [23] analyzed $SIQR - B$ (Susceptible, Infectious, Quarantine, Removed and Pathogen) model for transmission of cholera with saturated incidence rate and quarantine as measure of intervention. The study focused on effects of quarantine and incidence on the spread of cholera. Wang and Wang [30] Studied a cholera model that incorporates human behaviour via modelling disease prevalence depending on contact rate for direct and indirect transmissions and infectious host shedding. Other related delay model is presented by Prasenjit, *et al* in 2007, [24] that incorporated delay as time between infection and infectiousness for the reservoir hosts in the model of American Cutaneous Leishmaniasis originally formulated in [9].

Quarantine is a disease control strategy that has been adopted as a mean of separating people, animals and goods that may have been exposed to communicable diseases. The separation can be in form of isolation, sanitary cordons, bills of health issued to ships, fumigation, disinfection and regulation of groups of persons, amongst other strategies [20]. In [7], quarantine is defined loosely as the temporary removal (from their immediate abode or the general population) of people suspected of being exposed to a communicable disease. The Holling type II otherwise called saturated incidence function is used widely in mathematical epidemiology to describe a situation where a population is saturated with susceptibles or infectives or both - see for example [17, 25].

In this paper, we study the transmission dynamics of cholera in human population which is divided into four compartments, and the population of *Vibrio cholerae* pathogens concentration with time delay as incubation period. Furthermore, we use a saturated incidence function of Holling type II and quarantine of infected individuals inform of isolation/treatment as control measure. The main objective is to investigate the effects of quarantine and time delay on both dynamics and infectivity on the model. This research is extension of the work in [23, 27, 31] in the following sense.

1. In Nirwani *et al* [23], No time delay and global stabilities of equilibria.
2. In Sun *et al* [27], No time delay.
3. In Wang and Wei [31], No any control strategy.

2 Model Formulation

The human population is divided into four compartments at any time t given as Susceptible $S(t)$, Infectious $I(t)$, Quarantine $Q(t)$ and Removed $R(t)$, while the concentration of cholera bacterium in the environment as $B(t)$. The total human population at time t is given by

$N(t) = S(t) + I(t) + Q(t) + R(t)$. The susceptible humans compartment is increasing with constant recruitment at rate (A), decrease due to infection described by Holling type II saturated incidence rate $(\frac{\beta_1 S(t)B(t)}{1+\alpha_1 B(t)} + \frac{\beta_2 S(t)I(t-\tau)}{1+\alpha_2 I(t-\tau)})$ and by natural death at rate (μ_1), which is also applicable to all human compartments. The parameters β_1 and β_2 are the human-environment and human-human contact rates respectively. Here, τ is time delay representing the incubation period of cholera, while $e^{-\mu_1 \tau}$ is the probability that infectives will survive natural death over the period $0 \leq t \leq \tau$. Similarly, α_1 and α_2 are constants of the incidence rate that determine the rate of new infection. Infectious compartment is increasing due to infection at the rate $\left(\frac{\beta_1 S(t)B(t)}{1+\alpha_1 B(t)} + \frac{\beta_2 S(t)I(t-\tau)e^{-\mu_1 \tau}}{1+\alpha_2 I(t-\tau)}\right)$, decrease by deaths due to infection and naturally at rates (d_1) and (μ_1), respectively, natural recovery and quarantine at rates (α) and (δ), respectively. Similarly, the quarantine compartment increases by the rate of infectious individuals been quarantined at rate (δ), decreases by the rate of recovery of quarantined individuals, natural death and disease induced at rates (ϵ), (μ) and (d_2), respectively. The removed class is increased by the recoveries of infectious and quarantined individuals at rates (α) and (ϵ), respectively, and decrease by the natural death of humans at rate (μ_1). Finally, the *Vibro cholarae* is increased by the infectious human contribution to the environment at rate (η) and decreased by the natural death of pathogens at rate (μ_2).

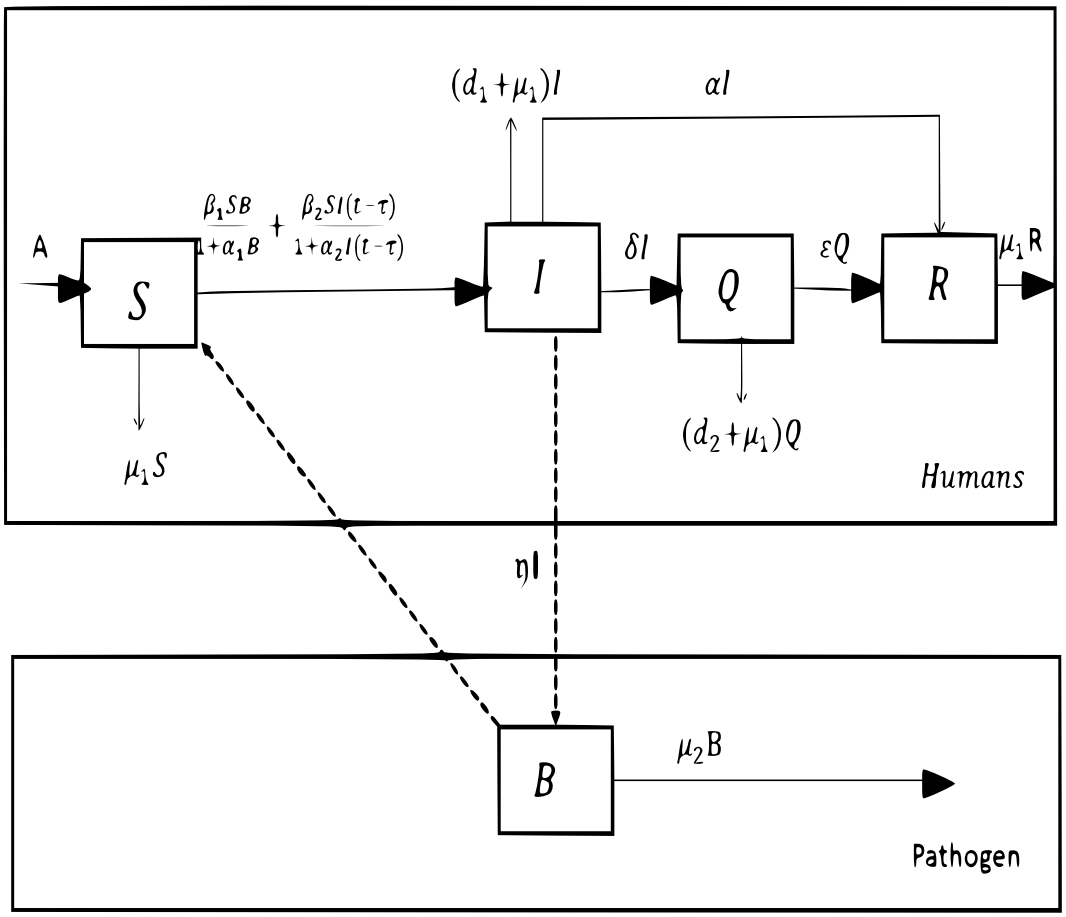


Figure 1: Schematic diagram for the model (2.1)–(2.5) illustrating movements between compartments for transmission of cholera.

It should be noted that in Figure 1, the solid arrows indicate movements among the human population due to change of status (compartment) in the course of infection or recovery, while the dotted arrows indicate interaction between human population and the cholera bacterium in

Variable/Parameter	Description	Units
S	Susceptible individuals	individual
I	Infectious individuals	individual
Q	Quarantine individuals	individual
R	Removed individuals	individual
B	Pathogen concentration in water	cell ml^{-1}
A	Recruitment of susceptible individuals	day^{-1}
μ_1	Natural death human of population	day^{-1}
μ_2	Death rate of pathogen in the environment	day^{-1}
β_1	Human-environment contact rate	$cell^{-1}\ ml^{-1}\ day^{-1}$
β_2	Human-human contact rate	$individual^{-1}\ day^{-1}$
d_1	Death rate of infected individuals due to disease	day^{-1}
d_2	Death rate of quarantine individuals due to disease	day^{-1}
δ	Quarantine rate of infected individuals	day^{-1}
ϵ	Rate of recovery of after quarantine	day^{-1}
α	Rate of recovery of infected individuals	day^{-1}
η	Infected human contributions to the pathogen	cell $ml^{-1}\ day^{-1}\ indl.^{-1}$
α_1	Determinant of new infections through Pathogen	day^{-1}
α_2	Determinant of new infections through infectious humans	day^{-1}

Table 1: Descriptions of Variables and Parameters for System (2.1)–(2.5).

the environment. The model is therefore described by the flow diagram Figure 1 and represented with the following system of delay differential equations:

$$\frac{dS(t)}{dt} = A - \frac{\beta_1 S(t)B(t)}{1+\alpha_1 B(t)} - \frac{\beta_2 S(t)I(t-\tau)e^{-\mu_1\tau}}{1+\alpha_2 I(t-\tau)} - \mu_1 S(t), \tag{2.1}$$

$$\frac{dI(t)}{dt} = \frac{\beta_1 S(t)B(t)}{1+\alpha_1 B(t)} + \frac{\beta_2 S(t)I(t-\tau)e^{-\mu_1\tau}}{1+\alpha_2 I(t-\tau)} - (d_1+\mu_1+\alpha+\delta)I(t), \tag{2.2}$$

$$\frac{dQ(t)}{dt} = \delta I(t) - (\epsilon+\mu_1+d_2)Q(t), \tag{2.3}$$

$$\frac{dB(t)}{dt} = \eta I(t) - \mu_2 B(t). \tag{2.4}$$

$$\frac{dR(t)}{dt} = \alpha I(t) + \epsilon Q(t) - \mu_1 R(t). \tag{2.5}$$

The model (2.1)–(2.5) satisfy the initial conditions

$$S(\theta) = \psi_1(\theta),\ I(\theta) = \psi_2(\theta),\ Q(\theta) = \psi_3(\theta),\ B(\theta) = \psi_4(\theta),\ R(\theta) = \psi_5(\theta), \tag{2.6}$$

for all $\theta \in [-\tau, 0]$. where $\psi_i(\theta)$, $i = 1,2,3,4,5 \in \mathcal{C}$, the Banach space $\mathcal{C}([-\tau,0],\mathbb{R}^5)$ of continuous functions mapping$[-\tau,0] \to \mathbb{R}^5$, with $\|\psi_i(\theta)\| = \sup_{-\tau\le\theta\le 0} |\psi_i|$, $i = 1,2,3,4,5$. We further assume that $\psi_i(\theta) \ge 0$ for $i = 1,...,5$.

3 Basic properties of the model

In this section, we present results for basic properties of the model such as existence, uniqueness, positivity and boundedness of solution. We also present existence and stability of equilibria.

Theorem 1 *The solution* $(S(t), I(t), Q(t), B(t), R(t))$ *of system* (2.1)–(2.5)*, exists and is bounded for all time* $t \geq 0$ *under the initial conditions* (2.6)*. Moreover, the solution is positive for all* $t > 0$ *and the region*

$$\Omega = \left\{ (S, I, Q, B, R) \in \mathbb{R}^5_+ : S + I + Q + R \leq \frac{A}{\mu_1}, B \leq \frac{K}{\mu_2} \right\}$$

is positive invariant, where $K = \eta \frac{A}{\mu_1}$.

Proof. We first prove that the solution $(S(t), I(t), Q(t), B(t), R(t))$ exists and is unique as shown below.
Let $X(t) = (S(t),\ I(t),\ Q(t),\ R(t),\ B(t))$. The system (2.1)–(2.5), can be written as

$$\frac{dX}{dt} = f(t, X_t),$$

where $X_t(\theta) = X(t + \theta)$, for $\theta \in [-\tau, 0]$, f is Lipschitz in X. It then follows from Theorems 2.1 and 2.3 in [11] that the system (2.1)–(2.5) has a unique solution $(S(t),\ I(t),\ Q(t),\ R(t),\ B(t))$ satisfying the initial data (2.6).

For the positivity of solution $(S(t),\ I(t),\ Q(t),\ R(t),\ B(t))$, we assume that the initial condition in (2.6) hold true, then we prove that $S(t) > 0$, $I(t) > 0$, $R(t) > 0$, $B(t) > 0$ for all time $t \in (0, \infty)$. We proceed by contradiction by assuming that the solution is non-positive. This will implies that the corresponding derivatives are also non-positive (≤ 0). Then there exists a time $t_1 > 0$ such that

$$\min\{S(t_1), I(t_1), R(t_1), B(t_1)\} = 0,$$

and

$$\min\{S(t), I(t), Q(t), R(t), B(t)\} > 0 \text{ for all } \ t \in [0, t_1).$$

If $\min\{S(t_1), I(t_1), Q(t_1), R(t_1), B(t_1)\} = I(t_1) = 0$, then from (2.4),

$$\frac{dB(t)}{dt} \ \geq \ -\mu_2 B(t), \text{ for all } \ t \in [0, \hat{t}],$$

hence

$$B(t_1) \ > \ B(0) \exp(-\mu_2 t_1) > 0,$$

which contradicts our earlier assumption. Hence there is no such time $t_1 > 0$, which implies that $B(t) > 0$ for all $t > 0$.

Similarly, from (2.3), we get

$$\frac{dQ(t)}{dt} \ \geq \ -(\epsilon + \mu_1 + d_2) Q(t), \text{ for all } \ t \in [0, t_1],$$

so that

$$Q(t_1) \ > \ Q(0) \exp(\epsilon + \mu_1 + d_2) t_1 > 0,$$

which also contradicts our earlier assumption. Hence there is no such time $t_1 > 0$, which implies that $Q(t) > 0$ for all $t > 0$.

Suppose also the $\min\{S(t_1), I(t_1), Q(t_1), R(t_1), B(t_1)\} = S(t_1) = 0$, then from (2.2) we have

$$\frac{dI(t)}{dt} \ \geq \ -(d_1 + \mu_1 + \alpha + \delta) I(t), \text{ for all } \ t \in [0, t_1],$$

hence

$$I(t_1) \quad > \quad I(0)\exp((d_1+\mu_1+\alpha+\delta)t_1) > 0.$$

This also contradicts our assumption. Hence there is no such time $t_1 > 0$, hence, $I(t) > 0$ for all $t > 0$. Similar approaches can be followed to show that $S(t)$, $R(t)$ are positive at all time $t > 0$.

Thus, starting with positive initial values, all solutions of the model (2.1)–(2.5) will be positive at all time $t > 0$.

For boundedness of solution, we prove that the total population of humans ($N(t)$) and the pathogen concentration ($B(t)$) at time t are bounded as shown below: Adding equations (2.1)–(2.3) and (2.5) we have

$$\frac{dN(t)}{dt} \leq A - \mu_1 N(t). \tag{3.1}$$

Solving (3.1) we get

$N(t) \leq \frac{A}{\mu_1} + \left[N(0) - \frac{A}{\mu_1}\right] e^{-\mu_1 t}$.
If $N(0) \leq \frac{A}{\mu_1}$, then
$0 \leq N(t) \leq \frac{A}{\mu_1}$.

Furthermore, it follows from equation (2.4) that since $I(t) \leq N(t) \leq \frac{A}{\mu_1}$, it implies that $I(t) \leq \frac{A}{\mu_1}$. Then

$$\frac{dB(t)}{dt} \leq K - \mu_2 B(t) \tag{3.2}$$

Using Gronwall's Inequality [10],

$0 \leq B(t) \leq \frac{K}{\mu_2}$.

This completes the proof of Theorem 1. ■

4 Equilibria points and Stability Analysis

At equilibrium points, $I(t) = I(t-\tau) = I^*$. It is observed that in system (2.1)–(2.5), $R(t)$ appear only in equation (2.4). Therefore, without loss of generality, the dynamics of the system can be considered by dropping (2.5).

To determine equilibria of the system, we set the right hand sides of equations (2.1)–(2.4) to zero. Thus

$$A - \frac{\beta_1 S(t)B(t)}{1+\alpha_1 B(t)} - \frac{\beta_2 S(t)I(t-\tau)e^{-\mu_1\tau}}{1+\alpha_2 I(t-\tau)} - \mu_1 S = 0, \tag{4.1}$$

$$\frac{\beta_1 S(t)B(t)}{1+\alpha_1 B(t)} + \frac{\beta_2 S(t)I(t-\tau)e^{-\mu_1\tau}}{1+\alpha_2 I(t-\tau)} - (d_1+\mu_1+\alpha+\delta)I = 0, \tag{4.2}$$

$$\delta I(t) - (\epsilon+\mu_1+d_1)Q(t) = 0, \tag{4.3}$$

$$\eta I(t) - \mu_2 B(t) = 0. \tag{4.4}$$

From equation (4.4),

$$B^* = \frac{\eta I^*}{\mu_2}. \tag{4.5}$$

Similarly, from (4.3),

$$Q^* = \frac{\delta I^*}{(\epsilon + \mu_1 + d_1)}. \tag{4.6}$$

Substituting (4.5) in (4.2) we have

$$\left[\frac{\beta_1\eta}{\mu_2 + \alpha_1\eta I^*} + \frac{\beta_2 e^{-\mu_1\tau}}{1 + \alpha_2 I^*}\right] S^* I^* - (d_1 + \mu_1 + \alpha + \delta)I^* = 0. \tag{4.7}$$

Adding (4.1) and (4.2) gives

$$S^* = \frac{A - (d_1 + \mu_1 + \alpha + \delta)I^*}{\mu_1}. \tag{4.8}$$

Substituting equation (4.8) into (4.7) we have

$$\left[\left(\frac{\beta_1\eta}{\mu_2 + \alpha_1\eta I^*} + \frac{\beta_2 e^{-\mu_1\tau}}{1 + \alpha_2 I^*}\right)\left(\frac{A - (d_1 + \mu_1 + \alpha + \delta)}{\mu_1}\right)\right] I^* - (d_1 + \mu_1 + \alpha + \delta)I^* = 0. \tag{4.9}$$

The trivial case, when $I^* = 0$, give rise to the disease free equilibrium (DFE) denoted by $E_1 = (S^0, I^0, Q^0, B^0)$ given by,

$$E_1 = \left(\frac{A}{\mu_1}, 0, 0, 0\right). \tag{4.10}$$

.

However, for non trivial solution, ($I^* \neq 0$), we get

$$\left[\frac{\beta_1\eta}{\mu_2 + \alpha_1\eta I^*} + \frac{\beta_2 e^{-\mu_1\tau}}{1 + \alpha_2 I^*}\right]\left[\frac{A - (d_1 + \mu_1 + \alpha + \delta)I^*}{\mu_1}\right] - (d_1 + \mu_1 + \alpha + \delta) = 0 \tag{4.11}$$

.

After simplifying equation (4.11), we obtain the following quadratic equation in I^*.

$$C_1(I^*)^2 + C_2 I^* + C_3 \quad = 0, \tag{4.12}$$

where $C_1 = [(\beta_1\alpha_2\eta + \beta_2\alpha_1\eta)(d_1 + \mu_1 + \alpha + \delta) + \alpha_1\alpha_2\eta\mu_1(d_1 + \mu_1 + \alpha + \delta)]$,
$C_2 = [(\beta_1\eta + \beta_2\mu_2)(d_1 + \mu_1 + \alpha + \delta) + (\mu_2\alpha_2 + \alpha_1\eta)(d_1 + \mu_1 + \alpha + \delta)\mu_1 - (\beta_1\alpha_2\eta + \beta_2\alpha_1\eta)A]$, and
$C_3 = -\mu_1\mu_2(d_1 + \mu_1 + \alpha + \delta)[\mathcal{R}_q - 1]$.

Here, we define

$$\mathcal{R}_q = \frac{A(\beta_1\eta + \beta_2\mu_2 e^{-\mu_1\tau})}{\mu_1\mu_2(d_1 + \mu_1 + \alpha + \delta)}, \tag{4.13}$$

to be the control reproduction number. The basic control reproduction number is defined as the expected number of secondary cases produced by introducing one infected person and cholera pathogens in a completely susceptible population in the presence of intervention. $\mathcal{R}_q$ can also be calculated using the next infection operator matrix as shown in [36, 37],

From (4.12), it can be observed that $C_1 > 0$, and $C_3 < 0$ if $\mathcal{R}_q > 1$, while C_2 can be > 0 or < 0. Therefore, irrespective of the sign of C_2, equation (4.12) will admit a unique positive endemic equilibrium in I^*.

Therefore, the endemic equilibrium (EE) is given by

$$E_2 = (S^*, I^*, Q^*, B^*),$$

where

$$S^* = \frac{(d_1+\mu_1+\alpha+\delta)}{\left[\frac{\beta_1\eta}{\mu_2+\alpha_1\eta I^*}+\frac{\beta_2 e^{-\mu_1\tau}}{1+\alpha_2 I^*}\right]},\ Q^* = \frac{\delta I^*}{(\epsilon+\mu_1+d_2)},\ B^* = \frac{\eta I^*}{\mu_2},$$

with I^* the unique positive root of equation (4.12). Thus the endemic equilibrium exists whenever $\mathcal{R}_q > 1$.

In order to study the stability of equilibria, we first linearize the system (2.1)–(2.4) about an arbitrary equilibrium to have,

$$\frac{dZ}{dt} = J_1 Z(t) + J_2 Z(t-\tau), \tag{4.14}$$

where $Z(t) = (S(t), I(t), Q(t), B(t))^T$ is a vector while J_1 and J_2 are the Jacobian matrices of the system given as

$$J_1 = \begin{pmatrix} -\frac{\beta_1 B(t)}{1+\alpha_1 B(t)} - \frac{\beta_2 I(t-\tau)e^{-\mu_1\tau}}{1+\alpha_2 I(t-\tau)} - \mu_1 & 0 & 0 & \frac{\alpha_1\beta_1 S(t)B(t) - (1+\alpha_1 B(t))\beta_1 S(t)}{(1+\alpha_1 B(t))^2} \\ \frac{\beta_1 B(t)}{1+\alpha_1 B(t)} + \frac{\beta_2 I(t-\tau)e^{-\mu_1\tau}}{1+\alpha_2 I(t-\tau)} & -(d_1+\mu_1+\alpha+\delta) & 0 & 0 \\ 0 & \delta & -(d_2+\mu_1+\epsilon) & 0 \\ 0 & \eta & 0 & -\mu_2 \end{pmatrix},$$

$$J_2 = \begin{pmatrix} 0 & \frac{\alpha_2\beta_2 S(t)I(t-\tau)e^{-\mu_1\tau} - \beta_2 S(1+\alpha_2 I(t-\tau)e^{-\mu_1\tau})}{(1+\alpha_2 I(t-\tau))^2} & 0 & 0 \\ 0 & \frac{\beta_2 S(1+\alpha_2 I(t-\tau)e^{-\mu_1\tau}) - \alpha_2\beta_2 SI(t-\tau)e^{-\mu_1\tau}}{(1+\alpha_2 I(t-\tau))^2} & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

Assuming a solution of the form

$$Y(t) = \mathbf{c}e^{\lambda t},$$

where $\mathbf{c}$ is a constant vector and λ is a complex eigenvalue.

For a non trivial solution ($ce^{\lambda t} \neq 0$) therefore, we have

$$J_1 + J_2 e^{-\lambda\tau} = 0, \tag{4.15}$$

as the transcendental equation.

4.1 Local stability of disease free equilibrium

To investigate the local stability of DFE E_1, we state and prove the following result.

Theorem 2 *The disease free equilibrium E_1 is absolutely stable if $\mathcal{R}_q < 1$ for all delay $\tau \geq 0$ and unstable otherwise.*

Proof. We substitute the disease free equilibrium E_1 into equation (4.15) to get the corresponding transcendental equation as

$$\begin{aligned} H_1(\lambda) = \quad & (\lambda+\mu_1)(\lambda+d_2+\mu_1+\epsilon)[(\lambda-\beta_2\tfrac{A}{\mu_1}e^{-\lambda\tau}+d_1+\mu_1+\alpha+\delta)(\lambda+\mu_2) \\ & -\eta\beta_1\tfrac{A}{\mu_1})] = 0. \end{aligned} \tag{4.16}$$

Clearly, H_1 has two negative real roots. Thus,

$\lambda_1 = -\mu_1$ and $\lambda_2 = -(d_2+\mu_1+\epsilon)$. Hence we concentrate on the remaining part of (4.16) defined by,

$$\begin{aligned} H_2(\lambda) = \lambda^2 &+ (d_1+\mu_1+\alpha+\delta+\mu_2-\beta_2\frac{A}{\mu_1}e^{-\lambda\tau})\lambda + (d_1+\mu_1+\alpha+\delta \\ &- \beta_2\frac{A}{\mu_1}e^{-\lambda\tau})\mu_2 - \eta\beta_1\frac{A}{\mu_1}. \end{aligned} \tag{4.17}$$

Assume $\tau = 0$. From (4.17) we have

$$\begin{aligned} H_2(\lambda) =& \lambda^2 + (d_1+\mu_1+\alpha+\delta+\mu_2-\beta_2\frac{A}{\mu_1})\lambda + (d_1+\mu_1+\alpha+\delta-\beta_2\frac{A}{\mu_1})\mu_2 - \eta\beta_1\frac{A}{\mu_1} \\ =& \lambda^2 + \lambda\left[d_1+\mu_1+\alpha+\delta+\mu_2-\frac{\beta_2\mu_2(d_1+\mu_1+\alpha+\delta)\mathcal{R}_q}{\beta_1\eta+\beta_2\mu_2}\right] \\ &+ \mu_2(d_1+\mu_1+\alpha+\delta)[1-\mathcal{R}_q] \\ =& \lambda^2 + \lambda\left[\mu_2+(d_1+\mu_1+\alpha+\delta)(1-\frac{\beta_2\mu_2\mathcal{R}_q}{\beta_1\eta+\beta_2\mu_2}\right] + \mu_2(d_1+\mu_1+\alpha+\delta)[1-\mathcal{R}_q]. \end{aligned}$$

This implies that, when $\mathcal{R}_q < 1$, the coefficient of λ and the constant term are positive. Therefore, by Descarte's rule of signs, $H_2(\lambda)$ has no positive real roots. Hence, $H_2(\lambda)$ is stable when $\tau = 0$.

If $\tau \neq 0$, then from (4.17), and substituting $\lambda = iy$ to be a root, where $y \in \mathbb{R}_+$, we have

$$\begin{aligned} F_1(y) = y^4 &+ \left[(d_1+\mu_1+\mu_2+\alpha+\delta)+\beta_2\frac{A}{\mu_1}\right]\left[\mu_2+(d_1+\mu_1+\alpha+\delta)(1-\frac{\beta_2\mu_2R_q}{\beta_1\eta+\beta_2\mu_2}\right]y^2 \\ &+ \left[(d_1+\mu_1+\alpha+\delta)\mu_1\mu_2+A(\eta\beta_1+\mu_2\beta_2)\right](d_1+\mu_1+\alpha+\delta)\mu_1\mu_2\left[1-R_q\right]. \end{aligned}$$

Thus, when $\mathcal{R}_q < 1$, the coefficient of y^2 and the constant term are positive. Therefore, by the application of Descarte's rule of sign, $F_1(y) = 0$ has no positive real root and there is no $y \in \mathbb{R}_+$ such that $\lambda = iy$ can be a root of $F_1(y)$. Hence, the disease free equilibrium E_1 is absolutely stable when $\mathcal{R}_q < 1$ and unstable otherwise. ■

4.2 Global stability of disease free equilibrium

In order to be certain about the eradication of cholera irrespective of the initial population started with, we prove the global attractiveness of the DFE as shown below.

Theorem 3 *The DFE E_1 is globally asymptotically stable for all delay $\tau \geq 0$ when $\mathcal{R}_q < 1$ and unstable otherwise.*

Proof. We assume a continuously differentiable Lyapunov function

$$V = \mu_2\eta I + \mu_2(d_1 + \mu_1 + \alpha + \delta)B. \tag{4.18}$$

Differentiating equation (4.18) along the solution of model (2.1)–(2.5), we have

$$V' = \mu_2\eta I' + \mu_2(d_1 + \mu_1 + \alpha + \delta)B'. \tag{4.19}$$

Substituting I', B' in (4.19) we get

$$\begin{aligned} V' =& \mu_2\eta\left[\frac{\beta_1 SB}{1+\alpha_1 B} + \frac{\beta_2 SIe^{-\mu_1\tau}}{1+\alpha_2 I} - (d_1+\mu_1+\alpha+\delta)I\right] + \mu_2(d_1+\mu_1+\alpha+\delta)\left[\eta I - \mu_2 B\right], \\ =& \frac{\mu_2\eta\beta_1 SB}{1+\alpha_1 B} + \frac{\mu_2\eta\beta_2 SIe^{-\mu_1\tau}}{1+\alpha_2 I} - \mu_2^2(d_1+\mu_1+\alpha+\delta)B. \end{aligned}$$

From Theorem 1, $I(t) \leq \frac{A}{\mu_1}$, $S(t) \leq \frac{A}{\mu_1}$ and $B \leq \frac{\eta A}{\mu_1\mu_2}$, thus

$$\begin{aligned} V' \leq& \frac{\eta^2\beta_1 AS}{\mu_1} + \frac{\mu_2\eta\beta_2 ASe^{-\mu_1\tau}}{\mu_1} - \frac{\mu_2\eta(d_1+\mu_1+\alpha+\delta)A}{\mu_1}, \\ \leq& \frac{\eta S}{\mu_1}\left(\eta\beta_1 A + \mu_2\beta_2 Ae^{-\mu_1\tau} - \mu_1\mu_2(d_1+\mu_1+\alpha+\delta)I\right) \\ \leq& \eta\mu_2(d_1+\mu_1+\alpha+\delta)S\left[\left(\frac{\eta\beta_1 A + \mu_2\beta_2 Ae^{-\mu_1\tau}}{\mu_1\mu_2(d_1+\mu_1+\alpha+\delta)}\right) - 1\right], \\ \leq& \eta\mu_2(d_1+\mu_1+\alpha+\delta)S\left(\mathcal{R}_q - 1\right). \end{aligned}$$

Thus,

$$V' \leq \eta\mu_2(d_1+\mu_1+\alpha+\delta)S\left(\mathcal{R}_q - 1\right). \tag{4.20}$$

All parameters and variables of the model are non-negative, therefore, $V' \leq 0$ when $\mathcal{R}_q < 1$ with equality if and only if $S = \frac{A}{\mu_1}$, $I = B = 0$. Hence, V is a Lyapunov function in the feasible region Ω, and it can easily be shown that E_1 is the largest invariant set in Ω. Hence by Lasalle's Invariance Principle [19], the disease free equilibrium is globally asymptotically stable when $\mathcal{R}_q < 1$ for all $\tau \geq 0$ and unstable if $\mathcal{R}_q > 1$. ■

4.3 Local stability of endemic equilibrium (EE)

Here we establish the local stability of endemic equilibrium point E_2 as follows.

Theorem 4 *The endemic equilibrium E_2, is locally asymptotically stable if $\mathcal{R}_q > 1$ for all $\tau \geq 0$ and unstable otherwise.*

Proof. To investigate the local stability of EE first we substitute E_2 into the Jacobian matrix (4.15) to get the transcendental equation as

$$\begin{aligned} H_3(\lambda) =& (\lambda + K_1 + \mu_1)(\lambda + d_2 + \mu_1 + \epsilon)[(\lambda + K_2e^{-\lambda\tau} + (d_1+\mu_1+\alpha+\delta))(\lambda+\mu_2) \\ &+ \eta K_3] = 0, \end{aligned} \tag{4.21}$$

where

$$\begin{aligned} K_1 &= \frac{\beta_1 B^*}{1+\alpha_1 B^*} + \frac{\beta_2 I^*}{1+\alpha_2 I^*},\ K_2 = \frac{\alpha_2\beta_2 S^* I^* - \beta_2 S^*(1+\alpha_2 I^*)}{(1+\alpha_2 I^*)^2} = -\frac{\beta_2 S^*}{(1+\alpha_2 I^*)^2}, \\ K_3 &= \frac{(1+\alpha_1 B^*)\beta_1 S^* - \alpha_1\beta_1 S^* B^*}{(1+\alpha_1 B^*)^2} = \frac{\beta_1 S^*}{(1+\alpha_1 B^*)^2}. \end{aligned}$$

Clearly, H_3 has two negative real roots: $\lambda_1 = -K_1 - \mu_1 < 0$ and $\lambda_2 = -(d_2 + \mu_1 + \epsilon) < 0$. Therefore, stability of E_2 depends on the remaining part of H_3 defined as

$$\begin{aligned} H_4(\lambda) =& \lambda^2 + (d_1 + \mu_1 + \mu_2 + \alpha + \delta + K_2 e^{-\lambda\tau})\lambda + \mu_2(d_1 + \mu_1 + \alpha + \delta) \\ &+ \mu_2 K_2 e^{\lambda\tau} + \eta K_3. \end{aligned} \tag{4.22}$$

When $\tau = 0$,

$$H_4(\lambda) = \lambda^2 + (d_1 + \mu_1 + \mu_2 + \alpha + \delta + K_2)\lambda + \mu_2(d_1 + \mu_1 + \alpha + \delta) + \mu_2 K_2 + \eta K_3.$$

It can be observed that all the coefficients of H_4 are positive. By Discarte's rule of sign, $H_4(\lambda)$ has no positive real roots, hence, it is stable.

However, when $\tau \neq 0$, using Theorem (1) in [6], and letting $\lambda = iy$ for $y \in \mathbb{R}_+$ as a root of H_4, we have

$$\begin{aligned} F_2(y) = y^4 &+ \left[(d_1 + \mu_1 + \mu_2 + \alpha + \delta) + \frac{\beta_2 S^*}{(1+\alpha_2 I^*)^2}\right]\left[(d_1 + \mu_1 + \mu_2 + \alpha + \delta) + K_2\right] y^2 \\ &+ \left[(d_1 + \mu_1 + \alpha + \delta)\mu_2 + \left[\frac{\eta\beta_1}{(1+\alpha_1 B^*)^2} + \frac{\mu_2\beta_2}{(1+\alpha_2 I^*)^2}\right] S^*\right] \\ &\left[(d_1 + \mu_1 + \alpha + \delta)\mu_2 + \left[\frac{\eta\beta_1}{(1+\alpha_1 B^*)^2} - \frac{\mu_2\beta_2}{(1+\alpha_2 I^*)^2}\right] S^*\right]. \end{aligned}$$

Whenever, $\mathcal{R}_q > 1$, the coefficient of y^2 and the constant term are positive values. Therefore, by the application of Descarte's rule of sign, $F_2(y) = 0$ has no positive real root. Therefore there is no $y \in \mathbb{R}_+$ such that $\lambda = iy$ can be a root of $F_2(y) = 0$. Hence, the endemic equilibrium E_2 is locally asymptotically stable when $\mathcal{R}_q > 1$ for all $\tau \geq 0$ and unstable otherwise. ■

4.4 Global stability of endemic equilibrium

In this section the global asymptotic stability for the endemic equilibrium E_2 is shown. This result will present the conditions for existence of endemic cholera in the population irrespective of initial populations started with.

Theorem 5 *If $\mathcal{R}_q > 1$, the endemic equilibrium E_2 is globally asymptotically stable for all delay $\tau \geq 0$ and unstable otherwise.*

Proof. Considering equations (2.1)–(2.4) of the model, it is observed that, equation (2.4) is independent of the other equations, hence can be drop. At equilibrium, from equations (2.1)–

(2.3), we have

$$A = \frac{\beta_1 S^* B^*}{1+\alpha_1 B^*} + \frac{\beta_2 S^* I^* e^{-\mu_1 \tau}}{1+\alpha_2 I^*} + \mu_1 S^*, \tag{4.23}$$

$$(d_1+\mu_1+\alpha+\delta) = \frac{1}{I^*}\left[\frac{\beta_1 S^* B^*}{1+\alpha_1 B^*} + \frac{\beta_2 S^* I^* e^{-\mu_1 \tau}}{1+\alpha_2 I^*}\right], \tag{4.24}$$

$$\eta = \frac{\mu_2 B^*}{I^*}. \tag{4.25}$$

We follow the approach in [22] and define a Lyapunov function as

$$\mathcal{F} = (S - S^* \ln S) + G(I - I^* \ln I) + H(B - B^* \ln B) \tag{4.26}$$

By definition $\mathcal{F} > 0$, where G and H are positive constants to be determined.

Differentiating $\mathcal{F}$ along the solution curves of the model, we have

$$\begin{aligned}
\mathcal{F}' &= \left(1-\frac{S^*}{S}\right)S' + G\left(1-\frac{I^*}{I}\right)I' + H\left(1-\frac{B^*}{B}\right)B' \\
&= \left(1-\frac{S^*}{S}\right)\left[A - \frac{\beta_1 SB}{1+\alpha_1 B} - \frac{\beta_2 SIe^{-\mu_1\tau}}{1+\alpha_2 I} - \mu_1 S\right] \\
&\quad + G\left(1-\frac{I^*}{I}\right)\left[\frac{\beta_1 SB}{1+\alpha_1 B} + \frac{\beta_2 SIe^{-\mu_1\tau}}{1+\alpha_2 I} - (d_1+\mu_1+\alpha+\delta)I\right] \\
&\quad + H\left(1-\frac{B^*}{B}\right)\left[\eta I - \mu_2 B\right].
\end{aligned}$$

Substituting equations (4.23)–(4.25) in $\mathcal{F}'$, we have

$$\begin{aligned}
\mathcal{F}' &= \left(1-\frac{S^*}{S}\right)\left[\frac{\beta_1 S^* B^*}{1+\alpha_1 B^*} + \frac{\beta_2 S^* I^* e^{-\mu_1\tau}}{1+\alpha_2 I^*)} + \mu_1 S^* - \frac{\beta_1 SB}{1+\alpha_1 B} - \frac{\beta_2 SIe^{-\mu_1\tau}}{1+\alpha_2 I} - \mu_1 S\right] \\
&\quad + G\left(1-\frac{I^*}{I}\right)\left[\frac{\beta_1 SB}{1+\alpha_1 B} + \frac{\beta_2 SIe^{-\mu_1\tau}}{1+\alpha_2 I} - \frac{I}{I^*}\left[\frac{\beta_1 S^* B^*}{1+\alpha_1 B^*} + \frac{\beta_2 S^* I^* e^{-\mu_1\tau}}{1+\alpha_2 I^*}\right]\right] \\
&\quad + H\left(1-\frac{B^*}{B}\right)\left[\frac{\mu_2 B^* I}{I^*} - \mu_2 B\right], \\
&= \left(1-\frac{S^*}{S}\right)\mu_1(S^*-S) + \left(1-\frac{S^*}{S}\right)\left[\frac{\beta_1 S^* B^*}{1+\alpha_1 B^*}\right] + \left(1-\frac{S^*}{S}\right)\left[\frac{\beta_2 S^* I^* e^{-\mu_1\tau}}{1+\alpha_2 I^*)}\right] \\
&\quad - \left(1-\frac{S^*}{S}\right)\left[\frac{\beta_1 SB}{1+\alpha_1 B}\right] - \left(1-\frac{S^*}{S}\right)\left[\frac{\beta_2 SIe^{-\mu_1\tau}}{1+\alpha_2 I} - \mu_1 S\right] + G\left(1-\frac{I^*}{I}\right)\left[\frac{\beta_1 SB}{1+\alpha_1 B}\right] \\
&\quad + G\left(1-\frac{I^*}{I}\right)\left[\frac{\beta_2 SIe^{-\mu_1\tau}}{1+\alpha_2 I}\right] - G(\frac{I}{I^*}-1)\left[\frac{\beta_1 S^* B^*}{1+\alpha_1 B^*}\right] - G(\frac{I}{I^*}-1)\left[\frac{\beta_2 S^* I^* e^{-\mu_1\tau}}{1+\alpha_2 I^*}\right] \\
&\quad + H\mu_2 B^*\left(1-\frac{B^*}{B}\right)\left[\frac{I}{I^*} - \frac{B}{B^*}\right], \\
&= -\mu_1\frac{(S-S^*)^2}{S} + \frac{\beta_1 S^* B^*}{1+\alpha_1 B^*}\left[\left(1-\frac{S^*}{S}\right) - G\left(\frac{I}{I^*}-1\right)\right] \\
&\quad + \frac{\beta_1 S^* B^*}{1+\alpha_1 B}\left[G\left(1-\frac{I^*}{I}\right)\frac{SB}{S^*B^*} - \left(1-\frac{S^*}{S}\right)\frac{SB}{S^*B^*}\right] + \frac{\beta_2 S^* I^* e^{-\mu_1\tau}}{1+\alpha_2 I^*}\left[\left(1-\frac{S^*}{S}\right) - G\left(\frac{I}{I^*}-1\right)\right] \\
&\quad + \frac{\beta_2 S^* I^* e^{-\mu_1\tau}}{1+\alpha_2 I}\left[G\left(1-\frac{I^*}{I}\right)\frac{SI}{S^*I^*} - \left(1-\frac{S^*}{S}\right)\frac{SI}{S^*I^*}\right] + H\mu_2 B^*\left(1-\frac{B^*}{B}\right)\left[\frac{I}{I^*} - \frac{B}{B^*}\right],
\end{aligned}$$

Let $x = \frac{S}{S^*}$, $y = \frac{B}{B^*}$, $z = \frac{I}{I^*}$ *and* $\beta_1 = \beta_2 = \beta$, such that

$$\begin{aligned}\mathcal{F}' =& -\mu_1\frac{(S-S^*)^2}{S} + \frac{\beta S^*B^*}{1+\alpha_1 B^*}\left[(1-\frac{1}{x}) - G(z-1)\right]\\ &+ \frac{\beta S^*B^*}{1+\alpha_1 B}\left[G(1-\frac{1}{z})xy - (1-\frac{1}{x})xy\right] + \frac{\beta S^*I^*e^{-\mu_1\tau}}{1+\alpha_2 I^*}\left[(1-\frac{1}{x}) - G(z-1)\right]\\ &+ \frac{\beta S^*I^*e^{-\mu_1\tau}}{1+\alpha_2 I}\left[G(1-\frac{1}{z})xz - (1-\frac{1}{x})xz\right] + H\mu_2 B^*(1-\frac{1}{y})(z-y),\end{aligned}$$

Now,

$$\mathcal{F}' = -\mu_1\frac{(S-S^*)^2}{S} + f(x,y,z,\beta), \tag{4.27}$$

where,

$$\begin{aligned}f(x,y,z,\beta) =& \frac{\beta S^*B^*}{1+\alpha_1 B^*}\left[(1-\frac{1}{x}) - G(z-1)\right] + \frac{\beta S^*B^*}{1+\alpha_1 B}\left[G(1-\frac{1}{z})xy - (1-\frac{1}{x})xy\right]\\ &+ \frac{\beta S^*I^*e^{-\mu_1\tau}}{1+\alpha_2 I^*}\left[(1-\frac{1}{x}) - G(z-1)\right] + \frac{\beta S^*I^*e^{-\mu_1\tau}}{1+\alpha_2 I}\left[G(1-\frac{1}{z})xz - (1-\frac{1}{x})xz\right]\\ &+ H\mu_2 B^*(1-\frac{1}{y})(z-y),\\ =& \frac{\beta S^*B^*}{1+\alpha_1 B^*}\left[(1-\frac{1}{x}) - G(z-1)\right] + \frac{\beta S^*B^*}{1+\alpha_1 B}\left[G(1-\frac{1}{z})xy - xy + y\right]\\ &+ \frac{\beta S^*I^*e^{-\mu_1\tau}}{1+\alpha_2 I^*}\left[(1-\frac{1}{x}) - G(z-1)\right] + \frac{\beta S^*I^*e^{-\mu_1\tau}}{1+\alpha_2 I}\left[G(1-\frac{1}{z})xz - xz + z\right]\\ &+ H\mu_2 B^*(1+z-y-\frac{z}{y}).\end{aligned}$$

Now, we can choose the values of G and H such that f is non-positive for all $x, y, z \in \mathbb{R}_+$. Assume $G = 1 \quad$ and $\quad H = \frac{1}{\mu_2 B^*}$, then

$$\begin{aligned}f(x,y,z,\beta) =& (2-\frac{1}{x}-z)\beta S^*\left[\frac{B^*}{1+\alpha_1 B^*} + \frac{I^*e^{-\mu_1\tau}}{1+\alpha_2 I^*}\right] + \beta S^*\left[\frac{B^*}{1+\alpha_1 B}(y-\frac{xy}{z}) + \frac{I^*e^{-\mu_1\tau}}{1+\alpha_2 I}(z-x)\right]\\ &+ (1+z-y-\frac{z}{y})\end{aligned} \tag{4.28}$$

Substituting $x = z = 1$ in equation (4.28) implies that

$$f(x,y,z,\beta) = (1+z-y-\frac{z}{y}),$$

which show that $f(x,y,z,\beta) \leq 0$ by the arithmetic mean - geometric mean inequality, and with equality to zero if $y = z = 1$.
Thus, $\mathcal{F} \leq 0$, with equality if and only if $S = S^*$. Hence, $\mathcal{F}$ is a Lyapunov function and it can also be shown that the largest invariant set in Ω is E_2. Thus by LaSalle's Invariance Principle, the endemic equilibrium is globally asymptotically stable for all $\tau \geq 0$ when $\mathcal{R}_q > 1$ and unstable otherwise. ■

5 Analysis for the effect of time delay

In this section, we will investigate the effect of delay (increase or decrease) on the infectivity of cholera in a population. To start with, we use the unique threshold quantity of the model

(control reproduction number, $\mathcal{R}_q$). The idea is to determine a critical delay value above (below) which the number of infected individuals will decrease (increase).

Since $\mathcal{R}_q = 1$ is a bifurcation parameter point where stability changes, we consider it a threshold value for infection and determine the critical delay as follows:

$$\begin{aligned}
&\frac{A(\eta\beta_1 + \mu_2\beta_2 e^{-\mu_1\tau})}{\mu_1\mu_2(d_1+\mu_1+\alpha+\delta)} = 1\\
&A(\eta\beta_1 + \mu_2\beta_2 e^{-\mu_1\tau}) = \mu_1\mu_2(d_1+\mu_1+\alpha+\delta),\\
&\mu_2\beta_2 e^{-\mu_1\tau} = \frac{\mu_1\mu_2(d_1+\mu_1+\alpha+\delta)}{A} - \eta\beta_1,\\
&e^{-\mu_1\tau} = \frac{\mu_1\mu_2(d_1+\mu_1+\alpha+\delta)}{A\mu_2\beta_2} - \frac{\eta\beta_1}{\mu_2\beta_2}.
\end{aligned}$$

Thus, solving for τ, we get the critical delay as

$$\tau_{crit} = \frac{ln\left[\frac{1}{\mu_2\beta_2}\left(\frac{\mu_1\mu_2(d_1+\mu_1+\alpha+\delta)}{A} - \eta\beta_1\right)\right]}{-\mu_1}. \tag{5.1}$$

To determine the nature of (4.13) as either increasing or decreasing, we differentiate it with respect to time delay parameter (τ).

$$\begin{aligned}
\frac{\partial R_q}{\partial\tau} &= \frac{\partial}{\partial\tau}\left[\frac{A(\eta\beta_1 + \mu_2\beta_2 e^{-\mu_1\tau})}{\mu_1\mu_2(d_1+\mu_1+\alpha+\delta)}\right]\\
&= \frac{\partial}{\partial\tau}\left[\frac{A\eta\beta_1}{\mu_1\mu_2(d_1+\mu_1+\alpha+\delta)}\right] + \frac{\partial}{\partial\tau}\left[\frac{A\mu_2\beta_2 e^{-\mu_1\tau}}{\mu_1\mu_2(d_1+\mu_1+\alpha+\delta)}\right]\\
&= -\left[\frac{A\beta_2 e^{-\mu_1\tau}}{(d_1+\mu_1+\alpha+\delta)}\right].
\end{aligned}$$

The negative sign of the derivative above, implies that, increasing time delay beyond the critical delay τ_{crit} with fixed values of all parameters involved will lead to the decrease in number of infectious individuals. Hence, this indicates that time delay has effect on the infectivity of cholera in the population. This result can be summarized as follows.

Proposition 6 *The increase (decrease) of time delay in the model* (2.1)–(2.5) *will reduce (increase) the infectivity of cholera whenever the delay is greater than the threshold value* τ_{crit}.

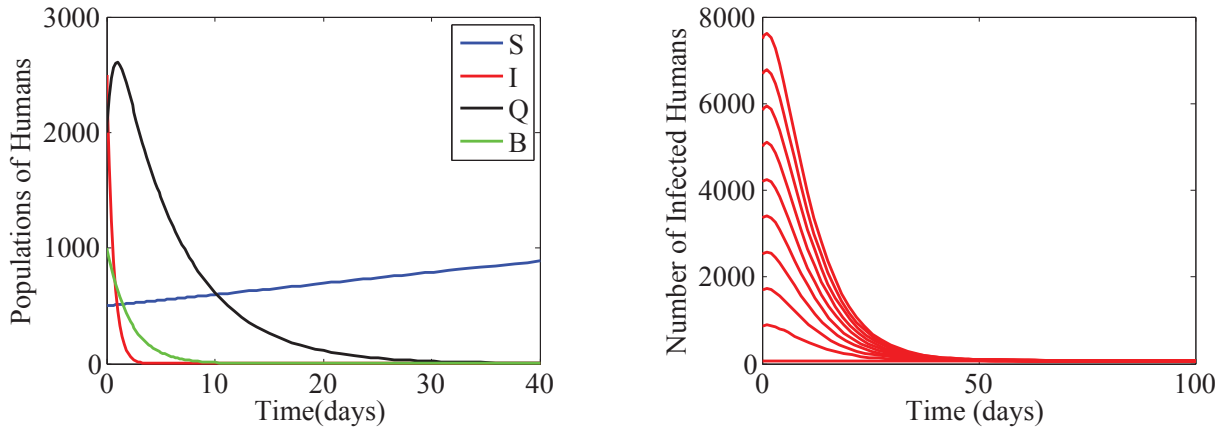
6 Numerical simulations

In this section, numerical simulations are conducted using MATLAB (R2014a) to illustrate the theoretical results proved in the previous sections, the effects of time delay and quarantine in the model. Parameter values from Table 2 are used as obtained from literature and some reasonable estimates.

Figure 2(a) illustrates that, starting with initial population close to disease free equilibrium E_1, the population will remain healthy as time progress (irrespective of the length of delay), this implies that E_1 is locally asymptotically stable as proved in Theorem 2. In Figure 2(b), it is shown that, irrespective of the initial population started with, the population will remain healthy as time progresses, the equilibrium E_1 is globally asymptotically stable as indicated in Theorem 5. In both Figures 2(a) and (b), the values of basic control reproductive number $\mathcal{R}_q$, are 0.8725 and 0.5412, (< 1) respectively for any value of τ.

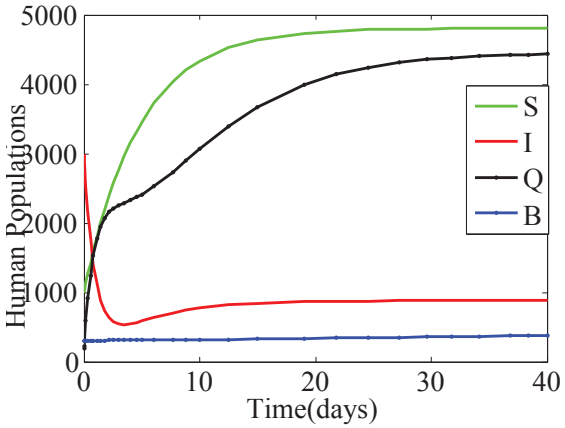
Parameter	Value	Unit	Reference
A	100	day^{-1}	Assumed
μ_1	0.000046	day^{-1}	$(WHO)(2016)$
μ_2	0.00046	day^{-1}	$(WHO)(2016)$
β_1	0.0000012	$individual^{-1}day^{-1}$	[28]
β_2	0.0000012	$individual^{-1}\ day^{-1}$	[28]
d_1	0.4	day^{-1}	[28]
d_2	0.2	day^{-1}	[28]
δ	0.0085	day^{-1}	[28]
α	0.0085	day^{-1}	[1]
ϵ	0.05	day^{-1}	[1]
η	0.036	$cellml^{-1}day^{-1}individual^{-1}$	Assumed
α_1	0.056	day^{-1}	Assumed
α_2	0.06	day^{-1}	Assumed

Table 2: Numerical values for Parameters of the model



(a) (b)

Figure 2: Numerical simulations showing (a) local and (b) global asymptotic stability of disease free equilibrium E_1 using parameter values in Table 2, except for $\tau = 3$, 10 respectively.



(a)

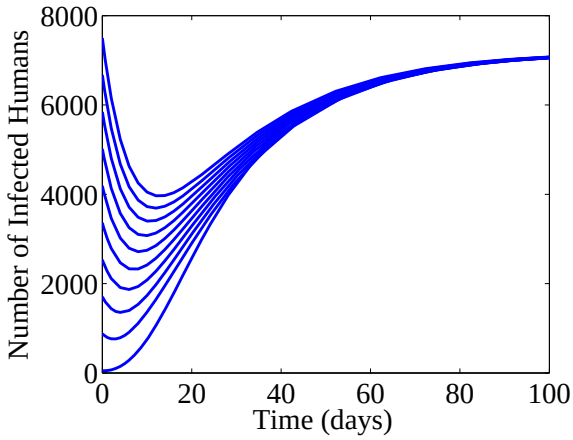
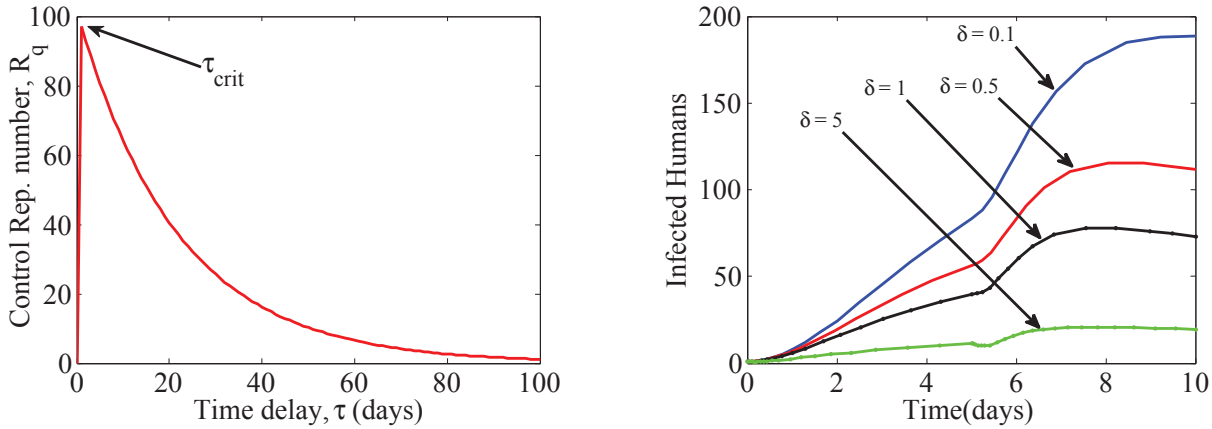


Figure 3: Numerical simulations showing (a) local and (b) global asymptotic stability of endemic equilibrium E_2 using parameter values from Table 2, except for $\beta_1 = 0.00012 = \beta_2$, $\tau = 3, 5$.



(a) (b)

Figure 4: Numerical simulations showing impacts of (a) time delay as a function of $\mathcal{R}_q$ and (b) quarantine on the model using parameter values from Table 2 with δ values as indicated.

The asymptotic stabilities of endemic equilibrium E_2 are shown in Figures 3 (a) and (b). It can be seen in Figure 3(a) that with initial data close to the endemic equilibrium and parameter values in Table 2, the subpopulations of human converge to E_2 asymptotically. Using $\beta_1 = 0.00012 = \beta_2$, $\tau = 3$, the value of $\mathcal{R}_q = 3.4175 > 1$. This illustrates the result in Theorem 4. Similarly, in Figure 3 (b), the global attractiveness of E_2 is shown as proved in Theorem 5. With parameter values from Table 2 except for $\beta_1 = 0.00012 = \beta_2$, $\tau = 10$, using different initial values, so that $\mathcal{R}_q = 2.8317 > 1$.

In Figure 4 (a), the control reproduction number $\mathcal{R}_q$ is plotted as a function of time delay to illustrates its impact on the infectivity of cholera in the population. It can be seen from the figure that initially $\mathcal{R}_q$ increases with increase in the time delay before τ_{crit} is reached. However, after passing τ_{crit}, as time delay τ increases, the value of $\mathcal{R}_q$ decreases drastically as stated in Preposition 6. This result tallies with the ones in [25, 31]. Similarly, the impact of quarantine is illustrated in Figure 4 (b). As shown in the figure, number of infected people decreases with increase in the quarantine rate δ.

7 Conclusion

A deterministic time delay Cholera model with quarantine as control strategy is formulated and analyzed. The main objectives are to investigate the effects of quarantine and time delay on the model with Holling type II incidence functional. The main results are summarized as follows:

(i) Basic properties of the model are proved and a Threshold quantity (Control Reproduction Number) $\mathcal{R}_q$ is obtained.

(ii) The model has a unique disease free equilibrium E_1, which is absolutely and globally asymptotically stable when $\mathcal{R}_q < 1$ for all delay $\tau \geq 0$. This result indicates that cholera

can be eradicated in the population whenever basic control reproduction number is brought and kept below unity.

(iii) When $\mathcal{R}_q > 1$, there exist an endemic equilibrium E_2, which is shown to be locally and globally asymptotically stable for all delay $\tau \geq 0$. This indicates that cholera will persists in the population.

(iv) Although time delay has no effect on the qualitative dynamics of the model, it however have effect on the disease burden whenever the time delay is above a threshold value (the critical delay value τ_{crit}).

(v) Quarantine intervention is also found to reduce the infectivity of cholera by increasing the quarantine rate. Indeed, cholera can be eradicated when at least 80% of infected individuals are quarantined in the given population.

(vi) Numerical simulations are used to illustrate our theoretical and numerical results.

In future work, we would like to investigate additional control strategies such as pulse vaccination for speedy eradication of cholera. Double patch model for the transmission of cholera with time delay would also be considered to investigate the effect of time delay in the presence of movement of individuals from one patch to another during epidemic.

Disclosure statement

The authors hereby declare that there is no conflicts of interest whatsoever.

References

[1] T. Berge, S. Bowong and J. M. S. Lubuma, Global stability of a two patch cholera model with fast and slow transmissions, Maths. and Computer in simulation, **133** 142–164 (2017).

[2] E. Beretta and Y. Kuang, Geometric Stability switch criteria in delay differential system with delay dependent parameters, SIANJ, Math. Anal. **13** 1144 - 1165 (2002).

[3] F. Brauer and C. Castillo-Chavez, Mathematical Models in Population Biology and Epidemiology, Vol. 2. New York: Springer, 2012.

[4] L. Cai, C. Modnak, J. Wang, An age-structured model for cholera control with vaccination, Applied Mathematics and Computation **299** 127–140 (2017)

[5] C. T. Codeco, Endemic and epidemic dynamics of cholera: the role of the aquatic reservoir, BMC Infec. Dis. **1** (1) 1–14 (2001).

[6] K. L. Cooke and P. van den Driesche, On Zeroes of Some Transcendental Equations, Funkcielaj Ekvacioj, **29** 77–90 (1986).

[7] A. De*á*nes, A. B. Gumel, Modeling the impact of quarantine during an outbreak of Ebola virus disease, Infectious Disease Modelling **4** 12–27 (2019).

[8] J. Dhar, A. K. Sharma, The role of viral infection in phytoplankton dynamics with the inclusion of incubation class, Nonlinear Analysis Hybrid Syst. **4** 9–15 (2010).

[9] B. Gontijor and L. de-Carvalho Mde, American Cutaneous Leishmaniasis, Rev. Soc. Bras. Med. Trop. **36** (1) 71–80 (2003).

[10] T. H. Gronwall, Note on the derivatives with respect to a parameter of the solutions of a system of differential equations, *Anal. Math.* 292–296 (1919).

[11] J. K. Hale and S. M. Verduyn Lunel, Introduction to Functional Differential Equations, Springer-Verlag New York Inc, 1993.

[12] D. M. Hartley1, J. G. Morris Jr.1, D. L. Smith, Hyperinfectivity: A Critical Element in the Ability of *V. cholerae* to Cause Epidemics?, PLoS Medicine **3** (1) 0063–0069 (2006).

[13] A. S. Hassan, Dynamical analysis and consistent numerics for a delayed model of viral infection in phytoplankton population, Afrika Mathematika, **29** (1 - 2), 277–294 (2018).

[14] A. S. Hassan and N. Hussaini, Analysis of an HIV - HCV simultaneous infection model with time delay, J. Nig. Soc. Phys. Sci., **3**, 1–11, 2021.

[15] M. W. Hirsch, and S. Smale, Differential Equations, Dynamical Systems, and Linear Algebra, Acad. Press, New York, (1974).

[16] G. Huang and Y. Takeuchi, Global analysis on delay epidemiological dynamic mode with nonlinear incidence, Journal of Mathematical Biology, **63** (1) 125–139 (2011).

[17] A. Kaddar, Stability analysis in a delayed SIR epidemic model with a saturated incidence rate, Nonlinear Analysis: Modelling and Control, **15** (3) 299–306, (2010).

[18] Y. Kuang, Delay differential equations with application in population dynamics, Mathematics in Science and Engineering, **191**, Arizona, 1993.

[19] J. P. LaSalle, The Stability of Dynamical Systems, Regional Conference Series in Applied Mathematics, SIAM, Philadelphia, 1976.

[20] A. P. Lemos-Paião, C. J. Silva, D. F. M. Torres, An epidemic model for cholera with optimal control treatment, Journal of Computational and Applied Mathematics, **318** 168–180 (2017).

[21] A. K. Misra, S. N. Mishra, A. L. Pathak, P. Misra, R. Naresh, Modeling the effect of time delay in controlling the carrier dependent infectious disease – Cholera, Applied Mathematics and Computation **218** 11547–11557 (2012).

[22] C. C. Mccluskey, Lyapunov Functions for Turberculosis Models with Fast and Slow Progression. Mathematical Biosciences and Engineering, **3** (4), 603 (2006).

[23] N. Nirwani, V. H. Badshah and R. Khandelwal, SIQR model for transmission of cholera, Advances in Applied Sciences Research, **6** (6) 181–186 (2015).

[24] D. Prasenjit, D. Mukherjee and A. K. Sarkar, Effect of Delay on the model of American Cutaneous Leishmaniasis, Journal of Biological System, **15**(2) 139–147 (2007).

[25] M. A. Safi, A. B. Gumel, The effect of incidence functions on the dynamics of a quarantine/isolation model with time delay, Nonlinear Analysis: Real World Applications **12** 215–235 (2011).

[26] M. A. Safi, D. Y. Melesse, A. B. Gumel, Dynamics Analysis of a Multi-strain Cholera Model with an Imperfect Vaccine, Bulletin of Mathematical Biology, **75**(7), 1104–1137 (2013).

[27] G. Q. Sun, J. H. Xie, S. H. Huang, Z. Jin, M. T. Li, and L. Liu. Transmission dynamics of cholera: Mathematical modeling and control strategies, Communications in Nonlinear Science and Numerical Simulation, **45** 235–244 (2017).

[28] L. Tiantian and Y. Xue, Global Stability Analysis of a Delayed SEIQR Epidemic model with Quarantine and Latent. Applied Mathematics, **4** 109–117 (2013).

[29] United Nations Office for the Coordination of Humanitarian Affairs (UNOCHA) https://www.unocha.org/ (Accessed in March 2018).

[30] X. Wang, D. Gao and J. Wang, Influence of human behavior on cholera dynamics, Mathematical Biosciences, **267** 41–52 (2015).

[31] Y. Wang, J. Wei, Global dynamics of Cholera model with time delay, Int. J. Biomath. **6** (1) 1–18 (2013).

[32] C. Wei and L. Chen, A Delay Model with Pulse Vaccination, Discrete Dynamics in Nature and Society, Article $ID746951, doi$: 10.1155/2008/746951, 1–12 (2008).

[33] WHO :Weekly epidemiological records, August, (2013).

[34] P. Yongzhen, L. Shaoying, G. Shujing, L. Shuping and L. changguo, A delayed SEIQR epidemic model with pulse vaccination and the quarantine measure, Computers and Mathematics with Applications, **58** 135–145 (2009).

[35] Z. Zhang and H. Yang, Hopf Bifurcation of an SIQR Computer Virus Model with Time Delay, Discrete dynamics in nature and society, **2015** 1–8 (2015).

[36] W. Zhen, Z. Xiao-Qiang, Global dynamics of a time-delayed dengue transmission model, Canadian Applied Mathematics Quartelry, **20** (1) 89–114 (2012).

[37] X. Zhiting, Z. Xiao-Qiang, A vector-bias malaria model with incubation period and diffusion, Discrete and Continuous Dynamical Systems - Series B, **17** (7) *doi* : 10.1371/*journal.pone*.0020891 (2012)

[38] X. Zhou, X. Shia, J. Cui, Stability and backward bifurcation on a cholera epidemic model with saturated recovery rate, Mathematical Methods in the Applied Sciences, **40**(4), 1288—1306 (2017).

[39] A. Zilinskas, J. Zilinskas, Adaptation of a one-step worst-case optimal university algorithm of bi-objective Lipschitz optimization to multidimentional problems. Communication in Nonlinear Science and Numerical simulation, **21** (1-3) 89–98 (2015).

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Mathematical model for the introduction of Wolbachia-infected mosquitoes to stop the spread of Yellow Fever

M. C. Anyanwu*and O. F. Anorue†

Abstract

In this paper, we model the use of wolbachia-infected aedes aegypti mosquitoes to control the spread of yellow fever. Yellow fever is spread through bites of infected and uninfected aedes aegypti mosquitoes. The model, which is a system of non-linear ordinary differential equations, describes the transmission dynamics of the disease in the human population, natural aedes aegypti mosquitoes population and wolbachia-infected mosquitoes used for control. The expression for the control reproduction number of the disease is derived through the next generation matrix approach. In the stability analysis, the Gershgorin's theorem is used to obtain the condition under which the disease-free equilibrium is locally asymptotically stable. Also, in the absence of wolbachia-infected mosquitoes, the disease-free equilibrium is locally asymptotically stable if the basic offspring number and the basic reproduction number are less than one. The presented numerical results show that the population of the wolbachia-free aedes aegypti mosquitoes diminishes over time as compared to the population of the wolbachia-infected mosquitoes. These results confirm that the use of wolbachia can be effective in combating the spread of yellow fever.

Keywords: yellow fever; aedes aegypti; wolbachia; offspring number

1 Introduction

Yellow fever, a hemorrhagic fever caused by Flavivirus, family Flaviviridae is primarily transmitted to human through the bite of an infected female aedes aegypti. This mosquito also transmits dengue, chikungunya and zika[8, 9]. The origin of the disease is Africa, from where it spreads to South America through the slave trade in the 17th century[12, 14]. The yellow fever was the first human virus discovered and its family comprises approximately 70 viruses[9, 7], most of which are transmitted through arthropod insects. For those infected, the disease incubates in the first 3-6 days of onset, after which there is abrupt " period of infection " of the intense viremia lasting for 2-4 days (fever, weakness, headache, nausea, muscle pain)[7]. This is followed by a period of remission in which the symptoms reduce and settle and most infected individuals recover at this stage. Thus some 85% of yellow fever infections are asymptomatic and then 15% of patients relapse and move to a "period of intoxication "characterized by abdominal pain, vomiting, jaundice (yellow skin and eyes) and often culminating in death. Recent developments in epidemiological studies have shown that mathematical modeling played a significant role in the fight against infectious diseases and incessant disease outbreaks [6]. However, the control of these diseases can be achieved by acting on the mosquito population and in absence of vaccine or curative treatment, control turns out to be an important tool in the mission of reducing

*Department of Mathematics, Michael Okpara University of Agriculture, Umudike; email: manyanwu71@yahoo.com

†Department of Mathematics, Michael Okpara University of Agriculture, Umudike

transmission. However, the traditional use of insecticides is often excessively expensive and environmentally undesirable and could lead to its resistance [20, 17].
In this work, we model the use of wolbachia bacterium which is a novel, natural and self- sustaining approach to reduce arboviral diseases such as Dengue, zika virus disease, etc, transmitted by aedes aegypti mosquitoes[4]. The symbolic Wolbachia is found naturally in over 60% of insect species, but not in aedes aegypti, which lives in the testes and ovaries of their hosts and is passed from one generation to the next through the eggs of mosquitoes[19]. Thus, they can interfere with the reproductive process of mosquitoes causing phenomena such as cytoplasmic incompatibility (C.I), parthenogenesis and fertilization of genetic males[4]. Appearances of these phenotypes depend on the host species and Wolbachia types. C.I causes uninfected Wolbachia females that mate with the infected Wolbachia males to rarely produce fertile eggs, while infected Wolbachia females are not affected. This gives the infected Wolbachia females an advantage and helps the bacteria to spread quickly through the mosquito population, which effectively block the reproduction of the vector mosquitoes[2].

2 Model Formulation

The mosquito population is made up of the wild(or wolbachia-free) (N) and wolbachia-infected aedes aegypti mosquitoes(W), with the classes Eggs(E_j), adult male mosquitoes(M_i), adult female mosquitoes that are not pregnant(F_i), and pregnant mosquitoes, which are either susceptible mosquitoes, (S_i),the exposed mosquitoes, (E_i) or infectious mosquitoes,(I_i), where $i = N, W$ and $j = 1, 2$. We assume that only the pregnant female mosquitoes bite humans since they need the blood to nourish their eggs after mating. Let $T_i = S_i + E_i + I_i$, be the total female pregnant mosquitoes. We assume that these pregnant mosquitoes lay eggs at the rate α, to produce the quantity of eggs, $\alpha F_i(1 - \frac{E_1+E_2}{K})$, where K is the carrying capacity of the environment. The laid eggs mature to either adult males (M_N) or adult females (F_N) in the numbers, $\epsilon m(1-c)E_1$ and $\epsilon(1-m)(1-c)E_1$, respectively, for wolbachia-free mosquitoes and $\epsilon m E_2$ and $\epsilon(1-m)E_2$, respectively, for adult male and female wolbachia-carrier mosquitoes, where ϵ is the rate of maturity of eggs into adult mosquitoes, m is the proportion of eggs that mature into adult males and c is the proportion of the eggs that are affected by cytoplasmic incompatibility(CI), hence, $(1 - c)$ is the proportion of the eggs that are not affected by CI. We take $c = 0$ for the case of wolbachia-infected mosquitoes, since their eggs are not affected by cytoplasmic incompatibility. The eggs are assumed to die at the rate,μ_0. The adult female mosquitoes comprise the female mosquitoes that have matured from eggs and the ones that migrated into the area at the recruitment level,π_1. The adult uninfected female mosquitoes become susceptible after mating with males of both species of mosquitoes. The process of mating and becoming pregnant is modeled through the expression $\rho F_i \frac{M_N+M_W}{M_N+M_W+M_\Theta}$, where ρ is the mating rate, and M_Θ is the number of male mosquitoes other than aedes aegypti. These male mosquitoes are assumed to interfere in the mating of aedes aegypti mosquitoes. The term $\frac{M_N+M_W}{M_N+M_W+M_\Theta}$ can be regarded as the probability of mating with wild male mosquitoes,M_N or wolbachia-infected males mosquitoes,M_W. Therefore, in the analysis and implementation of the model, we take $\frac{M_N}{M_N+M_W+M_\Theta} = p$ and $\frac{M_W}{M_N+M_W+M_\Theta} = q$ so that $\frac{M_N+M_W}{M_N+M_W+M_\Theta} = p+q$. The susceptible mosquitoes get exposed to the virus when they bite infectious humans at the rates, $b_1\alpha_{HN}$ and $b_1\alpha_{HW}$, respectively for wolbachia-free and wolbachia-carrier mosquitoes, respectively, where b_1 and b_2 are the biting rates of wolbachia-free and wolbachia-carrier mosquitoes, respectively, and α_{HN} and α_{HW} are the transmission probabilities of the virus from infected humans to wolbachia-free and wolbachia-carrier mosquitoes, respectively. The susceptible mosquitoes are also recruited through migration at the rate, π_3. The mosques become infectious at the incubation rates, β_N and β_W for wolbachia-free and wolbachia-carrier mosquitoes, respectively, where, $\beta_W \ll \beta_N$. The infectious mosquitoes remain so until they die naturally at the rate, μ_1. The susceptible class in the human population increases due to recruitment at the level, π_4, and those who

have recovered from the illness at the rate, η. This class decreases due to natural death of humans at the rate, μ_2 and when they are infected with yellow fever through the bites of infected wolbachia-free and wolbachia-carrier mosquitoes at the rates, $b_1\alpha_{NH}$ and $b_2\alpha_{WH}$, respectively, where α_{NH} and α_{WH} are the transmission probabilities of the virus from infected wolbachia-free and wolbachia-carrier mosquitoes, respectively to humans such trhat $\alpha_{WH} \lll \alpha_{NH}$. After contracting the virus, humans become infectious at the expiration of the incubation period, $\frac{1}{\beta_H}$, where, β_H is the incubation rate of the virus in humans. The infected humans are assumed to recover from the disease at the rate, γ. while the disease-induced death occurs at the rate, δ. The associated system of ordinary differential equations based on the interactions amongst the three populations is given by

$$\begin{aligned}
\frac{dE_1}{dt} &= \alpha T_N\left(1-\frac{E_1+E_2}{K}\right)-\epsilon(1-c)(1-m)E_1-\epsilon m(1-c)E_1-\mu_0E_1\\
\frac{dM_N}{dt} &= \epsilon m(1-c)E_1-\mu_1M_N\\
\frac{F_N}{dt} &= \pi_1+\epsilon(1-c)(1-m)E_1-\rho F_N\frac{M_N+M_w}{M_N+M_w+M_\theta}-\mu_1F_N\\
\frac{dS_N}{dt} &= \pi_2+\rho F_N\frac{M_N+M_w}{M_N+M_w+M_\theta}-b_1\alpha_{HN}S_NI_H-\mu_1S_N\\
\frac{dE_N}{dt} &= b_1\alpha_{HN}S_NI_H-(\beta_N+\mu_1)E_N\\
\frac{dI_N}{dt} &= \beta_NE_N-\mu_1I_N\\
\frac{dE_2}{dt} &= \alpha T_W\left(1-\frac{E_1+E_2}{K}\right)-\epsilon(1-m)E_2-\epsilon mE_2-\mu_1E_2\\
\frac{dM_W}{dt} &= \epsilon mE_2-\mu_1M_W\\
\frac{F_W}{dt} &= \pi_3+\epsilon(1-m)E_2-\rho F_N\frac{M_N+M_w}{M_N+M_w+M_\theta}-\mu_1F_W\\
\frac{dS_W}{dt} &= \rho F_W\frac{M_N+M_w}{M_N+M_w+M_\theta}-b_2\alpha_{HW}S_WI_H-\mu_1S_W\\
\frac{dE_W}{dt} &= b_2\alpha_{HW}S_WI_H-(\beta_W+\mu_1)E_W\\
\frac{dI_W}{dt} &= \beta_WE_W-\mu_1I_W\\
\frac{dS_H}{dt} &= \pi_4+\eta R_H-b_1\alpha_{NH}S_HI_N-b_2\alpha_{WH}S_HI_W-\mu_2S_H\\
\frac{dE_H}{dt} &= b_1\alpha_{NH}S_HI_N+b_2\alpha_{WH}S_HI_W-(\beta_H+\mu_2)E_H\\
\frac{dI_H}{dt} &= \beta_HE_H-(\gamma+\delta+\mu_2)I_H\\
\frac{dR_H}{dt} &= \gamma I_H-(\eta+\mu_2)R_H
\end{aligned} \tag{1}$$

with the initial condition $X_0 = (E_1^0, M_N^0, F_N^0, S_N^0, E_N^0, I_N^0, E_2^0, M_W^0, F_W^0, S_W^0, E_W^0, I_W^0, S_H^0, E_H^0, I_H^0, R_H^0)$ which are all nonnegative quantities. The domain of existence of solution to the IVP can be described as $\mathcal{D} = \mathcal{D}_1 \cup \mathcal{D}_2 \cup \mathcal{D}_3$, where

$$\mathcal{D}_1 = \{(E_1, M_N, F_N, S_N, E_N, I_N) \in \mathbb{R}_+^6 | E_1 + M_N + F_N + S_N + E_N + I_N \leq T_1\}$$

$$\mathcal{D}_2 = \{(E_2, M_W, F_W, S_W, E_W, I_W) \in \mathbb{R}_+^6 | E_2 + M_W + F_W + S_W + E_W + I_W \leq T_2\}$$

$$\mathcal{D}_3 = \{(S_H, E_H, I_H, R_H) \in \mathbb{R}_+^4 | S_H + E_H + I_H + R_H \leq T_3\}$$

where $T_1(t), T_2(t)$ and $T_3(t)$ are respectively, the total population of normal mosquitoes, wolbachia-infected mosquitoes and humans, at any time t.

2.1 Model Properties

2.1.1 Existence and Uniqueness of Model Solution

All functions in the right-hand of the model equation (1) have continuous partial derivatives with respect to the state variables on $\mathcal{D}$. Therefore, the model IVP possesses a unique solution.

2.1.2 Positivity of Model Solution and positive invariance

Here, we follow the method described in [5] to show that all the components of the solution are nonnegative $\forall t > 0$, and that all the trajectories enter and remain in $\mathcal{D}$ at all times, $t \geq 0$. Let $(E_1^*(t), M_N^*(t) \cdots, R_H^*(t))$ be a fixed solution to the IVP(1) through the initial solution, X_0, on $[0, \tau)$, for a real τ. By continuity of the solution on $[0, \tau)$, there exists a τ_1, $0 < \tau_1 < \tau$, such that $E_1^*(t') > 0, M_N^*(t') > 0 \cdots, R_H^*(t') > 0$ for any $t' \in [0, \tau_1]$. So on $[0, \tau_1]$, we have
$\frac{dE_1^*(t)}{dt} > -(\epsilon(1-c)+\mu_0)E_1^*(t) \implies E_1^*(t) > E_1(0)e^{-(\epsilon(1-c)+\mu_0)t} > 0$,
$\frac{dM_N^*(t)}{dt} > -\mu_1 M_N^*(t) \implies M_N^*(t) > M_N(0)e^{-\mu_1 t} > 0$. In this manner, all other components of the solution can be shown to be positive on $[0, \tau_1]$. Since the solution is continuous on $[0, \tau)$, we have that the solution is positive on $[0, \tau)$. So all the components of the solution are bounded below by a positive number on $[0, \tau)$. So, $\lim_{t \to \tau^-}(E_1^*(t), M_N^*(t) \cdots, R_H^*(t)) > 0$. This shows that all the solution components can be continuously extended to $[0, \tau]$, and $\mathcal{D}$ is invariant with respect to the semi-flow defined by the model system on $[0, \tau]$. Consequently, $[0, \infty)$ is the maximal interval of existence of the solution[11]. Hence, the solution is nonnegative at all times, and $\mathcal{D}$ is positively invariant.

3 Effective Reproduction Number

The effective reproduction number of a disease infection gives on average, the number of secondary infections that would be recorded when an index case is introduced in a purely susceptible population in the presence of any control measure applied to stop the spread of the disease. The control measure is effective if the effective reproduction number is less than one. Otherwise, the control measure is ineffective, and should be discarded. The method of determining the effective reproduction number, $\mathcal{R}_{eff}$ of the disease is based on the next generation matrix approach where the reproduction number is given by the spectral radius of the next generation matrix:$\mathcal{R}_{eff} = \rho(FV^{-1})$, where FV^{-1} is called the next generation matrix. Tthe matrices F and V are easily calculated from the model system as described in[1] and in other articles on infectious disease modeling.

Theorem 1 *Given the disease-free equilibrium* $\Gamma^0 = (E_1^*, M_N^*, F_N^*, S_N^*, 0, 0, E_2^*, M_W^*, F_W^*, 0, 0, 0, S_H^*, 0, 0, 0)$,
with $E_1^* = \frac{(K-E_2^*)\alpha S_N^*}{\alpha S_N^* + K\epsilon(1-c)(1-m)+\mu_0}$, $M_N^* = \frac{em(1-c)E_1^*}{\mu_1}$, $F_N^* = \frac{\pi_1+\epsilon(1-c)(1-m)E_1^*}{\rho(p+q)+\mu_1}$, $S_N^* = \frac{\pi_2+\rho(p+q)F_N^*}{\mu_1}$
$E_2^* = \frac{(K-E_1^*)\alpha S_W^*}{\alpha S_W^* + K\epsilon(1-m)+\mu_e}$, $M_W^* = \frac{\epsilon m E_2^*}{\mu_1}$, $F_W^* = \frac{\pi_3+\epsilon(1-m)E_2^*}{\rho(p+q)+\mu_2}$, $S_W^* = \frac{\rho(p+q)F_W^*}{\mu_1}, S_H^* = \frac{\pi_4}{\mu_2}$,
the model has a next generation matrix of the form

$$\mathcal{K} = \begin{pmatrix} 0 & \mathcal{K}_{NH} & \mathcal{K}_{WH} \\ \mathcal{K}_{HN} & 0 & 0 \\ \mathcal{K}_{HW} & 0 & 0 \end{pmatrix}, \tag{2}$$

and the effective reproduction number is

$$\mathcal{R}_{eff}^2 = \mathcal{K}_{NH}\mathcal{K}_{HN} + \mathcal{K}_{WH}\mathcal{K}_{HW} \tag{3}$$

where $\mathcal{K}_{NH} = \frac{\beta_N b_1 \alpha_{NH} S_H^*}{\mu_1(\beta_N+\mu_1)}$, $\mathcal{K}_{WH} = \frac{\beta_W b_2 \alpha_{WH} S_H^*}{\mu_1(\beta_W+\mu_1)}$, $\mathcal{K}_{HN} = \frac{\beta_H b_1 \alpha_{HN} S_N^*}{(\gamma+\delta+\mu_2)(\beta_H+\mu_2)}$, $\mathcal{K}_{HW} = \frac{\beta_H b_2 \alpha_{HW} S_W^*}{(\gamma+\delta+\mu_2)(\beta_H+\mu_2)}$

***proof*:** the size and the elements of the next generation matrix (2) are due to the three populations involved in the yellow fever dynamics as assumed in the model. Moreover, for the model,

$$F = \begin{pmatrix} 0 & 0 & 0 & b_1\alpha_{NH}S_H^* & 0 & b_2\alpha_{WH}S_H^* \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & b_1\alpha_{HN}S_N^* & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & b_2\alpha_{HW}S_W^* & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$V = \begin{pmatrix} \beta_H + \mu_2 & 0 & 0 & 0 & 0 & 0 \\ -\beta_H & \gamma + \delta + \mu_2 & 0 & 0 & 0 & 0 \\ 0 & 0 & \beta_N + \mu_1 & 0 & 0 & 0 \\ 0 & 0 & -\beta_N & \mu_1 & 0 & 0 \\ 0 & 0 & 0 & 0 & \beta_W + \mu_1 & 0 \\ 0 & 0 & 0 & 0 & -\beta_W & \mu_1 \end{pmatrix}$$

so that the next generation matrix becomes

$$\mathcal{K} = \begin{pmatrix} 0 & 0 & \frac{\beta_N b_1 \alpha_{NH} S_H^*}{\mu_1(\beta_N+\mu_1)} & \frac{b_1\alpha_{NH}S_H^*}{\mu_1} & \frac{\beta_W b_2 \alpha_{WH} S_H^*}{\mu_1(\beta_W+\mu_1)} & \frac{b_2\alpha_{WH}S_H^*}{\mu_1} \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{\beta_H b_1 \alpha_{HN} S_N^*}{(\gamma+\delta+\mu_2)(\beta_H+\mu_2)} & \frac{b_1\alpha_{HN}S_N^*}{(\gamma+\delta+\mu_2)} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ \frac{\beta_H b_2 \alpha_{HW} S_W^*}{(\gamma+\delta+\mu_2)(\beta_H+\mu_2)} & \frac{b_2\alpha_{HW}S_W^*}{(\gamma+\delta+\mu_2)} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

The multiplication of the form $A^T\mathcal{K}A$, where $A = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \end{pmatrix}^T$ is an auxiliary matrix, gives the desired structure(2). The largest eigenvalue of (2) is the effective reproduction number (3) of the model.□

4 Stability Analysis

In this section, we discuss the local asymptotic stability of the disease-free equilibrium for the complete system and in the absence of wolbachia-infected mosquitoes.

4.1 Local Stability of Γ^0 for the Complete System

The local asymptotic stability of the disease-free equilibrium is determined by the eigenvalues of the Jacobian matrix of the right-hand side of (1), evaluated at the disease-free equilibrium, Γ_0. Let $J(\Gamma^0)$ be the Jacobian matrix of the right-hand side of (1), evaluated at the disease-free equilibrium, Γ^0. If all the eigenvalues of $J(\Gamma^0)$ are negative or have negative real part, then Γ^0 is locally asymptotically stable. The disease-free equilibrium, Γ^0 is unstable if at least one eigenvalue of $J(\Gamma)$ is positive or have positive real part. From (1). we have that

$$J(\Gamma^0)=\begin{pmatrix}
-a_1 & 0 & 0 & a_2 & a_3 & a_4 & -a_5 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
a_6 & -a_7 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
c_1 & 0 & -c_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & d_1 & -d_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -d_3 & 0\\
0 & 0 & 0 & 0 & -e_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & e_2 & 0\\
0 & 0 & 0 & 0 & f_1 & -f_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
-g_1 & 0 & 0 & 0 & 0 & 0 & -g_2 & 0 & 0 & g_3 & g_4 & g_5 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & h_1 & -h_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & k_1 & 0 & -k_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -m_1 & -m_2 & 0 & 0 & 0 & 0 & -m_3 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -n_1 & 0 & 0 & 0 & -n_2 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & -q_1 & 0 & 0 & 0 & 0 & -p_2 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & -q_1 & 0 & 0 & 0 & 0 & 0 & -q_2 & -q_3 & 0 & 0 & q_4\\
0 & 0 & 0 & 0 & 0 & s_1 & 0 & 0 & 0 & 0 & 0 & s_2 & 0 & -s_3 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & t_1 & -t_2 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & u_1 & -u_2
\end{pmatrix}$$

where $a_1=\frac{\alpha S_N^*}{K}+e(1-c)(1-m)+\mu_0),\ a_2=a_3=a_4=\alpha\left(1-\frac{E_1^*+E_2^*}{K}\right),\ a_5=\frac{\alpha S_N^*}{K}$
$c_1=e(1-c)(1-m),\ c_2=\rho(p+q)+\mu_1,\ d_1=\rho(p+q),\ d_2=\mu_1,\ d_3=b_1\alpha_{HN}S_N^*,\ e_1=\beta_N+\mu_1$
$e_2=b_1\alpha_{HN}S_N^*,\ f_1=\beta_N,\ f_2=\mu_1,\ g_1=\frac{\alpha S_W^*}{K},\ g_2=\frac{\alpha S_W^*}{K}+e(1-m)+\mu_0,$
$g_3=g_4=g_5=\alpha\left(1-\frac{E_1^*+E_2^*}{K}\right),\ h_1=em,\ e_2=\mu_1,\ k_1=e(1-m),\ k_2=\rho(p+q)+\mu_0,$
$m_1=\rho(p+q),\ m_2=\mu_1,\ m_3=b_2\alpha_{HW}S_W^*,\ n_1=\beta_W+\mu_1,\ n_2=b_2\alpha_{HW}S_W^*,\ p_1=\beta_W,$
$p_2=\mu_1,\ q_1=b_1\alpha_{NH}S_H^*,\ q_2=b_2\alpha_{WH}S_H^*,\ q_3=\mu_2,\ q_4=\eta,\ s_1=b_1\alpha_{NH}S_H^*,$
$s_2=b_2\alpha_{WH}S_H^*,\ s_3=\beta_H+\mu_2,\ t_1=\beta_N,\ t_2=(\gamma+\delta+\mu_2),\ u_1=\gamma,\ u_2=\eta+\mu_2.$
The eigenvalues of $J(\Gamma^0)$ are $a_7<0,\ h_2<0,\ q_3<0,\ u_2<0$ and the eigenvalues of the submatrix

$$J'(\Gamma^0)=\begin{pmatrix}
-a_1 & 0 & a_2 & a_3 & a_4 & -a_5 & 0 & 0 & 0 & 0 & 0 & 0\\
c_1 & -c_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
0 & d_1 & -d_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -d_3\\
0 & 0 & 0 & -e_1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & e_2\\
0 & 0 & 0 & f_1 & -f_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0\\
-g_1 & 0 & 0 & 0 & 0 & -g_2 & 0 & g_3 & g_4 & g_5 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & k_1 & -k_2 & 0 & 0 & 0 & 0 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & -m_1 & -m_2 & 0 & 0 & 0 & -m_3\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -n_1 & 0 & 0 & -n_2\\
0 & 0 & 0 & 0 & 0 & -q_1 & 0 & 0 & 0 & -p_2 & 0 & 0\\
0 & 0 & 0 & 0 & s_1 & 0 & 0 & 0 & 0 & s_2 & -s_3 & 0\\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & t_1 & -t_2
\end{pmatrix} \tag{4}$$

The theorem below gives the condition under which all the eigenvalues of $J'(\Gamma^0)$ are negative.

Theorem 2 (Gershgorin) *Let $A=a_{ij}$ be a complex $n\times n$ matrix with eigenvalues, λ. For $i\in n$, let $R_i=\sum_{j\neq i}|a_{ij}|$ be the sum of the absolute values of the non-diagonal entries in the i^{th} row. Let $D(a_{ii},R_i):=|\lambda-a_{ii}|\leq R_i$ be a closed disc centered at a_{ii} with radius R_i. Then, the eigenvalues of A belong to the union of the discs, $D(a_{ii},R_i)$.*

From the Gershgorin's theorem, we have that all the eigenvalues, λ of $J'(\Gamma^0)$ lie in the union of the closed disc $|\lambda - a_{ii}| \leq \sum_{j\neq i} |a_{ij}|$, $i, j = 1, 2, 3 \cdots 12$. Hence, we have

$$\begin{gathered}
-(a_1 + a_2 + 3a_3) \leq \lambda \leq a_2 + 3a_3 - a_1, \\
-(c_1 + c_2) \leq \lambda \leq c_1 - c_2, \\
-(d_1 + d_2 + d_3) \leq \lambda \leq d_1 + d_3 - d_2, \\
-(e_1 + e_2) \leq \lambda \leq e_2 - e_1, \\
-(f_1 + f_2) \leq \lambda \leq f_1 - f_2, \\
-(g_1 + g_2 + 3g_3) \leq \lambda \leq g_1 + 3g_3 - g_2 \\
-(k_1 + k_2) \leq \lambda \leq k_1 - k_2, \\
-(m_1 + m_2 + m_3) \leq \lambda \leq m_1 + m_3 - m_2, \\
-(n_1 + n_2) \leq \lambda \leq n_2 - n_1, \\
-(p_1 + p_2) \leq \lambda \leq p_1 - p_2, \\
-(s_1 + s_2 + s_3) \leq \lambda \leq s_1 + s_2 - s_3, \\
-(t_1 + t_2) \leq \lambda \leq t_1 - t_2
\end{gathered} \tag{5}$$

Therefore, if $J'(\Gamma^0)$ is strictly diagonally dominant, then Gershgorin's theorem ensures that $\lambda \in [-\Theta_1, -\Theta_2]$, where $-\Theta_1$ and $-\Theta_2$ are respectively, the minimum and maximum of the left-hand and right-hand sides of the inequalities in (5). Therefore, the disease-free equilibrium Γ^0 is locally asymptotically stable if $J'(\Gamma^0)$ is strictly diagonally dominant(SDD).

4.2 Local Stability of Γ^0 in the wolbachia-free mosquito system

We consider the stability of Γ^0 when the wolbachia-infected mosquitoes have not been introduced in the population. In this case, the disease-free equilibrium is $(E_1^*, M_N^*, F_N^*, S_N^*, E_N^*, I_N^*, S_H^*, E_H^*, I_H^*, R_H^*)$, and the associated Jacobian matrix is

$$J''(\Gamma^0) = \begin{pmatrix}
-a_1 & 0 & 0 & a_2 & a_3 & a_4 & 0 & 0 & 0 & 0 \\
a_6 & -a_7 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
c_1 & 0 & -c_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & d_1 & -d_2 & 0 & 0 & 0 & 0 & -d_3 & 0 \\
0 & 0 & 0 & 0 & -e_1 & 0 & 0 & 0 & e_2 & 0 \\
0 & 0 & 0 & 0 & f_1 & -f_2 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & q_1 & -q_2 & 0 & 0 & q_3 \\
0 & 0 & 0 & 0 & 0 & s_1 & 0 & -s_2 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & t_1 & -t_2 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & u_1 & -u_2
\end{pmatrix} \tag{6}$$

Eliminating the rows and columns containing the entries $a_7 < 0, q_2 < 0, u_2 < 0$, and transforming the remaining submatrix to an upper traingular matrix, we find that all the eigenvalues of $J''(\Gamma^0)$ are negative if

$$K_{offN} < 1 \quad \text{and} \quad \mathcal{R}_0^2 < 1$$

where

$$K_{offN} = \frac{\alpha\left(1 - \frac{E_1^*}{K}\right)\epsilon(1-c)(1-m)\rho p}{\left(\frac{\alpha S_N^*}{K} + \epsilon(1-c)(1-m) + \mu_0\right)(\rho p + \mu_1)\mu_1}$$

is the basic offspring number of the mosquito, and

$$\mathcal{R}_0^2 = \frac{b_1\beta_H\alpha_{HN}S_N^*}{(\beta_H + \mu_2)(\gamma + \delta + \mu_2)} \frac{\beta_N b_1 \alpha_{NH} S_H^*}{\mu_1(\beta_N + \mu_1)}$$

is the basic reproduction number of the disease in the absence of wolbachia-infected mosquitoes used for control, Therefore, the disease-free equilibrium in the absence of wolbachia-infected mosquitoes is locally asymptotically stable if $K_{offN} < 1$ and $\mathcal{R}_0 < 1$, simultaneously. This shows that ther disease-free equilibrium is locally asymptotically stable if the average number of mosquito offspring produced by each adult female mosquito is less than one, and if the average number of persons infected by a single index case of yellow fever in a purely susceptible human and mosquito population is less than one.

5 Numerical Simulations

The simulation of the model is carried out with the following initial solution and the parameter values in Table 1. $E_1^0 = 1000, M_N^0 = 1000, F_N^0 = 1200, S_N^0 = 10000, E_N^0 = 1000, I_N^0 = 12000, E_2^0 = 0, M_W^0 = 100, F_W^0 = 1000, S_W = 10000, E_W^0 = 0, I_N^0 = 0, S_H = 10000, E_H^0 = 1300, I_H^0 = 1500, R_H^0 = 50, \Pi_1 = 150, \pi_2 = 150, \pi_3 = 10000, \pi_4 = 100, K = 20000$.In table 1, we chose parameters of the wolbachia-infected mosquitoes based on the parameters of the normal mosquitoes. For example, the incubation period of yellow fever virus in the normal mosquitoes is 12 days. Hence, we choose the incubation period of the virus in the wolbachia-infected mosquito to be double that of the normal mosquito, which is 24 days.This is because wolbachia increases the incubation period of the virus in its host mosquito. Also, the probability of transmission α_{WH} of the virus from wolbachia-infected mosquitoes is chosen so that it is much smaller than that of the normal mosquitoes, since wolbachia reduces the ability of the mosquitoes to transmit the virus to humans. The result of the numerical experiment is given in Figures 1-6. In the graphs, 'N' represents normal aedes aegypti mosquitoes, while 'W' represents wolbachia-infected aedes aegypti mosquitoes.

Parameter	*Value*	*Source*	*Parameter*	*Value*	*Source*
m	0.6	[3]	μ_2	3.5×10^{-5}	[13]
μ_0	0.0005	[10]	e	1/6.67	[10]
α_{HN}	0.175	[21]	γ	0.143	[13]
α_{HW}	0.175	[21]	α_{WH}	0.0005	assumed
μ_1	0.09	[13]	α_{NH}	0.175	[21]
β_H	1/5	[8]	q	0.25	assumed
b_1	0.004	assumed	η	0.015	assumed
b_2	0.7	[21]	p	0.58	assumed
β_N	1/12	[19]	δ	3.5×10^{-4}	[13]
β_W	1/24	$\frac{1}{2}$ of β_N	α	0.15	assumed
ρ	0.075	assumed	c	0.6	assumed

Table 1: Parameter Values used in this model

6 Results and Discussion

The graphs depict the impact of wolbachia-infected mosquitoes on the population of wolbachia-free mosquitoes. Figure 1 shows the quantity of eggs produced by the normal mosquitoes(N) and the wolbachia-infected mosquitoes(W) in a given period of time. From the graph, we see that the quantity of eggs produced by the normal mosquitoes rises slightly and begins to decrease as the eggs produced by the wolbachia-infected mosquitoes increase. The reduction in the quantity of eggs produced by the normal mosquitoes is attributed to cytoplasmic incompatibility, which prevents eggs produced by the normal female mosquitoes from hatching, when mated by

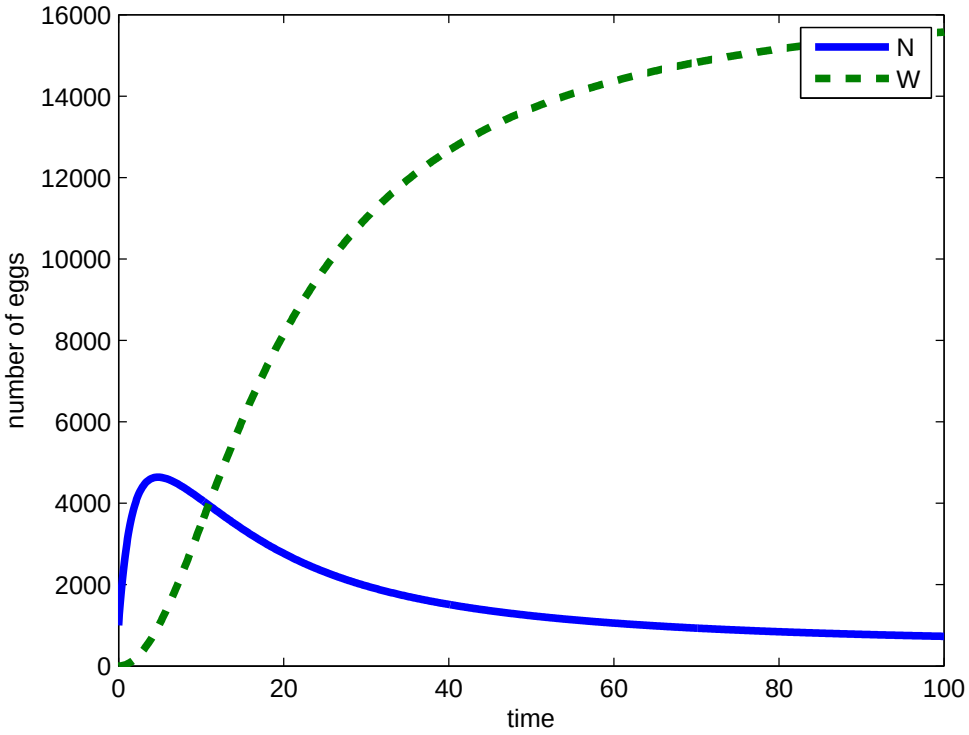

Figure 1: Quantity of Eggs produced by the mosquitoes

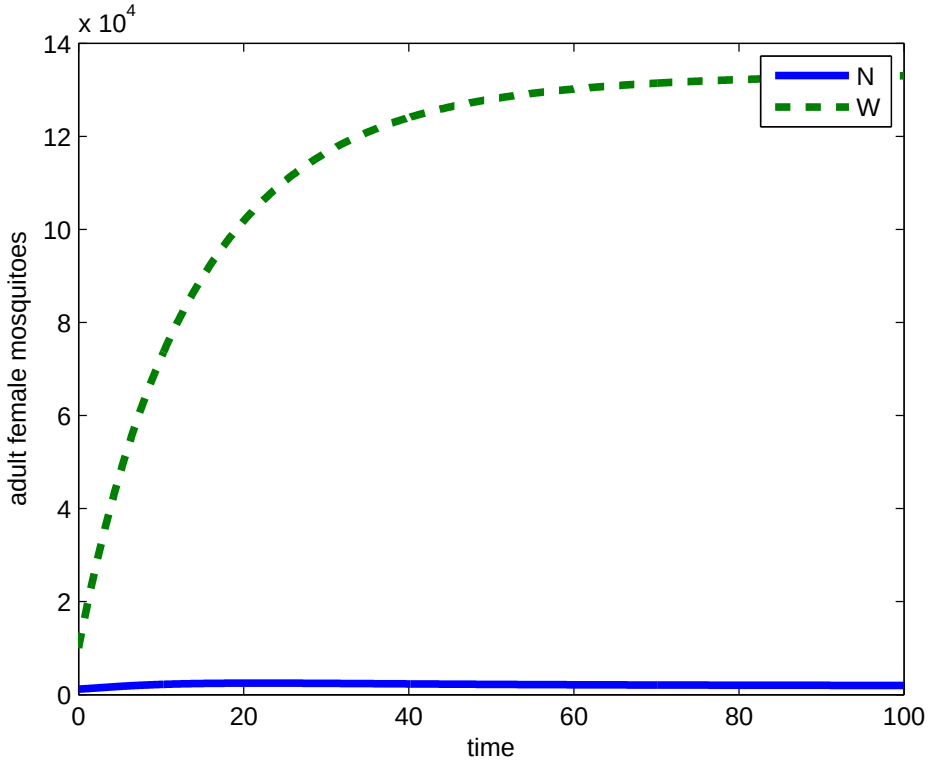

Figure 2: Number of adult female mosquitoes

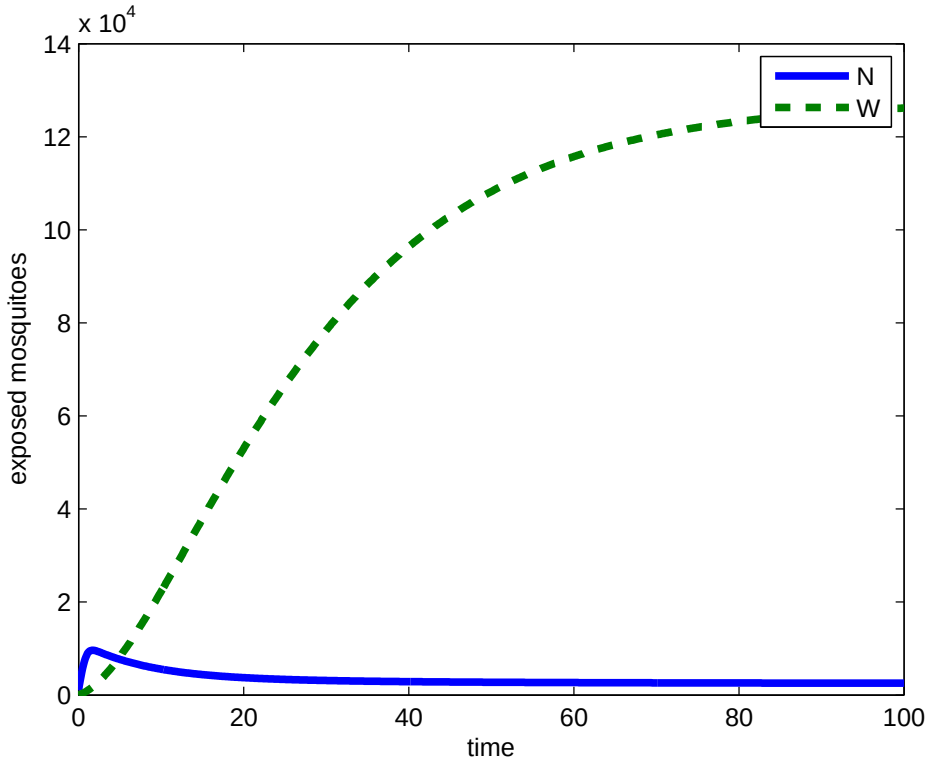

Figure 3: Number of exposed mosquitoes

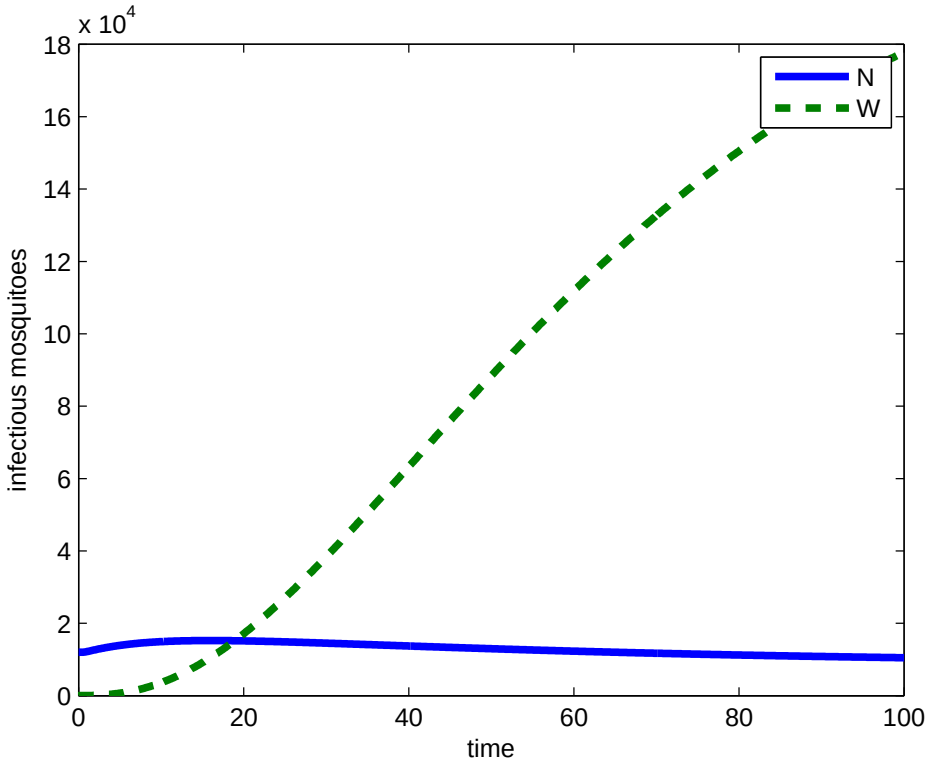

Figure 4: Number of infectious mosquitoes

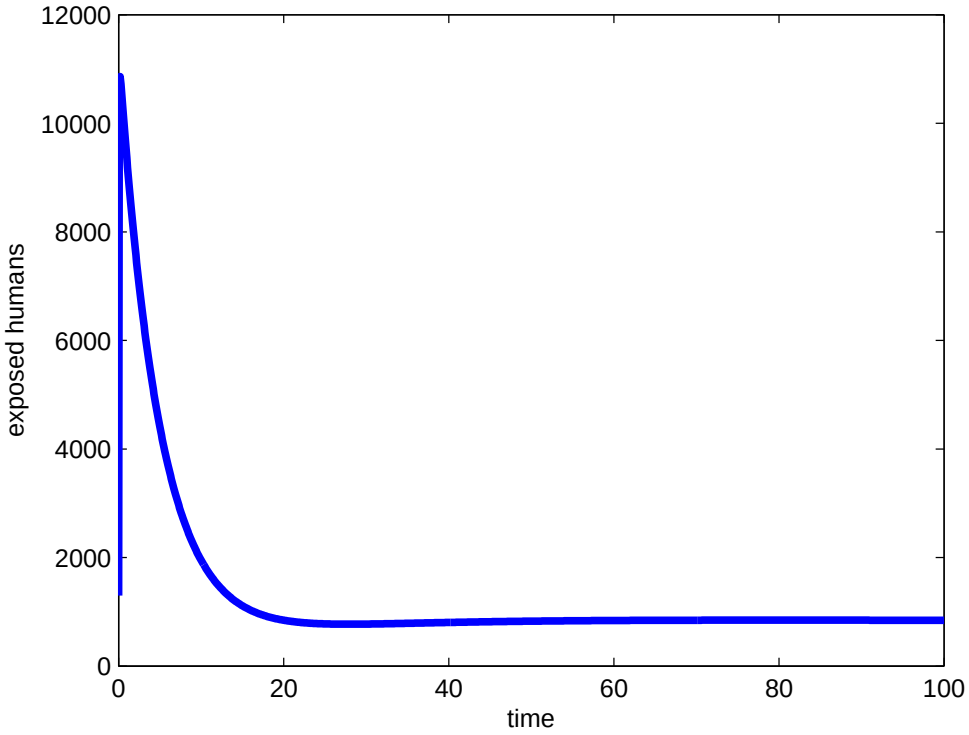

Figure 5: Number of exposed humans

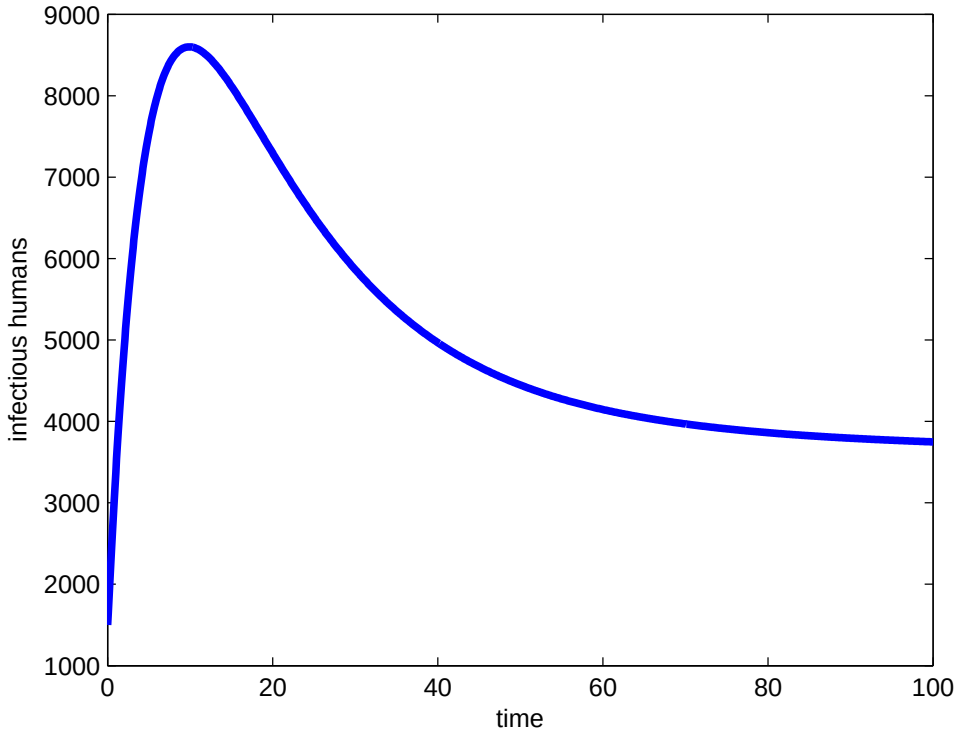

Figure 6: Number of infectious humans

wolbachia-infected male mosquitoes. The reduction in the number of eggs produced by the normal mosquitoes leads to reduction in the emerging normal adult female mosquitoes as shown in figure 2, figure 3 and figure 4. In figure 5 and figure 6, we notice an initial increase in the exposed and infectious human classes, which later decrease as time increases. The period of increase in the size of exposed and infectious humans can be regarded as the period when wolbachia-infected mosquitoes have not fully established in the population. In this case, more normal infectious mosquitoes are available to bite and infect humans with yellow fever.

7 Conclusion

We have modeled the introduction of wolbachia into aedes argypti mosquitoes in order to curb the spread of yellow fever. An application of Gershgorin's theorem gives the condition under which the disease-free equilibrium of the model is locally asymptotically stable. In the absence of the wolbachia-infected mosquitoes used for control, we derived that the disease-free equilibrium is locally asymptotically stable if the basic offspring number of the normal mosquitoes and the basic reproduction number of the disease are simultaneously less than one. This agrees with the use of wolbachia-infected mosquitoes as control since it reduces the basic offspring number of the wild mosquitoes through the action of cytoplasmic incompatibility and reduces the basic reproduction number through reduction in the incubation rate of the virus in the wolbachia-infected mosquitoes. Numerical simulations of the model also show that the population of the normal mosquitoes, including its eggs is reduced compared to the population of the wolbachia-infected mosquitoes which increases. This shows that the wolbachia-infected mosquitoes gradually replaces the normal mosquitoes in the area where yellow fever is endemic. In this case, less number of normal mosquitoes would be available to bite and transmit yellow fever virus to humans, and the more abundant wolbachia-infected mosquitoes would have less ability to transmit the disease to humans. We therefore conclude that releasing wolbachia-infected aedes aegypti mosquitoes in the area where yellow fever is endemic has the ability to prevent the disease from spreading in the population.

References

[1] Diekmann, O., Heesterbeek, J. A. P. & Roberts, M. G. (2010). The construction of next-generation matrices for compartmental epidemic models.Journal of Royal Society Interface, 7, 873–885.

[2] Hancock, P. A., Sinkins, S. P. & Godfray, H. J.(2011), Population Dynamic Models of the Spread of Wolbachia, The American Naturalist, 177(3) 323-333.

[3] Hickey, W.A and Craig, G. B.(1966). Genetic distortion of sex ratio in a mosquito, Aedes Aegypti, in Genetics, 53(6).

[4] Hughes, H. and Britton, N. F.(2013), Modelling the use of Wolbachia to control dengue fever transmission, Bulletin of Mathematical Biology, 75 (5) 796-818

[5] Katri, P.(2010), Modeling the Transmission Dynamics of the Dengue Virus. Open Access Dissertations, Paper 147.

[6] Luz, P.M., Struchiner, C.J., Galvani A.P. (2020). Modeling transmission dynamics and control of vector-borne neglected Tropical disease sPLOS Negl. Trop Dis.;4(10): e761. Dol:10.1371/journal.pntd. 000761.

[7] Monath, T.P. (2008). Treatment of Yellow fever. Antiviral Res. 2008, 78:116-24.http:doi org 110.1061j.10.009 PMID:18061688.

[8] Monath, T. P.(2001). Yellow fever: an update, The lancet infectious Diseases, Vol. 1., No. 1, pp. 11-20

[9] Moreno,E.S., Rocco, I.M., Bergo, E.S.(2011), Reemergence of yellow fever: detection of transmission in the state of Sao Paulo Brazil, 2008". Revista dasociedade Brasileira de medicina Tropical, vol .44, no 3. Pp 290-296

[10] Ndii, M. Z., Hickson, R. I. & Mercer, G. N. (2012). Modelling the Introduction of Wolbachia into Aedes Aegypti Mosquitoes to Reduce Dengue Transmission. *The ANZIAM Journal*, 53, 1-15.

[11] Perko, L., Differential equations and dynamical systems, Third, Texts in Applied Mathematics, vol. 7, Springer-Verlag, New York, 2001.

[12] Oldstone, M.(2009). Viruses, Plagues and history: past, present and future, Oxford University press, Oxford Uk

[13] Raimundo, S. M., Amaku, M. & Massad, E.(2015), Equilibrium Analysis of a Yellow Fever Dynamical Model with Vaccination, Computational and Mathematical Methods in Medcine, Volume 2015.

[14] Smith, B. G.(2013), The ship of Death: A voyage that changed the Atlantic, Yale University Press, Yale, Mich, USA.

[15] Tolle, M. A.(2009). Mosquito-born diseases, current problems in pediatric and Adolescent health care, vol. 39, No. 4, Pp. 97-140

[16] Twu, J., Peak, C. M., Leung, G. M. and Lipsitch, M.(2016). Fractional dosing of yellow fever vaccine to extend supply: A modlling study. Lancet;. Available: https://doi.org//01016/50140. 6736(16): 31838 - 4.

[17] Wang, L., Zhao, H., Munize, S. & Zhu, H.(2007). Modeling the transmission and control of zika in Brazil Scientifics Rports. www.nature.com/ scientific reports.

[18] WHO, Yellow fever fact sheet No. 100, World health Organization, 2013.

[19] WHO, Yellow fever fact sheet No. 100, World health Organization, 2013.

[20] Zhang, L., Qi, R., R.F. & Chi, C.(2008), Biological characteristics of dengue virus and potential targets for drug design.Acia: Biochimica Et Biophysica sonica 40, 91-101..

[21] Zha0, S., Stone, L., Gao, D.& He, D.(2018). Modeling the Large-Scale Yellow Fever Outbreak in Luanda, Angola, and the impact of Vaccination, PLoS Negl Trop.Dis. 12(1):e006158.

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Dynamical analysis of a two-strain treatment model for Anthrax in a population where it is deployed as bio-terrorism weapon

[*]P.O. Ameh, B.I. Omede and B. Bolaji[†]

Abstract

The major short coming associated with the use of antibiotics to combat anthrax in a population under the siege of its attack, is the emergence and transmission of anthrax that are resistant to these drugs. Consequently, our focus in this work is the formulation of a new deterministic treatment model which incorporates a wild (drug-sensitive) and drug-resistant strain for gaining insight into the dynamical features of the two strains of anthrax, with a view to determining result-oriented, and effective ways to control the spread of the disease and its treatment in this circumstance. Discoveries from both the qualitative and numerical analysis of the model, is that the model has two equilibria: the disease free equilibrium (DFE) which is locally asymptotically stable when a certain epidemiological threshold R_0^t (the associated reproduction number) is not up to unity, that is, $R_0^t \prec 1$ and the disease will persist in the community when the threshold exceeds unity, that is, $R_0^t \succ 1$. In addition, for the case where $R_0^t \succ 1$, it is shown that the model can have two co-existing endemic equilibria and there is occurrence of a phenomenon, competitive exclusion whenever the associated reproduction number of the drug-resistant strain (R_R^t) is greater than that of the wild strain (R_W^t). On the other hand, unlike in the treatment model, it is shown that the model without treatment can have a family of infinitely many endemic equilibria when its associated epidemiological threshold (R_0) exceeds unity. Whenever $R_W^t \succ R_R^t$ and $R_W^t \succ 1$, it is shown that widespread application of treatment regimen of combination of prophylaxis and antibiotics against the wild strain of the disease can lead to its elimination from the community if the associated reduction in infectiousness of infected individuals who were treated for the wild strain infection does not exceed a certain threshold value, which in this case, is the use of treatment expected to make $R_W^t \prec R_R^t$.

Keywords: Anthrax, wild, resistant, strains, equilibria, reproduction number, stability, treatment.

[*] P.O.A., B.I.O. and B.B.: Department of Mathematical Sciences, Kogi State University, Anyigba, Nigeria.
[†] Corresponding author: bolarinwa.s.bolaji@gmail.com

1 Introduction

Bacillus anthracis is the bacteria causing an acute infectious disease referred to as Anthrax. Anthrax causative bacterium, a non-motile, spore-forming bacterium, produces spores, small resistant cells that are capable of surviving for many years in the environment [1, 2]. The disease which commonly occur in wild or domesticated animals has an occurrence in humans due to exposure to infected animals or tissue from animals that have been infected with the disease or expose directly to Bacillus anthracis. There are basically three forms of occurrence: coetaneous, gastrointestinal, and inhalation [3]. The time between becoming infected and developing symptoms of the disease, - incubation period - is usually one to seven days, commonly but can be up to two months at times. The neurological symptoms of anthrax at prodromal stage are non-headache, such as fever, fatigue, and muscle aches. Strict adherence to prophylaxis during incubation stage will not lead to illness. The veterinary vaccine that is currently in use in the U.S. is a spore suspension from a virulent non-encapsulated strain [5, 6]. Original human anthrax vaccine have been developed in the 1950s. From the examination of the safety of the vaccine, [7] concluded that there is relatively minor individual reactions to it. Antibiotics such as Penicillin G., Amoxicillin, Doxycyline and Ciproflaxacin have been found to be effective for the treatment of anthrax [6, 7]. However, there is report that 20% of untreated people may die of the disease. A large numbers of humans and animals were killed by the disease in the middle ages when it swept across Europe [8]. With the industrialization of Europe, however, smaller outbreaks of anthrax began to occur in factories where imported animal hides and hair were processed [9]. It is pertinent to note that anthrax is a potential agent for use in biological warfare due to the fact that it has virulent characteristics that have made it attractive as a bio-weapon. Cases of use of anthrax as a bio-terrorism weapon has been reported by many researchers, which include [14-16, 34]. It should be noted that although, the scourge of anthrax can be combatted with vaccine and effective treatment with ciprofloxacin and doxycycline; however, with low dosage of antibiotics, treatment can fail [17]. There now abound evidences of development of resistance to Penicillin G., and Amoxicillin and other antibiotics used in the treatment of anthrax [18-20].

Mathematical models have been found to provide key insights into the causes of an outbreak of disease and help the management in the allocation of healthcare resources optimally by investigating the impact of alternative interventions [31]. In literature, there exist several attempts to study the dynamics of the transmission of anthrax in a population. [21] formulated a model considering only the susceptible animals, the environmental contamination and the number of carcasses of animals that may have died of anthrax. [22, 23] in their models investigated the contamination of environment and the contact between animal and infected carcasses, they discovered that if there is early and effective treatment, the infected animals can be cured. [24] formulated epidemic models on anthrax transmission in animals; they do not consider anthrax as a zoonotic disease. As a result of the renewed interest in anthrax, other researchers such as [24–28] provided comprehensive and complementary perspectives on this disease.

Arising from the reported cases of the deployment of anthrax as bio-terrorism weapon in literature, then the objective of this study, therefore, is to design a new deterministic treatment model which incorporates the drug-sensitive and drug-resistant strain into the transmission dynamics of anthrax in a population where it is deployed as bio-terrorism weapon such that the two strains of the disease are co circulating. We shall undergo rigorous analysis of the resulting deterministic system of non-linear differential equations with a view to gaining insight into its dynamical features towards exploring the strategies for its control and cure.

2 Model formulation

We split the total population of the people in the community at time t, denoted by $N(t)$, into mutually exclusive compartments of Susceptible people that are not on prophylactic treatment (usually called Prophylaxis) within 48 hours of case detection in their household $S_U(t)$, susceptible people that are on early Prophylaxis $S_{EP}(t)$, susceptible people that are on late Prophylaxis $S_{LP}(t)$, exposed people with wild strain of the disease $E_W(t)$, exposed people with resistance strain of the disease $E_R(t)$, asymptomatic infectious people with the wild strain $I_{AW}(t)$, symptomatic infectious people with the wild strain $I_{SW}(t)$, asymptomatic infectious people with the resistance strain $I_{AR}(t)$, symptomatic infectious people with the resistance strain $I_{SR}(t)$, the treated class $T_W(t)$ of the wild strain, and the recovered people $R(t)$, so that we have:

$$N(t) = S_U(t) + S_{EP}(t) + S_{LP}(t) + E_W(t) + E_R(t) + I_{AW}(t) + I_{SW}(t) + I_{AR}(t) + I_{SR}(t) + T_W(t) + R(t)$$

We generated the population of Susceptible people that are not on prophylaxis within 48 hours of case detection in their household $S_U(t)$, by the birth of children at a rate π and diminished by individuals who acquire infection following contact with infected individuals at the rate λ_W, primary infection with wild strain and λ_R, primary infection with resistant strain. There is a further reduction in this population by individuals who progressed at rate α to the class of susceptible on early prophylaxis and natural death (at a rate μ; natural death occur in all epidemiological compartments at this rate), so that we have:

$$\frac{dS_U}{dt} = \pi - (\lambda_W + \lambda_R)S_U - (\alpha + \mu)S_U$$

We generated the population of susceptible people that are on early Prophylaxis $S_{EP}(t)$, following the prophylaxis of the fraction, k, where $0 < k < 1$ of susceptible individuals not on prophylaxis at the rate $k\alpha$. This population is diminished by susceptible individuals who are on early prophylaxis who came in contact with infected individuals at the rate $(1-\varepsilon_1)\lambda_W$ and $(1-\varepsilon_1)\lambda_R$ (where ε_1 is the efficacy of the early prophylaxis) and natural death, so that we have:

$$\frac{dS_{EP}}{dt} = k\alpha S_U - (1-\varepsilon_1)(\lambda_W + \lambda_R)S_{EP} - \mu S_{EP}$$

We generated the population of susceptible people that are on late prophylaxis $S_{LP}(t)$, following the prophylaxis of the fraction, k, where 0 < k < 1 of susceptible individuals not on prophylaxis at the rate $(1-k)\alpha$. This population is diminished by susceptible individuals who are on late prophylaxis

who came in contact with infected individuals at the rate $(1-\varepsilon_2)\lambda_W$ and $(1-\varepsilon_2)\lambda_R$ (where ε_2 is the efficacy of the late prophylaxis) and $0 < \varepsilon_2 < \varepsilon_1$) and natural death, so that:

$$\frac{dS_{LP}}{dt} = (1-k)\alpha S_U - (1-\varepsilon_2)(\lambda_W + \lambda_R)S_{LP} - \mu S_{LP}$$

We generated the population of exposed individuals to the wild strain of the disease $E_W(t)$ by susceptible individuals not on prophylaxis who came in contact with those who are infected by the wild strain at the rate λ_W and susceptible individuals on early prophylaxis who came in contact with those who are infected by the wild strain of the disease at the rate $(1-\varepsilon_1)\lambda_W$ and susceptible individuals on late prophylaxis who came in contact with those who are infected by the wild strain of the disease at the rate $(1-\varepsilon_2)\lambda_W$. This population is diminished by exposed individuals who progressed to infected class with the wild strain of the disease at the rate σ_W and natural death, so that we have:

$$\frac{dE_W}{dt} = \{S_U + (1-\varepsilon_1)S_{EP} + (1-\varepsilon_2)S_{LP}\}\lambda_W + (\sigma_W + \mu)E_W$$

Likewise, we generated the population of exposed individuals to the resistance strain of the disease which is given by:

$$\frac{dE_R}{dt} = \{S_U + (1-\varepsilon_1)S_{EP} + (1-\varepsilon_2)S_{LP}\}\lambda_R + (\sigma_R + \mu)E_R$$

We generated the population of the asymptomatic infected class with the wild strain of the disease $I_{AW}(t)$ by the fraction, f_1, where $0 < f_1 < 1$ of individuals that progressed from exposed with wild strain to asymptotically infected with the wild strain at the rate $(1-f_1)\sigma_W$. This population is diminished by those who progressed to symptomatic infected class with the wild strain at the rate γ_W. This population is further reduced by disease-induced death at the rate δ_W and natural death, so that:

$$\frac{dI_{AW}}{dt} = (1-f_1)\sigma_W E_W - (\gamma_W + \delta_W + \mu)I_{AW}$$

We generated the population of the symptomatic infected class with the wild strain of the disease $I_{SW}(t)$ by the remaining fraction of those individuals that progressed from exposed wild strain to symptomatic infected individuals with the wild strain at the rate $f_1\sigma_W$ and individuals who progressed from infected asymptomatic wild strain to symptomatic infected individuals with the wild strain at the rate γ_W. This population is diminished by those who progressed to treatment class at the rate τ_W.

There is a further reduction in this population by disease-induced death at the rate δ_W and natural death, so that we have:

$$\frac{dI_{SW}}{dt} = f_1\sigma_W E_W + \gamma_W I_{AW} - (\tau_W + \delta_W + \mu) I_{SW}$$

We generated the population of the asymptomatic infected class with the resistance strain of the disease $I_{AR}(t)$ by the fraction, f_2 , where $0 < f_2 < 1$ of individuals that progressed from exposed with resistance strain to asymptotically infected with the resistance strain at the rate $(1-f_2)\sigma_R$; the population is further increased by the fraction f_3, where $0 < f_3 < 1$ of individuals who resisted treatment in the treatment class at the rate $f_3\psi_W$. This population is diminished by those who progressed to the class of symptomatic infected with resistance strain at the rate γ_R. This class is further reduced by disease-induced death at the rate δ_R and natural death, so that:

$$\frac{dI_{AR}}{dt} = (1-f_2)\sigma_R E_R + f_3\psi_W T_W - (\gamma_R + \delta_R + \mu) I_{AR}$$

We generated the population of the symptomatic infected class with the resistance strain of the disease $I_{SR}(t)$ by the remaining fraction of those individuals that progressed from exposed resistance strain to symptomatic infected individuals with the resistance strain at the rate $f_2\sigma_R$;this population is further increased by the remaining fraction $(1-f_3)$ of individuals who resisted treatment in the treatment class at the rate $(1-f_3)\psi_W$ that progressed to this class. There is further increment in this population by the individuals who progressed to this class from the asymptomatic infected class at the rate γ_R. This population is diminished by disease-induced death at the rate δ_R and natural death, so that we have:

$$\frac{dI_{SR}}{dt} = f_2\sigma_R + (1-f_3)\psi_W T_W + \gamma_R I_{AR} - (\delta_R + \mu) I_{SR}$$

We generated the population of the treated class $T_W(t)$ following the individuals who are symptomatic infected with the wild strain of the disease and progressed to the treatment class at the rate τ_W; but this population is diminished by those individuals who resist treatment at the rate ψ_W and progression from treated class to recovered class at the rate ν. There is a further reduction in population by disease-induced death at slower rate $\theta\delta_W$ and natural death, so that the treated class is given by:

$$\frac{dT_W}{dt} = \tau_W I_{SW} - (\psi_W + \nu + \theta\delta_W + \mu) T_W$$

We generated the population of the recovered class $R(t)$ by those who recovered from the disease due to treatment at the rate ν; while the population of the class is diminished by natural death; so that we have:

$$\frac{dR}{dt} = \nu T_W - \mu R$$

Based on the above formulations and assumptions, the model for the transmission dynamics of the two strains of anthrax is given by the following deterministic system of non-linear differential equations:

$$\begin{aligned}
\frac{dS_U}{dt} &= \pi - (\lambda_W + \lambda_R)S_U - (\alpha + \mu)S_U \\
\frac{dS_{EP}}{dt} &= (1-k)\alpha S_U - (1-\varepsilon_1)(\lambda_W + \lambda_R)S_{EP} - \mu S_{EP} \\
\frac{dS_{LP}}{dt} &= k\alpha S_U - (1-\varepsilon_2)(\lambda_W + \lambda_R)S_{LP} - \mu S_{LP} \\
\frac{dE_W}{dt} &= \{S_U + (1-\varepsilon_1)S_{EP} + (1-\varepsilon_2)S_{LP}\}\lambda_W - (\sigma_W + \mu)E_W \\
\frac{dE_R}{dt} &= \{S_U + (1-\varepsilon_1)S_{EP} + (1-\varepsilon_2)S_{LP}\}\lambda_R - (\sigma_R + \mu)E_R \qquad (1) \\
\frac{dI_{AW}}{dt} &= (1-f_1)\sigma_W E_W - (\gamma_W + \delta_W + \mu)I_{AW} \\
\frac{dI_{SW}}{dt} &= f_1\sigma_W E_W + \gamma_W I_{AW} - (\tau_W + \delta_W + \mu)I_{SW} \\
\frac{dI_{AR}}{dt} &= (1-f_2)\sigma_R E_R + f_3\psi_W T_W - (\gamma_R + \delta_R + \mu)I_{AR} \\
\frac{dI_{SR}}{dt} &= f_2\sigma_R E_R + (1-f_3)\psi_W T_W + \gamma_R I_{AR} - (\delta_R + \mu)I_{SR} \\
\frac{dT_W}{dt} &= \tau_W I_{SW} - (\psi_W + \nu + \theta\delta_W + \mu)T_W \\
\frac{dR}{dt} &= \nu T_W - \mu R
\end{aligned}$$

where $\lambda_W = \dfrac{\beta_W (I_{AW} + I_{SW})}{N}$ and $\lambda_R = \dfrac{\beta_R (I_{AR} + I_{SR})}{N}$

It should be noted that the effective contact rate with infected individuals having the wild strain and resistant strain of the disease is β_W and β_R respectively.

Below is the itemization of some of the main assumptions made in the formulation of the model:

(i) The disease-induced death rate in all the infected compartments and natural death rate in all the compartments are the same.

(ii) In the treatment class, infection takes place.

(iii) There cannot be natural recovery from the infection [17].

It is pertinent to note that model (1) is an extension of models for transmission of anthrax in the literature such as those in [11, 12, 16, 21, 22, 23] by inter alia:

(1) As against the transmission dynamics of anthrax in literature, including those in [11, 12, 16, 21, 22, 23], we considered the two strains of the disease that can co-circulate in a given population where anthrax is endemic, the drug-sensitive and drug-resistance strain. It should be noted that this was not done in any of the afore-mentioned works; they only considered a single strain of the disease. The motivating factor for incorporating the two strains into our model is the community – wide impact of the two strains of the disease co circulating in the community that now abounds [18, 19]; and there is need to qualitatively assess them;

(2) Including the dynamics of Exposed individuals to the dynamics of the disease by incorporating classes E_W & E_R. This is not included in any of the afore-mentioned models;

(3) Including a compartment for the treated individuals against the infection of anthrax, since there exist treatment for the disease as obtained in literature (see [6, 7]); however, it should be noted that this is not included in any of the afore-mentioned models.

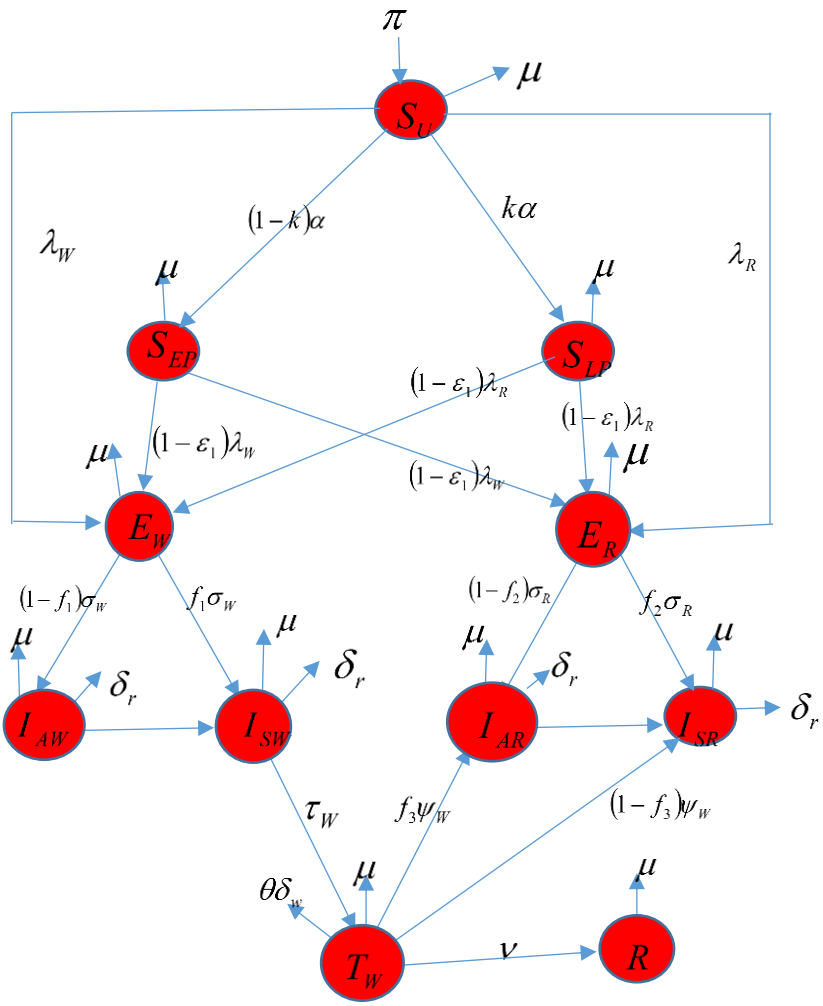

Figure 1: Schematic diagram of the model

Table 1. Description of variables and parameters for model (1)

Variables	**Interpretation**
S_U	Population of susceptible individuals not on prophylaxis
S_{EP}	Population of susceptible individuals on early prophylaxis
S_{LP}	Population of susceptible individuals on late prophylaxis
E_W	Population of exposed individuals to wild strain
E_R	Population of exposed individuals to resistance strain
I_{AW}	Population of asymptomatic infectious individuals with the wild strain
I_{SW}	Population of symptomatic infectious individuals with the wild strain
I_{AR}	Population of asymptomatic infectious individuals with the resistance strain
I_{SR}	Population of symptomatic infectious individuals with the resistance strain
T_W	Population of treated individuals who are infected with the wild strain
R	Population of the recovered individuals
Parameters	**Interpretation**
π	Recruitment rate
α	Progression rate of susceptible people not on prophylaxis to the class of susceptible people on early/late prophylaxis
$\lambda_W(\lambda_R)$	Force of infection for wild (resistance) strain
$\varepsilon_1/\varepsilon_2$	Efficacy of prophylaxis drug for early/late treatment respectively
μ	Natural death rate
$\sigma_W(\sigma_R)$	Progression rate of people in exposed class of wild (resistance) strain to infectious class of wild (resistance) strain
$\delta_W(\delta_R)$	Disease-induced death rate due to wild (resistance) strain of the disease
$\gamma_W(\gamma_R)$	Progression rate from asymptomatic infected people with wild (resistant) strain to symptomatic infected wild (resistant) strain
ψ_W	Progression rate of people who resist treatment (fail) to symptomatic or asymptomatic infected class
τ_W	Rate of treatment of symptomatic infected people with the wild strain of the disease

θ	Modification factor for progression to death by treated individuals
f	Fraction of people in exposed class of wild (resistance) strain who progressed to infectious classes
k	Fraction of people who are susceptible but not on prophylaxis who progressed to class of susceptible on early or late prophylaxis
$\beta_W(\beta_R)$	The effective contact rate with infected individuals having the wild strain (resistant strain) of the disease
ν	Rate of progression from treatment class to recovery class

2.1 Basic Properties

In order for the model (1) to be meaningful epidemiologically, there is the need to prove that all the state variables of the model are non-negative for all time *(t)*. So to say that the solution with positives of the model (1) with positive initial data will remain positive for all $t \geq 0$. We do this as follows:

Note that, initially,

$$S_U(t) + S_{EP}(t) + S_{LP}(t) + E_W(t) + E_R(t) + I_{AW}(t) + I_{SW}(t) + I_{AR}(t) + I_{SR}(t) + T_W(t) + R = N(t).$$

Thus, at any time *t,* $S_U(t) \leq N(t), S_{EP}(t) \leq N(t), S_{LP}(t) \leq N(t), E_W(t) \leq N(t), E_R(t) \leq N(t),$

$I_{AW}(t) \leq N(t), I_{SW}(t) \leq N(t), I_{AR}(t) \leq N(t), I_{SR}(t) \leq N(t), T_W(t) \leq N(t),$ and $R \leq N(t),$ so that

$$\frac{dS_U}{dt} = \pi - \lambda_W S_U - \lambda_R S_U - \alpha S_U - \mu S_U \geq -\lambda_W S_U - \lambda_R S_U - \alpha S_U - \mu S_U$$

$$\geq -2\beta S_U - 2\beta S_U - \alpha S_U - \mu S_U$$

$$\geq -\beta(4 + \alpha + \mu) S_U,$$

From here, it is clear that

$$S(t) \geq S(0)e^{-\beta(4+\alpha+\mu)t} \succ 0, \qquad \text{for } t \geq 0 \text{ and } S(0) \succ 0.$$

By using similar approach, it can equally be shown that $S_{EP}(t) \succ 0, S_{LP}(t) \succ 0, E_W(t) \succ 0,$ $E_R(t) \succ 0,$ $I_{AW}(t) \succ 0, I_{SW}(t) \succ 0, I_{AR}(t) \succ 0, I_{SR}(t) \succ 0, T_W(t) \succ 0,$ and $R \succ 0,$ respectively. Hence the solution of the model remains non-negative for all non-negative initial conditions.

Lemma 2.1

The region $D = \left\{ \left(S_U, S_{EP}, S_{LP}, E_W, E_R, I_{AW}, I_{SW}, I_{AR}, I_{SR}, T_W, R \right) \in R_+^{11} : N \leq \frac{\pi}{\mu} \right\}$ is positively-

invariant and attracts all the solution in R_+^{11}.

Proof: By adding the equations in the model system, we have:

$$\frac{dN}{dt} = \pi - \mu N - \delta_W \left(I_{AW} + I_{SW}\right) - \delta_R \left(I_{AR} + I_{SR}\right) - \theta \delta_W T_W \tag{2}$$

In the absence of disease, δ_W and δ_R equals zero; therefore equation (2) becomes:

$$\frac{dN}{dt} \le \pi - \mu N$$

Thus, whenever $N > \frac{\pi}{\mu}$ then $\frac{dN}{dt} < 0$. Hence, since it follows from the right hand side of the inequality that $\frac{dN}{dt}$ is bounded by $\pi - \mu N$, a standard comparison theorem can be used to show that:

$$N(t) \le N(0)e^{-\mu t} + \frac{\pi}{\mu}\left(1 - e^{-\mu t}\right).$$

If $N(0) \le \frac{\pi}{\mu}$, then $N(t) \le \frac{\pi}{\mu}$. Thus, D is a positively-invariant set under the flow described by model (1) so that no solution path leaves through the boundary of region D. Hence, it is sufficient to consider the dynamics of the model in region D. Thus, in this region, the model can be considered as been epidemiologically and mathematically well-posed [29].

This ends the proof.

3 Treatment-free model

For convenience we first study a version of model (1) in the absence of treatment by setting $T_W = \tau_W = \theta = \psi_W = 0$ before we proceed to analyze the treatment model (1); thus, we obtain a treatment-free model:

$$\frac{dS_U}{dt} = \pi - \left(\lambda_W + \lambda_R\right)S_U - \left(\alpha + \mu\right)S_U$$

$$\frac{dS_{EP}}{dt} = \left(1-k\right)\alpha S_U - \left(1-\varepsilon_1\right)\left(\lambda_W + \lambda_R\right)S_{EP} - \mu S_{EP}$$

$$\frac{dS_{LP}}{dt} = k\alpha S_U - \left(1-\varepsilon_2\right)\left(\lambda_W + \lambda_R\right)S_{LP} - \mu S_{LP}$$

$$\frac{dE_W}{dt} = \left\{S_U + (1-\varepsilon_1)S_{EP} + (1-\varepsilon_2)S_{LP}\right\}\lambda_W - (\sigma_W + \mu)E_W$$

$$\frac{dE_R}{dt} = \left\{S_U + (1-\varepsilon_1)S_{EP} + (1-\varepsilon_2)S_{LP}\right\}\lambda_R - (\sigma_R + \mu)E_R \quad (3)$$

$$\frac{dI_{AW}}{dt} = (1-f_1)\sigma_W E_W - (\gamma_W + \delta_W + \mu)I_{AW}$$

$$\frac{dI_{SW}}{dt} = f_1\sigma_W E_W + \gamma_W I_{AW} - (\delta_W + \mu)I_{SW}$$

$$\frac{dI_{AR}}{dt} = (1-f_2)\sigma_R E_R - (\gamma_R + \delta_R + \mu)I_{AR}$$

$$\frac{dI_{SR}}{dt} = f_2\sigma_R E_R + \gamma_W I_{AW} - (\delta_R + \mu)I_{SR}$$

$$\frac{dR}{dt} = -\mu R,$$

where $\lambda_W = \dfrac{\beta_W (I_{AW} + I_{SW})}{N}$ and $\lambda_R = \dfrac{\beta_R (I_{AR} + I_{SR})}{N}$.

For the treatment-free model (3), it can be shown that the following region is positively, invariant and attracting:

$$D_1 = \left\{(S_U, S_{EP}, S_{LP}, E_W, E_R, I_{AW}, I_{SW}, I_{AR}, I_{SR}, R) \in R_+^{10} : N \le \frac{\pi}{\mu}\right\}$$

So that it is sufficient to consider the dynamics of the treatment-free model (3) in D_1.

3.1 Local stability of disease-free equilibrium

For the treatment-free model (3), the disease-free equilibrium (DFE) is given by:

$$\varepsilon_0 = \left\{(S_U^*, S_{EP}^*, S_{LP}^*, E_W^*, E_R^*, I_{AW}^*, I_{SW}^*, I_{AR}^*, I_{SR}^*, R^*) = \left(\frac{\pi}{\alpha+\mu}, \frac{\pi k\alpha}{\mu(\alpha+\mu)}, \frac{\pi(1-k)\alpha}{\mu(\alpha+\mu)}, 0,0,0,0,0,0,0\right)\right\}$$

(4)

By using the notations in [30], using next generation operator method on the system (3), we establish the linear stability of ε_0, by obtaining the matrices F and V, for the new infection terms and the remaining transfer terms respectively, given by:

$$F = \begin{pmatrix} 0 & 0 & \frac{Q\beta_W}{S_U^* + S_{EP}^* + S_{LP}^*} & \frac{Q\beta_W}{S_U^* + S_{EP}^* + S_{LP}^*} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{Q\beta_R}{S_U^* + S_{EP}^* + S_{LP}^*} & \frac{Q\beta_R}{S_U^* + S_{EP}^* + S_{LP}^*} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

And $$V = \begin{pmatrix} B_5 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & B_6 & 0 & 0 & 0 & 0 & 0 \\ -B_7 & 0 & B_8 & 0 & 0 & 0 & 0 \\ -f_1\sigma_w & 0 & -\gamma_W & B_9 & 0 & 0 & 0 \\ 0 & -B_{10} & 0 & 0 & B_{11} & 0 & 0 \\ 0 & -f_2\sigma_R & 0 & 0 & -\gamma_R & B_{13} & 0 \\ 0 & 0 & 0 & 0 & 0 & -\nu & \mu \end{pmatrix}$$

Where $B_1 = \alpha + \mu$, $B_2 = (1-k)\alpha$, $B_3 = (1-\varepsilon_1)$, $B_4 = (1-\varepsilon_2)$, $B_5 = \sigma_W + \mu$,

$B_6 = \sigma_R + \mu$, $B_7 = (1-f_1)\sigma_W$, $B_8 = \gamma_W + \delta_W + \mu$, $B_9 = \tau_W + \delta_W + \mu$,

$B_{10} = (1-f_2)\sigma_R$, $B_{11} = \gamma_R + \delta_R + \mu$, $B_{12} = (1-f_3)\psi_W$,

$B_{13} = \delta_R + \mu$, and $Q = S_U + B_3 S_{EP} + B_4 S_{LP}$

It follows that the reproduction number, denoted by $R_0 = \rho\left(FV^{-1}\right)$, is given by:

$$R_0 = \max\{R_R, R_W\},$$

With $$R_W = \frac{\beta_W\left(B_2B_3 + k\alpha B_4 + \mu\right)\left(f_1\sigma_W B_8 + B_7B_9 + \gamma_W B_7\right)}{B_1B_5B_8B_9}$$

And $$R_R = \frac{\beta_R\left(B_2B_3 + k\alpha B_4 + \mu\right)\left(f_2\sigma_R B_{11} + B_{10}B_{13} + \gamma_R B_{10}\right)}{B_1B_6B_{11}B_{13}}$$

By subtituting back the values of B_1, B_2 e.t.c as defined earlier into each of the reproduction numbers above, we obtain:

$$R_W = \frac{\beta_W\left[\mu + (1-\varepsilon_1)k\alpha + (1-\varepsilon_2)(1-k)\alpha\right]\left[f_1\sigma_W(\gamma_W + \delta_W + \mu) + (1-f_1)\sigma_W(\tau_W + \delta_W + \mu) + \gamma_W(1-f_1)\sigma_W\right]}{(\alpha+\mu)(\sigma_W + \mu)(\gamma_W + \delta_W + \mu)(\tau_W + \delta_W + \mu)}$$

$$R_R = \frac{\beta_R\left[\mu + (1-\varepsilon_1)k\alpha + (1-\varepsilon_2)(1-k)\alpha\right]\left[f_2\sigma_R(\gamma_R + \delta_R + \mu) + (1-f_2)\sigma_R(\delta_R + \mu) + \gamma_R(1-f_2)\sigma_R\right]}{(\alpha+\mu)(\sigma_R+\mu)(\gamma_R+\delta_R+\mu)(\delta_R+\mu)}$$

where R_W and R_R are the basic Reproduction number for wild and drug-resistant strain of the disease. We define the basic reproduction number as the expected number of secondary cases of infection which would occur due to a primary case in a completely susceptible population [23]. This is a parameter useful in determining the stability of the disease-free equilibrium towards measuring the peak and final size of an epidemic. If $R_0 < 1$, then a few infected individuals introduced into a completely susceptible population will, on average, fail to replace themselves, and the disease will not spread. On the other hand, when $R_0 > 1$, then the number of infected individuals will increase with each generation and ultimately, the disease will spread.

3.1.1 Interpretation of the reproduction number

In this section, we proceed to give interpretation of the reproduction numbers computed above so that the heathcare practitioners can have a good understanding of what it stands for and how to apply them in their work on the curtailment and control of the disease.

For the reproduction number R_W for the wild strain, given as:

$$R_W = \frac{\beta_W\left[\mu + (1-\varepsilon_1)k\alpha + (1-\varepsilon_2)(1-k)\alpha\right]\left[f_1\sigma_W(\gamma_W + \delta_W + \mu) + (1-f_1)\sigma_W(\tau_W + \delta_W + \mu) + \gamma_W(1-f_2)\sigma_W\right]}{(\alpha+\mu)(\sigma_W+\mu)(\gamma_W+\delta_W+\mu)(\tau_W+\delta_W+\mu)}$$

Observe that at DFE,

$$\beta_W \frac{\left[S_U^* + (1-\varepsilon_1)S_{EP}^* + (1-\varepsilon_1)S_{LP}^*\right]}{N^*} = \frac{\beta_W\left[\mu + (1-\varepsilon_1)k\alpha + (1-\varepsilon_2)(1-k)\alpha\mu\right]}{\alpha+\mu}$$

Thus,

$$R_W = \beta_W \frac{\left[S_U^* + (1-\varepsilon_1)S_{EP}^* + (1-\varepsilon_1)S_{LP}^*\right]}{N^*} \times \frac{\left[f_1\sigma_W(\gamma_W + \delta_W + \mu) + (1-f_1)\sigma_W(\tau_W + \delta_W + \mu) + \gamma_W(1-f_2)\sigma_W\right]}{(\sigma_W+\mu)(\gamma_W+\delta_W+\mu)(\tau_W+\delta_W+\mu)}$$

$$R_W = \beta_W \frac{\left[S_U^* + (1-\varepsilon_1)S_{EP}^* + (1-\varepsilon_1)S_{LP}^*\right]}{N^*} \times \left[\frac{f_1\sigma_W}{(\sigma_W+\mu)(\tau_W+\delta_W+\mu)} + \frac{(1-f_1)\sigma_W}{(\sigma_W+\mu)(\gamma_W+\delta_W+\mu)} + \frac{\gamma_W(1-f_2)\sigma_W}{(\sigma_W+\mu)(\gamma_W+\delta_W+\mu)(\tau_W+\delta_W+\mu)}\right]$$

$R_W = [Infection\ rate\ at\ DFE]$ [(*Fraction that survives* E_W & *moves to* I_{AW} *class*)(*duration in* I_{AW} *class*)
+ (Fraction that survives E_W and moves to I_{SW} class)(*Duration in* I_{SW} *class)* +
(Fraction that survives E_W *and moves to* I_{AW} class)(fraction that survives I_{AW} and moves to I_{SW})(Duration in I_{SW} class)].

Likewise, we interprete the reproduction number for the drug-resistant strain, given as:

$$R_R = \frac{\beta_R\left[\mu+(1-\varepsilon_1)k\alpha+(1-\varepsilon_2)(1-k)\alpha\right]\left[f_2\sigma_R(\gamma_R+\delta_R+\mu)+(1-f_2)\sigma_R(\delta_R+\mu)+\gamma_R(1-f_2)\sigma_R\right]}{(\alpha+\mu)(\sigma_R+\mu)(\gamma_R+\delta_R+\mu)(\delta_R+\mu)}$$

Observe that at DFE,

$$\beta_W\frac{\left[S_U^*+(1-\varepsilon_1)S_{EP}^*+(1-\varepsilon_1)S_{LP}^*\right]}{N^*}=\frac{\beta_W\left[\mu+(1-\varepsilon_1)k\alpha+(1-\varepsilon_2)(1-k)\alpha\right]}{\alpha+\mu}$$

Thus,

$$R_R=\frac{\left[S_U^*+(1-\varepsilon_1)S_{EP}^*+(1-\varepsilon_1)S_{LP}^*\right]}{N^*}\frac{\left[f_2\sigma_R(\gamma_R+\delta_R+\mu)+(1-f_2)\sigma_R(\delta_R+\mu)+\gamma_R(1-f_2)\sigma_R\right]}{(\sigma_R+\mu)(\gamma_R+\delta_R+\mu)(\delta_R+\mu)}$$

$$R_R=\beta_R\frac{\left[S_U^*+(1-\varepsilon_1)S_{EP}^*+(1-\varepsilon_1)S_{LP}^*\right]}{N^*}\times\left[\frac{f_2\sigma_R}{(\sigma_R+\mu)(\delta_R+\mu)}+\frac{(1-f_2)\sigma_R}{(\sigma_R+\mu)(\gamma_R+\delta_R+\mu)}+\frac{\gamma_R(1-f_2)\sigma_R}{(\sigma_R+\mu)(\gamma_R+\delta_R+\mu)(\delta_R+\mu)}\right]$$

R_R = [Infection rate at DFE][(Fraction that survives E_R and moves to I_{AR} class)(Duration in I_{AR} class)+ (fraction that survives E_R class and moves to I_{SR} class)(Duration in I_{SR} class) + (fraction that survives E_R class and moves to I_{AR})(fraction that survives I_{AR} class and moves to I_{SR} class)(Duration in I_{SR} class)]

By using theorem 2 in [30], we establish the following result:
Lemma 2: The Disease-Free Equilibrium (DFE) of the treatment-free model (3), given by equation (4), is Locally Asymptotically Stable (LAS) if $R_0 < 1$, & unstable if $R_0 > 1$.

It should be noted that R_W is the basic reproduction number of the wild strain of the disease while R_R is the basic reproduction number of the resistance strain of the disease. It is worth stating that R_W and R_R measures respectively, the average number of new infections brought about by the introduction of a single infected individual with the wild or resistance strain of the disease to a completely susceptible population.
The meaning of Lemma 2 epidemiologically, is that the disease, anthrax (Anthraces Bacillus) can be eliminated from the community when $R_0 < 1$, if the initial sizes of the subpopulations of the model are in the basin of attraction of ε_0.
Remark:
However, in order to ensure that the elimination of the disease is independent of the initial sizes of the subpopulations, it is necessary to show that the DFE is Globally Asymptotically Stable (GAS) in D_1. This is as established below:

3.2 Global stability of Disease Free Equilibrium (DFE)

Theorem 1: The DFE of the model (3) given by equation (4) is Globally Asymptotically Stable (GAS) in D_1 whenever $R_0 \prec 1$.

Proof: we consider the following Lyapunov function:

$$F = \left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}(f_1\sigma_W B_8 + B_7 B_9 + \gamma_W B_7)\right]E_W + \left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}B_5(\gamma_W + B_9)\right]I_{AW} +$$

$$\left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}B_5 B_8\right]I_{SW} + \left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}(f_2\sigma_R B_{11} + B_{10}B_{13} + \gamma_R B_{10})\right]E_R +$$

$$\left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}B_6(\gamma_R + B_{13})\right]I_{AR} + \left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}B_6 B_{11}\right]I_{SR}$$

With Lyapunov derivative (where a dot represents differentiation with respect to time)

$$\dot{F} = \left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}(f_1\sigma_W B_8 + B_7 B_9 + \gamma_W B_7)\right]\dot{E_W} + \left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}B_5(\psi_W + B_9)\right]\dot{I}_{AW} +$$

$$\left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}B_5 B_8\right]\dot{I}_{SW} + \left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}(f_2\sigma_R B_{11} + B_{10}B_{13} + \gamma_R B_{10})\right]\dot{E}_R +$$

$$\left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}B_6(\gamma_R + B_{13})\right]\dot{I}_{AR} + \left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}B_6 B_{11}\right]\dot{I}_{SR}$$

By putting the values of $\dot{E_W}$, $\dot{I_{AW}}$, e.t.c into this we obtained:

$$\dot{F} = \left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}(f_1\sigma_W B_8 + B_7 B_9 + \gamma_W B_7)\right]\left[(S_U^* + (1-\varepsilon_1)S_{EP}^* + (1-\varepsilon_1)S_{LP}^*)\lambda_W - B_5 E_W\right] +$$

$$\left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}B_5(\gamma_W + B_9)\right]\left[f_1\sigma_W E_W - B_8 I_{AW}\right] +$$

$$\left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}B_5 B_8\right]\left[B_{10}E_W + \psi_W I_{AW} - B_9 I_{SW}\right] +$$

$$\left[\frac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}(B_{10}B_{13} + f_2\sigma_R B_{11} + \gamma_R B_{10})\right]\left[(S_U + (1-\varepsilon_1)S_{EP} + (1-\varepsilon_1)S_{LP})\lambda_R - B_6 E_R\right] +$$

$$\left[\frac{(\mu+k\alpha B_3+B_2B_3)}{\alpha+\mu}B_6(\gamma_R+B_{13})\right]\left[f_2\sigma_R\dot{E_R}-B_{11}I_{AR}\right]+$$
$$\left[\frac{(\mu+k\alpha B_3+B_2B_3)}{\alpha+\mu}B_6B_{11}\right]\left[f_2\sigma_R E_R+\gamma_R I_{AR}-B_{13}I_{SR}\right]$$

$$=\left[\frac{(\mu+k\alpha B_3+B_2B_3)}{\alpha+\mu}\right]\left[f_1\sigma_W B_8+B_7B_9+B_7\gamma_W\right]\left[\left(S_U+(1-\varepsilon_1)\dot{S_{EP}}+(1-\varepsilon_1)S_{LP}\right)\right]\lambda_W-$$
$$\left[\frac{(\mu+k\alpha B_3+B_2B_3)}{\alpha+\mu}B_5B_8B_9(I_{AW}+I_{SW})\right]+\left[\frac{(\mu+k\alpha B_3+B_2B_3)}{\alpha+\mu}\right]\left[f_2\sigma_W B_{11}+B_{10}B_{13}+B_{10}\gamma_R\right]$$
$$\times\left[\left(S_U+(1-\varepsilon_1)\dot{S_{EP}}+(1-\varepsilon_1)S_{LP}\right)\right]\lambda_R-\left[\frac{(\mu+k\alpha B_3+B_2B_3)}{\alpha+\mu}B_6B_{11}B_{13}(I_{AR}+I_{SR})\right]$$
$$\leq\left[\frac{(\mu+k\alpha B_3+B_2B_3)}{\alpha+\mu}B_5B_8B_9(I_{AW}+I_{SW})\right]$$
$$\times\left[\frac{\beta_W\left[f_1\sigma_W B_8+B_7B_9+B_7\gamma_W\right]\left(S_U+(1-\varepsilon_1)S_{EP}+(1-\varepsilon_1)S_{LP}\right)}{B_5B_8B_9N}-1\right]+$$
$$\left[\frac{(\mu+k\alpha B_3+B_2B_3)}{\alpha+\mu}B_6B_{11}B_{13}(I_{AR}+I_{SR})\right]\times\left[\frac{\beta_R\left[f_2\sigma_R B_{11}+B_{10}B_{13}+B_{10}\gamma_R\right]\left(S_U+(1-\varepsilon_1)S_{EP}+(1-\varepsilon_1)S_{LP}\right)}{B_6B_{11}B_{13}N}-1\right]$$

For $\quad\dfrac{S_U+(1-\varepsilon_1)S_{EP}+(1-\varepsilon_1)S_{LP}}{N}\leq 1$

Then

$$\dot{F}\leq\left[\frac{(\mu+k\alpha B_3+B_2B_3)}{\alpha+\mu}B_5B_8B_9(I_{AW}+I_{SW})\right]\left[\frac{\alpha+\mu}{(\mu+k\alpha B_3+B_2B_3)}R_W-1\right]+$$
$$\left[\frac{(\mu+k\alpha B_3+B_2B_3)}{\alpha+\mu}B_6B_{11}B_{13}(I_{AW}+I_{SW})\right]\left[\frac{\alpha+\mu}{(\mu+k\alpha B_3+B_2B_3)}R_R-1\right]$$

$$\dot{F}\leq\left[\frac{(\mu+k\alpha B_3+B_2B_3)}{\alpha+\mu}B_5B_8B_9(I_{AW}+I_{SW})\right]\left[\frac{\alpha+\mu}{(\mu+k\alpha B_3+B_2B_3)}R_W-1\right]+$$
$$\left[\frac{(\mu+k\alpha B_3+B_2B_3)}{\alpha+\mu}B_6B_{11}B_{13}(I_{AW}+I_{SW})\right]\left[\frac{\alpha+\mu}{(\mu+k\alpha B_3+B_2B_3)}R_R-1\right]$$

We rewrite this as follows:

$$\dot{F}\leq PB_5B_8B_9(I_{AW}+I_{SW})\left[\frac{1}{P}R_W-1\right]+PB_6B_{11}B_{13}(I_{AR}+I_{SR})\left[\frac{1}{P}R_R-1\right]$$

where $P = \dfrac{(\mu + k\alpha B_3 + B_2 B_3)}{\alpha + \mu}$,

$\dot{F} \le 0$ If $P \le 1$, $\dfrac{1}{P} R_W \le 1$ and $\dfrac{1}{P} R_R \le 1$

Since all the model parameters are non-negative, it follows that $\dot{F} \le 0$ for $R_0 \le 1$ with $\dot{F} = 0$ if and only if $E_W = E_R = 1_{AW} = 1_{SW} = 1_{AR} = 1_{SR} = 0$. Hence, F is a Lyapunov function on D_1. Therefore, by LaSalle's invariance principle [35], every solution to the equations in the treatment-free model (3), with initial conditions in D_1, approaches ε_0 as $t \to \infty$.

Thus, theorem 1 shows that the necessary and sufficient condition for the elimination of the disease from the community is the classical requirement that $R_0 \le 1$.

Epidemiologically, the implication of this theorem is that both strains will be eliminated from the community if the use of prophylaxis/antibiotics treatment can lead to a reduction of the maximum of the reproduction numbers of the two strains below unity.

3.3 Existence and local stability of boundary equilibria

The non-trivial equilibria of the treatment-free model (3) occur when at least one of the infected variables there in it is non-zero; as these cannot be cleanly expressed in closed form, we use the approach in [31] to explore the possibility of the existence and stability of the non-trivial equilibria. By inspection, the possible equilibria of the model (3) are as stated below:

(1) No resistance strain boundary equilibrium, wild strain-only

$$\varepsilon_W = \left(S_U^*, S_{EP}^*, S_{LP}^*, E_W^*, 0, I_{AW}^*, I_{SW}^*, 0, 0, R^*\right)$$

(2) No wild strain boundary equilibrium, drug-resistant strain-only

$$\varepsilon_R = \left(S_U^*, S_{EP}^*, S_{LP}^*, 0, E_R^*, 0, 0, I_{AR}^*, I_{SR}^*, R^*\right)$$

(3) Co-existence equilibrium, that is, the two strains co-exist,

$$\varepsilon_{WR} = \left(S_U^*, S_{EP}^*, S_{LP}^*, E_W^*, E_R^*, I_{AW}^*, I_{SW}^*, I_{AR}^*, I_{SR}^*, R^*\right)$$

By solving the treatment-free model (3) at steady state, we obtained:

$$S_U^{**} = \frac{\pi}{\lambda_W^{**} + \lambda_R^{**} + \alpha + \mu} \qquad S_{EP}^{**} = \frac{\pi(1-k)\alpha}{\left[(1-\varepsilon_1)(\lambda_W^{**} + \lambda_R^{**}) + \mu\right]\left[(\lambda_W^{**} + \lambda_R^{**}) + \alpha + \mu\right]},$$

$$S_{LP}^{**} = \frac{\pi k \alpha}{\left[(1-\varepsilon_2)(\lambda_W^{**} + \lambda_R^{**}) + \mu\right]\left[(\lambda_W^{**} + \lambda_R^{**}) + \alpha + \mu\right]}, \qquad E_W^{**} = A\frac{\lambda_W^{**}}{B_5}\left[\frac{\pi}{\lambda_W^{**} + \lambda_R^{**} + \alpha + \mu}\right],$$

$$E_R^{**} = A\frac{\lambda_R^{**}}{B_6}\left[\frac{\pi}{\lambda_W^{**}+\lambda_R^{**}+\alpha+\mu}\right], \qquad I_{AW}^{**} = A\frac{B_7\lambda_W^{**}}{B_5B_8}\left[\frac{\pi}{\lambda_W^{**}+\lambda_R^{**}+\alpha+\mu}\right],$$

$$I_{SW}^{**} = A\lambda_W^{**}\left[\frac{f_1\sigma_W B_8 + B_7\gamma_W}{B_5B_8B_9}\right]\left[\frac{\pi}{\lambda_W^{**}+\lambda_R^{**}+\alpha+\mu}\right], \qquad I_{AR}^{**} = A\frac{B_{10}\lambda_R^{**}}{B_6B_{11}}\left[\frac{\pi}{\lambda_W^{**}+\lambda_R^{**}+\alpha+\mu}\right],$$

$$I_{SR}^{**} = A\lambda_R^{**}\left[\frac{f_2\sigma_W B_{11} + B_{10}\gamma_R}{B_6B_{11}B_{13}}\right]\left[\frac{\pi}{\lambda_W^{**}+\lambda_R^{**}+\alpha+\mu}\right], \qquad \text{and } R^{**}=0 \tag{5}$$

Note that at endemic state, the expressions for λ_W and λ_R denoted by λ_W^{**} and λ_R^{**} are given by:

$$\lambda_W^{**} = \frac{\beta\left(I_{AW}^{**}+I_{SW}^{**}\right)}{N^{**}} \quad \text{and} \quad \lambda_R^{**} = \frac{\beta\left(I_{AR}^{**}+I_{SR}^{**}\right)}{N^{**}} \tag{6}$$

By substituting the expressions in equation (5) into (6) we obtained:

$$\lambda_W^{**} = \phi_1\left(\lambda_W^{**},\lambda_R^{**}\right) = \frac{\beta_W A\lambda_W^{**}\left[\frac{\pi}{\lambda_W^{**}+\lambda_R^{**}+\alpha+\mu}\right]\left[\frac{B_7B_9 + f_1\sigma_W B_8 + B_7\gamma_W}{B_5B_8B_9}\right]}{N^{**}}$$

$$\lambda_R^{**} = \phi_2\left(\lambda_W^{**},\lambda_R^{**}\right) = \frac{\beta_R A\lambda_R^{**}\left[\frac{\pi}{\lambda_W^{**}+\lambda_R^{**}+\alpha+\mu}\right]\left[\frac{B_{10}B_{13} + f_2\sigma_R B_{11} + B_{10}\gamma_R}{B_6B_{11}B_{13}}\right]}{N^{**}} \tag{7}$$

Where

$$N^{**} = \left[\frac{\pi}{\lambda_W^{**}+\lambda_R^{**}+\alpha+\mu}\right]\left[C + \left\{\frac{\mu B_8B_9 + \mu(1-f_1)\sigma_W B_7 + \mu f_1\sigma_W B_8 + \mu B_7\gamma_W}{B_5B_8B_9}\right\}A\lambda_W^{**} + \left\{\frac{\mu B_{11}B_{13} + \mu B_{13}B_{10} + \mu f_2\sigma_R B_{11} + \mu B_{10}\gamma_R}{B_6B_{11}B_{13}}\right\}A\lambda_R^{**}\right]$$

$$A = 1 + \frac{(1-\varepsilon_1)(1-k)\alpha}{(1-\varepsilon_1)\left(\lambda_W^{**}+\lambda_R^{**}\right)+\mu} + \frac{(1-\varepsilon_2)k\alpha}{(1-\varepsilon_2)\left(\lambda_W^{**}+\lambda_R^{**}\right)+\mu},$$

And $$C = 1 + \frac{(1-k)\alpha}{(1-\varepsilon_1)\left(\lambda_W^{**}+\lambda_R^{**}\right)+\mu} + \frac{k\alpha}{(1-\varepsilon_2)\left(\lambda_W^{**}+\lambda_R^{**}\right)+\mu},$$

The equilibria of the model can then be obtained by finding the fixed points of the system:

$$x = \phi(x) = \begin{pmatrix}\phi_1\left(\lambda_W^{**},\lambda_R^{**}\right)\\ \phi_2\left(\lambda_W^{**},\lambda_R^{**}\right)\end{pmatrix}, \qquad \text{where } x = \begin{pmatrix}\lambda_W^{**}\\ \lambda_R^{**}\end{pmatrix}, \tag{8}$$

as follows:

3.3.1. Existence and stability of wild strain-only equilibrium (ε_W)

We claim the following:

Theorem 2: The treatment-free model (3) has a unique positive wild strain-only boundary equilibrium ε_W, whenever $R_R \prec 1 \prec R_W$. This equilibrium is locally asymptotically stable whenever it exists.

Proof: Let $R_R \prec 1$. it can easily be shown that for $R_R \prec 1$, $(I_{AR}, I_{SR}) \to (0,0)\, t \to \infty$. In addition, it is clear from equation (7) that $\phi_2(\lambda_W^{**}, 0) = 0$. Thus a fixed point of $\phi_1(\lambda_W^{**}, \lambda_R^{**}) = 0$ is obtained by solving equation $\phi_1(\lambda_W^{**}, 0) = \lambda_W^{**}$. Hence, it follows that λ_W^{**} is the root of equation:

$$G_1(\lambda_W^{**3}) + G_2(\lambda_W^{**2}) + G_3(\lambda_W^{**}) + \mu^2[1 - R_W] = 0 \tag{9}$$

Where

$$G_1 = (1-\varepsilon_1)(1-\varepsilon_2)[\mu B_8 B_9 + \mu B_8 f_1 \sigma_W + \mu B_7 \gamma_W] \succ 0$$

$$G_2 = [(1-\varepsilon_1)(1-\varepsilon_2) + \mu(1-\varepsilon_1) + \mu(1-\varepsilon_2)][\mu B_8 B_9 + \mu B_8 f_1 \sigma_W + \mu B_7 \gamma_W + \mu(1-\varepsilon_1)(1-\varepsilon_2)]$$
$$[B_5 B_8 B_9 - \beta_W (B_7 B_9 + B_8 B_9 + B_7 \gamma_W)]$$

$$G_3 = [\mu^2 + \mu(1-\varepsilon_1)k\alpha + \mu\alpha(1-\varepsilon_2)(1-k)](\mu B_8 B_9 + \mu B_8 f_1 \sigma_W + \mu B_7 \gamma_W)$$
$$+ \mu B_5 B_8 B_9 [\alpha(1-k)(1-\varepsilon_1) + \mu(1-\varepsilon_2) + \alpha k(1-\varepsilon_2) - \beta_W [\alpha(1-k)(1-\varepsilon_1) + \mu(1-\varepsilon_1) + \mu(1-\varepsilon_2)]]$$
$$[B_7 B_8 + B_8 f_1 \sigma_W + B_7 \gamma_W]$$

From the polynomial above, regardless of the sign of G_3, the polynomial has a unique positive solution whenever $R_W \succ 1$. Furthermore, for the equilibrium ε_W to exist alone, it is necessary that the drug resistant strain of the disease does not exist, (that is $R_R \prec 1$). Thus, by putting all these together, it shows that a unique wild strain-only boundary equilibrium, ε_W exists, whenever $R_R \prec 1 \prec R_W$.

We now explore the local stability property of ε_W; we note that the Jacobian of the system (8) is given by:

$$J(\lambda_W^{**}, \lambda_R^{**}) = \begin{pmatrix} \dfrac{\partial \phi_1(\lambda_W^{**}, \lambda_R^{**})}{\partial \lambda_W^{**}} & \dfrac{\partial \phi_1(\lambda_W^{**}, \lambda_R^{**})}{\partial \lambda_R^{**}} \\ \dfrac{\partial \phi_2(\lambda_W^{**}, \lambda_R^{**})}{\partial \lambda_W^{**}} & \dfrac{\partial \phi_2(\lambda_W^{**}, \lambda_R^{**})}{\partial \lambda_R^{**}} \end{pmatrix}, \tag{10}$$

So that $$J(\lambda_W^{**}, 0) = \begin{pmatrix} \dfrac{1}{R_W} & \left.\dfrac{\partial \phi_1(\lambda_W^{**}, \lambda_R^{**})}{\partial \lambda_W^{**}}\right|_{(\lambda_W^{**}, 0)} \\ 0 & \dfrac{R_R}{R_W} \end{pmatrix}$$

From this equation, observe that the eigen values of $J(\lambda_W^{**},0)$ are $\lambda_1 = \frac{1}{R_W}$ and $\lambda_2 = \frac{R_R}{R_W}$, Then, if $R_R \prec 1$, from here, then it implies that the wild strain-only equilibrium , ε_W, is locally asymptotically stable whenever $\left|\frac{1}{R_R}\right| \prec 1$, (that is $R_W \succ 1$) and $\left|\frac{R_R}{R_W}\right| \prec 1$, (that is $R_R \prec R_W$). Hence, ε_W, is locally asymptotically stable whenever $R_R \prec 1 \prec R_W$.

3.3.2. Existence and stability of drug resistant strain-only equilibrium (ε_R)

We claim the following result.

Theorem 3: The treatment-free model (3) has a unique positive drug-resistant strain-only boundary equilibrium ε_R, whenever $R_W \prec 1 \prec R_R$. This equilibrium is locally asymptotically stable whenever it exists.

Proof: Let $R_W \prec 1$. so that $(I_{AW}, I_{SW}) \to (0,0)$ as $t \to \infty$. In addition, it is clear from equation (7) that $\phi_2(0, \lambda_R^{**}) = 0$. Thus a fixed point of $\phi_1(\lambda_W^{**}, \lambda_R^{**}) = 0$ is obtained by solving equation $\phi_2(0, \lambda_R^{**}) = \lambda_R^{**}$. Hence, it follows that λ_R^{**} is the root of equation:

$$G_{11}(\lambda_R^{**3}) + G_{12}(\lambda_R^{**2}) + G_{13}(\lambda_R^{**}) + \mu^2[1 - R_R] = 0 \tag{11}$$

Where

$$G_{11} = (1-\varepsilon_1)(1-\varepsilon_2)[\mu B_{11}B_{13} + \mu B_6 B_{10} B_{13} + \mu B_{11} f_2 \sigma_R] \succ 0$$

$$G_{12} = [\alpha(1-\varepsilon_1)(1-\varepsilon_2) + \mu(1-\varepsilon_1) + \mu(1-\varepsilon_2)]\left[\begin{pmatrix}\mu B_{11}B_{13} + \mu B_6 B_{10} B_{13} + \\ \mu B_{11} f_2 \sigma_R + \mu B_{10}\gamma_W\end{pmatrix} + \mu(1-\varepsilon_1)(1-\varepsilon_2)\right]$$
$$[B_6 B_{11} B_{13} - \beta_R(B_{10}B_{13} + B_{11} f_2 \sigma_R + B_{10}\gamma_R)]$$

$$G_{13} = \mu B_5 B_8 B_9[\alpha(1-\varepsilon_1)(\mu + k\alpha) + \mu(1-\varepsilon_1) + \alpha(1-\varepsilon_2)(1-k)] + [\mu^2 + \mu\alpha(1-\varepsilon_1)(1-k)]$$
$$(\mu B_{11}B_{13} + \mu B_6 B_{10} B_{13} + B_{11} f_1 \sigma_W + \mu B_{10}\gamma_W) - \beta_R(\alpha(1-\varepsilon_1)(1-\varepsilon_2) + \mu(1-\varepsilon_2))[B_{10}B_{13} + B_{11} f_2 \sigma_R + B_{10}\gamma_R]$$

It follows from the polynomial above, that regardless of the sign of G_{13}, the polynomial has a unique positive solution whenever $R_R \succ 1$. Furthermore, for the equilibrium ε_R to exist alone, it is necessary that the wild strain of the disease does not exist, (that is $R_W \prec 1$). Thus, by putting all these together, it shows that a unique drug resistant strain-only boundary equilibrium, ε_R exist, whenever $R_W \prec 1 \prec R_R$.

By evaluating J at $(0, \lambda_R^{**})$ we have:

$$J\left(0,\lambda_R^{**}\right)=\begin{pmatrix} \dfrac{R_W}{R_R} & 0 \\ \left.\dfrac{\partial\phi_1\left(\lambda_W^{**},\lambda_R^{**}\right)}{\partial\lambda_R^{**}}\right|_{\left(0,\lambda_R^{**}\right)} & \dfrac{1}{R_R} \end{pmatrix},$$

From here it follows that the local asymptotic stability of the equilibrium ε_R, requires $\left|\frac{1}{R_R}\right| \prec 1,$ (that is $R_R \succ 1$) and $\left|\frac{R_W}{R_R}\right| \prec 1, (R_W \prec R_R.)$. Thus, the drug resistant strain-only boundary equilibrium ε_R, is locally asymptotically stable provided that $R_W \prec 1 \prec R_R.$.

3.4 Existence and local stability of co-existence equilibria

We rewrite the expressions in equation (7) as follows:

$$\lambda_W^{**}=\frac{\beta\left(I_{AW}^{**}+I_{SW}^{**}\right)}{N^{**}}\equiv\frac{\lambda_W^{**}R_W}{1+D+\lambda_W^{**}L_1+\lambda_R^{**}L_2}$$

and

$$\lambda_R^{**}=\frac{\beta\left(I_{AR}^{**}+I_{SR}^{**}\right)}{N^{**}}\equiv\frac{\lambda_R^{**}R_R}{1+D+\lambda_W^{**}L_1+\lambda_R^{**}L_2} \tag{12}$$

Where $D=\dfrac{(1-k)\alpha}{(1-\varepsilon_1)\left(\lambda_W^{**}+\lambda_R^{**}\right)+\mu}+\dfrac{k\alpha}{(1-\varepsilon_2)\left(\lambda_W^{**}+\lambda_R^{**}\right)+\mu}$

$$L_1=\left\{\frac{\mu B_8B_9+\mu(1-f_1)\sigma_WB_7+\mu f_1\sigma_WB_8+\mu B_7\gamma_W}{B_5B_8B_9}\right\}A$$

$$L_2=\left\{\frac{\mu B_{11}B_{13}+\mu B_{13}B_{10}+\mu f_2\sigma_RB_{11}+\mu B_{10}\gamma_R}{B_6B_{11}B_{13}}\right\}A$$

It follows from equation (12) that

$$\lambda_W^{**}L_1+\lambda_R^{**}L_2=R_W-1,$$

$$\lambda_W^{**}L_1+\lambda_R^{**}L_2=R_R-1, \tag{13}$$

Since the left-hand sides of the expressions in equation (13) are always positive, it is necessary that $R_W \succ 1$ and $R_R \succ 1$. If $R_W \neq R_R$, then the system (13) is inconsistent, and there is no positive co-existence equilibrium in this case. Consequently, for equation (13) to be consistent, it is necessary that $R_W = R_R \succ 1$. There is a need to state that in this case, infinitely many equilibria (otherwise called a continuum of endemic equilibria) will arise. It should be noted that this phenomenon was observed

in a study of multi-strains model of HIV dynamics [31]. The implication of this is, is that by setting $R_W = R_R = R \succ 1$

$$\lambda_W^{**} L_1 + \lambda_R^{**} L_2 = R - 1, \tag{14}$$

So that $0 \prec \lambda_W^{**} \prec \dfrac{(R-1)}{L_1}$ and $0 \prec \lambda_R^{**} \prec \dfrac{(R-1)}{L_2}$.

We summarize the results below:

Theorem 4: There is a continuum of positive co-existence endemic equilibria, ε_{WR}^n $(n \in Z_+)$, for the treatment-free model (3), whenever the following conditions hold:

(a) $R_W = R_R = R \succ 1,$ (b) $0 \prec \lambda_W^{**} \prec \dfrac{(R-1)}{L_1},$

(c) $0 \prec \lambda_R^{**} \prec \dfrac{(R-1)}{L_2},$ (d) $\lambda_W^{**} = \dfrac{R - 1 - \lambda_R^{**} L_2}{L_2}$

And no co-existence endemic equilibria otherwise.

It should be noted that conditions (b) – (d) are needed to preserve the non-negativity of λ_W^{**} and λ_R^{**} in equation (13).

We then consider the stability of the continuum of positive co-existence endemic equilibria, ε_{WR}^n, is considered. For computational convenience, let

$$\text{Let } R_{WR}^n = \frac{T_0 + \sqrt{T_0^2 - 4T_1}}{2}, \quad n \in Z_+,$$

With $$T_0 = \left(\frac{\partial \varphi_1}{\partial \lambda_W^{**}} + \frac{\partial \varphi_2}{\partial \lambda_R^{**}} \right)\Bigg|_{(\lambda_W^{**}, \lambda_R^{**})} = \frac{1+R}{R},$$

and $$T_1 = \left(\frac{\partial \varphi_1}{\partial \lambda_W^{**}} \frac{\partial \varphi_2}{\partial \lambda_R^{**}} - \frac{\partial \varphi_1}{\partial \lambda_R^{**}} \frac{\partial \varphi_2}{\partial \lambda_W^{**}} \right)\Bigg|_{(\lambda_W^{**}, \lambda_W^{**})} = \frac{1}{R},$$

With $R_W = R_R = R$. We claim the following result.

Theorem 5: The continuum of positive co-existence endemic equilibria, ε_{WR}^n is neutrally stable whenever $R \succ 1.$

Proof: It can be shown that the eigenvalues of the Jacobian of ϕ at λ_W^{**} and λ_R^{**} in the region (b) to (c), given by equation (10), satisfy the following characteristics polynomial:

$$\chi^2 - \chi\left(\frac{\partial\varphi_1}{\partial\lambda_W^{**}} + \frac{\partial\vartheta_2}{\partial\lambda_R^{**}}\right)\Bigg|_{(\lambda_W^{**},\lambda_R^{**})} + \left(\frac{\partial\varphi_1}{\partial\lambda_W^{**}}\frac{\partial\varphi_2}{\partial\lambda_R^{**}} - \frac{\partial\varphi_1}{\partial\lambda_R^{**}}\frac{\partial\varphi_2}{\partial\lambda_W^{**}}\right)\Bigg|_{(\lambda_W^{**},\lambda_R^{**})} = 0$$

Which is equivalent to:

$$\chi^2 - \chi\left(\frac{1+R}{R}\right) + \frac{1}{R} = 0 \tag{15}$$

The roots of the quadratic equation (15) are $\chi = 1$ and $\chi = \frac{1}{R}$, so that the family of co-existence endemic equilibrium, ε_{WR}^n is neutrally stable (since $\chi = 1$ is an eigenvalue).

It is worthy of note that for the case R=*1, the solution of the system (13) is the trivial solution* $\left(\lambda_W^{**}, \lambda_R^{**}\right) = (0,0)$ corresponding to the disease-free equilibrium.

It is necessary to offer the following conjectures on competitive exclusion:

CONJECTURE 1: The treatment-free model (3) has a unique and locally asymptotically stable positive wild strain-only boundary equilibrium, ε_W, whenever $R_R \prec R_W$, and $R_W \succ 1.$

CONJECTURE 2: The treatment-free model (3) has a unique and locally asymptotically stable positive drug-resistant strain-only boundary equilibrium, ε_R, whenever $R_W \prec R_R$, and $R_R \succ 1.$

4 Analysis of Treatment model

4.1 Local stability of the Disease Free Equilibrium (DFE)

For the treatment-free model (1), it can be shown that the following region is positively, invariant and attracting:

$$D_1 = \left\{\left(S_U, S_{EP}, S_{LP}, E_W, E_R, I_{AW}, I_{SW}, I_{AR}, I_{SR}, T, R\right) \in R_+^{11} : N \le \frac{\pi}{\mu}\right\}$$

So that it is sufficient to consider the dynamics of the treatment-free model (1) in D_1.

The treatment-free model (1) has a disease-free equilibrium (DFE) given by:

$$\varepsilon_0^t = \left\{\left(S_U^*, S_{EP}^*, S_{LP}^*, E_W^*, E_R^*, I_{AW}^*, I_{SW}^*, I_{AR}^*, I_{SR}^*, T_W^*, R^*\right) = \left(\frac{\pi}{\alpha+\mu}.\frac{\pi k\alpha}{\mu(\alpha+\mu)}, \frac{\pi(1-k)\alpha}{\mu(\alpha+\mu)}, 0,0,0,0,0,0,0,0\right)\right\} \tag{16}$$

Likewise, as we did for the treatment-free model, the next generation matrices are given by:

$$F = \begin{pmatrix} 0 & 0 & \frac{Q\beta_W}{S_U^* + S_{EP}^* + S_{LP}^*} & \frac{Q\beta_W}{S_U^* + S_{EP}^* + S_{LP}^*} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & \frac{Q\beta_R}{S_U^* + S_{EP}^* + S_{LP}^*} & \frac{Q\beta_R}{S_U^* + S_{EP}^* + S_{LP}^*} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

$$V = \begin{pmatrix} B_5 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & B_6 & 0 & 0 & 0 & 0 & 0 & 0 \\ -B_7 & 0 & B_8 & 0 & 0 & 0 & 0 & 0 \\ -f_1\sigma_W & 0 & -\gamma_W & B_9 & 0 & 0 & 0 & 0 \\ 0 & -B_{10} & 0 & 0 & B_{11} & 0 & -f_3\psi_W & 0 \\ 0 & -f_2\sigma_R & 0 & 0 & -\gamma_R & B_{13} & -B_{12} & 0 \\ 0 & 0 & 0 & -\tau_W & 0 & 0 & B_{14} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -\nu & \mu \end{pmatrix}$$

Where $B_{11} = \alpha + \mu$, $B_{12} = (1-k)\alpha$, $B_{13} = (1-\varepsilon_1)$, $B_{14} = (1-\varepsilon_2)$,

$B_{15} = \sigma_W + \mu$, $B_{16} = \sigma_R + \mu$, $B_{17} = (1-f_1)\sigma_W$, $B_{18} = \gamma_W + \delta_W + \mu$,

$B_{19} = \tau_W + \delta_W + \mu$, $B_{20} = (1-f_2)\sigma_R$, $B_{21} = \gamma_R + \delta_R + \mu$, $B_{22} = (1-f_3)\psi_W$,

$B_{23} = \delta_R + \mu$, $B_{24} = \psi_W + \nu + \theta\delta_W + \mu$, and $Q = S_U + B_{13}S_{EP} + B_{14}S_{LP}$,

It follows that the reproduction number, denoted by $R_0^t = \rho(FV^{-1})$, is given by:

$$R_0^t = \max\{R_W, R_R\},$$

With $R_W^t = \dfrac{\beta_W(\mu + k\alpha B_{14} + B_{12}B_{13})(f_{11}\sigma_W B_{18} + B_{17}B_{19} + \gamma_W B_{17})}{B_{11}B_{15}B_{18}B_{19}}$

And $R_R^t = \dfrac{\beta_R(\mu + k\alpha B_{14} + B_{12}B_{13})(f_{22}\sigma_R B_{21} + B_{20}B_{23} + \gamma_R B_{20})}{B_{11}B_{16}B_{21}B_{23}}$

By subtituting back the values of B_{11}, B_{12} e.t.c as defined earlier into each of the reproduction numbers above, we obtain:

$$R_W^t = \frac{\beta_W\left[\mu+(1-\varepsilon_1)k\alpha+(1-\varepsilon_2)(1-k)\alpha\right]\left[f_1\sigma_W(\gamma_W+\delta_W+\mu)+(1-f_1)\sigma_W(\tau_W+\delta_W+\mu)+\gamma_W(1-f_1)\sigma_W\right]}{(\alpha+\mu)(\sigma_W+\mu)(\gamma_W+\delta_W+\mu)(\tau_W+\delta_W+\mu)}$$

$$R_R^t = \frac{\beta_R\left[\mu+(1-\varepsilon_1)k\alpha+(1-\varepsilon_2)(1-k)\alpha\right]\left[f_2\sigma_R(\gamma_R+\delta_R+\mu)+(1-f_2)\sigma_R(\delta_R+\mu)+\gamma_R(1-f_2)\sigma_R\right]}{(\alpha+\mu)(\sigma_R+\mu)(\gamma_R+\delta_R+\mu)((\delta_R+\mu))}$$

R_W^t and R_R^t are the basic Reproduction number for wild and drug-resistant strain of the disease.

4.1.1 Interpretation of the reproduction number

We proceed to give interpretation of the reproduction numbers computed above so that the heath care practitioners can have a good understanding of what it stands for and how to apply them in their work on the curtailment and control of the disease, this we do in this section, as follows:

For the reproduction number R_W^t for the wild strain, given as:

$$R_W^t = \frac{\beta_W\left[\mu+(1-\varepsilon_1)k\alpha+(1-\varepsilon_2)(1-k)\alpha\right]\left[f_1\sigma_W(\gamma_W+\delta_W+\mu)+(1-f_1)\sigma_W(\tau_W+\delta_W+\mu)+\gamma_W(1-f_2)\sigma_W\right]}{(\alpha+\mu)(\sigma_W+\mu)(\gamma_W+\delta_W+\mu)(\tau_W+\delta_W+\mu)}$$

Observe that at Disease Free Equilibrium (DFE),

$$\beta_W\frac{\left[S_U^*+(1-\varepsilon_1)S_{EP}^*+(1-\varepsilon_1)S_{LP}^*\right]}{N^*} = \frac{\beta_W\left[\mu+(1-\varepsilon_1)k\alpha+(1-\varepsilon_2)(1-k)\alpha\mu\right]}{\alpha+\mu}$$

Thus,

$$R_W^t = \beta_W\frac{\left[S_U^*+(1-\varepsilon_1)S_{EP}^*+(1-\varepsilon_1)S_{LP}^*\right]}{N^*}\times\frac{\left[f_1\sigma_W(\gamma_W+\delta_W+\mu)+(1-f_1)\sigma_W(\tau_W+\delta_W+\mu)+\gamma_W(1-f_2)\sigma_W\right]}{(\sigma_W+\mu)(\gamma_W+\delta_W+\mu)(\tau_W+\delta_W+\mu)}$$

$$R_W^t = \beta_W\frac{\left[S_U^*+(1-\varepsilon_1)S_{EP}^*+(1-\varepsilon_1)S_{LP}^*\right]}{N^*}$$
$$\times\left[\frac{f_1\sigma_W}{(\sigma_W+\mu)(\tau_W+\delta_W+\mu)}+\frac{(1-f_1)\sigma_W}{(\sigma_W+\mu)(\gamma_W+\delta_W+\mu)}+\frac{\gamma_W(1-f_2)\sigma_W}{(\sigma_W+\mu)(\gamma_W+\delta_W+\mu)(\tau_W+\delta_W+\mu)}\right]$$

$R_W^t = [Infection\ rate\ at\ DFE]$[(*Fraction that survives* E_W & *moves to* I_{AW} *class*)(*duration in* I_{AW} *class*)
+ (Fraction that survives E_W and moves to I_{SW} class)(*Duration in* I_{SW} *class)* +
(Fraction that survives E_W *and moves to* I_{AW} class)(fraction that survives I_{AW} and moves to I_{SW})(Duration in I_{SW} class)]

Likewise, we interprete the reproduction number for the drug-resistant strain, given as:

$$R_R^t = \frac{\beta_R\left[\mu+(1-\varepsilon_1)k\alpha+(1-\varepsilon_2)(1-k)\alpha\right]\left[f_2\sigma_R(\gamma_R+\delta_R+\mu)+(1-f_2)\sigma_R(\delta_R+\mu)+\gamma_R(1-f_2)\sigma_R\right]}{(\alpha+\mu)(\sigma_R+\mu)(\gamma_R+\delta_R+\mu)((\delta_R+\mu))}$$

Observe that at Disease Free Equilibrium DFE,

$$\beta_W\frac{\left[S_U^*+(1-\varepsilon_1)S_{EP}^*+(1-\varepsilon_1)S_{LP}^*\right]}{N^*}=\frac{\beta_W\left[\mu+(1-\varepsilon_1)k\alpha+(1-\varepsilon_2)(1-k)\alpha\right]}{\alpha+\mu}$$

Thus,

$$R_R^t = \frac{\beta_R\left[(1-k)\alpha(1-\varepsilon_1)+k\alpha(1-\varepsilon_2)+\mu\right]\left[f_2\sigma_R(\gamma_R+\delta_R+\mu)+(1-f_2)\sigma_R(\delta_R+\mu)+\gamma_R(1-f_2)\sigma_R\right]}{(\alpha+\mu)(\sigma_R+\mu)(\gamma_R+\delta_R+\mu)(\delta_R+\mu)}$$

$$R_R^t = \beta_R\frac{\left[S_U^*+(1-\varepsilon_1)S_{EP}^*+(1-\varepsilon_1)S_{LP}^*\right]}{N^*}$$
$$\times\left[\frac{f_2\sigma_R}{(\sigma_R+\mu)(\delta_R+\mu)}+\frac{(1-f_2)\sigma_R}{(\sigma_R+\mu)(\gamma_R+\delta_R+\mu)}+\frac{\gamma_R(1-f_2)\sigma_R}{(\sigma_R+\mu)(\gamma_R+\delta_R+\mu)(\delta_R+\mu)}\right]$$

R_R^t = [Infection rate at DFE][(Fraction that survives E_R and moves to I_{AR} class)(Duration in I_{AR} class) + (fraction that survives E_R class and moves to I_{SR} class)(Duration in I_{SR} class) + (fraction that survives E_R class and moves to I_{AR})(fraction that survives I_{AR} class and moves to I_{SR} class) (Duration in I_{SR} class)]

By using theorem 2 in [30], we establish the following result:

Lemma 3: The Disease-Free Equilibrium (DFE) of the treatment model (1), given by equation (16) is locally asymptotically stable (LAS) if $R_0^t \prec 0$ and unstable if $R_0^t \succ 0$

The implication of the above Lemma is that the use of antibiotics for treatment of the disease anthrax (Anthraces Bacillus) can be eliminated from the community when $R_0^t \prec 0$, if the initial sizes of the subpopulations of the model are in the basin of attraction of ε_0^t.

However, in order to ensure that the elimination of the disease is independent of the initial sizes of the subpopulations, it is necessary to show that the DFE of the model (1) is Globally Asymptotically Stable (GAS) in D_1. This is as established below:

4.2 Global stability of Disease Free Equilibrium (DFE)

Theorem 6: The DFE of the model (1) given by equation (16) is Globally Asymptotically Stable (GAS) in D_1 whenever $R_0^t \prec 0$.

Proof: the proof of this theorem is based on comparison theorem. We first rewrite the equations for the infected components in model (1) in compact form as follows:

$$\begin{pmatrix} \frac{dE_W(t)}{dt} \\ \frac{dE_R(t)}{dt} \\ \frac{dI_{AW}(t)}{dt} \\ \frac{dI_{SW}(t)}{dt} \\ \frac{dI_{AR}(t)}{dt} \\ \frac{dI_{SR}(t)}{dt} \\ \frac{dR(t)}{dt} \end{pmatrix} = (\text{F-V}) \begin{pmatrix} E_W(t) \\ E_R(t) \\ I_{AW}(t) \\ I_{SW}(t) \\ I_{AR}(t) \\ I_{SR}(t) \\ R(t) \end{pmatrix} - (1-\frac{1}{N}) \begin{pmatrix} 0 & 0 & P\beta_W & P\beta_W & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & P\beta_R & P\beta_R & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & \nu & -\mu \end{pmatrix} \begin{pmatrix} E_W(t) \\ E_R(t) \\ I_{AW}(t) \\ I_{SW}(t) \\ I_{AR}(t) \\ I_{SR}(t) \\ R(t) \end{pmatrix}$$

Where matrices F and V are as defined initially in section 4.1, and

$$P = \frac{\left[S_U^* + (1-\varepsilon_1)S_{EP}^* + (1-\varepsilon_1)S_{LP}^*\right]}{N^*},$$

Since $S(t) \le N(t)$ for all $t \ge N(t)$ in D, it follows that:

$$\begin{pmatrix} \frac{dE_W(t)}{dt} \\ \frac{dE_R(t)}{dt} \\ \frac{dI_{AW}(t)}{dt} \\ \frac{dI_{SW}(t)}{dt} \\ \frac{dI_{AR}(t)}{dt} \\ \frac{dI_{SR}(t)}{dt} \\ \frac{dR(t)}{dt} \end{pmatrix} \le (\text{F-V}) \begin{pmatrix} E_W(t) \\ E_R(t) \\ I_{AW}(t) \\ I_{SW}(t) \\ I_{AR}(t) \\ I_{SR}(t) \\ R(t) \end{pmatrix} \tag{17}$$

By using the fact that the eigen values of the matrix F - V all have negative real parts (see local stability result in lemma 3, where $\rho(\text{FV}^{-1}) \le 1$, if $R_0^t \prec 1$, which is equivalent to F-V having eigen values with negative real parts when $R_0^t \prec 1$, then it implies that the linearized differential inequality system (17) is stable whenever $R_0^t \prec 1$. Consequently, $(E_W(t), E_R(t), I_{AW}(t), I_{SW}(t), I_{AR}(t), I_{SR}(t), R(t)) \to (0,0,0,0,0,0,0)$ as $t \to \infty$. Hence, by comparison theorem (see for instance [31,32]) that $(E_W(t), E_R(t), I_{AW}(t), I_{SW}(t), I_{AR}(t), I_{SR}(t), R(t)) \to (0,0,0,0,0,0,0)$,

By substituting $E_W(t) = E_R(t) = I_{AW}(t) = I_{SW}(t) = I_{AR}(t) = I_{SR}(t) = R(t) = 0$ in the first expression of equation (1) we have: $(S_U(t) + S_{EP}(t) + S_{LP}(t)) \to \pi/\mu$ as $t \to \infty$. Thus,

$$(S_U(t), S_{EP}(t), S_{LP}(t), E_W(t), E_R(t), I_{AW}(t), I_{SW}(t), I_{AR}(t), I_{SR}(t), T(t), R(t)) \to \left(\frac{\pi}{\alpha+\mu}, \frac{\pi k\alpha}{\mu(\alpha+\mu)}, \frac{\pi(1-k)\alpha}{\mu(\alpha+\mu)}, 0,0,0,0,0,0,0,0\right)$$

as $t \to \infty$ for $R_0^t \prec 1$, so that ε_0 is globally asymptotically stable in D_1 if $R_0^t \prec 1$.

Epidemiologically, the implication of this theorem is that if the use of prophylaxis and treatment can lead to a reduction of the maximum of the reproduction numbers of the two strains of the disease below unity, then both strains will be eliminated from the community.

4.3 Existence and local stability of boundary equilibria

For model (1), we investigate the existence and stability of the equilibria associated with it here; we take note of the following points:

(i) The only way individuals are generated into the infected wild strain classes I_{AW} and I_{SW} is when susceptibles individuals acquire primary infection with the wild strain of the disease at the rate λ_W.

(ii) For the infected drug-resistant classes I_{AR} and I_{SR}, individuals are generated there only by these two ways:

(a) When Susceptible individuals acquire primary infection with the drug-resistant strain of the disease at the rate λ_R.

(b) When treated individuals infected with the wild strain of the disease develop resistant to treatment (that is, they fail treatment) at the rate τ_W.

Therefore, the possible equilibria of the model (1) by taking into account (i) and (ii) above are as follows:

(1) Drug resistant strain-only boundary equilibria $\varepsilon_R^I = \left(S_U^{**}, S_{EP}^{**}, S_{LP}^{**}, 0, E_R^{**}, 0, 0, I_{AR}^{**}, I_{SR}^{**}, 0, R^{**}\right)$ (no wild strain).

(2) Low endemicity co-existence equilibrium, that is the two strains co-exist, which is denoted by $\varepsilon_{WR1}^I = \left(S_U^{**}, S_{EP}^{**}, S_{LP}^{**}, E_W^{**}, E_R^{**}, I_{AS}^{**}, I_{SW}^{**}, I_{AR}^{**}, I_{SR}^{**}, T^{**}, R^{**}\right)$. There is occurrence of this equilibrium since there is no primary transmission of the resistant strain which is obtained by setting $\lambda_R = 0$ in model (1). It should however be noted that, even in the class, the sub populations I_{AR} and I_{SR} are non-zero, since treated individuals will develop resistance at a rate τ_W (except if $\lim_{t\to\infty} T_W = 0$) and move to the class I_{SR}. In other words, $\lim_{t\to\infty} I_{AR} = 0$ and $\lim_{t\to\infty} I_{SW} = 0$ even if $\lambda_R = 0$. In order to distinguish it from the other co-existence equilibrium for which primary transmission of the drug resistance strain of the disease occurs, this equilibrium is so called: low endemicity co-existence equilibrium.

(3) High endemicity co-existence equilibrium, meaning both strains co-exist, which is denoted by $\varepsilon_{WR2}^I = \left(S_U^{**}, S_{EP}^{**}, S_{LP}^{**}, E_W^{**}, E_R^{**}, I_{AS}^{**}, I_{SW}^{**}, I_{AR}^{**}, I_{SR}^{**}, T^{**}, R^{**}\right)$. Here we set $\lambda_R = 0$ in model (1), that is, primary transmission of the drug-resistant strain occurs.

However, it is important to emphasize that there cannot be a wild strain-only boundary equilibrium, for model (1), except $\lim_{t\to\infty} T_W = 0$, note that this is not feasible here since treatment is a must for infected individuals.

As we did before, by solving model (1) at steady state, in terms of the force of infection:

$$\lambda_W^{**} = \frac{\beta\left(I_{AW}^{**} + I_{SW}^{**}\right)}{N^{**}} \qquad \text{and} \qquad \lambda_R^{**} = \frac{\beta\left(I_{AR}^{**} + I_{SR}^{**}\right)}{N^{**}} \tag{18}$$

We obtain:

$$S_U^{**} = \frac{\pi}{\lambda_W^{**} + \lambda_R^{**} + \alpha + \mu}, \quad S_{EP}^{**} = \frac{\pi(1-k)\alpha}{\left[(1-\varepsilon_1)\left(\lambda_W^{**} + \lambda_R^{**}\right) + \mu\right]\left[\left(\lambda_W^{**} + \lambda_R^{**}\right) + \alpha + \mu\right]}, \quad E_W^{**} = A\frac{\lambda_W^{**}}{\gamma_R}\left[\frac{\pi}{\lambda_W^{**} + \lambda_R^{**} + \alpha + \mu}\right],$$

$$S_{LP}^{**} = \frac{\pi k\alpha}{\left[(1-\varepsilon_2)\left(\lambda_W^{**} + \lambda_R^{**}\right) + \mu\right]\left[\left(\lambda_W^{**} + \lambda_R^{**}\right) + \alpha + \mu\right]}, \qquad E_R^{**} = A\frac{\lambda_R^{**}}{B_{23}}\left[\frac{\pi}{\lambda_W^{**} + \lambda_R^{**} + \alpha + \mu}\right],$$

$$I_{AW}^{**} = A\frac{B_7\lambda_W^{**}}{B_{15}B_{18}}\left[\frac{\pi}{\lambda_W^{**} + \lambda_R^{**} + \alpha + \mu}\right], \qquad I_{SW}^{**} = A\lambda_W^{**}\left[\frac{f_1\sigma_W B_{18} + B_{17}\gamma_W}{B_{15}B_{18}B_{19}}\right]\left[\frac{\pi}{\lambda_W^{**} + \lambda_R^{**} + \alpha + \mu}\right],$$

$$I_{AR}^{**} = A\frac{B_{20}\lambda_R^{**}}{B_{16}B_{21}}\left[\frac{\pi}{\lambda_W^{**} + \lambda_R^{**} + \alpha + \mu}\right], \qquad I_{SR}^{**} = A\lambda_R^{**}\left[\frac{f_2\sigma_W B_{21} + B_{20}\gamma_R}{B_{16}B_{21}B_{23}}\right]\left[\frac{\pi}{\lambda_W^{**} + \lambda_R^{**} + \alpha + \mu}\right],$$

$$T_W^{**} = A\lambda_W^{**}\left[\frac{f_1\sigma_W B_{18}B_{24} + B_{17}B_{24}\gamma_W}{B_{16}B_{21}B_{23}\gamma_W}\right]\left[\frac{\pi}{\lambda_W^{**} + \lambda_R^{**} + \alpha + \mu}\right],$$

$$\& \quad R^{**} = A\frac{1}{\mu}\left[\frac{\pi}{\lambda_W^{**} + \lambda_R^{**} + \alpha + \mu}\right]\left[\left(\frac{f_1\sigma_W B_{22}B_{18} + B_{17}B_{22}\gamma_W}{B_{15}B_{18}B_{19}B_{23}}\right)\lambda_W^{**} + \left(\frac{f_1\sigma_W B_{23}B_{11} + B_{23}B_{10}\gamma_R}{B_{16}B_{19}B_{21}B_{23}}\right)\lambda_R^{**}\right] \tag{19}$$

By substituting the expressions in equation (19), the components of the equilibrium at steady state into the expressions in (18), by taking note that

$$N^{**} = S_U^{**}, S_{EP}^{**} + S_{LP}^{**} + E_W^{**} + E_R^{**} + I_{AS}^{**} + I_{SW}^{**} + I_{AR}^{**} + I_{SR}^{**} + T^{**} + R^{**}$$

we obtained a fixed point problem of the form:

$$x = \vartheta(x) = \begin{pmatrix} \vartheta_1\left(\lambda_W^{**}, \lambda_R^{**}\right) \\ \vartheta_2\left(\lambda_W^{**}, \lambda_R^{**}\right) \end{pmatrix}, \qquad \text{where} \quad x = \begin{pmatrix} \lambda_W^{**} \\ \lambda_R^{**} \end{pmatrix}, \tag{20}$$

Where ϑ_1 and ϑ_2 are defined as the right-hand sides of the equations for λ_W^{**} and λ_R^{**} in equation (18) respectively.

4.4 Existence and stability of drug resistant strain-only equilibrium $\left(\varepsilon_R^t\right)$

Theorem 7: The model (1) has a unique and locally asymptotical stability drug-resistant strain-only boundary equilibrium ε_R^t, whenever $R_W^t \prec 1 \prec R_R^t$, and no boundary equilibrium otherwise.

Proof: The proof is as in section 3.4. We set $\vartheta_1\left(0, \lambda_R^{**}\right) = 0$, so that the fixed point of $\vartheta_2\left(\lambda_W^{**}, \lambda_R^{**}\right) = 0$ is obtained by solving the equation $\vartheta_2\left(0, \lambda_R^{**}\right) = \lambda_R^{**}$. It follows that λ_R^{**} satisfies the equation:

$$G_{31}\left(\lambda_W^{**3}\right)+G_{32}\left(\lambda_W^{**2}\right)+G_{33}\left(\lambda_W^{**}\right)+\mu^2\left[1-R_R^t\right]=0$$

Where $G_{31}=(1-\varepsilon_1)(1-\varepsilon_2)\left[\mu B_{21}B_{16}+\mu B_{16}B_{20}B_{23}+\mu B_{21}f_2\sigma_R\right]\succ 0$

$$G_{32}=\left[\alpha(1-\varepsilon_1)(1-\varepsilon_2)+\mu(1-\varepsilon_1)+\mu(1-\varepsilon_2)\right]\left[\begin{pmatrix}\mu B_{21}B_{23}+\mu B_{16}B_{20}B_{23}+\\ \mu B_{21}f_2\sigma_R+\mu B_{20}\gamma_W\end{pmatrix}+\mu(1-\varepsilon_1)(1-\varepsilon_2)\right]$$
$$\left[B_{16}B_{21}B_{23}-\beta_R\left(B_{20}B_{23}+B_{21}f_2\sigma_R+B_{20}\gamma_R\right)\right]$$

$$G_{33}=\mu B_{15}B_{18}B_{19}\left[\alpha(1-\varepsilon_1)(\mu+k\alpha)+\mu(1-\varepsilon_1)+\alpha(1-\varepsilon_2)(1-k)\right]+\left[\mu^2+\mu\alpha(1-\varepsilon_1)(1-k)\right]$$
$$\left(\mu B_{21}B_{23}+\mu B_{16}B_{20}B_{23}+B_{21}f_1\sigma_W+\mu B_{20}\gamma_W\right)-\beta_R\left(\alpha(1-\varepsilon_1)(1-\varepsilon_2)+\mu(1-\varepsilon_2)\right)$$
$$\left[B_{20}B_{23}+B_{21}f_2\sigma_R+B_{20}\gamma_R\right]$$

It follows from the polynomial above, that regardless of the sign of G_{33}, the polynomial has a unique positive solution whenever $R_R^t\succ 1.$ Furthermore, for the equilibrium ε_R^t to exist alone, it is necessary that the wild strain of the disease does not exist, (that is $R_W^t\prec 1.$).

For the local stability of this equilibrium, ε_R^t; we note that the Jacobian of the system (20) is given by:

$$J\left(\lambda_W^{**},\lambda_R^{**}\right)=\begin{pmatrix}\dfrac{\partial\vartheta_1\left(\lambda_W^{**},\lambda_R^{**}\right)}{\partial\lambda_W^{**}} & \dfrac{\partial\vartheta_1\left(\lambda_W^{**},\lambda_R^{**}\right)}{\partial\lambda_R^{**}}\\ \dfrac{\partial\vartheta_2\left(\lambda_W^{**},\lambda_R^{**}\right)}{\partial\lambda_W^{**}} & \dfrac{\partial\vartheta_2\left(\lambda_W^{**},\lambda_R^{**}\right)}{\partial\lambda_R^{**}}\end{pmatrix},$$

So that
$$J\left(\lambda_W^{**},0\right)=\begin{pmatrix}\dfrac{R_W^t}{R_R^t} & 0\\ \left.\dfrac{\partial\vartheta_1\left(\lambda_W^{**},\lambda_R^{**}\right)}{\partial\lambda_R^{**}}\right|_{\left(\lambda_R^{**},0\right)} & \dfrac{1}{R_R^t}\end{pmatrix}$$

Thus, the local stability of drug-resistant strain-only, ε_R^t, is stable if $\frac{1}{R_R^t}\prec 1$ (that is $R_R^t\succ 1$) and

$\frac{R_W^t}{R_R^t}\prec 1$(that is $R_W^t\prec R_R^t$). By putting all these together, it shows that a unique drug-resistant strain-only boundary equilibrium, ε_R^t, is locally asymptotically stable provided $R_W^t\prec 1\prec R_R^t$. Note that, as earlier mentioned, a wild strain-only equilibrium is not feasible in this case except if $\lim_{t\to\infty}T_W=0$.

4.5 Existence and stability of co-existence equilibria

4.5.1. Existence and stability of the low-endemicity co-existence equilibrium $\left(\varepsilon_{WR1}^t\right)$

We claim the following:

Theorem 8: Let $R_W^{tt} = \dfrac{T_{10} + \sqrt{\left(T_{10}^2 - 4T_{20}\right)}}{2}$

with $T_{10} = \left(\dfrac{\partial \vartheta_1}{\partial \lambda_W^{**}} + \dfrac{\partial \vartheta_2}{\partial \lambda_R^{**}}\right)\Bigg|_{(\lambda_W^{**},0)}$ and $T_{20} = \left(\dfrac{\partial \vartheta_1}{\partial \lambda_W^{**}}\dfrac{\partial \vartheta_2}{\partial \lambda_R^{**}} - \dfrac{\partial \vartheta_1}{\partial \lambda_R^{**}}\dfrac{\partial \vartheta_2}{\partial \lambda_W^{**}}\right)\Bigg|_{(\lambda_W^{**},0)}$

The model (1) has a low-endemicity co-existence equilibrium, denoted by ε_{WR1}^t, whenever $R_W^t \succ 1$, in the absence of primary infection with the drug resistant strain $(\lambda_R = 0)$. This equilibrium is locally asymptotically stable whenever $R_W^{tt} \prec 1$.

Proof: By Letting $\lambda_R^{**} = 0$ in equation (19), accounting for the absence of the primary transmission of the drug resistant strain of the disease, we obtain:

$$S_U^{**} = \frac{\pi}{\lambda_W^{**} + \alpha + \mu} \qquad S_{EP}^{**} = \frac{\pi(1-k)\alpha}{\left[(1-\varepsilon_1)(\lambda_W^{**}) + \mu\right]\left[\lambda_W^{**} + \alpha + \mu\right]}, \qquad S_{LP}^{**} = \frac{\pi k\alpha}{\left[(1-\varepsilon_2)(\lambda_W^{**}) + \mu\right]\left[\lambda_W^{**} + \alpha + \mu\right]},$$

$$E_W^{**} = A\frac{\lambda_W^{**}}{\gamma_R}\left[\frac{\pi}{\lambda_W^{**} + \alpha + \mu}\right], \qquad E_R^{**} = A\frac{\lambda_R^{**}}{B_{23}}\left[\frac{\pi}{\lambda_W^{**} + \alpha + \mu}\right], \qquad I_{AW}^{**} = A\frac{B_7\lambda_W^{**}}{B_{15}B_{18}}\left[\frac{\pi}{\lambda_W^{**} + \alpha + \mu}\right],$$

$$I_{SW}^{**} = A\lambda_W^{**}\left[\frac{f_1\sigma_W B_{18} + B_{17}\gamma_W}{B_{15}B_{18}B_{19}}\right]\left[\frac{\pi}{\lambda_W^{**} + \alpha + \mu}\right], \qquad I_{SR}^{**} = A\lambda_R^{**}\left[\frac{f_2\sigma_W B_{21} + B_{20}\gamma_R}{B_{16}B_{21}B_{23}}\right]\left[\frac{\pi}{\lambda_W^{**} + \alpha + \mu}\right],$$

$$T_W^{**} = A\lambda_W^{**}\left[\frac{f_1\sigma_W B_{18}B_{24} + B_{17}B_{24}\gamma_W}{B_{16}B_{21}B_{23}\gamma_W}\right]\left[\frac{\pi}{\lambda_W^{**} + \alpha + \mu}\right], \qquad I_{AR}^{**} = A\frac{B_{20}\lambda_R^{**}}{B_{16}B_{21}}\left[\frac{\pi}{\lambda_W^{**} + \alpha + \mu}\right],$$

$$\& \quad R^{**} = A\frac{1}{\mu}\left[\frac{\pi}{\lambda_W^{**} + \alpha + \mu}\right]\left[\left(\frac{f_1\sigma_W B_{22}B_{18} + B_{17}B_{22}\gamma_W}{B_{15}B_{18}B_{19}B_{23}}\right)\lambda_W^{**}\right] \tag{21}$$

With A as previously defined in section 3.3. by substituting the expressions in equation (21) into the expression for λ_W^{**} in equation (18) and simplifying, we obtain the non-zero equilibrium of the model (1) satisfies:

$$G_{41}\left(\lambda_W^{**3}\right) + G_{42}\left(\lambda_W^{**2}\right) + G_{43}\left(\lambda_W^{**}\right) + \mu^2\left[1 - R_R\right] = 0 \tag{22}$$

Where

$$G_{41} = (1-\varepsilon_1)(1-\varepsilon_2)\begin{bmatrix}\mu B_{18}B_{19}B_{24} + \mu B_{17}B_{19}B_{24} + \mu B_{21}B_{24}f_2\sigma_R + B_{23}B_{17}B_{23} + \\ B_{18}B_{23}f_2\sigma_W + B_{17}B_{19}B_{23} + B_{17}B_{19}B_{24} + B_{17}B_{19}B_{23} + B_{17}B_{19}B_{23}\end{bmatrix} \succ 0$$

$$G_{42} = \left[\mu^2(1-\varepsilon_1) + \alpha\mu(1-\varepsilon_1)(1-\varepsilon_2)\right]\begin{bmatrix}\left(\mu B_{11}B_{13}B_{24} + \mu B_6B_{10}B_{24} + \mu B_{11}B_{24}f_2\sigma_R + B_{10}B_{24}\gamma_W + \right. \\ \left. B_{11}B_{13}B_{24} + B_{16}B_{10}B_{24} + B_{12}B_{13}B_{24} + B_{14}B_{10}B_{13}B_{24}\right) \\ + (1-\varepsilon_1)(1-\varepsilon_2)\end{bmatrix}$$
$$\left[B_{15}B_{11}B_{13} - \mu^2\beta_W\left(B_{10}B_{13}B_{24} + B_{11}B_{24}f_2\sigma_R + B_{24}B_{10}\gamma_R\right)\right]$$

$$G_{43} = \left[\mu^3 + \mu^2\alpha(1-\varepsilon_2)(1-k) + \mu^2 k\alpha(1-\varepsilon_1)\right]\left[\begin{matrix} B_{18}B_{19}B_{24} + B_{15}B_{19}B_{24} + B_{15}B_{14}B_{24} + B_{18}B_{16}B_{24} + \\ B_{15}B_{18}B_{23} + B_{15}B_{11}B_{23} + B_{13}B_{18}B_{24} + B_{15}B_{19}B_{24} \end{matrix}\right] +$$
$$\left[\mu(1-\varepsilon_1) + \mu(1-\varepsilon_2)\right]\left[B_{15}B_{16}B_{19}B_{24} - \mu^2\beta_W\left(B_{17}B_{19}B_{24} + B_{18}B_{24}f_1\sigma_W + B_{17}B_{24}\gamma_W\right)\right]$$

It follows from the polynomial in (22) above that regardless of the sign of G_{43}, the polynomial has a unique positive solution whenever $R_W^t \succ 1$ (so that $\lambda_W^{**} \succ 0$). With this, the existence of the low-endemicity co-existence equilibrium is proved.

To obtain the local stability of ε_{WR1}^t, we evaluate the Jacobian of the system at $(\lambda_W^{**},0)$, to obtain:

$$J(\lambda_W^{**},0) = \begin{pmatrix} \left.\dfrac{\partial \vartheta_1(\lambda_W^{**},\lambda_R^{**})}{\partial \lambda_W^{**}}\right|_{(\lambda_W^{**},0)} & \left.\dfrac{\partial \vartheta_1(\lambda_W^{**},\lambda_R^{**})}{\partial \lambda_R^{**}}\right|_{(\lambda_W^{**},0)} \\ \left.\dfrac{\partial \vartheta_2(\lambda_W^{**},\lambda_R^{**})}{\partial \lambda_W^{**}}\right|_{(\lambda_W^{**},0)} & \left.\dfrac{\partial \vartheta_2(\lambda_W^{**},\lambda_R^{**})}{\partial \lambda_R^{**}}\right|_{(\lambda_W^{**},0)} \end{pmatrix},$$

With eigenvalues satisfying:

$$\chi^2 - \chi\left(\frac{\partial \vartheta_1}{\partial \lambda_W^{**}} + \frac{\partial \vartheta_2}{\partial \lambda_R^{**}}\right)\Bigg|_{(\lambda_W^{**},0)} + \left(\frac{\partial \vartheta_1}{\partial \lambda_W^{**}}\frac{\partial \vartheta_2}{\partial \lambda_R^{**}} - \frac{\partial \vartheta_1}{\partial \lambda_R^{**}}\frac{\partial \vartheta_2}{\partial \lambda_W^{**}}\right)\Bigg|_{(\lambda_W^{**},0)} = 0$$

It is not difficult to show that the dominant eigenvalue of $J(\lambda_W^{**},0)$ is R_W^{tt}. It follows that, the low-endemicity equilibrium, ε_{WR1}^t, is locally asymptotically stable whenever $R_W^{tt} \prec 1$.

4.5.2 Existence and stability of the high-endemicity co-existence equilibrium (ε_{WR2}^t)

We rewrite the expressions in equation (18) as follows:

$$\lambda_W^{**} = \frac{\beta(I_{AW}^{**} + I_{SW}^{**})}{N^{**}} \equiv \frac{\lambda_W^{**}R_W}{1 + E + \lambda_W^{**}H_1 + \lambda_R^{**}H_2}$$

and
$$\lambda_R^{**} = \frac{\beta(I_{AR}^{**} + I_{SR}^{**})}{N^{**}} \equiv \frac{\lambda_R^{**}R_R}{1 + E + \lambda_W^{**}H_1 + \lambda_R^{**}H_2} \qquad (23)$$

Where $E = \dfrac{(1-k)\alpha}{(1-\varepsilon_1)(\lambda_W^{**} + \lambda_R^{**}) + \mu} + \dfrac{k\alpha}{(1-\varepsilon_2)(\lambda_W^{**} + \lambda_R^{**}) + \mu}$

$$H_1 = \left\{\begin{matrix} \dfrac{\mu B_{18}B_{19} + \mu(1-f_1)\sigma_W B_{17} + \mu f_1\sigma_W B_{18} + \mu B_{17}\gamma_W + \mu B_{14}B_{12}}{B_{15}B_{18}B_{19}} + \\ + \dfrac{f_1\sigma_W B_{18}B_{24} + B_{17}B_{24}\gamma_W}{B_{16}B_{21}B_{23}\gamma_W} + \dfrac{f_1\sigma_W B_{22}B_{18} + B_{17}B_{22}\gamma_W}{B_{15}B_{18}B_{19}B_{23}} \end{matrix}\right\} A$$

$$H_2 = \left\{ \frac{\mu B_{21} B_{23} + \mu B_{23} B_{20} + \mu f_2 \sigma_R B_{21} + \mu B_{20} \gamma_R}{B_{16} B_{21} B_{23}} \right\} A$$

It follows from equation (23) that

$$\lambda_W^{**} H_1 + \lambda_R^{**} H_2 = R_W - 1, \tag{24}$$

$$\lambda_W^{**} H_1 + \lambda_R^{**} H_2 = R_R - 1, \tag{25}$$

Since the left-hand sides of the expressions in equations (24) and (25) are always positive, it is necessary that $R_W^t \succ 1$ and $R_R^t \succ 1$ for consistency. It should be noted that for consistency of the two strains, the forces of infection λ_W^{**} and λ_R^{**}, at steady state, must ne non-zero. Consequently, we establish the following results:

Theorem 9: The model (1) has a positive high-endemicity co-existence endemic equilibrium, ε_{WR2}^t, whenever $R_W^t \succ R_R^t$ and $R_W^t \succ 1$.

Theorem 10: The positive high-endemicity co-existence endemic equilibrium of the model (1), given by ε_{WR2}^t, is locally asymptotically stable whenever $R_W^t \succ R_R^t$ and $R_W^t \succ 1$.

Proof: By evaluating the Jacobian of equation (20) at $\left(\lambda_W^{**}, \lambda_R^{**}\right)$, we have:

$$J\left(\lambda_W^{**}, \lambda_R^{**}\right) = \begin{pmatrix} \left.\frac{\partial \vartheta_1\left(\lambda_W^{**}, \lambda_R^{**}\right)}{\partial \lambda_W^{**}}\right|_{\left(\lambda_W^{**}, \lambda_R^{**}\right)} & \left.\frac{\partial \vartheta_1\left(\lambda_W^{**}, \lambda_R^{**}\right)}{\partial \lambda_R^{**}}\right|_{\left(\lambda_W^{**}, \lambda_R^{**}\right)} \\ \left.\frac{\partial \vartheta_2\left(\lambda_W^{**}, \lambda_R^{**}\right)}{\partial \lambda_W^{**}}\right|_{\left(\lambda_W^{**}, \lambda_R^{**}\right)} & \left.\frac{\partial \vartheta_2\left(\lambda_W^{**}, \lambda_R^{**}\right)}{\partial \lambda_R^{**}}\right|_{\left(\lambda_W^{**}, \lambda_R^{**}\right)} \end{pmatrix}, \tag{26}$$

With eigenvalues satisfying:

$$\chi^2 - \chi\left(\left.\frac{\partial \vartheta_1}{\partial \lambda_W^{**}} + \frac{\partial \vartheta_2}{\partial \lambda_R^{**}}\right|_{\left(\lambda_W^{**}, \lambda_R^{**}\right)} \right) + \left(\left.\frac{\partial \vartheta_1}{\partial \lambda_W^{**}} \frac{\partial \vartheta_2}{\partial \lambda_R^{**}} - \frac{\partial \vartheta_1}{\partial \lambda_R^{**}} \frac{\partial \vartheta_2}{\partial \lambda_W^{**}}\right|_{\left(\lambda_W^{**}, \lambda_R^{**}\right)} \right) = 0$$

From equation (26), it follows that the dominant eigenvalues of $J\left(\lambda_W^{**}, \lambda_R^{**}\right)$ is given by:

$$R_{WR}^t = \frac{T_{11} + \sqrt{T_{11}^2 - 4T_{21}}}{2},$$

Where $T_{11} = \left(\left.\frac{\partial \varphi_1}{\partial \lambda_W^{**}} + \frac{\partial \varphi_2}{\partial \lambda_R^{**}}\right|_{\left(\lambda_W^{**}, \lambda_R^{**}\right)} \right) = \frac{1 + R_R^t}{R_W^t},$ & $T_{21} = \left(\left.\frac{\partial \varphi_1}{\partial \lambda_W^{**}} \frac{\partial \varphi_2}{\partial \lambda_R^{**}} - \frac{\partial \varphi_1}{\partial \lambda_R^{**}} \frac{\partial \varphi_2}{\partial \lambda_W^{**}}\right|_{\left(\lambda_W^{**}, \lambda_R^{**}\right)} \right) = \frac{R_R^t}{\left(R_W^t\right)^2},$

By substituting the expressions of T_{11} and T_{21} into R_{WR}^t, shows that the roots of the quadratic equation (26) are $1/R_W^t$ and R_R^t/R_W^t. Thus, the required result follows.

A major revelation from the analysis of the two models (1) and (3) done so far, is that model (1) exhibits some dynamical features that are not present in the treatment-free model (3). While there is

exhibition of a continuum of co-existence equilibria when the reproduction numbers of the wild strain and that of drug resistant strain of the disease is greater than unity, for the treatment-free model (3), on the other hand, it is revealed that the treatment model (1) has a co-existence equilibrium of the two strains only when the reproduction number of the wild strain is greater than unity and exceeds that of the drug resistant strain of the disease.

A cursory look at equation (24), reveals that whenever $R_W^t = R_R^t = 1$, then $\lambda_W^{**} = 0$ and equation (24) reduces to:

$$\lambda_R^{**} H_2 = 0 \qquad \Rightarrow \lambda_R^{**} = 0.$$

Take note that H_2 is as previously defined in section 4.5.2. Consequently, if both the reproduction numbers are the same and equal to unity, then $\lambda_R^{**} = 0$ and $\lambda_W^{**} = 0$, corresponding to disease free equilibrium. By and large, in summary, while the treatment-free model (3) has a continuum of co-existence endemic equilibria, the treatment model (1) has a low-endemicity and high-endemicity co-existence equilibria.

5 Numerical simulations and discussions.

In this section, we carry out simulations whose main objective is to illustrate some of the theoretical results obtained in this work as done earlier in the analysis of the models. We carefully chose from literature a set of parameter values depicted in table 2 below, for this purpose for a population where anthrax is deployed as bio-terrorism weapon, where about one hundred million people (that is n = *100* million) inhabits.

Table 2: Parameter values for the models.

parameters	*nominal values*	*source*
π	1000	Assumed
α	0.1	[16]
β_w (β_R)	0.2 (0.1)	[11]
$\varepsilon_1/\varepsilon_2$	$1/90$	Variable
μ	0.0001	[11]
$\delta_w(\delta_R)$	0.102 (0.2)	Inferred from [16]
$\sigma_w(\sigma_R)$	0.2(0.1)	[16]
γ_w (γ_R)	0.1(0.12)	[11]
ψ_w	0.102	[11]
τ_w	0.2	Assumed
θ	0.1	Assumed

$f_1(f_2)$	$\frac{1}{3}(\frac{1}{3})$	Assumed
k	0.42	Assumed
v	0.5	Assumed

We carried out the simulations as follows:

Treatment-free model: we first simulated the treatment –free model (3). By using the parameters in table 2 above with $\beta_W = \beta_R = 0.05$, it follows that the reproduction number for the wild (drug-resistant) strain of the disease is given by $R_W = 0.7164$ ($R_R = 0.2469$), so that $R_0 = 0.7164 \prec 1$. This confirms theorem 1, that the disease-free equilibrium of the model is globally asymptotically stable. Under this scenario, with various initial conditions, figure 3 (a) depicts the simulation of the model, and this confirms the global asymptotic stability property of the model as initially proved qualitatively in section 3.2. We carried out additional simulations of the model for $R_i \succ R_j$ with $R_i \succ 1$ where $(i, j = W, R \; and \; i \neq j)$, these simulations are as shown in figures 3(b),(c) and (d) where we see that the strain with higher reproduction number drives out the other, a phenomenon commonly refers to as competitive exclusion. Note that this is in line with theorems 2 and 3 and conjectures 1 and 2.

Treatment model: we simulated the treatment model (1) next. By using the parameters in table 2 above with $\beta_W = \beta_R = 0.05$, figure 4(a) shows that the two strains of the disease dies out since the reproduction numbers are each less than one, confirming the global asymptotic stability of the treatment model (1). Further simulations as shown in figure 4(b), illustrate the fact that for $R_W^t \succ R_R^t \succ 1$ the drug-resistant strain dies out while for figure 4(c) for $R_R^t \succ R_W^t \succ 1$, the wild strain of the disease dies out. In other words, the wild strain of the disease will be eliminated from the community suffering from bio-terrorism attack via competitive exclusion if the use of prophylaxis and antibiotics can reduce R_W^t below R_R^t with $R_R^t \succ 1$. However, as can be seen from figure 4(d) for $R_R^t \prec 1 \prec R_W^t$, both strain co-exist in the community with the system converging to low-endemicity steady state.

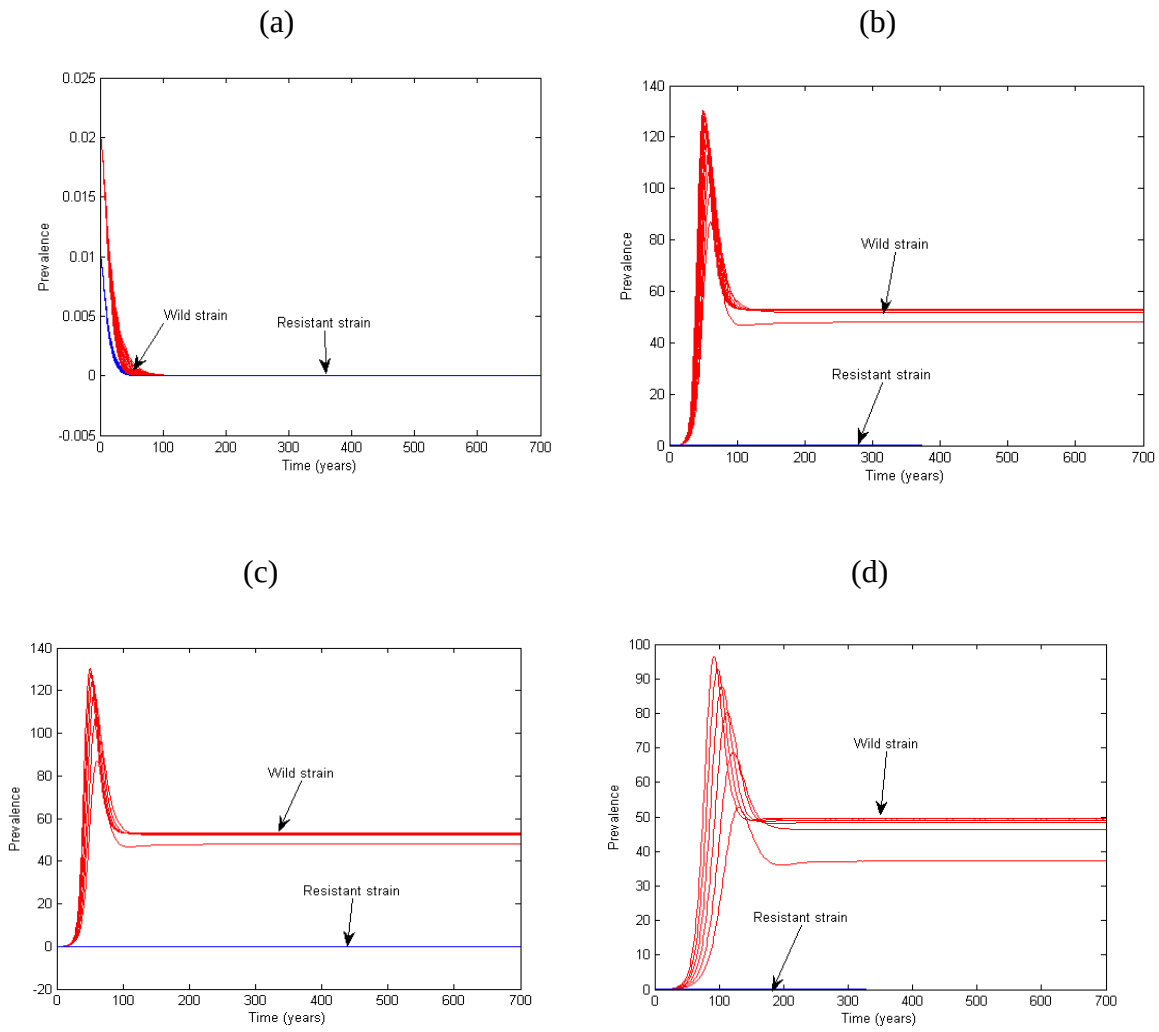

Figure 3. Prevalence given by total number of infected individuals divided by the total population of the community under the bio-terrorism attack as a function of time (years) for treatment-free model(3).3(a) $\beta_W = \beta_R = 0.05, R_W = 0.7164 \& R_R = 0.2469$;3(b) $R_W \succ R_R \succ 1$, $\beta_W = 0.8, \beta_R = 0.3$ 3(c) $R_R \succ R_W \succ 1, \beta_W = 0.2, \beta_R = 0.8$;3(d) $R_W \succ R_R, R_R \prec 1$ $\beta_W = 0.4, \beta_R = 0.1$.

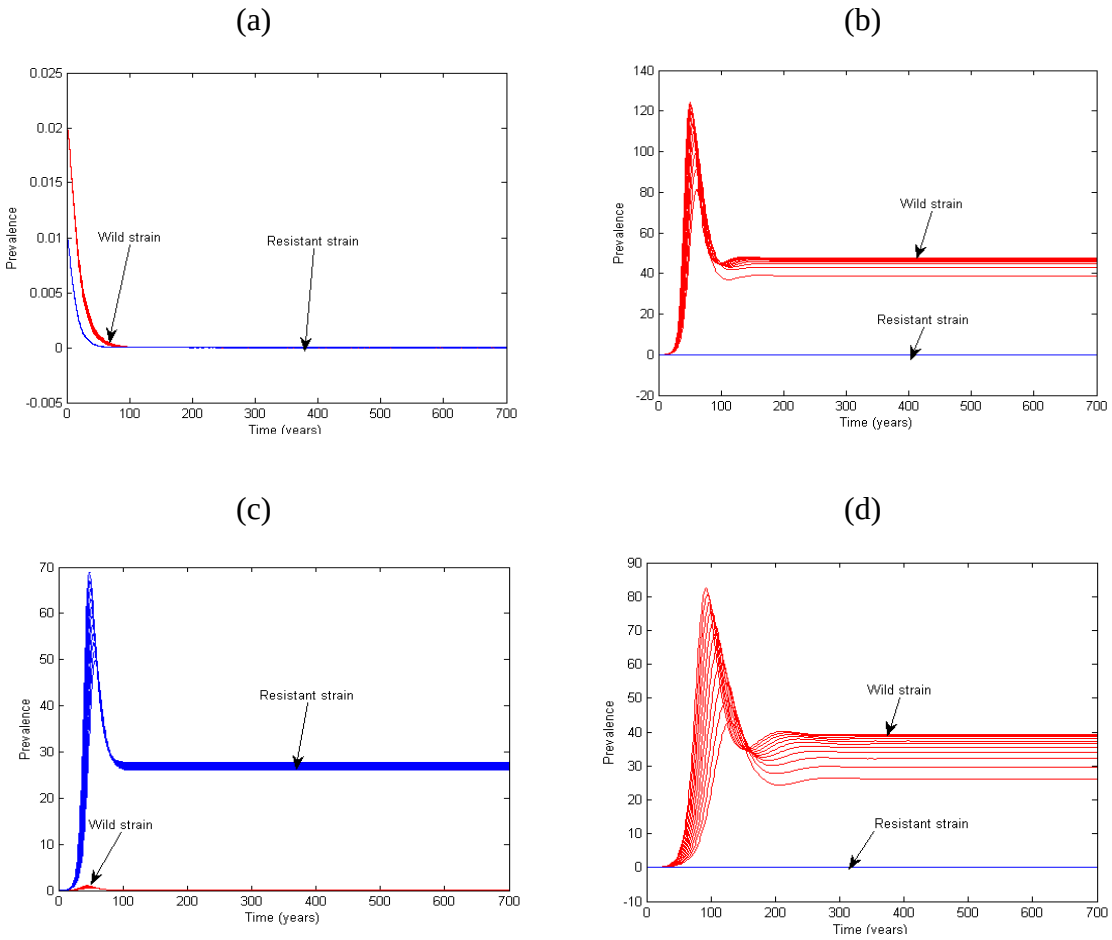

Figure 4. Prevalence given by total number of infected individuals divided by the total population of the community under bio-terrorism attack as a function of time (years) for treatment model (1).

4(a) $R_W^t \prec R_R^t \prec 1\, \beta_W = \beta_R = 0.05$; 4(b) $R_W^t \succ R_R^t \succ 1$, $\beta_W = 0.8, \beta_R = 0.3$; 4(c) $R_R^t \succ R_W^t \succ 1$, $\beta_W = 0.2, \beta_R = 0.8$; 4(d) $R_W^t \succ R_R^t, R_R^t \prec 1; \beta_W = 0.4, \beta_R = 0.1$.

(a) (b)

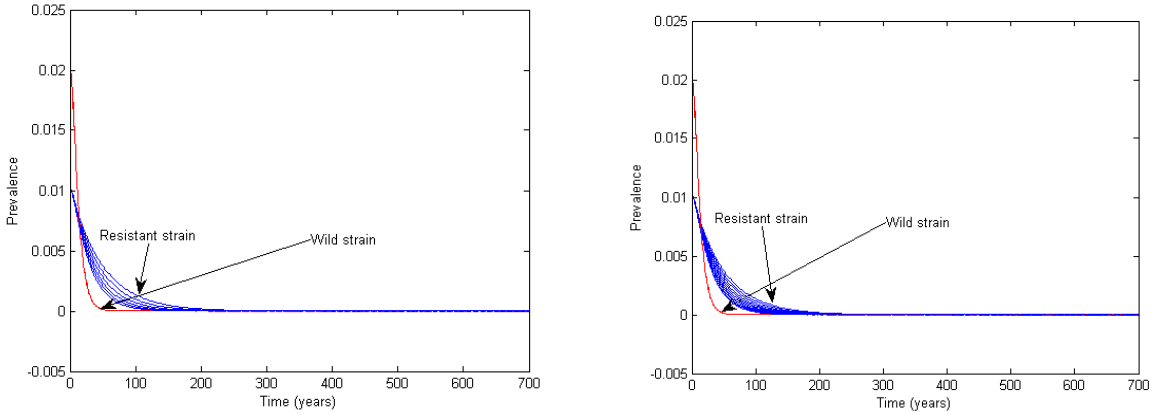

Figure 5. Prevalence given by total number of infected individuals divided by the total population of the community under bio-terrorism attack as a function of time (in years) 5(a) $R_R^t \prec R_W^t \prec 1$- for treatment-free model (3); 5(b) $R_R^t \prec R_W^t \prec 1$-for treatment model (1).

(a) (b)

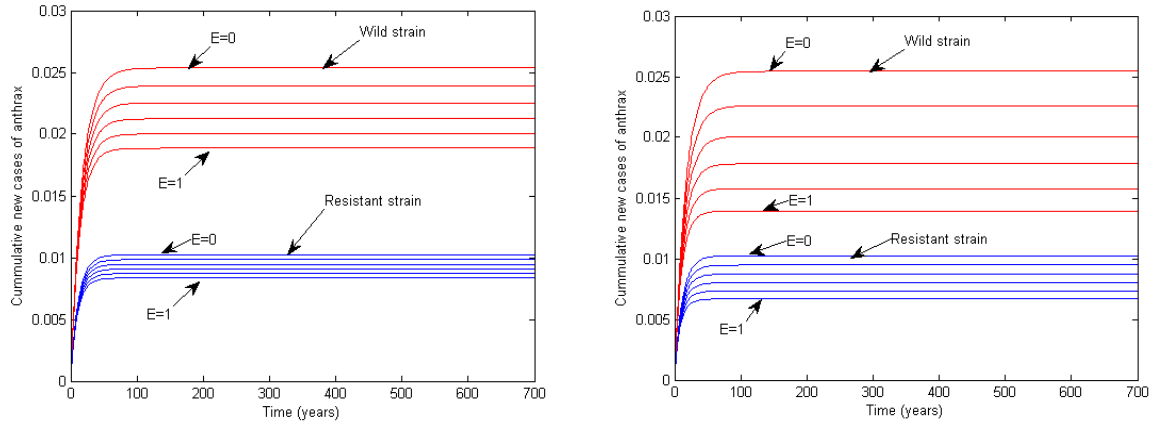

Figure 6. Cumulative number of new cases of anthrax by varying administration of prophylaxis plotted as a function of time (in years) for treatment model. 6(a) $R_R^t \prec R_W^t \prec 1$- varying early administration of prophylaxis (ε_1) represented by E on the graph; 6(b) $R_R^t \prec R_W^t \prec 1$- varying late administration of prophylaxis (ε_2) represented by E on the graph.

The effect of efficacy of early administration of prophylaxis, ε_1, on the cumulative number of new cases of anthrax in the community under reference, is assessed by simulating the model using various values of ε_1. The results obtained, depicted in Figure 6 (a) show a decrease in the cumulative number of new cases with increasing values of ε_1 for both strains of the disease. Similar conclusions were arrived at when examining the effect of late administration of prophylaxis, ε_2, on the cumulative number of new cases in the community, this is as depicted in Figure 6 (b). In both cases, we plotted cumulative number of new cases of the disease by varying early and late administration of prophylaxis ε_1 and ε_2 in the interval 0.2 for [0,1].

6 Conclusions

Summarily, from the qualitative analysis of the treatment-free model (3) and treatment model (1) and the numerical results, the main findings in this work are as follows:

(1) There exists a global asymptotical stable disease-free equilibrium whenever the maximum of the two reproduction numbers for each of the models (1) and (3) is less than unity, which implies that effective control or elimination of the bio-terrorism attack of the disease in the community under reference is feasible by applying a combination of prophylaxis and antibiotic treatment of individuals under attack of anthrax, if the application of this combination of regimen of treatment can make the maximum of the reproduction numbers less than unity.

(2) It is shown for the treatment-free model that the strain with higher reproduction number is always dominant of the other at steady state while the other strain dies out in the community.

(3) For the treatment-free model, there exists continuum of co-existence endemic equilibria when the two reproduction numbers are equal and greater than unity, while this feature is missing in the treatment model.

(4) For the treatment model, there exist competitive exclusion only when $R_R^t \succ 1$ and $R_R^t \succ R_W^t$.

(5) Quite unlike the treatment-free model, the treatment model, exhibits a low-endemicity and high-endemicity co-existence equilibria under some certain conditions.

(6) There can be elimination of wild strain of the disease from the community under the attack of anthrax as bio-terrorism weapon when there is wide spread use of treatment involving a combination of prophylaxis and antibiotics in the case when the reproduction number for the wild strain exceeds that of the drug resistant strain (and greater than unity) if infectiousness of infected individuals does not exceed a certain threshold.

Conclusively, this study reveals that the widespread use of treatment involving a combination of prophylaxis and antibiotics, despite the risk of the emergence and transmission of drug-resistant strain of the disease, can ultimately lead to a significant reduction in the disease burden or even complete

elimination of anthrax in the community under the siege of bio-terrorism attack, when certain conditions are met. To mitigate the effects of resistant to drug in the treatment of anthrax, it is hereby recommended that further study be focused on discovery and use of alternative drugs for treating the resistant strain of the disease.

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References

[1] K. A. Wenner, J. R. Kenner, Anthrax. Dermatol Clin. 22 (2004), pp. 247-256.

[2] P. A. Pinzon-Arango, *Investigation of the biological and physicochemical Properties of Bacillus anthracis spores during germination, virulence, and killing*. (2012). Retrieved from https://digitalcommons.wpi.edu/etd-dissertations/21

[3] F. John, M. D. Modlin, Dixie E. Snider, M. D, Junior, Use of Anthrax vaccine in the United United States. Recommendations of the advisory committee on immunization practices, Journal of Toxicology. 39 (1) (2000) pp. 85-100.

[4] Michelle Lee Houck, Compartmental and simulation modus for evaluating medkit prepositioning strategies for anthrax attack response. University of Maryland. (2011).

[5] D. C. Dragon, and R. P. Rennie, The ecology of anthrax spores: tough but not invincible. Can. Vet. J. 36 (1995), pp. 295–301.

[6] M. Sterne, The use of Anthrax vaccines prepared from a virulent (uncapsulated) variants of *Bacillus anthracis* onderstepoort. J. Vet. Sci. Animal Ind. 13 (1939) pp. 307–312.

[7] P. S. Brachman, H. P. Gold, S. A. Lotkin, F. R. Fekety, M, Werrin, N. R. Ingraham, Field evaluation of a human anthrax vaccine. Am J public Health Nations health. 52(4) (1962), pp. 632-645.

[8] P. C. Turnbull, Introduction: anthrax history, disease and ecology. In: Koehler T.M (eds), Anthrax, Current Topics in Microbiology & Immunology. Springer, Berlin, Heidelberg, 271 (2002).

[9] M. Hugh-Jones, Global anthrax report. J. Appl. Microbiol, 87 (1999), pp.189-191.

[10] F. A. Abramova, L. M. Grinberg, O. V. Yampolskaya, D. H. Walker, Pathology of

inhalational anthrax in 42 cases from the Sverdlovsk outbreak of 1979. Proc. Natl. Acad. Sci. USA, 90(6) (1993), pp. 2291-2294.

[11] S. Mushayabasa, Global stability of an anthrax model with environmental decontamination and time delay," Discrete Dynamics in Nature and Society, (2015).

[12] Z. M. Sinkie and N. S. Murthy, Modeling and simulation study of anthrax attack on environment, Journal of Multidisciplinary Engineering Science and Technology, 3(4) (2016), pp. 4574–4578.

[13] T. V. Inglesby, D. A. Henderson, J. G. Bartlett et al. Anthrax as a biological weapon: medical and public health management. JAMA 281 (1999), pp. 1735–45.

[14] J. A. Jernigan, D. S. Stephens, D. A. Ashford, C. menaca, M. S. Topiel, M. Galbraith, M. Tapper, T. L. Fisk, S. Zaki, T. Popovic, Bioterrorism-related inhalational anthrax: the first 10 cases reported in the united states. Emerg. Infect. Dis. 7 (2001), pp. 933–944.

[15] L.C. Hsu, S. R. Ali, S. McGillivray, P. H. Tseng, S. Mariathasan, E. W. Humke, L. Eckmann, J. J. Powell, V. Nizet, V. M. Dixit, A nod2-nalp1 complex mediates caspase-1-dependent il-1beta secretion in response to bacillus anthracis infection and muramyl dipeptide. Proc. Natl. Acad. Sci, USA 105 (2008), pp. 7803–7808.

[16] S. Mushayabasa, T. Marijani, M. Masocha, Dynamical analysis and control strategies in modeling anthrax. *Computational and Applied Mathematics*, (2015), pp. 1—16.

[17] Jean-Didier, C. Francoise, G. Monique, V. Josee, M. Michelle, and H. Eric, Antibiotic susceptibilities of 96 isolates of Bachillus anthracis isolated in France between 1994 and 2002. Antimicrobial Agents and Chemotherapy. 46(7) (2002), pp. 2307 -2309.

[18] C. H. Choe, S. S. Bouhaouala, I. Brook, T. B. Elliot, G. B. Knudson, In vitro development of resistance to ofloxacin and doxycycline in Bachillus anthracis sterne. Antimicrob. Agents Chemother. 44 (2000), pp. 1766 - 1702.

[19] A. P. Pomerantzev, N. A. Shishkova, L. I. Marinn, Comparison of the therapeutic effects of antibiotics of the tetracycline group in the treatment of anthrax caused by a strain inheriting tet-gene of plasmid Pbcib. Antibiotic. Khimister. 37 (1992), pp. 31-34.

[20] M. W. Odendaal, P. M. P, V. de Vos, A. D. Botha, The antibiotic sensitivity pattern of Baccillus anthracis isolated from the Kruger National park. J. Vet. Res. 58 (1991), pp. 17-18.

[21] B. D. Hahn, P. R. Furniss, A deterministic model of an anthrax epizootic: Threshold results. Ecol. Model. 20 (1983), pp. 233–241.

[22] P. R Furniss, B. D. Hahn, A mathematical model of an anthrax epizootic in the Kruger National Park. Appl Math Model. 5 (1981), 130–136.

[23] C. M. Saad-Roy, P. van den Driessche, Y. Abdul-Aziz, A Mathematical model of anthrax transmission in animal populations, bulletin of mathematical biology. (2017), pp 303- 324.

[24] T. C. Dixon, M. Meselson, J. Guillemin, P. C. Hanna, Anthrax. N Engl. J. Med., 341 (11) (1999), pp. 815-826.

[25] M. Mock, A. Fouet, Anthrax. Annu Rev. Microbiol. 55, (2001), pp. 647-671.

[26] J. Guarner, J. A. Jernigan, W. J. Shieh, K. Tatti, L. M. Flannagan, D. S. Stephens, T. Popovic, D. A. Ashford, B. A. Perkins, S. R. Zaki, Inhalational Anthrax Pathology Working Group. Pathology and pathogenesis of bioterrorism-related inhalational anthrax. Am. J. Pathol. 163 (2003), pp. 701–709.

[27] H. Khanna, Y. Singh, War against anthrax. Mol. Med. 7 (2001), pp. 795-796.

[28] S. Oncu, and S. Sakarya, Anthrax-an overview. *Med. Sci. Monit.* 9(11) (2003), pp. 276 – 283.

[29] H. W. Hethcote, The mathematics of infectious diseases, SIAM Rev. 42 (4) (2002), pp. 599-653.

[30] P. van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission., Math. Biosci. 180 (2002), pp. 29- 49.

[31] O. Sharomi, and A. B. Gumel, Dynamical analysis of a multi-strain model of HIV in the presence of anti-retroviral drugs., Journal of Biological Dynamics. 2(3) (2008), pp. 323-345.

[32] V. Lakshmikantham, S. Leela, and A. A. Martynyuk, Stability Analysis of non linear systems, Marcel Dekker, Inc., New York and Basel, (1989).

[33] Zerihun Mamo Sinkie1 and S. Narasimha Murthy, Modelling and simulation study of Anthrax attack on environment. Journal of Multidisciplinary Engineering Science and Technology. 3(4) (2016), pp. 4574-4578.

[34] T. V. Inglesby, T. O'Toole, D. A. Henderson, J. G. Bartlett, M. S. Ascher, E. Eitzen, A. M. Friedlander, J. Gerberding, J. Hauer, J. Hughes, Biodefense WGoC. Anthrax as a biological weapon, 2002: updated recommendations for management. JAMA 287 (2002), pp. 2236–2252.

[35] J. LaSalle, S. Lefschetz, The stability of dynamical systems, SIAM, Philadelphia, (1976).

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[2] Castillo-Chavez, C. and Song, B. (2004). Dynamical models of tuberculosis and their applications, *Math. Biosci. Eng.,* 1: 361-404.

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