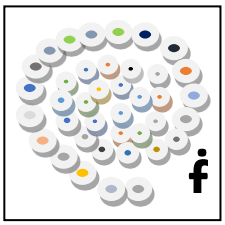

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Dynamical analysis of a two-strain treatment model for Anthrax in a population where it is deployed as bio-terrorism weapon

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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.

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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.

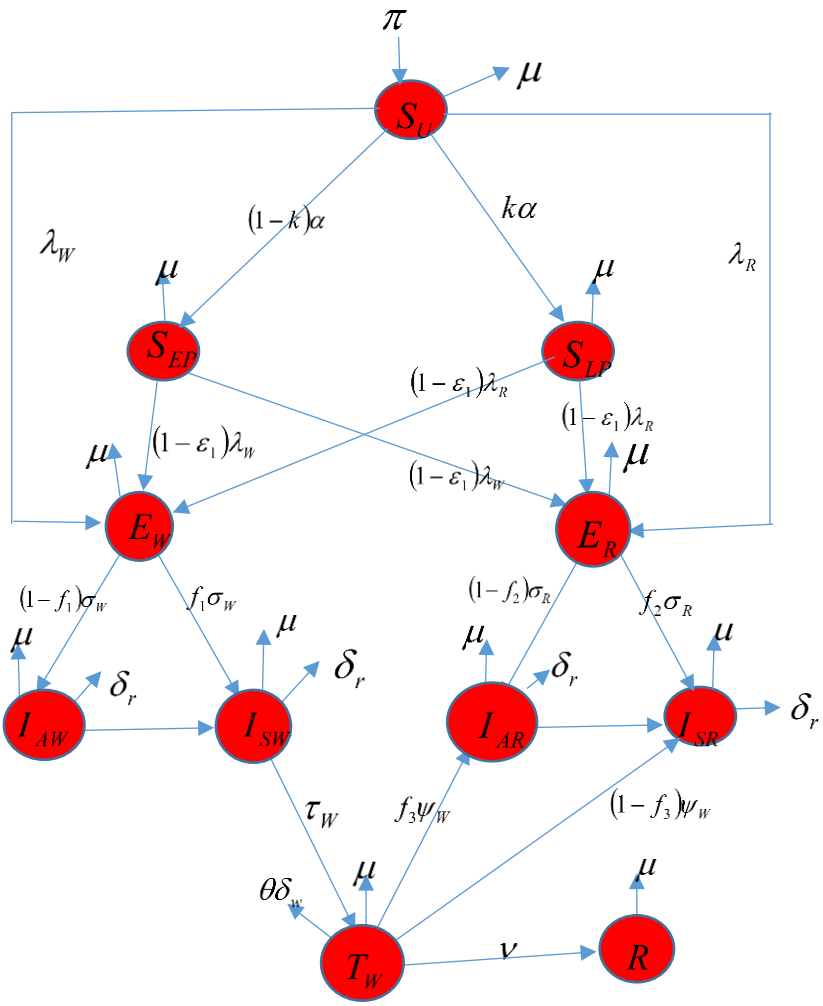

Figure 1: Schematic diagram of the model

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.

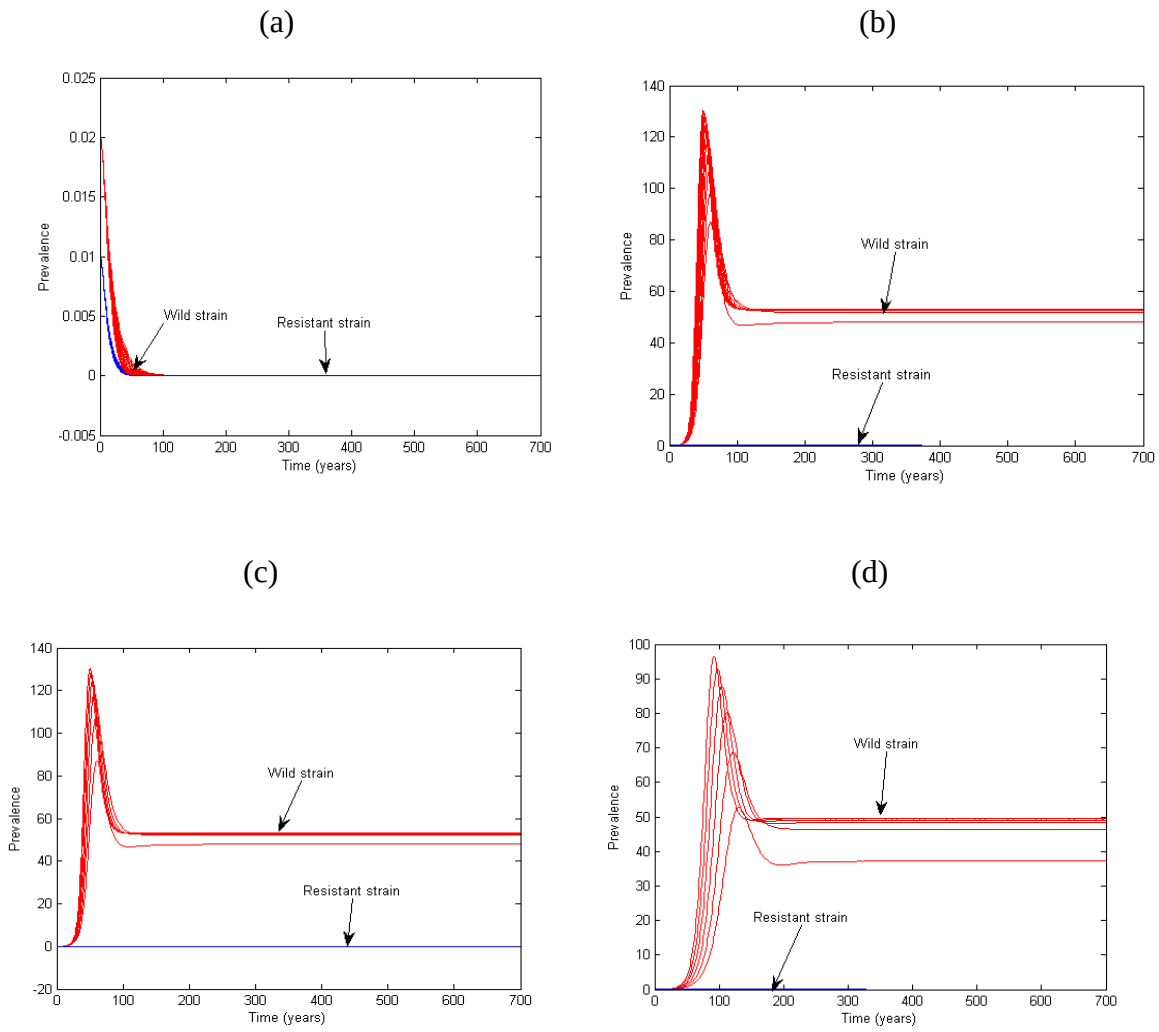

Figure 3. Prevalence given by total number of infected individuals divided by the total population of the community under the bio-terrorism attack as a function of time (years) for treatment-free model(3).3(a) $\beta_W = \beta_R = 0.05, R_W = 0.7164 \& R_R = 0.2469$;3(b) $R_W \succ R_R \succ 1$, $\beta_W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

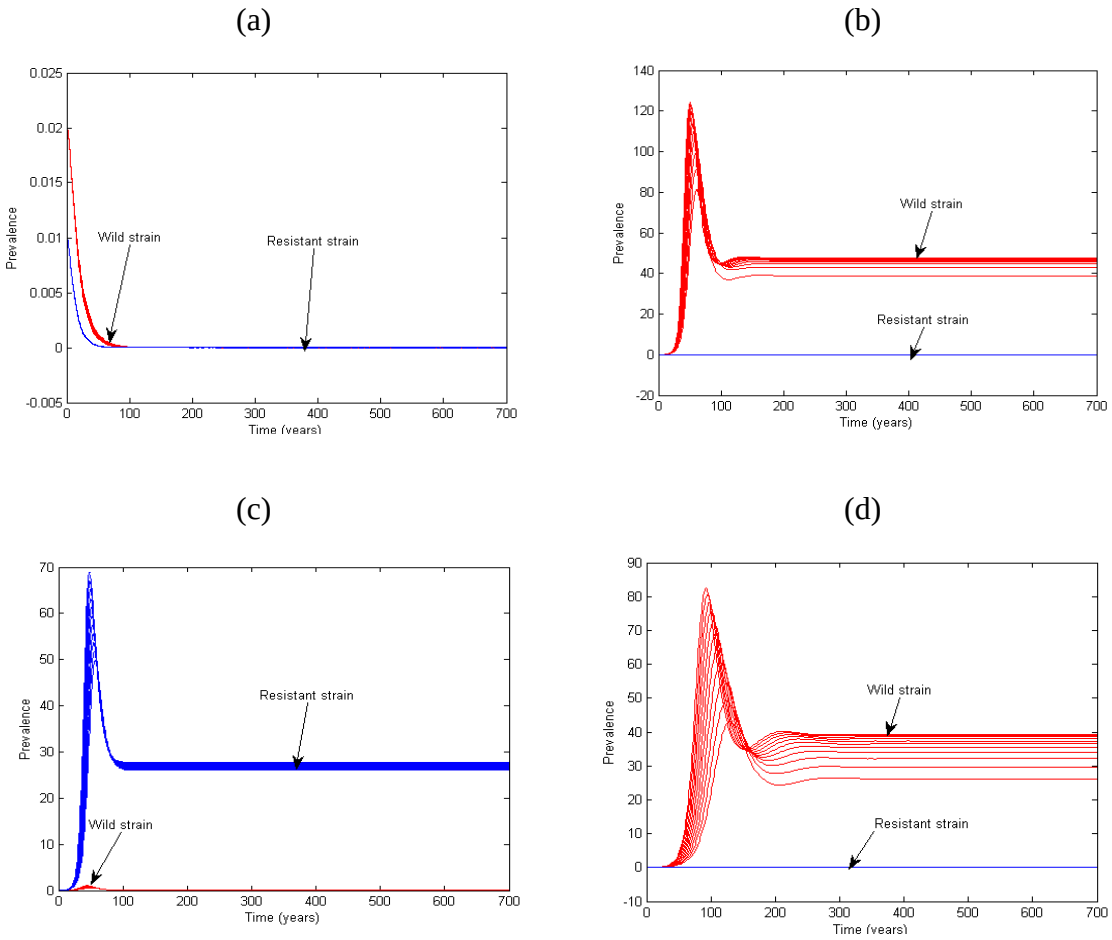

Figure 4. Prevalence given by total number of infected individuals divided by the total population of the community under bio-terrorism attack as a function of time (years) for treatment model (1).

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)

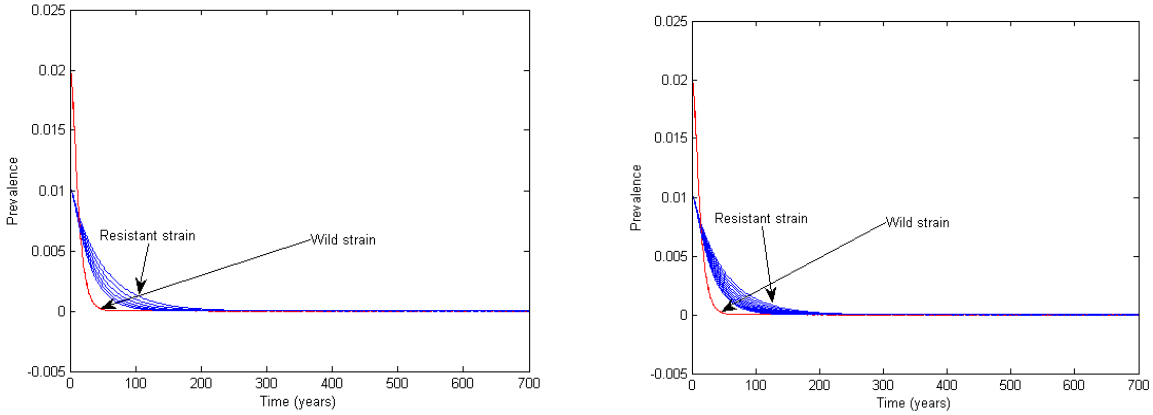

Figure 5. Prevalence given by total number of infected individuals divided by the total population of the community under bio-terrorism attack as a function of time (in years) 5(a) $R_R^t \prec R_W^t \prec 1$- for treatment-free model (3); 5(b) $R_R^t \prec R_W^t \prec 1$-for treatment model (1).

(a) (b)

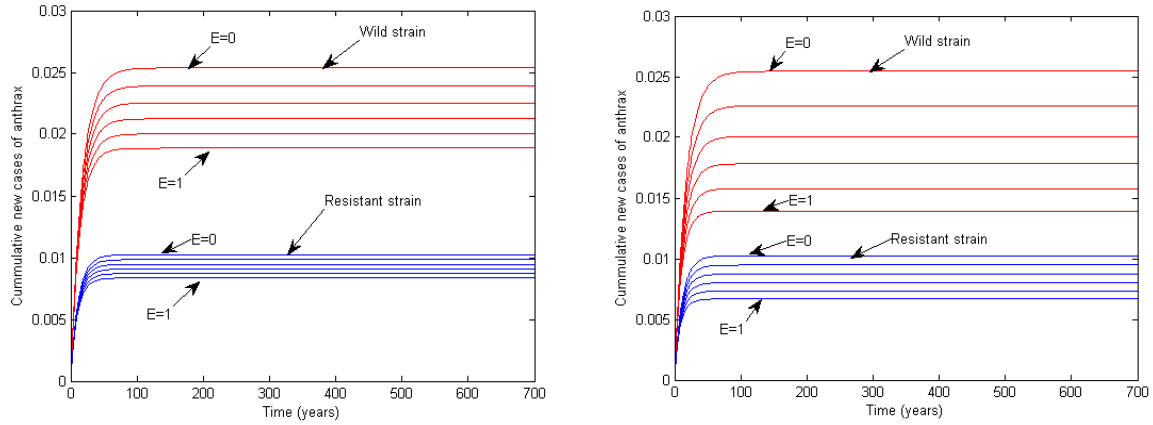

Figure 6. Cumulative number of new cases of anthrax by varying administration of prophylaxis plotted as a function of time (in years) for treatment model. 6(a) $R_R^t \prec R_W^t \prec 1$- varying early administration of prophylaxis (ε_1) represented by E on the graph; 6(b) $R_R^t \prec R_W^t \prec 1$-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