

Backward Bifurcation Analysis of Epidemic Model with Partial Immunity

Roumen Anguelov, Salisu M Garba, Salisu Usaini*

*Department of Mathematics and Applied Mathematics
University of Pretoria, South Africa*

Abstract

This paper presents a two stage SIS epidemic model in animal population with bovine tuberculosis (BTB) in African buffalo as a guiding example. The proposed model is rigorously analyzed. The analysis reveals that the model exhibits the phenomenon of backward bifurcation, where a stable disease-free equilibrium (DFE) coexists with a stable endemic equilibrium (EE) when the associated reproduction number (\mathfrak{R}_v) is less than unity. It is shown under two special cases of the presented model, that this phenomenon of backward bifurcation does not arise depending on vaccination coverage and efficacy of vaccine. Numerical simulations of the model show that, the use of an imperfect vaccine can lead to effective control of the disease if the vaccination coverage and the efficacy of vaccine are high enough.

Keywords: Buffalo, backward bifurcation, bovine tuberculosis, vaccine.

1. Introduction

Bovine tuberculosis (BTB) is a contagious disease caused by a bacterium called *mycobacterium bovis* (M. bovis), with a wide range of hosts such as domestic livestock, wildlife and humans. Some of such animals include cattle, goats, sheep, Badgers (*Meles meles*), brushtail possums (*Trichosurus vulpecula*), deer (*Odocoileus virginianus*), bison (*Bison bison*) and African buffalo

Email addresses: roumen.anguelov@up.ac.za (Roumen Anguelov),
salisu.garba@up.ac.za (Salisu M Garba), kunyasco@yahoo.com (Salisu Usaini*)

*Corresponding author

(*Syncerus caffer*) which can either be reservoir or spill-over [9]. A reservoir host maintains and spread infection whereas a spill-over host has a little or no consequence in the maintenance and spread of the infection. However, a spill-over host is referred to a dead-end host when it does not pass on the infection. BTB is a chronic and progressive disease in buffalo that leads to direct or indirect death. In buffalo herds, BTB has a high prevalence of 60% to 92% [7]. It was reported in [10] that the higher the prevalence rate the higher the disease-related mortality and hence a mortality of up to 10% was detected in buffalo herds having a BTB prevalence of at least 50%. The time from infection to death is not known but it varies and depends on the animal's immune response, which can wane by factors such as stress, drought or old age.

As in cattle the main source of BTB transmission in buffalo is by direct contact or by aerosol [10]. Vertical (intrauterine) and pseudo-vertical (through infected milk) transmissions are considered to be rare events in buffalo [7]. The mode of transmission and the route of infection within and between species are generally indicated by the locations of the tuberculous lesions in that species [9].

In Africa most animals infected with BTB show clinical signs only when the disease has reached an advanced stage. The clinical signs of BTB in buffalo at such stage include: coughing, debilitation, poor body condition or emaciation and lagging when chased by helicopter [9, 10].

Park management (Kruger National Park (KNP) and Hluhluwe-iMfolozi Park (HiP)) in South Africa have maintained some control measures such as culling, vaccination and some combination of them to control or eradicate BTB owing to its potential effects on buffalo and other host species [7, 18]. However, some modeling work on BTB on buffalo suggest that vaccination may be the best control measure option since BTB may persist in buffalo population even when the population is reduced to low densities [7]. In order to assess the effectiveness of a buffalo vaccination program in South Africa some age structured mathematical models have recently been developed [1, 7].

Since there is no clinical evidence which suggest that animals recover from BTB infection [7], we design a simple susceptible-infectious-susceptible (SIS) compartmental model based on the most assumptions of the two stage

bovine respiratory syncytial virus epidemic model presented in [13]. This is for the fact that BTB infection confers partial immunity and spreads among seropositive animals. The basic idea of their model is that for animal diseases which confer partial immunity from initial infection recovery, an animal may become lightly infected again without necessarily showing clinical symptoms of the disease. This appears for some diseases at which such seropositive animals may transmit the infection at a lower rate than animals experiencing the infection for the first time. Analysis of the two-stage model in [13] shows the possibility of backward bifurcation, and that the higher of the two subcritical equilibria (one with larger number of infective individuals) is stable whereas the lower one (one with smaller number of infective individuals) is unstable. It is argued in [14] that using two-stage model to incorporate the effect of successive exposure to infectious agents is an oversimplification. This is based on the suggestion in [23] that in some cases greater level of exposure to infectious organism may overcome the immune system and lead to a more subsequent transmission of the disease than a lower exposure. However, a three-stage model for the spread of Bovine respiratory syncytial virus in cattle may be more realistic than the two-stage one. The three-stage extended model considered in [14] is shown to exhibit more complex dynamics such as two subcritical endemic equilibria in the presence of forward bifurcation and multiple supercritical equilibria.

It is to be noted that both the two-stage and its three-stage extension in [13, 14] as well as the three compartmental model in [20] are restricted to the situations where the affected population is of constant size. This assumption is reasonable for diseases that either spread quickly (i.e. in less than one year) through the population or those that spread slowly (i.e. over many years) with births approximately balanced by the natural deaths [6, 17, 27]. However, for diseases with either high disease-related mortalities or in which the births are not balanced by the deaths, this assumption is not very realistic. Several examples of animal diseases in which disease-related deaths have drastically decreased the population sizes are given in [27]. The two-stage model presented here is an extension of the model presented in [13] by incorporating vital dynamics in a population with varying size which makes the model more realistic and practically relevant. It can also be considered

as an extension of the three compartmental model in [20] by considering both differential susceptibility and differential infectivity, respectively. We study this model with aim to identify causes of backward bifurcation and to assess vaccine impact in the transmission dynamics of an epidemic model with partial immunity and variable population.

A rigorous analysis of our model reveals some threshold values of the most important parameters in applications (i.e. reproduction number, vaccination coverage and vaccine efficacy). In fact, we obtained a critical value of the vaccinated reproduction number \mathfrak{R}_v , denoted by \mathfrak{R}_v^c , for the saddle-node bifurcation which is related with appearance and disappearance of the two endemic equilibria. In this setting, reducing \mathfrak{R}_v to a value less than one is no longer sufficient for disease eradication but below \mathfrak{R}_v^c . Threshold analysis of the minimum effort for disease eradication taking into account the existence of backward bifurcation is presented in [20, 21]. In this paper, we investigate thresholds of vaccination coverage (θ) and vaccine efficacy ($\phi = 1 - \alpha$) in relation to the coexistence region of the stable disease-free equilibrium and endemic equilibrium. These were not reported in [13, 14], even though their models exhibit backward bifurcations.

The paper is organized as follows. In Section 2, we formulate the mathematical model and present it's basic properties. Detailed analysis of the phenomenon of backward bifurcation and two significant special cases of the proposed model is presented in Section 3. In Section 4, the impact of vaccine is assessed via numerical simulations.

2. Mathematical model

2.1. Formulation of the model

It is well known that some animal infections may confer partial immunity and can spread among seropositive animals. Such type of disease can be modeled by the *SISI* (or $S_1I_1S_2I_2S_2$) compartmental type [13]. Following this approach, we divide the total population N of African buffalo, at time t into four distinct epidemiological classes, namely: those who have never been infected before ($S_1(t)$), those who have experienced at least one previous infection ($S_2(t)$), first time infectious ($I_1(t)$), and at least second time infectious ($I_2(t)$). Hence, the total population at any time t is given by

$$N(t) = S_1(t) + I_1(t) + S_2(t) + I_2(t).$$

The system of ordinary differential equations for the $S_1I_1S_2I_2S_2$ model is

$$\begin{aligned}\frac{dS_1}{dt} &= (1 - \theta)\Lambda - (\beta + \mu)S_1, \\ \frac{dI_1}{dt} &= \beta S_1 - (\gamma_1 + \mu + \tau_1)I_1, \\ \frac{dS_2}{dt} &= \theta\Lambda + \gamma_1 I_1 + \gamma_2 I_2 - (\alpha\beta + \mu)S_2, \\ \frac{dI_2}{dt} &= \alpha\beta S_2 - (\gamma_2 + \mu + \tau_2)I_2,\end{aligned}\tag{1}$$

with force of infection

$$\beta = \frac{\sigma_1 I_1 + \sigma_2 I_2}{N}.$$

In (1), the parameter Λ is the recruitment rate of susceptible buffalo. A fraction θ of these susceptible buffalo are vaccinated. Furthermore, the population of first time susceptible buffalo acquire infection, following effective contact with infectious buffalo at a rate β . The parameter σ_i ($i = 1, 2$) is the effective contact rate for the respective infectious class I_i , μ is the natural death rate in all classes. γ_i ($i = 1, 2$), is the recovery rate of infected buffalo from the I_i class. τ_i ($i = 1, 2$), is the disease induced death rate in each class I_i . It is assumed that second and subsequent times infected buffalo acquire natural immunity after recovery and move to S_2 class. Further, it is assumed that vaccine-induced immunity provides the same protection as the natural immunity. This is a simplifying assumption which helps keep mathematical complexity of the model at reasonable level, while the model is still relevant. Hence, the S_2 class can be referred to as vaccinated class as well. The population of vaccinated buffalo in S_2 acquire infection at the rate $\alpha\beta$ where $0 \leq \alpha \leq 1$. Thus α provides a measure of the efficacy of vaccine in a relative way so that $\alpha = 0$ means the vaccine is completely effective in preventing infection and $\alpha = 1$ means that the vaccine is ineffective. More precisely, in the absence of vaccine the force of infection is β , with vaccine

it becomes $\alpha\beta$. The relative reduction $\phi = \frac{\beta - \alpha\beta}{\beta} = 1 - \alpha$ of the force of infection is referred to as efficacy of the vaccine.

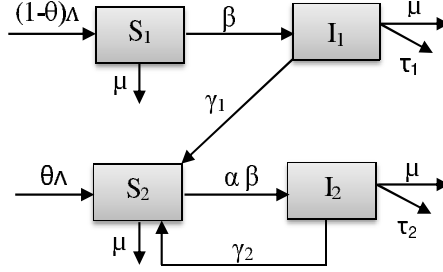


Figure 1: Schematic diagram of model (1)

2.2. Basic properties

The typical epidemiological questions, such as persistence/extinction of the infection, threshold values of the parameter, etc., are mathematically formulated in terms of the asymptotic behavior of the solution of (1) considered as a dynamical system as well as the bifurcations of this system.

It is easy to verify that the system of equations (1) defines a (positive) dynamical system on the domain

$$\Omega = \left\{ (S_1, I_1, S_2, I_2) \in \mathcal{R}_+^4 : S_1 + I_1 + S_2 + I_2 \leq \frac{\Lambda}{\mu} \right\}.$$

In fact, one can easily see that $\dot{S}_i \geq 0$, $\dot{I}_i \geq 0$ and $\dot{N} \leq 0$ when $S_i = 0$, $I_i = 0$ and $N = \lambda/\mu$, respectively. Therefore, at any point on the boundary the vector field is pointing inside Ω . Hence, the system (1) defines a dynamical system on Ω .

2.3. Existence and stability of equilibria

2.3.1. Disease-free equilibrium (DFE)

In the absence of the disease ($I_1 = I_2 = 0$), the DFE of the model (1) obtained at steady state is given by

$$\mathcal{E}_0 = (S_1^*, I_1^*, S_2^*, I_2^*) = \left(\frac{(1-\theta)\Lambda}{\mu}, 0, \frac{\theta\Lambda}{\mu}, 0 \right).$$

To establish conditions for the linear stability of \mathcal{E}_0 , the next generation operator method is applied to the system (1). Using the notation in [25], the matrices F (for the new infection terms) and V (of the transition terms) are given, respectively, by

$$F = \begin{bmatrix} \sigma_1(1-\theta) & \sigma_2(1-\theta) \\ \alpha\sigma_1\theta & \alpha\sigma_2\theta \end{bmatrix}, \quad V = \begin{bmatrix} \gamma_1 + \mu + \tau_1 & 0 \\ 0 & \gamma_2 + \mu + \tau_2 \end{bmatrix}.$$

The associated reproduction number denoted by \mathfrak{R}_v , is the spectral radius of the next generation matrix FV^{-1} , given by

$$\mathfrak{R}_v = \frac{\sigma_1 k_2 (1-\theta) + \alpha \sigma_2 k_1 \theta}{k_1 k_2}, \quad (2)$$

where $k_1 = \gamma_1 + \mu + \tau_1$ and $k_2 = \gamma_2 + \mu + \tau_2$.

The threshold quantity, \mathfrak{R}_v , represents the average number of secondary infections caused by a single infected buffalo in a susceptible buffalo population where a certain fraction of the population is vaccinated [12, 22]. Hence, using [25, Theorem 2], we obtain the following result.

Theorem 1. *The DFE, \mathcal{E}_0 of the model (1) is locally-asymptotically stable (LAS) if $\mathfrak{R}_v < 1$, and unstable if $\mathfrak{R}_v > 1$.*

The epidemiological implication of Theorem 1 is that if $\mathfrak{R}_v < 1$, the disease will be eliminated provided the initial sizes of the infected subpopulations of the model are sufficiently small so that the initial state of the system is in basin of attraction of the DFE (\mathcal{E}_0).

We note that this result does not exclude the possibility of coexistence of DFE with a stable endemic equilibrium. This coexistence, which results from a backward bifurcation at $\mathfrak{R}_v = 1$, is the main issue investigated in the sequel.

2.3.2. Endemic equilibria (EE)

The endemic equilibria of the model (1) are the steady states where the disease may persist in the population, that is when at least one of the infected compartments of the model is non-empty. Let $\mathcal{E}_1 = (S_1^{**}, I_1^{**}, S_2^{**}, I_2^{**})$ be an endemic equilibrium solution of model (1). Then, equating the right-hand side of (1) to zero, we obtain

$$\begin{aligned} S_1^{**} &= \frac{(1-\theta)\Lambda}{\beta^{**} + \mu}, \quad I_1^{**} = \frac{\beta^{**}(1-\theta)\Lambda}{k_1(\beta^{**} + \mu)}, \\ S_2^{**} &= \frac{k_2\Lambda[k_1\theta(\beta^{**} + \mu) + \gamma_1(1-\theta)\beta^{**}]}{k_1(\beta^{**} + \mu)[(\mu + \tau_2)(\alpha\beta^{**} + \mu) + \mu\gamma_2]}, \\ I_2^{**} &= \frac{\alpha\beta^{**}\Lambda[k_1\theta(\beta^{**} + \mu) + \gamma_1(1-\theta)\beta^{**}]}{k_1(\beta^{**} + \mu)[(\mu + \tau_2)(\alpha\beta^{**} + \mu) + \mu\gamma_2]}, \end{aligned} \quad (3)$$

where

$$\beta^{**} = \frac{\sigma_1 I_1^{**} + \sigma_2 I_2^{**}}{N^{**}} \quad (4)$$

and

$$N^{**} = S_1^{**} + I_1^{**} + S_2^{**} + I_2^{**}. \quad (5)$$

Equation (4) can be written in the form

$$S_1^{**} + \left(1 - \frac{\sigma_1}{\beta^{**}}\right) I_1^{**} + S_2^{**} + \left(1 - \frac{\sigma_2}{\beta^{**}}\right) I_2^{**} = 0. \quad (6)$$

Substituting equations in (3) into equation (6), gives the following equation for β^{**} .

$$\begin{aligned} \frac{(1-\theta)\Lambda}{\beta^{**} + \mu} + \left(1 - \frac{\sigma_2}{\beta^{**}}\right) \frac{\alpha\beta^{**}\Lambda[k_1\theta(\beta^{**} + \mu) + \gamma_1(1-\theta)\beta^{**}]}{k_1(\beta^{**} + \mu)[(\mu + \tau_2)(\alpha\beta^{**} + \mu) + \mu\gamma_2]} \\ + \frac{k_2\Lambda[k_1\theta(\beta^{**} + \mu) + \gamma_1(1-\theta)\beta^{**}]}{k_1(\beta^{**} + \mu)[(\mu + \tau_2)(\alpha\beta^{**} + \mu) + \mu\gamma_2]} + \left(1 - \frac{\sigma_1}{\beta^{**}}\right) \frac{\beta^{**}(1-\theta)\Lambda}{k_1(\beta^{**} + \mu)} = 0. \end{aligned} \quad (7)$$

Hence, the endemic equilibria of the model (1) correspond to positive solutions of the equation (7).

3. Backward bifurcation analysis

The phenomenon of backward bifurcation occurs in models that have multiple endemic equilibria when $\mathfrak{R}_v < 1$ [13, 14, 16]. In this case, the classical epidemiological requirement of having $\mathfrak{R}_v < 1$, is necessary but no longer sufficient for effective disease control or elimination.

3.1. Existence of endemic equilibria

Re-arranging and simplifying equation (7), gives the following quadratic equation in terms of β^{**}

$$a(\beta^{**})^2 + b\beta^{**} + c = 0, \quad (8)$$

where,

$$\begin{aligned} a &= \alpha[k_1\theta + (\gamma_1 + \mu + \tau_2)(1 - \theta)], \\ b &= k_1\alpha(\mu + \tau_2)(1 - \theta) + k_1\alpha\theta(\mu - \sigma_2) + k_2(1 - \theta)(\mu + \gamma_1) \\ &\quad + k_1k_2\theta - \sigma_1\alpha(\mu + \tau_2)(1 - \theta) - \sigma_2\gamma_1\alpha(1 - \theta), \\ c &= k_1k_2\mu(1 - \mathfrak{R}_v). \end{aligned} \quad (9)$$

Thus, the following result is established.

Theorem 2. *The model (1) has:*

- i. *a unique endemic equilibrium if $c < 0$,*
- ii. *a unique endemic equilibrium if $b < 0$ and $c = 0$ or $\Delta = b^2 - 4ac = 0$,*
- iii. *two endemic equilibria if $b < 0, c > 0$ and $\Delta > 0$,*
- iv. *no endemic equilibrium otherwise.*

If $\alpha > 0$, the proof follows easily from the properties of the roots of a quadratic equation. For $\alpha = 0$, one can verify the statements by inspection.

Note that a is always positive and c is positive or negative according as \mathfrak{R}_v is less than or greater than unity. It is clear from Case (i) of Theorem 2 that the model (1) has a unique endemic equilibrium whenever $\mathfrak{R}_v > 1$. Furthermore, the possibility of backward bifurcation (where a stable DFE

coexists with a stable EE see, for instance [5, 11, 13, 14, 15, 16, 19, 20, 21]) in model (1) is indicated by Case (iii) of Theorem 2. To check for the possibility of this phenomenon in (1), the discriminant Δ of the equation (8), is set to zero and solved for the critical value of \mathfrak{R}_v , denoted by \mathfrak{R}_v^c , given by

$$\mathfrak{R}_v^c = 1 - \frac{b^2}{4ak_1k_2\mu}.$$

It follows that backward bifurcation occurs for values of \mathfrak{R}_v such that $\mathfrak{R}_v^c < \mathfrak{R}_v < 1$ (see also [22]). This is illustrated on Figure 2 by simulating the model (1) with following set of parameter values : $\mu = 0.097, \sigma_1 = 0.5, \sigma_2 = 0.75, \alpha = 0.8, \tau_1 = 0.36, \tau_2 = 0.162, \gamma_1 = 0.52, \gamma_2 = 0.001$ and $\theta = 0.2$ (so that $\mathfrak{R}_v^c = 0.8646438738 < \mathfrak{R}_v = 0.8709550431 < 1$). Figure 2 clearly shows in this case the coexistence of two stable equilibria of the model (1) for $\mathfrak{R}_v^c < \mathfrak{R}_v < 1$.

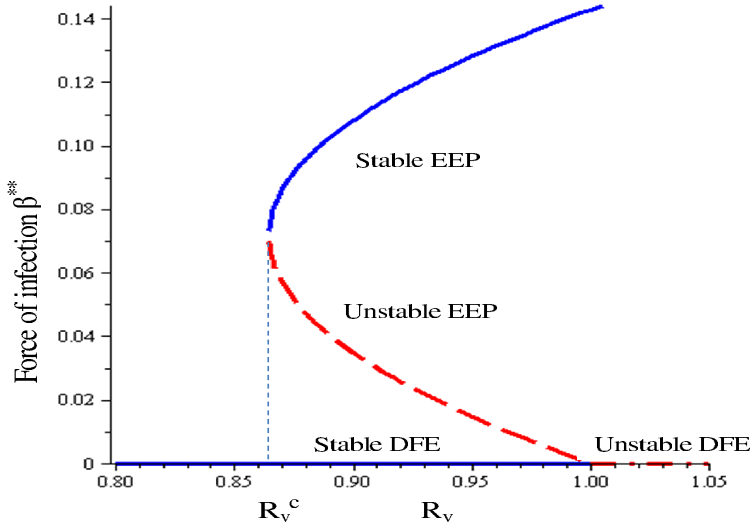


Figure 2: Graph of the force of infection β^{**} versus reproduction number \mathfrak{R}_v that shows a backward bifurcation diagram for the model (1).

3.2. Coexistence of stable DFE and EE

The parameters θ and α can be considered as controls in the model (1) due to their relation to vaccination rate and vaccine efficacy. With all other

parameters fixed, the coefficients a, b and c in equation (9) are functions of θ and α . Then it follows from Theorem 2 that a stable DFE coexists with an endemic equilibrium for values of θ and α in the region

$$M = \{(\theta, \alpha) \in [0, 1] \times [0, 1] : b < 0, c > 0, b^2 - 4ac > 0\}.$$

The graph of the coexistence region M on the (θ, α) plane is presented on Figure 3. One can observe that although the region covers wide range of values of θ and α , for any fixed value of one parameter the range of the other is rather small. Further, the curves $\Delta = 0$, $b = 0$ and $\mathfrak{R}_v = 1$ intersect at one point, say $P = (\hat{\theta}, \hat{\alpha})$. Indeed, it is easy to see that if two of the equations hold then so does the third one, e.g. $\Delta = 0, b = 0 \Rightarrow c = 0 \Leftrightarrow \mathfrak{R}_v = 1$.

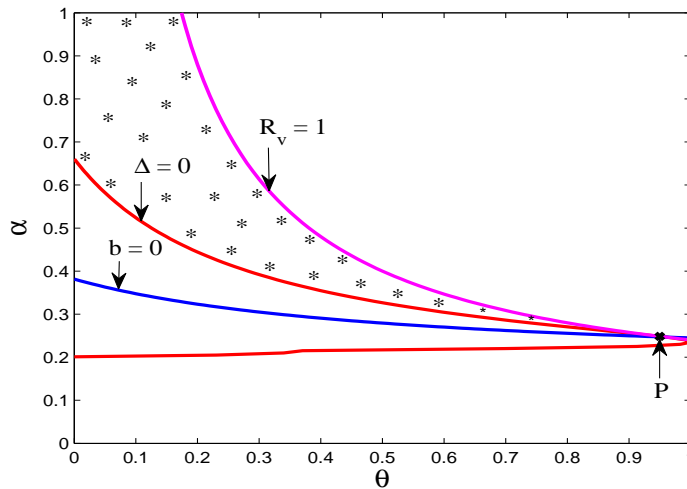


Figure 3: Region with stars in the (θ, α) space is defined by $\mathfrak{R}_v < 1, b < 0$ and $\Delta > 0$ where stable DFE and EE of model (1) coexist. Parameter values used are: $\mu = 0.01, \sigma_1 = 0.07, \sigma_2 = 0.5, \gamma_1 = 0.1, \gamma_2 = 0.01$ and $\tau_1 = \tau_2 = 0.1$.

Note that for values of θ larger than $\hat{\theta}$ or values of α smaller than $\hat{\alpha}$ there is no coexistence of DFE with any endemic equilibrium. Depending on the values of the other parameters the region M may vary in shape and size. However, we will show later that there are always threshold values $\hat{\theta}$ and $\hat{\alpha}$

with the above stated properties. The proof is based on the two special cases given in the next subsection.

3.3. Two special cases

3.3.1. All new recruits are vaccinated ($\theta = 1$)

In this case we have

$$\mathfrak{R}_v = \frac{\alpha\sigma_2}{k_2} \quad (10)$$

and the coefficients of equation (8) in (9) are now

$$a = \alpha, \quad b = \alpha\mu + k_2(1 - \mathfrak{R}_v), \quad c = k_2\mu(1 - \mathfrak{R}_v). \quad (11)$$

Then it follows from Theorem 2 that there is no endemic equilibrium when $\mathfrak{R}_v \leq 1$. The following theorem shows that if $\mathfrak{R}_v \leq 1$, the DFE is globally asymptotically stable on Ω .

Theorem 3. *The DFE (\mathcal{E}_0) of the model (1) is GAS on Ω whenever $\mathfrak{R}_v \leq 1$.*

Proof. Since for $\theta = 1$ there are no recruits in the compartment S_1 then both S_1 and I_1 approach zero as $t \rightarrow \infty$. This essentially means that the model is reduced to a two dimensional system given by

$$\begin{aligned} \frac{dS_2}{dt} &= \Lambda + \gamma_2 I_2 - \frac{\alpha\sigma_2 I_2}{N} S_2 - \mu S_2, \\ \frac{dI_2}{dt} &= \frac{\alpha\sigma_2 I_2}{N} S_2 - (\gamma_2 + \mu + \tau_2) I_2. \end{aligned} \quad (12)$$

This argument can be made precise by using LaSalle's Invariance Principle [2] with Lyapunov function

$$G(S_1, I_1, S_2, I_2) = S_1 + I_1.$$

Indeed, we have

$$\dot{G} = \frac{dS_1}{dt} + \frac{dI_1}{dt} = -\mu S_1 - (\gamma_1 + \mu + \tau_1) I_1 \leq 0$$

and

$$\dot{G} = 0 \Leftrightarrow S_1 = I_1 = 0.$$

It is easy to see that the largest invariant subset of

$$\begin{aligned} W &= \{(S_1, I_1, S_2, I_2) \in \Omega : \dot{G}(S_1, I_1, S_2, I_2) = 0\} \\ &= \{(S_1, I_1, S_2, I_2) \in \Omega : S_1 = I_1 = 0\} \end{aligned}$$

is the disease-free equilibrium \mathcal{E}_0 . Then it follows from LaSalle's Invariance Principle [2, Theorem 3.7.11, page 346] that \mathcal{E}_0 is globally asymptotically stable. ■

3.3.2. Recovery from infection confers permanent immunity ($\alpha = 0$)

In this case we have $\mathfrak{R}_v = \frac{\sigma_1(1-\theta)}{k_1}$ and the coefficients of (8) in equation (9) become

$$a = 0, \quad b = k_1\theta + (\mu + \gamma_1)(1 - \theta), \quad c = k_1\mu(1 - \mathfrak{R}_v). \quad (13)$$

It then follows from Theorem 2 that there is no endemic equilibrium when $\mathfrak{R}_v \leq 1$. Furthermore, the following theorem shows that if $\mathfrak{R}_v \leq 1$, the DFE is globally asymptotically stable on Ω .

Theorem 4. *The DFE (\mathcal{E}_0) of the model (1) is GAS on Ω whenever $\mathfrak{R}_v \leq 1$.*

Proof. Since for $\alpha = 0$ recovery from infection confers permanent immunity then the infected compartment I_2 approaches zero as $t \rightarrow \infty$. In fact, this reduces (1) to the following three dimensional system

$$\begin{aligned} \frac{dS_1}{dt} &= (1 - \theta)\Lambda - \frac{\sigma_1 I_1}{N} S_1 - \mu S_1, \\ \frac{dI_1}{dt} &= \frac{\sigma_1 I_1}{N} S_1 - (\gamma_1 + \mu + \tau_1) I_1, \\ \frac{dS_2}{dt} &= \theta\Lambda + \gamma_1 I_1 - \mu S_2. \end{aligned} \quad (14)$$

We make this statement precise by using LaSalle's Invariance Principle in a similar way as in the proof of Theorem 3. We consider the Lyapunov function

$$U(S_1, I_1, S_2, I_2) = \begin{cases} I_2 + \frac{1}{2}(\theta S_1 - (1 - \theta)S_2)^2 & \text{if } S_1 > \frac{1-\theta}{\theta} S_2, \\ I_2 & \text{if } S_1 \leq \frac{1-\theta}{\theta} S_2. \end{cases}$$

Then

$$\dot{U} = \begin{cases} \dot{I}_2 + (\theta S_1 - (1 - \theta)S_2)(\theta \dot{S}_1 - (1 - \theta)\dot{S}_2) & \text{if } S_1 > \frac{1-\theta}{\theta}S_2, \\ \dot{I}_2 & \text{if } S_1 \leq \frac{1-\theta}{\theta}S_2. \end{cases}$$

We have

$$\begin{aligned} \theta \dot{S}_1 - (1 - \theta)\dot{S}_2 &= -\mu(\theta S_1 - (1 - \theta)S_2) - \theta\beta S_1 - (1 - \theta)(\gamma_1 I_1 + \gamma_2 I_2) \\ &\leq -\mu(\theta S_1 - (1 - \theta)S_2). \end{aligned}$$

Therefore

$$\dot{U} \leq \begin{cases} -k_2 I_2 - \mu(\theta S_1 - (1 - \theta)S_2)^2 & \text{if } S_1 > \frac{1-\theta}{\theta}S_2, \\ -k_2 I_2 & \text{if } S_1 \leq \frac{1-\theta}{\theta}S_2. \end{cases}$$

Hence, $\dot{U} \leq 0$ with $\dot{U} = 0$ if and only if $I_2 = 0$ and $\theta S_1 - (1 - \theta)S_2 = 0$. Then it follows that

$$\check{\Omega} = \{(S_1, I_1, S_2, I_2) \in \Omega : \theta S_1 \leq (1 - \theta)S_2, I_2 = 0\}$$

is a stable and attractive invariant subdomain of Ω . Therefore, \mathcal{E}_0 is GAS equilibrium of (1) on Ω if it is GAS equilibrium of (1) on $\check{\Omega}$ or equivalently that $\bar{\mathcal{E}}_0 = (S_1^*, I_1^*, S_2^*) = \left(\frac{\Lambda(1-\theta)}{\mu}, 0, \frac{\Lambda\theta}{\mu}\right)$ is a GAS equilibrium of (14) on

$$\bar{\Omega} = \left\{ (S_1, I_1, S_2) \in \mathbb{R}_+^3 : S_1 + I_1 + S_2 \leq \frac{\Lambda}{\mu}, \theta S_1 \leq (1 - \theta)S_2 \right\}.$$

For the dynamical system defined by (14) on $\bar{\Omega}$, we consider the Lyapunov function $F(S_1, I_1, S_2) = \frac{1}{2}I_1^2$. Then

$$\dot{F} = I_1 \frac{dI_1}{dt} = I_1 \left(\frac{\sigma_1 I_1}{N} S_1 - k_1 I_1 \right) = I_1^2 \left(\frac{\sigma_1 S_1}{N} - k_1 \right).$$

But on $\check{\Omega}$, we have

$$S_1 = (1 - \theta)S_1 + \theta S_1 \leq (1 - \theta)S_1 + (1 - \theta)S_2 \leq (1 - \theta)(S_1 + S_2) \leq (1 - \theta)N.$$

Therefore

$$\dot{F} \leq I_1^2 \left(\frac{\sigma_1(1-\theta)N}{N} - k_1 \right) = I_1^2 k_1 (\mathfrak{R}_v - 1) \leq 0.$$

It is easy to see that $\dot{F} = 0$ if and only if $I_1 = 0$. Substituting $I_1 = 0$ in the first and third equations of (14) implies that S_1 approaches $\frac{\Lambda(1-\theta)}{\mu}$ and S_2 approaches $\frac{\Lambda\theta}{\mu}$ as $t \rightarrow \infty$. Hence, $\bar{\mathcal{E}}_0$ is GAS equilibrium of (14) on $\bar{\Omega}$ and subsequently \mathcal{E}_0 is GAS equilibrium of (1) on Ω . ■

3.4. Existence of thresholds for θ and α

The functions a, b and c in (9) used in the equations defining the coexistence region M are all continuous functions of θ and α . Therefore, the topological closure of M is

$$\bar{M} = \{(\theta, \alpha) : b \leq 0, c \geq 0, b^2 - 4ac \geq 0\}.$$

Let

$$\hat{\theta} = \max\{\theta \in [0, 1] : \exists \alpha \in [0, 1] : (\theta, \alpha) \in \bar{M}\}$$

and

$$\hat{\alpha} = \min\{\alpha \in [0, 1] : \exists \theta \in [0, 1] : (\theta, \alpha) \in \bar{M}\}.$$

Assume $\hat{\theta} = 1$, then there exists $\check{\alpha}$ such that $(1, \check{\alpha}) \in \bar{M}$. However, from the discussion in Subsection 3.3.1 we have $(1, \check{\alpha}) \notin M$. Therefore $b = 0$ at the point $(1, \check{\alpha})$ in Figure 3. Then it follows from (11) that $\alpha = 0$ and $\mathfrak{R}_v = 1$ which contradicts (10). Thus $\hat{\theta} < 1$. Similarly, using Subsection 3.3.2 we show that $\hat{\alpha} > 0$.

These results show that the backward bifurcation can be removed if either (i) significantly large proportion of the population are vaccinated or (ii) the vaccine efficacy $\phi = 1 - \alpha$ is high enough. Indeed, in the parameter regime of the coexistence region (Figure 3) $\hat{\alpha} = 0.25$ and $\hat{\theta} = 0.95$, so that at least 75% vaccine efficacy or 95% vaccination coverage is required to remove backward bifurcation.

4. Impact of vaccine

Since preliminary data from a previous study of African buffalo suggests that the Bacille Calmette-Guerin (BCG) vaccine was not effective [8] despite its potential impact in some alternative BTB hosts, it is useful to investigate whether or not the widespread application of such imperfect vaccine in free-ranging African buffalo will be beneficial or not.

To get a clear insight of vaccine impact in reducing the spread of infection at endemic state, a plot of the BTB prevalence as a function of time is depicted in Figure 4. It is evident from Figure 4, that prevalence decreases with decreasing value of the vaccinated reproduction number (\mathfrak{R}_v). It should be noted that the reproduction number before vaccination (\mathfrak{R}_0), is always greater than the reproduction number in the presence of vaccination (\mathfrak{R}_v) at the endemic state. Thus, vaccination reduces the prevalence of the disease.

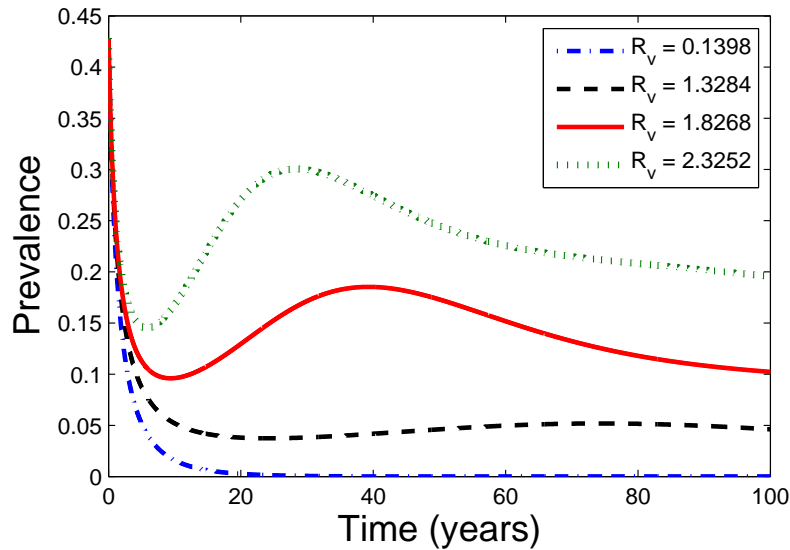


Figure 4: Prevalence as a function of time for model (1) showing positive impact of vaccine: when $\sigma_1 = 0.93$ then $\mathfrak{R}_v = 2.3252 < \mathfrak{R}_0 = 4.6350$; when $\sigma_1 = 0.73$ then $\mathfrak{R}_v = 1.8268 < \mathfrak{R}_0 = 3.6382$; when $\sigma_1 = 0.53$ then $\mathfrak{R}_v = 1.3284 < \mathfrak{R}_0 = 2.6414$; when $\sigma_1 = 0.053$ then $\mathfrak{R}_v = 0.1398 < \mathfrak{R}_0 = 0.2641$. Other parameter values used are as given in Table 2 with $\sigma_2 = 0.0034$.

A contour plot of the reproduction threshold \mathfrak{R}_v , as a function of vaccine efficacy (ϕ) and fraction of vaccinated buffalo (θ), is depicted in Figure 5. The contours indicate that for effective disease elimination, a vaccine efficacy (ϕ) and fraction of vaccinated susceptible buffalo (θ) are to be high enough. For instance, if 90% of susceptible African buffalo are vaccinated, an efficacy level of at least 85% would be required to eradicate the disease.

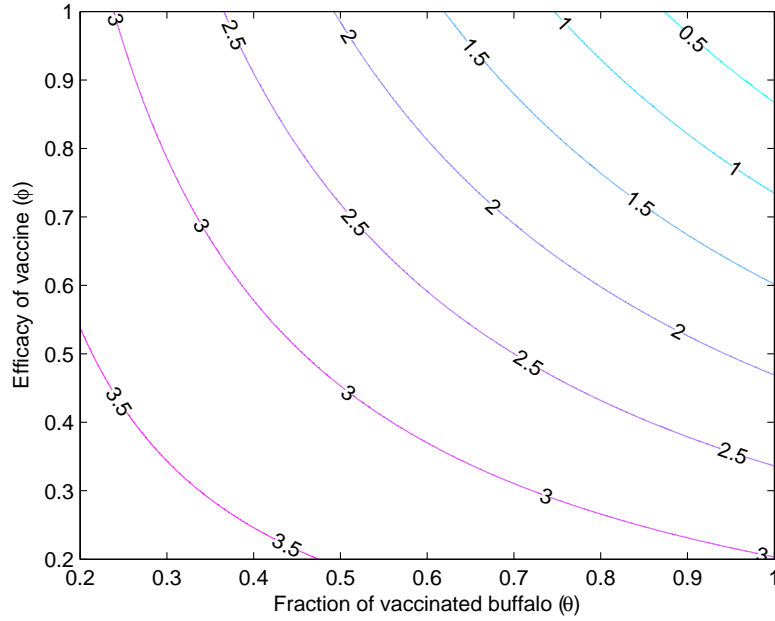


Figure 5: Contour plot of \mathfrak{R}_v of the model (1) as a function of vaccine efficacy (ϕ) and fraction of vaccinated susceptible buffalo (θ). Parameter values used are $\mu = 0.000648$, $\sigma_1 = 0.83$, $\sigma_2 = 0.3$, $\gamma_1 = 0.09$, $\gamma_2 = 0.01$, $\tau_1 = 0.12$, $\tau_2 = 0.069$. The reproduction number without vaccination is $\mathfrak{R}_0 = 3.94$ which indicates that vaccination always has positive impact.

Conclusion

A two-stage deterministic epidemic model in animal population with bovine tuberculosis in African buffalo as a guiding example, is designed and rigorously analyzed. Some of the main findings of the study are:

- (1) The presented model exhibits the phenomenon of backward bifurcation for certain values of the parameters.
- (2) The presence of backward bifurcation does not arise under each of the following scenarios:
 - (i) sufficiently large fraction (at least 95%) but not necessarily all of recruited buffalo are vaccinated,
 - (ii) if the efficacy of the vaccine is high enough (at least 75%), although it need not be perfect.
- (3) The disease-free equilibrium is proved to be globally-asymptotically stable whenever all new recruits are vaccinated ($\theta = 1$) or the vaccine is 100% effective ($\alpha = 0$).
- (4) Numerical simulations of the model demonstrate that, the use of an imperfect vaccine can lead to effective control of the disease if the vaccination coverage and the efficacy of vaccine are high enough, at least 90% each.
- (5) Vaccination with BCG is a means of reducing levels of bovine TB, thereby, diminishing the spread and severity of the disease in African buffalo population. This follows from the model result in the parameter regime of the coexistence region (Figure 3), that for effective disease eradication a high vaccination coverage or vaccine efficacy is required. But in the field high coverage is very challenging and efficacy of the BCG vaccine may wane with prior exposure to mycobacteria [3]. This conclusion is in line with the finding in [7] that eradication of BTB via vaccination alone may not be an effective control strategy .

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Table 1: Description of variables and parameters of the models (1).

Variable	Interpretation	
S_1	First time susceptible buffalo	
I_1	First time infectious buffalo	
S_2	Subsequent times susceptible buffalo	
I_2	Subsequent times infectious buffalo	
Parameter	Interpretation	Unit
Λ	Recruitment rate	year ⁻¹
θ	Fraction of newly-recruited buffalo vaccinated	year ⁻¹
μ	Natural death rate	year ⁻¹
σ_1, σ_2	Effective contact rates	year ⁻¹
γ_1, γ_2	Recovery rates	year ⁻¹
τ_1, τ_2	disease induced death rates	
$\alpha = 1 - \phi$	relative vaccine efficacy	

Table 2: Parameter Values

Parameter	nominal value	references
Λ	1000	[4]
θ	[0,1]	[7]
μ	0.000648	assumed
σ_1	0.053	[7]
σ_2	0.034	[7]
γ_1	0.1	assumed
γ_2	0.01	assumed
τ_1, τ_2	0.1	assumed
α	0.5	assumed