

Research Article

Mathematical Analysis of a General Two-Patch Model of Tuberculosis Disease with Lost Sight Individuals

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A two-patch model, $SE_{i1}, \dots, E_{in}I_iL_i$, $i = 1, 2$, is used to analyze the spread of tuberculosis, with an arbitrary number n of latently infected compartments in each patch. A fraction of infectious individuals that begun their treatment will not return to the hospital for the examination of sputum. This fact usually occurs in sub-Saharan Africa, due to many reasons. The model incorporates migrations from one patch to another. The existence and uniqueness of the associated equilibria are discussed. A Lyapunov function is used to show that when the basic reproduction ratio is less than one, the disease-free equilibrium is globally and asymptotically stable. When it is greater than one, there exists at least one endemic equilibrium. The local stability of endemic equilibria can be illustrated using numerical simulations. Numerical simulation results are provided to illustrate the theoretical results and analyze the influence of lost sight individuals.

1. Introduction

For a given system, the focus in qualitative mathematical epidemiology is the long-term dynamics. The simplest possible attractor is a globally and asymptotically stable equilibrium. Equilibrium can be shown to be globally and asymptotically stable, using Poincaré-Bendixson theory [1], Bendixson's negative criterion [2, 3], or the generalized version of Dulac [4]. Another method of Li and Muldowney [5–7] for demonstrating global stability in n dimensions has been developed more recently, with applications in three [8, 9] and four dimensions [10, 11]. For higher-dimensional systems, the theory of quadratic forms [12] or Lyapunov's method can be used [13, 14]. Lyapunov's method requires finding a function V such that the flow always crosses the level sets from higher values of V to lower values. When such

a function can be found, then any isolated minimum of the function is a stable equilibrium of the flow. In this paper, the stability of a $2n + 6$ -dimensions system is investigated using Lyapunov-LaSalle functions and quadratic forms. The function $V = \sum_{i=1}^n a_i(x_i - x_i^* \ln x_i)$ has a long story in epidemiology [15–20]. Volterra himself originally discovered this function, although he did not use the vocabulary and the theory of Lyapunov functions. Since epidemic models are Lotka-Volterra-like models, the pertinence of this function is not surprising.

The issue of modeling tuberculosis motivates the model studied in this paper. It is an extension with two patches and n latent classes of the SEIL model in [21], where L denotes the lost sight individuals. These lost sight individuals usually occur in sub-Saharan Africa. For example,

according to the Cameroonian National Program of Fight against Tuberculosis, about 10% of infectious individuals that begun their therapy treatment lost sight. Therefore, this fact cannot be neglected in the modeling of TB. By allowing for an arbitrary number of latently infected compartments, the model allows for the approximation of a wide class of distributions of latency durations. This is of particular importance for tuberculosis since latency may last for years or even decades.

In the model given here, there are migrations between people of two patches, who have the same epidemiological characteristics. We introduce a direct transfer from the class of susceptible individuals toward the compartment of infectious individuals in each patch. The reason is that there are some individuals with bad immune effector protection, due to many reasons. We also incorporate a transfer from the infectious class to the exposed class to take into account the fact that some infectious individuals apparently recover but actually harbor TB bacteria. Let us give now the outlines of the paper. In Section 2, the model is constructed; the variables and parameters of the model are explained. In Section 3, the mathematical properties of the model are given. We present the computation thresholds as basic reproduction numbers, which are bifurcation parameters R_0^i , using the same method as in [22]. The equilibria of the model are computed: equilibrium without disease, endemic equilibria, or coexistence equilibria. The stability of each equilibrium is investigated, using the bifurcation parameters R_0^i . In Section 4, numerical simulations are done to illustrate the results. In Section 5, we give the conclusion.

2. Model Construction

The model consisted of two patches. Each patch denotes a given population and the two populations are very much closed. Based on epidemiological status, the population of a given patch i ($i = 1, 2$) is divided into $n+3$ classes: susceptible (S_i), latently infected (E_i), infectious (I_i), and lost sight (L_i). All recruitments in a given patch i are into the susceptible class and occur at a constant rate Λ_i . The rate constant for nondisease related death is μ_i ; thus $1/\mu_i$ is the average lifetime. Infectious and lost sight classes of a patch i have addition death rates due to the disease with rates constants d_i and l_i , respectively. Since we do not know if lost sight class is recovered, died, or is still infectious, we assume that a fraction δ_i of them is still infectious and can transmit disease to susceptible class. Transmission of *Mycobacterium tuberculosis* occurs following adequate contacts between susceptible and infectious or lost sight classes that continue to have disease. We assume that infected individuals are not infectious and thus are not capable of transmitting bacteria. We use the universal incidence expressions $\beta_i S_i I_i / N_i$ and $\beta_i \delta_i S_i L_i / N_i$ to indicate successful transmission of *M. tuberculosis* due to nonlinear contacts dynamics in the population by infectious and lost sight classes, respectively. A fraction p_i of the newly infected individuals is assumed to undergo fast progression directly to the infectious class, while the remainder are latently infected and enter the latent class. Once latently

infected with *M. tuberculosis*, an individual will remain so for life unless reactivation occurs. To account for treatment, we define $r_{ij} E_i$, with $i = 1, 2$ and $j = 1, \dots, n$, as the fraction of infected individuals receiving effective chemoprophylaxis, and γ_i as the rate of effective per capita therapy. We assume that chemoprophylaxis of latently infected individuals E_{ij} reduces their reactivation at rate r_{ij} . Thus, a fraction $(1 - r_{ij}) E_i$ of infected individuals who do not receive effective chemoprophylaxis becomes infectious with a rate constant k_i , so that $1/k_i$ represents the average latent period. Thus, individuals leave the class E_{ij} to I_i at rate $k_i(1 - r_{ij})$. After receiving an effective therapy, infectious individuals can spontaneously recover from the disease with a rate constant γ_i , entering the infected class E_{in} . A fraction $s_i(1 - r_{ij}) I_i$ of infectious individuals that began their treatment will not return to the hospital for the examination of sputum. After some time, some of them will return to the hospital with the disease at a constant rate α_i . This can be the situation in many African countries or refugees camps in Africa or elsewhere.

The transfer diagram of the model is given by Figure 1.

This yields the following set of differential equations:

$$\begin{aligned} \frac{dS_1}{dt} &= \Lambda_1 - (\mu_1 + a_1) S_1 \\ &\quad - \beta_1 \frac{(I_1 + \delta_1 L_1) S_1}{N_1} + a_2 S_2, \\ \frac{dE_{11}}{dt} &= \beta_1 (1 - p_1) \frac{(I_1 + \delta_1 L_1) S_1}{N_1} \\ &\quad + b_{21} E_{21} - (\mu_1 + b_{11} + (1 - r_{11}) k_{11}) E_{11}, \\ \frac{dE_{12}}{dt} &= (1 - r_{11}) k_{11} E_{11} + b_{22} E_{22} \\ &\quad - (\mu_1 + b_{12} + (1 - r_{12}) k_{12}) E_{12}, \\ &\quad \vdots \\ \frac{dE_{1n}}{dt} &= (1 - r_{1,n-1}) k_{1,n-1} E_{1,n-1} + \gamma_1 I_1 \\ &\quad + b_{2n} E_{2n} - (\mu_1 + b_{1n} + (1 - r_{1n}) k_{1n}) E_{1n}, \\ \frac{dI_1}{dt} &= \beta_1 p_1 \frac{(I_1 + \delta_1 L_1) S_1}{N_1} + (1 - r_{1n}) k_{1n} E_{1n} \\ &\quad + \alpha_1 L_1 + c_2 I_2 - (\mu_1 + d_1 + \gamma_1 + (1 - v_1) s_1 + c_1) I_1, \\ \frac{dL_1}{dt} &= (1 - v_1) s_1 I_1 + f_2 L_2 \\ &\quad - (\mu_1 + l_1 + \alpha_1 + f_1) L_1, \\ \frac{dS_2}{dt} &= \Lambda_2 - (\mu_2 + a_2) S_2 \\ &\quad - \beta_2 \frac{(I_2 + \delta_2 L_2) S_2}{N_2} + a_1 S_1, \end{aligned}$$

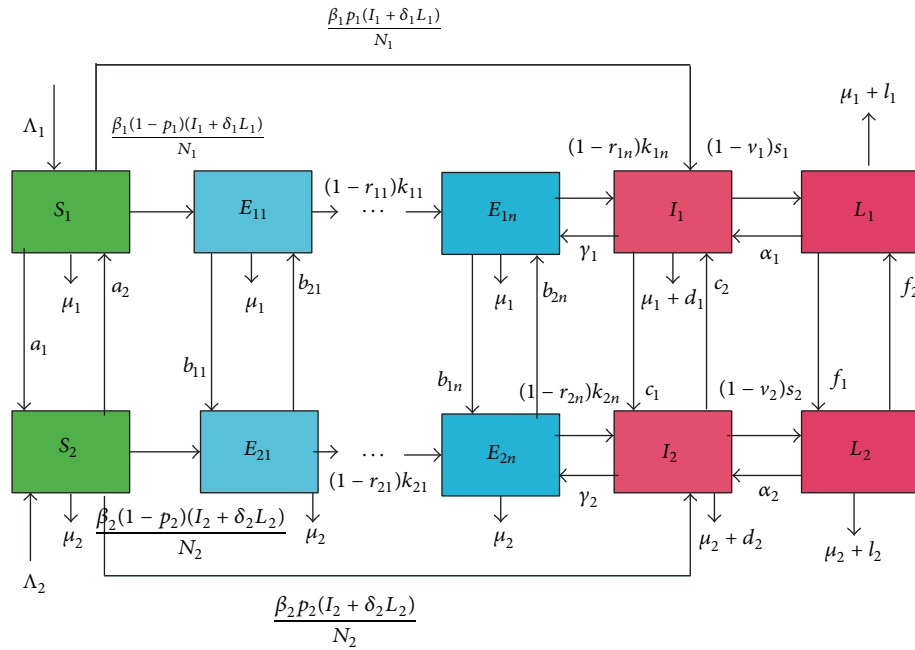


FIGURE 1: Flow chart of a two-patch model of tuberculosis with lost sight individuals in sub-Saharan Africa, with migrations at rate a_i between susceptible individuals of two populations, at rate b_{ij} between latently infected individuals of two populations, at rate c_i between infectious individuals in care centre, and at rate f_i for infectious lost sight individuals. An individual of a given population (patch) has contacts only with individuals of the same population.

$$\begin{aligned} \frac{dE_{21}}{dt} &= \beta_2(1-p_2) \frac{(I_2 + \delta_2 L_2) S_2}{N_2} \\ &\quad + b_{11} E_{11} - (\mu_2 + b_{21} + (1-r_{21})k_{21}) E_{21}, \\ \frac{dE_{22}}{dt} &= (1-r_{21})k_{21} E_{21} + b_{12} E_{12} \\ &\quad - (\mu_2 + b_{22} + (1-r_{22})k_{22}) E_{22}, \\ &\quad \vdots \\ \frac{dE_{2n}}{dt} &= (1-r_{2,n-1})k_{2,n-1} E_{2,n-1} \\ &\quad + \gamma_2 I_2 + b_{1n} E_{1n} \\ &\quad - (\mu_2 + b_{2n} + (1-r_{2n})k_{2n}) E_{2n}, \\ \frac{dI_2}{dt} &= \beta_2 p_2 \frac{(I_2 + \delta_2 L_2) S_2}{N_2} \\ &\quad + (1-r_{2n})k_{2n} E_{2n} + \alpha_2 L_2 + c_1 I_1 \\ &\quad - (\mu_2 + d_2 + \gamma_2 + (1-v_2)s_2 + c_2) I_2, \\ \frac{dL_2}{dt} &= (1-v_2)s_2 I_2 + f_1 L_1 - (\mu_2 + l_2 + \alpha_2 + f_2) L_2, \end{aligned}$$

(1)

where $N_1 = S_1 + E_{11} + \dots + E_{1n} + I_1 + L_1$ and $N_2 = S_2 + E_{21} + \dots + E_{2n} + I_2 + L_2$.

System (1) can also be written as

$$\begin{aligned} \frac{dx_1}{dt} &= \Lambda_1 - (\mu_1 + a_1) x_1 - \beta_1 \frac{x_1}{N_1} \left\langle e_{n+1}^{n+2} + \frac{\delta_1 e_{n+2}^{n+2}}{Y_1} \right\rangle, \\ \frac{dx_2}{dt} &= \Lambda_2 - (\mu_2 + a_2) x_2 - \beta_2 \frac{x_2}{N_2} \left\langle e_{n+1}^{n+2} + \frac{\delta_2 e_{n+2}^{n+2}}{Y_2} \right\rangle, \\ \frac{dY_1}{dt} &= \beta_1 \frac{x_1}{N_1} \left\langle e_{n+1}^{n+2} + \frac{e_{n+2}^{n+2}}{Y_1} \right\rangle Q_1 + A_{11} Y_1 + A_{12} Y_2, \\ \frac{dY_2}{dt} &= \beta_2 \frac{x_2}{N_2} \left\langle e_{n+1}^{n+2} + \frac{e_{n+2}^{n+2}}{Y_1} \right\rangle Q_2 + A_{21} Y_1 + A_{22} Y_2, \end{aligned} \tag{2}$$

where $\langle \cdot / \cdot \rangle$ is the scalar usual product in IR_+^{n+2} , $Q_1 = ((1-p_1), 0, \dots, 0, p_1)^T$, $Q_2 = ((1-p_2), 0, \dots, 0, p_2)^T$, $x = (x_1, x_2)^T$, $Y_1 = (E_{11}, \dots, E_{1n}, I_1, L_1)^T = (y_{11}, \dots, y_{1n}, y_{1,n+1}, y_{1,n+2})^T$, $Y_2 = (E_{21}, \dots, E_{2n}, I_2, L_2)^T = (y_{21}, \dots, y_{2n}, y_{2,n+1}, y_{2,n+2})^T$, (e_i^{n+2}) is the canonical basis of IR_+^{n+2} , the matrices A_{11} and A_{22} are Metzler stable [23], and A_{12} and A_{21} are Metzler stable and given, respectively, by

$$\begin{aligned}
 A_{11} &= \begin{pmatrix} -m_{11} & 0 & \cdots & 0 & 0 & 0 & 0 \\ (1-r_{11})k_{11} & -m_{12} & 0 & \cdots & 0 & 0 & 0 \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ 0 & \cdots & 0 & (1-r_{1,n-1})k_{1,n-1} & -m_{1n} & \gamma_1 & 0 \\ 0 & 0 & \cdots & 0 & (1-r_{1,n})k_{1,n} & -m_{L_1} & \alpha_1 \\ 0 & 0 & 0 & \cdots & 0 & (1-v_1)s_1 & -m_{L_1} \end{pmatrix}, \\
 A_{22} &= \begin{pmatrix} -m_{21} & 0 & \cdots & 0 & 0 & 0 & 0 \\ (1-r_{21})k_{21} & -m_{22} & 0 & \cdots & 0 & 0 & 0 \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ 0 & \cdots & 0 & (1-r_{2,n-1})k_{2,n-1} & -m_{2n} & \gamma_2 & 0 \\ 0 & 0 & \cdots & 0 & (1-r_{2,n})k_{2,n} & -m_{L_2} & \alpha_2 \\ 0 & 0 & 0 & \cdots & 0 & (1-v_2)s_2 & -m_{L_2} \end{pmatrix}, \\
 A_{12} &= \begin{pmatrix} b_{21} & 0 & 0 & \cdots & 0 & 0 \\ 0 & b_{22} & 0 & \cdots & 0 & 0 \\ 0 & \cdots & 0 & b_{2n} & 0 & 0 \\ 0 & \cdots & 0 & 0 & c_2 & 0 \\ 0 & \cdots & 0 & 0 & 0 & f_2 \end{pmatrix}, \\
 A_{21} &= \begin{pmatrix} b_{11} & 0 & 0 & \cdots & 0 & 0 \\ 0 & b_{12} & 0 & \cdots & 0 & 0 \\ 0 & \cdots & 0 & b_{1n} & 0 & 0 \\ 0 & \cdots & 0 & 0 & c_1 & 0 \\ 0 & \cdots & 0 & 0 & 0 & f_1 \end{pmatrix},
 \end{aligned} \tag{3}$$

where $m_{i1} = (\mu_i + b_{i1} + (1-r_{i1})k_{i1})$, $m_{in} = (\mu_i + b_{in} + (1-r_{in})k_{in})$, $m_{L_i} = (\mu_i + d_i + \gamma_i + (1-v_i)s_i + c_i)$, and $m_{L_i} = (\mu_i + l_i + \alpha_i + f_i)$, $i = 1, 2$.

Let us give another expression of system (1). System (2) can be written as

$$\begin{aligned}
 \frac{dx(t)}{dt} &= \Lambda + D_x x - \sum_{i=1}^2 \left\langle \frac{B_i}{y(t)} \right\rangle \frac{\langle e_i^2/x(t) \rangle}{N_i} e_i^2, \\
 \frac{dy(t)}{dt} &= \sum_{i=1}^2 \left\langle \frac{B_i}{y(t)} \right\rangle \frac{\langle e_i^2/x(t) \rangle}{N_i} K_i + A_y y,
 \end{aligned} \tag{4}$$

where $\langle \cdot / \cdot \rangle$ is now the usual scalar product in IR^{2n+4} , $x = (x_1, x_2)^T$, $e_1^2 = (1, 0)^T$, $e_2^2 = (0, 1)^T$, $\Lambda = (\Lambda_1, \Lambda_2)^T$, $y = (E_{11}, \dots, E_{1n}, I_1, L_1, E_{21}, \dots, E_{2n}, I_2, L_2)^T$, $D_x = \begin{pmatrix} -(\mu_1+a_1) & a_2 \\ a_1 & -(\mu_2+a_2) \end{pmatrix}$, $B_1 = \left(\underbrace{0, \dots, 0}_{n+2}, \underbrace{0, \dots, 0}_n, \beta_1, \beta_1 \delta_1, \underbrace{0, \dots, 0}_{n+2} \right)^T$, $B_2 = \left(\underbrace{0, \dots, 0}_{n+2}, \underbrace{0, \dots, 0}_n, \beta_2, \beta_2 \delta_2 \right)^T$, $K_1 = (1 - p_1, \underbrace{0, \dots, 0}_{n-1}, p_1, 0, \underbrace{0, \dots, 0}_{n+2})^T$, $K_2 = \left(\underbrace{0, \dots, 0}_{n+2}, 1 - p_2, \underbrace{0, \dots, 0}_{n-1}, p_2, 0 \right)^T$, and $A_y = \begin{pmatrix} A_{11} & A_{12} \\ A_{21} & A_{22} \end{pmatrix}$.

3. Mathematical Properties

3.1. Positivity of the Solutions. Since the variables considered here are nonnegative quantities, we have to be sure that their values are always nonnegative.

Theorem 1. *The nonnegative orthant IR_+^{2n+6} is positively invariant by (1). This means that every trajectory, which begins in the positive orthant, will stay inside.*

Proof. System (4) can be written in the following form:

$$\begin{aligned}
 \frac{dx(t)}{dt} &= \Lambda + D_x x - \sum_{i=1}^2 \left\langle \frac{B_i}{y(t)} \right\rangle \frac{\langle e_i^2/x(t) \rangle}{N_i} e_i^2, \\
 \frac{dy(t)}{dt} &= \left(\sum_{i=1}^2 B_i^T \frac{\langle e_i^2/x(t) \rangle}{N_i} K_i + A_y \right) y(t).
 \end{aligned} \tag{5}$$

Since $x(t) \geq 0$ and $N_i(t) \geq 0$, the matrix $(\sum_{i=1}^2 B_i^T (\langle e_i^2/x(t) \rangle / N_i) K_i + A_y)$ is Metzler. It is well known that linear Metzler system lets the nonnegative orthant invariant [23]. Moreover $dx(t)/dt \leq \Lambda + D_x x$ and D_x is a Metzler matrix. These prove the positive invariance of the nonnegative orthant IR_+^{2n+6} by (1). \square

3.2. Boundedness of the Trajectories

Lemma 2. *The simplex $\{(S_1, E_{11}, \dots, E_{1n}, I_1, L_1, S_2, E_{21}, \dots, E_{2n}, I_2, L_2) \in IR_+^{2n+6} / S_1 + E_{11} + \dots + E_{1n} + I_1 + L_1 + S_2 + E_{21} + \dots + E_{2n} + I_2 + L_2 \leq ((\Lambda_1 + \Lambda_2) / \mu) + \varepsilon\}$, is a compact forward and absorbing set for (1).*

Proof. From system (1), if $N(t) = N_1(t) + N_2(t)$ denotes the entire population of (1), one has $N(t) = S_1 + E_{11} + \dots + E_{1n} + I_1 + L_1 + S_2 + E_{21} + \dots + E_{2n} + I_2 + L_2$.

Then, the dynamics of $N(t)$ at any time t is given by

$$\frac{dN(t)}{dt} = \Lambda_1 + \Lambda_2 - \mu_1 N_1(t) - \mu_2 N_2(t) - d_1 I_1 - l_1 L_1 - d_2 I_2 - l_2 L_2. \tag{6}$$

Thus, $dN(t)/dt \leq \Lambda_1 + \Lambda_2 - \mu N(t)$, where $\mu = \min(\mu_1, \mu_2)$. It follows that $\limsup_{t \rightarrow +\infty} N(t) = (\Lambda_1 + \Lambda_2)/\mu$. \square

In the simplex Γ_e , (1) is mathematically well posed. The following lemma also holds.

Lemma 3. *The simplex $\gamma_e = \{(x, y) \in \Gamma_e / x \leq x^*\}$ is a compact forward invariant set for (1).*

3.3. Local Stability of the Disease-Free Equilibrium. Many epidemiological models have a threshold condition which can determine whether an infection will be eliminated from the population or become endemic. The basic reproduction number, R_0 , is defined as the average number of secondary infections produced by an infected individual in a completely susceptible population [16]. As discussed in [24, 25], R_0 is a simply normalized bifurcation (transcritical) parameter for epidemiological models, such that $R_0 > 1$ implies that the endemic steady state is stable (i.e., the infection persists), and $R_0 < 1$ implies that the uninfected steady state is stable (i.e., the infection can be eliminated from the population).

Equation (1) has a disease-free equilibrium given by $K_2 = (S_1^*, \underbrace{0, \dots, 0}_{n+2}, S_2^*, \underbrace{0, \dots, 0}_{n+2})^T$ which always exists in the nonnegative orthant IR_+^{2n+6} . The explicit expressions of S_1^* and S_2^* are

$$S_1^* = \frac{(\mu_2 + a_2)\Lambda_1 + a_2\Lambda_2}{\mu_1\mu_2 + \mu_1a_2 + \mu_2a_1}, \quad S_2^* = \frac{(\mu_1 + a_1)\Lambda_2 + a_1\Lambda_1}{\mu_1\mu_2 + \mu_1a_2 + \mu_2a_1}. \tag{7}$$

The disease-free equilibrium can also be denoted by $(x^*, 0)$ since it is the solution of equation $\Lambda + D_x x^* = 0$ of the compact system (5).

Lemma 4. *Using the same method as in [17], the basic reproduction ratio of (1) is $R_0 = \rho(K_1 B_1^T (-A_y)^{-1} + K_2 B_2^T (-A_y)^{-1})$, where ρ denotes the spectral radius.*

Proof. The expressions, which are coming from the other compartment, due to contamination, are given by the following matrix:

$$F = \frac{\partial}{\partial y} \left(\sum_{i=1}^2 \left\langle \frac{B_i}{y(t)} \right\rangle \frac{\langle e_i^2 / x(t) \rangle}{N_i} K_i \right)_{(x^*, 0)} \tag{8}$$

$$= \sum_{i=1}^2 \frac{\langle e_i^2 / x^* \rangle}{N_i^*} K_i B_i^T.$$

The expressions, which are coming from the other compartment, due to reasons different from contamination, are given

by $V = -A_y$. The next generation matrix, since $\langle e_i^2 / x^* \rangle = N_i^*$, is

$$FV^{-1} = \left(\sum_{i=1}^2 \frac{\langle e_i^2 / x^* \rangle}{N_i^*} K_i B_i^T \right) (-A_y)^{-1} \tag{9}$$

$$= \left(\sum_{i=1}^2 K_i B_i^T \right) (-A_y)^{-1}.$$

We can observe that, since R_0 is the largest eigenvalue of the next generation matrix,

$$R_0 = \rho(FV^{-1}) = \rho(K_1 B_1^T (-A_y)^{-1} + K_2 B_2^T (-A_y)^{-1}), \tag{10}$$

where ρ denotes the spectral radius. \square

Consequently, from Theorem 2 of [22], the following lemma holds.

Lemma 5. *The disease-free equilibrium of (1) is locally and asymptotically stable whenever $R_0 \leq 1$ and unstable if $R_0 > 1$.*

Remark 6. This lemma shows that if $R_0 \leq 1$, a small flow of infectious individuals will not generate large outbreaks of the disease. To control the disease independently of the initial total number of infectious individuals, a global asymptotic stability property has to be established for the DFE when $R_0 \leq 1$.

3.4. Global Stability of the Disease-Free Equilibrium. The following result helps to determine the stability and is related to LaSalle's principle [13]. Consider the differential equation

$$\frac{dx(t)}{dt} = X(x(t)), \tag{11}$$

$$X(x_0) = 0,$$

where X is a C^1 function defined on an open set of IR^n containing the closure $\bar{\Omega}$ of a positively invariant set Ω such that the equilibrium x_0 is in $\bar{\Omega}$. The following lemma holds.

Lemma 7. *We assume that system (11) is point dissipative [1] on Ω . In other words there exists a compact set $K \subset \Omega$ such that, for any $y \in \Omega$, there exists a time $t(y_0) > 0$ such that, for any time $t > t(y_0)$, the trajectory with initial condition y_0 is in the interior of K . If there exists a C^1 function $V \geq 0$ defined on $\bar{\Omega}$, then*

- (1) $dV(t)/dt = \langle \delta V(x) / X(x) \rangle \leq 0$, for all $x \in \Omega$;
- (2) the greatest invariant set L contained in $E = \{x \in \bar{\Omega}, dV(t)/dt = 0\}$ is contained in a positively invariant set on which the restriction of system (11) is globally and asymptotically stable on L at x_0 .

Then, x_0 is a globally and asymptotically stable equilibrium of system (11) on Ω .

Theorem 8. When $R_0 \leq 1$ (this implies $R_0^1 \leq 1$ and $R_0^2 \leq 1$, where R_0^i is the basic reproduction number for the patch i), the disease-free equilibrium (DFE), when it is unique, is globally and asymptotically stable in Γ_ε , since it is the unique equilibrium. This implies the global asymptotic stability of the DFE on the nonnegative orthant IR_+^{2n+6} ; that is, the disease dies out in both two populations.

Remark 9. At least one endemic equilibrium can exist and coexist with the disease-free equilibrium when $R_0 \leq 1$. In this case the DFE cannot be globally asymptotically stable.

Proof. Following the same method as in [23], system (4) can be written in a pseudotriangular form as

$$\begin{aligned} \frac{dx(t)}{dt} &= A_1(x, y)(x - x^*) + A_{12}(x, y)y = f(x, y), \\ \frac{dy(t)}{dt} &= A_2(x, y)y = g(x, y), \end{aligned} \tag{12}$$

where $f(x^*, 0) = \Lambda + D_x x^* = 0$, $g(x^*, 0) = 0$, $A_1(x, y) = D_x \in IR^{2 \times 2}$, $A_{12}(x, y) = -\sum_{i=1}^2 (\langle e_i^2/x(t) \rangle / N_i) e_i^2 B_i^T \in IR^{2 \times (2n+4)}$, and $A_2(x, y) = \sum_{i=1}^2 (\langle e_i^2/x(t) \rangle / N_i) K_i B_i^T + A_y \in IR^{(2n+4) \times (2n+4)}$. The Jacobian matrix of system (4) at disease-free equilibrium $(x^*, 0)$ is $A_2(x, y) = \sum_{i=1}^2 (\langle e_i^2/x(t) \rangle / N_i) K_i B_i^T + A_y \in IR^{(2n+4) \times (2n+4)}$. The Jacobian matrix of system (4) at disease-free equilibrium $(x^*, 0)$ is $J = \begin{pmatrix} A_1(x^*, 0) & A_{12}(x^*, 0) \\ 0 & A_2(x^*, 0) \end{pmatrix} = \begin{pmatrix} D_x & -\sum_{i=1}^2 e_i^2 B_i^T \\ 0 & \sum_{i=1}^2 K_i B_i^T + A_y \end{pmatrix}$. The matrix D_x is clearly a Metzler stable matrix and, using a result in [8], there exists a vector $u = (u_1, u_2) > 0$ such that $D_x u \leq 0$. The matrix $\bar{A}_2 = \sum_{i=1}^2 K_i B_i^T + A_y$ is a Metzler and irreducible matrix, which is stable if $R_0 \leq 1$. With this condition satisfied and using the same previous result in [22], the stability modulus $\alpha(\bar{A}_2)$ of the matrix is in the spectrum of \bar{A}_2 (Perron-Frobenius theorem, proof of Lemma 2) and there exists a vector $c > 0 \in IR^{2n+4}$ such that $c^T \bar{A}_2 = \alpha(\bar{A}_2) c^T$, with $\alpha(\bar{A}_2) \leq 0$. Let us show the global stability of the DFE.

System (12) is in pseudotriangular form since the matrix $A_2(x, y)$ depends on (x, y) . There are many results for the stability of triangular systems [21–25]. Using LaSalle’s principle [13] one can obtain attractivity of equilibrium. But, for nonlinear systems, attractivity does not generally implies stability. We can use now the result of Lemma 7. Let us consider the following candidate Lyapunov function:

$$V_{DFE}(x(t), y(t)) = \left\langle \frac{(0, c)}{(x(t), y(t))^T} \right\rangle. \tag{13}$$

The function $V_{DFE}(x(t), y(t))$ is positive and it is time derivative along the trajectories of (4) which gives

$$\begin{aligned} \frac{dV(x(t), y(t))}{dt} &= \left(\sum_{i=1}^2 \left\langle \frac{B_i}{y(t)} \right\rangle \frac{\langle e_i^2/x(t) \rangle}{N_i} K_i + A_y y \right) c \\ &\leq c^T \left(\sum_{i=1}^2 K_i B_i^T + A_y \right) y \\ &\leq c^T \alpha(\bar{A}_2) y. \end{aligned} \tag{14}$$

Then, $R_0 \leq 1$ ensures that $dV_{DFE}(x(t), y(t))/dt \leq 0$ for all $y \geq 0$ and that $dV_{DFE}(x(t), y(t))/dt = 0$ holds when $(x(t), y(t)) = (x^*, 0)$. This proves the global asymptotic stability on IR_+^{2n+6} [14]. This achieves the proof that the DFE is globally and asymptotically stable. \square

3.5. Existence of Endemic Equilibrium

Definition 10. An equilibrium for a multipatch model as (1) is called endemic equilibrium when the two populations coexist (the density of each compartment is different from zero) at this equilibrium.

Lemma 11. An endemic equilibrium (\bar{x}, \bar{y}) of (1) can be determined, using an equation $F(\bar{x}) = 1$.

Proof. An endemic equilibrium (\bar{x}, \bar{y}) of (1) is obtained by setting the right-hand side of (4) which equals zero, giving

$$\begin{aligned} \Lambda + D_x \bar{x} &= \sum_{i=1}^2 \left\langle \frac{B_i}{\bar{y}(t)} \right\rangle \frac{\langle e_i^2/\bar{x}(t) \rangle}{N_i} e_i^2, \\ \sum_{i=1}^2 \left\langle \frac{B_i}{\bar{y}(t)} \right\rangle \frac{\langle e_i^2/\bar{x}(t) \rangle}{N_i} K_i + A_y \bar{y} &= 0. \end{aligned} \tag{15}$$

Multiplying the second equation of (15) by $(-A_y)^{-1}$ gives

$$\begin{aligned} \bar{y} &= \left\langle \frac{B_1}{\bar{y}(t)} \right\rangle \frac{\langle e_1^2/\bar{x}(t) \rangle}{N_1} (-A_y)^{-1} K_1 \\ &+ \left\langle \frac{B_2}{\bar{y}(t)} \right\rangle \frac{\langle e_2^2/\bar{x}(t) \rangle}{N_2} (-A_y)^{-1} K_2. \end{aligned} \tag{16}$$

From (16),

$$\begin{aligned} \left\langle \frac{B_1}{\bar{y}} \right\rangle &= g_{11} \left\langle \frac{B_1}{\bar{y}} \right\rangle \frac{\langle e_1^2/\bar{x}(t) \rangle}{N_1} + g_{12} \left\langle \frac{B_2}{\bar{y}} \right\rangle \frac{\langle e_2^2/\bar{x}(t) \rangle}{N_2}, \\ \left\langle \frac{B_2}{\bar{y}} \right\rangle &= g_{21} \left\langle \frac{B_1}{\bar{y}} \right\rangle \frac{\langle e_1^2/\bar{x}(t) \rangle}{N_1} + g_{22} \left\langle \frac{B_2}{\bar{y}} \right\rangle \frac{\langle e_2^2/\bar{x}(t) \rangle}{N_2}, \end{aligned} \tag{17}$$

where

$$\begin{aligned}
 g_{11} &= \left\langle \frac{B_1}{(-A_y)^{-1}K_1} \right\rangle, & g_{12} &= \left\langle \frac{B_1}{(-A_y)^{-1}K_2} \right\rangle, \\
 g_{21} &= \left\langle \frac{B_2}{(-A_y)^{-1}K_1} \right\rangle, & g_{22} &= \left\langle \frac{B_2}{(-A_y)^{-1}K_2} \right\rangle.
 \end{aligned}
 \tag{18}$$

From the second equation of (17),

$$\left\langle \frac{B_2}{\bar{y}} \right\rangle = \frac{g_{21} \left(\langle e_1^2/\bar{x}(t) \rangle / \bar{N}_1 \right)}{1 - g_{22} \left(\langle e_2^2/\bar{x}(t) \rangle / \bar{N}_2 \right)} \left\langle \frac{B_1}{\bar{y}} \right\rangle.
 \tag{19}$$

Using the expression of $\langle B_2/\bar{y} \rangle$ in (16) gives

$$\begin{aligned}
 \bar{y} &= \left\langle \frac{B_1}{\bar{y}} \right\rangle \frac{\langle e_1^2/\bar{x}(t) \rangle}{\bar{N}_1} (-A_y)^{-1}K_1 \\
 &+ \frac{g_{21} \left(\langle e_1^2/\bar{x}(t) \rangle / \bar{N}_1 \right)}{1 - g_{22} \left(\langle e_2^2/\bar{x}(t) \rangle / \bar{N}_2 \right)} \left\langle \frac{B_1}{\bar{y}} \right\rangle \\
 &\times \frac{\langle e_2^2/\bar{x}(t) \rangle}{\bar{N}_2} (-A_y)^{-1}K_2.
 \end{aligned}
 \tag{20}$$

Then

$$\begin{aligned}
 \left\langle \frac{B_1}{\bar{y}} \right\rangle &= \left\langle \frac{B_1}{\bar{y}} \right\rangle \frac{\langle e_1^2/\bar{x}(t) \rangle}{\bar{N}_1} g_{11} \\
 &+ \frac{g_{21} \left(\langle e_1^2/\bar{x}(t) \rangle / \bar{N}_1 \right)}{1 - g_{22} \left(\langle e_2^2/\bar{x}(t) \rangle / \bar{N}_2 \right)} \left\langle \frac{B_1}{\bar{y}} \right\rangle \frac{\langle e_2^2/\bar{x}(t) \rangle}{\bar{N}_2} g_{12},
 \end{aligned}
 \tag{21}$$

where $g_{11} = \langle B_1/(-A_y)^{-1}K_1 \rangle$ and $g_{12} = \langle B_1/(-A_y)^{-1}K_2 \rangle$. \square

If $\langle B_1/\bar{y} \rangle = 0$, we obtain the disease-free equilibrium again. If not, the following equation holds:

$$\begin{aligned}
 1 &= \frac{\langle e_1^2/\bar{x}(t) \rangle}{\bar{N}_1} \\
 &\times \left[g_{11} + \frac{g_{21}g_{12}}{1 - g_{22} \left(\langle e_2^2/\bar{x}(t) \rangle / \bar{N}_2 \right)} \frac{\langle e_2^2/\bar{x}(t) \rangle}{\bar{N}_2} \right],
 \end{aligned}
 \tag{22}$$

which can also be written as

$$\left\langle \frac{e_2^2}{\bar{x}(t)} \right\rangle = \frac{\bar{N}_1\bar{N}_2 - g_{11}\bar{N}_2 \langle e_1^2/\bar{x}(t) \rangle}{g_{12}g_{21} \langle e_1^2/\bar{x}(t) \rangle + g_{22}\bar{N}_1 - g_{11}g_{22} \langle e_1^2/\bar{x}(t) \rangle}.
 \tag{23}$$

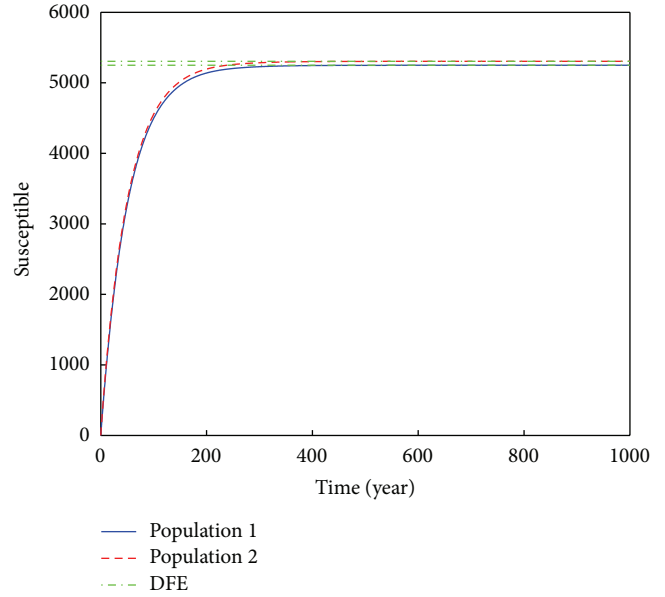


FIGURE 2: Trajectories of susceptible individuals of (1) for different initial conditions when $\beta_1 = 0.002$ and $\beta_2 = 0.003$ (such that $R_0^1 = 0.3691$ and $R_0^2 = 0.4980$). We can observe the global stability of DFE when $R_0 < 1$. All other parameters are as in Table 1.

This expression of $\langle e_2^2/\bar{x}(t) \rangle$ in (23) is positive when one of these conditions is satisfied:

$$\begin{aligned}
 \bar{N}_1 - g_{11} \left\langle \frac{e_1^2}{\bar{x}(t)} \right\rangle &> 0, \\
 \bar{N}_1 - g_{11} \left\langle \frac{e_1^2}{\bar{x}(t)} \right\rangle &< 0, \\
 g_{12}g_{21} \left\langle \frac{e_1^2}{\bar{x}(t)} \right\rangle + g_{22}\bar{N}_1 &< g_{11}g_{22} \left\langle \frac{e_1^2}{\bar{x}(t)} \right\rangle.
 \end{aligned}
 \tag{24}$$

Case 1. $\bar{N}_1 - g_{11} \langle e_1^2/\bar{x}(t) \rangle > 0$. This yields the condition

$$\left\langle \frac{e_1^2}{\bar{x}(t)} \right\rangle < \frac{\bar{N}_1}{g_{11}}.
 \tag{25}$$

Case 2. $\bar{N}_1 - g_{11} \langle e_1^2/\bar{x}(t) \rangle < 0$ and $g_{12}g_{21} \langle e_1^2/\bar{x}(t) \rangle + g_{22}\bar{N}_1 < g_{11}g_{22} \langle e_1^2/\bar{x}(t) \rangle$. This yields the condition

$$\begin{aligned}
 \left\langle \frac{e_1^2}{\bar{x}(t)} \right\rangle &> \max \left(\frac{\bar{N}_1}{g_{11}}, \frac{g_{22}\bar{N}_1}{g_{11}g_{22} - g_{12}g_{21}} \right) \\
 &\text{since } g_{11}g_{22} - g_{12}g_{21} > 0.
 \end{aligned}
 \tag{26}$$

In sum, $\langle e_2^2/\bar{x}(t) \rangle$ exists when $\langle e_1^2/\bar{x}(t) \rangle$ satisfies condition (25) or condition (26). Now, using the first equation of system (15) gives

$$\Lambda + D_x\bar{x} = \sum_{i=1}^2 \left\langle \frac{B_i}{\bar{y}(t)} \right\rangle \frac{\langle e_i^2/\bar{x}(t) \rangle}{\bar{N}_i} e_i^2.
 \tag{27}$$

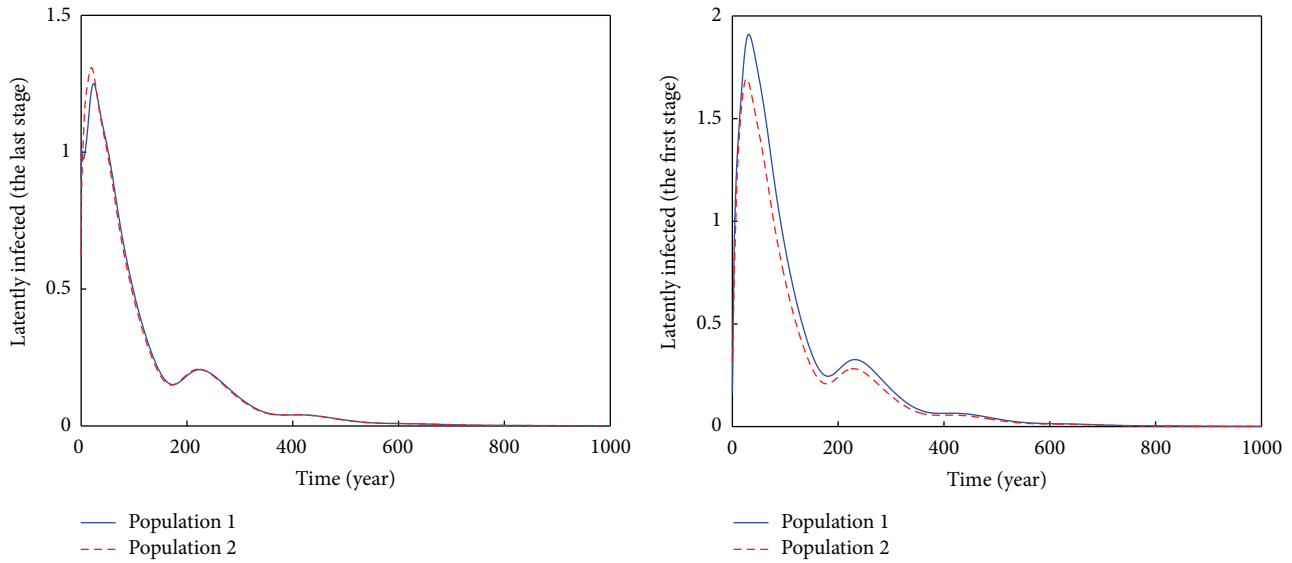


FIGURE 3: Trajectories of latently infected individuals of (1) for different initial conditions when $\beta_1 = 0.002$ and $\beta_2 = 0.003$ (such that $R_0^1 = 0.3691$ and $R_0^2 = 0.4980$). The latent classes disappear at the end and only susceptible classes persist when $R_0 < 1$. All other parameters are as in Table 1.

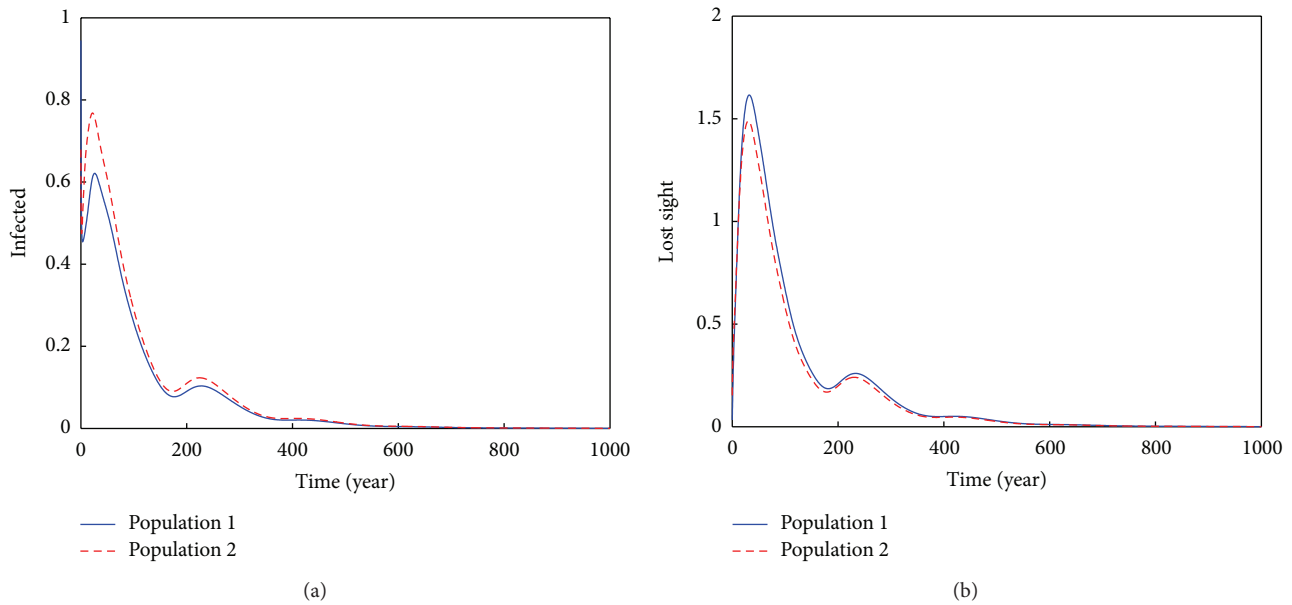


FIGURE 4: Trajectories of infectious individuals in care center (a) and lost sight individuals (b) of (1) for different initial conditions when $\beta_1 = 0.002$ and $\beta_2 = 0.003$ (such that $R_0^1 = 0.3691$ and $R_0^2 = 0.4980$). The infectious and lost sight classes disappear at the end and only susceptible classes persist when $R_0 < 1$. All other parameters are as in Table 1.

Then,

$$\frac{\langle B_1/\bar{y} \rangle}{\bar{N}_1} = \frac{\Lambda_1 - (\mu_1 + a_1)\bar{x}_1 + a_2\bar{x}_2}{\bar{x}_1} = \frac{\langle \Lambda + D_x\bar{x}/e_1^2 \rangle}{\langle e_1^2/\bar{x} \rangle},$$

$$\frac{\langle B_2/\bar{y} \rangle}{\bar{N}_2} = \frac{\Lambda_2 - (\mu_2 + a_2)\bar{x}_2 + a_1\bar{x}_1}{\bar{x}_2} = \frac{\langle \Lambda + D_x\bar{x}/e_2^2 \rangle}{\langle e_2^2/\bar{x} \rangle}. \tag{28}$$

Putting (28) into the first equation of (17) gives

$$\bar{N}_1 = \left\langle \frac{e_1^2}{\bar{x}(t)} \right\rangle \times \left[g_{11} \left\langle \Lambda + \frac{D_x\bar{x}}{e_1^2} \right\rangle + g_{12} \left\langle \Lambda + \frac{D_x\bar{x}}{e_2^2} \right\rangle \right] \times \left(\left\langle \Lambda + \frac{D_x\bar{x}}{e_1^2} \right\rangle \right)^{-1}. \tag{29}$$

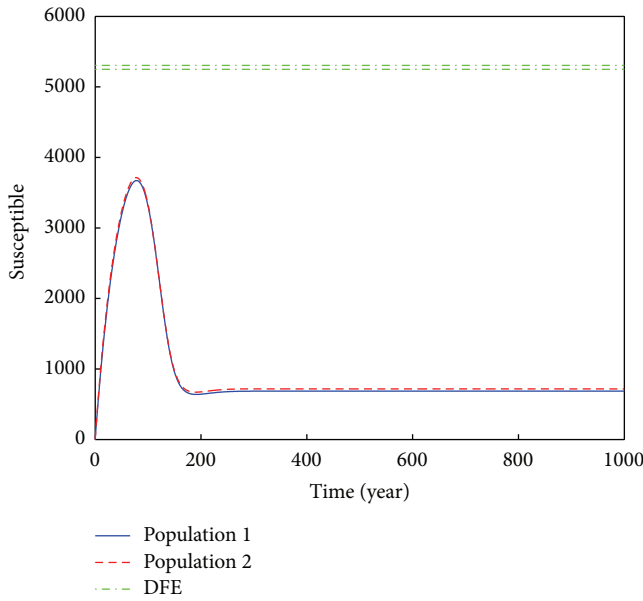


FIGURE 5: Trajectories of susceptible individuals of (1) for different initial conditions when $\beta_1 = 0.002$ and $\beta_2 = 0.003$ (such that $R_0^1 = 0.3691$ and $R_0^2 = 0.4980$). The DFE coexists with endemic equilibrium and is locally stable when $R_0 < 1$. All other parameters are as in Table 1.

Putting (28) into the second equation of (17) gives

$$\begin{aligned} \bar{N}_2 &= \left\langle \frac{e_2^2}{\bar{x}(t)} \right\rangle \\ &\times \left[g_{21} \left\langle \Lambda + \frac{D_x \bar{x}}{e_1^2} \right\rangle + g_{22} \left\langle \Lambda + \frac{D_x \bar{x}}{e_2^2} \right\rangle \right] \\ &\times \left(\left\langle \Lambda + \frac{D_x \bar{x}}{e_2^2} \right\rangle \right)^{-1}. \end{aligned} \tag{30}$$

Then, in the compact form,

$$\begin{aligned} \frac{\bar{N}_1}{\langle e_1^2/\bar{x}(t) \rangle} &= \frac{g_{11} \langle \Lambda + D_x \bar{x}/e_1^2 \rangle + g_{12} \langle \Lambda + D_x \bar{x}/e_2^2 \rangle}{\langle \Lambda + D_x \bar{x}/e_1^2 \rangle}, \\ \frac{\bar{N}_2}{\langle e_2^2/\bar{x}(t) \rangle} &= \frac{g_{21} \langle \Lambda + D_x \bar{x}/e_1^2 \rangle + g_{22} \langle \Lambda + D_x \bar{x}/e_2^2 \rangle}{\langle \Lambda + D_x \bar{x}/e_2^2 \rangle}. \end{aligned} \tag{31}$$

From (1),

$$\begin{aligned} \dot{N}_1 + \dot{N}_2 &= \Lambda_1 + \Lambda_2 - \mu_1 N_1 - \mu_2 N_2 - d_1 I_1 - l_1 L_1 - d_2 I_2 - l_2 L_2, \end{aligned} \tag{32}$$

which can be written in semicompact form as

$$\dot{N}_1 + \dot{N}_2 = \Lambda_1 + \Lambda_2 - \mu_1 N_1 - \mu_2 N_2 - \left\langle \frac{B_3}{y} \right\rangle - \left\langle \frac{B_4}{y} \right\rangle, \tag{33}$$

where $B_3 = (0, \dots, 0, d_1, l_1, 0, \dots, 0, 0, 0)^T$, $B_4 = (0, \dots, 0, 0, 0, \dots, 0, d_2, l_2)^T$, and $N = N_1 + N_2$.

At equilibrium,

$$\Lambda_1 + \Lambda_2 = \mu_1 \bar{N}_1 + \mu_2 \bar{N}_2 + \left\langle \frac{B_3}{y} \right\rangle + \left\langle \frac{B_4}{y} \right\rangle. \tag{34}$$

Using (16) in (34),

$$\begin{aligned} \Lambda_1 + \Lambda_2 &= \mu_1 \bar{N}_1 + \mu_2 \bar{N}_2 + \left\langle \frac{B_1}{y(t)} \right\rangle \frac{\langle e_1^2/\bar{x}(t) \rangle}{\bar{N}_1} h_{31} \\ &+ \left\langle \frac{B_2}{y(t)} \right\rangle \frac{\langle e_2^2/\bar{x}(t) \rangle}{\bar{N}_2} h_{32} \\ &+ \left\langle \frac{B_1}{y(t)} \right\rangle \frac{\langle e_1^2/\bar{x}(t) \rangle}{\bar{N}_1} h_{41} \\ &+ \left\langle \frac{B_2}{y(t)} \right\rangle \frac{\langle e_2^2/\bar{x}(t) \rangle}{\bar{N}_2} h_{42}, \end{aligned} \tag{35}$$

where $h_{31} = \langle B_3/(-A_y)^{-1}K_1 \rangle$, $h_{32} = \langle B_3/(-A_y)^{-1}K_2 \rangle$, $h_{41} = \langle B_4/(-A_y)^{-1}K_1 \rangle$, and $h_{42} = \langle B_4/(-A_y)^{-1}K_2 \rangle$. Using (28) in (35) gives

$$\begin{aligned} \Lambda_1 + \Lambda_2 &= \mu_1 \bar{N}_1 + \mu_2 \bar{N}_2 + \left\langle \Lambda + \frac{D_x \bar{x}}{e_1^2} \right\rangle h_{31} \\ &+ \left\langle \Lambda + \frac{D_x \bar{x}}{e_2^2} \right\rangle h_{32} \\ &+ \left\langle \Lambda + \frac{D_x \bar{x}}{e_1^2} \right\rangle h_{41} + \left\langle \Lambda + \frac{D_x \bar{x}}{e_2^2} \right\rangle h_{42}. \end{aligned} \tag{36}$$

Using (31) in (36) gives

$$\begin{aligned} 1 &= \frac{\mu_1}{\Lambda_1 + \Lambda_2} \left\langle \frac{e_1^2}{\bar{x}} \right\rangle \\ &\times \frac{g_{11} \langle \Lambda + D_x \bar{x}/e_1^2 \rangle + g_{12} \langle \Lambda + D_x \bar{x}/e_2^2 \rangle}{\langle \Lambda + D_x \bar{x}/e_1^2 \rangle} \\ &+ \frac{\mu_2}{\Lambda_1 + \Lambda_2} \left\langle \frac{e_2^2}{\bar{x}} \right\rangle \\ &\times \frac{g_{21} \langle \Lambda + D_x \bar{x}/e_1^2 \rangle + g_{22} \langle \Lambda + D_x \bar{x}/e_2^2 \rangle}{\langle \Lambda + D_x \bar{x}/e_2^2 \rangle} \\ &+ \frac{h_{31}}{\Lambda_1 + \Lambda_2} \left\langle \Lambda + \frac{D_x \bar{x}}{e_1^2} \right\rangle + \frac{h_{32}}{\Lambda_1 + \Lambda_2} \left\langle \Lambda + \frac{D_x \bar{x}}{e_2^2} \right\rangle \\ &+ \frac{h_{41}}{\Lambda_1 + \Lambda_2} \left\langle \Lambda + \frac{D_x \bar{x}}{e_1^2} \right\rangle + \frac{h_{42}}{\Lambda_1 + \Lambda_2} \left\langle \Lambda + \frac{D_x \bar{x}}{e_2^2} \right\rangle. \end{aligned} \tag{37}$$

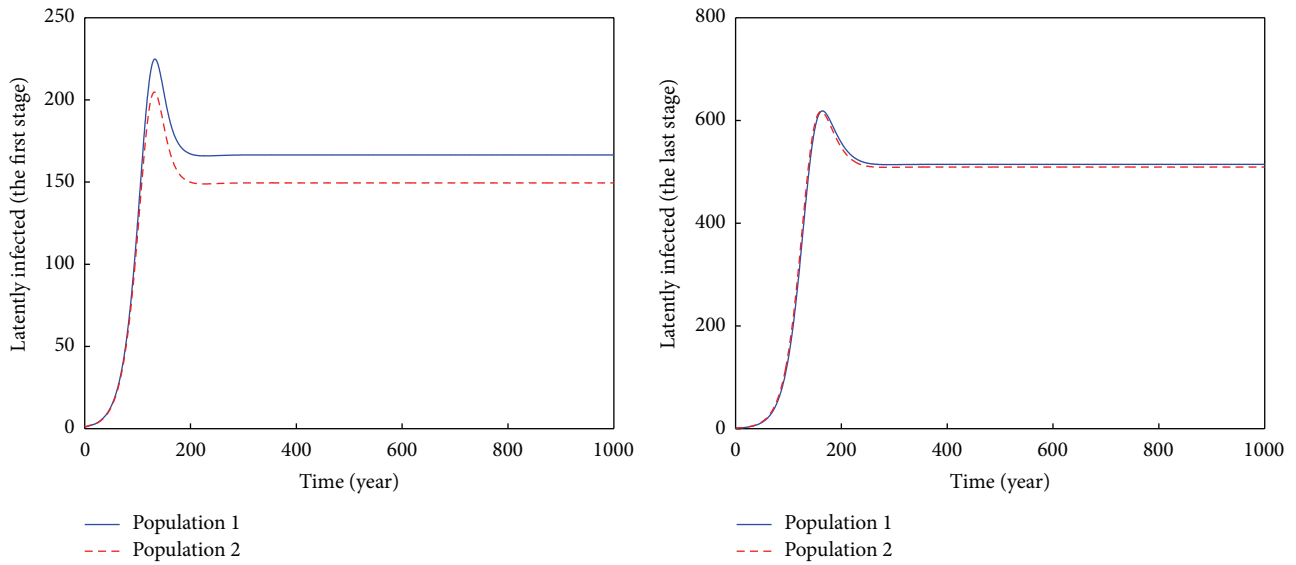


FIGURE 6: Trajectories of latently infected individuals of (1) for different initial conditions when $\beta_1 = 0.822$ and $\beta_2 = 0.943$ (such that $R_0^1 = 2.3601$ and $R_0^2 = 2.4910$). The endemic equilibrium is locally and asymptotically stable when $R_0 > 1$. All other parameters are as in Table 1.

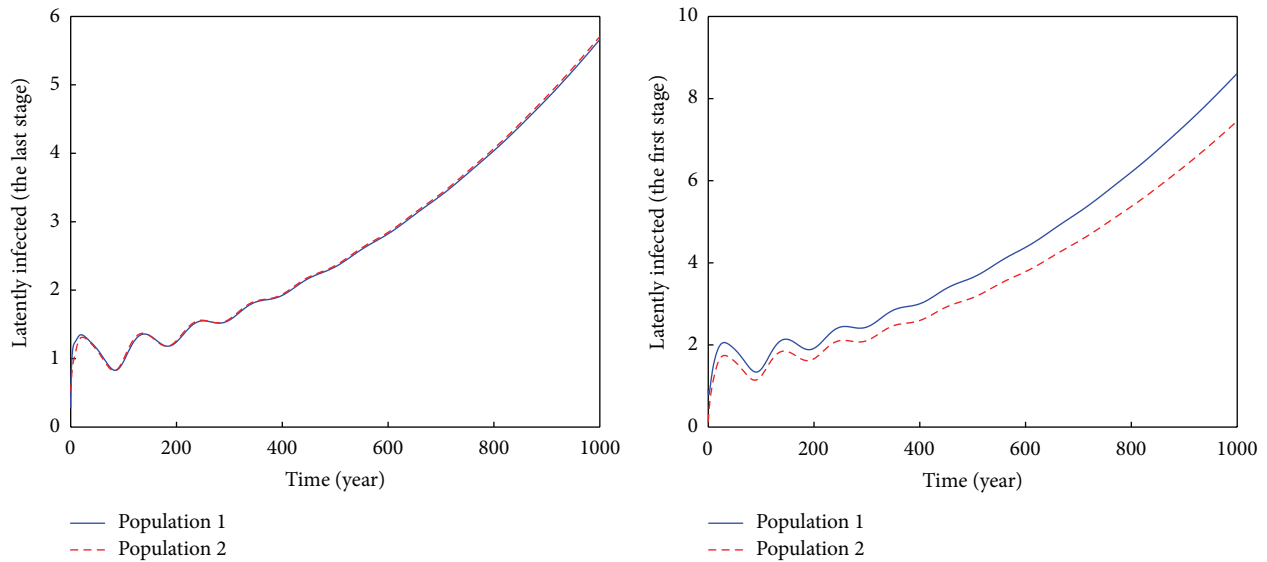


FIGURE 7: Trajectories of latently infected individuals of (1) for different initial conditions when $\beta_1 = 2.082$ and $\beta_2 = 2.173$ (such that $R_0^1 = 3.1492$ and $R_0^2 = 4.1085$). The endemic equilibrium is locally and asymptotically stable when $R_0 > 1$. In this case, the DFE is unstable. All other parameters are as in Table 1.

Let us set

$$\begin{aligned}
 F(\bar{x}) = & \frac{\mu_1}{\Lambda_1 + \Lambda_2} \left\langle \frac{e_1^2}{\bar{x}} \right\rangle \\
 & \times \frac{g_{11} \langle \Lambda + D_x \bar{x} / e_1^2 \rangle + g_{12} \langle \Lambda + D_x \bar{x} / e_2^2 \rangle}{\langle \Lambda + D_x \bar{x} / e_1^2 \rangle} \\
 & + \frac{\mu_2}{\Lambda_1 + \Lambda_2} \left\langle \frac{e_2^2}{\bar{x}} \right\rangle \\
 & \times \frac{g_{21} \langle \Lambda + D_x \bar{x} / e_1^2 \rangle + g_{22} \langle \Lambda + D_x \bar{x} / e_2^2 \rangle}{\langle \Lambda + D_x \bar{x} / e_2^2 \rangle}
 \end{aligned}$$

$$\begin{aligned}
 & + \frac{h_{31}}{\Lambda_1 + \Lambda_2} \left\langle \Lambda + \frac{D_x \bar{x}}{e_1^2} \right\rangle + \frac{h_{32}}{\Lambda_1 + \Lambda_2} \\
 & \times \left\langle \Lambda + \frac{D_x \bar{x}}{e_2^2} \right\rangle \\
 & + \frac{h_{41}}{\Lambda_1 + \Lambda_2} \left\langle \Lambda + \frac{D_x \bar{x}}{e_1^2} \right\rangle + \frac{h_{42}}{\Lambda_1 + \Lambda_2} \\
 & \times \left\langle \Lambda + \frac{D_x \bar{x}}{e_2^2} \right\rangle.
 \end{aligned}$$

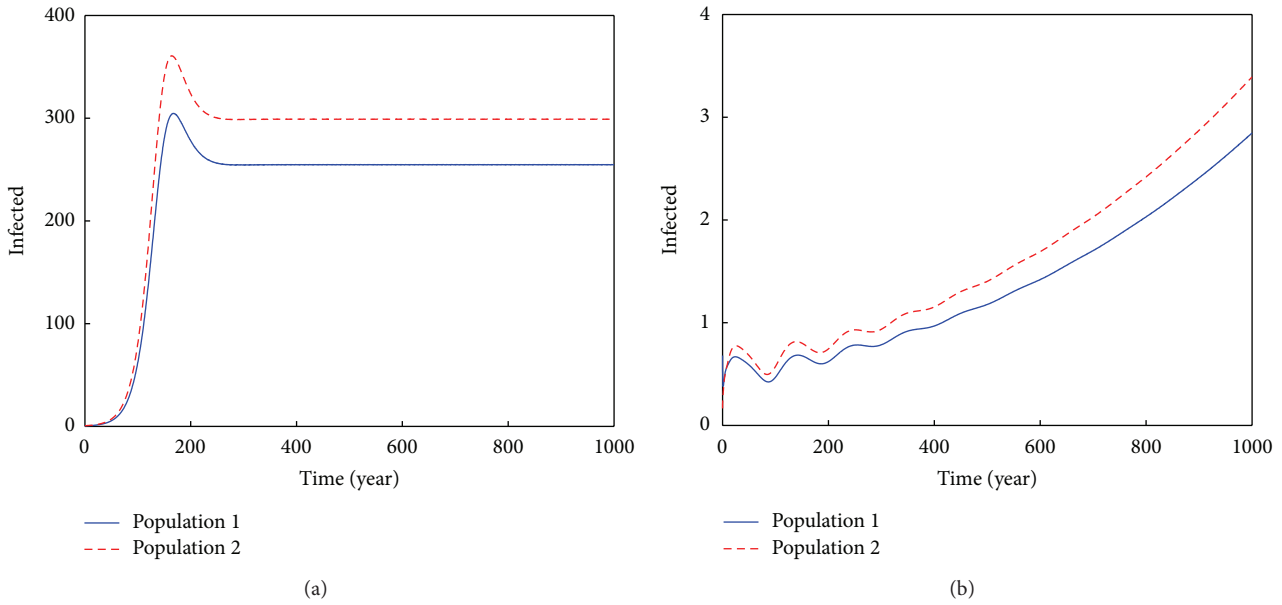


FIGURE 8: (a, b) Trajectories of infectious individuals in care center of (1) for different initial conditions. The endemic equilibrium exists and is stable when $R_0 > 1$; the DFE is unstable in this case.

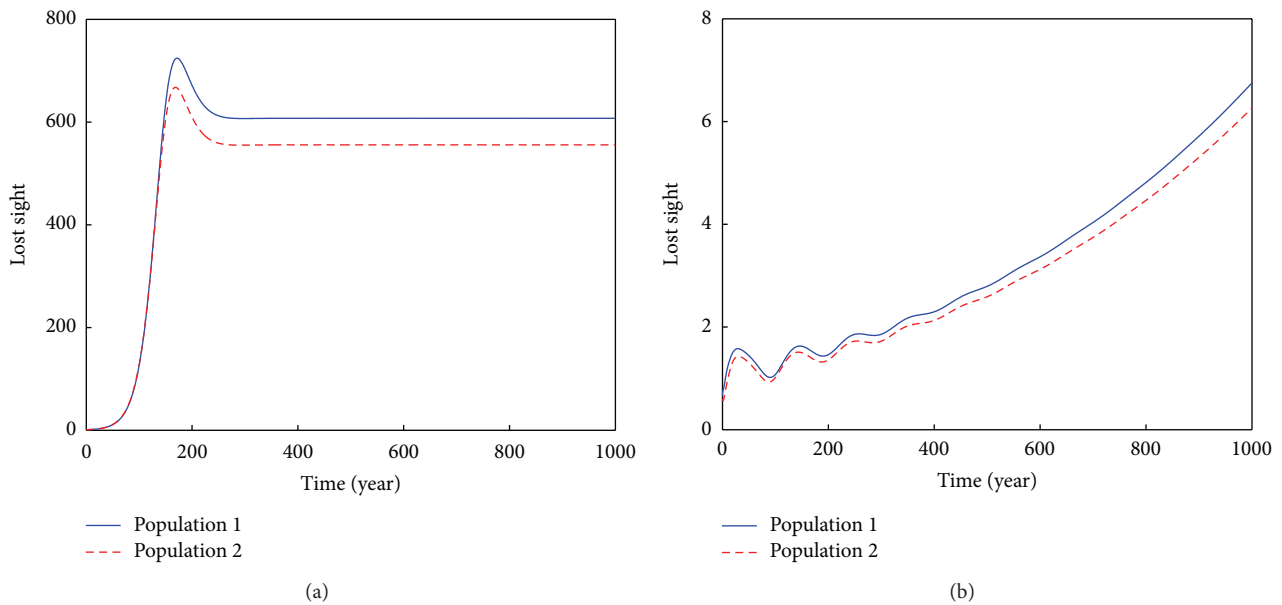


FIGURE 9: (a, b) Trajectories of lost sight individuals of (1) for different initial conditions. The endemic equilibrium exists and is stable when $R_0 > 1$; the DFE is unstable in this case.

One can observe that it is useful to analyze how many times the function $F(\bar{x})$ intersects the line $F(\bar{x}) = 1$ in the plane $(\bar{x}, F(\bar{x}))$. The monotony of the function F depends on the parameters of system (1). Then, the following lemma and theorem hold.

Lemma 12. *The function F satisfies the following properties.*

(1) *The limit when $\bar{x} \rightarrow 0$ is finite and is given by*

$$\begin{aligned} \lim_{\bar{x} \rightarrow 0} F(\bar{x}) &= \frac{h_{31}}{\Lambda_1 + \Lambda_2} \left\langle \frac{\Lambda}{e_1^2} \right\rangle + \frac{h_{32}}{\Lambda_1 + \Lambda_2} \left\langle \frac{\Lambda}{e_2^2} \right\rangle \\ &+ \frac{h_{41}}{\Lambda_1 + \Lambda_2} \left\langle \frac{\Lambda}{e_1^2} \right\rangle + \frac{h_{42}}{\Lambda_1 + \Lambda_2} \left\langle \frac{\Lambda}{e_2^2} \right\rangle = s_0. \end{aligned} \tag{39}$$

TABLE 1: Numerical values for the parameters of the model.

Parameters	Description	Estimated value/range	Reference
Λ_1	Recruitment rate into the S_1 class	100/yr	Assumed
Λ_2	Recruitment rate into the S_2 class	110/yr	Assumed
β_1	Transmission coefficient in patch 1	Variable	Assumed
β_2	Transmission coefficient in patch 2	Variable	Assumed
μ_1	Per capita death rate in patch 1	0.019896/yr	Estimated
μ_2	Per capita death rate in patch 2	0.019897/yr	Estimated
k_{1i}	Progression rate from E_{1i} to next class in patch 1	0.00013/yr	Assumed
k_{2i}	Progression rate from E_{2i} to next class in patch 2	0.00023/yr	Assumed
r_{1i}	Effective chemoprophylaxis in the E_{1i} class	0/yr	Estimated
r_{2i}	Effective chemoprophylaxis in the E_{2i} class	0/yr	Estimated
δ_1	Lost sight individuals still able to transmit disease in patch 1	0.46/yr	Estimated
δ_2	Lost sight individuals still able to transmit disease in patch 2	0.48/yr	Estimated
γ_1	Effective therapy in I_1 class	0.8182/yr	Estimated
γ_2	Effective therapy in I_2 class	0.8183/yr	Assumed
α_1	Return rate in care centre for patch 1	0.23/yr	Estimated
α_2	Return rate in care centre for patch 2	0.23/yr	Estimated
v_1	Infectious individuals in care centre of patch 1 who can stay in care centre	0.59/yr	Estimated
v_2	Infectious individuals in care centre of patch 2 who can stay in care centre	0.5903/yr	Estimated
s_1	Infectious individuals in care centre of patch 1 who disappear	0.019/yr	Estimated
s_2	Infectious individuals in care centre of patch 1 who disappear	0.01905/yr	Estimated
a_1	Migration rate of susceptible individuals from patch 1 to patch 2	0.07/yr	Assumed
a_2	Migration rate of susceptible individuals from patch 2 to patch 1	0.0701/yr	Assumed
b_{1i}	Migration rate from latent class E_{1i} to latent class E_{2i}	0.05/yr	Assumed
b_{2i}	Migration rate from latent class E_{2i} to latent class E_{1i}	0.0503/yr	Assumed
c_1	Migration rate of infectious individuals from patch 1 to patch 2	0.02/yr	Assumed
c_2	Migration rate of infectious individuals from patch 2 to patch 1	0.0201/yr	Assumed
d_1	Additional death rate in I_1	0.0575/yr	Assumed
d_2	Additional death rate in I_2	0.05751/yr	Assumed
l_1	Additional death rate in L_1	0.0565/yr	Assumed
l_2	Additional death rate in L_2	0.05651/yr	Assumed
p_1	Fast progression to the I_1 class	0.015/yr	Assumed
p_2	Fast progression to the I_2 class	0.016	Assumed

(2) The limit when $\bar{x} \rightarrow +\infty$ is infinite: $\lim_{\bar{x} \rightarrow +\infty} F(\bar{x}) = +\infty$.

Theorem 13. *These properties hold for system (1).*

- (1) *There is no boundary equilibrium. This means that the disease cannot persist in one patch while disappearing in the other one.*
- (2) *If $s_0 \leq R_0 \leq 1$, there exists at least one solution of $F(\bar{x}) = 1$, depending on the monotony of the function F , and therefore there exists at least one endemic equilibrium (\bar{x}, \bar{y}) for system (5) which coexists with the disease-free equilibrium. This situation corresponds to a backward bifurcation.*
- (3) *If $R_0 \leq s_0 \leq 1$, there exists at least one solution of $F(\bar{x}) = 1$, depending on the monotony of the function F , and therefore there exists at least one endemic equilibrium (\bar{x}, \bar{y}) for system (5) which coexists with the*

disease-free equilibrium. There is no backward bifurcation in this case since the endemic equilibrium no longer exists (it disappears as the disease-free equilibrium).

- (4) *If $R_0 \leq 1 \leq s_0$, at least one solution of $F(\bar{x}) = 1$ can exist, depending on parameters of system (1), since the monotony of the function F also depends on these parameters.*
- (5) *If $s_0 \leq 1 \leq R_0$, at least one solution of $F(\bar{x}) = 1$ can exist, depending on the monotony of the function F , and therefore there exists at least one endemic equilibrium (\bar{x}, \bar{y}) for system (5), which coexists with the disease-free equilibrium.*
- (6) *If $1 \leq R_0 \leq s_0$, at least one solution of $F(\bar{x}) = 1$ can exist, depending on parameters of system (1), since the monotony of the function F also depends on these parameters.*
- (7) *If $1 \leq s_0 \leq R_0$, at least one solution of $F(\bar{x}) = 1$ can exist, depending on parameters of system (1), since*

the monotony of the function F also depends on these parameters.

Proof. When an endemic equilibrium (\bar{x}, \bar{y}) for system (5) exists, \bar{x} is solution of $F(\bar{x}) = 1$. \bar{N}_1 and \bar{N}_2 are given by (31) as

$$\begin{aligned} \frac{\bar{N}_1}{\langle e_1^2/\bar{x}(t) \rangle} &= \frac{g_{11} \langle \Lambda + D_x \bar{x}/e_1^2 \rangle + g_{12} \langle \Lambda + D_x \bar{x}/e_2^2 \rangle}{\langle \Lambda + D_x \bar{x}/e_1^2 \rangle}, \\ \frac{\bar{N}_2}{\langle e_2^2/\bar{x}(t) \rangle} &= \frac{g_{21} \langle \Lambda + D_x \bar{x}/e_1^2 \rangle + g_{22} \langle \Lambda + D_x \bar{x}/e_2^2 \rangle}{\langle \Lambda + D_x \bar{x}/e_2^2 \rangle}. \end{aligned} \tag{40}$$

$\langle B_1/\bar{y} \rangle$ and $\langle B_2/\bar{y} \rangle$ are given by (16) as $\langle B_i/\bar{y} \rangle/\bar{N}_i = \langle \Lambda + D_x \bar{x}/e_i^2 \rangle/\langle e_i^2/\bar{x} \rangle$, $i = 1, 2$.

The expression of \bar{y} is given by (16) as

$$\begin{aligned} \bar{y} &= \left\langle \frac{B_1}{\bar{y}} \right\rangle \frac{\langle e_1^2/\bar{x}(t) \rangle}{\bar{N}_1} (-A_y)^{-1} K_1 \\ &+ \left\langle \frac{B_2}{\bar{y}} \right\rangle \frac{\langle e_2^2/\bar{x}(t) \rangle}{\bar{N}_2} (-A_y)^{-1} K_2. \end{aligned} \tag{41}$$

Since the function F is not strictly monotone, the number of solutions of $F(\bar{x}) = 1$ depends on the parameters of system (1). Therefore, there can be more than one endemic equilibrium. \square

Remark 14. In the second case of the theorem, we observe that at least one endemic equilibrium coexists with the disease-free equilibrium. Then, there can be a backward bifurcation in this case.

3.6. Stability of Endemic Equilibrium. The stability of endemic equilibrium is always a big challenge in epidemiology. The problem is more difficult here since we have $2n + 6$ equations. For multipatch and universal incidence law, results concerning the global stability of endemic equilibrium are limited. Next we will illustrate some results concerning our model.

4. Numerical Simulations

System (1) is simulated with parameter values presented in Table 1 using real data of the cities of Yaounde and Bafia [21].

Next we use the values in Table 1 to generate several curves (Figures 2, 3, 4, 5, 6, 7, 8, and 9) in order to illustrate our theoretical results.

5. Conclusion

The long-term dynamics of our system has been completely investigated. The model exhibits rich dynamics, depending on the values of the bifurcation parameters R_0^i , $i = 1, 2$, and R_0 . The influence of parameter R_0^i is significant on the spread of tuberculosis since it quantifies the intensity of pathogens

transmission. The stability of equilibria depends on these parameters. We have transcritical bifurcation parameters and backward bifurcation. When the basic reproduction number is less than unity, tuberculosis can be controlled in each population if the DFE is the unique equilibrium. It can be more difficult if the DFE coexists with at least one endemic equilibrium (this is the situation of backward bifurcation). In this case, the disease-free equilibrium can be locally and asymptotically stable, as well as the endemic equilibrium. When the basic reproduction number R_0 is greater than unity, tuberculosis is endemic and can be difficult to control in the population. The disease in our model cannot persist in one population while disappearing in the other one.

Disclosure

Part of this work was realized during the visit of Jean Jules Tewa at the UMI 209 UMMISCO Laboratory of University Cheikh Anta Diop, Dakar, Senegal.

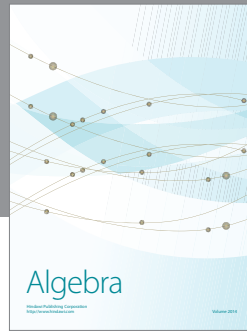
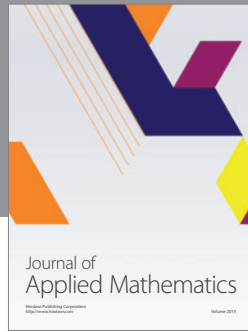
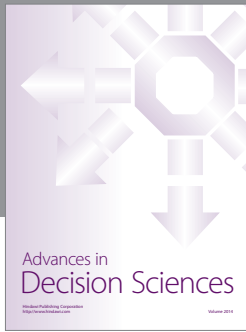
Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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