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Global Stability of a Susceptible-Infected-Recovered (SIR) Epidemic Model with Two Infectious Stages and Treatment

M. Elhia, A.E. Laaroussi, M. Rachik, Z. Rachik, E. Labriji

Laboratory of Analysis Modelling and Simulation
Department of Mathematics and Computer Science
Faculty of Sciences Ben M'Sik, Hassan II University
Mohammedia, BP 7955, Sidi Othman, Casablanca, Morocco

Abstract: ***In this paper, we study the global stability of an epidemic model that incorporates two infectious staged and treatment. The model allows for infected individuals on the second stage to move from treated to untreated class and vice-versa. The basic reproduction number R_0 is computed. If $R_0<1$, then the disease-free equilibrium (DFE) is globally asymptotically stable and the disease always dies out. If $R_0>1$, then there exists a unique endemic equilibrium (EE). This endemic equilibrium is shown to be globally asymptotically stable, under certain parameters restriction. The proof of global stability utilizes a Lyapunov function. To illustrate the theoretical results, numerical simulations are also provided.***

Keywords: global stability, SIR epidemic model, the basic reproduction number R_0, Lyapunov function, numerical simulation

1. Introduction

In epidemiology, there is a long and distinguished history of mathematical models. The earliest mathematical epidemic model was formulated and solved by Daniel Bernoulli in 1760 [4] in order to evaluate the effectiveness of variolation of healthy people with the smallpox virus. However, the first contributions to modern mathematical epidemiology are due to P.D. En'ko between 1873 and 1894 [8], and the foundations of the entire approach to epidemiology based on compartmental models were laid by Sir R.A. Ross, W.H. Hamer, A.G. McKendrick, and W.O. Kermack between 1900 and 1935 (see for example [18],[9],[16],[12]).

Since the middle of the 20th century, the world has seen a marked improvement of sanitary conditions and the development of more effective treatment (antibiotics, antivirals, vaccines ... etc), suggesting that infectious diseases would soon be eradicated. But this did not materialize, and conversely, new strains of old diseases, resistant to available drugs, have re-emerged, new diseases such as AIDS have taken hold and changes in lifestyle, particularly increased mobility, provide ample opportunities for new infectious diseases to emerge and spread very rapidly. For these reasons, theoretical epidemiology has witnessed numerous developments and the number of works on epidemic modelling has grown at an astonishing rate. Nowadays, mathematical epidemic models are a very important tool in understanding, analyzing and controlling infectious diseases. They are used in making prediction of disease outbreak and evaluations of prevention or intervention strategies. An overview of the use of mathematical models in infectious disease epidemiology, can be found in Baily [2], Anderson and May [1], Hethcote [10], Keeling and Rohani [11] and Brauer et al. [5].

Most models in mathematical epidemiology are compartmental models. The population is divided into various classes based on the stages of infection, with the assumptions about the nature and time rate of transfer from one compartment to another. For many models (see for instance [3],[19],[17],[15],[21],[6]), the population is divided into three disease-state compartments: susceptible individuals, people who can catch the disease; infectious (infective) individuals, people who have the disease and can transmit the disease; recovered individuals, people who have recovered from the disease. Once infected, each susceptible individual *(S)* instantaneously becomes infectious *(I)*, and later recovers *(R)* with a permanent immunity. These general models are called SIR models. The basic form of these models involves a single class for infectious individuals. While this is a practical assumption for diseases with short infectious periods, such as measles or influenza, it is not generally suitable for diseases for which the infectious period lasts many years. Moreover, this assumption overlooks that some infected individuals can be properly detected and treated, isolated or removed, whereas others remain undetected and untreated.

In this work, we propose to study the global dynamic of an SIR epidemic model with two infectious stages, namely the first stage of the disease and the worsened case. In the second stage of infection, we assume there are two subclasses, treated and untreated individuals. Furthermore, it is well known that among infectious individuals that begin treatment some of them will subsequently give up treatment. This can be due to negligence, lack of information about the disease, long duration of treatment, poverty, mentality, etc.. While some of the untreated individuals who are no longer able to stand the pain will join the treated class. So, in order to have a more realistic model we allow for infected individuals on the second stage to move from treated to untreated class and vice-versa. The proposed model allows highlighting the state of the disease and tracking changes in each compartment. It can be used to show the impact of detection and treatment strategies on spread of an epidemic.

This paper is organized as follows. In section 2, we present

our mathematical model. In section 3, we give some properties of solutions. In section 4, we derive the expression of the basic reproduction number R_0 and we analyze global behavior of disease-free and endemic equilibria by constructing suitable Lyapunov functional. Numerical studies are presented, in section 5, to validate the analytical results.

2. Mathematical model

In this section, we present the Susceptible-Infected-Recovered (SIR) epidemic model used in this paper. We consider two infectious stages, the infectious class is divided into three categories; infected individuals in the primary stage of the disease *(I)*, infected individuals in the worsened case who are not on treatment *(U)* and those how are under treatment *(T)*.

To build our model we make the following assumptions:

- All recruitment is into the susceptible class, and occurs at a constant rate Λ;
- Transmission of the disease occurs following adequate contacts between a susceptible individual and infectious in respectively the compartments *I*, *U* and *T*. The standard mass balance incidence expressions $\beta_1 SI$, $\beta_2 SU$, $\beta_3 ST$ are used to indicate successful transmission of disease, with $\beta_i \ (i=1,3)$ denote the per capita contact rate of the infectious in respectively the compartments I, U and T. Thus, the force of infection is given by
$$\lambda = \beta_1 I + \beta_2 U + \beta_3 T \qquad (1)$$
- In the second stage of disease, the rate at which individuals on treatment infect people with the disease is less in comparison to that of infectives who are not under treatment i.e. $\beta_2 > \beta_3$;
- Natural death rate, μ, is constant across all the classes;
- A fraction p $(0 \le p \le 1)$ of all infectives in the first stage of the disease i.e. $p\delta I$ goes to treated class *(T)* while the others i.e. $(1-p)\delta I$ join the untreated class *(U)*. Here δ is the rate of movement from infectious class *I*.
- Individuals in class *U* are treated at a per capita rate γ_1;
- Among treated individuals, some of them will subsequently give up treatment at a per capita rate γ_2;
- Treated and untreated infected individuals progress to the recovered class at respective rates α_1 and α_2;
- The disease is fatal to a proportion of those infected by it. Thus, we introduce additional death rates due to infection and disease with constant rates d_I, d_U, d_T;
- All the individuals recovered have permanent immunity.

The transfer diagram of our model is depicted in Figure 1:

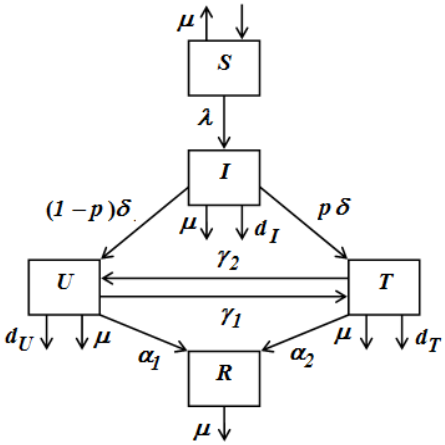

Figure 1: The basic model compartments and flow

The dynamics of the model are governed by the following system of differential equations:

$$\begin{cases} \dfrac{dS}{dt} = \Lambda - \lambda S - \mu S \\ \dfrac{dI}{dt} = \lambda S - (\mu + \delta + d_I) I \\ \dfrac{dU}{dt} = (1-p)\delta I - (\mu + \gamma_1 + \alpha_1 + d_U) U + \gamma_2 T \\ \dfrac{dT}{dt} = p\delta I + \gamma_1 U - (\mu + \gamma_2 + \alpha_2 + d_T) T \\ \dfrac{dR}{dt} = \alpha_1 U + \alpha_2 T - \mu R \end{cases} \qquad (2)$$

with

- $S(0) \ge 0, I(0) \ge 0, U(0) \ge 0, T(0) \ge 0$ and $R(0) \ge 0$ are given;
- $N(t) = S(t) + I(t) + U(t) + T(t) + R(t)$ is the total population number at time *t*.

Since the state variable *R* does not appear in the first four equations of the system (2), our analysis of the model shall be based on the system (3) below.

$$\begin{cases} \dfrac{dS}{dt} = \Lambda - \lambda S - \mu S \\ \dfrac{dI}{dt} = \lambda S - (\mu + \delta + d_I) I \\ \dfrac{dU}{dt} = (1-p)\delta I - (\mu + \gamma_1 + \alpha_1 + d_U) U + \gamma_2 T \\ \dfrac{dT}{dt} = p\delta I + \gamma_1 U - (\mu + \gamma_2 + \alpha_2 + d_T) T \end{cases} \qquad (3)$$

3. Properties of the model

Since the model (3) describes the evolution of a human population, it is important to prove the individual's number in each compartment should remain non negative and bounded. So, we establish, in this section, the positivity and the boundedness of solutions of model (3).

Let $x=S$, $y=(I,U,T)^T$ then the system (3) can be written under the following general form:

$$\begin{cases} \dot{x} = \varphi(x) - x\,\langle y, \eta \rangle \\ \dot{y} = x\,\langle y, \eta \rangle e_1 + Ay \end{cases} \quad (4)$$

Where $\varphi(x) = \Lambda - \mu x$, $\eta = (\beta_1, \beta_2, \beta_3)^T$, $e_1 = (1,0,0)^T$ $\langle \ , \ \rangle$, is the usual scalar product in $\mathbb{R}^3$ and A is a Metzler 3×3 matrix given by

$$A = \begin{pmatrix} -a_{11} & 0 & 0 \\ a_{21} & -a_{22} & a_{23} \\ a_{31} & a_{32} & -a_{33} \end{pmatrix} \quad (5)$$

With

$$a_{11} = \mu + \delta + d_I, \quad a_{21} = (1-p)\delta \ , \ a_{22} = \mu + \gamma_1 + \alpha_1 + d_U \ , \ a_{23} = \gamma_2 \quad (6)$$
$$a_{31} = p\delta \ , \ a_{32} = \gamma_1 \ , \ a_{33} = \mu + \gamma_2 + \alpha_2 + d_T$$

The compact form (4) will be very useful in the rest of this article. Particularly, the use of the Metzler matrix A will ensure the positivity of the basic reproduction number R_0 as $\left(-A^{-1}\right) \geq 0$ (see subsection 4.1).

3.1 Positive invariance of the nonnegative orthant

For system (4) to be epidemiologically meaningful, it is important to prove that all its state variables are non-negative for all time. In other word, solutions of system (4) with positive initial data remain positive for all time $t>0$. We have the following result:

Proposition 1 *The nonnegative orthant $\mathbb{R}^4_+$ is positively invariant for the system* (4).

Proof. To ensure the invariance of the positive orthant $\mathbb{R}^4_+$ it is necessary and sufficient to verify that the boundaries of $\mathbb{R}^4_+$ (i.e. hyperplanes $x_i=0$) are impassable by the trajectories of the system (4) initialized in $\mathbb{R}^4_+$. This can be verified as follows. For $x \geq 0$ the matrix $(xe_1\eta^T + A)$ is a linear Metzler matrix. Since it is well known that linear Metzler matrix let invariant the nonnegative orthant, this proves that the positive orthant $\mathbb{R}^3_+$ is positively invariant by $\dot{y} = (xe_1\eta^T + A)y$. For the variable x it is easy to check that it remain non negative for all $t>0$. Indeed, from the first equation of (4) we have

$$\frac{dx}{dt} = \Lambda - \mu x - \lambda x \quad (7)$$

Hence

$$\frac{dx}{dt} \geq -(\mu + \lambda)x \quad (8)$$

So that

$$\left[\frac{dx}{dt} + (\mu + \lambda)x\right] \exp\left(\mu t + \int_0^t \lambda(v)dv\right) \geq 0 \quad (9)$$

It follows

$$\frac{d}{dt}\left[x(t) \exp\left(\mu t + \int_0^t \lambda(v)dv\right)\right] \geq 0 \quad (10)$$

Finally

$$x(t) \geq x(0) \exp\left[-\left(\mu t + \int_0^t \lambda(v)dv\right)\right] \geq 0 \quad (11)$$

3.2 Boundedness of trajectories

The trajectories of the model (4) are bounded. Indeed, adding all equation of the model (4), one has

$$\frac{dN}{dt} \leq \Lambda - \mu N \quad (12)$$

Thus, one can deduce that

$$N(t) \leq \frac{\Lambda}{\mu} + N(0)e^{-\mu t} \quad (13)$$

It then follows that $0 \leq N(t) \leq \frac{\Lambda}{\mu}$, when $t \to +\infty$, and all possible solutions of the system (4) enter the region

$$\Omega = \left\{(S, I, U, T) \in \mathbb{R}^4_+ : N \leq \frac{\Lambda}{\mu}\right\} \quad (14)$$

Ω is a compact forward invariant set for the system (4) and so we limit our study to this simplex, where the model can be considered to be epidemiologically and mathematically well-posed.

4. Model Equilibria Analysis

In this section we analyze the model (4) using stability theory of differential equations.

4.1 The basic reproduction number

Global behavior of the model (4) crucially depends on the basic reproduction number R_0, that is, the average number of secondary cases produced by a single infective individual which is introduced into an entirely susceptible population.

The model has an evident equilibrium $P_0 = \left(\frac{\Lambda}{\mu}, 0\right) = \left(x^*, 0\right)$, called the disease free equilibrium (DFE). Using the Van Den Driesseche and Watmough next generation approach [20] and the techniques reported in [14] and [7], the expression of R_0 is given as follows:

Proposition 2 *The basic reproduction number of the system* (4) *is defined by*

$$R_0 = x^* \left\langle \left(-A^{-1}\right)e_1, \eta \right\rangle \quad (15)$$

and takes the form

$$R_0 = x^* \left(R_{01} + R_{02} + R_{03}\right) \quad (16)$$

Where

$$R_{01} = \frac{\beta_1}{\mu + \delta}$$
$$R_{02} = \frac{\beta_2\left[(1-p)\delta(\mu + \alpha_2) + \delta\gamma_2\right]}{(\mu+\delta)\left[(\mu + \gamma_1 + \alpha_1 + d_U)(\mu + \gamma_2 + \alpha_2 + d_T) - \gamma_1\gamma_2\right]} \quad (17)$$
$$R_{03} = \frac{\beta_3\left[p\delta(\mu + \alpha_1) + \delta\gamma_1\right]}{(\mu+\delta)\left[(\mu + \gamma_1 + \alpha_1 + d_U)(\mu + \gamma_2 + \alpha_2 + d_T) - \gamma_1\gamma_2\right]}$$

Proof. The next generation method consists in considering only the infected classes I, U and T. The variations of these infected variables are described by

$$\dot{y} = x\,\langle y, \eta \rangle e_1 + Ay \quad (18)$$

we put

$$\mathcal{F} = x\,\langle y,\eta\rangle e_1 \text{ and } \mathcal{V} = -Ay$$

where $\mathcal{F}$ is the rate of new infections in each class, and $\mathcal{V}$ describes the other flows in the infected classes.

The Jacobian matrix of $\mathcal{F}$ and $\mathcal{V}$ at the disease-free equilibrium P_0 are given by

$$F = \frac{\partial \mathcal{F}}{\partial y}(P_0) = x^* e_1 \eta^T \text{ and } V = \frac{\partial \mathcal{V}}{\partial y}(P_0) = -A$$

The basic reproduction number is defined, following Van den Driessche and Watmough [20], as the spectral radius of the next generation matrix, FV^{-1}. Since FV^{-1} is a rank one matrix, the only nonzero eigenvalue is given by

$$x^* \eta^T \left(-A^{-1}\right) e_1 \tag{19}$$

So

$$R_0 = x^* \left\langle \left(-A^{-1}\right) e_1, \eta \right\rangle \tag{20}$$

or, using the inner product and after the computation of $\left(-A^{-1}\right)$, the full expression of R_0 may be rewritten as (16)-(17).

4.2 Stability of the disease free equilibrium

Here we study the stability of the DFE $P_0 = \left(x^*, 0\right)$

Theorem 3 *The disease free equilibrium (DFE), P_0, of the model (4), is globally asymptotically stable (GAS) if $R_0<1$.*

Proof. Let us consider the following Lyapunov function:

$$V(x,y) = \left\langle \left(-A^{-T}\right)\eta, y \right\rangle \tag{21}$$

It is obvious that $V(x,y)>0$ for $(x,y) \neq P_0$ and $V(P_0) = 0$.

The time derivative of V along the solutions of system (4) satisfies

$$\begin{aligned}
\dot{V}(x,y) &= \left\langle -A^{-T}\eta, \dot{y} \right\rangle \\
&= \left\langle -A^{-T}\eta, x\,\langle y,\eta\rangle e_1 + Ay \right\rangle \\
&= x\,\langle y,\eta\rangle \left\langle -A^{-T}\eta, e_1 \right\rangle - \langle y,\eta\rangle \\
&= \langle y,\eta\rangle \left(x\left\langle -A^{-T}\eta, e_1 \right\rangle - 1 \right) \\
&= \langle y,\eta\rangle \left(\frac{x}{x^*} R_0 - 1 \right)
\end{aligned}$$

Therefore, $\dot{V}(x,y) \le 0$ for $R_0<1$. While $\dot{V}(x,y) = 0$ if and only if $(x,y) = P_0$. The maximal compact invariant set in $M = \left\{(x,y) : \dot{V} = 0\right\}$ is the singleton $\{P_0\}$. By the LaSalle's Invariance Principle [13], it follows that the DFE P_0, is globally asymptotically stable.

4.3 Stability of the endemic equilibrium

In the following, we study the existence and the stability of the endemic equilibrium P^*. The existence of P^* is given by the following result.

Proposition 4 *If $R_0<1$, then the point P^* does not exist and $P^*=P_0$ when $R_0=1$.*

If $R_0>1$, then there exists a unique endemic equilibrium $P^* = \left(\bar{S}, \bar{I}, \bar{U}, \bar{T}\right)$ where

$$\begin{aligned}
\bar{S} &= \frac{x^*}{R_0} \\
\bar{I} &= \frac{\Lambda - \mu\bar{S}}{\beta_1} R_{01} \\
\bar{U} &= \frac{\Lambda - \mu\bar{S}}{\beta_2} R_{02} \\
\bar{T} &= \frac{\Lambda - \mu\bar{S}}{\beta_3} R_{03}
\end{aligned} \tag{22}$$

Proof.

If $R_0<1$, it is easy to show that P^* does not exist and $P^*=P_0$ when $R_0=1$.

When $R_0>1$ the disease persists in the population i.e. $\bar{I} \neq 0$ so $\langle y,\eta\rangle \neq 0$. By setting the right-hand side of all equations in model (4) equal to zero, that is,

$$\begin{cases} \varphi(\bar{x}) - \bar{x}\,\langle \bar{y},\eta\rangle = 0 \\ \bar{x}\,\langle \bar{y},\eta\rangle e_1 + A\bar{y} = 0 \end{cases} \tag{23}$$

Form the second equation of (23), one has $\bar{y} = \bar{x}\,\langle \bar{y},\eta\rangle \left(-A^{-1}\right) e_1$. And replacing in $\langle \bar{y},\eta\rangle$ yields

$$\langle \bar{y},\eta\rangle = \bar{x}\,\langle \bar{y},\eta\rangle \left\langle \left(-A^{-1}\right) e_1, \eta \right\rangle \tag{24}$$

Since $\langle \bar{y},\eta\rangle \neq 0$, (24) implies $1 = \bar{x}\left\langle \left(-A^{-1}\right) e_1, \eta \right\rangle$ then

$$\bar{S} = \frac{x^*}{R_0} \tag{25}$$

From the first and the second equations of (23), one obtains

$$\bar{y} = \varphi(\bar{x}) \left(-A^{-1}\right) e_1 \tag{26}$$

When $R_0>1$ one has $\varphi(\bar{x}) > 0$. Further, since $\left(-A^{-1}\right) \ge 0$ we have $\bar{y} \ge 0$. Now, using the expression of $\varphi(\bar{x})$ and the expression of $\left(-A^{-1}\right)$ obtained after some calculations, the model (4) has a unique endemic equilibrium P^* given by (22).

Theorem 5 *If $R_0>1$ and $p > \frac{\gamma_1}{\gamma_1+\gamma_2}$, the positive endemic equilibrium P^* is globally asymptotically stable.*

Proof.

Before introducing the Lyapunov functional, we recall that for any $x>0$, the function g defined by

$$g(x) = x - 1 - \ln x \tag{27}$$

is non-negative and $g(x)=0$ if and only if $x=1$.

Moreover, note that $\bar{S}g\left(\frac{S}{\bar{S}}\right) \ge 0$, $\bar{I}g\left(\frac{I}{\bar{I}}\right) \ge 0$, $\bar{U}g\left(\frac{U}{\bar{U}}\right) \ge 0$ and $\bar{T}g\left(\frac{T}{\bar{T}}\right) \ge 0$.

Now, let consider the following Lyapunov function

$$V = \bar{S}g\left(\frac{S}{\bar{S}}\right) + b_1\bar{I}g\left(\frac{I}{\bar{I}}\right) + b_2\bar{U}g\left(\frac{U}{\bar{U}}\right) + b_3\bar{T}g\left(\frac{T}{\bar{T}}\right) \tag{28}$$

Where b_i *(i=1,2,3)* are positive, and left unspecified.

Differentiating the function V along with the solutions of system (3) with respect to time t gives

$$\dot{V}=\left(1-\frac{\bar{S}}{S}\right)\dot{S}+b_1\left(1-\frac{\bar{I}}{I}\right)\dot{I}+b_2\left(1-\frac{\bar{U}}{U}\right)\dot{U}+b_3\left(1-\frac{\bar{T}}{T}\right)\dot{T} \quad (29)$$

Substituting system (3) into the above equation yields

$$\begin{aligned}\dot{V}=&\left(1-\frac{\bar{S}}{S}\right)\left[\Lambda-\lambda S-\mu S\right]\\&+b_1\left(1-\frac{\bar{I}}{I}\right)\left[\lambda S-\left(\mu+\delta+d_1\right)I\right]\\&+b_2\left(1-\frac{\bar{U}}{U}\right)\left[(1-p)\delta I-\left(\mu+\gamma_1+\alpha_1+d_U\right)U+\gamma_2 T\right]\\&+b_3\left(1-\frac{\bar{T}}{T}\right)\left[p\delta I+\gamma_1 U-\left(\mu+\gamma_2+\alpha_2+d_T\right)T\right]\end{aligned} \quad (30)$$

Using the coefficients of the matrix A, $\dot{V}$ may be rewritten as

$$\begin{aligned}\dot{V}=&\left(1-\frac{\bar{S}}{S}\right)\left[\Lambda-\lambda S-\mu S\right]\\&+b_1\left(1-\frac{\bar{I}}{I}\right)\left[\lambda S-a_{11}I\right]\\&+b_2\left(1-\frac{\bar{U}}{U}\right)\left[a_{21}I-a_{22}U+a_{23}T\right]\\&+b_3\left(1-\frac{\bar{T}}{T}\right)\left[a_{31}I+a_{32}U-a_{33}T\right]\end{aligned} \quad (31)$$

Then

$$\begin{aligned}\dot{V}=&\Lambda-\lambda S-\mu S-\Lambda\frac{\bar{S}}{S}+\lambda\bar{S}+\mu\bar{S}\\&+b_1\lambda S-b_1a_{11}I-b_1\lambda S\frac{\bar{I}}{I}+b_1a_{11}\bar{I}\\&+b_2a_{21}I-b_2a_{22}U+b_2a_{23}T-b_2a_{21}I\frac{\bar{U}}{U}+b_2a_{22}\bar{U}-b_2a_{23}T\frac{\bar{U}}{U}\\&+b_3a_{31}I+b_3a_{32}U-b_3a_{33}T-b_3a_{31}I\frac{\bar{T}}{T}-b_3a_{32}U\frac{\bar{T}}{T}+b_3a_{33}\bar{T}\end{aligned} \quad (32)$$

Using the expression of λ, and rearranging the above equation, we have

$$\begin{aligned}\dot{V}=&\Lambda+\mu\bar{S}+b_1a_{11}\bar{I}+b_2a_{22}\bar{U}+b_3a_{33}\bar{T}\\&+\left(b_1-1\right)\left(\beta_1SI+\beta_2SU+\beta_3ST\right)\\&-\left(\mu+b_1\beta_1\bar{I}\right)\bar{S}\frac{S}{\bar{S}}+\left(-b_1a_{11}+b_2a_{21}+b_3a_{31}+\beta_1\bar{S}\right)\bar{I}\frac{I}{\bar{I}}\\&+\left(-b_2a_{22}+b_3a_{32}+\beta_2\bar{S}\right)\bar{U}\frac{U}{\bar{U}}+\left(b_2a_{23}-b_3a_{33}+\beta_3\bar{S}\right)\bar{T}\frac{T}{\bar{T}}\\&-\Lambda\frac{\bar{S}}{S}-b_1\beta_2\bar{S}\bar{U}\frac{S}{\bar{S}}\frac{U}{\bar{U}}\frac{\bar{I}}{I}-b_1\beta_3\bar{S}\bar{T}\frac{S}{\bar{S}}\frac{T}{\bar{T}}\frac{\bar{I}}{I}-b_2a_{21}\bar{I}\frac{I}{\bar{I}}\frac{\bar{U}}{U}\\&-b_2a_{23}\bar{T}\frac{\bar{U}}{U}\frac{T}{\bar{T}}-b_3a_{31}\bar{I}\frac{\bar{T}}{T}\frac{I}{\bar{I}}-b_3a_{32}\bar{U}\frac{\bar{T}}{T}\frac{U}{\bar{U}}\end{aligned} \quad (33)$$

By denoting $u_1=\frac{S}{\bar{S}}$, $u_2=\frac{I}{\bar{I}}$, $u_3=\frac{U}{\bar{U}}$ and $u_4=\frac{T}{\bar{T}}$, we obtain

$$\begin{aligned}\dot{V}=&\Lambda+\mu\bar{S}+b_1a_{11}\bar{I}+b_2a_{22}\bar{U}+b_3a_{33}\bar{T}\\&+\left(b_1-1\right)\left(\beta_1SI+\beta_2SU+\beta_3ST\right)\\&-\left(\mu+b_1\beta_1\bar{I}\right)\bar{S}u_1+\left(-b_1a_{11}+b_2a_{21}+b_3a_{31}+\beta_1\bar{S}\right)\bar{I}u_2\\&+\left(-b_2a_{22}+b_3a_{32}+\beta_2\bar{S}\right)\bar{U}u_3+\left(b_2a_{23}-b_3a_{33}+\beta_3\bar{S}\right)\bar{T}u_4\\&-\Lambda\frac{1}{u_1}-b_1\beta_2\bar{S}\bar{U}\frac{u_1u_3}{u_2}-b_1\beta_3\bar{S}\bar{T}\frac{u_1u_4}{u_2}-b_2a_{21}\bar{I}\frac{u_2}{u_3}\\&-b_2a_{23}\bar{T}\frac{u_4}{u_3}-b_3a_{31}\bar{I}\frac{u_2}{u_4}-b_3a_{32}\bar{U}\frac{u_3}{u_4}\end{aligned} \quad (34)$$

From the set

$$\left\{u_1,u_2,u_3,u_4,\frac{1}{u_1},\frac{u_1u_3}{u_2},\frac{u_1u_4}{u_2},\frac{u_2}{u_3},\frac{u_4}{u_3},\frac{u_2}{u_4},\frac{u_3}{u_4}\right\} \quad (35)$$

There are five groups such that the product of all functions within each group is unity. The five groups are, respectively,

$$\begin{aligned}&\left\{u_1,\frac{1}{u_1}\right\};\left\{\frac{u_4}{u_3},\frac{u_3}{u_4}\right\};\left\{\frac{1}{u_1},\frac{u_1u_3}{u_2},\frac{u_2}{u_3}\right\};\left\{\frac{1}{u_1},\frac{u_1u_4}{u_2},\frac{u_2}{u_4}\right\};\\&\left\{\frac{1}{u_1},\frac{u_1u_3}{u_2},\frac{u_4}{u_3},\frac{u_2}{u_4}\right\}\end{aligned} \quad (36)$$

Further, we rewrite $\dot{V}$ according to the above groups, as the following form

$$\begin{aligned}\dot{V}=&e_1\left(2-u_1-\frac{1}{u_1}\right)+e_2\left(2-\frac{u_4}{u_3}-\frac{u_3}{u_4}\right)+e_3\left(3-\frac{1}{u_1}-\frac{u_1u_3}{u_2}-\frac{u_2}{u_3}\right)\\&+e_4\left(3-\frac{1}{u_1}-\frac{u_1u_4}{u_2}-\frac{u_2}{u_4}\right)+e_5\left(4-\frac{1}{u_1}-\frac{u_1u_3}{u_2}-\frac{u_4}{u_3}-\frac{u_2}{u_4}\right)\end{aligned} \quad (37)$$

With the coefficients e_i($i=1,...,5$) left unspecified.

In the following, equating the coefficients of the like terms from (34) and (37) yields the following equations

$$\begin{cases}b_1-1=0\\-b_1a_{11}+b_2a_{21}+b_3a_{31}+\beta_1\bar{S}=0\\-b_2a_{22}+b_3a_{32}+\beta_2\bar{S}=0\\b_2a_{23}-b_3a_{33}+\beta_3\bar{S}=0\\e_1=\left(\mu+b_1\beta_1\bar{I}\right)\bar{S}\\e_2=b_3a_{32}\bar{U}\\e_3=b_2a_{21}\bar{I}\\e_4=b_1\beta_3\bar{S}\bar{T}\\e_4+e_5=b_3a_{31}\bar{I}\\e_1+e_3+e_4+e_5=\Lambda\\e_2+e_5=b_2a_{23}\bar{T}\\e_3+e_5=b_1\beta_2\bar{S}\bar{U}\\2e_1+2e_2+3e_3+3e_4+4e_5=\Lambda+\mu\bar{S}+b_1a_{11}\bar{I}+b_2a_{22}\bar{U}+b_3a_{33}\bar{T}\end{cases} \quad (38)$$

It follows from the four first equations that $b_1=1$ and the pair (b_2, b_3) is a solution of the following system

$$\begin{cases}b_2a_{21}+b_3a_{31}+\beta_1\bar{S}-a_{11}=0\\-b_2a_{22}+b_3a_{32}+\beta_2\bar{S}=0\\b_2a_{23}-b_3a_{33}+\beta_3\bar{S}=0\end{cases} \quad (39)$$

Note that when the first equation of (39) is satisfied, then all equations of (39) are also satisfied. Indeed, we know that for the endemic equilibrium $P^*=\left(\bar{S},\bar{I},\bar{U},\bar{T}\right)$ one has

$$\begin{cases} \Lambda-\beta_1\bar{S}\bar{I}-\beta_2\bar{S}\bar{U}-\beta_3\bar{S}\bar{T}-\mu\bar{S}=0 \\ \beta_1\bar{S}\bar{I}+\beta_2\bar{S}\bar{U}+\beta_3\bar{S}\bar{T}-a_{11}\bar{I}=0 \\ a_{21}\bar{I}-a_{22}\bar{U}+a_{23}\bar{T}=0 \\ a_{31}\bar{I}+a_{32}\bar{U}-a_{33}\bar{T}=0 \end{cases} \quad (40)$$

That is

$$\begin{cases} \Lambda=\beta_1\bar{S}\bar{I}+\beta_2\bar{S}\bar{U}+\beta_3\bar{S}\bar{T}+\mu\bar{S} \\ a_{11}\bar{I}=\beta_1\bar{S}\bar{I}+\beta_2\bar{S}\bar{U}+\beta_3\bar{S}\bar{T} \\ a_{21}\bar{I}=a_{22}\bar{U}-a_{23}\bar{T} \\ a_{31}\bar{I}=-a_{32}\bar{U}+a_{33}\bar{T} \end{cases} \quad (41)$$

Multiplying the first equation of (39) by $\bar{I}$ and using the expression of $a_{11}\bar{I}$, $a_{21}\bar{I}$ and $a_{31}\bar{I}$ defined in (41), one has

$$b_2a_{21}\bar{I}+b_3a_{31}\bar{I}+\beta_1\bar{S}\bar{I}-a_{11}\bar{I}=0 \quad (42)$$

That is

$$b_2\left(a_{22}\bar{U}-a_{23}\bar{T}\right)+b_3\left(-a_{32}\bar{U}+a_{33}\bar{T}\right)-\left(\beta_1\bar{S}\bar{I}+\beta_2\bar{S}\bar{U}+\beta_3\bar{S}\bar{T}\right)+\beta_1\bar{S}\bar{I}=0 \quad (43)$$

This gives

$$\left(b_2a_{22}-b_3a_{32}-\beta_2\bar{S}\right)\bar{U}+\left(-b_2a_{23}+b_3a_{33}-\beta_3\bar{S}\right)\bar{T}=0 \quad (44)$$

This proves that when the first equation of (39) is satisfied, then all equations of (39) are also satisfied. Therefore, b_2 and b_3 can be obtained by solving the following system

$$\begin{cases} -b_2a_{22}+b_3a_{32}+\beta_2\bar{S}=0 \\ b_2a_{23}-b_3a_{33}+\beta_3\bar{S}=0 \end{cases} \quad (45)$$

Thus

$$b_1=1$$

$$b_2=\frac{a_{33}\beta_2+a_{32}\beta_3}{a_{22}a_{33}-a_{23}a_{32}}\bar{S}=\frac{\left(\mu+\gamma_2+\alpha_2+d_T\right)\beta_2+\gamma_1\beta_3}{\left(\mu+\gamma_1+\alpha_1+d_U\right)\left(\mu+\gamma_2+\alpha_2+d_T\right)-\gamma_2\gamma_1}\bar{S}>0$$

$$b_3=\frac{a_{22}\beta_3+a_{23}\beta_2}{a_{22}a_{33}-a_{23}a_{32}}\bar{S}=\frac{\left(\mu+\gamma_1+\alpha_1+d_U\right)\beta_3+\gamma_2\beta_2}{\left(\mu+\gamma_1+\alpha_1+d_U\right)\left(\mu+\gamma_2+\alpha_2+d_T\right)-\gamma_2\gamma_1}\bar{S}>0 \quad (46)$$

In conclusion, our Lyapunov coefficients are all positive, which is necessary in ensuring that the candidate function, V, is positive definite. However, we still need to show that $\dot{V}\left(u_1,u_2,u_3,u_4\right)$ defined as in (37) is non-positive. From (38) one has

$$\begin{cases} e_1=\left(\mu+b_1\beta_1\bar{I}\right)\bar{S} \\ e_2=b_3a_{32}\bar{U} \\ e_3=b_2a_{21}\bar{I} \\ e_4=b_1\beta_3\bar{S}\bar{T} \\ e_5=b_3a_{31}\bar{I}-e_4=b_3a_{31}\bar{I}-b_1\beta_3\bar{S}\bar{T} \end{cases} \quad (47)$$

Note that $e_i>0(\ i=1,...,4)$. Now, using the expressions of e_4 as in (47), b_3 as in (46), system (41) and the hypothesis $\beta_2>\beta_3$ we can show that $e_5>0$ when $p>\frac{\gamma_1}{\gamma_1+\gamma_2}$.

So, the coefficients $e_i(\ i=1,...,5)$ are all positive.

At this point, we give the following lemma which is necessary to demonstrate that $\dot{V}\left(u_1,u_2,u_3,u_4\right)$ defined as in (37) is non-positive.

Lemma(Arithmetic-Geometric Means Inequality) *Let $z_1,...,z_w$ be positive real numbers. Then*

$$\sqrt[w]{z_1\ldots z_w}\le\frac{z_1+\ldots+z_w}{w} \quad (48)$$

Furthermore, exact equality only occurs if $z_1=\ldots=z_w$.

Thus $\left(2-u_1-\frac{1}{u_1}\right)$ is less than or equal to zero according to the previous lemma, with equality if and only if u_1=1. Also the expressions $\left(2-\frac{u_4}{u_3}-\frac{u_3}{u_4}\right)$, $\left(3-\frac{1}{u_1}-\frac{u_1u_3}{u_2}-\frac{u_2}{u_3}\right)$, $\left(3-\frac{1}{u_1}-\frac{u_1u_4}{u_2}-\frac{u_2}{u_4}\right)$ and $\left(4-\frac{1}{u_1}-\frac{u_1u_3}{u_2}-\frac{u_4}{u_3}-\frac{u_2}{u_4}\right)$ are also less than or equal to zeros by the arithmetic-geometric-means-inequality, with equality if and only if $u_2=u_3=u_4$.

This implies that $\dot{V}\le0$ with equality only if $S=\bar{S}$ and $\frac{I}{\bar{I}}=\frac{U}{\bar{U}}=\frac{T}{\bar{T}}$.

Since S must remain constant at $\bar{S}$, $\dot{S}$ is zero. We obtain that, $\frac{I}{\bar{I}}=\frac{U}{\bar{U}}=\frac{T}{\bar{T}}=1$. Thus, the maximal compact invariant set in $M=\left\{\left(S,I,U,T\right):\dot{V}=0\right\}$ is the singleton $\left\{P^*\right\}$. Using the LaSalle's invariance principle [13], it follows that the EE P^*, is globally asymptotically stable.

5. Numerical Simulations

In this section, we present numerical simulations to illustrate the various theoretical results previously obtained. Thus, we draw first the trajectories of system (3) for parameters verifying R_0 less than 1, and we shall do the same for parameters verifying R_0 upper to 1. All simulations are performed using the parameter values in Table 1. It is worthy to note that although carefully chosen our parameter values are theoretical and may not be biologically realistic.

Table 1: Parameter values used in the simulations

Parameter	*Description*	*Value*
Λ	Recruitment rate of susceptibles	1000 yr^{-1}
$\beta_i\ (i=1,2,3)$	Per capita contact rate of the infectious	variable
δ	The rate of movement from infectious class	0.4 yr^{-1}
μ	Natural per capita death rate	0.0101 yr^{-1}
γ_1	Progression rate to treated class for the untreated individuals	0.0087 yr^{-1}
γ_2	Rate of interrupting treatment	0.02 yr^{-1}
α_1	The recovery rate of untreated individuals	0.009 yr^{-1}
α_2	The recovery rate of treated individuals	0.8182 yr^{-1}
d_I	Disease induced rate for individuals in I class	0.001 yr^{-1}
d_U	Disease induced rate for individuals in U class	0.020 yr^{-1}
d_T	Disease induced rate for individuals in T class	0.002 yr^{-1}

Figure 2 presents the trajectories of the system (3) using various initial conditions when $\beta_1 = 0.0408 \times 10^{-6}$, $\beta_2 = 0.2879 \times 10^{-6}$, $\beta_3 = 0.0089 \times 10^{-6}$ which correspond to $R_0 = 0.5$. We have theoretically proved that, in this case, $R_0 < 1$, the disease free equilibrium is globally asymptotically stable. From this figure, we see that the trajectories converge to the disease free equilibrium. Thus the disease disappears in the host population.

Figure 3 provides the trajectories of the system (3) using various initial conditions when $\beta_1 = 0.0652 \times 10^{-5}$, $\beta_2 = 0.4607 \times 10^{-5}$, $\beta_3 = 0.0142 \times 10^{-5}$ and $p = 0.31$ which correspond to $R_0 = 8$. We have theoretically proved that, in this case, $R_0 > 1$ and $p > \frac{\gamma_1}{\gamma_1 + \gamma_2}$, the endemic equilibrium is globally asymptotically stable. From this figure, we see that the trajectories converge to positive and finite limit, which is the endemic equilibrium. Therefore, the disease will persist in the host population irrespective of the initial conditions. It is thus important to reduce the reproduction number to below unit in order to control the epidemic.

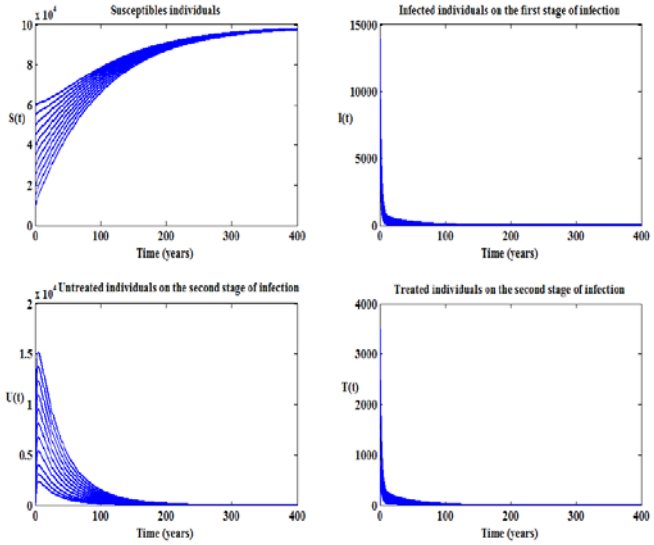

Figure 2: Trajectories of the system (3) for different initial conditions when $R_0 = 0.5$

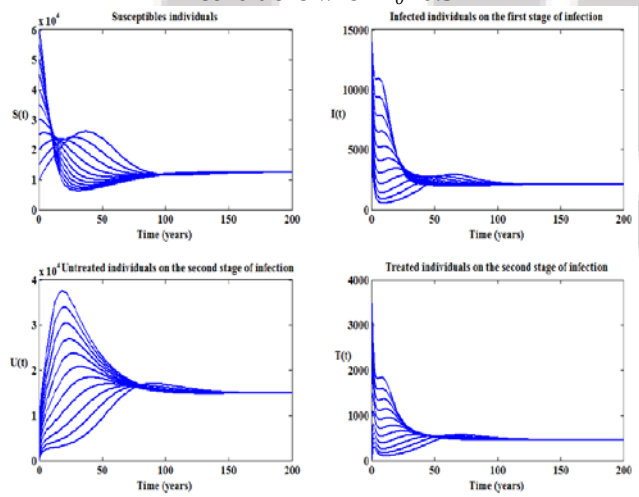

Figure 3: Trajectories of the system (3) for different initial conditions when $R_0 = 8$ and $p = 0.31$

6. Conclusion

In this paper we have carried out the global qualitative analysis of a realistic SIR model, which includes two infectious stages and treatment. The model allows, also, for infected individuals on the second stage to move from treated to untreated class and vice-versa. This model was studied theoretically, and it was found that the dynamic behavior of the model can be determined by its basic reproduction number R_0. When $R_0 < 1$, there exists no positive equilibrium and the disease free equilibrium is globally asymptotically stable. But when $R_0 > 1$, there exists a unique endemic equilibrium. Using a Lyapunov function, we have proved that the endemic equilibrium is globally asymptotically stable, under certain parameters restriction. The global stability of the disease free equilibrium state implies that for any initial condition, the disease will eventually dies out. While the global stability of endemic equilibrium implies that the disease will persist irrespective of the initial conditions. It is thus important to reduce the reproduction number to below 1 in order to control the epidemic. Numerical simulations were carried out using theatrical set of parameter to illustrate the analytical results.

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