Folia Mathematica
Vol. 20, No. 1, pp. 50–85
Acta Universitatis Lodziensis

SEIS MODEL WITH TREATMENT IN AN EXPONENTIALLY GROWING POPULATION

STANISLAS OUARO AND DÉSIRÉ OUEDRAOGO[‡]

Abstract. An SEIS deadly disease is introduced in an exponentially growing population. Without the treatment, three thresholds quantities R_0, R_1, R_2 determine the dynamic of the epidemic and that of the population. With the treatment, three other threshold quantities R_{0T}, R_{1T}, R_{2T} govern the dynamic of the epidemic and that of the population. We define the treatment effort and determine the critical treatment effort needed to prevent the disease to invade the population.

1. Introduction

Chronic diseases are responsible of most of the deaths in developed countries while infectious diseases are the first cause of deaths in developing countries. But, even in the developed countries, infectious diseases remain a serious threat due to the emergence of new diseases, the reemergence of old diseases and the immigrants coming from developing countries where diseases like tuberculosis are endemic.

Mathematical modelling of the dynamics of transmissible diseases is very useful, since it allows to understand and gives conditions to prevent and eradicate them. Most of mathematical epidemic models are compartmental. The population is divided in several compartments. Each compartment contains individuals with the same statue with respect to the disease. The number of compartments depends of the disease studied and the question in interest. Every model has at least the two following compartments. The compartment I of the infectious individuals who are infected and able to transmit the disease. The compartment S of the susceptible individuals who are not infected but can be infected through a contact with an infectious individual. Other compartments are the compartment E of the exposed or latent individuals who are infected but not yet able to transmit the disease;

[‡]*boratoire de Mathématiques et Informatique (LAMI),*
Département de Mathématiques, Unité de Formation et de Recherche en Sciences Exactes et Appliquées, Université Ouaga I Professeur Joseph Ki-Zerbo, 03 B.P.7021 Ouagadougou 03, Burkina Faso. E-mail: souaro@univ-ouaga.bf, ouaro@yahoo.fr.

Key words and phrases: SEIS model, threshold quantities, treatment effort, numerical simulations.

the compartment R of those who have a permanent or non-permanent immunity, the compartment M of infants born with passive and temporary immunity, transmitted by infected mothers; the compartment T of treated individuals or individuals under treatment. In [11] Mena-Lorca and Hethcote, studied the dynamic of SIRS epidemics with varying population sizes and found that the disease can play the role of regulator of the population. In [3] Castillo-Chavez and Sung studied tuberculosis models with treatment. Castillo and Feng studied in [4] a tuberculosis model with treatment in a population with a constant recruitment rate. Ssematimba *et al.* studied a tuberculosis model with treatment in [15]. In [8], Hui and Zhu studied the dynamics of SEIS epidemic models with varying population size and vertical transmission, assuming that all the offspring of the infected individuals are exposed. Meng et *al.* studied in [12] the dynamic of an SEIS model with treatment in a population with a constant recruitment rate. Zhang et *al.* studied an SEIS epidemic model with a general saturation incidence in a population with a constant recruitment rate [17]. In [10], A. Jabarri et *al.* studied a two-strain TB model with multiple latent stages. Zhang et *al.* studied a delayed SIV model with direct and environmental transmissions in [18]. In [13] Meng et *al.* studied the dynamics of a stochastic SIS model with double epidemic hypothesis. Yang et *al.* studied a diffusive within-host dynamics in [16].

The basic reproduction number R_0 is defined as the average number of secondary case generated by the introduction of one infectious individual in a fully susceptible population. For many epidemiological models, R_0 is the threshold quantity. If R_0 is less than one, then the disease cannot invade the population. Otherwise, the disease will invade and persist in the population. For epidemiology models with a disease free equilibrium, R_0 is the spectral radius of the next generation matrix [6, 5]. For models with closed population, the dynamic of the epidemic in term of the numbers of individuals and that in term of the proportions in the epidemiological classes are identical. But for epidemics with varying population size, the number of infected people could go to infinity even though the proportion of the infected goes to zero if the population grow faster than the epidemic. Furthermore, the proportions of the infected could remain positive, while the number of infected vanishes, if the population is decaying to zero. Thus, it is important when studying an epidemic in a population with varying size to consider the proportions and also the sizes of the epidemiological classes.

In this paper, we study an SEIS epidemic in a population that is growing exponentially without the disease. We consider a population with a birth rate b, and a death rate μ, such that $b > \mu$, that is the population is growing

exponentially with rate $b - \mu$. In this population, a mortal and non immunizing infectious disease is introduced. With the introduction of the disease, the population is divided in three classes: S, E and I. The class S contains susceptible individuals that is, those who are not infected but who can be infected through contact with an infectious. When there is an adequate contact of a susceptible with an infectious so that transmission occurs, then the susceptible enters the exposed class E of those in latent period, who are infected but not yet infectious. If the conditions are favorable for the development of the disease agent, the exposed individual become infectious, entering the class I. When the infectious period end, the individual become again susceptible, since the disease does not confer immunity. So, we have an endemic SEIS model. We assume that there is no vertical transmission that is all newborns are susceptible. This model fit with diseases like tuberculosis and gonorrhea. The disease induce an additional rate of death d in the class I. The population is homogeneously mixing with average contact rate c per unit time. The probability of the disease transmission during a contact between a susceptible and an infectious is β. Thus, the incidence is the standard form $c\beta SI/N$. With the treatment a fourth compartment T of the individuals under treatment is introduced. We assume that during the treatment, the treated person is not infectious. This assumption is justified because during the treatment, the action of the medicine can reduce the capacity of the disease agent and more, during the treatment, the person may be quarantined and then has no contact with the susceptible. The treatment rates of the latent and the infectious are respectively r_1 and r_2. A treated individual recover with the rate m, that is the average time of the treatment is $1/m$. The summary of the notations used in this paper is given in Table 1. Our treatment model is different from the treatment model studied by Castillo and Feng in [4, section 5] by the fact that, they assumed that T is the compartment of the individuals recovered by treatment. We consider first the model without treatment. Three threshold parameters R_0, R_1, R_2 determine the dynamic of the epidemic and the dynamic of the population. Further, we consider the model with treatment that is governed by three others threshold parameters R_{0T}, R_{1T}, R_{2T}. We define the treatment effort and determine the critical treatment effort as the minimal treatment effort required to prevent the disease to invade the population.

The rest of the paper is structured as follow. In Section 2, we consider the case where there is no treatment. Section 3 is dedicated to the study of the case were there is a treatment for the infectious and for the latent . In Section 4, we simulate some epidemics to illustrate the results of the previous sections. We end the paper in Section 5 by a conclusion and some perspectives.

N	The population size
S	Susceptible
E	Exposed people in the latent period
I	Infectious
T	People in treatment
s, e, i, τ	proportions of the population in the classes S,E,I,T
β	Probability of transmitting the disease in a contact
c	Contact rate
b	Birth rate
μ	Natural death rate
d	Disease induced death rate
k	Transfer rate from E to I
r_1	Treatment rate of the latent
r_2	Treatment rate of the infectious
δ	Natural recovering rate
m	Recovering rate of the treated
R_0	Basic reproduction number

Table 1. Summary of notations.

2. The model without treatment

In this section, we consider the SEIS model without treatment. The population is divided in three compartments S, E and I. The transfer diagram of the model is given by Figure 1. We introduce first, the model then, we consider the dynamic of the proportions and therefore study the asymptotic behavior of the sizes of the compartments and the population size.

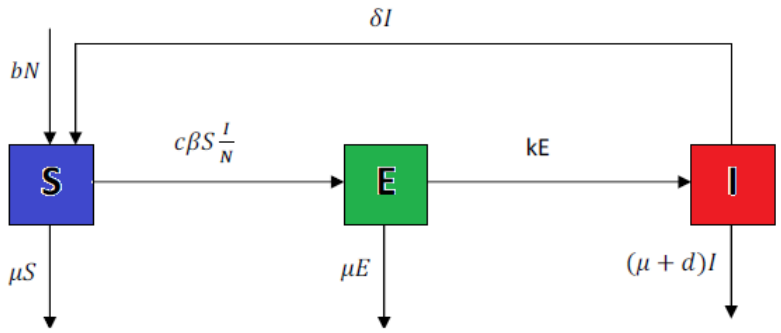


FIGURE 1. The transfer diagram of the SEIS model with the susceptible class S, the exposed class E and the infectious class I.

2.1. **The model.** Without treatment, we have an SEIS model given by the following system.

$$
(1) \qquad \begin{cases} \dfrac{dS}{dt} = bN + \delta I - c\beta S\dfrac{I}{N} - \mu S \\ \dfrac{dE}{dt} = c\beta S\dfrac{I}{N} - (k+\mu)E \\ \dfrac{dI}{dt} = kE - (\delta + \mu + d)I \\ N(t) = S(t) + E(t) + I(t) \\ S(0) \geq 0, E(0) \geq 0, I(0) \geq 0. \end{cases}
$$

From (1) we have : $dN/dt = (b-\mu)N - dI$. Since i is the proportion of the infectious ($i = I/N$), $dN/dt = (b - \mu - id)N$. Then the population will be increasing if $i < (b-\mu)/d$, and decreasing if $i > (b-\mu)/d$. Therefore if $(b-\mu)/d > 1$ (i.e $b > \mu + d$), then the population will always be increasing. System (1) has a trivial solution that is $(0, 0, 0)$. But this solution is not interesting because it is not relevant to consider an empty population. Further if we assume that $E(0) = I(0) = 0$, then $E(t) = I(t) = 0$ and $S(t) = N(t) = N(0)e^{(b-\mu)t}$, for all $t > 0$. Thus, System (1) does not admit a non trivial disease free equilibrium since we assume that $b > \mu$. Therefore, the next generation matrix (NGM) method (see [5, 6]) does not fit to derive its basic reproduction number R_0.

Theorem 1. *$N(t)$ is positive and constant ($N(t) = N(0) > 0, \forall t \geq 0$) if and only if the parameters satisfy*

$$kc\beta[db + \delta(b-\mu)] - (k+\mu)(\delta+\mu+d)[c\beta(b-\mu) + d\mu] = 0, \tag{2}$$

and the initial values verify

$$\begin{cases} S(0) = (kc\beta)^{-1}(k+\mu)(\delta+\mu+d)N_0, \\ E(0) = (kd)^{-1}(\delta+\mu+d)(b-\mu)N_0, \\ I(0) = d^{-1}(b-\mu)N_0, \\ \text{with } N_0 > 0. \end{cases} \tag{3}$$

Proof. By using successively the derivatives of N, I and E; N is constant if and only if I, E, S are constant with $I = d^{-1}(b-d)N$, $E = (kd)^{-1}(\delta + \mu + d)(b-\mu)N$ and $S = (kc\beta)^{-1}(k+\mu)(\delta+\mu+d)N$. By setting $dS/dt = 0$ and substituting S, E and I by their respective values in function of N, simplifying by N as it is assumed to be positive, and multiplying by $kc\beta d$, one gets Eq. (2) □

Generally, (2) and (3) are not satisfied, therefore $N(t)$ is not constant. Thus in the following, we assume that $N(t)$ is not constant.

2.2. **Study of the proportions.** We consider the proportions of individuals in the three compartments, $s = S/N$, $e = E/N$ and $i = I/N$. By System (1) and the derivative of N, we get the following system.

$$\begin{cases} \dfrac{ds}{dt} = b - bs + \delta i - (c\beta - d)si \\ \dfrac{de}{dt} = c\beta si - (b+k)e + dei \\ \dfrac{di}{dt} = ke - (b+\delta+d)i + di^2. \end{cases} \tag{4}$$

Remark 1. *The natural death rate μ is absent in System (4). It has no effect on the dynamic of the proportions since it is the same in all the three compartments.*

As $s+e+i=1$, by substituting s by $1-e-i$ in the derivative of e, one gets

$$\begin{cases} \frac{de}{dt} = -(b+k)e + c\beta i + (d-c\beta)ei - c\beta i^2, \\ \\ \frac{di}{dt} = ke - (b+\delta+d)i + di^2. \end{cases} \tag{5}$$

The suitable set is

$$D = \{(e,i)/e \geq 0, i \geq 0, e+i \leq 1\}. \tag{6}$$

Theorem 2. *The domain D is positively invariant for System (5).*

Proof. If $i(t)=0$ for a given time $t \geq 0$, then $\frac{di}{dt}(t) = ke(t) \geq 0$.
If $e(t)=0$ for a given time $t \geq 0$, then $\frac{de}{dt}(t) = c\beta s(t)i(t) \geq 0$.
If $e(t)+i(t)=1$ for a given time $t \geq 0$, then $\frac{d(e+i)}{dt}(t) = -b-\delta i(t) < 0$.
Thus no solution path starting in D, leaves D. □

The dynamic of System (5) is determined by the threshold quantity R_1 given by

$$R_1 = \frac{kc\beta}{(b+k)(b+\delta+d)}. \tag{7}$$

It is obvious that $(0,0)$ is the unique disease free equilibrium (DFE) of System (5).

Theorem 3. *The disease free equilibrium $(0,0)$ of System (5), is globally asymptotically stable (GAS) in D if $R_1 \leq 1$ and unstable if $R_1 > 1$.*

Proof of Theorem 3 (See Appendix A).

Theorem 4. *If $R_1 > 1$, then System (5) has a unique endemic equilibrium that is globally asymptotically stable in $D - \{(0,0)\}$.*

Proof of Theorem 4 (see Appendix B).

The dynamic of the proportions model is fully determined by the threshold quantity R_1. If R_1 is less or equal one, then the disease free equilibrium is globally asymptotically stable in the feasible region D. If $R_1 > 1$, then the disease free equilibrium is unstable and System (5) admits an a unique endemic equilibrium that is globally asymptotically stable in $D - \{(0,0)\}$. Biologically, this means that if R_1 is less or equal one, the disease cannot invade the population in term of proportions. But, if R_1 is greater than one, then the disease will remain endemic in the population. Due to the variation of the population size, the knowledge of the dynamic of the proportions

is not enough. Because the proportion of the infected may vanishes while the number of the infected goes to ∞, if the population size goes to ∞. In the other hand, the proportion of the infected individuals may remain positive with their number vanishing if the population vanishes. Thus in the following, we study the asymptotic behavior of $N(t), E(t), I(t)$ and $S(t)$.

2.3. **The asymptotic behavior of** $N(t), E(t), I(t), S(t)$**.** Now, we study the asymptotic behavior of the population size and that of the compartments. These behaviors are determined by the threshold parameters R_0 and R_2 given by

$$R_0 = \frac{kc\beta}{(k+\mu)(\mu+\delta+d)} \text{ and } R_2 = \frac{b}{\mu+di^*} \text{ if } R_1 > 1.$$

where i^* is the asymptotic proportion of the infectious individuals.

Remark 2. *R_0 is the product of the contact rate c, the probability of transmitting the disease during a contact between a susceptible and an infectious β, the average infectious period $1/(\mu+\delta+d)$, the probability for an exposed individual to become infectious $k/(k+\mu)$. Thus R_0 is basic reproduction number, that is the average number of secondary infections due to an infected individual during the infectious period, in a susceptible population.*

Theorem 5. *Let $(S(t), E(t), I(t))$ be a solution of System (1) with $N(0) > 0$.*

(1) *If $R_0 < 1$, then $(S(t), E(t), I(t)) \longrightarrow (\infty, 0, 0)$,*
(2) *if $R_0 = 1$, then $(S(t), E(t), I(t)) \longrightarrow (\infty, E^*, I^*)$,*
(3) *if $R_1 \leq 1 < R_0$, then $(S(t), E(t), I(t)) \longrightarrow (\infty, \infty, \infty)$,*
(4) *if $R_1 > 1$ and $R_2 > 1$ then $(S(t), E(t), I(t)) \longrightarrow (\infty, \infty, \infty)$,*
(5) *if $R_1 > 1$ and $R_2 = 1$ then $(S(t), E(t), I(t)) \longrightarrow (S^*, E^*, I^*)$,*
(6) *if $R_1 > 1$ and $R_2 < 1$ then $(S(t), E(t), I(t)) \longrightarrow (0, 0, 0)$.*

Proof of Theorem 5. See appendix C.

Remark 3. *If $R_1 > 1$, then R_2 is the asymptotic reproduction number of the population and $\alpha := b - \mu - di^*$ is its asymptotic exponential growth rate. An alternative way is to set $R_2 = (b-\mu)/di^*$ as in* [3] *or $R_2 = (b - di^*)/\mu$. The result will be the same, but R_2 will not get a biological interpretation.*

We have

$$R_0 = \frac{kc\beta}{(\mu+k)(\mu+\delta+d)} \text{ and } R_1 = \frac{kc\beta}{(b+k)(b+\delta+d)}.$$

Thus $R_1 < R_0$, since we assume that $b > \mu$. Therefore to prevent the invasion of the population by the disease one should focus on the basic reproduction number R_0.

In this section we have studied the dynamic of an SEIS epidemic introduced in a population with an exponentially growing size. The dynamic of the epidemic and that of the population is governed by three threshold quantities R_0, R_1 and R_2. If $R_0 < 1$, then the disease cannot invade the population. When $R_0 = 1$, the number of latent individuals and that of infectious individuals go to positive numbers, while the population keep on growing exponentially. If $R_1 \leq 1 < R_0$, then the number of infected individuals grow exponentially, but with a lower rate than the population growth rate, so that the proportion of infected individuals vanishes. When $R_1 > 1$, then the proportions go to an endemic equilibrium, and the dynamic of the population is determined by R_2. If $R_2 < 1$, then the population size goes to zero. If $R_2 = 1$, then the population stabilizes and if $R_2 > 1$, then the population grows exponentially but with a lower rate than its initial growth rate. The summary of the results of this section is given in Table 2.

R_1	R_2	R_0	$(N, S, E, I) \to$	$(s, e, i) \to$
≤ 1	> 1	< 1	$(\infty, \infty, 0, 0)$	$1, 0, 0$
≤ 1	> 1	$= 1$	$(\infty, \infty, E^*, I^*)$	$1, 0, 0$
≤ 1	> 1	> 1	$(\infty, \infty, \infty, \infty)$	$1, 0, 0$
> 1	< 1	> 1	$(0, 0, 0, 0)$	(s^*, e^*, i^*)
> 1	$= 1$	> 1	(N^*, S^*, E^*, I^*)	(s^*, e^*, i^*)
> 1	> 1	> 1	$(\infty, \infty, \infty, \infty)$	(s^*, e^*, i^*)

TABLE 2. Summary of results for the SEIS model

3. The model with treatment

Now we assume that there is a treatment for the latent and the infectious individuals. Hence we have a fourth compartment T of those in treatment. As for the preceding model, we present first the model, then we study the dynamic of the proportions and finish by studying the asymptotic behavior of the numbers.

3.1. **The model.** As in [3, 15] we consider an SEIS model with treatment for the latent and for the infectious individuals. But instead of considering T as the compartment of treated and healed individuals, we assume that it is the compartment of those in treatment. We assume that an individual in treatment is no more infectious and has not a disease related death rate. Since the recovery from the disease does not confer immunity, we assume that at the end of the treatment, the treated individual becomes susceptible, unless he dies during this period from other causes. We neglect death due to

the disease, for the treated individuals, and also transmission of the disease to susceptible by treated individuals. In the following, we shall refer to this model as the SEITS model. The transfer diagram of the SEITS model is given by Figure 2. With the treatment and the hypothesis above, the model

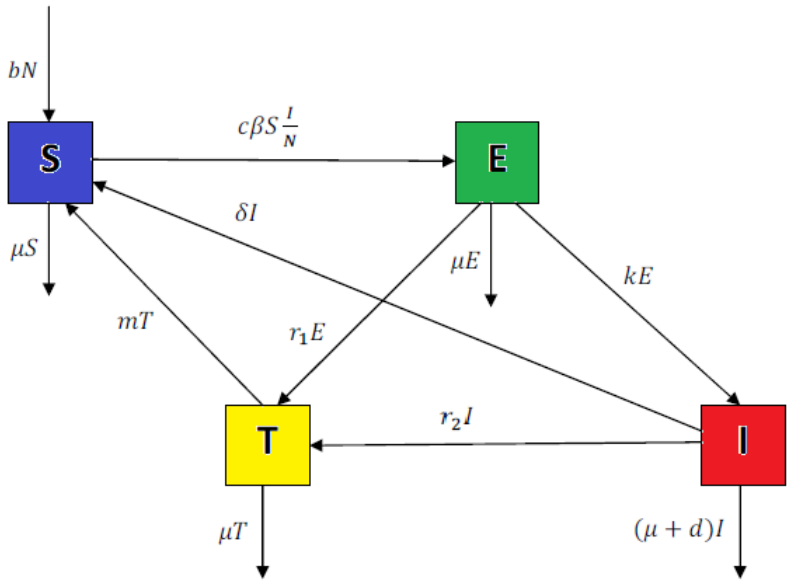


FIGURE 2. *The transfer diagram of the SEITS model with the susceptible class S, the exposed class E, the infectious class I, and the treatment class T.*

is given by the following system.

$$
(8)\qquad \begin{cases} \dfrac{dS}{dt} = bN + mT + \delta I - c\beta S\dfrac{I}{N} - \mu S, \\ \dfrac{dE}{dt} = c\beta S\dfrac{I}{N} - (k + r_1 + \mu)E, \\ \dfrac{dI}{dt} = kE - (r_2 + \delta + \mu + d)I, \\ \dfrac{dT}{dt} = r_1E + r_2I - (m + \mu)T = 0, \\ N = S + E + I + T, \\ S(0) \geq 0, E(0) \geq 0, I(0) \geq 0, T(0) \geq 0. \end{cases}
$$

By summing the four derivatives in (8), one gets

$$
(9)\qquad \frac{dN}{dt} = (b - \mu)N - dI
$$

Remark 4. *By setting $r_1 = \delta = 0$ and $T = R$, we get a model that is equivalent to an SEIRS model. Thus the SEITS model, studied here is more general than the SEIRS model.*

Theorem 6. *$N(t)$ is positive and constant ($N(t) = N(0) > 0, \forall t \geq 0$) if and only if the parameters satisfy the following equality :*

$$
(10)\qquad \begin{aligned} &(m + \mu)kc\beta[db + \delta(b - \mu)] + mc\beta[r_1(r_2 + \delta + \mu + d) + r_2k](b - \mu) \\ &\qquad -(m + \mu)(k + r_1 + \mu)(r_2 + \delta + \mu + d)[c\beta(b - \mu) + \mu d] = 0 \end{aligned}
$$

and the initial values satisfy

$$
(11)\qquad \begin{cases} S(0) = (kc\beta)^{-1}(k + r_1 + \mu)(r_2 + \delta + \mu + d)N_0, \\ E(0) = (kd)^{-1}(r_2 + \delta + \mu + d)(b - \mu)N_0, \\ I(0) = d^{-1}(b - \mu)N_0, \\ T(0) = (kd(m + \mu))^{-1}[r_1(r_2 + \delta + \mu + d) + r_2k](b - \mu)N_0, \\ \text{with } N_0 > 0. \end{cases}
$$

Proof. The proof of this theorem is similar to that of Theorem 1 mutatis mutandis. □

Remark 5. *If we set $r_1 = r_2 = m = 0$ in Eq. (10), then we retrieve Eq. (2)*

3.2. **Study of the proportions.** Let's consider the proportions in the epidemiological classes, $s = S/N, e = E/N, i = I/N, \tau = T/N$. By System 8 and Eq. 9, we get the following system.

$$\begin{cases} \frac{ds}{dt} = b + m\tau + \delta i - bs - (c\beta - d)si, \\ \frac{de}{dt} = c\beta si - (b + k + r_1)e + dei, \\ \frac{di}{dt} = ke - (b + \delta + r_2 + d)i + di^2, \\ \frac{d\tau}{dt} = r_1 e + r_2 i - (b + m)\tau + d\tau i. \end{cases} \tag{12}$$

As $s(t) + e(t) + i(t) + \tau(t) = 1$, by substituting τ by $1 - s - e - i$ in the derivative of s, we get

$$\begin{cases} \frac{ds}{dt} = b + m + (\delta - m)\, i - me - (b + m)s - (c\beta - d)si, \\ \frac{de}{dt} = c\beta si - (b + k + r_1)e + dei, \\ \frac{di}{dt} = ke - (b + \delta + r_2 + d)i + di^2. \end{cases} \tag{13}$$

The suitable set is

$$D_T = \{(s, e, i)/s \geq 0, e \geq 0, i \geq 0, s + e + i \leq 1\}.$$

Theorem 7. *The domain D_T is positively invariant for the System (13).*

Proof. The proof of Theorem 7 is similar to that of Theorem 2 □

If $e = i = 0$ then, $de/dt = di/dt = 0$ and $ds/dt = (b+m)(1-s)$. Therefore $(1, 0, 0)$ is the unique disease free equilibrium (DFE) of System (13).

The dynamic of System (13) is determined by the threshold quantity R_{1T} given by

$$R_{1T} = \frac{kc\beta}{(b + k + r_1)(b + \delta + r_2 + d)}. \tag{14}$$

Theorem 8. *The disease free equilibrium of System (13) is globally asymptotically stable in D_T when $R_{1T} \leq 1$ and unstable if $R_{1T} > 1$.*

Proof of Theorem 8 (See Appendix D).

The threshold parameter R_{1T} can be written as follow

$$\begin{aligned} R_{1T} &= \frac{kc\beta}{(b+r_1+k)(b+r_2+\delta+d)} \\ &= \frac{b+k}{b+r_1+k} \times \frac{b+\delta+d}{b+r_2+\delta+d} \times \frac{kc\beta}{(b+k)(b+\delta+d)} \\ &= (1-\tau_1^b)(1-\tau_2^b)R_1, \end{aligned}$$

with $\tau_1^b = r_1/(b+r_1+k)$ and $\tau_2^b = r_2/(b+r_2+\delta+d)$. by substituting b by μ in the expressions of τ_1^b and τ_2^b, one gets respectively the treated fraction among the latent individuals and the treated fraction among the infectious individuals. We define the pseudo treatment effort γ^b by

$$\gamma^b = 1 - \sqrt{(1-\tau_1^b)(1-\tau_2^b)}. \tag{15}$$

To prevent the disease to invade the population in term of the proportions, the pseudo treatment effort γ^b must be greater than the quantity $1-\sqrt{1/R_1}$.

When $R_{1T} > 1$ the disease free equilibrium is unstable. We did not show but the simulations results show that in this case there is an endemic equilibrium that is globally asymptotically stable (Figure 9). Therefore, we make the following conjecture.

Conjecture 1. *If $R_{1T} > 1$, then System (13) has one and only one endemic equilibrium, that is globally asymptotically stable in the interior of D_T.*

In this subsection we have studied the model with proportions of the SEITS model. Its dynamic is determined by the threshold quantity R_{1T}, given by Eq. (14). Then the disease free equilibrium is globally asymptotically stable in the feasible region, if $R_1 \leq 1$ and unstable if $R_{1T} > 1$. Biologically this means that the disease cannot invade the population in term of the proportions if $R_{1T} \leq 1$. While it will persist in the population if $R_{1T} > 1$.

3.3. **Asymptotic behavior of $N(t), S(t), E(t), I(t)$ and $T(t)$.** Now, we study the asymptotic behavior of the population size $N(t)$, and that of the compartments. That behaviors are determined by the threshold parameters R_{0T} and R_{2T} given by

$$R_{0T} = \frac{kc\beta}{(k+r_1+\mu)(\mu+r_2+\delta+d)} \text{ and } R_{2T} = \frac{b}{\mu+di_T^*},$$

where i_T^* is the asymptotic positive infectious proportion when it exists.

Remark 6. *R_{0T} is the product of the contact rate c, the probability of transmitting the disease during a contact between a susceptible and an infectious β, the average infectious period $1/(\mu+r_2+\delta+d)$, and the probability for*

R_{1T}	R_{0T}	$N, S, E, I, T \to$	$s, e, i, \tau \to$
≤ 1	< 1	$\infty, \infty, 0, 0, 0$	$1, 0, 0, 0$
≤ 1	$= 1$	$\infty, \infty, E^*, I^*, T^*$	$1, 0, 0, 0$
≤ 1	> 1	$\infty, \infty, \infty, \infty, \infty$	$1, 0, 0, 0$

TABLE 3. Summary of the results for the SEIS model with treatment when $R_{1T} \leq 1$.

an exposed individual to become infectious $k/(k + r_1 + \mu)$. Thus, R_{0T} is the average number of secondary infections due to an infectious during the infectious period, in a susceptible population.

Theorem 9. *Let $(S(t), E(t), I(t), T(t))$ be a solution of System (8).*

(1) *If $R_{0T} < 1$, then $(S(t), E(t), I(t), T(t)) \longrightarrow (\infty, 0, 0, 0)$,*
(2) *if $R_{0T} = 1$, then $(S(t), E(t), I(t), T(t)) \longrightarrow (\infty, E^*, I^*, T^*)$,*
(3) *if $R_{1T} \leq 1 < R_{0T}$, then $S(t), (E(t), I(t), T(t)) \longrightarrow (\infty, \infty, \infty, \infty)$.*

The threshold parameter R_{0T} can be written as follow

$$\begin{aligned} R_{0T} &= \frac{kc\beta}{(\mu + k + r_1)(\mu + \delta + r_2 + d)}, \\ &= \frac{(\mu + k)}{(\mu + k + r_1)} \times \frac{(\mu + \delta + d)}{(\mu + \delta + r_2 + d)} \times \frac{kc\beta}{(\mu + k)(\mu + \delta + d)}, \\ &= (1 - \tau_e)(1 - \tau_i)R_0, \end{aligned}$$

where τ_e and τ_i are respectively the proportion of the treated individuals among the latent and the proportion of the treated individuals among the infectious. We define the treatment effort by $\gamma = 1 - \sqrt{(1 - \tau_e)(1 - \tau_i)}$. $R_{0T} < 1 \iff \sqrt{(1 - \tau_e)(1 - \tau_i)} < \sqrt{1/R_0}$, then to prevent the disease to invade the population, the geometric mean of the proportions of the untreated among the latent and the infectious individuals must be less than $\sqrt{1/R_0}$, equivalently, the treatment effort γ must be greater than $1 - \sqrt{1/R_0}$. Let's set γ_c the critical treatment effort, the minimal treatment effort needed to prevent the invasion of the population by the disease. We have

$$\gamma_c = \begin{cases} 0, \text{ if } R_0 \leq 1, \\ 1 - \sqrt{1/R_0}, \text{ if } R_0 > 1. \end{cases}$$

Theorem 10. *let's assume that System (13) has a unique endemic equilibrium (s_T^*, e_T^*, i_T^*), that is globally asymptotically stable in $\overset{o}{D}_T$ and, set $R_{2T} = b/(\mu - di_T^*)$.*

(1) *if $R_{2T} > 1$, then $(S, E, I, T) \longrightarrow (\infty, \infty, \infty, \infty)$,*

(2) *if* $R_{2T} = 1$ *, then* $(S, E, I, T) \longrightarrow (S^*, E^*, I^*, T^*)$,
(3) *if* $R_{2T} < 1$ *, then* $(S, E, I, T) \longrightarrow (0, 0, 0, 0)$.

Proof. Let's assume that System (13) has an endemic equilibrium (s_T^*, e_T^*, i_T^*) that is globally asymptotically stable in $\overset{o}{D}_T$. Then,

$$\frac{dN}{dt} \longrightarrow (b - \mu - di_T^*)N \text{ when } t \longrightarrow \infty.$$

Set $\alpha_{2T} = b - \mu - di_T^*$ and $R_{2T} = b/(\mu - di_T^*)$. Thus, the asymptotic exponential growth rate of the population size $N(t)$ is α_T , its asymptotic reproduction number is R_{2T} and we have the sign relation $sign(\alpha_T) = sign(R_{2T} - 1)$. Thus, the result follows. □

In this section, we have studied the dynamic of an SEIS disease introduced in a population that was initially growing exponentially, assuming that there is a treatment for latent individuals and infectious individuals. As for the model without treatment, the dynamic of the SEIST model is determined by three threshold quantities, R_{0T}, R_{1T} and R_{2T}. We have defined the treatment effort γ and the critical treatment effort γ_c. To prevent the disease to invade the population the treatment effort, must be larger than the quantity $1 - \sqrt{1/R_0}$.

4. Simulations

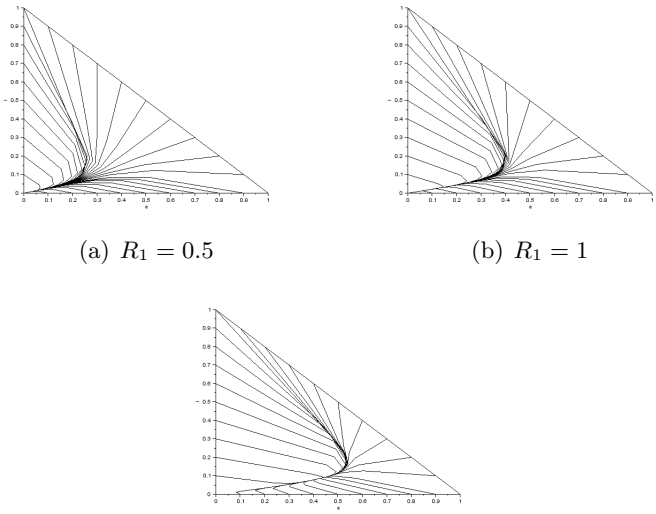
In this section, we illustrate the dynamics of the previous systems by numerical simulations. We set $\mu = 1$, that is the time unit is the life expectancy. We choose arbitrary the other parameters values to cover the different scenarios given by the theoretical results.

4.1. **Simulations of the model without treatment.**

We simulate first the model without treatment to validate the results of Section 2.
Figure 3 shows phase portraits for system (5). When $R_1 = 0.5$ or $R_1 = 1$, the disease free equilibrium $(0, 0)$ is globally asymptotically stable in the feasible region D. For $R_1 = 2$, the disease free equilibrium is unstable and there is an endemic equilibrium that is globally asymptotically stable in $D - \{(0, 0)\}$. These simulations confirm Theorems 3 and 4.

In Figure 4, the proportions go to an endemic equilibrium, while the sizes of all the compartments grow exponentially, but with a lower rate than the initial growth rate of the population.

In Figure 5, the proportions go to an endemic equilibrium and the sizes also go to an endemic equilibrium. The disease has stopped the growth of the population. The parameters verify Equality (2).



(a) $R_1 = 0.5$ (b) $R_1 = 1$

(c) $R_1 = 2$

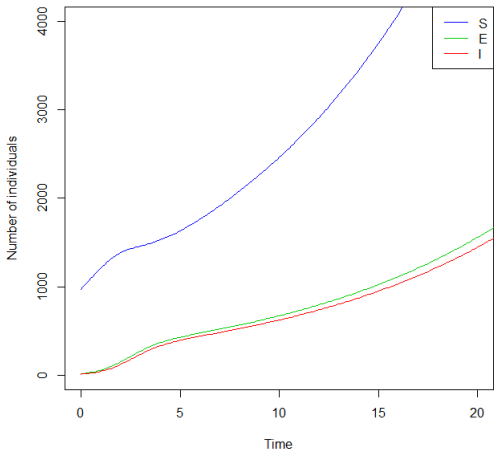
FIGURE 3. Phase plane portraits for the system (5) with different values of R_1. For all cases $b = 4, k = 2, \delta = 4, d = 2$; for (a) $c\beta = 15$, for (b) $c\beta = 30$ and $c\beta = 60$ for (c), that gives respectively $R_1 = 0.5$, $R_1 = 1$ and $R_1 = 2$.

In Figure 6, we have the worst case scenario. The disease turned the exponential growth of the population to an exponential decay. The population vanishes and the disease with. But the proportions go to an endemic equilibrium.

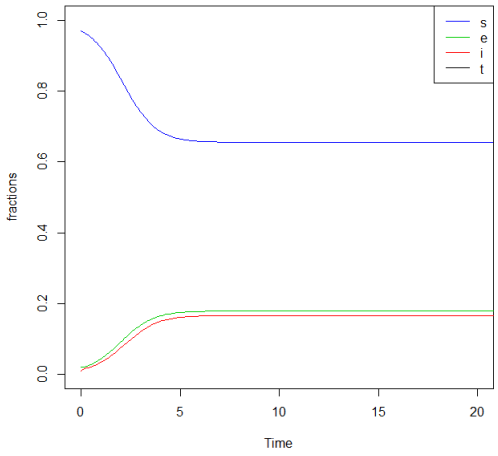
We have simulated different scenarios of the SEIS model without treatment. The findings confirm the results that we have in Section 2.

4.2. **Simulations for the model with treatment.** Now we simulate some SEITS epidemics using different values of the parameters to cover the different cases that we have in Section 3. We start by simulating a situation where the conditions in Theorem 8 hold. We have solution with constant population size in Figure 7. In Figure 8 we have the solutions paths of System (12) with different initial values. This simulations confirm that if $R_{1T} \leq 1$ then the disease free equilibrium is globally asymptotically stable in D_T, confirming Theorem 8.

In Figure 9, we have two cases where R_{1T} is greater than 1, in each case all the solutions approach the same endemic equilibrium. Showing that the disease free equilibrium is unstable and that there is an endemic equilibrium

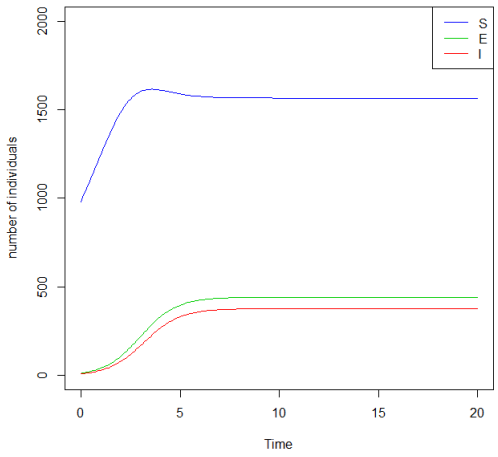


(a) Numbers

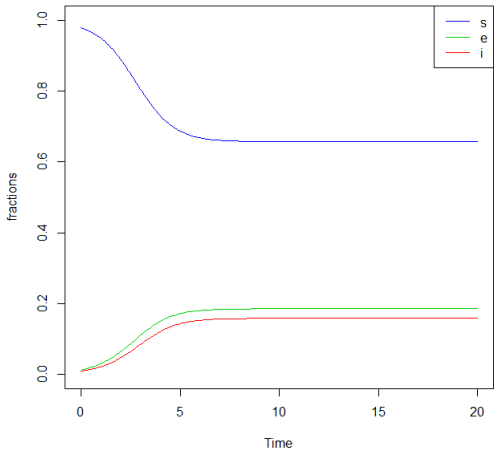


(b) proportions

FIGURE 4. SEIS curves with $b = 1.3, \mu = 1, c\beta = 10, k = 5, d = 1.3, \delta = 3$ that gives $R_1 = 1.417, R_0 = 1.572, i^* = 0.1660424, \alpha_T = 0.084, R_2 = 1.069$, where the initial values are $(S(0), E(0), I(0)) = (970, 20, 10)$. The proportions approach an endemic equilibrium, while the sizes grow exponentially.

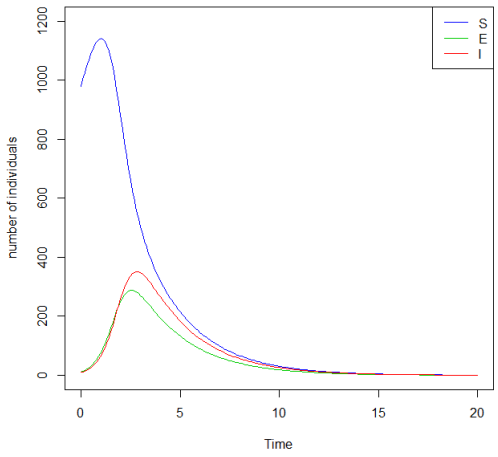


(a) Numbers

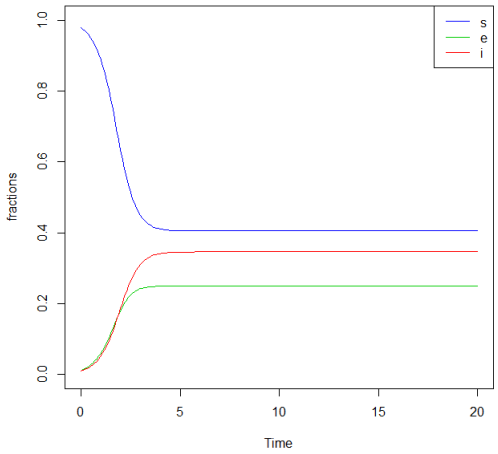


(b) proportions

FIGURE 5. SEIS curves with $b = 1.3, \mu = 1, c\beta = 10, k = 4.609756, d = 1.9, \delta = 2.5$ that gives $R_1 = 1.368, R_0 = 1.522, i^* = 0.158, \alpha_T = 0, R_2 = 1$, where the initial values are $(S(0), E(0), I(0)) = (980, 10, 10)$. The sizes of all the compartments stabilize.



(a) Numbers



(b) proportions

FIGURE 6. SEIS curves with $b = 1.3, \mu = 1, c\beta = 10, k = 5, d = 2, \delta = 1$ that gives $R_1 = 1.846, R_0 = 2.083, i^* = 0.346, \alpha_T = -0.391, R_2 = 0.769$, where the initial values are $(S(0), E(0), I(0)) = (980, 10, 10)$. The fractions approach an endemic equilibrium, while the population vanishes.

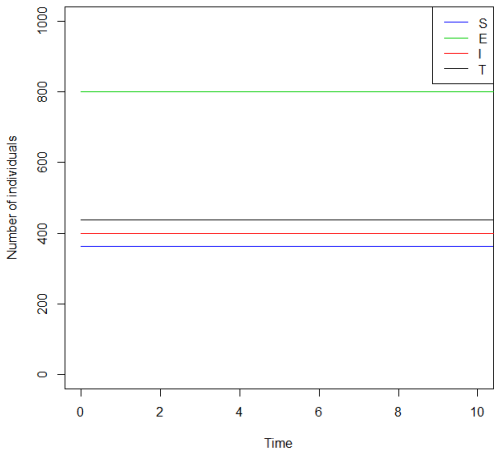


FIGURE 7. SEIST curves with $b = 3, \mu = 1, c\beta = 154, k = 10, d = 10, \delta = 3, r_1 = 3, r_2 = 6, m = 10$, the parameters and the initial values are chosen such that the equalities in Theorem 6 are verified.

that is globally asymptotically stable in the interior of the feasible region. The endemic equilibrium in (a) is different to that in (b), hence the endemic equilibrium depends on the parameters values. This simulations confirms conjecture 1.

In Figure 10, we have $R_{0T} < 1$. Then, the number of the infected individuals goes to zero and the population keep on growing exponentially.

In Figure 11, we have $R_{1T} < 1$ and $R_{0T} = 1$, the population keep on growing exponentially while the numbers of the latent, of the infectious and of the treated go to positive values. In term of the proportions, the epidemic dies out. But in term of the numbers, the disease is endemic, although rare in population.

In Figure 12, we have the situation where $R_{2T} > 1$. All the compartments grow exponentially but with a lower rate than the initial growth rate of the population. The epidemic has slowed the growth of the population.

For Figure 13, the parameters are chosen such that Eq. (10) is verified. The epidemic has stopped the growth of the population. In this case, we get $R_{2T} = 1$.

In Figure 14, we have the worst situation. In spite of the treatment, the disease induced death rate turned the population exponential growth to an exponential decay.

The simulations of the SEITS model, studied in Section 3 confirm the theoretical results. If the parameters and the initial values verify the hypotheses of Theorem 6, then $S(t), E(t), I(t), T(t)$ are constant (Figure 7). For the proportions, if $R_{1T} \leq 1$, then the disease free equilibrium is globally asymptotically stable (Figure 8); if $R_{1T} > 1$, then the disease free equilibrium is unstable and there is an endemic equilibrium that is globally asymptotically stable in the interior of the feasible region (Figure 9). If $R_{0T} < 1$, then the number of the infected individuals go to zero (Figure 10). If $R_{0T} = 1$, the number of the infected individuals goes to a positive and finite number, while the population size goes to infinity (Figure 11). If $R_{1T} \leq 1 < R_{0T}$, then the infected compartments grow exponentially, but with a lower rate than that of the population (Figure 12). If $R_{1T} > 1$, then at the beginning of the epidemic, the number of the infected grows exponentially with a rate that is greater than the population growth rate. In this case, the asymptotic behavior of the population depends on the threshold quantity R_{2T}. If $R_{2T} > 1$, then all the compartments grow asymptotically exponentially with a lower rate than the initial growth rate of the population (Figure 12). If $R_{2T} = 1$, then the population stabilizes (Figure 13). If $R_{2T} < 1$, then the population vanishes (Figure 14).

5. Conclusion

We have studied the dynamic of an infectious disease with latent period which does not confer immunity at recovery, in a population that initially grows exponentially. We considered first the model without treatment. Thus, we studied the model with treatment for the exposed and for the infectious. Therefore we validated the theoretical results by numerical simulations.

For the model without treatment, three thresholds quantities R_0, R_1, R_2 govern the asymptotic behavior of the disease and that of the population. If $R_0 < 1$ then the disease cannot invade the population ($(E, I) \longrightarrow (0, 0)$) and the population keep on growing exponentially. If $R_1 \leq 1 < R_0$, then the number of the infected grow exponentially but with a lower rate than that of the population, hence the proportion of the infected vanishes. If $R_1 > 1$, then the number of the infected grow initially quickly than the population, and three scenarios are possible. i) The population keep on growing exponentially and the epidemic with, but with a lower rate; ii) The population stabilizes; iii) the population vanishes. Therefore, when studying the dynamic of an infectious disease in a population with varying

population size, it is not enough to control the proportion of the infected individuals in the population. It is important to study also the dynamic of the number of the infected individuals.

For the model with treatment, its dynamic is similar to that of the model without treatment with the thresholds quantities R_{0T}, R_{1T} and R_{2T}. The treatment can prevent the disease to invade the population if its effort is large enough. In order to perform this, the treatment effort must be greater than $1 - \sqrt{1/R_0}$. Unless, the number of individuals in treatment can grow exponentially with the population. That is not realistic because the capacity of the hospitals, and the availability of the drugs are often limited. The treatment effort is a symmetric function of the proportions treated among the latent and among the infectious. Thus, treating the infectious or the exposed will have the same effect. But it depends on the respective numbers of exposed individuals and infectious individuals. For tuberculosis for instance, it is known that one third of the world population is contaminated but few $(5 - 10\%)$ of the infected will become infectious (see [7]). Thus, to have the same proportion of the infectious and the latent, the corresponding number of the latent will be at least ten times the number of the infectious. Hence, the treatment effort should be focused on the infectious.

For both models, we found that the epidemic can slow down, stop or turn the exponential growth of the population to an exponential decay. That is the disease can play the role of regulator of the population. The size of the susceptible compartment has the same asymptotic behavior than that of the population size in all the cases. That is understandable since in the model, all the new born are susceptible.

One perspective is to show the existence, the uniqueness and the global stability of an endemic equilibrium, when $R_{1T} > 1$. Another one is to consider multiple latent stages (see [10]), since it is known that for tuberculosis, the risk to become infectious is not the same for a the latent individuals. In fact the majority of the infectious, develops TB disease that is become infectious, within the first five years after initial infection (see [7]).

Appendix A. Proof of Theorem 3

Proof. Let $f(e, i)$ be the RHS of System (5). The Jacobian of f at the disease free equilibrium is

$$Df(0,0) = \begin{pmatrix} -(b+k) & c\beta \\ k & -(b+\delta+d) \end{pmatrix}.$$

The characteristic polynomial of the Jacobian above is

$$P(x) = x^2 + (2b + k + \delta + d)x + (b + k)(b + \delta + d) - kc\beta.$$

By the Routh-Hurwitz criterion (see [14, page 11]), all the roots of $P(x)$ have negative real parts if and only if $(b+k)(b+\delta+d)-kc\beta>0$. Note that $(b+k)(b+\delta+d)-kc\beta>0$ if and only if $R_1<1$. Thus by the Poincaré-Lyapunov theorem of linearization, the disease free equilibrium $(0,0)$ is locally asymptotically stable (LAS) if $R_1<1$ and unstable when $R_1>1$. For the global stability, let us consider the function L defined on D by $L(e,i)=ke+(b+k)i$.

$$\begin{aligned}\dot{L}\,(e,i) &= k[c\beta(1-e-i)i-(b+k-di)e]+(b+k)[ke-(b+\delta+d-di)i]\\ &= i[kc\beta-(b+k)(b+\delta+d)+(kd-kc\beta)e+((b+k)d-kc\beta)i]\\ &= iH(e,i)\end{aligned}$$

with $H(e,i)=kc\beta-(b+k)(b+\delta+d)+k(d-c\beta)e+((b+k)d-kc\beta)i$.
As H is affine, its maximum in the closed set D is achieved in the extremal points of the boundary of D. The values of H at these points are $H(0,1)=-(b+k)(b+\delta)$,
$H(1,0)=-[(b+k)(b+\delta)+bd]$ and $H(0,0)=(b+k)(b+\delta+d)(R_1-1)$. Then, $max(H)\leq 0$ if $R_1\leq 1$. Thus, $\dot{L}\leq 0$ when $R_1\leq 1$. Therefore, L is a Lyapunov function for System (5). The set where $\dot{V}=0$ is the face of D with $i=0$, but if $i=0$ then $di/dt=ke$, so that i leaves this face unless $e=0$. Thus $\{(0,0)\}$ is the only positively invariant subset of the set with $\dot{L}=0$. It follows from the Lasalle Invariance Principle (see [9, p. 200]) that, all paths in D approach the origin. Then the disease free equilibrium is globally asymptotically stable in D when $R_1\leq 1$. □

Appendix B. Proof of Theorem 4

Proof. If $R_1\leq 1$, the disease free equilibrium is globally asymptotically stable in D, that precludes the existence of an endemic equilibrium. let's assume that $R_1>1$. At an equilibrium, we have

$$-(b+k)e+c\beta i+(d-c\beta)ei-c\beta i^2=0, \tag{16}$$

$$-(b+\delta+d)i+ke+di^2=0. \tag{17}$$

The Eq. (16) is equivalent to $ke=(b+\delta+d-di)i$. Multiplying Eq. (17) by k, substituting ke by $(b+\delta+d-di)i$, simplifying by i (as we are looking for an endemic equilibrium), developing and reducing, one gets

$$kc\beta-(b+k)(b+\delta+d)-[(c\beta-d)(b+k+\delta+d)-bd]i+d(c\beta-d)i^2=0.$$

Then, (s^*,e^*,i^*) is an endemic equilibrium of (4) if and only if i^* is a root in $(0,1)$ of the polynomial

$$p(x)=kc\beta-(b+k)(b+\delta+d)-[(c\beta-d)(b+k+\delta+d)-bd]x+d(c\beta-d)x^2$$

and $e^* = k^{-1}(b+\delta+d-di^*)i^*$; $s^* = (kc\beta)^{-1}(b+k-di^*)(b+\delta+d-di^*)$. As $p(x)$ is a second degree polynomial, then $p(x)$ has one and only one root in $(0,1)$ if and only if $p(0)p(1)<0$.
We have

$$p(0) = kc\beta - (b+k)(b+\delta+d) = (b+k)(b+\delta+d)(R_0-1) > 0 \text{ as } R_1 > 1;$$
$$p(1) = -(b+k+c\beta-d)(b+\delta).$$

Thus $p(0)p(1)<0$ if and only if $b+k+c\beta-d>0$. But

$$\begin{aligned} R_1 > 1 &\Leftrightarrow kc\beta > (b+k)(k+\delta+d) \\ &\Leftrightarrow kc\beta > k(b+k+\delta+d)+b(\delta+d) \\ &\Rightarrow kc\beta > k(b+k+\delta+d) \\ &\Rightarrow c\beta > b+k+\delta+d \\ &\Rightarrow c\beta > d \\ &\Rightarrow b+k+c\beta-d>0 \end{aligned}$$

Then if $R_1>1$, $p(x)$ has one and only one root in $(0,1)$. let i^* be this root and set
$e^* = k^{-1}(b+\delta+d-di^*)i^*$, $s^* = (kc\beta)^{-1}(b+k-di^*)(b+\delta+d-di^*)$. We have $s^*+e^*+i^*=1$ and $e^*>0$. To show that $s^*>0$, note first that $s^*>0 \Leftrightarrow b+k-di^*>0$. We have $p(\frac{b+k}{d}) = -c\beta(\delta k+\delta b+db)<0$. This imply that $\frac{b+k}{d} > i^*$. Then, (5) has a unique endemic equilibrium. By Theorem 3, the disease free equilibrium is unstable in D as $R_1>1$. Busenberg and van den Driessche have shown that System (5) has no periodic solution [1, 2]. Thus by the Poincaré- Bendixson Theorem, the unique endemic equilibrium is globally asymptotically stable in $D-\{(0,0)\}$. □

Appendix C. Proof of Theorem 5

Proof.

Lemma 1. *If $R_1 \le 1$, then*

$$\frac{E}{I} \longrightarrow \frac{\delta+d-k+\sqrt{\Delta}}{2k}, \text{ when } t \longrightarrow \infty, \text{ with } \Delta = (\delta+d-k)^2+4kc\beta.$$

Proof.

$$\left(\frac{E}{I}\right)' = \frac{E'I-I'E}{I^2} = c\beta s + (\delta+d-k)\frac{E}{I} - k\left(\frac{E}{I}\right)^2.$$

Then, if $R_1 \leq 1$,

$$\left(\frac{E}{I}\right)' \longrightarrow c\beta + (\delta + d - k)\frac{E}{I} - k\left(\frac{E}{I}\right)^2, \text{ when } t \longrightarrow \infty.$$

$$y' = c\beta + (\delta + d - k)y - ky^2 \tag{18}$$

is a Riccati's equation. Its solution is

$$y : t \longmapsto \left(Ce^{\sqrt{\Delta}t} - \frac{k}{\sqrt{\Delta}}\right)^{-1} + \frac{\delta + d - k + \sqrt{\Delta}}{2k}, \text{ with } C > 0 \text{ and } \Delta = (\delta + d - k)^2 + 4kc\beta.$$

Then,

$$\frac{E}{I} \longrightarrow \frac{\delta + d - k + \sqrt{\Delta}}{2k}, \text{ when } t \longrightarrow \infty.$$

□

We have $R_1 = kc\beta/(b + k)(b + \delta + d)$ and $R_0 = kc\beta/(\mu + k)(\mu + \delta + d)$, with $b > \mu$. Thus $R_1 < R_0$.

Let's assume first that $R_1 \leq 1$. Then, the disease free equilibrium of the model with proportions, is globally asymptotically stable in its feasible region, that is $(s, e, i) \longrightarrow (1, 0, 0)$. $dN/dt \longrightarrow (b - \mu)N$, thus $N \longrightarrow \infty$, since $b > \mu$. Therefore $S \longrightarrow \infty$, since $s \longrightarrow 1$.

$$\frac{dI}{dt} = kE - (\mu + \delta + d)I = \left[k\frac{E}{I} - (\mu + \delta + d)\right] I.$$

As $R_1 \leq 1$, by Lemma 1,

$$\frac{E}{I} \longrightarrow \frac{\delta + d - k + \sqrt{\Delta}}{2k}, \text{ when } t \longrightarrow \infty, \text{ with } \Delta = (\delta + d - k)^2 + 4kc\beta.$$

Therefore,

$$\frac{dI}{dt} \longrightarrow \left[\frac{\delta + d - k + \sqrt{\Delta}}{2} - (\mu + \delta + d)\right] I = \alpha I,$$

with $\alpha = (\sqrt{\Delta} - k - \delta - d - 2\mu)/2$.
As $S/N \longrightarrow 1$, $E/I \longrightarrow (\delta + d - k + \sqrt{\Delta})/2k$, by using the derivative of E, we get $dE/dt \longrightarrow \alpha E$. Thus, α is the common asymptotic exponential growth rate of the infected compartments E and I when R_1 is less than one.

We have

$$\begin{aligned}\alpha \geq 0 &\Longleftrightarrow \delta + d - k + \sqrt{\Delta} \geq 2(\mu + \delta + d)\\ &\Longleftrightarrow \sqrt{\Delta} \geq 2\mu + \delta + d + k\\ &\Longleftrightarrow \Delta \geq (2\mu + \delta + d + k)^2\\ &\Longleftrightarrow 4kc\beta \geq (2\mu + \delta + d + k)^2 - (\delta + d - k)^2\\ &\Longleftrightarrow kc\beta \geq (k + \mu)(\mu + \delta + d)\\ &\Longleftrightarrow R_0 \geq 1.\end{aligned}$$

Thus it follows the sign relation $sign(R_0 - 1) = sign(\alpha)$.
Therefore, $(E, I) \longrightarrow (0, 0)$ when $R_0 < 1$, $(E, I) \longrightarrow (E^*, I^*)$ when $R_0 = 1$ and
$(E, I) \longrightarrow (\infty, \infty)$ when $R_1 \leq 1 < R_0$.

Let's assume now that $R_1 > 1$. Then, the system with proportions admits a unique endemic equilibrium (s^*, e^*, i^*) that is globally asymptotically stable. Therefore, all the compartments have the same asymptotic behavior than that of the population size N. We have
$dN/dt = (b - \mu - di)N$. Then, $dN/dt \to (\mu + di^*)(R_2 - 1)N$. Therefore, $N(t) \to 0$ if $R_2 < 1$, $N(t) \to N^* > 0$ if $R_2 = 1$ and $N(t) \to \infty$ when $R_2 > 1$. □

Appendix D. Proof of Theorem 8

Proof. Let $g(e, s, i)$ be Rhs of System (13). The Jacobian of g at the disease free equilibrium is

$$Dg(1, 0, 0) = \begin{pmatrix} -m - b & -m & -m + \delta - c\beta + d \\ 0 & -(b + k + r_1) & c\beta \\ 0 & k & -(b + \delta + r_2 + d) \end{pmatrix}.$$

The characteristic polynomial of $Dg(1, 0, 0)$ is

$$U(x) = (-m-b-x)\left[x^2 + (2b + k + r_1 + r_2 + \delta + d)x + (b + k + r_1)(b + \delta + r_2 + d) - kc\beta\right].$$

It is obvious that $-(m+b)$ is a negative root of $U(x)$. By the Routh-Hurwitz criterion [14, page 11], all the roots of $U(x)$ have negative real parts if and only if $(b + k + r_1)(b + \delta + r_2 + d) - kc\beta > 0$. Note that

$$(b + k + r_1)(b + \delta + r_2 + d) - kc\beta > 0 \Longleftrightarrow R_{1T} < 1.$$

Thus, by the Poincaré-Lyapunov linearization Theorem, the disease free equilibrium $(1, 0, 0)$ is locally asymptotically stable (LAS) if $R_{1T} < 1$ and unstable when $R_{1T} > 1$. To show that the disease free equilibrium is globally

asymptotically stable in D_T when $R_{1T} \leq 1$, let's consider the function V defined by $V(s,e,i) = ke + (b+k+r_1)i$.

$$\begin{aligned}\dot{V}(s,e,i) &= k\frac{de}{dt} + (b+k+r_1)\frac{di}{dt} \\ &= k[c\beta si - (b+k+r_1-di)\,e] + (b+k+r_1)[ke - (b+\delta+r_2+d-di)\,i] \\ &= i[kc\beta s - (b+k+r_1)(b+\delta+r_2+d) + kde + (b+k+r_1)di] \\ &= iW(s,e,i),\end{aligned}$$

with $W(s,e,i) = kc\beta s - (b+k+r_1)(b+\delta+r_2+d) + kde + (b+k+r_1)di$. The affinity of W implies that it achieves its maximum in the extremal points of the boundary of D_T, and, we have

$$\begin{aligned}W(0,0,0) &= -(b+k+r_1)(b+\delta+r_2+d), \\ W(1,0,0) &= (b+k+r_1)(b+\delta+r_2+d)(R_{1T}-1), \\ W(0,1,0) &= -[(b+k+r_1)(b+\delta+r_2) + (r_1+b)d], \\ W(0,0,1) &= -(b+k+r_1)(b+\delta+r_2).\end{aligned}$$

Then, $max(W) \leq 0$ if $R_{1T} \leq 1$. Thus $\dot{V} \leq 0$ when $R_{1T} \leq 1$. Therefore, V is a Lyapunov function. Furthermore, $\{(1,0,0)\}$ is the only positively invariant subset of the set with $\dot{V} = 0$. It follows from LaSalle invariance principle [9, p. 200], that the disease free equilibrium is globally asymptotically stable in D_T when $R_{1T} \leq 1$. □

Appendix E. Proof of Theorem 9

Proof.

Lemma 2. *If $R_{1T} \leq 1$, then*

$\frac{E}{I} \longrightarrow \frac{\delta+d+r_2-k-r_1+\sqrt{\Delta_T}}{2k}$, *when* $t \longrightarrow \infty$, *with* $\Delta_T = (\delta+d+r_2-k-r_1)^2+4kc\beta$.

Proof. The proof of Lemma 2 is similar to that of Lemma 1. □

$dN/dt = (b-\mu-di)N$ and $i \longrightarrow 0$, when $R_{1T} \leq 1$. Then $dN/dt \longrightarrow (b-\mu)N$, when $t \longrightarrow \infty$. Therefore, $N(t) \longrightarrow \infty$ since we assume that $b > \mu$.

$$\begin{aligned}\frac{dI}{dt} &= kE - (\mu+r_2+\delta+d)I \\ &= \left[k\frac{E}{I} - (\mu+r_2+\delta+d)\right]I.\end{aligned}$$

Thus, by applying Lemma 2 one gets

$$\frac{dI}{dt} \longrightarrow \left[\frac{\delta + d + r_2 - k - r_1 + \sqrt{\Delta_T}}{2} - (\mu + r_2 + \delta + d)\right] I = \alpha_T I,$$

with

$$\alpha_T = \frac{\sqrt{\Delta_T} - 2\mu - \delta - r_2 - d - k - r_1}{2}.$$

As $dE/dt = c\beta\frac{S}{N}I - (k + r_1 + \mu)E, S/N \longrightarrow 1$ and $E/I \longrightarrow (\delta + d + r_2 - k - r_1 + \sqrt{\Delta_T})/2k$ when $t \longrightarrow \infty$, one gets also that $dE/dt \longrightarrow \alpha_T E$. Then, the infected compartments E and I have the same asymptotic growth rate α_T, and

$$\begin{aligned}
\alpha_T \geq 0 &\Longleftrightarrow \sqrt{\Delta_T} \geq 2\mu + \delta + d + k + r_1 + r_2 \\
&\Longleftrightarrow \Delta_T \geq (2\mu + \delta + d + k + r_1 + r_2)^2 \\
&\Longleftrightarrow kc\beta \geq (k + r_1 + \mu)(\mu + r_2 + \delta + d) \\
&\Longleftrightarrow R_{0T} \geq 1.
\end{aligned}$$

Thus, we have $sign(\alpha_T) = sign(R_{0T} - 1)$. Therefore,

$$\begin{aligned}
&(E, I) \longrightarrow (0, 0) \text{ if } R_{0T} < 1, \\
&(E, I) \longrightarrow (E^*, I^*) \text{ with } E^* > 0 \text{ and } I^* > 0 \text{ if } R_{0T} = 1, \\
&(E, I) \longrightarrow (\infty, \infty) \text{ if } R_{0T} > 1.
\end{aligned}$$

For the number T of treated individuals, its derivative ($dT/dt = r_1 E + r_2 I - (m + \mu)T$) shows that T has the same asymptotic behavior than that of E and I. □

References

[1] S. Busenberg and P. van den Driessche, *Analysis of a Disease Transmission Model in a Population with Varying Size*, DMS-504-IR April 1989.

[2] S. Busenberg and P. van den Driessche, Nonexistence of periodic solutions for a class of epidemiological models, in *Biology, and Ecology* (Lect. Notes Biomath. 92), S. Busenberg and M Martelli, Eds., Springer-Verlag, Berlin, 1991, pp. 70-79.

[3] C. Castillo-Chavez and B. Sung *Dynamical Models of Tuberculosis and their Applications* Mathematical Biosciences and Engineering,1 (2004), pp. 361-404

[4] C. Castillo-Chavez and Z. Feng, *To treat or not to treat: The case of Tuberculosis*, J. Math. Biol.35 (1997): 629-646

[5] O. Diekmann, H. Heesterbeek and M. G. Roberts, *The construction of next-generation matrices for compartment epidemic models*, J. R. Soc. Interface (2010) 7, 873-885

[6] P. van den Driessche and J. Watmough, *Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission*, Mathematical Biosciences 180 (2002), pp. 29-48.

[7] *Guidelines on the Management of Latent Tuberculosis Infection*, 2015. Available from: http://apps.who.int/medicinedocs/documents/s21682en/s21682en.pdf

[8] J. Hui and D. Zhu, *Dynamics of SEIS Epidemic Models with varying population size*, International Journal of Bifurcation and chaos, 17 (2007), pp. 1513-1529.

[9] M. W. Hirsh, S. Smale, R. L. Devaney *Differential Equations, Dynamical Systems and an Introduction to Chaos* Elsivier Academic Press, 2004.

[10] A. Jabbari, C. Castillo-Chavez, F. Nazari, B. Song and H. Kheiri *a two-strain TB model with multiple latent stages*, Mathematical Bioscience and engineering, 13 (2016), pp. 741-785.

[11] J. Mena-Lorca, H. W. Hethcote, *Dynamic models of infectious diseases as regulators of population sizes*, J. Math. Biol., 30(1992), pp. 693-716.

[12] X. Meng, Z. Wu and T. Zhang, *The Dynamics and Therapeutic Strategies of a SEIS Epidemic Model*, Int. J. Biomath. 06 (2013)

[13] X. Meng, S. Zhao, T. Feng and T. Zhang, *Dynamics of a novel nonlinear stochastic SIS epidemic model with double hypothesis*, J. Math. Appl. 433 (2016), pp. 227-242.

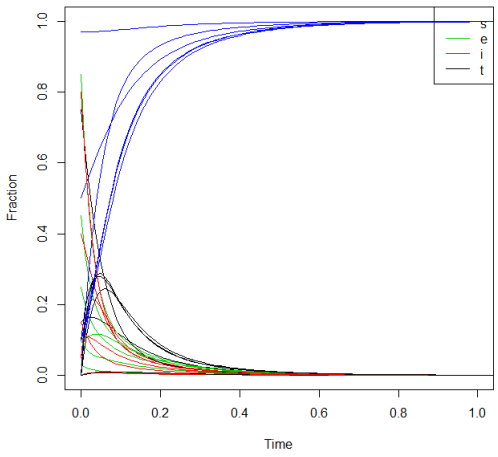
[14] Routh, Edward John *A Treatise on the Stability of a Given State of Motion: Particularly Steady Motion*, Macmillan and Company, 1877.

[15] A. Ssematimba, J. Y. T. Mughisa and L.S. Luboobi, *Mathematical model for the dynamics of tuberculosis in density dependent population: The case of Internally deplaced peoples Camps(IDPCs) in Uganda*, Journal of Mathematics and Statistics 1(3) (2005), pp.217-224.

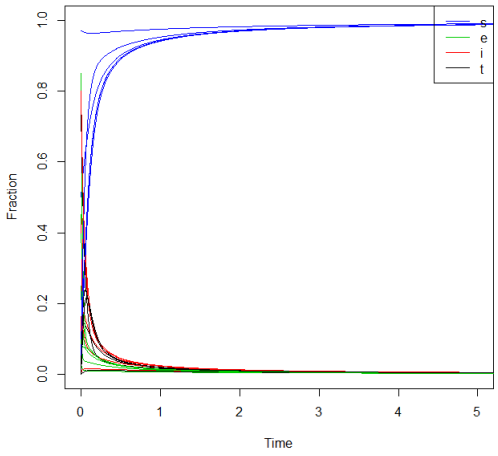
[16] Y. Yang, J. Zhou, X. Ma and T. Zhang, *Nonstandard finite difference scheme for a diffusive within-host virus dynamics model with both virus-to-cell and cell-to-cell transmissions*, Computers and Mathematics with Applications, Vol. 72 (2016), pp. 1013-1020.

[17] H. Zhang, L. Yingqi and W. Xu, *Global Stability of an SEIS Epidemic Model With Saturation Incidence*, Hindawi Publishing Corporation, ISRN Applied Mathematics Vol 2013 (2013), Article ID 710643.

[18] T. Zhang, X. Meng and T. Zhang, *Global Analyis for a delayed SIV model with Direct and Environmental Transmissions* Journal of Applied Analysis and Computation, Volume 6, Number 2 (2016), pp. 479-491.

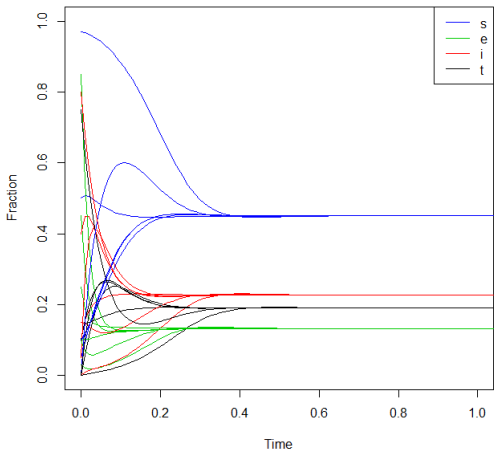


(a) $R_{1T} = 0.74$

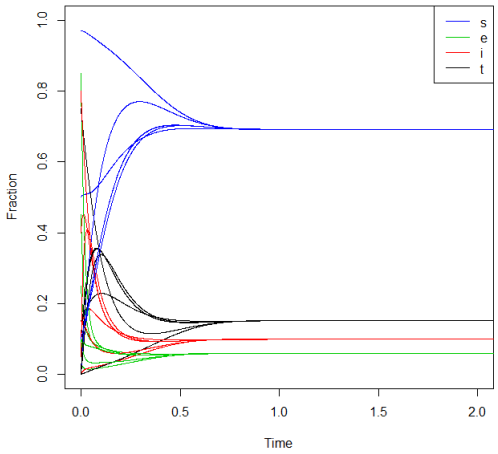


(b) $R_{1T} = 1$

FIGURE 8. seits curves with $R_{1T} \leq 1$. For (a), we used $b = 2, \mu = 1, c\beta = 40, k = 20, d = 8, \delta = 4, r_1 = 10, r_2 = 20, m = 20$ to get $R_{1T} = 0.735$. For (b) we used $b = 3, \mu = 1, c\beta = 30, k = 40, d = 3, \delta = 4, r_1 = 5, r_2 = 15, m = 20$ that gives $R_{1T} = 1$. In both cases, all solutions paths approach the disease free equilibrium (DFE) $(1, 0, 0, 0)$.

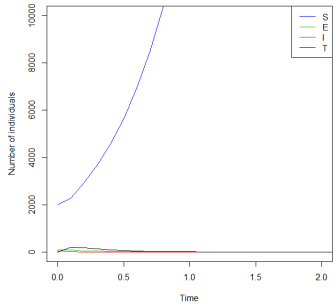


(a) $R_{1T} \approx 2.128$

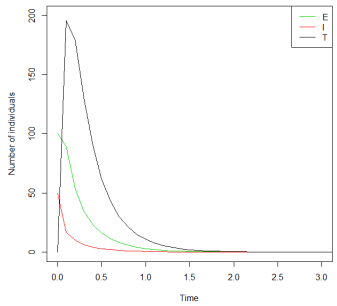


(b) $R_{1T} \approx 1.418$

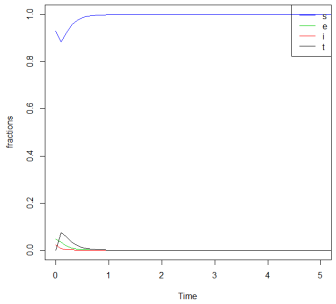
FIGURE 9. seits curves with $R_{1T} > 1$. For (a) we used $b = 2, \mu = 1, c\beta = 60, k = 40, d = 3, \delta = 4, r_1 = 5, r_2 = 15, m = 20$ to get $R_{1T} \approx 2.128$. For (b) we used the parameters values except that we set $c\beta = 40$ and get $R_{1T} \approx 1.418$. In (a) all the solutions paths approach the same endemic equilibrium $(s^*, e^*, i^*, \tau^*) \approx (0.450, 0.132, 0.227, 0.191)$. In (b) all the solutions paths approach the same endemic equilibrium $(s^*, e^*, i^*, \tau^*) \approx (0.691, 0.058, 0.099, 0.151)$.



(a) Numbers

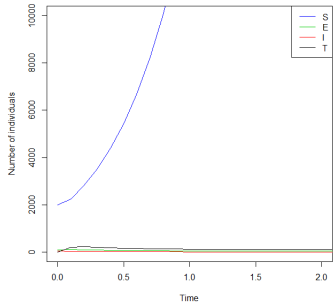


(b) Numbers

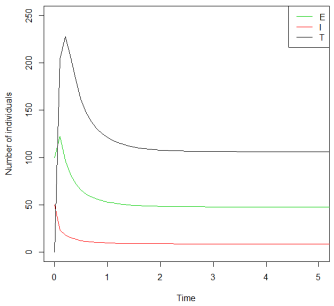


(c) proportions

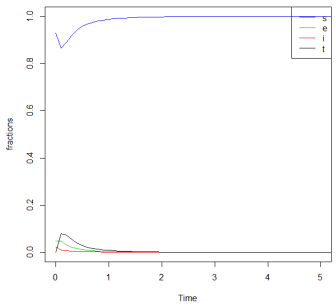
FIGURE 10. SEITS curves with $b = 3, \mu = 1, c\beta = 154, k = 10, d = 10, \delta = 3, r_1 = 17, r_2 = 41, m = 10$ that gives $R_{1T} = 0.765, R_{0T} = 0.842$. The initial values are $(S(0), E(0), I(0), T(0)) = (2000, 100, 50, 0)$. The proportions and the numbers of the infected individuals go to zero while the population grows exponentially.



(a) Numbers

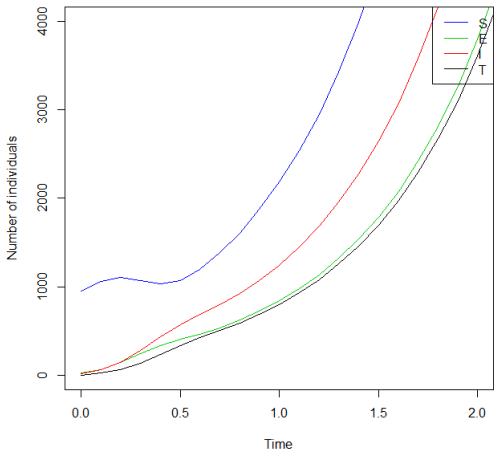


(b) Numbers

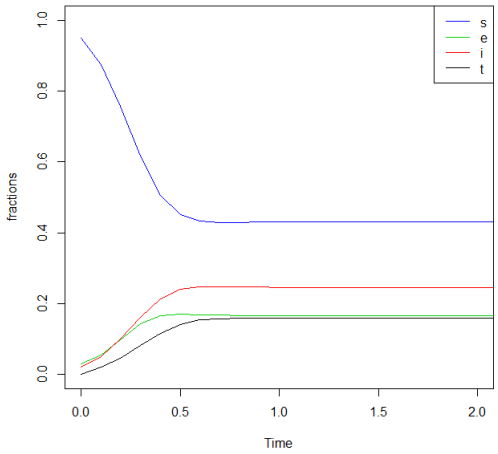


(c) proportions

FIGURE 11. SEITS curves with $b = 3, \mu = 1, c\beta = 154, k = 10, d = 10, \delta = 3, r_1 = 17, r_2 = 41, m = 10$ that gives $R_{1T} = 0.901, R_{0T} = 1$. The initial values are $(S(0), E(0), I(0), T(0)) = (2000, 100, 50, 0)$. $R_{1T} < 1$ thus, the proportions go to the disease free equilibrium. $R_{0T} = 1$, then the numbers of the infected and treatment compartments stabilize to positive values, while the population grows exponentially.

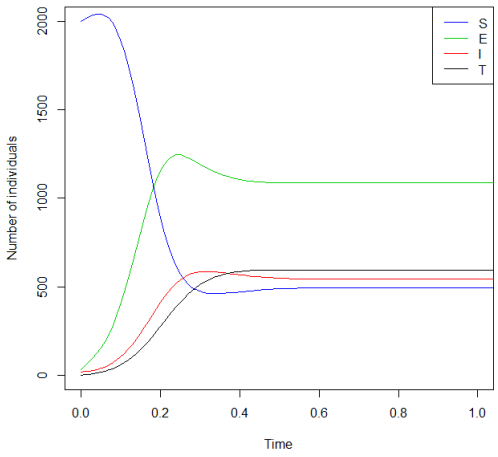


(a) Numbers

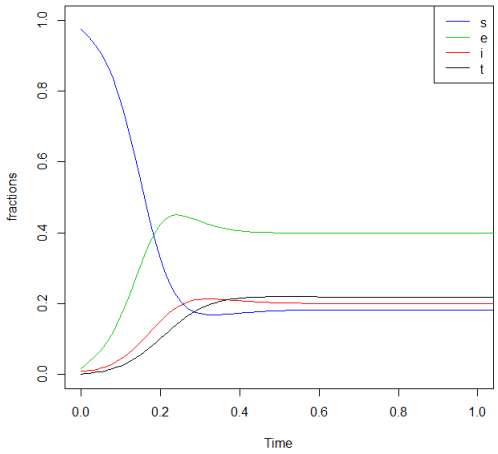


(b) proportions

FIGURE 12. SEITS curves with $b = 3, \mu = 1, c\beta = 40, k = 20, d = 2, \delta = 3, r_1 = 3, r_2 = 6, m = 10$ that gives $R_{1T} = 2.198, R_{0T} = 2.778, i^* = 0.346, \alpha_T = 1.509, R_{2T} = 2.012$, where the initial values are $(S(0), E(0), I(0), T(0)) = (950, 30, 20, 0)$. The proportions go to an endemic equilibrium, while the number of individuals in each compartment grow exponentially.

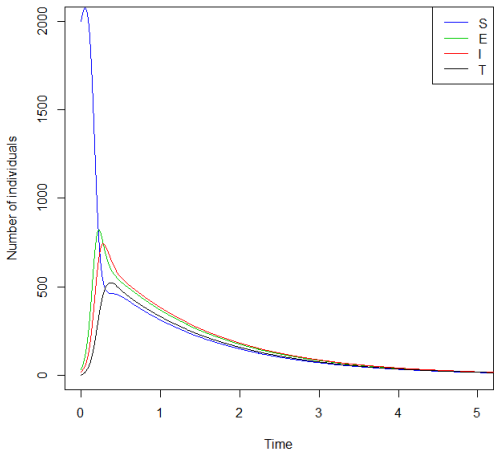


(a) Numbers

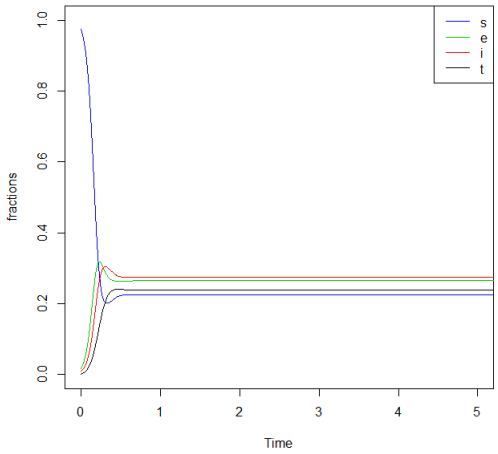


(b) proportions

FIGURE 13. SEITS curves with $b = 3, \mu = 1, c\beta = 154, k = 10, d = 10, \delta = 3, r_1 = 3, r_2 = 6, m = 10$ that gives $R_{1T} \approx 4.38, R_{0T} = 5.5, s^* \approx 0.18, e^* = 0.4, \tau^* \approx 0.22, i^* = 0.2, \alpha_T = 0, R_{2T} = 1$. The initial values are $(S(0), E(0), I(0), T(0)) = (2000, 30, 20, 0)$. The proportions go to an endemic equilibrium and the numbers also go to an endemic equilibrium.



(a) Numbers



(b) proportions

FIGURE 14. SEITS curves with $b = 3, \mu = 1, c\beta = 100, k = 20, d = 10, \delta = 3, r_1 = 3, r_2 = 6, m = 10$ that gives $R_{1T} \approx 3.50, R_{0T} \approx 4.17, s^* = 0.22, e^* = 0.26, \tau^* = 0.24, i^* = 0.27, \alpha_T = -0.74, R_{2T} \approx 0.80$. The initial values are $(S(0), E(0), I(0), T(0)) = (2000, 30, 20, 0)$. The proportions approach an endemic equilibrium, while the sizes vanish.