Available online at http://scik.org
Commun. Math. Biol. Neurosci. 2017, 2017:23
ISSN: 2052-2541

SEIS MODEL WITH MULTIPLE LATENT STAGES AND TREATMENT IN AN EXPONENTIALLY GROWING POPULATION

STANISLAS OUARO *, DESIRE OUEDRAOGO

LAboratoire de Mathématiques et Informatique (LAMI), Université Ouaga I Pr Joseph Ki-Zerbo, Unité de Formation et de Recherche en Sciences Exactes et Appliquées, Département de Mathématiques, 03 B.P.7021 Ouagadougou 03, Burkina Faso

Communicated by L. Chen

Abstract. An SE^nIS epidemiological model with vital dynamics in an exponentially growing population is discussed. Without treatment three threshold parameters R_0, R_1 and R_2 determine the dynamic of compartments sizes and that of the fractions. With the treatment the dynamics of the population and that of the epidemic depend on three other threshold parameters R_T, R_{1T} and R_{2T}. We made a link between the models with one latent stage and the models with multiple latent stages by defining and deriving the "effective" activation rate and the "effective" treatment rate for the latent individuals. We defined the treatment force, the relative treatment force and deduced the critical treatment force needed to eradicate the disease. The theoretical results are validated by numerical simulations.

Keywords: mathematical model; epidemiological model; Lyapunov function; numerical simulations.

2010 AMS Subject Classification: 37B25, 40C05, 92C42, 92B05.

1. Introduction

Bame et *al.* studied SEIS models with n Latent classes in [1] assuming that an infected individual passes through n latent classes before becoming infectious. In [2] Bowong et *al.* studied a

*Corresponding author

E-mail addresses: souaro@univ-ouaga.bf, ouaro@yahoo.fr

Received July 20, 2017

Tuberculosis model with two differential infectivity and n latent classes. Moualeu et *al.* studied a Tuberculosis Model with n latent classes in [11]. For these models an individual can become infectious from any latent class. Jabbari et *al.* studied a two-strain TB model with multiple latent stages in [9]. In [10] Meng et *al.* studied the dynamics of an SEIS model with therapeutic strategies. For these models the population has a constant recruitment rate and the incidence is the simple mass action.

In this paper we study an SEIS model with n latent classes. The population has an individual birth rate b and an individual death rate μ such that $b > \mu$, that is the population is growing exponentially without the epidemic. With the introduction of the disease, the population is split into $n+2$ compartments. The compartment S of susceptible individuals, the compartments $\mathrm{E}_1, ..., \mathrm{E}_\mathrm{n}$ of individuals in n different latent stages, and the compartment I of infectious individuals. $S, E_1, \cdots, E_n, I$ denote the numbers of individuals in the corresponding compartments. We consider serial latent stages that is individual pass successively in the compartments E_1,...,E_n. We assume that an individual in the latent class E_m can become infectious with rate k_m or be transferred into $\mathrm{E}_{\mathrm{m+1}}$ with rate ν_m for $m = 1, \cdots, n-1$. The contact rate is c and the probability of infection during a contact of an infectious with a susceptible is β. Thus the effective contact rate is $c\beta$ and the incidence is $c\beta SI/N$, where N denotes the total population size ($N = S + E_1 + ... + E_n + I$). An infectious individual recovers with rate δ. In that case, he becomes susceptible again. The disease induces an additive death rate d to the infectious individuals. We assume afterward that there is a treatment for latent individuals and infectious individuals. With the treatment a new compartment T of the individuals under treatment is added. The treatment rate for an individual in the latent class E_m is r_m, $m = 1, \cdots, n$ and that for an infectious individual is r. A treated individual recovers with rate θ. All the parameters listed above are positive. The summary of the notations used in this paper is given in Table 1. Our model is different from that listed above since we consider a population that grows exponentially in absence of the disease, instead of a population with a constant recruitment rate. Furthermore we have a standard incidence instead of the simple mass incidence. This model fits for tuberculosis.

Our paper is organized as follow. In Section 2 we study the dynamic of the model without treatment. Section 3 is dedicated to the study of the model with treatment. We validate the

N	The population size
S	Susceptible
$\mathrm{E_m}$	Exposed people in the m^{th} latent class, $m = 1,...,n$
I	Infectious
T	People under treatment
$S, E_1, \cdots, E_n, I, T$	Compartments sizes
s, e_m, i	Fractions of the population in the classes S,$\mathrm{E_m}$,I
β	Probability of transmitting the disease during a contact
c	Contact rate
b	Birth rate
μ	Natural death rate
d	Disease induced death rate
k_m	Transfer rate from $\mathrm{E_m}$ into I
ν_m	Transfer rate from $\mathrm{E_m}$ into $\mathrm{E_{m+1}}$, $m = 1, \cdots, n-1$
r_m	Treatment rate of a latent in $\mathrm{E_m}$
r	Treatment rate of an infectious
δ	Natural recovering rate
θ	Recovering rate of a treated individual
R_0	Basic reproduction number
R_T	Initial reproduction number (with treatment)

Table 1. Summary of notations

theoretical results by simulations in Section 4. Thereafter we conclude the paper and discuss some perspectives in Section 5.

2. The model without treatment

In this section we study the dynamic of the model without treatment. We give the system of the model, then we derive its basic reproduction number and compare hence the multiple latent stages model to the unique latent stage model, give conditions for endemic equilibria,

therefore we study the dynamic of the fractions and hence deduce the asymptotic behaviour of the compartments sizes. The diagram of the SE^{n}IS model is given in Figure 1.

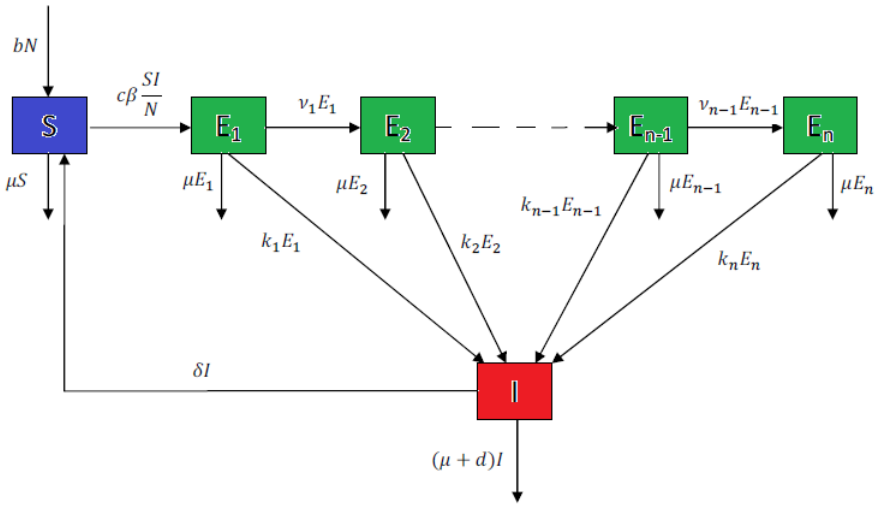


Figure 1. The transfer diagram of the SE^{n}IS model with the susceptible class S, the n exposed classes E_1,...,E_n and the infectious class I

2.1. The model

The model without treatment is given by the following system of ordinary differential equations (ODE).

$$
\begin{cases}
\frac{dS}{dt} = bN + \delta I - c\beta S\frac{I}{N} - \mu S, \\
\frac{dE_1}{dt} = c\beta S\frac{I}{N} - (k_1+\nu_1+\mu)E_1, \\
\frac{dE_m}{dt} = \nu_{m-1}E_{m-1} - (k_m+\nu_m+\mu)E_m, m = 2,\cdots,n-1, \\
\frac{dE_n}{dt} = \nu_{n-1}E_{n-1} - (k_n+\mu)E_n, \\
\frac{dI}{dt} = \sum_{m=1}^{m=n} k_mE_m - (\delta+\mu+d)I, \\
N(t) = S(t) + \sum_{m=1}^{m=n} E_m(t) + I(t), \\
S(0) > 0, E_1(0) \geq 0, \cdots, E_n(0) \geq 0, I(0) \geq 0.
\end{cases}
\tag{2.1}
$$

Remark 2.1. *By setting $\nu_n = 0$ in System (2.1), the formula $dE_m/dt = \nu_{m-1}E_{m-1} - (k_m + \nu_m + \mu)E_m$ applies also for $m = n$. Thus to simplify the formulas we set $\nu_n = 0$ in the following.*

From System (2.1) we have $dN/dt = (b-\mu)N - dI = (b-\mu-di)N$, where $i = I/N$ is the fraction of the infectious. Then the population will go on growing whenever the fraction i of infectious individuals is less than $(b-\mu)/d$. But the population would decrease if i grows beyond $(b-\mu)/d$.

2.2. The basic reproduction number

The basic reproduction R_0 is defined as the average number of new cases of an infection caused by one typical infected individual, in a population consisting of susceptibles only [4].

Theorem 2.2. *The basic reproduction number R_0 of the epidemic defined by System (2.1) is given by*

$$R_0 = \frac{c\beta}{\mu+d+\delta} \sum_{m=1}^{m=n} \frac{k_m}{\mu+\nu_m+k_m} \prod_{l=1}^{l=m-1} \frac{\nu_l}{\mu+\nu_l+k_l}. \tag{2.2}$$

Proof. R_0 is the product of the contact rate c, the probability to transmit the disease during a contact β, the average infectious time $1/(\mu+d+\delta)$ and the probability for the newly exposed individual to become infectious $\sum_{m=1}^{m=n} \frac{k_m}{\mu+\nu_m+k_m} \prod_{l=1}^{l=m-1} \frac{\nu_l}{\mu+\nu_l+k_l}$. The latter is the sum of the probabilities to become infectious from the different latent compartments. More precisely $\frac{k_m}{\mu+\nu_m+k_m} \prod_{l=1}^{l=m-1} \frac{\nu_l}{\mu+\nu_l+k_l}$ is the probability for the individual to become infectious while being in the compartment E_m. □

If $R_0 \leq 1$, then the epidemic cannot invade the population. But if $R_0 > 1$, then the epidemic will invade the population.

Theorem 2.3. *If $k_1 = k_2 = \cdots = k_n = k$ then*

$$R_0 = \frac{kc\beta}{(k+\mu)(\mu+d+\delta)}. \tag{2.3}$$

Proof. Let's note first that if $k_1 = k_2 = \cdots = k_n = k$ then Equation (2.3) is equivalent to

$$\frac{c\beta}{\mu+d+\delta} \sum_{m=1}^{m=n} \frac{k}{\mu+\nu_m+k} \prod_{l=1}^{l=m-1} \frac{\nu_l}{\mu+\nu_l+k} = \frac{kc\beta}{(\mu+k)(\mu+d+\delta)}.$$

Then it is enough to show that

$$\sum_{m=1}^{m=n} \frac{k}{\mu+\nu_m+k} \prod_{l=1}^{l=m-1} \frac{\nu_l}{\mu+\nu_l+k} = \frac{k}{\mu+k}. \tag{2.4}$$

Let's assume first that $n=2$ then

$$\begin{aligned}\frac{k}{\mu+\nu_1+k} + \frac{k}{\mu+k}\frac{\nu_1}{\mu+\nu_1+k} &= \frac{k}{\mu+\nu_1+k}\left[1+\frac{\nu_1}{\mu+k}\right] \\ &= \frac{k}{\mu+\nu_1+k}\frac{\mu+\nu_1+k}{\mu+k} \\ &= \frac{k}{\mu+k}.\end{aligned}$$

Thus Equation (2.4) is verified if $n=2$. Let's assume now that the result is true for $n=p$ for a given integer $p \geq 2$, that is

$$\sum_{m=1}^{m=p} \frac{k}{\mu+\nu_m+k} \prod_{l=1}^{l=m-1} \frac{\nu_l}{\mu+\nu_l+k} = \frac{k}{\mu+k}.$$

Thus we have

$$\begin{aligned}\sum_{m=1}^{m=p+1} \frac{k}{\mu+\nu_m+k} \prod_{l=1}^{l=m-1} \frac{\nu_l}{\mu+\nu_l+k} &= \frac{k}{\mu+\nu_1+k} + \frac{\nu_1}{\mu+\nu_1+k} \sum_{m=2}^{m=p+1} \frac{k}{\mu+\nu_m+k} \prod_{l=2}^{l=m-1} \frac{\nu_l}{\mu+\nu_l+k} \\ &= \left[\frac{k}{\mu+\nu_1+k} + \frac{\nu_1}{\mu+\nu_1+k}\frac{k}{\mu+k}\right] \\ &= \frac{k}{\mu+k}.\end{aligned}$$

Thus we have shown by induction that R_0 satisfies (2.3) when $k_1 = k_2 = \cdots = k_n = k$, for all $n \geq 2$. □

Remark 2.4. *$kc\beta/[(\mu+k)(\mu+d+\delta)]$ is the basic reproduction number of the SEIS model with one latent stage, where k is the activation rate (the transfer rate from the latent compartment E into the infectious compartment I)*[12].

Now to make a link between the model with multiple latent stages and the model with one latent stage [12], we define the "effective" activation rate as the rate k_e that satisfies Equation (2.3). The "effective" activation rate is then the transfer rate from the latent stage to the infectious stage of the model with one latent stage which has the same basic reproduction number

as that of the model with n latent stages. By equations (2.2) and (2.3) one gets the following result.

Theorem 2.5. *The "effective" activation rate of the epidemic defined by System (2.1) is given by*

$$k_e = \frac{\mu \sum_{m=1}^{m=n} \frac{k_m}{\mu+\nu_m+k_m} \prod_{l=1}^{l=m-1} \frac{\nu_l}{\mu+\nu_l+k_l}}{1-\sum_{m=1}^{m=n} \frac{k_m}{\mu+\nu_m+k_m} \prod_{l=1}^{l=m-1} \frac{\nu_l}{\mu+\nu_l+k_l}}. \tag{2.5}$$

2.3. Equilibria

If $I=0$ then $dN/dt=(b-\mu)N$. Therefore the population will grow if the disease dies out as we assume that $b>\mu$. Thus, System (2.1) does not admit a disease free equilibrium. The following result gives necessary and sufficient conditions for endemic equilibria.

Theorem 2.6. *Let $X(t)=(S(t),E_1(t),\cdots,E_n(t),I(t))$ be a solution of System (2.1). $X(t)$ is constant if and only if the parameters satisfy*

$$\begin{aligned} &\left(\frac{bd}{b-\mu}+\delta\right)\frac{1}{\delta+\mu+d}\left(k_n+(k_n+\mu)\sum_{m=1}^{m=n-1}\frac{k_m}{\nu_m}\prod_{l=m+1}^{l=n-1}\frac{k_l+\nu_l+\mu}{\nu_l}\right) \\ &-\left(1+\frac{d\mu}{c\beta(b-\mu)}\right)\left(\prod_{l=1}^{l=n-1}\frac{k_l+\nu_l+\mu}{\nu_l}\right)(k_n+\mu)=0 \end{aligned} \tag{2.6}$$

and the initial values satisfy

$$\begin{aligned} S(0) &= \frac{1}{c\beta}\frac{d}{b-\mu}\left(\prod_{l=1}^{l=n-1}\frac{k_l+\nu_l+\mu}{\nu_l}\right)(k_n+\mu)E_n(0), \\ E_m(0) &= \frac{1}{\nu_m}\left(\prod_{l=m+1}^{l=n-1}\frac{k_l+\nu_l+\mu}{\nu_l}\right)(k_n+\mu)E_n(0), \forall m=1,\cdots,n-1, \\ I(0) &= \frac{1}{\delta+\mu+d}\left(k_n+(k_n+\mu)\sum_{m=1}^{m=n-1}\frac{k_m}{\nu_m}\prod_{l=m+1}^{l=n-1}\frac{k_l+\nu_l+\mu}{\nu_l}\right)E_n(0), \\ E_n(0) &> 0. \end{aligned} \tag{2.7}$$

Proof. By using successively the derivatives of $E_n, E_{n-1}, \cdots, E_1, I, S$, one gets that $E_n, \cdots, E_1$, I, S are constant if and only if the parameters satisfy Equation (2.6) and the initial values satisfy System (2.7). □

Remark 2.7. *If the parameters values satisfy Equation (2.6) then for every positive number E_0, one gets an endemic equilibrium by setting $E_1(0) = E_0$ and deducing the other initial values from System (2.7). Therefore, System (2.1) admits an infinite endemic equilibrium and there is no stability.*

2.4. The dynamic of the fractions

For epidemics in populations that grow exponentially in the absence of the disease, it is common to study the fractions of individuals in the different compartments [3, 7, 12, 5]. Let's consider the fractions $s = S/N$, $e_m = E_m/N, m = 1, \cdots, n$ and $i = I/N$. By System (2.1), one gets

$$
\left\{
\begin{array}{l}
\dfrac{ds}{dt} = b - bs + \delta i - (c\beta - d)si, \\
\dfrac{de_1}{dt} = c\beta si - (k_1 + \nu_1 + b)e_1 + die_1, \\
\dfrac{de_m}{dt} = \nu_{m-1}e_{m-1} - (k_m + \nu_m + b)e_m + die_m, m = 2, \cdots, n, \\
\dfrac{di}{dt} = \displaystyle\sum_{m=1}^{m=n} k_m e_m - (b + \delta + d)i + di^2, \\
\text{with } s + \displaystyle\sum_{m=1}^{m=n} e_m + i = 1, \\
s(0) > 0, e_1(0) \geq 0, \cdots, e_n(0) \geq 0, i(0) \geq 0.
\end{array}
\right. \tag{2.8}
$$

Remark 2.8. *As for other models the natural death rate μ does not appear in System (2.8). That is understandable since all the individuals of the population have the same natural death rate. Thus the natural death does not affect the fractions.*

as $s = 1-(\sum_{m=1}^{m=n} e_m + i)$ one gets

$$\begin{cases} \dfrac{de_1}{dt} = c\beta i - (k_1+\nu_1+b-di)\,e_1 - \displaystyle\sum_{m=1}^{m=n} c\beta e_m i - c\beta i^2, \\ \dfrac{de_m}{dt} = \nu_{m-1}e_{m-1} - (k_m+\nu_m+b)e_m + die_m, m = 2,\cdots,n, \\ \dfrac{di}{dt} = \displaystyle\sum_{m=1}^{m=n} k_m e_m - (b+\delta+d)i + di^2, \\ s(0) > 0, e_1(0) \geq 0, \cdots, e_n(0) \geq 0, i(0) \geq 0, \end{cases} \tag{2.9}$$

with $s(t) = 1-\sum_{m=1}^{m=n} e_m(t) - i(t)$.

The suitable set is $D = \{(e_1,\cdots,e_n,i)/e_1 \geq 0,\cdots,e_n \geq 0, i \geq 0, \sum_1^n e_m + i \leq 1\}$.

Theorem 2.9. *The domain D is positively invariant for System (2.9).*

Proof. If $i(t) = 0$ at a given time $t \geq 0$, then $\dfrac{di}{dt}(t) = \displaystyle\sum_{m=1}^{m=n} k_m e_m(t) \geq 0$.

If $e_1(t) = 0$ at a given time $t \geq 0$, then $\dfrac{de_1}{dt}(t) = c\beta\left(1 - \displaystyle\sum_{m=2}^{m=n} e_m(t) - i(t)\right) i(t) \geq 0$.

If $e_m(t) = 0$ at a given time $t \geq 0$, then $\dfrac{de_m}{dt}(t) = \nu_{m-1}e_{m-1}(t) \geq 0, m = 2,\cdots,n$.

If $\displaystyle\sum_{m=1}^{m=n} e_m(t) + i(t) = 1$ at a given time $t \geq 0$, then $\dfrac{d(\sum_{m=1}^{m=n} e_m + i)}{dt}(t) = -b - \delta i(t) \leq 0$.

Thus all solution of System (2.9) starting in D remains in D for all $t > 0$. □

In the following we use the method of the next generation matrix described in [6] to derive a threshold parameter R_1 with threshold value equals 1 for System (2.9). It is obvious that $x_0 = (0,\cdots,0,0)$ is the unique disease free equilibrium (DFE) of System (2.9). Let's set

$$\mathscr{F}(e_1,\cdots,e_n,i) = \begin{pmatrix} c\beta i - \sum_{m=1}^{m=n} c\beta e_m i - c\beta i^2 \\ 0 \\ \vdots \\ 0 \end{pmatrix},$$

$$\mathscr{V}(e_1,\cdots,e_n,i)=\begin{pmatrix} -a_1e_1+die_1 \\ \vdots \\ \nu_{m-1}e_{m-1}-a_me_m+die_m \\ \vdots \\ \sum_{m=1}^{m=n}k_me_m-a_{n+1}i+di^2 \end{pmatrix},$$

with $a_m=k_m+\nu_m+b, m=1,\cdots,n; a_{n+1}=b+\delta+d$. Let F and V be the respective jacobians at the DFE of $\mathscr{F}$ and $\mathscr{V}$, that is $F=D\mathscr{F}(0,\cdots,0,0)$ and $V=D\mathscr{V}(0,\cdots,0,0)$, and set $R_1=\rho(-FV^{-1})$. After some calculus, one gets

$$R_1=\frac{c\beta}{(b+\delta+d)}\sum_{m=1}^{m=n}\frac{k_m}{b+\nu_m+k_m}\prod_{l=1}^{l=m-1}\frac{\nu_l}{b+\nu_l+k_l}. \tag{2.10}$$

Remark 2.10. *One gets R_1 by substituting μ by b in the expression of R_0 in Equation (2.2). Thus as $b>\mu$, we have $R_1<R_0$.*

Following Odo et *al.* [5, Page 89], we refer to R_1 as the relative basic reproduction.

Theorem 2.11. *The disease free equilibrium $(0,\cdots,0,0)$ of System (2.9) is globally asymptotically stable (GAS) in D if $R_1\leq 1$ and unstable if $R_1>1$.*

Proof. By Theorem 2 in [6], the disease free equilibrium is asymptotically stable if $R_1<1$ and unstable if $R_1>1$. To show its global stability, let L be the function defined on D by $L(e_1,\cdots,e_n,i)=\sum_{m=1}^{m=n}x_me_m+i$, with x_m defined by

$$x_m=\sum_{j=m}^{j=n}\frac{k_j}{a_j}\prod_{l=m}^{l=j-1}\frac{\nu_l}{a_l}, m=1,\cdots,n. \tag{2.11}$$

By Equation (2.11) we have $x_n = k_n/a_n$ and $x_{m-1} = (x_m\nu_{m-1} + k_{m-1})/a_{m-1}, m = 2,\cdots,n$. The time derivative of L evaluated along a solution of System (2.9) is

$$\begin{aligned}
\dot{L}(e_1,\cdots,e_n,i) &= \sum_{m=1}^{m=n} x_m \frac{de_m}{dt} + \frac{di}{dt} \\
&= x_1\left[c\beta i - (a_1 - di)e_1 - \sum_{m=1}^{m=n} c\beta e_m i - c\beta i^2\right] \\
&+ \sum_{m=2}^{m=n} x_m\left[\nu_{m-1}e_{m-1} - a_m e_m + die_m\right] \\
&+ \left[\sum_{m=1}^{m=n} k_m e_m - a_{n+1}i + di^2\right] \\
&= \left[x_1 c\beta - a_{n+1} + \sum_{m=1}^{m=n}(x_m d - x_1 c\beta)e_m + (d - x_1 c\beta)i\right] i \\
&= iW(e_1,\cdots,e_n,i),
\end{aligned}$$

with, $W(e_1,\cdots,e_n,i) = x_1c\beta - a_{n+1} + \sum_{m=1}^{m=n}(x_m d - x_1 c\beta)e_m + (d - x_1 c\beta)i$. W is an affine function. Thus, it reaches its maximum on the extreme points of the closed set D. We have

$W(0,\cdots,0,0) = x_1c\beta - a_{n+1} = a_{n+1}(R_1 - 1)$,

$W(0,\cdots,0,1) = x_1c\beta - a_{n+1} + (d - x_1c\beta) = -(a_{n+1} - d) = -(b+\delta) < 0$,

$W(e_m = 1) = x_1c\beta - a_{n+1} + (x_m d - x_1 c\beta) = -a_{n+1} + x_m d = -b - \delta - d(1 - x_m), m = 1,\cdots,n$.

But, $x_n = k_n/a_n = k_n/(k_n + b) < 1$. Furthermore if we assume that for a given integer $m \in (1,n]$, we have $x_m < 1$, then $x_{m-1} = (x_m\nu_{m-1} + k_{m-1})/a_{m-1} < (\nu_{m-1} + k_{m-1})/a_{m-1} < 1$, since $a_{m-1} = \nu_{m-1} + k_{m-1} + b$. Thus, by backward induction we have proved that $x_m < 1$, for all $m = 1,\cdots,n$. Therefore, $W(e_m = 1) < 0, m = 1,\cdots,n$.

Then, $W(e_1,\cdots,e_n,i) \leq 0, \forall (e_1,\cdots,e_n,i) \in D$. Thus $\dot{L}(e_1,\cdots,e_n,i) \leq 0, \forall (e_1,\cdots,e_n,i) \in D$ when $R_1 \leq 1$. Therefore L is a Lyapunov function for System (2.9). Moreover, the only invariant subset of the set $\{\dot{L} = 0\}$ is $\{(0,\cdots,0,0)\}$. It follows from the Lasalle Invariance Principle [8, p. 200] that, all paths in D approach the origin. Then the disease free equilibrium is globally asymptotically stable in D when $R_1 \leq 1$. □

Remark 2.12. *Biologically, Theorem 2.11 means that when $R_1 \leq 1$, the fraction of infected individuals vanishes, but when $R_1 > 1$ it will remain positive.*

When $R_1 > 1$, the disease free equilibrium of System (2.9) is unstable. We conjecture that in this case System (2.9) admits an endemic equilibrium that is globally asymptotically stable in the interior of D. This conjecture is confirmed by simulations (Figure 4 (b) and (c)).

2.5. The asymptotic behaviour of the compartments sizes

For models with varying population size, the knowledge of the dynamic of the fractions is not enough. In fact, if a fraction go to 0 or to a positive number, there are three possible cases for the size. It may go to ∞, go to a positive number, or go to 0. Then it is important to study also the dynamics of the compartments sizes. We consider first the situation where the fractions disease free equilibrium is globally asymptotically stable in its feasible region, that is when $R_1 < 1$. In this case the fraction of infected individuals goes to zero, while that of susceptible individuals goes to 1. Therefore $dN/dt \longrightarrow (b-\mu)N$, and then $N \longrightarrow \infty$ when $t \longrightarrow \infty$. Thus, $S(t) \longrightarrow \infty$ when $R_1 \leq 1$. Due to the results for the model with a unique latent class [12] and the simulations results (figures 5, 6, 7), we made the following conjecture.

Conjecture 2.13. *Let $(S(t), E_1(t), \cdots, E_n(t), I(t))$ be a solution of System (2.1).*

(1) If $R_0 < 1$, then $(S(t), E_1(t), \cdots, E_n(t), I(t)) \longrightarrow (\infty, 0, \cdots, 0, 0)$, when $t \longrightarrow \infty$;

(2) If $R_0 = 1$, then $(S(t), E_1(t), \cdots, E_n(t), I(t)) \longrightarrow (\infty, E_1^*, \cdots, E_2^*, I^*)$, when $t \longrightarrow \infty$, with $E_1^* > 0, \cdots, E_n^* > 0, I^* > 0$;

(3) If $R_1 \leq 1 < R_0$, then $(S(t), E_1(t), \cdots, E_n(t), I(t)) \longrightarrow (\infty, \infty, \cdots, \infty, \infty)$, when $t \longrightarrow \infty$.

The proof of Conjecture 2.13 for a unique latent stage ($n = 1$) is done in [12].

Now we consider the case where the fractions admits an endemic equilibrium that is globally asymptotically stable in the interior of its feasible region.

Theorem 2.14. *Let's assume that $R_1 > 1$ and that System (2.8) admits an endemic equilibrium $(s^*, e_1^*, \cdots, e_n^*, i^*)$ which is globally asymptotically stable in the interior of D and set*

$$R_2 = \frac{b}{\mu + di^*}. \tag{2.12}$$

Let $(S(t), E_1(t), \cdots, E_n(t), I(t))$ be a solution of System (2.1).

(1) If $R_2 > 1$, *then* $(S(t), E_1(t), \cdots, E_n(t), I(t)) \longrightarrow (\infty, \infty, \cdots, \infty, \infty)$, *when* $t \longrightarrow \infty$;

(2) If $R_2 = 1$, *then* $(S(t), E_1(t), \cdots, E_n(t), I(t)) \longrightarrow (S^*, E_1^*, \cdots, E_2^*, I^*)$, *when* $t \longrightarrow \infty$, *with* $S^* > 0, E_1^* > 0, \cdots, E_n^* > 0, I^* > 0$;

(3) If $R_2 < 1$, *then* $(S(t), E_1(t), \cdots, E_n(t), I(t)) \longrightarrow (0, 0, \cdots, 0, 0)$, *when* $t \longrightarrow \infty$.

Proof. Let's assume that $R_1 > 1$ and System (2.9) admits and endemic equilibrium $(s^*, e_1^*, \cdots, e_n^*, i^*)$ which is globally asymptotically stable in the interior of D. Then we have $dN/dt \longrightarrow (b - \mu - di^*)N$. The asymptotic growth rate of the population is $\alpha = b - \mu - di^*$. We have the sign relation $sign(\alpha) = sign(R_2 - 1)$. Therefore, if $R_2 > 1$, then $N(t) \longrightarrow \infty$; if $R_2 = 1$, then $N(t) \longrightarrow N^* > 0$; if $R_2 < 1$, then $N(t) \longrightarrow 0$. As the fractions approach an endemic equilibrium that is in the interior of D, the results follow. □

Remark 2.15. *Biologically,* R_2 *is the asymptotic reproduction number of the population, since the birth rate is b and the asymptotic death rate is* $\mu + di^*$.

We have derived three threshold parameters R_0, R_1 and R_2 that determine the dynamic of the fractions and that of the compartments sizes. The summary of the results is given in Table 2.

R_1	R_0	R_2	$(s, e_1, \cdots, e_n, i) \longrightarrow$	$(S, E_1, \cdots, E_n, I) \longrightarrow$
< 1	< 1		$(1, 0, \cdots, 0, 0)$	$(\infty, 0, \cdots, 0, 0)$
< 1	$= 1$		$(1, 0, \cdots, 0, 0)$	$(\infty, E_1^*, \cdots, E_n^*, I^*)$
≤ 1	> 1		$(1, 0, \cdots, 0, 0)$	$(\infty, \infty, \cdots, \infty, \infty)$
> 1	> 1	> 1	$(s^*, e_1^*, \cdots, e_n^*, i^*)$	$(\infty, \infty, \cdots, \infty, \infty)$
> 1	> 1	$= 1$	$(s^*, e_1^*, \cdots, e_n^*, i^*)$	$(S^* E_1^*, \cdots, E_n^*, I^*)$
> 1	> 1	< 1	$(s^*, e_1^*, \cdots, e_n^*, i^*)$	$(0, 0, \cdots, 0, 0)$

Table 2. Summary of the results for SE^{n}IS model

3. The model with treatment

Now we consider the model with treatment. To the $n+2$ compartments of the model above, we add the compartment T of the individual under treatment. We assume that the individuals

in T are not infectious and have not an additive death rate as those in I. The model diagram is given in Figure 2.

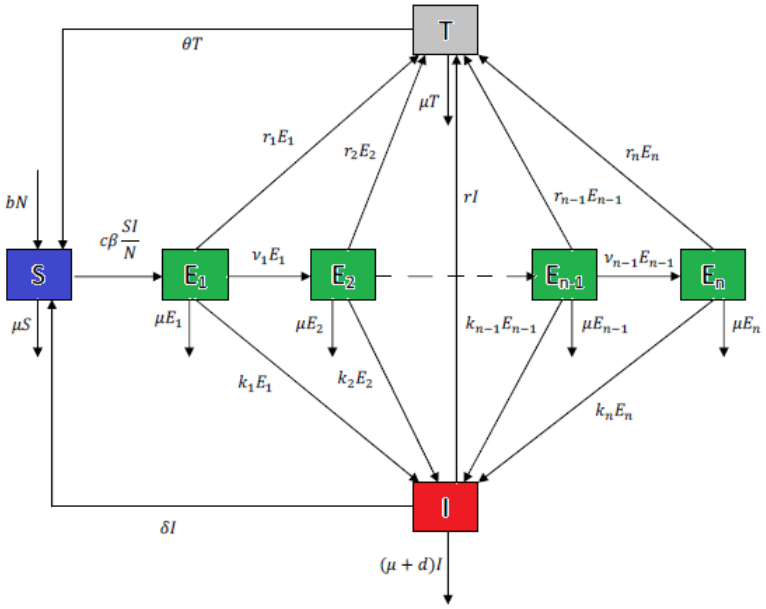


Figure 2. The transfer diagram of the SE^{n}ITS model with the susceptible class S, the n exposed classes E_1, E_2,...,E_n, the infectious class I and the treatment class T

3.1. The model

The model with treatment is given by the following ODE system.

$$
\begin{cases}
\dfrac{dS}{dt} = bN + \delta I + \theta T - c\beta S\dfrac{I}{N} - \mu S, \\
\dfrac{dE_1}{dt} = c\beta S\dfrac{I}{N} - (r_1 + k_1 + \nu_1 + \mu)E_1, \\
\dfrac{dE_m}{dt} = \nu_{m-1}E_{m-1} - (r_m + k_m + \nu_m + \mu)E_m, m = 2, \cdots, n, \\
\dfrac{dI}{dt} = \sum_{m=1}^{m=n} k_m E_m - (r + \delta + \mu + d)I, \\
\dfrac{dT}{dt} = \sum_{m=1}^{m=n} r_m E_m + rI - (\theta + \mu)T, \\
N(t) = S(t) + \sum_{m=1}^{m=n} E_m(t) + I(t) + T(t), \\
S(0) > 0, E_1(0) \geq 0, \cdots, E_n(0) \geq 0, I(0) \geq 0.
\end{cases}
\tag{3.1}
$$

3.2. The initial reproduction number

Theorem 3.1. *The initial reproduction number R_T of the epidemic defined by System (3.1) is given by*

$$R_T = \frac{c\beta}{\mu+d+\delta+r}\sum_{m=1}^{m=n}\frac{k_m}{\mu+\nu_m+k_m+r_m}\prod_{l=1}^{l=m-1}\frac{\nu_l}{\mu+\nu_l+k_l+r_l}. \tag{3.2}$$

Proof. R_T is the product of the contact rate c, the probability to transmit the disease during a contact β, the average infectious time $1/(r+\mu+d+\delta)$ and the probability for the exposed individual to become infectious $\sum_{m=1}^{m=n}\frac{k_m}{r_m+\mu+\nu_m+k_m}\prod_{l=1}^{l=m-1}\frac{\nu_l}{r_l+\mu+\nu_l+k_l}$. The latter is the sum of the probabilities to become infectious from the different latent compartments. More precisely $\frac{k_m}{r_m+\mu+\nu_m+k_m}\prod_{l=1}^{l=m-1}\frac{\nu_l}{r_l+\mu+\nu_l+k_l}$ is the probability for the individual to become infectious while being in the compartment E_m. □

Remark 3.2. *One gets R_T from the formula that gives R_0 (Equation (2.2)) by substituting $\mu+d+\delta$, $\mu+\nu_m+k_m, m=1,\cdots,n$, respectively by $\mu+d+\delta+r$, $\mu+\nu_m+k_m+r_m, m=1,\cdots,n$. Thus, we have $R_T < R_0$, the treatment reduces the reproduction number.*

Let $\tau_1,\cdots,\tau_n,\tau_i$ be the respective fractions of the treated individuals in the compartments $E_1,\cdots,E_n,I$. Thus we have

$$\begin{aligned}
\frac{c\beta}{\mu+d+\delta+r} &= \frac{\mu+d+\delta}{\mu+d+\delta+r}\frac{c\beta}{\mu+d+\delta} = (1-\tau_i)\frac{c\beta}{\mu+d+\delta},\\
\frac{k_m}{\mu+\nu_m+k_m+r_m} &= \frac{\mu+\nu_m+k_m}{\mu+\nu_m+k_m+r_m}\frac{k_m}{\mu+\nu_m+k_m} = (1-\tau_m)\frac{k_m}{\mu+\nu_m+k_m}, m=1,\cdots,n;\\
\frac{\nu_l}{r_l+\mu+\nu_l+k_l} &= \frac{\mu+\nu_l+k_l}{r_l+\mu+\nu_l+k_l}\frac{\nu_l}{\mu+\nu_l+k_l} = (1-\tau_l)\frac{\nu_l}{\mu+\nu_l+k_l}, l=1,\cdots,n.
\end{aligned}$$

Therefore R_T can be written as follow

$$\begin{aligned}
R_T &= (1-\tau_i)\frac{c\beta}{\mu+d+\delta}\sum_{m=1}^{m=n}(1-\tau_m)\frac{k_m}{\mu+\nu_m+k_m}\prod_{l=1}^{l=m-1}(1-\tau_l)\frac{\nu_l}{\mu+\nu_l+k_l}\\
&= (1-\tau_i)\frac{c\beta}{\mu+d+\delta}\sum_{m=1}^{m=n}\frac{k_m}{\mu+\nu_m+k_m}\prod_{l=1}^{l=m}(1-\tau_l)\prod_{l=1}^{l=m-1}\frac{\nu_l}{\mu+\nu_l+k_l}.
\end{aligned}$$

R_T is the sum of n terms. $(1-\tau_i)$ and $(1-\tau_1)$ are factors of all the n terms. While $(1-\tau_m)$ is factor of $n-m+1$ terms, $m=2,\cdots,n$. For instance $1-\tau_n$ is a factor of the last term only.

The biological meaning of this is that the treatment of an infectious individual or an individual in the latent class E_1 has an impact on all the infected compartments. While the treatment of an individual in the latent class E_m has a direct impact on E_m and the infected classes that come after E_m only. Therefore, for an optimal strategy of treatment, the priority is to treat the infectious individuals and the people in the earliest stage of latency.

Let's define the treatment force γ by setting $\gamma = 1 - R_T/R_0$. We have $R_T = (1-\gamma)R_0$, thus

$$R_T \leq 1 \Longleftrightarrow \gamma \geq 1 - \frac{1}{R_0}.$$

The critical treatment force to eradicate the epidemic is $\gamma_c := 1 - 1/R_0$. If $\gamma > \gamma_c$, then the epidemic will dies out. But if $\gamma < \gamma_c$, then the epidemic will go on in spite of the treatment.

Theorem 3.3. *If $k_1 = k_2 = \cdots = k_n = k$ and $r_1 = r_2 = \cdots = r_n = r_e$ then*

$$R_T = \frac{kc\beta}{(\mu + k + r_e)(\mu + \delta + d + r)}. \tag{3.3}$$

Proof. The proof of Theorem 3.3 is similar to that of Theorem 2.3. □

Remark 3.4. *The RHS of Equation (3.3) is the basic reproduction number of the SEIS model with one latent stage and treatment where k and r_e denote respectively the activation rate and the treatment rate of the latent individuals* [12].

Let k_e be the "effective" activation rate given by Equation (2.5). We define the effective "treatment" rate for latent individuals as the treatment rate r_e for the treatment model with one latent stage with activation rate k_e that has the same treatment initial reproduction number as that of the treatment model with n latent stages. By equations (3.2) and (3.3), one gets the following result.

Theorem 3.5. *The effective treatment rate of the latent individuals is*

$$r_e = \frac{k_e - (\mu + k_e)\displaystyle\sum_{m=1}^{m=n} \frac{k_m}{\mu + \nu_m + k_m + r_m} \prod_{l=1}^{l=m-1} \frac{\nu_l}{\mu + \nu_l + k_l + r_l}}{\displaystyle\sum_{m=1}^{m=n} \frac{k_m}{\mu + \nu_m + k_m + r_m} \prod_{l=1}^{l=m-1} \frac{\nu_l}{\mu + \nu_l + k_l + r_l}} \tag{3.4}$$

3.3. Equilibria

As we assume that the population is growing in absence of the disease ($b > \mu$), System (3.1) has no disease free equilibrium. The following result give the conditions for endemic equilibria.

Theorem 3.6. *Let $X(t) = (S(t), E_1(t), \cdots, E_n(t), I(t))$ be a solution of System (3.1). $X(t)$ is constant if and only if the parameters satisfy*

$$\left(\frac{bd}{b-\mu}+\delta\right)\frac{1}{r+\delta+\mu+d}\left(k_n+(r_n+k_n+\mu)\sum_{m=1}^{m=n-1}\frac{k_m}{\nu_m}\prod_{l=m+1}^{l=n-1}\frac{r_l+k_l+\nu_l+\mu}{\nu_l}\right)$$

$$+\frac{\theta}{\theta+\mu}\left[(r_n+k_n+\mu)\sum_{m=1}^{m=n-1}\left(r_m+\frac{rk_m}{r+\delta+\mu+d}\right)\frac{1}{\nu_m}\prod_{l=m+1}^{l=n-1}\frac{r_l+k_l+\nu_l+\mu}{\nu_l}\right. \tag{3.5}$$

$$\left.+r_n+\frac{rk_n}{r+\delta+\mu+d}\right]-\left(1+\frac{d\mu}{c\beta(b-\mu)}\right)(r_n+k_n+\mu)\prod_{l=1}^{l=n-1}\frac{r_l+k_l+\nu_l+\mu}{\nu_l}=0$$

and the initial values satisfy

$$\begin{cases} S(0)=\frac{1}{c\beta}\frac{d}{b-\mu}\left(\prod_{l=1}^{l=n-1}\frac{r_l+k_l+\nu_l+\mu}{\nu_l}\right)(r_n+k_n+\mu)E_n(0), \\ E_m(0)=\frac{1}{\nu_m}\left(\prod_{l=m+1}^{l=n-1}\frac{r_l+k_l+\nu_l+\mu}{\nu_l}\right)(r_n+k_n+\mu)E_n(0), m=1,\cdots,n-1, \\ I(0)=\frac{1}{r+\delta+\mu+d}\left(k_n+(r_n+k_n+\mu)\sum_{m=1}^{m=n-1}\frac{k_m}{\nu_m}\prod_{l=m+1}^{l=n-1}\frac{r_l+k_l+\nu_l+\mu}{\nu_l}\right)E_n(0), \\ T(0)=\frac{1}{\theta+\mu}\left[(r_n+k_n+\mu)\sum_{m=1}^{m=n-1}\left(r_m+\frac{rk_m}{r+\delta+\mu+d}\right)\frac{1}{\nu_m}\prod_{l=m+1}^{l=n-1}\frac{r_l+k_l+\nu_l+\mu}{\nu_l}\right. \\ \qquad \left.+r_n+\frac{rk_n}{r+\delta+\mu+d}\right]E_n(0), \\ E_n(0)>0. \end{cases} \tag{3.6}$$

Proof. We have $dN/dt = (b-\mu)N - dI$. Thus, $N(t)$ is constant if and only if $I(t)$ is constant and $N = (b-\mu)^{-1}dI$.

By the derivative of I, $I(t)$ is constant if and only if $I = (\delta+\mu+d)^{-1}\sum_{m=1}^{m=n}k_mE_m$. By using

successively the derivative of $E_n, E_{n-1}, \cdots, E_1, I, T$ and S, one gets that $X(t)$ is constant if and only if the initial values satisfy System (3.6) and the parameters satisfy Equation (3.5). □

Remark 3.7. *When the parameters satisfy Equation (3.5), System (3.1) admits infinite equilibria and there is no stability.*

3.4. The dynamic of the fractions

Now we consider the fractions of the populations in the different compartments, $s = S/N, e_1 = E_1/N, \cdots, e_n = E_n/N, i = I/N$ and $\tau = T/N$. By System (3.1) one gets

$$
\begin{cases}
\dfrac{ds}{dt} = b - bs + \delta i + \theta\tau - (c\beta - d)si, \\
\dfrac{de_1}{dt} = c\beta si - (r_1 + k_1 + \nu_1 + b)e_1 + die_1, \\
\dfrac{de_m}{dt} = \nu_{m-1}e_{m-1} - (r_m + k_m + \nu_m + b)e_m + die_m, m = 2, \cdots, n, \\
\dfrac{di}{dt} = \displaystyle\sum_{m=1}^{m=n} k_m e_m - (r + b + \delta + d)i + di^2, \\
\dfrac{d\tau}{dt} = \displaystyle\sum_{m=1}^{m=n} r_m e_m + ri - (\theta + b)\tau + di\tau, \\
\text{with } s + \displaystyle\sum_{m=1}^{m=n} e_m + i + \tau = 1, \\
s(0) > 0, e_1(0) \geq 0, \cdots, e_n(0) \geq 0, i(0) \geq 0, \tau(0) \geq 0.
\end{cases} \tag{3.7}
$$

As $\tau = 1 - (s + \sum_{m=1}^{m=n} e_m + i)$, it is enough to consider

$$
\begin{cases}
\dfrac{ds}{dt} = b + \theta - (b + \theta)s + (\delta - \theta)i - \theta \displaystyle\sum_{m=1}^{m=n} e_m - (c\beta - d)si, \\
\dfrac{de_1}{dt} = c\beta si - (r_1 + k_1 + \nu_1 + b)e_1 + die_1, \\
\dfrac{de_m}{dt} = \nu_{m-1}e_{m-1} - (r_m + k_m + \nu_m + b)e_m + die_m, m = 2, \cdots, n, \\
\dfrac{di}{dt} = \displaystyle\sum_{m=1}^{m=n} k_m e_m - (r + b + \delta + d)i + di^2, \\
\text{with } s + \displaystyle\sum_{m=1}^{m=n} e_m + i \leq 1, \\
s(0) > 0, e_1(0) \geq 0, \cdots, e_n(0) \geq 0, i(0) \geq 0, \tau(0) \geq 0.
\end{cases} \tag{3.8}
$$

The feasible region is

$$
\Delta = \left\{ (s, e_1, \cdots, e_n, i)/s \geq 0, e_1 \geq 0, \cdots, e_n \geq 0, i \geq 0, s + \sum_{m=1}^{m=n} e_m + i \leq 1 \right\}.
$$

It is obvious that $(1,0,\cdots,0,0)$ is the unique disease free equilibrium of System (3.8). The dynamic of System (3.8) depends on the threshold parameter R_{1T} given by

$$R_{1T} = \frac{c\beta}{b+d+\delta+r}\sum_{m=1}^{m=n}\frac{k_m}{b+\nu_m+k_m+r_m}\prod_{l=1}^{l=m-1}\frac{\nu_l}{b+\nu_l+k_l+r_l}. \tag{3.9}$$

Theorem 3.8. *The disease free equilibrium* $(1,0,\cdots,0,0)$ *of System (3.8) is globally asymptotically stable in* Δ *if* $R_{1T} \leq 1$ *and unstable when* $R_{1T} > 1$.

Proof. The proof of Theorem 3.8 is similar to that of Theorem 2.11 □

Biologically Theorem 3.9 means that if the relative treatment reproduction number R_{1T} is below one then the fraction of infected individuals will be negligible, while it will persist if R_{1T} is larger than one. Let's define the relative treatment force γ_1 by setting $\gamma_1 = 1 - R_{1T}/R_1$. We have

$$R_{1T} \leq 1 \Longleftrightarrow \gamma_1 \geq 1 - 1/R_1.$$

The critical relative treatment force is $\gamma_{1c} = 1 - 1/R_1$. If $\gamma_1 \geq \gamma_{1c}$ then the fraction of infected individuals in the population vanishes, while it persists if $\gamma_1 < \gamma_{1c}$.

When $R_{1T} > 1$ the disease free equilibrium of System (3.8) is unstable. The simulations that we made show that in this case there is one endemic equilibrium that is globally asymptotically stable in the interior of Δ (Figure 12 (c) and (d)).

Conjecture 3.9. *If* $R_{1T} > 1$*, then System (3.8) admits one and only one endemic equilibrium that is globally asymptotically stable in the interior of* Δ.

3.5. The asymptotic behaviour of the sizes

For the asymptotic behaviour of the compartments sizes we have similar results as that of the model without treatment. The treatment compartment size T have the same behaviour as that of the infected compartments sizes.

Conjecture 3.10. *Let* $(S(t),E_1(t),\cdots,E_n(t),I(t),T(t))$ *be a solution of System (3.1).*

(1) If $R_T < 1$*, then* $(S(t),E_1(t),\cdots,E_n(t),I(t),T(t)) \longrightarrow (\infty,0,\cdots,0,0,0)$.

(2) If $R_T = 1$*, then* $(S(t),E_1(t),\cdots,E_n(t),I(t),T(t)) \longrightarrow (\infty,E_1^*,\cdots,E_n^*,I^*,T^*)$, *with* $E_1^* > 0,\cdots,E_n^* > 0, I^* > 0, T^* > 0$.

(3) If $R_{1T} < 1 < R_T$, *then* $(S(t), E_1(t), \cdots, E_n(t), I(t), T(t)) \longrightarrow (\infty, \infty, \cdots, \infty, \infty, \infty)$.

Now let's assume that $R_{1T} > 1$ and that System (3.8) admits an endemic equilibrium that is globally asymptotically stable in the interior of Δ. In this case as the fractions approach an endemic equilibrium, the sizes of all the compartments have the same behaviour as that of the population size $N(t)$.

Theorem 3.11. *Let's assume that* $R_{1T} > 1$ *and that System (3.8) admits an endemic equilibrium* $(s^*, e_1^*, \cdots, e_n^*, i^*, \tau^*)$ *that is globally asymptotically stable in the interior of* Δ *and set* $R_{2T} = b/(\mu + di^*)$. *Let* $(S(t), E_1(t), \cdots, E_n(t), I(t), T(t))$ *be a solution of System (3.1).*

(1) If $R_{2T} > 1$, *then* $N(t) \longrightarrow \infty$;

(2) If $R_{2T} = 1$, *then* $N(t) \longrightarrow N^* > 0$;

(3) If $R_{2T} < 0$, *then* $N(t) \longrightarrow 0$;

Proof. The proof of Theorem 3.11 is similar to that of Theorem 2.14 □

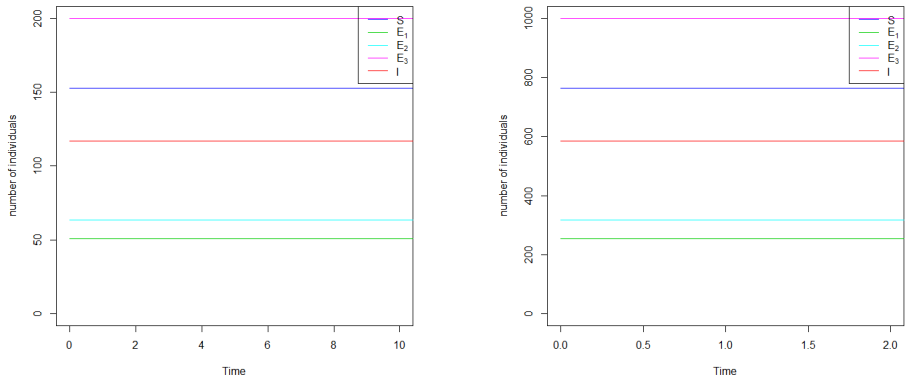
In this section we have studied the dynamic of the SEIS model with n latent classes with treatment (SE^nITS model). The dynamic of the epidemic and that of the population depend on three threshold parameters R_T, R_{1T} and R_{2T}. If $R_T < 1$ then the disease cannot invade the population. If $R_T = 1$ then the number of infected stabilizes. $R_T > 1$ then the epidemic will invade the population and the dynamic of the proportions depends on R_1. If $R_{1T} \leq 1$, then the proportion of infected individuals remains negligible. If $R_{1T} > 1$, then the proportion of the infected individuals will be important and the epidemic will affect the dynamic of the population. We defined the treatment force γ and the relative treatment force γ_1. They satisfy respectively $R_T = (1-\gamma)R_0$ and $R_{1T} = (1-\gamma_1)R_1$. The critical treatment force $\gamma_c := 1 - 1/R_0$ is the minimal treatment force needed to eradicate the disease. The relative critical treatment force $\gamma_{1c} := 1 - 1/R_1$ is the minimal relative treatment force needed to eradicate the disease in term of the proportions. The recovery rate θ of the treated individuals does not intervene in the thresholds parameters R_T and R_{1T}.

4. Simulations

In this section we make numerical simulations to validate the theoretical results. We set $n = 3, \mu = 1$, that is we assume that there are 3 latent classes and the life expectancy is the time unit. The other parameters and the initial values are chosen arbitrary to cover all the different scenarios that we have in the previous section. We use the software R and particularly the package deSolve [13] to integrate the ODE systems.

4.1. Simulations of the model without treatment

Let's consider first the case with constant solution for System (2.1). For Figure 3, the parameters values satisfy equation (2.6), and the initial values satisfy System (2.7). In fact for the initial values we have deduced $S(0), E_1(0), E_2(0)$ and $I(0)$ from $E_3(0)$, by System (2.7). In (a) as in (b) the sizes of all the compartments are constant. This confirms Theorem 2.6.



(a) Dynamics of compartments sizes (b) Dynamics of compartments sizes

Figure 3. SE^{3}IS curves with $b = 3, \mu = 1, c\beta = 60, \nu_1 = 30, \nu_2 = 20, k_1 = 5, k_2 = 3, k_3 = 1, \delta = 2, d = 10$. By Equation (2.6) we deduce $k_3 = 5.367041$. For (a) the initial values satisfy System (2.7) with $E_3(0) = 200$. For (b) the initial values satisfy System (2.7) with $E_3(0) = 1000$. In (a) and in (b) the sizes of the 5 compartments are constant.

We simulate now cases with varying population sizes. We start by integrating the fractions system. In Figure 4 we have in each case 10 solutions paths of System (2.8) starting at different

initial values. In (a) and (b) where $R_1 \approx 0.58$ and $R_1 \approx 0.98$ respectively, all the 10 solutions paths approach the disease free equilibrium. This validates that when $R_1 \leq 1$, the fractions disease free equilibrium is globally asymptotically stable in its feasible region. For (d) and (c), where $R_1 \approx 2.88$ and $R_1 \approx 4.32$, respectively, all the 10 solutions paths approach an endemic equilibrium. These results confirm that when $R_1 > 1$, the disease free equilibrium is unstable and that there is an endemic equilibrium that is globally asymptotically stable in the interior of the feasible region. The endemic equilibrium in (c) is different of that in (d). Thus, the endemic equilibrium depends on the parameters values.

Now we integrate System (2.1) to validate the results on the asymptotic behaviour of the compartments sizes. We set $(S(0), E_1(0), E_2(0), E_3(0), I(0)) = (1000, 200, 100, 200, 100)$ for the initial values.

In Figure 5 we have the best scenario, the epidemic dies out, while the population goes on growing exponentially. The parameters values satisfy $R_0 \approx 0.82$. It confirm that the epidemic cannot invade the population when the basic reproduction number is below one ($R_0 < 1$). It validates also Conjecture 2.13 (1).

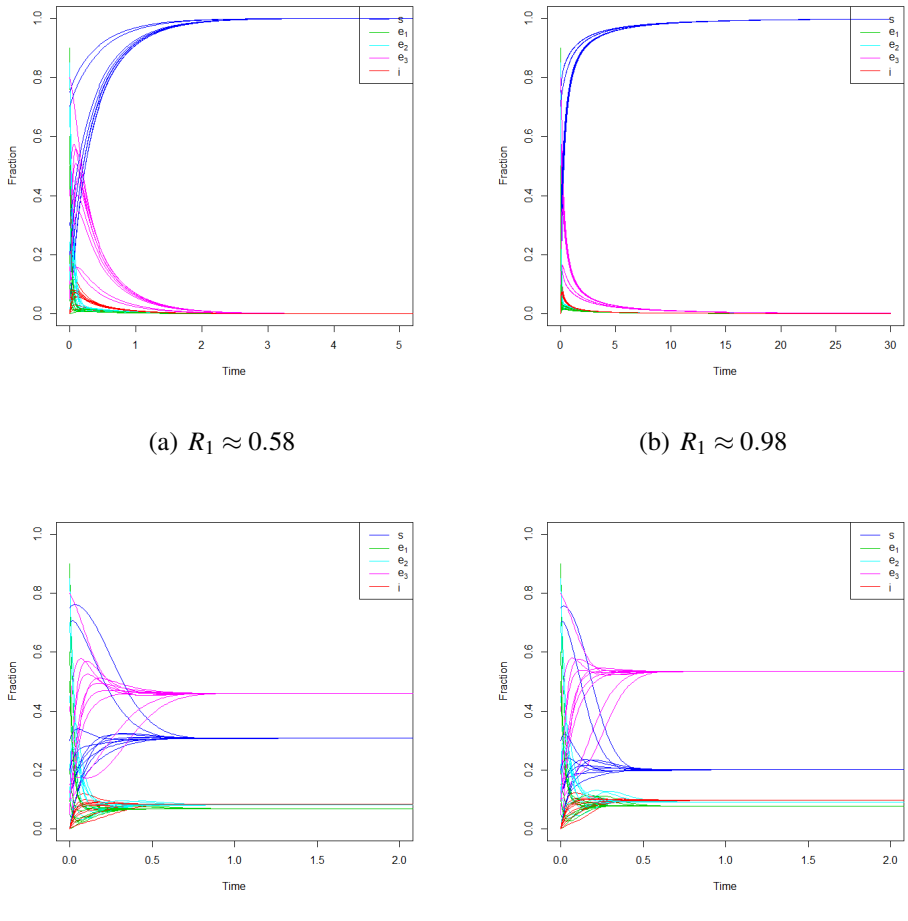
In Figure 6 we have the case with $R_0 = 1$. We get $R_0 = 1$ by deducing $c\beta$ from the other parameters and using equation (2.2). The population grow exponentially, while the infected compartments sizes go to positive numbers. This simulation confirms Conjecture 2.13 (2).

In Figure 7 all the compartments grow exponentially. But the population growth rate is larger. Therefore, the fractions approach the disease free equilibrium. we have $R_0 \approx 1.24$ and $R_1 \approx 0.84$. Thus this result confirms Conjecture 2.13 (3).

In Figure 8 all the compartments grow exponentially, while the fractions approach an endemic equilibrium. We have $R_0 \approx 3.55$ and $R_1 \approx 2.35$. The asymptotic reproduction number of the population is $R_2 \approx 1.50$. Thus this result complies with Theorem 2.14 (1).

In Figure 9 we have a case with $R_0 \approx 6.18$ and $R_1 \approx 3.84$. The fraction approach an endemic equilibrium such that the asymptotic growth rate of the population $R_2 = 1$. To get this, we have chosen the parameters values such that they satisfy Equation (2.6). All the compartments sizes stabilize. The epidemic has stopped the growth of the population. Thus Theorem 2.14 (2) is confirmed.

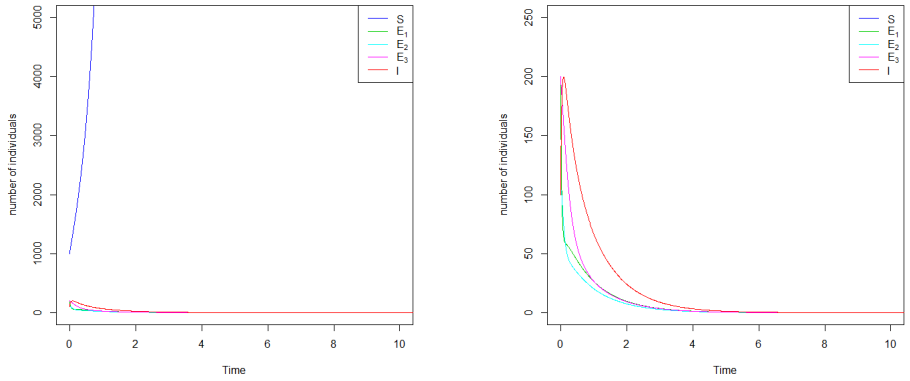
In Figure 10 we have the worse scenario, the population vanishes. The fraction approach an endemic equilibrium such that the asymptotic growth rate of the population is below one



(a) $R_1 \approx 0.58$ (b) $R_1 \approx 0.98$

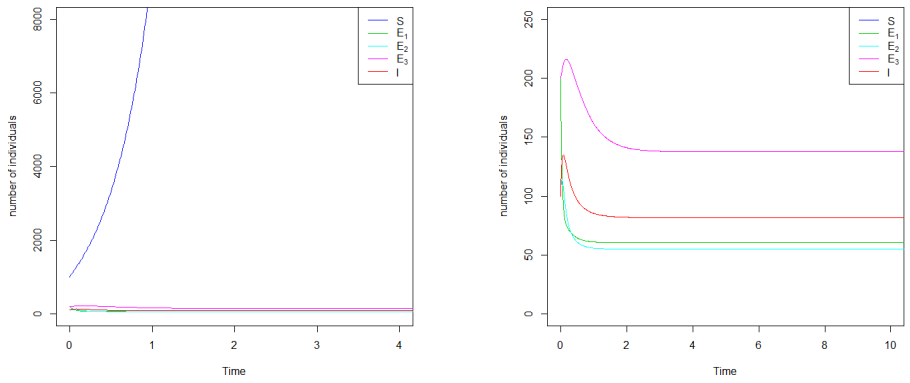
(c) $R_1 \approx 2.88$ (d) $R_1 \approx 4.32$

Figure 4. In each case we have 10 solutions paths of System (2.8) with different initial values. The parameters values are $b = 3, \mu = 1, \nu_1 = 30, \nu_2 = 20, k_1 = 5, k_2 = 3, k_3 = 1, \delta = 4, d = 6$. For (a) $c\beta = 20$, that gives $R_1 \approx 0.58$. For (b) $c\beta = 34$, that gives $R_1 \approx 0.98$. In (a) and in (b) all the solutions approach the disease free equilibrium $(1,0,0,0,0)$. For (c) $c\beta = 100$, that gives $R_1 \approx 2.88$; all the solutions approach the same endemic equilibrium $(s^*, e_1^*, e_2^*, e_3^*, i^*) \approx (0.31, 0.07, 0.09, 0.46, 0.08)$. For (d), we have $c\beta = 150$ that gives $R_1 \approx 4.32$; all the solutions approach the same endemic equilibrium $(s^*, e_1^*, e_2^*, e_3^*, i^*) \approx (0.20, 0.08, 0.09, 0.53, 0.10)$.



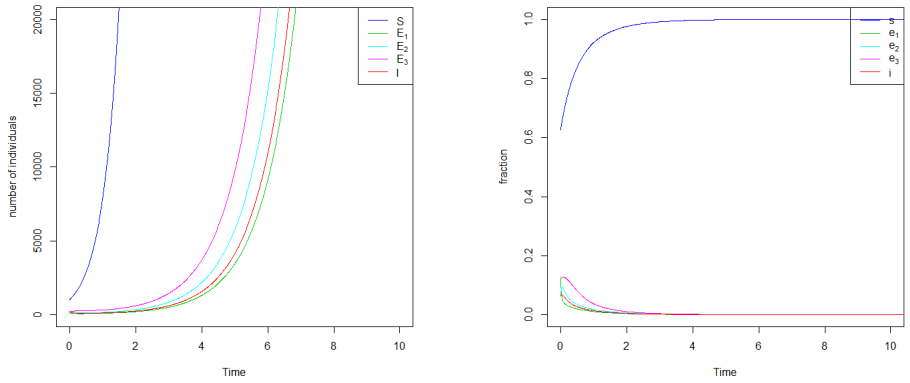
(a) Dynamics of the compartments sizes (b) Dynamics of the compartments sizes

Figure 5. SE^{3}IS curves with $b = 3, \mu = 1, c\beta = 10, \nu_1 = 10, \nu_2 = 5, k_1 = 15, k_2 = 8, k_3 = 4, \delta = 4, d = 6$, that gives $R_0 \approx 0.82$. The infected compartments vanish, while the population goes on growing exponentially. In (b) we made a zoom to show the dynamics of the sizes of the infected compartments.



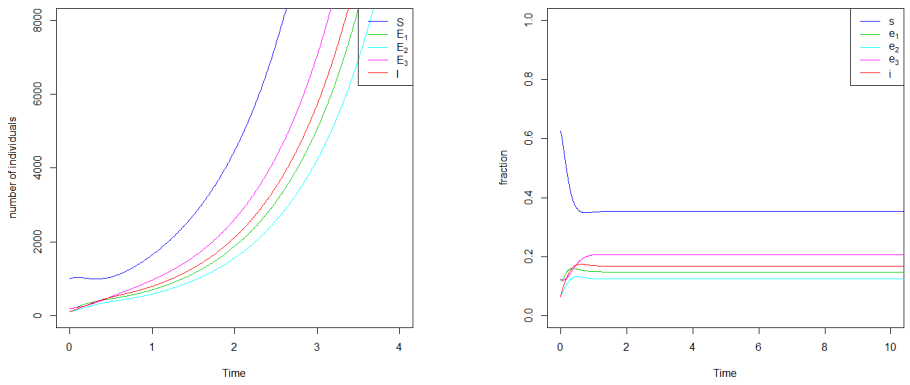
(a) Dynamics of compartments sizes (b) Dynamics of the compartments sizes

Figure 6. SE^{3}IS curves with $b = 3, \mu = 1, c\beta = 14.10429, \nu_1 = 10, \nu_2 = 5, k_1 = 8, k_2 = 5, k_3 = 1, \delta = 4, d = 6$, that gives $R_0 \approx 1$ and $R_1 \approx 0.66$. The population grow exponentially, while the sizes of the infected compartments approach positive values $(E_1^*, E_2^*, E_3^*, I^*) \approx (61, 55, 137, 81)$. In (b) we made a zoom to show the dynamics of sizes of the infected compartments.



(a) Dynamics of compartments sizes (b) Dynamics of the fractions

Figure 7. SE^{3}IS curves with $b = 3, \mu = 1, c\beta = 25, \nu_1 = 20, \nu_2 = 5, k_1 = 8, k_2 = 5, k_3 = 1, \delta = 4, d = 10$, that gives $R_0 \approx 1.24$ and $R_1 \approx 0.84$. All the compartments grow exponentially. But the fractions approach the disease free equilibrium $(1,0,0,0,0)$.



(a) Dynamics of compartments sizes (b) Dynamics of the fractions

Figure 8. SE^{3}IS curves with $b = 3, \mu = 1, c\beta = 50, \nu_1 = 10, \nu_2 = 5, k_1 = 8, k_2 = 5, k_3 = 1, \delta = 4, d = 6$, that gives $R_0 \approx 3.55$ and $R_1 \approx 2.35$. All the compartments grow exponentially, while the fractions approach an endemic equilibrium $(s^*, e_1^*, e_2^*, e_3^*, i^*) \approx (0.35, 0.15, 0.12, 0.21, 0.17)$. The asymptotic reproduction number of the population is $R_2 \approx 1.50$ and its asymptotic growth rate is $\alpha \approx 0.99$.

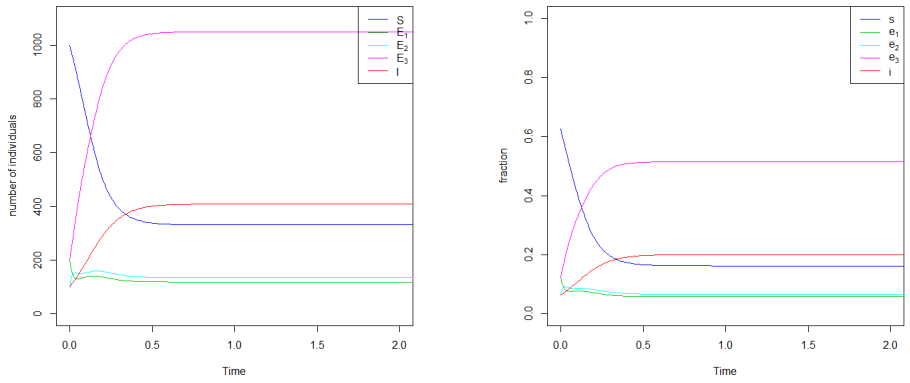
($R_2 \approx 0.86$). The epidemic has turned the exponential growth of the population to an exponential decay. This result confirms Theorem 2.14 (3).

In this subsection we have integrated numerically System (2.1) and System (2.8) for different values of the parameters. The numerical results comply with the theoretical ones.

4.2. Simulation of the model with treatment

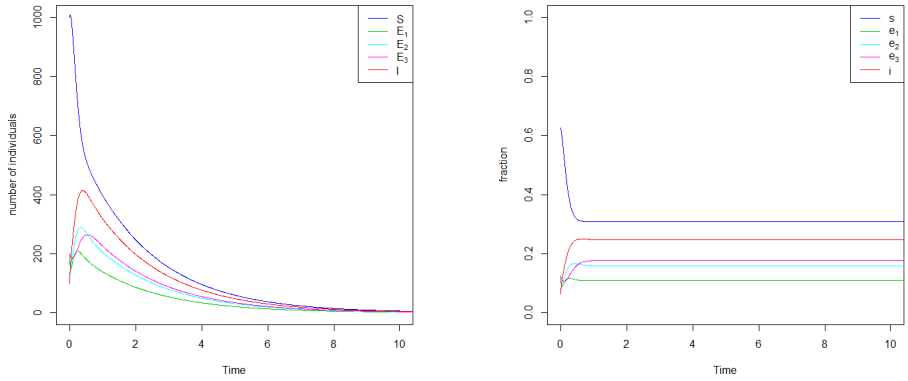
Now we simulate the model with treatment to illustrate and validate the theoretical results of Section 3.

Let's consider first the case with constant solution for System (3.1). For Figure 11, the parameters values satisfy Equation (3.5), and the initial values satisfy System (3.6). In fact for the initial values we have deduced $S(0), E_1(0), E_2(0)$, $I(0)$ and $T(0)$ from $E_3(0)$ by System (3.6). In (a) as in (b) the sizes of all the compartments are constant. Thus simulation confirms Theorem 3.6.



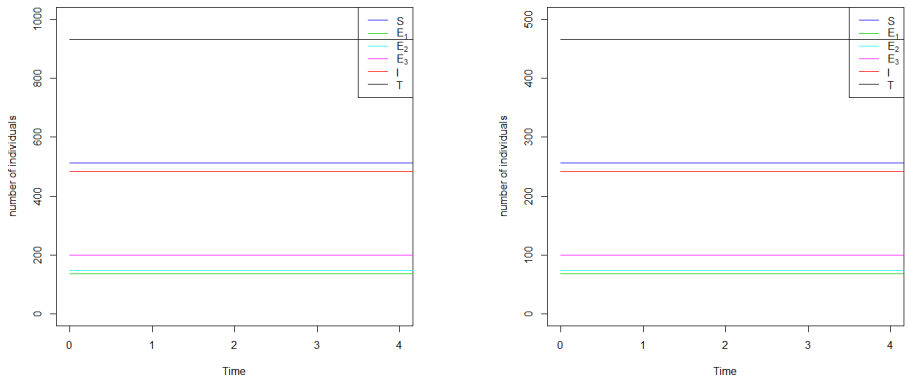
(a) Dynamics of compartments sizes (b) Dynamics of the fractions

Figure 9. SE^{3}IS curves with $b = 3, \mu = 1, c\beta = 100, \nu_1 = 50, \nu_2 = 40, k_1 = 5, k_2 = 3, \delta = 4, d = 10$. By Equation (2.6) we get $k_3 = 4.107866$, that gives $R_0 \approx 6.18$ and $R_1 \approx 3.84$. The sizes of the compartment approach an endemic equilibrium $(S^*, E_1^*, E_2^*, E_3^*, I^*) \approx (331, 118, 134, 1051, 408)$.The fractions approach an endemic equilibrium $(s^*, e_1^*, e_2^*, e_3^*, i^*) \approx (0.16, 0.06, 0.07, 0.51, 0.20)$. The asymptotic growth rate of the population is $\alpha = 0$ and its asymptotic reproduction number is $R_2 = 1$.



(a) Dynamics of compartments sizes (b) Dynamics of the fractions

Figure 10. SE^{3}IS curves with $b = 3, \mu = 1, c\beta = 50, \nu_1 = 20, \nu_2 = 5, k_1 = 15, k_2 = 8, k_3 = 4, \delta = 4, d = 10$, that gives $R_0 \approx 2.98$ and $R_1 \approx 2.21$. The fractions approach an endemic equilibrium $(s^*, e_1^*, e_2^*, e_3^*, i^*) \approx (0.31, 0.11, 0.16, 0.18, 0.25)$. The asymptotic growth rate of the population is $\alpha \approx -0.48$ and its asymptotic reproduction number is $R_2 \approx 0.86$. Thus it vanishes.



(a) Dynamics of compartments sizes (b) Dynamics of compartments sizes

Figure 11. SE^{3}IS curves with $b = 6, \mu = 1, c\beta = 200, \nu_1 = 100, \nu_2 = 50, k_1 = 40, k_2 = 35, \delta = 4, d = 25, \theta = 5, r_1 = 10, r_2 = 7, r_3 = 4, r = 5$. By Equation (2.6) we deduce $k_3 = 31.55076$. For (a) the initial values satisfy System (3.6) with $E_3(0) = 200$. For (b) the initial values satisfy System (2.7) with $E_3(0) = 100$. In (a) and in (b) the sizes of the 6 compartments are constant.

We simulate the fractions system (3.7) to validate the results on the dynamic of the fractions. In Figure 12 we have in each case 10 solutions paths of System (3.7) starting at different initial values. In (a) and in (b) where we have respectively $R_{1T} \approx 0.45$ and $R_{1T} \approx 0.99$, all the 10 solutions approach the disease free equilibrium. these simulations confirm that if $R_{1T} < 1$ or equivalently if $\gamma_1 \geq \gamma_{1c}$ then the fractions disease free equilibrium is globally asymptotically stable in Δ. In (c) and (d) where $R_{1T} > 1$ the 10 solutions approach an endemic equilibrium. Thus it confirm that if $R_{1T} > 1$ or equivalently if $\gamma_1 < \gamma_{1c}$ then the fractions disease free equilibrium is unstable and there is an endemic equilibrium which is globally asymptotically stable in the interior of the feasible set Δ. These simulations validate Theorem 3.8 and Conjecture 3.9.

In Figure 13 we have the best scenario, the epidemic dies out, while the population goes on growing exponentially. The parameters values satisfy $R_0 \approx 3.55$ and $R_T \approx 0.92$. It confirm that the epidemic cannot invade the population when $R_T < 1$. It validates Conjecture 3.10 (1).

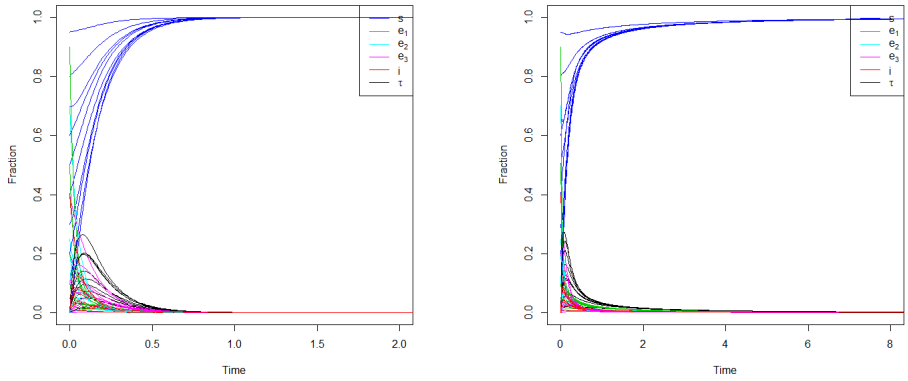
In Figure 14 all the compartments grow exponentially. But the population growth rate is larger. Therefore, the fractions approach the disease equilibrium. We have $R_0 \approx 4.25$ and $R_1 \approx 2.81$. With the treatment we have $R_T \approx 1.11$ and $R_{1T} \approx 0.91$. Thus this result confirms Conjecture 3.10 .

In Figure 15 all the compartments grow exponentially, while the fractions approach an endemic equilibrium. We have $R_0 \approx 7.09, R_1 \approx 4.69, R_T \approx 1.85$ and $R_{1T} \approx 1.52$. The asymptotic reproduction number of the population is $R_{2T} \approx 2.37$. Thus this result complies with Theorem 3.11 (3).

In Figure 16 the fractions approach an endemic equilibrium such that $R_{2T} = 1$. The sizes of all the compartments stabilize. In spite of the treatment, the epidemic has stopped the growth of the population. Thus this result complies with Theorem 3.11 (1).

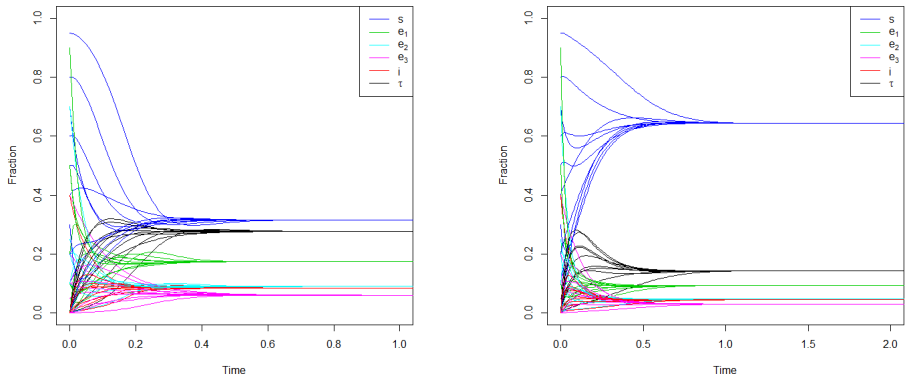
In Figure 17 the fractions approach an endemic equilibrium such that $R_{2T} = 0.97$. The population vanishes. In spite of the treatment, the epidemic has turned the exponential growth of the population to an exponential decay. Thus this result complies with Theorem 3.11 (3).

Now we simulate two epidemics with two different recovery rate θ for the treated individuals in order to check its impact on the epidemic. In Figure 18 we have two cases where all the parameters have the same values except that we set respectively $\theta = 15$ and 150 in (a) and in



(a) $R_{1T} \approx 0.45$

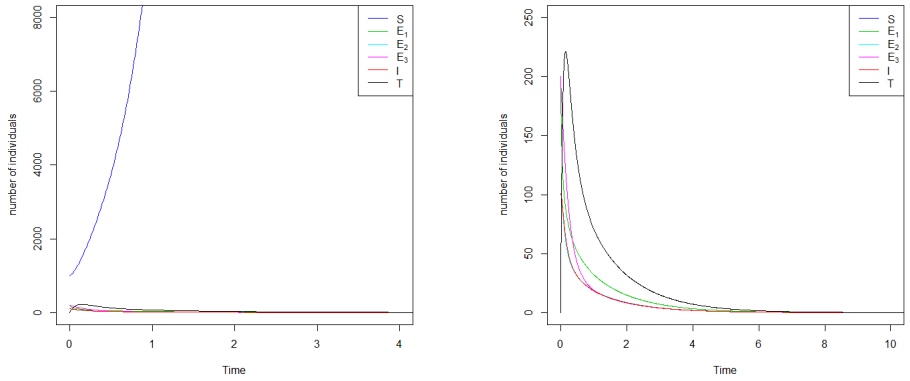
(b) $R_{1T} \approx 0.99$



(c) $R_{1T} \approx 3.03$

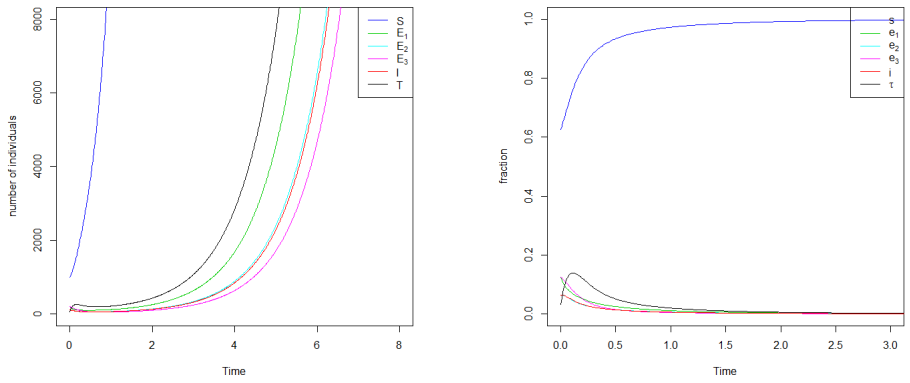
(d) $R_{1T} \approx 1.52$

Figure 12. In each case we have 10 solutions paths of System (3.7) with different initial values. The parameters values are $b = 3, \mu = 1, \nu_1 = 10, \nu_2 = 5, k_1 = 8, k_2 = 5, k_3 = 1, \delta = 4, d = 6, \theta = 10, r_1 = 10, r_2 = 7, r_3 = 4, r = 10$. For (a) $c\beta = 30$, that gives $R_{1T} \approx 0.45$. For (b) $c\beta = 65$, that gives $R_{1T} \approx 0.99$. In (a) and in (b) all the solutions approach the disease free equilibrium $(1,0,0,0,0,0)$. For (c) $c\beta = 200$, that gives $R_{1T} \approx 3.03$; all the solutions approach the same endemic equilibrium $(s^*, e_1^*, e_2^*, e_3^*, i^*, \tau^*) \approx (0.31, 0.17, 0.09, 0.06, 0.08, 0.28)$. For (d), we have $c\beta = 100$ that gives $R_{1T} \approx 1.52$; all the solutions approach the same endemic equilibrium $(s^*, e_1^*, e_2^*, e_3^*, i^*, \tau^*) \approx (0.64, 0.09, 0.05, 0.03, 0.04, 0.14)$.



(a) Dynamics of the compartments sizes (b) Dynamics of the compartments sizes

Figure 13. SE^{3}ITS curves with $b = 3, \mu = 1, c\beta = 50, \nu_1 = 10, \nu_2 = 5, k_1 = 8, k_2 = 5, k_3 = 1, \delta = 4, d = 6, \theta = 10, r_1 = 10, r_2 = 7, r_3 = 4, r = 10$, that gives $R_0 \approx 3.55, R_1 \approx 2.35, R_T \approx 0.92$ and $R_{1T} \approx 0.76$. The infected compartments vanish, while the population goes on growing exponentially. In (b) we made a zoom to show the dynamics of the infected compartments.



(a) Dynamics of compartments sizes (b) Dynamics of the fractions

Figure 14. SE^{3}ITS curves with $b = 3, \mu = 1, c\beta = 60, \nu_1 = 10, \nu_2 = 5, k_1 = 8, k_2 = 5, k_3 = 1, \delta = 4, d = 6, \theta = 10, r_1 = 10, r_2 = 7, r_3 = 4, r = 10$, that gives $R_0 \approx 4.25, R_1 \approx 2.81, R_T \approx 1.11$ and $R_{1T} \approx 0.91$. All the compartments grow exponentially. But the fractions approach the disease free equilibrium.

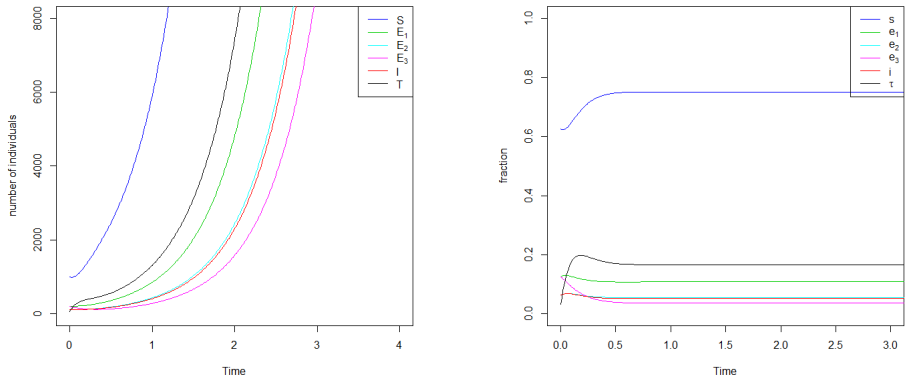
(b). In each case the fractions approach an endemic equilibrium. The asymptotic infectious fraction is respectively 0.05 and 0.8. The asymptotic reproduction number of the population is respectively $R_2 \approx 2.273$ and $R_2 \approx 2.06$. The asymptotic fraction of infectious individuals increases then with the recovery rate of the treated individuals.

The simulations of the treatment model agree with the theoretical results found in Section 3.

In this section we have integrated numerically the different system studied in the previous section. The simulations results validate the theoretical results. Beyond the validations of the theorems, the conjectures are confirmed.

5. Discussions and conclusion

We have studied an SEIS model with n serial latent classes with a standard incidence in a population that grows exponentially before the introduction of the disease. The disease induces an additive death rate d for the infectious, affecting hence the dynamic of the population. We



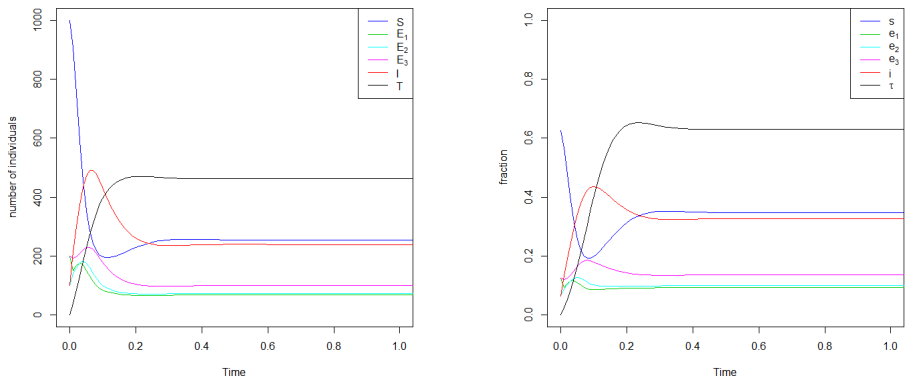
(a) Dynamics of compartments sizes (b) Dynamics of the fractions

Figure 15. SE^{3}ITS curves with $b = 3, \mu = 1, c\beta = 100, \nu_1 = 10, \nu_2 = 5, k_1 = 8, k_2 = 5, k_3 = 1, \delta = 4, d = 6, \theta = 10, r_1 = 10, r_2 = 7, r_3 = 4, r = 10$, that gives $R_0 \approx 7.09, R_1 \approx 4.69, R_T \approx 1.85$ and $R_{1T} \approx 1.52$. All the compartments grow exponentially, while the fractions approach an endemic equilibrium $(s^*, e_1^*, e_2^*, e_3^*, i^*, \tau^*) \approx (0.64, 0.09, 0.05, 0.03, 0.04, 0.14)$. The asymptotic reproduction number of the population is $R_2 \approx 2.37$ and its asymptotic growth rate is $\alpha \approx 1.73$.

have studied first the model without treatment and thereafter we have considered the model with treatment.

We derived the basic reproduction number R_0, the relative basic reproduction number R_1. When $R_0 < 1$ then the epidemic cannot invade the population that go on growing exponentially. If $R_0 > 1$ then the epidemic will invade the population and the behaviour of the fraction infected is determined by R_1. If $R_1 < 1$, then the fraction of infected remains negligible. If $R_1 > 1$ then the infected fraction persists and the asymptotic behaviour of the population relies on a third threshold parameter R_2. If $R_2 > 1$, then the population goes on growing exponentially with a lower rate than its initial rate. If $R_2 = 1$, then the population stabilizes. If $R_2 < 1$, then the population vanishes.

The dynamic of the model with treatment is determined by three threshold parameters R_T, R_{1T} and R_{2T}. The treatment reduces the threshold parameters, that is $R_T < R_0$ and $R_{1T} < R_1$. We



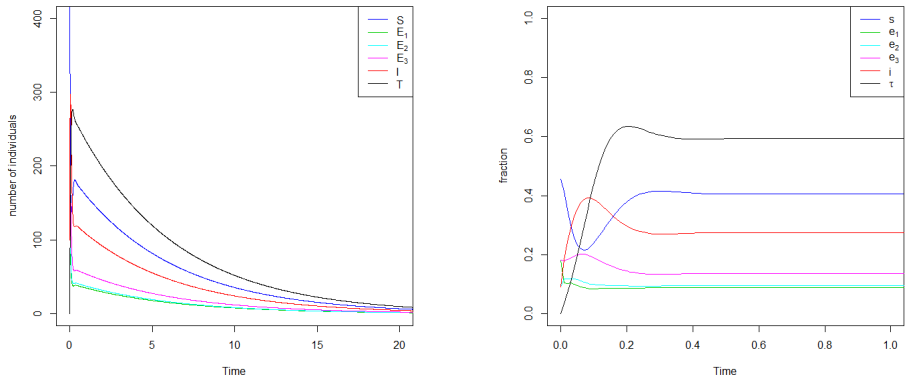
(a) Dynamics of compartments sizes (b) Dynamics of the fractions

Figure 16. SE^{3}ITS curves with $b = 6, \mu = 1, c\beta = 200, \nu_1 = 100, \nu_2 = 50, k_1 = 40, k_2 = 35, k_3 = 31.55076, \delta = 4, d = 25, \theta = 5, r_1 = 10, r_2 = 7, r_3 = 4, r = 5$, that gives $R_0 \approx 6.48, R_1 \approx 4.88, R_T \approx 4.69$ and $R_{1T} \approx 3.66$. The compartments sizes approach an endemic equilibrium $(S^*, E_1^*, E_2^*, E_3^*, I^*, T^*) \approx (255, 67, 73, 99, 239, 462)$, while the fractions approach an endemic equilibrium $(s^*, e_1^*, e_2^*, e_3^*, i^*, \tau^*) \approx (0.21, 0.06, 0.06, 0.08, 0.2, 0.39)$. The asymptotic reproduction number of the population is $R_2 = 1$.

have defined the treatment force γ and the relative force γ_1. Hence we deduced the critical treatment force γ_c and the relative critical treatment force γ_{1c}. If $\gamma > \gamma_c$ the epidemic dies out. But if $\gamma < \gamma_c$ then the epidemic will continue in spite of the epidemic. An optimal treatment strategy is to treat in priority the infectious individuals and the individuals in the earliest stage of latency. All the theoretical results are validated by numerical simulations.

The recovery rate θ of the individuals in the compartment T does not intervene in the threshold parameters R_T and R_{1T}. One may think that a high recovery rate (or equivalently a short period of treatment) is better for tackling the epidemic. But in fact when people recover from disease, they join the susceptible compartment increasing hence the number of new infectious contacts. The simulations we made confirm that in the case of endemicity, the fraction of infectious individuals increases with θ. But a long period of treatment means also more expenses, more places, and more personal in hospitals.

Some authors assume that the disease induces additive death rates for latent individuals and treated individuals [1, 2]. If we assume that the disease induces an additive death rate d_m for individuals in the latent compartment E_m, $m = 1, \cdots, n$ and an additive death rate d_T for



(a) Dynamics of compartments sizes (b) Dynamics of the fractions

Figure 17. SE^{3}ITS curves with $b = 6, \mu = 1, c\beta = 190, \nu_1 = 100, \nu_2 = 50, k_1 = 40, k_2 = 35, k_3 = 30, \delta = 4, d = 25, \theta = 5, r_1 = 10, r_2 = 7, r_3 = 4, r = 5$, that gives $R_0 \approx 5.27, R_1 \approx 4.04, R_T \approx 3.89$ and $R_{1T} \approx 3.08$. The fractions approach an endemic equilibrium $(s^*, e_1^*, e_2^*, e_3^*, i^*, \tau^*) \approx (0.25, 0.06, 0.06, 0.09, 0.17, 0.37)$. The asymptotic reproduction number of the population is $R_2 = 0.97$. The population goes extinct.

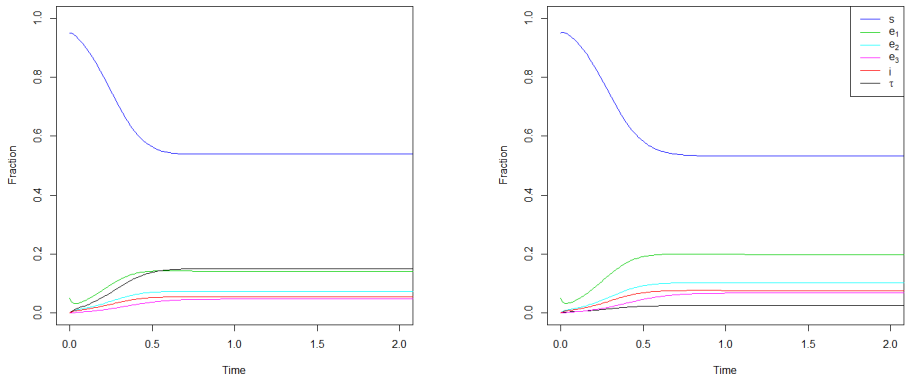
individuals in the compartment T, then the results are similar to that above. The difference is that the formula of the thresholds change as follow. One gets the new expressions of R_0 and R_T by substituting $k_m+\nu_m+\mu, m=1,\cdots,n$ respectively by $k_m+\nu_m+\mu+d_m, m=1,\cdots,n$ in their expressions. For the fractions threshold parameters R_1 and R_{1T}, one gets them by substituting μ by b in the preceding formulas. Therefore, the thresholds parameters for the models with disease induced death rates to latent individuals and treated individuals are given by

$$R_0 = \frac{c\beta}{\mu+d+\delta}\sum_{m=1}^{m=n}\frac{k_m}{\mu+\nu_m+k_m+d_m}\prod_{l=1}^{l=m-1}\frac{\nu_l}{\mu+\nu_l+k_l+d_l},$$

$$R_1 = \frac{c\beta}{b+\delta+d}\sum_{m=1}^{m=n}\frac{k_m}{b+\nu_m+k_m+d_m}\prod_{l=1}^{l=m-1}\frac{\nu_l}{b+\nu_l+k_l+d_l},$$

$$R_T = \frac{c\beta}{\mu+d+\delta+r}\sum_{m=1}^{m=n}\frac{k_m}{\mu+\nu_m+k_m+r_m+d_m}\prod_{l=1}^{l=m-1}\frac{\nu_l}{\mu+\nu_l+k_l+r_l+d_l},$$

$$R_{1T} = \frac{c\beta}{b+d+\delta+r}\sum_{m=1}^{m=n}\frac{k_m}{b+\nu_m+k_m+r_m+d_m}\prod_{l=1}^{l=m-1}\frac{\nu_l}{b+\nu_l+k_l+r_l+d_l}.$$



(a) Dynamics of the fractions (b) Dynamics of the fractions

Figure 18. se^{3}its curves with $b=6, \mu=1, c\beta=150, \nu_1=10, \nu_2=5, k_1=8, k_2=5, k_3=1, \delta=10, d=6, r_1=10, r_2=7, r_3=4, r=10$, that gives $R_{1T}\approx 1.80$. In (a) $\theta=15$ the fractions approach an endemic equilibrium $(s^*, e_1^*, e_2^*, e_3^*, i^*, \tau^*)\approx(0.54, 0.14, 0.07, 0.05, 0.05, 0.15)$ and the asymptotic reproduction number of the population is $R_2\approx 2.273$. In (b) $\theta=150$ the fractions approach an endemic equilibrium $(s^*, e_1^*, e_2^*, e_3^*, i^*, \tau^*)\approx(0.53, 0.20, 0.10, 0.07, 0.08, 0.02)$ and the asymptotic reproduction number of the population is $R_2\approx 2.06$.

Similarly to the recovery rate of the treated individuals, the additive death rate d_T induced by the disease to the treated individuals does not intervene in these formula.

Our model ignore the limitations of the means of treatment. We have studied the epidemic using only a deterministic model. But a deterministic model fits only when we have a large number of individuals. Therefore, the situation where the population vanishes must be taken with caution. Because when the number of individuals in the population become small, the deterministic setting does not fit anymore. What happens then is very stochastic. The most realistic scenario is that the epidemic dies out first, and the population regrows thereafter.

Conflict of Interests

The authors declare that there is no conflict of interests.

REFERENCES

[1] N. Bame, S. Bowong, J. Mbang, G. Sallet, J. J. Tewa, Global Stability for SEIS models with *n* latent classes, *Math. Biosci. Eng.* 5(2008), pp. 20-33.

[2] S. Bowong, Y. Emvudu, D. P. Moualeu and J. J. Tewa, Mathematical properties of a tuberculosis model with two differential infectivity and *n* latent classes, *J. Nonlinear Syst. Appl.*, 1 (2010), 13-26.

[3] S. Busenberg and P. van den Driessche, Analysis of a disease transmission model in a population with varying size, *J. Math. Biol.* 28 (1990), Article ID 257.

[4] O. Diekmann, J. A. P. Heesterbeek and M. G. Roberts, The Construction of next-generation matrices for compartmental epidemic models, *J. R. Soc. Interface* 7 (2010), 873-885.

[5] O. Diekmann, H. Heesterbeek and T. Britton, *Mathematical Tools for Understanding Infectious Disease Dynamics*, Princeton University Press (2013).

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

[7] H. W. Hethcothe, The mathematics of infectious diseases, *SIAM Review*, 42 (4) (2000), 599-653.

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

[9] A. Jabbari, C. Castillo-Chavez, F. Nazari, B. Song and H. Kheiri, a two-strain TB model with multiple latent stages, *Math. Biosci. Eng.*, 13 (2016), 741-785.

[10] X. Meng, Z. Wu and T. Zhang, The dynamics and therapeutic strategies of a SEIS epidemic model, *Int. J. Biomath.*, 06 (2013), Article ID 1350029.

[11] D. P. Moualeu, S. Bowong, Y. Emvudu, Global Stability of a Tuberculosis Model with *n* Latent Classes, *J. Appl. Math. Inform.* 29 (5 - 6) (2011), 1097 - 1115.

[12] S. Ouaro and D. Ouédraogo, SEIS epidemic model with treatment in an exponentially growing population, *Folia Mathematica*, in press.

[13] K. Soetaert, T. Petzoldt, R. W. Setzer , Solving Differential Equations in R: Package deSolve, *J. Stat. Softw.*, 33 (9) (2010), 1-25.