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Exogenous re-infection does not always cause backward bifurcation in TB transmission dynamics

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ABSTRACT

Models for the transmission dynamics of mycobacterium tuberculosis (TB) that incorporate exogenous re-infection are known to induce the phenomenon of backward bifurcation, a dynamic phenomenon associated with the existence of two stable attractors when the reproduction number of the model is less than unity. This study shows, by way of a counter example, that exogenous re-infection does not always cause backward bifurcation in TB transmission dynamics. In particular, it is shown that it is the transmission ability of the re-infected individuals, and not just the re-infection process, that causes the backward bifurcation phenomenon. When re-infected individuals do not transmit infection, the disease-free equilibrium of the model is shown to be globally-asymptotically stable (GAS) when the associated reproduction number is less than unity. The model has a unique endemic equilibrium whenever the reproduction threshold exceeds unity. It is shown, using a Lyapunov function, that the unique endemic equilibrium is GAS for the special case with no disease-induced mortality and no transmission by re-infected individuals. It is further shown that even if re-infected individuals do transmit infection, backward bifurcation only occurs if their transmissibility exceeds a certain threshold. Sensitivity analyses, with respect to the derived backward bifurcation threshold, show that the phenomenon of backward bifurcation is more likely to occur if the rates of re-infection and transmissibility of re-infected individuals are sufficiently high. Furthermore, it is likely to occur if the fraction of slow progressors (to active TB) is increased or if the rates of treatment (of symptomatic cases) and disease-induced mortality are increased. On the other hand, backward bifurcation is less likely to occur for increasing rates of endogenous re-activation of latent TB cases.

1. Introduction

Standard Kermarck–McKendrick models for the spread of emerging and re-emerging diseases in a population typically exhibit a forward bifurcation when the associated reproduction number (denoted by $\mathcal{R}_0$) of the model equals unity (see, for

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Table 1
Description of parameters of the model (2.1).

Variable	Description
S	Population of susceptible individuals
E	Population of exposed (infected but not symptomatic) individuals
I	Population of primary-infected symptomatic individuals
I_R	Population of re-infected symptomatic individuals
T	Population of effectively-treated individuals
Parameter	**Desciption**
Π	Recruitment rate into the population
μ	*Per capita* natural mortality rate
β	Effective contact rate for TB infection
η_R	Modification parameter for relative infectiousness of re-infected individuals
f	Proportion of slow progressors
$1-f$	Proportion of fast progressors
$1-\psi$	Reduction of exogenous re-infection rate
σ	Endogenous re-activation rate of exposed individuals
$\tau_I(\tau_R)$	Effective treatment rate of primary-infected (re-infected) symptomatic individuals
$\delta_I(\delta_R)$	Disease-induced mortality rate of primary-infected (re-infected) symptomatic individuals

instance, [2,8,12,14,21]). For such models, the disease typically dies out when $\mathcal{R}_0$ is less than unity and persists in the population when it exceeds unity (in other words, a small influx of new cases will not generate a large outbreak of the disease). Other models of disease transmission, particularly those associated with the phenomenon of exogenous re-infection of individuals with latent *mycobacterium tuberculosis* (TB) infection or the use of an imperfect vaccine [1,7,9–12,15,17–19], are known to undergo another type of bifurcation known as backward bifurcation. A unique feature of the backward bifurcation phenomenon is the co-existence of multiple stable attractors when $\mathcal{R}_0 < 1$, the consequence of which is that effective disease control is dependent on initial sizes of the sub-populations (state variables) considered in the model (thereby making effective disease control difficult). Numerous causes of backward bifurcation in disease transmission models have been identified (see, for instance, [12] and some of the references therein).

The purpose of the current study is to further theoretically explore the role of exogenous re-infection on the phenomenon of backward bifurcation in the transmission dynamics of TB (one of the world's deadliest communicable diseases [22]). In particular, this study will provide insight into the role of disease transmission by re-infected individuals on the backward bifurcation phenomenon theoretically observed in TB transmission dynamics. To achieve this objective, a deterministic model for TB spread in a population will be designed and rigorously analyzed. The model is formulated in Section 2, and its qualitative features are analyzed in Section 3. Biological plausibility of backward bifurcation, as well as sensitivity of some of the parameters of the models to the backward bifurcation phenomenon, are also explored. The theoretical results obtained are summarized in Section 4.

2. Model formulation

The model to be considered in this study is based on stratifying the total population at time t, denoted by $N(t)$, into mutually-exclusive compartments for susceptible ($S(t)$), exposed (infected but not symptomatic) ($E(t)$), symptomatic primary-infected ($I(t)$), symptomatic re-infected ($I_R(t)$) and effectively-treated ($T(t)$) individuals, so that

$$N(t) = S(t) + E(t) + I(t) + I_R(t) + T(t).$$

The basic model is given by the following deterministic system of non-linear differential equations (a flow diagram of the model is depicted in Fig. 1, and the state variables and parameters of the model are tabulated in Table 1):

$$\begin{aligned}
\frac{dS}{dt} &= \Pi - \beta\left(\frac{I+\eta_R I_R}{N}\right)S - \mu S,\\
\frac{dE}{dt} &= f\beta\left(\frac{I+\eta_R I_R}{N}\right)S - \beta(1-\psi)\left(\frac{I+\eta_R I_R}{N}\right)E - (\sigma+\mu)E,\\
\frac{dI}{dt} &= (1-f)\beta\left(\frac{I+\eta_R I_R}{N}\right)S + \sigma E - (\tau_I+\mu+\delta_I)I,\\
\frac{dI_R}{dt} &= \beta(1-\psi)\left(\frac{I+\eta_R I_R}{N}\right)E - (\tau_R+\mu+\delta_R)I_R,\\
\frac{dT}{dt} &= \tau_I I + \tau_R I_R - \mu T,
\end{aligned} \tag{2.1}$$

where Π is the recruitment rate, β is the effective contact rate, $\eta_R > 0$ is the relative infectiousness of re-infected individuals in comparison to primary-infected symptomatic individuals and μ is the natural death rate (assumed to be the same in all epidemiological compartments). Furthermore, the fraction f accounts for slow disease progression, while