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An agent-based computational model for tuberculosis spreading on age-structured populations

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HIGHLIGHTS

- TB with the population aging reproduces the coexistence of states.
- Public health policies against TB can lead to the emergence of resistant pathogens.
- Different treatment efficacies explain the patterns of age incidence of TB.

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ABSTRACT

In this work we present an agent-based computational model to study the spreading of the tuberculosis (TB) disease on age-structured populations. The model proposed is a merge of two previous models: an agent-based computational model for the spreading of tuberculosis and a bit-string model for biological aging. The combination of TB with the population aging, reproduces the coexistence of health states, as seen in real populations. In addition, the universal exponential behavior of mortalities curves is still preserved. Finally, the population distribution as function of age shows the prevalence of TB mostly in elders, for high efficacy treatments.

1. Introduction

Tuberculosis (TB) is an ancient infectious disease transmitted by *M. tuberculosis* bacteria. It is estimated that one-third of the world population is infected with TB [1] which is the second leading causes of deaths due to one infectious disease [2,3]. In some regions of the world, such as Europe and Southeast Asia, studies show that the tuberculosis incidence is higher in older people (ages $\geq$ 50 years) in opposition to younger people in Africa as reported by Refs. [4,5]. Although TB can infect people at any age, sex and socioeconomic conditions, it does it in different levels. Ref. [6] have already shown how age-structure can strongly affect the outcomes of mathematical models for epidemiological diseases, by comparing constant mortalities and Gompertz-like ones for age-structured populations. Therefore, to understand how TB is spread in certain strata of a population it is an important task for planning its control and treatment.

A recent work [7] that compares the incidence rates between USA and Africa, alerts to the fact of TB affects ages depending on the level of treatment, what justifies the importance of the study of aging effects on tuberculosis. In USA, TB incidence

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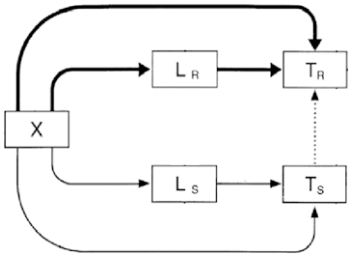

Fig. 1. Simplified schematic model showing interactions between compartments from Ref. [12]. For the sake of simplicity, only a few interactions are shown.

increases monotonically with age, whereas in Africa there is a peak between ages from 25 to 44. In low prevalence regions as USA, TB affects elderly people whereas in high prevalence countries, it seems to affect individuals belonging to the most productive age. There are some factors that could explain the increase of TB prevalence with age. For instance, if the exposure to the pathogen occurred when TB prevalence was much higher than today, it is expected to have a higher incidence in advanced ages. In addition, an accumulation of cases in the older age groups could happen if the fraction of susceptible individuals is higher than the one that die from TB. Other age-specific effects such as a higher susceptibility to the disease due to the decrease of the immune response in older people may also be important factors.

Here, we propose an agent-based model (ABM) to study the effects of aging on tuberculosis. We are interested on how the public health policies may affect the age prevalence of the TB in a population. The model is built based on two models: an agent-based model (ABM) for TB spread and a biological aging model. The first model proposes an ABM to simulate the spread of tuberculosis in a population considering the emergence of drug resistance [8]. The second one is an age structured population computational model based on cumulative mutations in individuals' genome [9]. The combination of this two approaches in a single model allows us study the spread of tuberculosis in a system in which the population is subject to aging.

This paper is organized as follows. Section 2 is intended for description of the agent-based model for TB. In Section 3, we review some features of the model for age structured populations. The computational model for the effect of age on tuberculosis is presented and discussed in Section 4. Computational implementation of the model as well as results are discussed in Section 5. Concluding remarks and possible extensions of this work are in Section 6.

2. Agent-based model of the spread of tuberculosis

A mathematical model to study the spread of tuberculosis has been proposed by *Blower* et al. [3,10–12]. It is a compartmental model in which the dynamics is governed by eight ordinary differential equations. Individuals belonging to a given compartment may be classified as susceptible (X), latent (L_i), latently infected that effectively received chemoprophylaxis (C_S), infectious (T_i) and effectively treated (E_i). The subscript i defines the type of bacteria, sensitive (S) or resistant (R) to antibiotics, carried by latent and infectious individuals. Fig. 1 shows the transitions between tuberculosis states according to the model proposed in Ref. [3]. Further details regarding this model can be found in Refs. [3,10–12].

Based on the work of *Blower* et al., an agent-based model to study TB spread has been proposed in Ref. [8]. In this new approach, each individual of the population is placed on one site of a square lattice of size $L \times L$. Each site (individual) is characterized by one of the accessible states of TB, namely: susceptible (X), latent (L_i) or infectious (T_i), where $i = \{S, R\}$. Susceptible individuals, X, are clear of TB pathogens and they may acquire these bacteria due to the contact with individuals in the states T_S and/or T_R. Latent individuals, L_S and L_R, are those who host TB pathogens but they are not symptomatic. In other words, latent individuals are not sick and they also do not transmit the disease to others. T_S and T_R individuals are ill and they can transmit the disease if they are not under treatment with antibiotics.

Contagion of a X individual depends on the health state of his/her neighbors. The contagion may be due to local (neighbors) and/or global (remaining sick individuals in the lattice) sources. A susceptible individual will be locally infected with probability

$$P_{L_i} = 1 - (1 - \beta_i)^{N_{T_i}}, \tag{1}$$

where β_i is the infectivity of type $i = \{S, R\}$ pathogen and N_{T_i} is the number of infectious neighbors in state T_i. Type S and R pathogens have their infectivities related by $\beta_R = \alpha\beta_S$, with $0 < \alpha < 1$ [8]. Thus, the total local infection probability due to both types of pathogens is given by

$$P_L = P_{L_S} + P_{L_R} - P_{L_S}P_{L_R}. \tag{2}$$

The probability of infection due to global sources is

$$P_{G_i} = \beta_i T_{T_i}/N, \tag{3}$$

where T_{T_i} is the total number of infectious individuals T_i in the lattice without treatment, with $i = \{S, R\}$, and N is the total population. Then, the total probability of global infection is assessed by

$$P_G = P_{G_S} + P_{G_R} - P_{G_S}P_{G_R}. \tag{4}$$