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Transmission dynamics of two dengue serotypes with vaccination scenarios

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ABSTRACT

In this work we present a mathematical model that incorporates two Dengue serotypes. The model has been constructed to study both the epidemiological trends of the disease and conditions that allow co-existence in competing strains under vaccination. We consider two viral strains and temporary cross-immunity with one vector mosquito population. Results suggest that vaccination scenarios will not only reduce disease incidence but will also modify the transmission dynamics. Indeed, vaccination and cross immunity period are seen to decrease the frequency and magnitude of outbreaks but in a differentiated manner with specific effects depending upon the interaction vaccine and strain type.

1. Introduction

Dengue is a vector-borne disease with more than 50 million cases per year [16]. The major vector, *Aedes aegypti*, is located in tropical regions, mainly in urban areas that provide water holding containers that function as breeding sites. There are four dengue serotypes (DEN-1, DEN-2, DEN-3 and DEN-4) that coexist in many endemic areas [21]. Dengue is an emergent infectious disease that can be very severe. Dengue Hemorrhagic fever (DHF) is a life-threatening condition whose development is not well known [6]. One of the main hypothesis that have been put forward to explain it is Antibody Dependent Enhancement (ADE) whereby previous exposure to a Dengue infection may generate a very strong immune response on a secondary infection, thus triggering DHF [19]. In recent years, the development of dengue vaccines has dramatically accelerated [14,24] given the frequent epidemics and morbidity and DHF mortality rates around the world. Vaccination is a cost-effective measure of control and prevention but its development is challenged by the existence of the four viral serotypes, the possibility of ADE and therefore of DHF [22].

Previous mathematical models have incorporated the effect of immunological interactions between the different dengue serotypes in disease dynamics. Infection with a particular serotype is believed to result in life-long immunity to that serotype and temporal cross-protection to the other serotypes. There exists many different models on Dengue population dynamics (e.g. [1,5,13,15,22,23,31]). In a recent paper Coudeville and Garnett [9], propose a compartmental, age structured model with four serotypes that incorporates cross protection and the introduction of a vaccine. Likewise Rodriguez–Barraquer et al. [27], use an age-stratified dengue transmission model to assess the impact of partially effective vaccines through a tetravalent vaccine with a protective effect against only 3 of the 4 serotypes. Other compartmental and agent-based models [8] have found that vaccines with efficacies of 70 – 90% against all serotypes have the potential to significantly reduce the frequency and magnitude of epidemics on a short to medium term.

Many of the published mathematical models include the four dengue serotypes (e.g. [15,17,23]) and deal with the full complexity of the population dynamics that this diversity triggers. In this paper the potential impact of a vaccine is studied through the use of a mathematical model of transmission for two dengue serotypes. In the Americas, Dengue has a typical pattern of presenting a dominant serotype while the others circulate at low densities and in very localized regions of the continent [11]. Dengue epidemics come sequentially thus reducing the basic population dynamics to the competition between two viral strains: the invading and the resident. This is the justification of the model that we study in this paper. On the other hand the introduction of vaccination is founded in the imminent release of a vaccine that has the characteristic of having high efficacy for only three of the four serotypes [6]. In our setting, the vaccination programs that we

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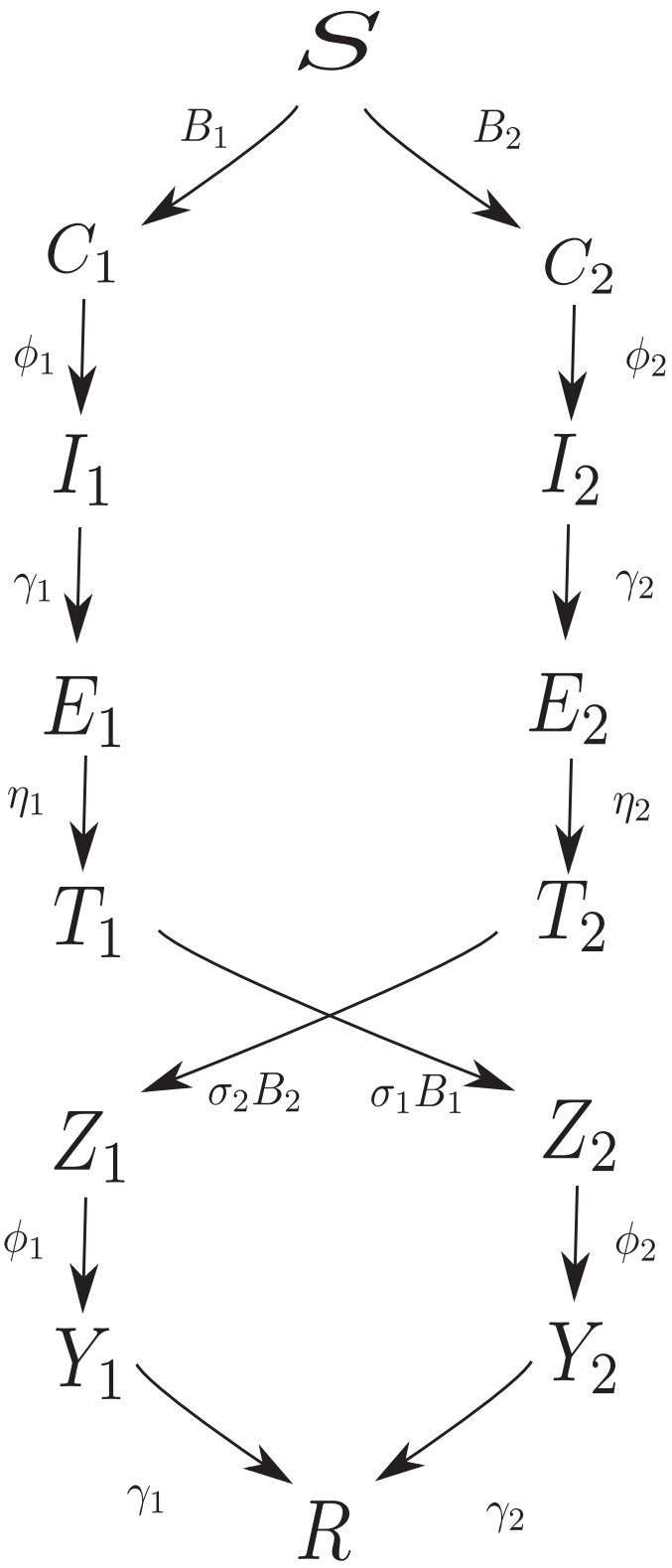

Fig. 1. Basic model without vaccination. S susceptible, C_i infectious in latent stage, I_i infected contagious, E_i temporary cross immunity, T_i susceptibles to strain j already recovered from strain i, Z_i infectious with secondary infection, Y_i infectious and contagious with a secondary infection, R immune to both strains.

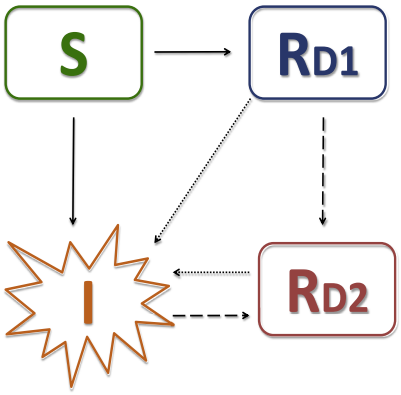

Fig. 2. Basic model with vaccination. D_1 and D_2 doses are applied sequentially; unvaccinated individuals follow a natural route of infection (see Fig. 3). The compartment I represents all infections. The dotted lines represent infections due to failure of the first and second vaccine application. The dashed lines represents the application of the second dose to all susceptible individuals (including those who recovered from a first infection).

study consider the application of one or two doses in the presence of cross protection. In our model the vaccine is assumed to confer higher protection to one serotype than to the second one. The paper is organized as follows. In Section 2 we present a mathematical model for Dengue and the incorporation of the vaccine. In Section 3 we explain the vaccination strategies. In Sections 4 and 5, we present and discuss the numerical results of the vaccination scenarios with different cross immunity periods. In Section 6 we present a statistics summary. Finally, in Section 7 we draw some conclusions about this work.

2. Mathematical model

A basic model for Dengue

In this section we describe the mathematical model for dengue transmission in the presence of vaccination and two co-circulating strains. All human newborns are susceptible to both dengue strains.

The model that we present considers a human host population classified in compartments according to Dengue infection status. We consider the population of individuals that are all fully susceptible to both strains of Dengue. At time $t = 0$ a few infected individuals are introduced and infection process is then triggered.

We call primary infections to those infections that occur in individuals with no previous exposure to either strain; we call secondary infections to those infections that occur in individuals that have been previously exposed to one of the two strains. Let S represents the susceptible individuals, C_i, Z_i the individuals in the latent period of primary or secondary infections for each strain, $i = 1, 2,$ respectively. Likewise, I_i, Y_i are individuals with primary and secondary infections for each of the two strains respectively. E_i are individuals in the state of temporary cross-immunity (temporary immune protection to both strains independent of the strain causing the immediate previous infection), respectively, T_i are susceptible population to dengue strain $j (j \neq i)$. Note that T_i individuals have already recovered from and infection by dengue strain i.

Infection with one serotype has been shown to provide lifelong immunity to that serotype but short-term cross-protection to the other serotypes [7,16]. R represents the immune population to both infections (see Fig. 1).

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