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A comparative analysis of three different methods for the estimation of the basic reproduction number of dengue

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ABSTRACT

The basic reproduction number, R_0, is defined as the expected number of secondary cases of a disease produced by a single infection in a completely susceptible population, and can be estimated in several ways. For example, from the stability analysis of a compartmental model; through the use of the matrix of next generation, or from the final size of an epidemic, etc. In this paper we applied the method for estimating R_0 of dengue fever from the initial growth phase of an outbreak, without assuming exponential growth of cases, a common assumption in many studies. We used three different methods of calculating R_0 to compare the techniques' details and to evaluate how these techniques estimate the value of R_0 of dengue using data from the city of Ribeirão Preto (SE of Brazil) in two outbreaks. The results of the three methods are numerically different but, when we compare them using a system of differential equations developed for modeling only the first generation time, we can observe that the methods differ little in the initial growth phase. We conclude that the methods predict that dengue will spread in the city studied and the analysis of the data shows that the estimated values of R_0 have an equal pattern overtime.

1. Introduction

One of the main variables of interest with respect to infectious diseases epidemiology is the competency of the infection to establish itself in the host population (its potential of transmission). This potential of transmission is normally represented by the Basic Reproduction Number, R_0, which is very important in studies about epidemics, specially to evaluate the efficiency of control strategies (Heesterbeeck, 1992; Massad et al., 1994). In addition, R_0 can be used to estimate the herd immunity threshold, that is, the proportion, p, of the population that should be immunized to control a disease. When p is greater than $1-1/R_0$, the infection cannot establish itself in the host population, and it will die out over time (Nishiura, 2010; Roberts and Heesterbeek, 2003).

The basic reproduction number, R_0, is defined as the expected number of secondary infections produced by a single infective person in a completely susceptible population during his/her infectious period (Diekmann, Heesterbeeck and Metz, 1990; Heesterbeek, 1992; Massad et al., 1994; van den Driessche & Watmough, 2002). In diseases transmitted by insect

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vectors, R_0 can be defined as expected number of people that will be infected by one person initially infected by a vector (Lopez et al., 2002; Massad et al., 2010).

It is important to note that it is possible to have a transitory outbreak even if $R_0 < 1$. In this case it is observed that the number of infected people start increasing but after a short period of time this number decreases until the disease dies out (Heesterbeek, 1992).

There are several ways to estimate R_0, for example, from the stability analysis of a compartmental model, through the matrix of next generation, from final size of an epidemic, from the initial growth rate, etc (Smith, 2008). In this work we study the method to estimate R_0 from the initial growth phase of the outbreak in diseases caused by vectors, without assuming an exponential growth of the number of cases.

One of the first studies to address R_0 of dengue using epidemic data was carried out by Koopman et al. (1991). In this paper the basic reproduction number was calculated using the final size of an epidemic in Mexico (Nishiura, 2006).

Massad et al. (2001) calculated the value of R_0 considering just the initial growth phase of dengue, proposing a modification of the method proposed by Marques, Forattini, and Massad (1994). Massad et al. (2001) obtained $R_0 = \left(1 + \frac{r}{\gamma}\right)\left(1 + \frac{r}{\mu_V}\right)$, where r is the exponential growth rate of the epidemic curve, μ_V is the mortality rate of the vectors and γ is the dengue recovery rate of humans. In this work, Massad et al. (2001) calculated the value of R_0 of dengue and yellow fever. Some years later, Favier et al. (2006) improved this method by including an intrinsic incubation period of dengue. Favier et al. (2006) formula is $R_0 = \left(1 + \frac{r}{\gamma}\right)\left(1 + \frac{r}{\mu_V}\right)e^{r(\tau_e+\tau_i)}$, where τ_e and τ_i are the extrinsic and the intrinsic periods of dengue, respectively. As mention in Massad et al. (2001), all these methods performed well, but it is implicit in all of them the exponential growth of cases.

In this paper we studied the methods proposed by Ross (1911) and Macdonald (1952), Nishiura (2010), and White & Pagano (2008). The Ross (1911) model is specific for diseases caused by vectors and was originally formulated for malaria; the methods proposed by Nishiura (2010) and White & Pagano (2008), are likelihood-based methods, and are not specific for diseases caused by vectors. None of these methods assume an exponential growth of the number of cases.

Dengue is a vector-born disease caused by dengue fever virus, with four serotypes, namely, DENV-1, DENV-2, DENV-3 and DENV-4, which belong to genus *Flavivirus* family *Flaviviridae* (Gubler, 1998). Dengue is an urban disease and its viruses are kept in a lifecycle that involves humans and mosquitoes *Aedes* (Chowell and Clark, 1995). Dengue is transmitted to humans through bite of an infected female of *Aedes aegypti* (Coura, 2005; Gubler, 1998; Guzman and Istúriz, 2010).

The clinical picture of dengue ranges from asymptomatic infection or mild febrile illness and even lethal disease (Teixeira and Barreto, 2009). However, the general symptoms are: high fever, tiredness, muscle pain, lack of appetite, etc (Guzman & Istúriz, 2010). It is believed that people infected by one serotype acquire long-live immunity only to this serotype, and temporary cross-immunity to the other three serotypes (Simmons, Farrar, Chau, & Wills, 2012). Our objective is to compare different techniques and to evaluate how these techniques estimate the value the R_0, applying them to diseases caused by vectors without assuming exponential growth of cases. In this particular case we used data of dengue provided by the Brazilian Ministry of Health.

2. Methods

In this section we present description of the methods studied by Ross (1911) and Macdonald (1952), Nishiura (2010) and White & Pagano (2008) to estimate the basic reproduction number of dengue, without assuming an exponential growth for the initial phase of the outbreak.

2.1. Description of the Ross-Macdonald's method

The first method presented in this section is the Ross-Macdonald's model. The basic reproduction number, R_0, was presented for the first time in a paper wrote by George Macdonald in 1952. In it Macdonald proposed a threshold for Malaria spread and persistence based in a previous work made by Sir Ronald Ross (1911). The concept proposed by Ross and Macdonald (Macdonald, 1952) was used by many researches like Anderson and May (1992) or Aron and May (1982). Some improper notational mistakes in the original formulation related with the R_0 dimension were years later fixed (Massad & Coutinho, 2012). Hereafter we show the model studied by Massad et al. (2010), where these authors used the R_0 expression given by the Ross-Macdonald model (Macdonald, 1952) without assuming an exponential form for the initial growth phase of the outbreak, and they showed that even when R_0<1, an auto-limited outbreak can happen.

The following equations describe the dynamics of the disease, where the involved populations are divided into humans host population $N_H(t)$ and vector population $N_V(t)$. The human host population, in turn, is divided into susceptible S_H, infected, $I_H(t)$ and recovered hosts, $R_H(t)$. The total vector population, $N_V(t)$ is divided into susceptible, $S_V(t)$, latent, $L_V(t)$, and infected vectors, $I_V(t)$.