

Dengue

- Dengue is a vector-borne disease caused by dengue fever virus, with 4 serotype, namely, DEN-1, DEN-2, DEN-3 and DEN-4;
- Dengue is an urban disease and its virus is kept in a lifecycle that involves humans and mosquitoes;
- The transmission cycles occur in this way: the female of *Aedes* feeds of an infected person and after an extrinsic incubation period, about 7 to 12 days this mosquitoes can transmit dengue to another uninfected people.

Dengue

- Infected people presents a clinical picture that ranges from asymptomatic infection or mild febrile illness and even lethal disease;
- People infected by one serotype acquire lifelong immunity only to this serotype, thus people can be infected by four dengue serotypes during their lifetime.

Basic Reproduction Number, R_0

- In works about infectious diseases one of the main goals is: to evaluate the potential transmission of this diseases;
- R_0 is defined as the expected number of secondary infections produced by a single infective person in a completely susceptible population;
- If $R_0 > 1$ on average each infected individual will cause more than one infection. If $R_0 < 1$ on average each infected individual will not to cause more than one infection.

Basic Reproduction Number, R_0

- There are several ways to estimate R_0 ;
- In diseases caused by vectors R_0 is defined as the expected number of people who would be infected from a single person initially infected by a vector;
- According to some works, if a proportion of the population greater than $1 - 1/R_0$ is constantly protected, the disease cannot spread. Another case that we can use R_0 is to check if a control mechanism is working or not.

Objective

Our aim is to evaluate which technique best estimates the R_0 in diseases caused by vectors without assuming exponential growth of cases. The methods used in this work to evaluate R_0 , are given by Macdonald(1925) and studied by Massad et. al (2010) and Nishiura(2010).

Mathematical Model studied by Massad et. al. (2010).

$$\left\{ \begin{array}{l} \frac{dS_H(t)}{dt} = -abl_V(t) \frac{S_H(t)}{N_H(t)} + \mu_H(N_H(t) - S_H(t)) \\ \frac{dI_H(t)}{dt} = abl_V(t) \frac{S_H(t)}{N_H(t)} - (\mu_H + \gamma)I_H(t) \\ \frac{dR_H(t)}{dt} = \gamma I_H(t) - \mu_H R_H(t) \\ \frac{dS_V(t)}{dt} = -acS_V(t) \frac{I_H(t)}{N_H(t)} + \mu_V(N_V(t) - S_V(t)) \\ \frac{dL_V(t)}{dt} = acS_V(t) \frac{I_H(t)}{N_H(t)} - \mu_V L_V(t) \\ \frac{dI_V(t)}{dt} = acS_V(t - \tau) \frac{I_H(t - \tau)}{N_H(t - \tau)} e^{-\mu_V \tau} - \mu_V I_V(t) \end{array} \right. \quad (1)$$

$$N_H = S_H + I_H + R_H.$$

$$N_V = S_V + L_V + R_V.$$

Mathematical Model studied by Massad et. al. (2010).

Table: Biological meaning of the parameters used in the model (1).

Parameter	Biological meaning
a	Biting rate by <i>A. aegypti</i> .
γ	Recovery rate for dengue.
μ_H	Natural mortality rate of humans.
c	Probability that a vector becomes infected.
b	Probability that a host becomes infected.
μ_V	Mortality rate of <i>A. aegypti</i> .
τ	Extrinsic incubation period of the parasite.

Mathematical Model studied by Massad et. al. (2010).

Macdonald demonstrated the existence of a threshold, the basic reproduction number,

$$R_0 = \frac{N_V}{N_H} \frac{a^2 b c e^{-\mu_V \tau}}{(\gamma + \mu_H) \mu_V} \quad (2)$$

Estimating R_0 studied by Massad et al (2010).

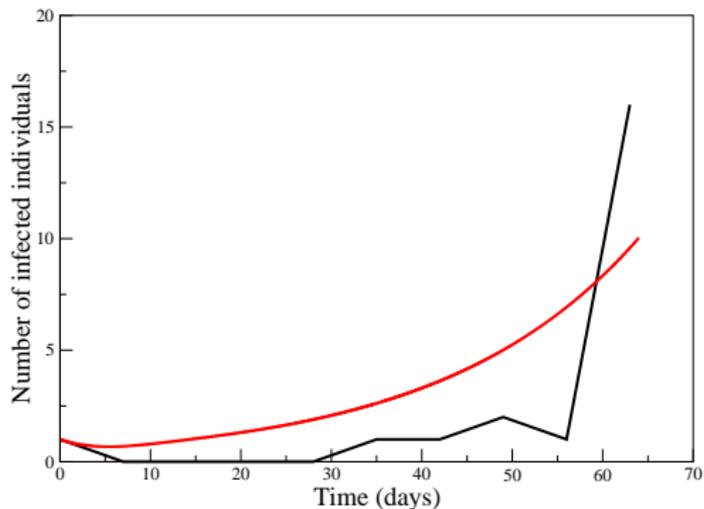
For estimating the value of R_0 by Macdonald's Method, we need information about some parameters, as death rate of humans, recovery rate of dengue, etc, however some parameters are hard to estimate, as biting rate (a), probability that a host to get infected (b), probability that a vector to get infected (c).

In order to determine the values of this parameters, we fitted the curve of model given by system (1) to real data, for this we used the maximal likelihood function:

$$L(m(x), \sigma^2 | d) = \prod_i \frac{1}{\sqrt{2\pi\sigma^2}} \exp \frac{-(d_i - m_i)^2}{2\sigma^2} \quad (3)$$

where d is a vector of real data, and m is a vector of model.

São Paulo



In the black line the real data, and in the red line the fitted data.

Mathematical Model studied by Nishiura (2010).

Nishiura(2010) presents a correction of the actual reproduction number (R_a), which is defined as the product of the average duration of infectiousness and the ratio of incidence to prevalence.

Estimating R_0 using Nishiura's Method.

$$R_0 = \frac{\sum_{t=1}^T J_t}{\sum_{t=1}^T \sum_{s=0}^{\min(k,t)} g_s J_{t-s}}, \quad (4)$$

where J_t is the incidence data and g_s is the generation interval, the numerator represents the total number of incidence data, and the denominator is the total numbers of effective contacts made by primary cases.

Estimating R_0 using Nishiura's Method.

We assumed that g_s is given by a cumulative gamma distribution,

$$g_s = \frac{\lambda^\alpha}{\Gamma(\alpha)} \int_s^{s+n} x^{\alpha-1} e^{-\lambda x} dx. \quad (5)$$

Mathematical Model studied by Nishiura (2010).

The generation interval for dengue ranges from 14 to 18 days, we took the generation interval for dengue virus in 14 days comprising intrinsic (within human) and extrinsic (within mosquito) periods with 7 days duration each, and we assumed the standard deviation of 5 days.

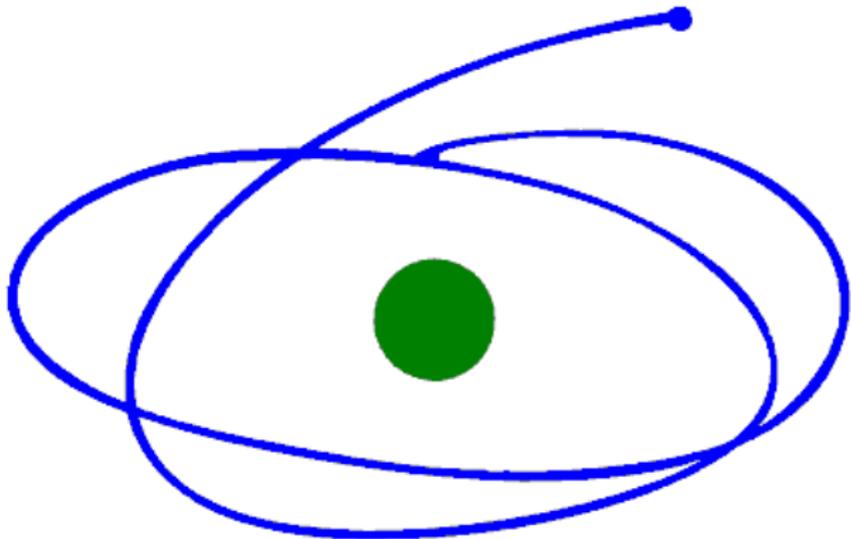
Table: Estimation of R_0 by Nishiura's Method and Macdonald's Method.

Massad et. at. (2003)	Nishiura's Method	Macdonald's Method.
6.59	6.33	5.25

- The method proposed by Nishiura(2010) does not require a large computational effort, it only requires tools for calculating the generation interval;
- In the method studied by Massad et. al. (2010), are necessary few information but it demands a hard computational effort;
- Therefore we can conclude in this first study that: what it may define which is the best method to estimate the value of R_0 , are the information we have available for making this calculation.

References

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C A P E S

Thank you!!!