Estimating the Size of Aedes aegypti Populations from Dengue Incidence Data: Implications for the risk of Yellow Fever, Zika Virus and Chikungunya Outbreaks.

Eduardo Massad¹,²,³,* , Marcos Amaku¹, Francisco Antonio Bezerra Coutinho¹, Claudio José Struchiner⁴, Luis Fernandez Lopez¹, Annelies Wilder-Smith⁵,⁶,⁷,⁸ and Marcelo Nascimento Burattini¹,⁹

¹School of Medicine, University of Sao Paulo, Brazil.
²London School of Hygiene and Tropical Medicine, UK.
³College of Life and Natural Sciences, The University of Derby, UK.
⁴Programme of Scientific Computation, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil.
⁵Li Ka Shing Knowledge Institute, St Michael’s Hospital, Toronto, Canada.
⁶Institute of Public Health, University of Heidelberg, Germany.
⁷Department Public Health and Clinical Medicine, Epidemiology and Global Health, Umeå University, SE-901 85 Umeå, Sweden.
⁸Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore.
⁹Hospital São Paulo, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brazil.
*Correspondence to: edmassad@usp.br

Abstract

In this paper we present a model to estimate the density of aedes mosquitoes in a community affected by dengue. The model is based on the fitting of a continuous function to the incidence of dengue infections, from which the density of infected mosquitoes is derived straightforwardly. Further derivations allows the calculation of the latent and susceptible mosquitoes' densities, the sum of the three equals the total mosquitoes' density. The model is illustrated with the case of the risk of urban yellow fever resurgence in dengue infested areas but the same methods apply for other aedes-transmitted infections like Zika and chikungunya viruses.

keywords: Aedes aegypti, mosquitoes' densities, dengue, zika virus, yellow fever.
1. Introduction

The main components of the Ross-Macdonald model for vector-borne infections have been estimated with reasonable degree of accuracy (Coutinho et al., 2006; Massad et al., 2011; Massad & Coutinho 2012; Amaku et al., 2013, 2016; Lopez et al., 2016). Values for mosquitoes' biting and mortality rates, extrinsic incubation periods, probabilities of transmission from mosquitoes-to-humans and vice-versa, human recovery and mortality rates from infection, are found in the specialized literature (Liu-Helmerson et al., 2016). Mosquitoes' densities, however, vary from place to place and with time and are extremely difficult to estimate (Adams and Kaplan, 2009). Empirical efforts (Maciel-de-Freitas, Eiras, and Lourenço de Oliveira, 2008) to determine the actual size of the mosquitoes populations in affected areas are limited in number and very laboriously done. Even these are limited in space and time due to regional and seasonal variations.

*Aedes aegypti* is known to transmit several infections like dengue virus, yellow fever virus, chikungunya virus, and Zika virus (ECDC, 2017). Some authors (Larsen & Ashley, 1971) suggested to be a potential vector of Venezuelan Equine Encephalitis virus and vector competency studies have shown *Ae. aegypti* is capable of transmitting West Nile virus. West Nile virus has also been isolated from this mosquito species in the field (Turell et al., 2005).

In this paper we propose a method to indirectly estimate the density of aedes mosquitoes in dengue affected areas. The method is based on incidence data of dengue infections and an application is illustrated with the case of the risk of urban yellow fever in a dengue infested area of Brazil. It serves, however, for the estimation of the risk of any aedes-transmitted disease outbreak, like Zika virus, chikungunya, Mayaro, among others (ECDC, 2017).

2. Materials and Methods

2.1. Formalism
2.1.1. The Ross-Macdonald Model

We use a variant of the classical Ross-Macdonald model, described in details in (Coutinho et al., 2006; Amaku et al., 2015, 2016).

The populations involved in the transmission are human hosts and mosquitoes. Therefore, the population densities are divided into the following compartments: susceptible humans denoted $S_H$; infected humans, $I_H$; recovered (and immune) humans, $R_H$; total humans, $N_H$; susceptible mosquitoes, $S_M$; infected and latent mosquitoes, $L_M$; infected and infectious mosquitoes, $I_M$. The variables and parameters appearing in the model are defined in Tables 1 and 2, respectively.

The model is defined by the following equations:

$$\frac{dS_H}{dt} = -abI_M \frac{S_H}{N_H} + \mu_H (N_H - S_H)$$

$$\frac{dI_H}{dt} = abI_M \frac{S_H}{N_H} - (\mu_H + \gamma_H)I_H$$

$$\frac{dR_H}{dt} = \gamma_H I_H - \mu_H R_H$$

$$\frac{dS_M}{dt} = -acS_M \frac{I_H}{N_H} + \mu_M (L_M + I_M) + \frac{dN_M}{dt}$$

$$\frac{dL_M}{dt} = acS_M \frac{I_H}{N_H} - \gamma_M L_M - \mu_M L_M$$

$$\frac{dI_M}{dt} = \gamma_M L_M - \mu_M I_M$$

$$\frac{dN_M}{dt} = \begin{cases} 
\mu_M S_M \text{ for constant population size} \\
\Omega \cos(2\pi t + \varphi) N_M(t) \text{ for seasonal variation}
\end{cases}$$

$$N_H = S_H + I_H + R_H$$

$$N_M = S_M + L_M + I_M$$

(1)
Remark 1: This model differs from the classical Ross-Macdonald model because the extrinsic incubation period in the classical Ross-Macdonald model is assumed to last $\tau$ days, whereas in model (1) we assumed an exponential distribution for the latency in the mosquitoes. The classical Ross-Macdonald model can be obtained from system (1) by replacing the fifth and sixth equations by (Amaku et al., 2015):

\[
\frac{dL_M}{dt} = acS_M \frac{I_H}{N_H} - \mu_M L_M - acS_M (t-\tau)\frac{I_H(t-\tau)}{N_H(t-\tau)} e^{-\mu_M \tau}
\]

\[
\frac{dI_M}{dt} = acS_M (t-\tau)\frac{I_H(t-\tau)}{N_H(t-\tau)} e^{-\mu_M \tau} - \mu_M I_M + p c_S(t) I_E
\]

where $\tau$ is the extrinsic incubation period and $\mu_M$ is the mosquito mortality rate. The expressions developed below in this paper with equations (1) can be replaced by the corresponding expressions of the classical Ross-Macdonald model described above by replacing $\frac{\gamma_M}{\gamma_M + \mu_M}$ by $e^{-\mu_M \tau}$. $\gamma_M$ is related to $\tau$ by $\tau = -\frac{1}{\mu_M} \ln \left[ \frac{\gamma_M}{\gamma_M + \mu_M} \right]$.

First we identify a dengue outbreak. For the purposes of this paper, an outbreak is defined as beginning at the moment $t_i$, when the epidemic curve is at its lowest values, that is, when $\frac{d}{dt} I_H(t_i) = 0$. The outbreak ends at time $t_f$, when $\frac{d}{dt} I_H(t_f) = 0$ again.

2.1.2. Calculating Dengue incidence from notification data in a population previously unexposed to dengue viruses.

Second, having identified a dengue outbreak, we fitted a continuous function to the number of actually reported dengue cases multiplied by 4 to take into account the 4:1 asymptomatic:symptomatic ratio (Ximenes et al., 2016), which has the form:

\[
Incidence_{DENV}(t) = c_1 \exp \left[ -\frac{(t-c_2)^2}{c_3} \right] + c_4
\]
representing the time-dependent dengue infection incidence. In equation (2) $c_1$ is a scale parameter that determines the maximum incidence, $c_2$ is the time at which the maximum incidence is reached, $c_3$ represents the width of the time-dependent incidence function and $c_4$ is just another scaling parameters. Equation (2) is intended to reproduce a "Gaussian" curve and so $c_1$ and $c_4$ are just scale parameters but $c_2$ represents the "mean" (and mode or maximum) time and $c_3$ represents the "variance" of the time distribution of cases. All parameters $c_i, i = 1,..., 4$ were fitted to model (2) so that the force of infection when applied to the dynamical model described below reproduces the observed incidence of dengue for a given outbreak in a region preferably small.

The first term of the first equation in system of equations (1) models the number of new infections per time unit. In terms of the classical notation of vector-borne infections (Coutinho et al., 2006) it is equal to the product of the force-of-infection, $\lambda(t)$ times the number of susceptible humans, denoted $S_H(t)$. As is well known, the force-of-infection in vector-borne infections is the product of the biting rate times the probability of transmission from infected mosquitoes to the human hosts, times the number of infected mosquitoes divided by the total number of humans (20). In terms of the variables of the model, the force of infection is defined as follows.

Let $S_H$ and $I_H$ represent the susceptible and infected humans, respectively, and $\lambda(t)$ be the force of infection (or incidence-density rate) which, as mentioned above, represents the product of the mosquitoes biting rate, $a$, the probability of transmission from mosquitoes to humans, $b$, and the number of infected mosquitoes with respect to humans, $\frac{I_M}{N_H}$, and is normally denoted as $\lambda = ab \frac{I_M}{N_H}$. Note, however, that none of these parameters/variables have been estimated in this paper. Also, as mentioned in the subheading of this section, all individuals in this population are considered susceptible to dengue, that is, $S_H(0) = N_H$. 


Remark 2: Note that $\lambda(t)S_H(t)$ is the dengue incidence. Or in detail,

$$\text{Incidence}(t) = \lambda(t)S_H(t) = ab\frac{I_M(t)}{N_H}S_H(t).$$

By numerically adjusting model (2) to the actual data we found the values of the parameters $c_i, i = 1,...,4$ that generate $\lambda(t)S_H(t)$, that is, the incidence data (reported cases); in other words, the fitted function $\text{Incidence}_{DENV}(t)$ (equation (2)) is simultaneously used to the system of equations (1) in order to obtain the incidence $\lambda(t)S_H(t)$.

The fitted incidence $\lambda(t)S_H(t)$, (taking into account the 4:1 asymptomatic:symptomatic ratio (Ximenes et al., 2016)), for two neighborhoods of the city of Rio de Janeiro in 2011-2012, using the parameters values shown in Table 2, are shown in Figs. 1 and 2.

3. Calculating the density of mosquitoes from the incidence of a dengue outbreak

In order to calculate the density of mosquitoes, we shall need the expression and derivatives of the incidence calculated as in the previous section.

3.1 Calculating the derivatives of $\text{Incidence}_{DENV}(t)$

From equation (2), we have:

$$\frac{d}{dt} \text{Incidence}_{DENV}(t) = -2c_1\left[\frac{(t-c_2)}{c_3}\right]\exp\left[-\left(\frac{(t-c_2)}{c_3}\right)^2\right]$$

(3)

$$\frac{d^2}{dt^2} \text{Incidence}_{DENV}(t) = -\frac{2c_1}{c_3}\left\{1 - \left[\frac{2(t-c_2)}{c_3}\right]\right\}\exp\left[-\left(\frac{(t-c_2)}{c_3}\right)^2\right]$$

(4)

$$\frac{d^3}{dt^3} \text{Incidence}_{DENV}(t) = 4\frac{c_1}{c_3^2}(t-c_2)\left[3 - \frac{2(t-c_2)^2}{c_3}\right]\exp\left[-\left(\frac{(t-c_2)}{c_3}\right)^2\right]$$

(5)

3.2 Calculating the derivatives of $S_H(t)$
From the first equation of the Ross-Macdonald model for the susceptible humans we obtain:

\[
\frac{d}{dt} S_H(t) = -ab \frac{I_M(t)}{N_H} S(t) + \mu_H (N_H - S_H(t)) \tag{6}
\]

But, as mentioned above, \(\text{Incidence}_{DENV}(t) = \lambda(t) S_H(t) = ab \frac{I_M(t)}{N_H} S(t)\). Hence:

\[
\frac{d}{dt} S_H(t) = -\text{Incidence}_{DENV}(t) + \mu_H (N_H - S_H(t)) \tag{7}
\]

Therefore:

\[
S_H(t) = N_H \left[1 - \exp(-\mu_H t)\right] + \exp(-\mu_H t) \left\{ S_H(0) - \int_0^t \exp(-\mu_H s) \text{Incidence}_{DENV}(s) ds \right\} \tag{8}
\]

or, in terms of the parameters of equation (2):

\[
S_H(t) = e^{-\mu_H t} S_H(0) - c_4 \left(1 - e^{-\mu_H t}\right) + N_H \left(1 - e^{-\mu_H t}\right) - \frac{c_3 \sqrt{c_2 c_3}}{2} e^{-\mu_H t} \right]
\]

\[
\times \left\{ \text{erf} \left[ \frac{1}{\sqrt{c_3}} + \sqrt{c_2} \left( -\frac{c_2}{c_3} + \frac{\mu_H}{2} \right) \right] - \text{erf} \left[ \sqrt{c_3} \left( -\frac{c_2}{c_3} + \frac{\mu_H}{2} \right) \right] \right\} \tag{9}
\]

For the numerical simulations, we used \(S_H(0) = N_H\). This is consistent with the case when the population do not have a history of previous exposure to dengue.

Hence:

\[
\frac{d^2}{dt^2} S_H(t) = -\frac{d}{dt} \text{Incidence}_{DENV}(t) - \mu_H \frac{d}{dt} S_H(t) \tag{10}
\]

\[
\frac{d^3}{dt^3} S_H(t) = -\frac{d^2}{dt^2} \text{Incidence}_{DENV}(t) - \mu_H \frac{d^2}{dt^2} S_H(t) \tag{11}
\]

3.3 Calculating the derivatives of \(I_H(t)\)
From the second equation of the Ross-Macdonald model for the infected humans we obtain:

\[
\frac{d}{dt} I_H(t) = ab \frac{I_M(t)}{N_H} S(t) - (\mu_H + \gamma_H) I_H(t) = Incidence_{DENV}(t) - (\mu_H + \gamma_H) I_H(t) \quad (12)
\]

which can be solved by standard methods resulting in:

\[
I_H(t) = I_H(0)e^{-(\mu_H + \gamma_H)t} + \int_0^t e^{(\mu_H + \gamma_H)(x-t)} Incidence_{DENV}(x)dx \quad (13)
\]

For the numerical simulations, we used \( I_H(0) = \frac{Incidence_{DENV}(0)}{(\mu_H + \gamma_H)} \). Note that when the population do not have a history of previous exposure to dengue, \( Incidence_{DENV}(0) = 1 \), meaning that one case was introduced in the population.

3.4 Calculating the number of mosquitoes \( N_M(t) = S_M(t) + L_M(t) + I_M(t) \)

3.4.1 Infective mosquitoes \( I_M(t) \)

We know that:

\[
Incidence_{DENV}(t) = \lambda(t) S_H(t) = ab \frac{I_M(t)}{N_H} S(t) \quad (14)
\]

Therefore:

\[
I_M(t) = \frac{N_H}{S_H(t)} \frac{Incidence_{DENV}(t)}{ab} \quad (15)
\]

\[
\frac{d}{dt} I_M(t) = \frac{N_H}{S_H(t)} \frac{1}{ab} \left[ \frac{d}{dt} Incidence_{DENV}(t) - \frac{Incidence_{DENV}(t)}{S_H(t)} \frac{d}{dt} S_H(t) \right] \quad (16)
\]
\[
\frac{d^2}{dt^2} I_M(t) = \frac{N_H}{S_H(t)} \frac{1}{ab} \left\{ \frac{2 \text{Incidence}_{DENV}(t)}{(S_H(t))^2} \left( \frac{d}{dt} S_H(t) \right)^2 - \frac{\text{Incidence}_{DENV}(t)}{S_H(t)} \frac{d^2}{dt^2} S_H(t) \right\} \\
- \frac{2}{S_H(t)} \frac{d}{dt} S_H(t) \frac{d}{dt} \text{Incidence}_{DENV}(t) + \frac{d^2}{dt^2} \text{Incidence}_{DENV}(t) \right\} \\
\]

\[ (S17) \]

\[
\frac{d^3}{dt^3} I_M(t) = \frac{N_H}{S_H(t)} \frac{1}{ab} \left\{ - \frac{6}{(S_H(t))^3} \left( \frac{d}{dt} S_H(t) \right)^3 \text{Incidence}_{DENV}(t) \right\} \\
+ \frac{5}{(S_H(t))^2} \left( \frac{d}{dt} S_H(t) \right)^2 \frac{d}{dt} \text{Incidence}_{DENV}(t) \\
+ \frac{4}{(S_H(t))^2} \left( \frac{d}{dt} S_H(t) \right) \left( \frac{d^2}{dt^2} S_H(t) \right) \text{Incidence}_{DENV}(t) \\
- \frac{3}{(S_H(t))^2} \frac{d^2}{dt^2} S_H(t) \frac{d}{dt} \text{Incidence}_{DENV}(t) \\
- \frac{3}{(S_H(t))} \frac{d}{dt} S_H(t) \frac{d^2}{dt^2} \text{Incidence}_{DENV}(t) \\
- \frac{\text{Incidence}_{DENV}(t)}{(S_H(t))} \frac{d^3}{dt^3} S_H(t) + \frac{d^3}{dt^3} \text{Incidence}_{DENV}(t) \right\} \\
\]

\[ (18) \]

### 3.4.2 Latent mosquitoes \( L_M(t) \)

From the sixth equation of the Ross-Macdonald model for the infected mosquitoes we obtain:

\[
\frac{d}{dt} I_M(t) = \gamma_M L_M(t) - \mu_M I_M(t) \\
\]

\[ (19) \]

Therefore:

\[
L_M(t) = \frac{1}{\gamma_M} \left[ \frac{d}{dt} I_M(t) + \mu_M I_M(t) \right] \\
\]

\[ (20) \]

Hence:

\[
\frac{d}{dt} L_M(t) = \frac{1}{\gamma_M} \left[ \frac{d^2}{dt^2} I_M(t) + \mu_M \frac{d}{dt} I_M(t) \right] \\
\]

\[ (21) \]
\[
\frac{d^2}{dt^2} L_M(t) = \frac{1}{\gamma_M} \left[ \frac{d^3}{dt^3} I_M(t) + \mu_M \frac{d^2}{dt^2} I_M(t) \right]
\]  

(22)

3.4.3 Susceptible mosquitoes \( S_M(t) \)

From the fifth equation of the Ross-Macdonald model for latent mosquitoes we obtain:

\[
\frac{d}{dt} L_M(t) = ac \frac{I_H(t)}{N_H} S_M(t) - (\mu_M + \gamma_M) L_M(t)
\]  

(23)

Therefore:

\[
S_M(t) = \frac{N_H}{acI_H(t)} \left[ \frac{d}{dt} L_M(t) + (\mu_M + \gamma_M) L_M(t) \right]
\]  

(24)

Hence:

\[
\frac{d}{dt} S_M(t) = \left\{ \frac{N_H}{acI_H(t)} \left[ \frac{d^2}{dt^2} L_M(t) + (\mu_M + \gamma_M) \frac{d}{dt} L_M(t) \right] \right. \\
- \left. \frac{N_H}{acI_H^2(t)} \frac{d}{dt} I_H(t) \left[ \frac{d}{dt} L_M(t) + (\mu_M + \gamma_M) L_M(t) \right] \right\}
\]  

(25)

The total size of the mosquitoes population, \( N_M(t) \) is given by:

\[
N_M(t) = S_M(t) + L_M(t) + I_M(t)
\]  

(26)

or

\[
N_M(t) = \left\{ \frac{N_H}{acI_H(t)} \left[ \frac{d}{dt} L_M(t) + (\mu_M + \gamma_M) L_M(t) \right] + \frac{1}{\gamma_M} \left[ \frac{d}{dt} I_M(t) + \mu_M I_M(t) \right] \right. \\
+ \left. \frac{N_H}{S_H(t)} \frac{Incidence_{DENV}(t)}{ab} \right\}
\]  

(27)

4. Illustrating the method

4.1. Example of applications
4.1.1. Testing the model's consistency

In order to test the model's accuracy, we applied the formalism above to the borough of Olaria in Rio de Janeiro. Olaria is located at the north of the city of Rio de Janeiro and is a traditional suburban residential area of the city. In the 2000 census, Olaria had an estimated population of 62,509 inhabitants in an area of around 3.7 km². This borough was chosen because in 2007 Maciel-de-Freitas, Eiras and Lourenço-de-Oliveira (2008) carried out a study in the area, in which they estimated, through the MosquiTrap and aspirator method, the population of *Aedes aegyptii*. In the estimated 0.79 km² area covering the average flight range of aedes mosquitoes, the authors found 3,505 and 4,828 female mosquitoes in the MosquiTrap and aspirator, respectively, totaling 8,333.

Using the data from dengue in the same period, the model estimated a total aedes population in the 0.79 km² area of Olaria in a period of two weeks as 8,145±12 female mosquitoes, which is a good approximation to the empirical data.

4.1.2. The case of dengue in two other neighborhoods of Rio de Janeiro

After fitting the dengue incidence in a given outbreak for a specific region, we used the above formalism to calculate the total mosquito density by simulating system (1). For this, we need, in addition to the parameters values as in Table 2, the initial condition for the susceptible mosquitoes, \( S_M(0) \).

4.1.2.1. Botafogo

Botafogo is a beachfront neighborhood of the city of Rio de Janeiro, Southeastern Brazil. It is essentially an upper middle class with small commerce community, with a population of about 83000 people, distributed in an area of 479.90 ha.

We used dengue data for the period between October 2011 and December 2012, comprising 3140 infections. Figure 1 shows the fitting of equation (2) to the monthly
number of dengue infections in Botafogo. The parameters values used in the calculations are shown in Table 2.

4.1.2.2. São Cristóvão

São Cristóvão is a traditional neighborhood located in the Central area of Rio de Janeiro, Brazil. With a population of about 26000 people distributed in an area of 410.56 ha, São Cristóvão experienced 3248 dengue infections in the period between October 2011 and December 2012.

Figure 2 shows the fitting of equation (2) to the monthly number of dengue infections in São Cristóvão.

In Fig. 3 we show the result of the calculation of the total number of Aedes mosquitoes in both neighborhoods, using the parameters as in Table 2.

4.1.2.3. Combining the data from both neighborhoods

In this section, we show that the method can be used for small geographical areas where the infection transits by mosquitoes’ movements but can also be applied for larger aggregated areas, where the infection transits by infected humans movements.

Let us call the incidence in areas 1 and 2 as Incidence$_1(t)$ and Incidence$_2(t)$, respectively, and defined as:

\[
Incidence_1(t) = abI_{M_1}(t) \frac{S_{H_1}(t)}{N_{H_1}(t)},
\]

and

\[
Incidence_2(t) = abI_{M_2}(t) \frac{S_{H_2}(t)}{N_{H_2}(t)},
\]

\[
Incidence_{1,2}(t) = ab \left[ I_{M_1}(t) \frac{S_{H_1}(t)}{N_{H_1}(t)} + I_{M_2}(t) \frac{S_{H_2}(t)}{N_{H_2}(t)} \right]
\]

If we define:
\[ I_{M_1}(t) = qI_M(t), \]
\[ I_{M_2}(t) = (1-q)I_M(t), \]
\[ S_{H_1}(t) = pS_H(t), \]
\[ S_{H_2}(t) = (1-p)S_H(t), \]
\[ N_{H_1}(t) = pN_H(t), \text{ and} \]
\[ N_{H_2}(t) = (1-p)N_H(t), \]

then:

\[
Incidence_{i=2}(t) = ab \left[ qI_M(t) \frac{pS_H(t)}{pN_H(t)} + (1-q)I_M(t) \frac{(1-p)S_H(t)}{(1-p)N_H(t)} \right]
\]

(29)

and the fractions \( q, (1-q), p \) and \( (1-p) \) cancel out, reducing equation (29) to equation (14).

Remark 3: About the above calculation, one should note that: (1) the values of \( p \) and \( q \) can be time-dependent; (2) the formalism can be extended to any number of sites.

Figure 4 illustrates this reasoning for the neighborhoods of Botafogo and São Cristóvão combined.

Note that the numerical simulation is a good approximation of the sum of the number of mosquitoes of each borough.

5. Calculating Dengue incidence from notification data in a population previously exposed to dengue viruses

The only modification necessary for this case from the previous discussed formalism occurs when we test the model’s consistency. When the population has been previously exposed to dengue, the boundary conditions have to be modified. In this case only a fraction \( p \) of the human population is susceptible to dengue due to previous epidemics, that is \( S_H(0) \to pN_H - I_H(0) \) and \( R_H(0) \to (1-p)N_H \) in the initial conditions of system (1). Remember that in this case \( I_H(0) = \frac{Incidence_{DENV}(0)}{(\mu_H + \gamma_H)} \) and \( Incidence_{DENV}(0) \neq 0 \).
The implications of this is as follows.

First, consider the Effective Reproduction Number, $R_{\text{eff}}(t)$ (Massad and COutinho 2012) of system (1):

$$R_{\text{eff}}(t) = \frac{a^2 b c \gamma_m^* N_m(t)}{\mu_M (\mu_H + \gamma_H)(\mu_M + \gamma_M) N_H} \frac{pS_H^*(t)}{N_H}$$

(30)

where $S_H^*(0) = N_H$. There is a threshold $p_{th}$ that makes $R_{\text{eff}}(t) < 1$ for $t > 0$.

When $p \to p_{th}$, then it is necessary a larger mosquitoes population to explain the same number of infections observed. When $p < p_{th}$, then it is impossible to have an outbreak in these places and the formalism breaks down. When $p = 1$, then we have a minimum mosquitoes population that reproduces the observed number of cases. In contrast, when $p \to p_{th}$, the mosquitoes population tends to its maximum size. This maximum size is calculated using the expression of $R_0 = 1$. Therefore, in the case where the population has been previously exposed to dengue, the total size of the mosquitoes population is bounded by $(p \to p_{th}) < 1$ and $p = 1$.

6. Digging a little bit more on the methodology proposed

In this section, we examine how the method proposed in the main text deals with an artificially constructed outbreak. To artificially construct an outbreak of a hypothetical vector-borne infection we specify a function $N_M(t)$ (see below) and use it in a conventional Ross-Macdonald model.

We know (Coutinho et al., 2006; Amaku et al., 2015, 2016) that a pure Ross-Macdonald model usually produces a single outbreak with a narrow and high peak in the incidence of cases. In nature, this is seldom observed because, as explained in (Amaku et al., 2016) the outbreak is produced in waves, that is, the disease travels throughout a geographical area. The Ross-Macdonald model only reproduces an outbreak if we concentrate in a very small area.
We produced two pure Ross-Macdonald models, one with a constant mosquito population and one in which the mosquito population oscillates with time. In both cases, we discovered that we could not fit the outbreak with the 'Gaussian' type of function as in equation (2). The resulting fit was always broad and the mosquito’s population retrieved was in complete disagreement with the artificial input. To solve this problem, we replace equation (2) with (28):

\[ \text{Incidence} = c \text{sech}^2(c_2 t + c_3) + c_4 \]  

(31)

Since this outbreak is artificial, we can use two methods to retrieve the mosquito population that we pretend not to know. The first method is the one described in the main text, that is, calculating from the fitting of the outbreak the value of \( I_M(t) \) as in equation (7) and, by differentiating it, calculate the values of \( L_M(t) \) and \( S_M(t) \). In the second method, we use the value of the incidence to calculate the human prevalence \( I_H(t) \) as in equation (18) and then \( I_M(t) \), \( L_M(t) \) and \( S_M(t) \) by using the Ross-Macdonald model. Since we pretend not to know the actual mosquito population, the value of \( S_M(0) \) is varied until the human prevalence from equation (18) matches that obtained from the Ross-Macdonald. Note that, as mentioned above, this second method cannot be applied to natural outbreaks, unless the outbreak occurs in a very limited geographical area, where the infection transits by infected mosquitoes movements.

In Fig. 5 we show the calculated number, by both methods, of mosquitoes populations as compared with that generated by a Ross-Macdonald model assuming a constant mosquitoes population.

The difference observed between the two methods is due to the limited quality of the fitting between the constructed incidence and the one fitted.

In Fig. 6 we show the calculated number, by both methods, of mosquitoes populations as compared with that generated by a Ross-Macdonald model assuming an oscillating mosquitoes population, obtained by the equation:
Again, the difference observed between the two methods is due to the limited quality of the fitting between the constructed incidence and the one fitted.

2. Estimating the risk of urban yellow fever resurgence in dengue endemic cities

2.1. Calculating the probability that one infected traveler arriving in an aedes infested area generates at least one autochthonous case of yellow fever.

Having calculated the total number of mosquitoes, $N_M(t)$, from the above formalism, we can calculate the probability that a number of infected travelers arriving at time $t = t_0$, $I^T_H(t_0)$, in a city infested by Aedes aegypti will generate at least one autochthonous yellow fever case in this city. This probability we call the 'risk of urban yellow fever resurgence' ($Risk_{UYFR}(t)$).

We begin by calculating the number of local mosquitoes that are infected by infective travelers that arrived at time $t = t_0$, $I^T_H(t_0)$. It is important to note that these infected travelers arriving at time $t = t_0$, $I^T_H(t_0)$, will remain infected for a period

$$\frac{1}{\Lambda} = \frac{1}{\mu_H + \gamma_H + \alpha_H},$$

after which they either recover, or die by other causes or die by the disease, that is:

$$I^T_H(t) = I^T_H(0) \exp\left[- \left(\mu_H + \gamma_H + \alpha_H\right) t\right]$$  \hspace{1cm} (33)

These infective travelers firstly infect local susceptible mosquitoes, which will become infected but not infective, called 'latent' mosquitoes, as expressed in the fifth equation of the Ross-Macdonald model described in equation (1):
\[ \frac{dL_M'(t)}{dt} = acS_M'(t) \frac{I_H^T(t)}{N_H} - (\mu_M + \gamma_M)L_M'(t) \] (34)

where \( I_H^T(t) \) as in equation (33). Equation (34) can be solve analytically by standard methods resulting in:

\[ L_M'(t) = ac \frac{N_M I_H^T(0)}{N_H} \exp \left[ -(\mu_M + \gamma_M) t \right] \frac{1}{(\mu_H + \gamma_H + \alpha_H) - (\mu_M + \gamma_M)} \left[ \exp \left[ -(\mu_H + \gamma_H + \alpha_H) t \right] \exp \left[ -(\mu_M + \gamma_M) t \right] \right] \] (35)

After surviving through the extrinsic incubation period, these late mosquitoes become infective, as expressed in the sixth equation of the Ross-Macdonald (S1), that is:

\[ \frac{dI_M'(t)}{dt} = \gamma_M L_M'(t) - \mu_M I_M'(t) \] (36)

which, in turn, can also be solved by standard techniques, resulting in:

\[ I_M'(t) = \frac{ac \gamma_M I_H^T(0)}{(\mu_H + \gamma_H + \alpha_H) - (\mu_M + \gamma_M)} \frac{N_M I_M'(t)}{N_H} \left[ \frac{e^{-\mu_M t} - e^{-(\mu_H + \gamma_H + \alpha_H) t}}{\gamma_M} + \frac{\mu_M - \mu_M^{-\mu_H t} - e^{-(\mu_H + \gamma_H + \alpha_H) t}}{(\mu_H + \gamma_H + \alpha_H)} \right] \] (37)

These infectious mosquitoes will generate a local force of infection, \( \lambda_L(t) \), which takes the form:

\[ \lambda_L(t) = \frac{abI_M'(t)}{N_H} \] (38)

where \( I_M'(t) \) as in equation (37).

Now we can calculate the probability that the infected travelers that arrived at time \( t = t_0 \), \( I_H^T(t_0) \), generate at least one local latent mosquito in the period between \( t \) and \( t + \Delta t \), \( L_M'(t) \). This probability satisfies the following equation:
\[
P_{\ell_{\text{lat}}} (t + \Delta t) = P_{\ell_{\text{lat}}} (t) \left[ 1 - ac \frac{N_M}{N_H} I_H^T (t_0) \Delta t \right] + P_{\ell_{\text{lat}}-1} (t) ac \frac{N_M}{N_H} I_H^T (t_0) \Delta t
\]  

(39)

Defining a mosquito's force of infection, that is, the incidence density of yellow fever to the local mosquitoes generated by the infected travelers as \( \lambda_M = ac \frac{N_M}{N_H} I_H^T (t_0) \)

and the mosquitoes densities with respect to the local human population \( m = \frac{N_M}{N_H} \), we can write (39) as:

\[
P_{\ell_{\text{lat}}} (t + \Delta t) = P_{\ell_{\text{lat}}} (t) (1 - \lambda_M \Delta t) + P_{\ell_{\text{lat}}-1} (t) \lambda_M \Delta t
\]

(40)

From equation (40), we write the Kolmogorov forward equation for the desired probability:

\[
\frac{d}{dt} P_{\ell_{\text{lat}}} (t) = -\lambda_M P_{\ell_{\text{lat}}} (t) + \lambda_M P_{\ell_{\text{lat}}-1} (t)
\]

(41)

Now, to calculate the probability that the infected travelers arriving at time \( t = t_0 \), \( I_H^T (t_0) \), will generate at least one local latent mosquito we first calculate the probability that these travelers will generate zero latent mosquitoes, that is, we set the term \( P_{\ell_{\text{lat}}-1} (t) \) in equation (41) as equal to zero. This results in:

\[
\frac{d}{dt} P_{\ell_{\text{lat}}=0} (t) = -\lambda_M (t) P_{\ell_{\text{lat}}} (t)
\]

(42)

Solving (42), we obtain:
\[ P_{I_{m}=0}(t) = \exp\left[ - \int_{t_0}^{t} \hat{\lambda}_M(t) \, dt \right] \] (43)

where \( \frac{1}{\Lambda} = \frac{1}{\mu_H + \gamma_H + \alpha_H} \).

Note that we did not include mosquitoes mortality in equation (43). This could be easily done by making the exponent in equation (43) as equal to \( - (\hat{\lambda}_M + \mu_M) t \).

The probability that one infected traveler arriving at time \( t = t_0 \), will generate at least one local latent mosquito is, therefore:

\[ P_{I_{m}=2}(t) = 1 - \exp\left[ - \int_{t_0}^{t} \hat{\lambda}_M(t) \, dt \right] \] (44)

The next step is the calculation of the probability that one infected traveler arriving at time \( t = t_0 \), will generate at least one local infected mosquito in the period between \( t \) and \( t + \Delta t \), \( I_{m}^{t}(t) \). For this we first write:

\[ P_{I_{m}^{t+\Delta t}}(t) = P_{I_{m}^{t}}(t)(1 - \phi_{M}(\Delta t)) + P_{I_{m}^{t-1}}(t)\phi_{M}(\Delta t) \] (45)

where the term \( \phi_{M} \) refers to the time evolution from the latent to the infective stages, that is:

\[ \phi_{M} = \gamma_M \Delta t [P_{I_{m}=1}(t) + P_{I_{m}=2}(t)] + o(\Delta t^2) \] (46)

where \( o(\Delta t^2) \) are terms of superior order that can be neglected. Therefore:

\[ P_{I_{m}^{t+\Delta t}}(t) = P_{I_{m}^{t}}(t)\left[ 1 - \gamma_M \Delta t (1 - e^{-\frac{t_0 + \Delta t}{\gamma_M} \hat{\lambda}_M(t) \, dt}) \right] + P_{I_{m}^{t-1}}(t)\gamma_M \Delta t (1 - e^{-\frac{t_0 + \Delta t}{\gamma_M} \hat{\lambda}_M(t) \, dt}) \] (47)
From equation (47), we write the Kolmogorov forward equation:

\[
\frac{d}{dt} P_{t_0} (t) = -\gamma_M \Delta t (1 - e^{-\int_0^{\gamma_M} \lambda_M(t) dt}) P_{t_0} (t) + P_{t_0 - t} (t) \gamma_M (1 - e^{-\int_0^{\gamma_M} \lambda_M(t) dt})
\]  

(48)

As before, we first calculate the probability that the local traveler will generate zero infective mosquitoes, that is, we make the term \( P_{t_0 - t} (t) \) in equation (41) as equal to zero. This results in:

\[
\frac{d}{dt} P_{t_0 = 0} (t) = -\gamma_M \Delta t (1 - e^{-\int_0^{\gamma_M} \lambda_M(t) dt}) P_{t_0 = 0} (t)
\]  

(49)

which, after integration gives:

\[
P_{t_0 = 0} (t) = \exp(-\gamma_M t) \exp \left[ \gamma_M \left( 1 - e^{-\int_0^{\gamma_M} \lambda_M(t) dt} \right) \right]
\]  

(50)

Finally, the probability that one infected traveler arriving at time \( t = t_0 \), will generate at least one local infective mosquito is

\[
P_{t_0 \geq 1} (t) = 1 - \exp(-\gamma_M t) \exp \left[ \gamma_M \left( 1 - e^{-\int_0^{\gamma_M} \lambda_M(t) dt} \right) \right]
\]  

(51)

We can now calculate the probability that one infected traveler arriving at time \( t = t_0 \), \( I^T_H(t_0) \), will generate at least one autochthonous yellow fever case in a city infested by *Aedes aegypti*. For this we first calculate the probability that one infected traveler
arriving at time $t = t_0$, $I_H^T(t_0)$, will generate none autochthonous yellow fever case, that is:

$$P_{I_H}(t + \Delta t) = P_{I_H}(t) \left(1 - abm\left[1 - P_{I_H=0}(t)\Delta t\right]\right) + P_{I_H}(t) \left(abm\left[1 - P_{I_H=0}(t)\right]\Delta t\right)$$

(52)

From equation (46), we write the Kolmogorov forward equation:

$$\frac{d}{dt} P_{I_H}(t) = -abm\left[1 - P_{I_H=0}(t)\right]P_{I_H}(t) + abm\left[1 - P_{I_H=0}(t)\right]P_{I_H-1}(t)$$

(53)

As before, we first calculate the probability that the traveler will generate zero autochthonous yellow fever case, that is, we set the term $P_{I_H-1}(t)$ in equation (53) as equal to zero. This results in:

$$\frac{d}{dt} P_{I_H}(t) = -abm\left[1 - P_{I_H=0}(t)\right]P_{I_H}(t)$$

(54)

which, after integration and rearrangement gives:

$$P_{I_H=0}(t) = \exp\left[-abm\int_0^t 1 - \exp(-\gamma_M s) \exp\left[\gamma_M \left(1 - e^{-\int_{s_0}^{s_1} \lambda_M(w)dw} \right) \right] ds \right]$$

(55)

So the probability that one infected traveler arriving at time $t = t_0$ will generate at least one autochthonous yellow fever case is

$$P_{I_H \geq 1}(t) = 1 - \exp\left[-abm\int_0^t 1 - \exp(-\gamma_M s) \exp\left[\gamma_M \left(1 - e^{-\int_{s_0}^{s_1} \lambda_M(w)dw} \right) \right] ds \right]$$

(56)
which, as mentioned above is our definition of risk of yellow fever resurgence in aedes infested cities.

**Remark 4:** The above results can be numerically calculated using the deterministic Ross-Macdonald model. The results obtained agree with the results using (56).

### 6.3. Calculating the risk of yellow fever resurgence in the its two neighborhoods of Rio de Janeiro analyzed above.

In this section, we calculate the risk of yellow fever resurgence and the expected number of autochthonous cases in the neighborhoods of Botafogo and São Cristóvão analysed in section 4.1.2.

We simulated model (1) with the parameter related to yellow fever for the dengue season of 2011-2012 and as initial conditions for the susceptible individuals equal to the respective populations of Rio's neighborhoods.

Then, we calculate the number of mosquitoes from dengue incidence from equation (27), the first derivative of which can be used in the fourth equation of system (1), so that:

\[
\frac{dS_M}{dt} = -ac_{yf}S_M \frac{I_H(0)}{N_H} + \mu_M (L_M + I_M) + \frac{dN_M}{dt}
\]

where \( \frac{dN_M}{dt} \) is the sum of equations (16), (21) and (25).

For the neighborhood of Botafogo, the maximum number of autochthonous cases is reached when the imported infection arrives at around 7 months after October 2011, with the number of yellow fever infections peaking between 5 and 11 and serious cases peaking between 1 and 2 (Fig. 7).

For the neighborhood of São Cristóvão, the maximum number of autochthonous cases is reached when the imported infection arrives at around 4 months after October
2011, with the number of yellow fever infections peaking between 5 and 11 and serious cases peaking between 1 and 2 (Fig. 8).

To complete the above analysis, we calculated the probability that one infected traveler arriving in February 2012 would generate at least one autochthonous yellow fever case.

As mentioned above, the risk of urban yellow fever resurgence depends on the size of the aedes mosquitoes population and its vectorial competence. As explained in the main text, this is defined as the relative reduction in the parameters $c$ and $b$ specific for yellow fever with respect to those specific for dengue. Hence, for instance, we used the value 0.6 for both parameters in the case of dengue and multiplied $c$ and $b$ for yellow fever by a factor varying from 0 to 1. Note that we assumed that the local aedes mosquitoes are always more competent to transmit dengue than yellow fever (Massad et al., 2001).

We then calculated:

1) the risk of yellow fever introduction (the probability of at least one autochthonous cases in the first generation of infective travelers) by one infective traveler to the neighborhoods of Rio de Janeiro arriving in February 2012. We remind that there was a huge outbreak of dengue in this dengue year of 2011-2012; and
2) the expected number of YF infections in the worst scenario after one year, that is, when the traveler arrives in the month of February 2012, both as a function of the local aedes vector competence.

7. Discussion and Conclusions

In this paper we present a model to estimate the density of aedes mosquitoes in a community affected by dengue. The model is based on the fitting of a continuous function to the incidence of dengue infections, from which the density of infected mosquitoes is derived straightforwardly. Further derivations allows the calculation of the latent and susceptible mosquitoes' densities, the sum of the three equals the total mosquitoes' density. The model is illustrated with the case of the risk of urban yellow
fever resurgence in dengue infested areas but the same methods apply for other aedes-transmitted infections like Zika and chikungunya viruses.

The model demonstrated to be reliable as the example of the Olaria neighborhood shows. It retrieved the actual number of mosquitoes collected in the area with good accuracy.

One caveat is worth noting; the Ross-Macdonald model assumes homogenously mixing population and one infected individual when introduced into a virgin population is homogeneously distribute over the whole area (Amaku et al., 2016). Therefore, the smaller the area we apply the model, the more reliable the results are.

The conclusion of the above analysis is that there is a positive and non-negligible risk of urban yellow fever resurgence in some dengue endemic areas due to their high aedes mosquitoes densities. The actual risk will be dependent on the probability that at least one infective human arrives at the right moment of the year, that is, when the local population of aedes mosquitoes is increasing in size and also on their vector competence. The examples provided in this paper are only intended to illustrate the method and more accurate parameters estimations are necessary for the true estimation of the risk of resurgence of urban yellow fever in those areas infested by *Aedes aegypti*. Finally, estimating the risk of urban yellow fever resurgence is central for the designing of an optimum vaccination strategy due to the yellow fever vaccine adverse events (Massad et al., 2005).
Fig. 1. Fitting a continuous function to the incidence of dengue infection in the period between October 2011 and December 2012 in Botafogo, Rio de Janeiro. Dots represent the actual notified data (x 4, see main text), continuous line the mean incidence and dotted line the 95% Confidence Interval.
Fig. 2. Fitting a continuous function to the incidence of dengue infection in the period between October 2011 and December 2012 in São Cristóvão, Rio de Janeiro. Dots represent the actual notified data (x 4, see main text), continuous line the mean incidence and dotted line the 95% Confidence Interval.
Fig. 3. Estimation of the size of the aedes mosquitoes’ population from the incidence of dengue infection in the period between October 2011 and December 2012 in Botafogo (red lines) and São Cristóvão (black lines) Rio de Janeiro. Continuous line the mean mosquitoes’ population size and dotted line the 95% Confidence Interval.
Fig. 4. Estimation of the size of the aedes mosquitoes’ population from the incidence of dengue infection in the period between October 2011 and December 2012 in Botafogo and São Cristóvão. Black lines represent the sum of both neighborhoods and red line the combination of them. Continuous line the mean mosquitoes’ population size and dotted line the 95% Confidence Interval.
Fig. 5. Calculated number, by both methods above, of mosquitoes populations (black line) as compared with that generated by a Ross-Macdonald model assuming a constant mosquitoes population (red line).
Fig. 6. Calculated number, by both methods, of mosquitoes populations (black lines) as compared with that generated by a Ross-Macdonald model assuming an oscillating mosquitoes population (red line).
Fig. 7. Cases of yellow fever in the neighborhood of Botafogo.
Fig. 8. Cases of yellow fever in the neighborhood of São Cristóvão.

Table 1.
Model variables and their biological meanings.

| Variable | Biological Meaning               |
|----------|----------------------------------|
| $S_H$    | Density of susceptible humans    |
| $I_H$    | Density of infected humans       |
| $R_H$    | Density of recovered humans      |
| $S_M$    | Density of uninfected mosquitoes |
| $L_M$    | Density of latent mosquitoes     |
| $I_M$    | Density of infected mosquitoes   |
Table 2.
Model parameters, their biological meanings and values used.

| Parameter | Meaning                                      | Value         | Value         |
|-----------|----------------------------------------------|---------------|---------------|
|           |                                              | Dengue        | Yellow Fever  |
| $a$       | Average daily rate of biting                 | 10 month$^{-1}$ | 10 month$^{-1}$|
| $b$       | Fraction of bites actually infective         | 0.6           | variable      |
| $\mu_H$   | Human natural mortality rate                 | $1.19 \times 10^3$ month$^{-1}$ | $1.19 \times 10^3$ month$^{-1}$ |
| $\gamma_H$| Human recovery rate                          | 4.0 month$^{-1}$ | 6.0 month$^{-1}$ |
| $\gamma_M$| Latency rate in mosquitoes                   | 5.6 month$^{-1}$ | 4.0 month$^{-1}$ |
| $\mu_M$   | Natural mortality rate of mosquitoes         | 5.6 month$^{-1}$ | 5.6 month$^{-1}$ |
| $c$       | Dengue susceptibility of A. aegypti          | 0.6           | variable      |
References

Adams B, Kapan DD (2009) Man Bites Mosquito: Understanding the Contribution of Human Movement to Vector-Borne Disease Dynamics. PLoS ONE 4(8): e6763. doi:10.1371/journal.pone.0006763

Amaku M, Burattini MN, Coutinho FA, Lopez LF, Massad E. Maximum equilibrium prevalence of mosquito-borne microparasite infections in humans. Comput Math Methods Med. 2013;2013:659038. doi: 10.1155/2013/659038.

Amaku M, Azevedo F, Burattini MN, Coutinho FA, Lopez LF, Massad E. Interpretations and pitfalls in modelling vector-transmitted infections. Epidemiol Infect. 2015 Jul;143(9):1803-15. doi: 10.1017/S0950268814002660.

Amaku M, Azevedo F, Burattini MN, Coelho GE, Coutinho FA, Greenhalgh D, Lopez LF, Motitsuki RS, Wilder-Smith A, Massad E. Magnitude and frequency variations of vector-borne infection outbreaks using the Ross-Macdonald model: explaining and predicting outbreaks of dengue fever. Epidemiol Infect. 2016 Aug 19:1-16

Coutinho FA, Burattini MN, Lopez LF, Massad E. Threshold conditions for a non-autonomous epidemic system describing the population dynamics of dengue. Bull Math Biol. 2006 Nov;68(8):2263-82.

Larsen JR, Ashley RF. Demonstration of Venezuelan equine encephalomyelitis virus in tissues of Aedes Aegypti. Am J Trop Med Hyg. 1971 Sep;20(5):754-60.

Liu-Helmersson J, Quam M, Wilder-Smith A, Stenlund H, Ebi K, Massad E, Rocklöv J. Climate Change and Aedes Vectors: 21st Century Projections for Dengue Transmission in Europe. EBioMedicine. 2016 May;7:267-77. doi: 10.1016/j.ebiom.2016.03.046.

Lopez LF, Amaku M, Coutinho FA, Quam M, Burattini MN, Struchiner CJ, Wilder-Smith A, Massad E. Modeling Importations and Exportations of Infectious Diseases via Travelers. Bull Math Biol. 2016 Feb;78(2):185-209. doi: 10.1007/s11538-015-0135-z.

ECDC 2017. European Centre for Disease Prevention and Control. Aedes aegypti - Factsheet for experts. Available at https://ecdc.europa.eu/en/disease-vectors/facts/mosquito-factsheets/aeedes-aegypti. Accessed in 6th September 2017

Maciel-de-Freitas, R. , A. E. Eiras, R. Lourenço-de-Oliveira. Calculating the survival rate and estimated population density of gravid Aedes aegypti (Diptera, Culicidae) in Rio de Janeiro, Brazil. Cad. Saude Publica. 24 (12), 2747-2754 (2008).

Massad E, Coutinho FA, Burattini MN, Lopez LF. The risk of yellow fever in a dengue-infested area. Trans R Soc Trop Med Hyg. 2001 Jul-Aug;95(4):370-4.
Massad E, Coutinho FA. Vectorial capacity, basic reproduction number, force of infection and all that: formal notation to complete and adjust their classical concepts and equations. Mem Inst Oswaldo Cruz. 2012 Jun;107(4):564-7.

Massad E, Coutinho FA, Lopez LF, da Silva DR. Modeling the impact of global warming on vector-borne infections. Phys Life Rev. 2011 Jun;8(2):169-99. doi: 10.1016/j.plrev.2011.01.001.

Massad, M., F. A. B. Coutinho, M. N. Burattini, L. F. Lopez, C. J. Struchiner. Yellow fever vaccination: how much is enough? Vaccine 23(30), 3908-3914 (2005).

Massad E, Coutinho FA, Burattini MN, Lopez LF, Struchiner CJ. Yellow fever vaccination: how much is enough? Vaccine. 2005 Jun 10;23(30):3908-14

Turell MJ, Dohm DJ, Sardelis MR, Oguinn ML, Andreadis TG, Blow JA. An update on the potential of north American mosquitoes (Diptera: Culicidae) to transmit West Nile virus. J Med Entomol. 2005 Jan;42(1):57-62.

Ximenes, R., M. Amaku, L. F. Lopez, F. A. B. Coutinho, M. N. Burattini, D. Greenhalgh, A. Wilder-Smith, C. J. Struchiner, E. Massad. The risk of dengue for non-immune foreign visitors to the 2016 summer olympic games in Rio de Janeiro, Brazil. BMC Infect. Dis. 16, 186 (2016). doi: 10.1186/s12879-016-1517-z