

Numerical Analysis of the Prevention with Vaccination Against Zika Virus (ZIKV)

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Abstract

A model for the transmission of the ZIKV is formulated, which includes the vaccination strategy of susceptible individuals at any age and time, from which there are determined the basic reproduction number R_0^η in function of the vaccination rate η , the vaccination criterion for the virus extinction, and the coverage for the reduction of the prevalence of the disease in an endemic state. It is also shown the prevention inequation and the graph of the region of values for a process free of infection and with infection.

Keywords: Basic reproduction number, Vaccination criteria, Prevalence, Endemic state

1 Introduction

ZIKV fever is a viral disease caused by a virus member of the Flaviridae family and the genus Flavivirus. [4]. The virus was detected for the first time in a research program on yellow fever in Uganda in the body of a primate in the forest that would give his name, Zika. The virus spread to Africa and in 1954 the first outbreak was detected in Nigeria. From here the disease spread through Southeast Asia and Africa. In 2015, the first confirmed infection in Latin America occurred in Brazil, according to WHO data. It has spread endemically to countries such as Colombia, Venezuela, Mexico, Costa Rica, which set off alarms, alerting countries to monitor the disease and notify the

authorities of cases of infected people [5].

The ZIKV can be transmitted through vectors, mainly mosquitoes that belong to the *Aedes* family, and in fact it is the most efficient way of transmitting the virus. However, it is not the only form of transmission for this virus, there have been cases of sexual transmission and the virus has been found in body fluids such as semen. There have been reports of transmission of the virus from a mother who has infected her child, through the placenta (vertical transmission) and has even found the presence of the virus in breast milk [5].

Currently several pharmaceutical companies and research institutes are working on the development of vaccines against Zika; According to WHO, the growing public concern about this rapidly expanding virus lies in its relationship with the birth of children with microcephaly, whose consequences can be serious brain damage or even death [6].

Scientists at Beth Israel Deaconess Medical Center, Walter Reed Army Institute of Research and the University of Sao Paulo have reported three vaccines against ZIKA protect monkeys as well as being safe, according to studies published in the journal Science. These results can pave the way for a vaccine in humans, their study began in 2017. One of them contains a whole Zika virus, another contains only DNA and the third contains fragments of viral DNA embedded in a vector. In 2016 three experimental vaccines were created Zika protected monkeys against the virus, an encouraging sign while investigations now pass to studies with people [7]. Some mathematical modeling studies that integrate vaccination are found in [1, 2, 3].

2 The model

A population model with ordinary nonlinear differential equations is presented, which interprets the dynamics of the ZIKV, including a constant vaccination rate of susceptible people at any time and age. It assumes a constant host population, considering the balance between birth and natural mortality, as well as a constant flow of female mosquitoes.

The variables and parameters of the model are: x_1 the average number of susceptible people, x_2 the average number of infectious people, $x_3(t)$ the average number of people immune from having suffered the infection and having been vaccinated, $N = x_1 + x_2 + x_3$ the human population (host) constant, at a time t respectively.

In the population of the vector, namely *Aedes aegypti*, the total mosquito pop-

ulation $M(t) = y_1 + y_2$ is divided by $y_1(t)$ the average number of mosquitoes not carriers of ZIKV, $y_2(t)$ the average number of mosquitoes carrying ZIKV at a time t , respectively.

The parameters of the model are μ the constant birth rate equal to the natural mortality rate of the host, ρ the constant flow of non-carrier vectors that reach the adult stage, β the probability of transmission of ZIKV from the carrier mosquito to the human, σ the probability of transmission of ZIKV from infectious persons to non-carrier mosquito, ϵ the mortality rate of mosquitoes by natural conditions, θ the constant recovery rate of people suffering from the infection, and η the constant vaccination rate of susceptible people over time and at any age. The objective of this study is to determine the vaccination coverage needed to reduce the prevalence to zero.

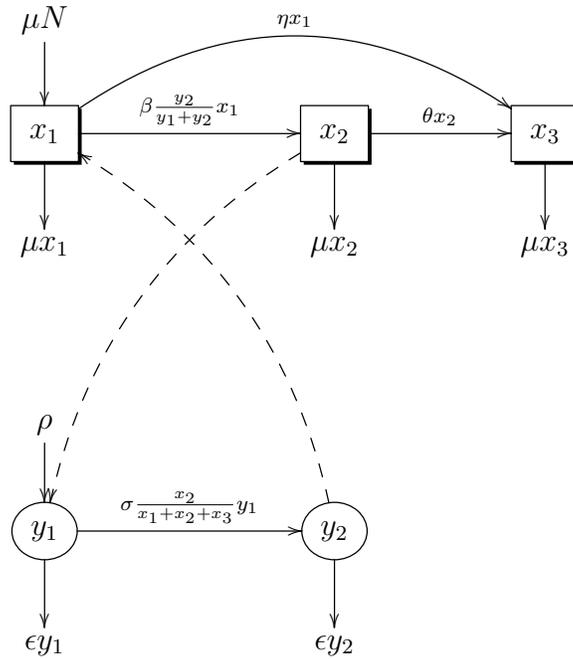


Figure 1: Diagram of the infectious process of the ZIKV with vaccination.

$$\frac{dx_1}{dt} = \mu N - \beta \frac{y_2}{y_1 + y_2 + y_3} x_1 - \mu x_1 - \eta x_1 \quad (1)$$

$$\frac{dx_2}{dt} = \beta \frac{y_2}{y_1 + y_2 + y_3} x_1 - \mu x_2 - \theta x_2 \quad (2)$$

$$\frac{dx_3}{dt} = \eta x_1 + \theta x_3 - \mu x_3 \quad (3)$$

$$\frac{dy_1}{dt} = \rho - \sigma \frac{x_2}{x_1 + x_2 + x_3} y_1 - \epsilon y_1 \quad (4)$$

$$\frac{dy_2}{dt} = \sigma \frac{x_2}{x_1 + x_2 + x_3} y_1 - \epsilon y_2 \quad (5)$$

with initial conditions $x_1(0) = x_{10}$, $x_2(0) = x_{20}$, $x_3(0) = x_{30}$, $y_1(0) = y_{10}$, $y_2(0) = y_{20}$ and $\epsilon, \mu, \theta, \rho, \eta > 0$, $y_1 > 0$, $0 < \beta, \sigma < 1$.

3 Main Results: Vaccination coverage criteria

The basic reproduction number R_0 , is defined as the average number of new cases that an infectious person can cause during the average time of infection (infectious period) in a susceptible population [8, 9]. This epidemiological threshold is determined as a function of the vaccination rate η , using previous biological definition with equations (1) - (5),

$$R_0^v(\eta) = \beta \sigma E[y_1] E[x_2] \frac{\mu}{\mu + \eta} = \frac{\beta \sigma \mu}{\epsilon(\mu + \eta)(\mu + \theta)} \quad (6)$$

where,

$$E[y_1] = \int_0^\infty t e^{-\epsilon t} dt \quad , \quad E[x_2] = \int_0^\infty t e^{-(\theta + \mu)t} dt.$$

To calculate the average life of the mosquito and the infectious period, we use the mathematical theory of epidemics in which many *life events* are the transition from a susceptible state (S) to a latent state (E), or a latent state to a state infectious (I) or from an infectious state to a state of removal (R), each with a certain probability of occurrence, which does not depend on how long it has persisted in the initial state, this dynamic is called **Process of Poisson** [8, 9].

Given the following consideration: if the infectious state x_2 persists even in $t + \Delta t$, then it has also persisted in t , and also there was no transition between t and $t + \Delta t$. These two events have probability $x_2(t)$ and $1 - (\theta + \mu)\Delta t$, respectively and are independent. Hence,

$$x_2(t + \Delta t) = (1 - (\theta + \mu)\Delta t)x_2(t)$$

That is,

$$x_2(t + \Delta t) - x_2(t) = -(\theta + \mu)x_2(t)\Delta t$$

from where,

$$\lim_{\Delta t \rightarrow 0} \frac{x_2(t + \Delta t) - x_2(t)}{\Delta t} = -(\theta + \mu)x_2(t)$$

Hence,

$$\frac{dx_2(t)}{dt} = -(\theta + \mu)x_2(t) \quad (7)$$

The expression (7) is an ordinary differential equation of separable variables and has the general solution $x_2(t) = ce^{-(\theta+\mu)t}$, Under the initial condition that $x_2(0) = 1$. That is, if the process starts at $t = 0$ in the state x_2 , then

$$x_2(t) = e^{-(\theta+\mu)t} \quad (8)$$

which is the probability of being infectious at a time t .

To calculate the average duration of the state x_2 we must apply the concepts of distribution and probability density of a random variable (v.a). These two functions are:

$$F(t) = 1 - e^{-(\theta+\mu)t}$$

and the probability density function by

$$f(t) = \frac{dF(t)}{dt} = (\theta + \mu)e^{-(\theta+\mu)t}$$

The average or expected value of x_2 is defined by:

$$E[x_2] = \int_0^{\infty} tf(t)dt$$

And considering the duration of the state x_2 as a random variable, we have

$$E[x_2] = \int_0^{\infty} t(\theta + \mu)e^{-(\theta+\mu)t}dt$$

This improper integral has solution $1/\theta+\mu$. We summarize the above reasoning in the following result:

Proposition 3.1. *If the transition from a state x_2 (infectious) to a state x_3 (removal) is a Poisson process with recovery rate θ and a death state with rate μ , then the average duration of the state x_2 is $E[x_2] = \frac{1}{\theta+\mu}$.*

In a similar way, the following proposition is proved:

Proposition 3.2. *If the transition of the mosquito state not carrying ZIKV y_1 or mosquito carrying ZIKV y_2 to the state of natural death due to environmental conditions, is a Poisson process with death rate ϵ , then the average life duration (life expectancy) of the state y_1 or y_2 is $E[y_i] = \frac{1}{\epsilon}$, $i = 1, 2$.*

The threshold $R_0^v(\eta)$, can be expressed in terms of the threshold without vac-

ination,

$$R_0^v(\eta) = \frac{\mu}{\mu + \eta} R_0 \quad (9)$$

where,

$$R_0 = \frac{\beta\sigma}{\epsilon(\theta + \mu)} = \left(\frac{\beta}{\theta + \mu} \right) \left(\frac{\sigma}{\epsilon} \right) \quad (10)$$

The first factor indicates the new cases in the host and the second factor the new cases in the vector.

Using the expression (9), the criterion for a vaccination coverage sufficient and necessary for virus extinction is determined,

$$R_0^v(\eta) < 1 \iff \frac{\mu}{\mu + \eta} R_0 < 1 \iff \eta > \mu(R_0 - 1) \quad (11)$$

when $R_0 > 1$.

The simulations are done with the Maple software, using the values in Table 1 and for different vaccination coverages.

Table 1: Model parameters.

Parameter	β	σ	ϵ	μ	θ
Value	0.7913	0.7730	0.0352	0.010	0.0500

In the first graph of Figure 2, the region of values for an efficient prevention with vaccination is shown and in the second graph, the population of infectious persons is simulated depending on the percentage of vaccination over time.

4 Conclusion

In the development of this research the importance of the Poisson Process application in epidemiology is shown, in particular in the interpretation of the threshold basic reproductive number R_0 and in the deduction of the epidemiological periods and average life times. It is also deduced that the coverage criterion of prevention with vaccination for the control of the virus and the region of values for an efficient control of the infection.

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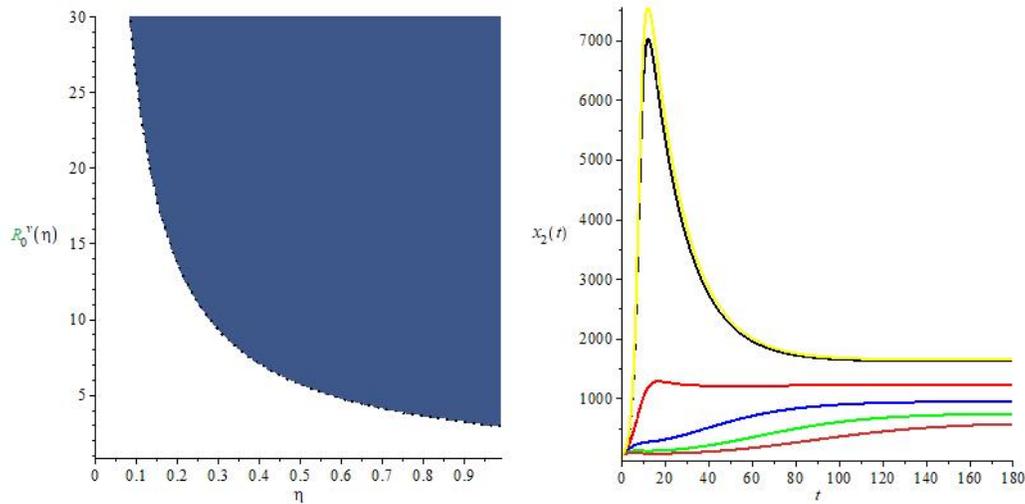


Figure 2: Regime of control coverage and behavior of the population infectious disease with respect to the following prevention coverages (η): 0% (yellow line), 0.9% (black line), 20% (red line), 40% (blue line), 60% (green line), 80% (orange line).

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