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Spatio-Temporal Modelling of Vector-borne Diseases in the Brazilian Amazon

A View on Dengue and Malaria Burden

by

Erick Albacharro Chacon Montalvan

Supervisor:

Dr. Benjamin Taylor

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Chapter 1

Introduction

1.1 Overview

Vector-borne diseases are a main world concern, representing 17% of all infectious diseases and more than 1 million deaths annually. These can be transmitted from humans or animals to humans by the so called vectors. Although there are several species of vectors, the most effective vector is the mosquito that become a host after feeding from a infected person and then spread the disease-causing pathogen to uninfected people. The main population affected are those living in the tropical region. Particularly, dengue and malaria, transmitted by mosquitoes, are the most sensible vector-borne diseases because the former has the highest incidence growth in the last 50 years (30-fold) with a 2.5 billion people at risk and the second has the highest morbidity incidence with an estimated of 627 thousand deaths in 2012. World Health Organisation (2014a)

The presence and incidence of vector-borne diseases are determined by the vector-pathogen-host relationship, where the environment and the socio-economic factors play a main role Tabachnick (2010). For the dengue case, the climate (temperature and precipitation), population growth, international travel, poverty and lack of sustained programmes are the main factors of incidence Guzman and Istúriz (2010); Gubler (2006). Similarly for malaria, climate (temperature, rainfall and relative humidity), sustained programmes, social and economic status are major factors Huang et al. (2011). However, due to the different behaviour of the vectors, these common factors could have different influences in the incidence of dengue and malaria.

Brazil, a tropical country with the highest population in Latin America zone, has favourable climate conditions for mosquito vectors being one of the most affected countries by arboviral diseases. For instance, it is the country with highest incidence of dengue with peaks from December to May because of climate conditions Amâncio et al. (2015). Specifically, the geographic, climatic and socio-economic features of the Amazon region make of this a susceptible and endemic area of vector-borne diseases. More than 95% of the viruses responsible of vector-borne diseases of the country has been isolated in the Amazon region Paula et al. (2015). In addition, while some diseases has been successfully controlled in the rest of Brazil, they are still a main concern in the Amazon basin; this is the case of the malaria disease Achcar et al. (2011).

Actions to control malaria and dengue were mainly focus on the reduction of the vector population and in education of the community about these diseases Marzochi (1994); Barat (2006). For dengue, in Brazil and the Americas, there was a successful program to eradicate the vector which explain the absence of dengue outbreaks between 1923-1981; however, due to the discontinuance of the program, the vector reinvaded the country becoming a today burden Figueiredo (1996); Gubler (2006). Similarly, in 1940 satisfactory results were obtained in the campaign against a main malaria vector in Northeastern Brazil and currently a significant reduction of cases has been reported in the country; nevertheless, the same success was not obtained in the Amazon region Coura et al. (2006). Despite the efforts to control dengue and malaria, these vector-borne diseases are still affecting the population and their quality of life; even worse, dengue is showing new trends that could aggravate the situation like hyper-endemicity and increased genetic diversity Figueiredo (2012).

In this context, the prediction of incidence is a need to improve control programs in order to prevent outbreaks with an efficient distribution of logistics and human resources to the affected zones within a reasonable time. Although, several attempts to predict epidemics has been made, the influence of the risk factors, the spatial variation and time evolution are not still fully understood. In part it this due to the complexity of vector-pathogen-host ecosystem with emerging patterns in dengue disease Paula et al. (2015), but the high computationally cost that is required for sophisticated spatio-temporal models for disease mapping and prediction has been a limiting factor.

In order to determine the main risk factors affecting malaria and dengue incidence in the Brazilian Amazon between 2006-2013 and to propose a predictive spatio-temporal model, Bayesian hierarchical techniques in the framework of latent Gaussian models were used through the novel INLA (Integrated Nested Laplace Approximation) inference approach Rue et al. (2009). The area of study covers 310 municipalities of 6 Federative Units and the considered factors include climatic and socio-economic variables in space, time and space-time domains. An additional goal was also to assess the efficiency of the INLA approach in comparison with Markov Chain Monte Carlo (MCMC) methods for spatial models.

This dissertation continues by providing major information about the epidemiology features of dengue and malaria join with a discussion of the literature review of spatio-temporal modelling of dengue and malaria incidence in this chapter. An exploratory analysis of the covariates and an initial analysis of the temporal, spatial and spatio-temporal patterns are presented in chapter 2. It will then go on to the explanation of the Laplace Approximation and the Bayesian inference in latent Gaussian models through the Integrated Nested Laplace Approximation in chapter 3. Chapters 4, 5 and 6 contain the dengue and malaria incidence modelling joint with the comparison of models and diagnostics for the temporal, spatial and spatio-temporal domains respectively. Finally, concluding remarks of the study are presented in chapter 7.

1.2 Epidemiology of Dengue and Malaria

This section covers the main features of dengue and malaria vector-borne diseases; with a focus on the such as the history, vector, pathogen, infection, symptoms and associated factors.

1.2.1 Dengue: Vector, Pathogen, Symptoms and Risk Factors

Dengue viruses were initially located in the jungle, then they spread to rural environments probably due to the clearing of the forests for the development of human settlements Gubler (2006). All dengue viruses belong to one of the four serotypes (DENV-1, -2, -3 and -4); the infection of one of them provide immunity for that serotype, but not against the others Gubler (1997). It is thought that initially, these viruses were transmitted by peri-domestic mosquitoes such as *Aedes albopictus* and then with major efficiency by the domestic mosquito *Aedes aegypti* Gubler (2006). This last prefers to lay its eggs in artificial containers around homes, to rest indoors and feeding during daylight Gubler (2006). Female *Aedes aegypti* is a nervous feeder that disrupts its meal with a slight movement to, then, return to the same or a different person being able of infecting several people in just one meal Gubler (2006). The infection could be asymptomatic, mild dengue fever (DF), dengue haemorrhagic fever (DHF), or dengue shock syndrome (DSS); although the last two has major severity, the mechanics to develop severe dengue is not clear Wilder-Smith et al. (2010). Symptoms include fever, myalgia, frontal headache, retro-orbital pain, arthralgia, rash, haemorrhagic manifestations and low white blood cell count Amâncio et al. (2015); Gubler (1997). Another symptoms related with a severe case are hypothermia, abdominal pains, rapid breathing and persistent vomiting World Health Organisation (2014a).

Between the environmental and socio-economic factors that affect the dengue incidence, the humidity, temperature and precipitation are a strong influencers because they impact in the population density of the *Aedes aegypti* mosquito Guzman and Istúriz (2010); Murray et al. (2013). On the other hand, the lack of basic resources and the deficiency of low water supply, sewer and waste management systems are of consideration because they are related with the presence of artificial habitat for the incubation of the mosquito eggs Gubler (2006); Morato et al. (2015). The efficiency of control programs also play an important role, but the level of information and participation of the communities are a key aspect Marzochi (1994). In addition, natural disaster such as drought or flood could have a strong impact Rajeswari et al. (2015).

1.2.2 Malaria: Vector, Pathogen, Symptoms and Risk Factors

It is thought that species of human malaria parasite has spread from Africa to other continents Carter and Mendis (2002). These parasites belong to four species of the genus Plasmodium (*P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*); however, human infectious with *P. knowlesi*, a monkey parasite, has been found in forested areas of South-East Asia World Health Organisation (2014b). The main malaria pathogens in Brazil are *P. vivax* and *P. falciparum* Carter and Mendis (2002); de Andrade et al. (1995), which are transmitted mainly by the female *Anopheles darlingi* vector Oliveira-Ferreira et al. (2010). It is important to emphasize that this mosquito is found in around the 80% of Brazil, but malaria is almost restricted to the Amazon region covering around the 99.8% of the cases Oliveira-Ferreira et al. (2010). It is know, at least out of Africa, that the female mosquito of malaria prefer to feed on animals rather than humans Carter and Mendis (2002), and that shallow groundwater and river edges are common places of breeding for this vector Cruz Marques (1987). Usually, the symptoms appears between 10 and 15 days after the infection, depending of the *Plasmodium* specie and the partial immunity of the host Bruce-Chwatt (1971). They can include fever, chills, rigors, sweating, body aches, headache and nausea; and life-threatening conditions in *P. falciparum* malaria Carter and Mendis (2002). Occurrence of these symptoms in cycles is a high indicator of malaria; nonetheless, this cycle pattern is not common in *P. falciparum* malaria Bruce-Chwatt (1971).

Similarly than dengue, environmental and socio-economic conditions are the main risk factors of malaria. Climate variables such as temperature and relativity humidity impact in the biology of the mosquito, whereas rainfall and floodplain areas could increase of reduce possible breeding sites Cruz Marques (1987); Huang et al. (2011). Low levels of education and poverty are also associated with the presence of malaria Carter and Mendis (2002); World Health Organisation (2014b). In addition, the efficiency of malaria control programs are a main factor due to the fact that some countries, including Brazil, have obtained satisfactory results against malaria with the available control tools Barat (2006). Finally, extreme events influence the development of the vector: for instance, floods could increase the number of breeding sites Sewe et al. (2015).

1.3 Literature Review

Chapter 2

Exploratory Analysis

2.1 Data

2.2 Temporal

2.2.1 Dengue

2.2.2 Malaria

2.3 Spatial

2.3.1 Dengue

2.3.2 Malaria

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2.4 Spatio Temporal

2.4.1 Dengue

2.4.2 Malaria

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