# Toward an early warning system for dengue prevention: modeling climate impact on dengue transmission

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**Abstract** Dengue fever is the most prevalent mosquito-borne viral disease of humans in tropical lands. As an efficient vaccine is not yet available, the only means to prevent epidemics is to control mosquito populations. These are influenced by human behavior and climatic conditions and thus, need constant effort and are very expansive. Examples of succeeded prevention are rare because of the continuous reintroduction of virus or vector from outside, or growing resistance of mosquito populations to insecticides. Climate variability and global warming are other factors which may favour epidemics of dengue. During a pilot study in Claris EC project, a model for the transmission of dengue was built, to serve as a tool for estimating the risk of epidemic transmission and eventually forecasting the risk under climatic change scenarios. An ultimate objective would be to use the model as an early warning system with meteorological forecasts as input, thus allowing better decision making and prevention.

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**Abbreviations**
EWS   Early warning systems
GCM   Global circulation models

## 1 Introduction

There is now a scientific consensus on the reality of climate change (Oreskes 2004) and it is clear that this change will have an impact on human health (Githeko et al. 2000; Patz et al. 2005; McMichael et al. 2006). Besides the impact on extreme weather events or on food supply, a major concern is the potential spread of climate-related infectious diseases and their emergence in previously spared areas (Shope 1992). Among them, tropical mosquito-borne diseases (malaria, yellow fever or dengue) have attracted most attention (Gubler et al. 2001; Hales et al. 2002; Unnasch et al. 2005). Their transmission depends on mosquito biology and population dynamics, which itself depends on climate. Warm temperature and high humidity favor longevity and shortens incubation and blood-feeding intervals (Christophers 1960). Climate change is expected to widen the warm regions and consequently vector distribution areas (Duvallet 2006). Based on the current distribution of dengue, these studies model the climatic domain for its occurrence, either by using statistical approaches deriving a probability of epidemic occurrence from climate variables (Rogers et al. 2006) or by using a mechanistic approach parameterizing the vector biology (Hopp and Foley 2003). The spatial distribution of the disease incidence is then redrawn for future climate, as projected by GCM. These studies thus rely on the strong assumption that the current and future disease distributions are dependent on climate only, which may be abusive as it fails to consider that the relations between man, the vector and the environment also matter for disease transmission (Burnett and Matthews 1997; Reiter 2001).

A striking example has been, from the late 1940s and on, the emergence of dengue, the most important arthropod-borne viral disease and a major global concern for international health organizations (Gubler 2002). This spread has been driven mainly by the changing habits of humans: population growth, urbanization and living standards have favoured the proliferation of the vector while the increase of air travel has facilitated the transport of dengue serotypes (Mairuhu et al. 2004). Dengue is typical of the complex interaction between climate, environment and man at the origin of epidemics (Guzmán and Kouri 2002). Its main vector, *Aedes* (*Stegomyia*) *aegypti* (L.), is closely related to human societies as it mainly bites humans and breeds preferentially in artificial water-holding containers (Hopp and Foley 2001). The availability and the nature of these water-holding containers exert therefore a primary control on the vector population and can be referred to as "environmental" controls (Favier et al. 2006). Similarly, temperature, humidity and rainfall can be referred to as "climatic" controls. To establish how climate change is likely to modify dengue occurrence patterns, it is necessary to define a measure of how environment acts to sustain epidemics under a determined climate, rather than trying to establish an unequivocal relationship between climate and incidence. After a short review of statistical models, we will consider mechanistic models to relate the transmission potential $R_0$ not only to climate, through the climatic dependence of biological stages, but also to the environment.

Due to the nature of the dengue transmission cycle—anthropic mosquitoes, viruses and human beings—key factors should be studied and selected among all those which regulate (1) the mosquito distribution, populations and vectorial capacity, (2) the virus multiplication and transmission, and (3) human behaviour. These factors are interconnected and are mainly influenced by changes in the global and local climate. A model of dengue epidemic risk would thus integrate all key factors of dengue fever transmission and estimate local risk indexes, according to climate variability and climate change projections.

## 2 Statistical versus mechanistic models

Statistical models are built from correlations between predictors and predistands. However the very nature of causal relationship between the two remains unknown. Basing their model on the relationships between seasonal climate forecasts and malaria incidence in Botswana, Thomson et al. (2006) developed a model to forecast the risk of malaria transmission. This statistical modelling approach has also been used for many other mosquito-borne diseases (Maelzer et al. 1999). In the case of Dengue fever, either the distribution of the disease or infestation levels of its main vector *Aedes aegypti* (L.) are corrrelated with global climate variables and represent first steps toward forecasting epidemic risks (Hales et al. 2002; Corrêa et al. 2005; Nakhapakorn and Tripathi 2005). Statistical methods, allied with processing of georeferenced data, are also commonly used to identify environmental factors of risk (Heukelbach et al. 2001; Hay et al. 2002; Barcellos et al. 2005; Rogers et al. 2006; Almeida et al. 2007). Thus, they allow a better and more target-specific allocation of ressources for the mosquito control and prevention in heterogeneous environments (Kolivras 2006). More simply, correlation analysis has attempted to show some associations between climate variables and dengue incidence (Depradine and Lovell 2004). In particular, El Niño phenomena (ENSO) has received special attention as it may be highly correlated with episodes of diseases transmission and spread (Hales et al. 1999; Kovats et al. 2003).

Mechanistic or dynamic models are reproducing with more or less details the biological processes which result in transmission of pathogens (Morse et al. 2005). The great majority of these models are adopting the principles of Ross-MacDonald as explained by Anderson (1981) and Dietz (1974). At diverse temporal scale, these models evaluate the fluctuations of mosquito densities and/or dengue cases according to climate seasonal or global variability. Global-scale models are those developed for dengue by Hopp and Foley (2003). Such models may accept a variety of driving climate values, like the CRU historical and present data or the SRES scenarios of future climate change (Martens et al. 1997; Arnell et al. 2004). At regional scale, many models have been described (Focks 1988; Bartley et al. 2002; Otero et al. 2005).

## 3 Early warning systems (EWS): the necessary link between scientific and operational research

Public health decision-making generally needs early warning output from systems which are based on uncertain data (Kuhn et al. 2005). The output of these EWS is
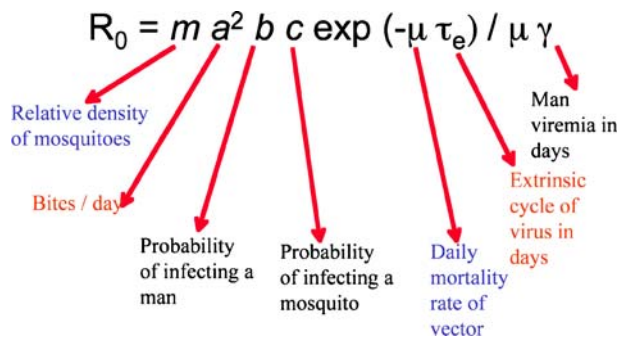
generally evaluated as a risk assessment (Eisenberg et al. 2002). The concept of transmission risk is mostly based on the paradigm of basic reproduction rate of the disease ($R_0$; Lieshout et al. 2004; Cruz-Pacheco et al. 2005), which arose initially in demography (Nishiura and Inaba 2007). Operationally, methods are being developed for mosquito density monitoring, in order to survey the effects of prevention (Nogueira et al. 2005). The quick detection of dengue cases is also of first importance (Beckett et al. 2005).

## 4 An example: the Claris dengue risk model

The model mimics the transmission of dengue virus by female mosquitoes from one infected human to an uninfected one. It evaluates a risk index, based on the suitability of the climate for the mosquito cycle to complete and for the virus to be transmitted from one human to another. The parameters which are included in the model as constant or variable quantities, as well as their relations, are showed in Fig. 1. The relative density of mosquitoes $m$ is exprimed in number of pupae per habitant, as this measure is considered the best estimate of productivity of the environment (Focks et al. 2006) and may be rather easily counted in the field. The daily number of bites is elevated at power two because it includes both the numbers of infective bites from mosquito to man and from sick man to mosquitoes, with probability of infection $b$ and $c$, respectively. The duration of viremia in the host ($\gamma$) is considered as a constant. Other important parameters are the mortality rate of adult female mosquitoes (the only which have a role as vectors; $\mu$) and the duration of the extrinsic cycle or multiplication of the virus in the mosquito ($\tau_e$). $R_0$ is put to 1 and $m$ is then estimated with the other parameters calculated with the climate input. A recent development of the model integrates a weighting of $m$ according to the suitability of the climate to the breeding of the mosquito.

Climate is currently represented by monthly means of the pressure vapour deficit and temperature and thus, the risk index is estimated for each month. A cut-off value of the risk is when it allows an epidemic to occur, i.e. when the $R_0 > 1$. However this model doesn't take into account the differences of human environment or human behavior, control activities etc. (Favier et al. 2005b). Spatially, the model is constrained by the scale of the climatic data: at this time, it was run on three grid scales: $2.5° \times 2.5°$ (world), $1° \times 1°$ (South America) and $6 \times 6$ km (New Caledonia).



**Fig. 1** Relations between the parameters (constant and variables) included in the risk model. According to *colour*, some variables are influenced either by both temperature and hygrometry (*in blue*) or temperature alone (*in red*). Others are considered constant or not climate dependent
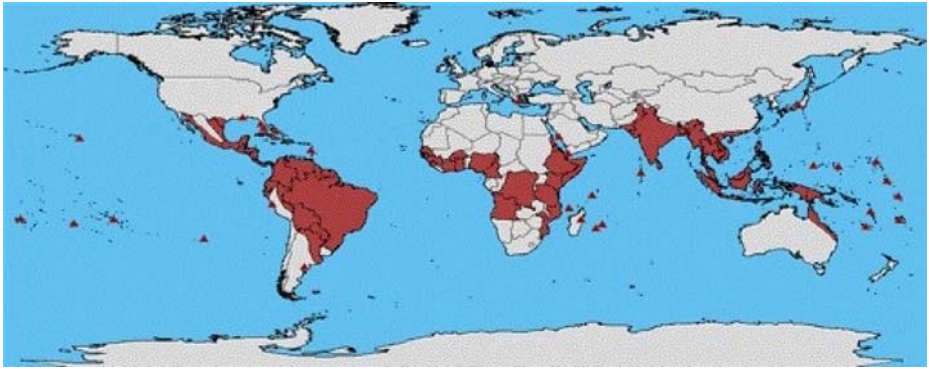
$$R_0 = m\, a^2\, b\, c\, \exp\left(-\mu\, \tau_e\right) / \mu\, \gamma$$

Relative density of mosquitoes

Bites / day

Probability of infecting a man

Probability of infecting a mosquito

Daily mortality rate of vector

Man viremia in days

Extrinsic cycle of virus in days

**Fig. 2** Present and past distribution of dengue fever (last 40 years)

Its validation was first done globally by checking the epidemic risk map against the known distributional map of dengue fever. In Fig. 2 is reported the known distribution of dengue fever during the last 40 years. The distribution of the risk of epidemics, calculated by the model with the mean climate of the same period (Fig. 3), corresponds fairly well with the actual distribution of dengue fever. Only China, the Arabic peninsula, and south of USA show a more extant dengue risk area than actually registered. This may be due to uncertainties in the climate data (case of China and Arabic Peninsula) or good environmental management activities (case of USA). On a more local scale and during some well-documented epidemics, the curves of variation of the incidence of dengue cases were compared with those of the risk given by the model (Fig. 4). In the case of the Athens epidemic in 1928, the peak of number of cases corresponds with the maximum of the risk index. In the other cases (Brazil and Thailand), the risk index changes are preceding by 1–2 months the changes in dengue prevalence. This is probably due to the necessary biological delay between growing up of populations of vectors and effective transmission of the viruses.
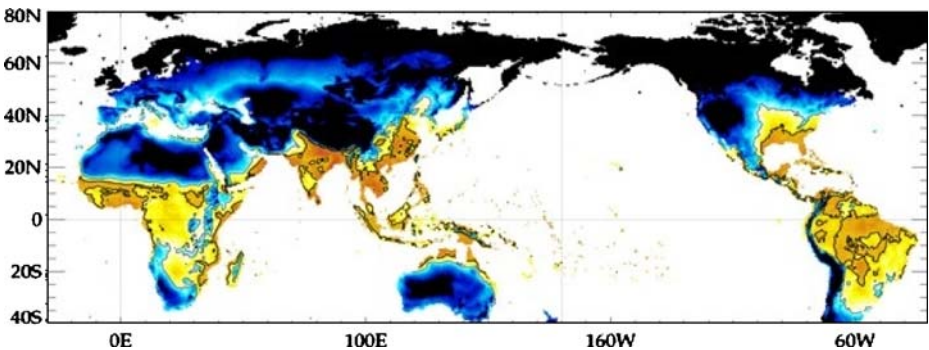


**Fig. 3** Map of risk of dengue transmission, computed by the model with the climatology of 1970–2000 from ERA40 reanalyses. *Dark* and *light-coloured risk areas* represent endemic and epidemic dengue-prone areas, respectively
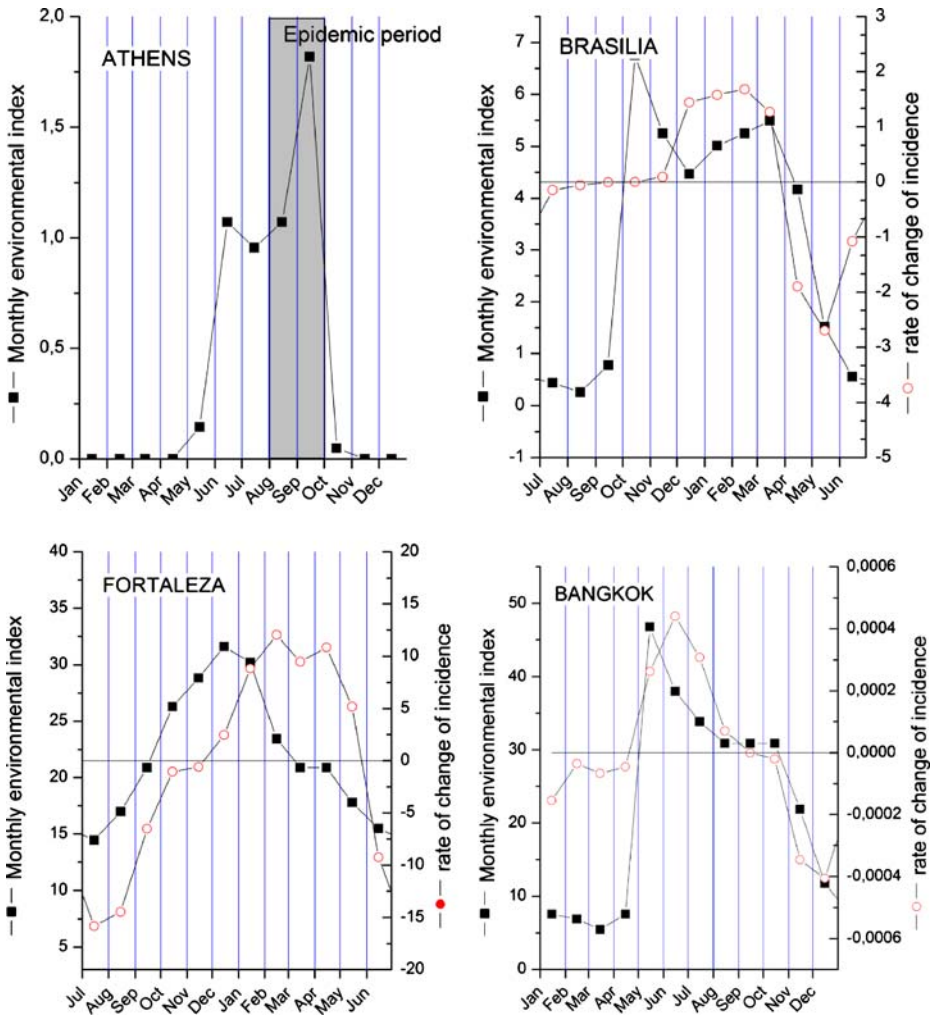
**Fig. 4** Evolution of the monthly risk index computed with 1970–2000 climatology from ERA40 reanalyses during the epidemics of **a** Athens, 1927–28; **b** Brasilia, DF Brazil, 2000–03 average; **c** Fortaleza, CE Brazil, 2001–03 average; **d** Bangkok, Thailand, 1983–96 average. Threshold values are indicated by a *horizontal line*

Outputs of the model may be shown as maps of risk: for given climate conditions, the risk index is proportionate to the density of mosquitoes to be attained to ensure an $R_0$ above 1, i.e. epidemic transmission (Degallier et al. 2005, 2006; Figs. 5, 6 and 7). During the austral summer (Fig. 5: January), greater part of tropical SA is under risk. The southeast limit corresponds with the risk maps given for Argentina by Carbajo et al. (2001). Great seasonal variation in the extension of risk areas is shown when comparing Fig. 6 with Fig. 5. It is interesting to note that, excepted the Amazonian basin, Northeastern Brazil would also be favourable for dengue transmission, although with lower risk during austral winter (July). Interannual climate variations may favour winter transmission in these regions. Seasonality of dengue

**Fig. 5** Map of the risk index for transmission of dengue fever in South America, computed for the mean climate of January (1981–90) CRU data
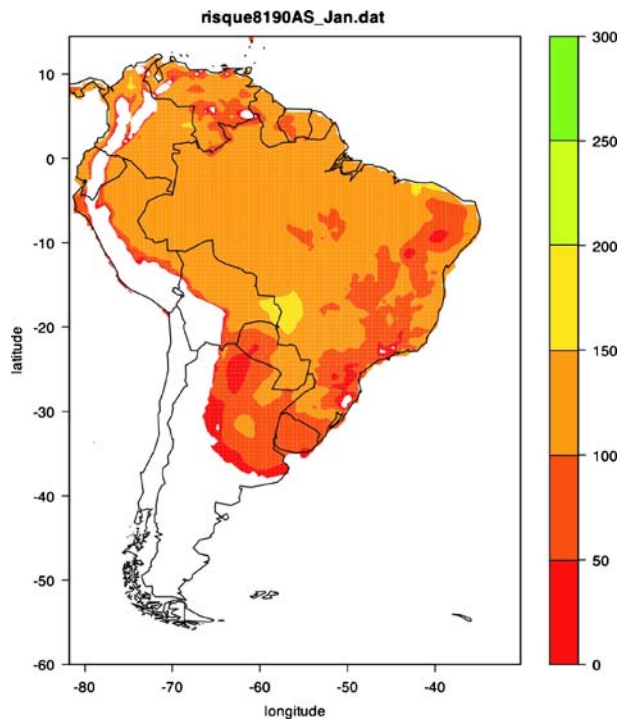


**Fig. 6** Map of the risk index for transmission of dengue fever in South America, computed for the mean climate of July (1981–90) CRU data
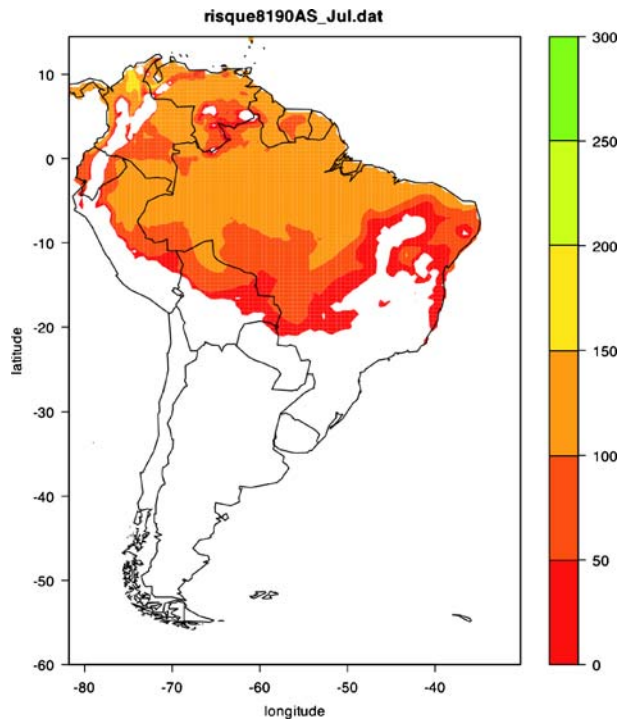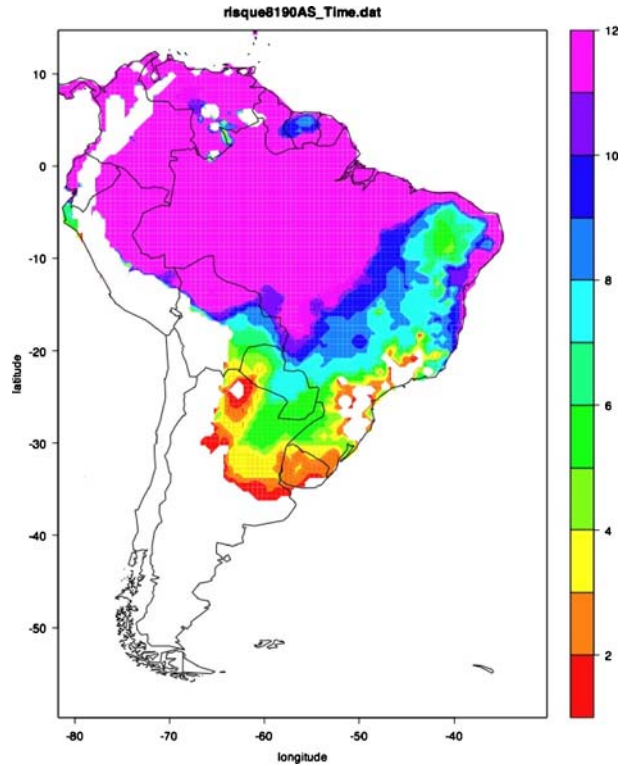
**Fig. 7** Map of the months
of maximum risk index for
transmission of dengue fever
in South America, computed
for the mean climate in CRU
data (1981–90)



transmission risk is well exemplified by the month when the risk index is maximum
(Fig. 7). This approach may serve as a preliminary EWS, indicating the months when
prevention activities should be intensified, according to each region.

**Fig. 8** Scatterplot of climate
risk index against dengue
fever prevalence (2000–2005)
according to population
density (*coloured scale*)
in a 0.5° × 0.5° gridded
representation of Brazil
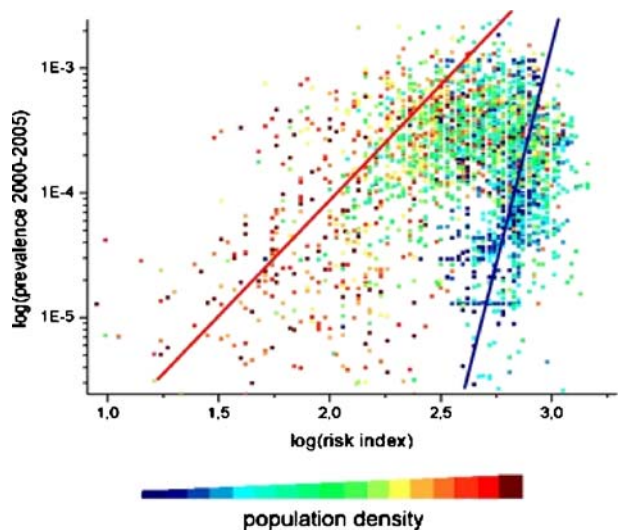
However, aspects which are not related to climate have been ignored in the model, and it can be seen in Fig. 8 that prevalence of the disease is not exclusively correlated to climate conditions but also to the density of human population and other environmental factors. When population density is low, climate should always be very suitable for dengue epidemics to occur. On the other hand, in big cities or densely populated States, disease prevalence grows up as climate risk becomes higher.

## 5 Discussion and conclusions

Influence of climate change (e. g. global warming) or variability (ENSO influence) on the spread of mosquito-borne diseases has been questioned (Burnett and Matthews 1997; Cazelles et al. 2005) despite numerous signs of an effective impact of climate change on the distribution of the vectors (Epstein et al. 1998). However, the importance of the human way of life and behaviour on the distribution of diseases should not be under estimated (Lifson 1996; Reiter 2001; Norris 2004; Sutherst 2004). Various methodologies and tools are available to forecast and eventually prevent epidemics but actually no one may be sufficient by itself. Thus, statistical and mathematical methods should be associated with data mining and geoprocessing (Barcellos et al. 2005; Almeida et al. 2007). Anyway, some limitations are yet met while modelling (Favier et al. 2005a), and the quality of data, mainly climatical, epidemiological and entomological, is of prime importance for building good models (Degallier et al. 2004). The development of reliable EWSs for dengue epidemics would allow to lowering the economic impact of the disease (Clark et al. 2005) and better evaluation of the outcomes of prevention programmes by the community (Marzochi 1994; Kay and Nam 2005). Future works should concentrate on including into the Claris model some non-climate parameters in order to cope with historical (immunization rate of population, level and efficiency of control and prevention measures), regional environmental, and socio-cultural (risky behaviours) factors.

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