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Analysis of a temperature- and rainfall-dependent model for malaria transmission dynamics

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ABSTRACT

A new non-autonomous model is designed and used to assess the impact of variability in temperature and rainfall on the transmission dynamics of malaria in a population. In addition to adding age-structure in the host population and the dynamics of immature malaria mosquitoes, a notable feature of the new model is that recovered individuals do not revert to wholly-susceptible class (that is, recovered individuals enjoy reduced susceptibility to new malaria infection). In the absence of disease-induced mortality, the disease-free solution of the model is shown to be globally-asymptotically stable when the associated reproduction ratio is less than unity. The model has at least one positive periodic solution when the reproduction ratio exceeds unity (and the disease persists in the community in this case). Detailed uncertainty and sensitivity analysis, using mean monthly temperature and rainfall data from KwaZulu-Natal province of South Africa, shows that the top three parameters of the model that have the most influence on the disease transmission dynamics are the mosquito carrying capacity, transmission probability *per* contact for susceptible mosquitoes and human recovery rate. Numerical simulations of the model show that, for the KwaZulu-Natal province, malaria burden increases with increasing mean monthly temperature and rainfall in the ranges ([17–25]°C and [32–110] mm), respectively (and decreases with decreasing mean monthly temperature and rainfall values). In particular, transmission is maximized for mean monthly temperature and rainfall in the ranges [21–25]°C and [95–125] mm. This occurs for a six-month period in KwaZulu-Natal (hence, this study suggests that anti-malaria control efforts should be intensified during this period). It is shown, for the fixed mean monthly temperature of KwaZulu-Natal, that malaria burden decreases whenever the amount of rainfall exceeds a certain threshold value. It is further shown (through sensitivity analysis and numerical simulations) that incorporating host age-structure and reduced susceptibility due to prior malaria infection has marginal effect on the transmission dynamics of the disease.

1. Introduction

A number of recent studies have established the significant direct role climate variables, such as temperature and rainfall, play on the transmission dynamics of vector-borne diseases (VBDs) [1,29,32,42,49,51,52,54,57,59,67,74,75]. Furthermore, changing wind patterns has been shown to have significant impact on the dynamics of some vectors [25]. Malaria, being the most important VBD [27], receives the most attention (half the world's population are at risk of malaria infection. The disease, which is spread in humans following an effective bite by an infected adult female Anopheles mosquito (the malaria vector), accounts for 250 million infections and approximately one million mortality annually, with 85% of the mortality occurring in children under the age of five [27,73]).

The specific role temperature plays on the dynamics of malaria takes many different forms. For example, increases in temperature generally causes the malaria vector to feed more frequently [26]. Furthermore, the average lifespan of the vector decreases rapidly (from the average 21 days) for higher temperatures (beyond [30–32]°C) [20]. The temperature sensitivity of malaria parasites to mosquito hosts has long been established [9,15,38]. Recent studies have shown that the maturation rate of the malaria parasite (*Plasmodium*) inside the host significantly decreases with increasing temperature (for example, as noted by Macdonald [38], the maturation rate decreases from 19 days at 22°C to 8 days at 30°C) [20]. Warmer temperature (warmer waters) also leads to faster maturation of the mosquito larvae [26]. Mosquito survival is greatly impacted at excessive temperatures [22]. Finally, in addition to its direct effects on vector and parasite development,

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temperature can also have a profound effect on vector physiology and immune responses [46,47,66].

The effect of rainfall on malaria transmission dynamics is directly tied to the availability of mosquito breeding sites (the use of precipitation as an empirical predictor of incidence, in addition to its direct impact on mosquito abundance, is well established [54]). Although total rainfall generally increases the availability and productivity of mosquito breeding sites (immature stages of the mosquito are aquatic, hence increasing rainfall increases breeding habitats and, consequently, mosquito abundance) [40], excessive rainfall can lead to washout effect of the breeding sites [40]. Hence, the timing, frequency and quantity of precipitation are important, and likely differ for different mosquito species [54]. Furthermore, as noted by Parham et al. [54], total rainfall is expected to have a highly nonlinear effect on mosquito production (in particular, having qualitatively different effects on container-breeding versus seasonal or permanent wetland breeding species).

Although climatic variability, especially changes in temperature and rainfall, influences the dynamics of malaria and other VBDs, this influence may be affected by non-climatic factors, such as epidemiological, environmental, socio-economic and demographic factors (see [54] and some of the references therein). Hence, as noted in [54], quantifying the impact of climate change on the dynamics of VBDs requires a better understanding of the role these non-climatic factors (and their combinations) have on the overall vector-pathogen-host dynamics. The purpose of the current study is to model the population-level effect of variabilities in temperature and rainfall patterns on the transmission dynamics of malaria.

Numerous mathematical models have been designed and used to quantify the impact of climate variables on the transmission dynamics of VBDs. These models fall in two main categories, namely mechanistic or process-based models (which represent the dynamics of the disease using differential equations) and statistical models (which are typically based on the use of regression models adapted to time-series data to describe the correlation or relationship between VBDs and environmental indicators of climate, climate change, meteorological factors and extreme weather events [2,3,7,10,14,54,58,62]).

Using a semi-parametric model, Egbendewe-Mondzozo et al. [20] showed that a marginal increase in temperature and precipitation could cause a significant change in malaria cases in many African countries. Blanford et al. [5] modeled the role of diurnal temperature range and mean temperature on the extrinsic incubation period of the malaria parasite. Lunde et al. [37] compared temperature-dependent mortality models for Anopheles gambiae sensu stricto. Mordecai et al. [45] showed, using a non-linear thermal response model, that the optimal temperature for malaria transmission is 25°C and decreases significantly beyond 28°C. Using a mechanistic repeated exposure malaria model, which also explicitly modeled the aquatic stages of the malaria vector, Agusto et al. [1] showed that the optimal temperature for malaria transmission in 67 cities in sub-Saharan Africa lies in the range [16–28]°C. A delay differential equation temperature-dependent malaria model was developed by Beck-Johnson et al. [4]. Using a mechanistic model which incorporates temperature, rainfall and other environmental variables (such as wind speed and relative humidity), Parham et al. [53] showed that these abiotic factors play significant roles in vector abundance.

As noted by Parham et al. [53], although statistical models have been useful in providing insight into the correlation between environmental variables and transmission intensity, the fundamental importance of mechanistic (process-based) models cannot be over-emphasized. For instance, unlike in the case of statistical models, mechanistic models allow for deeper understanding of the role of internal (due to biological processes) versus external (such as those due to changes in environmental variables) drivers of transmission (these biological processes, which drive the malaria transmission dynamics, are coupled within a dynamically-changing environment over a range a timescales [53]). The overwhelming majority of the VBD mechanistic modeling work that incorporate environmental variables published so far in the investigated the impact of variability in temperature only. To the authors' knowledge, the model in [53] is the only mechanistic modeling study to combine the effect of temperature and rainfall on malaria transmission dynamics. Consequently, the objective of the current study is to extend the work in [53] by designing a new temperature and rainfall-dependent mechanistic malaria model that incorporates some more pertinent climatic and non-climatic features and factors not considered in [53] (such as host age-structure, dynamics of immature mosquitoes, reduced susceptibility due to prior malaria infection etc.). The model to be developed in this paper is formulated in Section 2. The autonomous version of the model is analyzed in Section 3. The full non-autonomous model is analyzed and simulated in Section 4. Uncertainty and sensitivity analyses are carried out on the parameters of the model in Section 5. Numerical simulation results are also reported.

2. Model formulation

The total human population at time t, denoted by $N_h(t)$, is split into sub-populations of children (typically under the age of 17) and adults. The total sub-population of children at time t, denoted by $N_c(t)$, consists of children who are wholly susceptible ($S_c(t)$), susceptible with some immunity due to recovery from prior malaria infection ($S_{cr}(t)$), exposed ($E_c(t)$), exposed with prior immunity ($E_{cr}(t)$), infectious ($I_c(t)$), infectious with prior immunity ($I_{cr}(t)$), recovered ($W_c(t)$) and recovered with prior immunity ($W_{cr}(t)$). Similarly, the total sub-population of adults at time t, denoted by $N_a(t)$, is split into adults who are wholly susceptible ($S_a(t)$), susceptible with some immunity due to recovery from prior malaria infection ($S_{ar}(t)$), exposed ($E_a(t)$), exposed with prior immunity ($E_{ar}(t)$), infectious ($I_a(t)$), infectious with prior immunity ($I_{ar}(t)$), recovered ($W_a(t)$) and recovered with prior immunity ($W_{ar}(t)$). Thus, $N_h(t) = N_c(t) + N_a(t)$, where:

$$\begin{aligned} N_c(t) &= S_c(t) + S_{cr}(t) + E_c(t) + E_{cr}(t) + I_c(t) + I_{cr}(t) \\ &\quad + W_c(t) + W_{cr}(t), \\ N_a(t) &= S_a(t) + S_{ar}(t) + E_a(t) + E_{ar}(t) + I_a(t) + I_{ar}(t) \\ &\quad + W_a(t) + W_{ar}(t). \end{aligned}$$

The total mosquito population at time t, denoted by $N_v(t)$, is subdivided into sub-populations of immature mosquitoes (egg, larva and pupa stages), denoted by ($M_a(t)$), and adult mosquitoes (denoted by $N_m(t)$), so that

$$N_v(t) = M_a(t) + N_m(t),$$

where $N_m(t)$ as the sum of uninfected adult mosquitoes ($M_s(t)$) and infected adult mosquitoes ($M_i(t)$) (i.e., $N_m(t) = M_s(t) + M_i(t)$).

The non-autonomous age-structured model for malaria transmission dynamics in a population is given by the following deterministic system of non-linear differential equations (a flow diagram of the model is depicted in Fig. 1; the state variables and parameters of the model are described in Table 1):

$$\begin{aligned} \frac{dS_c(t)}{dt} &= \Pi_c - \lambda_c(T)S_c - (\xi_h + \mu_h)S_c, \\ \frac{dS_{cr}(t)}{dt} &= \psi_c\left(W_c + \theta_{cr}W_{cr}\right) - (1-\epsilon_c)\lambda_c(T)S_{cr} - (\xi_h + \mu_h)S_{cr}, \\ \frac{dE_c(t)}{dt} &= \lambda_c(T)S_c - (\sigma_c + \mu_h)E_c, \\ \frac{dE_{cr}(t)}{dt} &= (1-\epsilon_c)\lambda_c(T)S_{cr} - (\sigma_{cr} + \mu_h)E_{cr}, \end{aligned}$$

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