Chapter 13

Modelling Climate Change and Malaria Transmission

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Abstract

The impact of climate change on human health has received increasing attention in recent years, with potential impacts due to vector-borne diseases only now beginning to be understood. As the most severe vector-borne disease, with one million deaths globally in 2006, malaria is thought most likely to be affected by changes in climate variables due to the sensitivity of its transmission dynamics to environmental conditions. While considerable research has been carried out using statistical models to better assess the relationship between changes in environmental variables and malaria incidence, less progress has been made on developing process-based climate-driven mathematical models with greater explanatory power. Here, we develop a simple model of malaria transmission linked to climate which permits useful insights into the sensitivity of disease transmission to changes in rainfall and temperature variables. Both the impact of changes in the mean values of these key external variables and importantly temporal variation in these values are explored. We show that the development and analysis of such dynamic climate-driven transmission models will be crucial to understanding the rate at which *P. falciparum* and *P. vivax* may either infect, expand into or go extinct in populations as local environmental conditions change. Malaria becomes endemic in a population when the basic reproduction number R_0 is greater than unity and we identify an optimum climate-driven transmission window for the disease, thus providing a useful indicator for determing how transmission risk may change as climate changes. Overall, our results indicate that considerable work is required to better understand ways in which global malaria incidence and distribution may alter with climate change. In particular, we show that the roles of seasonality, stochasticity and variability in environmental variables, as well as ultimately anthropogenic effects, require further study. The work presented here offers a theoretical framework upon which this future research may be developed.

Introduction

The potential effects of global climate change and ozone depletion on human health have received increasing attention in recent years, with those due to changes in vector-borne disease (VBD) incidence and distribution thought to represent one of a range of major direct and indirect effects.[1-6] Malaria has arguably attracted the most attention of all VBDs,[4,7-9] due to both the sensitivity of its transmission dynamics to changes in environmental variables and its status as one of the biggest causes of worldwide mortality due to infectious disease, with an estimated 247 million cases in 2006.[10,11]

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Climate change may affect malaria transmission via changes in the ecology and behaviour of humans, *Anopheles* mosquitoes and *Plasmodium* parasites.[11] Perhaps the most important effect will be on the vector population itself. Immature stages of the lifecycle are aquatic and increasing rainfall, leading to increased availability of breeding sites, is a strong driver of abundance. The use of precipitation as an empirical predictor of incidence,[12-16] besides its direct impact on vector abundance,[17-22] is well-established. The role of temperature has also been considered in terms of its effects on vector abundance (as a physiological factor affecting the development rate of larvae, adult daily survival probability and biting rates due to increased processing rate of blood meals), local dispersal, parasite dynamics (such as reproduction rates as a function of temperature) and human behaviour.[4,23-25]

Given the links between malaria incidence and variation in environmental variables, mathematical models incorporating climate variables have been developed in recent years.[7,20,26-28] The growing importance of these models derives from the fact that while statistical models have been useful in elucidating relationships between environmental variables and transmission intensity,[9] process-based mathematical models permit a more explanatory understanding of the role of internal (due to biological processes) versus external (such as those due to changes in environmental variables) drivers of transmission. Dynamical models are fundamentally important, since the biological processes driving malaria transmission are embedded within a dynamically changing environment on a range of timescales. Moreover, to meaningfully capture the emergence of new outbreaks (e.g., due to changing climate making areas previously unsuitable for transmission more favourable, human movement or mosquito dispersal to previously disease-free regions), a dynamic model is required to capture invasion dynamics.

The modelling work to date incorporating environmental variables into dynamic transmission models has almost entirely focussed on the impact of changes in temperature (although see ref. 20). Most of the attention of previous modelling work has also been on capturing equilibrium dynamics based on derivation and analysis of static quantities such as R_0, the basic reproduction number of the disease. In this chapter, we firstly consider how rainfall may be incorporated within a dynamic transmission model and secondly highlight how important disease transmission issues not examined to date can only be addressed within such a dynamic modelling framework. More specifically, we examine the impact of climate change on mosquito (and hence malaria) extinction due to changes in environmental conditions, malaria invasion dynamics in previously disease-free regions and the effects of temporal variability in climate variables on mosquito population dynamics, invasion behaviour and endemic prevalence.

Mathematical Model Development

In terms of developing a dynamic framework for understanding the impact of climate change on malaria transmission, a deterministic or stochastic transmission model may be developed, embedded within an environment assumed static or fluctuating over the timescale of interest. Arguably, the most realistic framework is a stochastic transmission model within dynamic environmental conditions, in which the inclusion of environmental forcing would be key to obtaining a better understanding of the effects of climate change on the spread and control of malaria. Despite this, little research to date has examined the effects of temporal forcing by climate (i.e., variability in environmental variables occurring at intra-annual (seasonal), inter-annual, decadal and longer timescales) on malaria transmission, despite receiving attention for other infectious diseases.[29,30] Understanding the dynamical impact of trends and variability in climate over the next 40 years, for instance, may affect a goal of malaria eradication by 2050. Thus, although a more thorough theoretical study of the effects of temporal forcing is beyond the scope of this chapter, a key objective of the work presented here is to begin considering how seasonality effects may be incorporated into models and may impact vector population dynamics, invasion behaviour and changes in the R_0 of malaria.

We assume a deterministic model, which despite making simple biological assumptions, is expected to be sufficiently realistic to permit valuable insights into climate-driven malaria transmission dynamics. Let S_M, E_M and I_M represent the number of susceptible, exposed (but

Table 1. Malaria model parameters

Parameter	Definition (and Units)
$b(R,T)$	Adult mosquito birth rate (per day)
$\mu(T)$	Adult mosquito per capita death rate (per day)
$a(T)$	Mosquito biting rate (per day)
b_1	Proportion of bites by susceptible mosquitoes on infected humans that produce infection
$\tau_M(T)$	Duration of the sporogonic cycle (days)
$l_M(T)$	Survival probability of infected mosquitoes over the incubation period of the parasite
b_2	Proportion of bites by infectious mosquitoes on susceptible humans that produce infection
τ_H	Latent period of infection within humans (days)
$1/\gamma$	Human average duration of infectiousness (days)
$M(t)$	Total number of mosquitoes ($S_M(t) + E_M(t) + I_M(t)$)
N	Total number of humans ($S_H(t) + I_H(t) + R_H(t)$)

not infectious) and infectious mosquitoes respectively, along with S_H and I_H representing the analogous categories in humans (where we assume a fixed latent period of duration τ_H in humans). All model parameters, functional forms and baseline values assumed in this analysis are summarised in Tables 1-3. The model is described by the ordinary differential equations

$$\begin{aligned}
\frac{dS_M}{dt} &= b - ab_1\left(\frac{I_H}{N}\right)S_M - \mu S_M,\\
\frac{dE_M}{dt} &= ab_1\left(\frac{I_H}{N}\right)S_M - \mu E_M - ab_1\left(\frac{I_H(t-\tau_M)}{N}\right)S_M(t-\tau_M)l(\tau_M),\\
\frac{dI_M}{dt} &= ab_1\left(\frac{I_H(t-\tau_M)}{N}\right)S_M(t-\tau_M)l(\tau_M) - \mu I_M,\\
\frac{dS_H}{dt} &= -ab_2\left(\frac{I_M}{N}\right)S_H,\\
\frac{dI_H}{dt} &= ab_2\left(\frac{I_M(t-\tau_H)}{N}\right)S_H(t-\tau_H) - \gamma I_H,
\end{aligned} \tag{1}$$

where the total mosquito population $M(t) = S_M(t) + E_M(t) + I_M(t)$ and human population $N(t) = S_H(t) + I_H(t) + R_H(t)$.

Functional Forms for Incorporating Temperature and Rainfall Effects and the Derivation of R_0

We assume that the mosquito birth rate b depends on rainfall (through the dependence on breeding site availability) and temperature. Let us write the birth rate as

$$b(R,T) = \frac{B_E p_E(R) p_L(R,T) p_P(R)}{\tau_E + \tau_L(T) + \tau_P}, \tag{2}$$

Table 2. Functional forms for parameters appearing in Equation (1)

Parameter	Functional Form	Units	Reference
$a(T)$	$\frac{T - T_1}{D_1}$	Per day	34
$p(T)$	$e^{\frac{-1}{AT^2+BT+C}}$	Dimensionless	4
$\tau_M(T)$	$\frac{DD}{T - T_{min}}$	Days	35

where B_E is the number of eggs laid per adult per oviposition, $p_E(R)$, $p_L(R,T)$ and $p_p(R)$ are the daily survival probabilities of eggs, larvae and pupae, τ_E, τ_L (T) and τ_p are the duration of each development stage, $1/\gamma$ is the average duration of infectiousness in humans and we highlight the parameter dependence on daily temperature T (in °C) and rainfall R (in mm). The average larval duration depends on temperature as $\tau_L(T) = 1/(c_1T + c_2)$,[28,31] corresponding to larval daily survival probability $p_L(T) = e^{-(c_1T+c_2)}$, while the development rate of eggs and pupae is relatively independent of temperature.[32] While rainfall has been shown to positively correlate with malaria incidence, it has also been suggested that excessive rainfall may flush out larvae and breeding sites[31,33] and we assume a quadratic relationship between the daily survival probabilities of eggs, larvae and pupae and rainfall. For larvae, we assume

$$p_L(R) = \left(\frac{4p_{ML}}{R_L^2}\right) R(R_L - R) \tag{3}$$

where p_{ML} is the maximum daily survival probability (i.e., when there is optimum rainfall for mosquito breeding) and R_L is the rainfall limit beyond which breeding sites get flushed out and no immature stages survive. We assume an analogous expression for eggs and pupae. We also assume that temperature and rainfall act independently on the survival probability of larvae such that $p_L(R,T) = p_L(R)\, p_L(T)$, although this is likely to be an approximation in reality. Increased evaporation of breeding sites or the melting of snow packs as temperatures increase provide two examples of this. Substituting these expressions into (2) gives the birth rate as a function of temperature and rainfall and this functional form is plotted in Figure 1.

As well as $b(R,T)$, the biting rate $a(T)$, mosquito mortality hazard $\mu(T)$ and probability $l(\tau_M)(T)$ of a mosquito surviving the duration of the sporogonic cycle also depend on temperature.[4] These are summarised in Table 2 and plotted in Figure 2, where we additionally note that $\mu(T) = -ln\, p(T)$ and $l(\tau_M)(T) = p(T)^{\tau_M(T)}$. Note that the expression in ref. 4 for $p(T)$ is true only at favourable humidities for mosquito development. Survival drops off rapidly at relative humidities below 50-60%,[36] highlighting that $p(T)$ is also indirectly dependent on rainfall through its impact on relative humidity and illustrates again the interdependence of temperature and rainfall. We assume that the proportions of bites by susceptible mosquitoes on infectious humans (b_1) and infectious mosquitoes on susceptible humans (b_2) that produce infection are independent of environmental conditions.

Arguably, one of the most important concepts in infectious disease epidemiology is that of the basic reproduction number R_0, defined as the average number of secondary cases generated per infectious individual over their duration of infectiousness in an entirely susceptible population.[37] This may be similarly defined for VBDs as the product of the number of vectors infected per person and the number of people infected per vector (over their respective infectious periods). While R_0 may be calculated in a variety of ways for infectious disease models, calculation for models assuming homogeneous mixing is relatively straight forward. The transmission model (1) has two equilibrium

Table 3. Baseline parameter values assumed for model simulations

Parameter	Assumed Value	Units
B_E	200	Dimensionless
p_{ME}	0.9	Dimensionless
p_{ML}	0.25	Dimensionless
p_{MP}	0.75	Dimensionless
R_L	50	mm
τ_E	1	days
c_1	0.00554	(°C days)$^{-1}$
c_2	–0.06737	(days)$^{-1}$
τ_P	1	days
T_1	19.9	°C
D_1	36.5	°C days
b_1	0.04	Dimensionless
A	–0.03	(°C^2 days)$^{-1}$
B	1.31	(°C days)$^{-1}$
C	–4.4	days^{-1}
b_2	0.09	Dimensionless
τ_H	10	days
DD	111 (*P. falciparum*)	°C days
	105 (*P. vivax*)	
T_{min}	16 (*P. falciparum*)	°C
	14.5 (*P. vivax*)	
γ	1/120	days^{-1}

states, namely the disease-free state and the endemic equilibrium. In the latter case, it is readily shown that the prevalence in mosquitoes is given by

$$I_M^* = \frac{M(R_0 - 1)}{\left(\frac{R_0}{l(\tau_M)}\right) + \left(\frac{ab_2 M}{\gamma N}\right)}, \tag{4}$$

while for the human population

$$I_H^* = \frac{N(R_0 - 1)}{R_0 + \left(\frac{ab_1}{\mu}\right)} \tag{5}$$

where (ab_1/μ) is Macdonald's index of stability.[35] Stability analysis about the endemic state demonstrates that malaria will persist when $R_0 > 1$ where

$$R_0 = \frac{Ma^2 b_1 b_2 l(\tau_M)}{\gamma \mu N}, \tag{6}$$

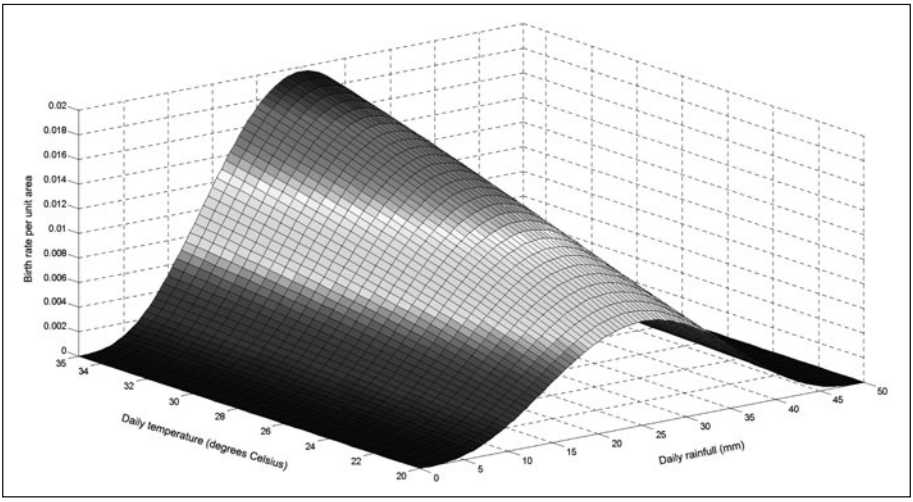

Figure 1. Mosquito birth rate b (R,T) as a function of daily rainfall R (in mm) and temperature T (in °C).

although note that this is conditional on assuming static environmental conditions. The expression for R_0 when we account for fluctuations in temperature and rainfall is considerably more complex[38-40] and we postpone a more theoretical discussion of the implications of environmental variability on R_0 (and transmission dynamics more generally) to future work.

Vector Population Dynamics

The dependence on mosquito abundance in the nonlinear vector-human transmission term of (1) results in considerable sensitivity of the model to vector population dynamics. Thus, understanding the dependence of $M(t)$ on temperature and rainfall (and seasonality therein) is key.

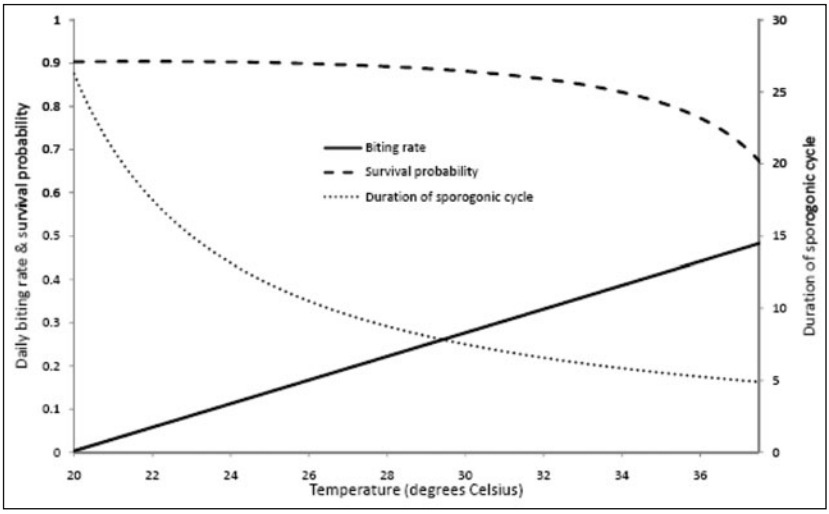

Figure 2. *Anopheles* biting rate and survival probability and *Plasmodium* incubation period as a function of temperature.

Adding equations in (1) related to the mosquito population gives the deterministic model for the vector population

$$\frac{dM(t)}{dt} = b(R,T) - \mu(T)M. \tag{7}$$

In reality, mosquito population dynamics behave stochastically and a full understanding of the impact of the mosquito population on transmission dynamics requires the stochastic equivalent of (7). If $p_M(t)$ denotes the probability of having $M(t)$ mosquitoes at time t, the master equation is

$$\frac{dp_M(t)}{dt} = b(t)p_{M-1}(t) + \mu(t)(M+1)p_{M+1}(t) - (b(t)+\mu(t)M)p_M(t) \tag{8}$$

for $M(t) = 0,1,2,...$ and where $p_{-1}(t) = 0$. If we define the probability generating function to be

$$G(z,t) = \sum_{i=0}^{\infty} p_i z^i ,$$

it is readily shown by successively multiplying (8) by z_i for each i and adding, we can convert (8) into a partial differential equation for $G(z,t)$ as

$$\frac{\partial G(z,t)}{\partial t} = b(t)(z-1)G(z,t) - \mu(t)(z-1)\frac{\partial G(z,t)}{\partial z}, \tag{9}$$

which can be solved using a variety of methods. We are interested in the dependence of the mosquito population on temperature and rainfall and their seasonal variability, a full understanding of which may be obtained by solving (9). The full solution of (9), however, for the case of general $b(t)$ and $\mu(t)$ is complex, so we simplify the analysis by considering only the dependence of the dynamics on the mean values of these environmental factors, not their variability.

We consider the mosquito population in Tanzania where malaria is highly-endemic, but the conclusions drawn about the effects of seasonality in environmental factors are general. Using temperature and rainfall data from WorldClim[41] (http://www.worldclim.org) and averaging across all regions in Tanzania, we fit the temporal profiles

$$T(t) = T_1(1 + T_2\cos(\omega_1 t - \Phi_1)) \tag{10}$$

and

$$R(t) = R_1(1 + R_2\cos(\omega_2 t - \Phi_2)), \tag{11}$$

giving the values in Table 4 (with the profiles plotted in Figure 3A. Substituting (10) and (11) into the earlier expressions for $b(R,T)$ and $\mu(T)$ and solving (7) gives the mean population dynamics plotted in Figure 3B, with the amplitude and frequency of vector oscillations strongly dependent on the seasonality factors T_2 and R_2. To better understand the sensitivity to variability in temperature and rainfall, Figure 3C plots the mean and standard deviation in mosquito numbers as a function of T_2 and R_2. Increasing seasonality in rainfall about a fixed mean (below the level at which flushing out occurs), broadly corresponding to more breeding sites, is found to always increase the mean size of the mosquito population, while increasing seasonality in temperature always reduces the vector population. Large amplitude variability in temperature is also found to drive mosquito populations to extinction, thus suggesting that extinction dynamics are more sensitive to changes in temperature than rainfall. This highlights that while understanding predicted changes in environmental variables from climate models is important, it is just as important to understand the impact of global warming on changes in the variability of climate variables.

Solution of (9) for general $b(t)$ and $\mu(t)$ would permit insight into the effects of climate variability on the stochastic population dynamics, but the complex and theoretical nature of the problem is beyond the scope of this chapter. Instead, we consider the extinction dynamics as a function of changes in mean temperature, fixing rainfall to simplify matters, but the analysis is

Table 4. Fitted temperature and rainfall seasonality parameters for Tanzania

Parameter	Definition	Fitted Value	Units
T_1	Mean temperature in the absence of seasonality	23.2	˚C
T_2	Amplitude of seasonal variability in temperature	0.07	Dimensionless
ω_1	(Angular) frequency of seasonal oscillations in temperature	0.67	months^{-1}
Φ_1	Phase lag of temperature variability	1.53	Dimensionless
R_1	Mean monthly rainfall in the absence of seasonality	85.9	mm
R_2	Amplitude of seasonal variability in rainfall	0.98	Dimensionless
ω_2	(Angular) frequency of seasonal oscillations in rainfall	0.65	months^{-1}
Φ_2	Phase lag of rainfall variability	1.99	Dimensionless

readily extended to include changes in rainfall at fixed temperature. When $b(t) = b$ and $d(t) = d$, (9) can be solved using Laplace Transforms or characteristics.[42] If we assume M_0 initial mosquitoes, solution of (9) gives

$$G(z,t) = e^{\frac{b}{\mu}(z-1)(1-e^{-\mu t})}(1+(z-1)e^{-\mu t})^{M_0}, \tag{12}$$

whereupon substituting $z = 0$ gives, as a function of temperature and rainfall, the probability that the mosquito population fades out at or before time t as

$$p_0(t) = e^{-\frac{b(R,T)}{\mu(T)}(1-e^{-\mu(T)t})}(1-e^{-\mu(T)t})^{M_0}. \tag{13}$$

At extreme temperatures, mosquitoes are more likely to fade-out (e.g., due to thermal death at temperatures beyond around 40˚C),[31] although the risk decreases with increasing rainfall when $R < R_L$. Beyond these early stages of mosquito invasion, the probability that the population ultimately fades out is $e^{-\frac{b(R,T)}{\mu(T)}}$. Thus, reliable estimates of parameters included within the birth and death models (e.g., the rainfall threshold beyond which breeding sites are washed out) will enable robust conclusions not only about when and where mosquitoes may be driven to extinction, but also the implications for malaria transmission. While a full analysis of malaria fade-out requires a stochastic transmission model, the proportionality of vector abundance and R_0 means that the above analysis yields useful insight into the impact of changes in climate variables on malaria elimination.

Invasion Dynamics

As well as providing a useful framework for understanding how the stochastic dynamics of mosquitoes may lead to the establishment of malaria as environmental conditions change, dynamical models are vital for capturing the invasion dynamics in previously susceptible populations. In addition to the direct effects of climate change on transmission, indirect effects such as those on malnutrition, poverty or the more frequent occurrence of extreme weather events (e.g., floods or heat waves) may also contribute to changing distributions of incidence, as human and animal ecosystems and habitats become more susceptible. However, while malaria is, in general, most prevalent in the tropics and subtropics, predictions that increases in global temperatures may lead to emergence in currently temperate regions and at higher altitudes[27] are not universally accepted.[43] Nonetheless, it is well-accepted that changes in climate variables influential in malaria transmission are likely to cause the global distribution of incidence to change over the next 100 years. Thus, understanding the invasion behaviour into new regions represents a key challenge and one which has considerable public health implications.

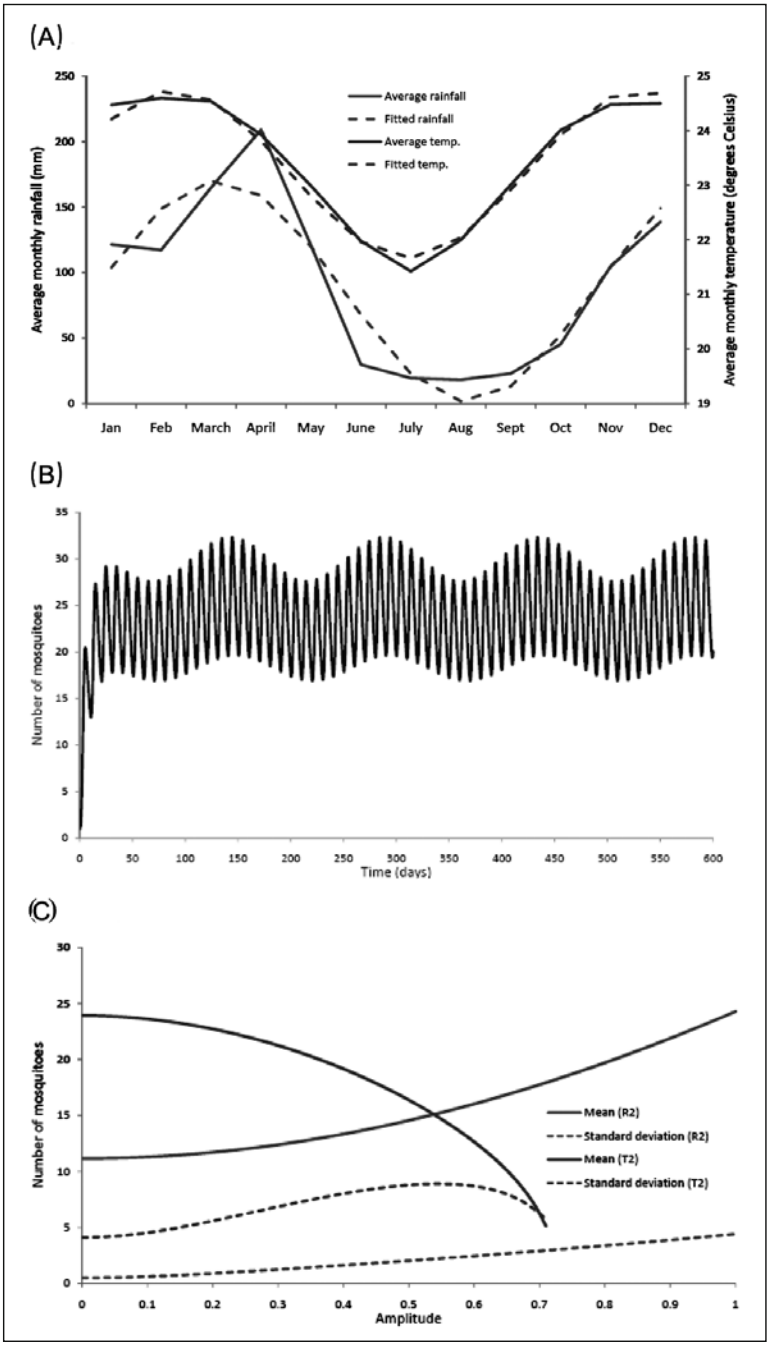

Figure 3. A) Annual temperature and rainfall profiles (10) and (11) fitted to WorldClim data[41] (http://www.worldclim.org) averaged across Tanzania, (B) predicted mosquito population dynamics for Tanzania from the solution to (7) (with parameters from Tables 2 and 3) and (C) the solution to (7) as a function of increasing seasonality in temperature (T_2) and rainfall (R_2).

Again, a more detailed stochastic transmission model, incorporating seasonally-varying environmental variables, is required for a more thorough understanding of invasion dynamics, but considerable progress about the expected behaviour can be obtained from (1). When most of the population are initially susceptible, $S_H(t-\tau_H) \approx N$ and $S_M(t-\tau_M) \approx M$, whereupon substituting into (1), the invasion dynamics are described by

$$\frac{dI_M}{dt} \approx ab_1\left(\frac{I_H(t-\tau_M)M}{N}\right)l(\tau_M) - \mu I_M, \tag{14}$$

$$\frac{dI_H}{dt} \approx ab_2 I_M(t-\tau_H) - \gamma I_H \tag{15}$$

and we look to solve for the growth rate of $I_H(t)$. We approach this problem in a way that allows illustration of the method and thus how to apply the technique to more complex transmission models.

In essence, we look to rewrite the system as a single equation in $I_H(t)$ and its derivatives, which we note currently depend on factors proportional to 1, $I_M(t)$, $I_M(t-\tau_H)$ and $dI_H(t)/dt$. Here, we have a dependence on four factors, but only two independent equations. However, a third independent equation may be obtained by differentiating (14), since this will depend on some combination of the same four factors. Considering the resultant equation, together with (14), at time $t+\tau_H$ gives the three independent equations

$$\begin{aligned}
&\frac{dI_H(t+\tau_H)}{dt} = ab_2 I_M(t) - \gamma I_H(t+\tau_H),\\
&\frac{dI_M(t)}{dt} = \left(\frac{ab_1 M}{N}\right) I_H(t-\tau_M)l_{\tau_M} - \mu I_M,\\
&\frac{d^2 I_H(t+\tau_H)}{dt^2} = \left(\frac{a^2 b_1 b_2 M}{N}\right) I_H(t-\tau_M)l_{\tau_M} - ab_2\mu I_M(t) - \gamma \dot{I}_H(t+\tau_H),
\end{aligned} \tag{16}$$

so that $I_H(t)$ and its derivatives now depend on three factors and we have three independent equations. If $\mathbf{J}$ is the 3 × 3 matrix with elements containing factors proportional to $I_H(t)$ and its derivatives, we can rewrite (16) as the matrix equation

$$\mathbf{J}\begin{pmatrix} 1 \\ I_M(t) \\ \dfrac{dI_M(t)}{dt} \end{pmatrix} = 0, \tag{17}$$

whereupon solving $\det \mathbf{J} = 0$ leads to

$$\ddot{I}_H(t+\tau_H) + (\mu+\gamma)\dot{I}_H(t+\tau_H) + \mu\gamma(I(t+\tau_H) - R_0 I(t-\tau_M)) = 0 \tag{18}$$

for the number of infectious humans. Substituting the trial solution $I_H(t) = e^{rt}$ gives

$$r^2 e^{r\tau_H} + (\mu+\gamma)re^{r\tau_H} + \mu\gamma(e^{r\tau_H} - R_0 e^{-r\tau_M}) = 0, \tag{19}$$

where r is the real-time growth rate and the solution reduces to the standard growth rate equation for an SEIR model (with analytical solutions) when $\tau_H = \tau_M = 0$. Substituting parameters and functional forms from earlier, Tables 2 and 3 allow numerical solution of (19) and Figure 4A plots the outbreak doubling time $T_D = 1n(2)/r$ as a function of temperature at different mosquito densities. The rate of spread into a susceptible population is found to be extremely sensitive to temperature, with a clear window around 32-33°C where the doubling time is shortest. At lower

temperatures, fewer mosquitoes survive long enough for the sporogonic cycle to complete, while at higher temperatures, mosquito survival probability drops off rapidly. Invasion dynamics are also found to be strongly dependent on vector abundance, itself driven by rainfall, with doubling times around 4-6 weeks at vector densities typical of rainy seasons and increasing to the order of months at lower abundances typical of dry seasons.

A more theoretical analysis of the effects of seasonality in the vector population on the growth rate has been considered elsewhere[40] and the applicability of such methods to more complex

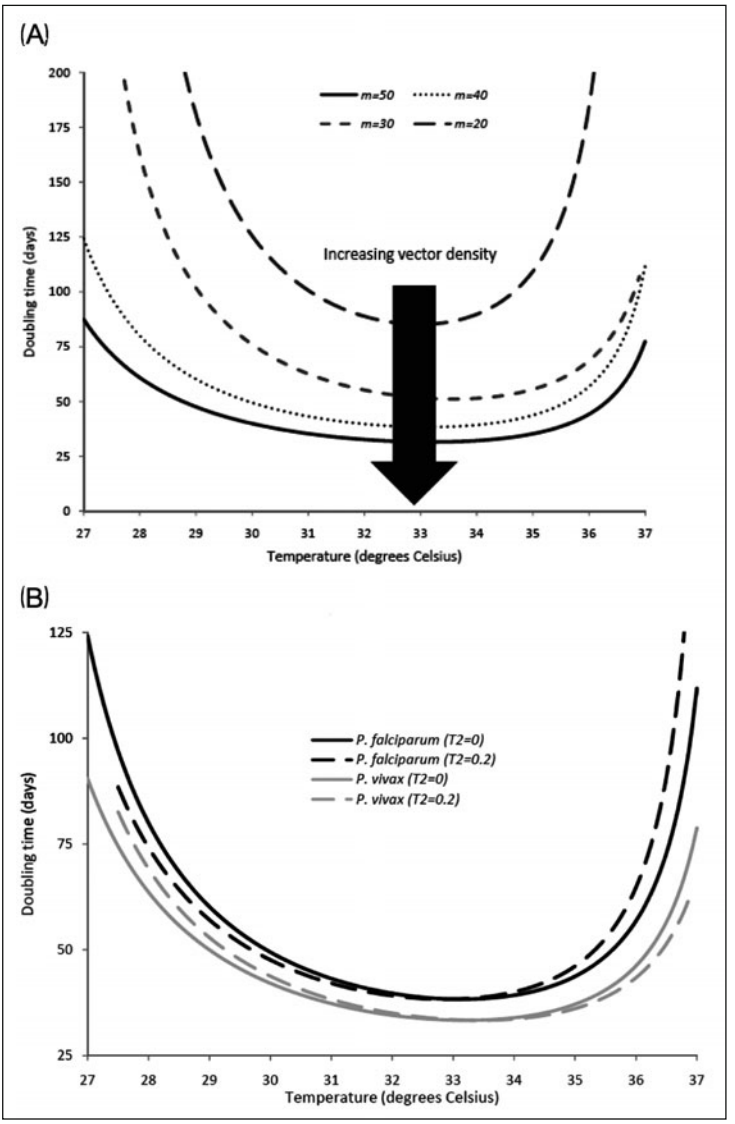

Figure 4. A) Doubling times of a *P. falciparum* outbreak as a function of temperature and mosquito density at fixed rainfall (and in the absence of seasonality). B) Predicted doubling times for *P. falciparum* and *P. vivax* with and without seasonality in temperature (where m = 40 and all other parameters as per (A)).

systems is beyond the scope of this chapter. However, approximate preliminary insight may be obtained by substituting (10), with parameter values given in Table 4, into (19) for parameters that depend on temperature and the results are shown in Figure 4B for *P. falciparum* and *P. vivax*. In the absence of seasonality, there is little difference between *P. falciparum* and *P. vivax*, with the latter spreading marginally quicker and potentially resulting in a greater outbreak threat at higher altitudes given the lower critical temperature for transmission (around 14.5°C and 16°C for *P. vivax* and *P. falciparum* respectively). Figures 4A,B combined also highlight that malaria invasion is considerably more sensitive to vector density than the strain of *Plasmodium* parasite. The crude inclusion of moderate seasonality in temperature, around three times greater than seasonality observed across Tanzania, is found to have little effect on the doubling times, although a more thorough analysis is required to fully understand the effects of variability in environmental variables on malarial invasion.

Implications for R_0 and Mapping Risk

It is readily shown from (1) that successful establishment and invasion of malaria into a previously unaffected population will lead to endemicity when $R_0 > 1$. Given the dependence of the vector population dynamics on temperature and rainfall, together with the functional forms contributing to R_0 in Table 2, an analytical expression for R_0 as a function of mean temperature and rainfall may be derived by substituting into (6). For the purpose of this analysis, we assume that the vector population is in equilibrium, so that $M(R,T) = b(R,T)/\mu(T)$ and there is no seasonality in rainfall nor temperature (so $R_2 = T_2 = 0$). For brevity, we do not write down the full expression, but R_0 as a function of these two variables is plotted in Figure 5.

Parameter uncertainty in the vector population model means that while precise quantitative conclusions should not be drawn from Figure 5, the qualitative dependence of R_0, capturing both the population risk of malaria becoming endemic and individual infection risk, on temperature and rainfall remains robust to these uncertainties. As with the invasion dynamics, we observe a clear window for optimum malaria transmission around 32-33°C, corresponding to where the balance between mosquitoes surviving long enough for completion of the sporogonic cycle and the rapid decline in mosquito survival at high temperatures is optimised. The approximate quadratic dependence of R_0 on temperature also offers insight into the question of how changes in local transmission risk may shift due to increases in temperature. Consider an endemic region currently at mean temperature T experiencing an increase in temperature by an amount ΔT. If

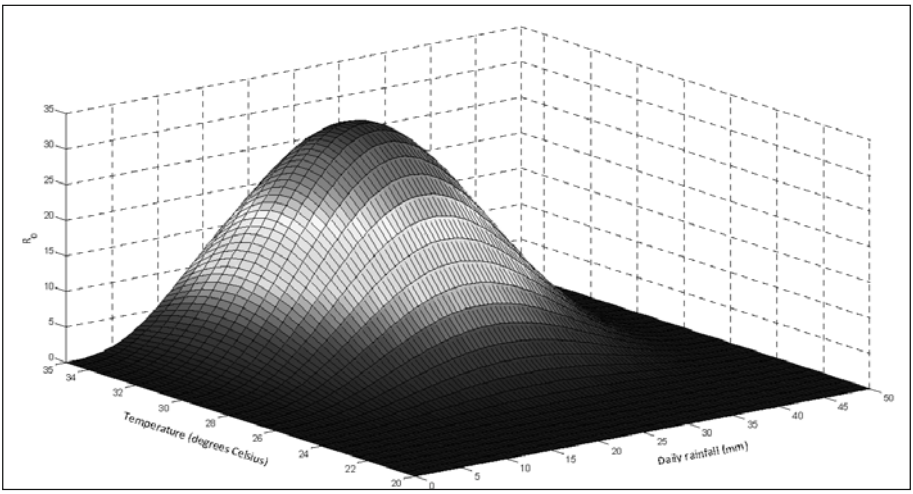

Figure 5. The dependence of R_0 on temperature and rainfall.

T_{max} represents the temperature at which the $R_0(T)$ profile peaks, it is clear that if $T + \Delta T < T_{max}$, malaria prevalence will get significantly worse in that region, while if $T > T_{max}$, global warming will lead to a decline in mosquito survival and a reduction in transmission.

For the case of Tanzania, Figure 6 plots the predicted mean temperature distribution for April (when rainfall peaks) under the A2a emission scenario[6] (data from WorldClim and where the calculation of mean temperature assumes uniformly distributed temperatures between monthly maxima and minima). Analysis of the expression quantifying the relationship between R_0 and temperature, and substitution of parameter values in Table 3, shows that T_{max} is around 32.9°C for *P. falciparum* and *P. vivax*. Temperature data presented in Figure 6 shows that the maximum mean temperature is predicted to be around 32.6°C for Tanzania and thus, given the monotonic relationship between R_0 and prevalence from (5) and the fact that we are in the regime $T + \Delta T < T_{max}$, we predict malaria prevalence to increase across Tanzania around the peak rainy season. The severity of the increase, however, will be regionally dependent and this highlights the need for implementation of control and mitigation strategies at a local level. Improvements in parameterisation of the model will lead to improved ability to make quantitative predictions about spatiotemporal dynamics and control, as well as addressing how changes in rainfall distribution, as well as temperature, may lead to changes in transmission risk. The impact of excessive rainfall, for instance, on vector abundance and transmission is only qualitatively captured here. Such an analysis also highlights the usefulness of assessing control strategies within a dynamic framework. Questions such as the relative magnitude and timing of interventions, as well as the impact of parameter uncertainty, variability and heterogeneity, be they human, mosquito or parasite, may also be considered, along with evaluating such questions within the context of limited resources. The direct impact of seasonality in vector dynamics on R_0 has been considered from a theoretical perspective elsewhere and we postpone a more thorough analysis of the dependence of control on variability in environmental conditions to future work.

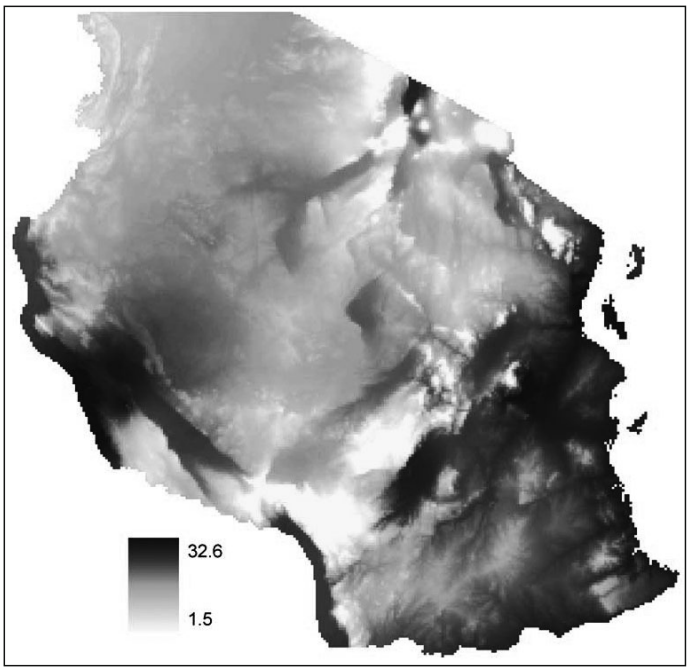

Figure 6. Predicted mean temperature distribution across Tanzania in April under the A2a emission scenario (data from WorldClim).

Conclusion

The complex transmission dynamics of malaria are strongly influenced by environmental conditions, with temperature, rainfall, humidity, wind speed and altitude, among others, shown to affect incidence. However, despite the opinion that malaria may represent one of the most sensitive VBDs to climate change over the next 100 years, most previous work on interactions between climate and malaria has been largely based on the use of statistical modelling approaches with little corresponding work carried out on using mathematical models to better understand the dynamical effects of this influence on disease transmission dynamics. Such process-based models may not only represent powerful tools for understanding how future trends and variability in key climate variables may affect global changes in malaria risk via their capacity to deal with the likely nonlinear and complex feedbacks in climate-pathogen relationships, but when combined with the ability to simulate 'what-if' scenarios, they may also represent valuable tools for policy-makers and future public health planning.[1,7,11]

In this chapter, we have shown the crucial need for the development of dynamic modelling frameworks to better understand the dependence of malaria transmission on changes in temperature and rainfall. The most general and probably most realistic modelling framework one could develop here would be a stochastic transmission model incorporating key environmental variables that are continuously changing. While we expect the field to undoubtedly progress towards this end, it is invaluable at the early stages of our understanding to construct simpler climate-linked transmission models that permit an understanding of how global warming may affect the burden of disease. Thus, using a relatively simple deterministic transmission model, we have been able to demonstrate the importance of accounting for the dependence of mosquito abundance on temperature and rainfall, which by entering the dynamical model through the nonlinear transmission term, we show can strongly influence the establishment probability of malaria in previously disease-free regions. The potential for mosquito extinction with large seasonality in temperature highlights a second key result, namely that it is important not only to examine the effects of future average trends in climate variables, but also the variability about these trends.

In reality, this variability may represent genuine fluctuations of climate variables or uncertainty from climate model predictions or human behaviour (corresponding to a range of possible emission scenarios). Indeed, it is clear from this chapter that seasonality and variability in climate on longer timescales can have profound effects on establishment, invasion and persistence and this remains a priority area for future research. Changes in patterns of malaria incidence due to changes in environmental conditions on longer timescales, e.g., due to the effects of El Niño-Southern Oscillation (ENSO), have been considered in the literature[44-47] and this continues to merit further research. Similarly, it is clear that when these studies are combined with corresponding concepts from infection system dynamics, such as the dependence of R_0 on temperature and rainfall and the identification of an optimal transmission window, such integrated analyses will prove crucial to improving understanding about how long-term global climate change will affect local environmental conditions and, in turn, whether a region is likely to experience a worsening or improvement in prevalence as global warming becomes more severe.

The results also highlight that considerable work, experimental, theoretical, modelling and policy-based, still remains to be statisfactorily carried out and modelled in an integrated fashion if we are to more realistically capture the impact of climate change on disease transmission. Although certain aspects of transmission dynamics are physiological (and therefore deterministic) drivers of transmission, it is clear that heterogeneities across the human, mosquito and parasite populations introduce considerable uncertainty into the system. It should also be borne in mind that a more realistic modelling approach should take spatial heterogeneities into account and thus realistic transmission models need to be spatial if they are to better predict spatiotemporal disease persistence and spread. A key challenge in incorporating environmental variables into malaria models is also selecting the appropriate scale at which to model, not only spatially, but over the most appropriate timescale and hierarchical level.[48] This is driven not only by the resolution of available climate data (either from remote sensing or output from climate models), but also from the knowledge that modelling at too fine a scale may translate poorly into global observables, while oversimplifying

local heterogeneities may neglect key environmental or biological processes influencing observations. Another challenge is how best to integrate ecological drivers with sociological processes of disease transmission in vulnerable communities, an area only now beginning to be examined.[1,2,23,25,26,43]

The quality of incidence data, as well as the reliability and depth of experimental knowledge on the effects of environmental variables on the transmission cycle, also requires considerable research and this remains an important priority. The impact of excessive rainfall, for instance, on vector abundance and transmission is only qualitatively captured here. Mathematical models can thus act as a useful guide for data collection by identifying areas where improvements in data quality may lead to substantial improvements in their explanatory power.

Finally, our results also underscore the usefulness of assessing control strategies within a dynamic framework. In particular, we suggest that only such frameworks will allow fuller exploration of key questions such as the relative magnitude and timing of interventions, as well as the impact of parameter uncertainty, variability and heterogeneity, be they human, mosquito or parasite, along with reliable evaluation of these questions within the context of limited resources. The dynamical modelling approach described here may thus provide a useful framework not only for obtaining a better understanding of the integrated impact of climate change on disease transmission dynamics, but also to serve as a tool for policy-makers developing mitigation and intervention strategies that may be used to tackle the potentially tough challenges that lie ahead.

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