Malaria dynamics and climate change

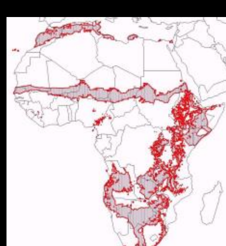
Mercedes Pascual

University of Michigan
and
Howard Hughes Medical Institute

UNIVERSITY OF MICHIGAN

HHMI HOWARD HUGHES MEDICAL INSTITUTE

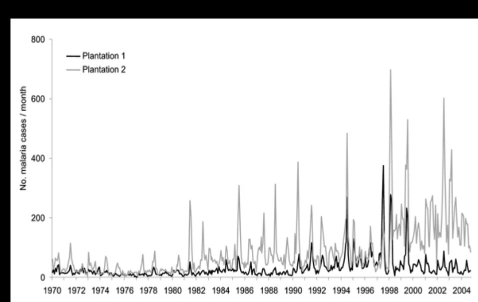
Highland malaria and climate change



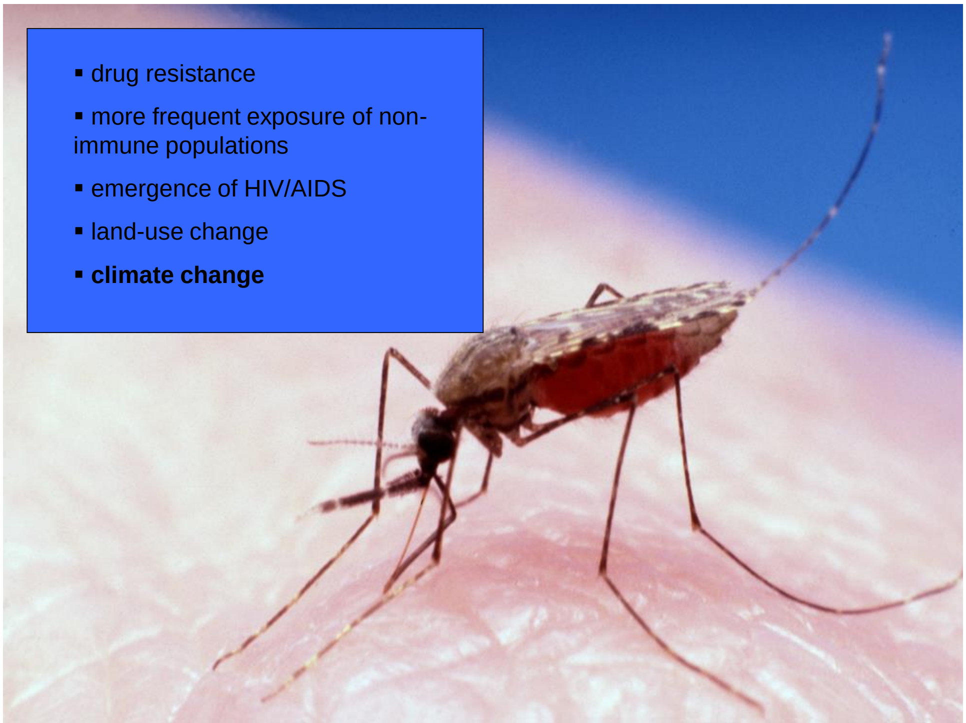
Areas at risk of epidemic malaria
From Grover-Kopec et al, Mal. J. 2005

~ 110 million Africans live in areas at risk of epidemic malaria

Estimated 110 000 deaths each year (Africa Malaria Report)



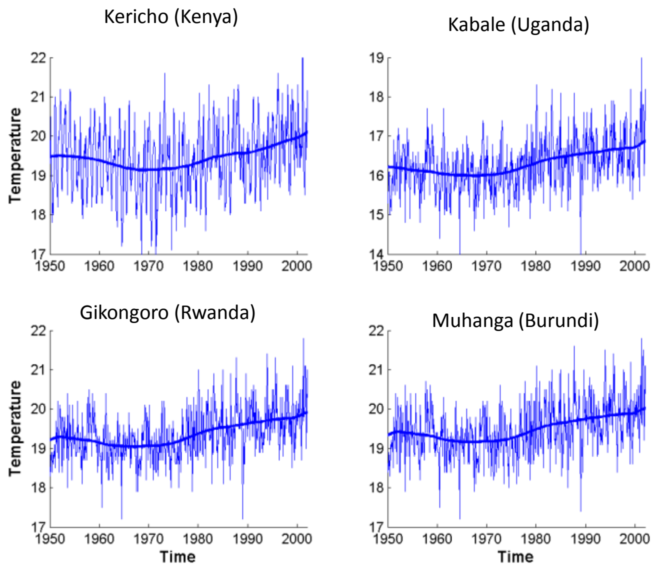
From Shanks et al. EID 2005



Highland malaria and climate change

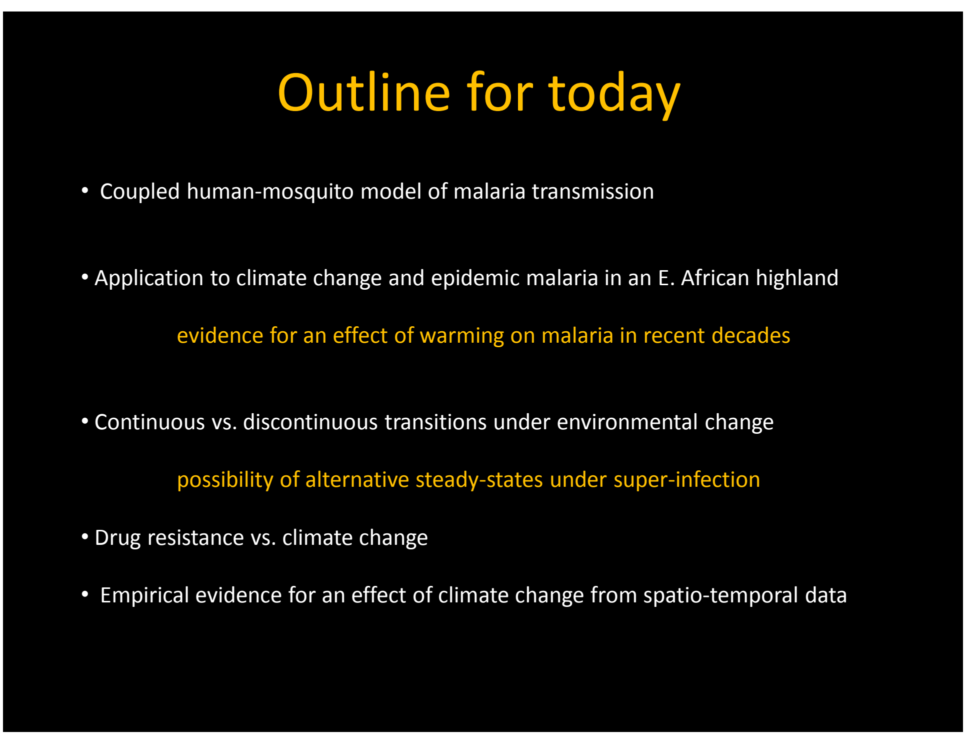
- Long-term trends in malaria cases in highland regions can be the result of many other factors. It is a challenge to adjudicate trends to particular underlying causes.
- Among alternative factors, drug resistance has been proposed as the main driver of decadal increases in incidence (Shanks *et al.*, EID 2005).
- Others have argued that socio-economic development is a more powerful 'force' than climate change and that the effect of climate change is negligible by comparison (e.g. Gething et al., Nature 2010).

This argument has been made with global maps that lack the spatial resolution to properly interpolate limited survey data in highland regions with rapidly changing elevation (and therefore temperature). (Bouma *et al.,* Trends in Parasitology 2011)



Pascual, Ahumada, Chaves, Rodo, Bouma (PNAS, 2006)

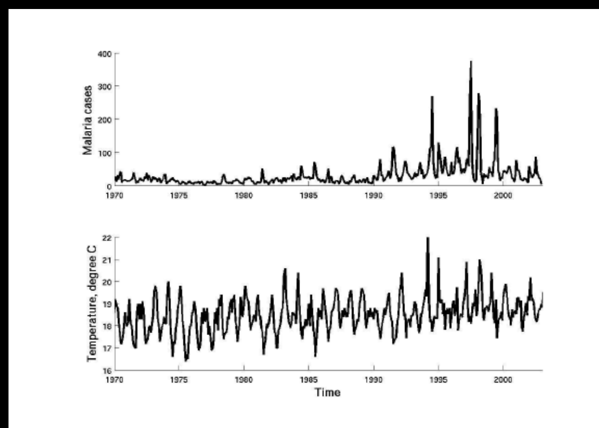
Data: CRU TS2.0 Tyndall Centre for Climate Change Research



Epidemic malaria in a Kenyan highland

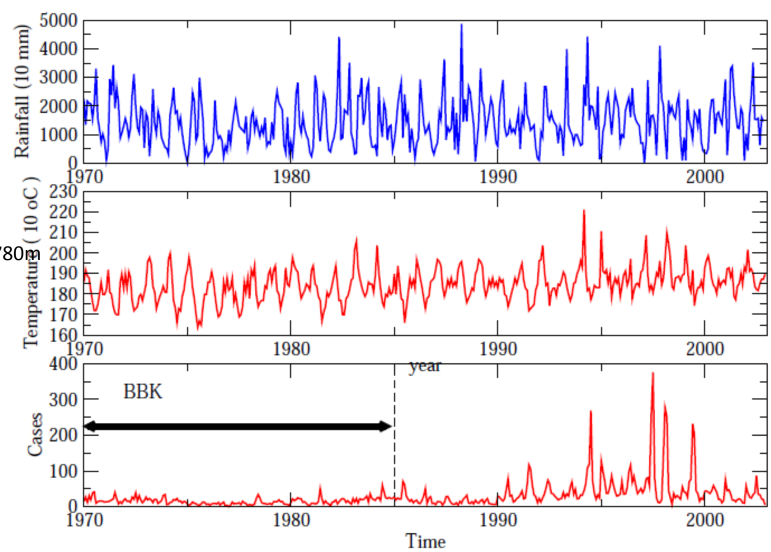
Tea estates (Brooke Bond Farms, Kericho, altitude: 1780-2225 m)

Two local meteorological stations 1780m



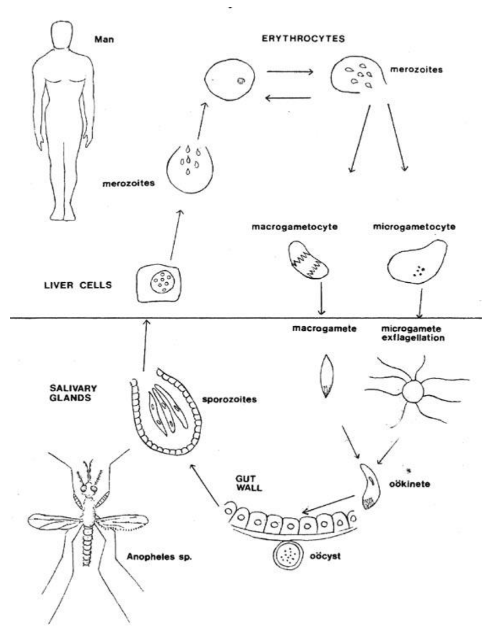
Empirical data: Rain, Temperature, and Cases

1780m



Model by Ross and McDonald (1916-1957)

- proportion of the human population infected
- proportion of the female mosquito population infected



<u>Ross-McDonald model:</u>

Number of mosquitoes

Success of bites

Recovery rate

$$dx/dt = (abM/N)\,y(1-x) - rx$$

Number of hosts

Biting rate

$$dy/dt = ax(1-y) - \mu y$$

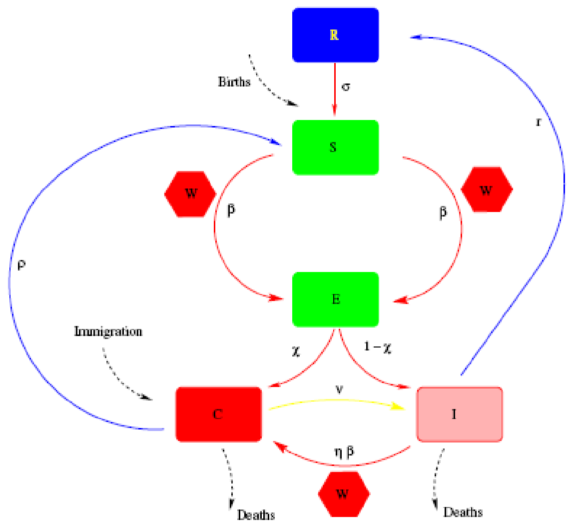
Mosquito death rate

Proportion mosquitoes infected, y

Proportion humans infected, x

Coupled mosquito-human transmission model

- Larvae
- Adults in three classes:
  - uninfected
  - exposed
  - infectious



Human model: β, the force of infection

$$
\begin{aligned}
\frac{dS}{dt} &= B - \beta\, S + \sigma R - \delta\, S + \rho\, C \\
\frac{dE}{dt} &= \beta\, S - \delta\, E - \gamma\, E \\
\frac{dI}{dt} &= (1-\xi)\,\gamma\, E - \eta\,\beta\, I + \nu\, C - r\, I - \delta\, I \\
\frac{dR}{dt} &= -\sigma R + r\, I - \delta\, R \\
\frac{dC}{dt} &= \xi\,\gamma\, E + \eta\,\beta\, I - \nu\, C - \rho\, C - \delta\, C
\end{aligned}
$$

$$\beta = b\, a\, \frac{W}{H} + \beta_0$$

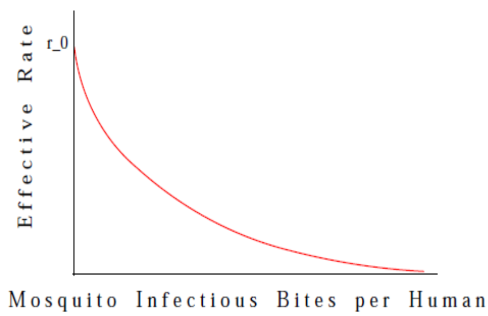
Human immunity

- The rate of loss of immunity, σ, and the recovery rate, r are related to the intensity of disease transmission.
- If the frequency of infective bites increases both the recovery rate r and the loss of immunity rate, σ, tend to decrease.
- These rates can be considered to be a decreasing function of the rate at which infectious bites per human arrive, $\Lambda = aW/N$:

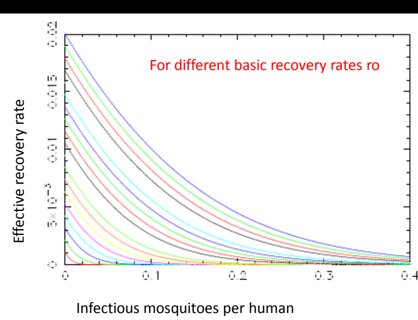
$$\sigma(\Lambda) = \frac{\Lambda}{\exp(\Lambda/\sigma_0) - 1}$$

$$r(\Lambda) = \frac{\Lambda}{\exp(\Lambda/r_0) - 1}$$

Dietz 1979; Aron and May 1982



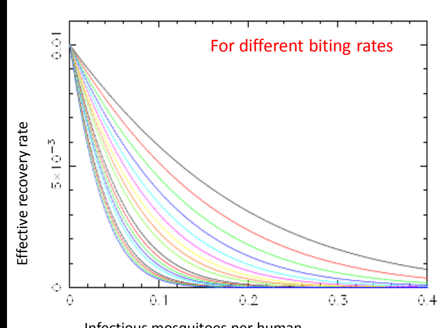
Superinfection: mean duration of infection (1/r)



$$r(\Lambda; r_0) = \frac{\Lambda}{\exp\left(\frac{\Lambda}{r_0}\right) - 1}$$

Dietz , Molineaux and Thomas (Bull. WHO, 1974)

Aron and May (1982)



Mosquito model: Population dynamics

L, larval stage and M adult stage

$$\begin{aligned}\frac{dL}{dt} &= f\,M\left(\frac{K-L}{K}\right)-\delta_L\,L-d_L\,L\\ \frac{dM}{dt} &= d_L\,L-\delta\,M\end{aligned}$$

Ahumada and Dobson 2009

Mosquito carrying capacity is controlled by water availability...

$$\frac{dK}{dt}=K_A\,p-K_E\,K$$

Mosquito sub-model:

$$\begin{aligned}\frac{dL}{dt} &= f\,M\left(\frac{K-L}{K}\right)-\delta_L\,L-d_L\,L\\ \frac{dX}{dt} &= -c\,a\,y\,X-\delta_M\,X+d_L\,L\\ \frac{dV}{dt} &= +c\,a\,y\,X-\gamma_P\,V-\delta_M\,V\\ \frac{dW}{dt} &= \gamma_P\,V-\delta_M\,W\end{aligned}$$

where y is the fraction of infectious humans:

$$y=\frac{C+I}{H}$$

Mosquito model: temperature-driven parameters

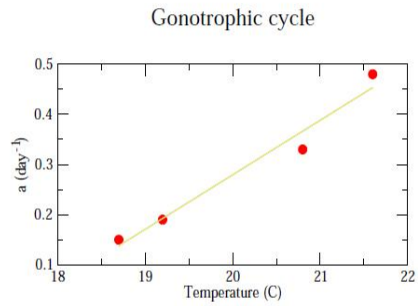
- Larva development, d_L
- *Plasmodium development*, γ_P
- Adult and larval survival, δ_M, δ_L
- Biting rate, a

$$f = F\,a$$

where F is the number of eggs per female.

Effective temperature:

$$T_e = T_o + (1-x)\,\Delta T$$



Afrane, Y. A., B. W. Lawson, A. K. Githeko and G. Yan 2005 Effects of Microclimatic changes caused by land use and land cover on duration of Gonotrophic cycle of *Anopheles gambiae* in Western Kenya Highlands. J. Med. Entomology 42(6): 974-980.

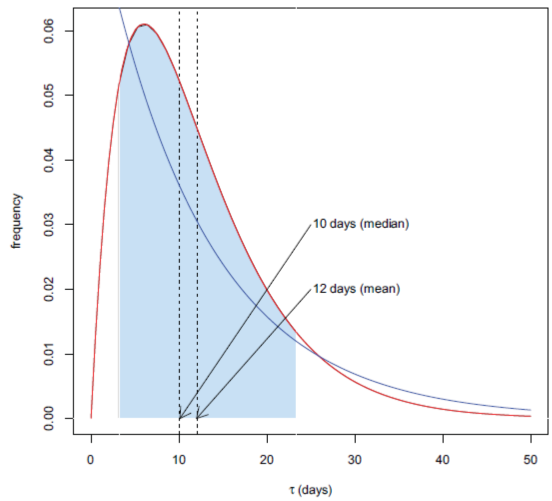
$$\begin{aligned}
\frac{dL}{dt} &= f\,M\left(\frac{K-L}{K}\right) - \delta_L\,L - d_L\,L \\
\frac{dX}{dt} &= -c\,a\,y\,X - \delta_M\,X + d_L\,L \\
\frac{dV_1}{dt} &= +c\,a\,y\,X - n_P\,\gamma_P\,V_1 - \delta_M\,V_1 \\
\frac{dV_2}{dt} &= n_P\,\gamma_P\,V_1 - n_P\,\gamma_P\,V_2 - \delta_M\,V_2 \\
\dots &\;\;\dots\;\;\dots \\
\frac{dV_n}{dt} &= n_P\,\gamma_P\,V_{n-1} - n_P\,\gamma_P\,V_n - \delta_M\,V_n \\
\frac{dW}{dt} &= n_P\,\gamma_P\,V_n - \delta_M\,W
\end{aligned}$$

$$\begin{aligned}
\frac{dS}{dt} &= B - \beta\,S + \sigma R - \delta\,S + \rho\,C \\
\frac{dE_1}{dt} &= \beta\,S - \delta\,E_1 - n_H\gamma_H\,E_1 \\
\frac{dE_2}{dt} &= n_H\gamma_H\,E_1 - n_H\gamma_H\,E_2 - \delta_H\,E_2 \\
\dots &= \dots \\
\frac{dE_n}{dt} &= n_H\gamma_H\,E_{n-1} - n_H\gamma_H\,E_n - \delta_H\,E_n \\
\frac{dI}{dt} &= (1-\xi)\,n_H\gamma_H\,E_n - \eta\,\beta\,I + \nu\,C - r\,I - \Psi\,I - \delta\,I \\
\frac{dR}{dt} &= -\sigma R + r\,I - \delta\,R \\
\frac{dC}{dt} &= \xi\,n_H\gamma_H\,E_n + \eta\,\beta\,I - \nu\,C - \rho\,C - \alpha\,C - \delta C
\end{aligned}$$

$$f_H(\tau) = \frac{n_H\,\gamma_H}{\Gamma(n_H)}\exp(-n_H\,\gamma_H\,\tau)\,\tau^{n_P-1}$$

of average $1/\gamma_H$ and variance $1/(n_H\,\gamma_H^2)$.

Gamma distributed 'incubation' time



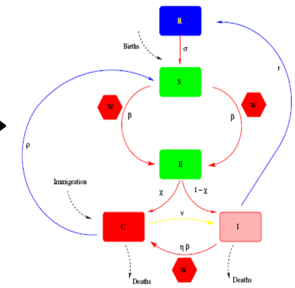
$$\Delta T \longrightarrow \Delta C$$

Can the observed ΔT
explain
the observed increase
in malaria cases?

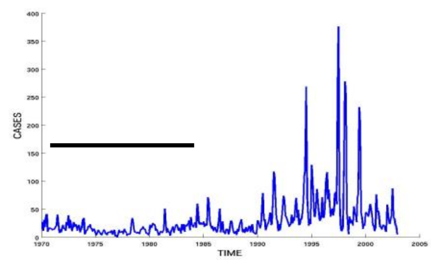
Temperature

Rainfall

- larva development (T)
- Plasmodium development (T)
- Adult and larval survival (T, R)
- Gonotrophic Cycle (biting rate , T)
- Carrying capacity (R)

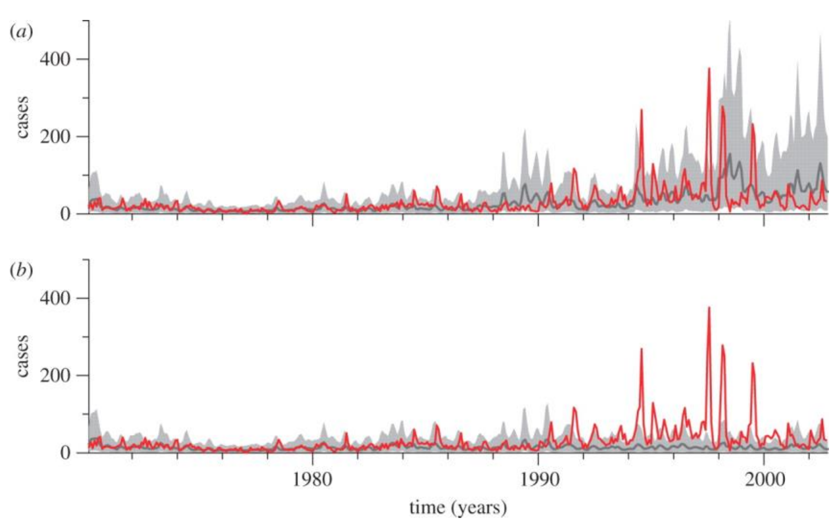


Model fitted to the observed cases from 1970 to 1985 by max. likelihood with a genetic algorithm



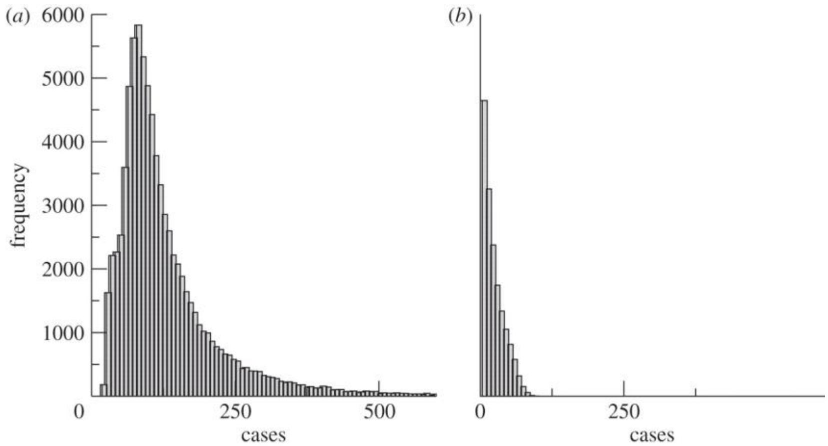
Alonso, Bouma and Pascual, *Proc. R. Soc. London B 2011*

Numerical simulations of the model (a) with and (b) without the trend in temperature.



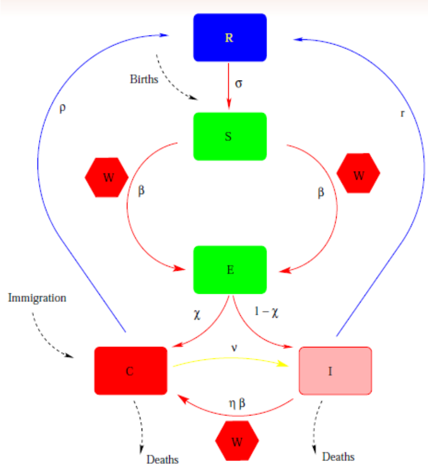
Alonso D et al. Proc. R. Soc. B 2011;278:1661-1669

Histograms of predicted cases at the seasonal peaks for the model (a) with and (b) without the trend in temperatures.

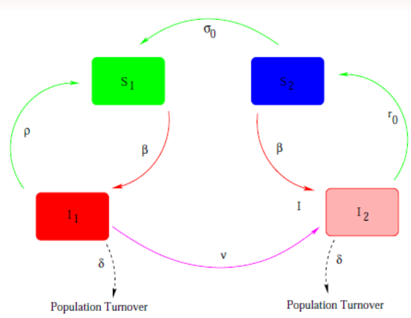


Alonso D et al. Proc. R. Soc. B 2011;278:1661-1669

Robustness to changes in model structure I



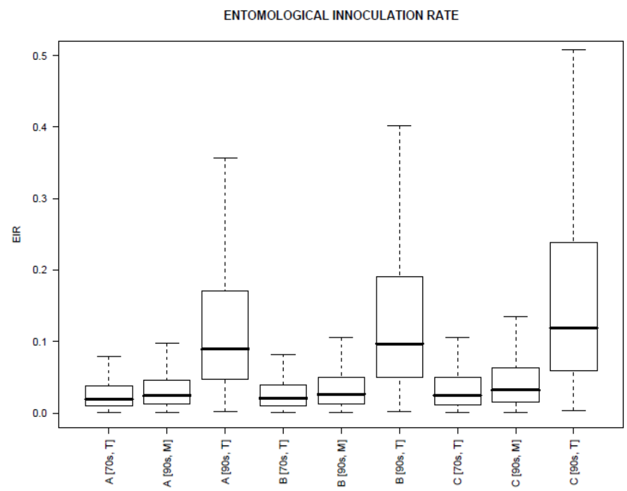
Model B



Model C

Klein, E. Y., Smith, D. L., Boni, M. F. & Laxminarayan, R. (2008). Clinically immune hosts as a refuge for drug-sensitive malaria parasites. Malaria journal, 7, 67

Robustness to changes in model structure III



Boxplot distributions for the entomological innoculation rate (number of infectious bites per human per year), for models A, B, and C for the first period (1970-85, labelled as the "70s") and the second period (1988-2003, labelled as the "90s") and the two temperature regimes (T *vs* M in the "90s").

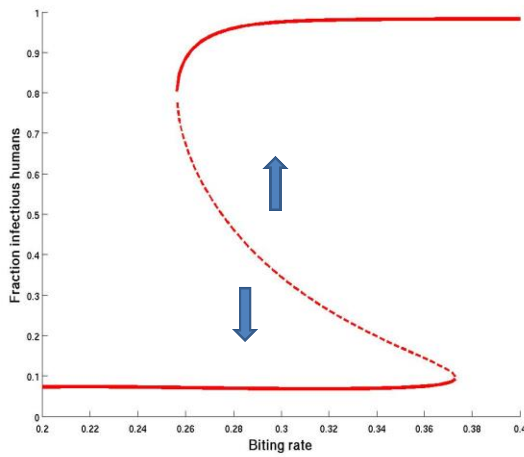
- Evidence for an effect of warmer temperatures on highland malaria in this region from the 1970s to the 1990s. (Warmer temperatures can explain a significant increase relative to the no-trend scenario)

- However, the temperature trend cannot explain in the model the full extend of the increase : this is consistent with other factors such as land-use change and drug resistance also playing a role

Artzy et al. (PloS One 2010): synergy between drug resistance and climate change

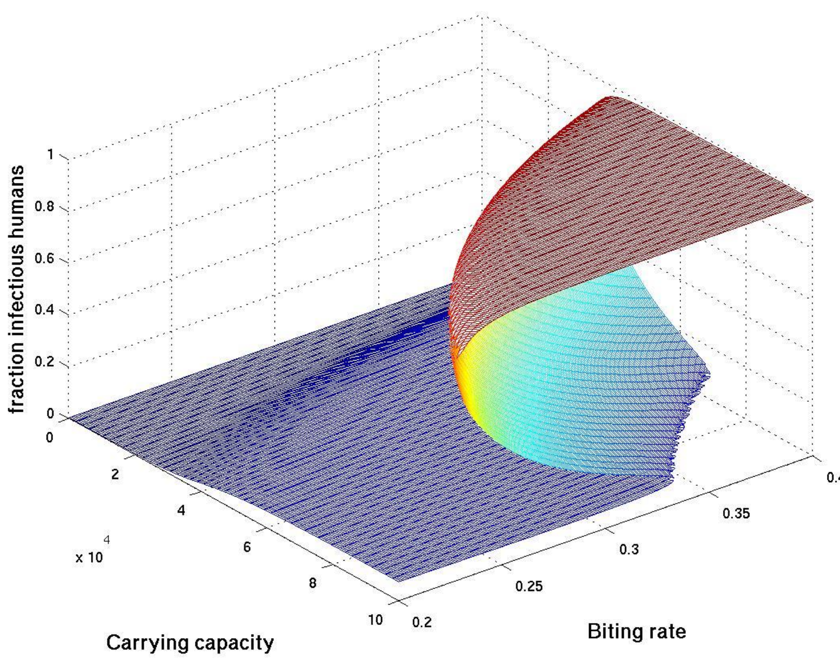
- Influence of (decreasing or increasing) trends on the dynamics of the disease are not sufficiently understood in the models themselves

A continuous or discontinuous response?

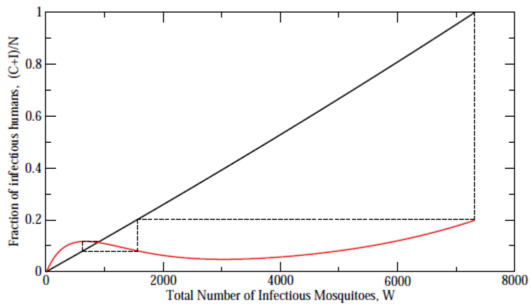


Alonso, Dobson and Pascual*, in prep.*

A **critical transition** that depends on including super-infection in the model



Equilibrium points: a semi-analytical approach



1) Solve for the equilibrium number of infectious mosquitoes, W*, as a function of the eq. number of infectious humans y*

$$W^\star = \frac{a\,c\,y^\star}{\delta_M + a\,c\,y^\star}\left[\frac{n_P\,\gamma_P}{n_P\,\gamma_P + \delta_M}\right]^{n_P} M^\star$$

$$M^* = K\,\frac{d_L}{\delta_M}\,\frac{f - \delta_M\,(1 + \frac{\delta_L}{d_L})}{f}$$

2) Solve for y* as a function of W*

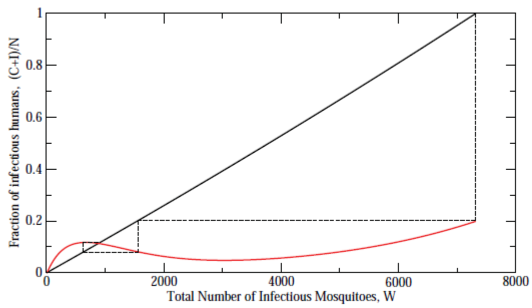
$$y \equiv \frac{I + C}{N} = \beta\,\frac{\nu + (1-\xi)\,(\rho + \delta_H) + \eta\beta + \xi\,(r + \delta_H)}{q\,(1+z)}\,[\theta_H]^{n_H}$$

where the constants θ_H, z, q, are defined as:

$$\begin{aligned}
\theta_H &= \frac{n_H\,\gamma_H}{n_P\,\gamma_H + \delta_H} \\
q &= \eta\,\beta\,(\rho + \delta_H) + (r + \delta_H)\,(\nu + \rho + \delta_H) \\
z &= \frac{\beta}{\delta_H} + \beta\left[\frac{\nu + (1-\xi)\,(\rho+\delta_H)}{q}\left\{1 + \frac{r}{\sigma + \delta_H}\right\}\right. \\
&\quad \left. + \frac{\eta\beta + \xi\,(r + \delta_H)}{q} - \frac{1}{\delta_H}\right][\theta_H]^{n_H}
\end{aligned}$$

Equilibrium points: a semi-analytical approach

$$\begin{aligned} y &= \mathcal{F}(W) \\ W &= \mathcal{G}(y) \end{aligned} \quad \Longrightarrow \quad y = \frac{\delta_M}{c\,a} \frac{[\theta_P]^{-n_P}\ w}{1 - [\theta_P]^{-n_P}\ w} \qquad \text{where } w \equiv W/M^{\star}$$



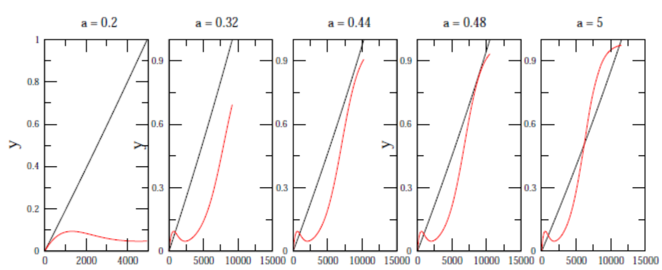
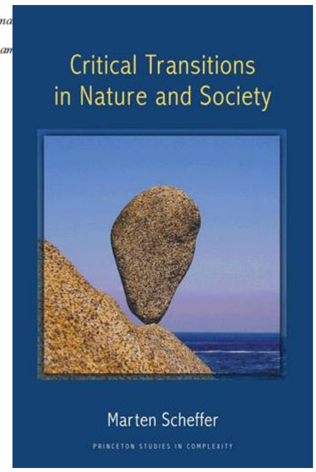


Figure 2: **Multiplicity of stationary states.**

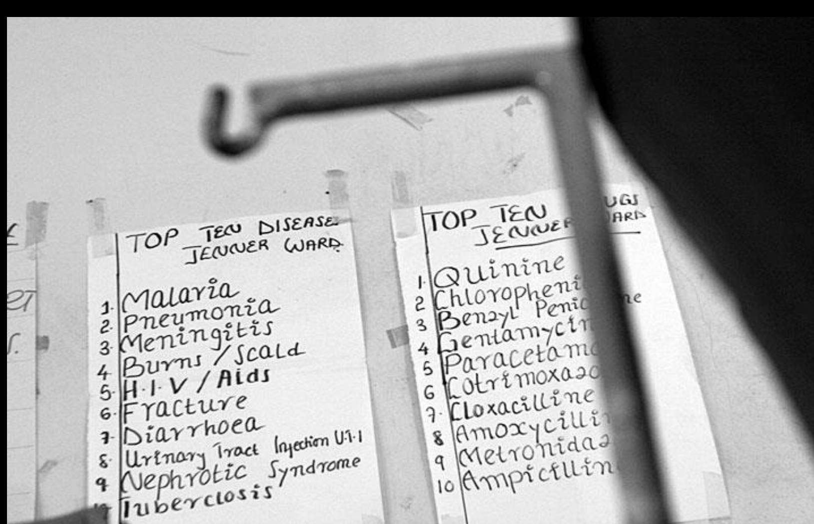
Regime shifts and heterogeneous trends in malaria time series from Western Kenya Highlands

LUIS FERNANDO CHAVES[1,2]*, MASAHIRO HASHIZUME[3], AKIKO SATAKE[1] and NOBORU MINAKAWA[3]

[1] Graduate School of Environmental Sciences and Global Center of Excellence Program on Integrated Field Environmental Science, Hokkaido University, Sapporo, Japan
[2] Programa de Investigación en Enfermedades Tropicales, Escuela de Medicina Veterina
Costa Rica
[3] Institute of Tropical Medicine (NEKKEN) and Global Center of Excellence Progran
Diseases, Nagasaki University, Nagasaki, Japan



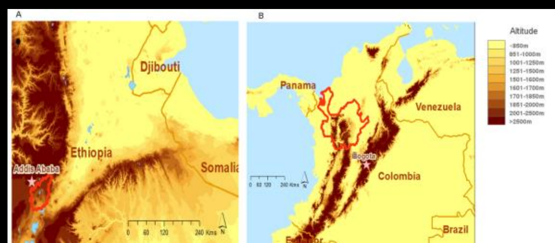
Synergy between increase transmission due to **climate change** and the evolution of **drug resistance**?



Photograph / SAMANTHA APPLETON

Taking advantage of high-resolution spatio-temporal data and climate variability to address climate change

1993-2005



1990-2005

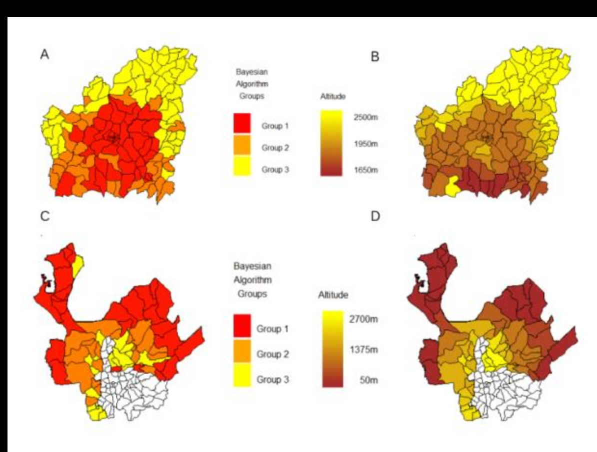
Confirmed monthly cases before major interventions of last decade

Siraj, Santos *et al.*, Science 2014

Clusters of similar temporal dynamics in the malaria data reflect variation in elevation

159 kebeles

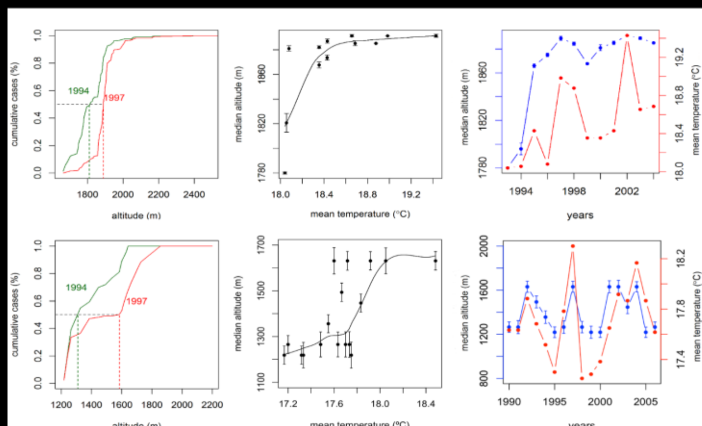
124 municipalities



The spatial distribution of the disease expands upwards in warmer years

Ethiopia

Colombia

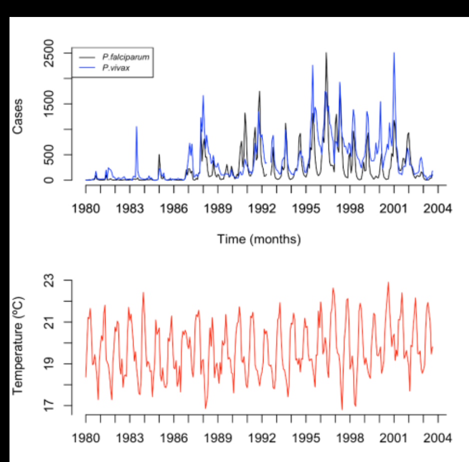


Is interannual variation consistent with the long-term trend?

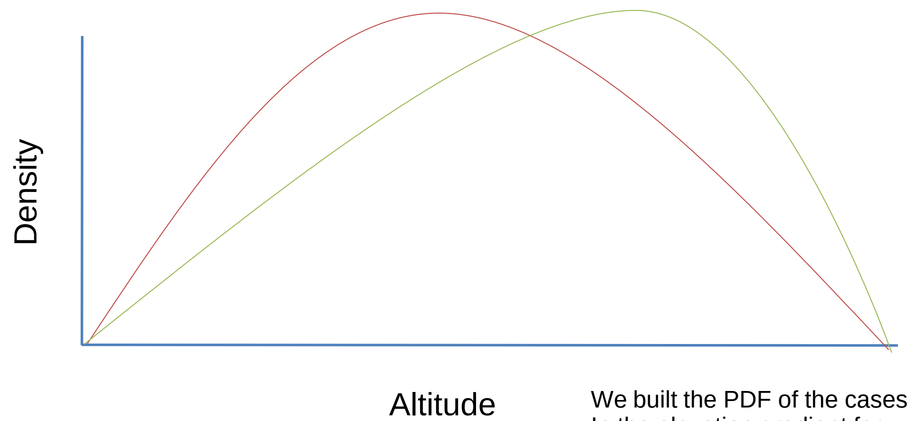
From spatio-temporal data and interannual variation

⇨ 2400 cases /degree C

From longer temporal trend ⇨ 2166 cases / degree C

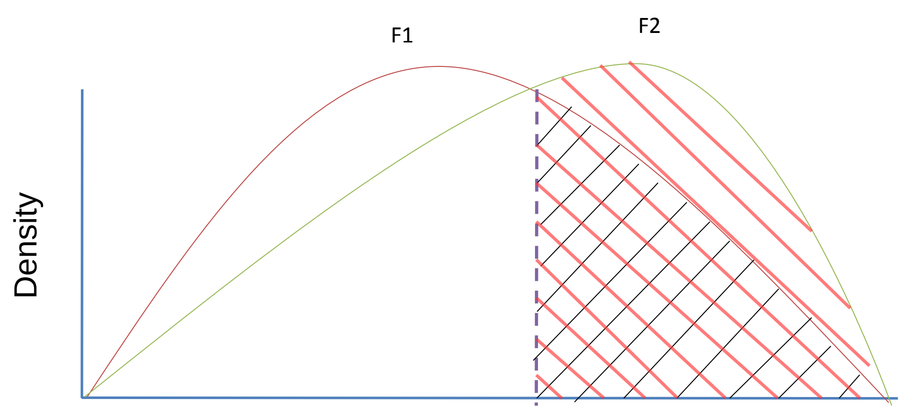


Changes in number of cases given a spatial expansion



We built the PDF of the cases
In the elevation gradient for
Every year (Y1, Y2....Fn)

Changes in number of cases given a spatial expansion



For both pdfs we compute the respective fractions above that altitude and call these f1 and f2 →

We transform the fractions into cases:

C2=Cases above alt_c in year 2= f2*total cases in year 2

C1= Cases above alt_c in year 1= f1* total cases in year 1

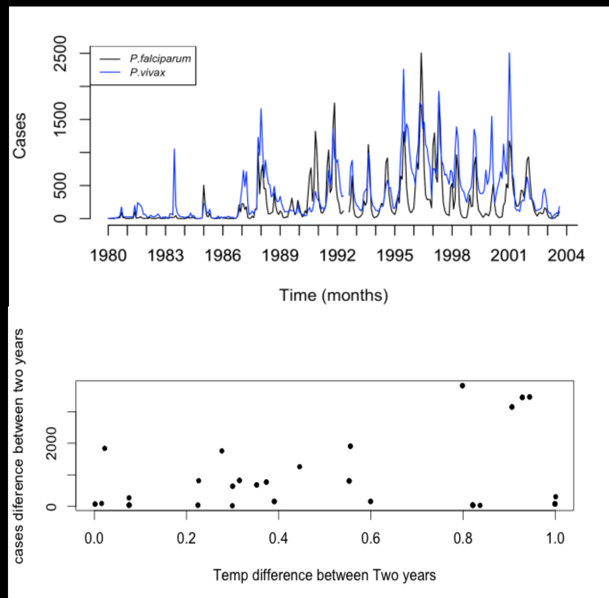
Is the long term trend consistent with the altitudinal expansion?

From movement in altitudinal distribution

~1980 cases/degree C

From fit linear trend

~2166 cases /degree C



Some conclusions

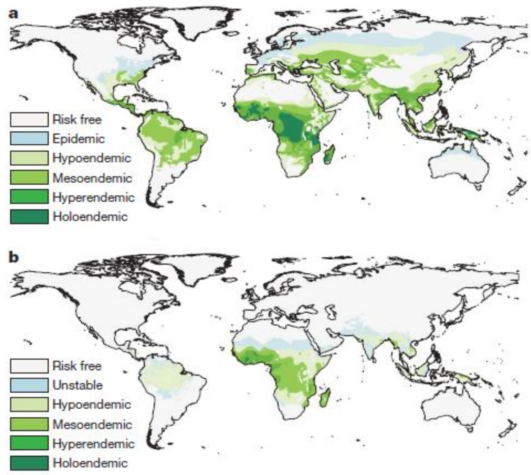
- We provided evidence for an upward expansion of malaria's elevation distribution in warmer years.
- This implies that climate change will, without mitigation, result in an increase of the malaria burden in the densely populated highlands of Africa and South America.
- For Ethiopia, we estimated a potential addition of 4.9 to 6.1 million cases to the annual national burden from the 1970s to the mid 2000s (Bouma and Pascual, 2014, *in press* in Butler *et al*. eds.)
- Similar trends in *P. falciparum* and *P. vivax* malaria are not consistent with drug resistance driving these patterns.

nature Vol 465|20 May 2010|doi:10.1038/nature09098

LETTERS

Climate change and tl

Peter W. Gething[1], David L. Smith[2,3], Anand P.



"Predictions of an intensification of malaria in a warmer world , based on extrapolated empirical relationships or biological mechanisms, must be set against a context of a century of warming that has seen marked global declines in the disease and a substantial weakening of the global correlations between malaria endemicity and climate "

Editorial commentary, Nature 2010

NEWS

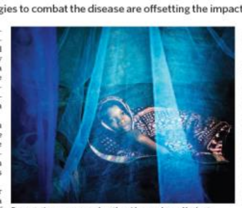
Malaria may not rise as world warms

Studies suggest that strategies to combat the disease are offsetting the impact of climate change.

Of the many climate-change catastrophes facing humankind, the anticipated spread of infectious tropical diseases is one of the most frequently cited — and most alarming. But a paper in this week's *Nature* adds to the growing voice of dissent from epidemiologists who challenge the prediction that global warming will fuel a worldwide increase in malaria.

On the surface, the connection between malaria and climate change is intuitive: higher temperatures are known to boost mosquito populations and the frequency with which they bite. And more mosquito bites mean more malaria.

Yet when epidemiologists Peter Gething and Simon Hay of the Malaria Atlas Project at the University of Oxford, UK, and their colleagues com-



Preventative measures such as the widespread use of bed nets have outweighed the effects of climate warming on malaria.

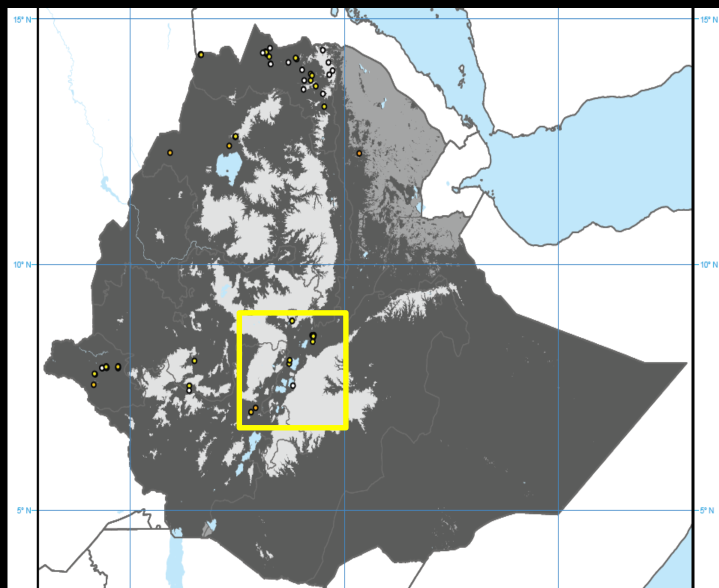
change per se is not something that should be central to the discussion. The risks have been overstated."

Some earlier analyses painted a dire picture of a malaria-ridden future, but these models often exclusively evaluated the impact of warmer temperatures without taking other factors into consideration, says Paul Reiter, an entomologist at the Pasteur Institute in Paris. The latest assessment of the Intergovernmental Panel on Climate Change noted these concerns: "Despite the known causal links between climate and malaria transmission dynamics, there is still much uncertainty about the potential impact of climate change on malaria at local and global scales."

Gething and colleagues' study is the first of its kind to provide a detailed sta-

But climate change will imply higher control efforts in these regions.

ETHIOPIA



Gething *et al.*, Nature 2010

Nature 2002

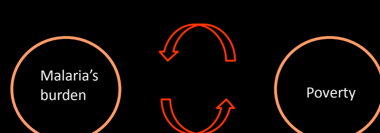

insight review articles

The economic and social burden of malaria

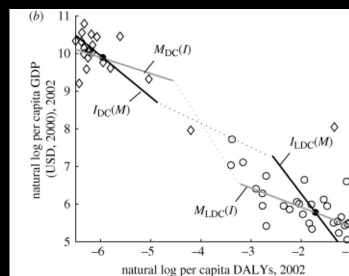
Jeffrey Sachs*† & Pia Malaney*

*Center for International Development, John F. Kennedy School of Government, Harvard University, 79 John F. Kennedy St., Cambridge, Massachusetts 02138, USA (e-mail: pia_malaney@harvard.edu)
†Commission on Macroeconomics and Health, World Health Organization, Avenue Appia 20, 1211 Geneva 27, Switzerland

Where malaria prospers most, human societies have prospered least. The global distribution of per-capita gross domestic product shows a striking correlation between malaria and poverty, and malaria-endemic countries also have lower rates of economic growth. There are multiple channels by which malaria impedes development, including effects on fertility, population growth, saving and investment, worker productivity, absenteeism, premature mortality and medical costs.



Poverty trap formed by the ecology of infectious diseases:



Bonds M H et al. Proc. R. Soc. B 2010

GRACIAS

Mauricio
Santos
Vega
UM

Yael Artzy
UM > U. of Amsterdam

Amir Siraj, DU

Menno J. Bouma, LSHTM

Graham Environmental Sustainability Institute (GESI, UM)
Howard Hugues Medical Institute
NOAA (Oceans and Health)