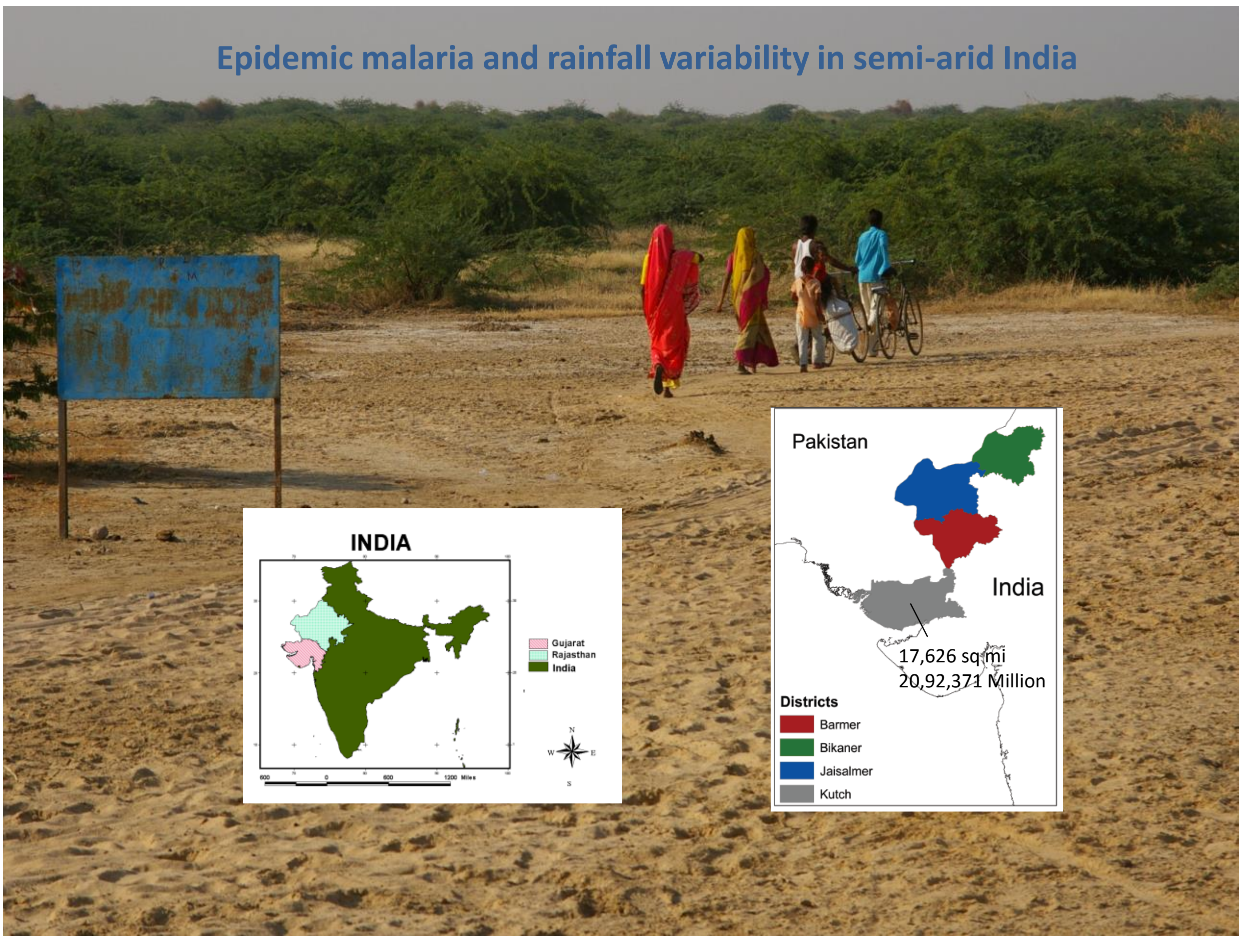
Climate forcing and malaria dynamics

Mercedes Pascual

University of Chicago

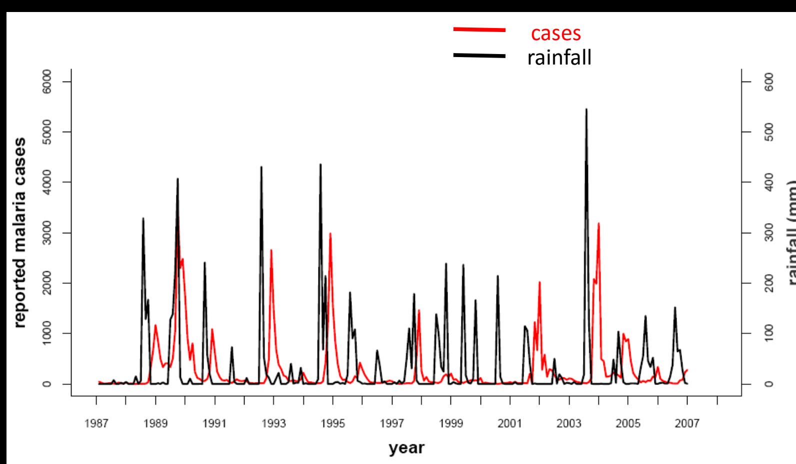
and

The Santa Fe Institute


Epidemic malaria and rainfall variability in semi-arid India
INDIA
Gujarat
Rajasthan
India
Pakistan
India
17,626 sq mi
20,92,371 Million
Districts
Barmer
Bikaner
Jaisalmer
Kutch

Typical epidemic behavior of *P. falciparum* cases

District of Kutch:
30 years
monthly cases

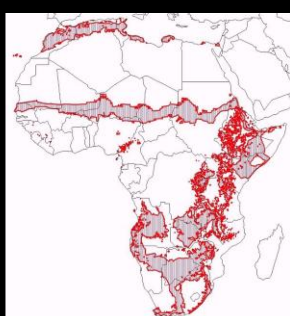


Laneri *et al.* PloS Computational Biology 2010

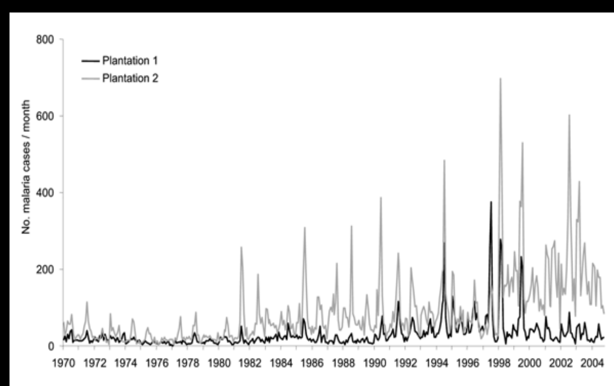
Highland malaria and climate change

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

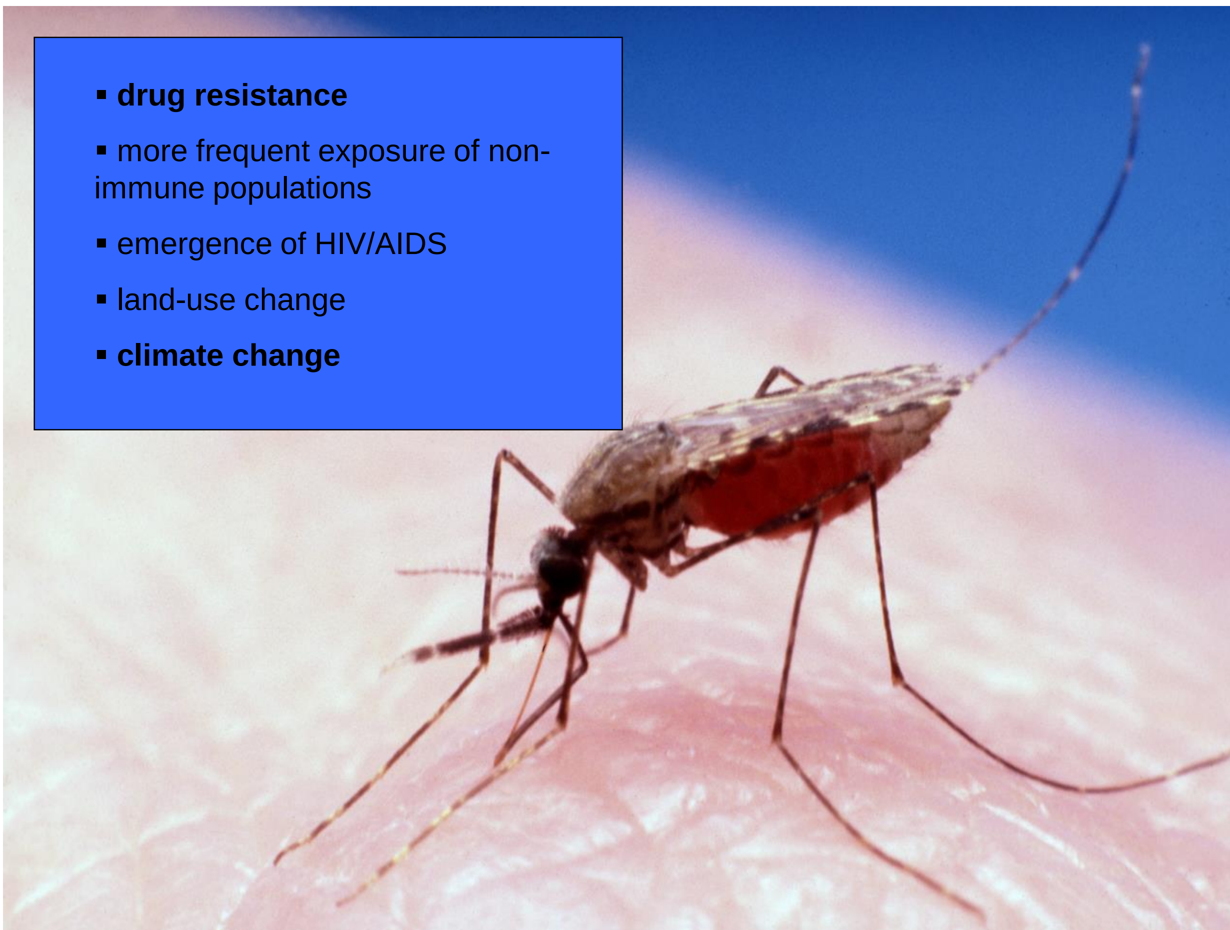
Estimated 110 000 deaths each year (Africa Malaria Report)



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



From Shanks et al. EID 2005


▪ **drug resistance**
▪ more frequent exposure of non-immune populations
▪ emergence of HIV/AIDS
▪ land-use change
▪ **climate change**

Testing hypotheses on disease dynamics and climate forcing by comparing mechanistic models

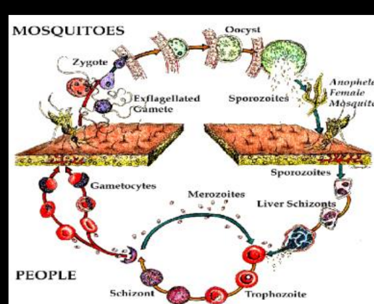
Best disease models

with no climate

↔

Best disease models

with climate variability



Conceptual outline

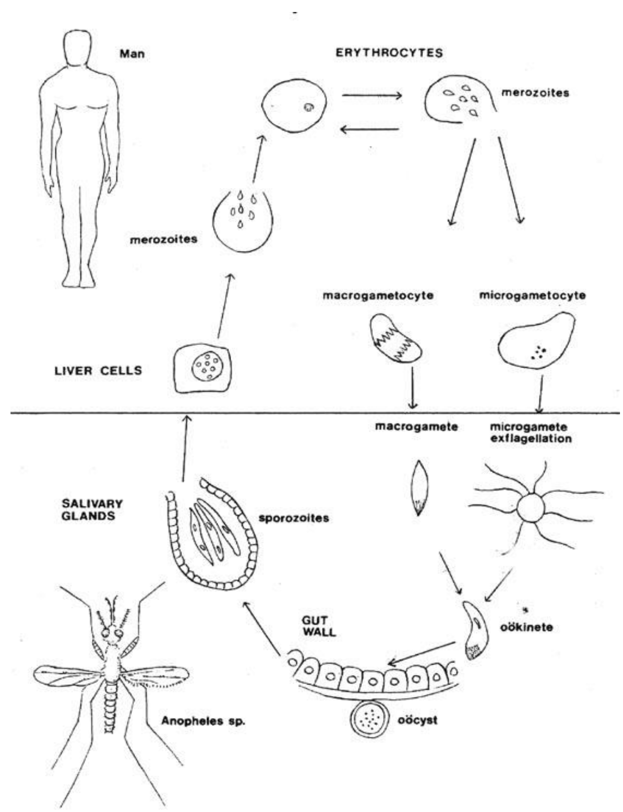
- The effect of climate forcing will be most apparent where climate factors act as strong limiting factors (at the edge of the spatial distribution of the disease, in highland and semi-arid regions). But here, by definition, transmission is low, and therefore, population immunity, is most <u>unlikely</u> to play a strong dynamical role.

- We will see that epidemiological processes matter primarily at seasonal and not interannual scales, and that 'reactive control' can act as a nonlinear feedback and generate multiannual cycles.

- Prediction needs to take into account non-stationary conditions.

Model by Ross and McDonald (1916-1957)

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



Ross-McDonald model:

Proportion mosquitoes infected, y

Success of bites

Number of mosquitoes

Recovery rate

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

Biting rate

Number of hosts

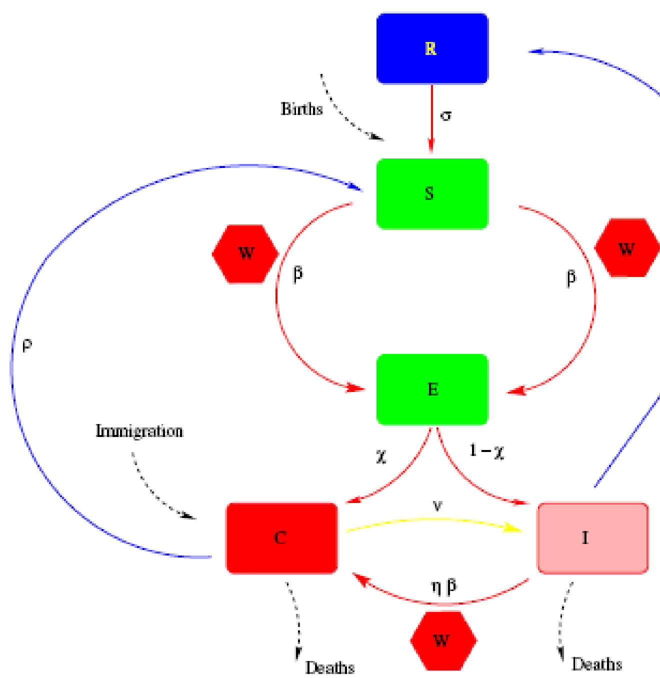
$$dy/dt = ax(1-y) - \mu y$$

Mosquito death rate

Proportion humans infected, x

Coupled mosquito-human transmission model

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



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

Human model: β, the force of infection

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

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

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:

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

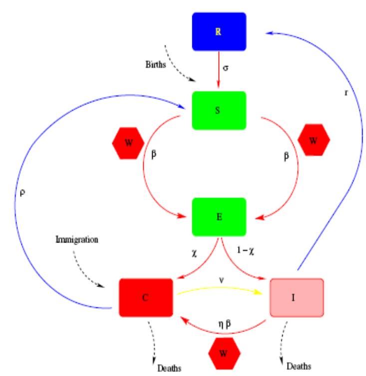
where y is the fraction of infectious humans:

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

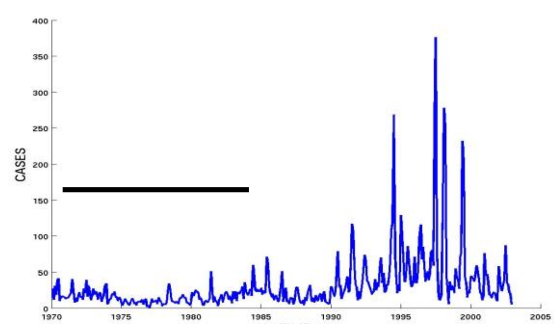
Temperature

Rainfall

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



See E. Mordecai, Ecology Letters 2013: Optimal temperature for malaria transmission is dramatically lower than previously predicted



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

$$\frac{dS}{dt} = B - \beta\, S + \sigma R - \delta\, S + \rho\, C$$

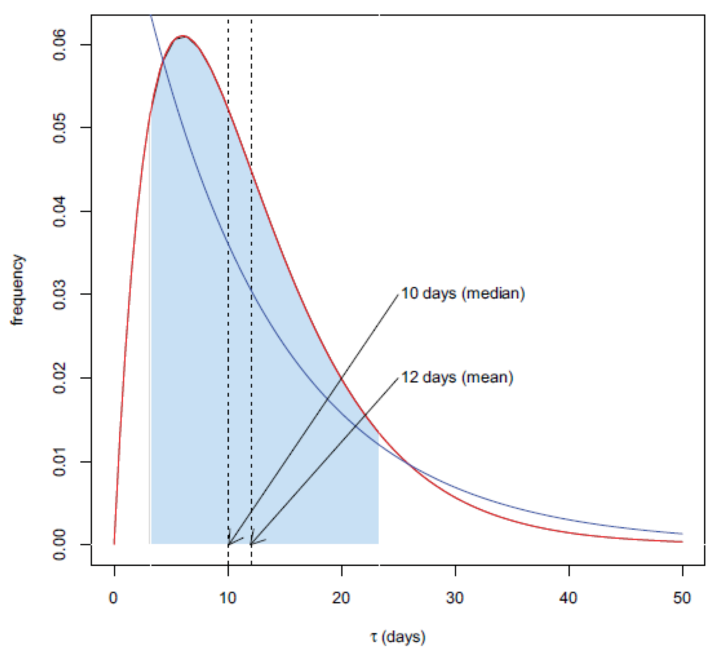
$$\begin{aligned}
\frac{dE_1}{dt} &= \beta\, S - \delta\, E_1 - n_H \gamma_H\, E_1 \\
\frac{dE_2}{dt} &= n_H \gamma_H\, E_1 - n_H \gamma_H\, E_2 - \delta_H\, E_2 \\
\dots &= \dots \\
\frac{dE_n}{dt} &= n_H \gamma_H\, E_{n-1} - n_H \gamma_H\, E_n - \delta_H\, E_n \\
\frac{dI}{dt} &= (1-\xi)\, n_H \gamma_H\,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

$(\delta = \delta_H)$

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

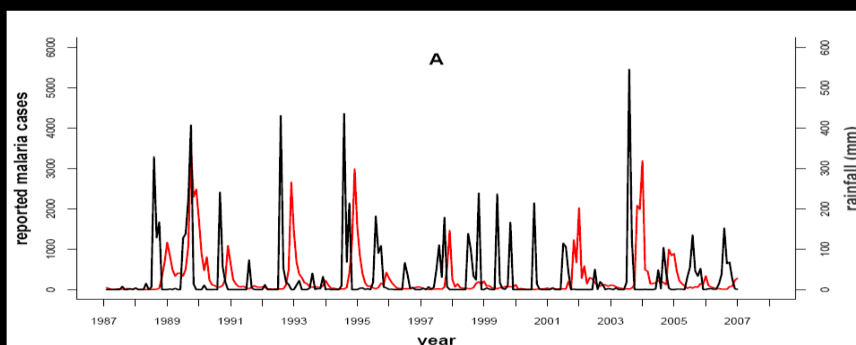
of average $1/\gamma_H$ and variance $1/(n_H\, \gamma_H^2)$.

Gamma distributed ‘incubation’ time



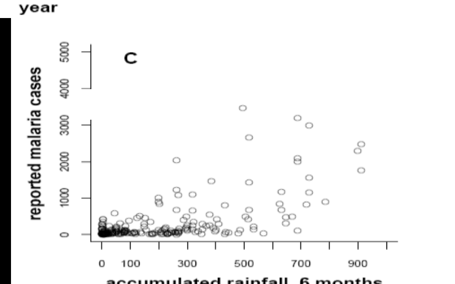
$$
\begin{aligned}
\frac{dL}{dt} &= f\, M \left(\frac{K-L}{K}\right) - \delta_L\, L - d_L\, L \\
\frac{dX}{dt} &= -c\, a\, y\, X - \delta_M\, X + d_L\, L \\
\frac{dV_1}{dt} &= +c\, a\, y\, X - n_P\, \gamma_P\, V_1 - \delta_M\, V_1 \\
\frac{dV_2}{dt} &= n_P\, \gamma_P\, V_1 - n_P\, \gamma_P\, V_2 - \delta_M\,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

A simple ‘coupled’ model: malaria in Kutch, India



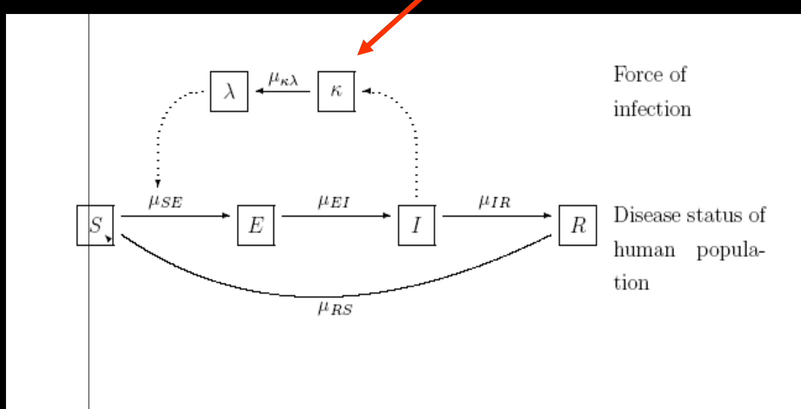
- does population immunity play a role in the response to climate variability?

- how predictable is the size of outbreaks based on transmission models driven by climate?



Malaria model

$$f(t) = \frac{I(t)}{N(t)} \exp\{\beta_{seas} + \beta.Rain(t)\} Noise$$



Latent force of infection

Force of infection

$$\kappa = \lambda_0 \Rightarrow \lambda_1 \Rightarrow \lambda_2 \Rightarrow \lambda$$

Parasite's development in surviving mosquitoes

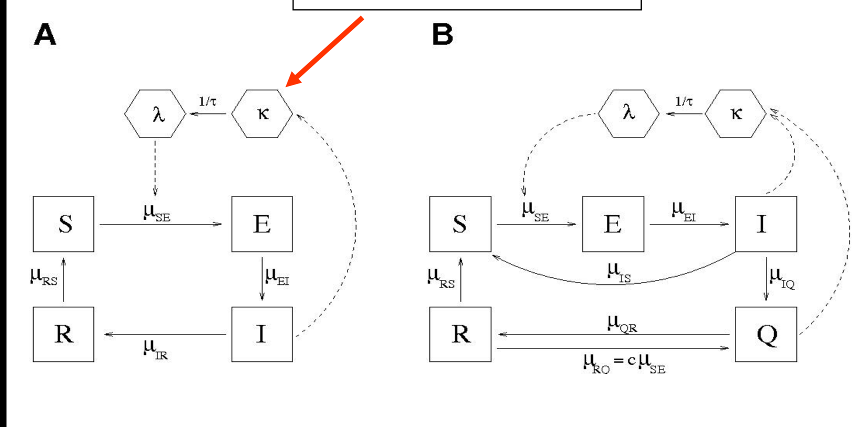
Two possible structures for human component

Force of infection:
a function of rainfall

$$f(t) = \frac{I(t)}{N(t)} \exp\{\beta_{seas} + \beta.Rain(t)\} Noise$$

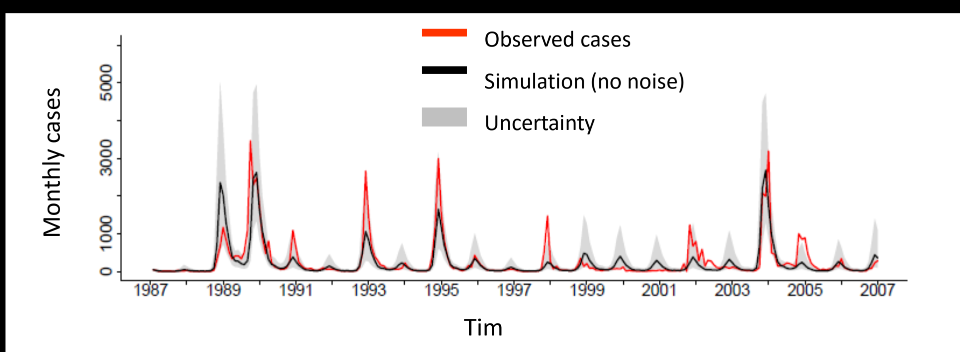
mosquitoes

hosts



Both rainfall and clinical immunity are included in the 'best' model

- Clinical immunity is important at seasonal scales
- This model outperforms a 'standard' non-mechanistic, linear autoregressive, model that includes rainfall



Laneri *et al.* PloS Computational Biology 2010
Bhadra *et al*. J. American Statistical Association 2011

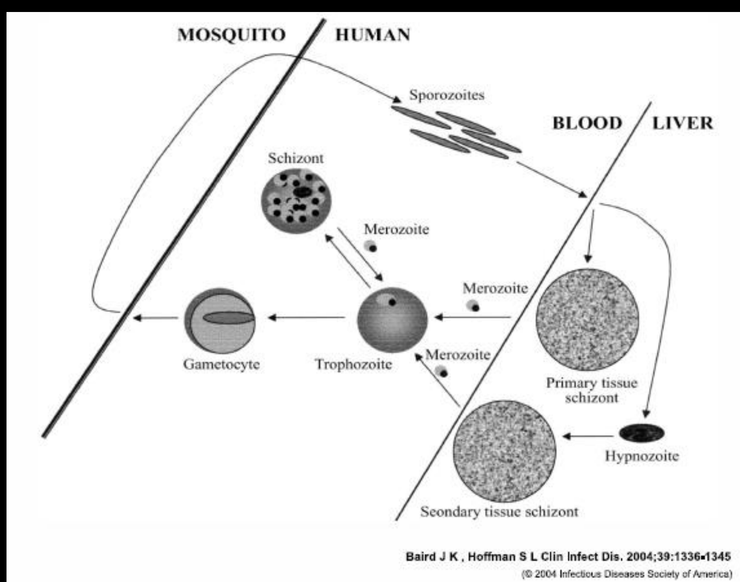
Model comparison

Table S1. Table of log-likelihood (ℓ) and AIC of the fitted models for Kutch and Barmer.

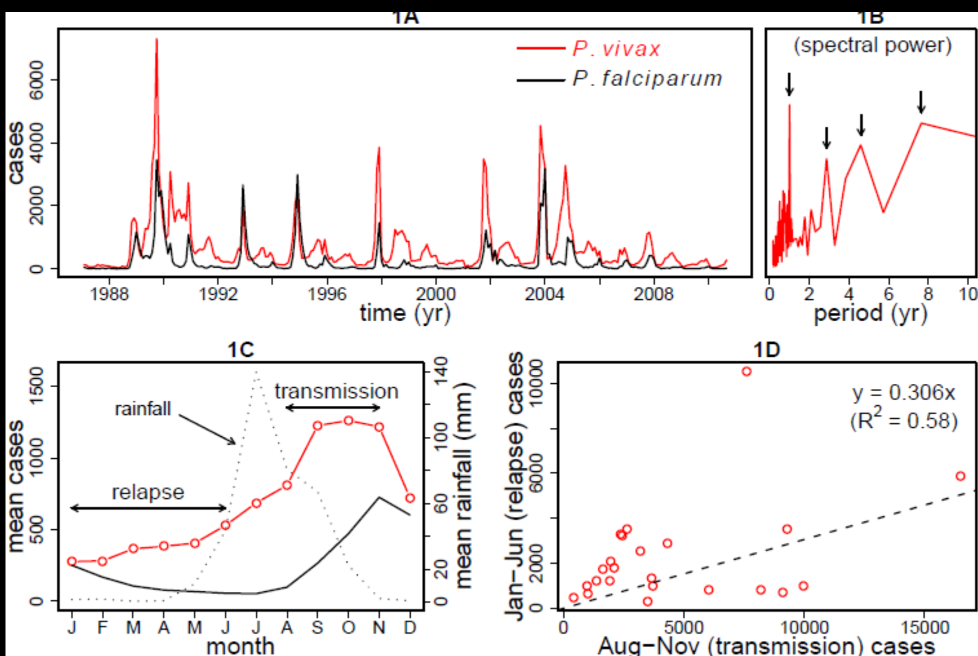
model	p	log-likelihood (ℓ)		AIC	
		Kutch	Barmer	Kutch	Barmer
VSEIRS model without rainfall	19	-1275.0	-984.1	2588.0	2006.2
VSEIRS model with rainfall	20	-1265.0	-978.6	2570.0	1997.2
VS^2EI^2 model without rainfall	24	-1261.1	-975.3	2570.2	1998.6
VS^2EI^2 model with rainfall	25	-1251.0	-970.5	2552.0	1991.0
SARIMA $(1,0,1) \times (1,0,1)_{12}$ without rainfall	6	-1329.0	-983.7	2670.0	1979.4
SARIMA $(1,0,1) \times (1,0,1)_{12}$ with rainfall	7	-1322.6	-977.0	2659.2	1968.0

In the table "p" denotes the number of parameters for each model. AIC is computed by the formula AIC $= -2\ell + 2p$. The SARIMA model was fitted to the data on the log scale (see the supplement of [2] for a detailed description of this procedure).

P. vivax malaria : relapses, rainfall and treatment

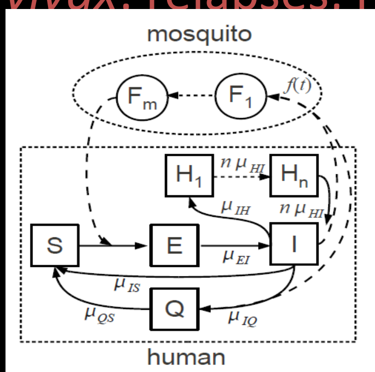


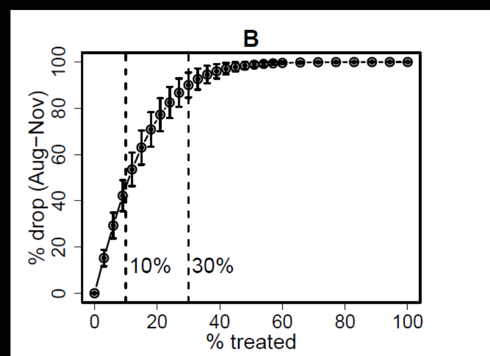
Inference on importance and duration of relapses for the population dynamics of the disease
Potential implications for treatment that focuses on this stage of the disease

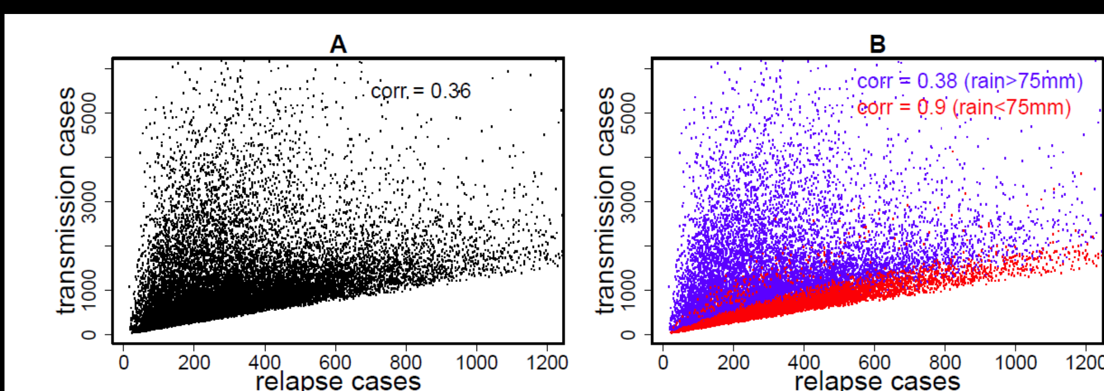


1A
P. vivax
P. falciparum
cases
time (yr)
1B
(spectral power)
period (yr)
1C
transmission
rainfall
relapse
mean cases
mean rainfall (mm)
month
1D
y = 0.306x
(R^2 = 0.58)
Jan−Jun (relapse) cases
Aug−Nov (transmission) cases

P. vivax: relapses, rainfall, and treatment





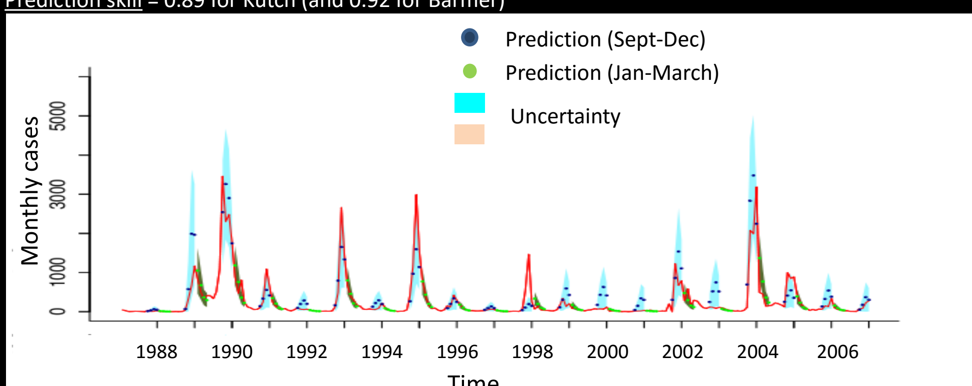


Roy *et al*, PloS Neglected Tropical Diseases, *PloS NTD*

Prediction

The rainfall-driven transmission model exhibits high prediction skill (retrospectively)

Prediction skill = 0.89 for Kutch (and 0.92 for Barmer)



Prediction performance: 4 months

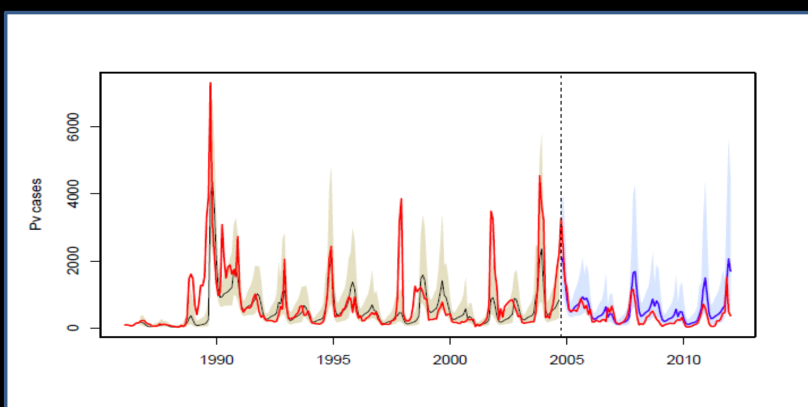
$$\text{skill} = 1 - \frac{\sum_{i=1987}^{2006} (y_i - \hat{y}_i)^2 w_i}{\sum_{i=1987}^{2006} (y_i - \mu)^2 w_i}$$

- w_i inverse of the prediction variance for the year i
- $\hat{y}_i$ and y_i are the predicted and observed cases, accumulated over September to December for the year i
- μ : 20 year mean of the observed cases accumulated between September and December

skill $\longrightarrow$ 1 Good Prediction
skill $\longrightarrow$ 0 Bad Prediction

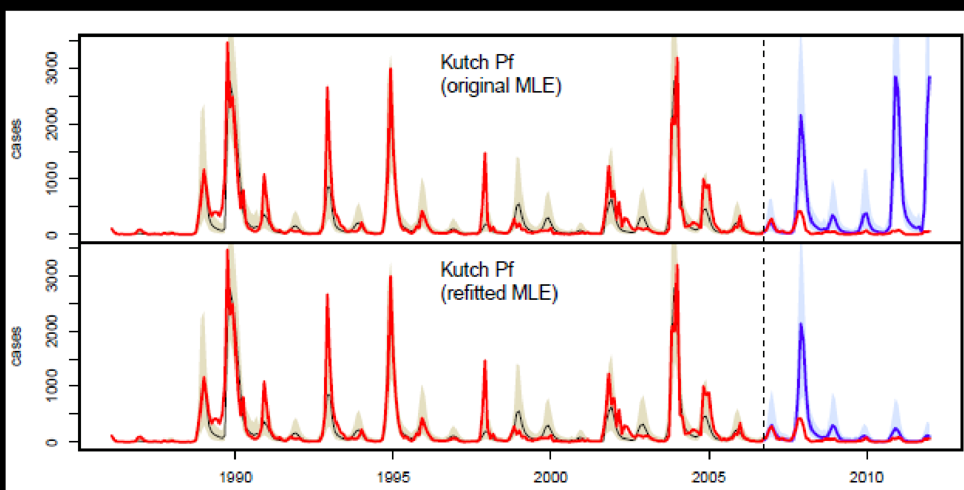
Predictability

- High prediction skill retrospectively (e.g. 0.9 for *P. falciparum* in Kutch)
- Also prospectively: illustrated here *for P. vivax*

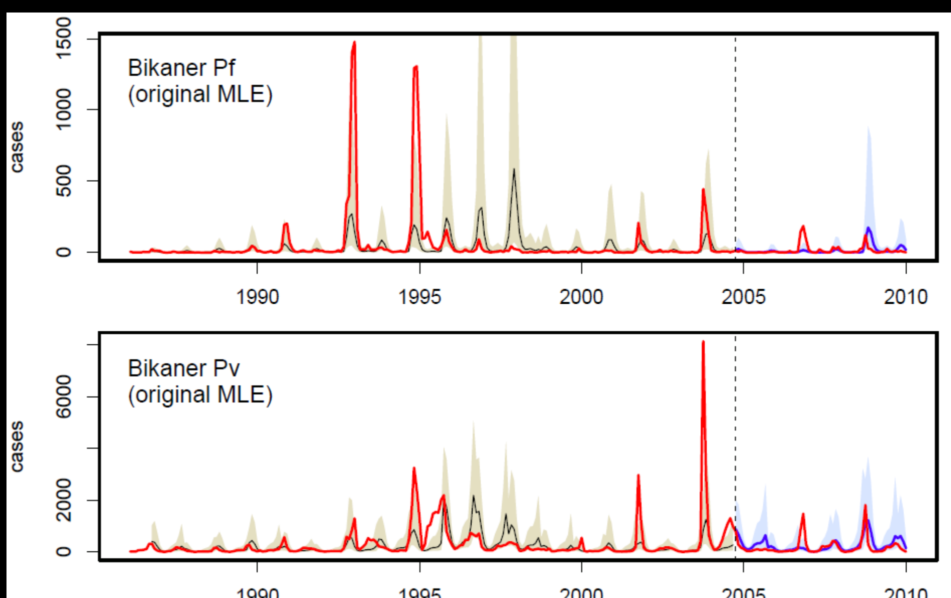


Roy *et al.* , *in review*

“’Prediction’ in the presence of non-stationarity



In this other district, we can see that the recent decrease in cases can completely be explained by the lack of rains



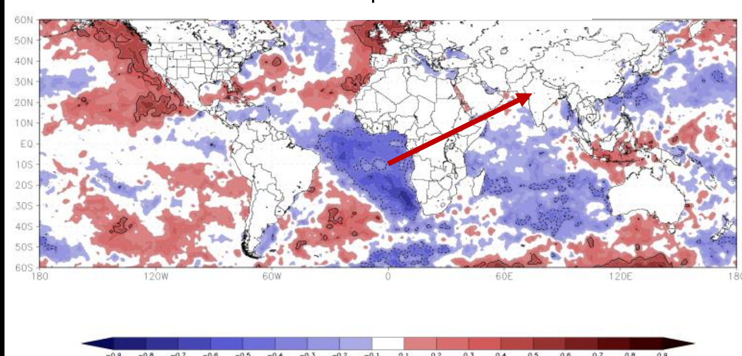
Ocean temperatures in the Tropical South Atlantic influence malaria epidemics in NW India

Sea Surface Temperatures (Atlantic)

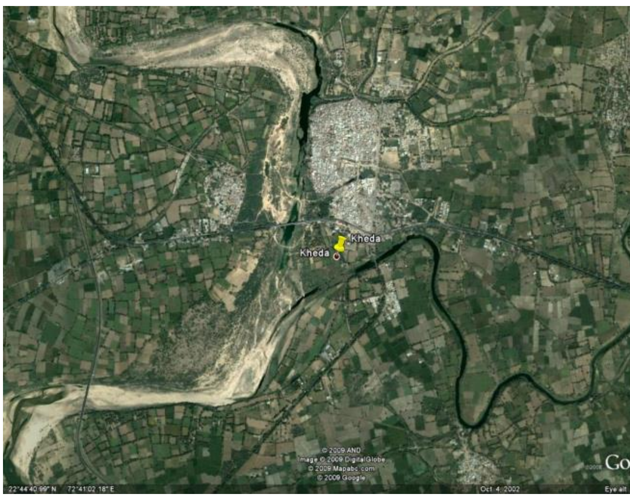
Rainfall NW India

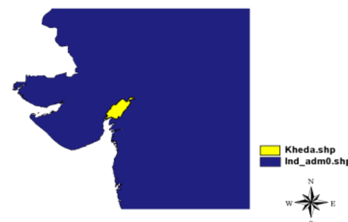
Malaria risk

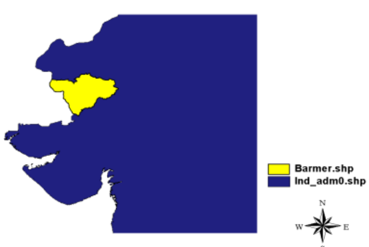
Lag (ranked) correlation between
Kutch cases in October and
Sea Surface Temperatures in June



Cash *et al.* Nature Climate Change 2013


Kheda
Kheda

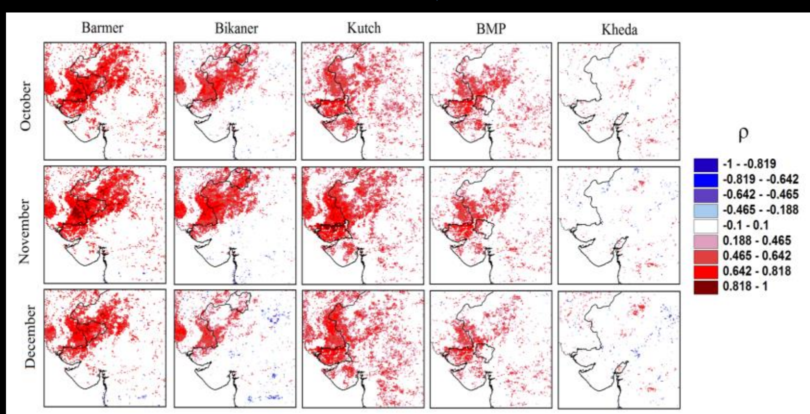

Kheda.shp
Ind_adm0.shp
N
W
E
S


Barmer.shp
Ind_adm0.shp
N
W
E
S


Barmer, India
Google

Association with climate breaks down along an irrigation gradient

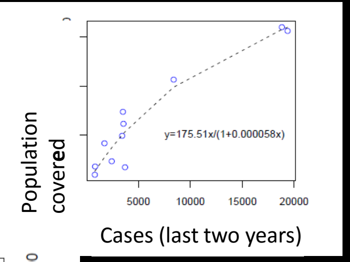
More irrigated land (more mosquito habitat / more wealth)

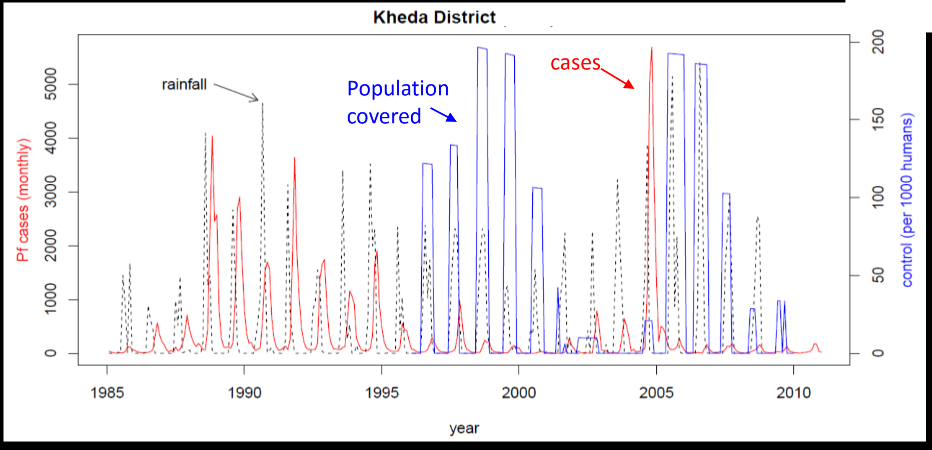


Rank correlation maps with vegetation index from remote sensing

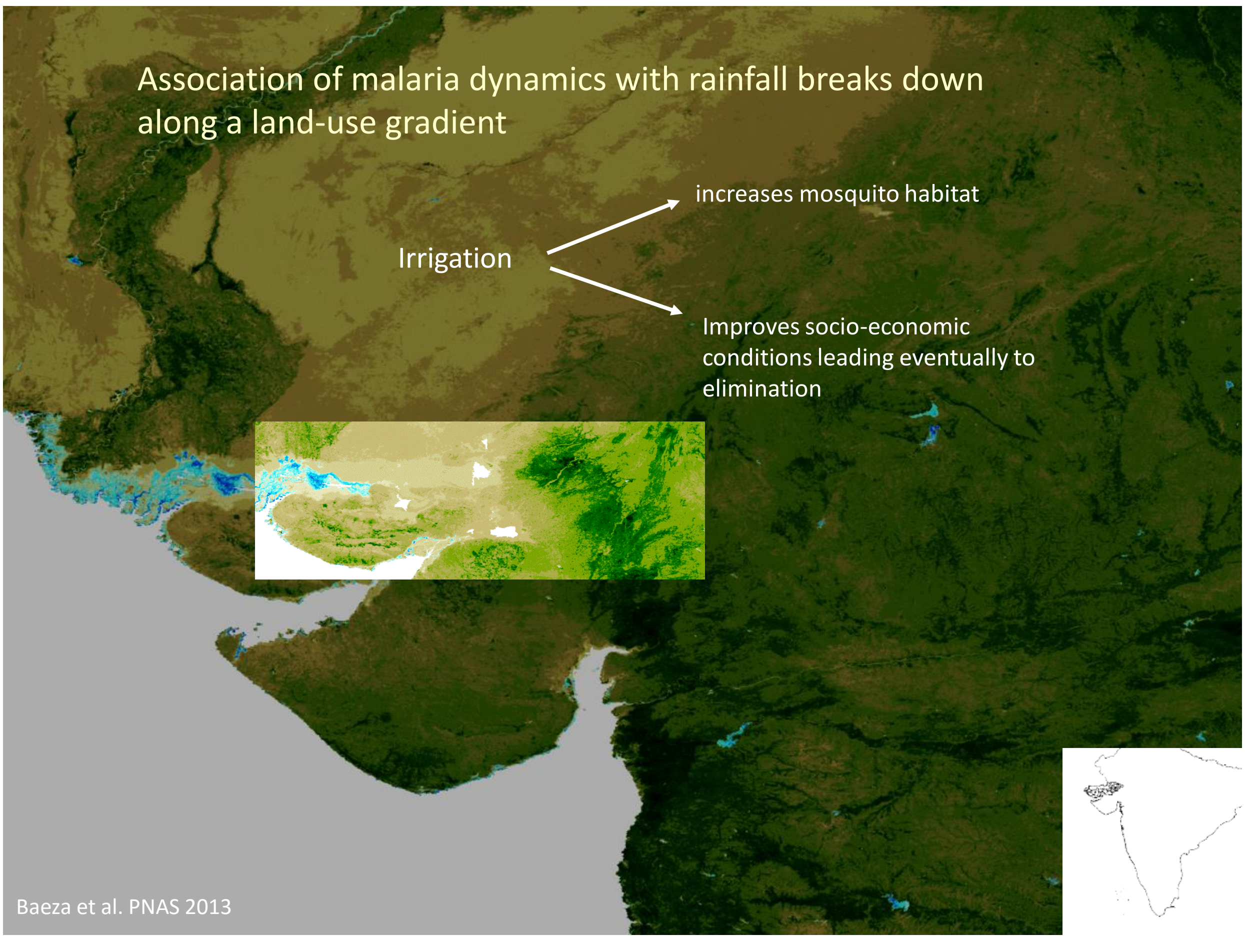
Baeza *et al.*, Malaria Journal 2011

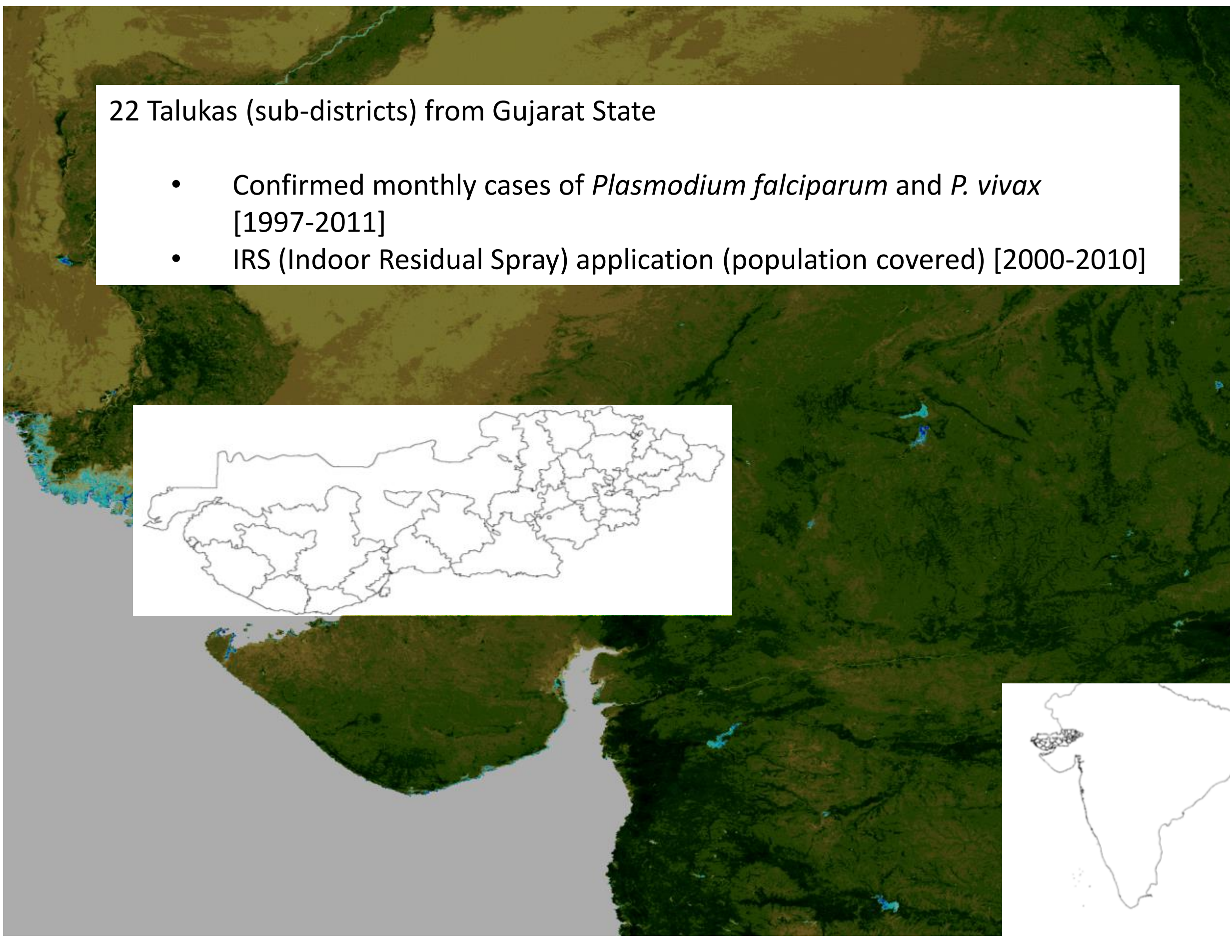
"Reactive" control policy
generates cycles and unexpected epidemics, precluding elimination



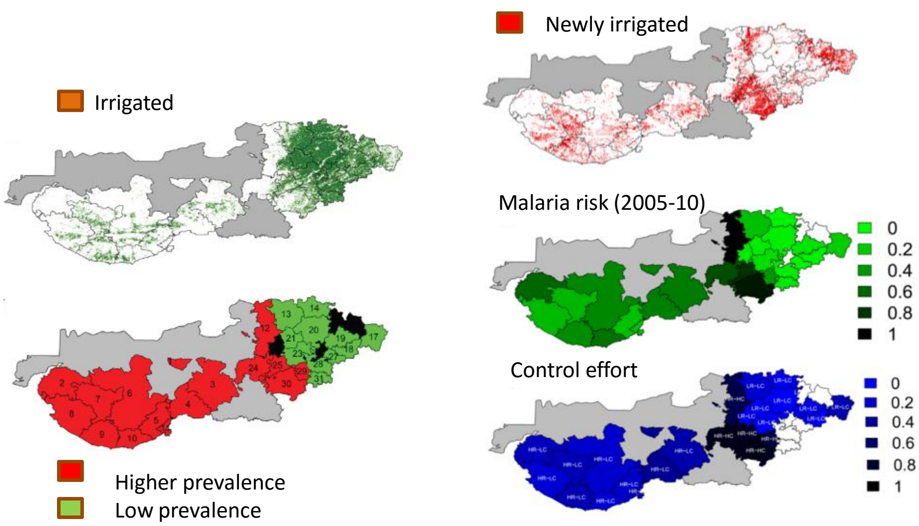


Baeza *et al*. Acta Tropica 2013
Baeza *et al*., PNAS 2013


Association of malaria dynamics with rainfall breaks down along a land-use gradient
Irrigation
increases mosquito habitat
Improves socio-economic conditions leading eventually to elimination
Baeza et al. PNAS 2013

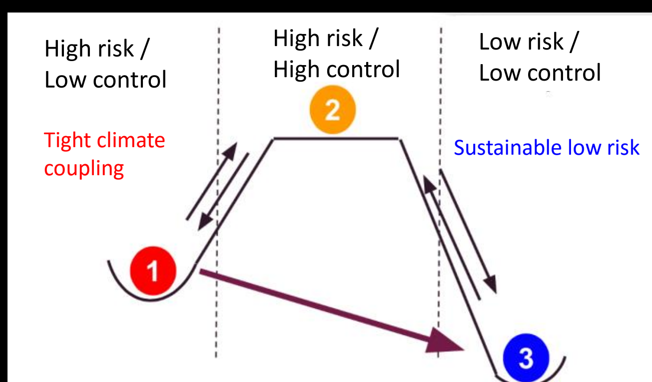

22 Talukas (sub-districts) from Gujarat State
• Confirmed monthly cases of *Plasmodium falciparum* and *P. vivax* [1997-2011]
• IRS (Indoor Residual Spray) application (population covered) [2000-2010]

Transition between epidemic malaria and elimination can be long-lasting (more than a decade) despite forceful control efforts



Baeza *et al*. PNAS 2013

Three distinct regimes: the transition regime can be long lasting (over a decade)



Baeza *et al.* PNAS 2013

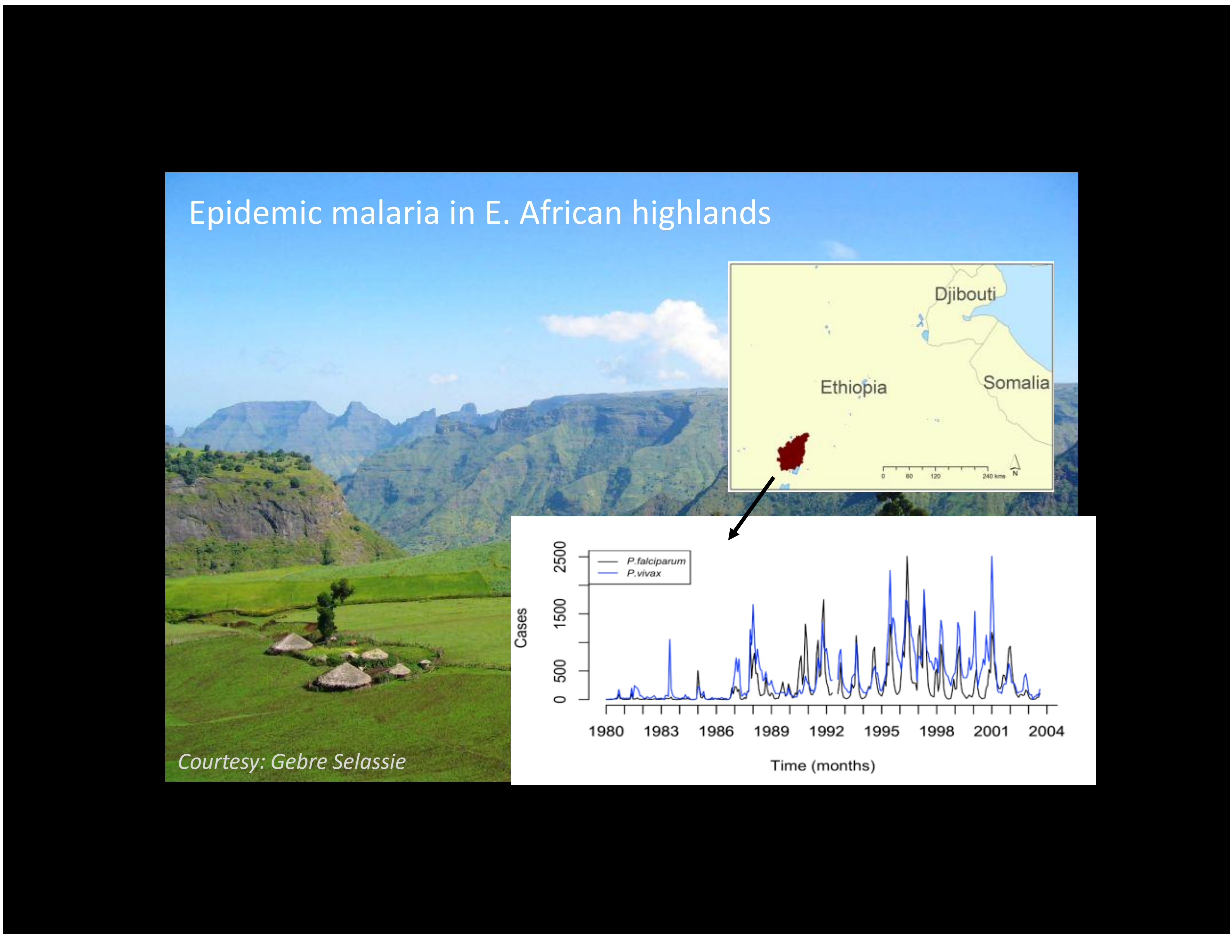
So far:

- Clear signature of climate forcing in epidemic regions.

- Nonlinear responses are not seen in terms of cycles. The depletion of the resource and therefore the strength of 'competition' for hosts is too low.

- Consideration of population dynamics (including immunity) remains important, especially for persistence during inter-epidemic periods.

- Interannual cycles can be generated when the epidemiological system includes intervention feedbacks, and these cycles can interact with climate anomalies to delay or impede elimination.

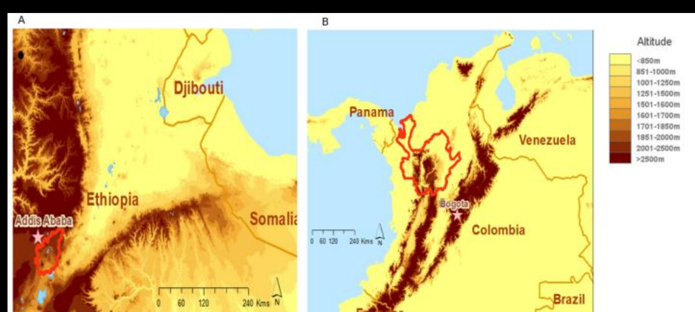

Epidemic malaria in E. African highlands
Djibouti
Ethiopia
Somalia
P.falciparum
P.vivax
Cases
0
500
1500
2500
1980
1983
1986
1989
1992
1995
1998
2001
2004
Time (months)
Courtesy: Gebre Selassie

Climate change vs.

- Evolution of drug resistance (Shanks et al. EID 2005)
- More frequent exposure of non-immune populations
- Emergence of HIV/AIDS
- Land-use change
- Breakdown of public health systems

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

1993-2005

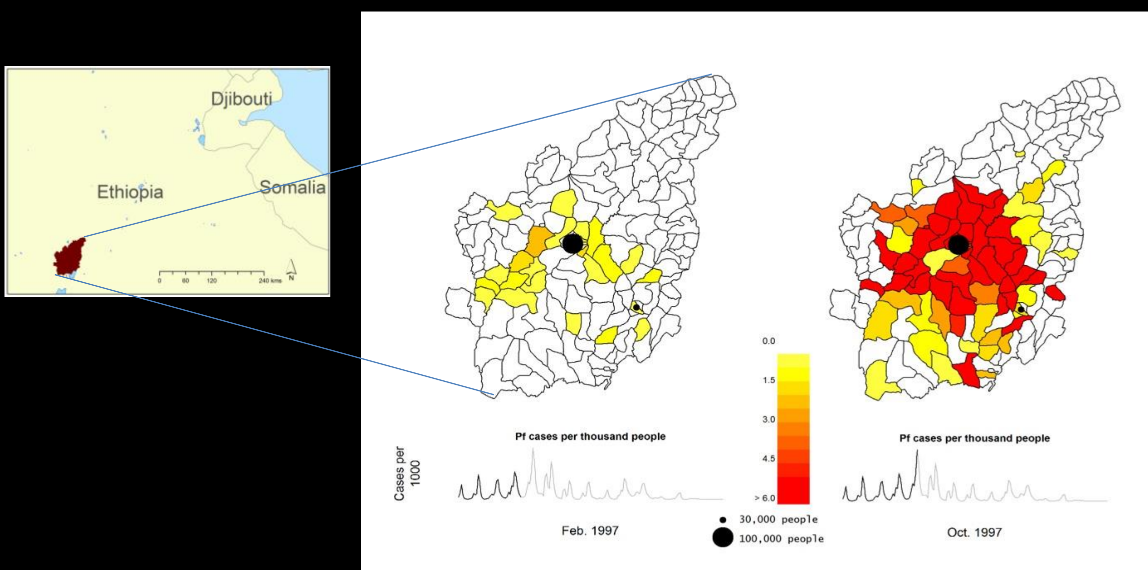


1990-2005

Confirmed monthly cases before major interventions of last decade

Siraj, Santos *et al.*, Science 2014

Expansion of the spatial distribution

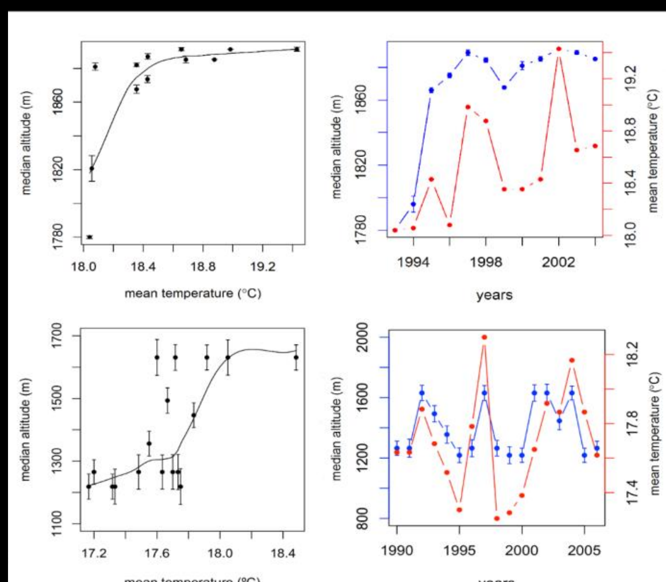


Siraj, Santos-Vega *et al., Science 2014*

The spatial distribution of the disease expands upwards in warmer years

Ethiopia

Colombia



Siraj, Santos-Vega *et al., Science 2014*

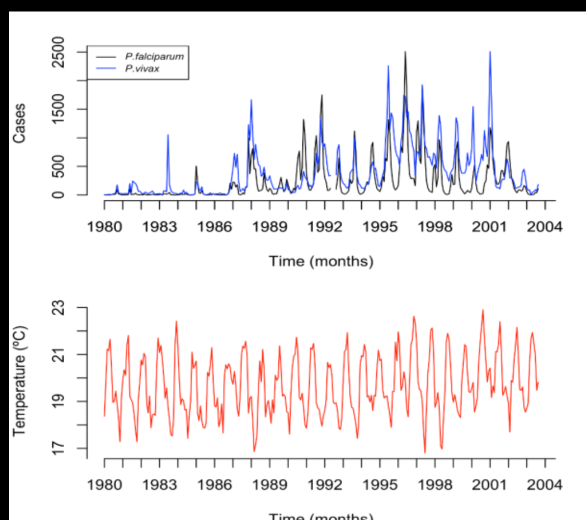
Is the long-term trend consistent with the magnitude of the altitudinal expansion?

From movement in altitudinal distribution

⇨ ~ 1980 cases / degree C

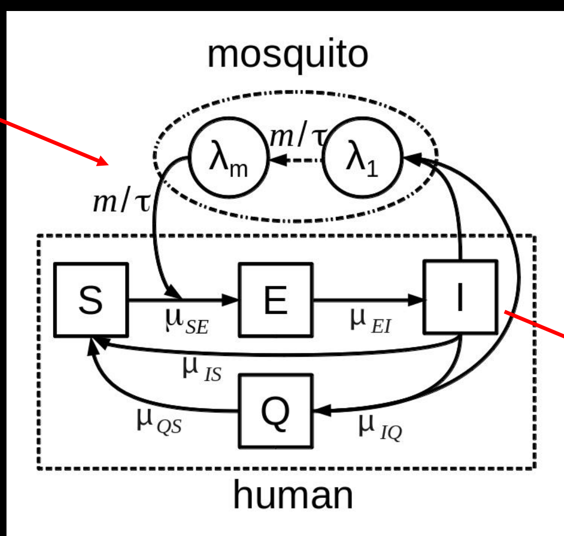
From longer temporal trend

⇨ ~2166 cases / degree C



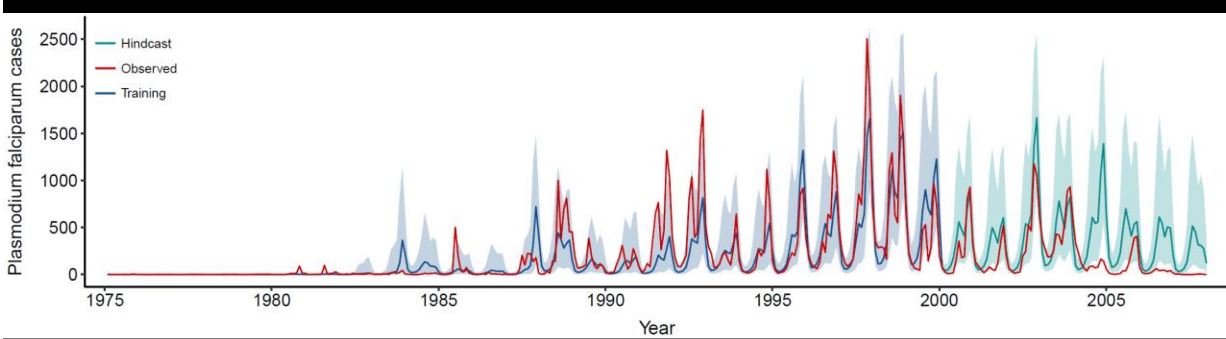
Transmission model

Force of Infection
(depends on
temperature,
season,
infection levels
and noise)



Reported cases + error
(under-reporting)

Likelihood maximization by iterated filtering



Pascual *et al., in prep.*

Gracias

Andres Baeza

Menno Bouma LSHTM

Ben Cash (COLA; IGES); Xavier Rodo (IC3); and Manojit Roy (UM)


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