Journey of Malaria Modelling: Tracing the Footsteps of Ronald Ross

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28 November 2023

What is epidemic modelling?

- A way of capturing natural history and transmission of disease
- A way of capturing how interventions shape transmission
- A framework for quantifying *costs* and *epidemiological impact*

Caution:

- A model is no substitute for surveillance and primary data!
- Offers a framework for
  - **making sense** of this data, and simulating **potential control policies**

Outline

- Ronald Ross and the story of first Malaria model
- McKendric and Kermack
- Malaria models: Past to present
- Conclusions

Story of Ronald Ross

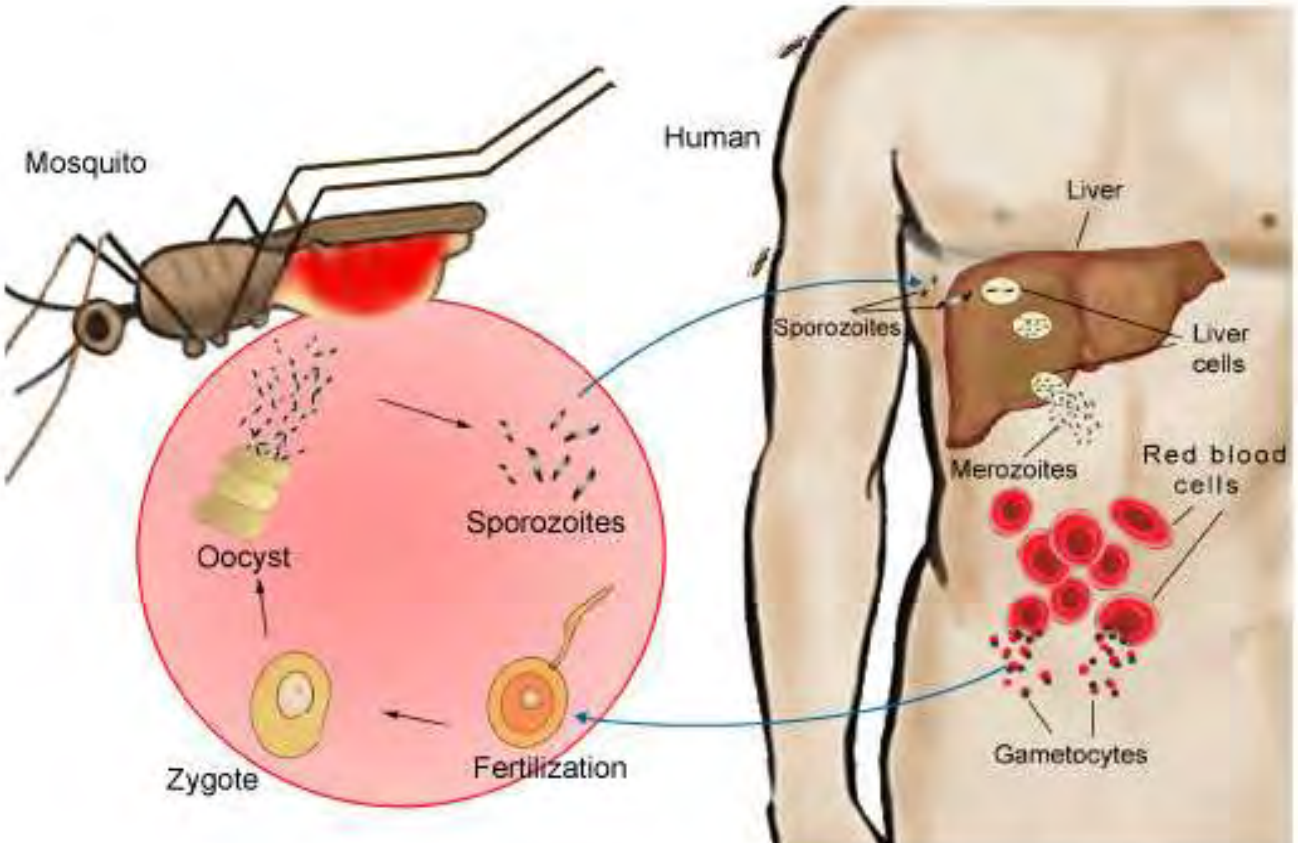
Sir Ronald Ross

1857 - 1932

India chapter

- Indian Medical Service (1881)
- Bangalore life (1883)
- First experiment with mosquitoes
- ‘Mosquitoes carry malaria just as they carry *filariae*’ - Patrick Manson.
- Second experiment in Bangalore
- Third experiment (on birds)
- Nobel Prize (1902)

Life cycle of Plasmodium parasite

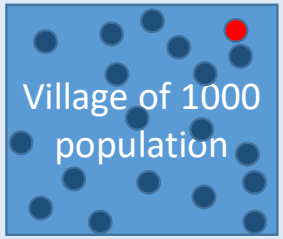


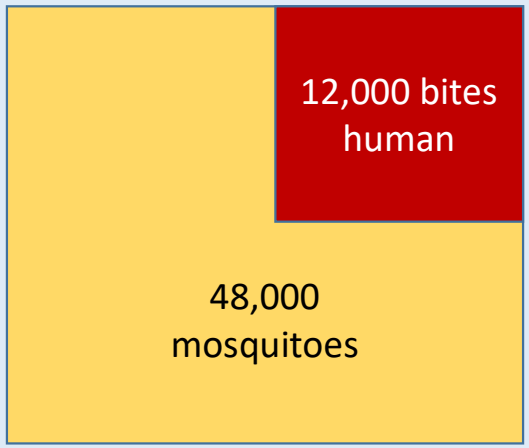
Two stages of Parasite life cycle

Link between insects and infections

- Ross's hypothesis - Removing mosquitoes was the key to controlling malaria
  - Practical experience – Sierra Leone (a country in West Africa), 1901
  - Experience during Suez Canal Project –Ismailia (Egypt)
- This was against popular wisdom – It was impossible to get rid of every last mosquito, which meant there would always be some insects left, and hence potential for malaria to spread.
- Need a stronger argument to persuade Ross's idea of mosquito control

Was it really possible to control malaria without removing every mosquito?





Assumptions:

- 1 in 4 mosquitoes would manage to bite someone
  - 1 of 3 mosquitoes survived to be infectious

12

Among all bites only 12 bites would be such that they can pick up the parasite

4

Survives to be infectious

1

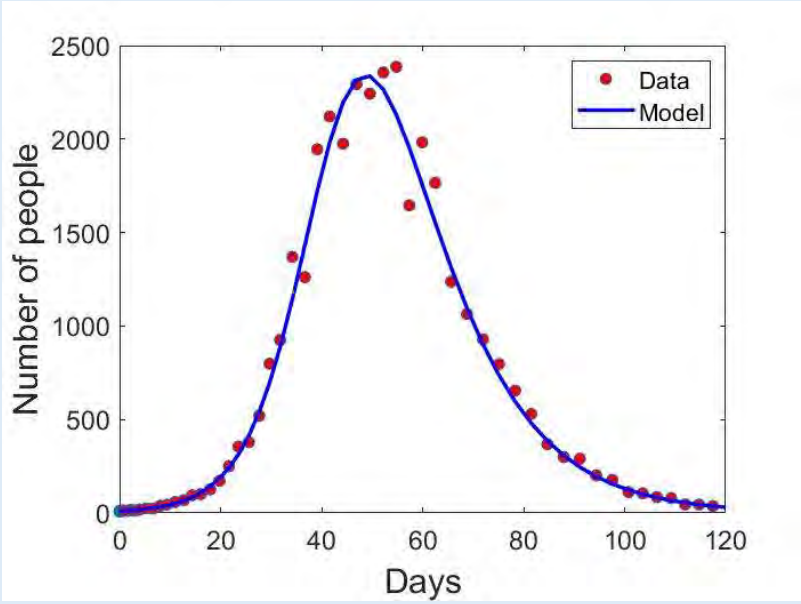
Bites another human

Even if there were 48,000 mosquitoes in the area, on average they would generate only one new human infection.

Two ways to approach disease analysis

Descriptive methods

- This involved starting with real life data and working backwards to identify predictable patterns.
- Example: William Farr's analysis of London smallpox outbreak, in 1830 and in 1840.
- Farr's method focused what shape epidemics take, not why they take the shape.



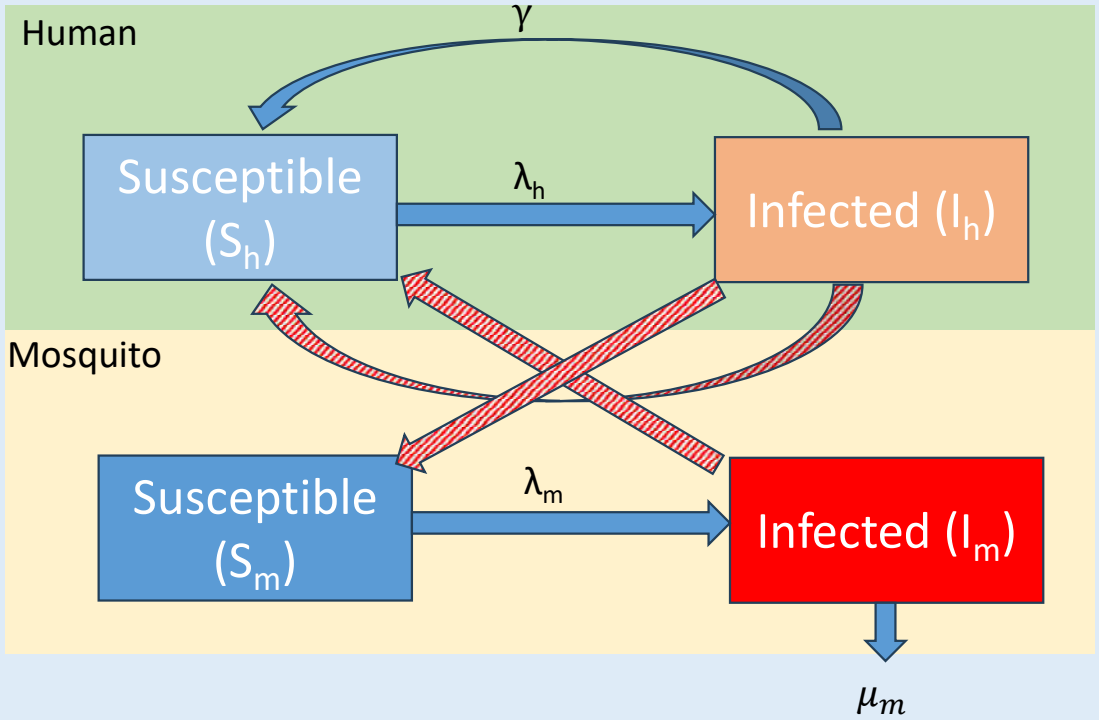
Mechanistic methods

- This started outlining the main processes that influenced transmission.
- Example: Ross's analysis by applying the knowledge of malaria transmission.
- Ross's conceptual model of transmission using mathematical equations, to make conclusions about likely outbreak patterns. It can answer 'what if' without doing real experiments.

Mechanistic approach of modelling malaria

Ross model

Ross model (1911)



$$\frac{dI_h}{dt} = \lambda_h S_h - \gamma I_h$$

$$\frac{dI_m}{dt} = \lambda_m S_m - \mu_m I_m$$

λ_h= biting rate $*$ probalility of infection $to\ human$ $*$ $relative\ mosquito\ population$ $* \left(\frac{I_m}{N_m}\right)$

λ_m= biting rate $*$ probalility of infection $to\ mosquito$ $*$ $* \left(\frac{I_h}{N_h}\right)$

Concluding analyses

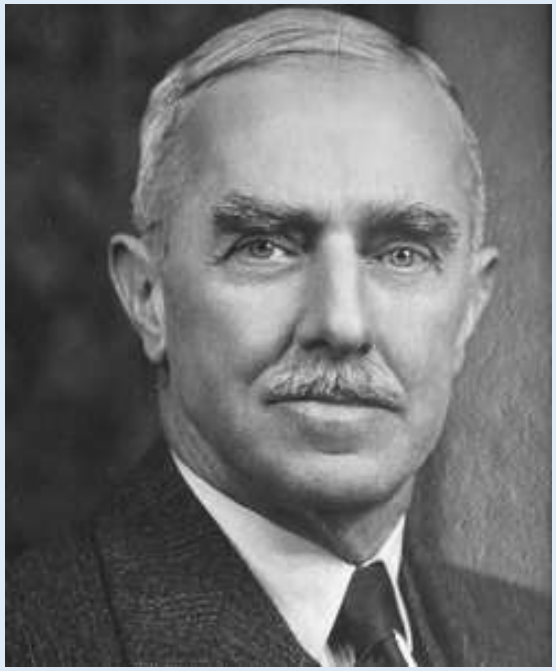
- More mosquitoes/more infected human → more new infections per month
- Process to counteracts the number → Estimated around 20% of humans infected with malaria would recover each month
- Condition for malaria to remain endemic in the population:

  Infection and recovery would need to balance each other
- If the recoveries outpaced the rate of new infections, the level of disease eventually would decline to zero.

"Malaria cannot persist in a community unless the *Anopheles* are so numerous that the number of new infections compensates for the number of recoveries." – *The Prevention of Malaria* (1910)

McKendrick and Kermack: Mathematics of disease

Anderson Gray McKendrick



1876 - 1943

William Kermack

1898 - 1970

Extended Ross's ideas to look at epidemics in general

Mathematical model of disease transmission

What causes epidemics to end?

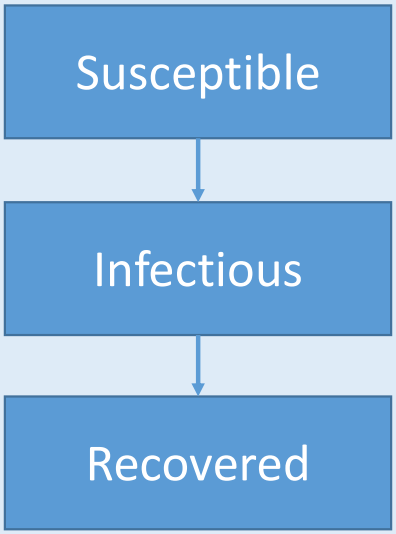
Two popular explanations:

- Transmission ceased because there were no susceptible people left to infect
- Pathogen itself became less infectious as the epidemic progressed

Neither explanation was correct

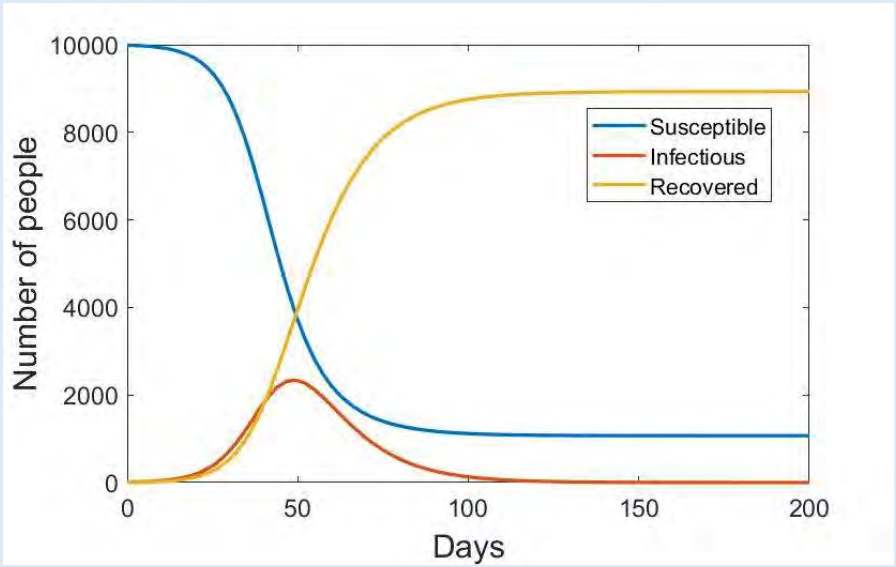
Mathematical model of disease transmission

Compartments according to disease status



SIR Model

Simulated outbreak using SIR model



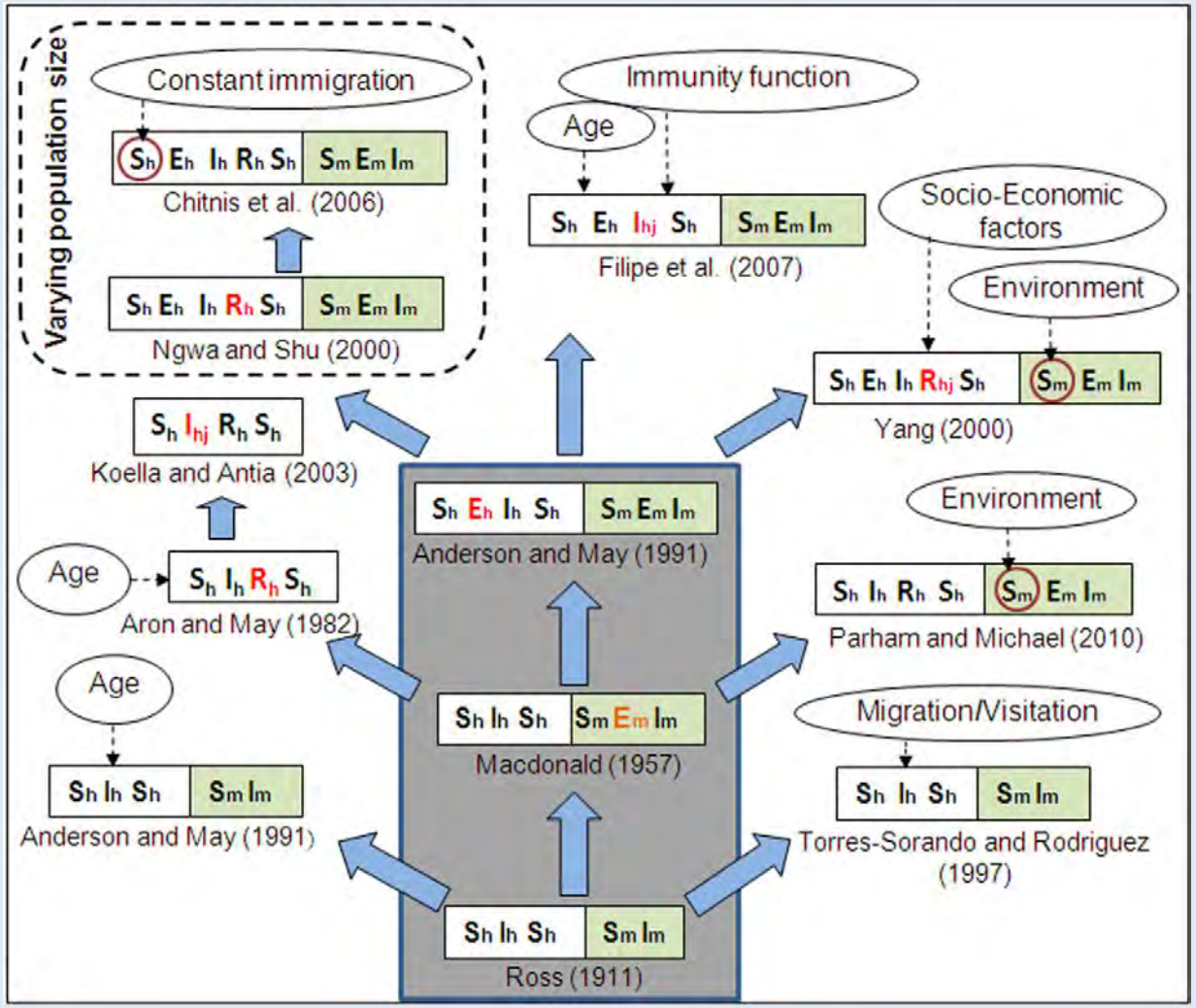
"An epidemic, in general comes to an end before the susceptible population has been exhausted" – Kermack and McKendrick

Mechanistic approach of modelling

Different types of theoretical approaches are used in epidemiological modelling

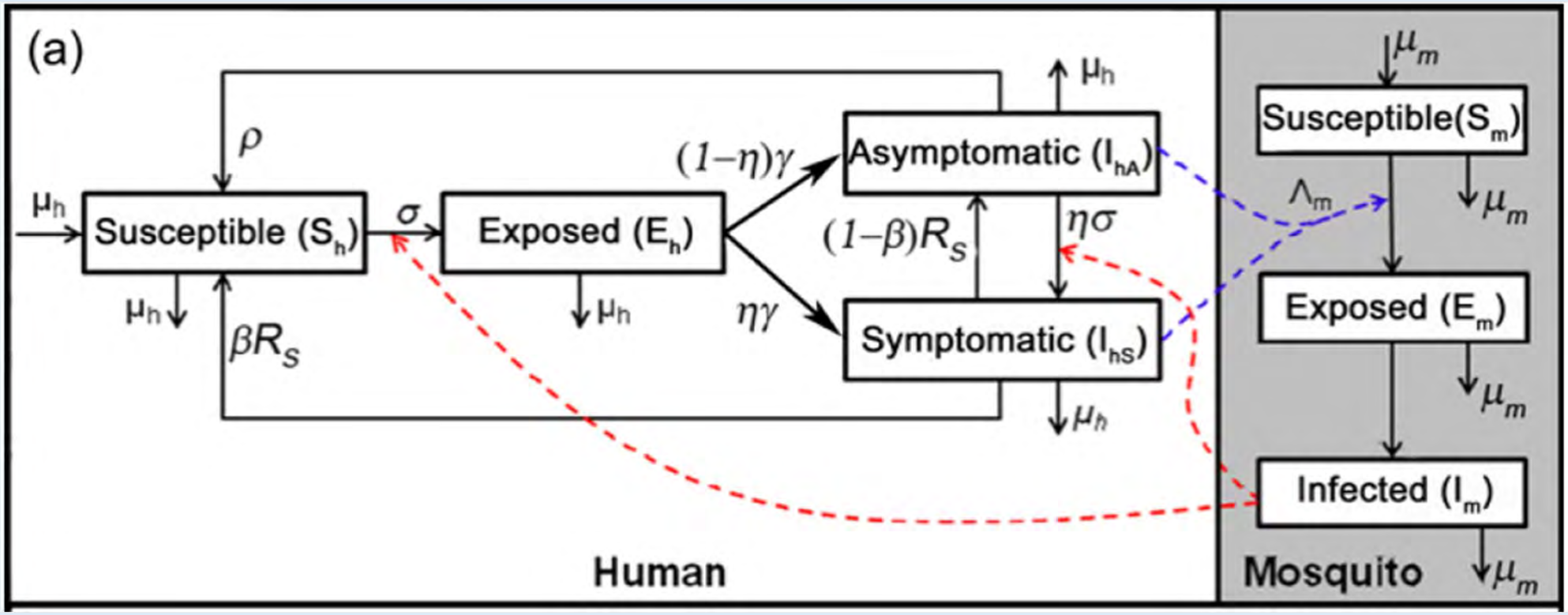
1) Differential equation-based SIR type models
2) Discrete models using generic host parasite population growth models
3) Network-based models – SIR or individuals
4) Lattice based models – continuous or discrete
5) Agent-based models

Evolution and grouping of different malaria models



Ref. Mandal et al. , *Malaria Journal*, 2011

Malaria model including mosquito dynamics



Ref. Mandal, *et al*, Bull Math. Biol. 2013

(a) For Human hosts

7 VARIABLES
AND
15 PARAMETERS

$$\frac{dS_h}{dt} = \mu_h + \beta R_S I_{hS} + \rho I_{hA} - \sigma I_m S_h - \mu_h S_h$$

$$\frac{dE_h}{dt} = \sigma I_m S_h - \eta\gamma E_h - (1-\eta)\gamma E_h - \mu_h E_h$$

$$\frac{dI_{hS}}{dt} = \eta\gamma E_h + \eta\sigma I_m I_{hA} - \beta R_S I_{hS} - (1-\beta) R_S I_{hS} - \mu_h I_{hS}$$

$$\frac{dI_{hA}}{dt} = (1-\eta)\gamma E_h + (1-\beta) R_S I_{hS} - \eta\sigma I_m I_{hA} - \rho I_{hA} - \mu_h I_{hA}$$

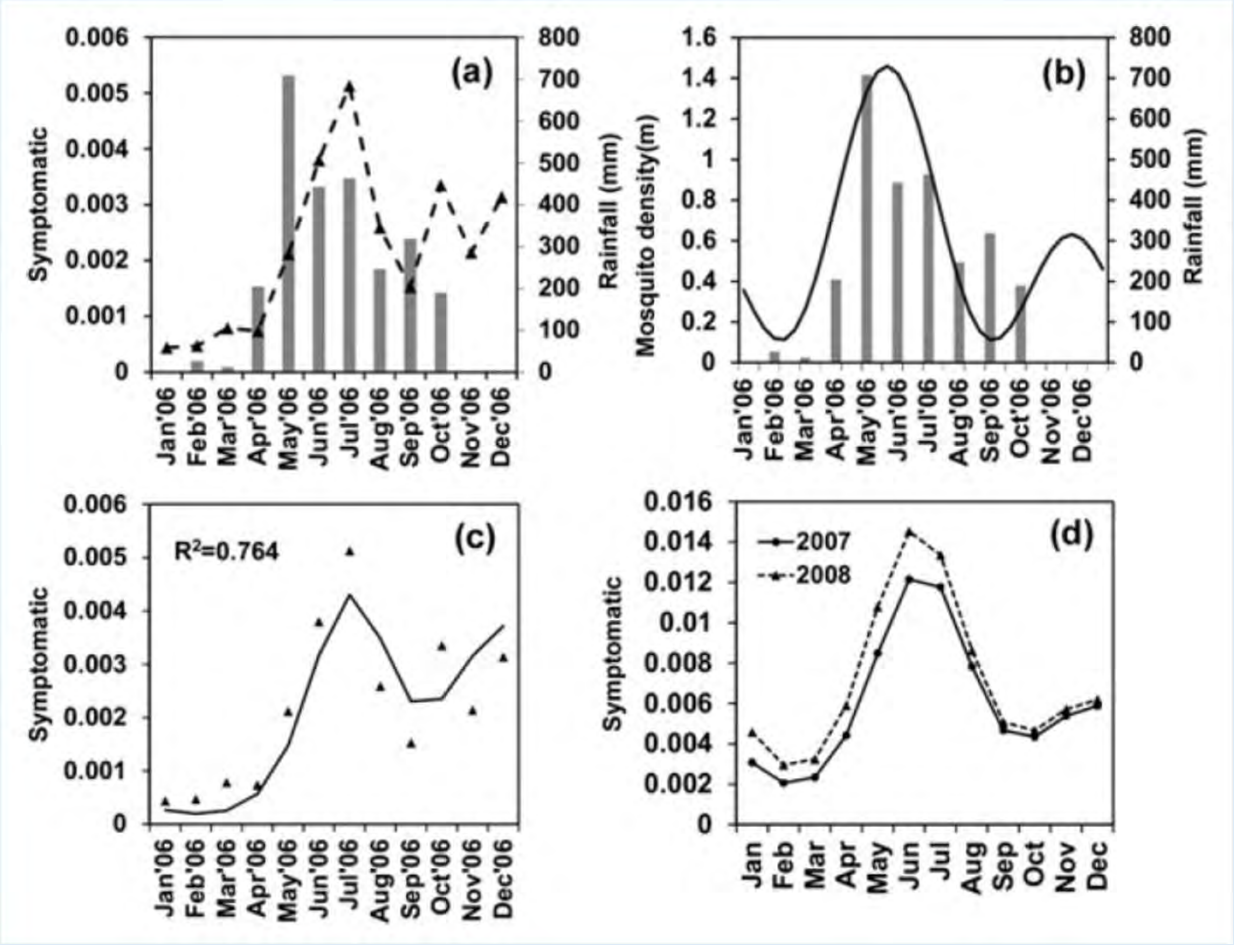
(b) For Mosquitoes (vectors/carriers)

$$\frac{dS_m}{dt} = \mu_m - \Lambda_m S_m - \mu_m S_m$$

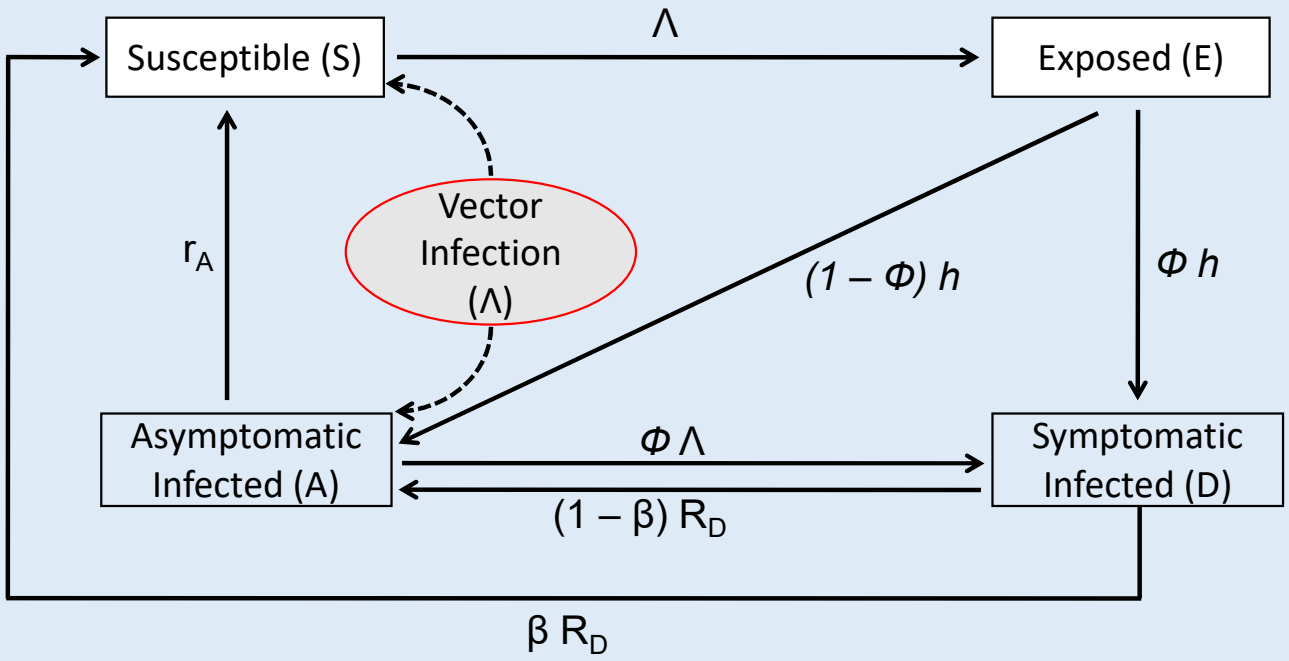
$$\frac{dE_m}{dt} = \Lambda_m S_m - \psi \Lambda_m (t-\tau) S_m (t-\tau) - \mu_m E_m$$

$$\frac{dI_m}{dt} = \psi \Lambda_m (t-\tau) S_m (t-\tau) - \mu_m I_m$$

Malaria cases in West Garo Hill district, Meghalaya, India in 2006 (Model projection)



Malaria model excluding mosquito population dynamics



Φ = susceptibility to clinical disease (depends on immunity)
h^{-1} = time duration in exposed class

r_A = recovery rate from asymptomatic to susceptible (depends on immunity)

R_D = recovery rate from symptomatic to susceptible class
β = proportion of diseased class that directly goes to susceptible class

Some reasons for changing force of infection (Λ)

- Stagnant water: (required for larval development of mosquito)
- Humidity: (life span of mosquito depends on humidity)
- Temperature: (number of days required for sporogony of parasites varies with temperature)

Introduction of environmental factors

$$\Lambda(\alpha)=[EIR\ b]\ (1- e^{-\alpha/\alpha_0})$$

$$\Downarrow$$

$$\Lambda(\alpha,t)=[EIR\ b\ Env(t)]\ (1- e^{-\alpha/\alpha_0})$$

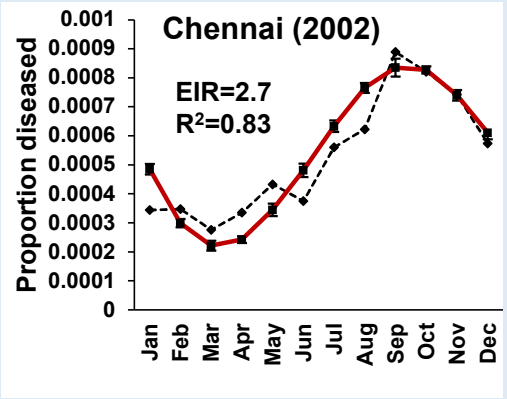
Env → average yearly variation + short random fluctuation

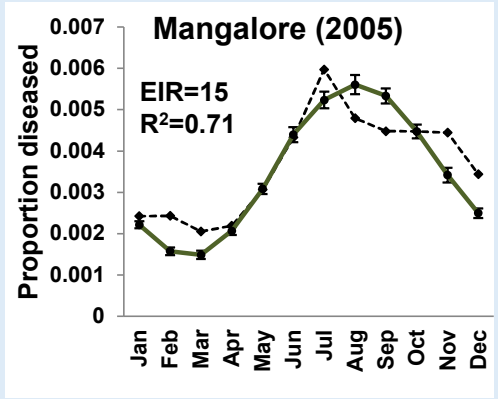
$$Env\ (t) = a_1\ e^{-\frac{(t+t_m)^2}{d_1}} + a_2\ e^{-\frac{(t-t_0)^2}{d_2}} + \xi$$

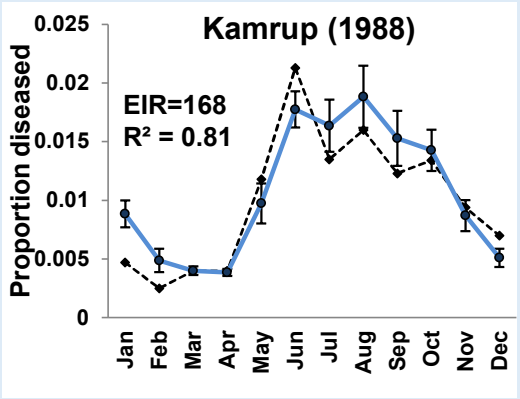
ξ = random noise chosen from scaled rainfall distribution

Malaria cases at different regions and Model result

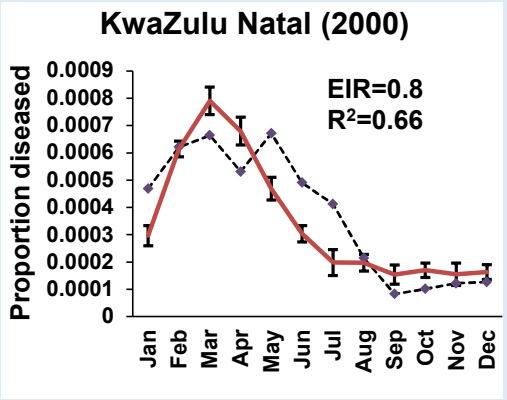
India

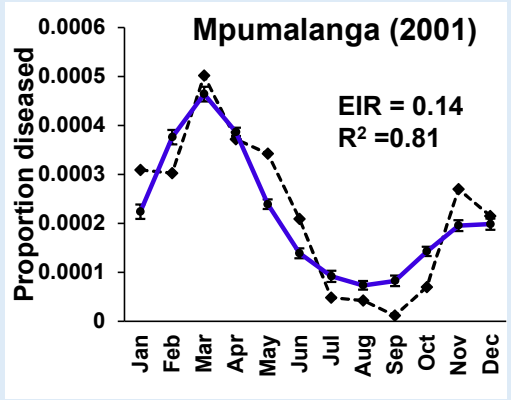


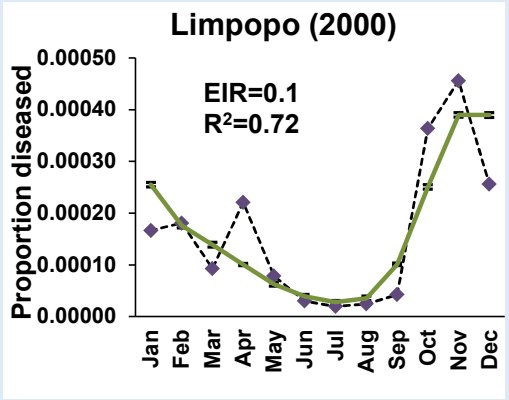




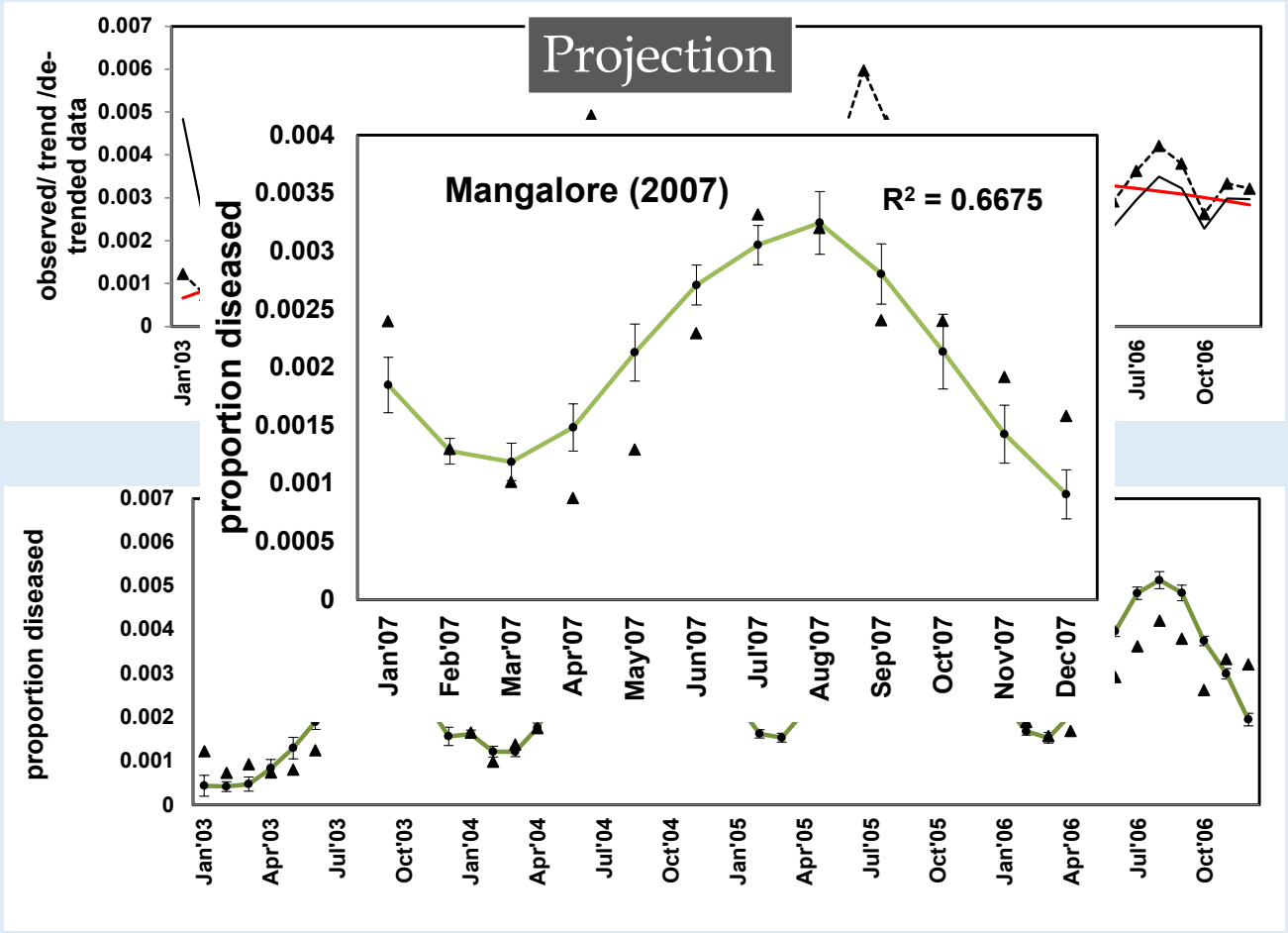
South Africa



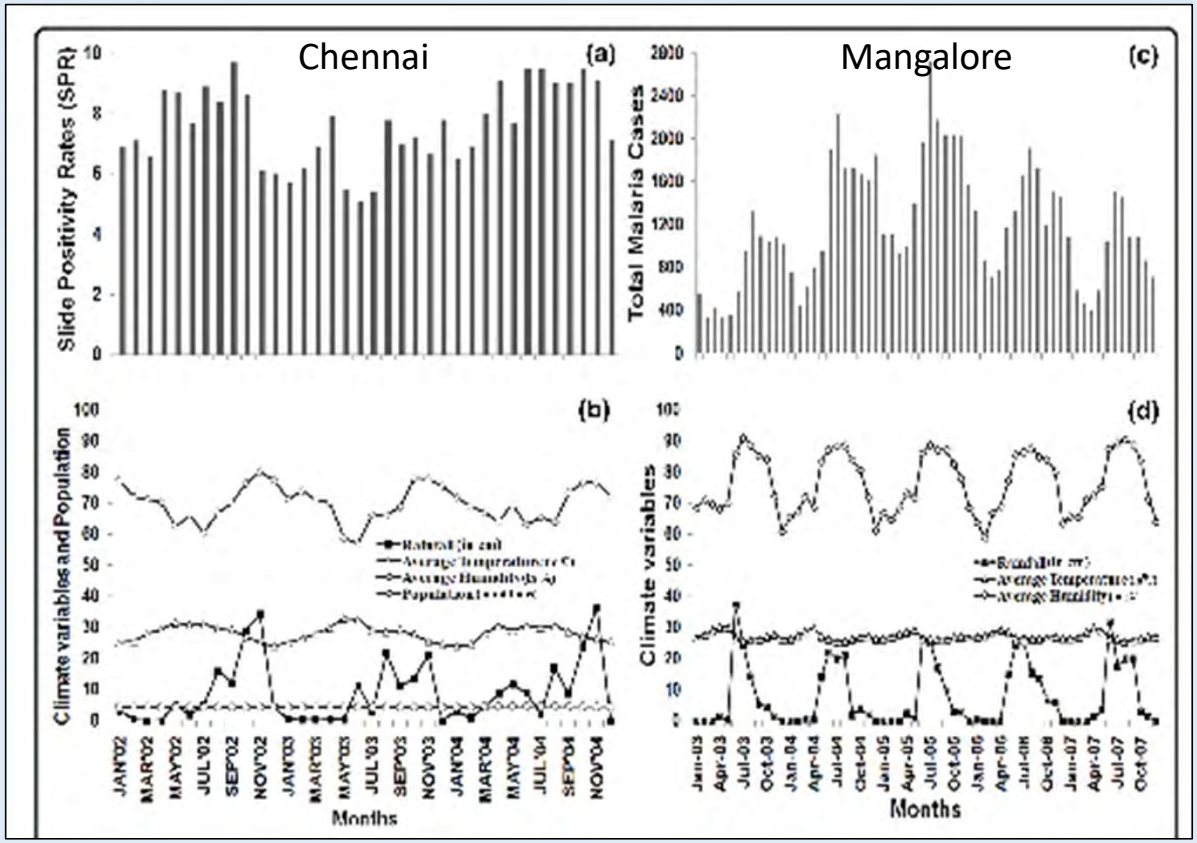




Long time series analysis: Mangalore, India (2003-2006)



Example of data-based *Statistical Modelling*



Malaria incidence and climate data.

(a) SPR (%) values in Chennai, during January 2002 - December 2004, and

(c) TMC values in Mangalore, during January 2003 - December 2007. The climate variables**, Rainfall (cm), Temperature (°C), Humidity (%), and Population (in millions)** are appropriately scaled to fit in the same plot

The Garki Project (1969 – 1976)

Aimed to study the effectiveness of various malaria control strategies, primarily focusing on vector control methods.

- A study conducted by the World Health Organization and Govt. of Nigeria in the Garki District, Nigeria.
- Malaria model was first systematically validated through the data generated through this Project*

- **Assessing Intervention Impact**: interventions like bed net distribution, indoor residual spraying, drug administration.
- **Targeting Interventions**: strategically targeted to maximize their effectiveness.
- **Evidence-based recommendations to policymakers**

*Ref. Dietz K, Molineaux L, Thomas A. A malaria model tested in the African savannah. *Bull WHO*, 1974, 50:347–357.

OpenMalaria
(A simulator of malaria epidemiology and control)

- Individual-based model of malaria transmission dynamics

- This model is an open-source tool for simulating the dynamics of malaria transmission and epidemiology, and the impact of interventions on health and economic outcomes.

Limitations of modelling approaches

Not a 'crystal ball'

- Model outcomes can depend sensitively on the assumptions
- Always important to know <u>why</u> a model suggests certain conclusions

- Better to think of a model as *bringing together* our best understanding of an epidemic (biology, epidemiology, existing care, etc), and
- *Projecting* their implications under given future scenarios

- 'Project' rather than 'predict'

Thank you