Modelling malaria transmission and control

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Objectives of this lecture

- **Become familiar with the Ross-MacDonald model for malaria transmission**
- **Appreciate the key features of malaria epidemiology and how these affect transmission dynamics**
- **Understand the basic reproductive ratio of malaria and how its components are linked to control**

Ronald Ross

* 1857, Almora, India
† 1932, London

1897: Malaria in mosquito
1902: Nobel Prize

"...With tears and toiling breath,
I find thy cunning seeds,
O million-murdering Death."

Ronald Ross

A priori method

"we assume a knowledge of the causes, construct our differential equations on that supposition, follow up the logical consequences, and finally test the calculated results by comparing them with the observed statistics."

A posteriori method

"we commence with observed statistics, endeavour to fit analytical laws to them, and so work backwards to the underlying cause."

Ross (1916-1917)
An application of the theory of probabilities to the study of a priori pathometry. I-III
Philos Trans R Soc Lond A

George MacDonald

* 1903, Sheffield
† 1967, London

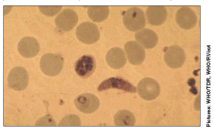
An overview of malaria

- **Malaria parasite = the protozoan *Plasmodium***
- **5 species which infect humans:**
  - *P. falciparum:* most dangerous (cerebral malaria/severe anaemia)
  - *P. vivax:* milder disease but still significant (relapsing)
  - *P. ovale* (relapsing), *P. malariae:* rarer, mostly benign disease
  - *P. knowlesi:* zoonosis from monkeys (Singh & Cox-Singh 2004)
- **Ancient disease, ~50,000-100,000 years old**
  - Strong force in human evolution

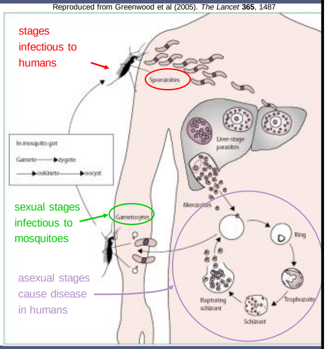
Lifecycle of the malaria parasite

- *Anopheles* mosquitoes
  - around 70 / 422 species are able to transmit the parasite

position. Below: Microscopist's view of Plasmodium Falciparum.



Reproduced from Greenwood et al (2005). *The Lancet* **365**, 1487



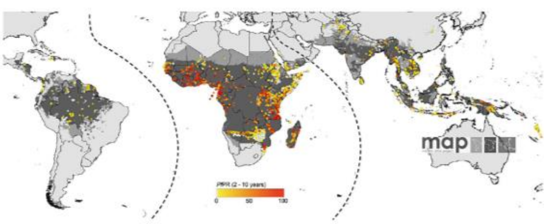
Disease burden

- *P. falciparum:*
  - Uncomplicated clinical episodes (fever, headache, nausea/vomiting, weakness)
  - Severe disease: mortality rate ~15-20%
- **Annually:**
  - 250 million disease episodes
  - ~ 0.5 million deaths
- **Medium to high transmission settings: ~4% children die of malaria before age 5yrs.**
- **Humans develop only partial immunity**

WHO malaria factfile

Worldwide distribution of *Pf* malaria

Constructed using prevalence surveys and climate data



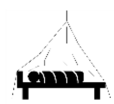
Hay et al. 2009 PLoS Med

stable transmission

unstable transmission

Malaria control interventions

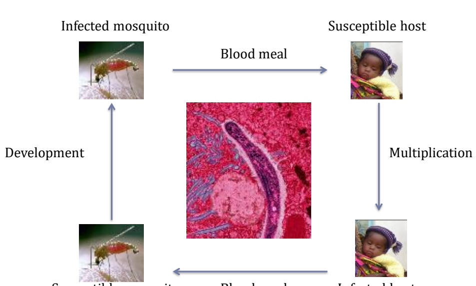
- **Targeting vectors:**
  - Indoor residual spraying
  - Insecticide treated bednets
  - Larval control



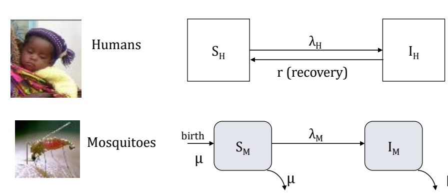
- **Targeting the parasites in humans:**
  - Antimalarial treatment of symptomatic cases
  - Prophylaxis (intermittent preventive treatment, post-treatment prophylaxis)
  - Mass treatment
  - Vaccines?

Ross-MacDonald model

Pathogen lifecycle in the Ross-MacDonald model



Ross-MacDonald model



- **Ronald Ross, early 1900's, India**
  - Refined by George Macdonald (1950s, a few metres from this room)

Equations of a basic Ross-MacDonald model

$$\begin{cases} \frac{dS_H}{dt} = rI_H - \lambda_H S_H \\ \frac{dI_H}{dt} = \lambda_H S_H - rI_H \end{cases}$$

λ_H: force of infection on humans
r: recovery rate from Malaria

S_H, I_H, S_M, I_M are the proportions of humans/mosquitoes that are susceptible/infected, i.e., I_H is the prevalence of infection in humans.

$$\begin{cases} \frac{dS_M}{dt} = \mu - \lambda_M S_M - \mu S_M \\ \frac{dI_M}{dt} = \lambda_M S_M - \mu I_M \end{cases}$$

λ_M: force of infection on mosquitoes
μ: mosquito death rate

Force of infection: humans

λ_H

From the viewpoint of a susceptible human:
The rate at which I'll get infected with malaria

= (rate at which infected mosquitoes bite me and transmit infection)

= (rate at which I get bitten by mosquitoes) ·
(proportion of mosquitoes that are infected) ·
(probability that I get infected when bitten by an infected mosquito)

= (rate at which one mosquito bites) · (number of mosquitoes) ·
(probability that a biting mosquito chooses me) ·
(proportion of mosquitoes that are infected) ·
(probability that I get infected when bitten by an infected mosquito)

Force of infection: humans

λ_H

From the viewpoint of a susceptible human:
The rate at which I'll get infected with malaria

$$\lambda_H = aM\frac{1}{H}I_M b$$

= (rate at which one mosquito bites) · (number of mosquitoes) ·
(probability that a biting mosquito chooses me) ·
(proportion of mosquitoes that are infected) ·
(probability that I get infected when bitten by an infected mosquito)

Force of infection: humans

Entomological inoculation rate (EIR)

$$\lambda_H = amI_M b$$

Where

- a = biting rate
  (number of bites taken on humans per mosquito per time unit)
- m = number of mosquitoes per human (m=M/H)
- I_M = prevalence of infection in mosquitoes
- b = probability that a bite by an infectious mosquito leads to successful mosquito-to-human transmission

Force of infection on humans depends on prevalence in mosquitoes

Equations of a basic Ross-MacDonald model

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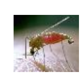
λ_M: force of infection on mosquitoes
μ: mosquito death rate

Force of infection: mosquitoes

λ_M

From the viewpoint of a susceptible mosquito:
The rate at which I'll get infected with malaria



= (rate at which I bite infectious humans and become infected)

= (rate at which I bite humans) ·
(probability that a human is infected) ·
(probability that I become infected through the bite)

$$\lambda_M = aI_H c$$

Force of infection: mosquitoes

$$\lambda_M = acI_H$$

Where

- a = biting rate (as above)
- c = probability that a bite taken on infectious human leads to successful human-to-mosquito transmission
- I_H = prevalence of infectious humans

Force of infection on mosquitoes depends on prevalence in humans

Equations of a basic Ross-MacDonald model

$$\begin{cases} \dfrac{dS_H}{dt} = rI_H - \lambda_H S_H \\ \dfrac{dI_H}{dt} = \lambda_H S_H - rI_H \end{cases}$$

S_H, I_H, S_M, I_M are the proportions of humans/mosquitoes that are susceptible/infected, i.e., I_H is the prevalence of infection in humans.

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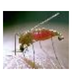
Equations of a basic Ross-MacDonald model

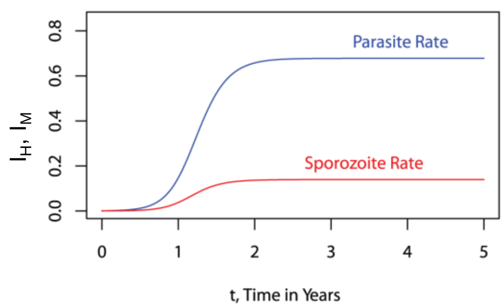
$$\begin{cases} \dfrac{dS_H}{dt} = rI_H - amI_M bS_H \\ \dfrac{dI_H}{dt} = amI_M bS_H - rI_H \end{cases}$$

S_H, I_H, S_M, I_M are the proportions of humans/mosquitoes that are susceptible/infected, i.e., I_H is the prevalence of infection in humans.

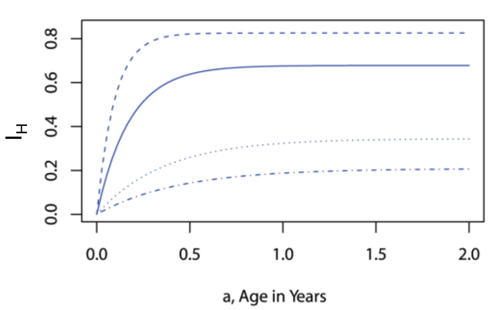


$$\begin{cases} \dfrac{dS_M}{dt} = \mu - acI_H S_M - \mu S_M \\ \dfrac{dI_M}{dt} = acI_H S_M - \mu I_M \end{cases}$$

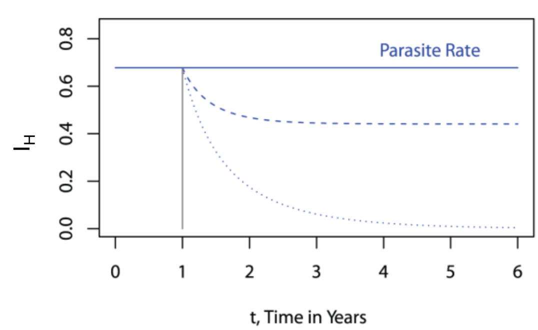
Model dynamics



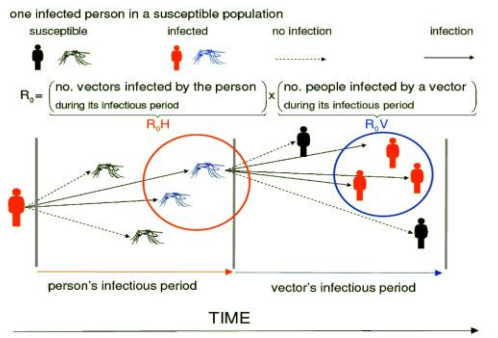
Model age at infection



Model impact of control



The basic reproductive ratio



Modelling malaria transmission and control

Heuristic derivation of R_0

HUMAN TO MOSQUITO: Number of new infections in mosquitoes caused by one infectious human

How many bites on one human per day?
= ma
What proportion of those bites will result in mosquito infection?
= c
How many days does a human remain infectious?
= 1/r

$$R_0 = \underbrace{\frac{mac}{r}}_{} \cdot \underbrace{\frac{ab}{m}}_{} = \frac{ma^2bc}{rm}$$

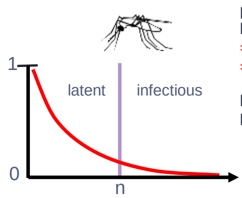
MOSQUITO TO HUMAN: Number of new infections in humans caused by one infectious mosquito

How many bites does a mosquito take per day?
= a
What proportion of those bites will result in human infection?
= b
How many days does a mosquito remain infectious?
= 1/μ

Modelling malaria transmission and control

Mosquito latent period

assuming constant mortality rate μ:



probability of surviving after infection

time since infection

probability of surviving after latent period (n days)
$= e^{-\mu n}$
$= p^n$

$p = e^{-\mu}$
prob. of surviving a day

Modelling malaria transmission and control

Basic reproductive number, including latent period

effective contact rates

mosquito latent period

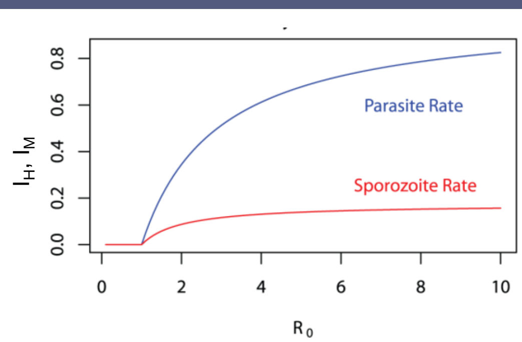
$$R_0 = \frac{ma^2bcp^n}{r\mu}$$

durations of infection

Without latent period: $R_0 = \dfrac{ma^2bc}{rm}$

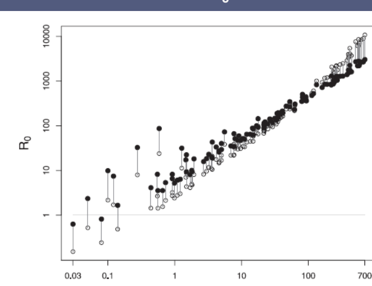
Modelling malaria transmission and control

Model steady states



Modelling malaria transmission and control

What is the R_0 for malaria?



Smith, D (2007) PLoS Biol

Figure 2. R_0 Estimates for 121 African Populations

Compare with e.g. flu, chickenpox, measles where R_0 ~2-14

Modelling malaria transmission and control

Using R_0 to assess control

Vaccination or prophylaxis to block infection

Larval control

$$R_0 = m\frac{a^2}{m}p^n bc\frac{1}{r}$$

Treating infection

Drugs or vaccines that block transmission

Adult vector control

$$R_0 = \frac{ma^2bcp^n}{rm}$$

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Smith DL et al. (2012).
Ross, Macdonald, and a Theory for the Dynamics and Control of Mosquito-Transmitted Pathogens. PLoS Pathog 8(4): e1002588. http://dx.doi.org/10.1371/journal.ppat.1002588