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Structured population models

Malaria along the endemicity gradient

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4000 years of mathematics

Arithmetics | Pure mathematics | Renaissance

2000 BC | **1000 BC** | **1000 AD** | **2000 AD**

Babylon
Egipt
India
China

Greece

Arabia

Europe

First mathematical model for malaria transmission (Ross)

Ronald Ross
1857-1932

Discovery mosquitoes transmit malaria
(Ross – Nobel Prize 1902)

China | *Rome* | *China*

2000 AD | **1000 AD** | **1000 BC** | **2000 BC**

Discovery of the parasite in blood of patient (Laveran – Nobel Prize 1907)

Medicinal plants

Association between malaria and swamps

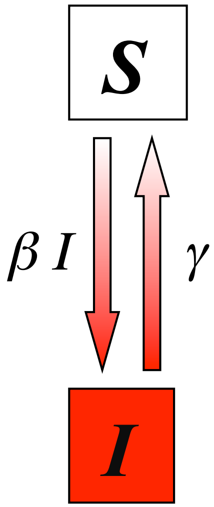
First reports of malaria symptoms

DDT
Global Eradication Campaign
1955-1978

4000 years of malaria

SIS model

Appropriate for infections that induce no effective immunity (e.g. malaria).



$$\frac{dS}{dt} = -\beta I S + \gamma I$$

$$\frac{dI}{dt} = \beta I S - \gamma I$$

β – transmission coefficient

γ – recovery rate

SIS model

As $S + I = 1$, the model is one dimensional and represented by the equation

$$\frac{dI}{dt} = \beta I(1-I) - \gamma I$$

This is a type of growth law known as *logistic growth*, and it appears commonly in population dynamics models in the form

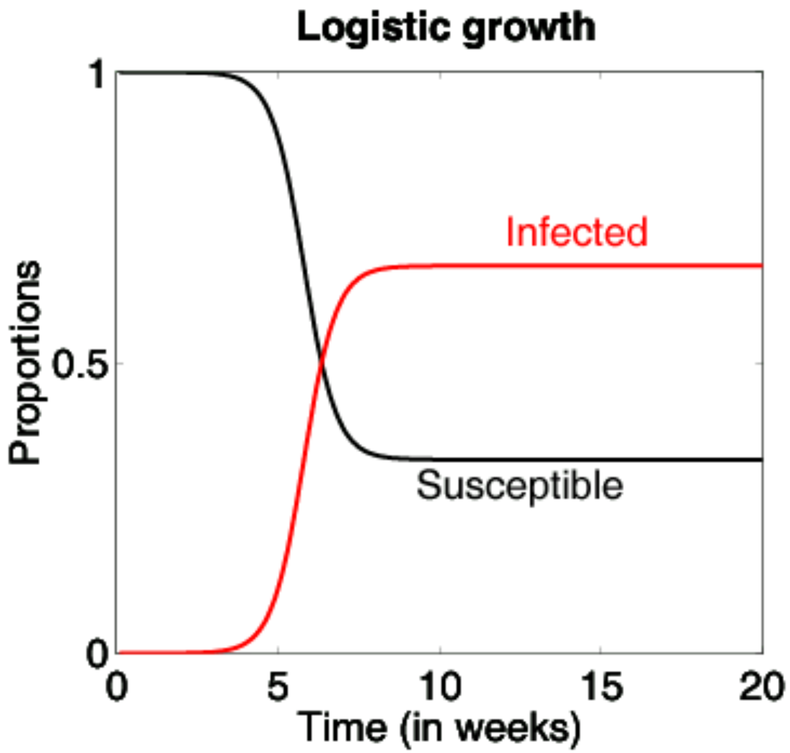
$$\frac{dI}{dt} = (\beta-\gamma) \left(1-\frac{I}{1-\gamma/\beta}\right) I$$

The solution can be obtained analytically

$$I(t) = \frac{I(0) \left(1-\gamma/\beta\right)}{I(0) + \left(1-\gamma/\beta-I(0)\right) e^{-(\beta-\gamma)t}}$$

SIS model

Given an initial condition, $I(0) = 10^{-6}$, the proportion of infected individuals grows as



Steady states:

1. Disease free equilibrium

$$I = 0, \quad S = 1$$

2. Endemic equilibrium

$$I = 1 - \frac{\gamma}{\beta}, \quad S = \frac{\gamma}{\beta}$$

Parameters: $\beta = 3$, $\gamma = 1$

Basic reproduction number, R_0

The basic reproduction number is defined as the

average number of secondary infections produced by an average infectious individual, during its entire infectious period, in a totally susceptible population

The basic reproduction number is calculated as

R_0 = (rate of transmission from an infectious individual) x (infectious period)

$$= \beta \times (1 / \gamma) = \beta / \gamma$$

Disease	R_0
Smallpox	4
Measles	17
Rubella (England and Wales) Rubella (Gambia)	6 15
Malaria	?

R_0 is a nondimensional number, and depends on both the environment (physical and social) and the disease.

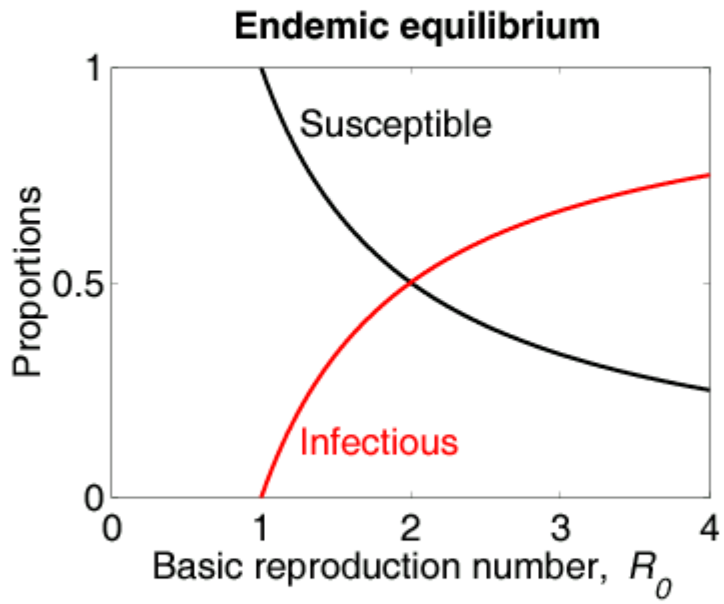
Nondimensional SIS model

If time is measured in units of infectious period, $1/\gamma$, then the SIS model becomes

$$\frac{dI}{dt} = R_0(1-I)I - I$$
$$= R_0\left(1-\frac{1}{R_0}-I\right)I$$

The endemic equilibrium is rewritten as

$$I = 1-\frac{1}{R_0}, \quad S = \frac{1}{R_0}$$



Epidemic threshold: Infection can invade a totally susceptible population if and only if

$$R_0 > 1$$

Heterogeneity in individual susceptibility

Natural exposure model:

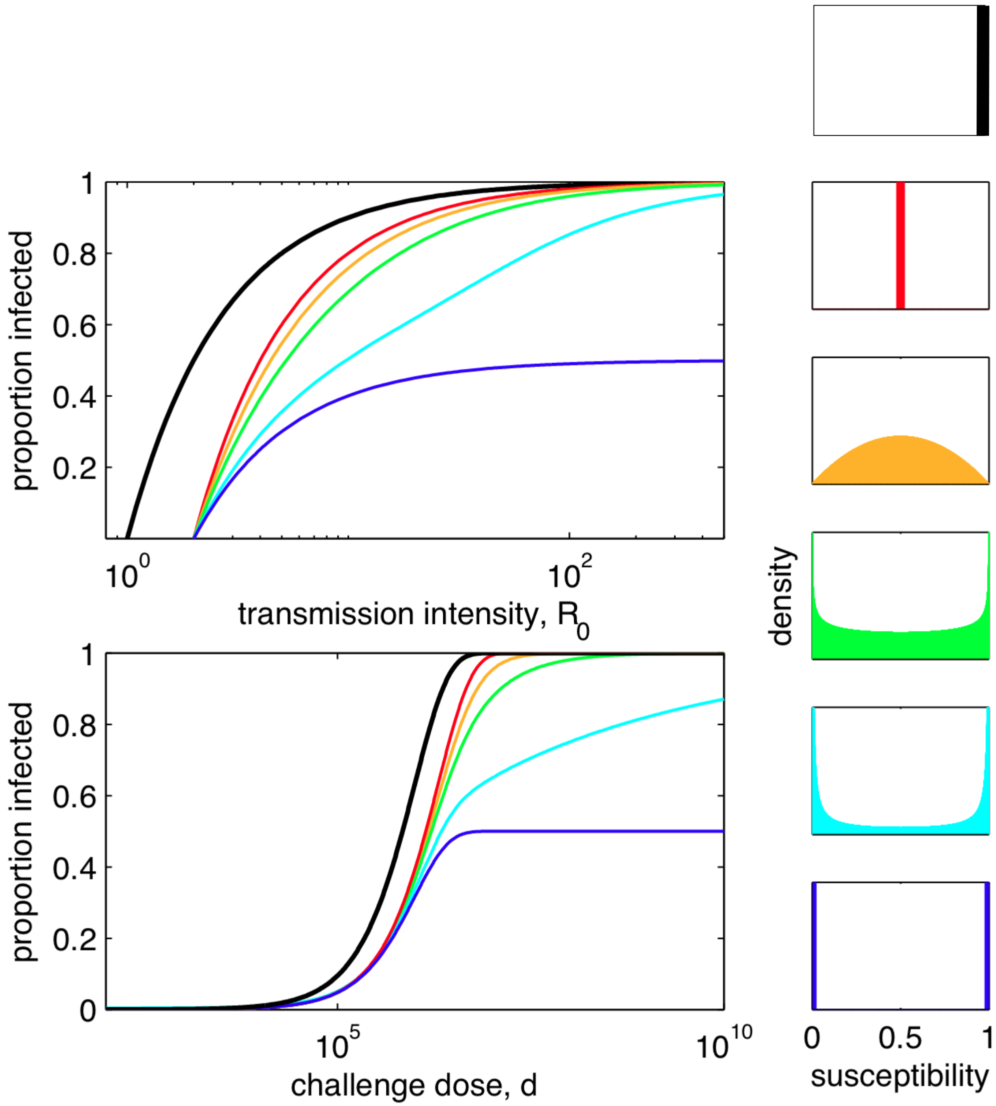
$$\frac{dS(x)}{dt} = q(x)\mu - x\lambda S(x) + \gamma I(x),$$

$$\frac{dI(x)}{dt} = x\lambda S(x) - (\gamma + \mu)I(x),$$

$$\lambda = \beta \int_0^1 I(x)dx.$$

Experimental challenge model:

$$I = 1 - \int_0^1 e^{-xpd} q(x)dx.$$



Gomes MGM, Lipsitch M, Wargo AR, Kurath G, Rebelo C, Medley GF, Coutinho A 2014 A missing dimension in measures of vaccination impacts. PLOS Pathog 10: e1003849.

Inference from multi-population studies

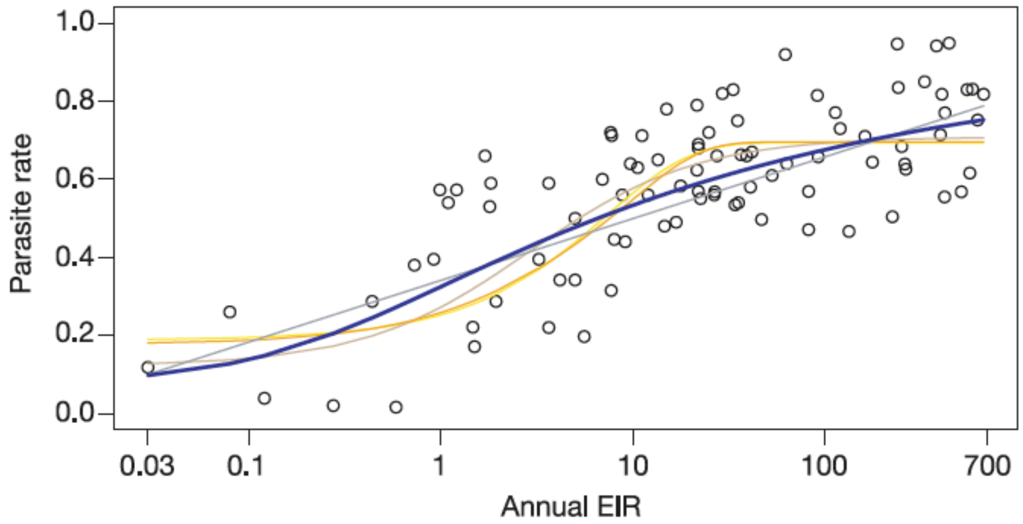
Heterogeneous susceptibility in malaria:

$$\frac{dS(x)}{dt} = q(x)\mu - x\lambda S(x) + f(x\lambda,\gamma)I(x),$$

$$\frac{dI(x)}{dt} = x\lambda S(x) - \left(f(x\lambda,\gamma) + \mu\right)I(x),$$

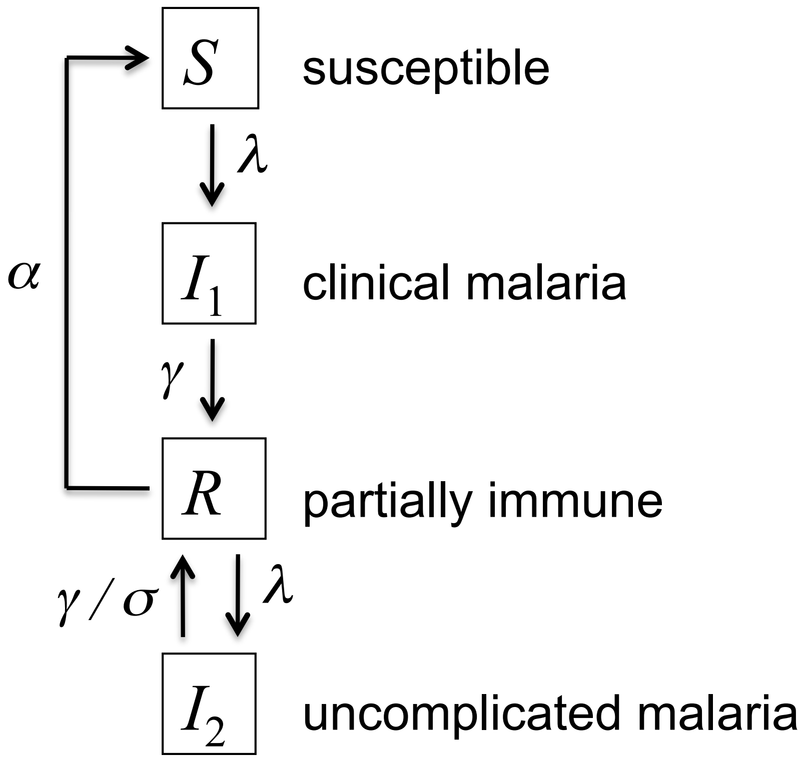
$$\lambda = \beta\int_0^1 I(x)dx.$$

Fitting to parasite rates from 90 communities



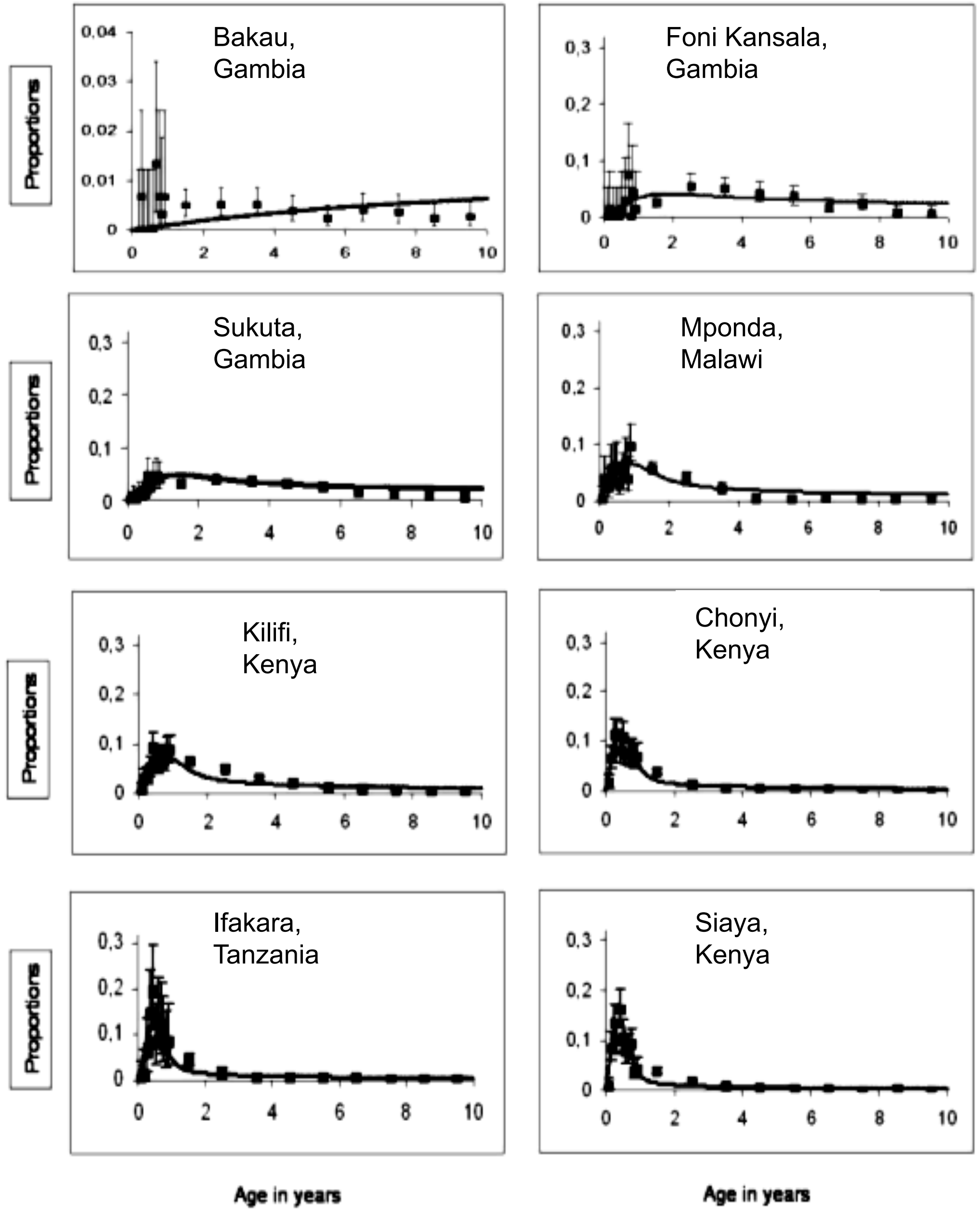
Smith DL, Dushoff J, Snow RW, Hay SI 2005 The entomological inoculation rate and Plasmodium falciparum infection in African children. Nature 438: 492.

Fitting age profiles of clinical malaria



Force of infection:

$$\lambda = \beta\left(I_1 + I_2\right)$$



Aguas R, White LJ, Snow RW, Gomes MGM (2008) Prospects for malaria eradication in sub-Saharan Africa. PLoS ONE 3: e1767.

System of partial differential equations (SIRI-like for malaria)

$$\frac{\partial S}{\partial t} + \frac{\partial S}{\partial a} = \alpha R - S(\lambda + \mu)$$

$$\frac{\partial I_1}{\partial t} + \frac{\partial I_1}{\partial a} = \lambda S - I_1(\gamma + \mu)$$

$$\frac{\partial R}{\partial t} + \frac{\partial R}{\partial a} = \gamma\left(I_1 + \frac{1}{\sigma} I_2\right) - R(\lambda + \alpha + \mu)$$

$$\frac{\partial I_2}{\partial t} + \frac{\partial I_2}{\partial a} = \lambda R - I_2\left(\frac{\gamma}{\sigma} + \mu\right)$$

Boundary conditions:

$$S(t,0) = \mu \qquad R(t,0) = I_1(t,0) = I_2(t,0) = 0$$

Model fitting and parameter estimation for malaria

Global parameters:

average duration of clinical malaria ~ 1 month
[$\gamma = 14.12 \text{ yr}^{-1}$]

average duration of uncomplicated malaria ~ 6 month
[$\sigma = 6.33$]

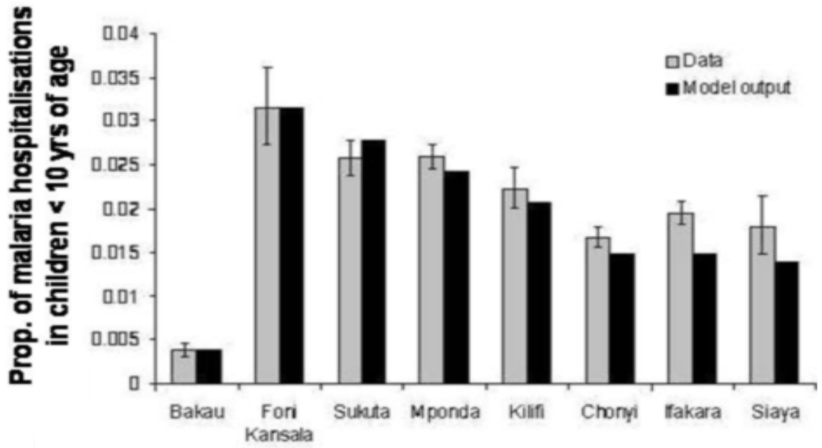
average duration of partial immunity ~ 12 month
[$\alpha = 1.07 \text{ yr}^{-1}$]

Local parameters:

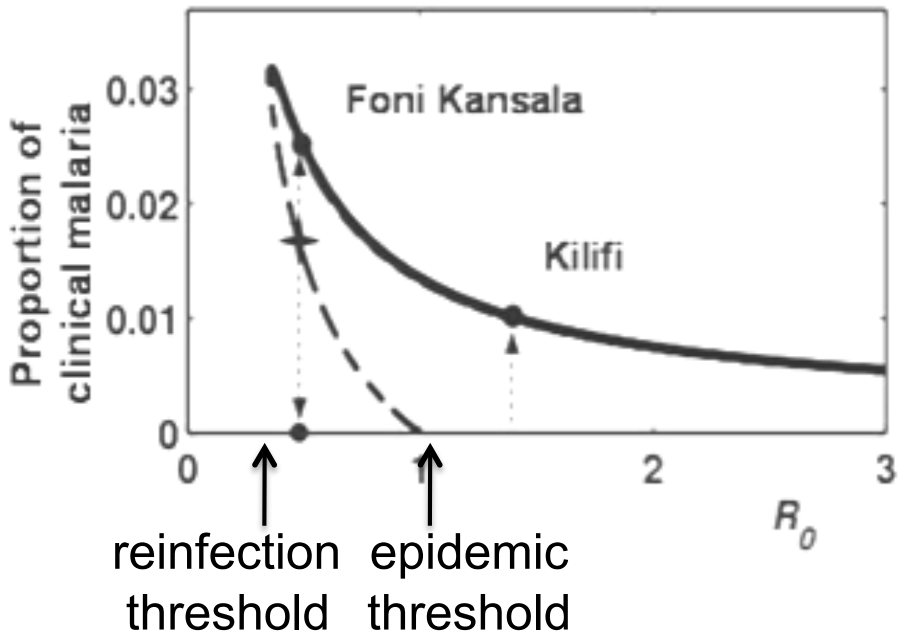
Region	λ_0 (95% c.i.)	Λ	β	R_0
Bakau	0.14 (−0.09–0.37)	0.12	*NA*	*NA*
Foni Kansala	4.86 (4.63–5.09)	4.26	6.99	0.49
Sukuta	6.70 (6.47–6.93)	5.87	8.48	0.60
Mponda	14.96 (14.73–15.19)	13.10	15.52	1.10
Kilifi	19.87 (19.64–20.10)	17.40	19.77	1.40
Chonyi	47.21 (46.98–47.44)	41.35	43.66	3.08
Ifakara	50.16 (49.93–50.40)	43.94	46.25	3.27
Siaya	71.02 (70.79–71.25)	62.21	64.53	4.56

$$R_0 = \beta/\gamma$$

Multi-population malaria trends

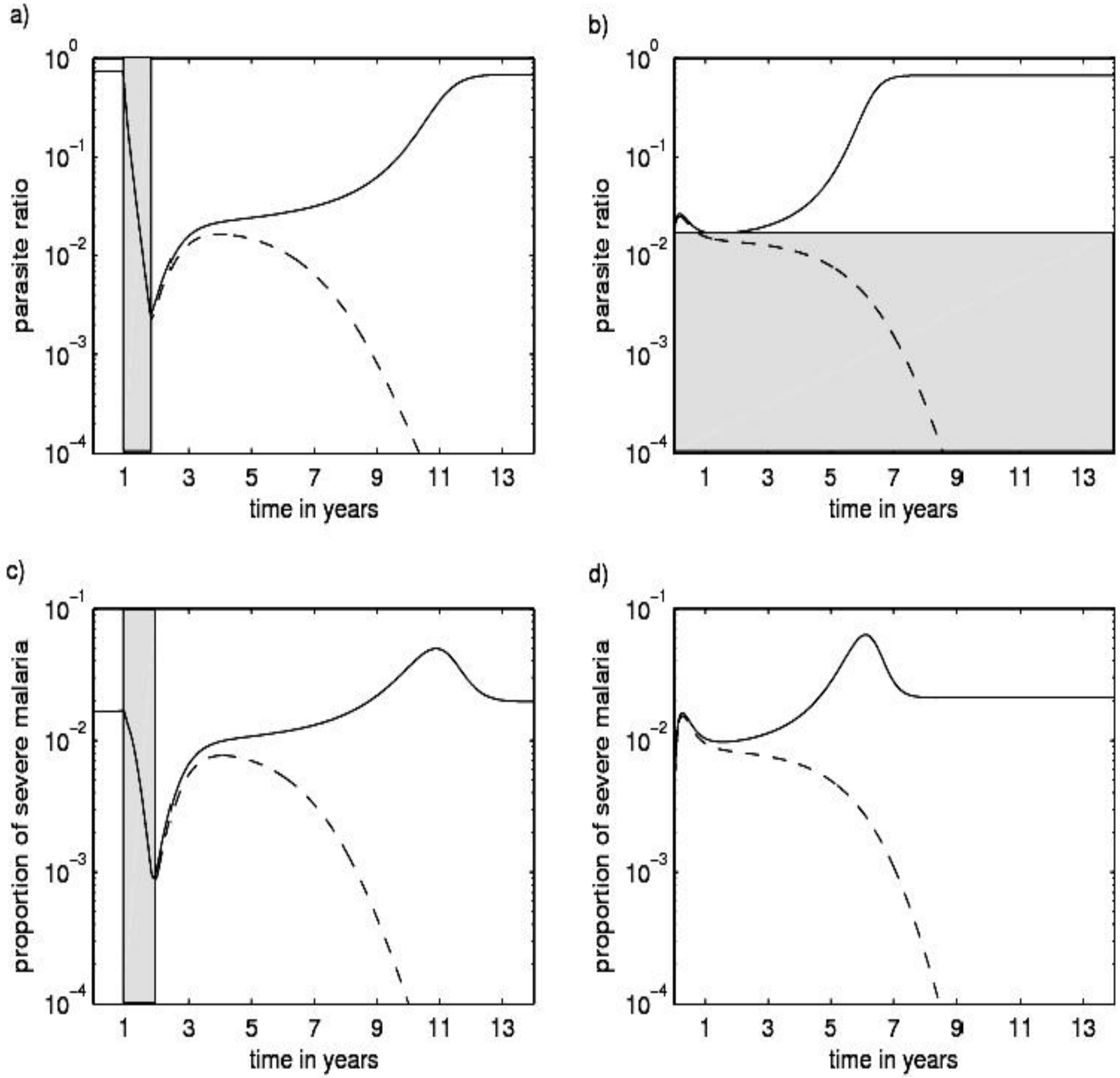


Decreasing disease with increasing transmission



Sustainable transmission for $R_0 < 1$ (hysteresis)

Bistable regime with implications for malaria elimination and resurgence



Chiyata C, Tatem AJ, Cohen JM, Gething PW, Johnston G, Gosling R, Laxminarayan R, Hay SI, Smith DL 2013 The stability of malaria elimination. Science 339: 909.