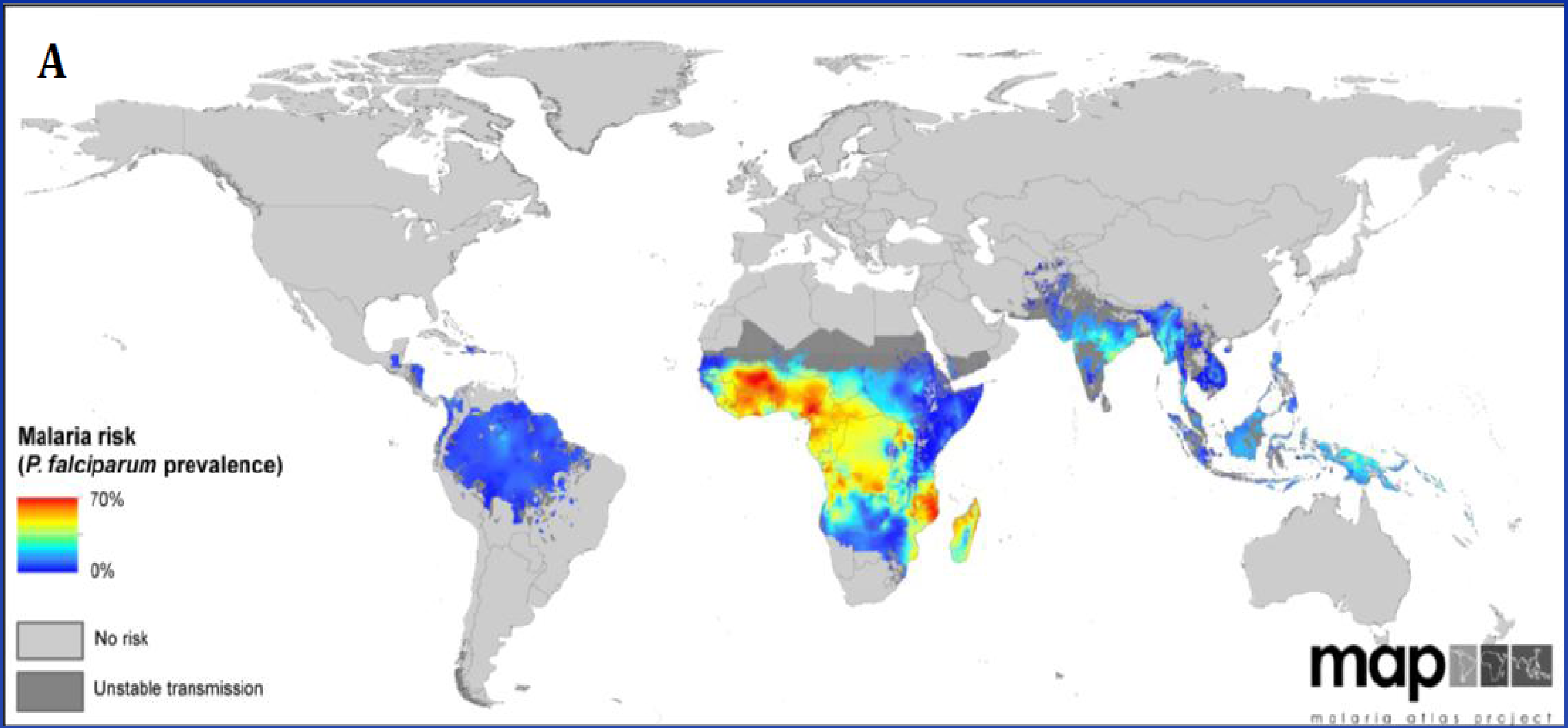
Malaria Risk Maps:

Quantifying Risk from Endemic Prevalence

Eduardo Massad
University of São Paulo, Brazil
edmassad@usp.br



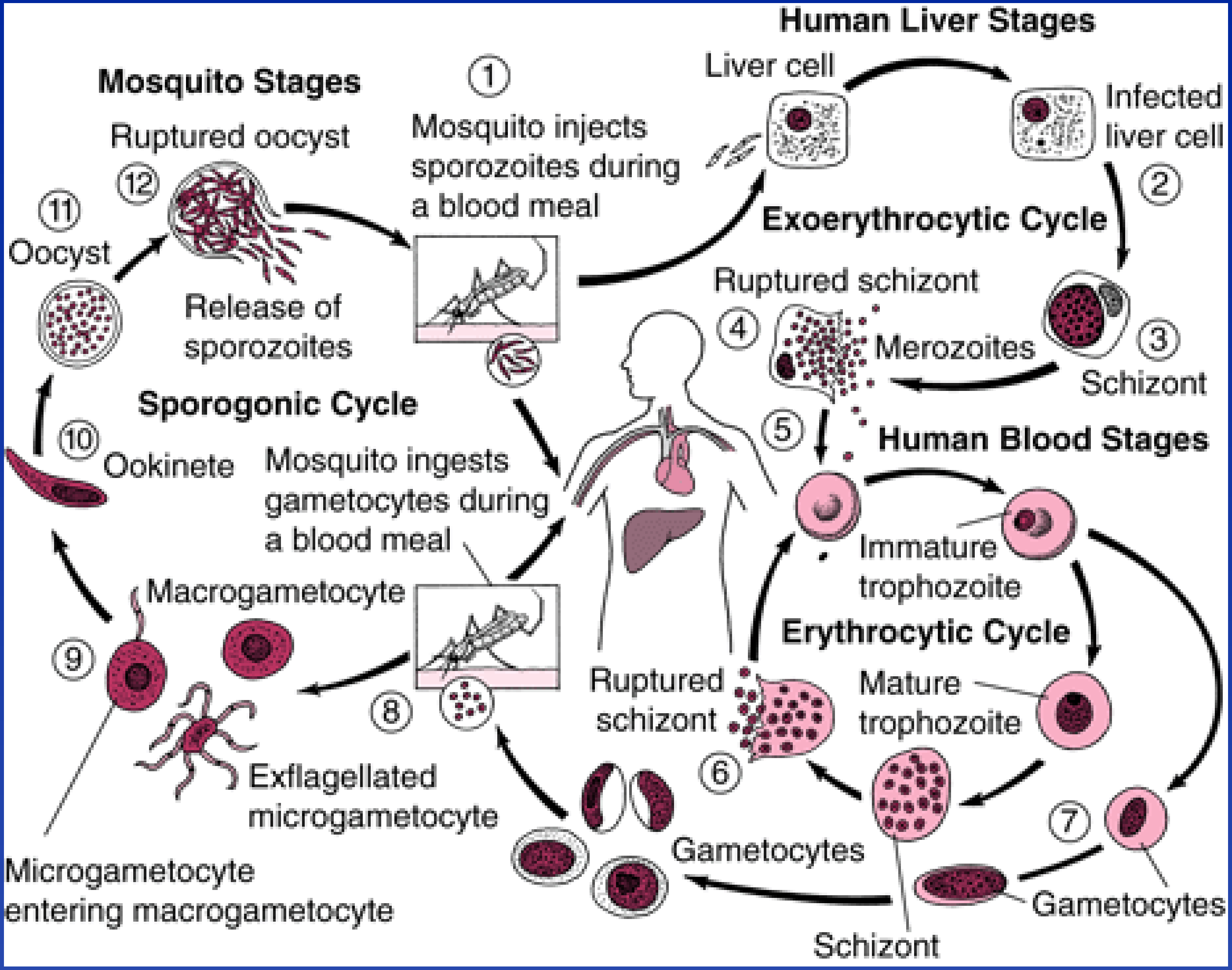
Credit: Malaria Atlas Project, University of Oxford

Inverse problems

An inverse problem is a general framework that is used to convert observed measurements into information about a physical object or system that we are interested in.

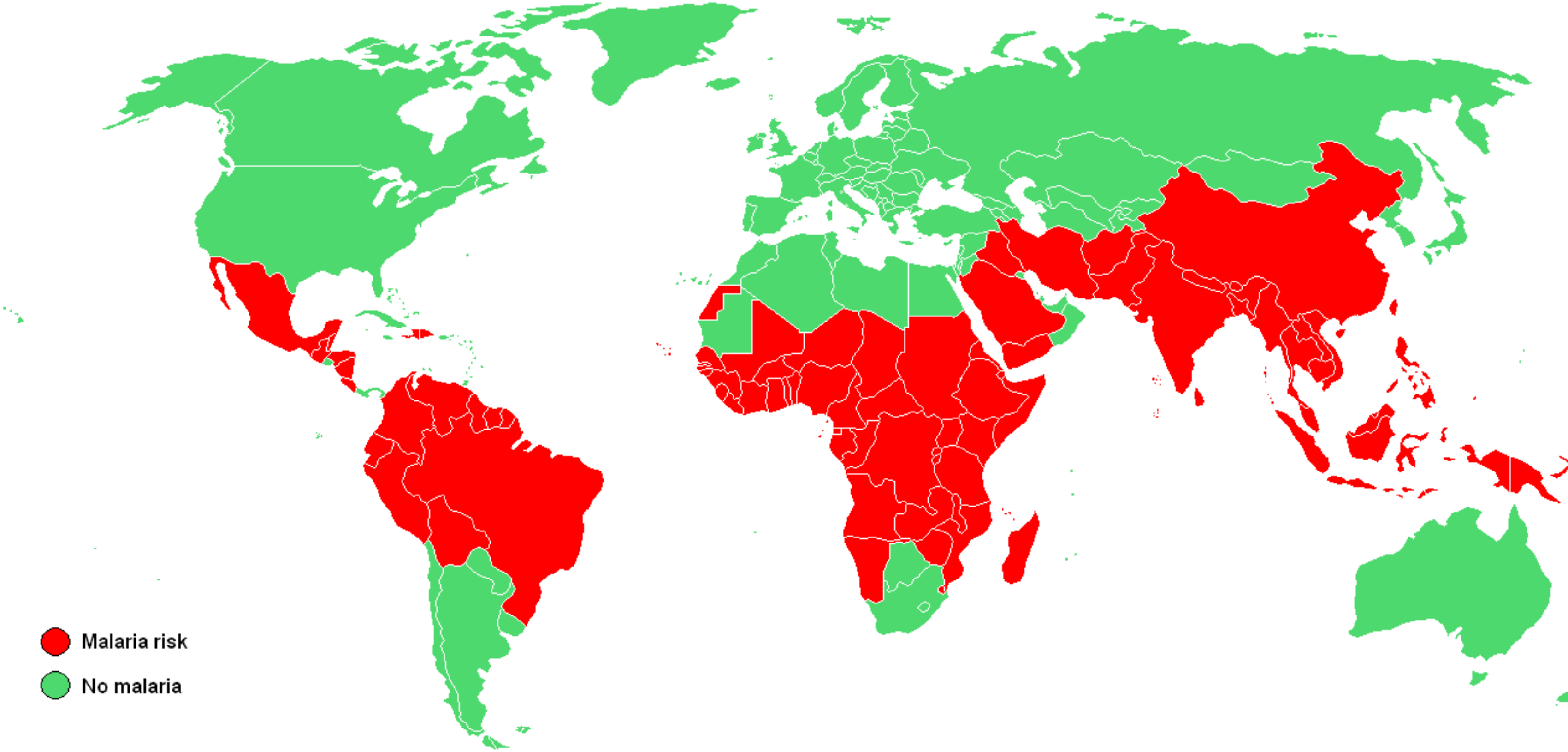
http://www.scienceworldreport.com/articles/4012/20121012/cell-phones-used-to-control-spread-of-malaria.htm

http://english.prolasa.org/malaria-prevention/



http://www.merckmanuals.com/professional/infectious_diseases/extraintestinal_protozoa/malaria.html

http://www.coolinfographics.com/blog/tag/airplane



http://en.wikipedia.org/wiki/File:Malaria_map.PNG

FIGURE 1. Global distribution (Robinson projection) of dominant or potentially important malaria vectors.

http://www.medicalecology.org/diseases/malaria/malaria.htm

risk (Oxford English Dictionary) Pronunciation: /risk/

Definition of risk

noun

•**a situation involving exposure to danger:** ***flouting the law was too much of a risk all outdoor activities carry an element of risk***

•***[in singular]*** **the possibility that something unpleasant or unwelcome will happen:** ***reduce the risk of heart disease [as modifier]: a high consumption of caffeine was suggested as a risk factor for loss of bone mass***

•***[usually in singular with adjective]*** **a person or thing regarded as likely to turn out well or badly, as specified, in a particular context or respect:** ***Western banks regarded Romania as a good risk***

•***[with adjective]*** **a person or thing regarded as a threat or likely source of danger:** ***she's a security risk gloss paint can burn strongly and pose a fire risk***

•**(usually risks) a possibility of harm or damage against which something is insured.**

•**the possibility of financial loss:** ***[as modifier]: project finance is essentially an exercise in risk management***

Risk = Likelihood x Impact

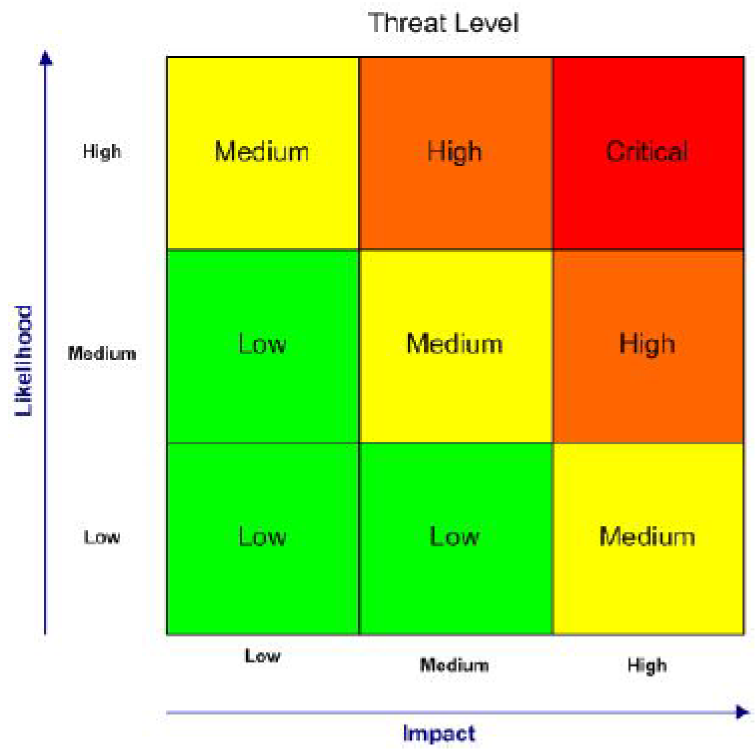
Assessment of the Risk involved in this Research Protocol:

NO RISK	☐		
MINIMUM RISK	☐	MEDIUM RISK	☐
LOW RISK	☐	HIGH RISK	☐

Assessment of the Risk involved in this Research Protocol:

NO RISK	☐		
MINIMUM RISK	☐	MEDIUM RISK	☐
LOW RISK	☐	HIGH RISK	☐

Risk Heat Maps and Profiles



Risk = Likelihood x Impact

http://www.agenarisk.com/resources/Using_Risk_Maps.pdf

"Relax pal, I'm only Micromort.
Wait till you see Big Mort."

http://www.prospectmagazine.co.uk/magazine/in-fact-20/

Table 1-1 Risks that Increase Chance of Death by 0.000001 (One in One Million, or 10^{-6})

Smoking 1.4 cigarettes	Cancer, heart disease
Drinking 1/2 liter of wine	Cirrhosis of the liver
Spending 1 hour in a coal mine	Black lung disease
Spending 3 hours in a coal mine	Accident
Living 2 days in New York or Boston	Air pollution
Traveling 6 minutes by canoe	Accident
Traveling 10 miles by bicycle	Accident
Traveling 300 miles by car	Accident
Flying 1000 miles by jet	Accident
Flying 6000 miles by jet	Cancer caused by cosmic radiation
Living 2 months in Denver	Cancer caused by cosmic radiation
Living 2 months in average stone or brick building	Cancer caused by natural radiation
One chest X-ray taken in a good hospital	Cancer caused by radiation
Living 2 months with a cigarette smoker	Cancer, heart disease
Eating 40 tablespoons of peanut butter	Liver cancer caused by aflatoxin B
Drinking Miami drinking water for 1 year	Cancer caused by chloroform
Drinking 30 12 oz. cans of diet soda	Cancer caused by saccharin
Living 5 years at site boundary of a typical nuclear power plant in the open	Cancer caused by radiation
Drinking 1000 24 oz. soft drinks from recently banned plastic bottles	Cancer from acrylonitrile monomer
Living 20 years near PVC plant	Cancer caused by vinyl chloride (1976 standard)
Living 150 years within 20 miles of nuclear power plant	Cancer caused by radiation
Eating 100 charcoal broiled steaks	Cancer from benzopyrene
Risk of accident by living within 5 miles of a nuclear reactor for 50 years	Cancer caused by radiation

From: Kammen DM and Hassenzahl (1999). *Should We Risk It? Exploring Environmental, Health and Technological Problem Solving.* Princeton. Princeton University Press.

Risk quantifiers in the Epidemiological Tradition

Transmission Probability (SAR)

$$p = \frac{\#\ \text{infections}}{\#\ \text{potentially infectious contacts}}$$

Hazard Rate Incidence (events per person-time)

$$\lambda(t) = \underset{\text{contacts per time}}{c} \times \underset{\text{transmission probability}}{p} \times \underset{\text{prevalence}}{P(t)}$$

Cumulative Incidence (event by time t; yes or no)

$$CI(t) = 1 - e^{-\int_0^t \lambda(u)du} = 1 - e^{-\int_0^t c\, p\, P(u)du}$$

From: Halloran ME, Longini Jr I, Struchiner CJ (2010). *Design and Analysis of Vaccine Studies. New York*. Springer-Verlag

$$Risk = \frac{\#\ \text{affected}}{\#\ \text{exposed}}$$

- Constant population
- No competitive risks

A Stochastic SI Model

$$P_y^I(t+\Delta t) = P_y^I(t)(1-\lambda x \Delta t) + P_{y-1}^I \lambda (x+1)\Delta t$$

The Kolmogorov equation is

$$\frac{dP_y^I(t)}{dt} = -\lambda(N-y)P_y^I(t) + \lambda(N-y+1)P_{y-1}^I$$

$$G(z,t) = \sum_{y=0}^{N} z^y P_y^I(t)$$

$$G(z,t) = \left[z - (z-1)\exp(-\lambda t) \right]^N$$

$$\left.\frac{\partial G(z,t)}{\partial z}\right|_{z=1} = N\left[1-\exp(-\lambda t)\right]$$

Average probability of infection

$$\pi_d(t) = \left[1-\exp(-\lambda t)\right]$$

$$N\sigma 2 = \left.\frac{\partial^2 G(z,t)}{\partial z^2}\right|_{z=1} + \left.\frac{\partial G(z,t)}{\partial z}\right|_{z=1} - \left[\left.\frac{\partial G(z,t)}{\partial z}\right|_{z=1}\right]^2$$

$$\sigma^2(t) = \exp(-\lambda t)\left[1 - \exp(-\lambda t)\right]$$

$$Risk = \frac{\#\, affected}{\#\, \exp osed}$$

- Constant population
- No competitive risks

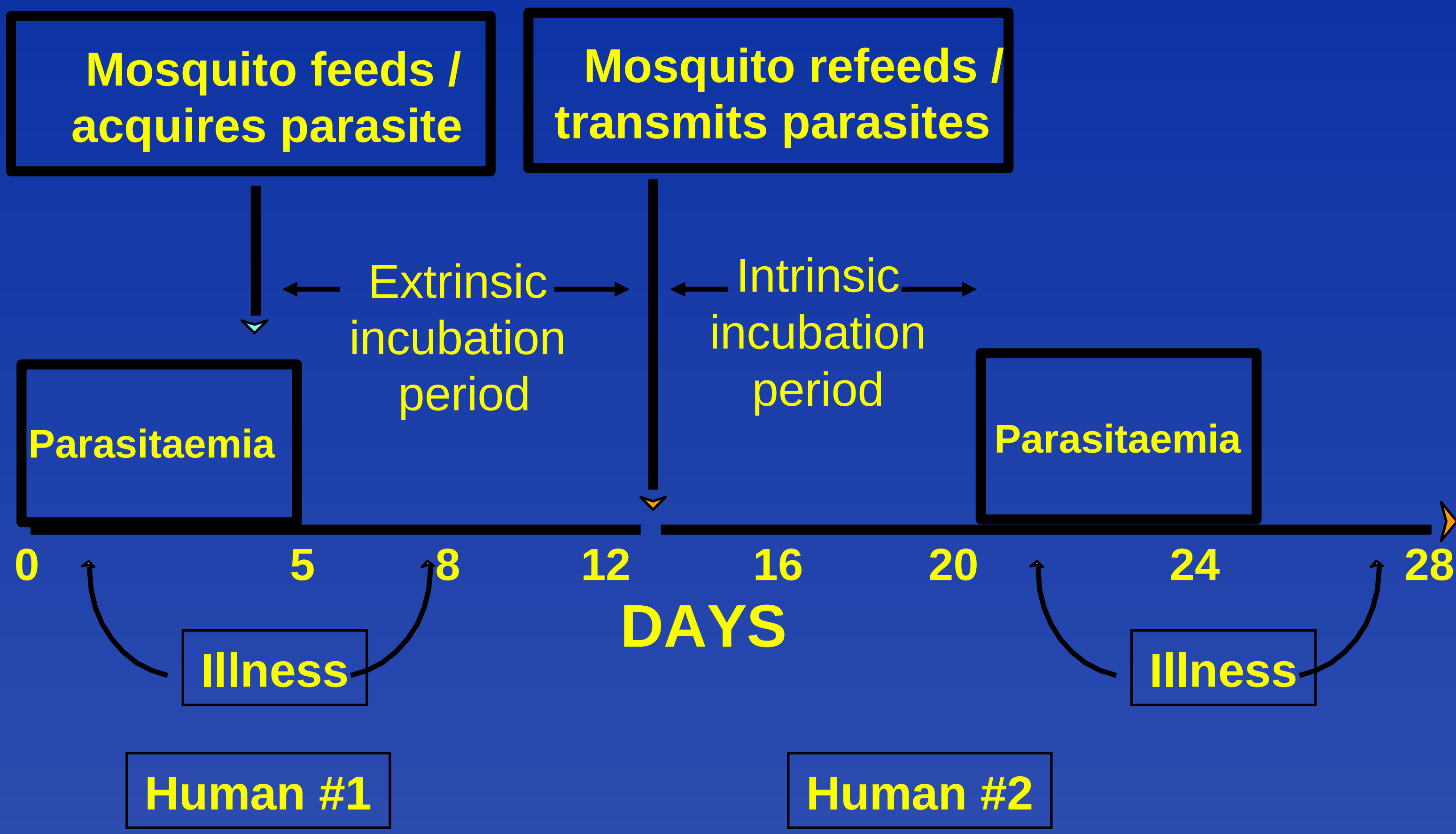
$$\frac{dS_H}{dt} = -abI_M \frac{S_H}{N_H} - (1-b)aI_M \frac{S_H}{N_H}$$

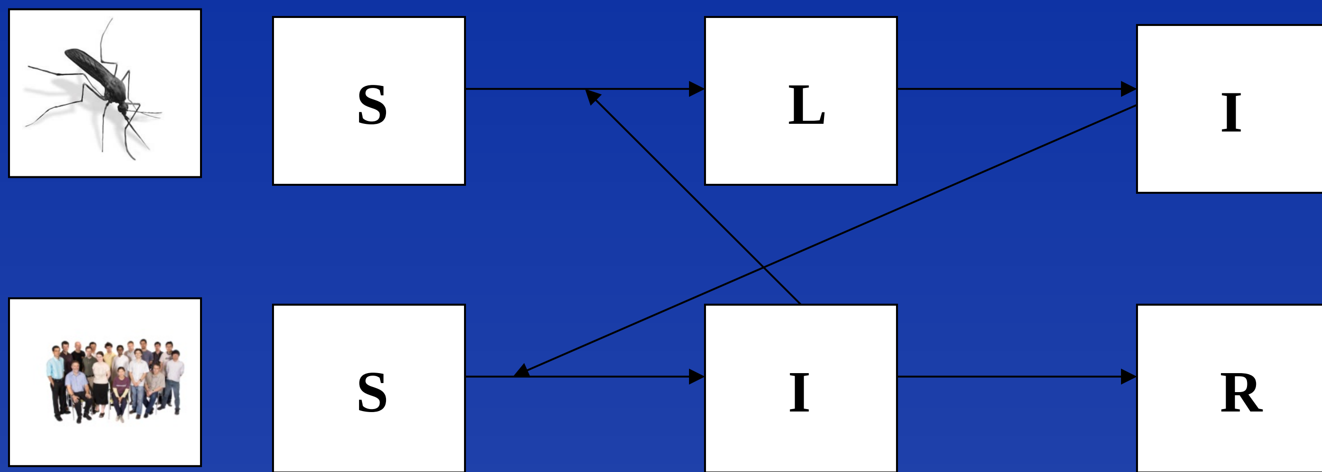
$$\frac{dI_H}{dt} = abI_M \frac{S_H}{N_H}$$

$$\frac{B_H}{dt} = abI_M \frac{S_H}{N_H} + (1-b)aI_M \frac{S_H}{N_H}$$

$$Risk = \frac{abI_M \frac{S_H}{N_H}}{\left[abI_M \frac{S_H}{N_H} + (1-b)aI_M \frac{S_H}{N_H} \right]} = b$$

Transmission of Malaria by *Anopheles* mosquitoes




S
L
I
S
I
R

$$\frac{dS_H}{dt} = -abI_M \frac{S_H}{N_H} - \mu_H S_H + r_H N_H \left(1 - \frac{N_H}{\kappa_H}\right) + \sigma_H R_H + \theta_H I_H$$

$$\frac{dL_H}{dt} = abI_M \frac{S_H}{N_H} - (\mu_H + \delta_H) L_H$$

$$\frac{dI_H}{dt} = \delta_H L_H - \left(\mu_H + \alpha_H + \gamma_H + \theta_H\right) I_H$$

$$\frac{dR_H}{dt} = \gamma_H I_H - \mu_H R_H - \sigma_H R_H$$

$$\frac{dS_M}{dt} = pc_S(t) S_E - \mu_M S_M - acS_M \frac{I_H}{N_H}$$

$$\frac{dL_M}{dt} = acS_M \frac{I_H}{N_H} - \gamma_M L_M - \mu_M L_M$$

$$\frac{dI_M}{dt} = \gamma_M L_M - \mu_M I_M + pc_S(t) I_E$$

$$\frac{dS_E}{dt} = \left[r_M S_M + \left(1 - g\right) r_M (I_M + L_M)\right] \left(1 - \frac{\left(S_E + I_E\right)}{\kappa_E}\right) - \mu_E S_E - pc_S(t) S_E$$

$$\frac{dI_E}{dt} = \left[g r_M (I_M + L_M)\right] \left(1 - \frac{\left(S_E + I_E\right)}{\kappa_E}\right) - \mu_E I_E - pc_S(t) I_E$$

The Force of Infection

Incidence density rate: Per capita number of new case per unit time

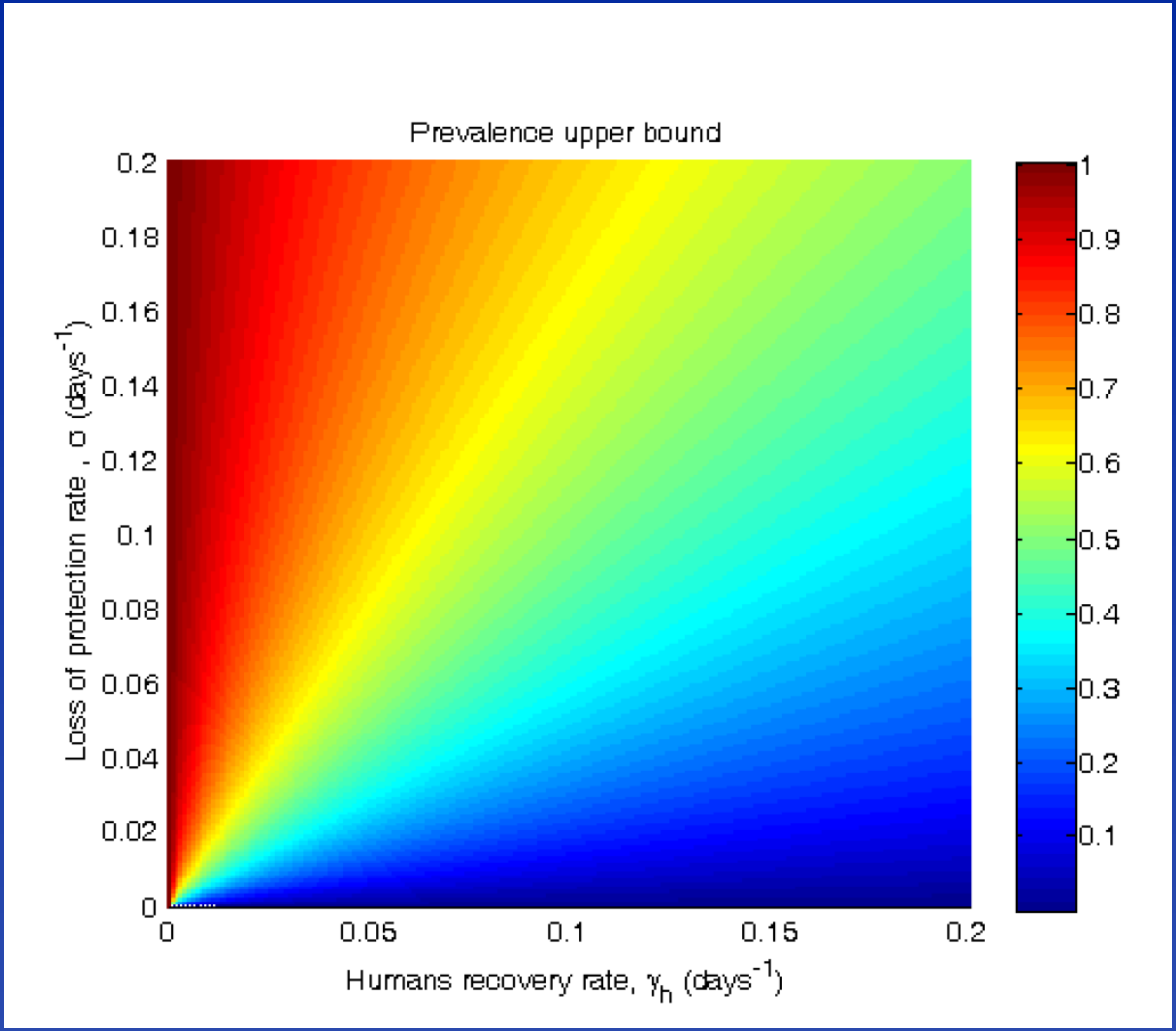
$$\lambda = ab\frac{I_M}{N_H}$$

$$\lambda_H^* = ab\frac{I_M^*}{N_H^*}$$

$$I_M^* = \frac{(\delta_H + \mu_H)(\mu_H + \gamma_H + \alpha_H + \sigma_H)I_H^*}{ab\delta_H\left(1 - \left(\frac{(\mu_H + \sigma_H)(\mu_H + \gamma_H + \alpha_H + \delta_H + \theta_H) + \gamma_H\delta_H}{\delta_H(\mu_H + \sigma_H)}\right)\frac{I_H^*}{N_H^*}\right)}$$

$$\lambda_H^* = \frac{\left(\delta_H + \mu_H\right)\left(\mu_H + \gamma_H + \alpha_H + \sigma_H\right)\dfrac{I_H^*}{N_H^*}}{\delta_H\left(1 - \left(\dfrac{\left(\mu_H + \sigma_H\right)\left(\mu_H + \gamma_H + \alpha_H + \delta_H + \theta_H\right) + \gamma_H\delta_H}{\delta_H\left(\mu_H + \sigma_H\right)}\right)\dfrac{I_H^*}{N_H^*}\right)}$$

$$\left(\frac{I_H^*}{N_H^*}\right)_{MAX} = \frac{\delta_H\left(\mu_H + \sigma_H\right)}{\left(\mu_H + \sigma_H\right)\left(\mu_H + \gamma_H + \alpha_H + \delta_H + \theta_H\right) + \gamma_H \delta_H}$$


Prevalence upper bound
Loss of protection rate , σ (days-1)
Humans recovery rate, γh (days-1)
0.2
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0
0.05
0.1
0.15
0.2
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1

A proposed expression for the probability of infection

$$\pi(t) = \frac{\int_{t_1}^{t_2} \lambda(s) S^{'}(t) ds}{N_H^{'}(0)}$$

$$\frac{dS_H}{dt} = -abI_M \frac{S_H}{N_H} - \mu_H S_H + r_H N_H \left(1 - \frac{N_H}{\kappa_H}\right) + \sigma_H R_H$$

$$\frac{dI_H}{dt} = abI_M \frac{S_H}{N_H} - (\mu_H + \alpha_H + \gamma_H) I_H$$

$$\frac{dR_H}{dt} = \gamma_H I_H - \mu_H R_H - \sigma_H R_H$$

$$\frac{dS_M}{dt} = p_S c_S(t) S_E - \mu_M S_M - acS_M \frac{I_H}{N_H}$$

$$\frac{dL_M}{dt} = acS_M \frac{I_H}{N_H} - \gamma_M L_M - \mu_M L_M$$

$$\frac{dI_M}{dt} = \gamma_M L_M - \mu_M I_M$$

$$\frac{dS_E}{dt} = [r_M S_M]\left(1 - \frac{(S_E)}{\kappa_E}\right) - \mu_E S_E - p_S c_S(t) S_E$$

$$N_H = S_H + I_H + R_H$$

$$N_M = S_M + L_M + I_M$$

$$\frac{dS'_H}{dt} = (-a'b'I_M \frac{S'_H}{N_H})\theta(t - t_0)$$

$$a' = POISSON(0.3)$$

$$b' = GAMMA(0.088, 0.017)$$

$$I_M^* = \frac{\left(\mu_H + \gamma_H + \alpha_H\right) I_H^*}{ab\left(1 - \left(1 + \frac{\gamma_H}{\mu_H + \sigma_H}\right)\frac{I_H^*}{N_H^*}\right)}$$

$$\left(\frac{I_H^*}{N_H^*}\right)_{MAX} = \left(1 + \frac{\gamma_H}{\mu_H + \sigma_H}\right)^{-1}$$

Estimating the force of infection from equilibrium prevalence

$$\lambda^* = \frac{\left(\mu_H + \gamma_H + \alpha_H\right)\dfrac{I_H^*}{N_H^*}}{ab\left(1 - \left(1 + \dfrac{\gamma_H}{\mu_H + \sigma_H}\right)\dfrac{I_H^*}{N_H^*}\right)}$$

A Stochastic SIS Model

$$P_x^S(t+\Delta t) = P_x^S(t)(1-\lambda x\Delta t - \gamma(N-x)\Delta t)$$
$$+ P_{x+1}^S\lambda(x+1)\Delta t + P_{x-1}^S\gamma(N-(x-1))\Delta t$$

The Kolmogorov equation is

$$\frac{dP_x^S(t)}{dt} = -(\lambda-\gamma)xP_x^S(t) - \gamma NP_x^S + \gamma NP_{x-1}^S$$
$$-\gamma(x-1)P_{x-1}^S + \lambda(x+1)P_{x-1}^S$$

$$G(z,t) = \sum_{y=0}^{N} z^y P_y^I(t)$$

$$G(z,t) = \left[\frac{\gamma}{\gamma+\lambda} \left(z + \frac{\lambda}{\gamma} \right) + \frac{\lambda}{\gamma+\lambda} (z-1) \exp(-(\lambda+\gamma)t) \right]^N$$

$$\left.\frac{\partial G(z,t)}{\partial z}\right|_{z=1} = \frac{N}{\gamma+\lambda}\left[\gamma + \exp(-(\lambda+\gamma)t)\right]$$

Average probability of infection

$$\pi_d(t) = \frac{N\lambda}{\gamma+\lambda}\left[1 - \exp(-(\lambda+\gamma)t)\right]$$

$$N\sigma 2 = \left.\frac{\partial^2 G(z,t)}{\partial z^2}\right|_{z=1} + \left.\frac{\partial G(z,t)}{\partial z}\right|_{z=1} - \left[\left.\frac{\partial G(z,t)}{\partial z}\right|_{z=1}\right]^2$$

$$\sigma^2(t) = N\,\frac{\lambda\gamma[1-\exp(-(\lambda+\gamma)t)] + \lambda^2\exp(-(\lambda+\gamma)t)[1-\exp(-(\lambda+\gamma)t)]}{(\gamma+\lambda)^2}$$

Deterministic SIS Model

$$\frac{dS_H}{dt} = -abI_M \frac{S_H}{N_H} + \gamma_H I_H$$

$$\frac{dI_H}{dt} = abI_M \frac{S_H}{N_H} - \gamma_H I_H$$

$$\frac{dS_M}{dt} = p_S c_S(t) S_E - \mu_M S_M - acS_M \frac{I_H}{N_H}$$

$$\frac{dL_M}{dt} = acS_M \frac{I_H}{N_H} - \gamma_M L_M - \mu_M L_M$$

$$\frac{dI_M}{dt} = \gamma_M L_M - \mu_M I_M$$

$$\frac{dS_E}{dt} = [r_M S_M]\left(1 - \frac{(S_E)}{\kappa_E}\right) - \mu_E S_E - p_S c_S(t) S_E$$

Latin hypercube sampling

Latin hypercube sampling (LHS) is a statistical method for generating a sample of plausible collections of parameter values from a multidimensional distribution.

In the context of statistical sampling, a square grid containing sample positions is a Latin square if (and only if) there is only one sample in each row and each column. A Latin hypercube is the generalization of this concept to an arbitrary number of dimensions, whereby each sample is the only one in each axis-aligned hyperplane containing it.

$$\pi(t) = \frac{N\lambda}{\gamma + \lambda}\left[1 - \exp(-(\lambda + \gamma)t)\right] = 0.043$$

$$\pi(t) = \frac{\int_{t_1}^{t_2} \lambda(s) S^{'}(t) ds}{N_H^{'}(0)} = 0.040$$

Risk = Likelihood x Impact

Impact = probability of dying

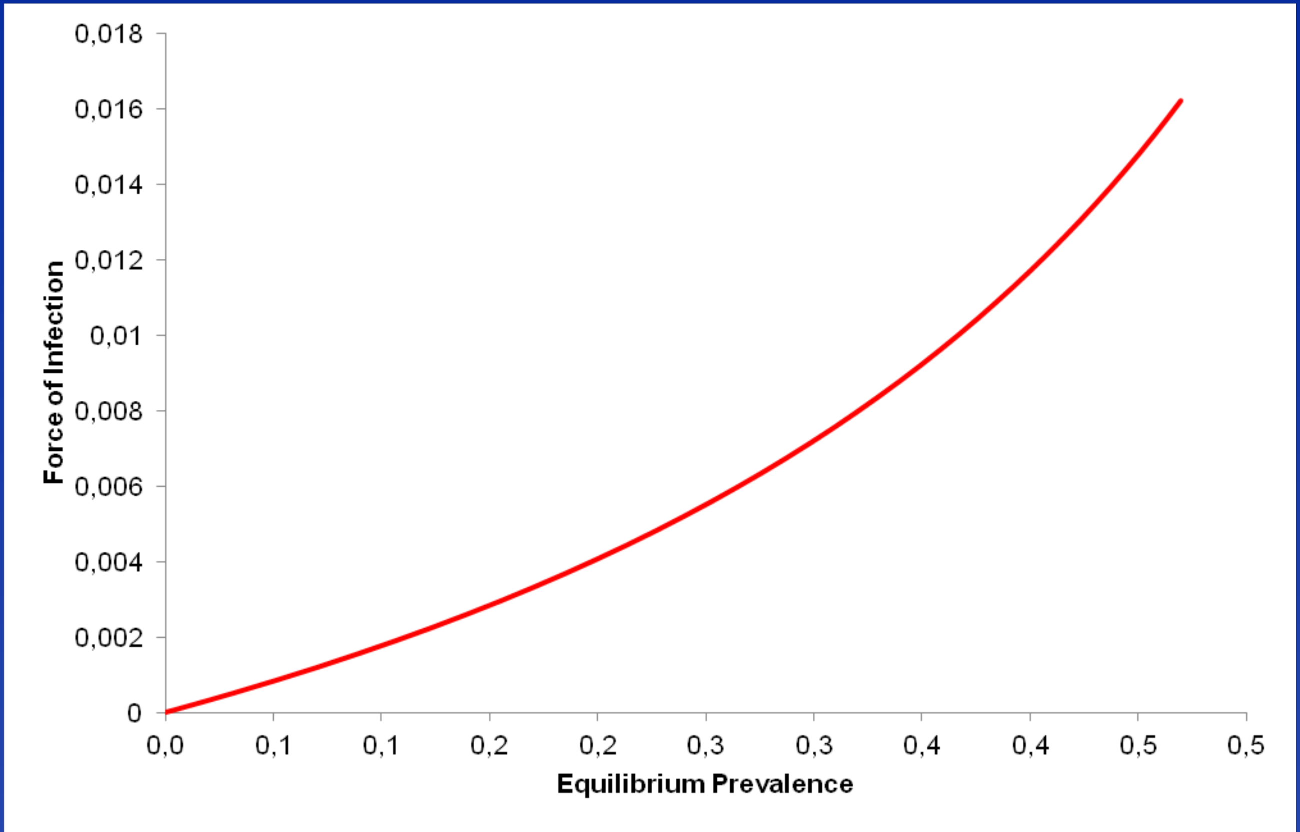
$$p_d(t) = \left[1 - \exp(-\alpha t)\right]$$

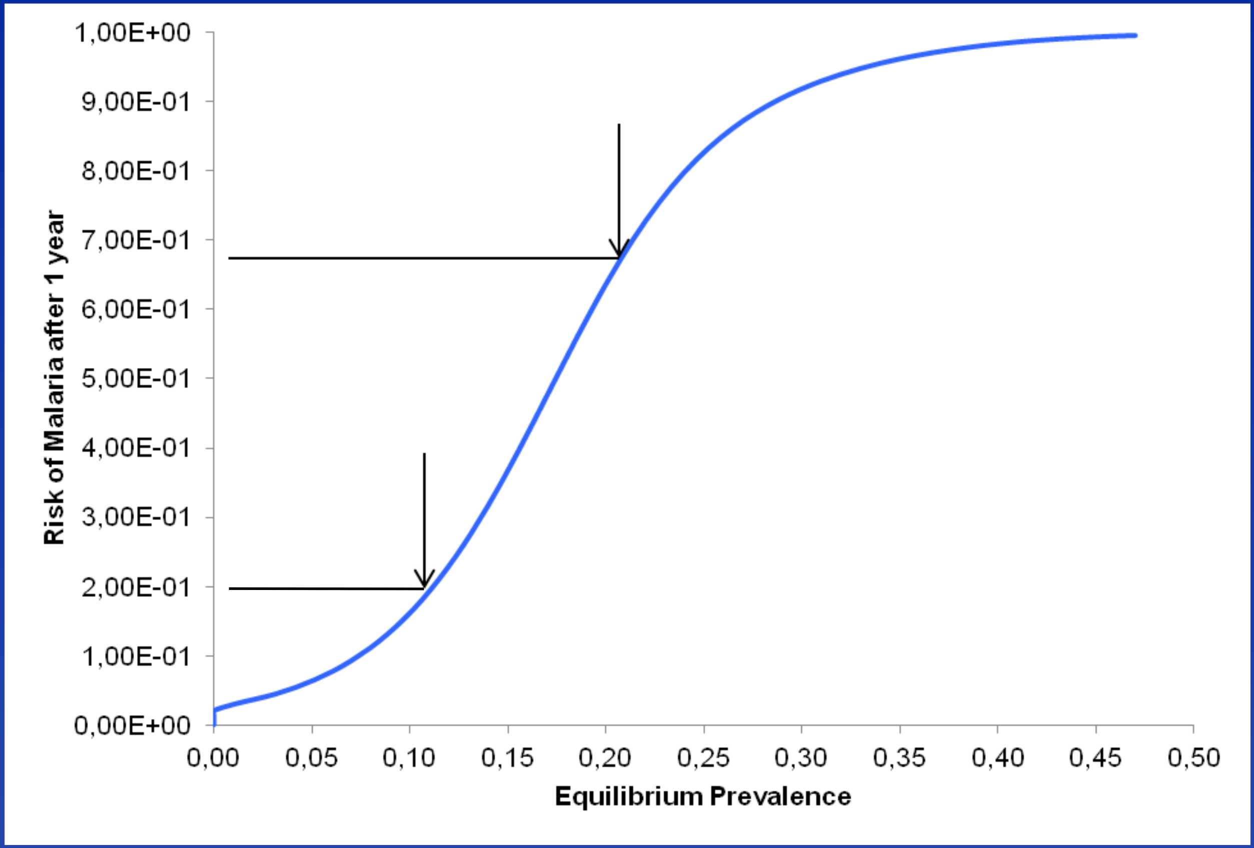
Risk = Probability of infection x probability of dying

$$Risk(t) = \frac{\int_{t_1}^{t_2} \lambda(s) S'(t) ds}{N'_H(0)} \times \left[1 - \exp(-\alpha t)\right]$$

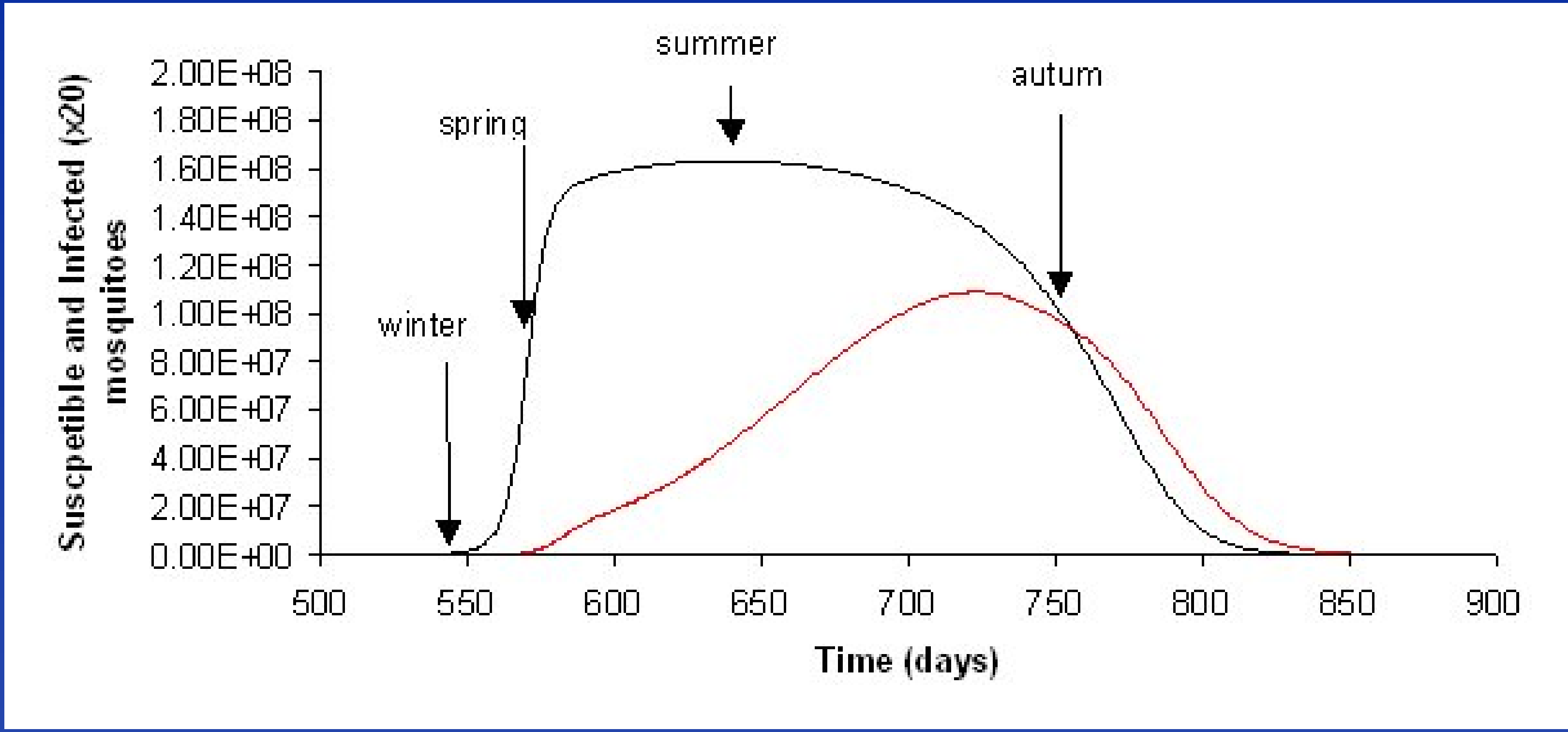
Mind you: the force of infection λ is an explicity function of the mortality rate α!

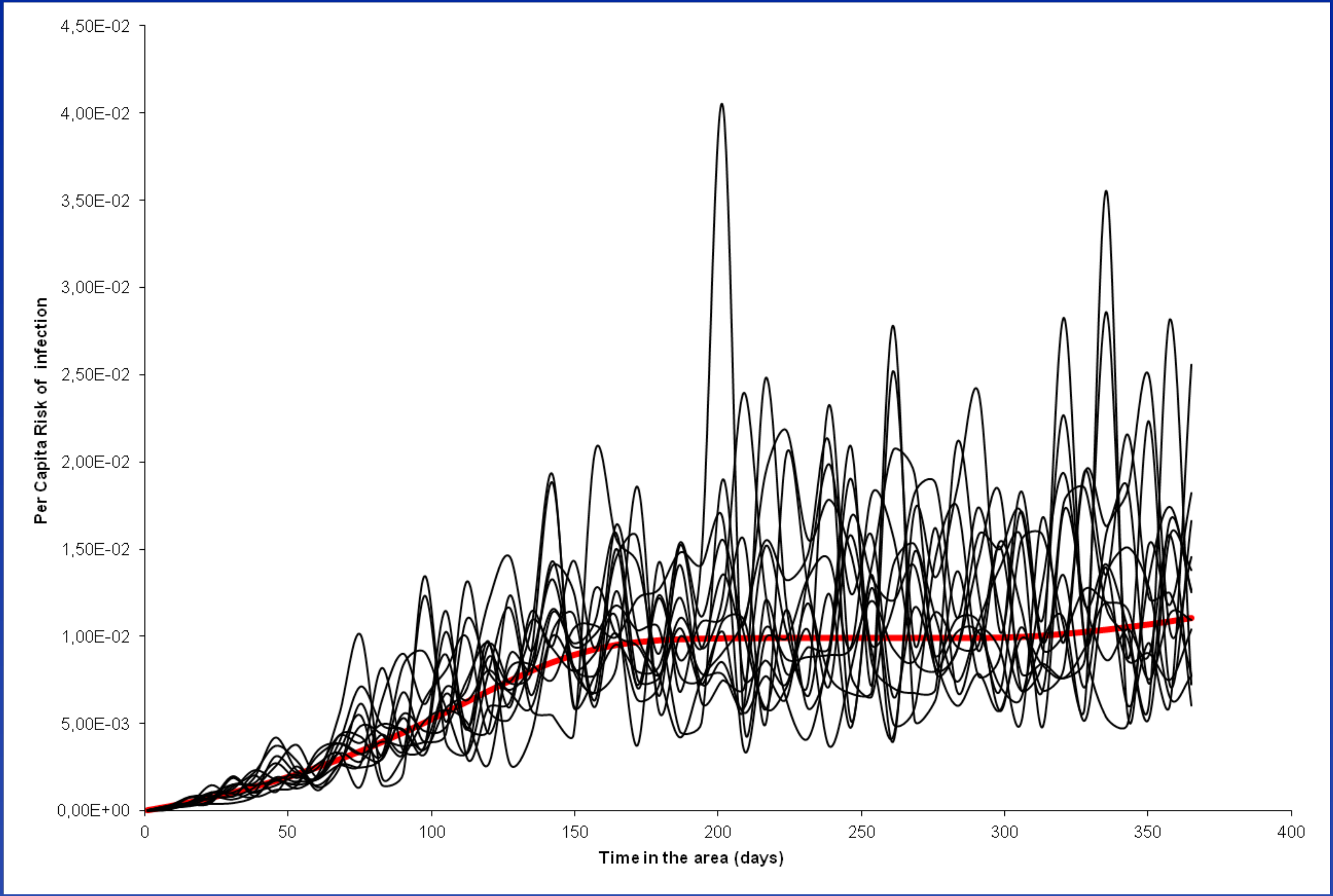
$$\lambda_H^* = \frac{\left(\delta_H + \mu_H\right)\left(\mu_H + \gamma_H + \alpha_H + \sigma_H\right)\dfrac{I_H^*}{N_H^*}}{\delta_H\left(1 - \left(\dfrac{\left(\mu_H + \sigma_H\right)\left(\mu_H + \gamma_H + \alpha_H + \delta_H + \theta_H\right) + \gamma_H\delta_H}{\delta_H\left(\mu_H + \sigma_H\right)}\right)\dfrac{I_H^*}{N_H^*}\right)}$$

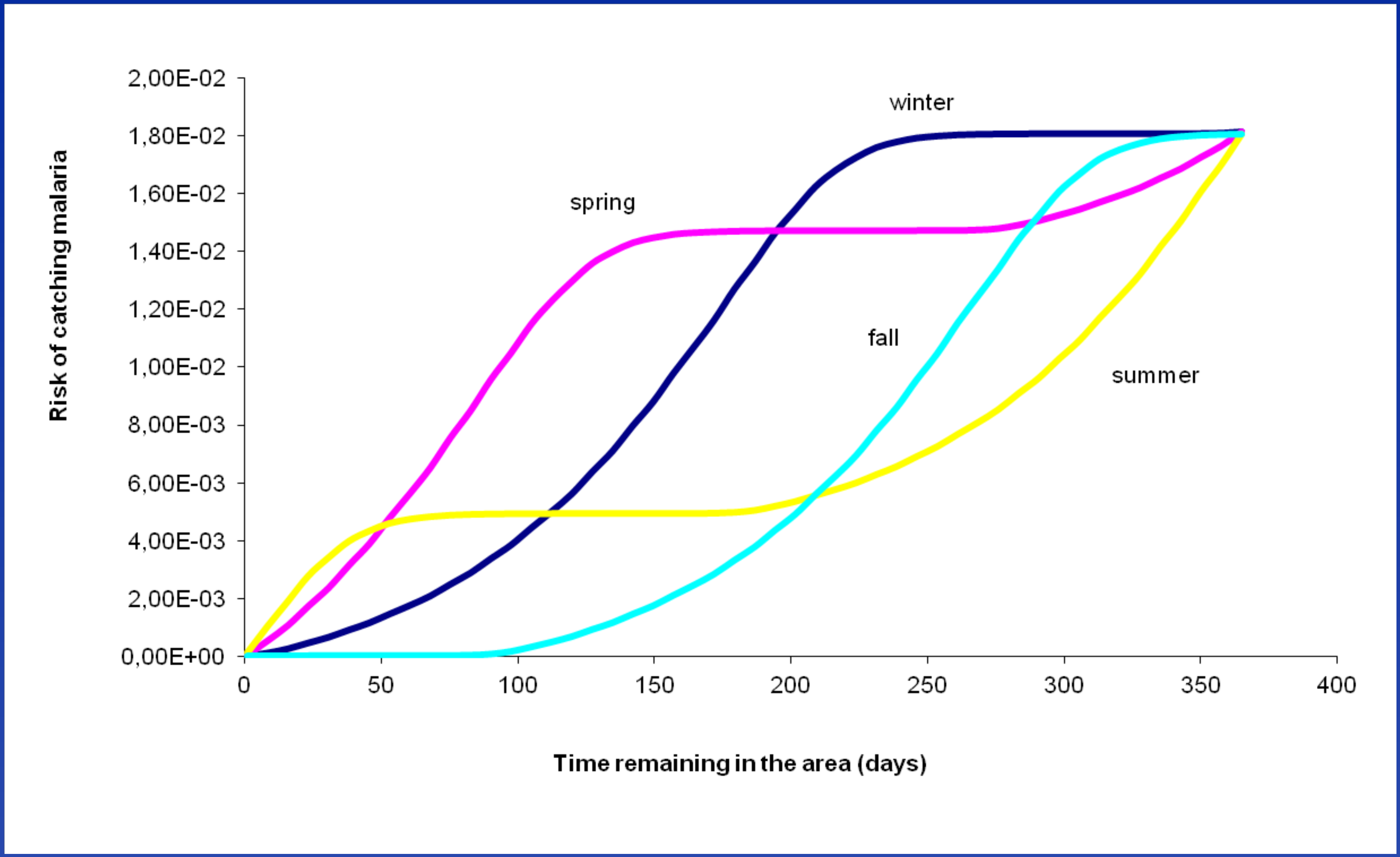

0,018
0,016
0,014
0,012
0,01
0,008
0,006
0,004
0,002
0
Force of Infection
0,0
0,1
0,1
0,2
0,2
0,3
0,3
0,4
0,4
0,5
0,5
Equilibrium Prevalence

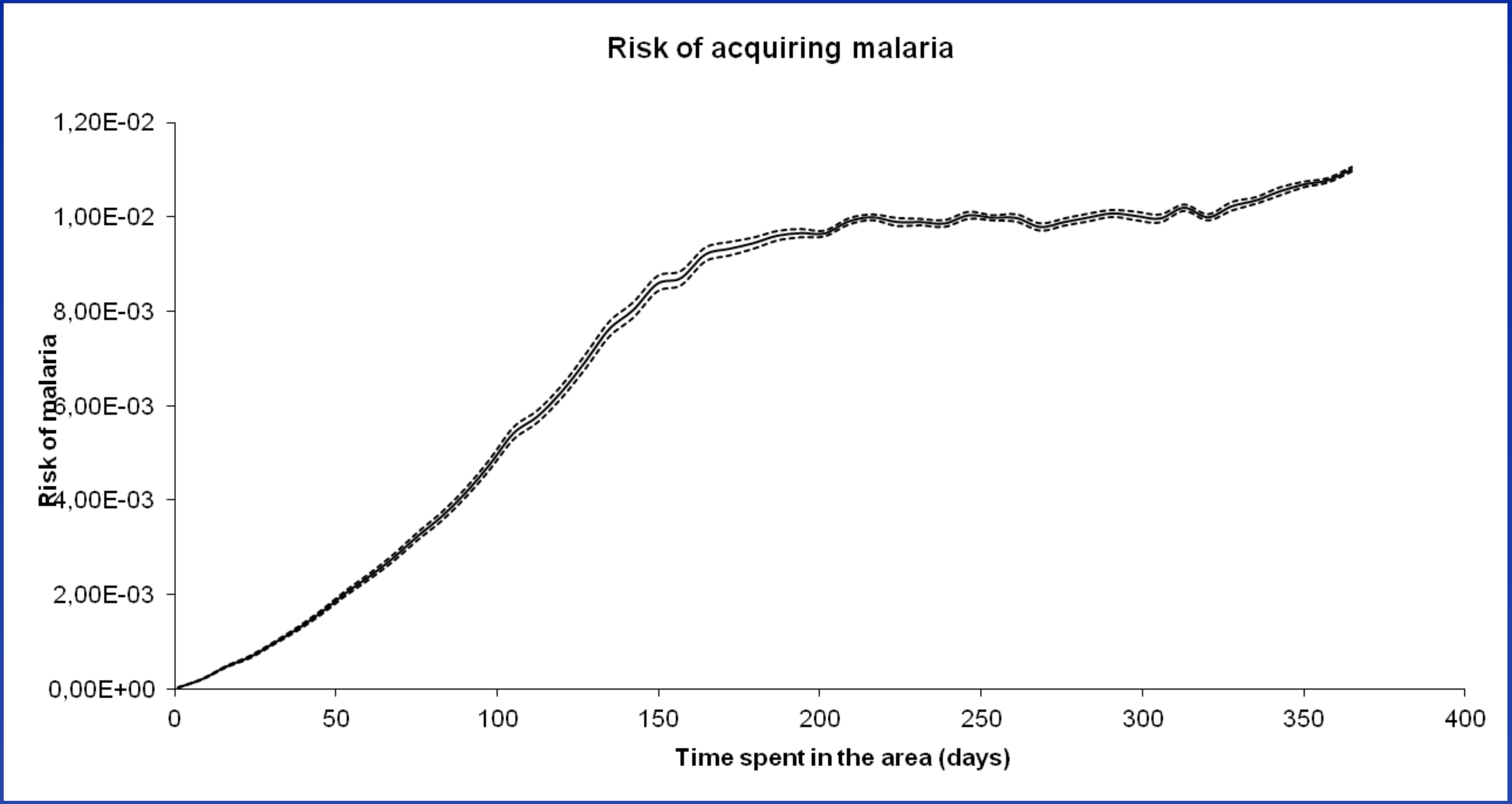

1,00E+00
9,00E-01
8,00E-01
7,00E-01
6,00E-01
5,00E-01
4,00E-01
3,00E-01
2,00E-01
1,00E-01
0,00E+00
Risk of Malaria after 1 year
0,00
0,05
0,10
0,15
0,20
0,25
0,30
0,35
0,40
0,45
0,50
Equilibrium Prevalence

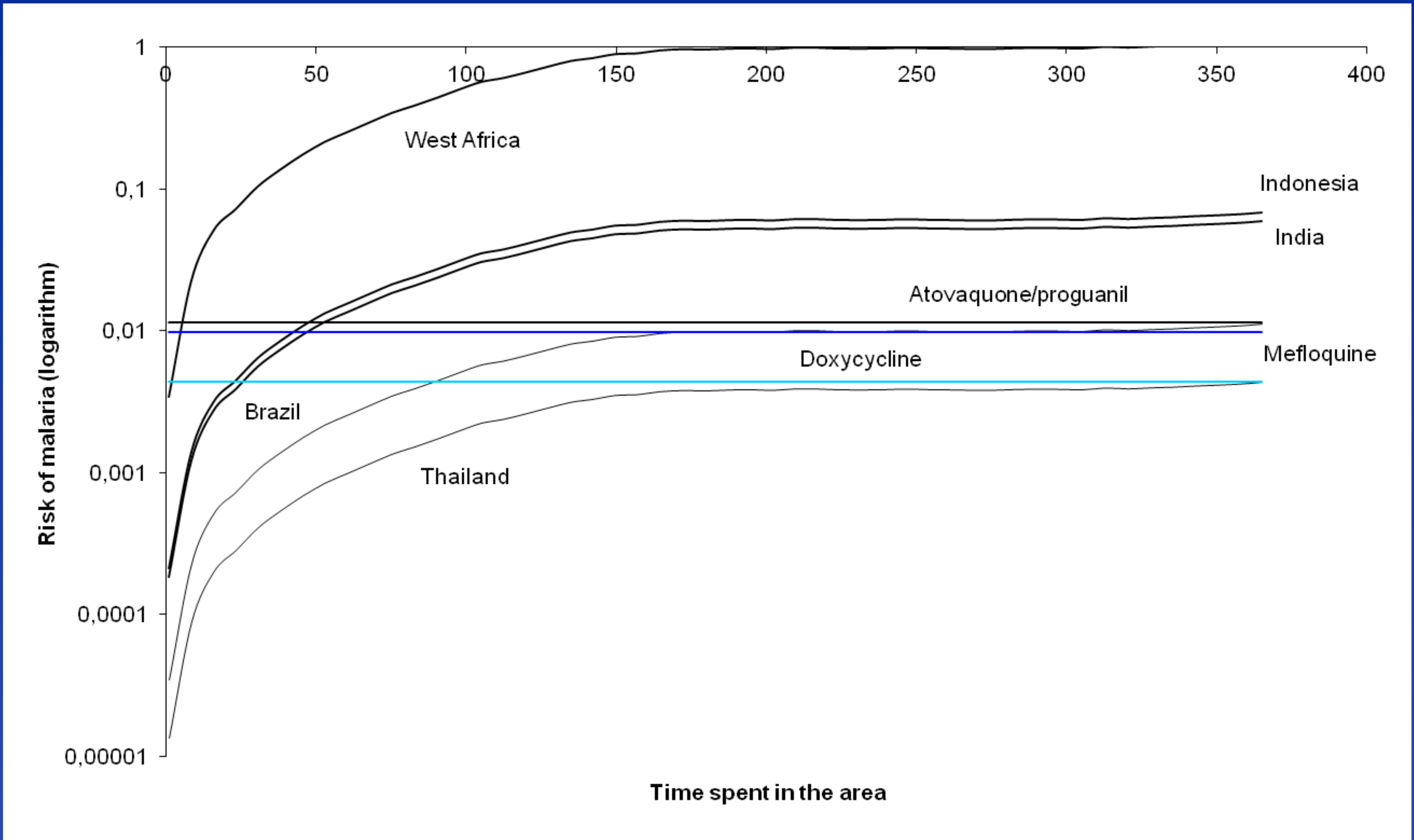
Applications


Susceptible and Infected (x20) mosquitoes
2.00E+08
1.80E+08
1.60E+08
1.40E+08
1.20E+08
1.00E+08
8.00E+07
6.00E+07
4.00E+07
2.00E+07
0.00E+00
summer
autum
spring
winter
500
550
600
650
700
750
800
850
900
Time (days)


Per Capita Risk of infection
Time in the area (days)
4,50E-02
4,00E-02
3,50E-02
3,00E-02
2,50E-02
2,00E-02
1,50E-02
1,00E-02
5,00E-03
0,00E+00
0
50
100
150
200
250
300
350
400


winter
spring
fall
summer
Risk of catching malaria
2,00E-02
1,80E-02
1,60E-02
1,40E-02
1,20E-02
1,00E-02
8,00E-03
6,00E-03
4,00E-03
2,00E-03
0,00E+00
0
50
100
150
200
250
300
350
400
Time remaining in the area (days)


Risk of acquiring malaria
1,20E-02
1,00E-02
8,00E-03
6,00E-03
4,00E-03
2,00E-03
0,00E+00
Risk of malaria
0
50
100
150
200
250
300
350
400
Time spent in the area (days)



1
0,1
0,01
0,001
0,0001
0,00001
0
50
100
150
200
250
300
350
400
Risk of malaria (logarithm)
Time spent in the area
West Africa
Indonesia
India
Atovaquone/proguanil
Doxycycline
Mefloquine
Brazil
Thailand

Collaborators:

Francisco Antonio Bezerra Coutinho
Marcos Amaku
Luis Fernandez Lopez
Marcelo Nascimento Burattini
Claudio José Struchiner