INSTITUTO GULBENKIAN de CIÊNCIA

Prospects for malaria eradication in Sub-Saharan Africa

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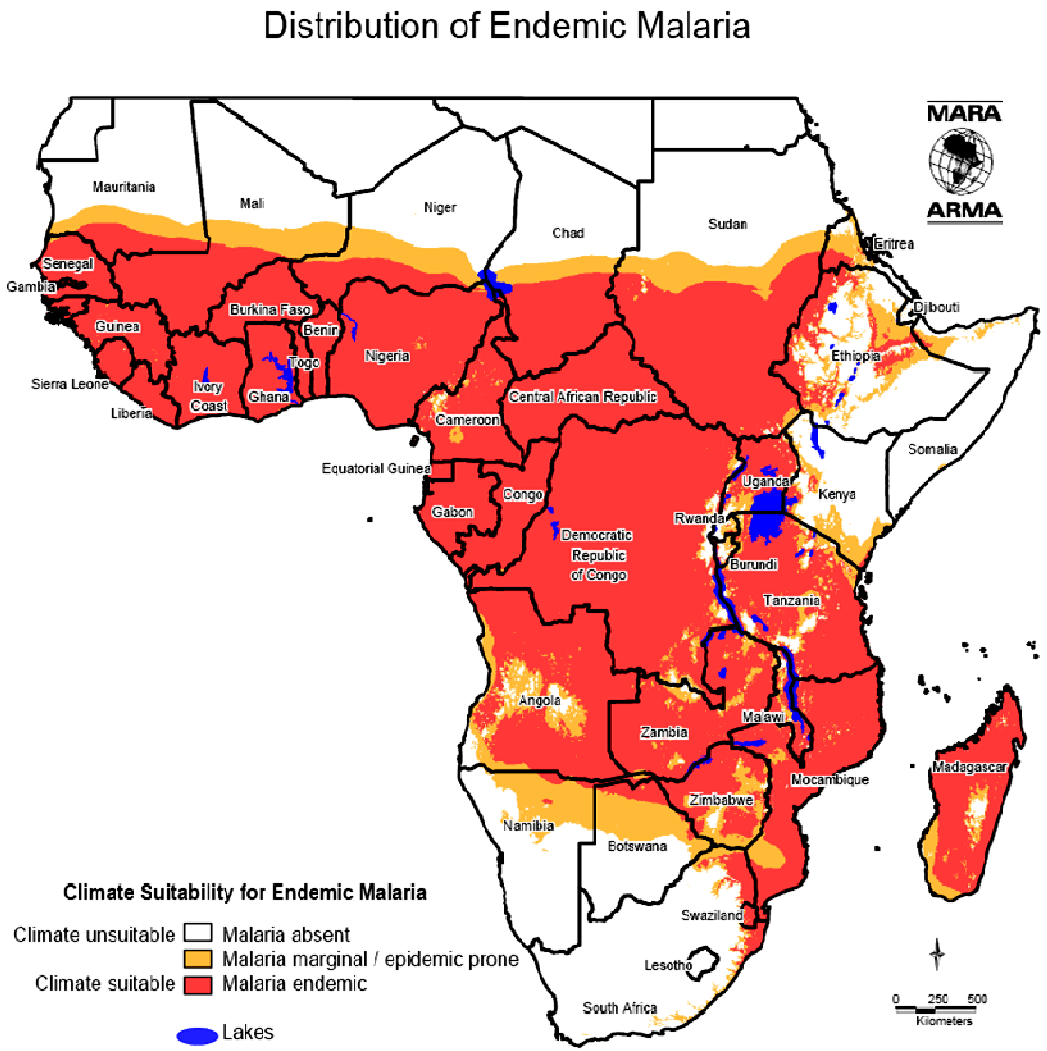
COLLABORATIVE RESEARCH PROGRAMME

Background

Heavy burden

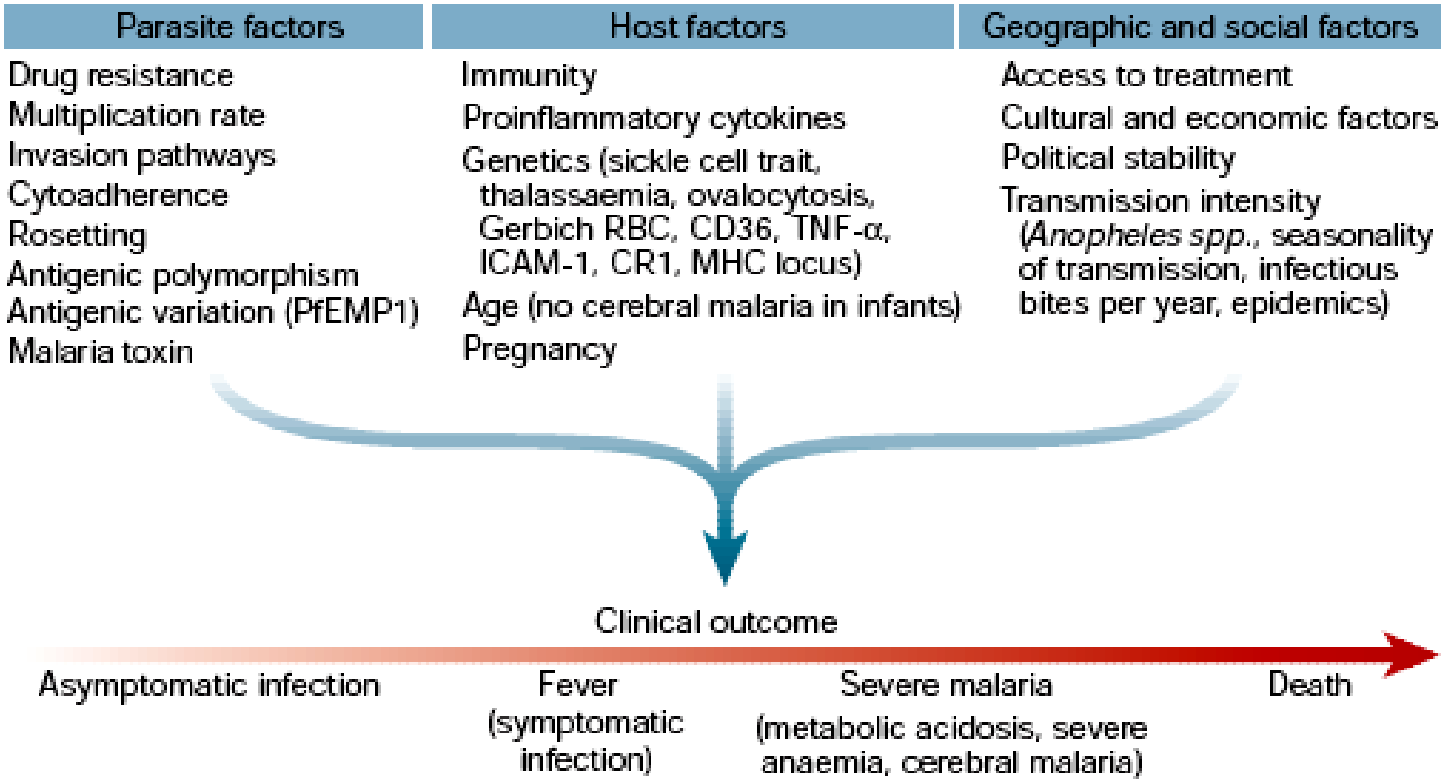


http://www.mara.org.za

- ~3.2 billion people are affected by malaria in 107 endemic countries.
- In Africa, 500 million clinical cases and over 1 million fatalities are registered every year.

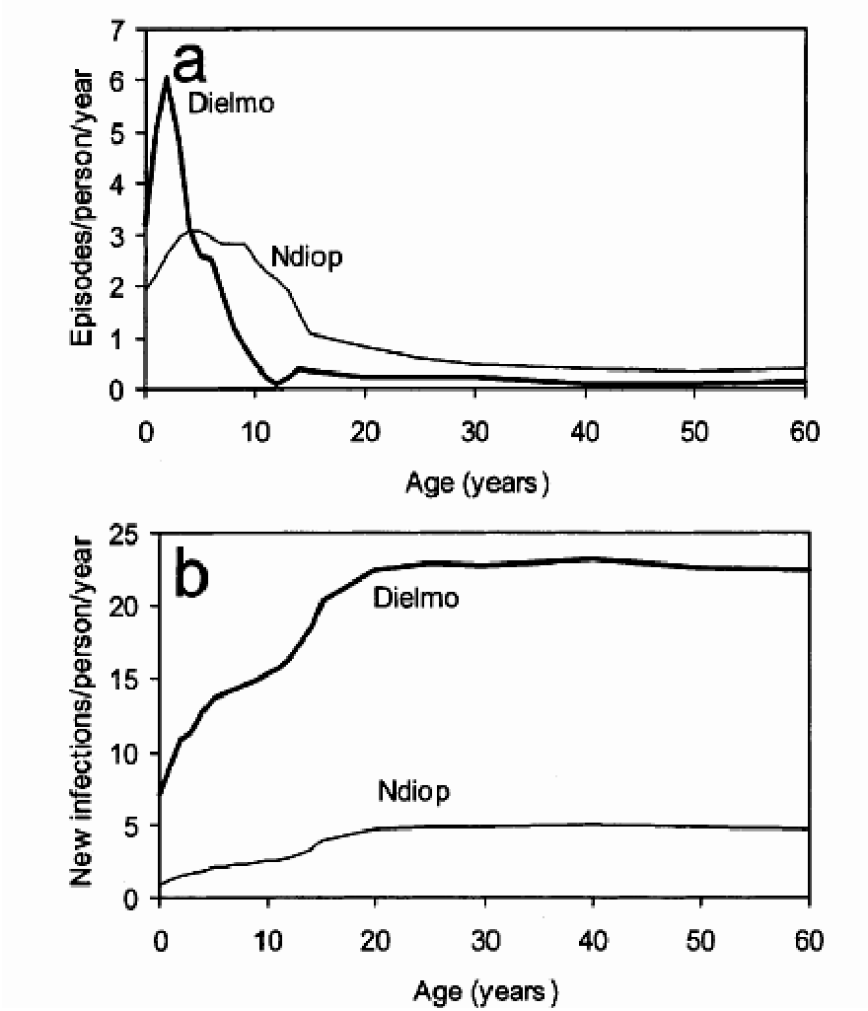
Snow *et al.*, 2005

Infection outcome



Miller et al., 2002

Intrinsic age profiles

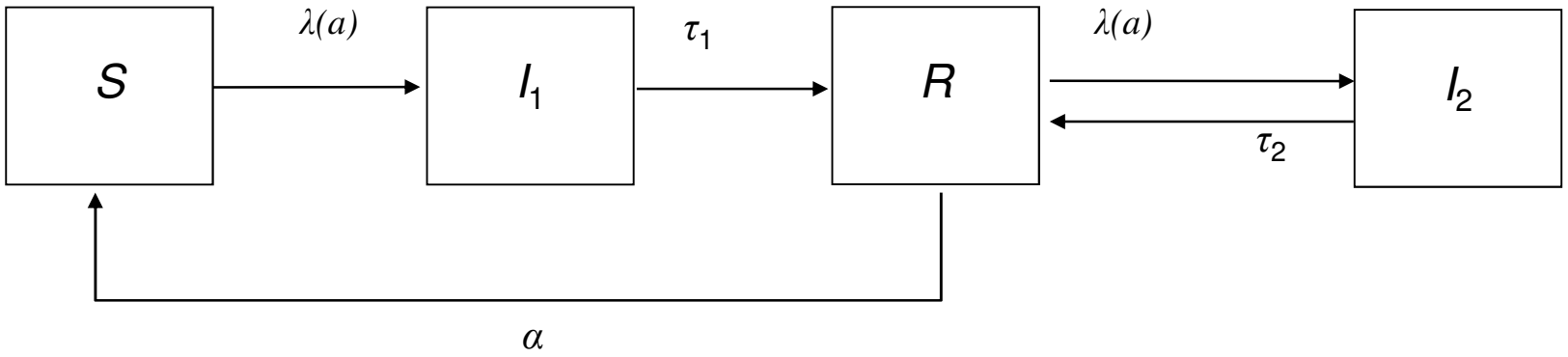


Smith *et al.*, 2004

- Even after many exposures, humans are not refractory to malaria parasites.
  - Clinical immunity prevents symptomatic disease.
- Malaria age profiles show the typical decrease in average age at infection with increasing transmission.

Candidate Model

The simplest possible



$$\lambda(a) = \lambda_0\left(1 - ce^{-ka}\right)$$

$$\Lambda = \int \lambda(a) P(a) da$$

$$\beta = \Lambda / \left(I_1 + \phi I_2\right)$$

$$R_0 = \beta / \left(\tau_1 + \mu\right)$$

Data

“For real progress, the mathematical modeller as well as the epidemiologist must have mud on his boots” Bradley 1982

Summary

	Bakau, The Gambia	*Foni Kansala, The Gambia*	*Sukuta, The Gambia*	*Mponda, Malawi*	*Kilifi, Kenya*	*Chonyi, Kenya*	*Siaya, Kenya*	*Ifakara, Tanzania*
Surveillance period	1.91-12.94 **(4 years)**	1.94-12.95 **(2 years)**	1.92-12.94 **(4 years)**	1.95-12.95 **(1 year)**	11.90-10.95 **(5 years)**	6.92-5.96 **(4 years)**	1.92-12.92 & 11.94-10.96 **(3 years)**	5.91-4.92 **(1 year)**
Total severe malaria admissions	**108**	**193**	**605**	**356**	**1358**	**766**	**719**	**144**
All cause malaria rate 0-9 years p.a.	**3.89** (108/27792)	**31.49** (193/6129)	**25.78** (605/23468)	**22.30** (356/15966)	**25.88** (1363/52675)	**16.66** (766/45967)	**17.95** (719/40064)	**19.51** (144/7380)
Median age months (IQR) of malaria admissions 0-9 years	**41.5** (23.5, 75.5)	**36** (24, 60)	**36** (22, 60)	**21** (11, 31)	**24** (12, 40)	**11** (6, 21)	**11** (5, 23)	**10** (6, 18)
Parasite ratio in childhood and approximate endemicity class	**2%** Hypoendemic	**31%** Mesoendemic	**37%** Mesoendemic	**40%** Mesoendemic	**49%** Meso-hyperendemic	**74%** Hyper-holoendemic	**83%** Holoendemic	**90%** Holoendemic

Model Fit

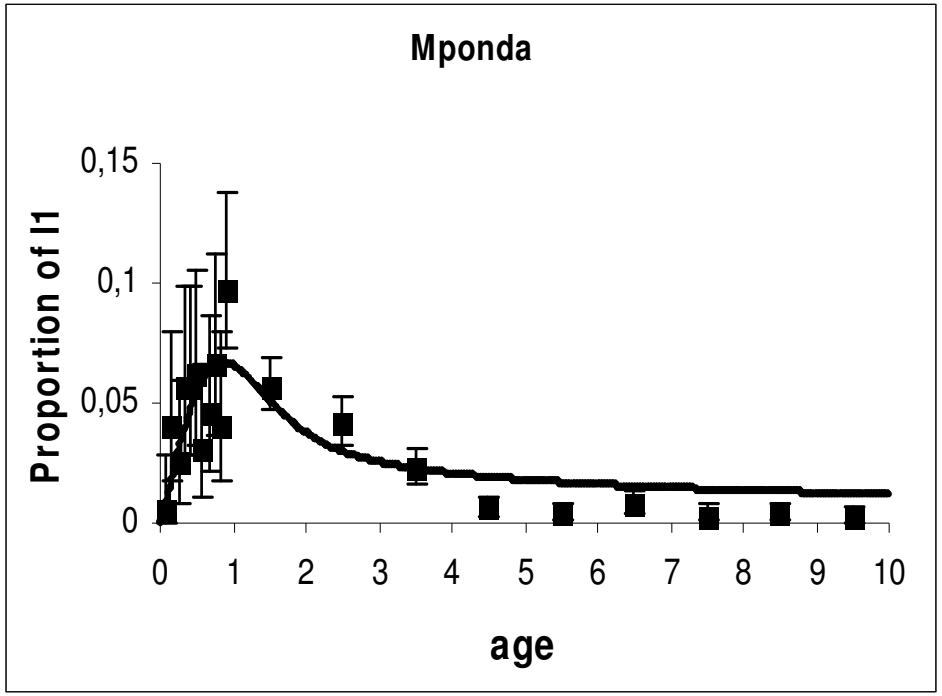
Fitting methods

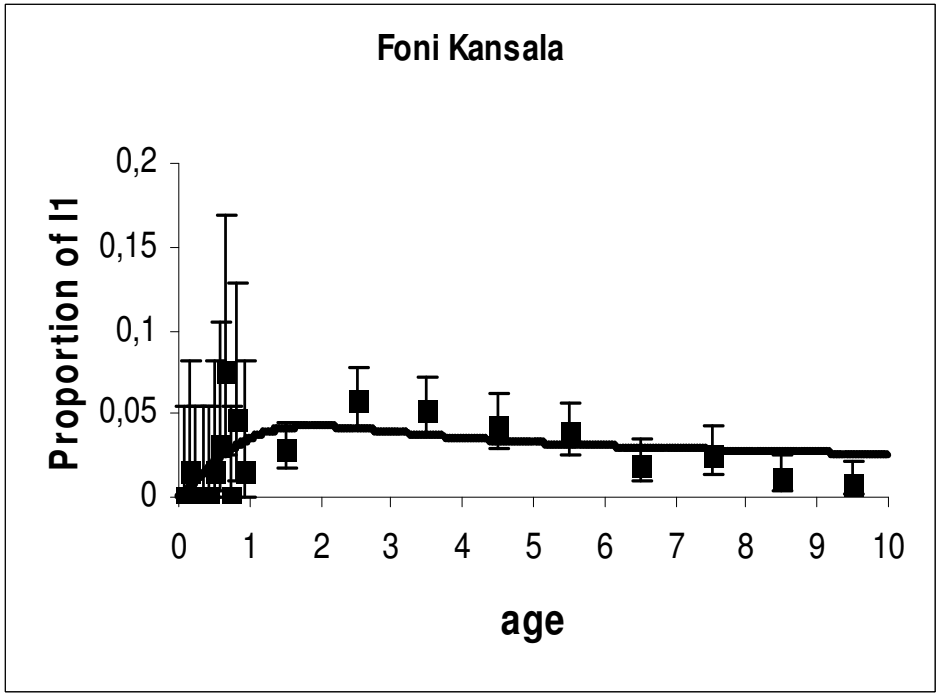
- Aggregate the data in such a way as to be comparable to the model output.

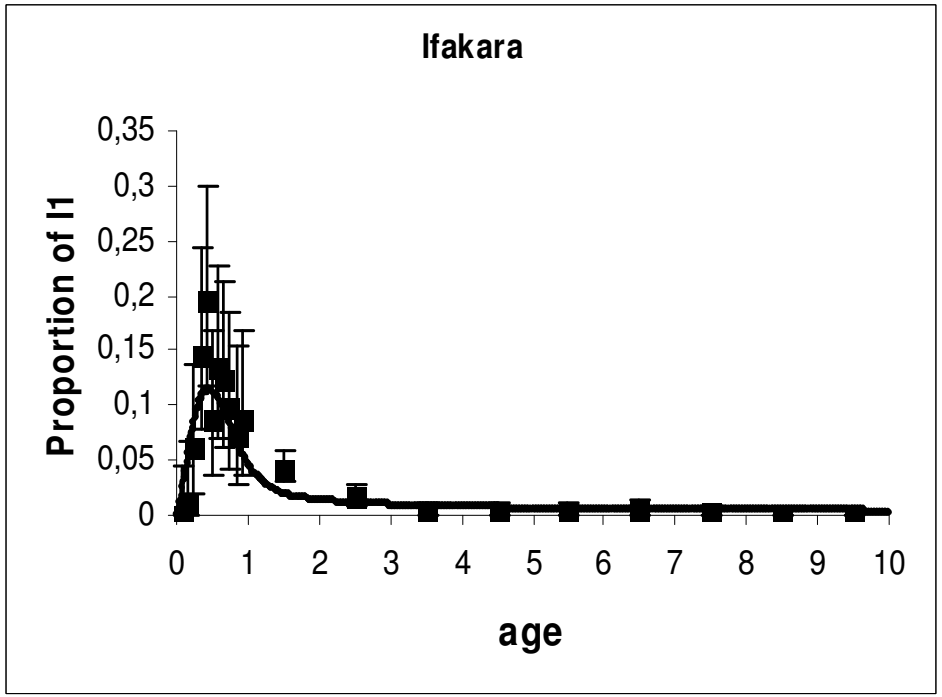
Define severe disease

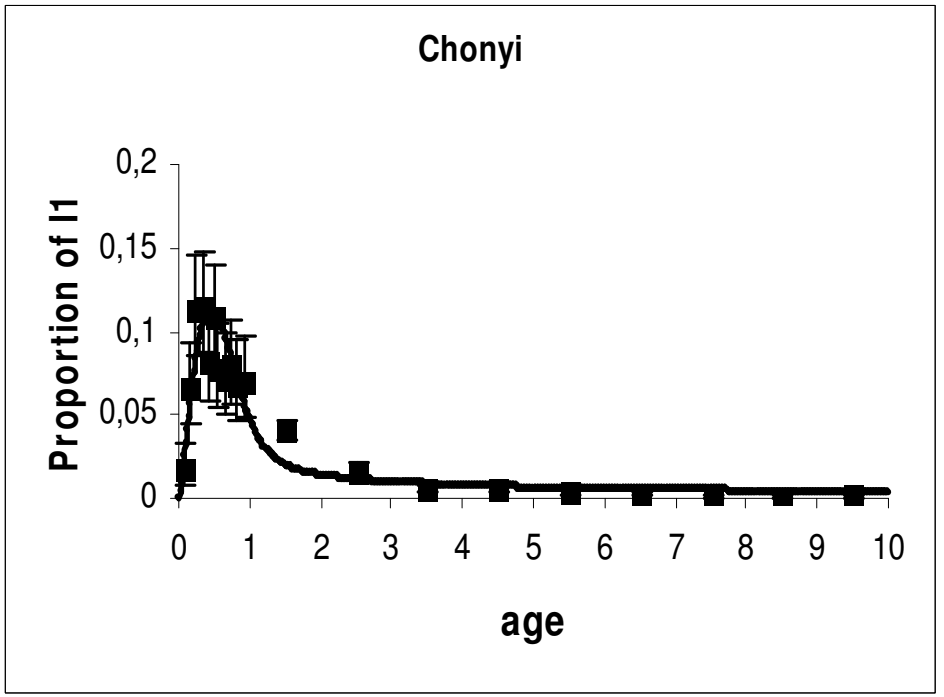
  - Introduce a parameter (η) to account for the percentage of clinical cases that are severe enough as to require hospitalisation.

- Fit all data sets simultaneously using a least squares minimization method.
  - We assumed that transmission intrinsic parameters such as the recovery form infection and loss of immunity would be the same for all regions;
  - The force of infection is the only parameter allowed to vary between regions accounting for region specific properties.


Mponda
Proportion of I1
0,15
0,1
0,05
0
0 1 2 3 4 5 6 7 8 9 10
age


Foni Kansala
Proportion of I1
0,2
0,15
0,1
0,05
0
0 1 2 3 4 5 6 7 8 9 10
age


Ifakara
Proportion of I1
0,35
0,3
0,25
0,2
0,15
0,1
0,05
0
0 1 2 3 4 5 6 7 8 9 10
age


Chonyi
Proportion of I1
0,2
0,15
0,1
0,05
0
0 1 2 3 4 5 6 7 8 9 10
age

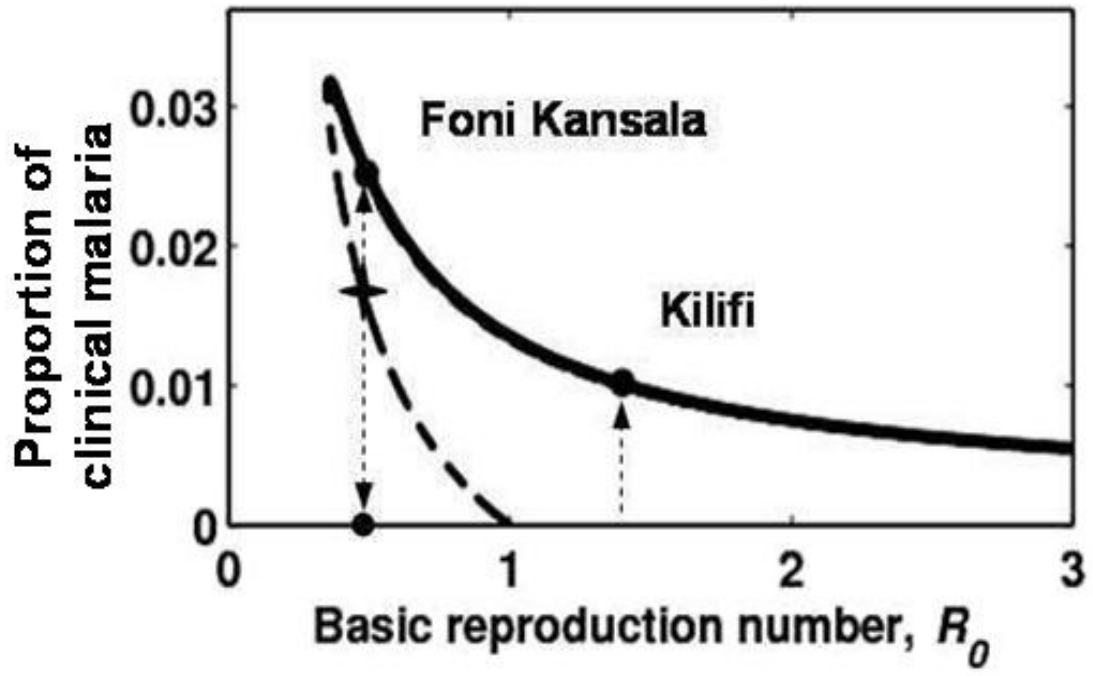
Fitted parameters

Parameter	Fitted value
k	**0.14** (-0.09 – 0.37)
c	**0.99** (0.77 – 1.23)
τ_1	**14.12** (13.90 – 14.36)
τ_2	**2.23** (2.00 – 2.46)
α	**1.07** (0.84 – 1.30)

Region	λ_0 **(95% c.i.)**	Λ	β	R_0
Bakau	0.14 (-0.09 – 0.37)	0.12	9.41	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

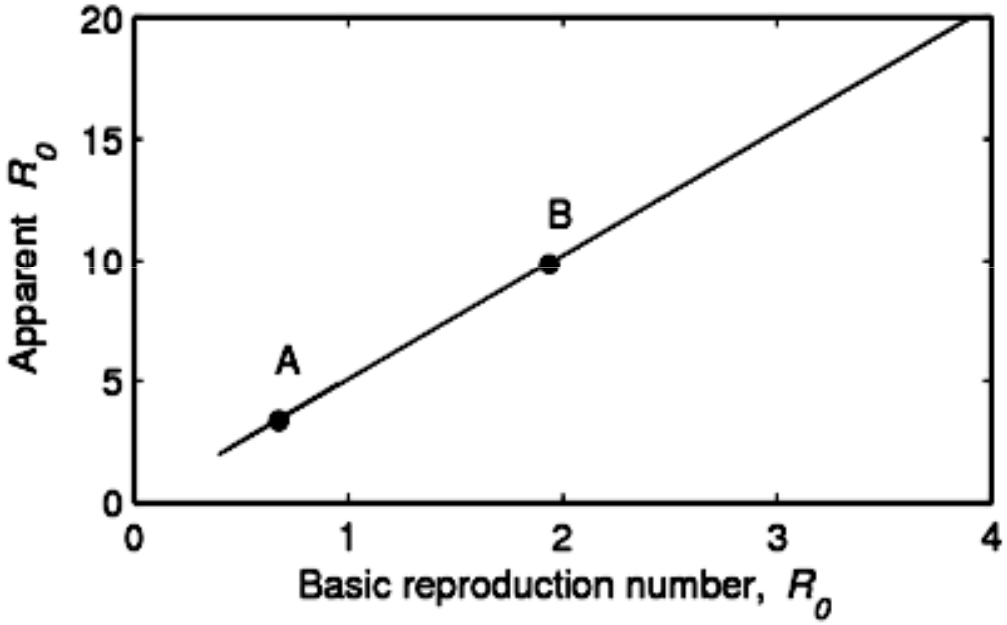
Epidemiological significance

Equilibrium analysis



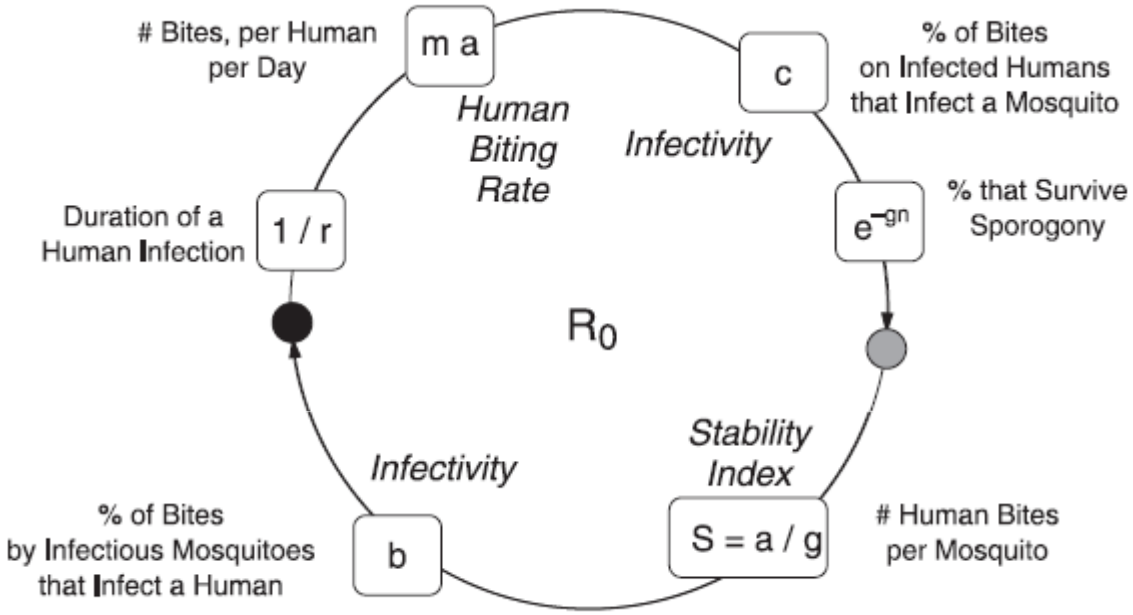
Making sense of R_0

$$R_0 = \beta\left((1-p)\tau_1 + p\tau_2\right)^{-1}$$



$$R_0 = \beta(\tau_1)^{-1}$$

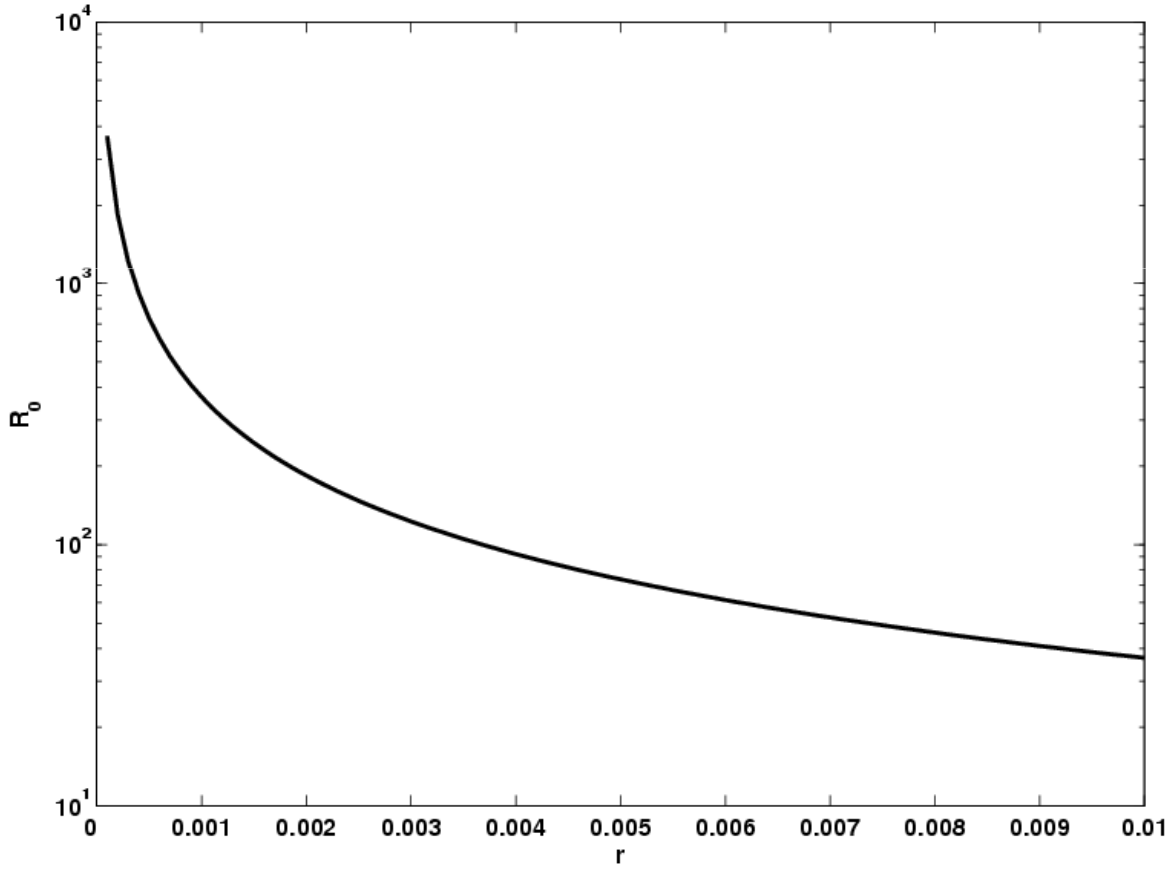
Closer look at transmission



$$R_0 = \frac{bma^2ce^{-gn}}{gr} \qquad \beta = \frac{bma^2ce^{-gn}}{g} \qquad D = \frac{1}{r}$$

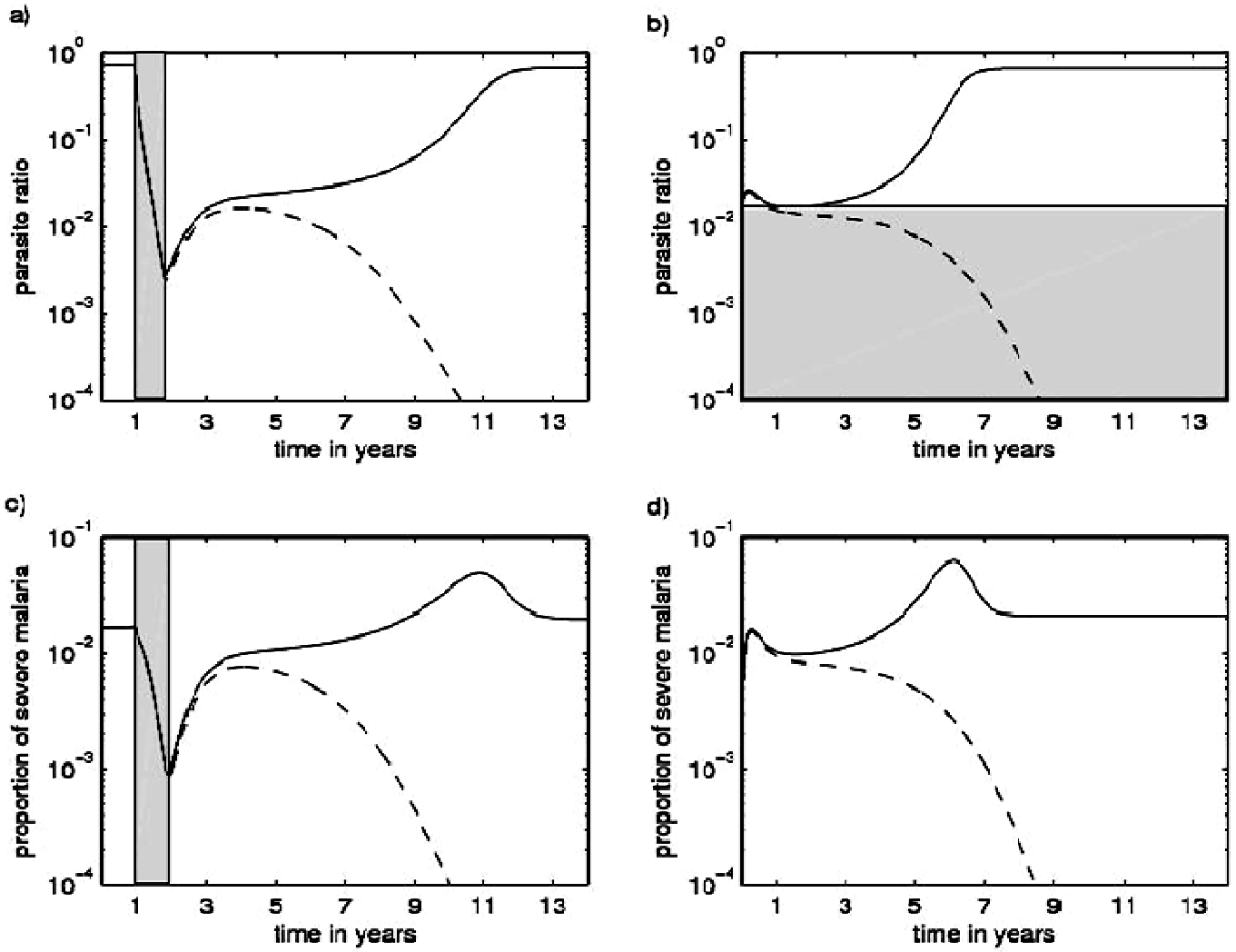
Simulating interventions (drugs)

$$R_0 = \frac{bma^2 ce^{-gn}}{gr}$$



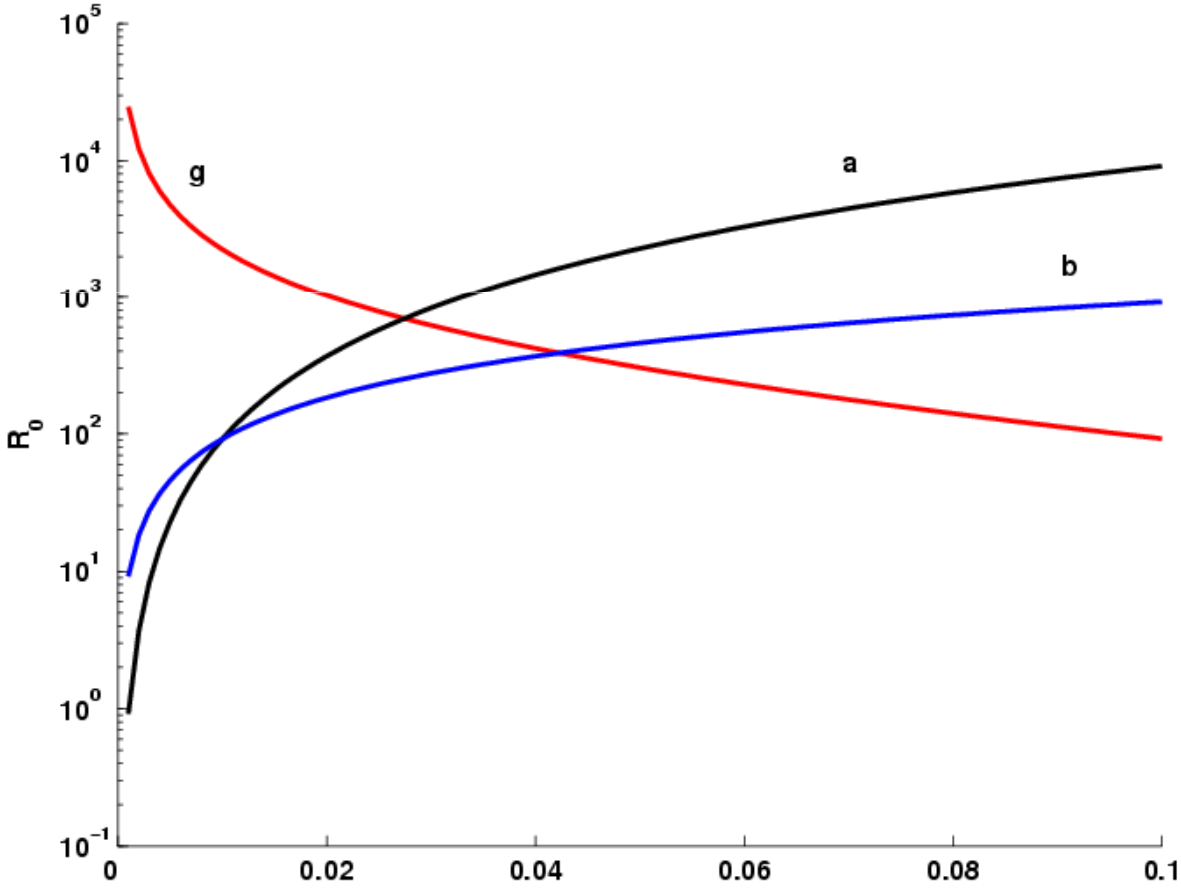
Simulating interventions (drugs)

Deacreasing D 6.3x



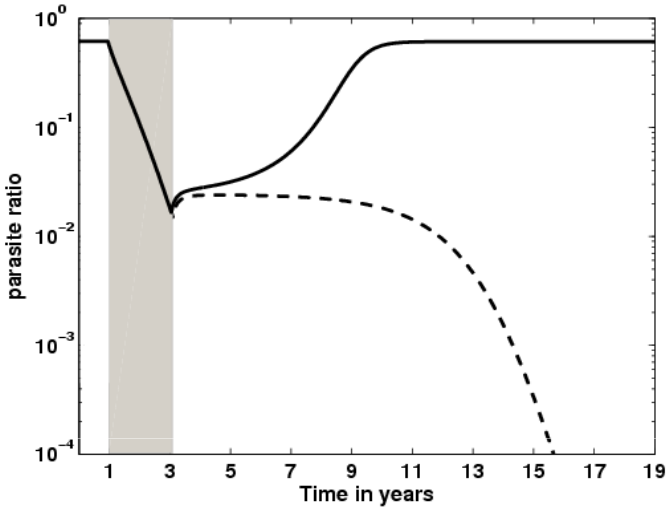
Simulating interventions (mosquitoes)

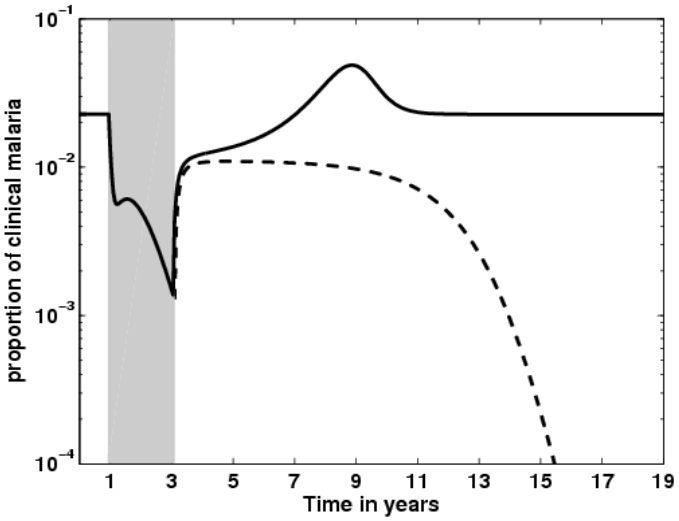
$$R_0 = \frac{bma^2 ce^{-gn}}{gr}$$



Simulating interventions (mosquitoes)

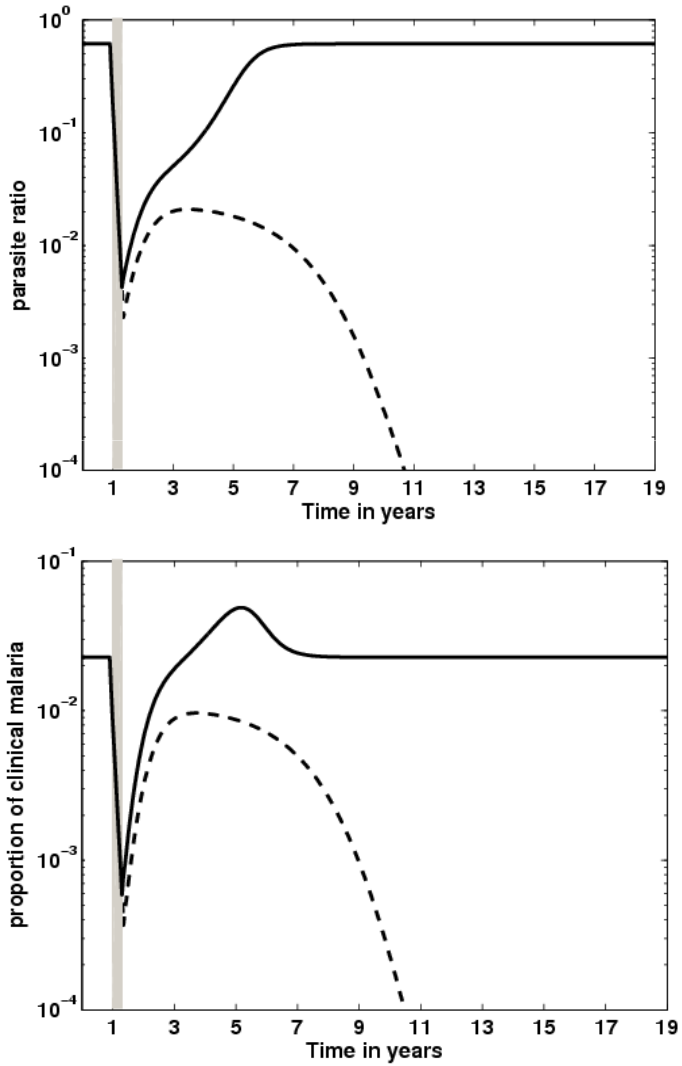
Deacreasing β 6.3x



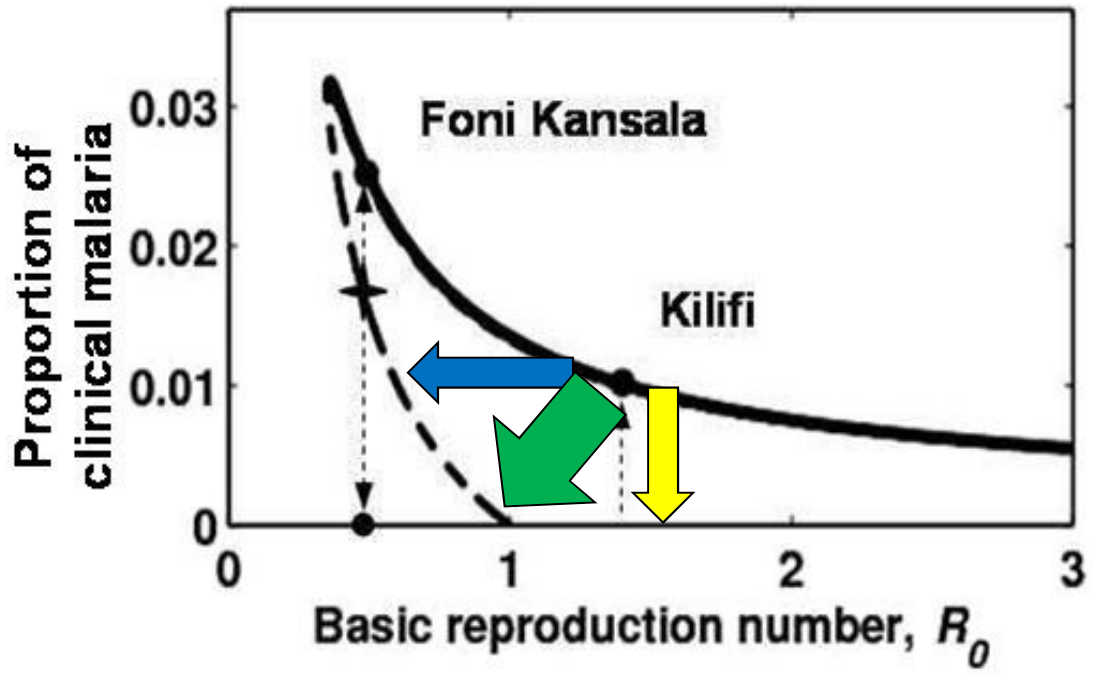


Integrated approach

Deacreasing both β *and D* 6.3x



Integrated approach



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