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Designing disease control strategies using models and data from multiple sources

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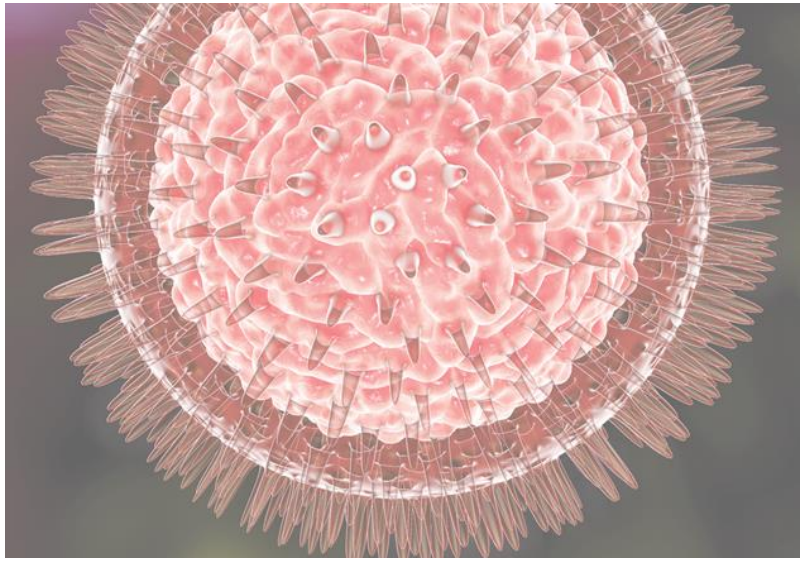
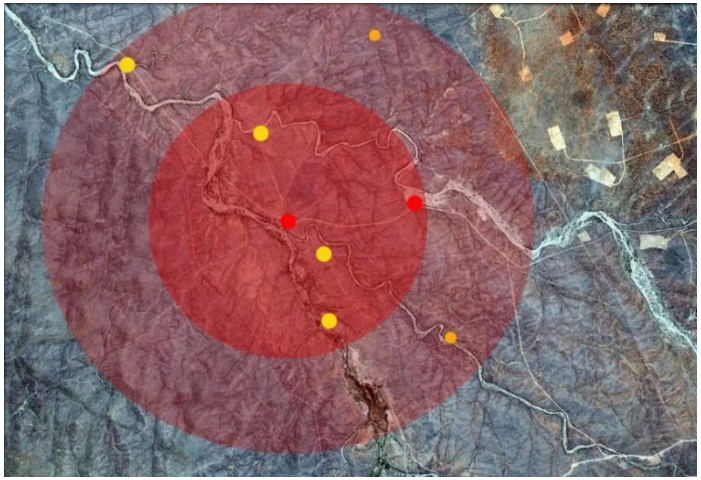




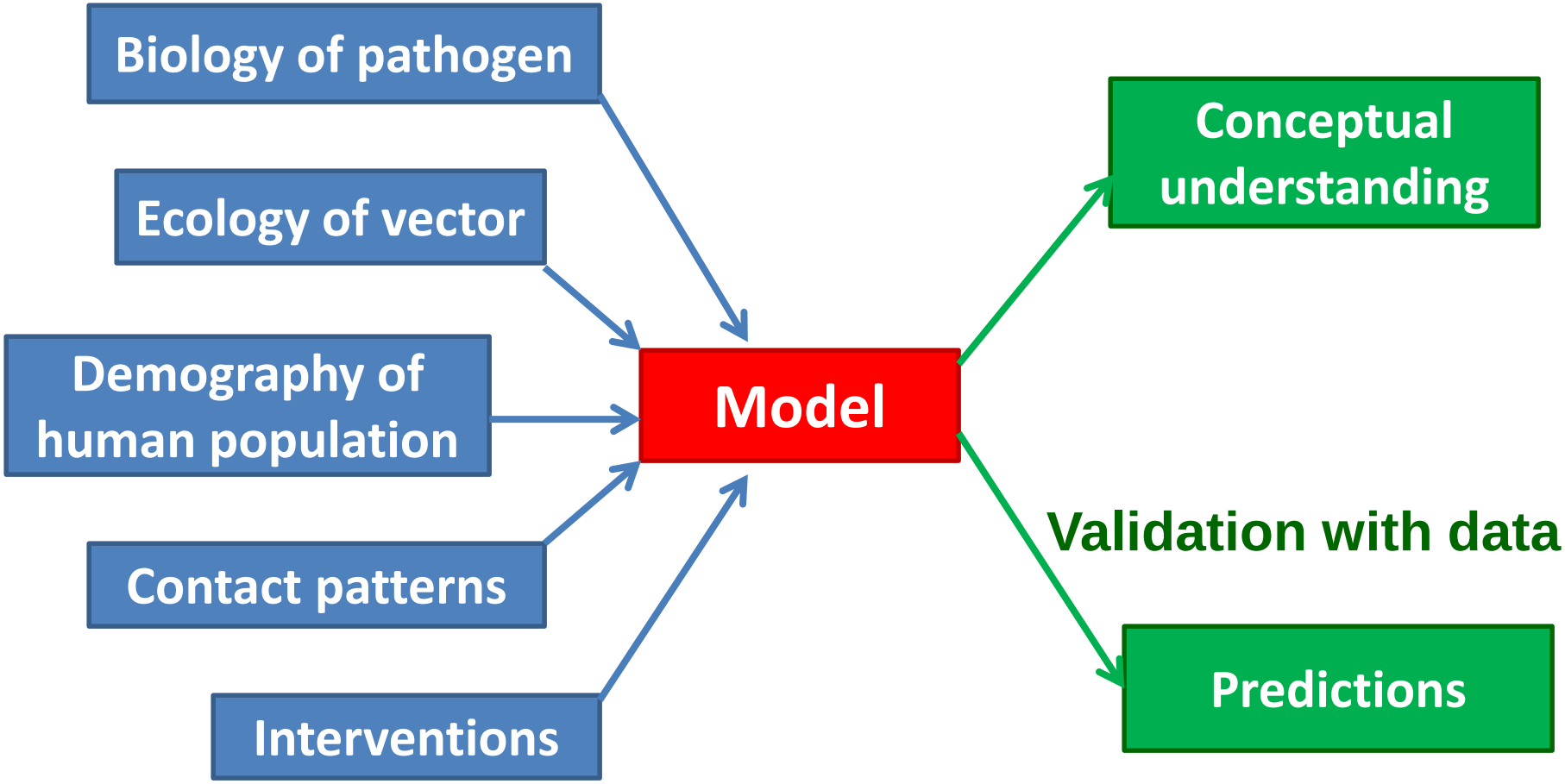
Berkeley School of Public Health

Overview of talk

1. Zika virus:
   - Questions that modeling can help us to address
   - Results from recent modeling papers

2. Malaria in elimination settings:
   - Importance of understanding heterogeneity
   - Quantifying geographic heterogeneity using risk maps
   - Predicting the impact of elimination strategies using mathematical models

Why model?


Biology of pathogen
Ecology of vector
Demography of human population
Contact patterns
Interventions
Model
Conceptual understanding
Validation with data
Predictions

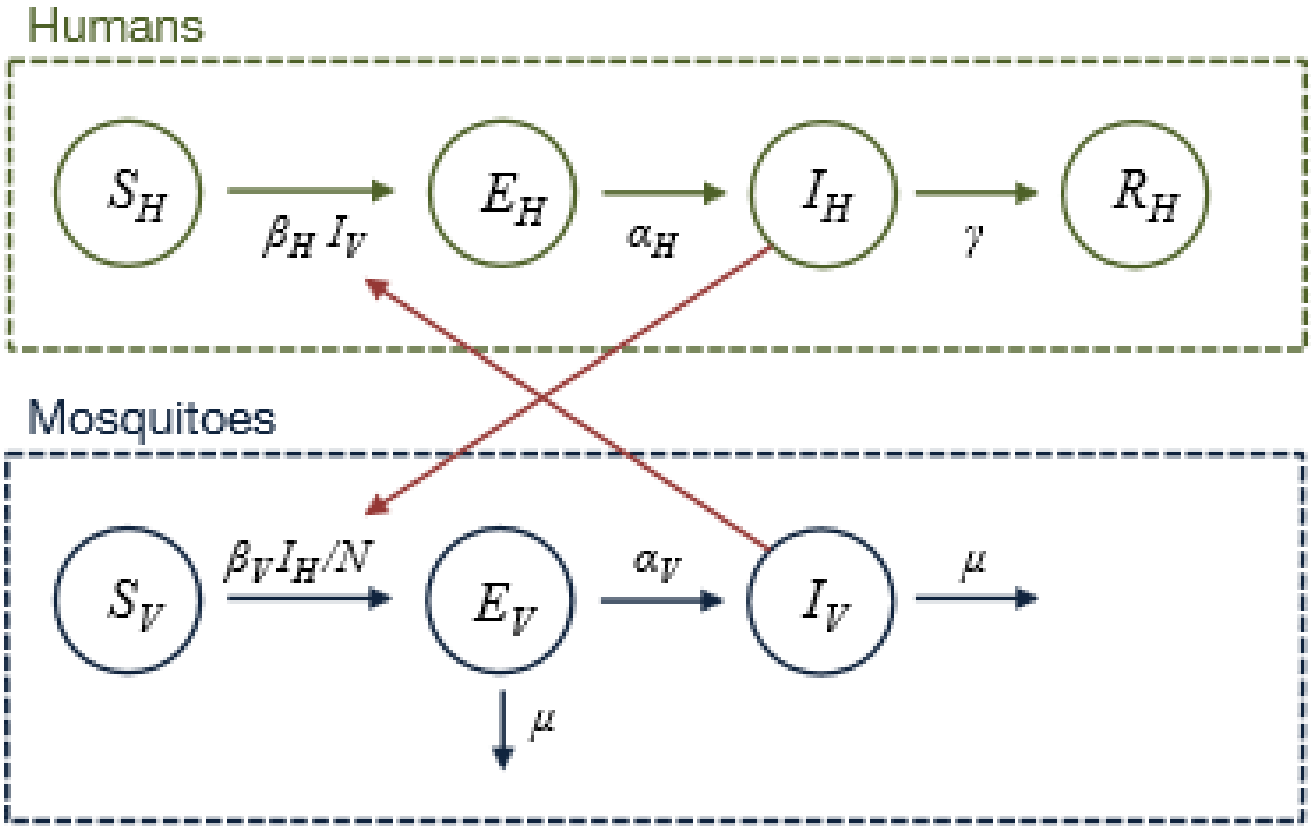
Zika questions that modeling may help to inform

1. What implications does the current outbreak in Latin America have for the US?
2. What is the expected time course of the current outbreak in Latin America?
3. Is Zika here to stay? What are the expected long-term dynamics of Zika in Latin America?
4. What impact can we expect vector control to have on Zika incidence and the incidence of Zika-induced microcephaly?
5. What about a Zika vaccine, if it becomes available?
6. What implications does the sexual transmission of Zika have on the population-wide dynamics?

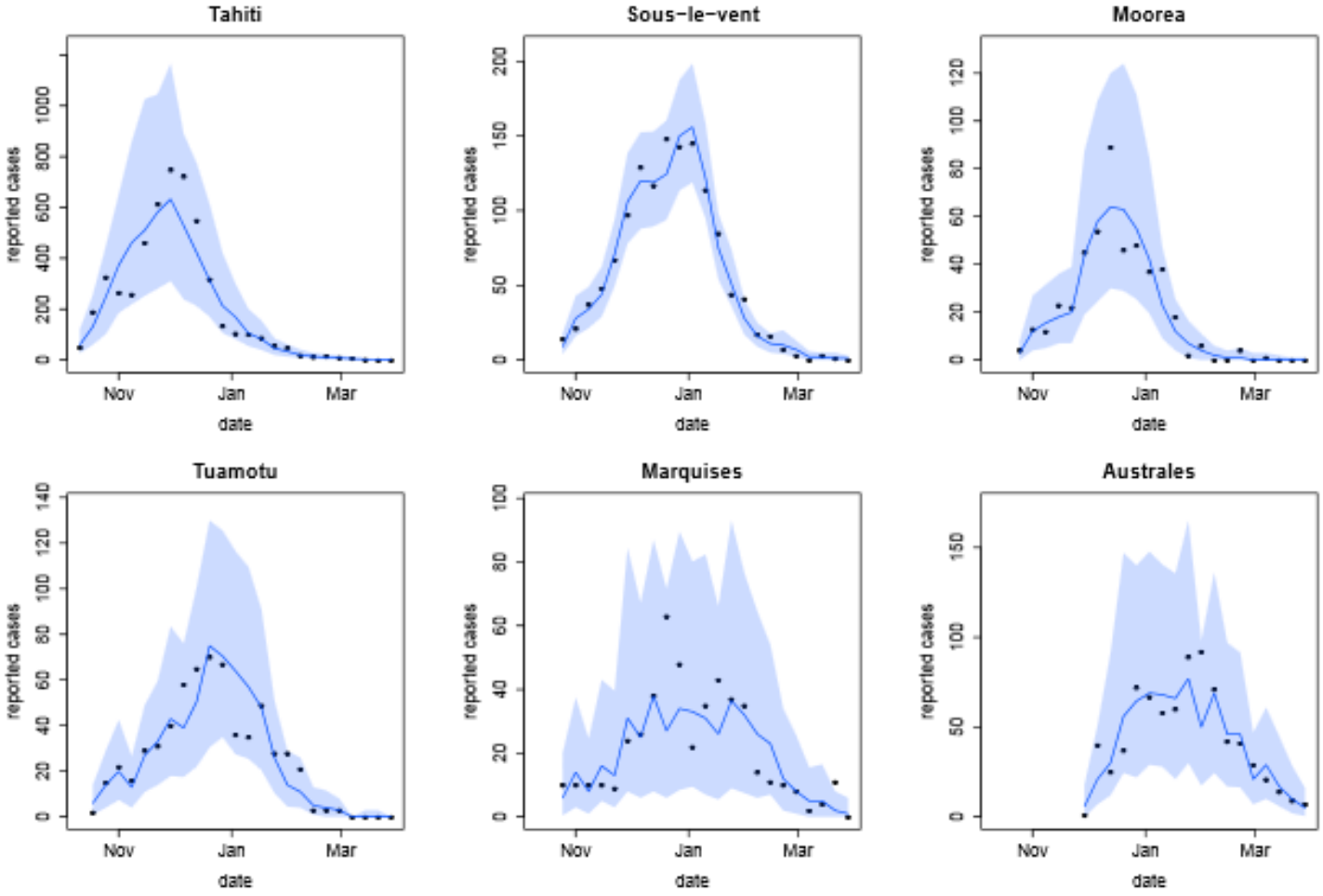
Compartmental model of Zika virus

Transmission dynamics of Zika virus in island populations: a modelling analysis of the 2013–14 French Polynesia outbreak

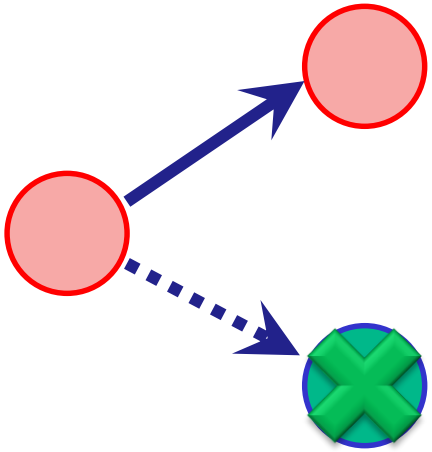
Adam J. Kucharski[1,*], Sebastian Funk[1], Rosalind M. Eggo[1], Henri-Pierre Mallet[2], W. John Edmunds[1], Eric J. Nilles[3]



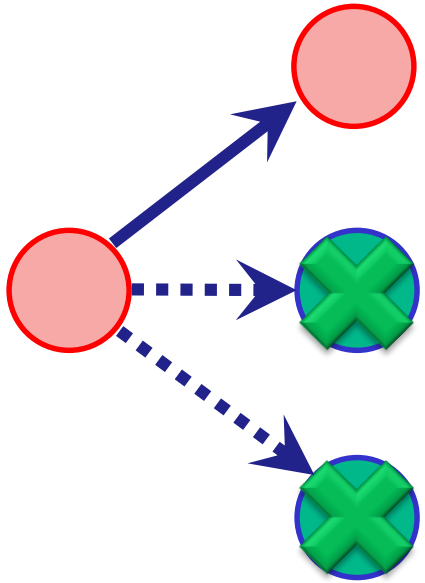
Fitting compartmental models to incidence data using Bayesian MCMC



Outbreak size seems to be determined by herd immunity threshold (HIT), itself determined by R_0



- $R_0 = 2$
- Outbreak slows down after 1/2 of population has been infected



- $R_0 = 3$
- Outbreak slows down after 2/3 of population has been infected

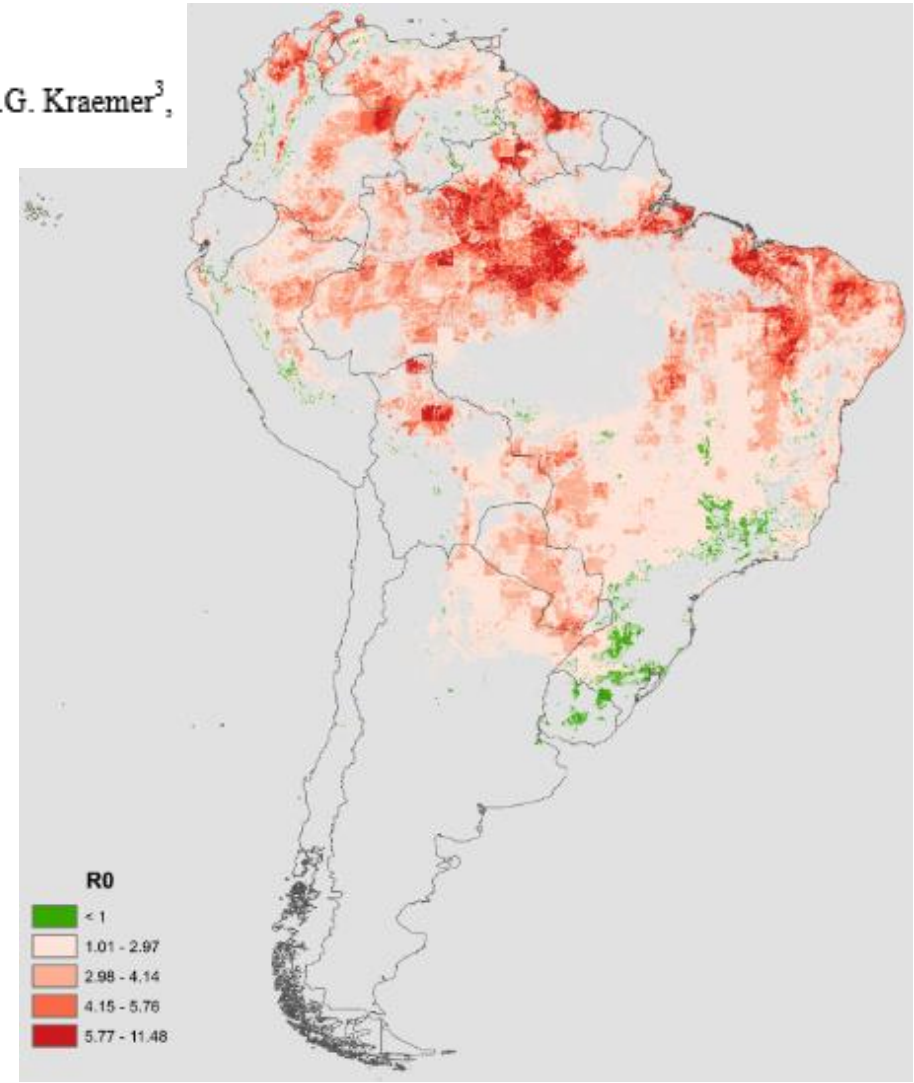
Implications for Latin America

Model-based projections of Zika virus infections in childbearing women in the Americas

T. Alex Perkins[1*], Amir S. Siraj[1], Corrine Warren Ruktanonchai[2], Moritz U.G. Kraemer[3], Andrew J. Tatem[2,4]

$$R_0(T) = \frac{mbca^2 e^{-\mu(T)n(T)}}{\mu(T)r}$$

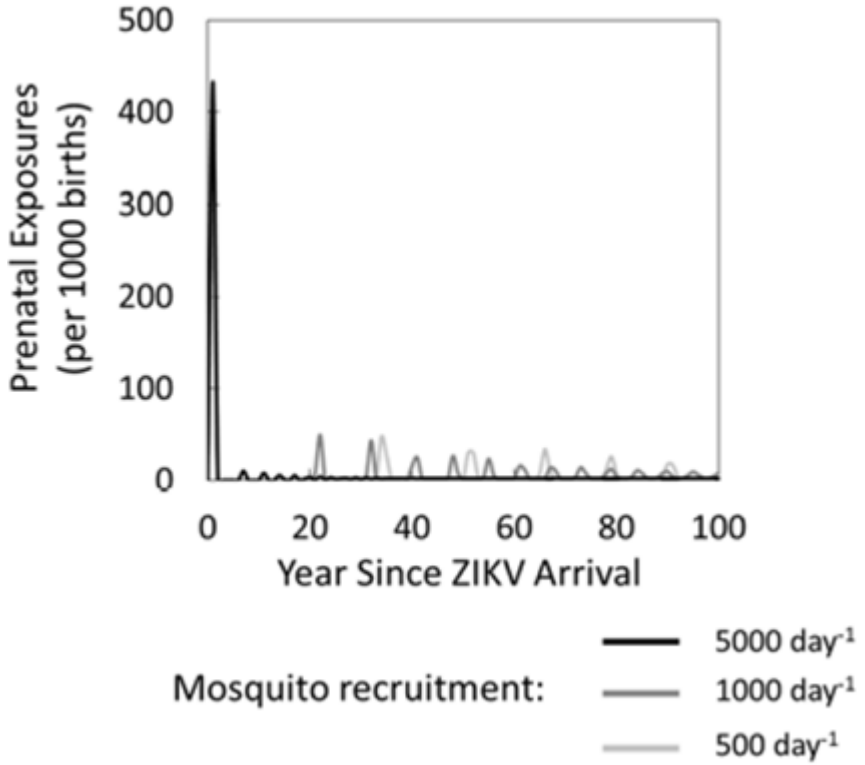
- m = Number of mosquitoes per person (derived from species mapping with correction factor from economic index)
- $\mu(T)$ = Mosquito death rate (function of temperature)
- $n(T)$ = Virus incubation period in mosquito (function of temperature)



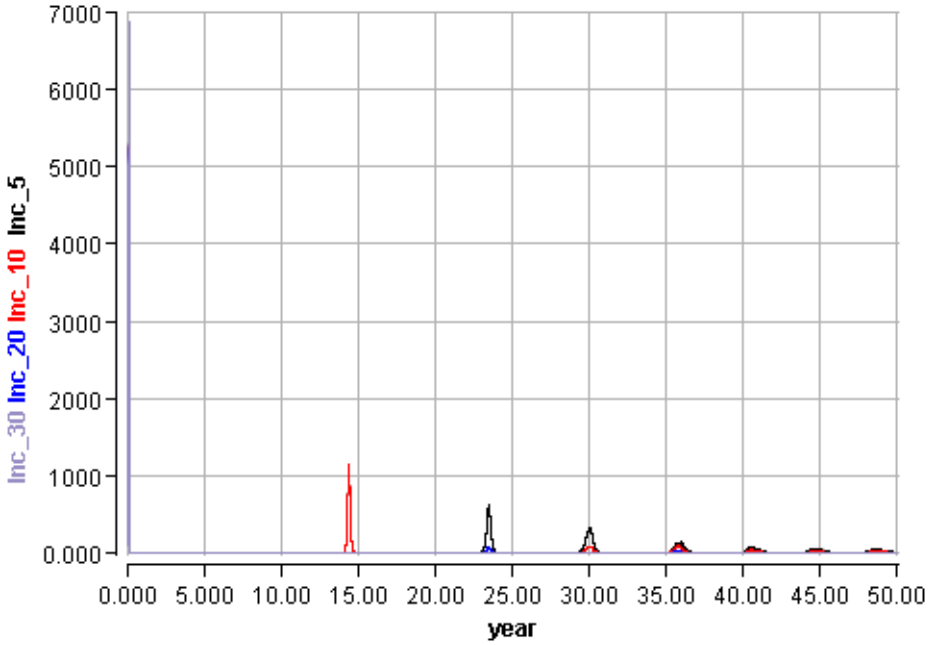
Is Zika here to stay?

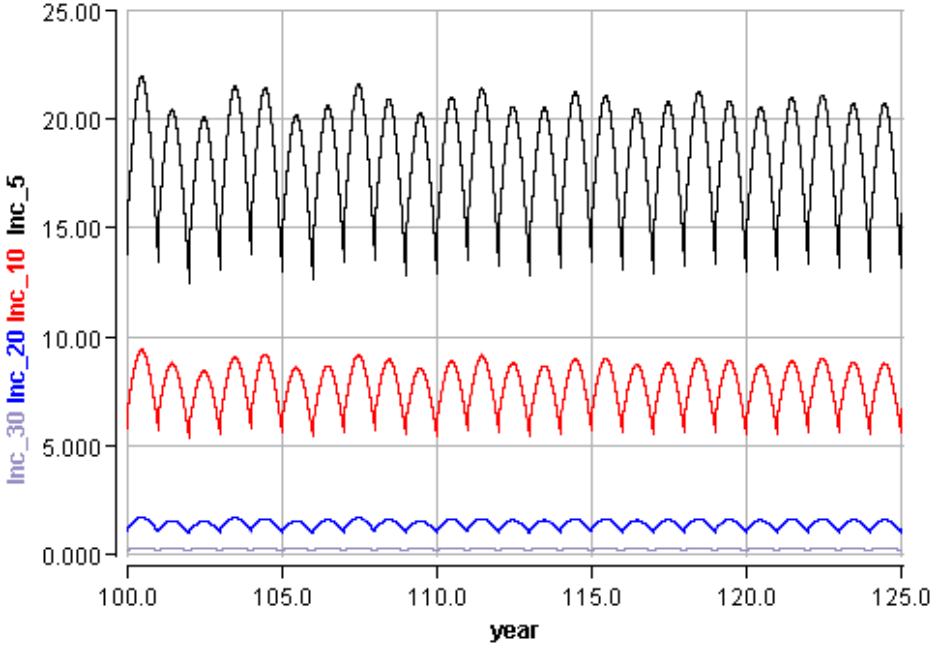
Zika Virus: Endemic Versus Epidemic Dynamics and Implications for Disease Spread in the Americas

Sharon Bewick[1], William F. Fagan[2], Justin Calabrese[2], Folashade Agusto[3,*]



Long-term dynamics of an immunizing infection (the endemic state) c.f. Rubella

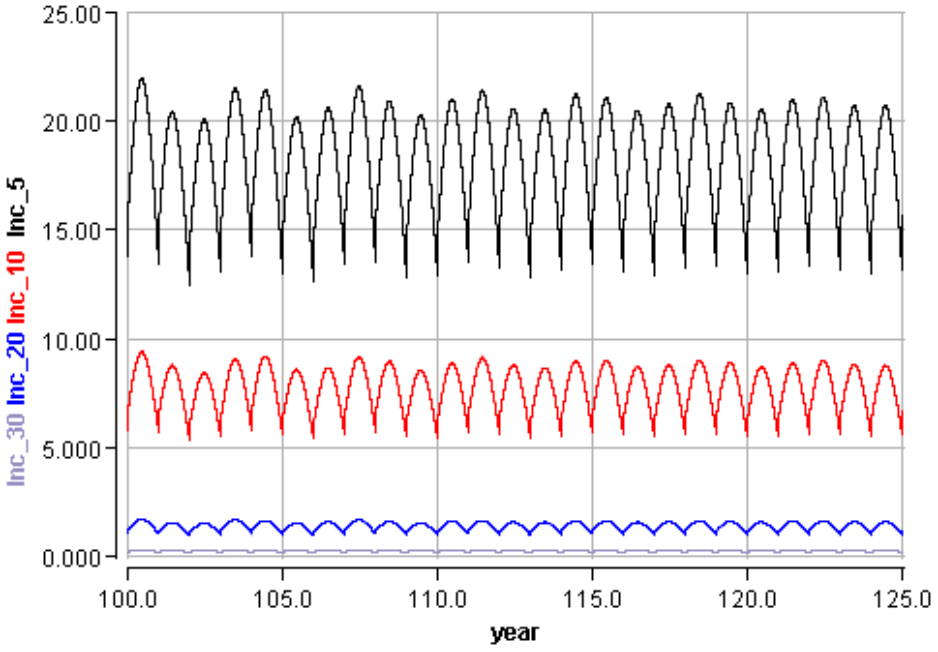


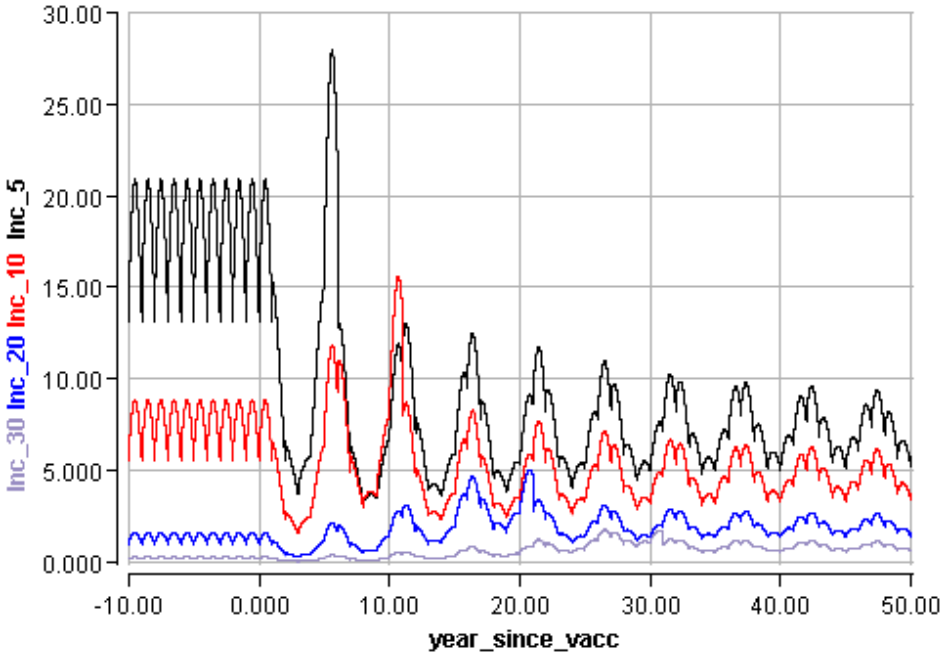


- Huge first outbreak with spread across all age-groups
- Progressively smaller outbreaks concentrated mostly among younger age-groups

- Incidence in the endemic state is ~0.0025 that of the first outbreak
- Incidence in the endemic state is concentrated mostly among younger age-groups

Vaccinating can have counterintuitive effects among older age groups (c.f. Rubella)





Vaccination campaign (50% coverage):

- Reduces proportion susceptible among younger age groups
- But decreases exposure rate and hence increases average age of exposure
- Possible to actually result in higher incidence among women of child-bearing age

Implications for vector control

$$R_0(T) = \frac{mbca^2 e^{-\mu(T)n(T)}}{\mu(T)r}$$

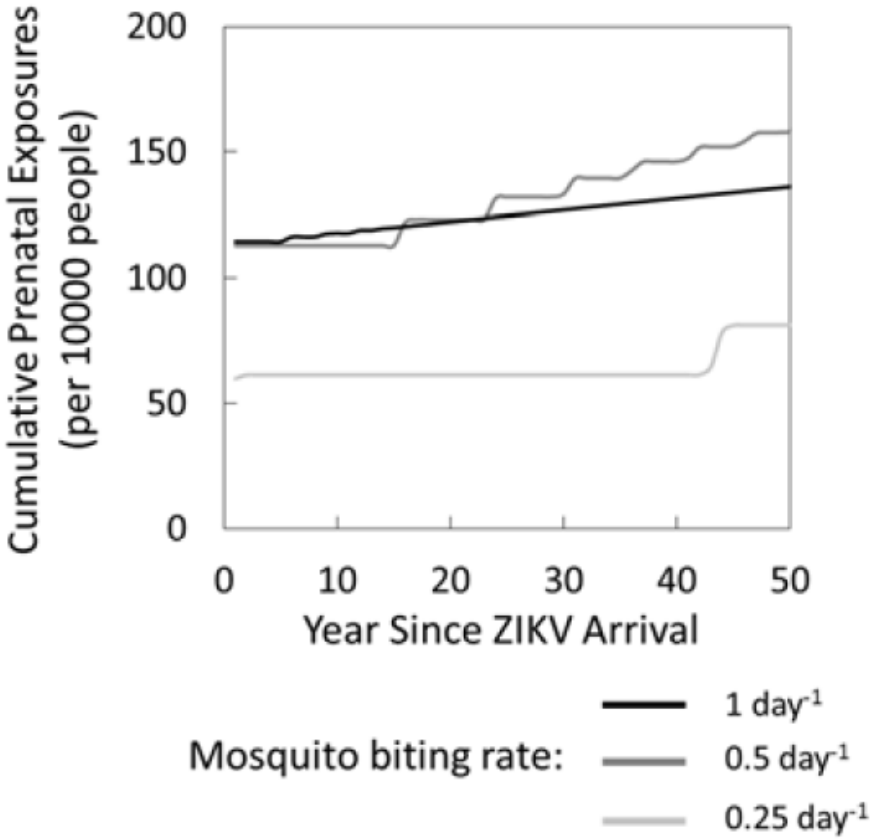
Vector control may reduce:

- *m* = Number of mosquitoes per person
- *a* = Mosquito biting rate

And may increase:

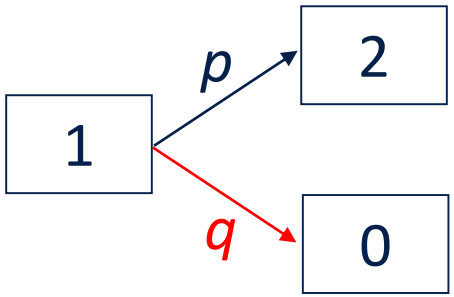
- μ = Mosquito death rate

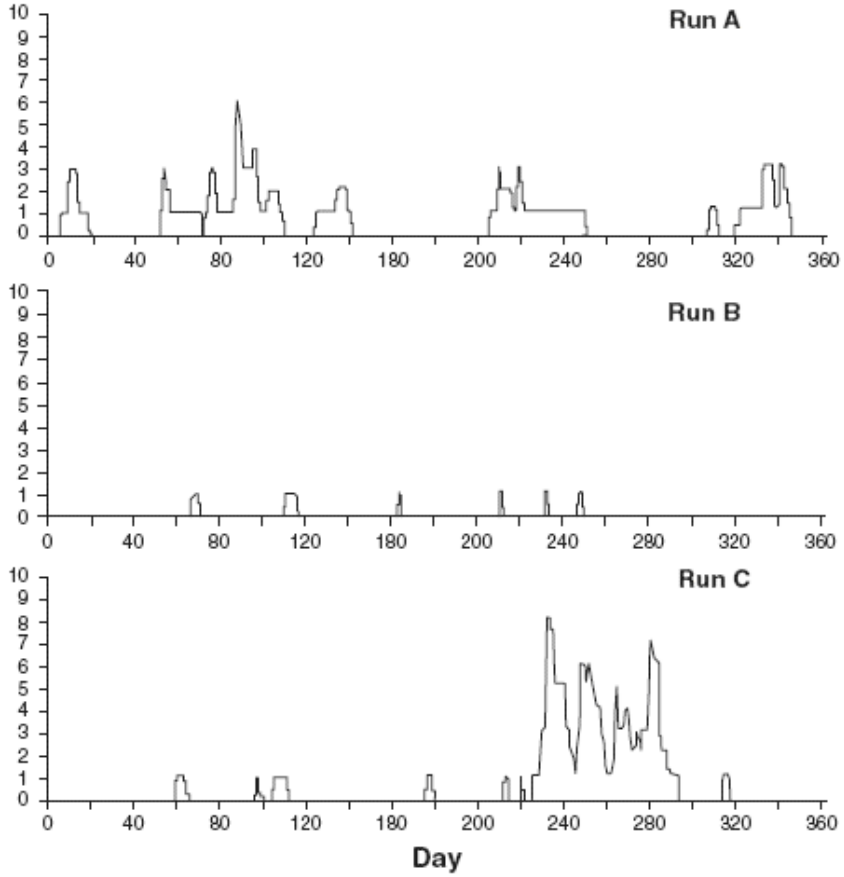
But may also delay infection to child-bearing ages

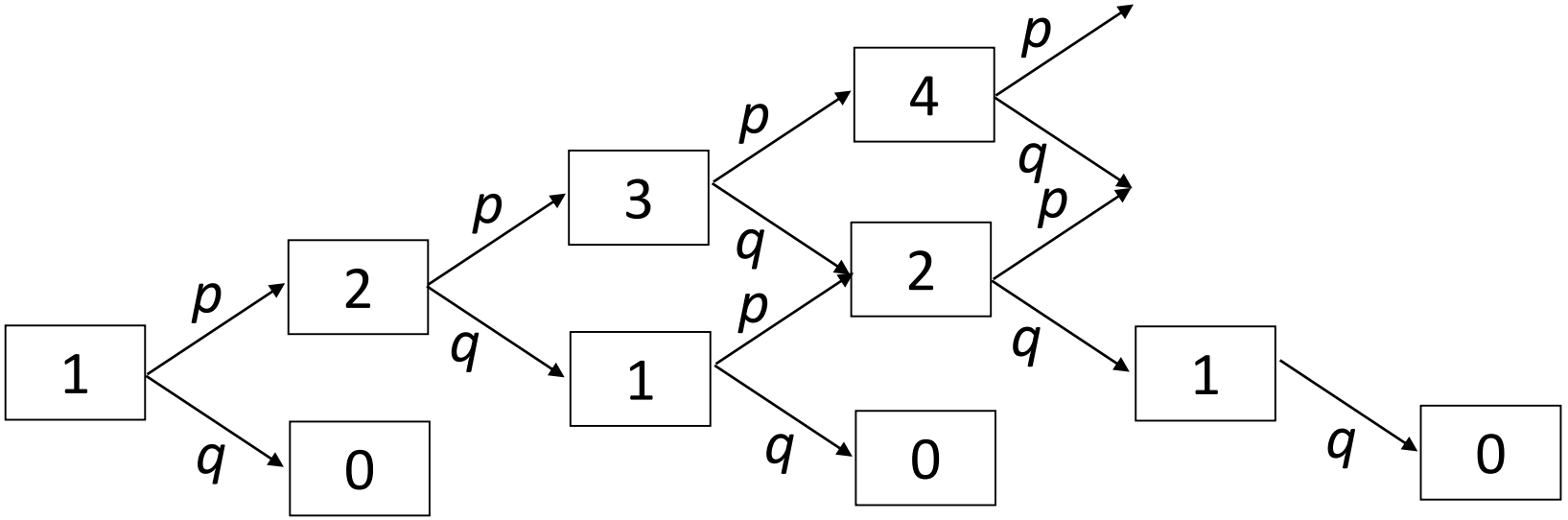


Implications for the US

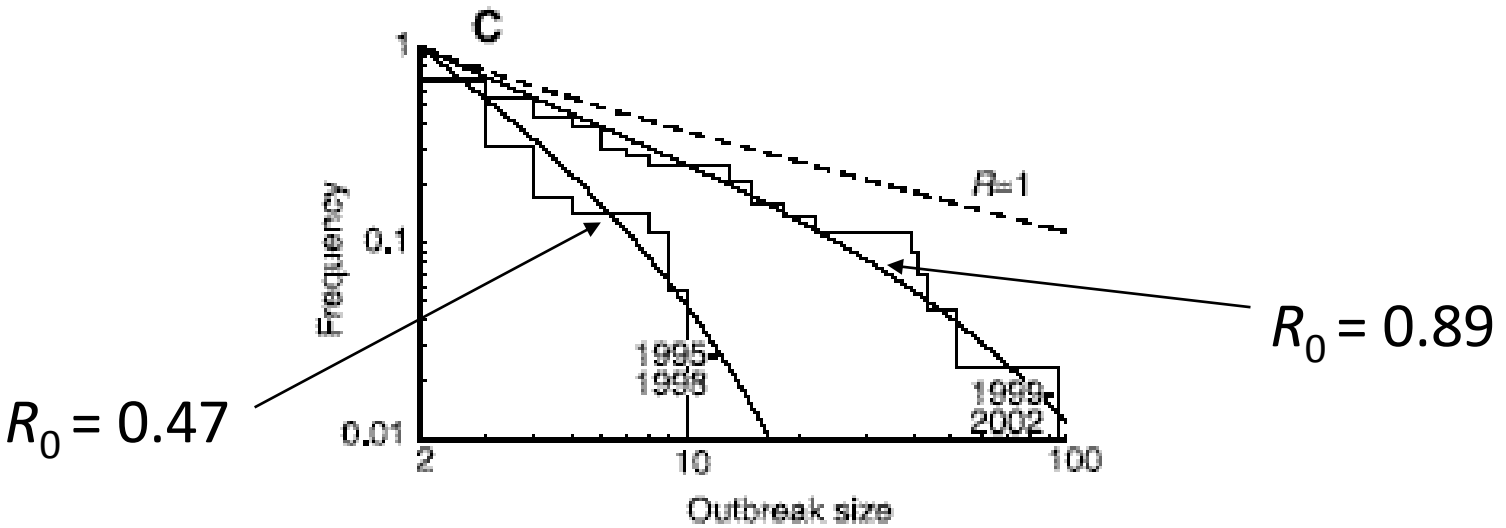
- $R_0 < 1$ so outbreaks are stochastic events





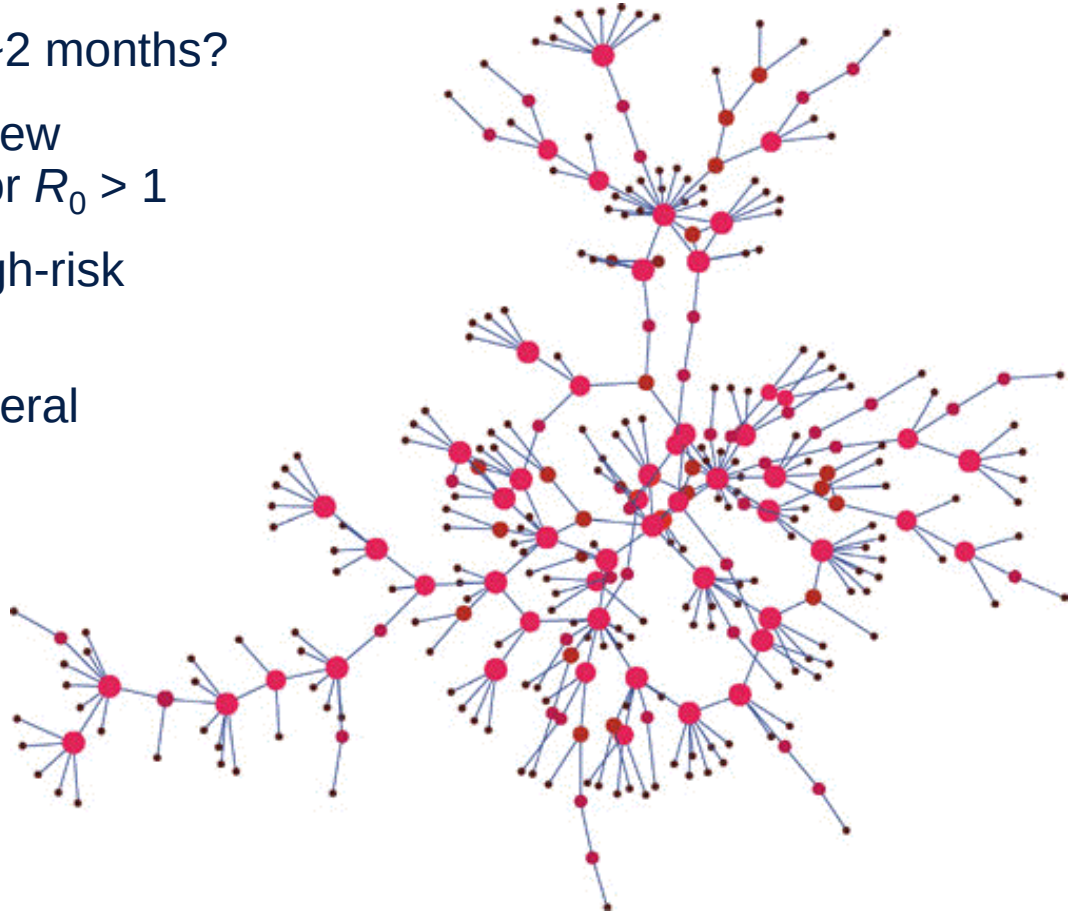


The probability of a final outbreak of size n is: $R_0^{n-1} e^{-Rn} n^{n-2} / (n-1)!$

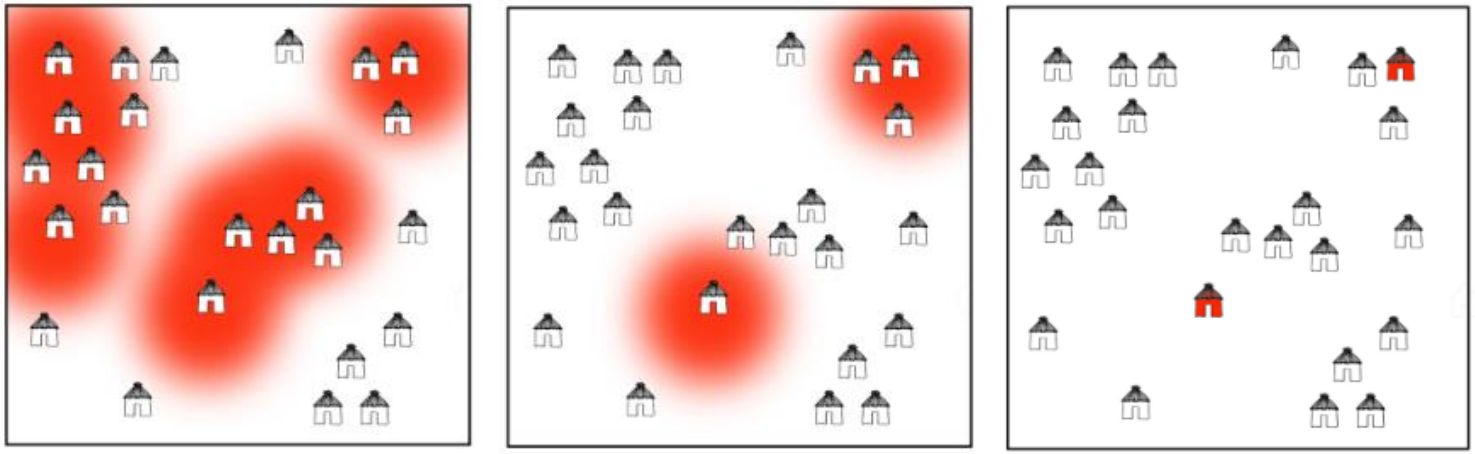


Implications of sexual transmission

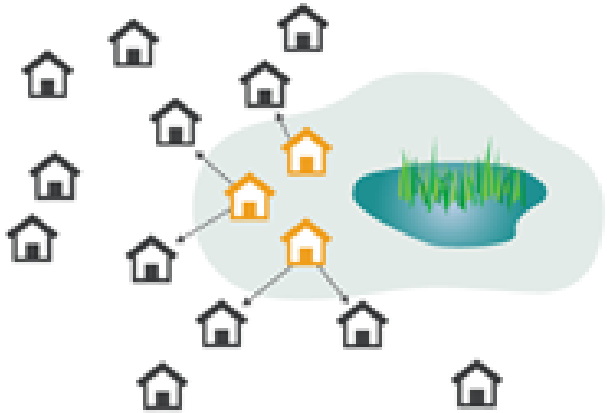
- R_0 = Number of partners per year
  x Probability of transmission per partnership
  x Duration of infectiousness
- Duration of infectiousness = ~2 months?
- Therefore need at least one new partnership every 2 months for $R_0 > 1$
- Potential to spread among high-risk groups
- Unlikely to persist among general population



Malaria elimination



- As malaria prevalence declines in many areas, it becomes increasingly focal and heterogeneous
- Understanding this heterogeneity is important for predicting the impact of elimination strategies
- Importance of using data to quantify heterogeneity



Bousema *et al.* (2010) PLoS Med.

Gonorrhea Transmission Dynamics and Control

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considered. Let the average durations of infection, d_1 and d_2, both be 25 days. Here we assume that all new encounters are adequate contacts so that $q_1 = q_2 = 1$. Thus the core-noncore model is an initial value problem with the differential equations

$$\frac{dI_i}{dt} = \frac{k_i}{d_i}(b_1I_1+b_2I_2)(1-I_i) - \frac{I_i}{d_i} \qquad [4.1]$$

for i = 1,2. A flow diagram for this model is given in figure 4.1.

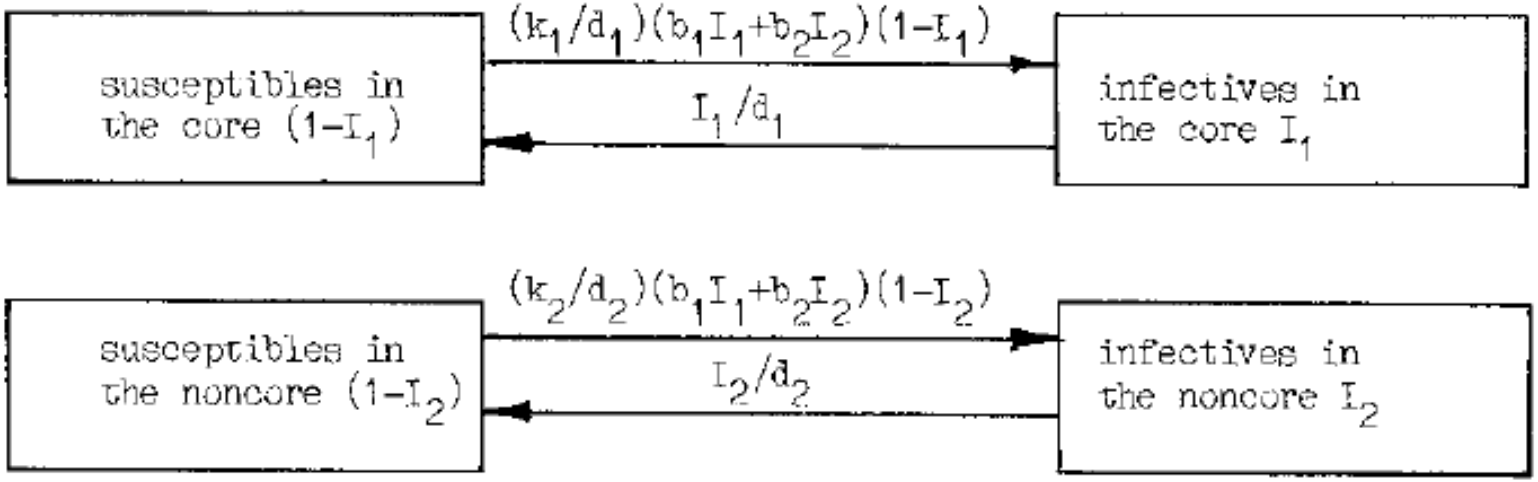
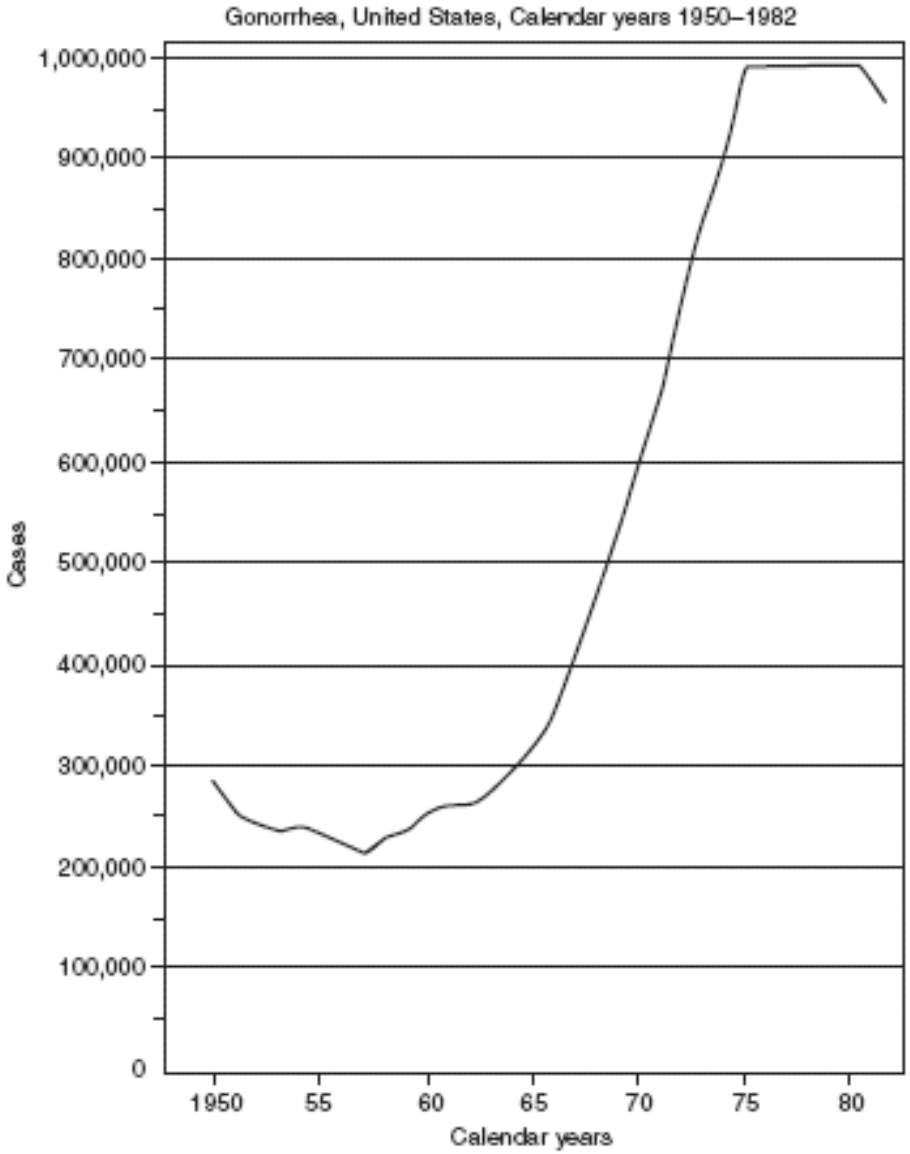
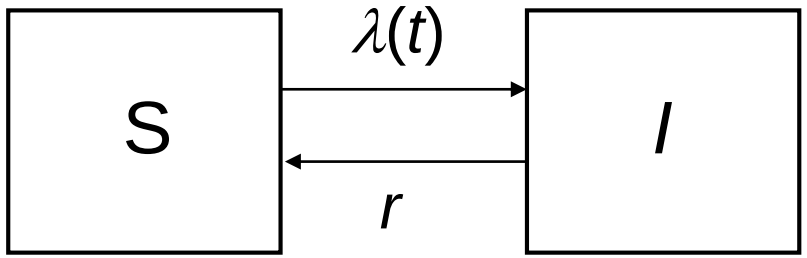
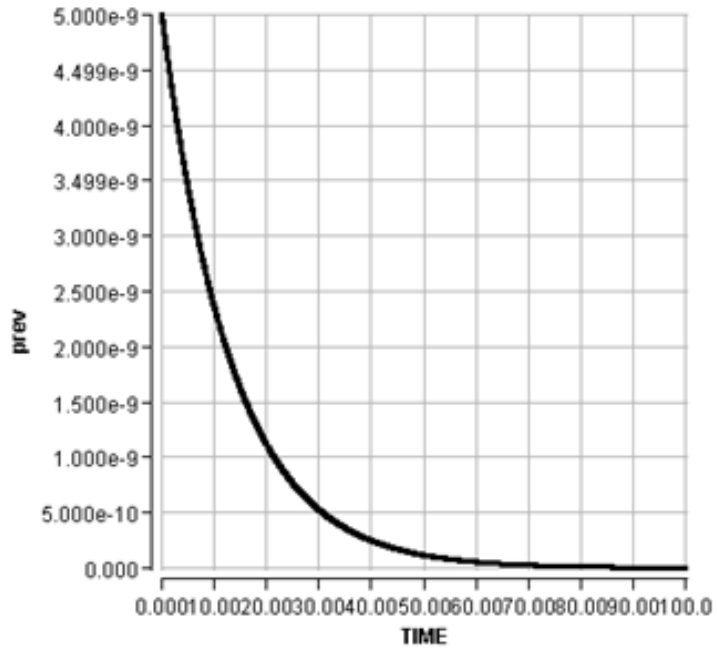


Figure 4.1 Flow diagram for the core-noncore model.

Hethcote-Yorke model of gonorrhea

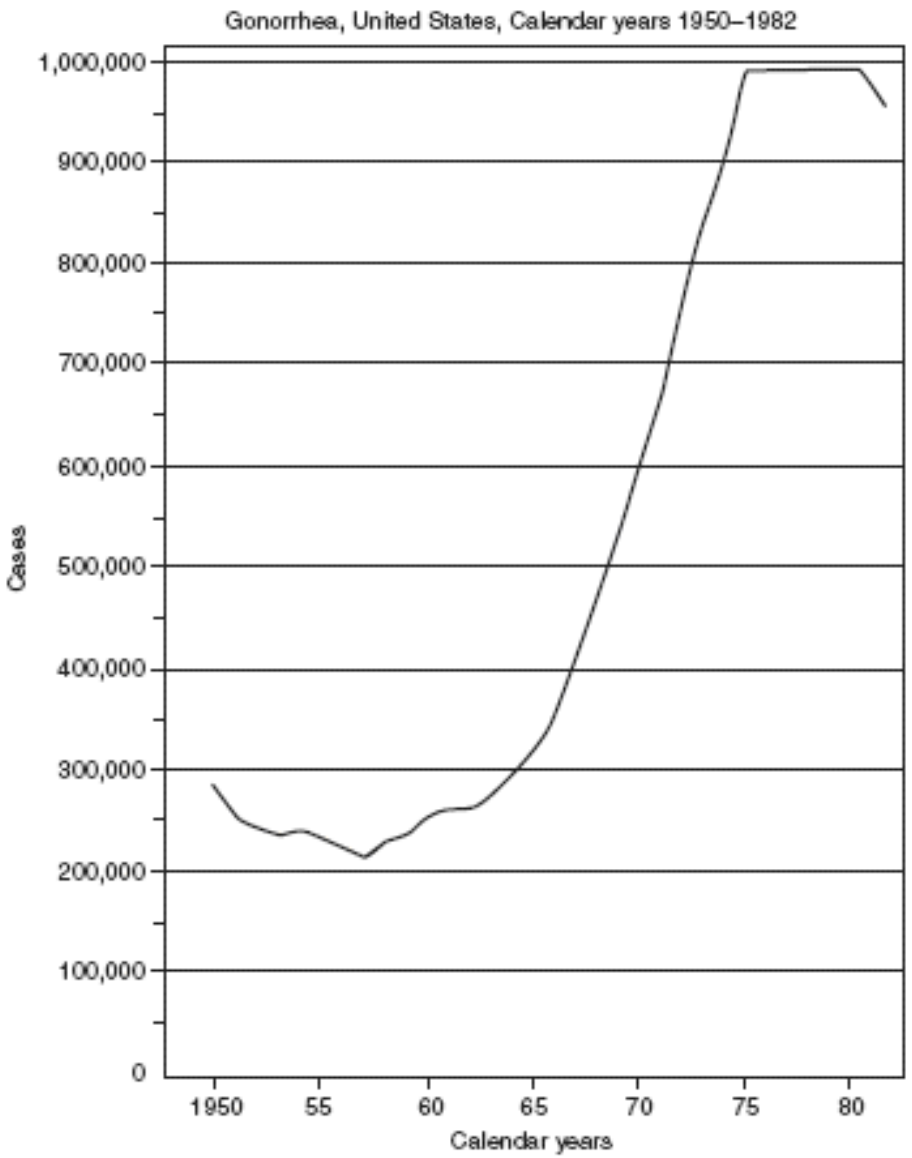


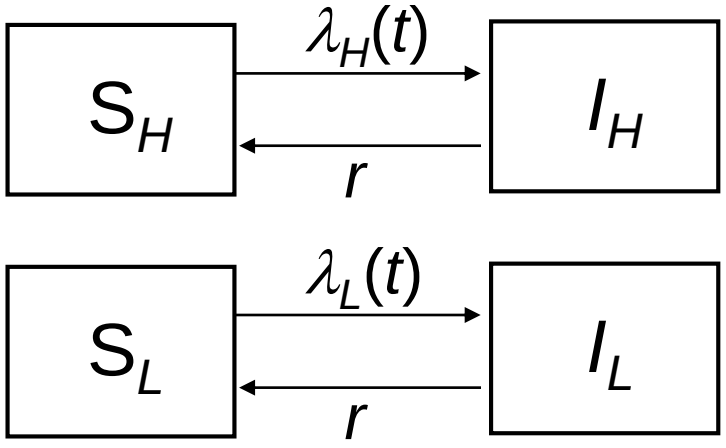


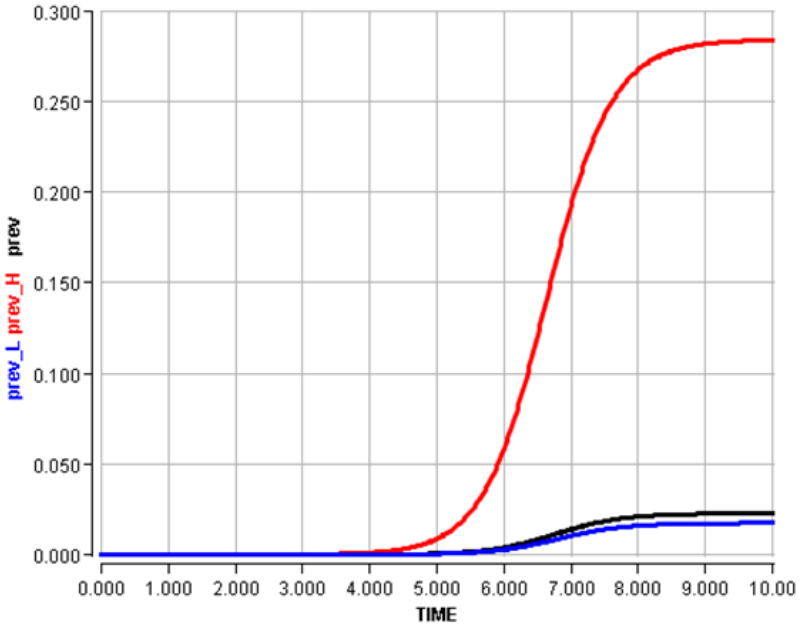


Hethcote & Yorke (1984)

Hethcote-Yorke model of gonorrhea





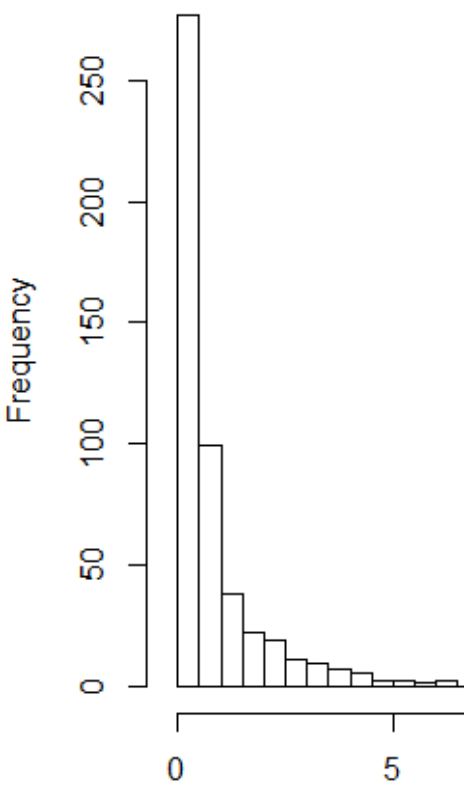


Hethcote & Yorke (1984)

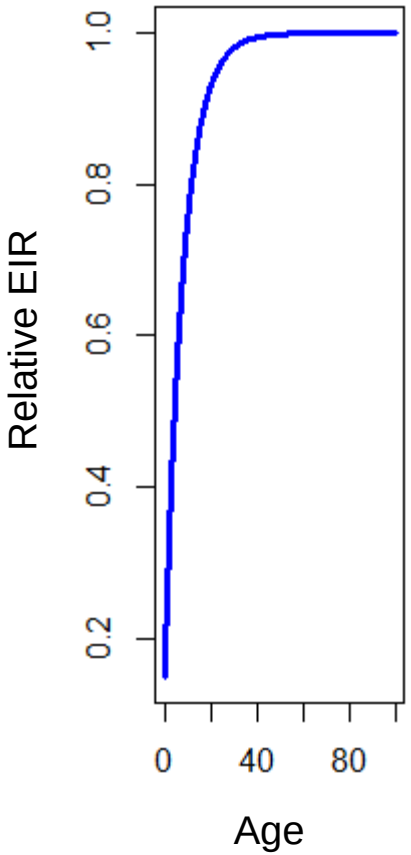
Heterogeneity in the entomological inoculation rate (EIR)

$$EIR = EIR_0 \times \zeta \times (1 - \rho e^{-a/a_0}) \times \psi$$

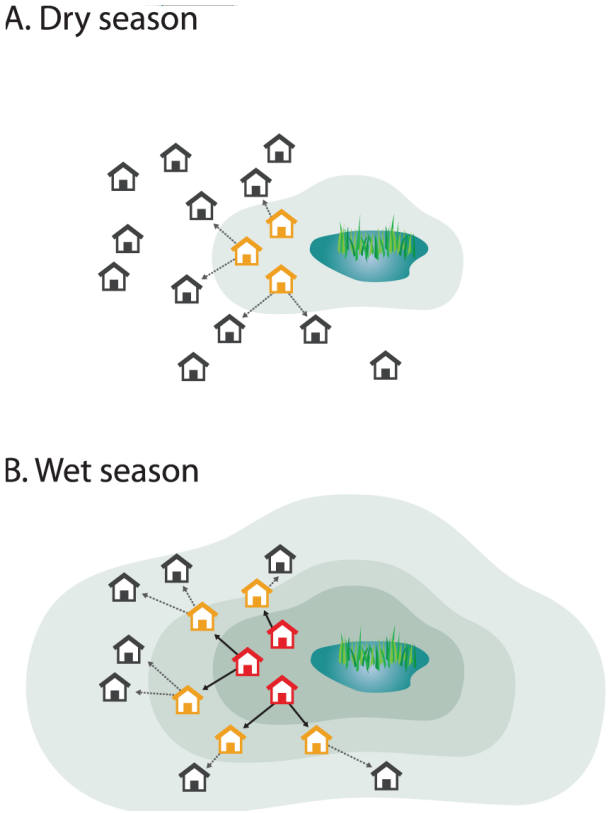
ζ = Individual variation in biting rates



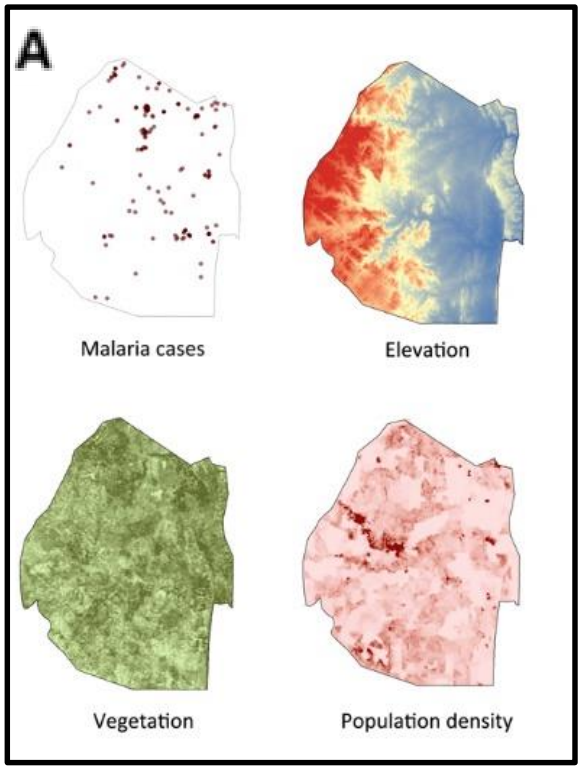
Variation with age

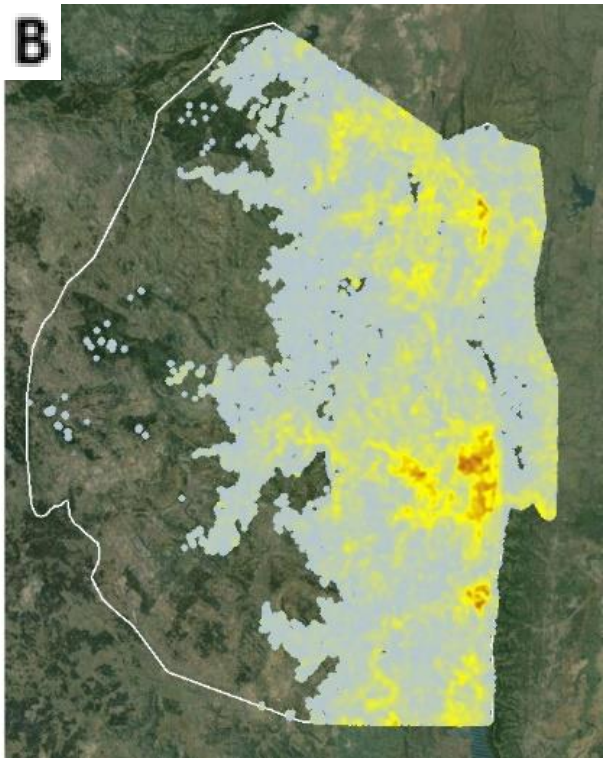


Ψ = Geographical variation



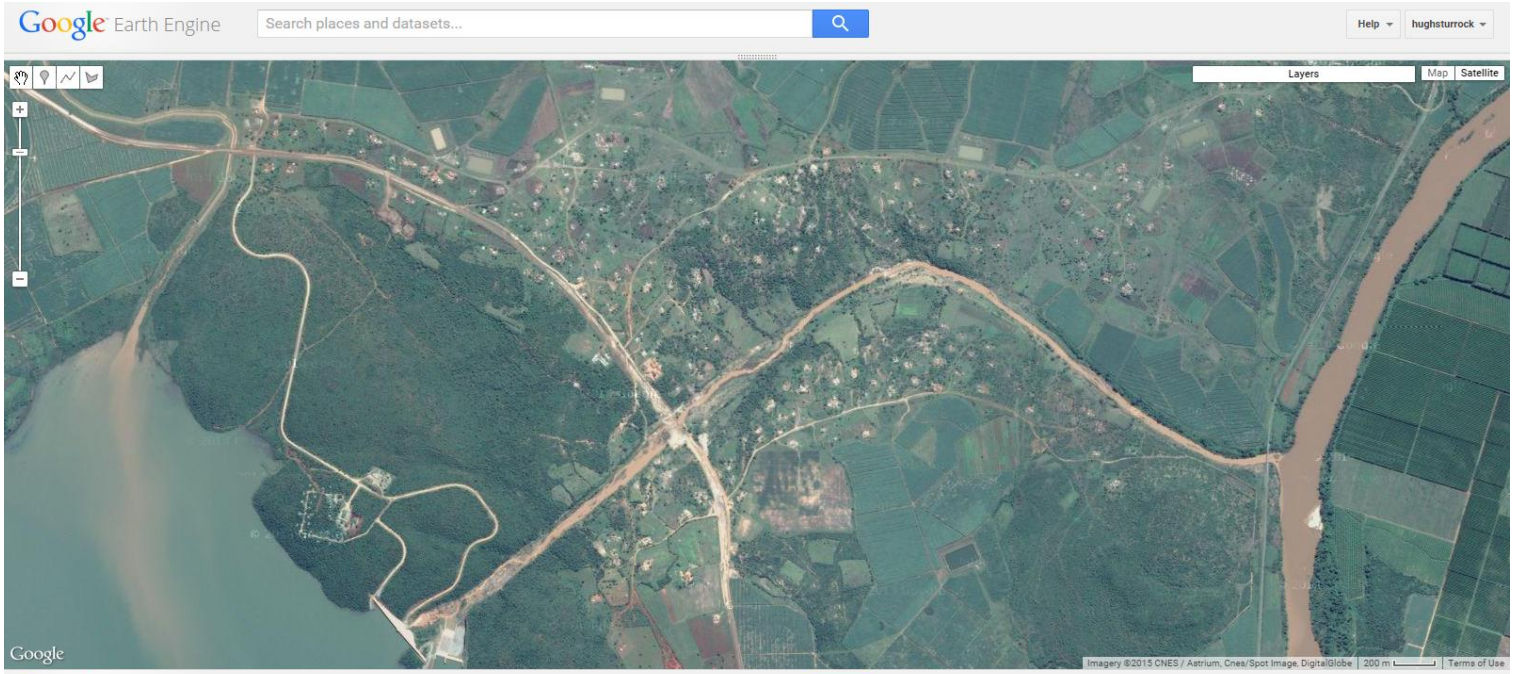
Estimating geographical heterogeneity in the EIR

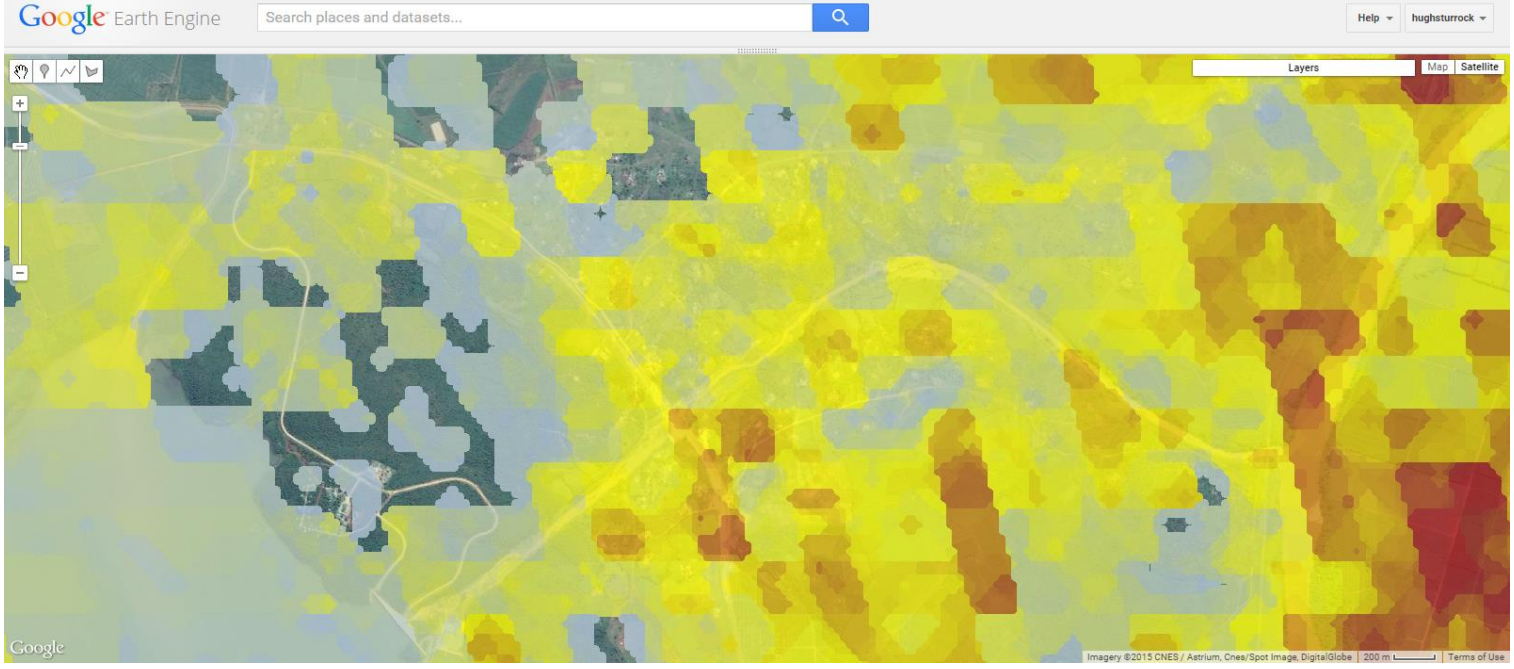




- **A:** Maps of:
  - health-facility level malaria case data
  - Environmental covariates (elevation and vegetation shown here)
  - Population density
- **B:** Used to create fine-scale risk maps for Swaziland at the national scale
- **C:** And also at the village scale

Google Earth demonstration…





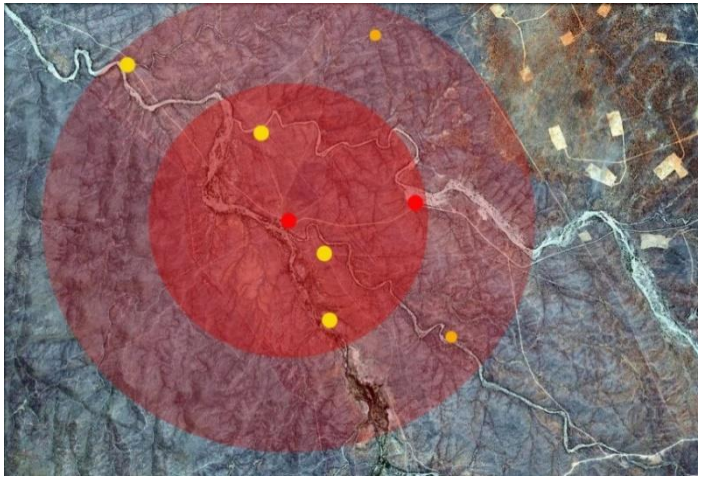
What we're deciding between…

Anti-parasite interventions & delivery strategies:

In high transmission settings:	
MDA	Mass Drug Administration
MSAT	Mass Screening and Treatment

In low transmission settings:	
Focal MDA	Focal Mass Drug Administration
RACD	Reactive Case Detection

Anti-vector interventions:	
LLINs	Long Lasting Insecticide-treated Nets
IRS	Indoor Residual Spraying with insecticides



Operational questions:

- Diagnostics (microscopy, RDTs, PCR)
- Treatment (ACTs, PQ)
- Radius of testing and treatment
- Desired coverage level

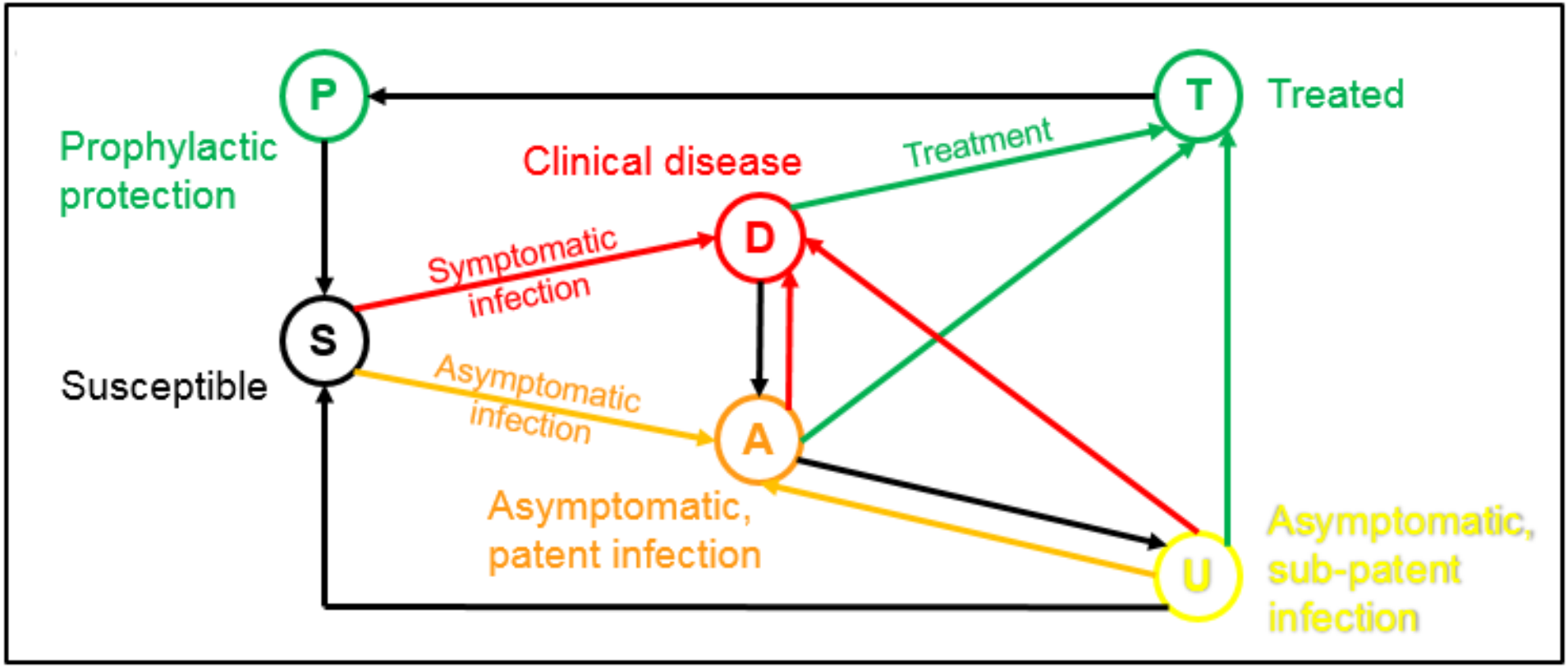
Constraints

- Currently being quantified from observational studies & clinical trials…

Types of constraints:	
Technical	Inherent in the mathematical modeling framework, describe limitations of currently-available tools to reduce transmission
Operational	Defined by logistical considerations (e.g. human resources, transport, ability of national organizations to carry out the program, etc.)
Financial	Defined by program costs and funds available over a sustained period

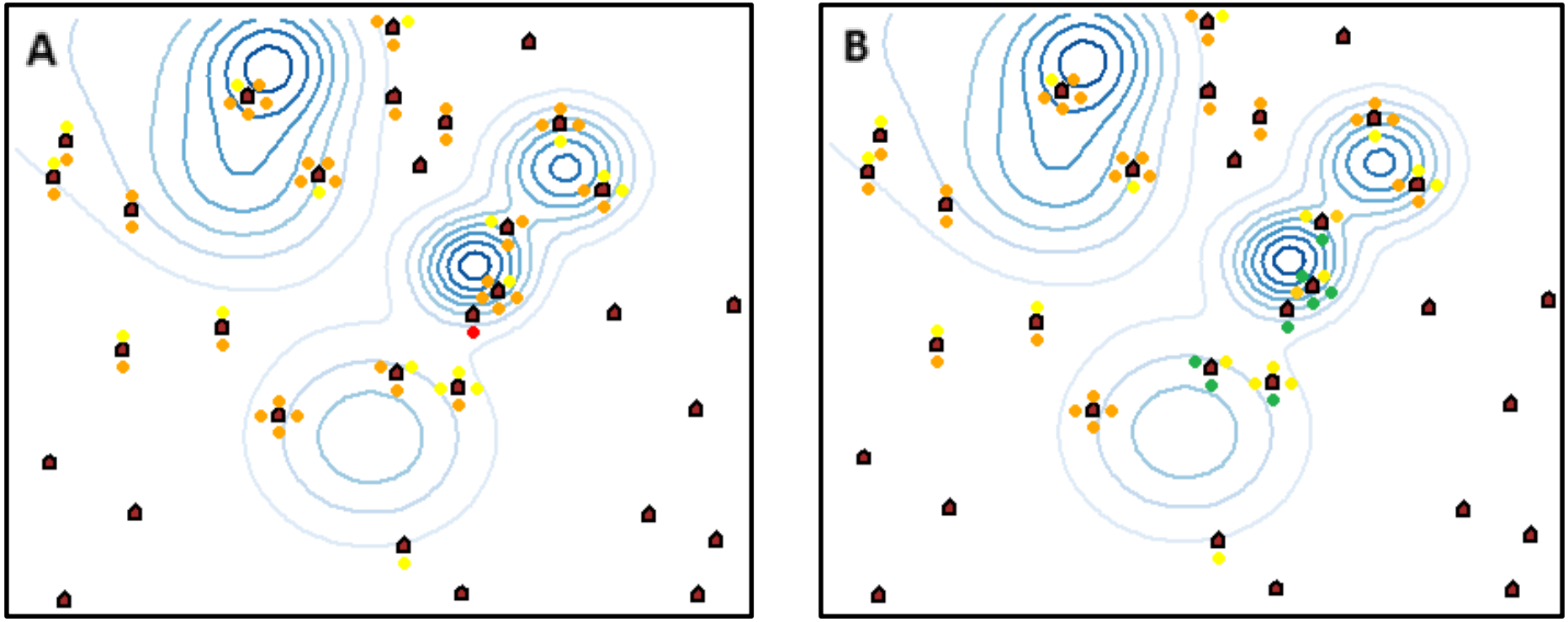
- Constrained optimization problem in which a desired outcome (e.g. clinical incidence) is minimized by exploring available intervention parameters subject to the above constraints.

Compartmental model of malaria



Griffin *et al.* (2010) PLoS Med.

Malaria model demonstration…



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