THE UNIVERSITY OF STRATHCLYDE

Remodeling selection to optimize disease forecasts and policies

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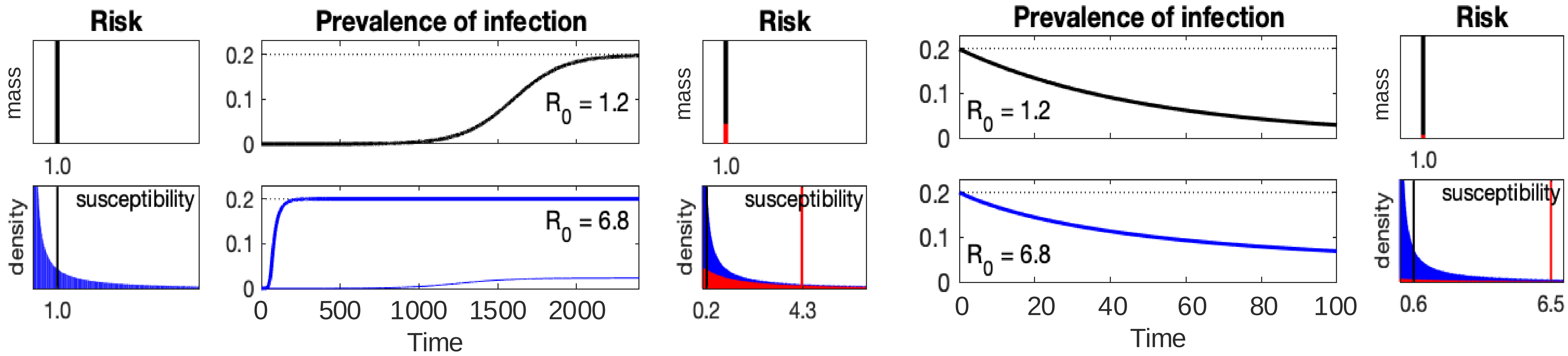
Background:

When variation in susceptibility is accounted for…

- estimated reproduction numbers are higher
- predicted impact of uniform control measures is lower

SI model and selective depletion bias:

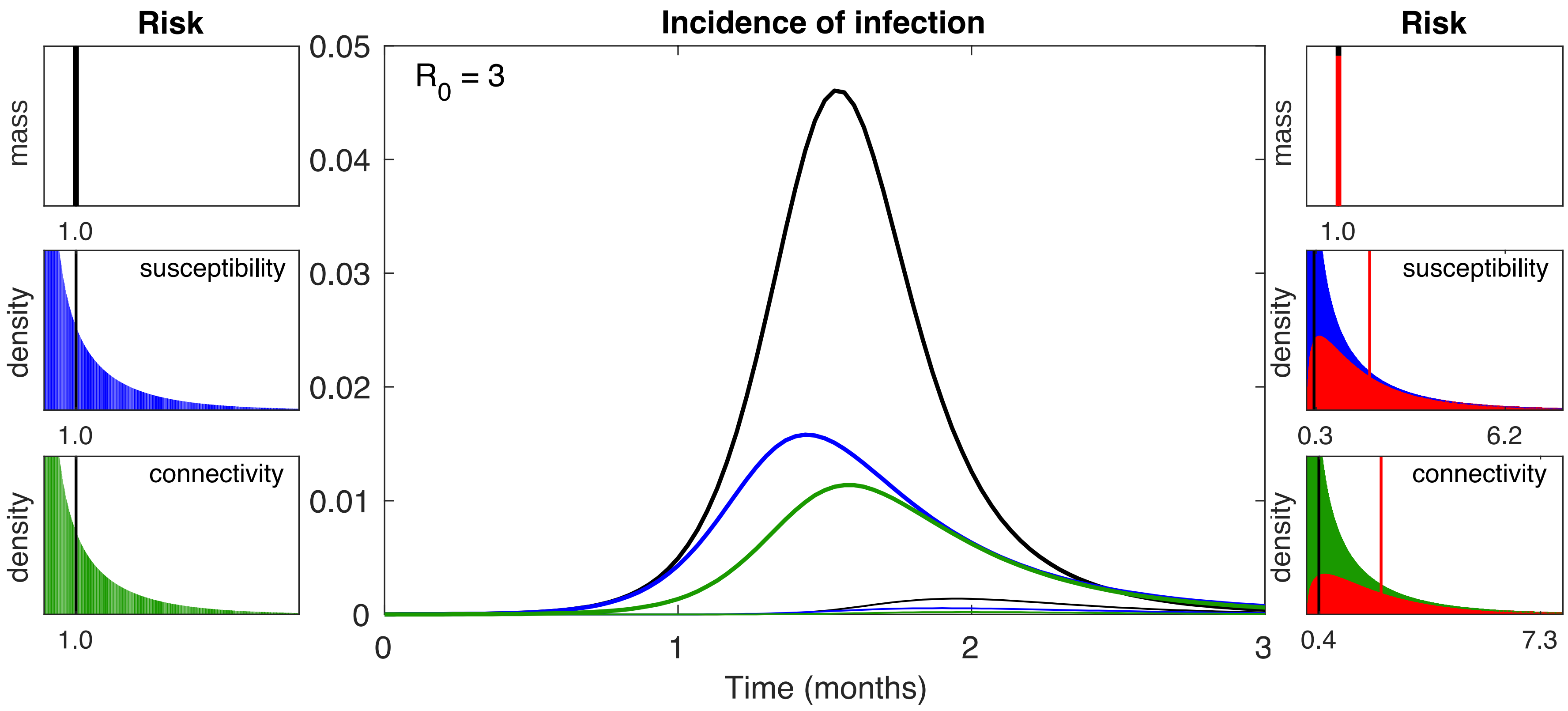
$$\frac{dS(x)}{dt} = q(x)\mu - \beta \int I(u)du\, xS(x) - \mu S(x), \qquad \frac{dI(x)}{dt} = \beta \int I(u)du\, xS(x) - \mu I(x), \qquad \mathcal{R}_0 = \frac{\beta}{\mu}$$



MGMG, AM Blagborough, KE Langwig, B Ringwald 2024 Remodelling selection to optimise disease forecasts and policies. *J Phys A: Math Theor 57*:103001.

SIR model and selective depletion bias:

$$\frac{dS(x)}{dt} = -\beta \int I(u)du\, xS(x), \qquad \frac{dI(x)}{dt} = \beta \int I(u)du\, xS(x) - \gamma I(x), \qquad \mathcal{R}_0 = \frac{\beta}{\mu}$$

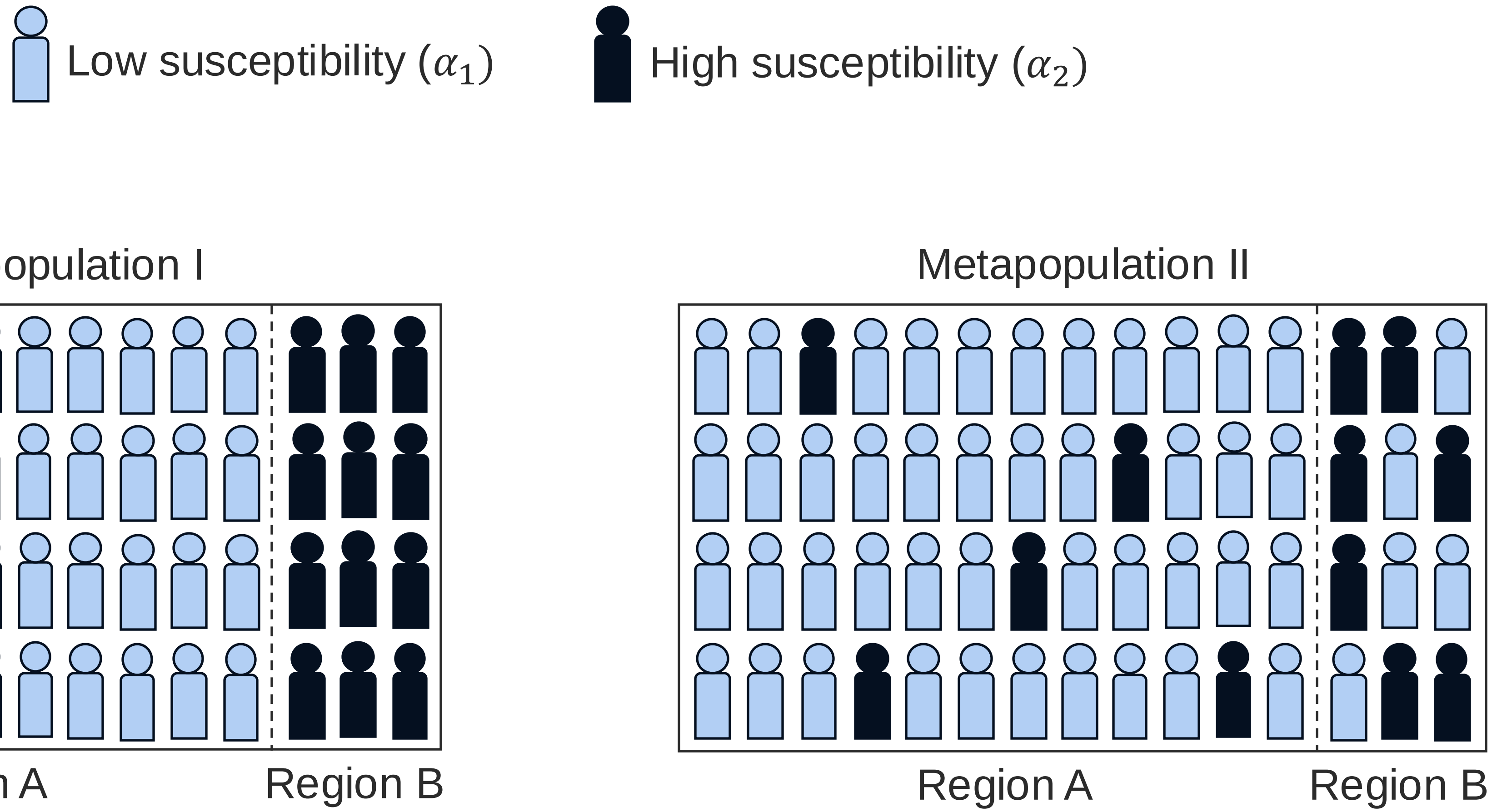


This talk:

Variation in susceptibility can be estimated by remodeling selection when…

- observational data can be stratified over selection gradients
- experimental data can be generated over selection gradients

Observational data stratified by region:



SI metapopulation model:

$$\frac{dS_{A1}}{dt} = (1 - q_A)\mu - \beta(I_{A1} + I_{A2})\alpha_1 S_{A1} - \mu S_{A1}$$

$$\frac{dI_{A1}}{dt} = \beta(I_{A1} + I_{A2})\alpha_1 S_{A1} - \mu I_{A1}$$

$$\frac{dS_{A2}}{dt} = q_A\mu - \beta(I_{A1} + I_{A2})\alpha_2 S_{A2} - \mu S_{A2}$$

$$\frac{dI_{A2}}{dt} = \beta(I_{A1} + I_{A2})\alpha_2 S_{A2} - \mu I_{A2}$$

$$\frac{dS_{B1}}{dt} = (1 - q_B)\mu - \beta(I_{B1} + I_{B2})\alpha_1 S_{B1} - \mu S_{B1}$$

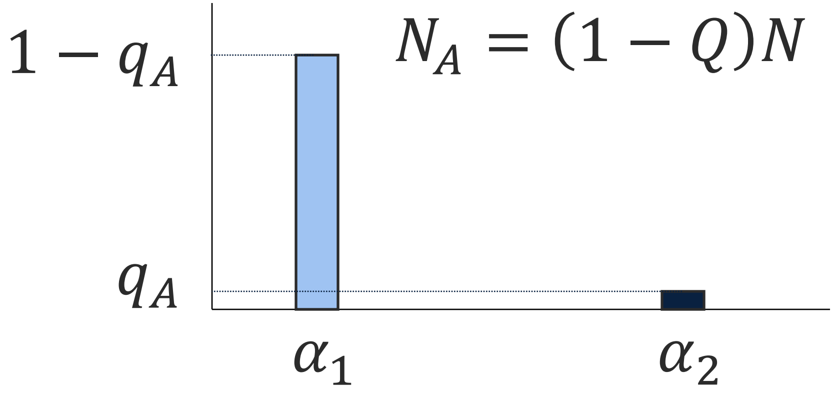
$$\frac{dI_{B1}}{dt} = \beta(I_{B1} + I_{B2})\alpha_1 S_{B1} - \mu I_{B1}$$

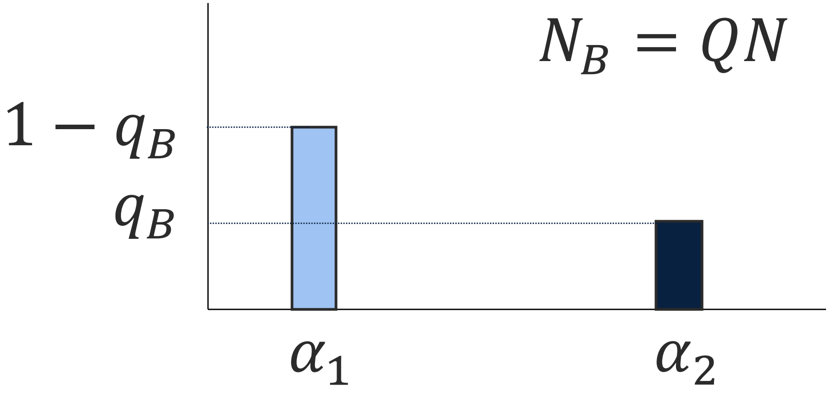
$$\frac{dS_{B2}}{dt} = q_B\mu - \beta(I_{B1} + I_{B2})\alpha_2 S_{B2} - \mu S_{B2}$$

$$\frac{dI_{B2}}{dt} = \beta(I_{B1} + I_{B2})\alpha_2 S_{B2} - \mu I_{B2}$$

$$\mathcal{R}_{0A} = [(1 - q_A)\alpha_1 + q_A\alpha_2]\frac{\beta}{\mu}$$

$$\mathcal{R}_{0B} = [(1 - q_B)\alpha_1 + q_B\alpha_2]\frac{\beta}{\mu}$$



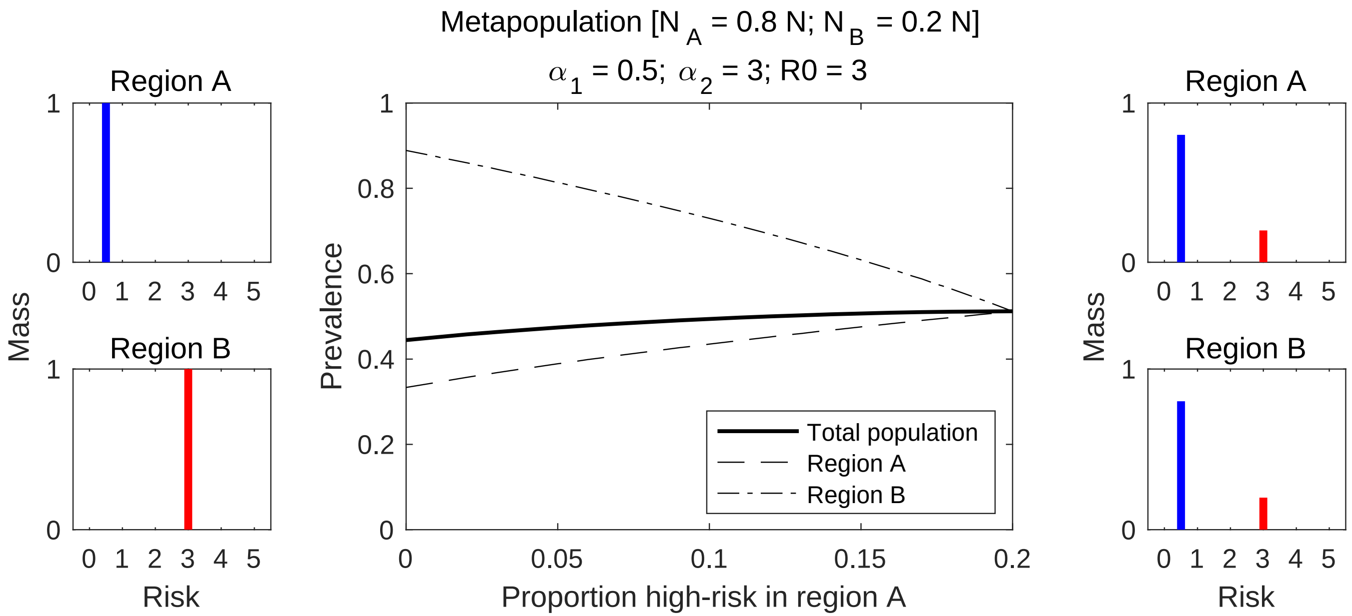


$$Q = (1-Q)q_A + Qq_B$$

$$\mathcal{R}_0 = (1-Q)\mathcal{R}_{0A} + Q\mathcal{R}_{0B} = \frac{\beta}{\mu}$$

$$\text{Mean}(\alpha) = (1-Q)\alpha_1 + Q\alpha_2 = 1$$

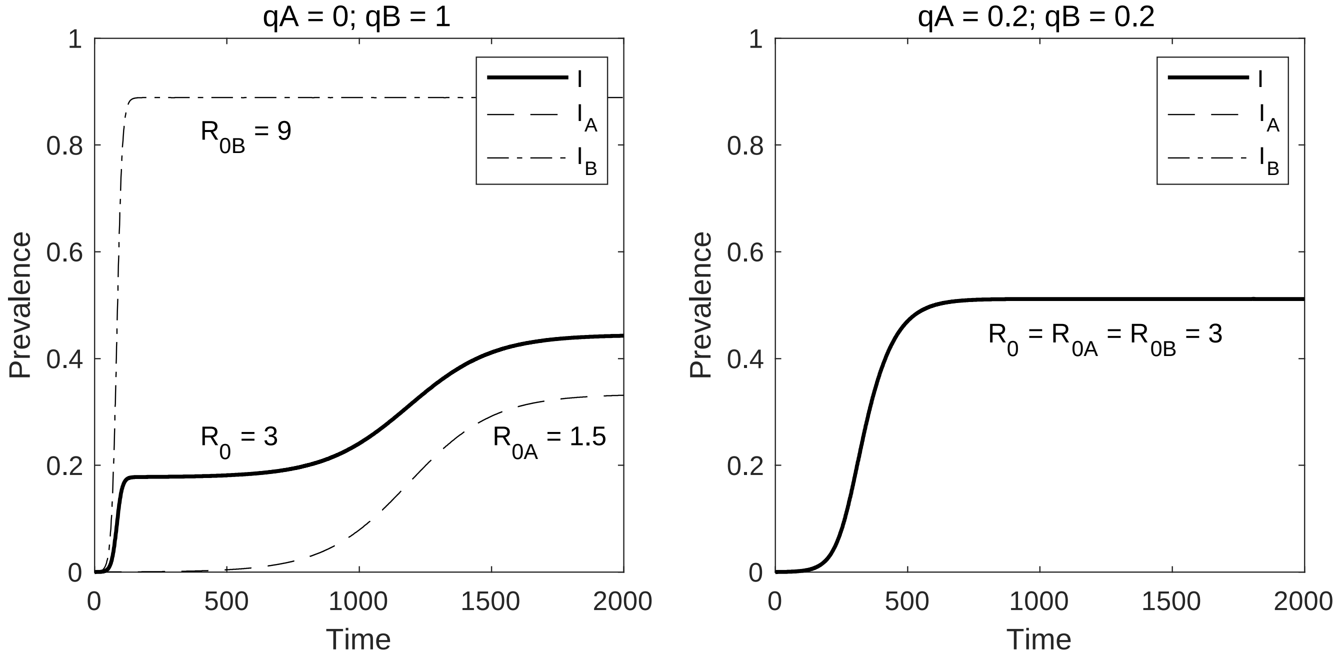
$$\text{Var}(\alpha) = (1-Q)(\alpha_1-1)^2 + Q(\alpha_2-1)^2$$



Endemic equilibrium:

$$\frac{\alpha_1(1-q_A)}{\beta I_A\alpha_1+\mu} + \frac{\alpha_2 q_A}{\beta I_A\alpha_2+\mu} = \frac{1}{\beta}$$

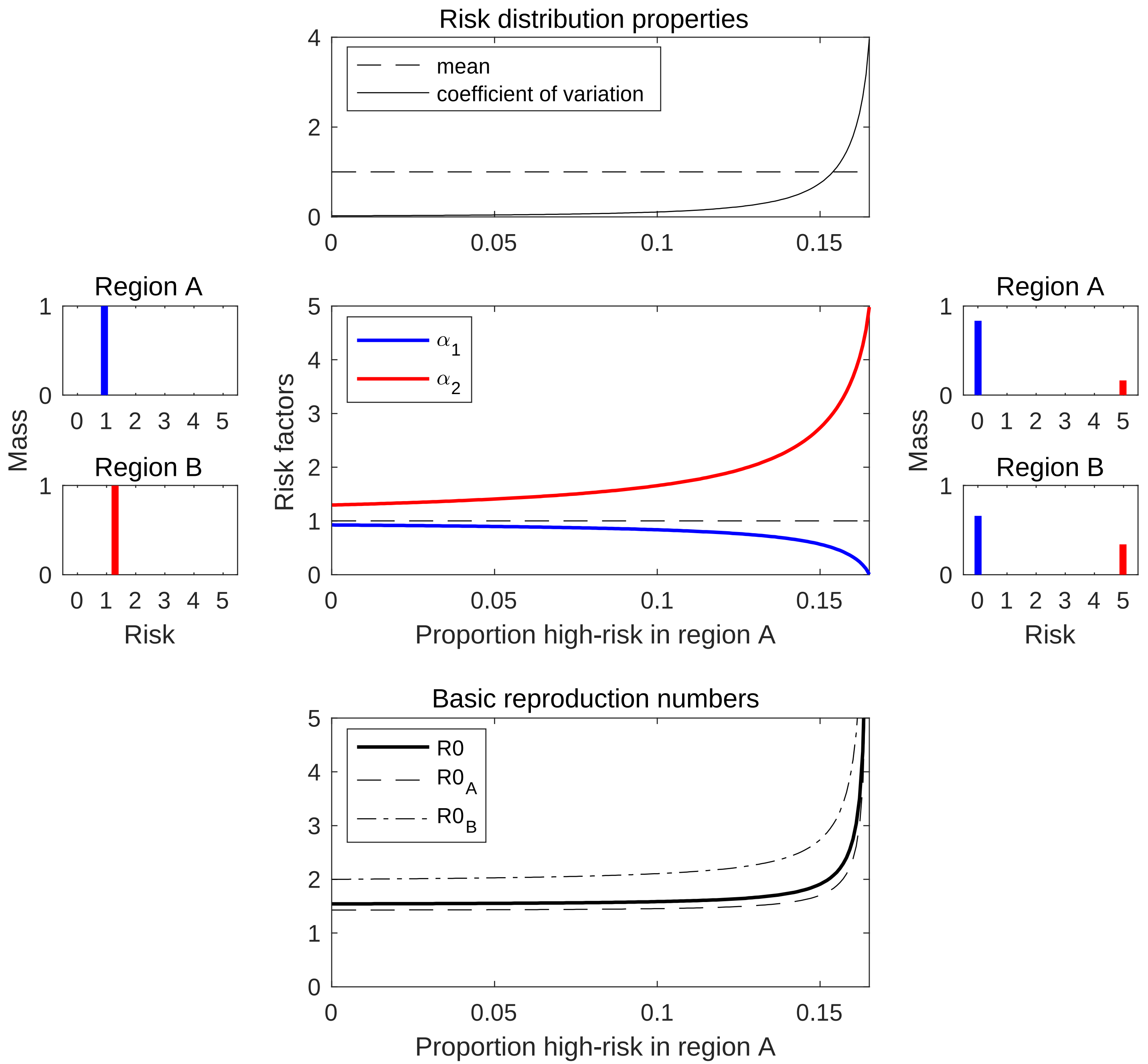
$$\frac{\alpha_1(1-q_B)}{\beta I_B\alpha_1+\mu} + \frac{\alpha_2 q_B}{\beta I_B\alpha_2+\mu} = \frac{1}{\beta}$$

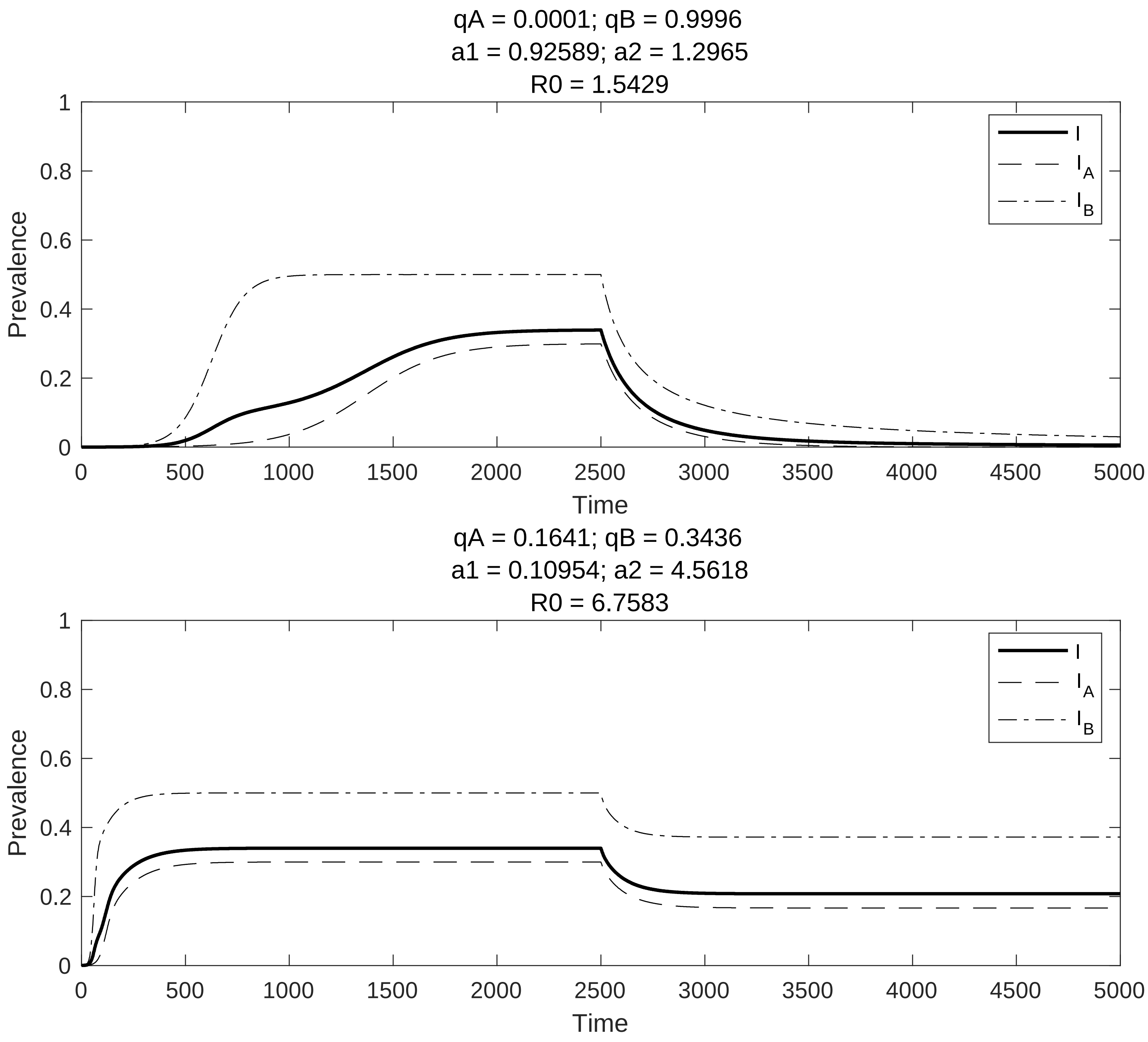


Given I_A and I_B the inverse problem can be solved exactly given the proportion high risk in one of the regions:

$$I_A = 0.3$$

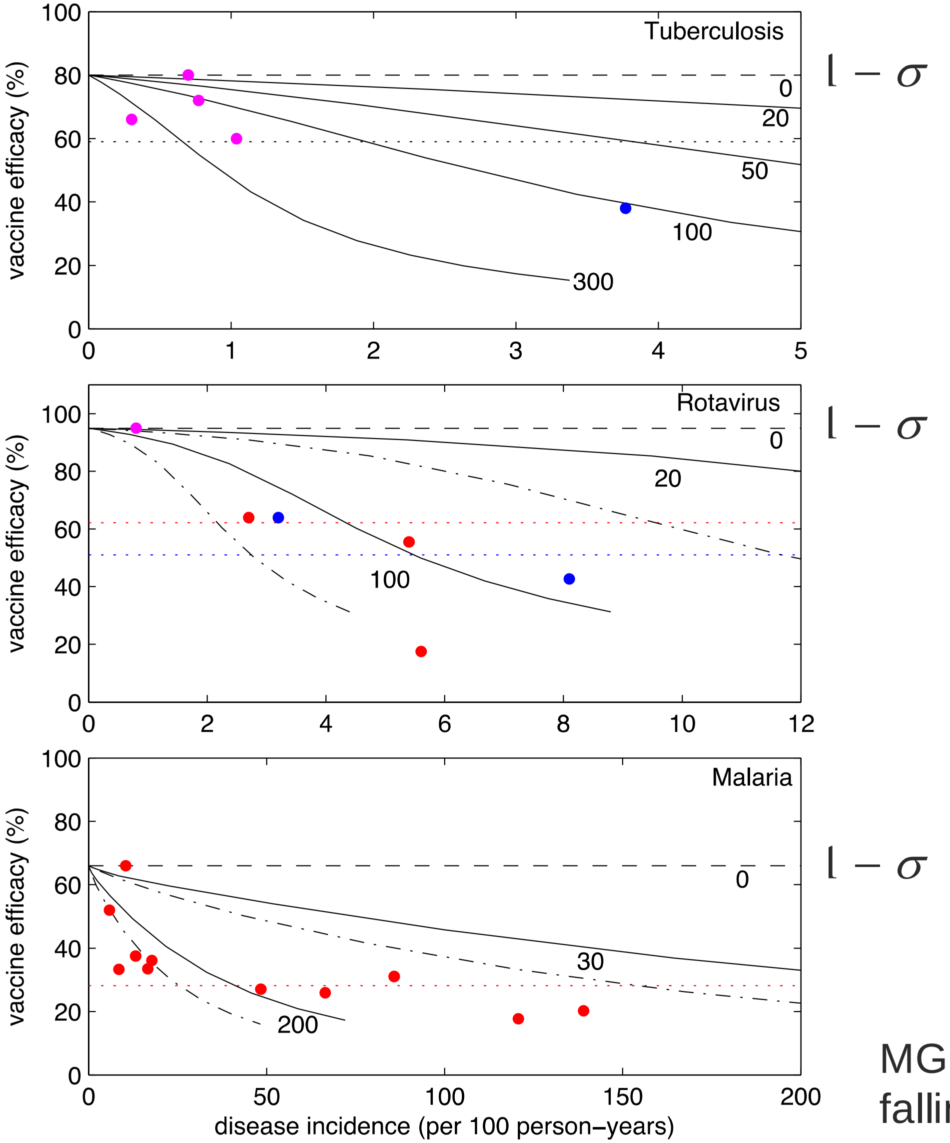
$$I_B = 0.5$$



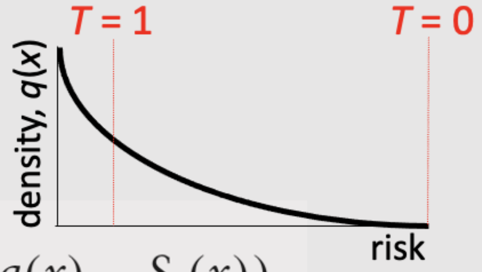


A classical metapopulation model would overpredict the impact of an intervention that uniformly reduces susceptibility, such as a vaccine

Vaccine trials (low efficacy under high exposure):



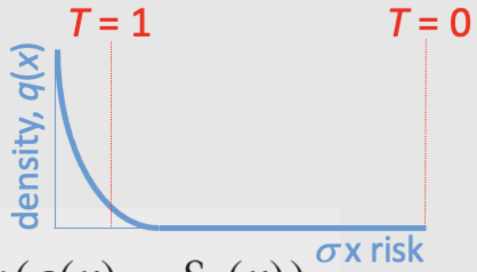
Control group:



$$\frac{dS_c}{dt}(x) = -\lambda x S_c(x) + \gamma(q(x) - S_c(x)),$$

$$\frac{dI_c}{dt}(x) = \lambda x S_c(x),$$

Vaccine group:



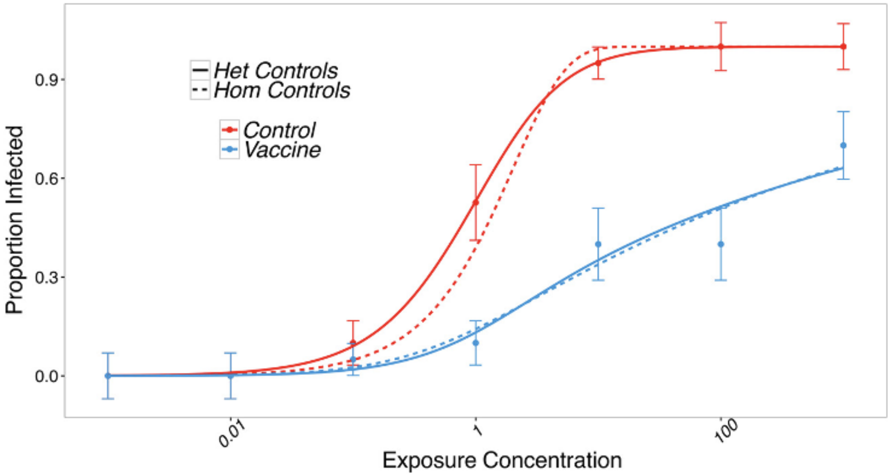
$$\frac{dS_v}{dt}(x) = -\sigma\lambda x S_v(x) + \gamma(q(x) - S_v(x)),$$

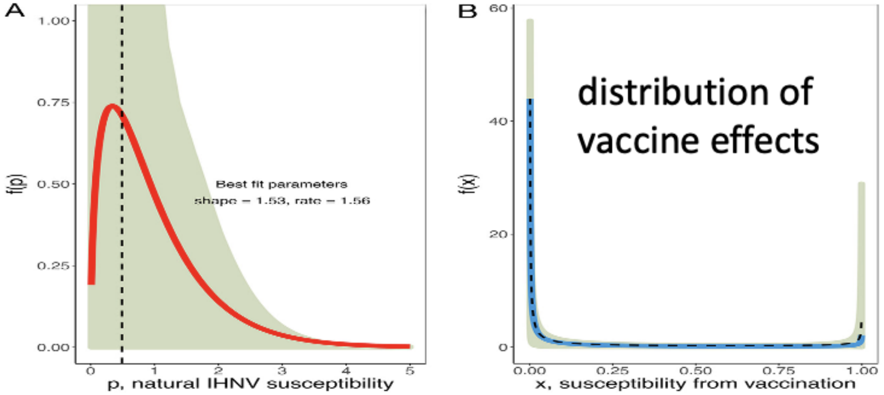
$$\frac{dI_v}{dt}(x) = \sigma\lambda x S_v(x).$$

MGMG, SB Gordon, DG Lalloo 2016 Clinical Trials: The mathematics of falling vaccine efficacy with rising disease incidence. *Vaccine* 34:3007.

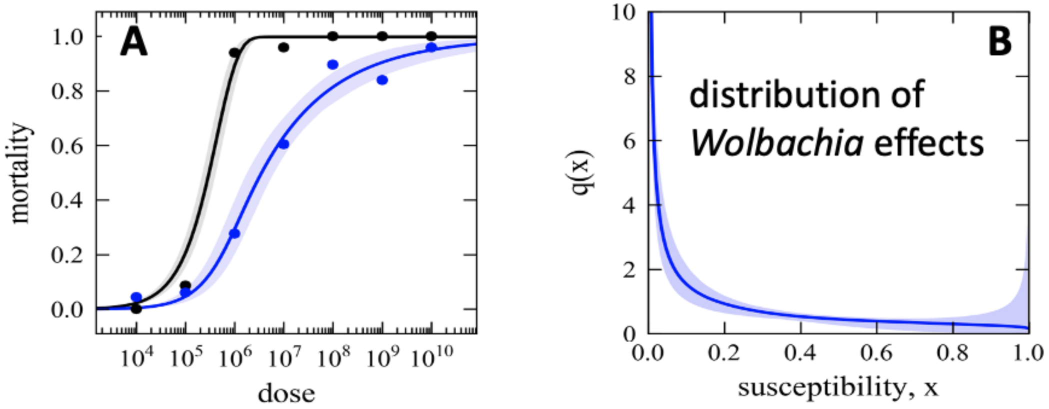
Dose-response infection experiments:

Fish (trout)

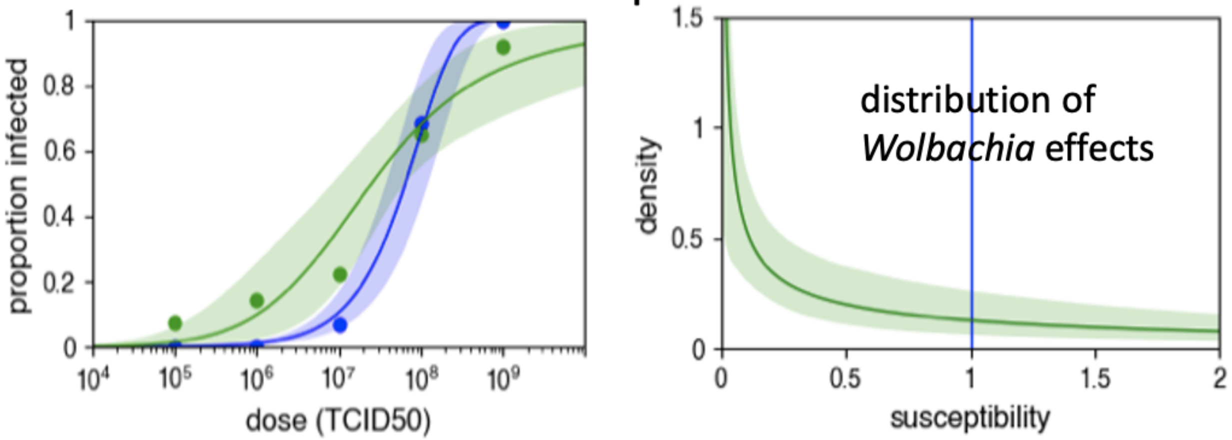




Fruit flies



Mosquitoes



KE Langwig *et al* 2017 *mBio* 8:e00796-17.
KE Langwig *et al* 2019 *Sci Rep* 9:3203.

D Pessoa *et al* 2014 *PLOS Comput Biol* 10:e1003773.
JG King *et al* 2018 *Nat Commun* 9:1483.

Summary:

- “Selective depletion bias” applies generally when the population mean value of a trait (such as susceptibility) changes over time or across environments due to selective depletion of the frailest (most susceptible) individuals, and this is misinterpreted as individuals (rather than population composition) changing.
- “Remodeling selection” is a novel approach (method) to infer unobserved variation from its effects on observational or experimental data collected over selection gradients.