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Risk inequality metrics in population health and disease

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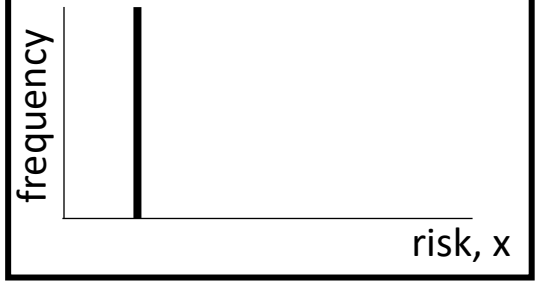
Risk inequality in the susceptible-infected (SI) model

Homogeneous risk
(susceptibility x connectivity):

$$\frac{dS}{dt} = \mu - \beta IS - \mu S$$

$$\frac{dI}{dt} = \beta IS - \mu I$$

$$\mathcal{R}_0 = \frac{\beta}{\mu}$$

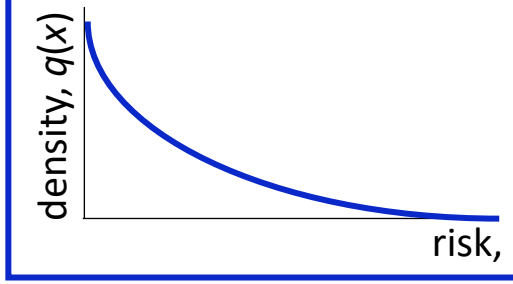


Heterogeneous susceptibility:

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

$$\frac{dI(x)}{dt} = \beta \int I(u)du\, xS(x) - \mu I(x)$$

$$\mathcal{R}_0 = \frac{\beta}{\mu}$$

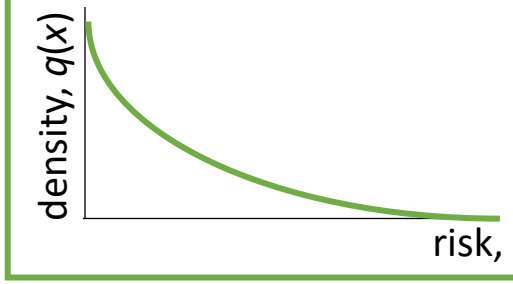


Heterogeneous connectivity:

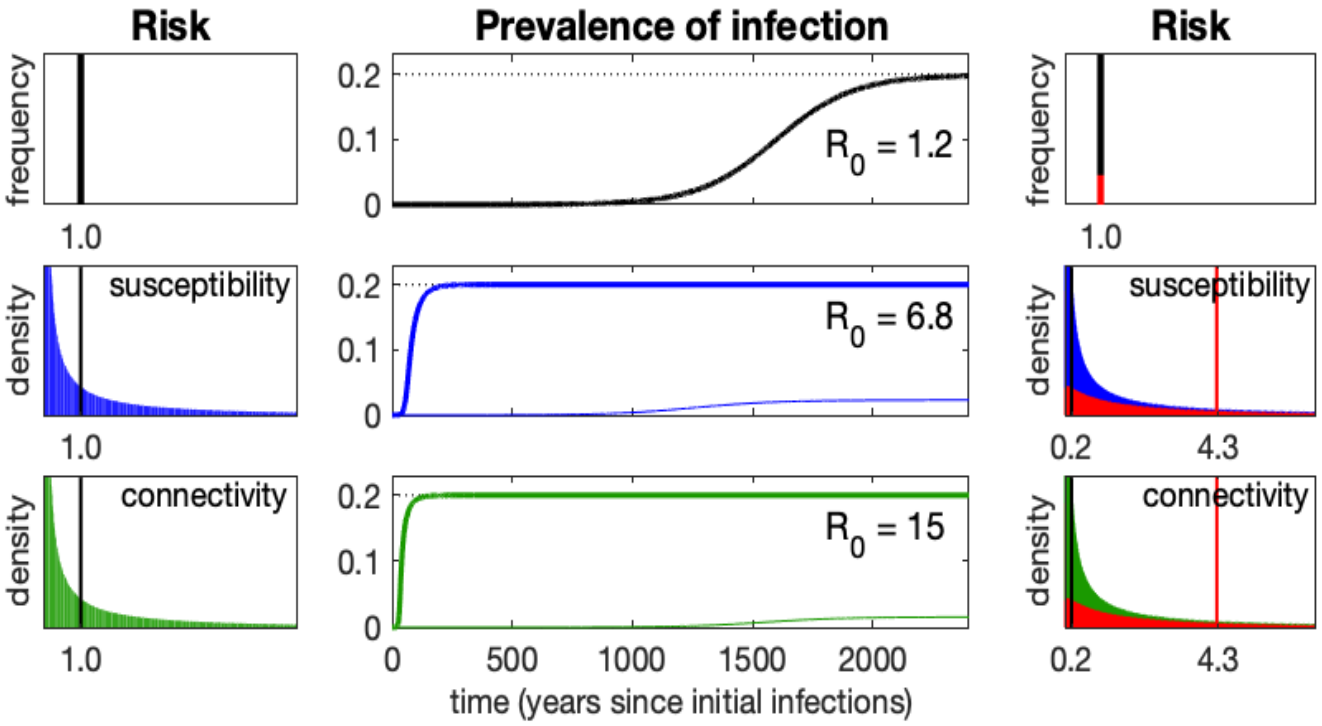
$$\frac{dS(x)}{dt} = q(x)\mu - \beta \int uI(u)du\, xS(x) - \mu S(x)$$

$$\frac{dI(x)}{dt} = \beta \int uI(u)du\, xS(x) - \mu I(x)$$

$$\mathcal{R}_0 = \frac{\beta}{\mu} \int x^2 q(x)dx$$

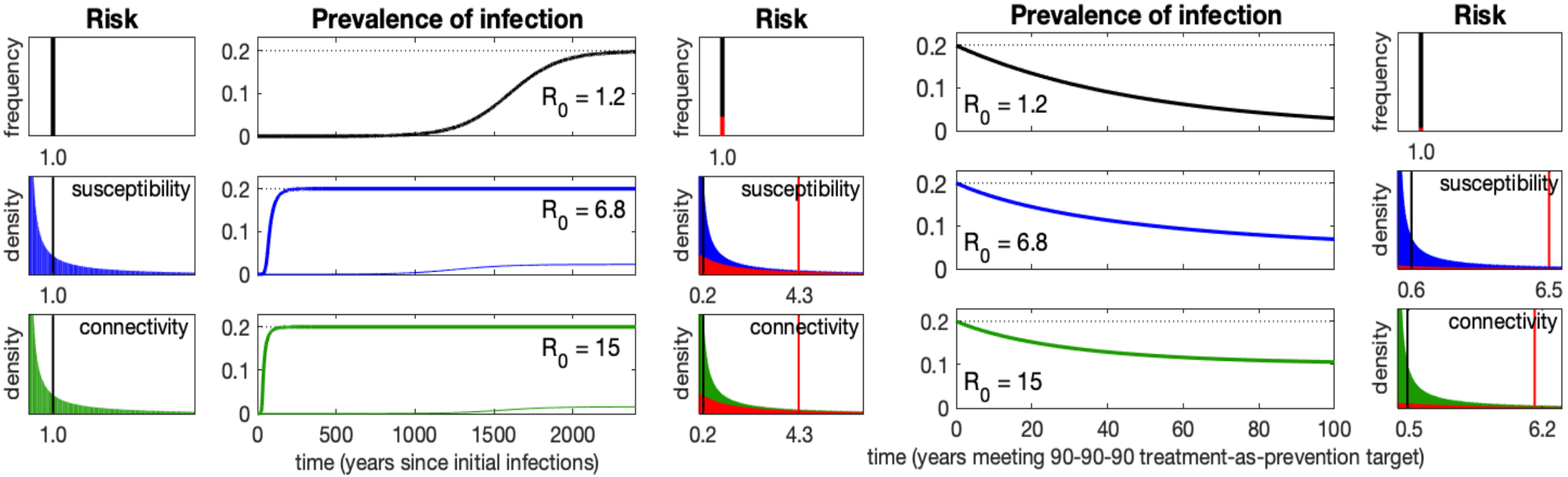


False homogeneity causes underestimation of reproduction numbers from endemic states



MGMG 2018 On the mathematics of populations. *CIM Bulletin* 40:21-27.

False homogeneity causes underestimation of reproduction numbers from endemic states and overoptimism about interventions



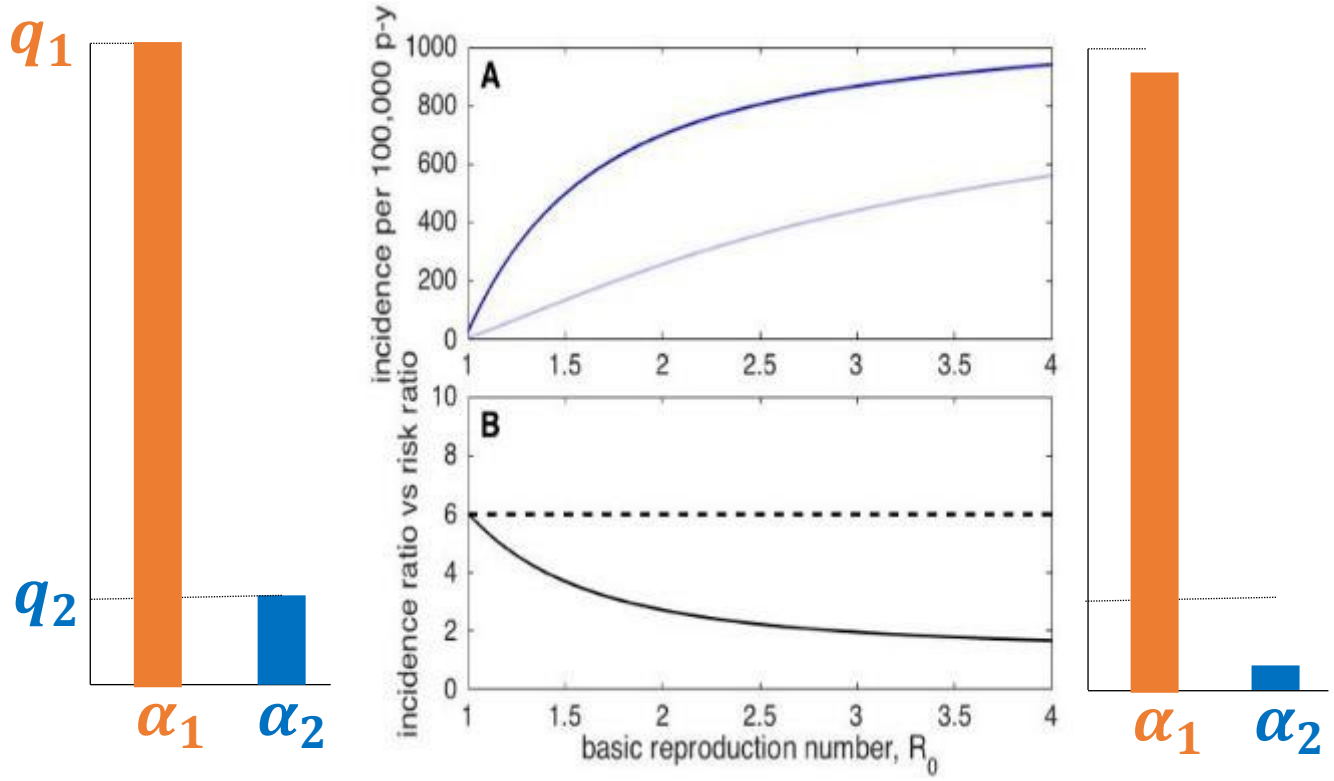
MGMG 2018 On the mathematics of populations. *CIM Bulletin* 40:21-27.

Individual variation in susceptibility/connectivity responds to selection making *risk mean* and *risk variance* appear lower (SIRS model)

$$\frac{dS_i}{dt} = -\alpha_i \beta (I_1 + I_2) S_i + \theta (q_i - S_i)$$

$$\frac{dI_i}{dt} = \alpha_i \beta (I_1 + I_2) S_i - \tau I_i$$

$$R_0 = \frac{\beta}{\tau}$$



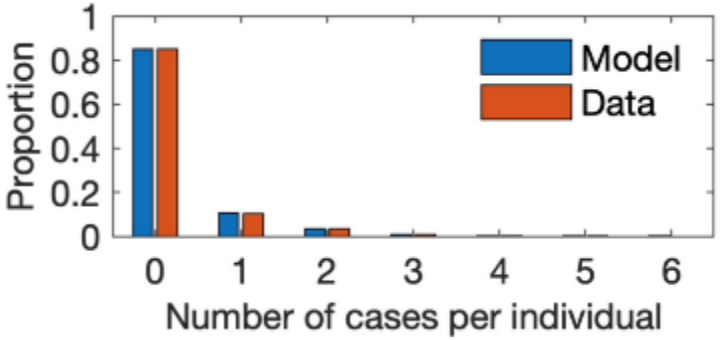
Aalen OO, Valberg M, Grotmol T, Tretli S 2015 Understanding variation in disease risk: the elusive concept of frailty. *Int J Epidemiol* 44:1408–1421.

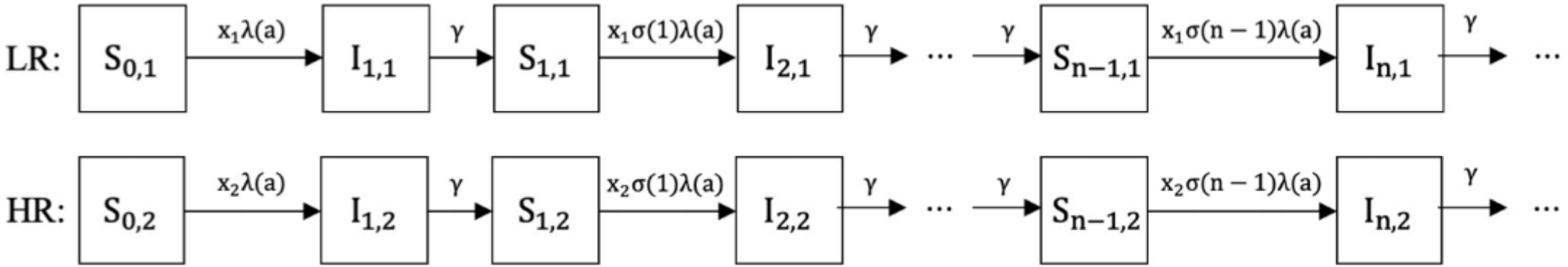
Incidence rate ratios are not directly informative for transmission modeling.

We propose new methods involving ReModeling Selection (RMS) in study design and analysis.

The method of choice will depend on the disease and research question.

Suppose an SIS endemic infection with individuals being infected at high frequency (e.g., malaria)





Corder RM, Ferreira MU, MGMG 2020 Modelling the epidemiology of residual *Plasmodium vivax* malaria in a heterogeneous host population: A case study in the Amazon Basin. *PLOS Comput Biol 16*:e1007377.

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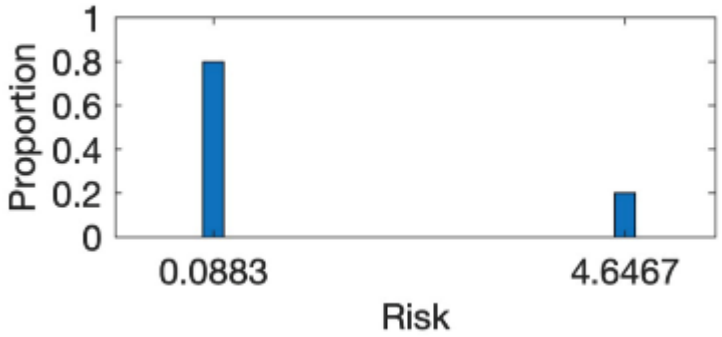

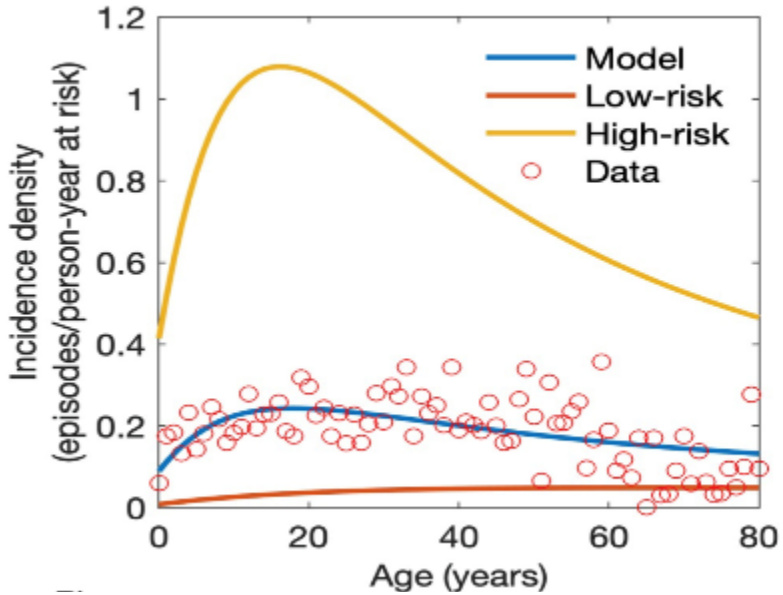

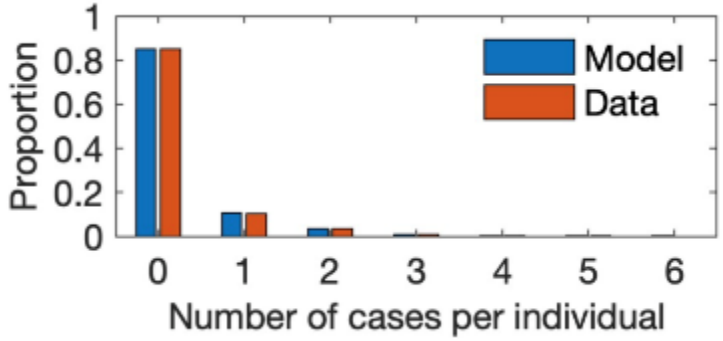

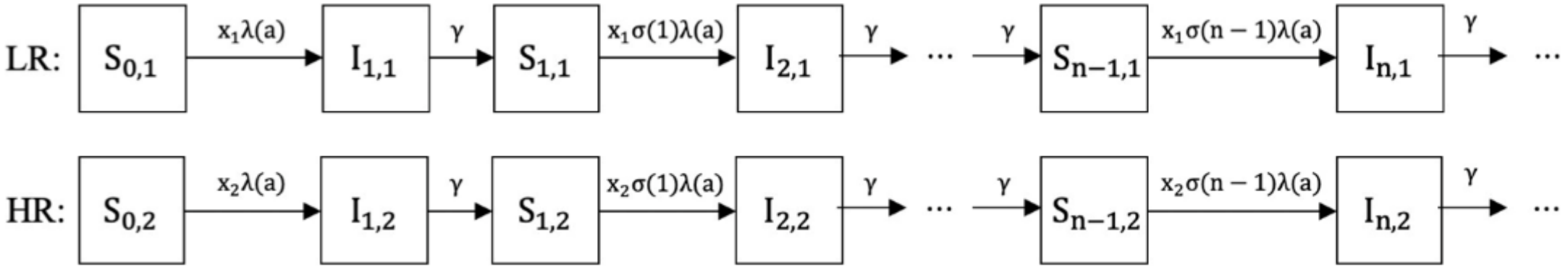

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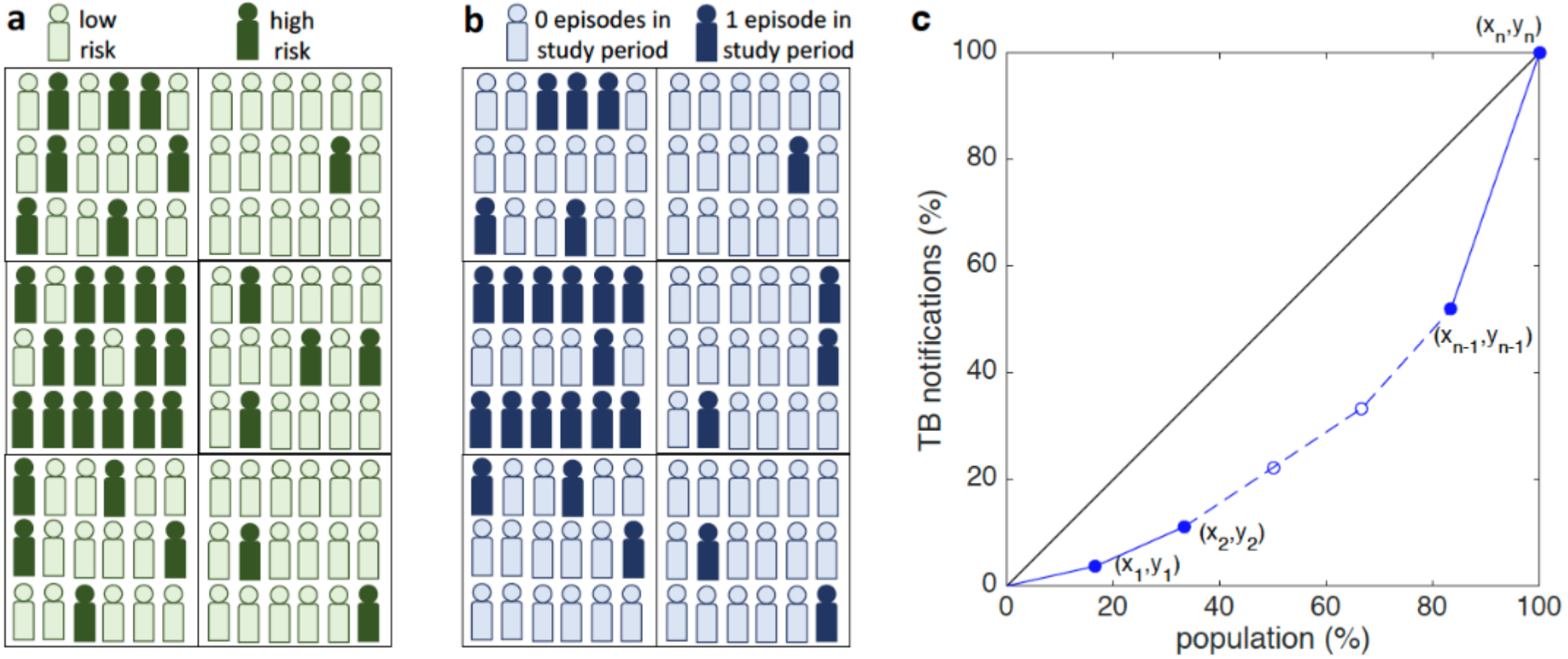
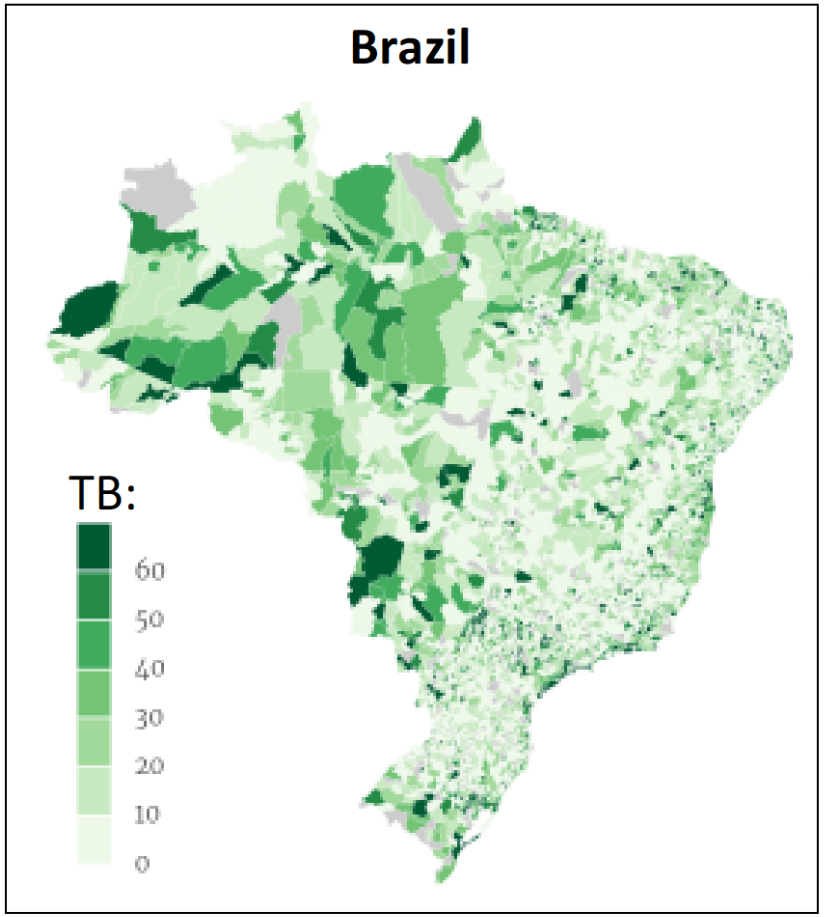
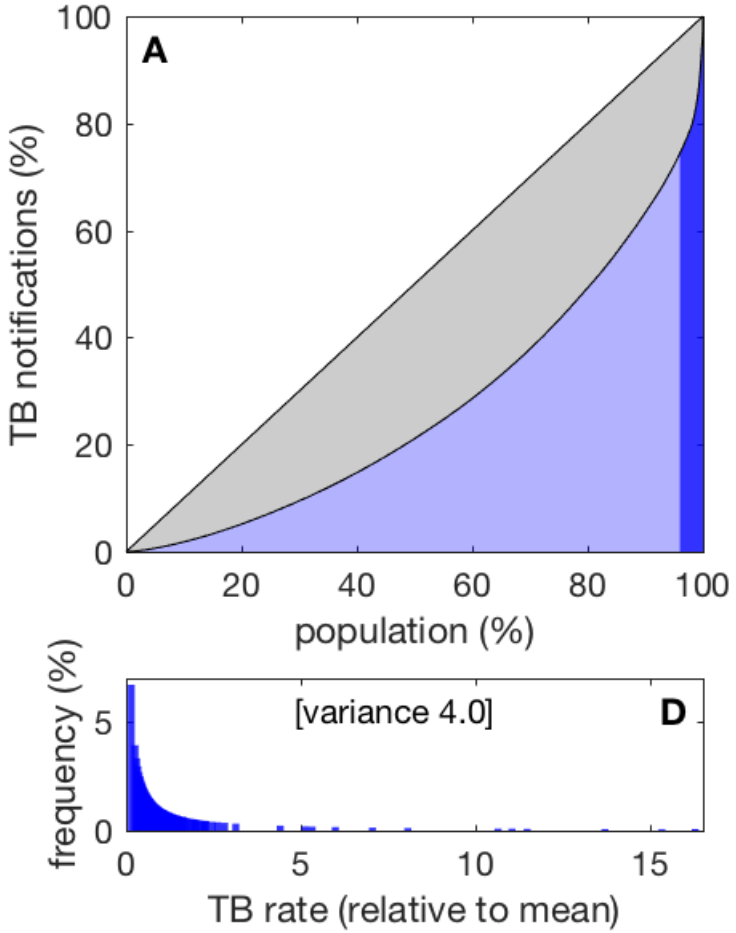
Now consider a not so frequent SIRS endemic infection (e.g., tuberculosis)



Estimation of risk distributions





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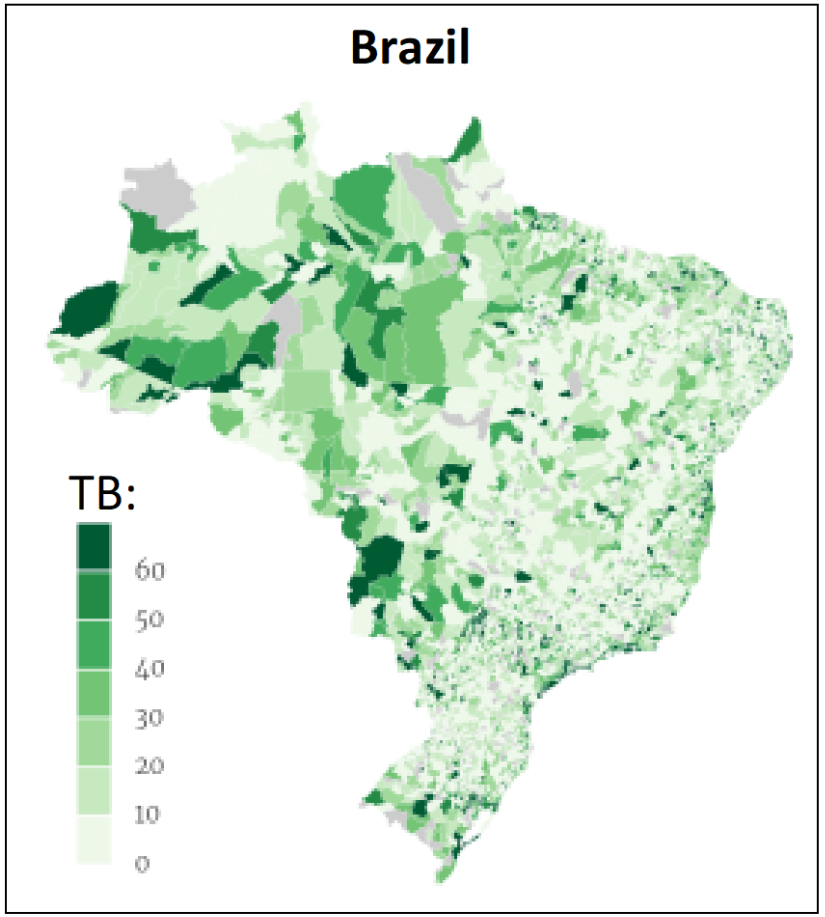
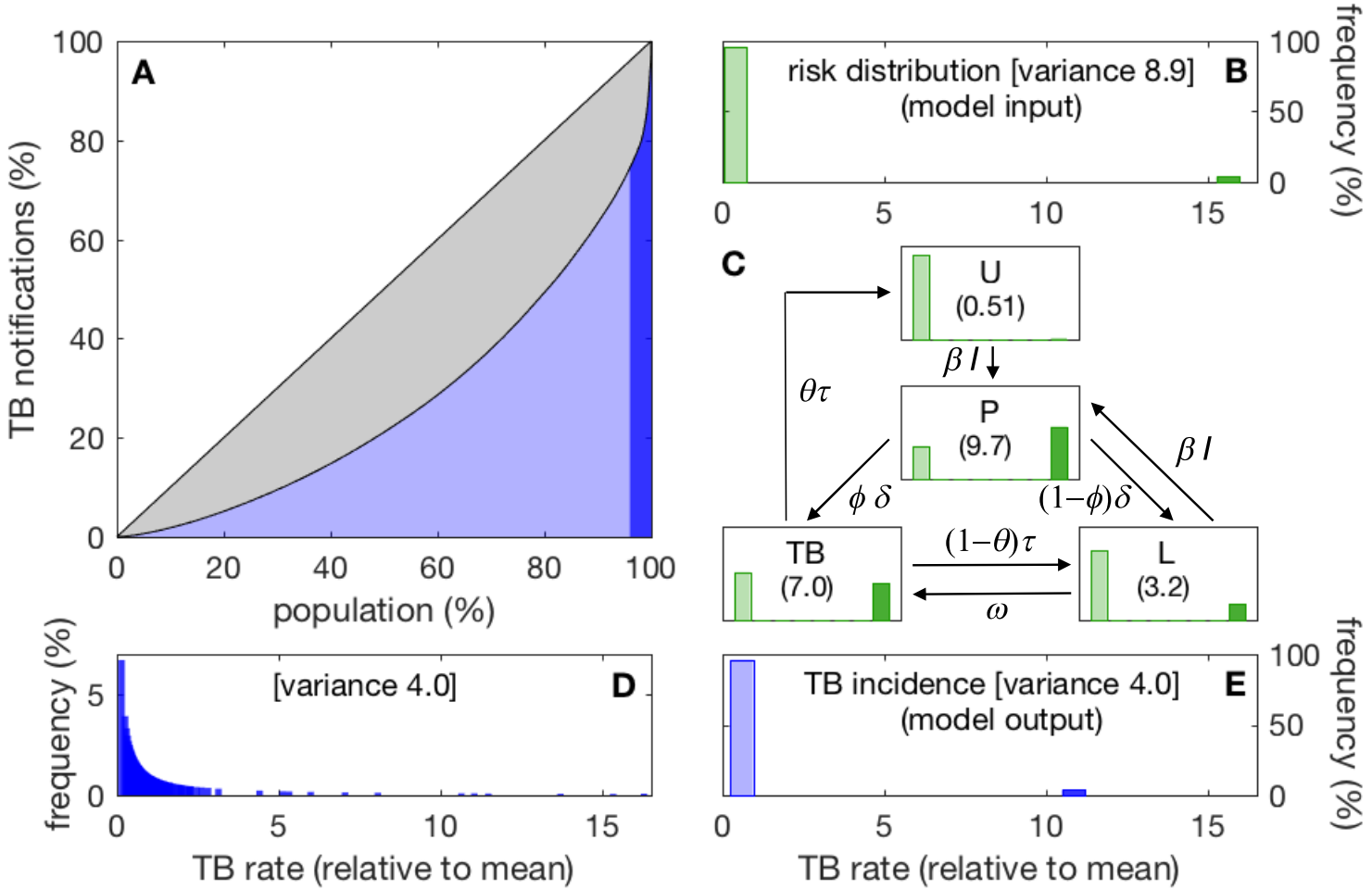
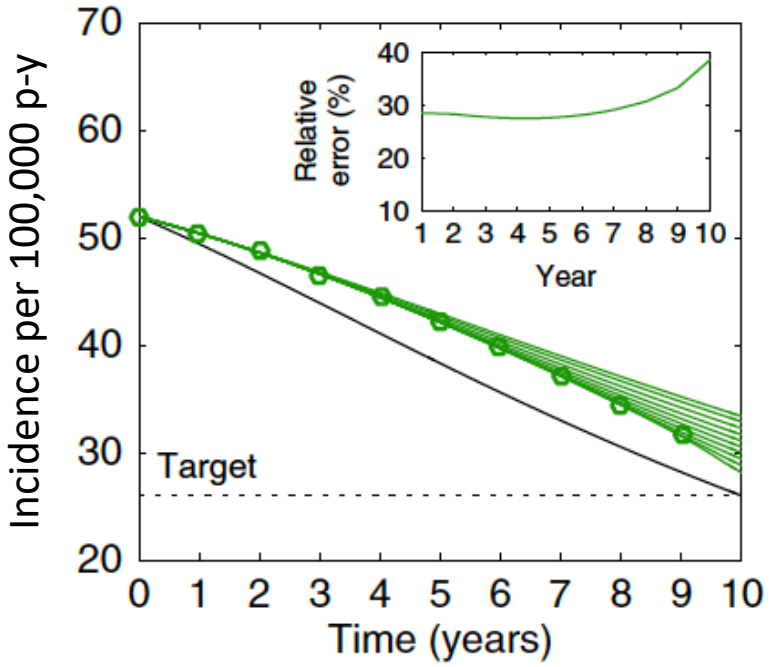




The nuisance of moving targets in TB control

a) Use ”an insufficiently heterogeneous model” to estimate the required control effort to meet a stipulated target;
b) Apply the control in a heterogeneous population, recognize its underperformance (**quantify the error after the first year**), and use the model a second time to re-estimate the required effort;
c) Increase the control effort accordingly in the heterogeneous population, recognize again that it underperforms (**quantify the error after the second year**), and re-estimate the required effort a third time;
d) Etc.



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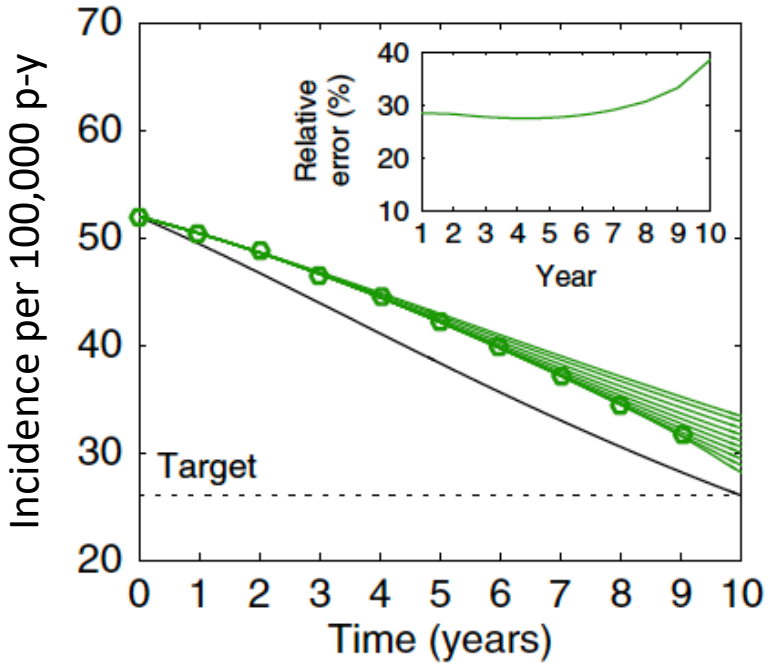
Not only control lags behind the prediction, but the relative error increases from year to year (**inset**);

i.e., the target appears to me moving when observed from a homogeneous frame.



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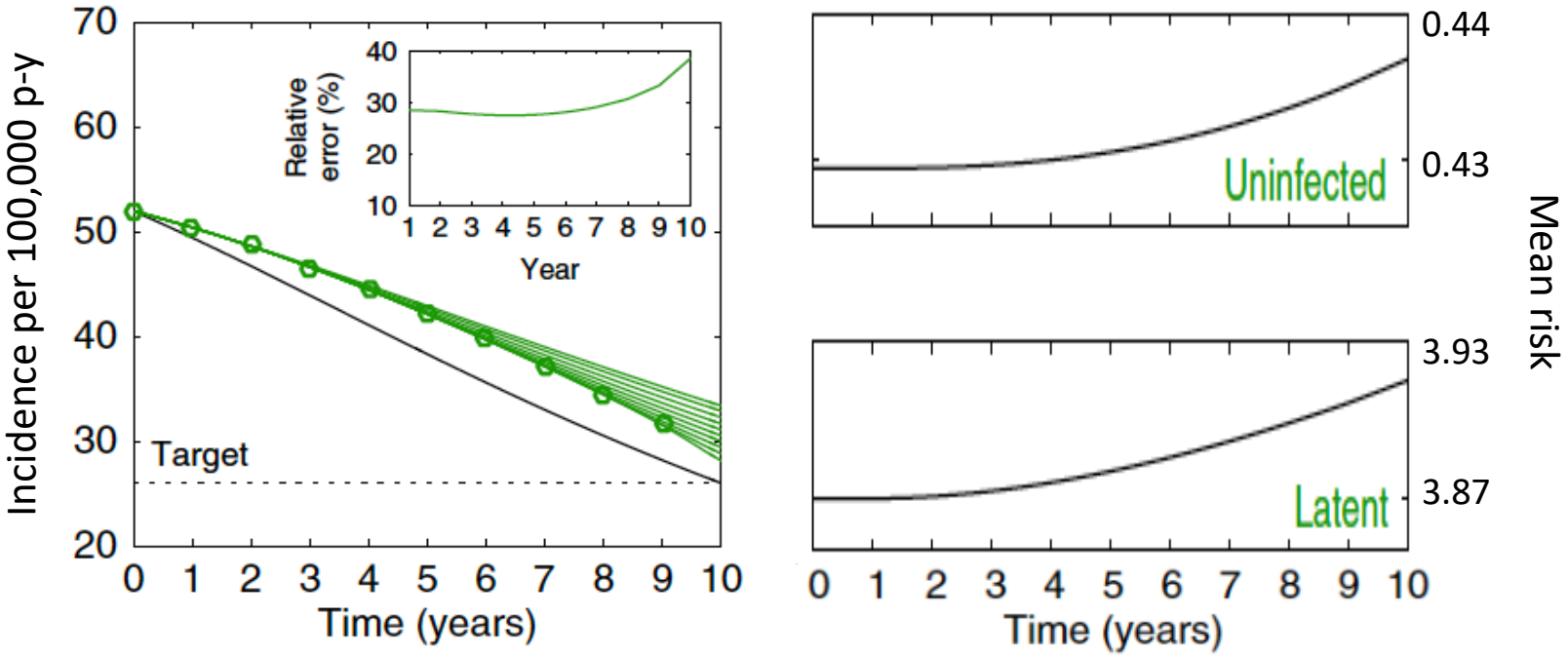
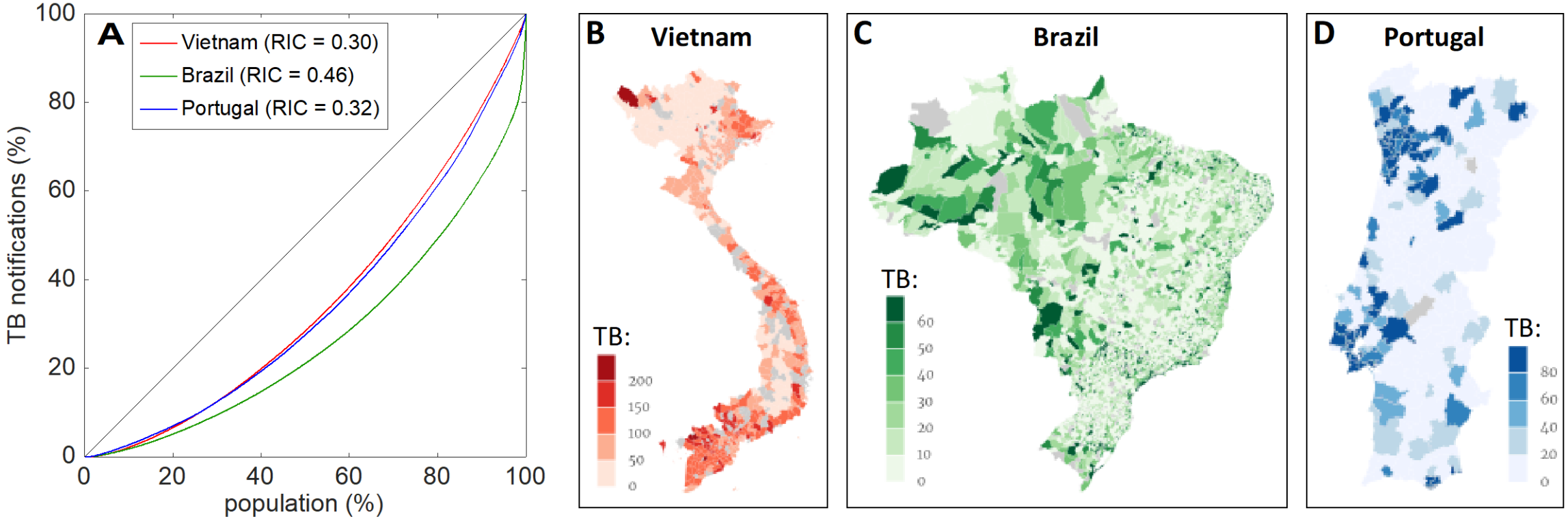


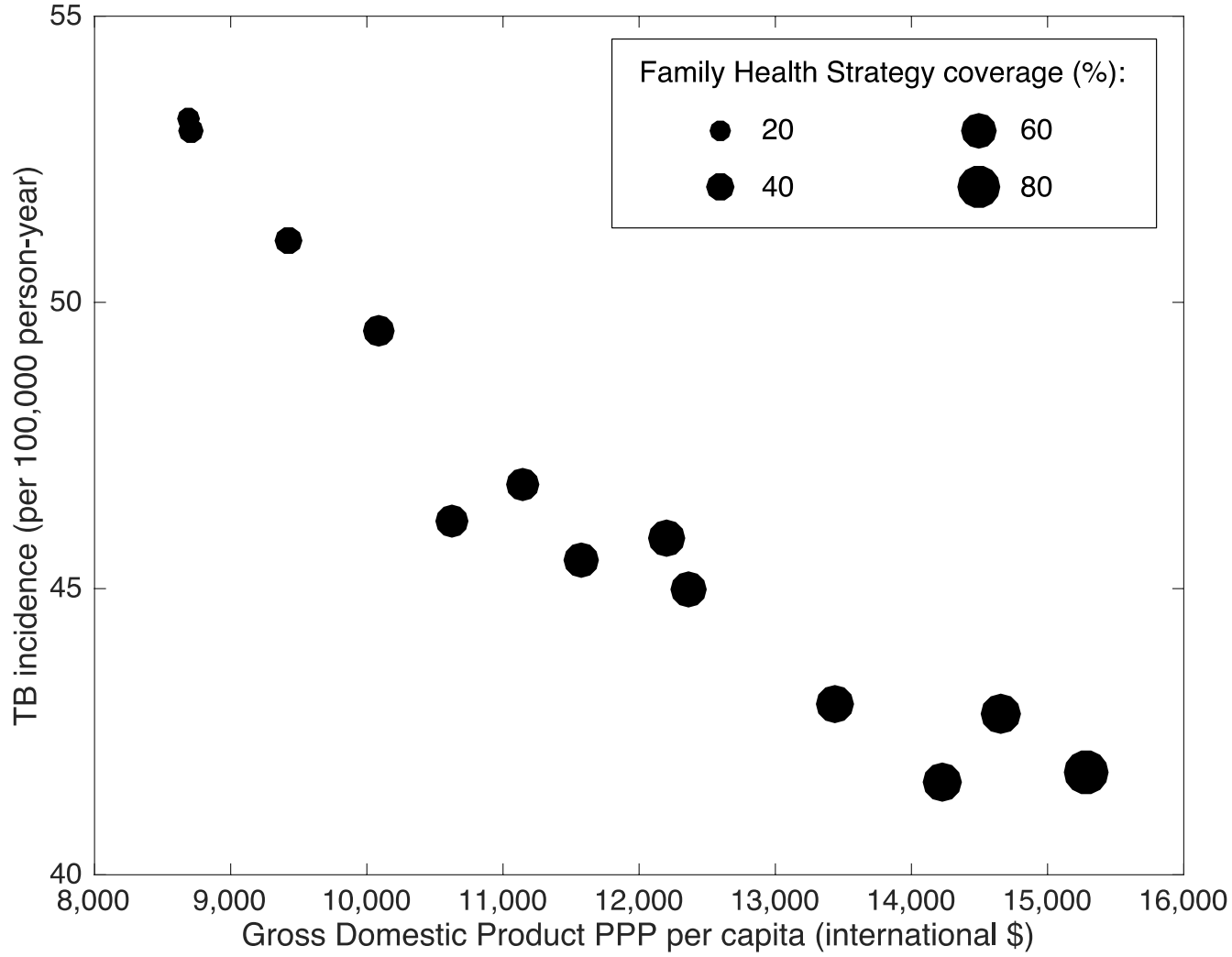
Risk Inequality Coefficient (RIC)



Gini Coefficient according to World Bank: Vietnam (0.38); Brazil (0.51); Portugal (0.32)

MGMG, Oliveira JF, Bertolde A, Nguyen TA, Maciel EL, Duarte R, Nguyen BH, Shete P, Lienhardt C 2018 Introducing risk inequality metrics in tuberculosis policy development *Nat Commun* 10:2480.

In further work we might stratify the population according to econometric indicators (rather than municipality)



Each dot is a year between 2002-1015

Further areas of RMS research and development (based on selection gradients):

- Epidemics (e.g., COVID-19)

- Efficacy estimation for susceptibility modifying interventions such as vaccines and *Wolbachia*

- Estimation of microbial fitness and evolution (relevant to AMR)

In conclusion

1) Misrepresentation of heterogeneity in risk of infection biases data interpretation and compromises intervention impact modeling;
2) Risk distributions can be estimated by remodeling selection (RMS);
3) Early work addressed malaria, tuberculosis, COVID-19 in humans, vaccine efficacy in fish, *Wolbachia* efficacy in flies and mosquitoes;
4) Ongoing work concerns vaccines in humans, fitness and evolution in bacteria.

SEVENTH FRAMEWORK PROGRAMME
AXA Research Fund
CAPES
FCT Fundação para a Ciência e a Tecnologia
NIH
BILL & MELINDA GATES foundation