PREDICTION IN LEPTOSPIROSIS RESEARCH AND ACTION

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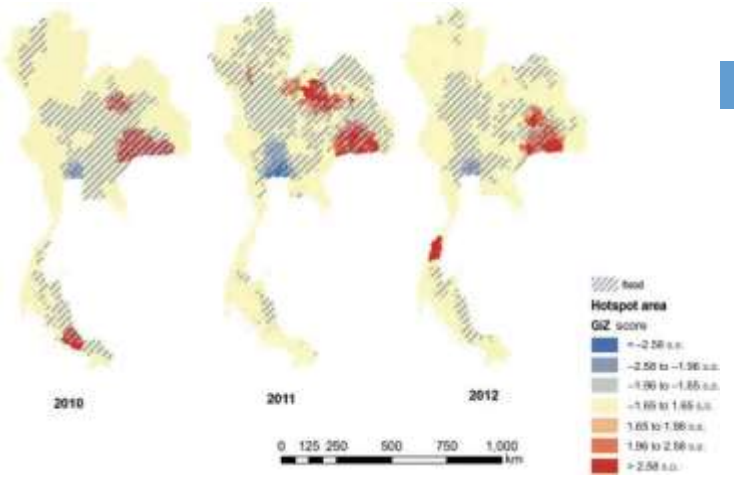
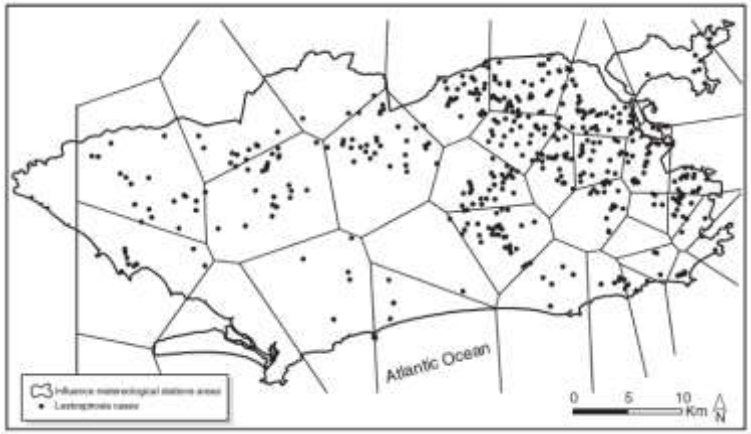
Observed patterns of leptospirosis

Some of this heterogeneity will be spatially structured and explained by various socio-ecological factors interactions that are themselves structured



Epidemiol. Infect. (2015), 143, 2106–2115. © Cambridge University Press 2015
doi:10.1017/S0950268815000205

Spatio-temporal patterns of leptospirosis in Thailand: is flooding a risk factor?



Detection and modelling of case clusters for urban leptospirosis

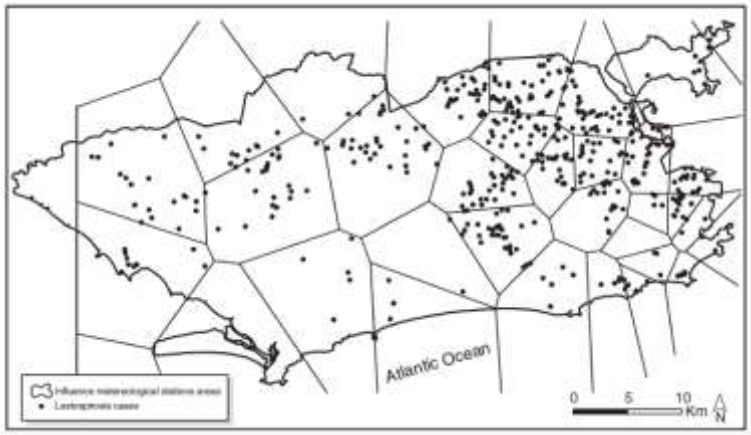
Tropical Medicine and International Health

VOLUME 13 NO 4 PP 503–512 APRIL 2008

Observed patterns of leptospirosis

We want to identity clusters and where they are

Also want to understand why cases tend to be clustered



Detection and modelling of case clusters for urban leptospirosis

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Goal of Epidemiological Research and Prediction

Data→ Statistical analyses → Set of variables that explain the data

- Improved understanding of the observed spatial-temporal patterns of infection and cases and the processes behind them
- This can improve our understanding of increased incidence and of outbreaks
- Knowledge can inform targeted interventions in a effective and timely manner
- Given a robust understanding, it can help predict patterns and distributions of cases in unsampled areas

Importance of scale

Need to distinguish between:

- Large-scale trends: deterministic trends

Dependence over large spatial scales may suggest the influence of major “external” factors (e.g. climate factors, seasons)

El Niño Southern Oscillation and Leptospirosis Outbreaks in New Caledonia

Daniel Weinberger[1], Noémie Baroux[2], Jean-Paul Grangeon[3], Albert I. Ko[1,4,5], Cyrille Goarant[2]*

Data:

- Cases from surveillance (date of first sample)
- El Niño Southern Oscillation (ENSO) and other climate variables
- Predictive (multivariable) model

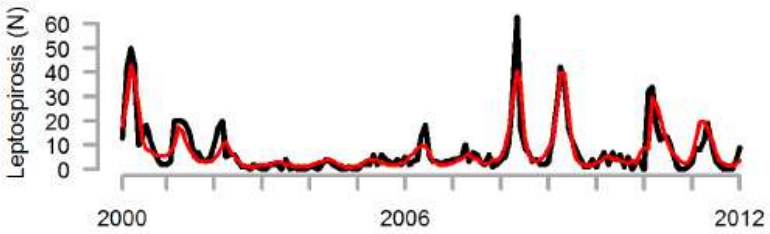


Figure 2. Observed (grey) and predicted (red) cases of leptospirosis occurring in each month in New Caledonia, 2000–2012.
doi:10.1371/journal.pntd.0002798.g002

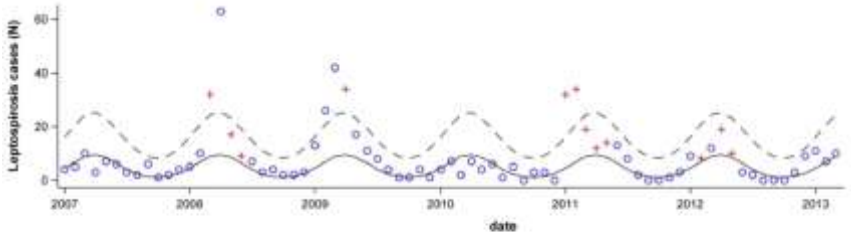


Figure 3. Seasonal baseline (solid line) and upper limit of the 95% confidence interval (dashed line). The observed number of leptospirosis cases in each month is shown for 2007–2012. Blue circles indicate months that had been forecasted to be below the epidemic threshold and red crosses indicate months where the forecast predicted an epidemic. When the red crosses are above the 95% confidence interval, this indicates that the forecast had correctly predicted an epidemic intensity in that month.
doi:10.1371/journal.pntd.0002798.g003

Forecastin
g

Importance of scale

Need to distinguish between:

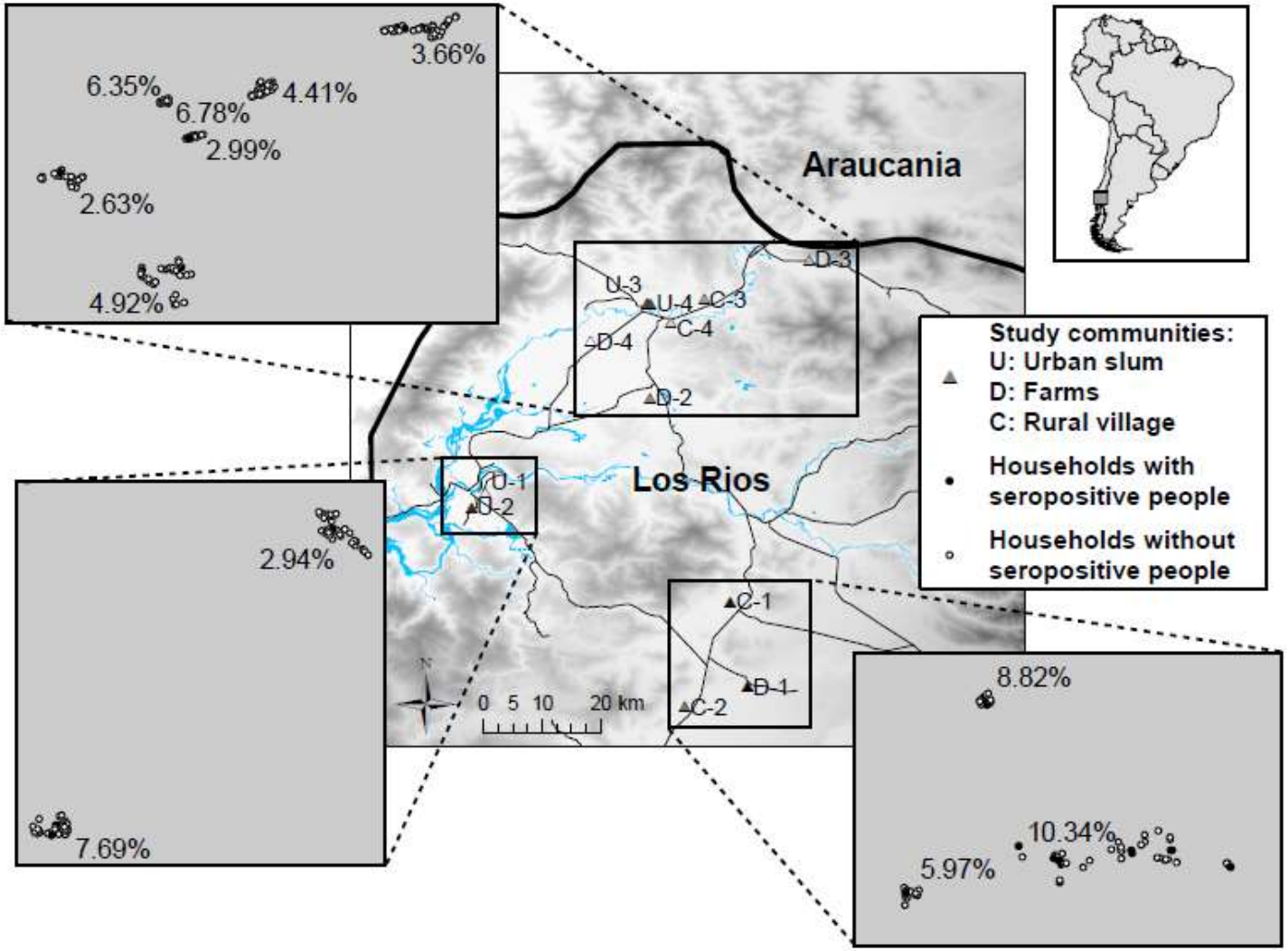
- Large-scale trends: deterministic trends

Dependence over large spatial scales may suggest the influence of major “external” factors (e.g. climate factors, seasons)

- Small-scale trends: stochastic effects

Dependence between near locations may suggest local, micro-environmental factors

Los Rios region, Chile: Individual-level seroprevalence in people



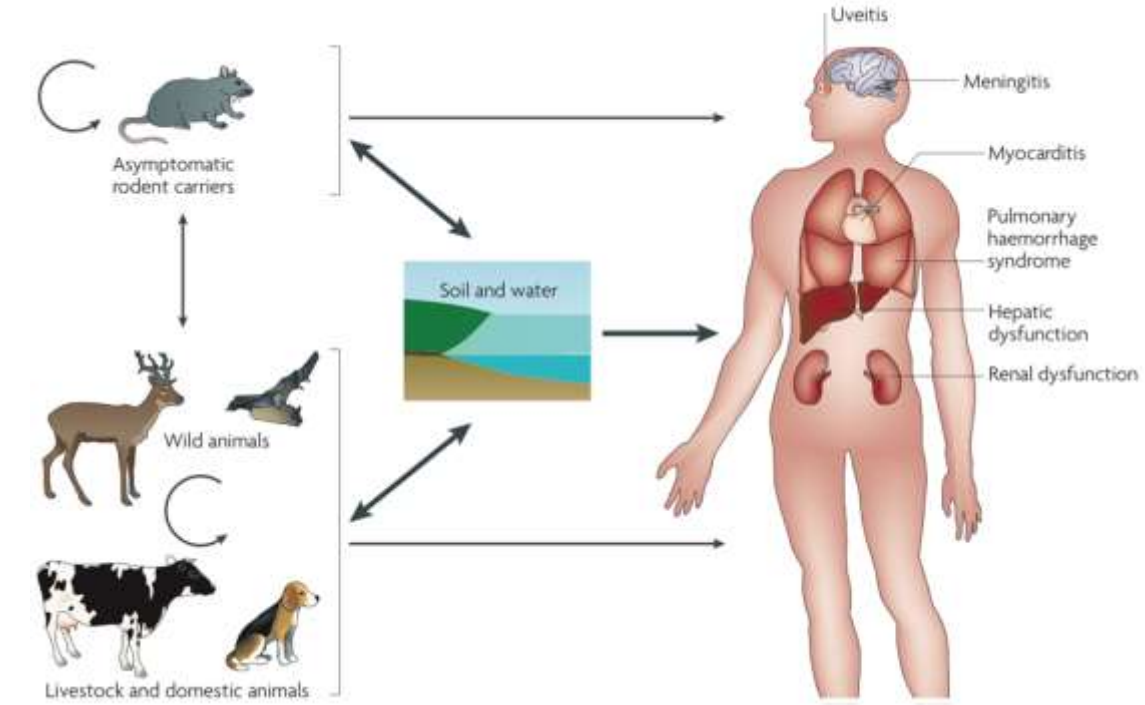
Small-scale analysis: Heterogeneity

- Analysis of community-level risk factors and point-level outcomes, we assume that the effect of the variable operates through its area-level average
- Community-level exposure-response relationships may not accurately reflect associations at the household level (ecological fallacy or bias)
  - Similar issue when analyzing province-level, county-level variables.
- The magnitude of the ecological bias depends on the degree of within-area variability in exposures and confounders

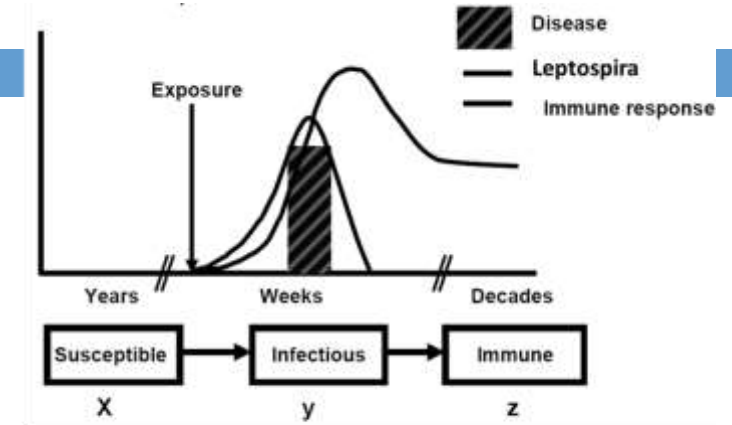
Small-scale analysis: Heterogeneity

- Why is this important? For interventions … a community-level intervention may also affect the people who did not participate on the intervention (was not invited or non-compliance).
- In my Chile example:
  - Community-level prevalence of rodent infection was associated with higher prevalence in people
  - Community-level rodent control program would reduce infection risk in the entire community ..??

Mathematical modeling



Ko AI, Goarant C, Picardeau M. Nature reviews. Microbiology. 2009;7(10):736–47.



Flow diagram of the natural history of the infection

Mathematical model

Set of equations which are the "mathematical translation" of hypotheses (or assumptions)

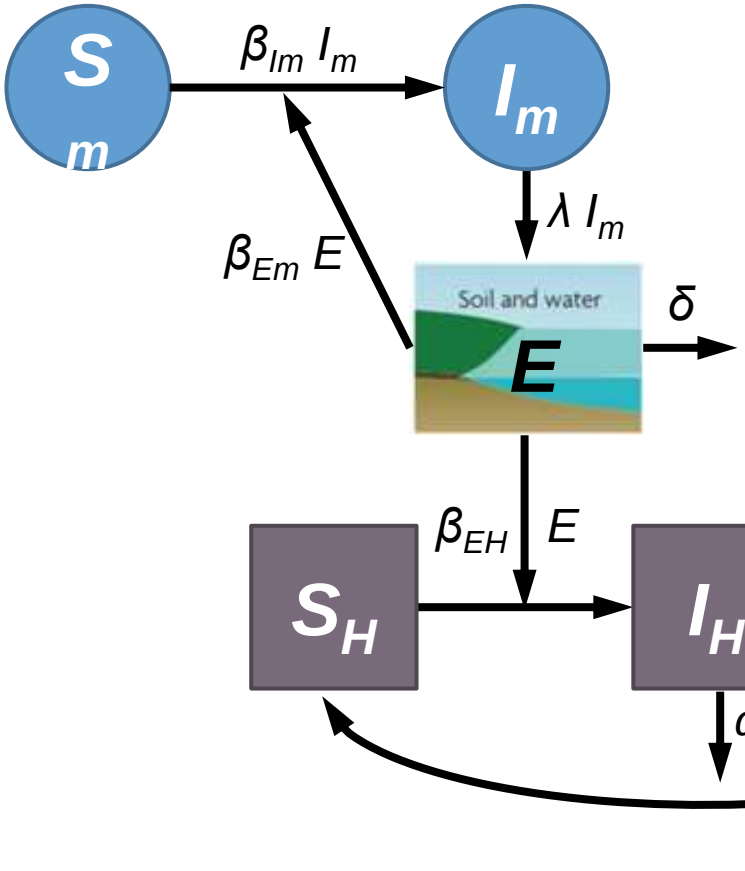
Mathematical modeling of *Leptospira* transmission and intervention strategies

Specific studies currently in development include:

- Large scale spatial-temporal modeling of leptospirosis incidence and early warning system for leptospirosis outbreaks
- A multi-host multi-strain model to investigate the patterns of strain dominance and source attribution of infection in animals and in people
- An eco-epidemiological model to investigate the role of species diversity, density, and ecological conditions on infection transmission
- Effectiveness and impact of chemoprophylaxis as an intervention for infection risk reduction
- Optimal and cost-effective diagnostic algorithms for early detection of leptospirosis cases
- A portfolio management model to compare interventions and identify optimal choices under different conditions

NIMBioS
National Institute for Mathematical and Biological Synthesis

Example: Models to examine interventions



β_{lm} = rate of direct transmission between rodents,
β_{Em} = rate of transmission from environment to rodents,
λ = excretion rate of leptospires,
δ = decontamination rate of leptorpires,

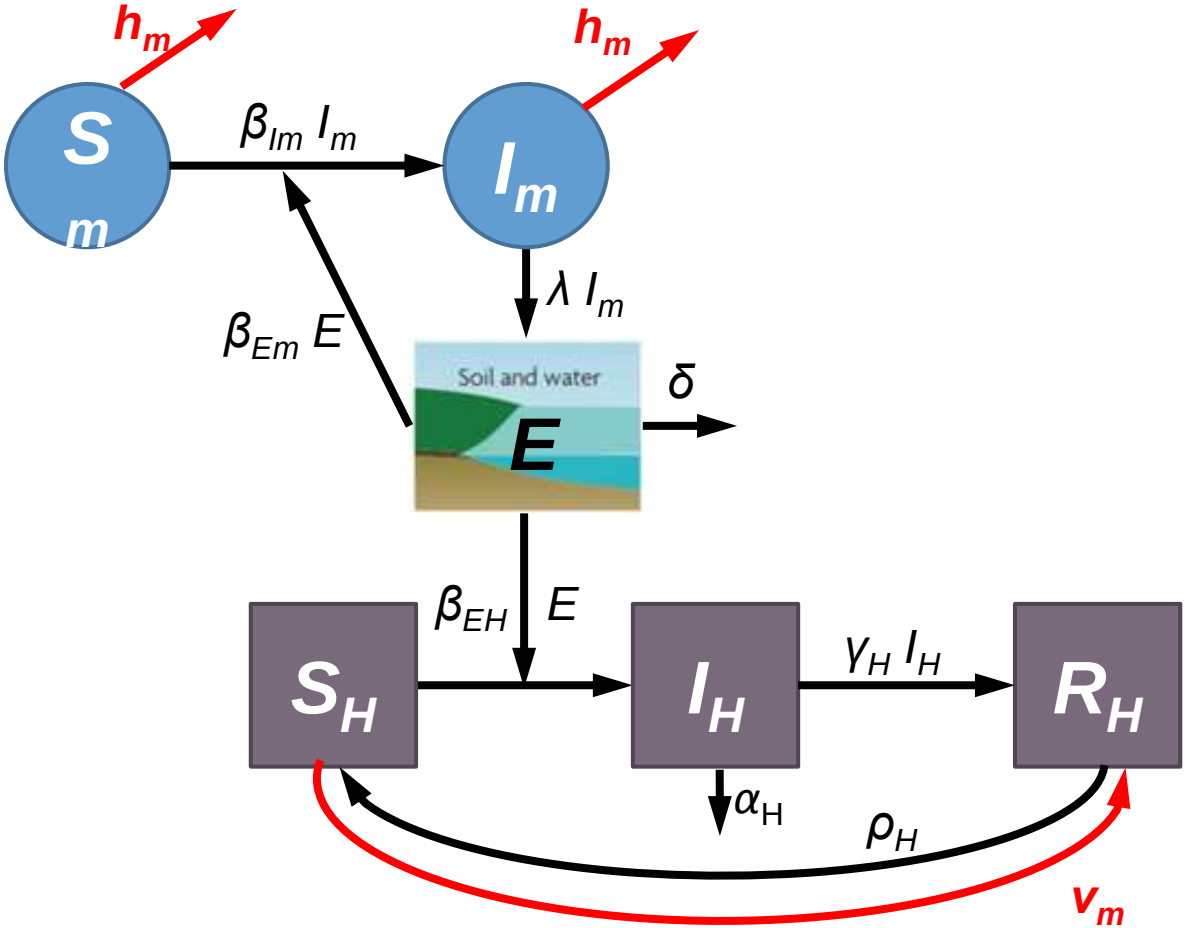
β_{EH} = rate of transmission from environment to humans,
α_H = virulence rate due to infection in humans,
γ_H = recovery rate in humans,
ρ_H = rate of immunity loss

Investigating interventions

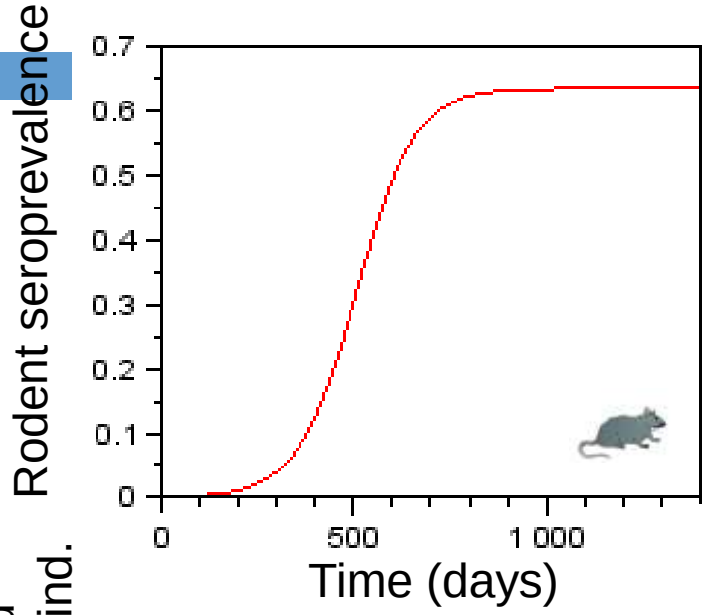
- **Rodent control at rate h_m**

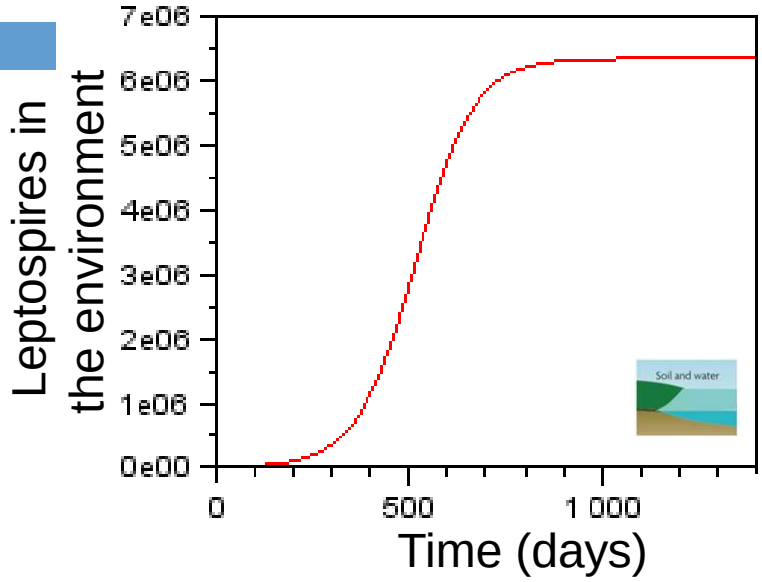
- **Human vaccination at rate v_m**

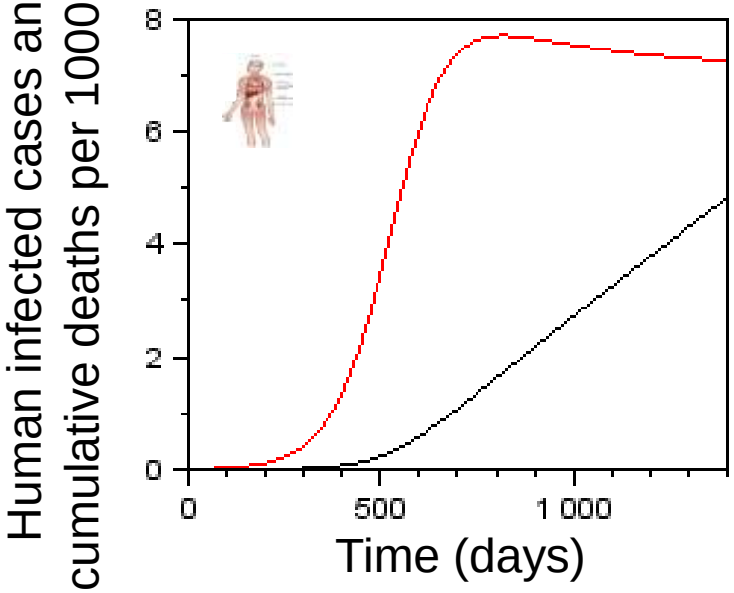
Asymptomatic rodent carriers

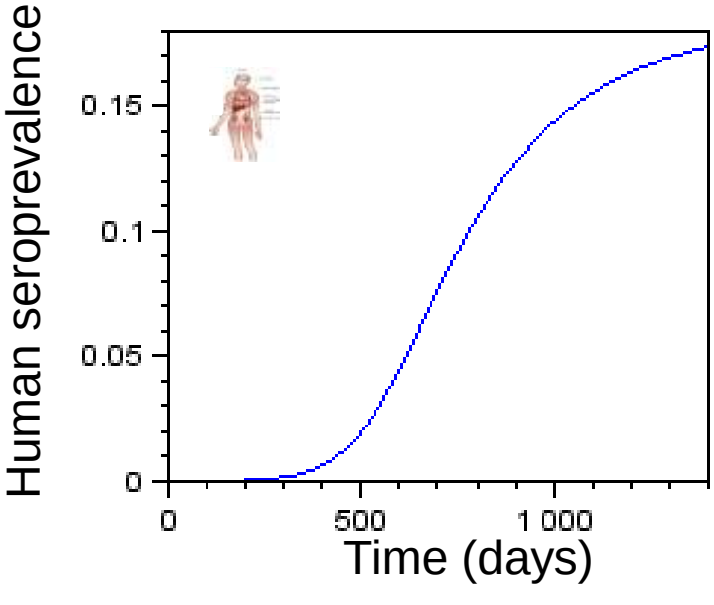


Baseline Predictions

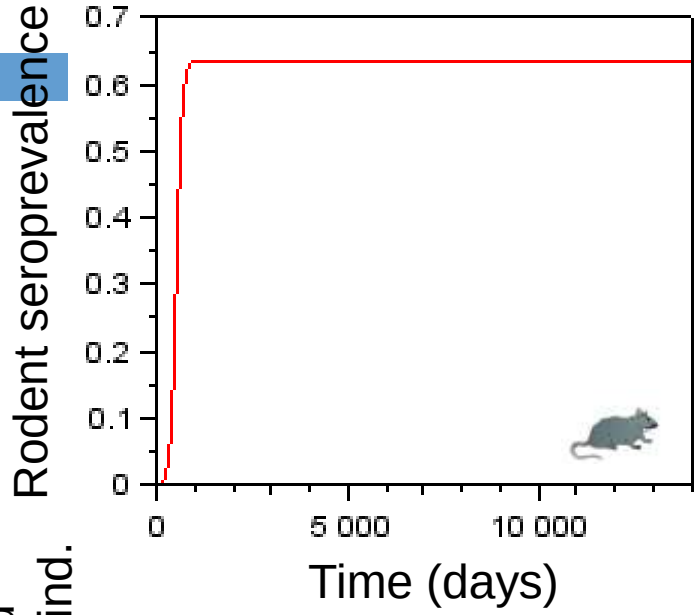


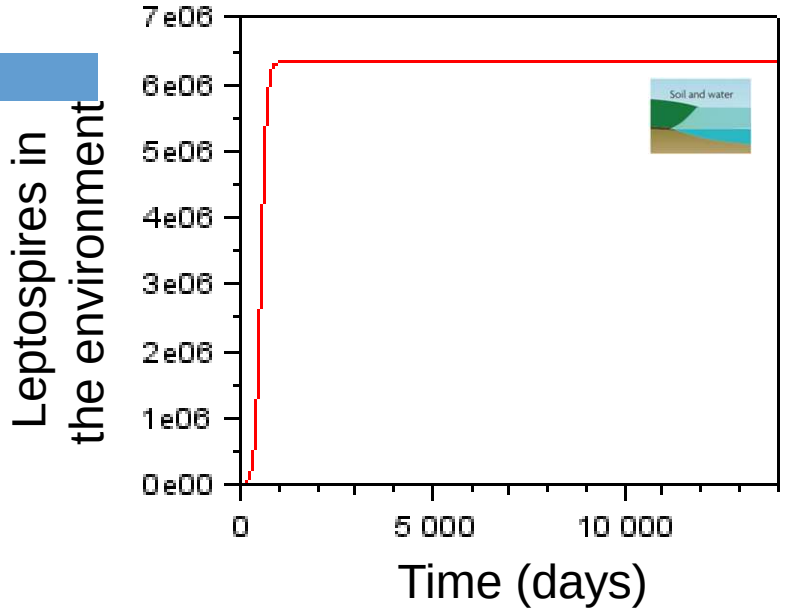


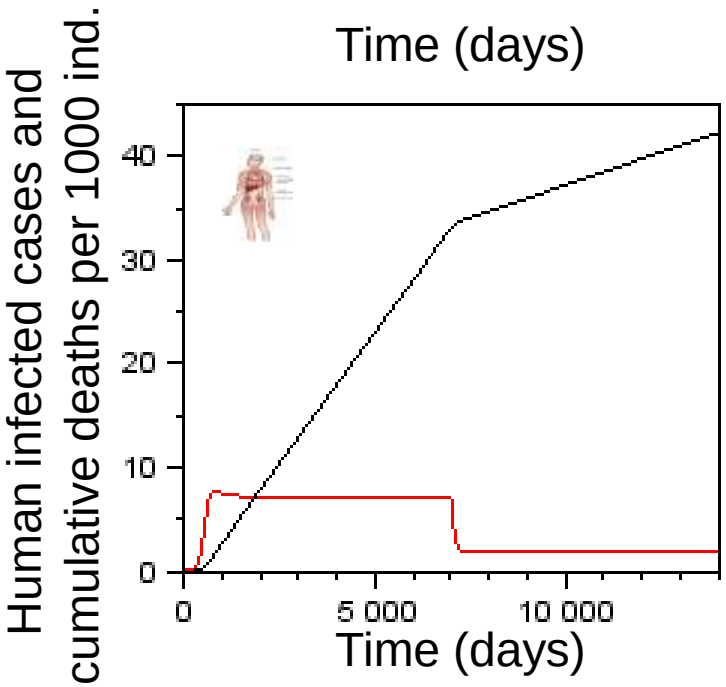


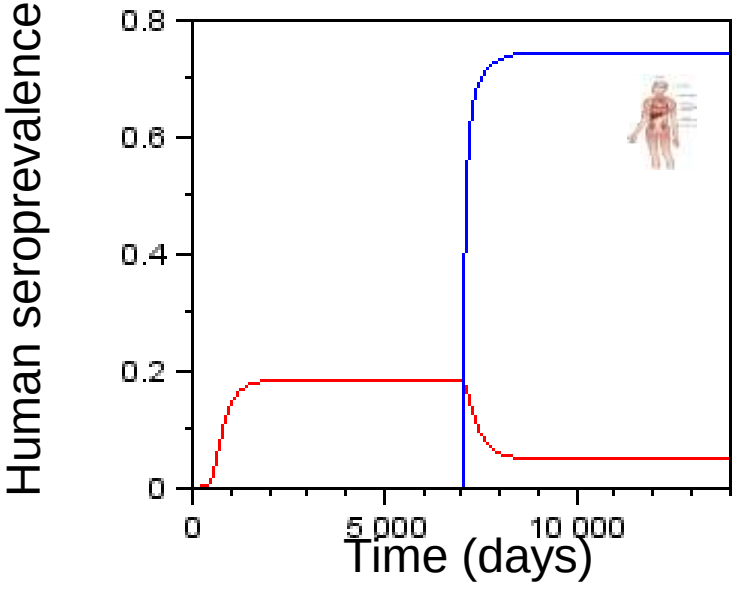


Vaccination in people

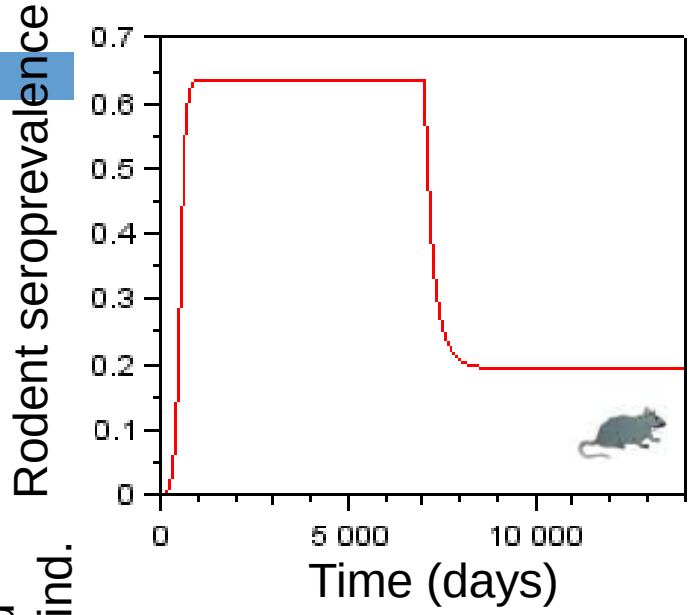


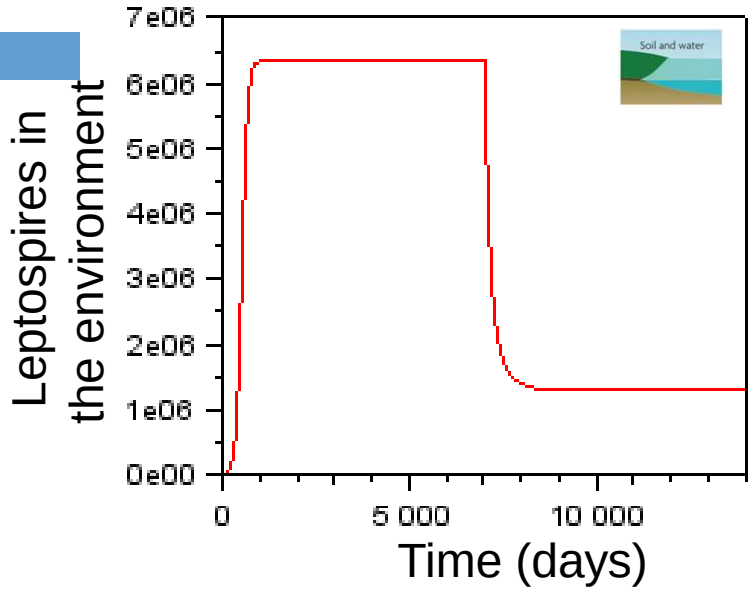


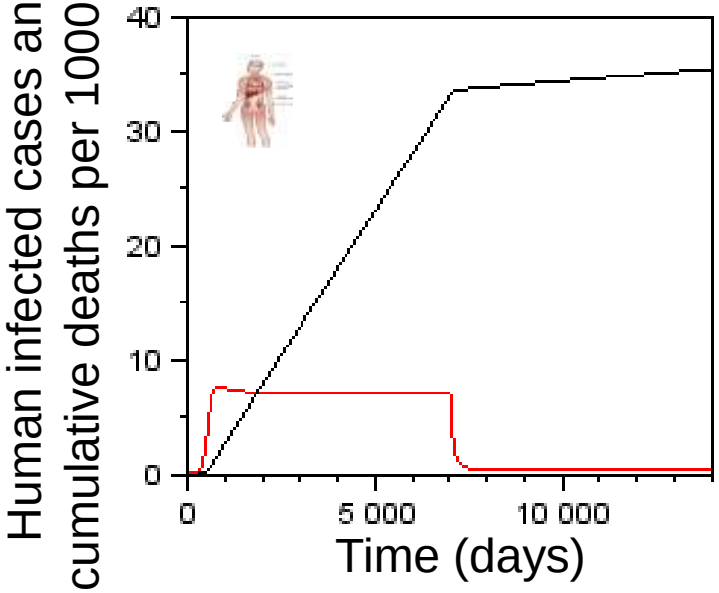


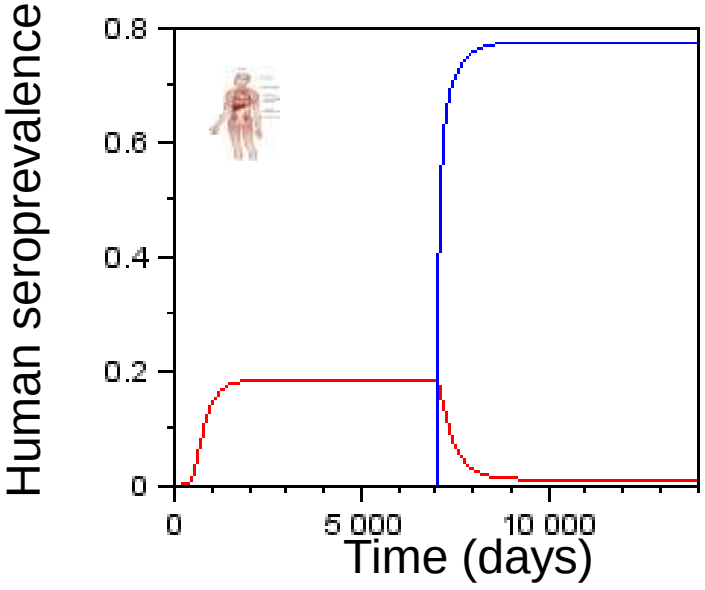


Rodent control + Vaccination









Challenge, gaps

- Improved and consistent methodology to accomplish different goals:
- Large-scale, aggregate level data:
  - Identification of high risk areas and time periods and influential factors
- Small-scale, individual-level data:
  - Understand transmission process
  - Identification of interventions
- Modeling: parameters, long-term and complete data for validation