Identification of hotspots of rat abundance and their effect on human risk of leptospirosis in a Brazilian slum community

Poppy Miller [1] Kate Hacker [2] Peter Diggle [1] Mike Begon [3] James Childs [2] Albert Ko [2] Federico Costa [2] Mitermayer Reis [2] Chris Jewell [1]

[1] **Lancaster University**

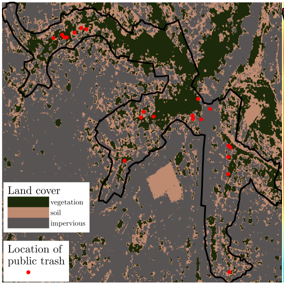
[2] **Yale University**

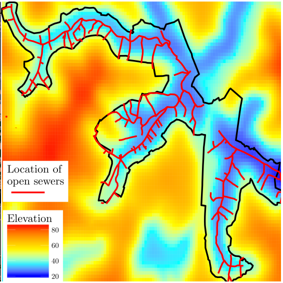
[3] **Liverpool University**

April 16, 2018

Study area: Pau da Lima, Salvador, Brazil

- Urban slum (0.17 km^2)
- high population density (88% squatters, low income and education level)
- lack of structural planning and basic sanitation
- high levels of many diseases (often spread by rats) e.g. leptospirosis





Background

Rats:

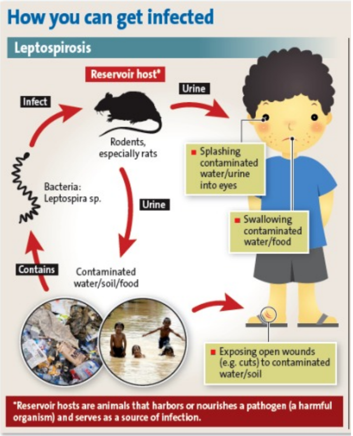
- abundant in urban slums
- reservoir hosts for many diseases

Leptospira:

- survive months in environment
- asymptomatic in reservoir hosts
- spread via shedding in urine

Leptospirosis:

- infection via skin/ mucous membranes
- estimated 1.03 million cases annually
- 90-95% cases are mild
- 10-50% mortality for severe form



Motivation

Pau da Lima:

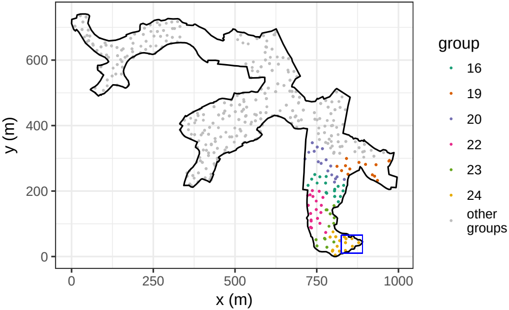
- high levels of human leptospirosis
- chronic leptospirosis infection of Norway rat

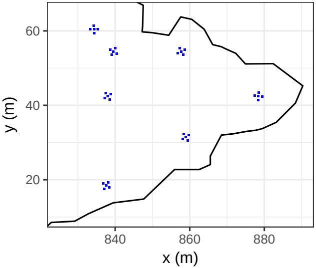
Rodent control is largely ineffective at reducing the burden of leptospirosis in urban slum environments where Norway rats are the primary reservoir hosts.

Reliable estimates of rat abundance and distribution are critical to mounting adequate rodent control in complex urban settings

Rat prevalence: study design

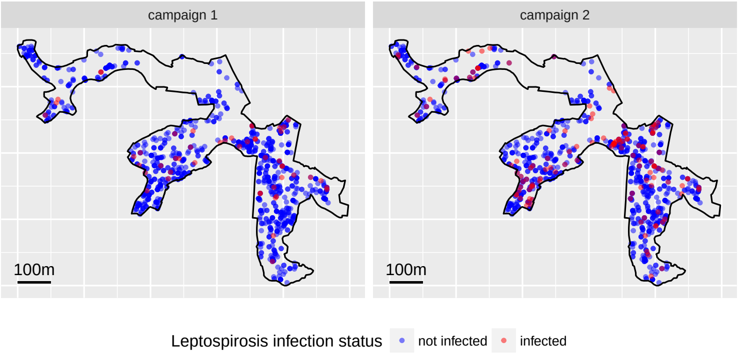
- 3 valleys, 0.17 km^2
- spatially constrained random sample of 340 points + 100 close range points
- 24 groups of points; sampled three groups per week
- 5 tracking plates per location; measured twice (2 consecutive days)
- repeated for dry and wet seasons



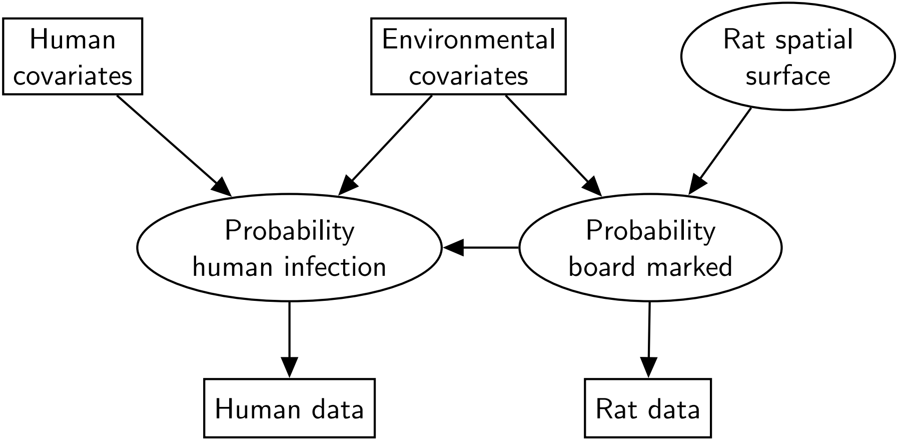


Human leptospirosis prevalence: study design and covariates

- 1110 residents in the study area
- MAT titres measured before and after each rat tracking campaign
- pairs of titres determine residents infection status



Model overview



Rat model

$$m_{ic} \sim \text{Binomial}\left(p_{ic}, n_{ic}\right)$$
$$\text{cloglog}\left(p_{ic}\right) = x_{ic}^T\beta + S_{ic} + \log\left(\text{T}_{ic}\right)$$

$$S_c \sim \text{MVN}\left(0, \tau^2 + \Sigma_c\right)$$
$$\Sigma_{cws} = \sigma^2\left(1 + V_c\right)\exp\left(-V_c\right)$$
$$V_c = \left(\sqrt{3}b_{cws}\right)/\phi$$

- S_c : Matern 3/2 spatially correlated random effects (separate surface for each campaign)
- b_{cws} : distance between points w and s in campaign c (meters)

- m_{ic} boards positive for rat marks out of n_{ic} total for location i, and campaign c
- p_{ic} : probability of rat marks
- T_{ic} : offset (number of nights board exposed)
- X : rat covariate matrix
- Priors:
  $\beta_k \sim \text{Normal}\left(0, 100\right)$
  $\tau^2, \sigma^2 \sim \text{Gamma}\left(2, 0.5\right)$
  $\phi \sim \text{Gamma}\left(1.5, 0.05\right)$

Human Model

$$y_{jc} \sim \text{Bernoulli}\left(\pi_{jc}\right)$$
$$\text{logit}\left(\pi_{jc}\right) = z_{kjc}^{T}\gamma + \theta\left(x_{j}^{T}\beta + S_{jc}\right) + \delta_{k}$$

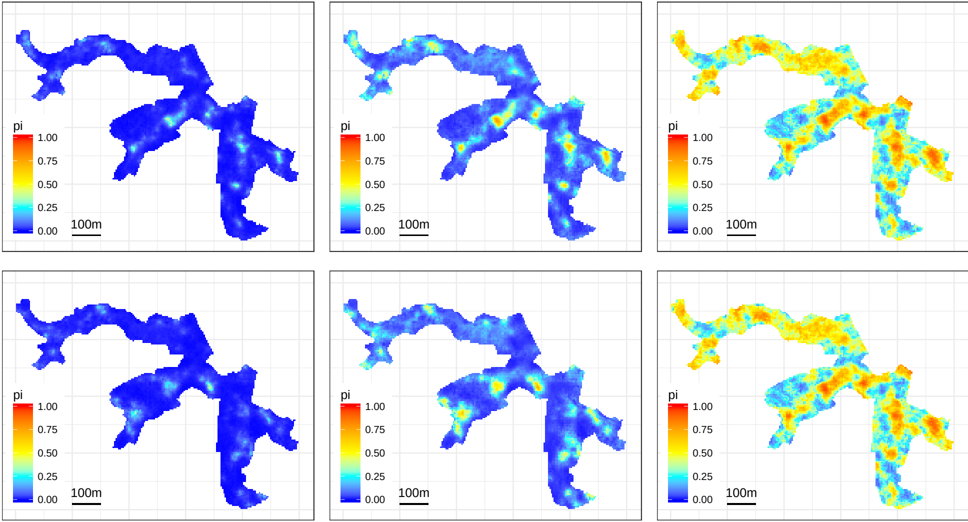
- y_{kjc} : human infection status for location j
- π_{kjc} : probability of human infection

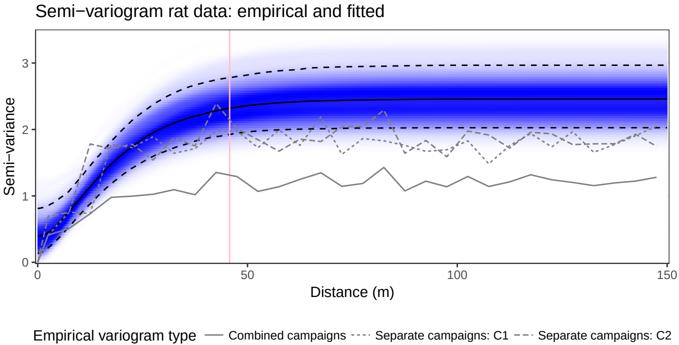
- Z : human covariate matrix
- X : rat covariate matrix at human locations
- S_{jc} : predicted spatial random effect at human locations
- γ, θ : coefficients
- δ_k : random effect for each individual k

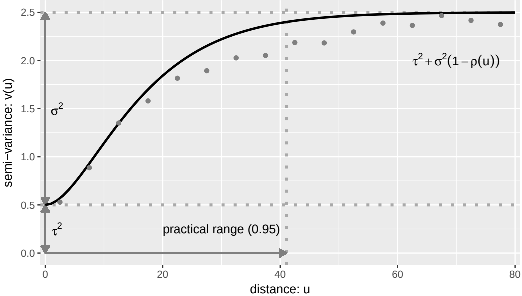
- Priors: $\gamma_k \sim \text{Normal}\left(0, 100\right)$, $\delta_i \sim \text{Normal}\left(0, \sigma_H\right)$, $\sigma_H \sim \text{Gamma}\left(2, 0.5\right)$

Predictive rat surfaces for campaigns 1 and 2

Lower (0.05), median and upper (0.95) predictive probabilities of rat marks







	Median (CI)
ϕ	17.31 (12.85, 22.86)
σ^2	2.03 (1.40, 2.71)
τ^2	0.39 (0.08, 0.85)

Rate ratios: rat model

Interpretation: The rate of rat mark deposition at the upper quartile value of a covariate is $RR_{U/L}$ multiplied by the rate at the lower quartile of the covariate.

	Rate ratio$_{U/L}$	**Data LQ**	**Data UQ**
Continuous variables			
Mean rainfall (mm)	1.46 (1.26, 1.66)	0.3	6.8
Distance 3d public dump (m)	0.60 (0.38, 0.82)	30.5	96.6
Distance 3d open sewer (m)	0.76 (0.60, 0.96)	9.6	17.6
Ground cover % soil	1.49 (0.95, 2.26)	6	41
Ground cover % vegetation	0.71 (0.43, 1.07)	0	57
Binary variables	**Rate ratio$_{1/0}$**		
Domestic / non-domestic	1.14 (0.82, 1.45)		

Odds ratios: leptospirosis model (significant variables)

Interpretation: The odds of being infected with leptospirosis for a person with a covariate value at the upper quartile for that covariate are $OR_{U/L}$ times those at the lower quartile for that covariate.

	Odds ratio$_{U/L}$	**Data LQ**	**Data UQ**
Continuous variables			
Distance public dump (m)	0.44 (0.27, 0.63)	32.7	90.6
Log income (reias/month)	0.64 (0.30, 1.09)	log(1)	log(728)
Cumulative rainfall (m)	4.12 (2.45, 6.33)	0.56	1.70
Age (years)	13.28 (5.38, 27.01)	15	42
Rat linear predictor	1.03 (1.00, 1.07)	0.033	0.214
Binary variables	**Odds ratio**$_{1/0}$		
Male / Female	3.78 (1.96, 6.33)		

Practical implications

Target interventions to decrease leptospirosis risk:

- why does increasing rainfall increase risk?
- why are men and young people more at risk?
- increase incomes?
- remove or cover public dumps
- decrease rat numbers

Target interventions to reduce rat numbers:

- cover open sewers
- remove or cover public dumps
- rodenticide campaigns targeting rat hotspots

Current and future work

- Incorporate uncertainty in human infection status
- Extend model to more campaigns worth of data when available
  - Add campaign as a random effect
  - Add temporal correlations
- Formal model selection

Thank you for your attention!

Contact: p.miller@lancaster.ac.uk

Significant covariate effects: leptospirosis model

Parameter	Median	(CI)	Prob <0	Prob >0
Dist public dump (km)	-14.31	(-21.69, -7.51)		**1.000**
Total rainfall (m)	1.24	(0.85, 1.66)	**1.000**	
Age	0.18	(0.12, 0.23)	**1.000**	
Age >30 years	-0.18	(-0.25, -0.11)		**1.000**
Sex (male = 1)	1.33	(0.78, 1.90)	**1.000**	
Log income	0.25	(0.02, 0.49)	**0.982**	
Log income >40 reais/month	-0.73	(-1.24,-0.20)		**0.997**
Rat linear predictor	0.18	(-0.02, 0.38)	**0.966**	
σ (individual level random effect)	1.72	(1.13, 2.31)		

Odds ratios: leptospirosis model continuous variables

Interpretation: The odds of being infected with leptospirosis for a person with a covariate value at the upper quartile for that covariate are $OR_{U/L}$ times those at the lower quartile for that covariate.

	Odds ratio$_{U/L}$	**Data LQ**	**Data UQ**
Ground cover % soil	1.09 (0.70, 1.56)	3	37
Ground cover % vegetation	1.15 (0.95, 1.38)	0	17
Cumulative rainfall (m)	4.12 (2.45, 6.33)	0.56	1.70
Distance public dump (m)	0.44 (0.27, 0.63)	32.7	90.6
Distance open sewer (m)	1.12 (0.97, 1.29)	6.2	16.9
Age (years)	13.28 (5.38, 27.01)	15	42
Log income (reias/month)	0.64 (0.30, 1.09)	log(1)	log(728)
Rat linear predictor	1.03 (1.00, 1.07)	0.033	0.214

Odds ratios: leptospirosis model binary variables

	Odds ratio$_{1/0}$
Male / Female	3.78 (1.96, 6.33)
Ethnicity 2 / Ethnicity 1	1.57 (0.28, 4.62)
Ethnicity 3 / Ethnicity 1	1.64 (0.34, 4.87)
Ethnicity 4 and 7 / Ethnicity 1	3.77 (0.00, 54.66)
Literate / Illiterate	0.89 (0.45, 1.48)
Sewer exposed / not exposed	1.54 (0.81, 2.58)
Mud exposed / not exposed	1.24 (0.64, 2.07)
Flood exposed / not exposed	1.00 (0.51, 1.63)

Covariate effects: rat model

Parameter	Median	(CI)	Prob <0	Prob >
Intercept	-3.06	(-3.52, -2.61)		**1.000**
Area soil	0.87	(-0.15, 2.00)	*0.943*	
Area soil squared	-3.76	(-6.89, -1.04)		**0.994**
Area veg 5m	-0.52	(-1.28, 0.17)		*0.934*
Area veg 5m squared	2.42	(0.04, 4.50)	**0.984**	
Mean rainfall	58.32	(38.14, 80.39)	**1.000**	
Dist dump	-16.11	(-26.50, -5.45)		**0.999**
Dist dump >70m	20.52	(6.14, 36.22)	**0.998**	
Domestic	0.13	(-0.17, 0.39)	0.795	
Dist open sewer	-19.87	(-38.14, -3.29)		**0.983**
Dist open sewer >40m	51.69	(12.29, 84.97)	**0.997**	
phi	17.31	(12.85, 22.86)		
sigmasq	2.03	(1.40, 2.71)		
tausq	0.39	(0.08, 0.85)		

Why the cloglog link?

Boards are marked at rate λ_i (Poisson process):

- p_i: probability that the number of rat marks is ≥ 1 in time period $[0, T_i]$
- $1 - p_i$: Prob (0 marks) in time period $[0, T_i]$

$$1 - p_i = \frac{\left\{\int_0^{T_i} \lambda_i dt\right\}^0 e^{-\int_0^{T_i} \lambda_i dt}}{0!} = e^{-\int_0^{T_i} \lambda_i dt} = e^{-\lambda_i T_i}$$

Rearrange to get cloglog link function:

$$\begin{aligned}
\log\left(-\log\left(1 - p_i\right)\right) &= \log\left(\lambda_i T_i\right) \\
&= \log \lambda_i + \log T_i \\
&= d\left(x_i\right)' \beta + S\left(i\right) + \log T_i \\
&= \eta_i
\end{aligned}$$