Model-based geostatistical inference with low prevalence data: a case study on lymphatic filariasis

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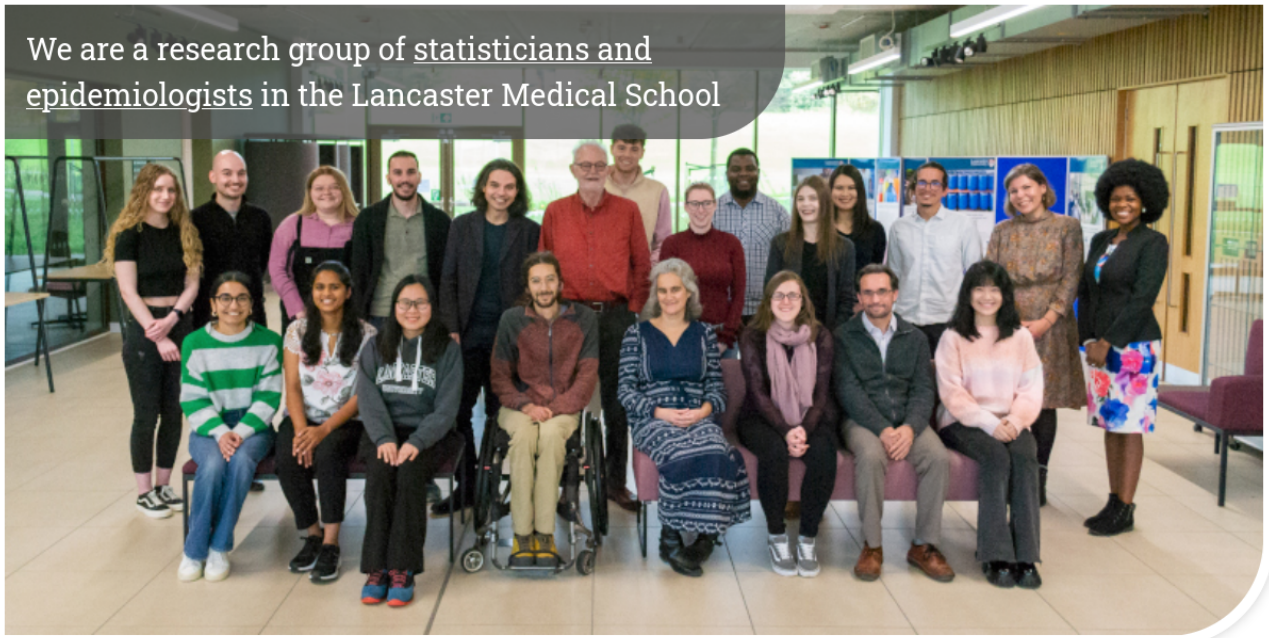

WHO Collaborating Centre

Current NTD Projects

- Brazilian Leptospirosis Study : Ecoepidemiology of Leptospirosis in the Urban Slums of Brazil
- Geostat NTD Hub : A Geostatistical Web Framework for Prevalence Surveys for Neglected Tropical Diseases
- Loa-loa Mapping : Developing methods to combine prevalence data from multiple diagnostics
- National Snakebite Study in Sri Lanka : Developing a Risk Map for Snakebites
- Neglected Tropical Disease Modelling Consortium : Survey Design and Analysis for Disease Prevalence

Overview of the talk

- Part 1: Introduction to Neglected Tropical Diseases
- Part 2: Model-based geostatistics for disease mapping
- Part 3: Case studies on lymphatic filariasis

Acknowledgements

- Lucinda Hadely (Senior Research Associate)
- Funders: TaskForce for Global Health and USAID

Neglected tropical diseases

Disease	CDC	WHO
Buruli ulcer (*Mycobacterium ulcerans* infection)	+	+
Chikungunya [a]	–	+
Chagas disease	+	+
Cysticercosis	+	+
Dengue fever	+	+
Dracunculiosis (or guinea worm disease) [b]	+	+
Echinococcosis	+	+
Fascioliasis	+	+
Foodborne trematodiasis [a]	–	+
Human African trypanosomiasis (or sleeping sickness)	+	+
Leishmaniasis (or kala-azar)	+	+
Leprosy	+	+
Lymphatic filariasis [b]	+	+
Mycetoma	+	+
Onchocerciasis (or river blindness) [b]	+	+
Rabies	+	+
Schistosomiasis [b]	+	+
Soil-transmitted helminthiasis [b]	+	+
Trachoma [b]	+	+
Yaws	+	+

Data source: CDC, 2017 [10]; WHO, 2017 [3]; [a] Not mentioned under CDC list of neglected tropical diseases (NTDs); [b] Diseases that can be controlled or eliminated through mass drug administration (MDA), or other interventions.

Common features of NTDs

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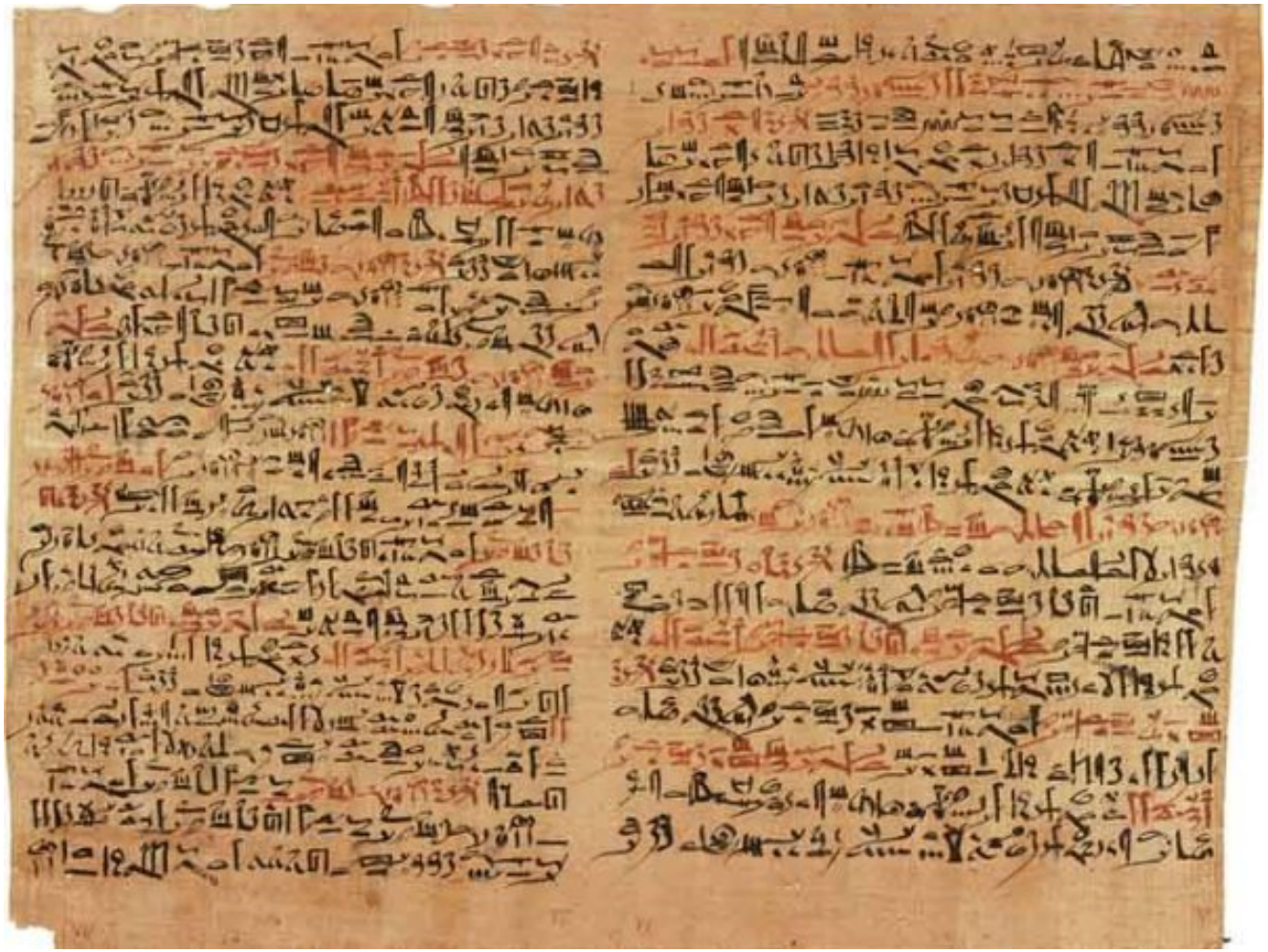

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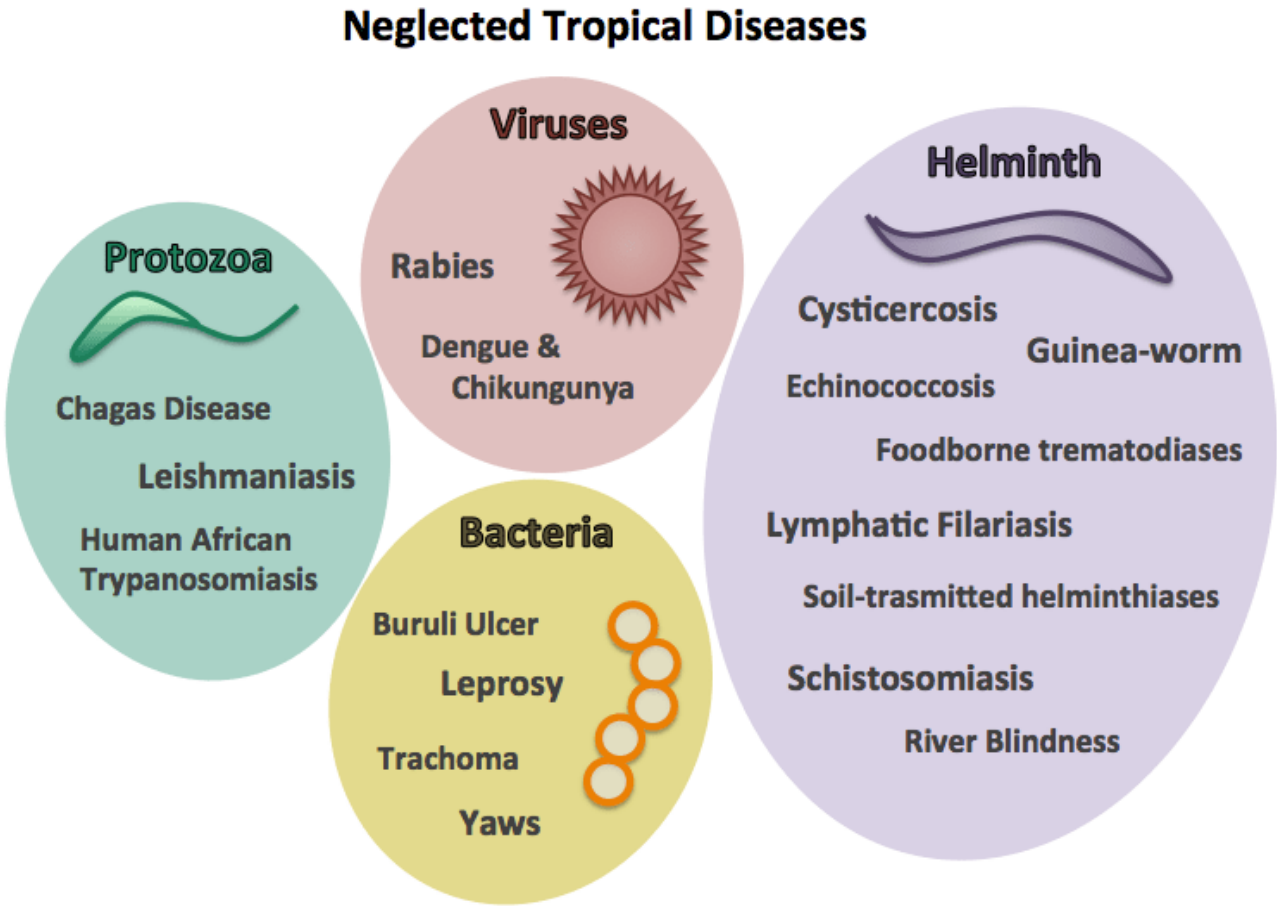
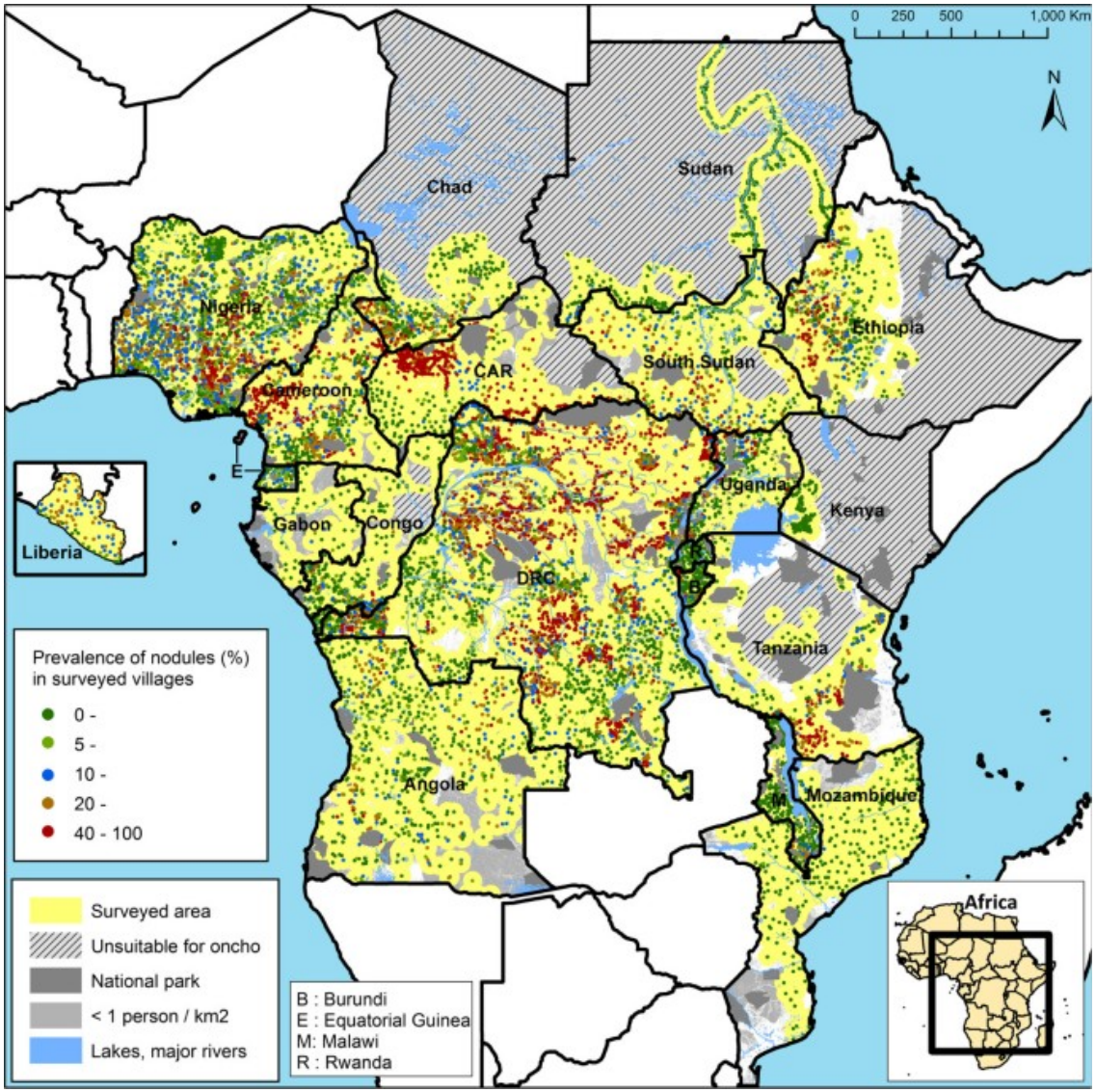


How can we map NTDs?



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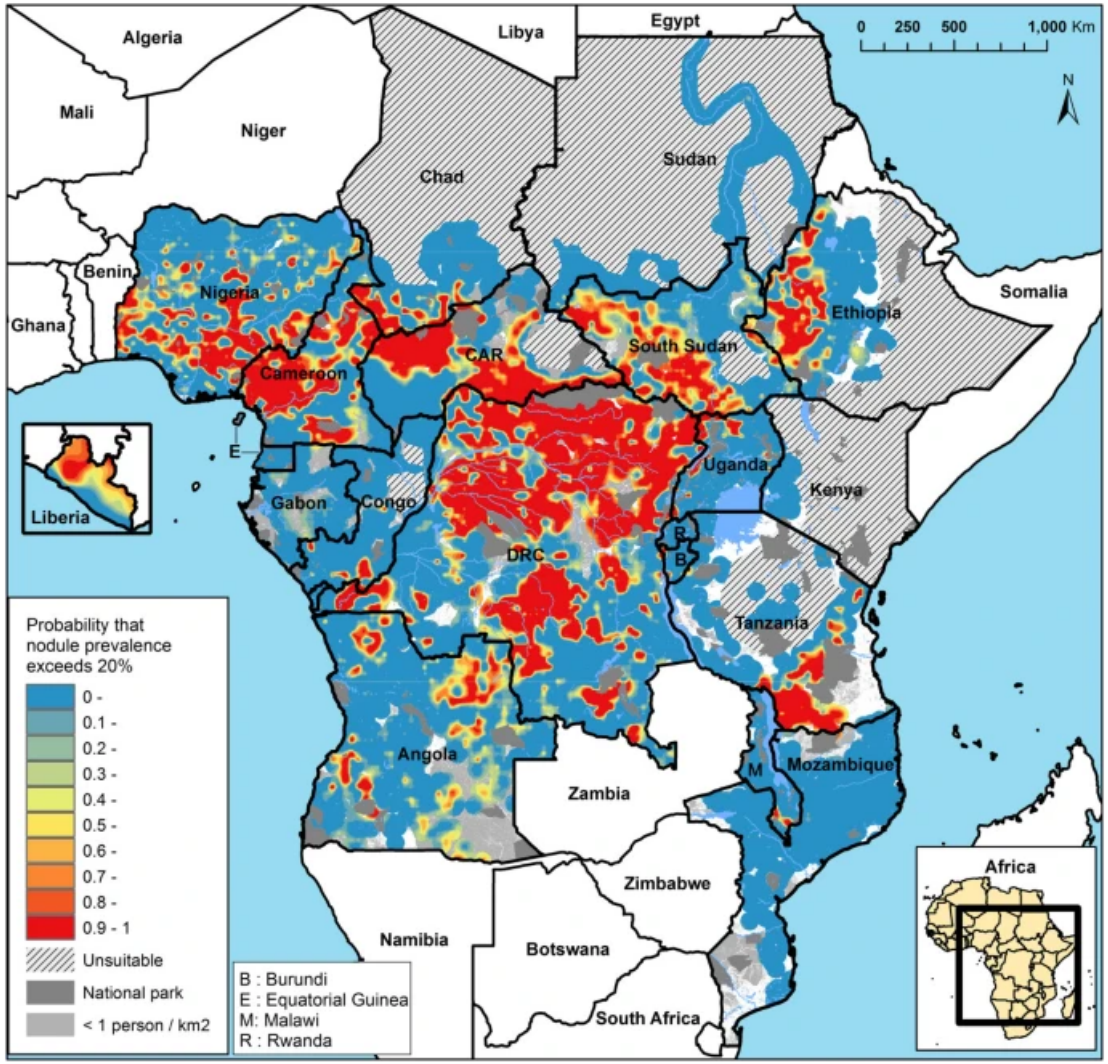

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Problem

1. How can we predict $p(x)$ using (x_i, n_i, y_i)?
2. How can we use $d(x)$ to improve our predictive inferences on $p(x)$?

Defining geostatistical problems

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- Y = data
- A statistical model $[S, Y] = [S] \times [Y|S]$

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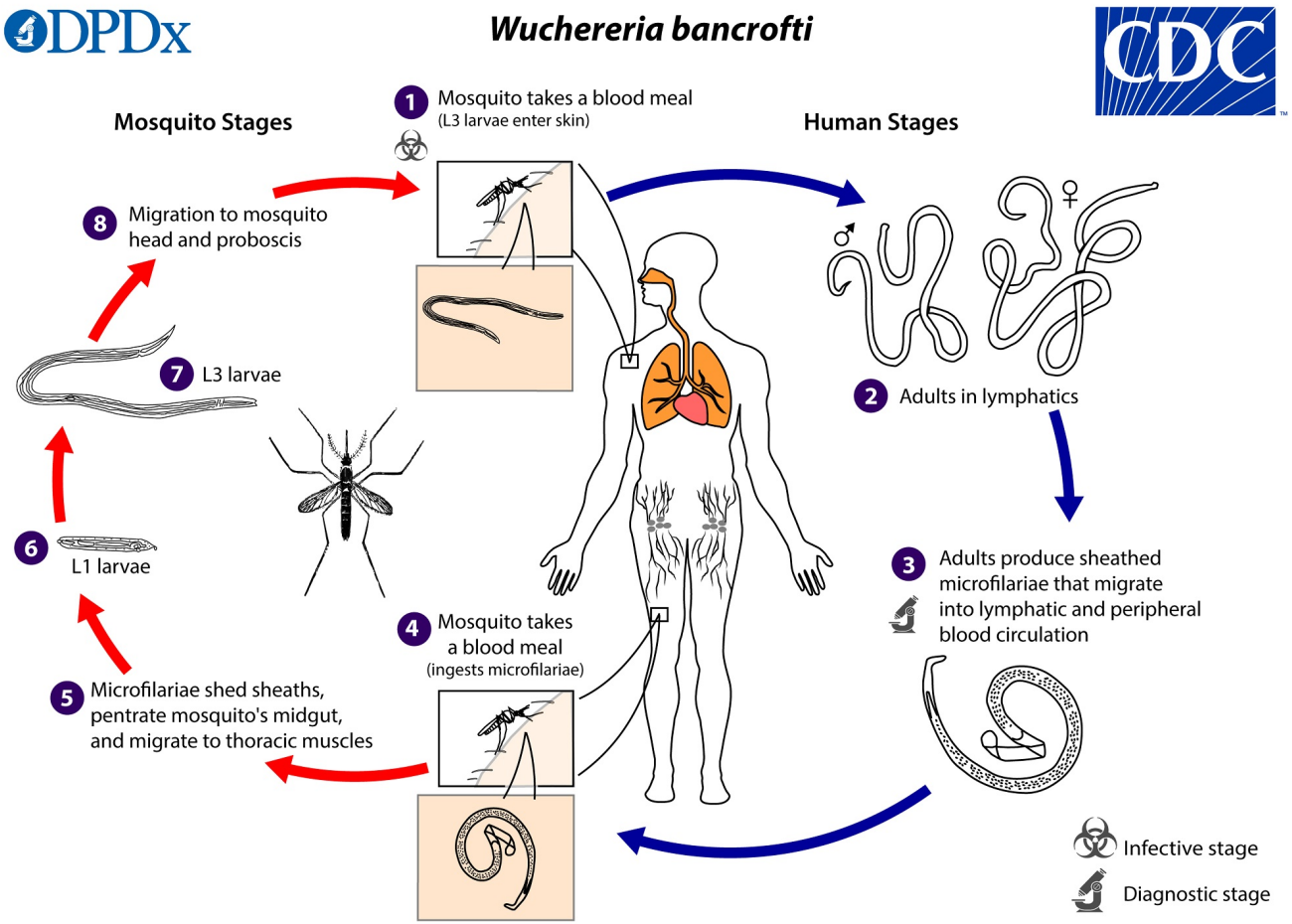
- $d(x_i)$ = vector covariates
- $S(x)$ = spatial stochastic process
- Z_i = unstructured random effects
- Assumption: $Y_i|S(x_i), Z_i \sim \text{Bin}(n_i, p(x_i))$

$$\log\left\{\frac{p(x_i)}{(1-p(x_i)}\right\} = d(x_i)^\top\beta + S(x_i) + Z_i$$

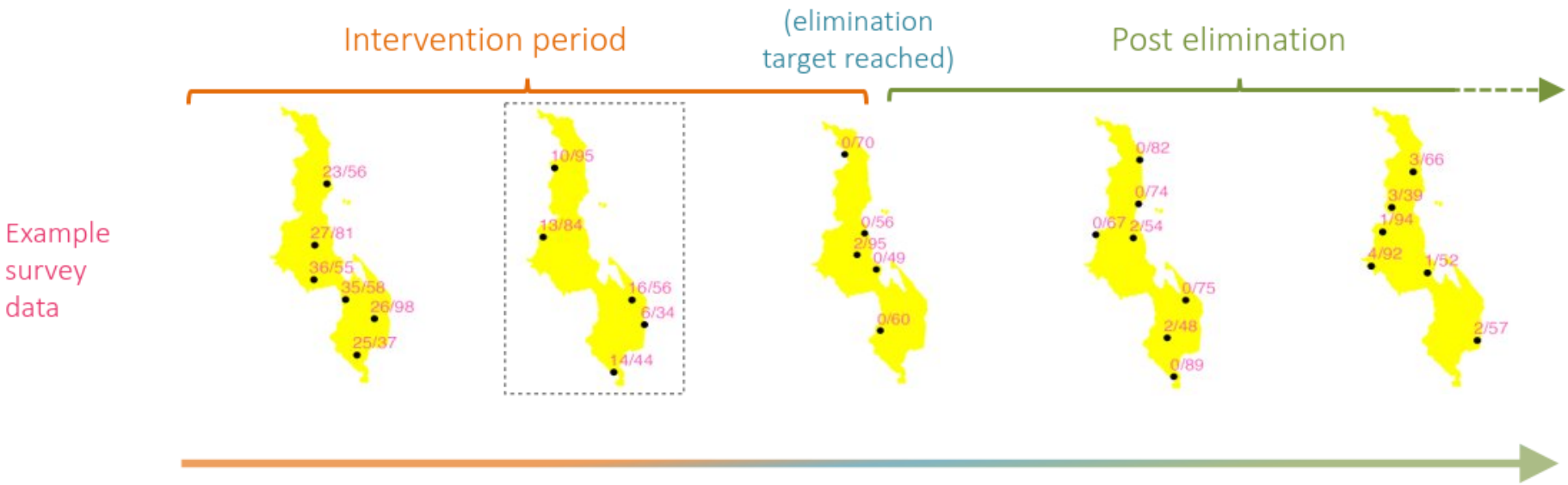
To predict or to explain?

- **Explanatory modelling:** emphasis is placed on understanding the relationships between the health outcome and risk factors
- **Predictive modelling:** maximize the predictive performance of the model

Lymphatic filariasis



LF prevalence surveys



- Elimination is declared when the district-wide is below 1%.
  - Questions: 1) How can we use these data to design a surveillance system in a post-elimination setting? 2) Where should we place the sentinel sites and how many?

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- Assumption 1: $[Y_t | \mathcal{S}_t(X_t)]$ is Binomial with linear predictor

$$\log\left\{\frac{p_t(x_{t,i})}{1 - p_t(x_{t,i})}\right\} = \alpha_t + S_t(x_{t,i})$$

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- Problem: inferring γ and α_t from the data may not empirically feasible.

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- We maximize $L(Y_0, \ldots, Y_k; \theta_{-\gamma})$ with respect to $\theta_{-\gamma})$ using Monte Carlo maximum likelihood.

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- Defining are suitable prior for γ (the temporal correlation parameter) and for α_t (the overall average prevalence).
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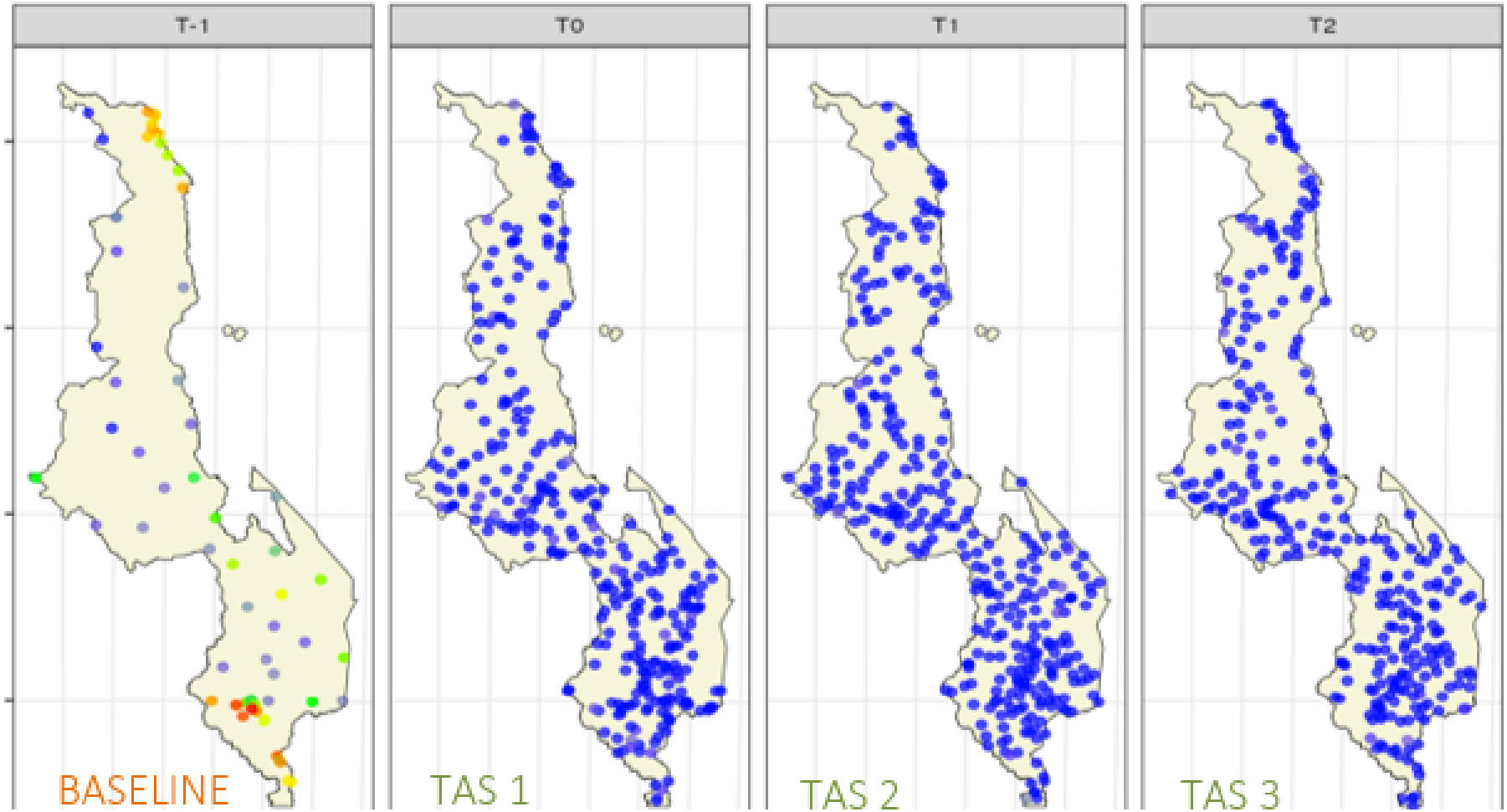
- $\mathcal{Y}_t = \{Y_k : k = 0, \dots, t\}$ (data collected from time 0 to time t)
- At time t, we then sample from $[\mathcal{S}_t|\mathcal{Y}_t]$ to assess the likelihood of resurgence (prevalence above 1%)

Setting up a simulation study

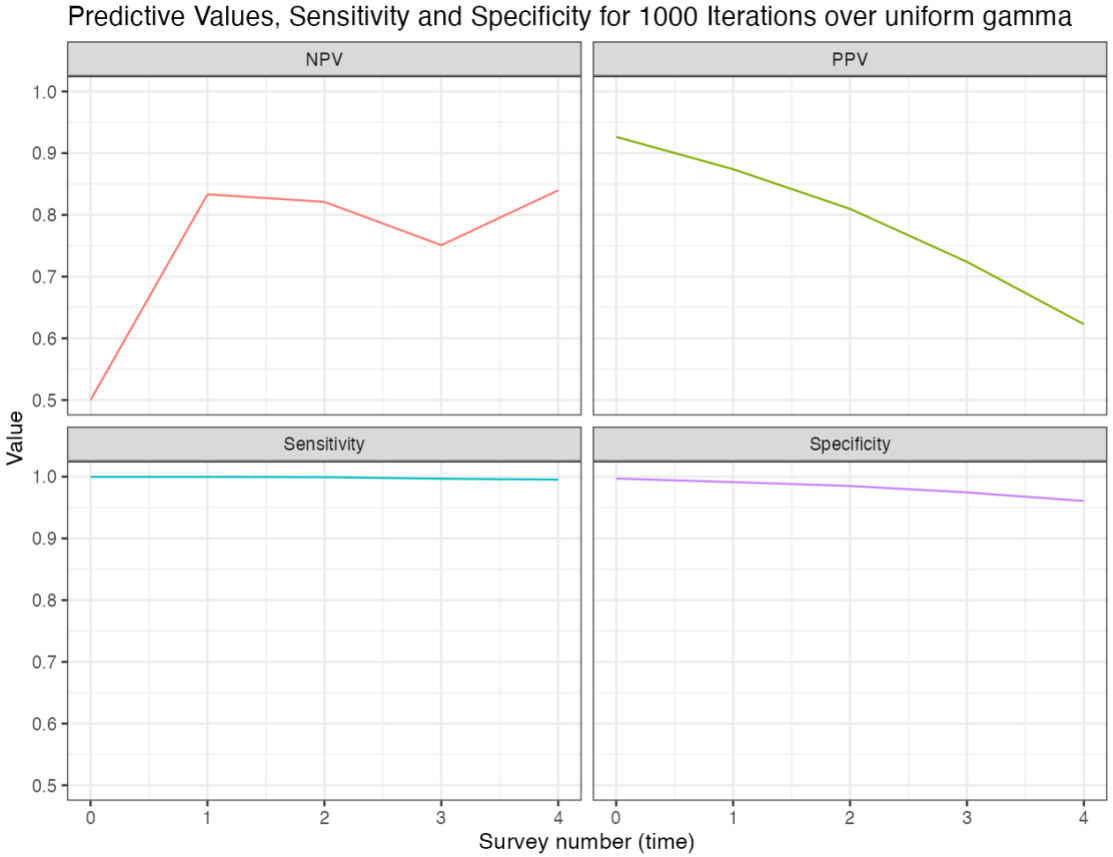
- Objective of the simulation: assess if the modelling framework can detect LF resurgence.
- Parameters of the simulation:
  1) where to place the sentinel sites
  2) how many sentinel sites per district
  3) the resurgence rate
  4) frequency of the sampling at sentinel sites.

LF in Malawi



Inital results from a simulation study

Parameters of the simulation: 1) allocate sentinel sites to locations with highest prevalence; 2) 2 sentinel sites per district; 3) resurgence rate of 5% prevalence increase every year; 4) sampling once per year.



Discussion

- We should also account for heterogeneous intervention coverage (TRANSFIL model)
- Computationally more efficient methods of inference (Kalman filter approximation for Binomial counts?)
- Generalizable to other NTDs.

References

- Galit Shmueli (2010) *To Explain or to Predict?.* Statistical Science 25 (3) 289 - 310 https://doi.org/10.1214/10-STS330
- Giorgi, E., Fronterre, C., Macharia, P., Alegana, V., Snow, R., Diggle, P. (2021) *Model building and assessment of the impact of covariates for disease prevalence mapping in low-resource settings: to explain and to predict.* Journal of the Royal Society Interface. 18:20210104. http://doi.org/10.1098/rsif.2021.0104
- Puranik, A., Diggle, P. J., Odiere, M. R., Gass, K., Kepha, S., Okoyo, C., Mwandawiro, C., Wakesho, F., Omondi, W., Sultani, H. M., Giorgi, E., *Understanding the impact of covariates on the classification of implementation units for soil-transmitted helminths control: A case study from Kenya.* BMC Methodology Research (Under Review). Pre-print available at: https://www.researchsquare.com/article/rs-3334755/v1