Understanding spatial patterns of NTD transmission using multiplex serological assays

Kimberly Fornace

NTD Detection and Diagnostics
6 June 2019

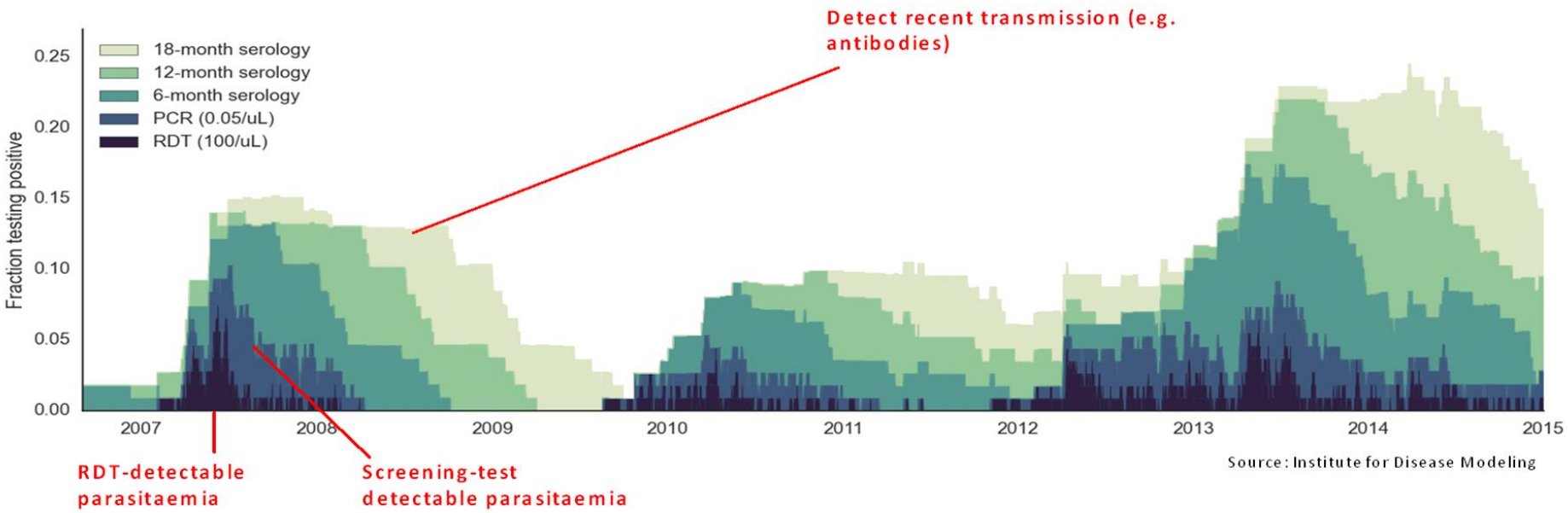
LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Serological data for surveillance

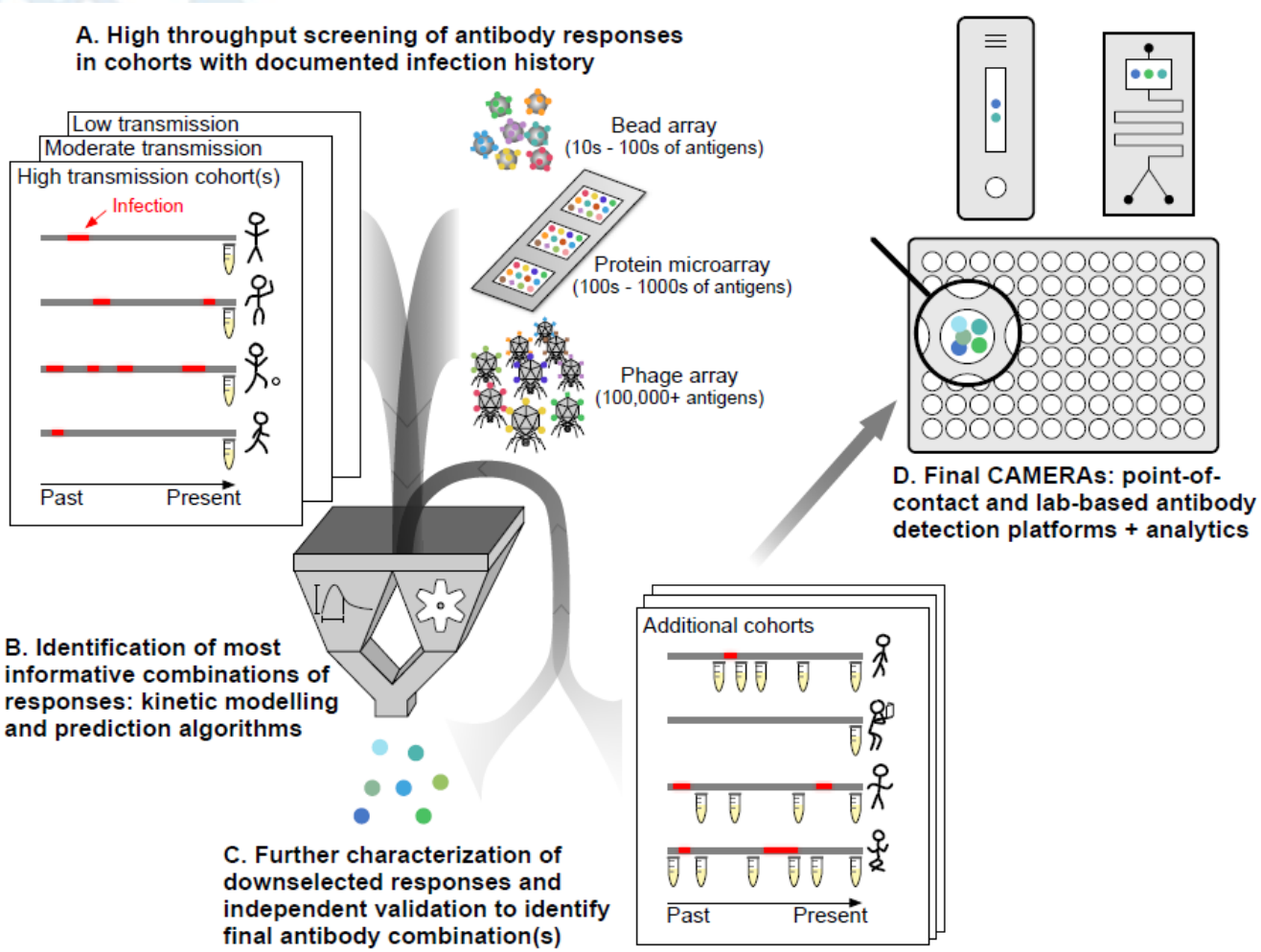
- Antibody levels reflect exposure to infection
- Utility in low transmission and elimination settings

Ability of various tests to detect foci of transmission

Simulated 'hot-spot' village in area with tenuous transmission



Multiplex serological platforms

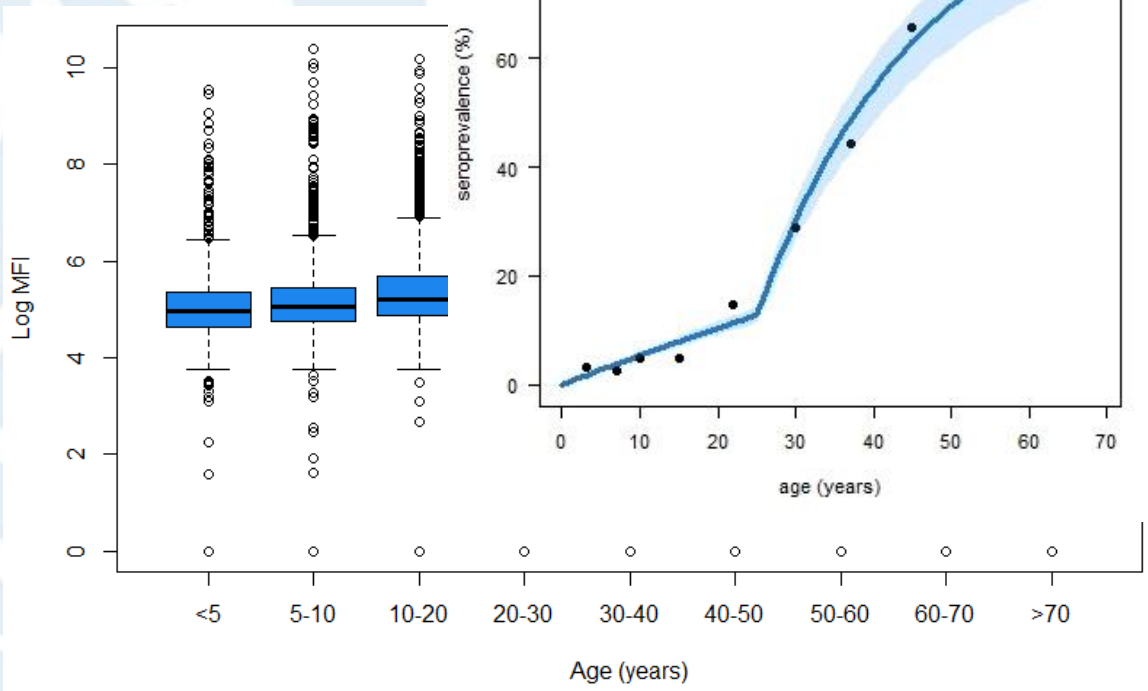


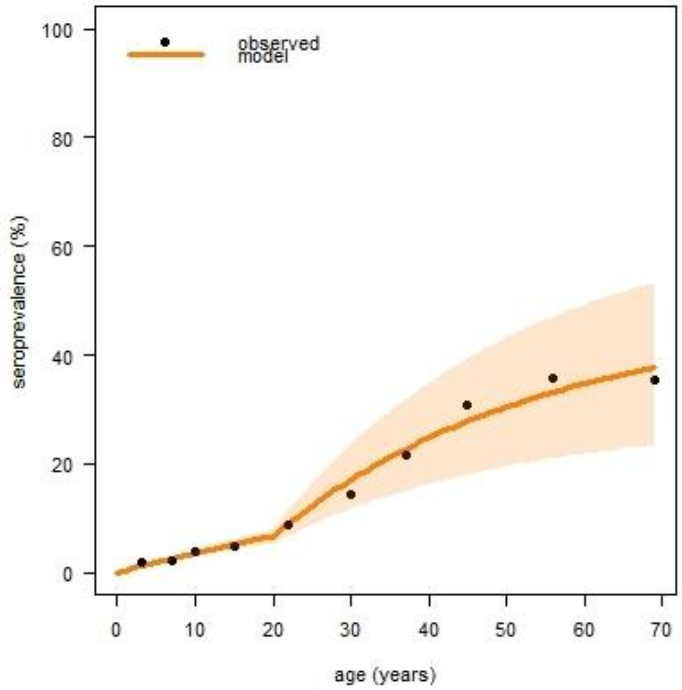
- Development of multiplex platforms
- Relatively low cost
- Operationally feasible

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Historical patterns of transmission

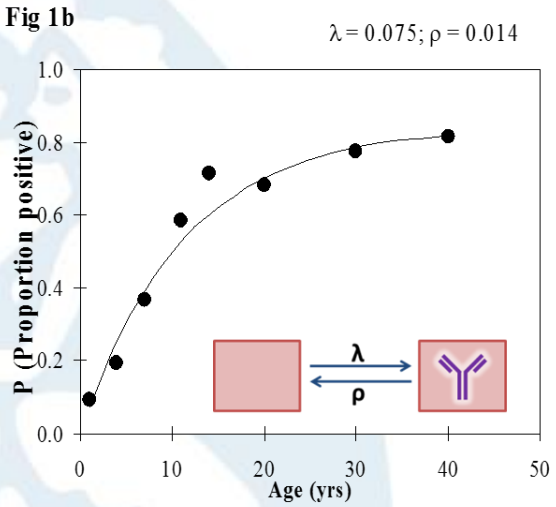
- Duration of antibody response allows estimation of force of infection and historical transmission



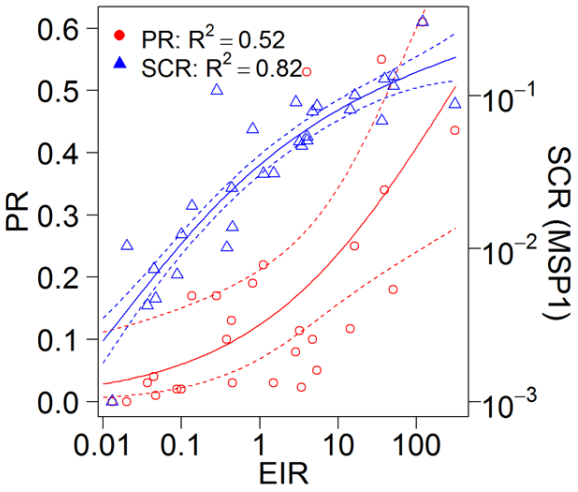


LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

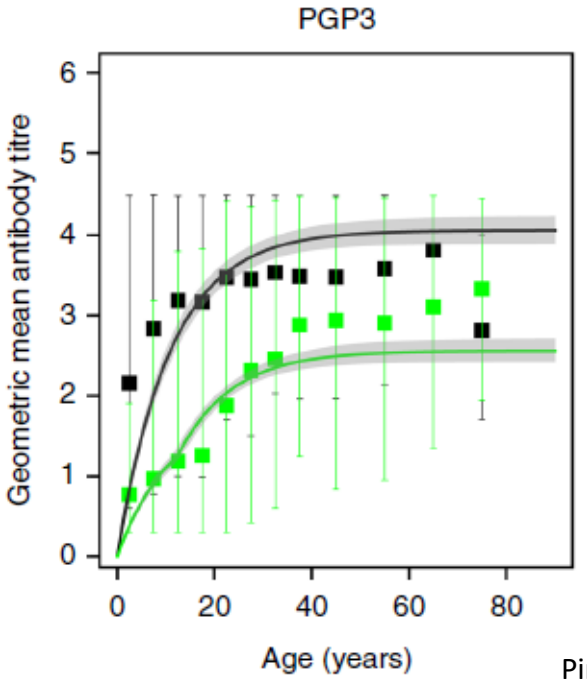
Correlation with other metrics

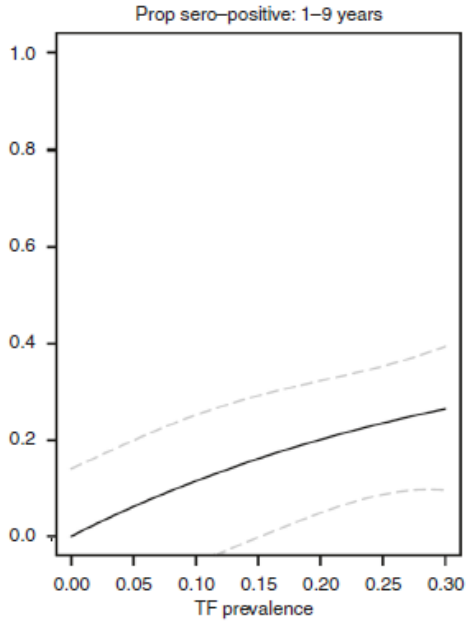


Drakeley et. al



- Seroprevalence and seroconversion rates correlate with other metrics
- Examples from malaria and trachoma





Pinsent et. al, 2018, *Nat Comm*

Spatial patterns of transmission

- Mismatch between temporal and spatial patterns

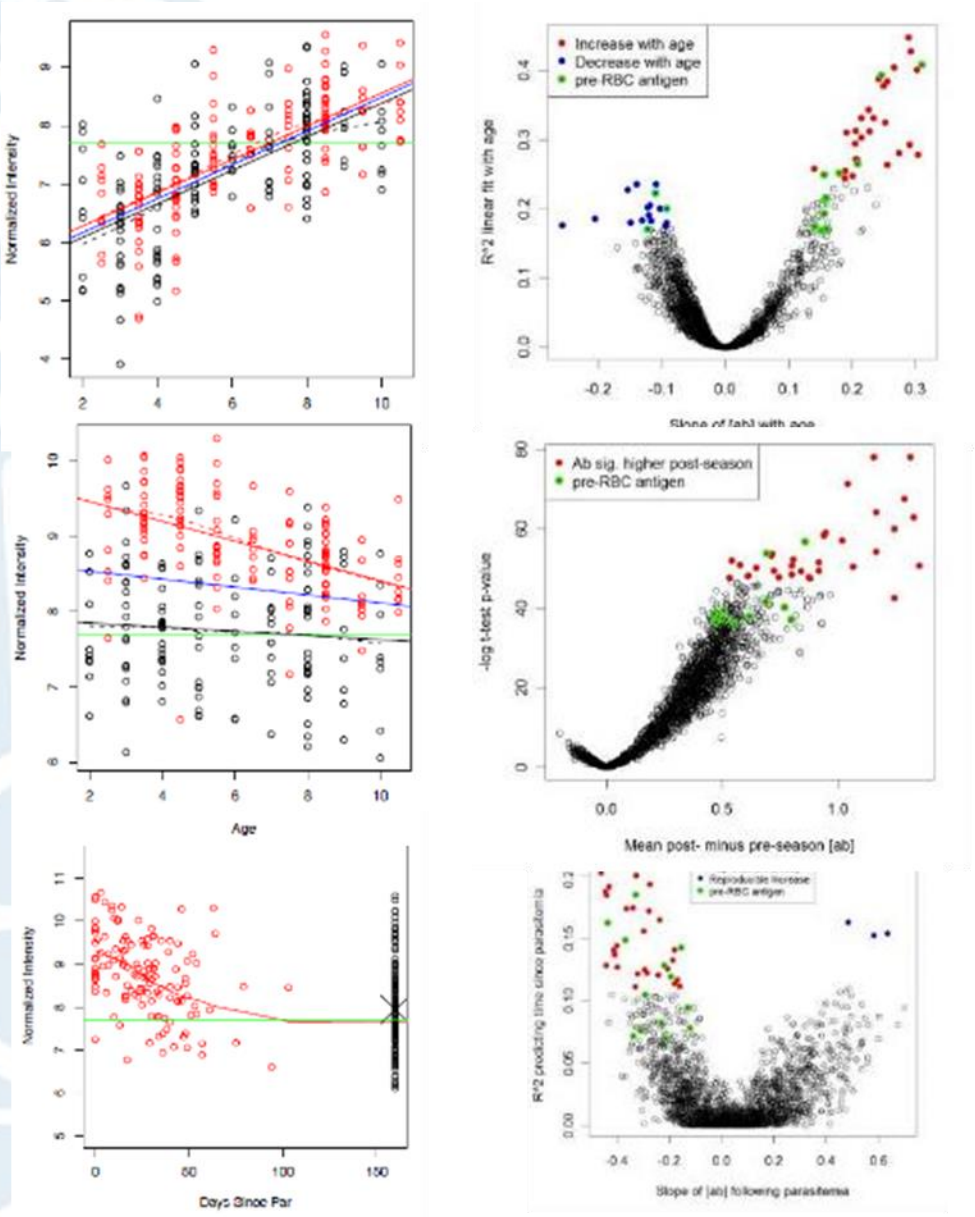
1. Model seroconversion rates or antibody acquisition
   - Requires aggregating data across households – loss of spatial resolution

2. Model recent exposure

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Differences in antibody kinetics

Example from *P. falciparum* – screening 1000+ antigens



Cumulative exposure
Change with age

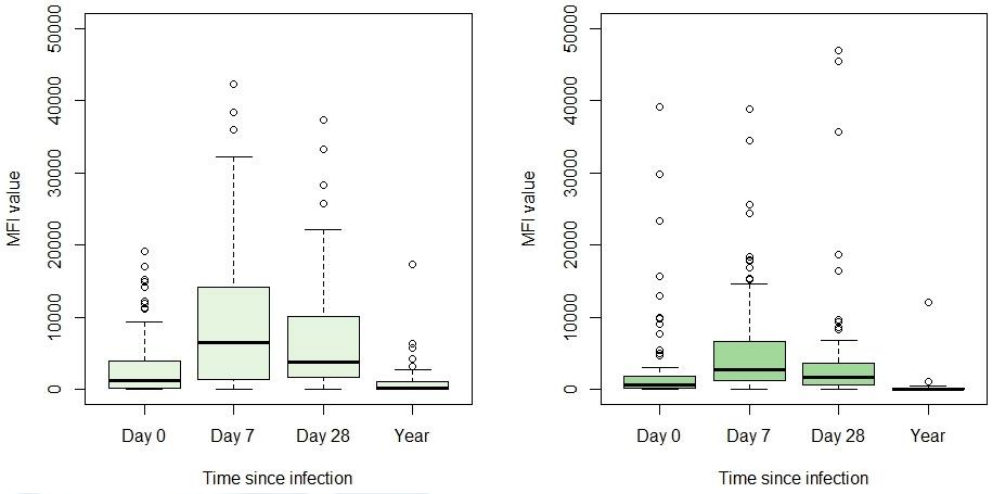
Recent exposure
Mean drop over season

Sero-incidence
Time since parasitaemia

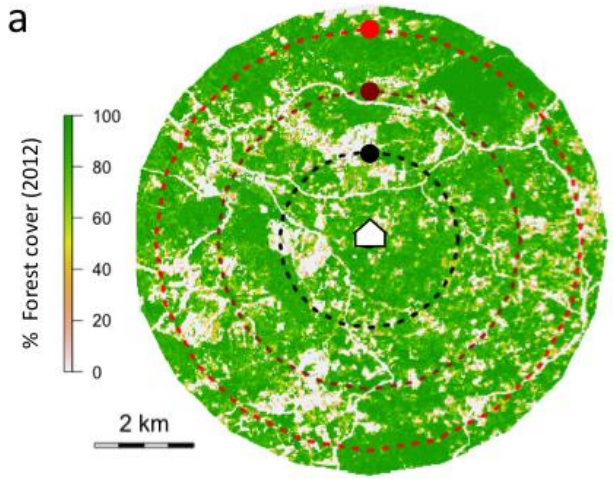
Helb, et al PNAS

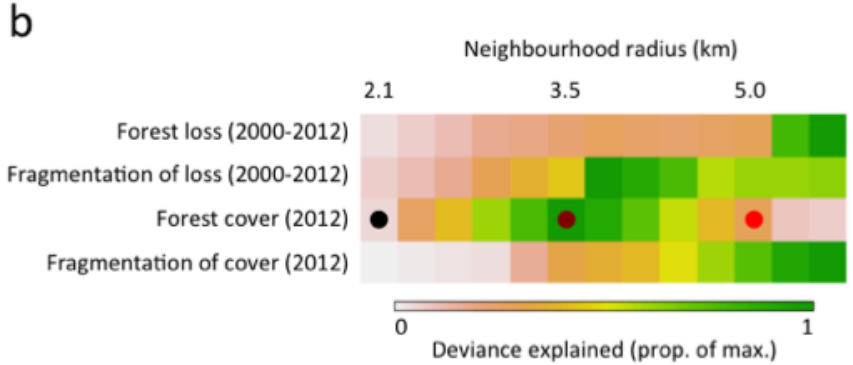
LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Modelling recent exposure to *P. knowlesi*



- Low infection prevalence
- Requires longitudinal data on antibody responses
- Identifying environmental risk factors for the zoonotic malaria *P. knowlesi*

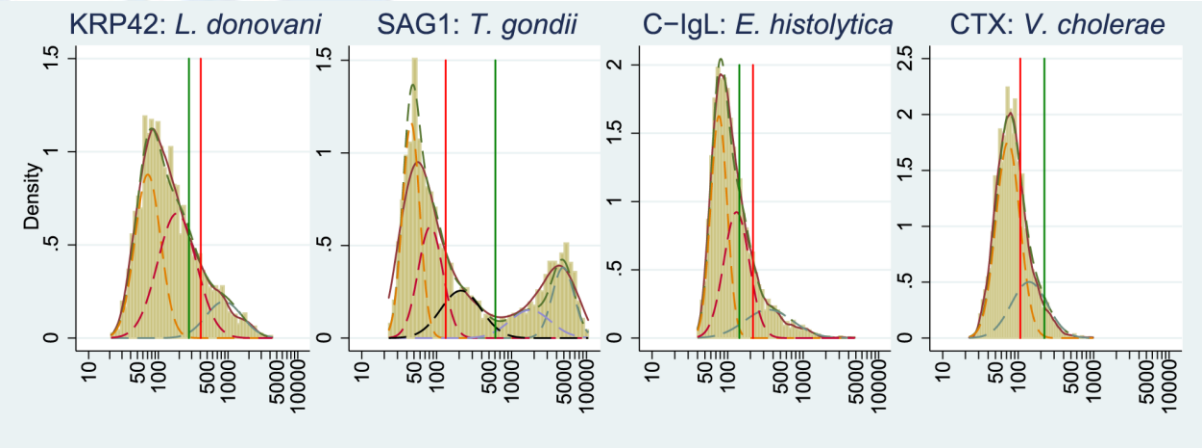




LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Classification methods

- Most NTDs lack longitudinal data
- Common methods – fit mixture models or use known negative population (e.g. UK or US)
- Extend to model recent exposure (high responses)



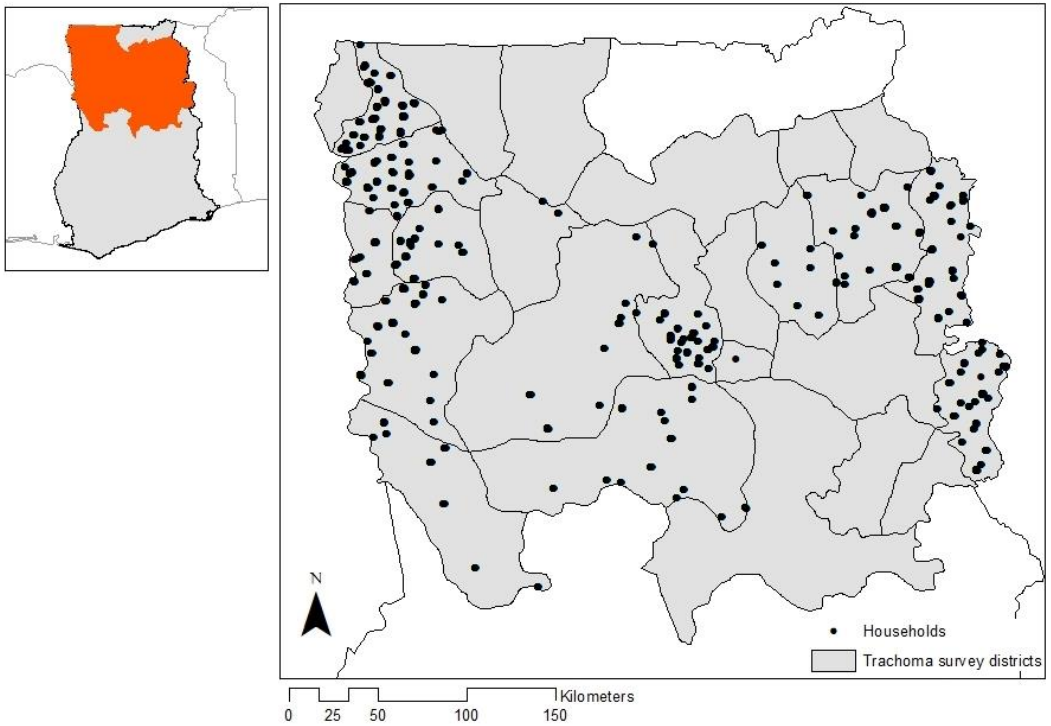
Green represents cutoff for healthy volunteers

Red based on finite mixture models

Fujii et. al, PLoS NTDs

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

NTD Transmission in Northern Ghana



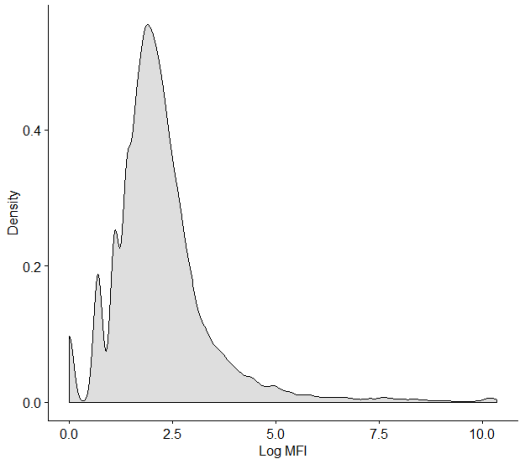
- Randomised cross-sectional survey for trachoma in Ghana
- ~10,000 children ages 1-9
- Very low infection prevalence detected

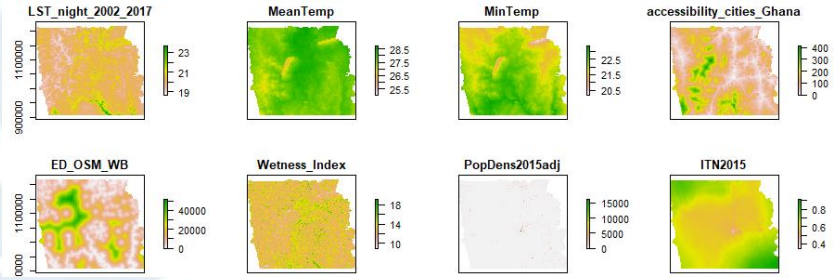
LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Spatial modelling of filariasis in Northern Ghana

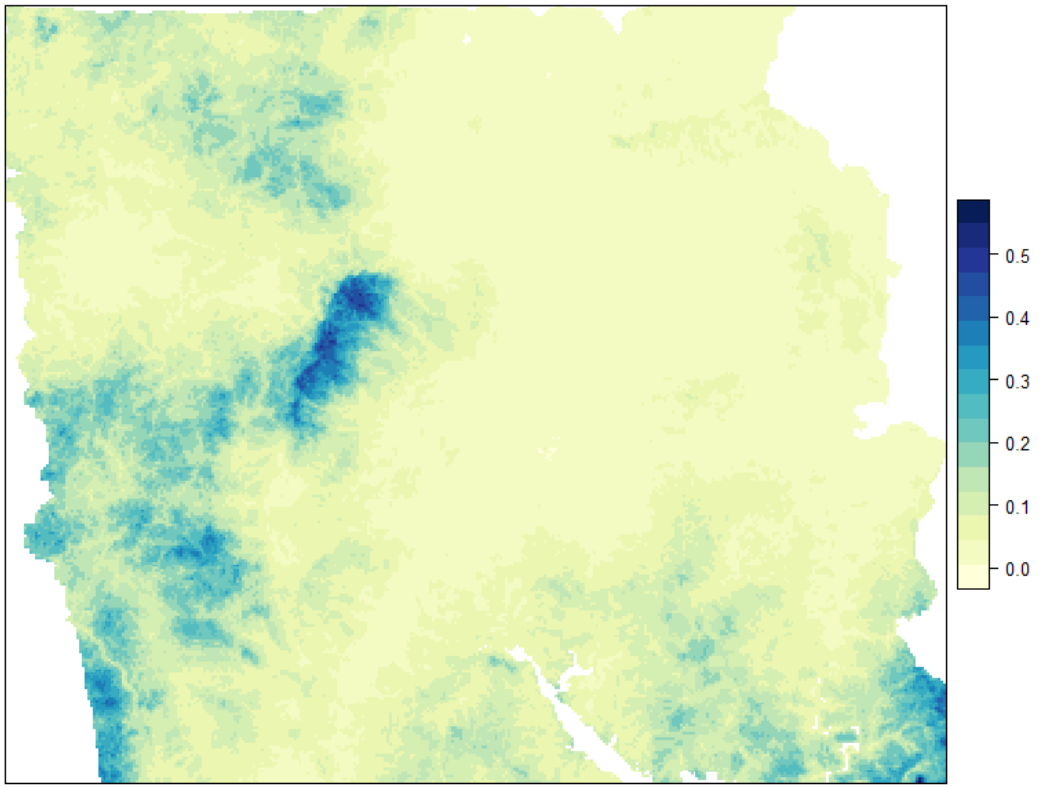
- Estimation of probability of recent exposure to filariasis
- Identification of high risk areas, key environmental risk factors

Density of antibody responses to Lf



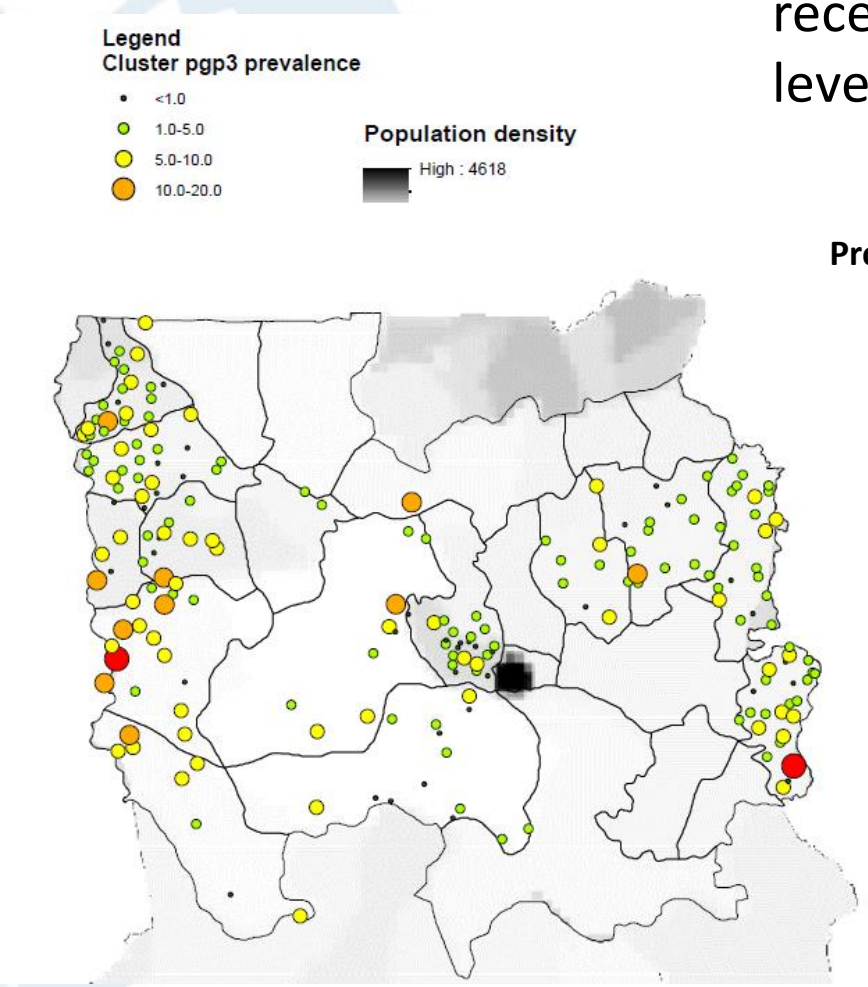


Probability 1 or more individuals in a household recently exposed

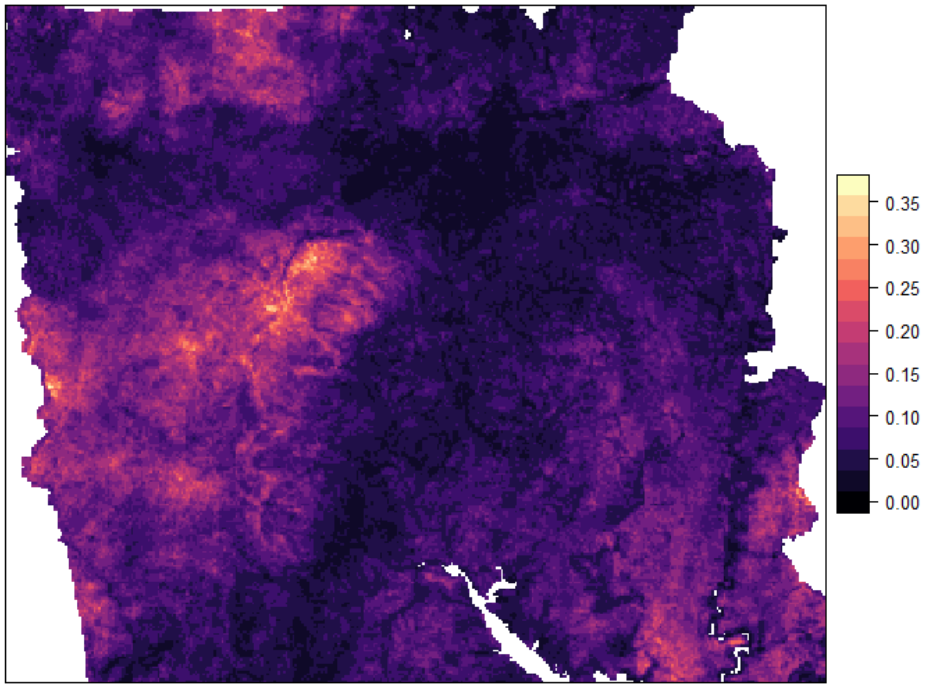


Identifying operationally useful indicators

- Comparison of modelled probability of recent exposure with estimates of cluster level seroprevalence for Trachoma pgp3



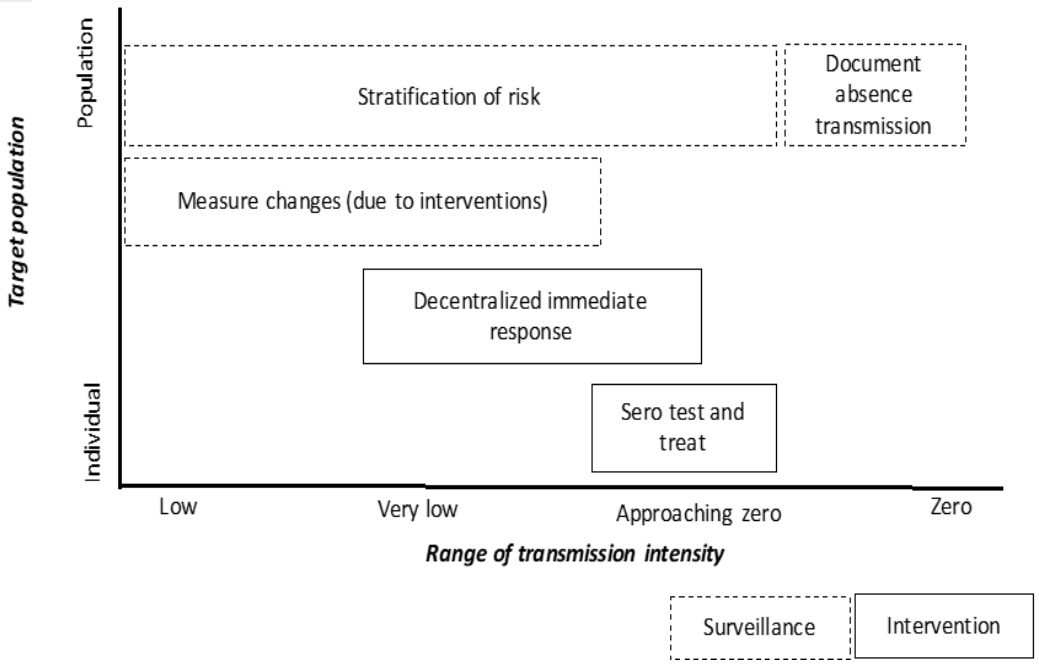
Probability 1 or more individuals in a household recently exposed



Incorporating spatial models of serological data into control and elimination activities

- Purpose of sampling defines types of data needed

- Need for longitudinal data on duration and intensity of antibody responses in different populations and transmission settings



LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Thank you

LSHTM

- Chris Drakeley
- Rachel Pullan
- Kevin Tetteh
- Lou Herman
- Nuno Sepulveda

Sightsavers

- Laura Senyonjo

Universiti Malaysia Sabah

- Tock Hing Chua
- Sylvia Daim
- Redley Yambun
- Dellroy Donny
- Tommy Rowel Abidin
- Lina Marlina

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE