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Simulating the Interruption of Transmission on Bioko Island

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TAG Meeting

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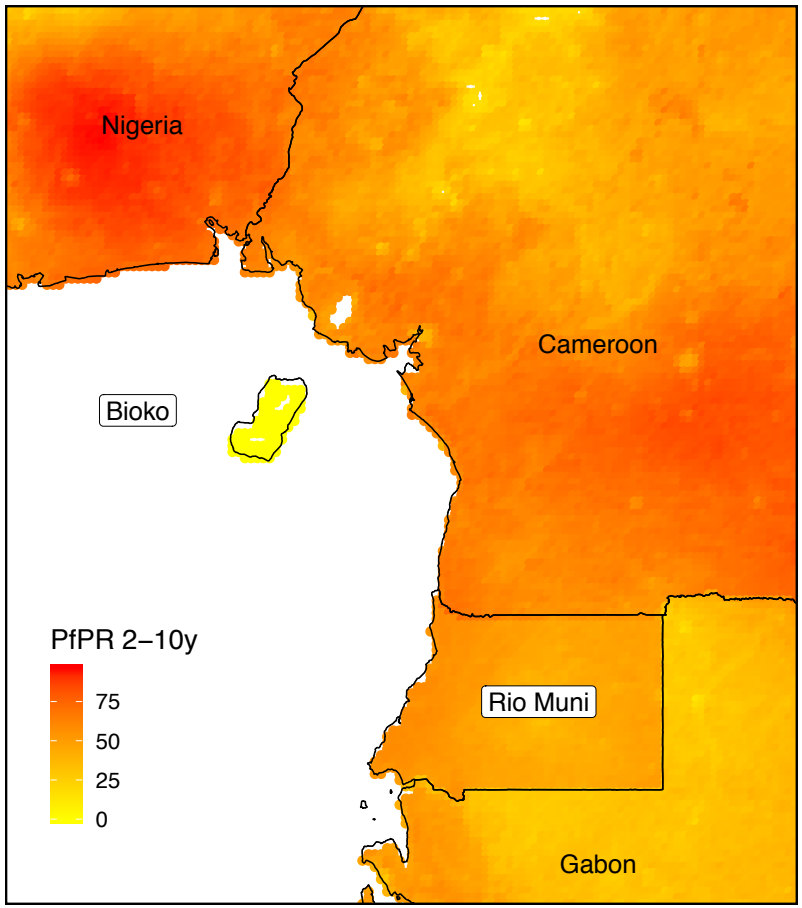
Background – BI Malaria Elimination Program

- From 2004 – Bioko PR ~ 40%
- 15-year heroic intervention program
  - Extensive IRS
  - Extensive LLIN distribution
  - Urban development
- From 2015 – Bioko PR ~ 10%
- Progress has plateaued - why?

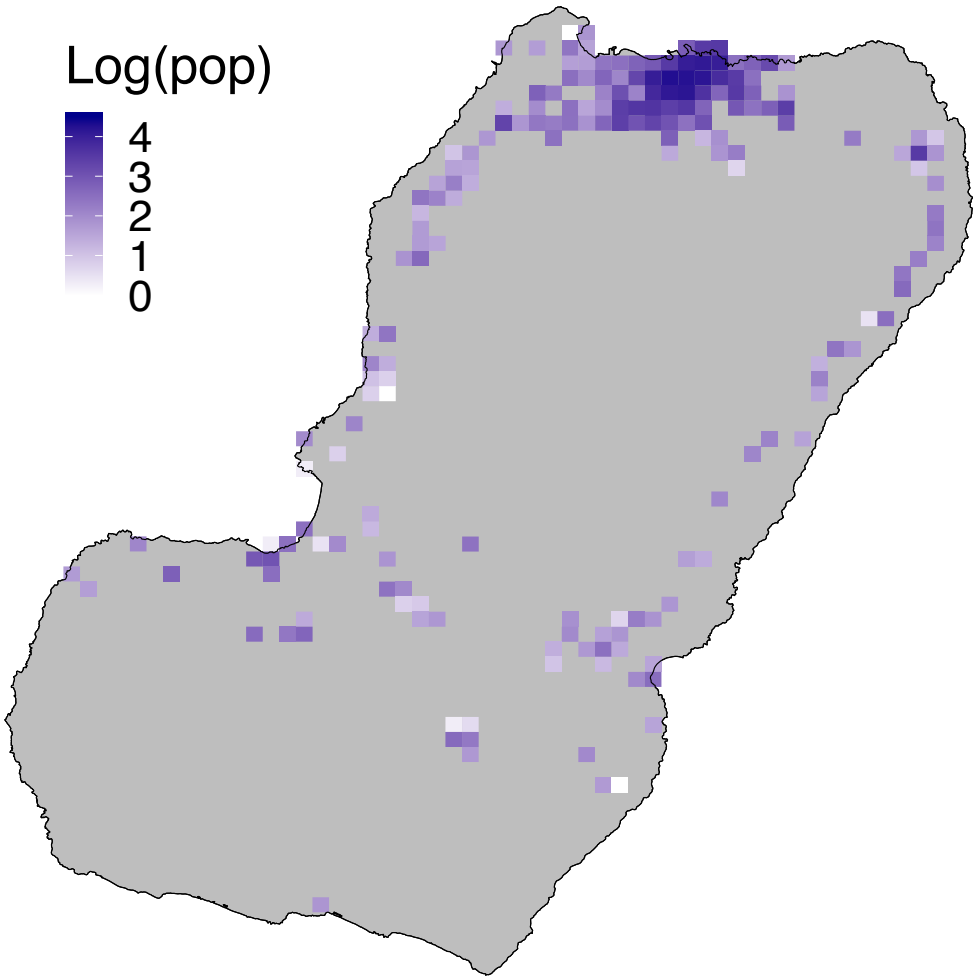


Background - Malaria Indicator Surveys

- 3 years of data: 2015-2017
  - ~15k people surveyed across Bioko
  - Survey period covers 8 weeks (June-August)
  - Prevalence and treatment
    - Number RDT+
    - Number of fevers and symptomatic cases treated
  - Travel history
    - Did you spend one or more nights away from home?
    - Where did you go? (Mainland EG, another location on-island)

Population Distribution

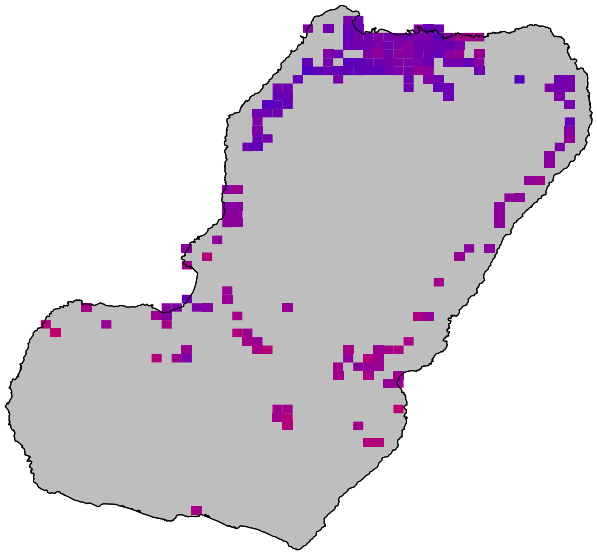
- Malabo (capitol city) in north
  - ~190,000 people
  - Urban, developed
- Volcanoes/reserves in center
- Small communities around rim



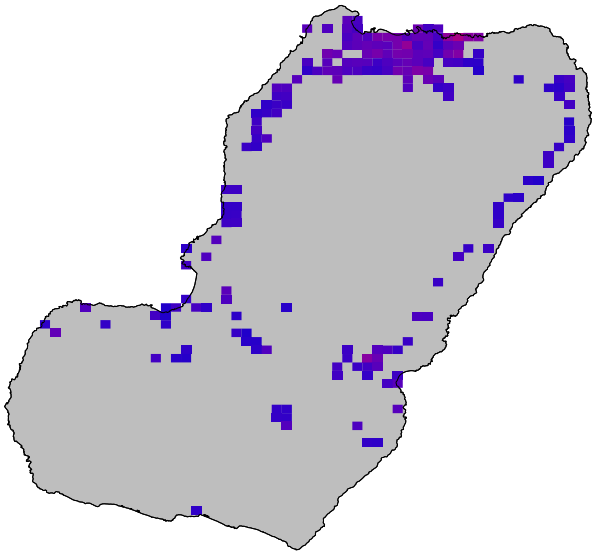
Travel "Prevalence"

- Geospatial modeling estimates of probability of travel
- Off-island travel concentrated in north (urban Malabo)
- On-island travel concentrated in south

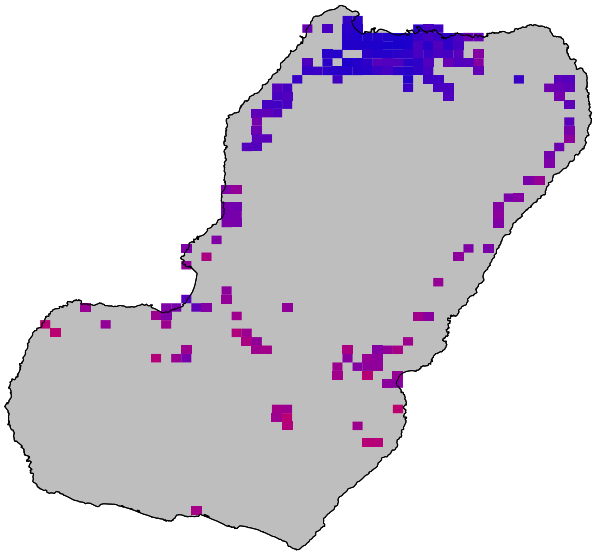
All Travel



Off-Island Only



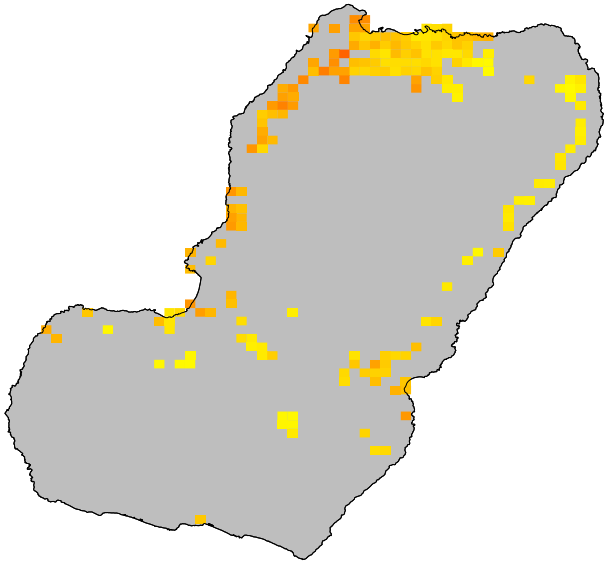
On-Island Only



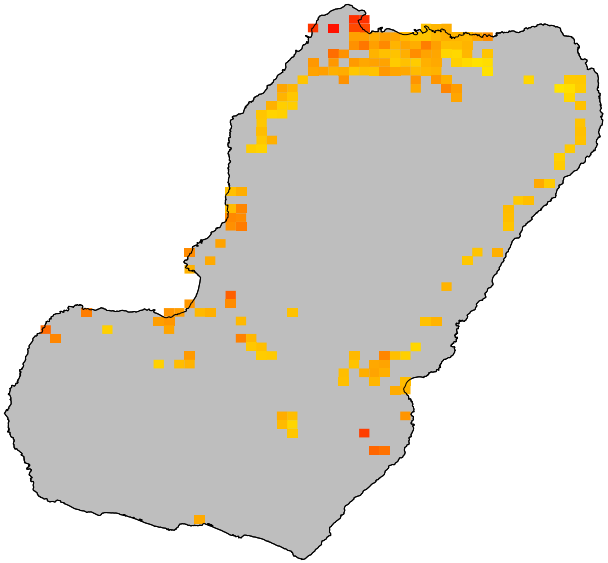
Parasite Rate

- Broken down by travel history
- Off-Island travelers have higher prevalence
- Consistent with other studies of travelers)

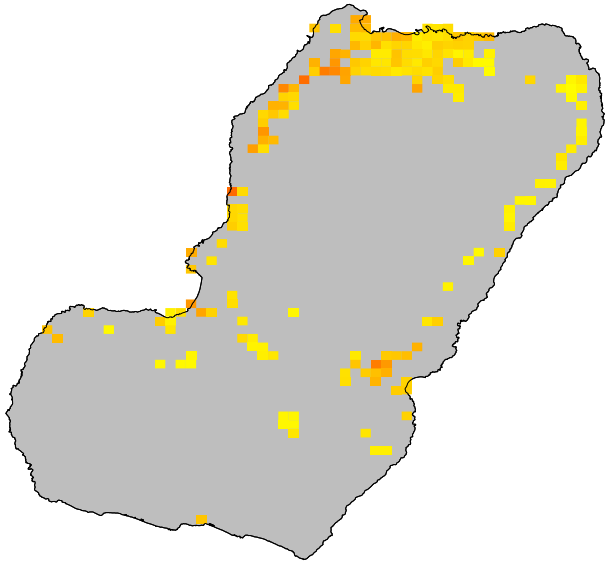
All



Off-Island Travelers

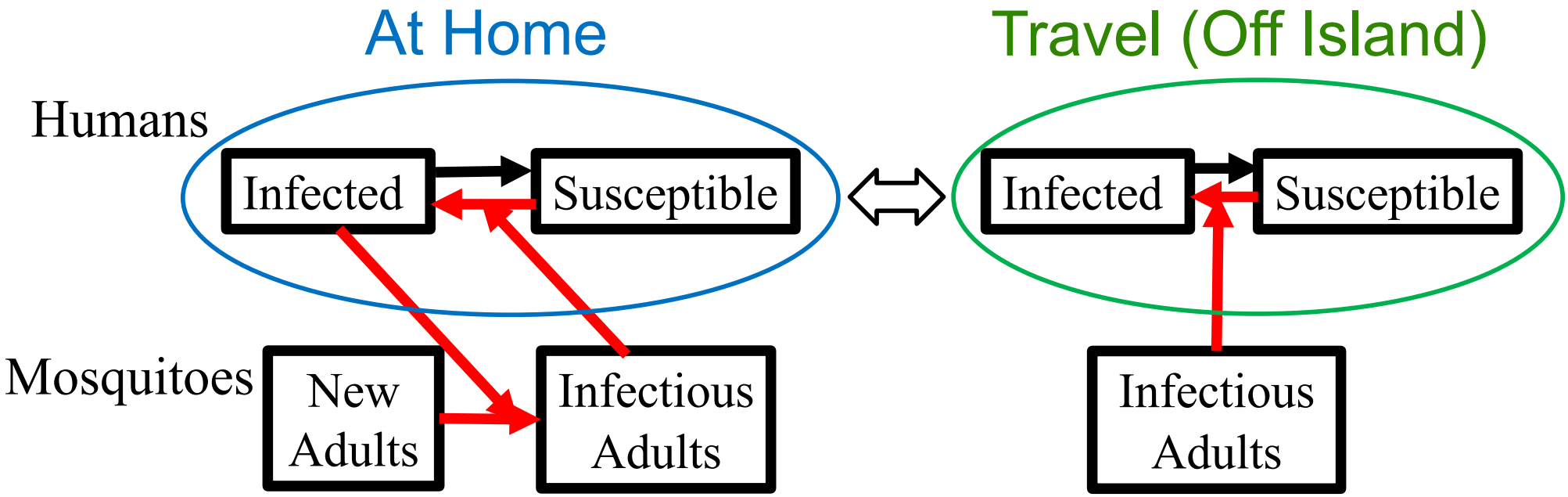


On-Island Travelers



Our Model

- Based on Ross-Macdonald
- Include human travel to other locations, imported infections



Generalized Ross-Macdonald Spatial model

$$\frac{dx}{dt} = h(1-x) - rx$$

$$\frac{d\vec{x}}{dt} = \psi \cdot \vec{h}\,(1-\vec{x}) - r\vec{x}$$

$\vec{x} =$ PR, vectorized across each map area

$\vec{h} =$ FOI

$\psi =$ Time at Risk matrix

$\psi_{i,j} = \mathbb{P}\,(\text{found at } j \mid \text{home at } i)$

Model Calibration – area by area

Calibrate model for each 1km^2 area on Bioko Island

Features		**Data Inputs**
• Population	←	Population Census
• Prevalence	←	Geospatial estimates, PR
• Travel frequency	←	Geospatial estimates, travel
• Local Transmission	←	Geospatial estimates, PR & Travel
• Risk while traveling	←	Bata PR estimate (Ncogo et al. 2015)

Calibrating Time at Risk Matrix

- $\psi_{i,j}$ - Fraction of time spent at *j*, given home is at *i*
- Mover-stayer model
  - Probability of leaving home
    - From travel "prevalence"
  - Choice of destination
    - Have regional destination data
    - Multinomial regression model
- Time spent while traveling
  - Missing from data set
  - Average 3 days for on-island travel
  - Average 10 days for off-island travel

Calibrating to PR

- $\psi_{i,j}$ - For each person living at *i*, distribute FOI according to time spent in different locations
- Allows for risk of infection while traveling
- Assume equilibrium
- Solve for FOI based on mean PR and travel estimates

$$0 = \psi \cdot \vec{h}\,(1 - \vec{x}) - r\vec{x}$$

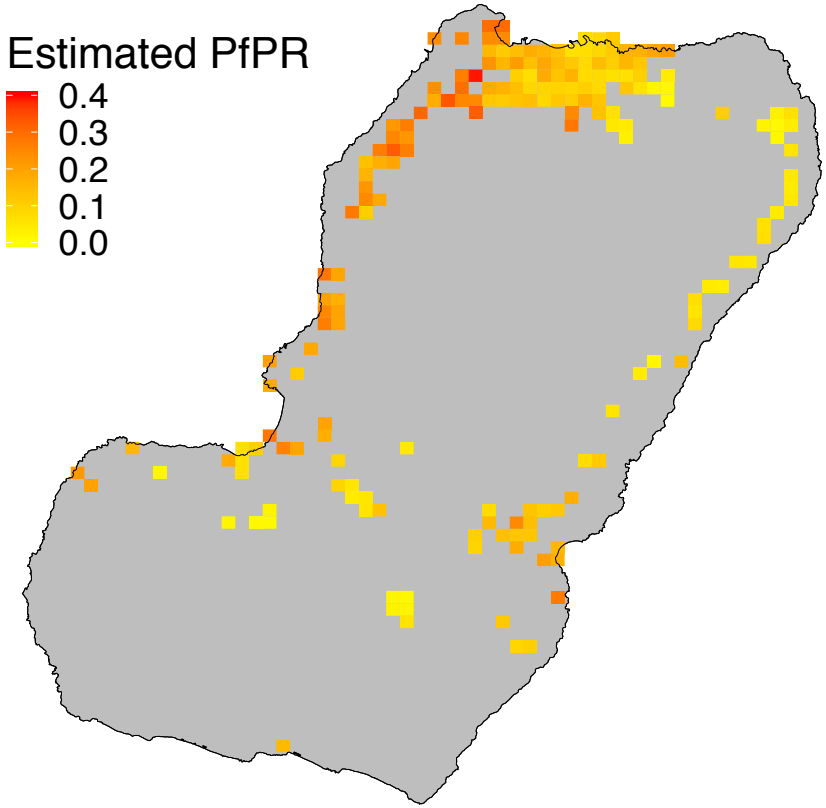
$$\vec{h} = \psi^{-1}\left(\frac{r\vec{x}}{1 - \vec{x}}\right)$$

Our Simulation Model

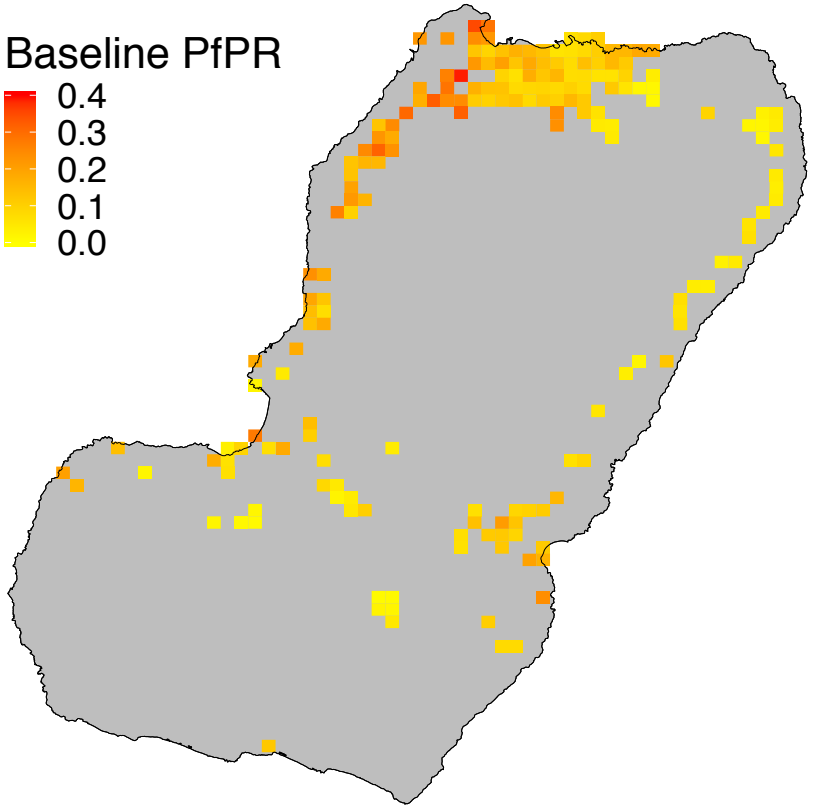
- MASH-MACRO
  - Individual-based Model of individual human movement
  - Calibrate emergence rate of mosquitoes to match FOI
  - Calibrate FOI to match PR estimate
  - Calibrate travel model to match Time at Risk matrix ψ
- Features not present:
  - Detailed care-seeking behavior (lack of subject history in data)
  - Detailed immune model – currently SIS
  - Age and demographics
  - Seasonality – mosquito breeding and travel
  - Poor matching with HLC data

Model Calibration – Matching PR

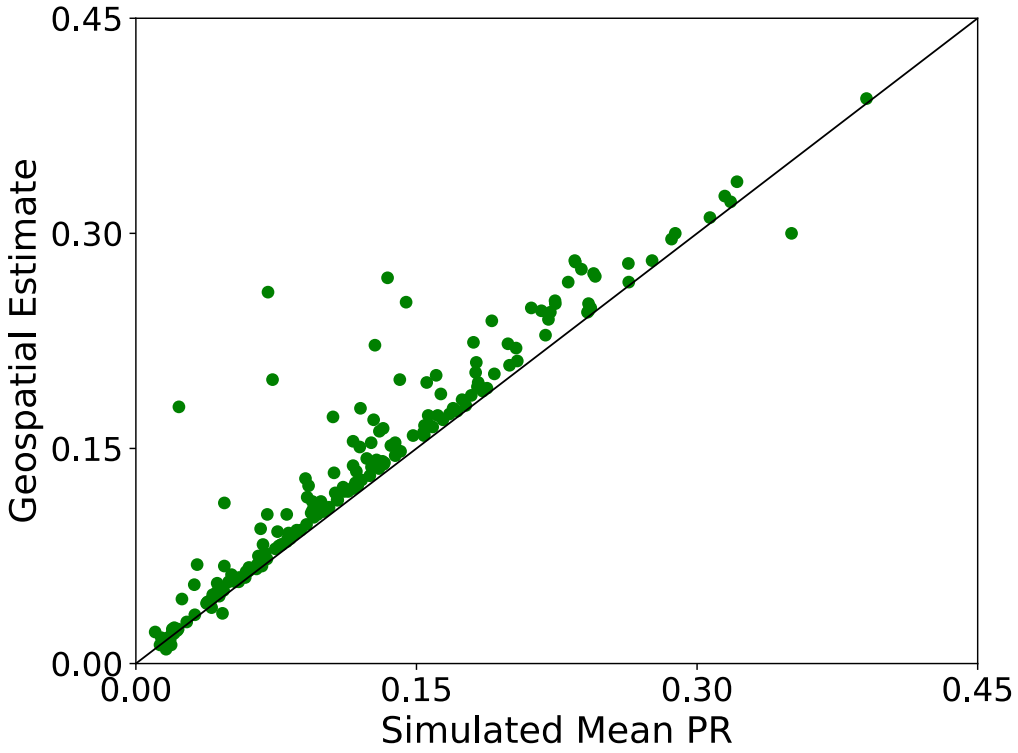
Geospatial Estimate Mean PR



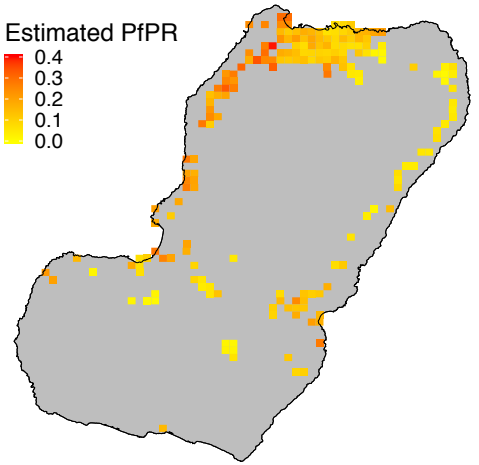
Calibrated Model Mean PR



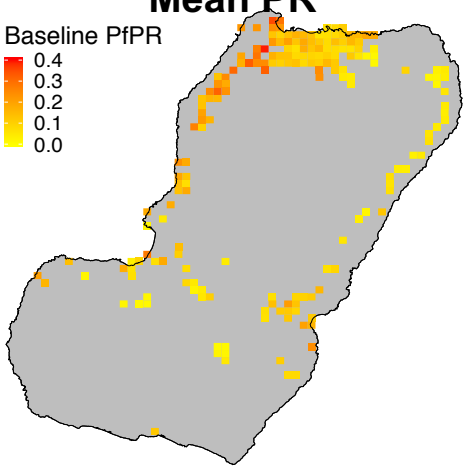
Model Calibration



Geospatial Estimate Mean PR



Calibrated Model Mean PR

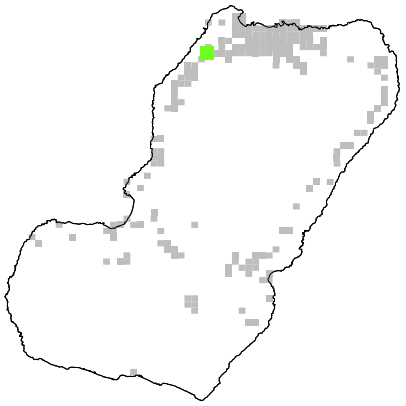


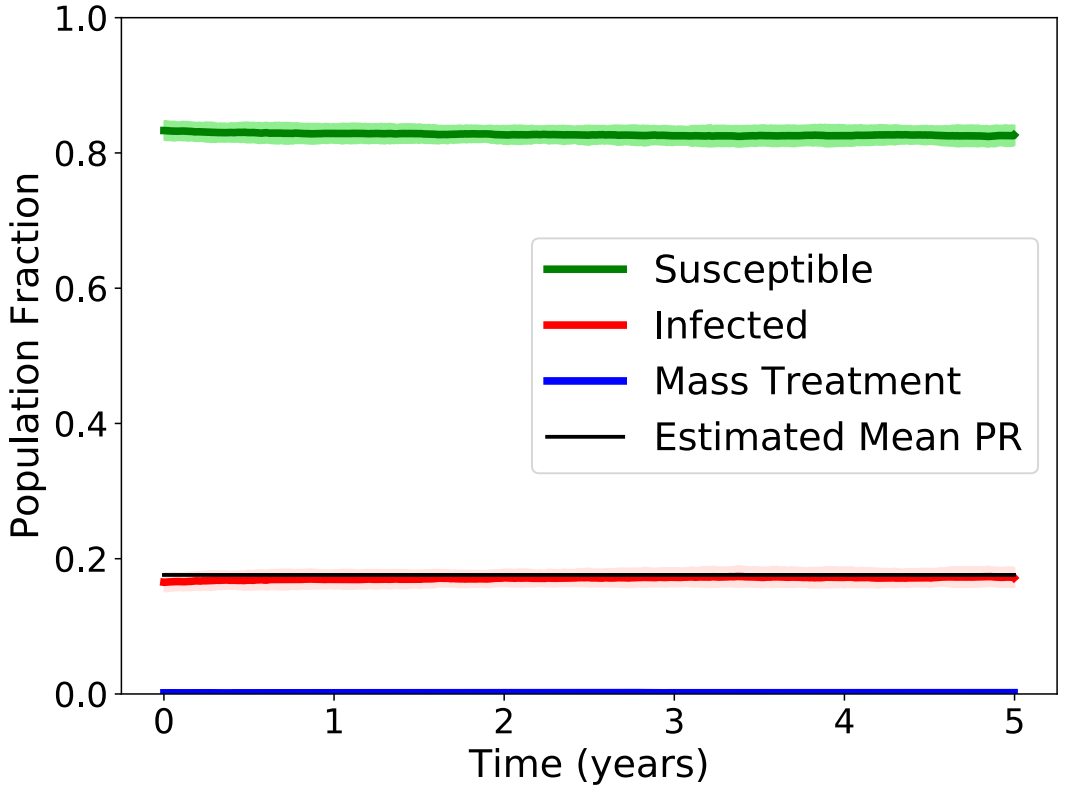
Vaccine Effectiveness

- Sanaria has partnered with BIMEP to implement vaccine
  - Clinical trials on the island
  - 2019 – Phase III trial designed to assess community protection
  - 202? – Step-wedge trial leading to full island coverage
- PfSPZ Vaccine properties
  - Irradiated sporozoite vaccine
  - Pre-erythrocytic - blocks liver stage infections
  - Not a silver bullet – efficacy is partial, temporary
- Will Sanaria's vaccine be sufficient to halt local transmission on Bioko Island?

Simulation results

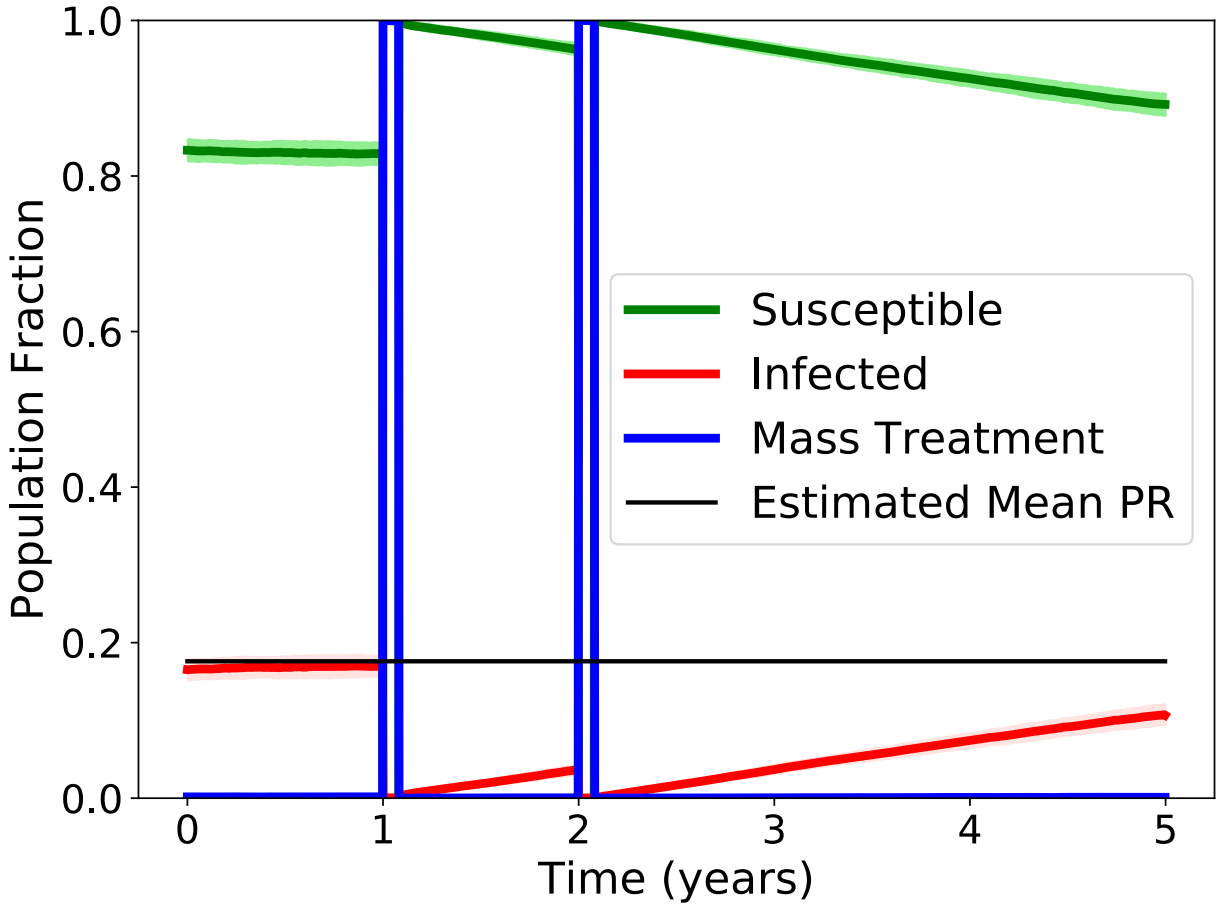
- Example: Basupu – 2028 people, PR = .18
- Baseline case with no interventions
- Ensemble of 100, plotting mean behavior





Adding Mass Treatment

- Mass treatment scheduled at start of years 2 and 3
- Clears infections, prevents new infections, lasts 30 days

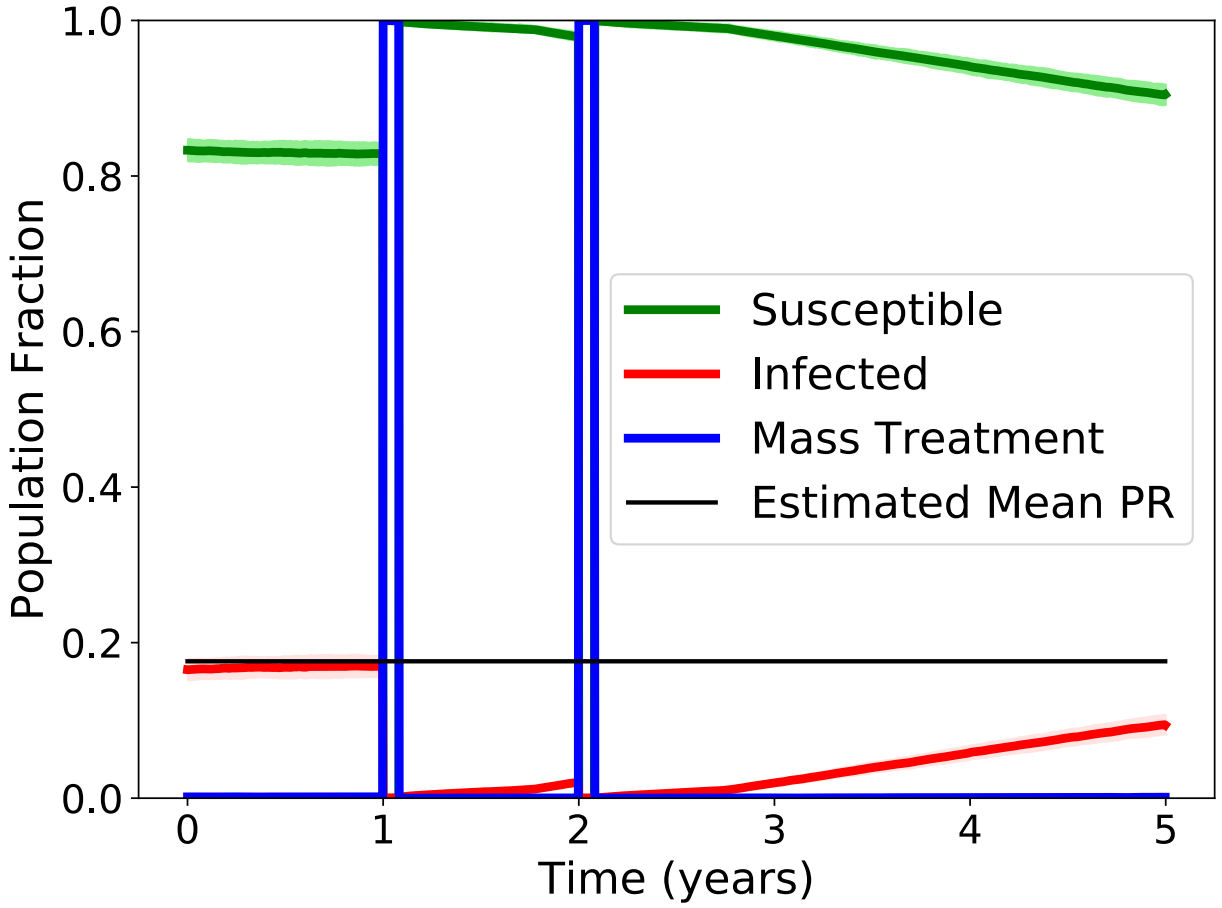


Simulated PfSPZ Vaccine

- Schedule
  - Vaccinate at years 2 and 3
  - Accompany with mass treatment
- Assumptions
  - Vaccine remains effective for 9 months
  - 100% coverage – all people vaccinated
  - 50% of recipients granted 100% personal protective efficacy

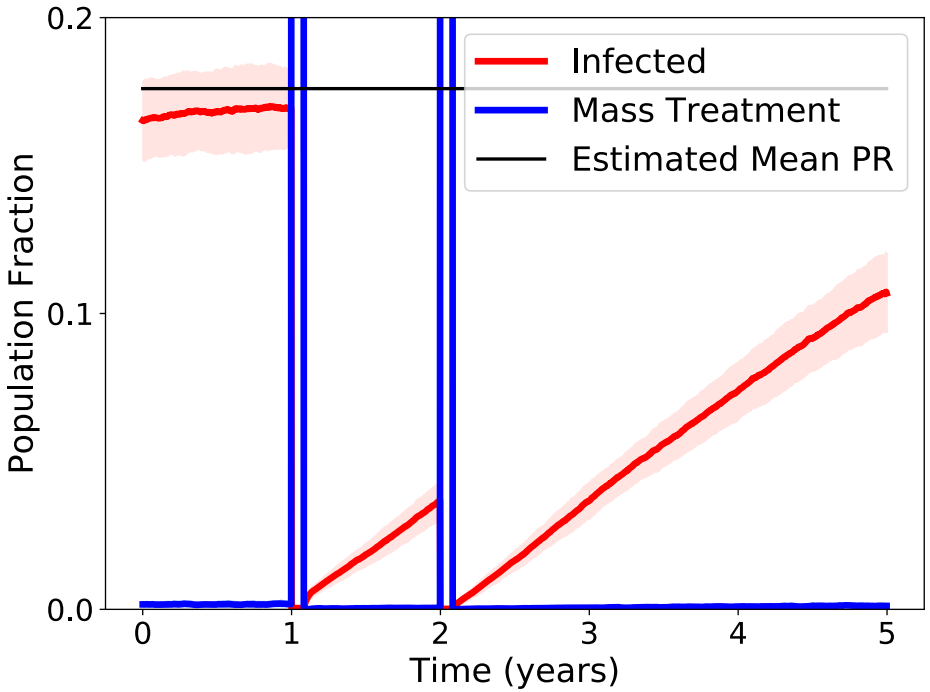
Adding Vaccination

- 50% of recipients granted 100% personal protective efficacy

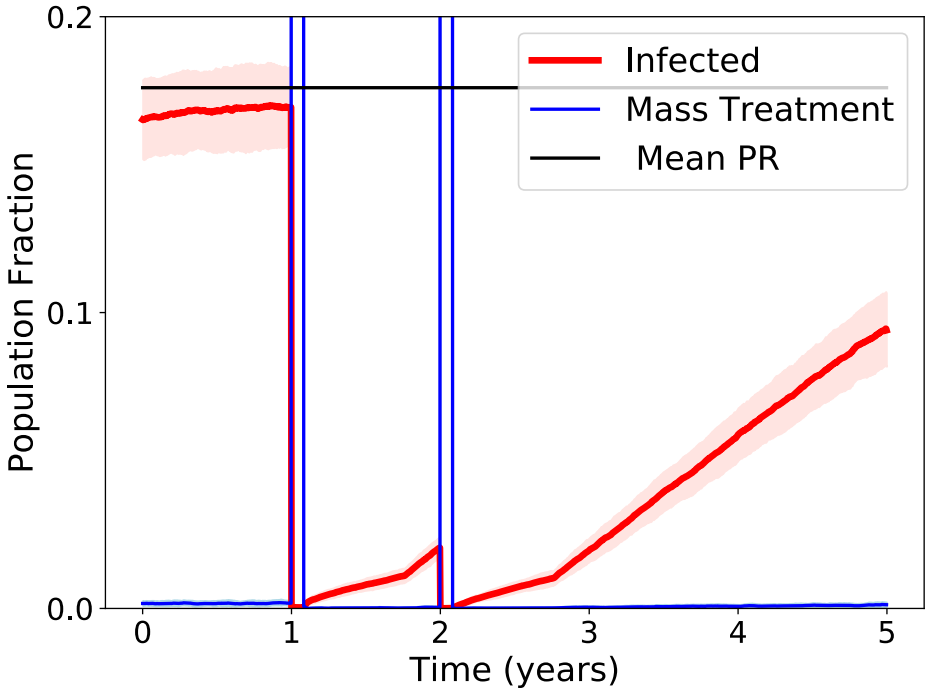


Adding Vaccination

Mass Treatment Only

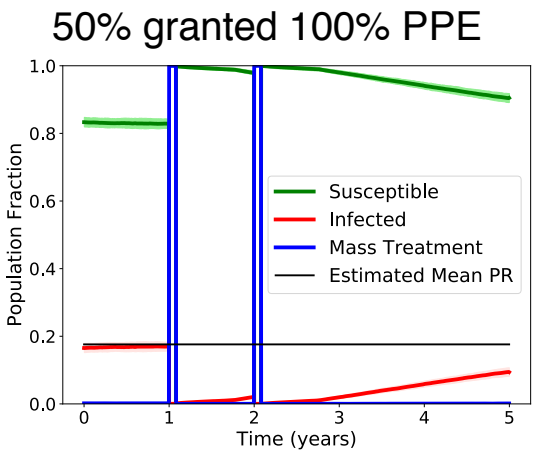


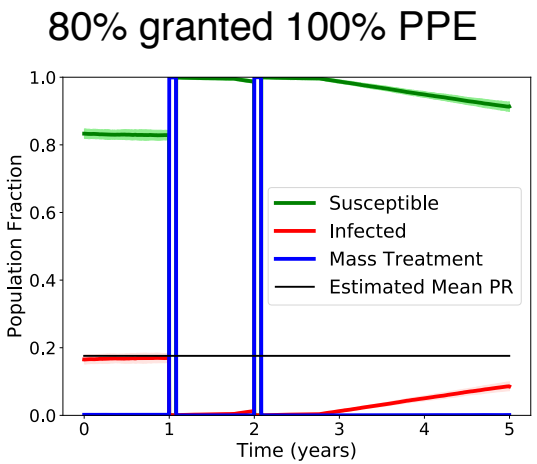
Adding Vaccination

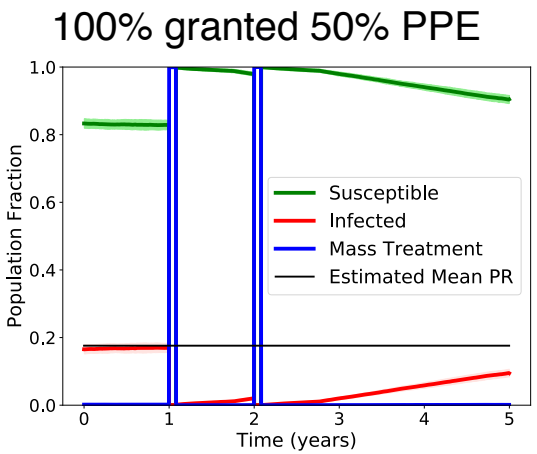


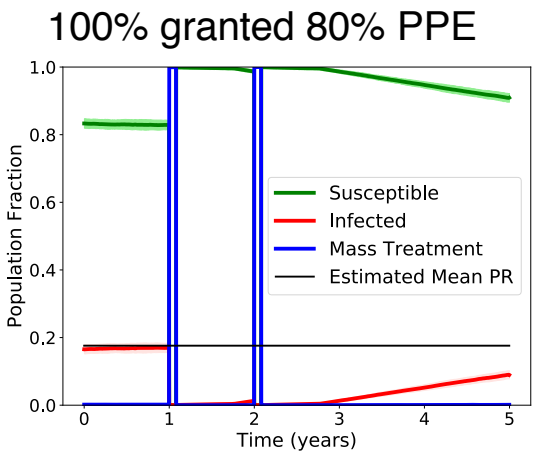
- Improvement – slows down rate of new cases
- Not a permanent fix

Results Robust to Varying Vaccine Efficacy







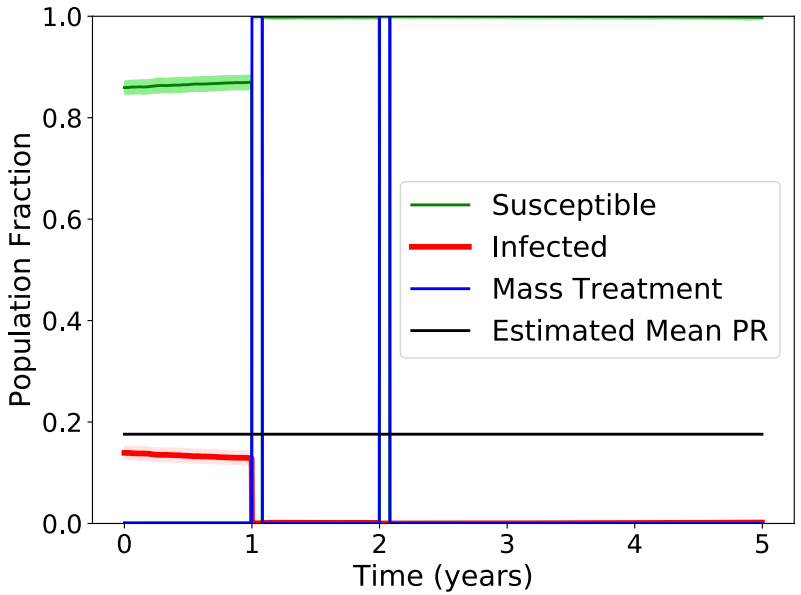


- Temporary protection limits long-term efficacy
- Reintroduction through importation occurs in all cases

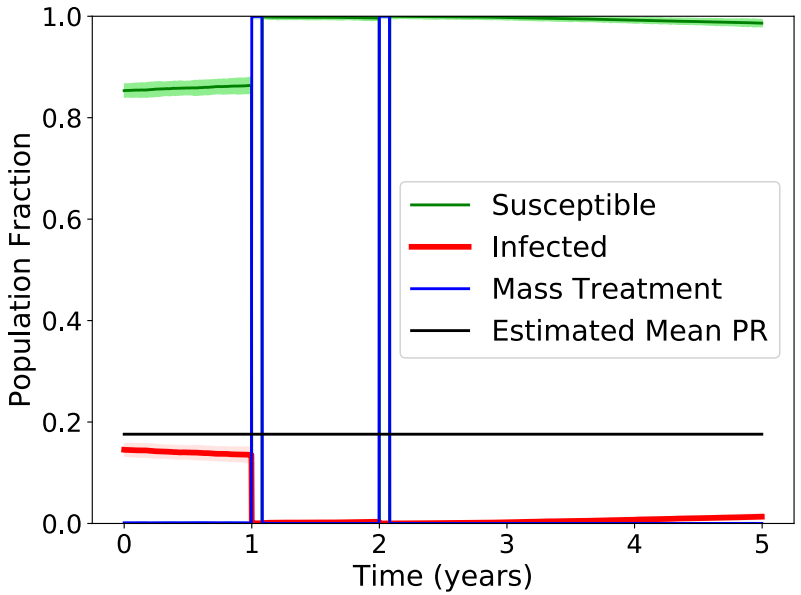
Reducing Imported Cases

- Reduce number of imported infections
- Following vaccination, importations drive return of PR

100% Reduction



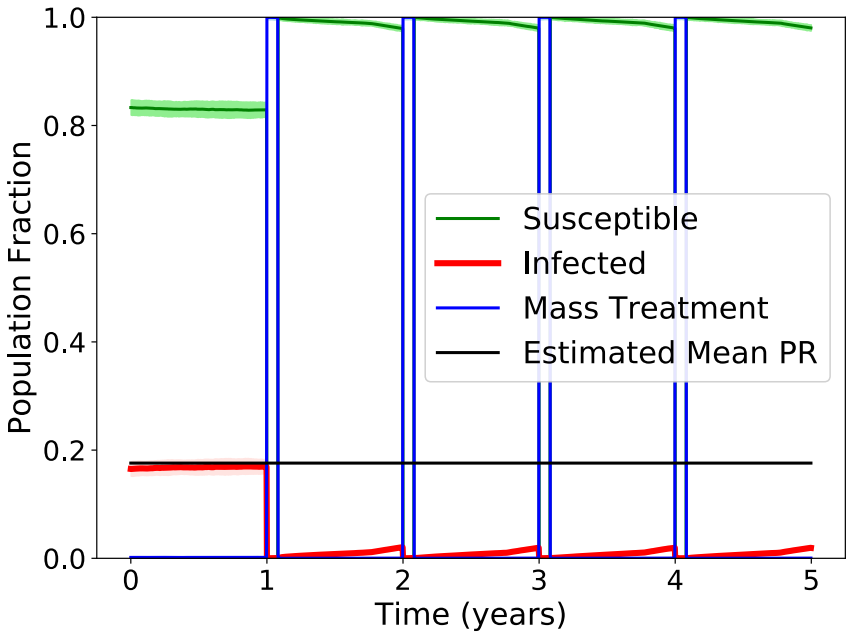
90% Reduction



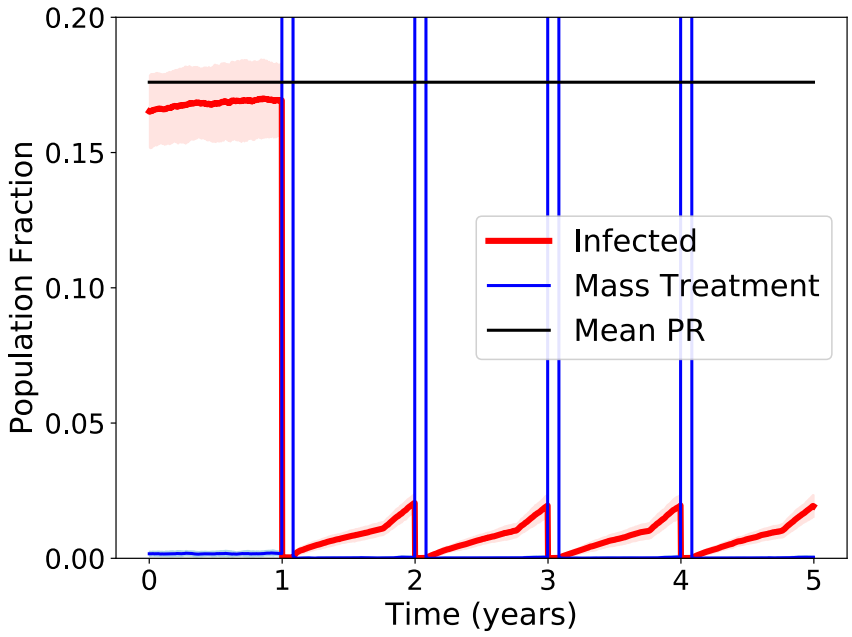
Annual Distribution of Vaccine

- Vaccine slows rate of new cases in short term
- Possible that periodic re-distribution could contribute to sustaining reduced prevalence

Full Time Series



Close-up Detail

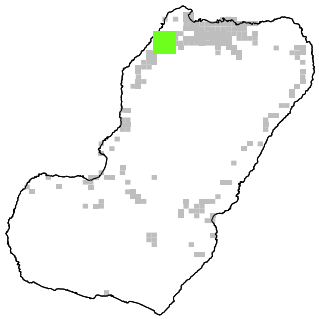


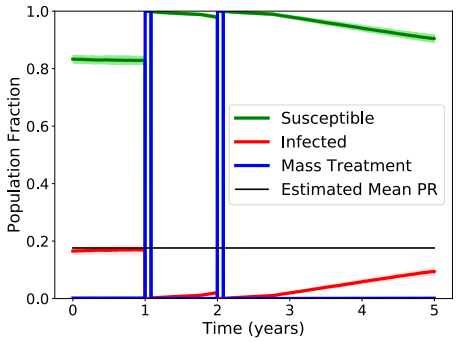
Conclusion

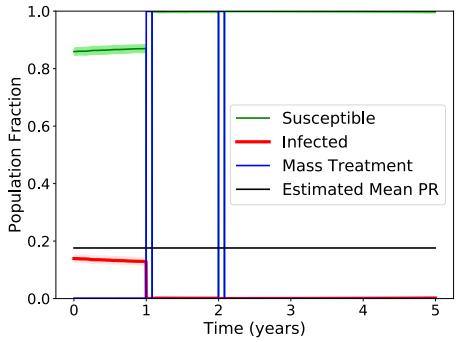
- Is the PfSPZ Vaccine sufficient to interrupt local transmission?
- Our results:
  - Vaccine slows but does not stop transmission over long-term
  - Volume of imported cases appears to be too high
  - Reducing importations, or frequently re-distributing vaccine may hold transmission near zero

Results Robust Across Different Areas

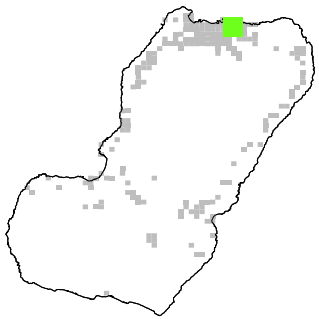
Basupu

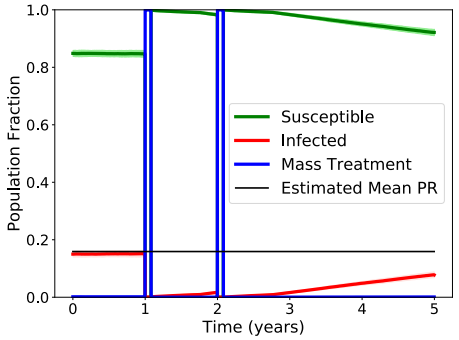


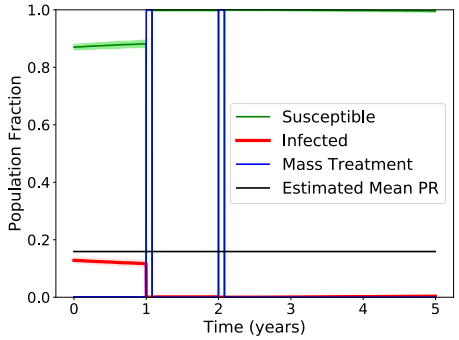




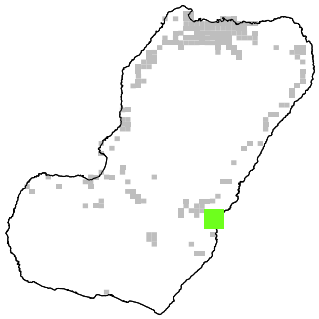
Malabo

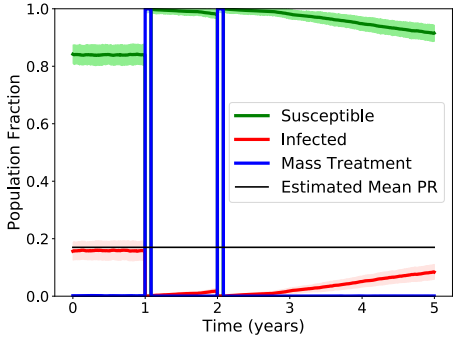


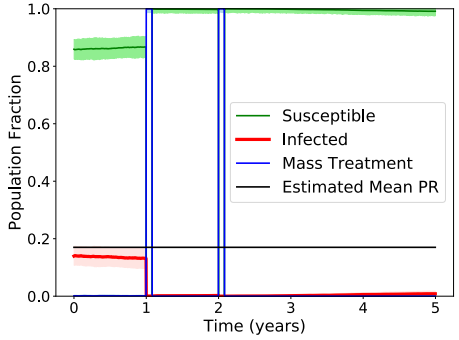




Riaba







Mosquito Density

- Mosquitoes/Human, calibrated to PR using Ross-Macdonald
- Accounts for PR attributable to importations
  - Lower: East, Malabo, Moka
  - Higher: Northwest