Agent-Based Modeling for Malaria Policy:
Applications, Challenges, and Lessons Learned

Daniel T. Citron, PhD

Malaria Elimination Team, IHME

Presentation Outline

- Malaria Basics

- Describe agent-based modeling application
  - Bioko Island Malaria Elimination Program
  - Analytical methodology
  - How we build our models

- Four lessons learned about the challenges presented when trying to use agent-based models to make robust policy recommendations
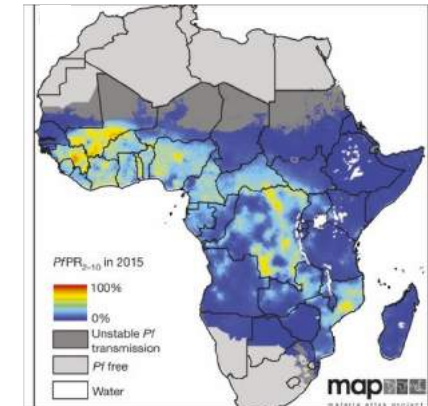
Malaria

- Vector borne parasitic disease
- Transmitted by *Anopheles* mosquitoes
- Tropical climates
- Disease burden
  - Estimated 200 million cases per year
  - Estimated 400,000 deaths per year
  - Disproportionately affecting children
  - Concentrated in sub-Saharan Africa

Parasite Life Cycle
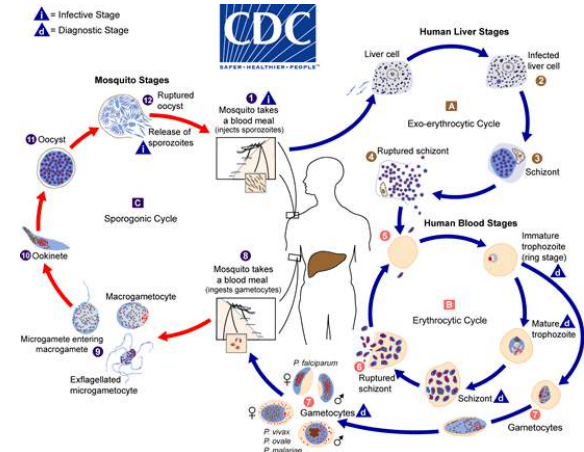
Parasite Distribution, Africa 2015

Heterogeneous Aspects of Malaria

- Malaria dynamics – nonlinear, multicomponent, heterogeneous
- Two examples:
  - Transmission is heavily dependent on mosquito ecology
    - Local mosquito habitats and mosquito activity
    - Seasonal changes to temperature and rainfall
    - Vector control – nets and insecticides
  - Human exposure risk and immunity
    - Immune response and symptoms sensitive to lifetime exposure history
    - Regular and irregular travel to high- or low-risk areas
    - Treatment seeking behavior in response to symptoms

# Agent-Based Models (ABMs) for Malaria

- Possible to write-down simpler mechanistic models
  - Family of Ross-Macdonald compartmental models
  - Difficult to account for heterogeneities
  - Fails to account for heterogeneous exposure
  - Fails to account for immune response variability
- ABMs can capture the many heterogeneities inherent to malaria transmission in ways that other modeling tools cannot
- ABMs are one of the best tools for exploring complicated data sets, and understanding which aspects of the data are most important

Challenges Posed by ABMs for Policy Analysis

- Robust policy recommendations require characterization of uncertainty
  - Uncertainty reflected in underlying data
  - Uncertainly inherent in choice of mechanistic model
- Made more difficult when using ABMs
  - Extensive and detailed data sets required
  - Enormous parameter space makes it difficult to calibrate
  - Vast set of possible models of individual behavior to choose from
- ABMs can be unwieldy to set up, use, and interpret

An Application: Bioko Island

- Island Population: ~250,000
- Malabo Population: ~190,000

Bioko Island Census Map

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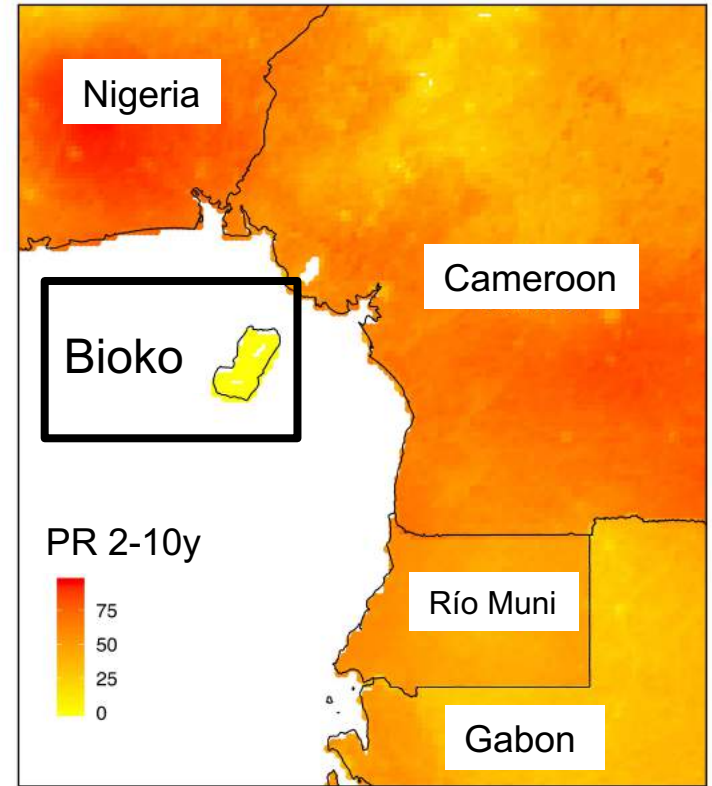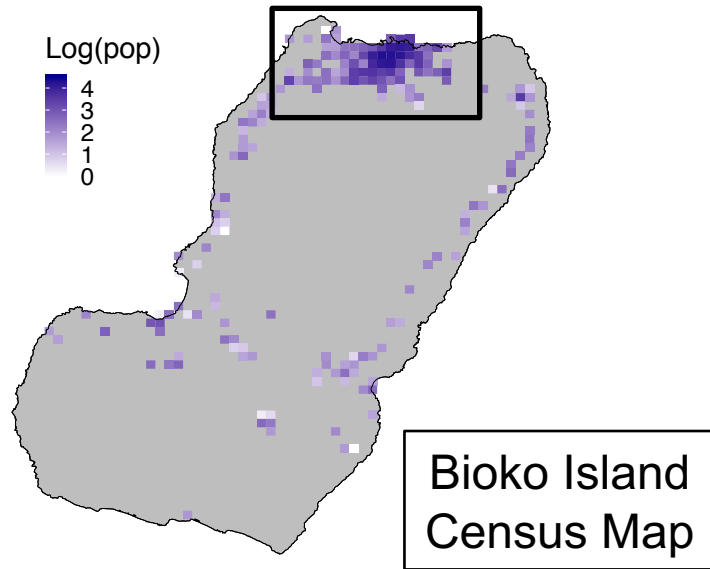
Bioko Island Epidemiological History

- PR = Parasite Rate, a measure of prevalence
- High risk region
- 2004 – Bioko PR ~ 40%
- 15-year control program, including:
  - Extensive surveillance
  - Extensive vector control
  - Freely available treatment
  - Capacity building
- Since 2015 – Bioko PR ~ 10%

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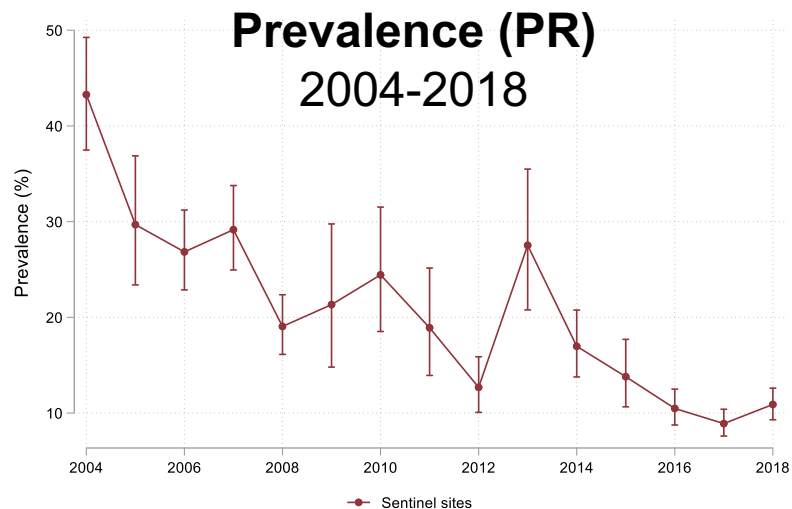Institute for Health Metrics and Evaluation
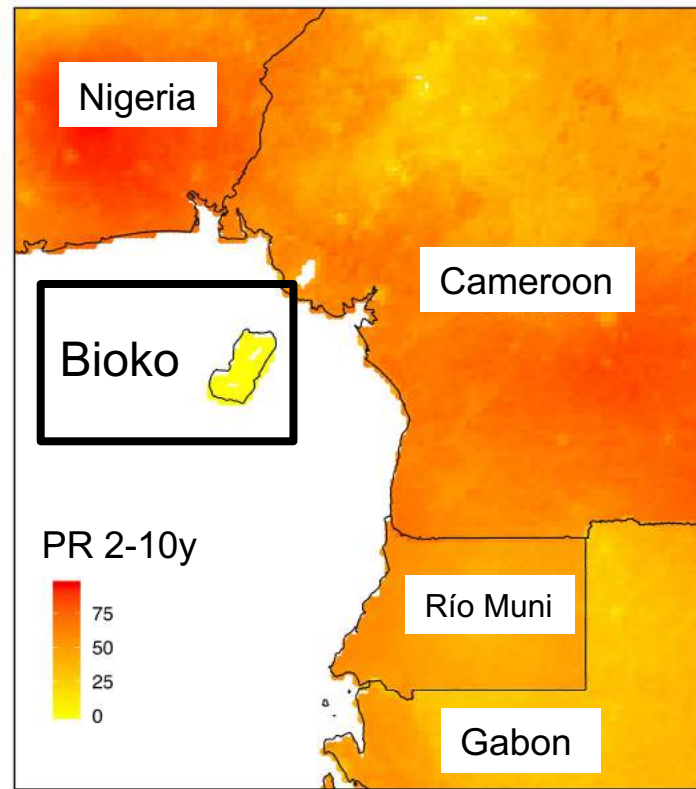
Bioko Island Malaria Elimination Program

- Program managed by MCDI

- Collect data in Malaria Indicator Survey:
  - Annual survey of ~15,000 residents
  - Parasite Rate
  - Treatment seeking and case history
  - Travel history

- Close collaboration was crucial for understanding transmission environment

Bioko Island: Key Questions

- No improvements to PR since 2015
- Why has progress stalled in recent years?
- What is role of off-island transmission?
- Will adding a vaccine to the current intervention package result in halting transmission on Bioko Island?

Prevalence (PR)
2004-2018

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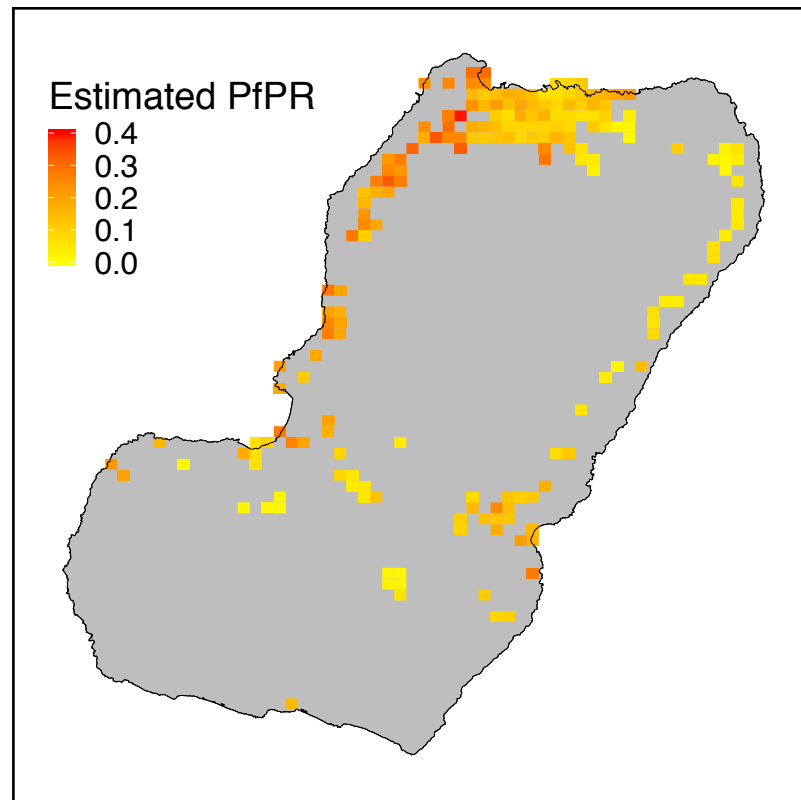
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Modeling Methodology

- Create geostatistical map of estimated PR

- Calibrate all mechanistic models to match PR in each map-area

- Analysis
  - Quantify influence of cases acquired off-island with simple dynamical model
  - Simulate vaccination deployment scenarios with ABM

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Mapping Malaria Prevalence

- Geostatistical prevalence mapping
  - Census
  - Survey data
  - Environmental covariates
- Estimate prevalence in each map-area
  - Captures km^2-scale variability in PR
  - Highest PR along northwest coast
  - ~10-14% in Malabo

Estimated PfPR
0.4
0.3
0.2
0.1
0.0

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Prevalence Conditioned on Travel History

- Map PR, this time conditioning on recent travel
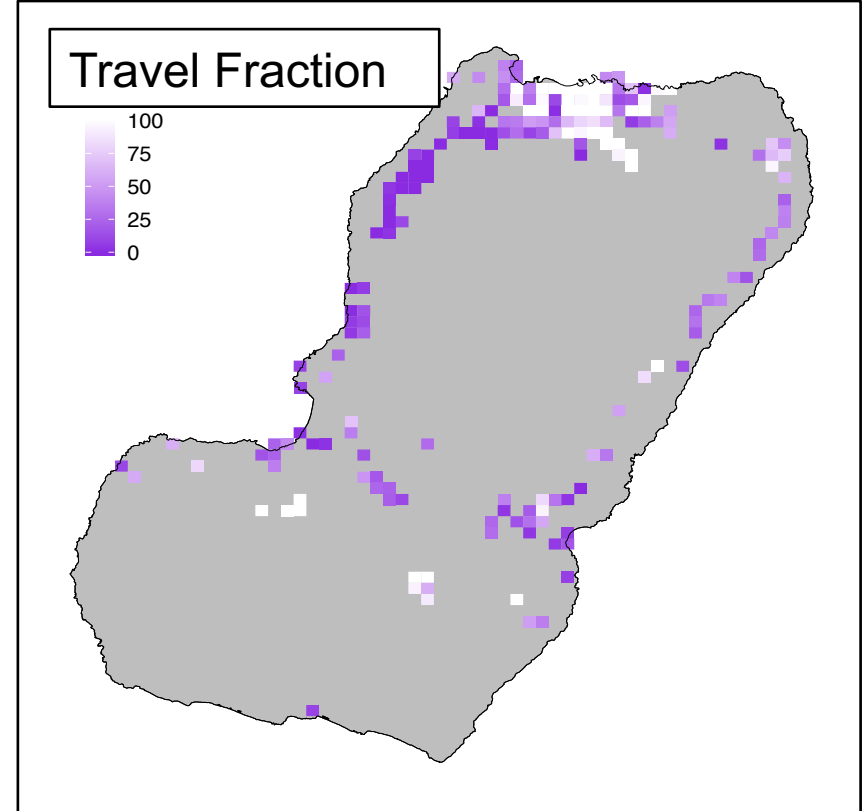- Higher risk of malaria among those who traveled off-island
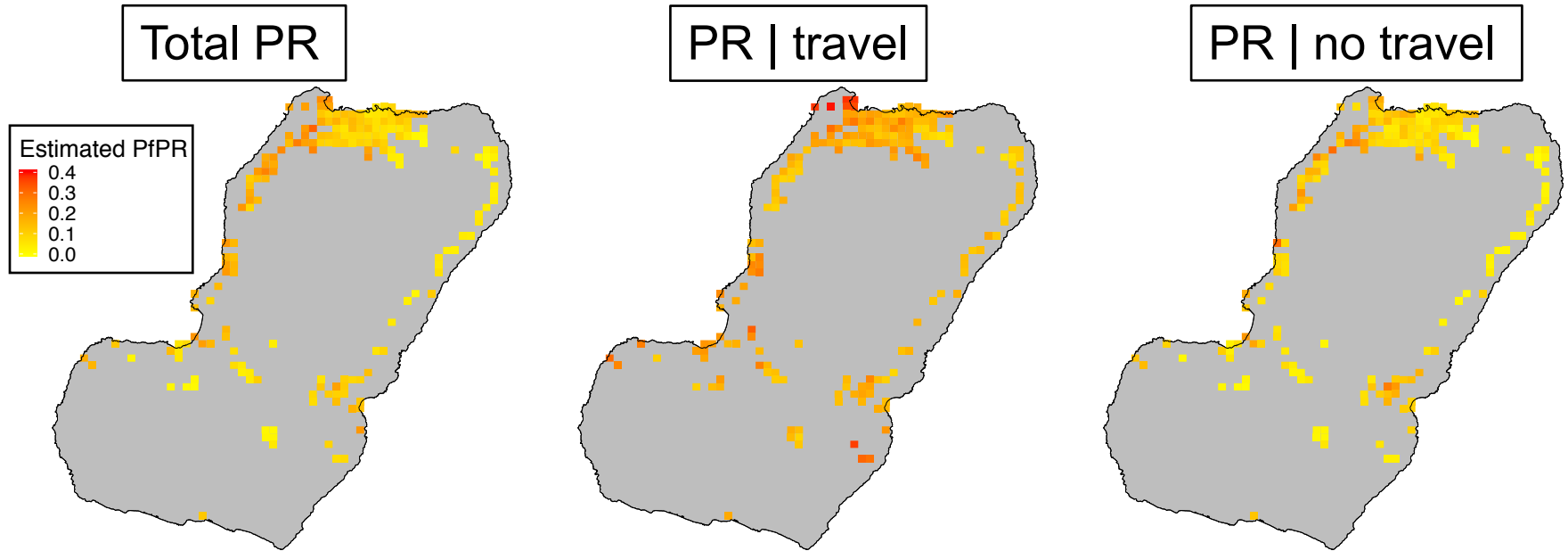
Influence of Off-Island Transmission

- Mainland EG has very high transmission risk
- Frequent off-island travel from Malabo
- How much of the prevalence seen on the island is attributable to travel?
- Use simple dynamical model
  - Ross-Macdonald
  - Include off-island infections
  - Calibrate based on PR + travel survey
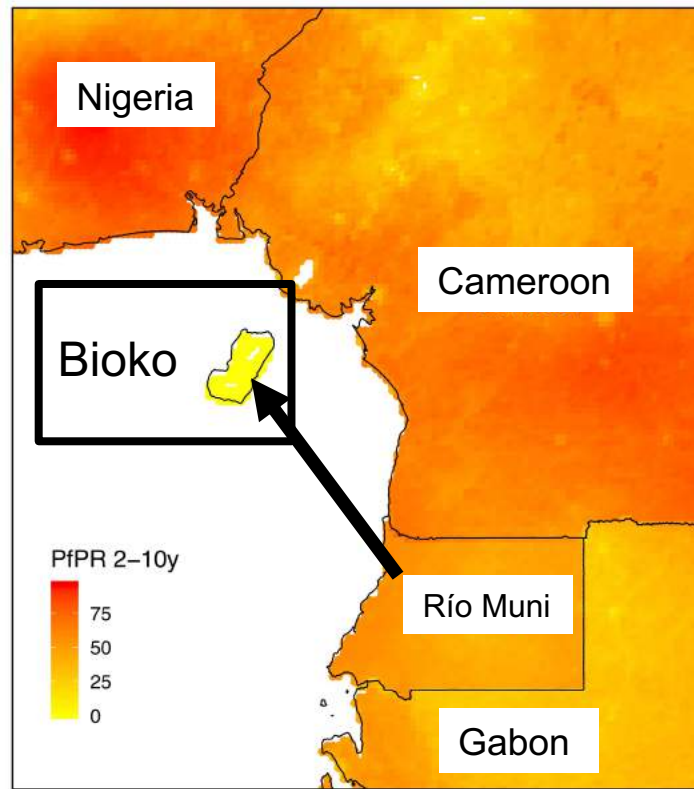
Influence of Off-Island Transmission

- Travel Fraction: % cases attributable to off-island transmission

- Malabo
  - High travel fraction (white)
  - Infections not occurring locally
  - Explains high prevalence and few viable vectors in urban area

- Malaria cases acquired off-island maintain prevalence in parts of Bioko

Travel Fraction

100
75
50
25
0

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Lesson 1: ABMs Are Not Always Necessary

- Using the simple dynamical model we were able to answer important questions about drivers of prevalence on Bioko Island

- Wanted a map of attributable cases – individual-level detail unnecessary:

  o More difficult to build

  o More difficult to calibrate

  o More difficult to interpret

  o Would not give us different results (effect size is very strong)

- ABMs more suited to exploring effects of individual-level heterogeneity

Agent-Based Modeling for Bioko Island

- What would be the impact of deploying a vaccine?
- Modeling vaccination requires individual-level heterogeneity
  - Vaccine coverage and distribution – whether someone receives the vaccine
  - Vaccine efficacy – whether the vaccine lends protection
  - Variable efficacy – fraction of new infections blocked by each individual
- Use simulation to measure population-level effects of protection

MACRO: Our Agent-Based Model

- Humans treated as individual agents
  - Populate island with individuals based on census data
  - Allow individuals to travel, based on travel survey data
 - Individuals in contact with mosquitoes, can become infected
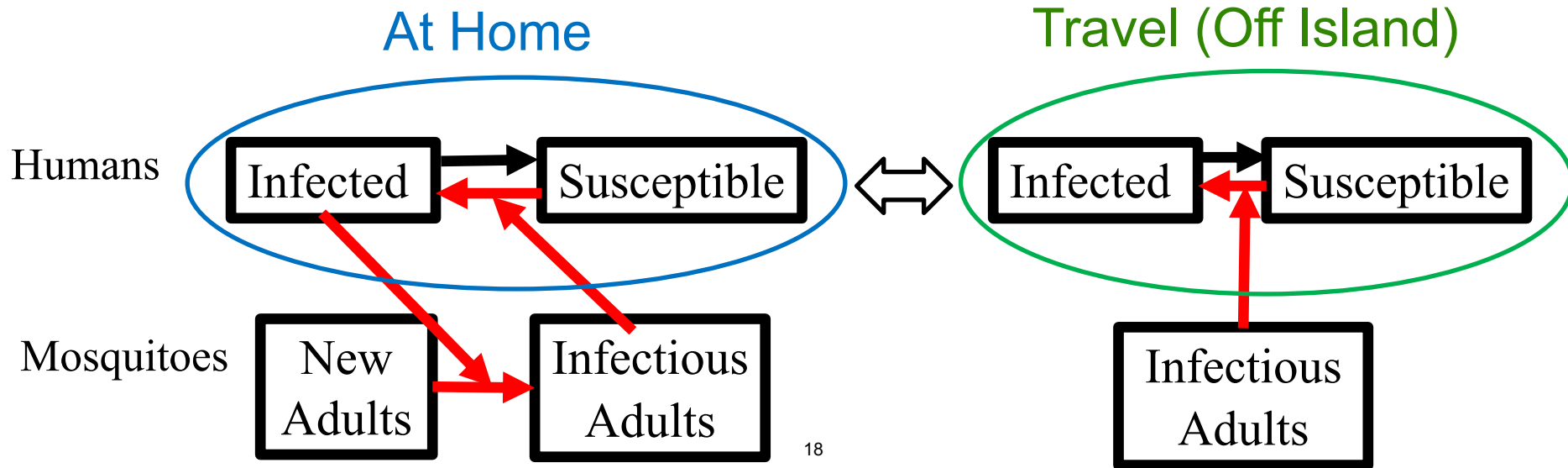
Lesson 2: Challenge of Verifying ABMs

- ABM outputs are very complicated

- How do I know the simulation is doing what I designed it to do?

- No accepted standards for ABM verification
  - Difficult to argue to others whether the model can be trusted

MACRO Verification

- Dynamics based on Ross-Macdonald Model
- Create hierarchy of related models
- Can show that MACRO aligns with Ross-Macdonald under special circumstances
- Challenges:
  - Time consuming
  - Unsure how to verify with heterogeneity
- Upsides :
  - Now can quantify importance of heterogeneity by comparing with non-homogeneous case
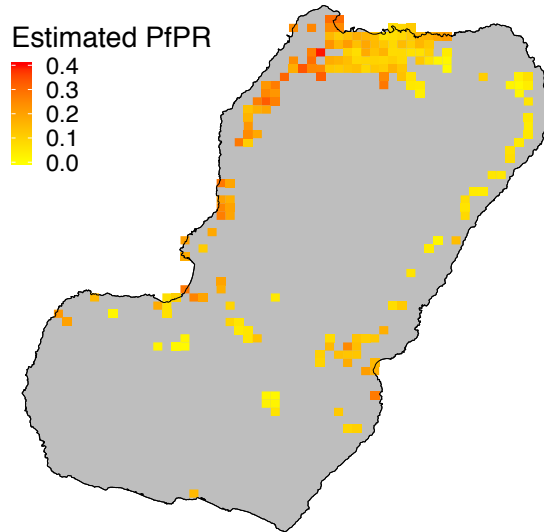 - Not just a theoretical exercise
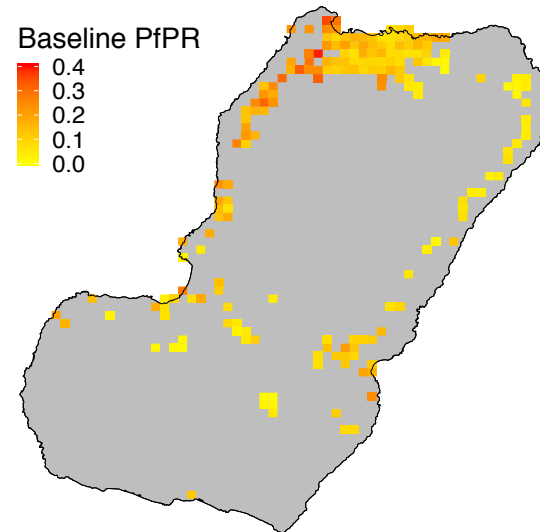
Comparing 4 related models
PR vs EIR
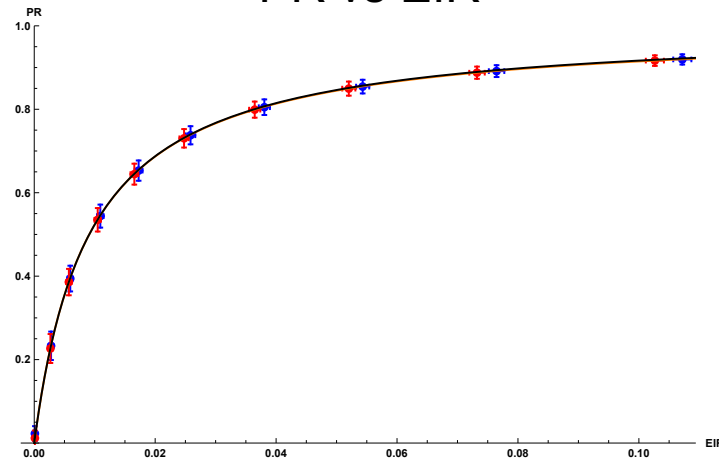
Agent-Based Modeling Results

- Establishing a baseline, calibrating to geostatistical PR map
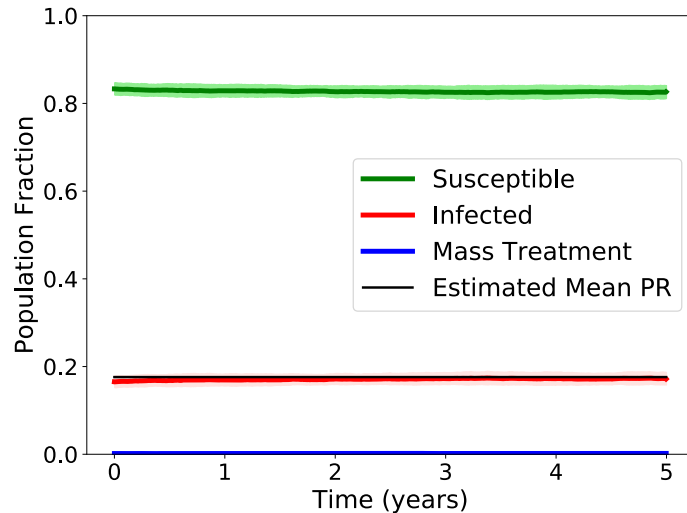
**Geospatial Estimate
Mean PR**

**Calibrated Model
Mean PR**

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Evaluation

Agent-Based Modeling Results

- Baseline: what would happen with no additional interventions
- Red: tracking mean prevalence over time

Baseline

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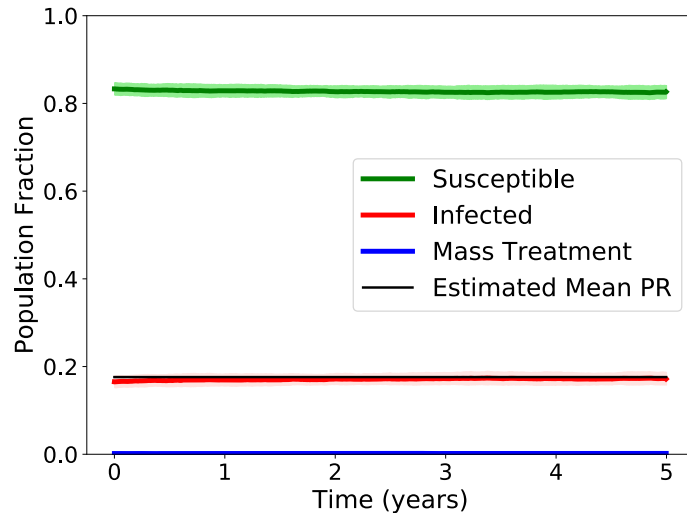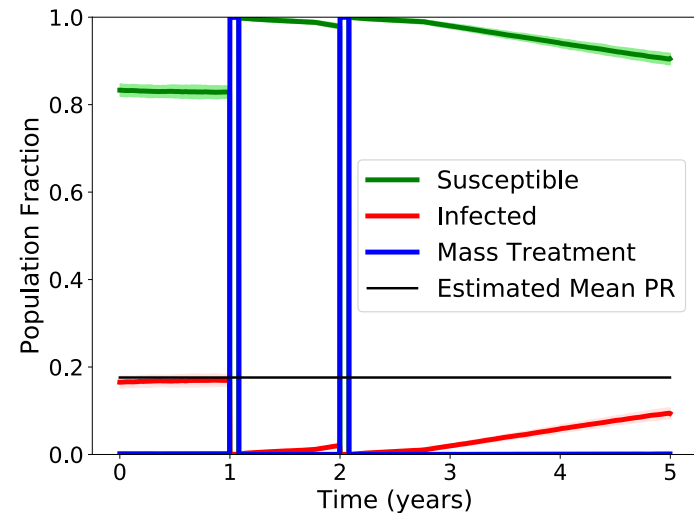
Agent-Based Modeling Results

- Adding vaccine + treatment, as a best-case scenario
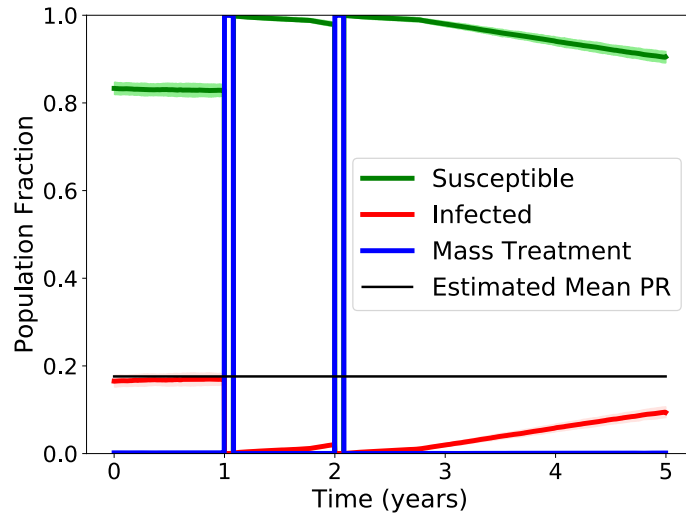- Malaria returns after a few years – unlikely to eliminate
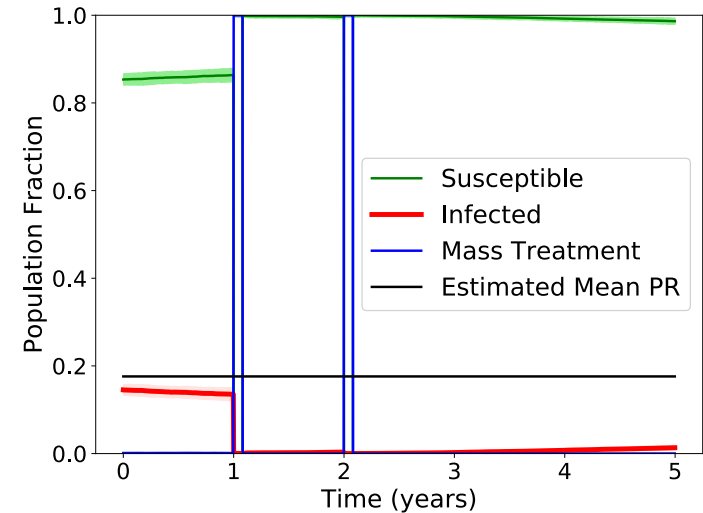

Baseline

Vaccination

Agent-Based Modeling Results

- Simulated reducing risk of acquiring infections off-island
- Addressing imported cases of malaria may be more effective


Vaccination

Reduced Off-Island Risk

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Lesson 3: Tool for Exploring Data

- ABMs show which features of complicated data sets are most important
  - Performed sensitivity analysis on vaccine efficacy and coverage
  - All results the same: malaria resurgence driven by off-island transmission
  - Focus on travel survey data as important for understanding patterns on BI
  - Recommend improvements to future surveys

Vaccination

Reduced Off-Island Risk

nd Evaluation
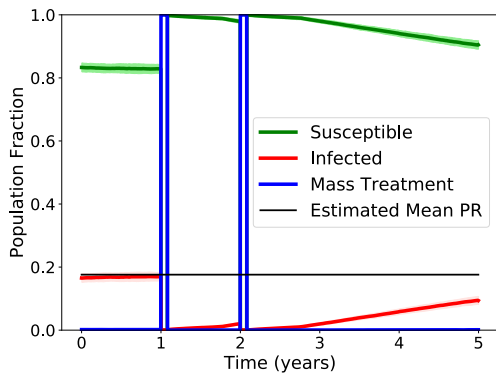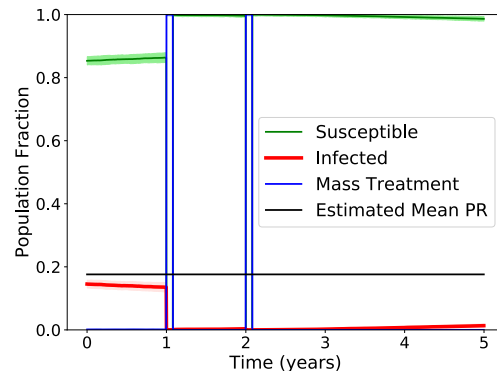
Lesson 4: Communicating with Policy Makers

- Large difference in training/expertise between modelers and policy makers
- When should policy makers trust modeling results?
- What evidence should modelers provide that their model results are useful?
- No standard practices for this

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ABMs - Worth the Trouble

- Why do we keep returning to ABMs?
  - Malaria modeling requires considering many heterogeneous components
  - No other known way of analyzing malaria data
  - No other known way of simulating for predictions and contingency planning
  - Indispensable for quantifying which aspects of the data matter and which do not
- Just because ABMs can be challenging to work with, does not at all mean we need to avoid them – no other options when dealing with highly complex and heterogeneous problems

Acknowledgments

- Bill & Melinda Gates Foundation
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