Projected impact of dengue vaccination and vector control in Yucatán, Mexico

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DENGUE VACCINE INITIATIVE
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Research questions

- Will vaccination be effective?
  - 1 licensed, 5 others in dev
- Should we expect vector control to work?
  - It often appears not to
  - Singapore: >$100 mil/year
  - “Revenge against the grandchildren”
- Beneficial synergy?

PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

Projected Impact of Dengue Vaccination in Yucatán, Mexico

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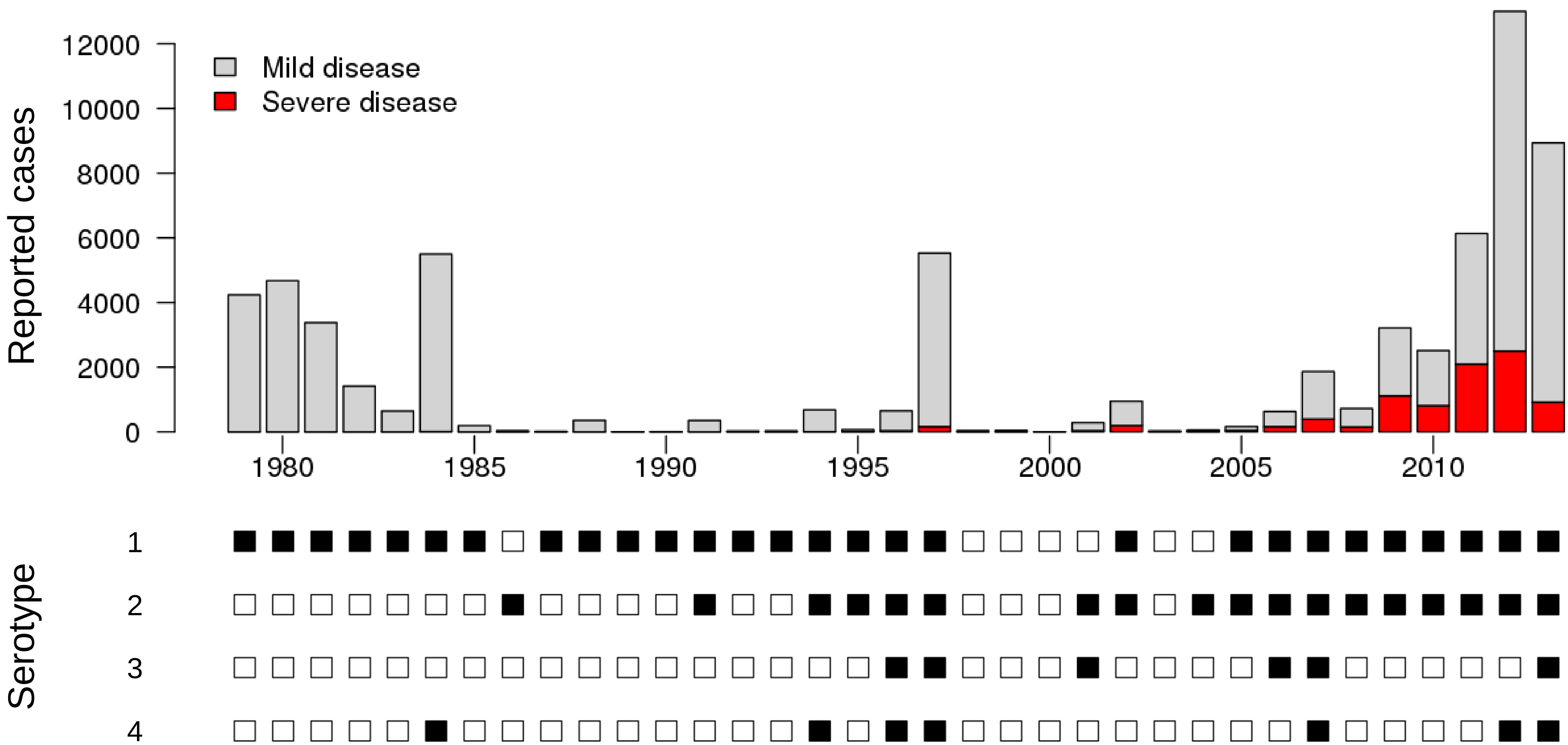
Abstract

CMDVI: Jit *et al.* (in review)

- Comparative modelling of dengue vaccine public health impact (CMDVI), sponsored by WHO
- Members of CMDVI (in authorship order, with joint first authors starred): Mark Jit*, Stefan Flasche*, Isabel Rodríguez-Barraquer*, Laurent Coudeville*, Mario Recker*, Katia Koelle*, George Milne*, Thomas Hladish*, Alex Perkins*, Derek Cummings, Ilaria Dorigatti, Daniel Laydon, Guido España, Joel Kelso, Ira Longini, Jose Lourenco, Carl A.B. Pearson, Robert C. Reiner, Luis Mier-y-Terán-Romero, Kirsten Vannice, Neil Ferguson
- Provide information to WHO/SAGE for use in developing recommendations on the use of dengue vaccine
- Understand the key features of dengue vaccine models that influence modelling results
- Help country-level decision makers interpret the results of modelling evidence.

Dengue in Yucatan, 1979-2013



Hladish *et al*. PLOS NTDs (2016)

Agent based model

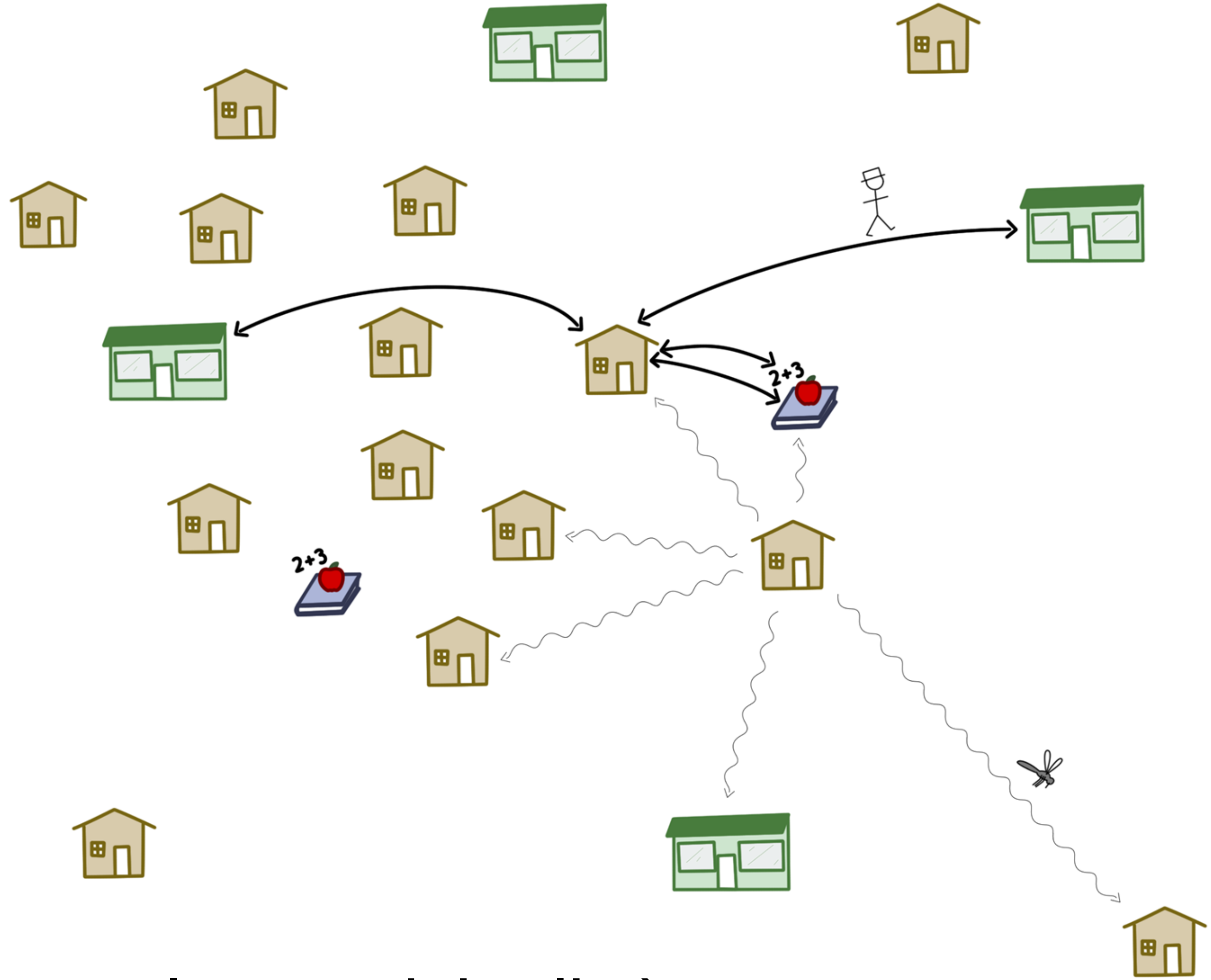
People

- Home
- Day location
- Age
- Infection state
- Immune state
- May stay home if sick

Mosquitoes

- Location
- Age
- Infection state
- May move once per day

Dengue model overview



1.82 million people

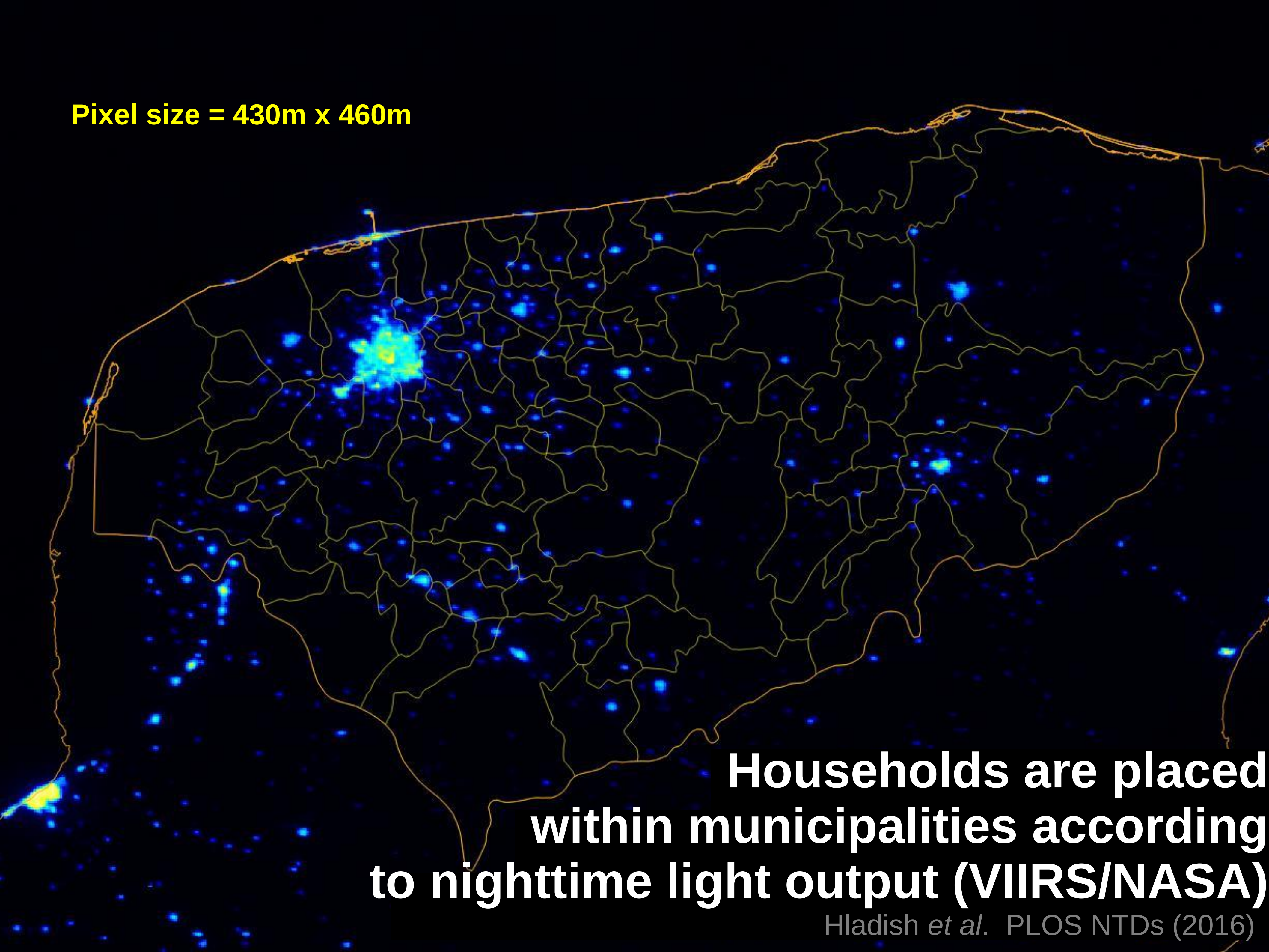
- 38% employed
- 28% in school
- 34% stay at home

376k Households (5% sample, municipality)

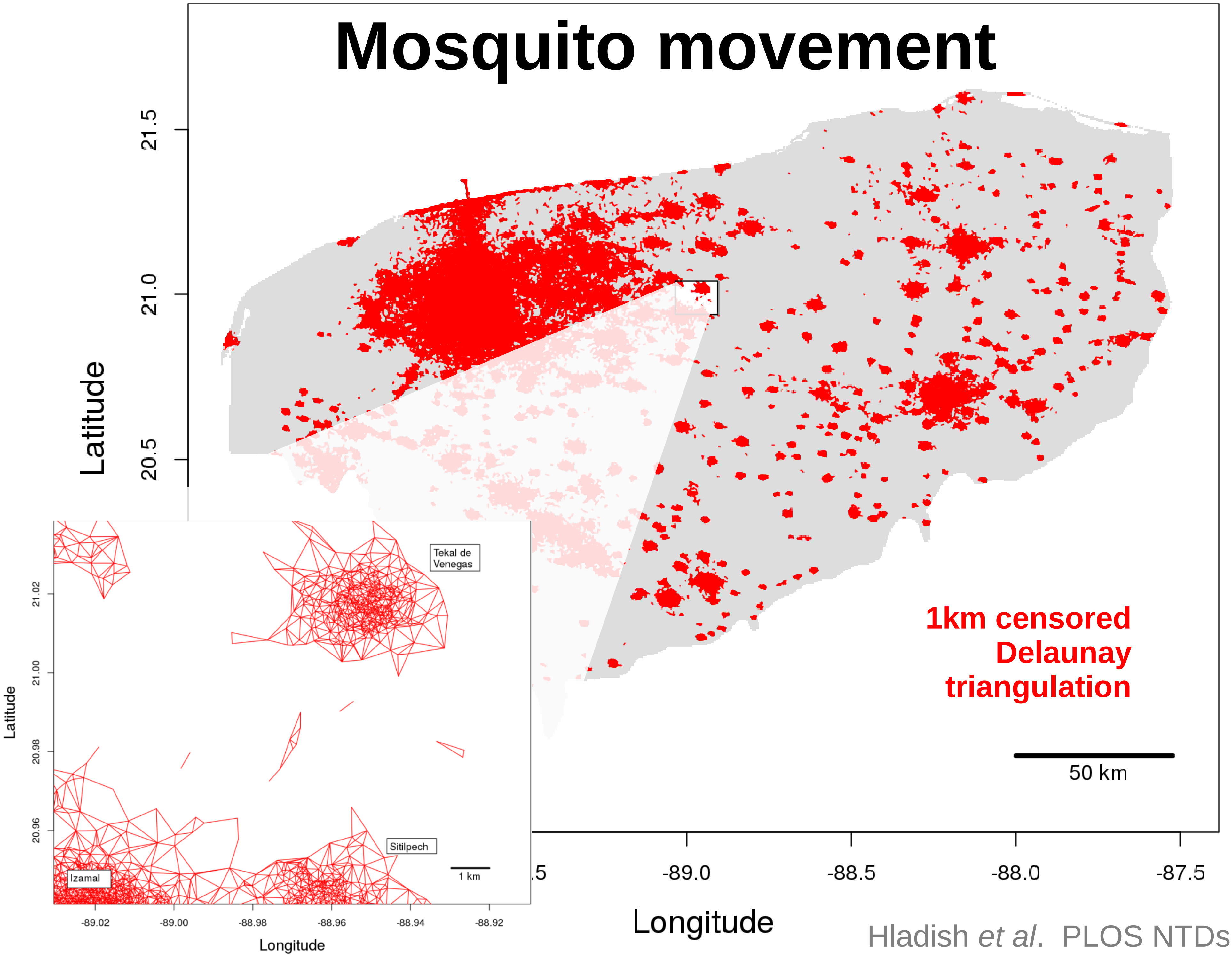
96k Workplaces (size, postal code)

3.4k Schools (postal code)

Hladish *et al*. PLOS NTDs (2016)

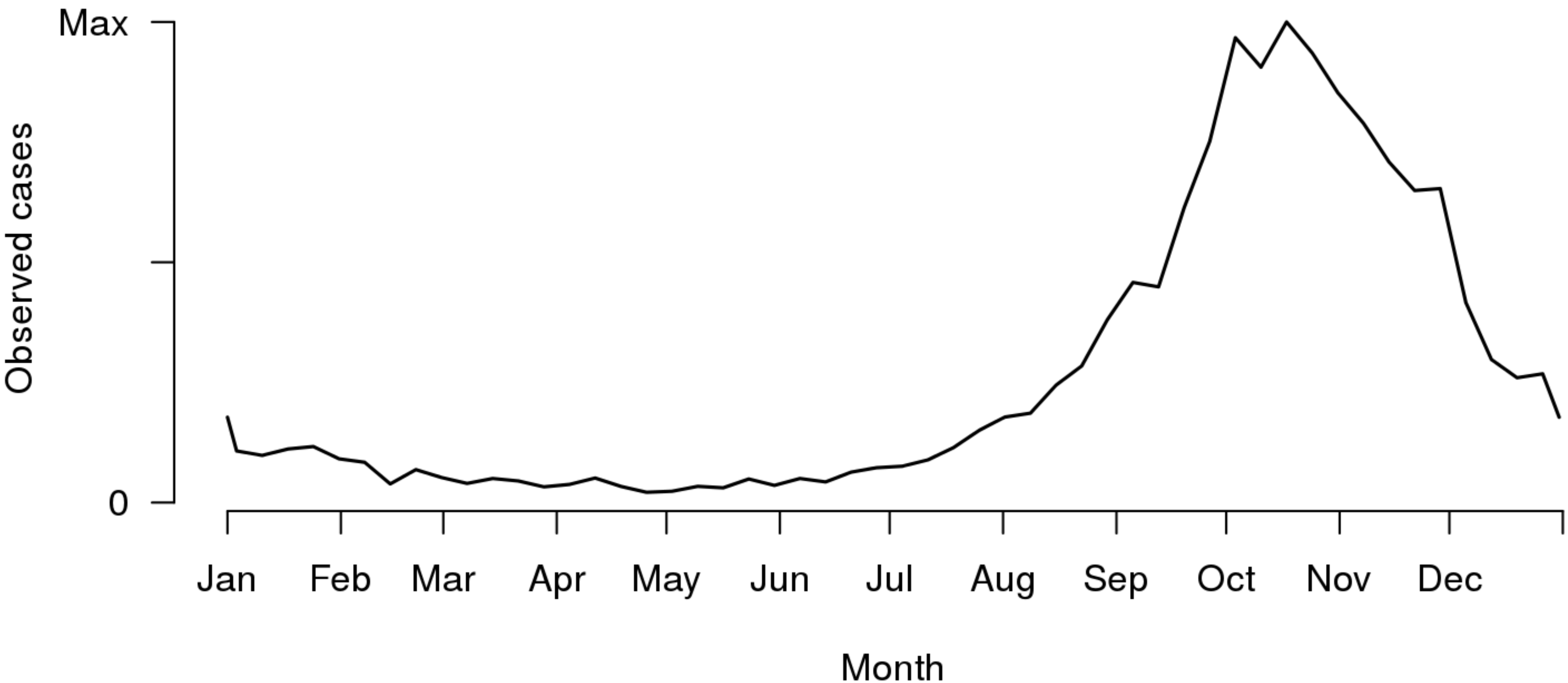

Pixel size = 430m x 460m
Households are placed
within municipalities according
to nighttime light output (VIIRS/NASA)
Hladish et al. PLOS NTDs (2016)

Mosquito movement



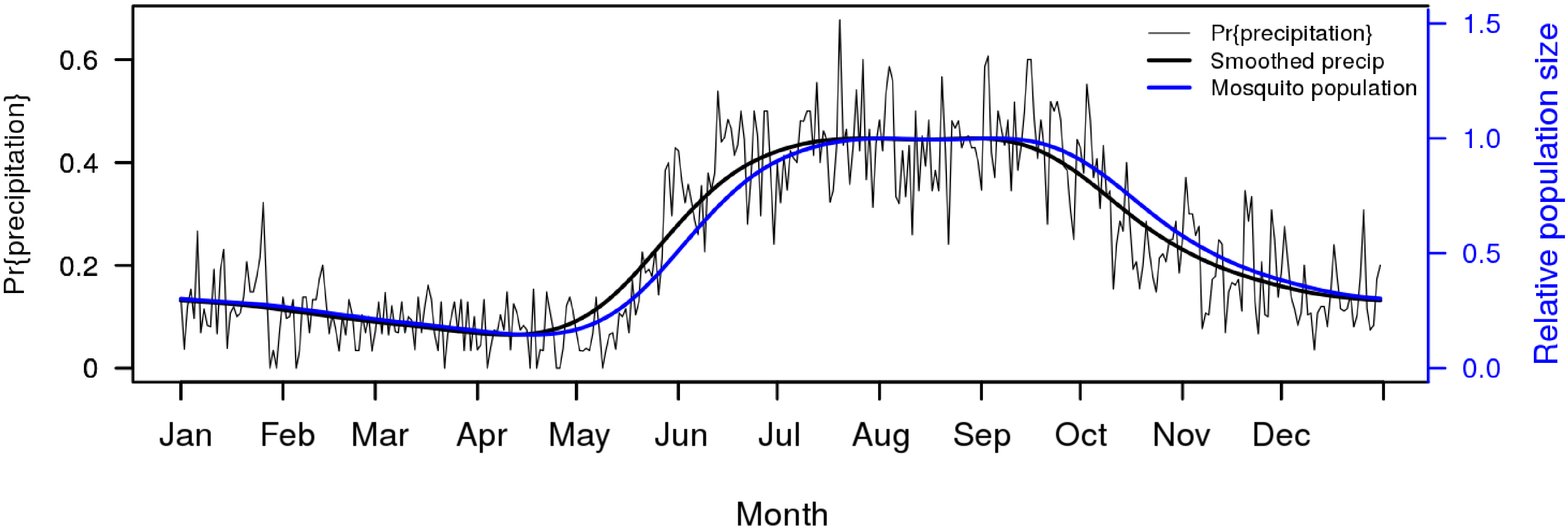
Hladish *et al*. PLOS NTDs (2016)

Observed seasonality (1995-2011)



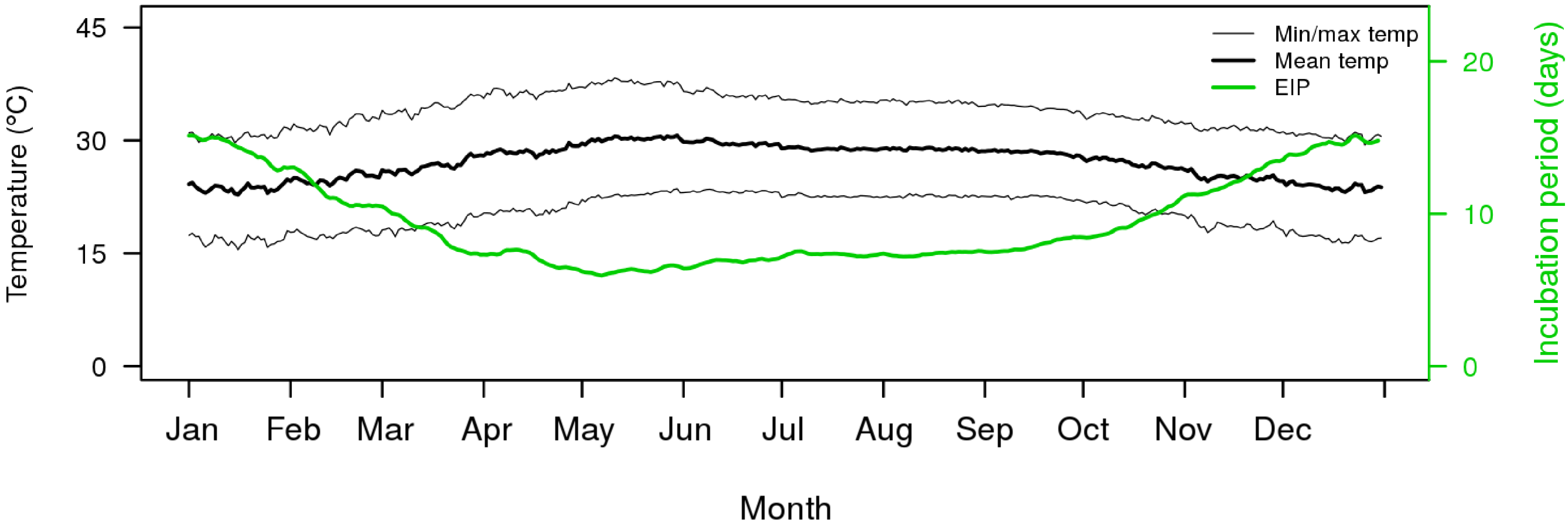
Hladish *et al*. PLOS NTDs (2016)

Rainfall → Mosquito population



Hladish *et al*. PLOS NTDs (2016)

Temperature → Incubation Period

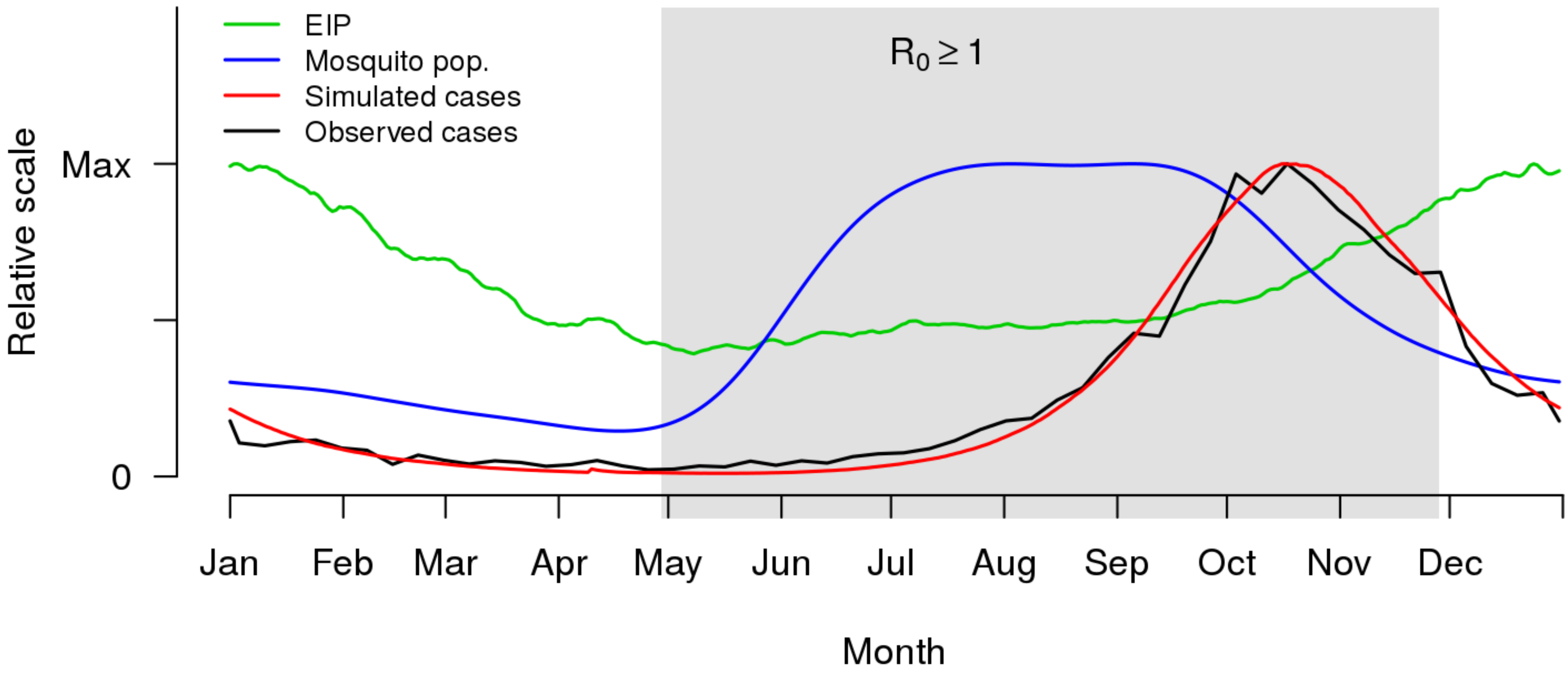


Log-normal EIP distribution based on hourly temperatures in Merida, 1995-2011

$EIP(T) = e^{\left[\left(e^{2.9-0.08T}\right)+0.1\right]}$, after Chan and Johansson (2012)

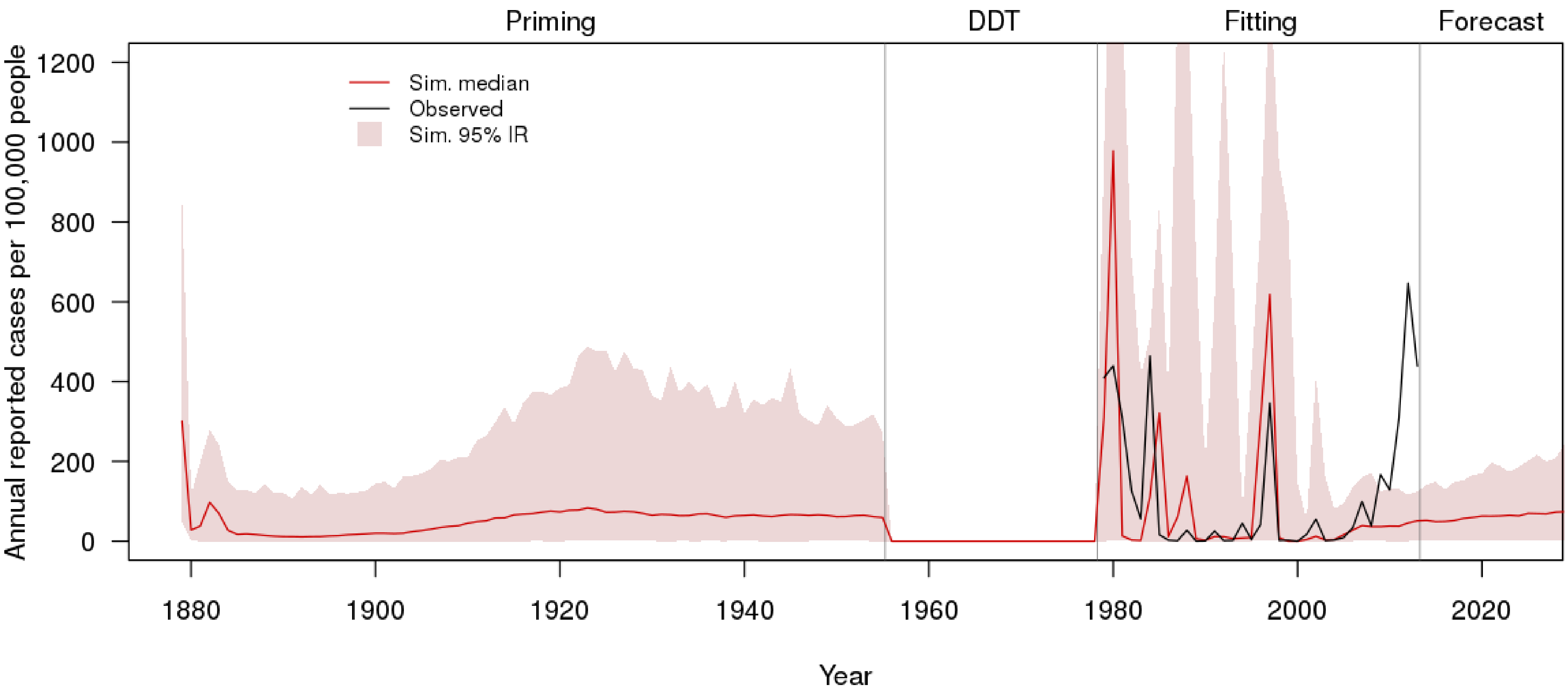
Hladish *et al*. PLOS NTDs (2016)

Emergent seasonality



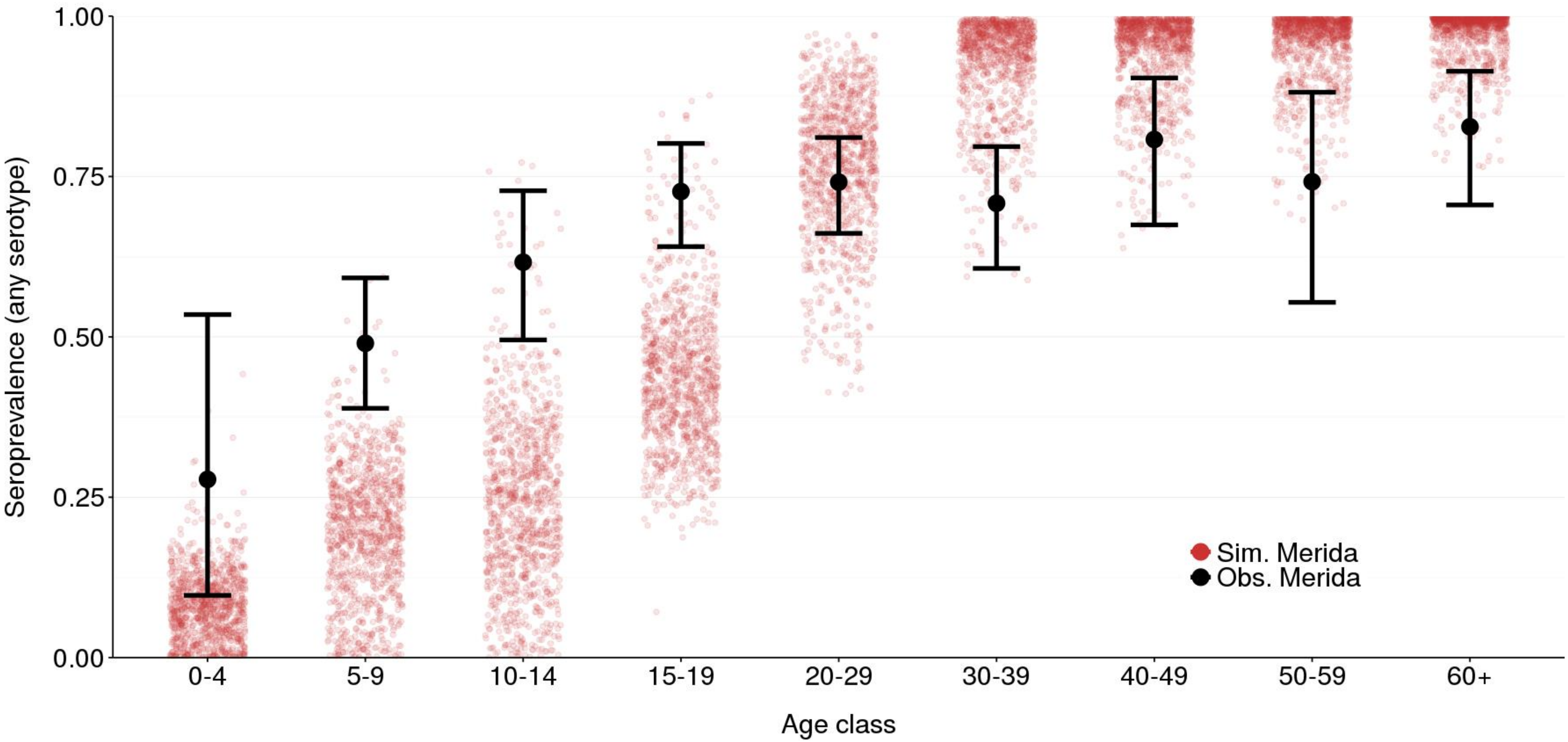
Hladish *et al*. PLOS NTDs (2016)

Reconstruct the past, forecast the future



Hladish *et al*. PLOS NTDs (2016)

Immune profile validation



95% CI bars on empirical data

Hladish *et al*. PLOS NTDs (2016)

Vaccine mechanisms

Simple Efficacy
- Serotype-specific
- Moderately efficacious
- Protects against infection
- Leaky
- Durable

Described in

Hladish *et al. PLOS NTDs* (2016)

Vaccine Replaces Infection
- Serotype-nonspecific
- Initial 100% efficacy
- Wanes to 0% over 2 years
- Replaces infection

Described in

Jit *et al* (in review)

"Simple efficacy" assumptions

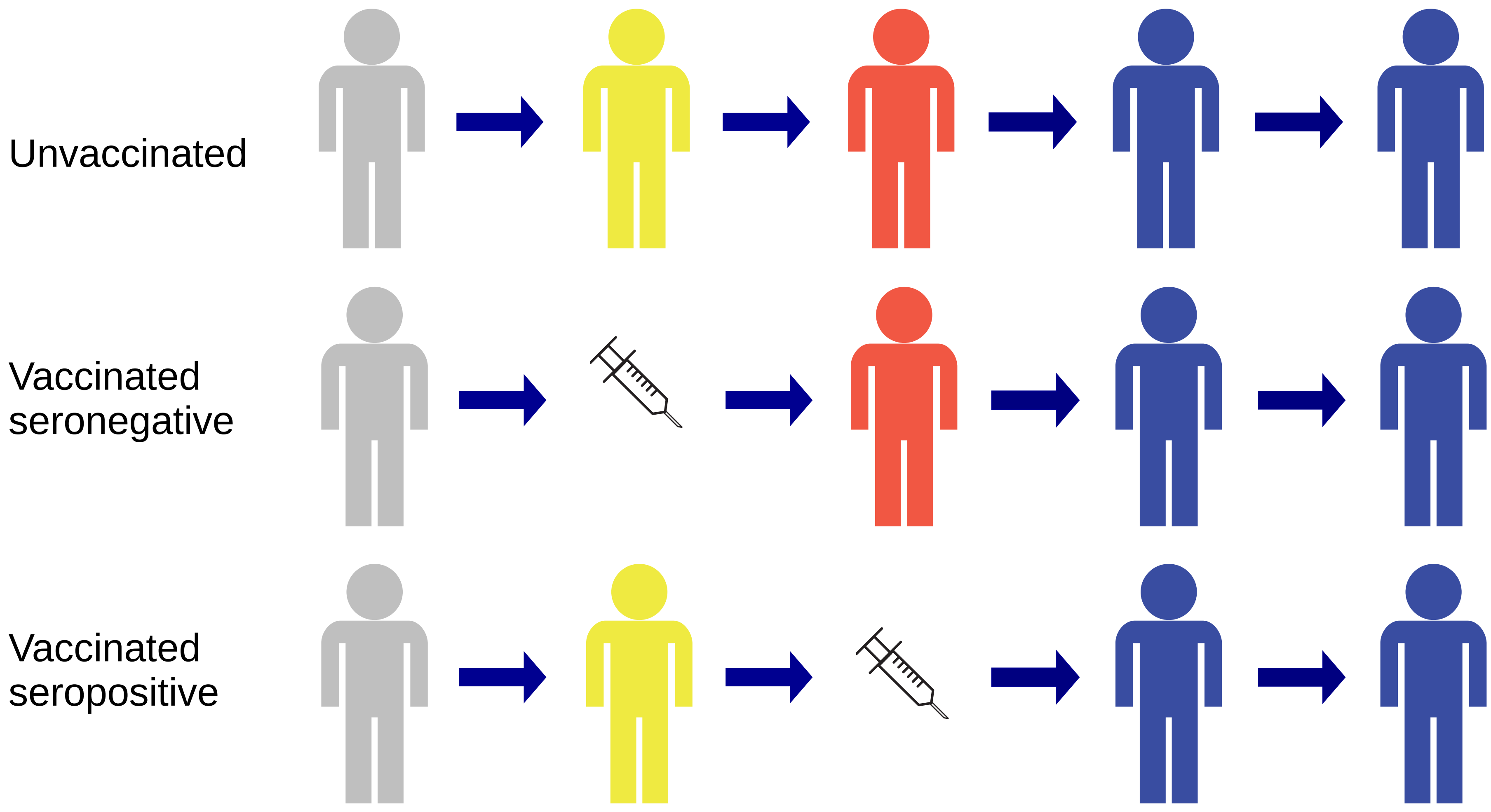
(Efficacy: direct, individual effect)

Serotype	Vaccine Efficacy*		
	Antibody positive	Antibody negative	Overall**
1	60	30	50
2	54	27	42
3	90	45	74
4	95	48	78

* Assuming leaky vaccine effect

** Based on 60% antibody positive

“Vaccine replaces infection” assumptions



Probability of severe disease upon infection

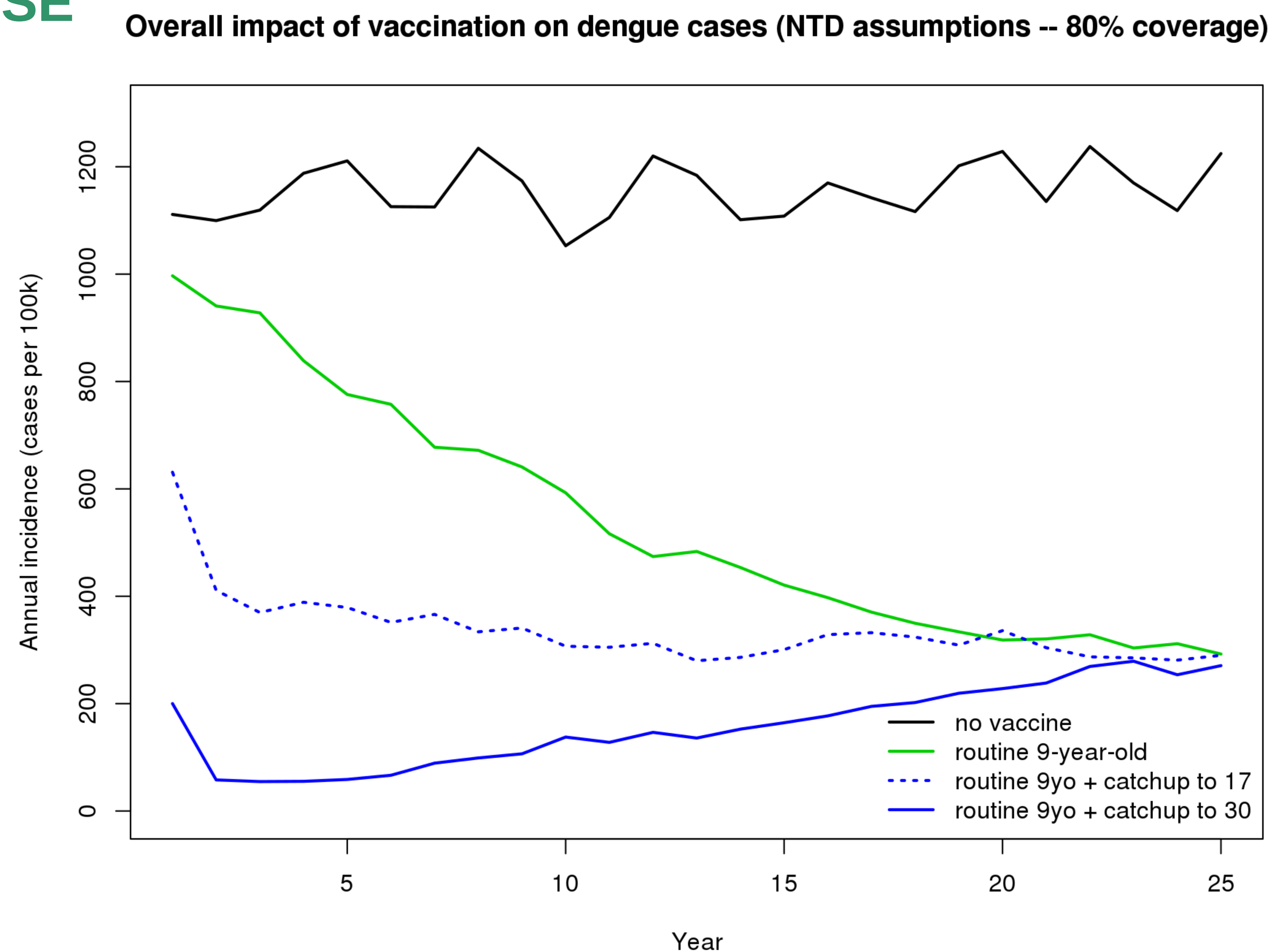
Low High

Ferguson *et al*. Science (2016), Jit *et al.* (in review)

Vaccination strategies

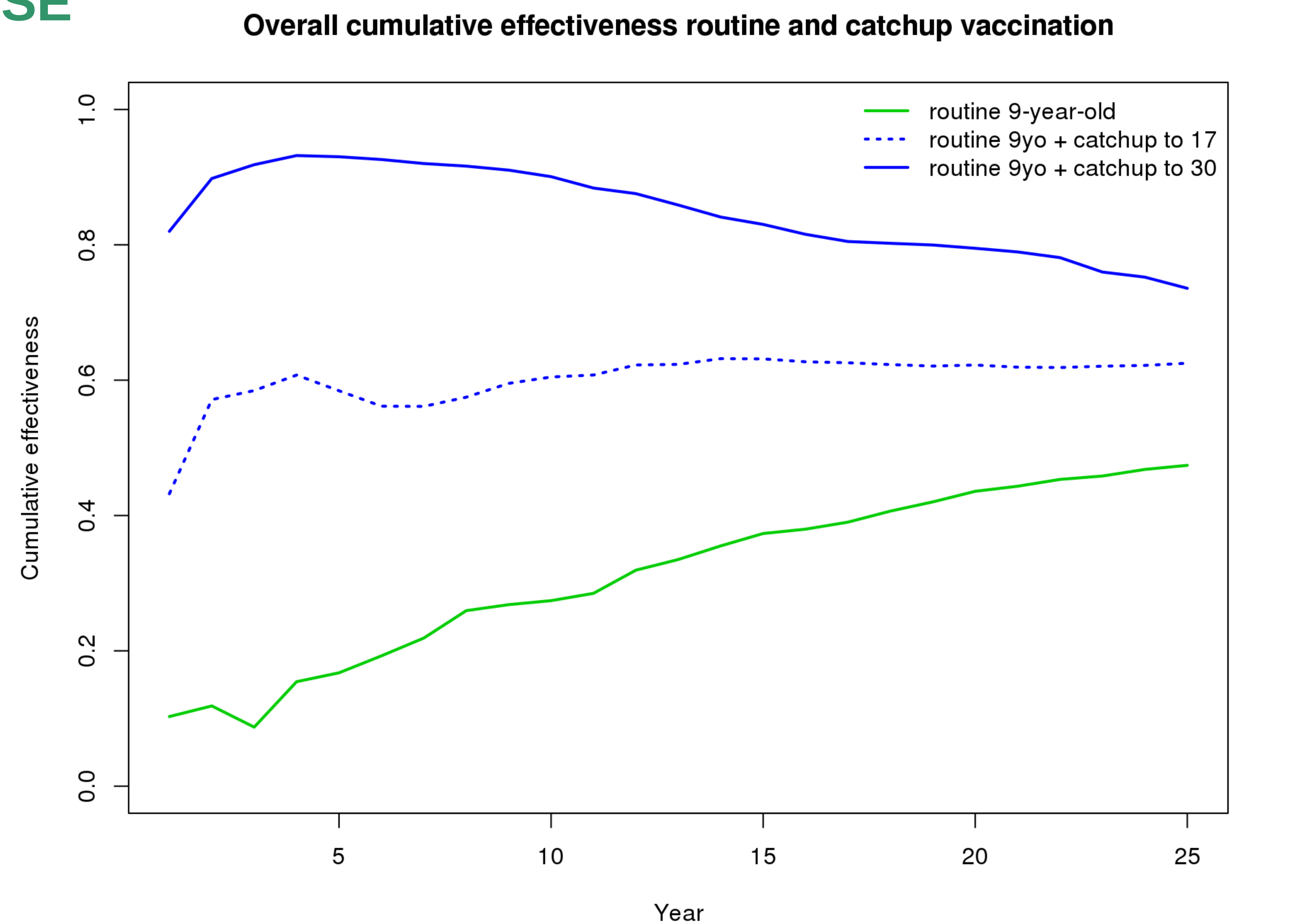
- Routine vaccination
  - Routine vaccination of 9 year-olds every year
- Routine vaccination with one-time catchup
  - One time catch-up up to 17 or 30 year-olds
- 80% coverage in all cases

SE

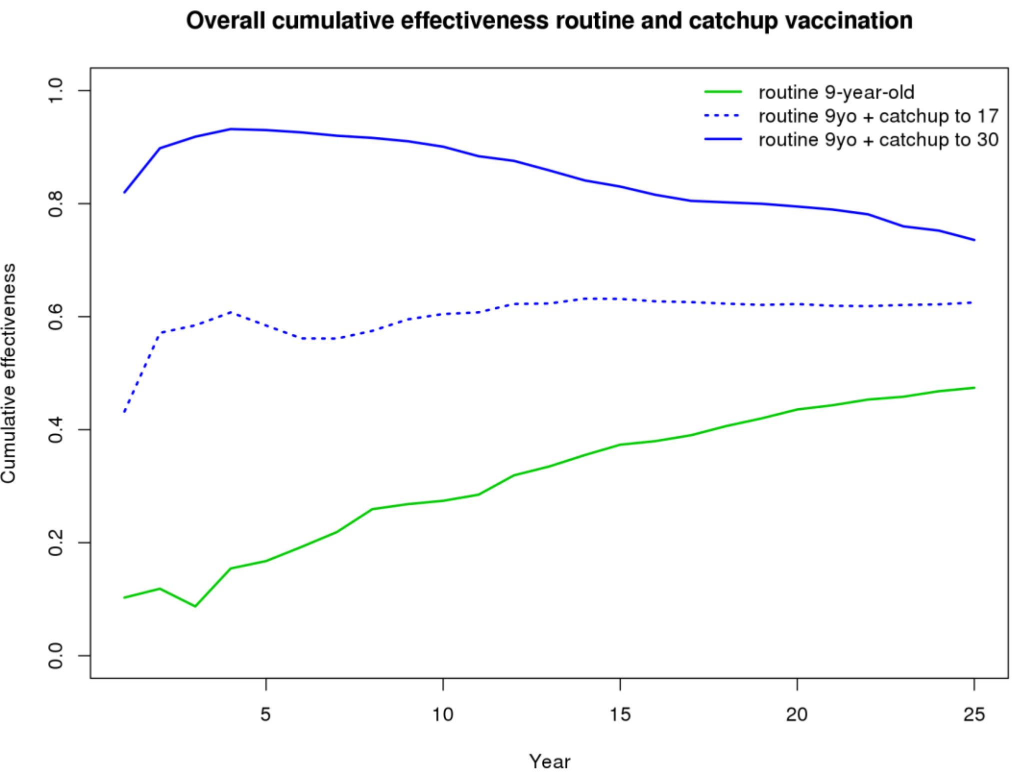


Overall impact of vaccination on dengue cases (NTD assumptions -- 80% coverage)
Annual incidence (cases per 100k)
0
200
400
600
800
1000
1200
5
10
15
20
25
Year
no vaccine
routine 9-year-old
routine 9yo + catchup to 17
routine 9yo + catchup to 30

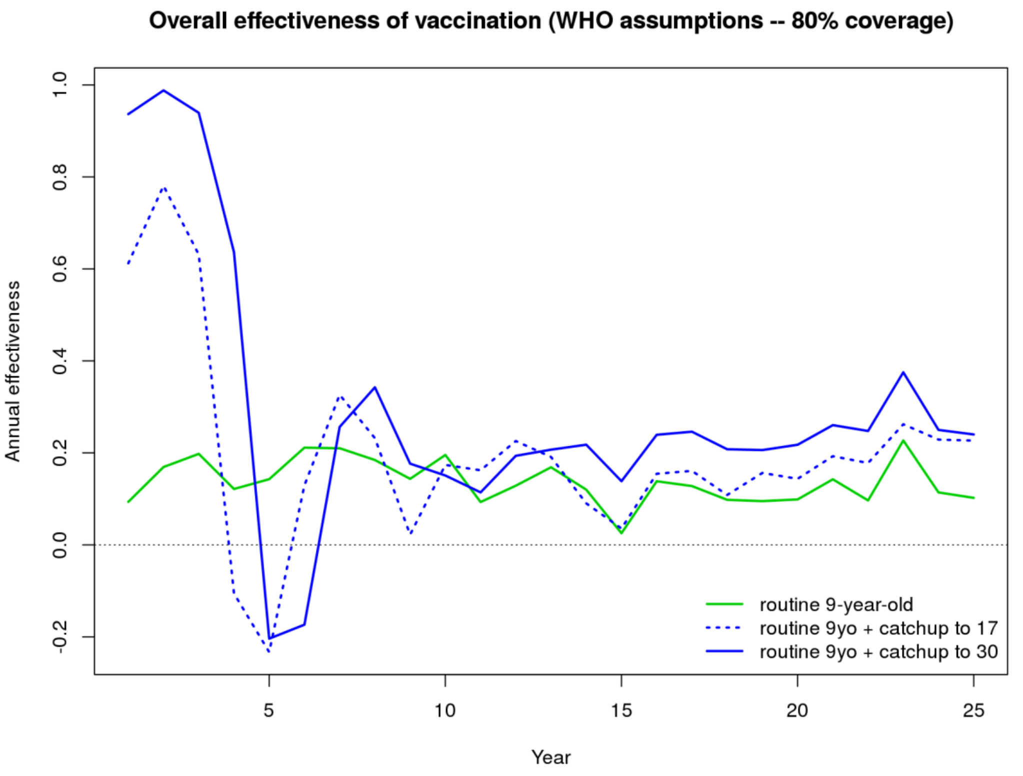
SE


Overall cumulative effectiveness routine and catchup vaccination
routine 9-year-old
routine 9yo + catchup to 17
routine 9yo + catchup to 30
Cumulative effectiveness
0.0
0.2
0.4
0.6
0.8
1.0
5
10
15
20
25
Year

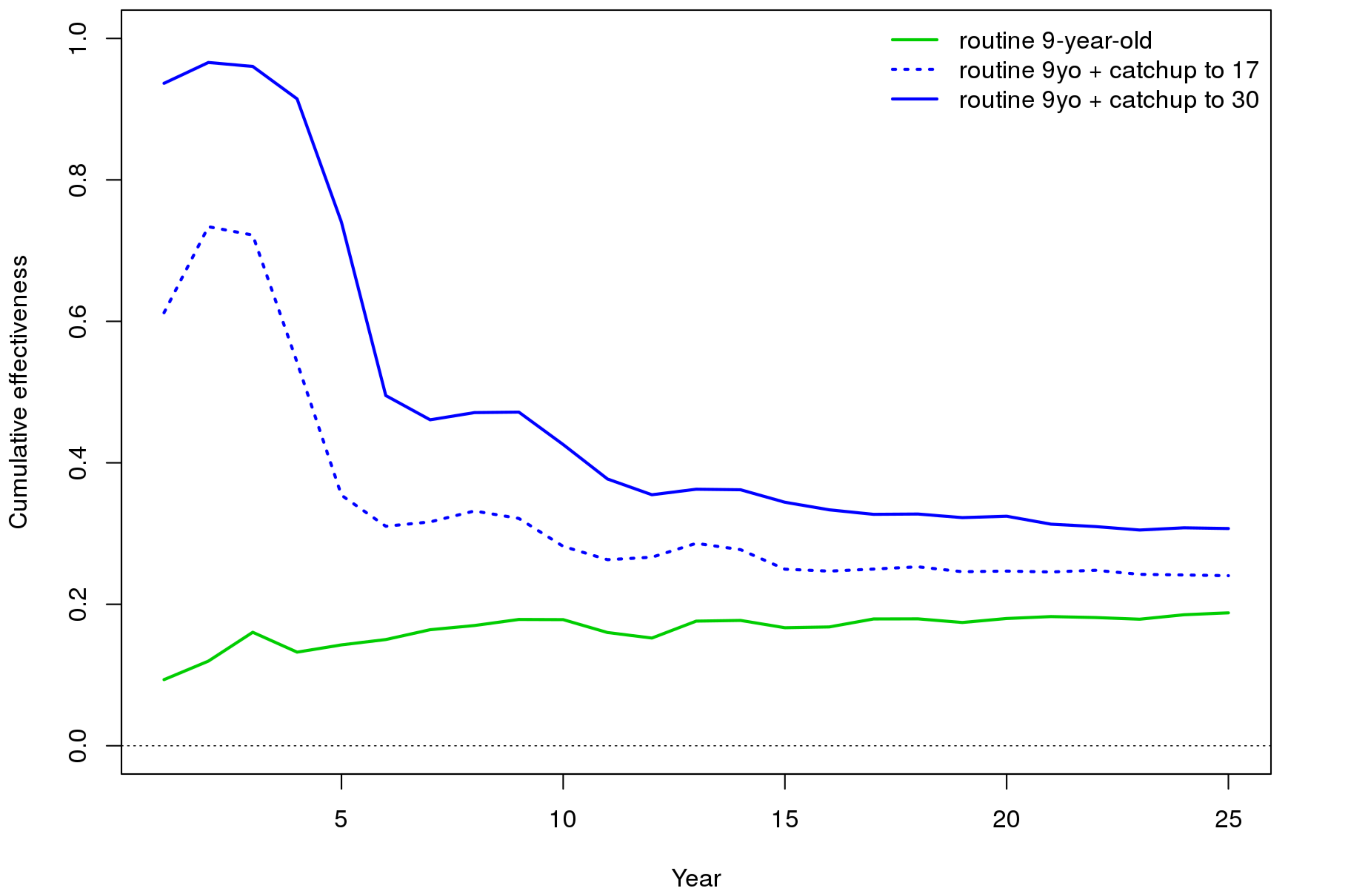
SimpleEfficacy

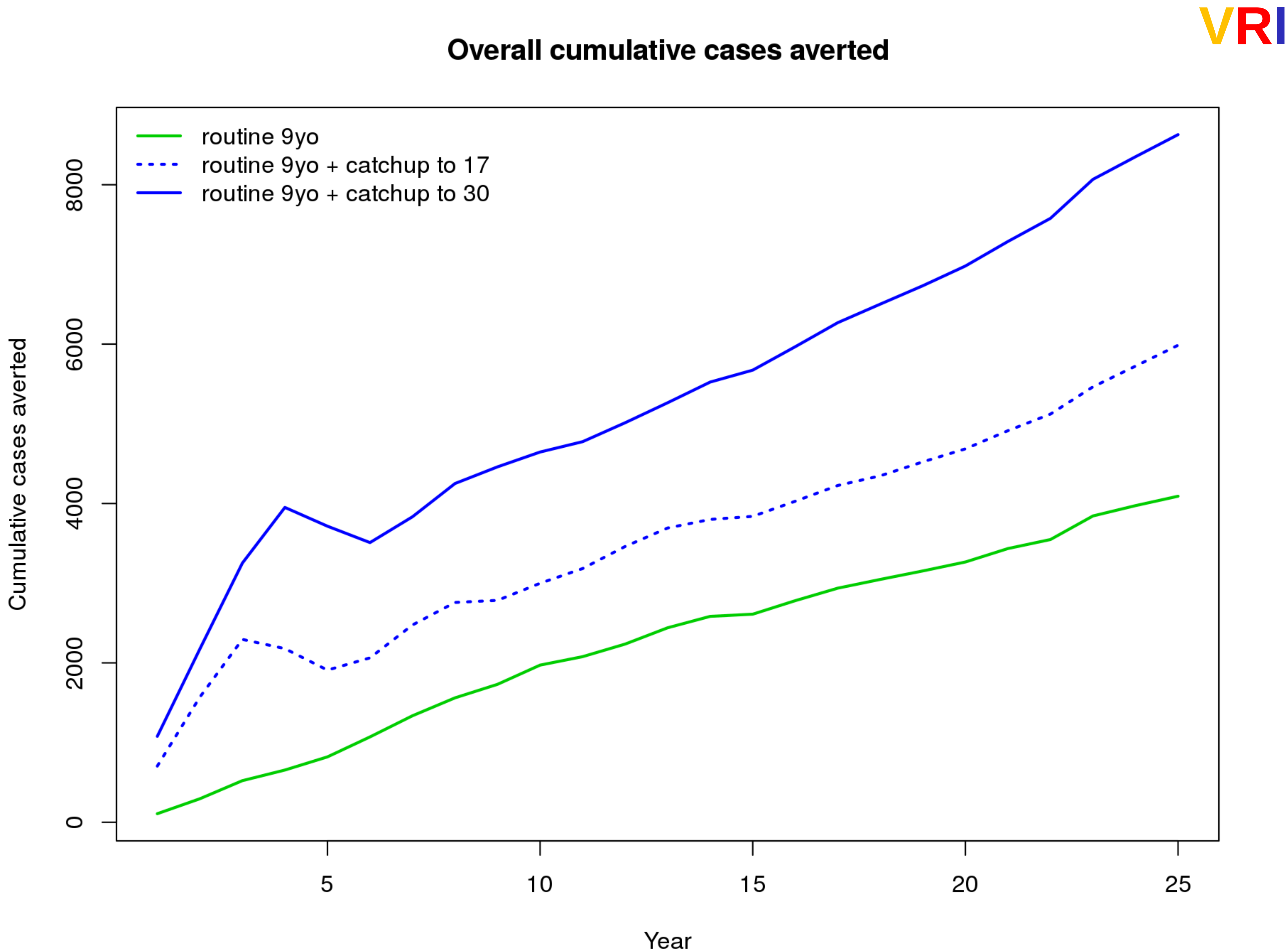


VaccineReplacesInfection



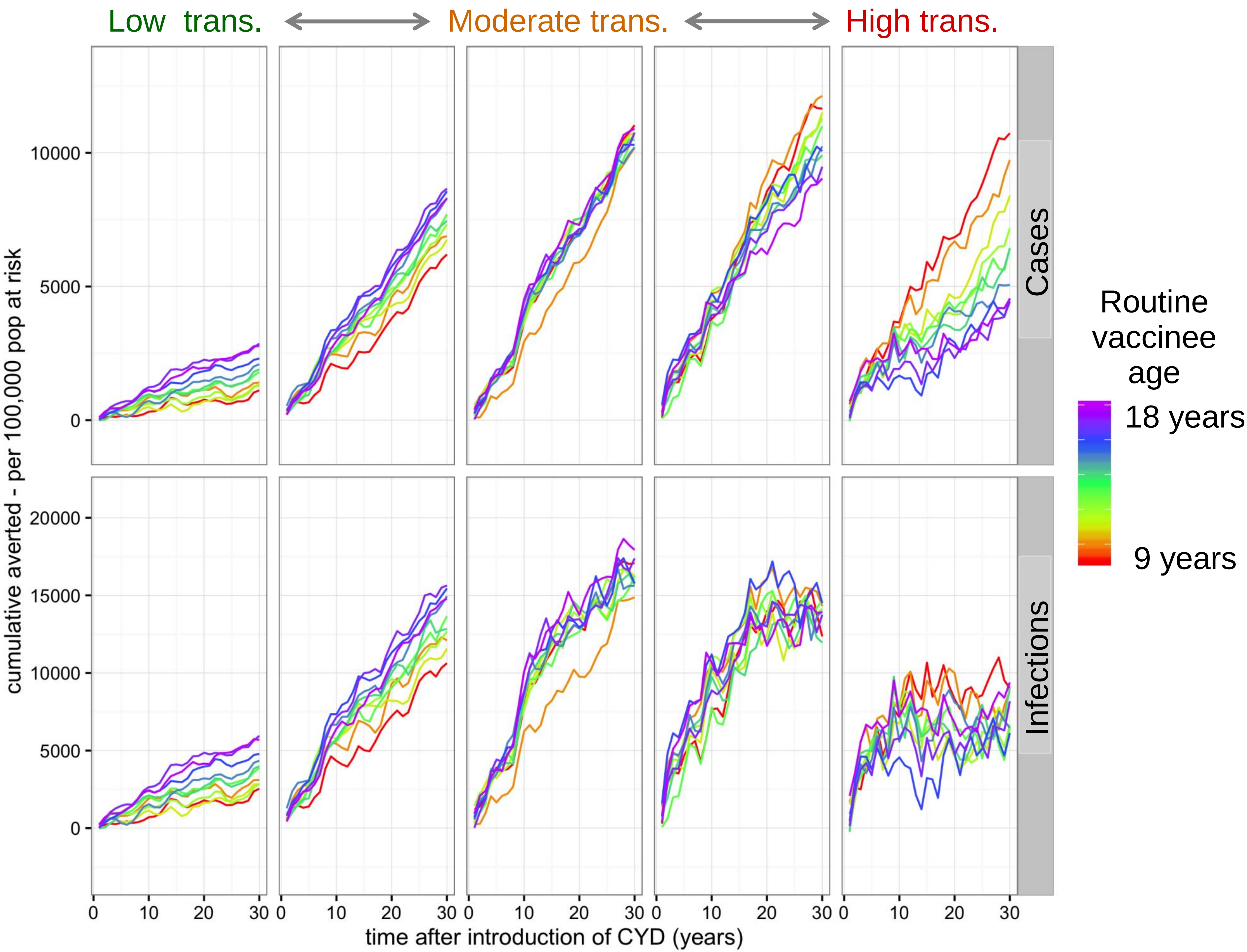
Overall cumulative effectiveness routine and catchup vaccination





VRI
Overall cumulative cases averted
routine 9yo
routine 9yo + catchup to 17
routine 9yo + catchup to 30
Cumulative cases averted
0
2000
4000
6000
8000
5
10
15
20
25
Year

Effect of vaccinee age on overall cumulative cases averted



Effects of
new vector reduction
plus vaccination

Indoor residual spraying*

Assume 25% of houses are randomly selected & treated during July-September

Efficacy = 80% (reduction in equilibrium pop size in treated houses)

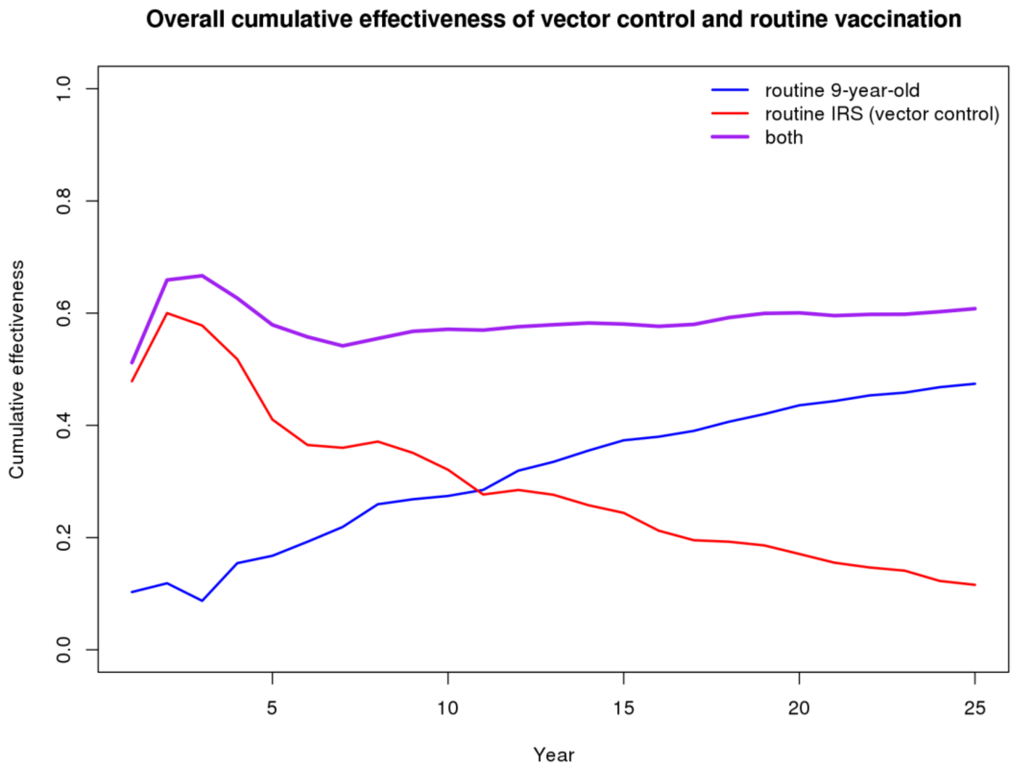
Corresponds to 13% daily mortality due to IRS

Treatment lasts 90 days

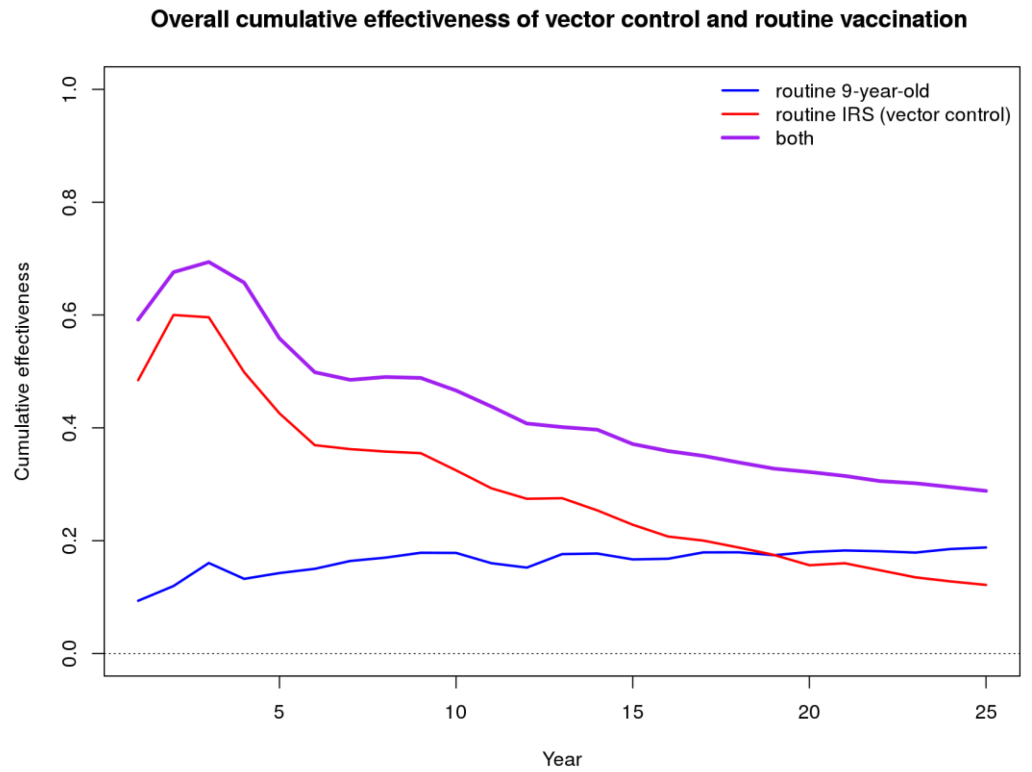
*Efficacy & durability based on unpublished data from

Gonzalo Vazquez Prokopec, Emory University

SimpleEfficacy

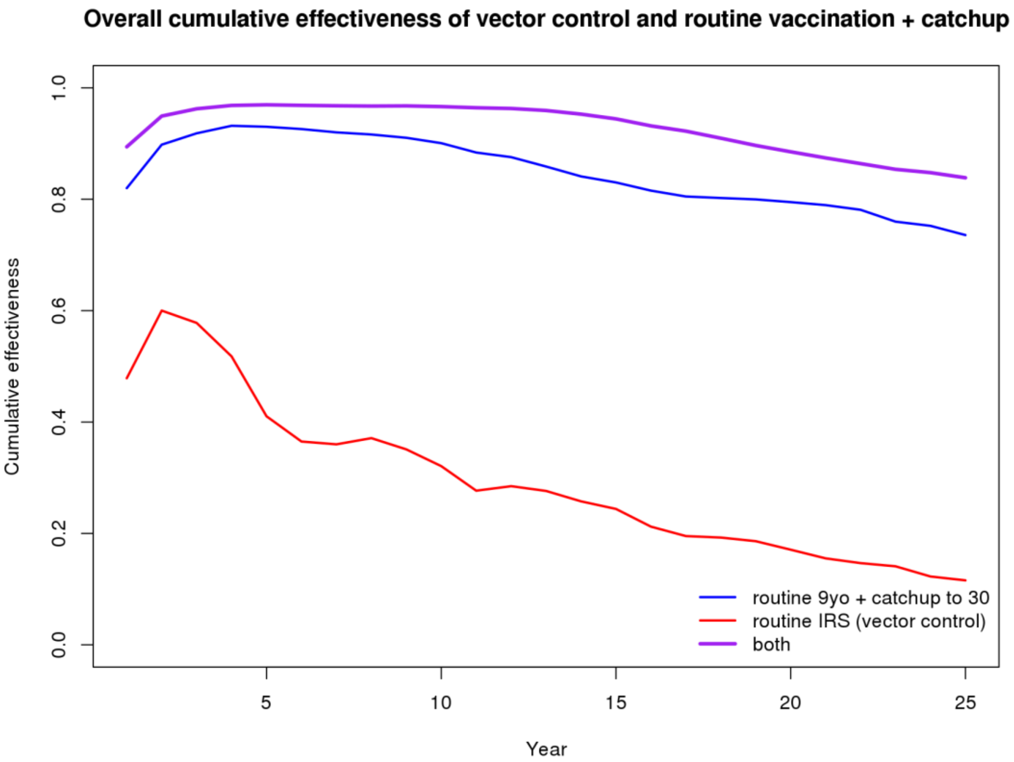


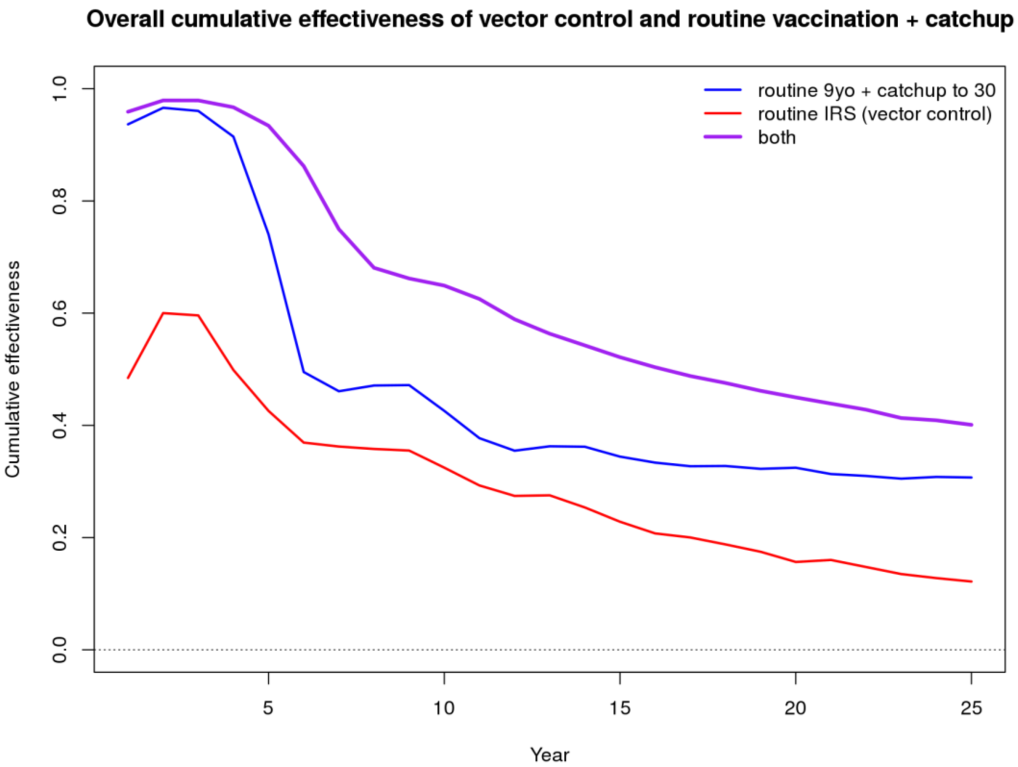
VaccineReplacesInfection



SimpleEfficacy

VaccineReplacesInfection





Overall conclusions (1 of 2)

- Short-term effectiveness good
- Long-term effectiveness may be modest – data needed
- Cumulative effectiveness always positive
- Modest interventions not bad, not impressive
- Noisy empirical data may obscure effectiveness
- Waning vaccine & IRS effectiveness don’t persist
  - Vac: Population loses vaccine-induced immunity
  - IRS: Population acquires less natural immunity
- Elimination unlikely

Overall conclusions (2 of 2)

- Catchup and IRS can have major near-term (~5 years) benefit
  - Some years may have > baseline burden
  - Some years with larger-than-normal epidemics are possible
  - Cumulative effectiveness & cases averted always positive
- Cost-benefit analysis needed to find balance

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- Dennis Chao

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- Gabriel Recchia

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