Dengue dynamics and projected effectiveness of vaccination and vector control in Yucatan, Mexico

Thomas Hladish *et al*

University of Florida

csquid
CENTER FOR STATISTICS & QUANTITATIVE INFECTIOUS DISEASES

National Institute of Public Health

NSF

Model described/used in:

Chao, DL, et al. "Controlling dengue with vaccines in Thailand." *PLOS Neglected Tropical Diseases* 6.10 (2012): e1876.

Hladish, TJ, et al. "Projected impact of dengue vaccination in Yucatán, Mexico." *PLOS Neglected Tropical Diseases* 10.5 (2016): e0004661.

Flasche, S, et al. "The long-term safety, public health impact, and cost-effectiveness of routine vaccination with a recombinant, live-attenuated dengue vaccine (Dengvaxia): a model comparison study." *PLOS Medicine* 13.11 (2016): e1002181.

Hladish, TJ, et al. "Forecasting the effectiveness of indoor residual spraying for reducing dengue burden." *PLOS Neglected Tropical Diseases* 12.6 (2018): e0006570.

Dengue at a glance

Flavivirus

Aedes aegypti, A. albopictus

390 million infections

96 million cases

> 100 countries

Typical symptoms:

- Often none
- Fever (DF), up to 106 F (41 C)
- Rash
- Muscle, bone, joint pain

DHF / DSS

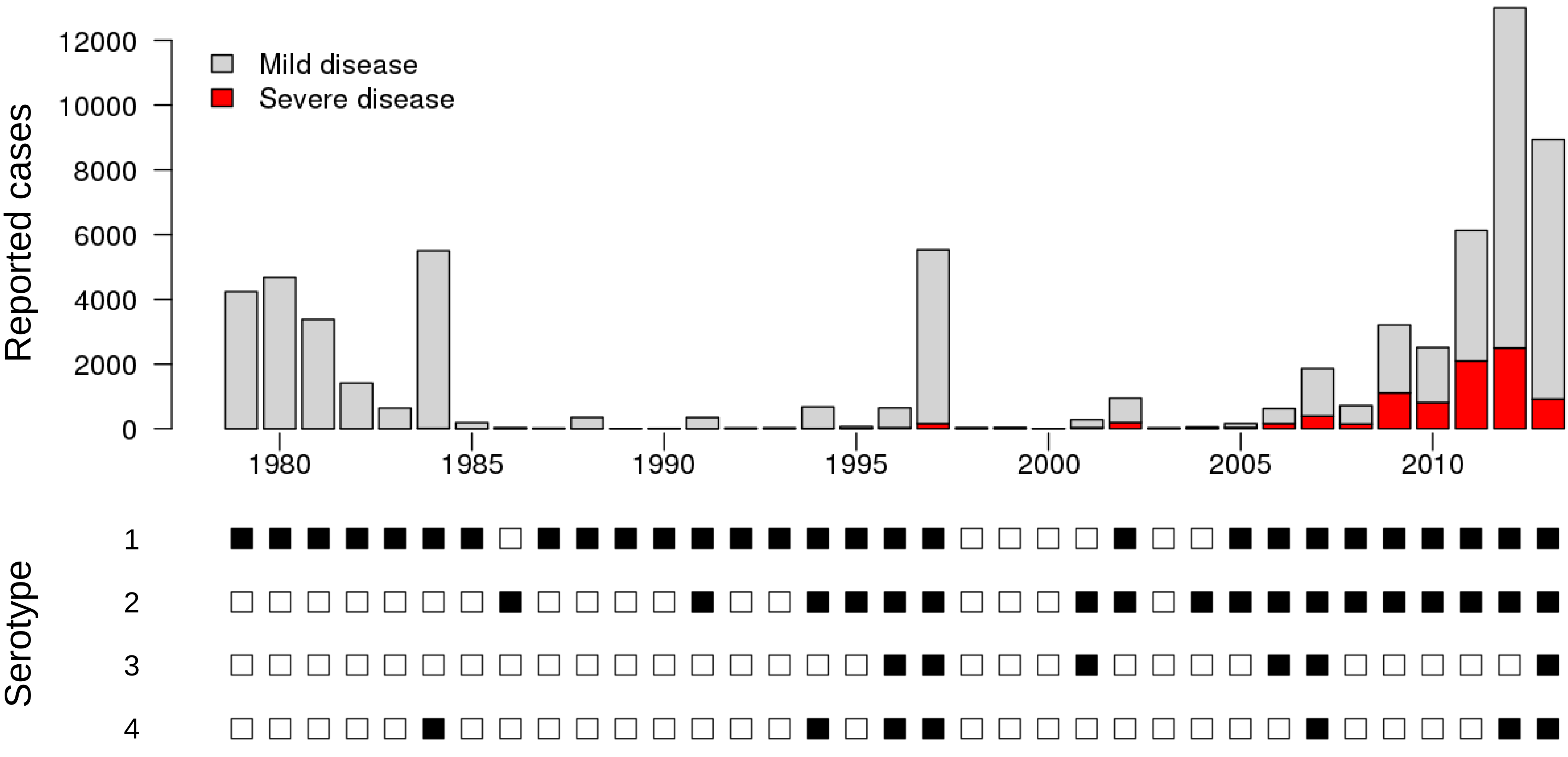
4 Serotypes

Temporary cross-protection, followed by enhancement

Research questions

- What benefit should be expected from the Sanofi-Pasteur vaccine?
- Why does killing mosquitoes seem ineffective?
- Given realistic options, how should vector control be done?
- Do combination strategies have synergistic benefits?

Dengue in Yucatan, 1979-2013



Hladish *et al*. PLOS NTDs (2016)

Agent based model

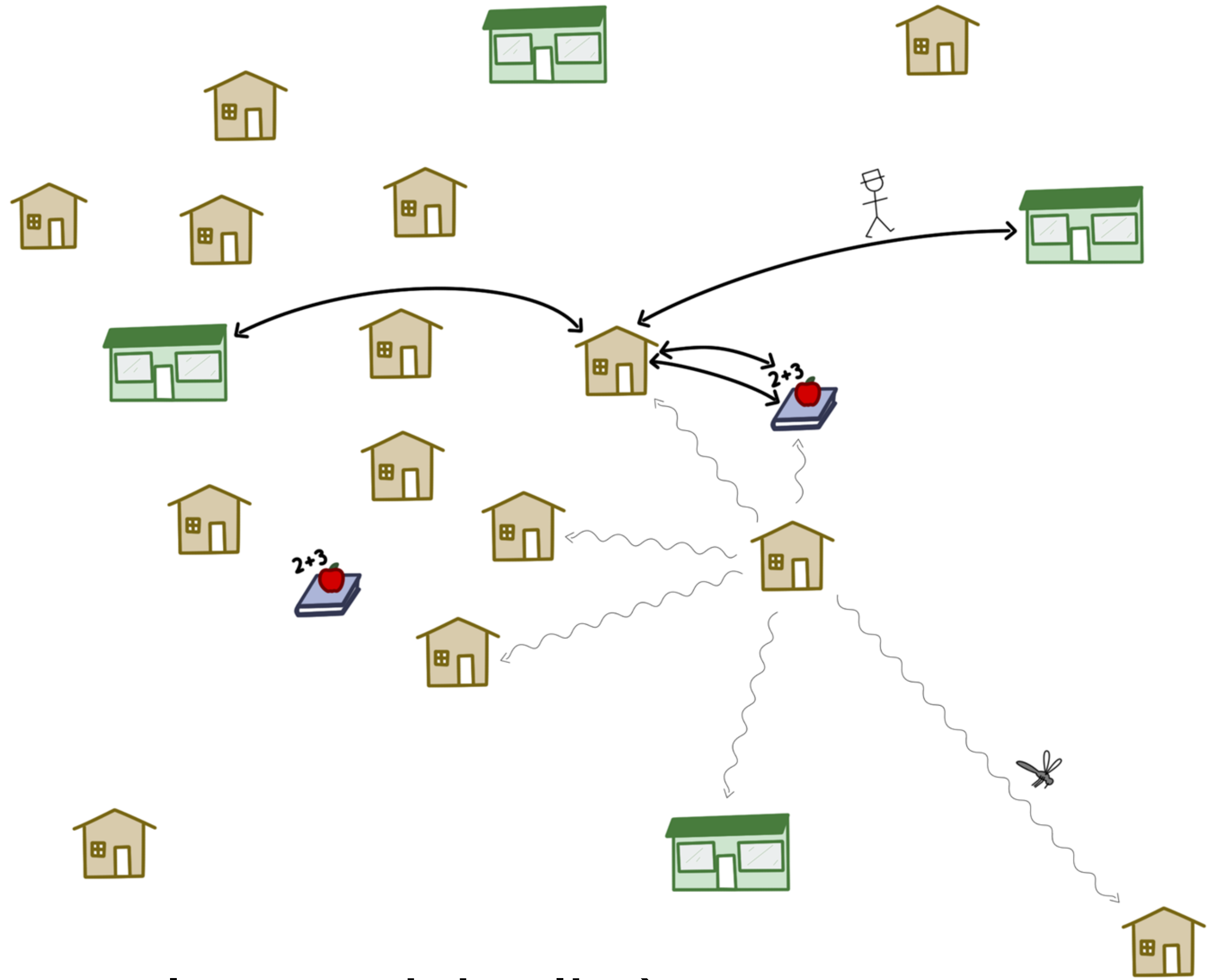
People

- 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

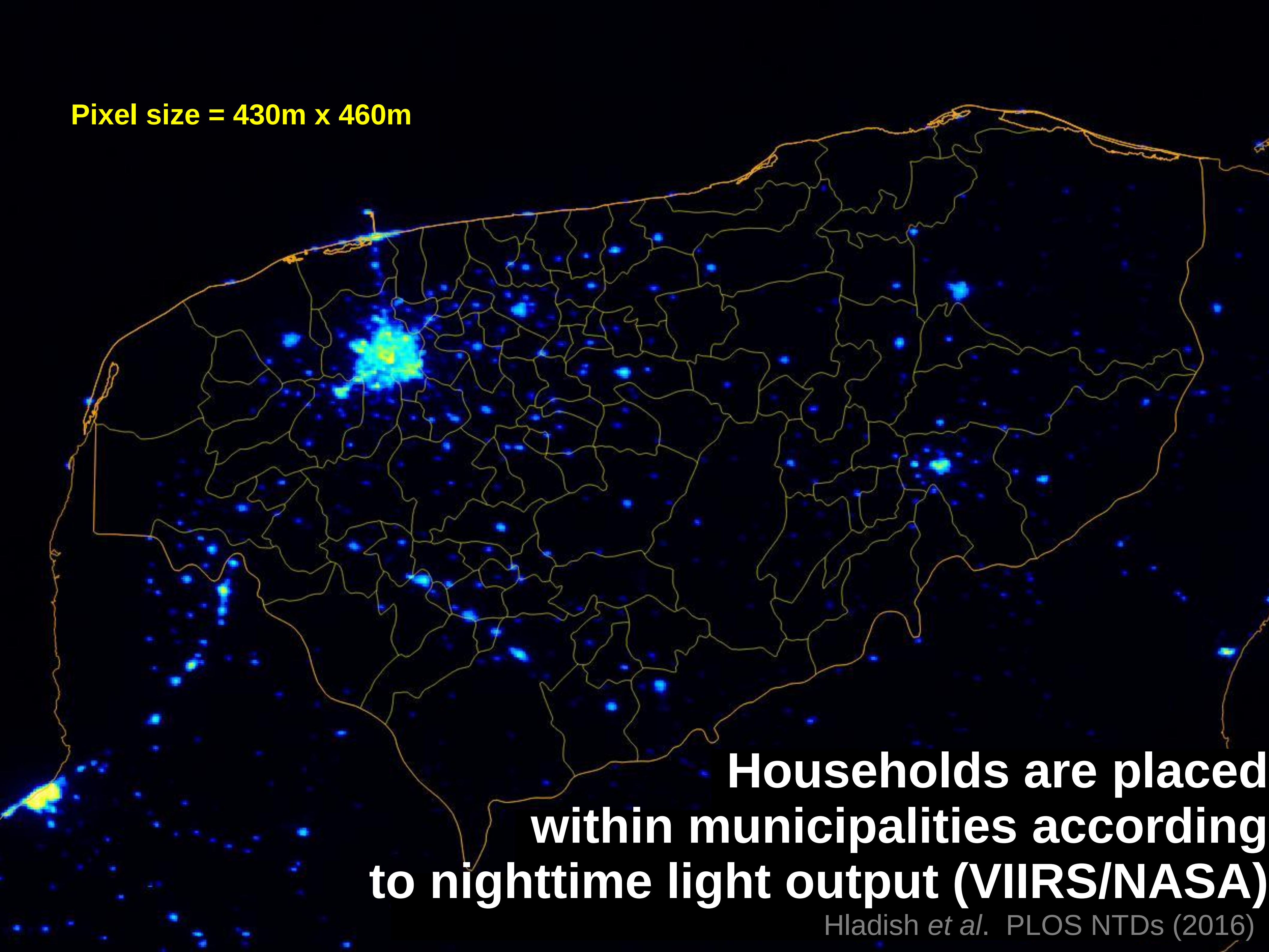
- 38% employed
- 28% in school
- 34% stay at home

376k Households (5% sample, municipality)

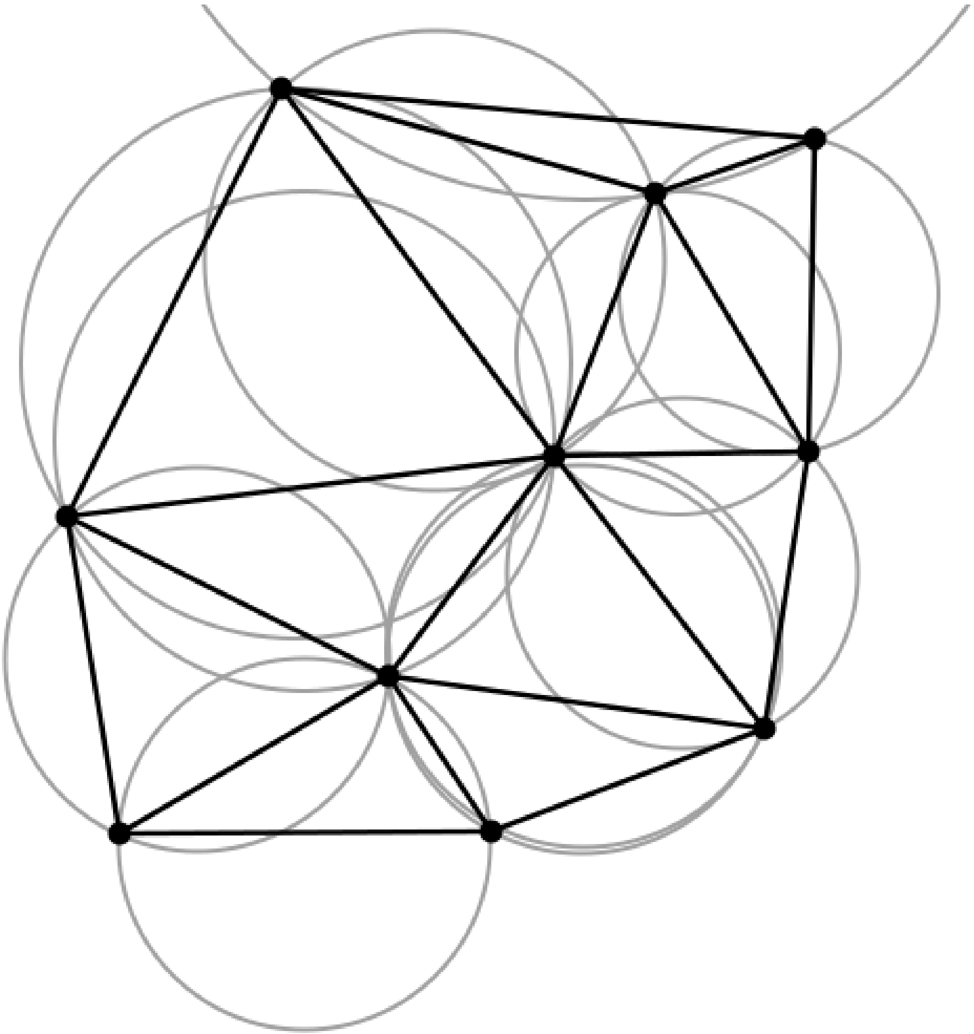
96k Workplaces (size, postal code)

3.4k Schools (postal code)

Hladish *et al*. PLOS NTDs (2016)

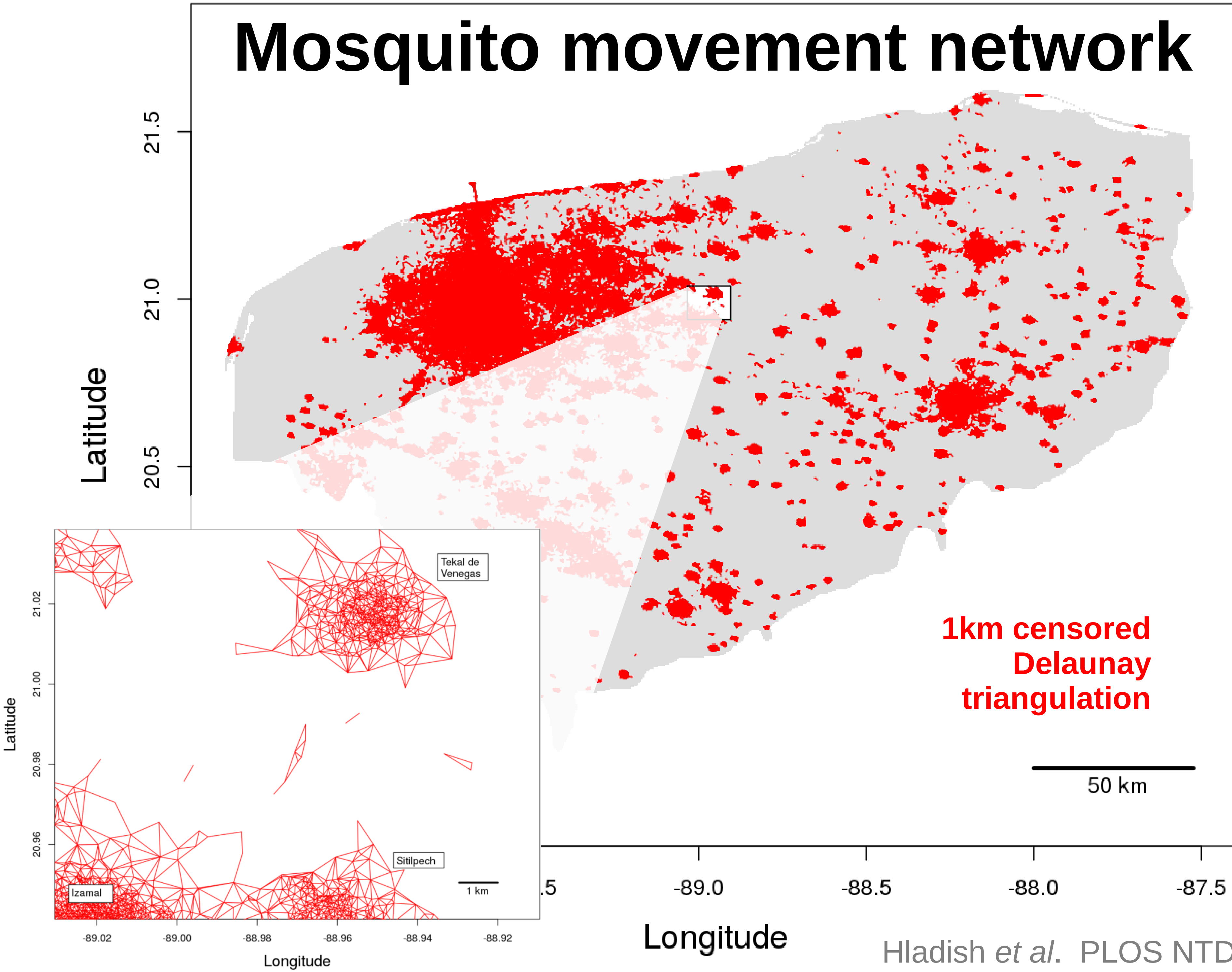

Pixel size = 430m x 460m
Households are placed
within municipalities according
to nighttime light output (VIIRS/NASA)
Hladish *et al*. PLOS NTDs (2016)

Mosquitoes movement:
Delaunay triangulation of locations



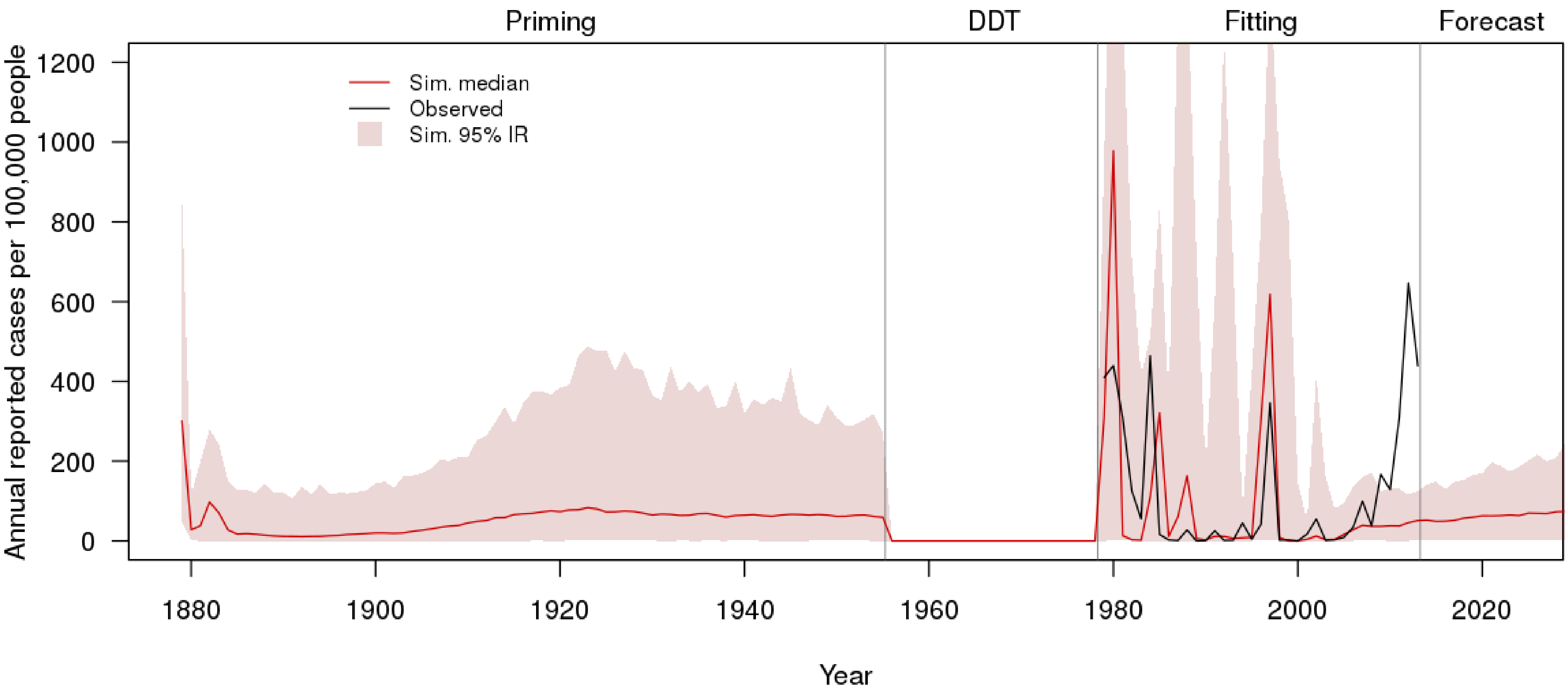
- Nodes are houses, workplaces and schools with (lat, long) coordinates
- Include all triangles whose circumscribed triangles contain no other nodes
- Remove edges longer than 1 km

Mosquito movement network



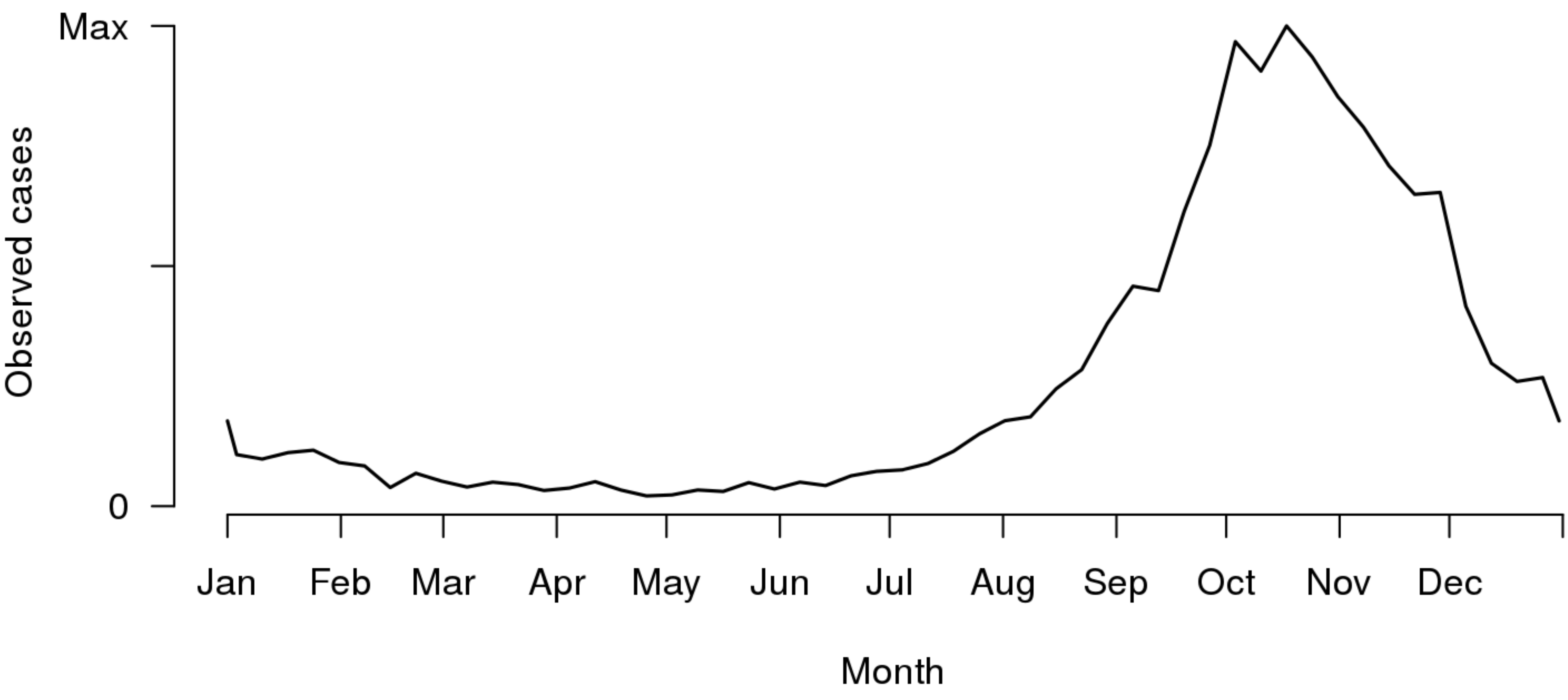
Hladish *et al*. PLOS NTDs (2016)

Reconstruct the past, forecast the future

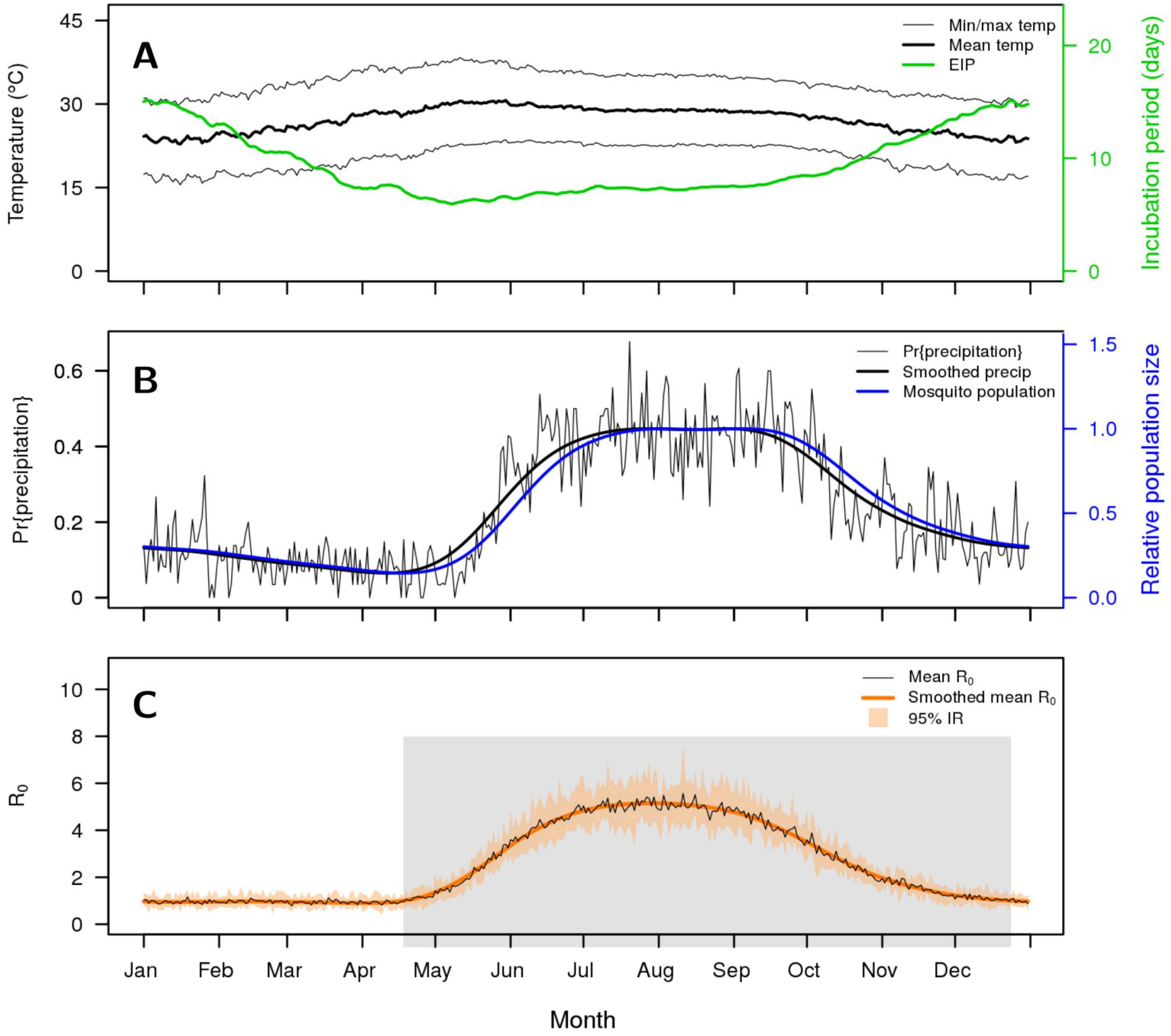


Hladish *et al*. PLOS NTDs (2016)

Observed seasonality (1995-2011)

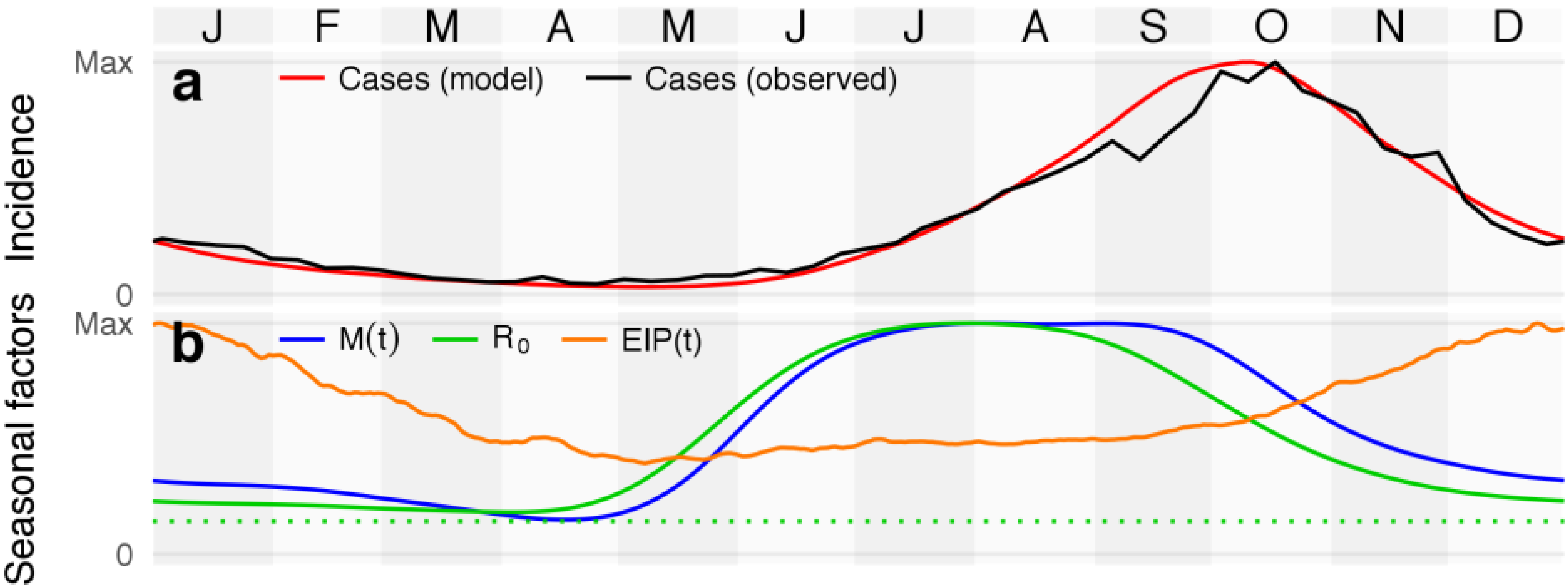


Hladish *et al*. PLOS NTDs (2016)



A
Min/max temp
Mean temp
EIP
Temperature (°C)
Incubation period (days)
45
30
15
0
20
10
0
B
Pr{precipitation}
Smoothed precip
Mosquito population
Pr{precipitation}
Relative population size
0.6
0.4
0.2
0
1.5
1.0
0.5
0.0
C
Mean R_0
Smoothed mean R_0
95% IR
R_0
10
8
6
4
2
0
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Month

Observed & modeled seasonality (1995-2015)



Indoor residual spraying*

Coverage: Treat 25/50/75% of houses per year

Efficacy: 80% reduction in equilibrium pop size in treated houses

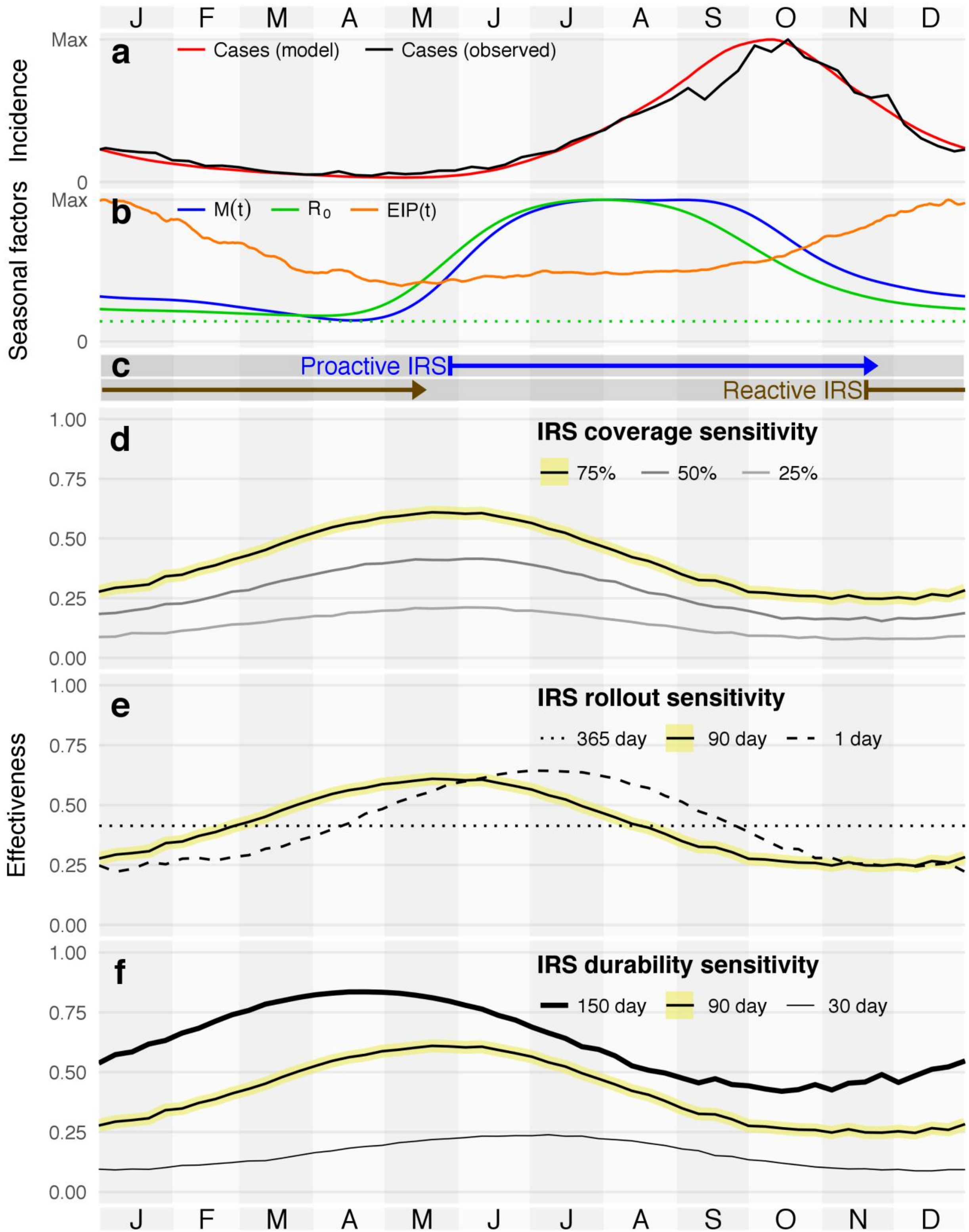
- Corresponds to 13% daily mortality due to IRS

Treatment lasts 90 days

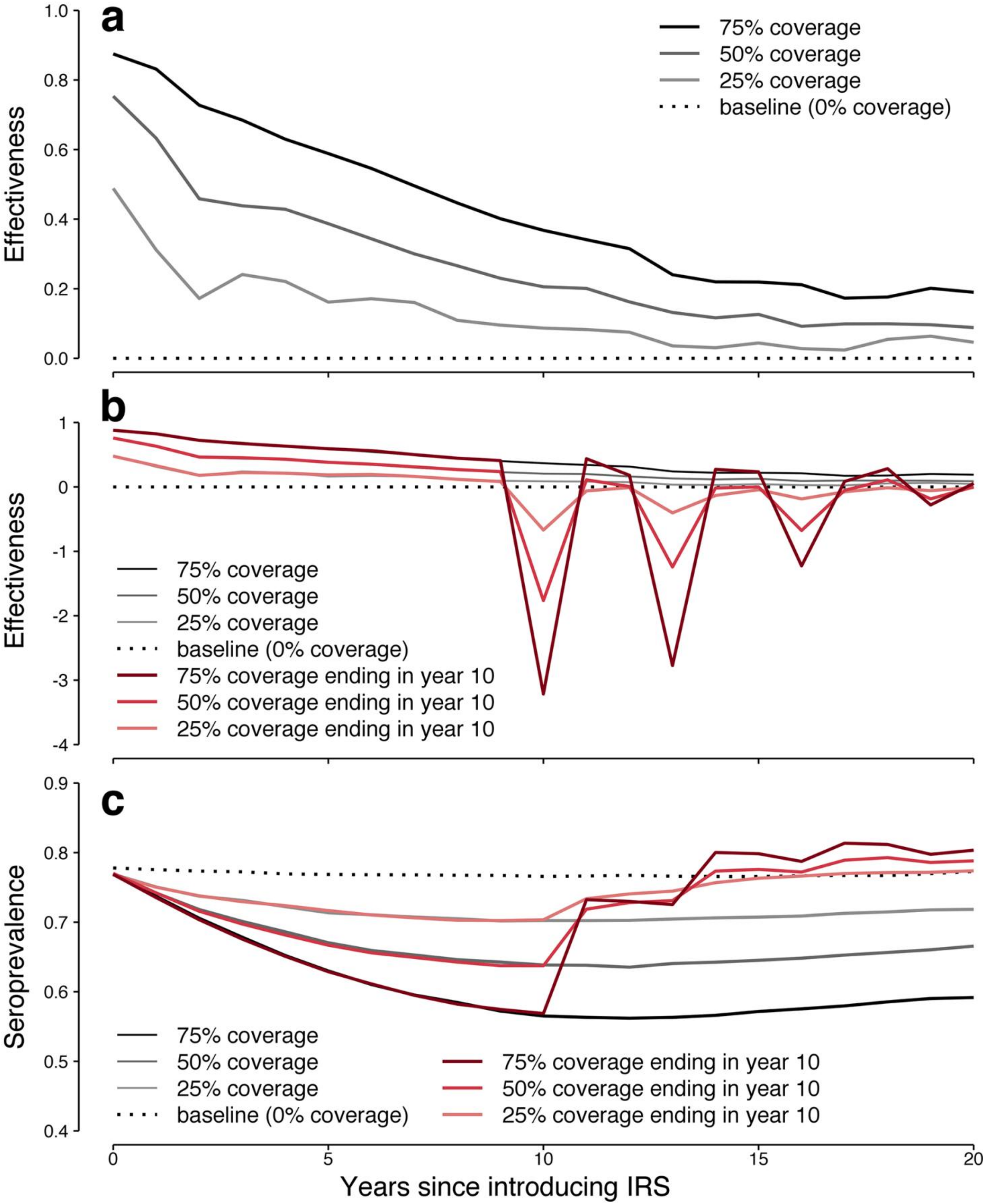
Campaigns last 1/90/365 days

52 different start dates (1 and 90 day campaigns)

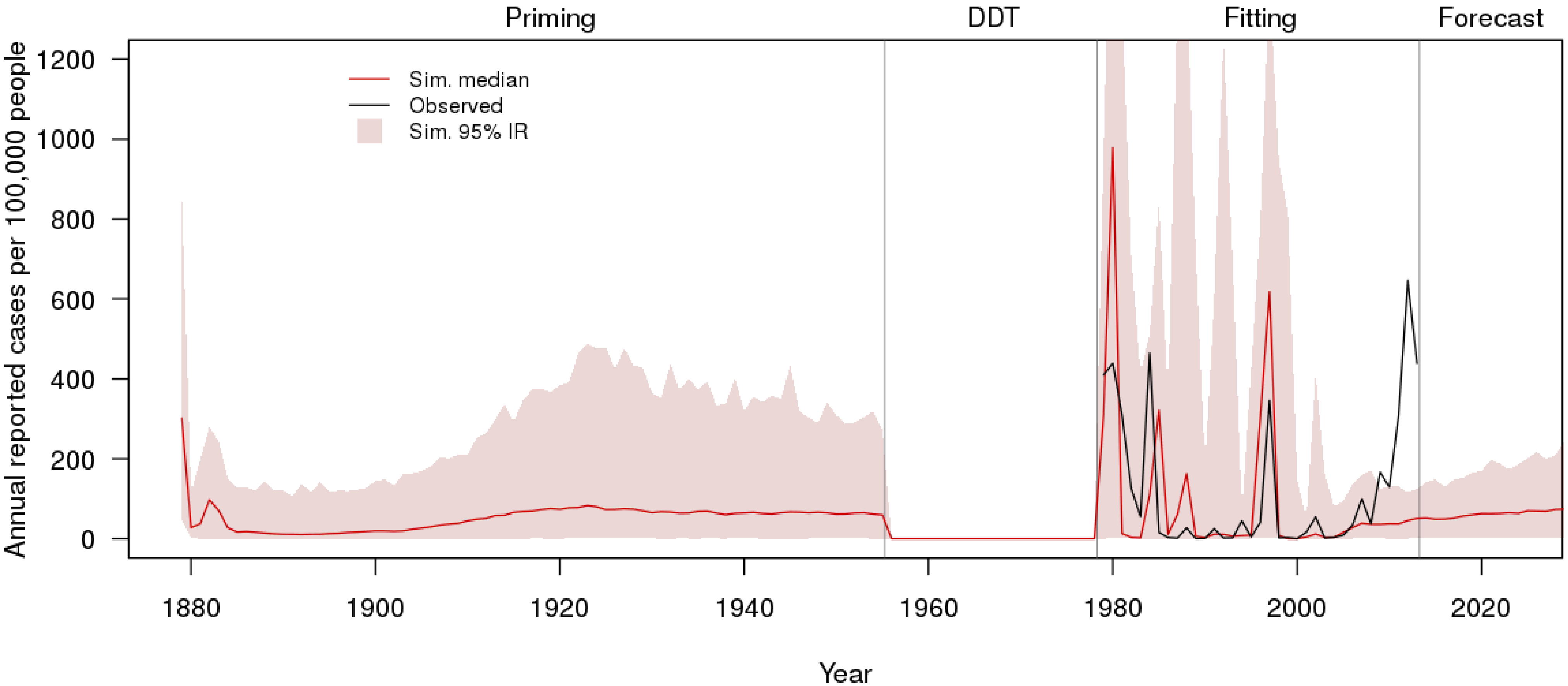
*Efficacy & durability based on Vazquez-Prokopec et al, *Science Advances* (2017)



J F M A M J J A S O N D
Max
a
Incidence
0
Cases (model)
Cases (observed)
Max
b
Seasonal factors
0
M(t)
R_0
EIP(t)
c
Proactive IRS
Reactive IRS
d
IRS coverage sensitivity
75%
50%
25%
e
IRS rollout sensitivity
365 day
90 day
1 day
f
IRS durability sensitivity
150 day
90 day
30 day
Effectiveness
1.00
0.75
0.50
0.25
0.00

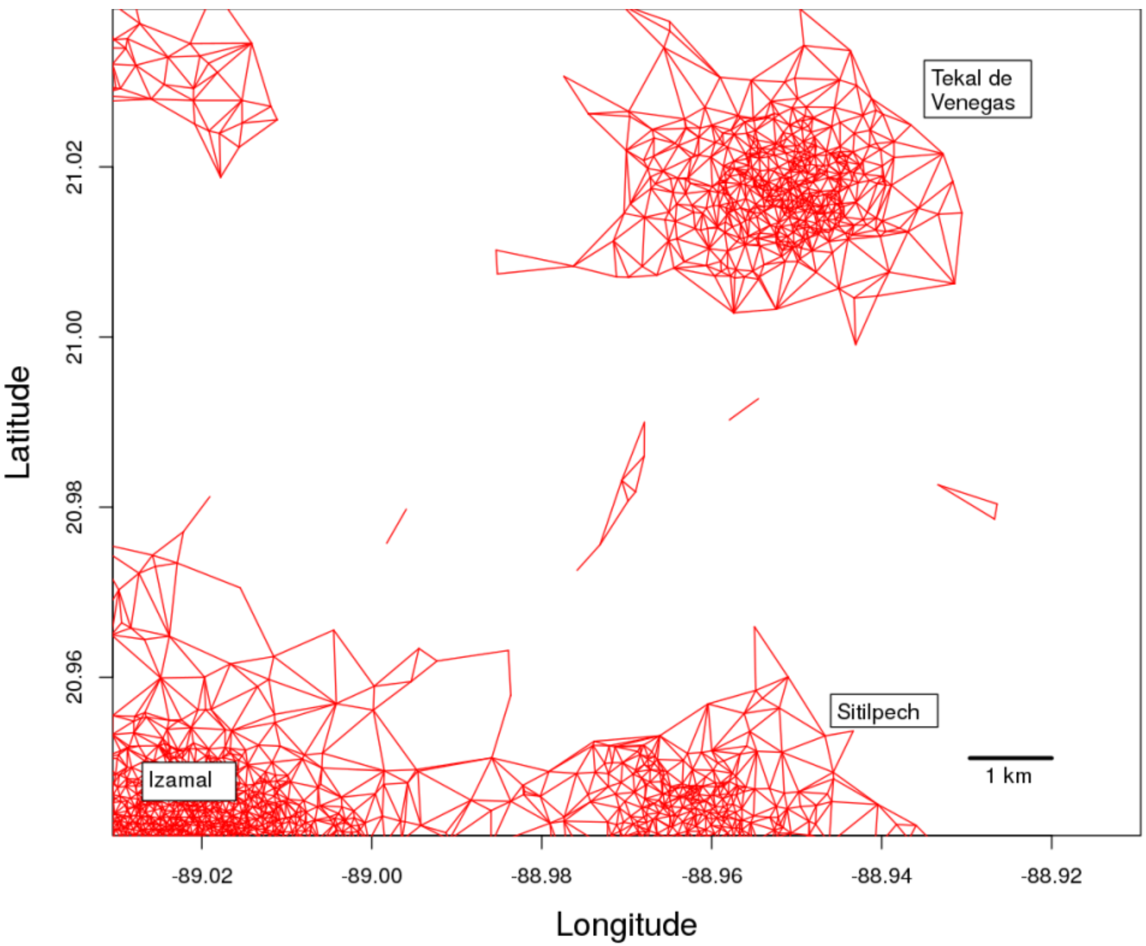

a
b
c
75% coverage
50% coverage
25% coverage
baseline (0% coverage)
75% coverage ending in year 10
50% coverage ending in year 10
25% coverage ending in year 10
Effectiveness
Seroprevalence
Years since introducing IRS

What happened in ~1980 and ~2012?



- Missing data from 1970's?
- Spatial distribution of *Aedes*

Proposed mosquito spread model



- Locations each have a distinct, seasonally varying carrying capacity
- Mosquitoes could spread along Delaunay network, seeding new locations
- Long distance mosquito movement enabled by humans

ToDo:

- Implement mosquito spread model
- Re-fit using AbcSmc to historical data
- Project effectiveness of combined strategies
- Simulate IRS trial design for Yucatan