Serosurveillance

Henrik Salje

University of Cambridge

20 June 2022

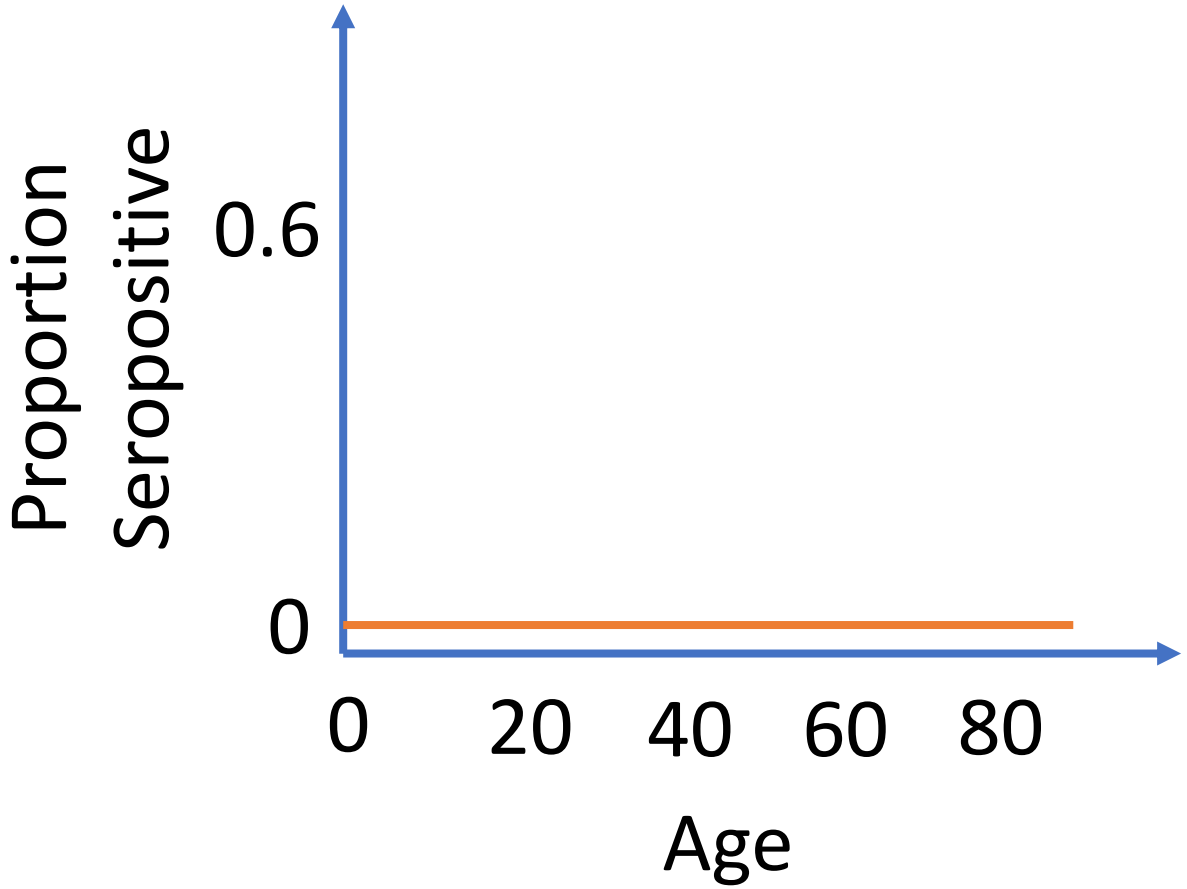
What is serosurveillance?

Why is it useful as compared to case-based surveillance?

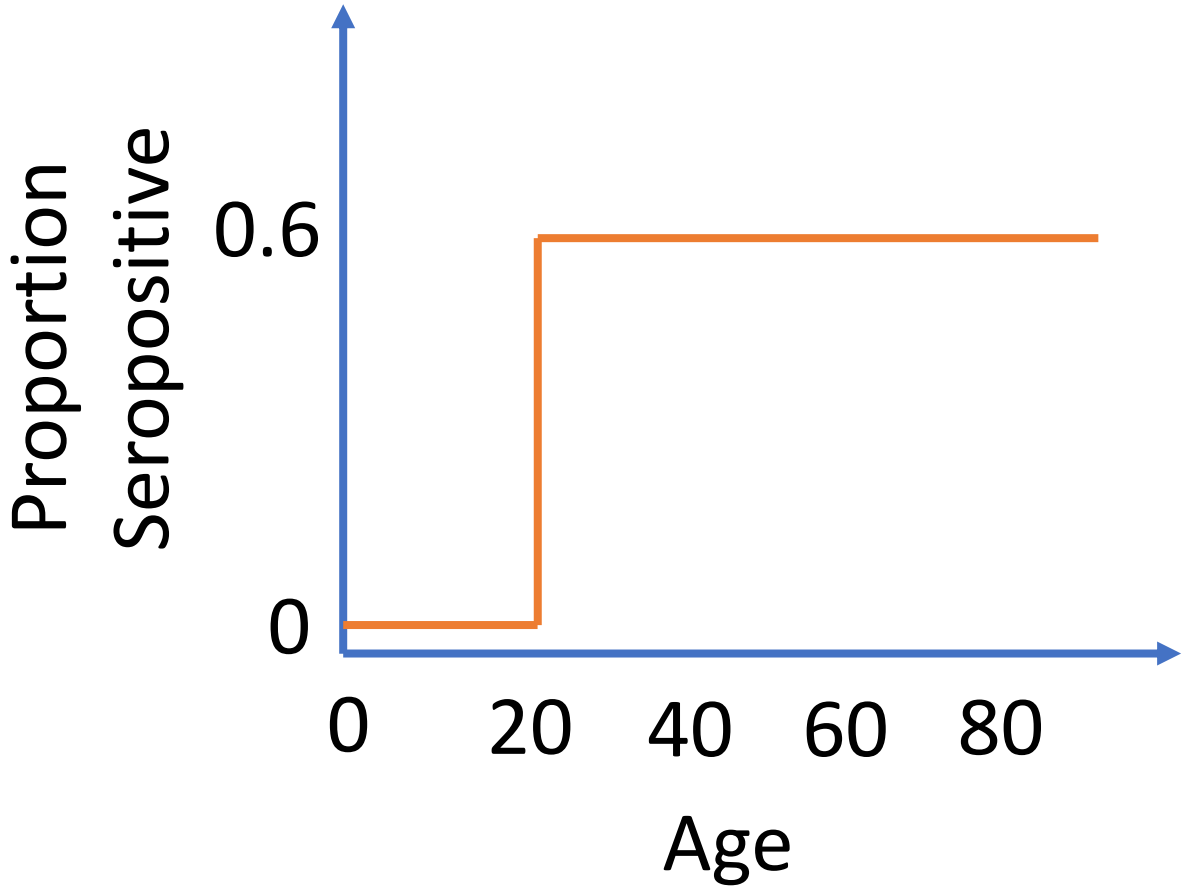
Potential sources of sera

Different assays

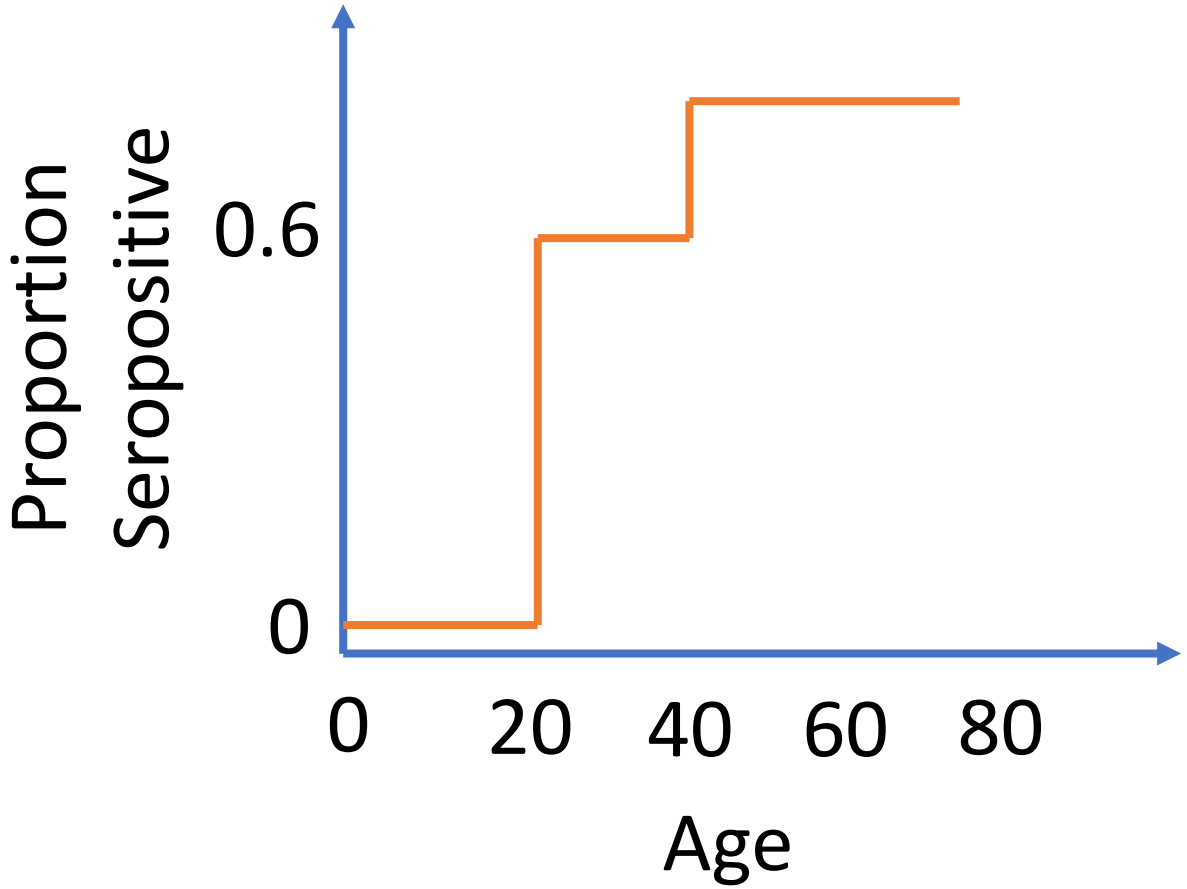
How would you interpret this?



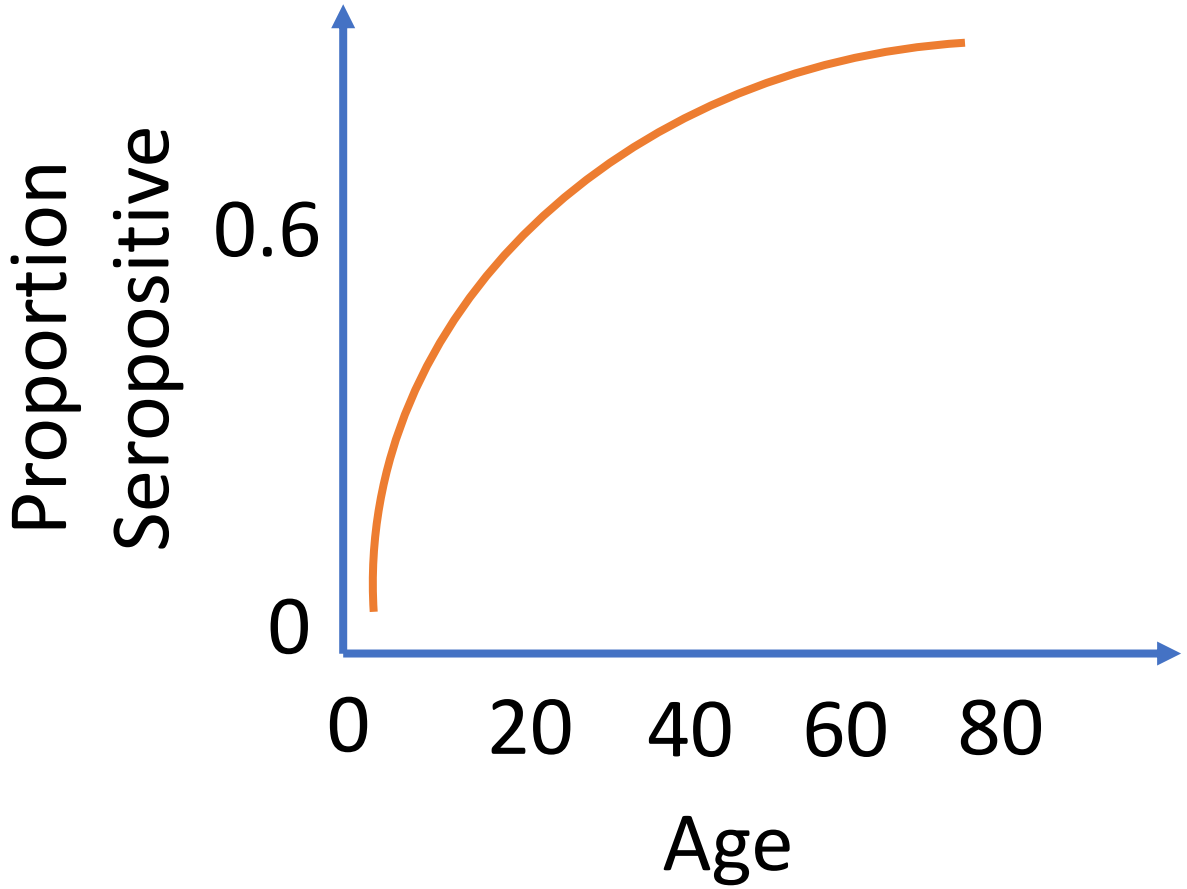
How would you interpret this?



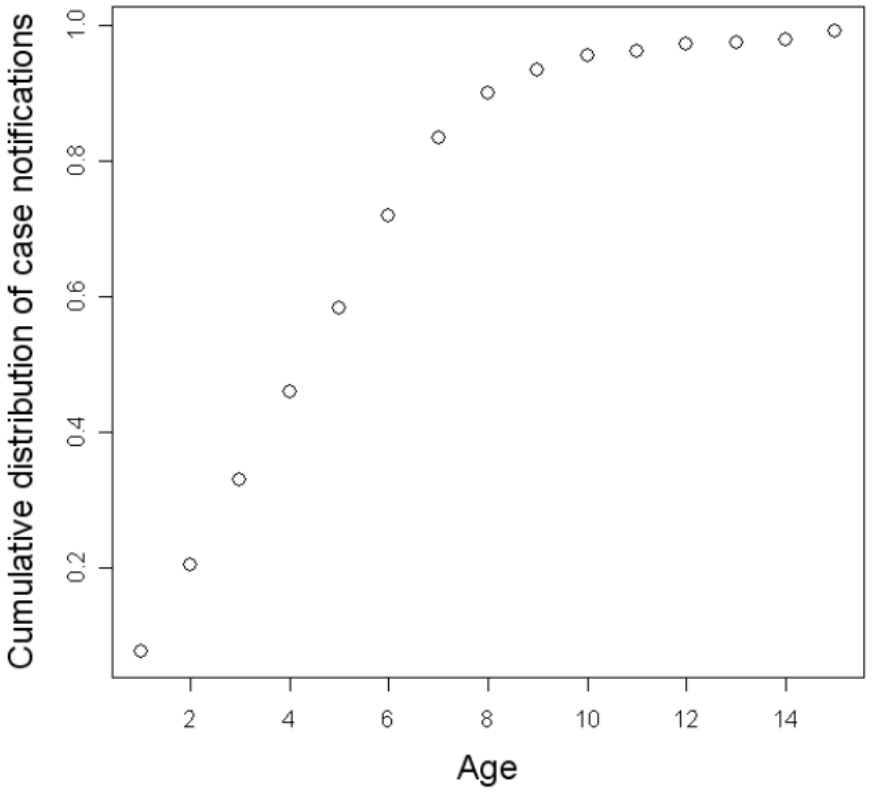
How would you interpret this?



How would you interpret this?



Age-specific Seroprevalence

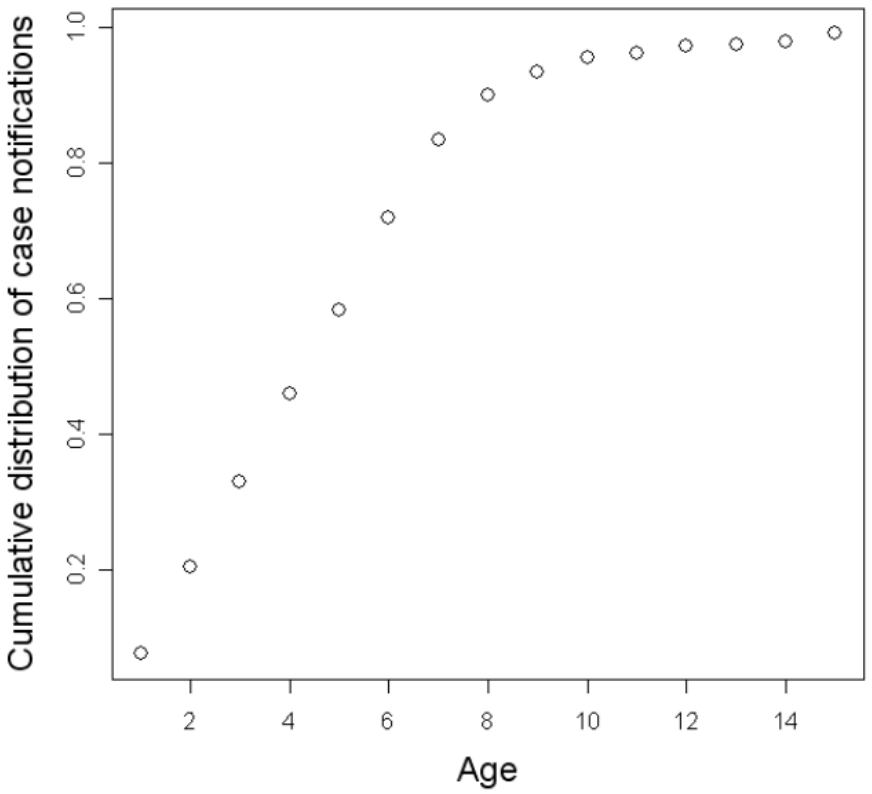


- Seroprevalence of measles in Aberdeen, UK
  - age-specific seroprevalence
  - this can be used to learn additional details about the disease dynamics
- What is the force of infection for this group?

Force of Infection

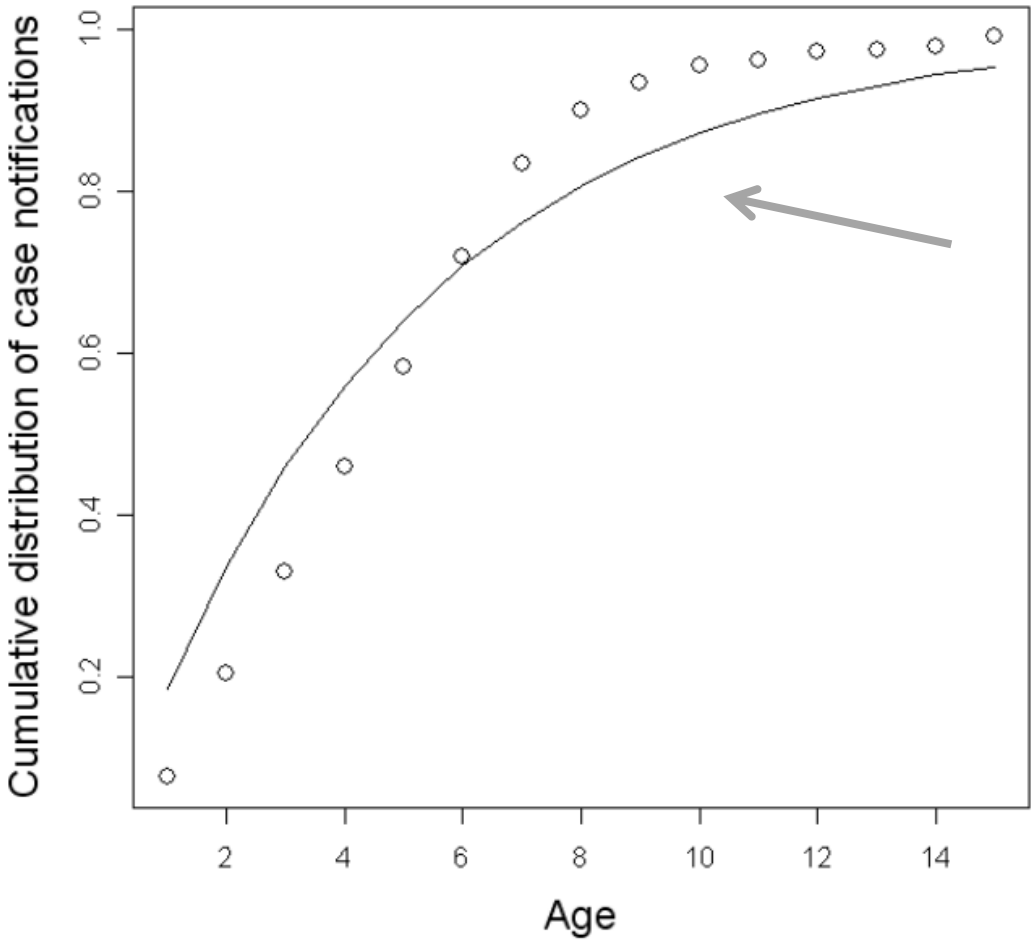
- Force of infection
  - FOI
  - Hazard of infection
  - the per capita rate at which people acquire infection
  - usually symbolized with λ
  - in an SEIR model, equivalent to βI

FOI for Measles in Aberdeen



What is the force of infection for this group?

FOI for Measles in Aberdeen



- What is the force of infection for this group?
- If we fit a constant force of infection, we see the fit is not very good
  - $\lambda=0.21$
  - 21% chance of becoming infected each year

Force of Infection

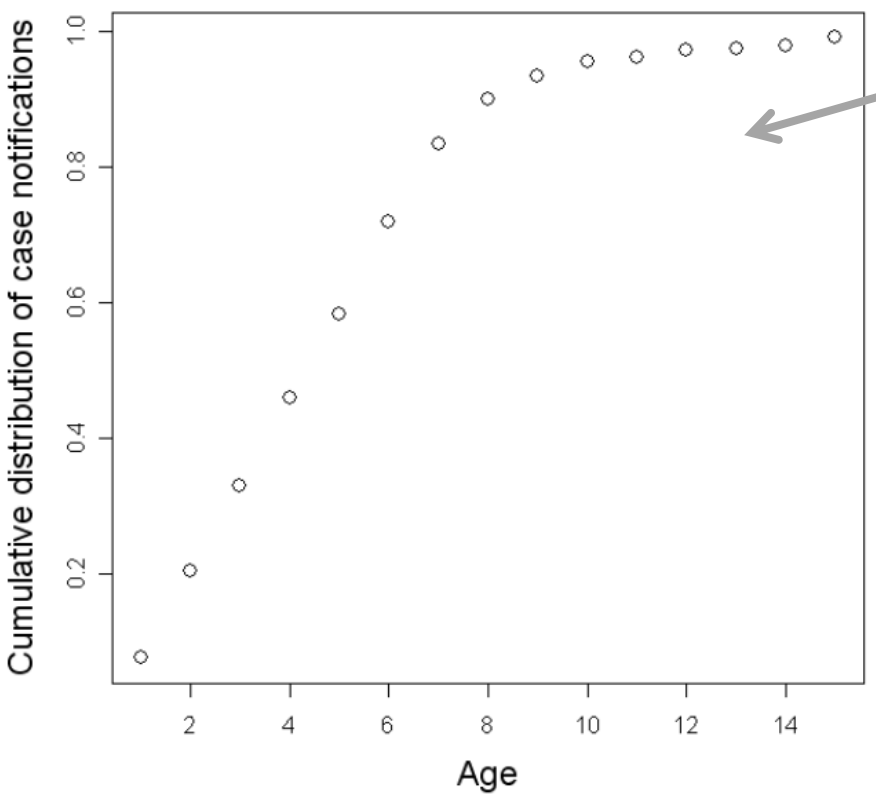
- Force of infection
  - the per capita rate at which people acquire infection
- FOI unlikely to be constant with age
  - infection risk changes with age
  - school entry, sexual activity, specific job exposures
- FOI likely to change over time
  - changes in contact rates, pathogen circulation

Force of Infection

- Force of infection
  - the per capita rate at which people acquire infection
- FOI unlikely to be constant with age
  - infection risk changes with age
  - school entry, sexual activity, specific job exposures
- FOI likely to change over time
  - changes in contact rates, pathogen circulation

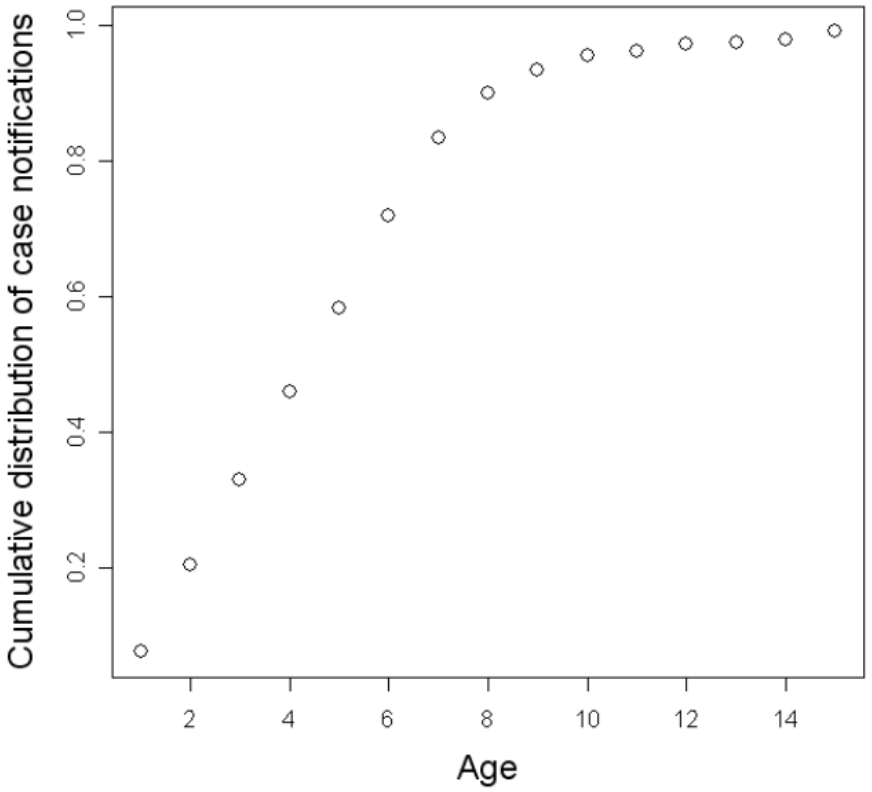
- These factors indicate that constant FOI is a poor assumption
- Age-specific FOI would be much better and age-specific seroprevalence can help estimate this!

Force of Infection



- As age increases, the proportion who are seronegative decreases
  - we expect more people to become seropositive over time
  - proportion of individuals who are **seronegative** at a given age (x(a)) is related to force of infection λ

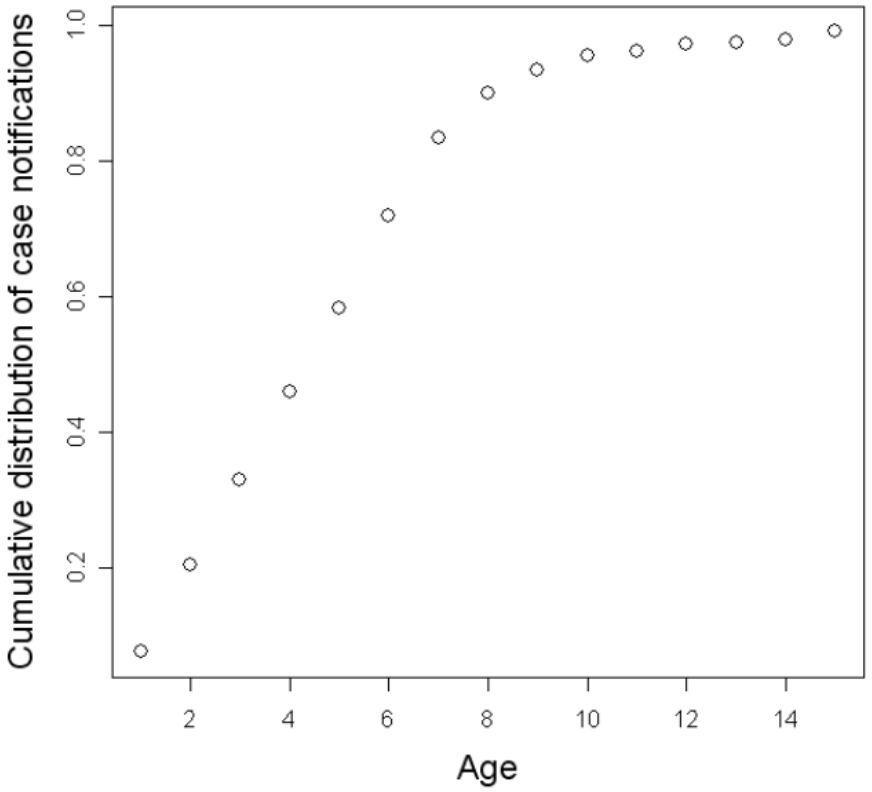
Force of Infection



As age increases, the proportion who are seronegative decreases

- we expect more people to become seropositive over time
- proportion of individuals who are seronegative at a given age (x(a)) is related to force of infection λ
  - $x(a) = e^{-\lambda a}$

Force of Infection



- As age increases, the proportion who are seronegative decreases
  - we expect more people to become seropositive over time
  - proportion of individuals who are seronegative at a given age (x(a)) is related to force of infection λ
    - $x(a) = e^{-\lambda a}$
  - proportion of individuals who are **seropositive** at a given age (y(a)) can then be calculated
    - $y(a) = 1 - x(a)$

Force of Infection

- Cumulative incidence by age (F(a)) is equivalent to seroprevalence
  - assumes permanent immunization
  - $F(a) = 1 - e^{-\lambda a} \approx y(a)$

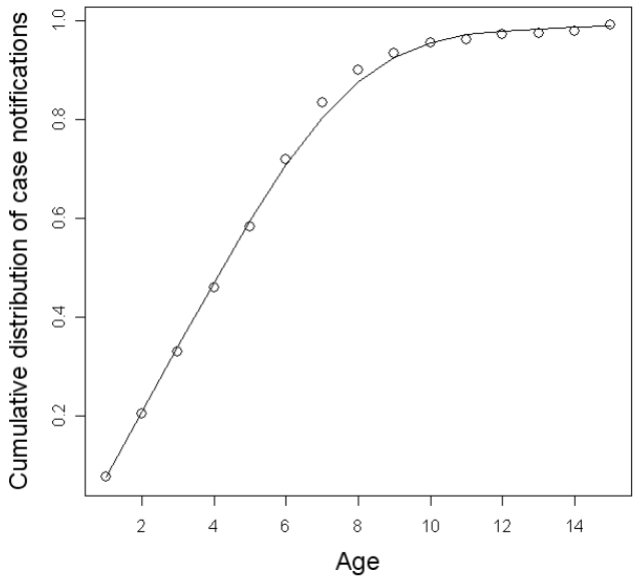
- As age increases, the proportion who are seronegative decreases
  - we expect more people to become seropositive over time
  - proportion of individuals who are seronegative at a given age (x(a)) is related to force of infection λ
    - $x(a) = e^{-\lambda a}$
  - proportion of individuals who are **seropositive** at a given age (y(a)) can then be calculated
    - $y(a) = 1 - x(a)$

Force of Infection

- Cumulative incidence by age (F(a)) is equivalent to seroprevalence
  - assumes permanent immunization
  - $F(a) = 1 - e^{-\lambda a} \approx y(a)$

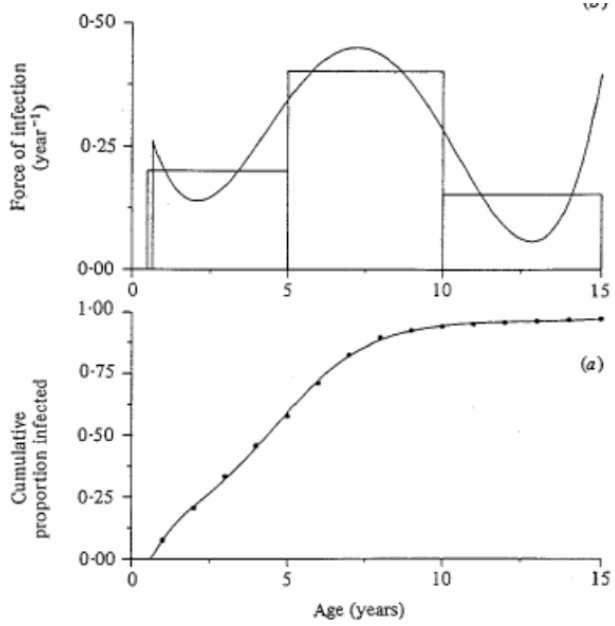
- We can use a binomial (statistical) framework to relate the seroprevalence to force of infection
- we are estimating a joint likelihood
- by using this statistical method, we can:
  - account for the different sample sizes among age groups
  - calculate confidence intervals for our estimate of FOI

FOI for Measles in Aberdeen



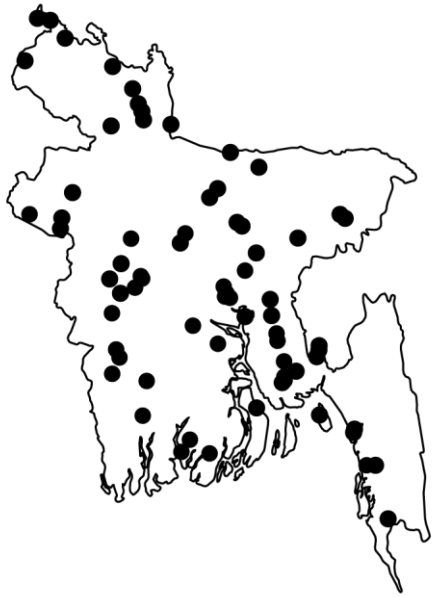
- What is the force of infection for this group?
- If we fit age-specific force of infection, we see the fit is excellent
  - three separate FOIs for three age groups

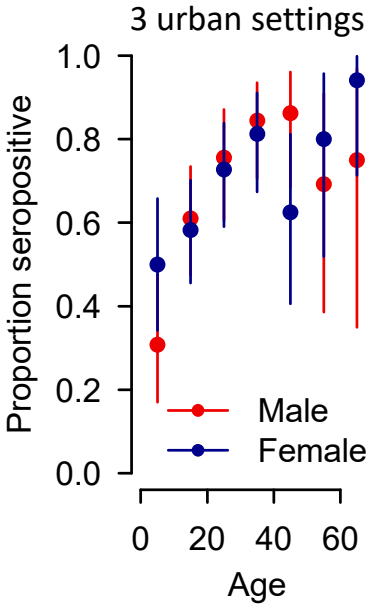
FOI for Measles in Aberdeen

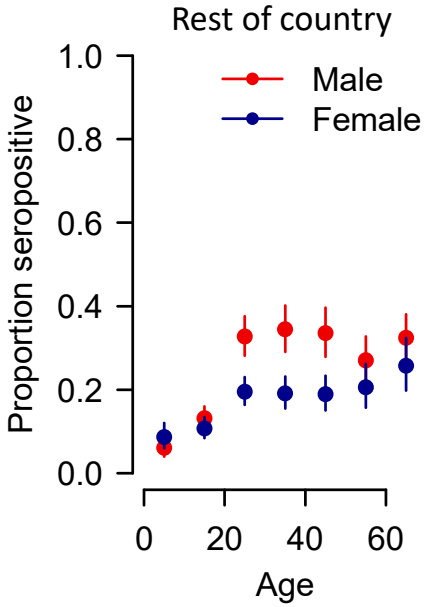


- What is the force of infection for this group?
- If we fit age-specific force of infection, we see the fit is excellent
  - three FOIs for three age groups
  - pre-school (<5 years old): 0.18
  - early school (5-10 years old): >0.3
  - late school (10-15 years old): <0.18

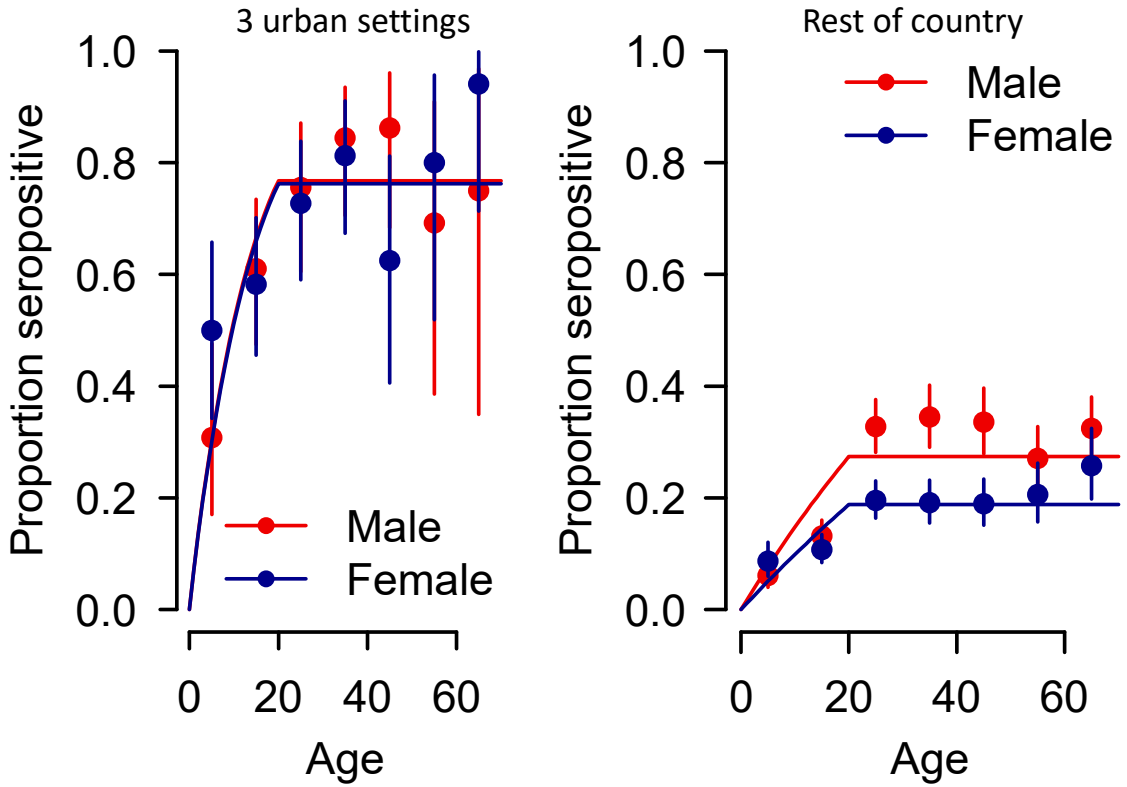
Serosurveillance for dengue virus in Bangladesh





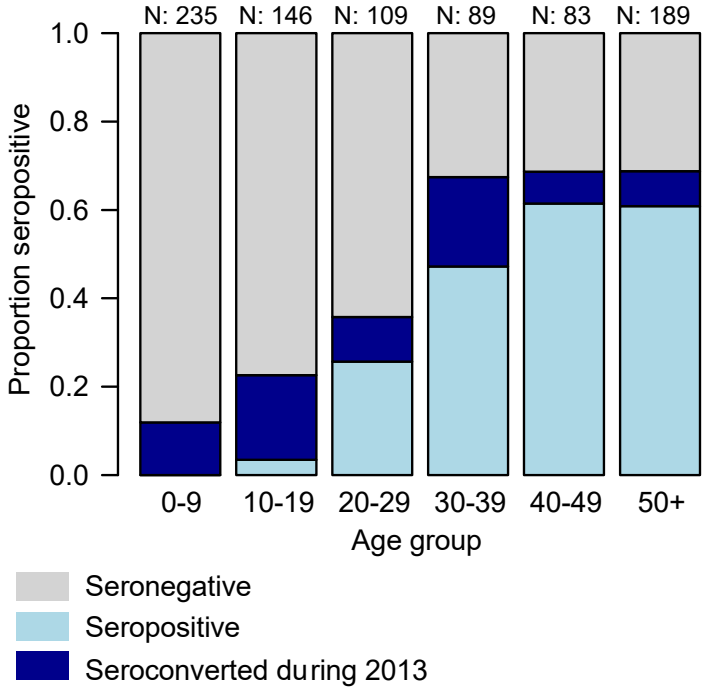


What did we assume here to fit these FOIs for DENV in Bangladesh?



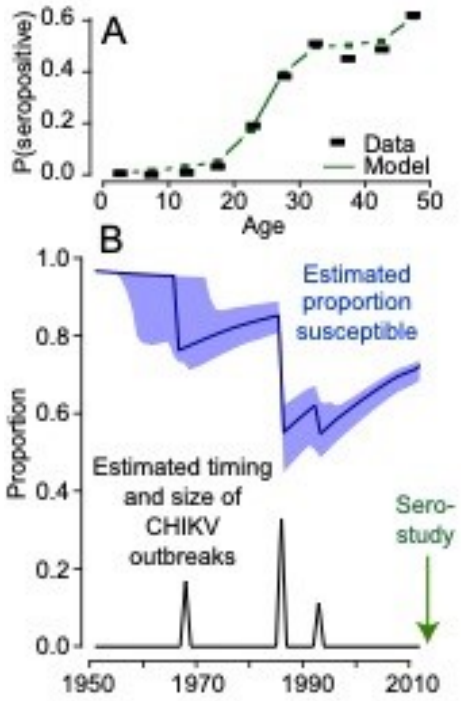
- Using serocatalytic models, we estimated that 40 million [34.3–47.2] people have been infected nationally (24% population), with 2.4 million ([1.3–4.5]) annual infections.
- 0.6% of participants reported having had dengue, of which half didn't actually have antibodies

We can also identify more complex past infection histories – example with chikungunya



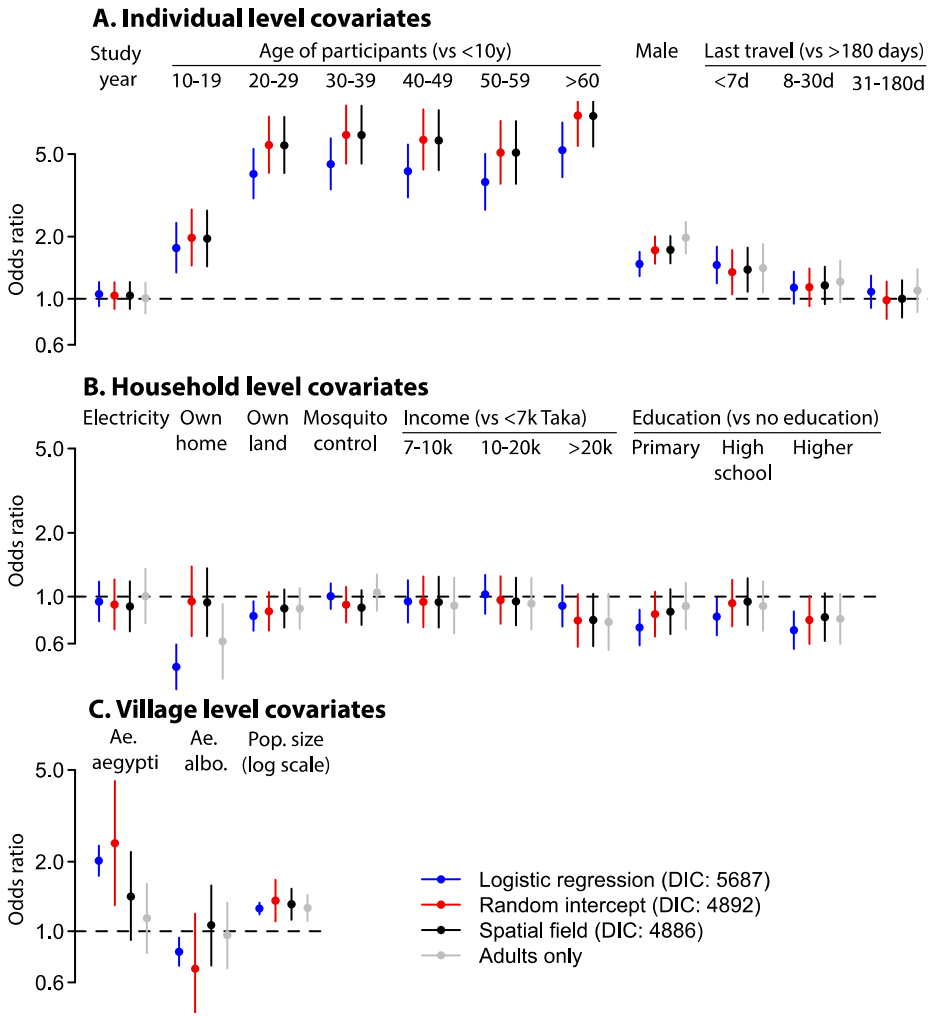
- In 2012 AFRIMS set up a cohort for chikungunya in Cebu, Philippines.
- No case of chikungunya had ever been reported in Cebu

We can also identify more complex past infection histories

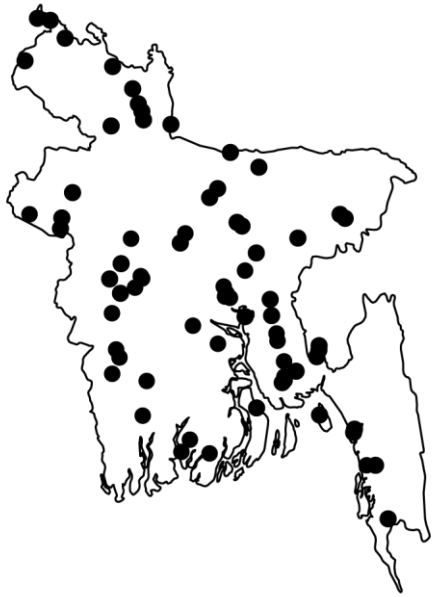


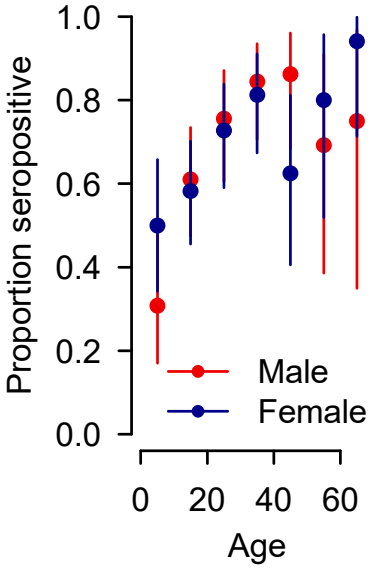
- This single seroprevalence study could identify that there had been three outbreaks in Cebu
- Using information on how the demography has changed in Cebu we could identify how many people had ever been infected (~350,000) and the changing level of immunity in the population.

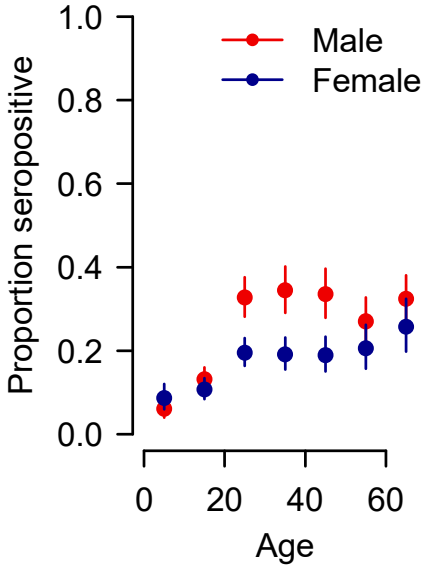
We can identify risk factors for infection



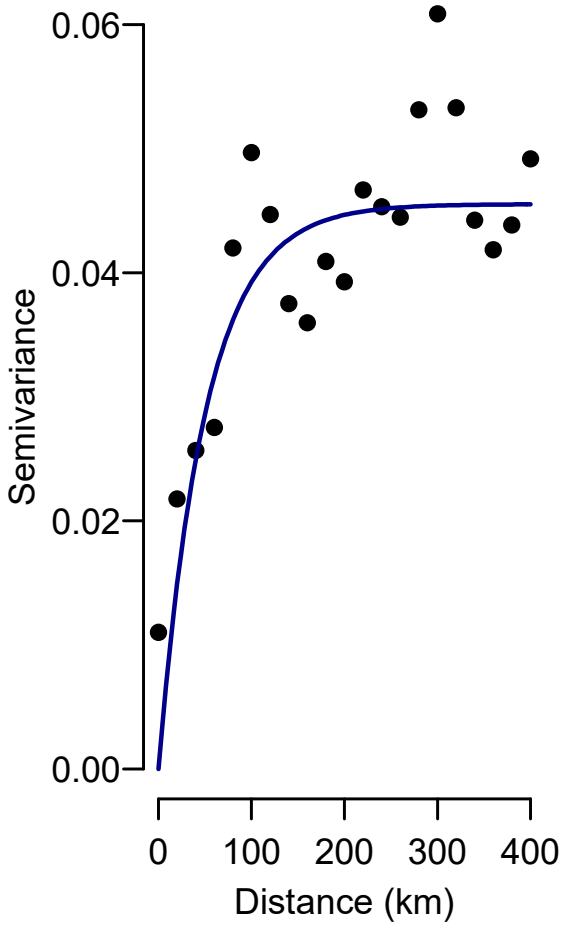
What about places we didn't sample?

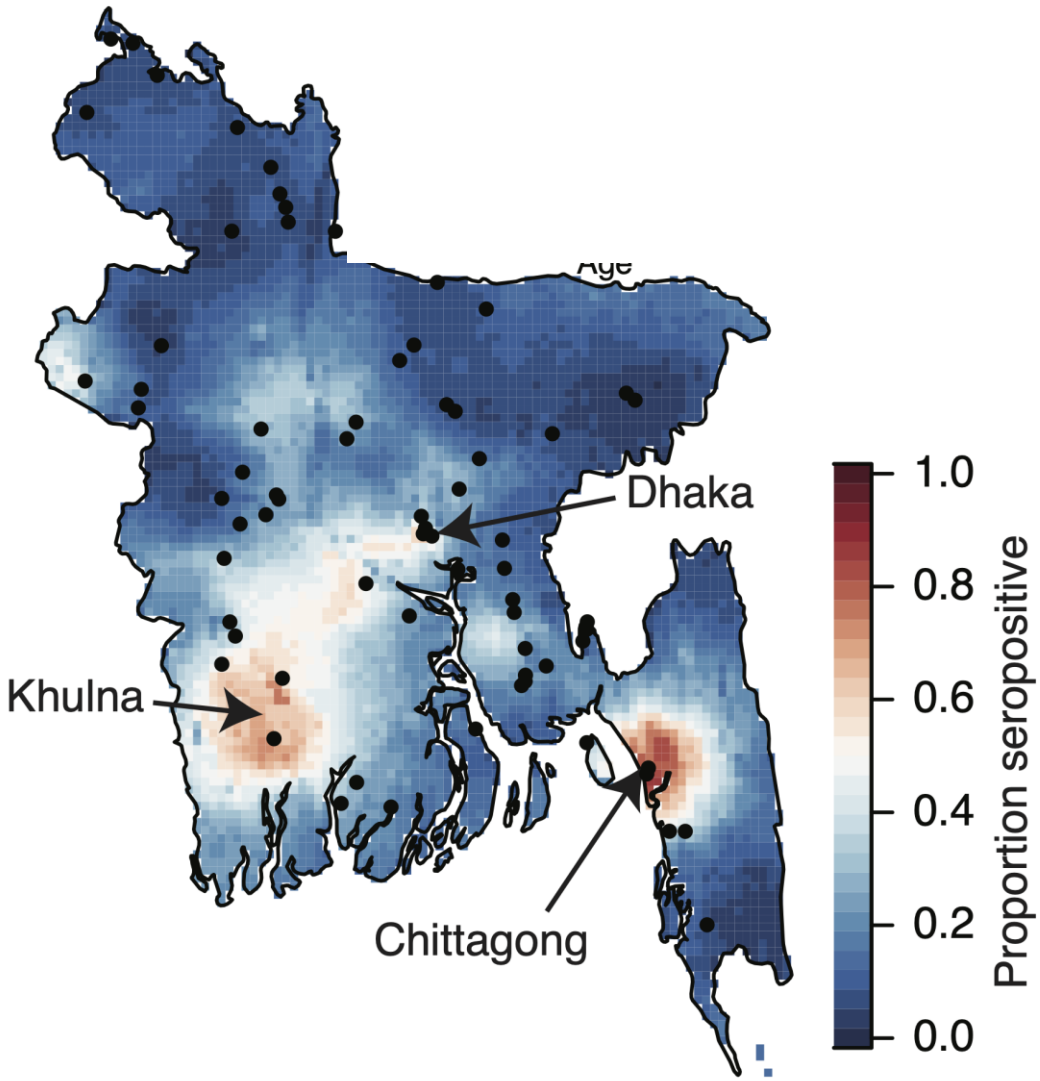




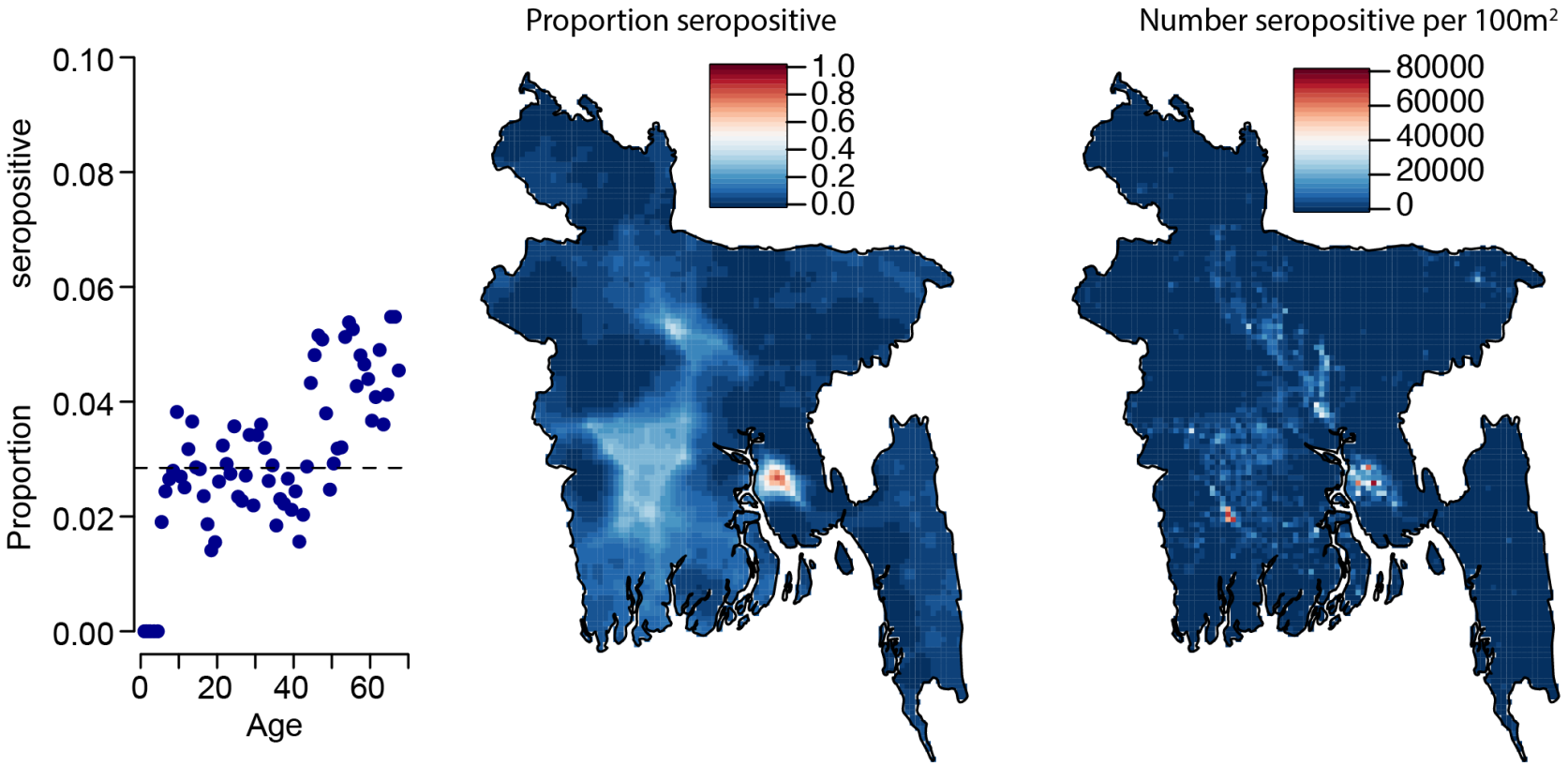


We can use spatial correlation

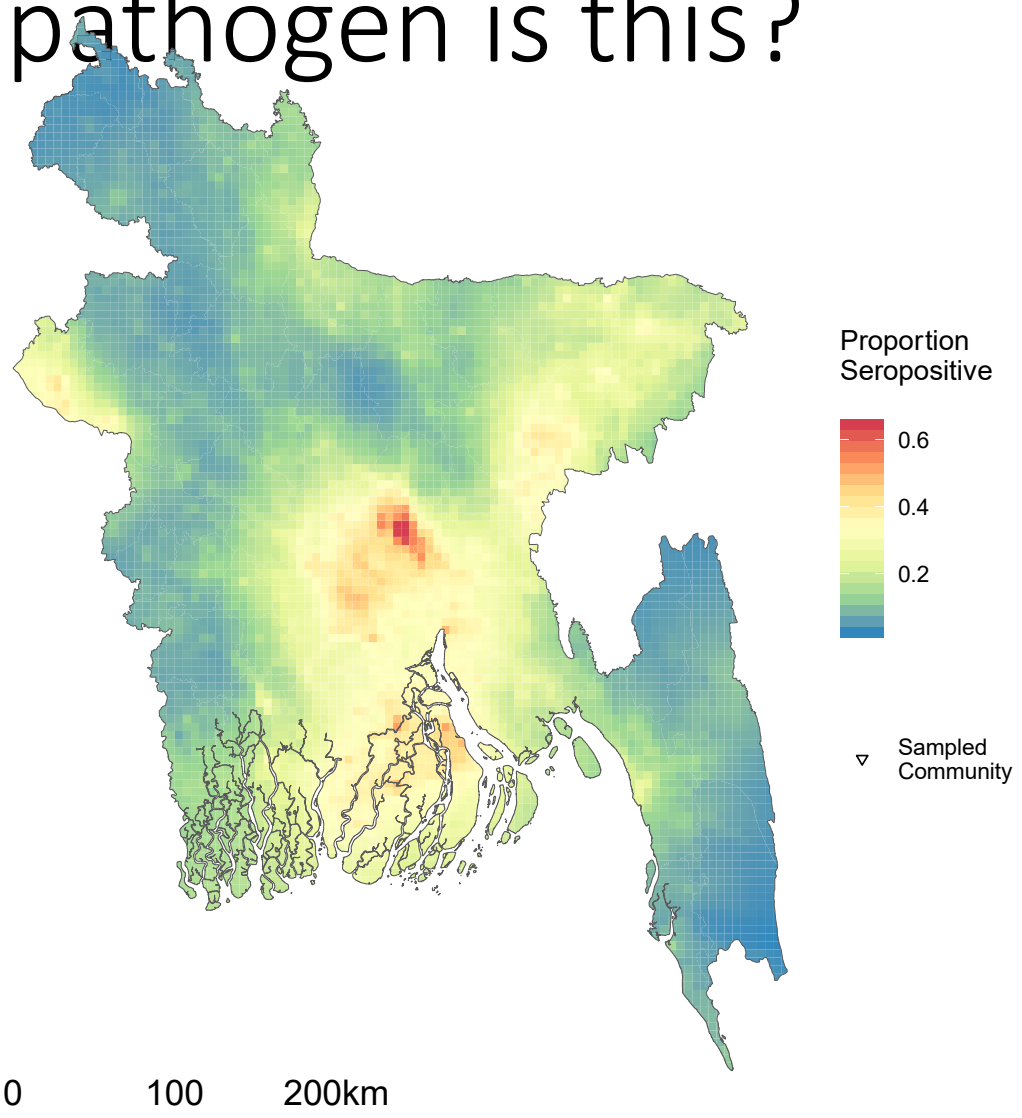



Dhaka
Khulna
Chittagong
1.0
0.8
0.6
0.4
0.2
0.0
Proportion seropositive

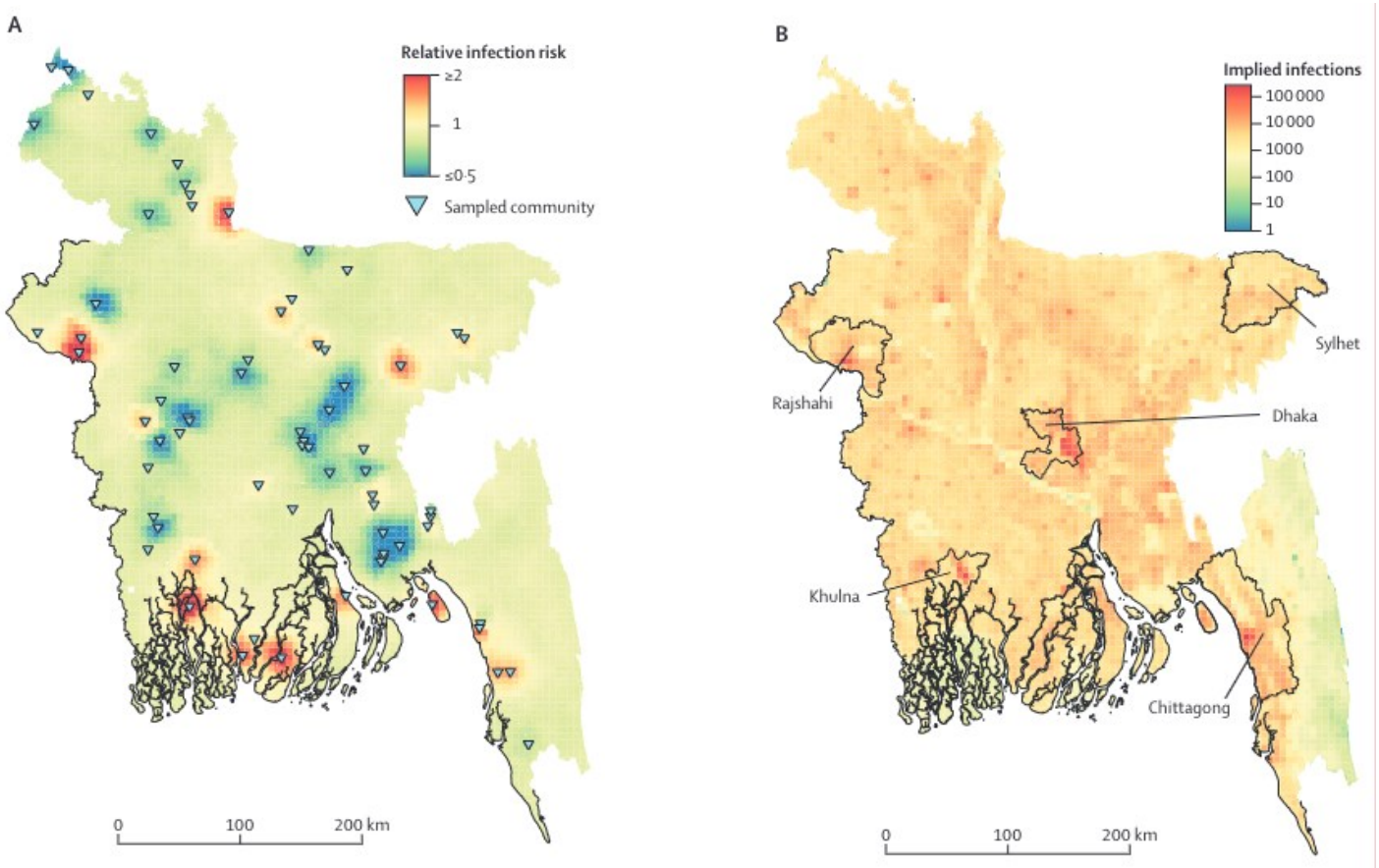
What pathogen is this?



What pathogen is this?

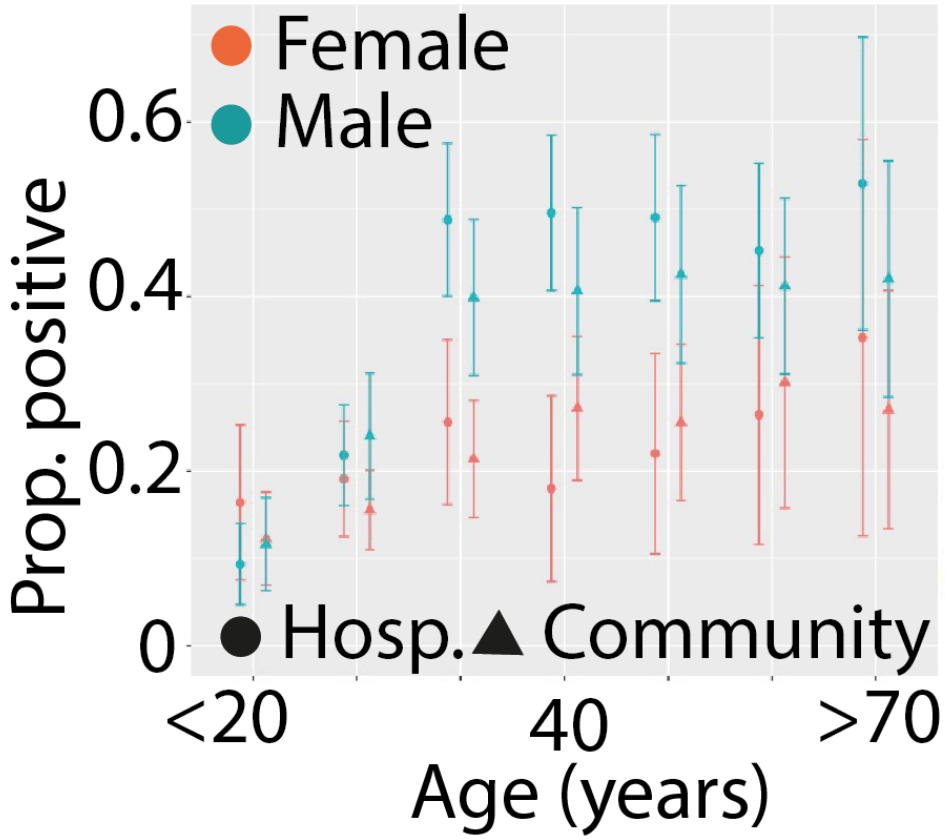


What pathogen is this?



Alternatives to community-based studies

What about using sera anyway collected in hospitals?



Conclusions

- Serosurveillance is an excellent way of understanding underlying level of infection
- Mathematical models can help maximise inferences, including the development of risk maps
- Need careful consideration of:
  - How antibodies behave post infection
  - Cross-reactivity
  - Biases in source of samples