

# Lecture 6

## Inferring transmission dynamics from seroprevalence data

May 23<sup>rd</sup>, 2025

Seroanalytics Training  
Blantyre, Malawi

# Lecture Outline

- Understanding what age-specific patterns of seroprevalence can tell us about past transmission
- Non-endemic transmission
  - Timing and magnitude of past outbreaks
- Endemic transmission
  - Force of infection

# Population transmission dynamics

*How has the pathogen spread in a given population?*

# Population transmission dynamics

*How has the pathogen spread in a given population?*

## Endemic

- Sustained/persistent transmission
- Can have epidemic or seasonal cycles

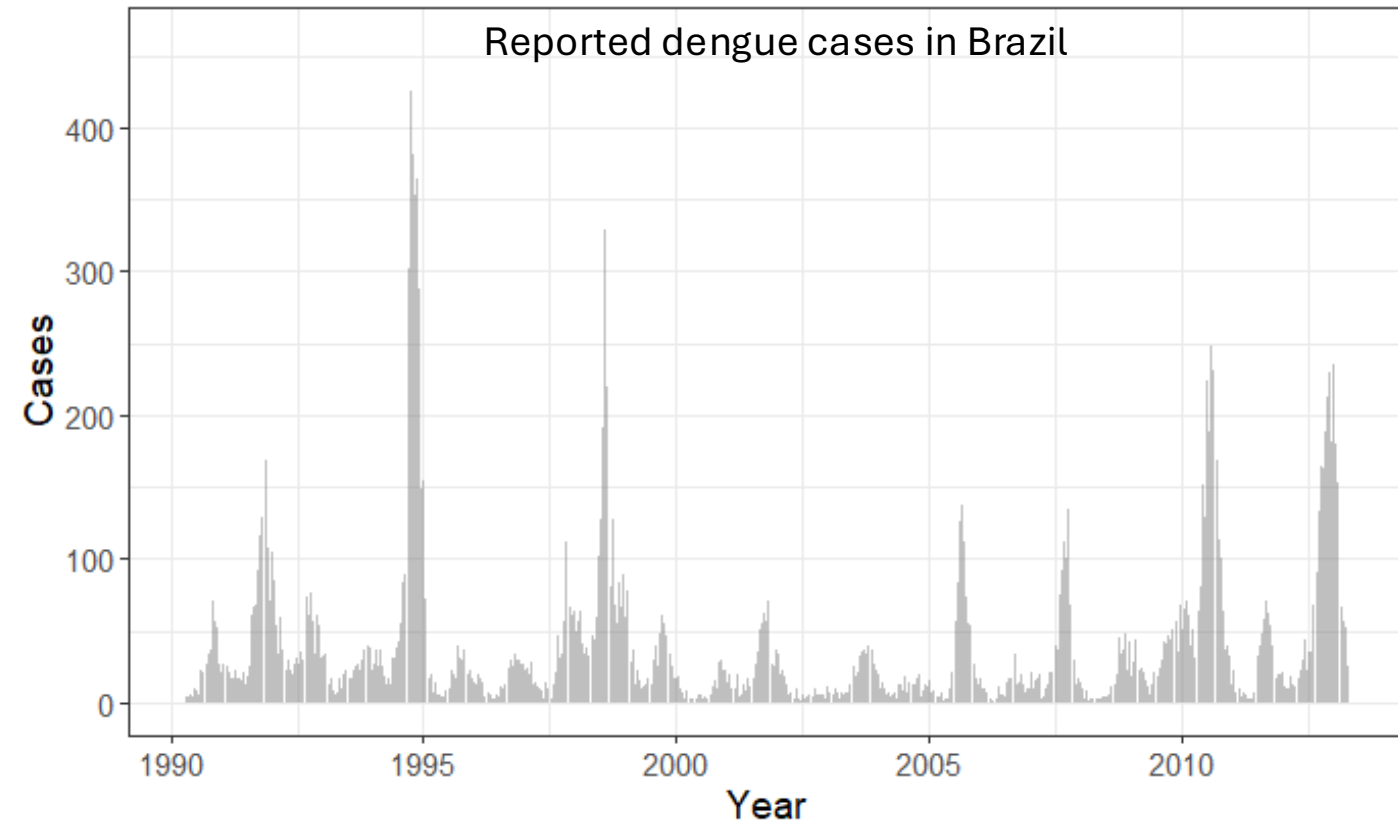
## Non-Endemic

- Sporadic outbreaks
- Transmission is not continuous

# Population transmission dynamics

## Endemic

- Sustained/persistent transmission
- Can have epidemic or seasonal cycles





# Why is this useful?

- Many infections can be missed by disease surveillance systems
  - Asymptomatic and mild infections
- To understand when in the past these infections occurred
- Quantifying annual risks of infection or average outbreak size
  - Valuable for planning control & prevention efforts

# Age = time spent at risk of infection

As we get older, we are more likely to have encountered more pathogens

- Age = time spent at risk of infection
- Age is therefore a proxy for time

Age-specific seroprevalence can help tell us what has happened in the past



# When is this applicable?

i.e. when can age tell us about past transmission?

**When seroprevalence  $\approx$  ever infected**

## **Pathogen:**

- Must be a pathogen that induces long-term antibody response

## **Antibody isotype:**

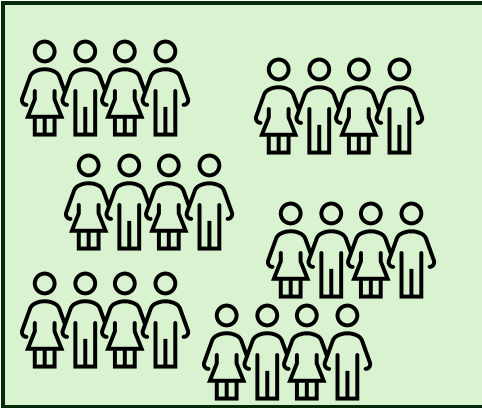
- IgG (longest-lived isotype)

## **Study type:**

- Cross-sectional seroprevalence studies
  - One time-point, single sample per person
- Sometimes, data from cohort or other studies can be used
  - E.g. the first sample from each participant (if taken around the same timeframe)

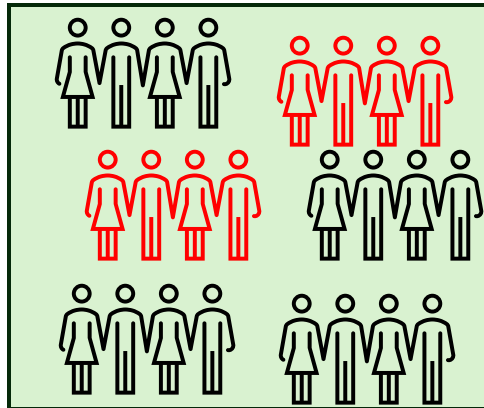
# Example

<5 years old



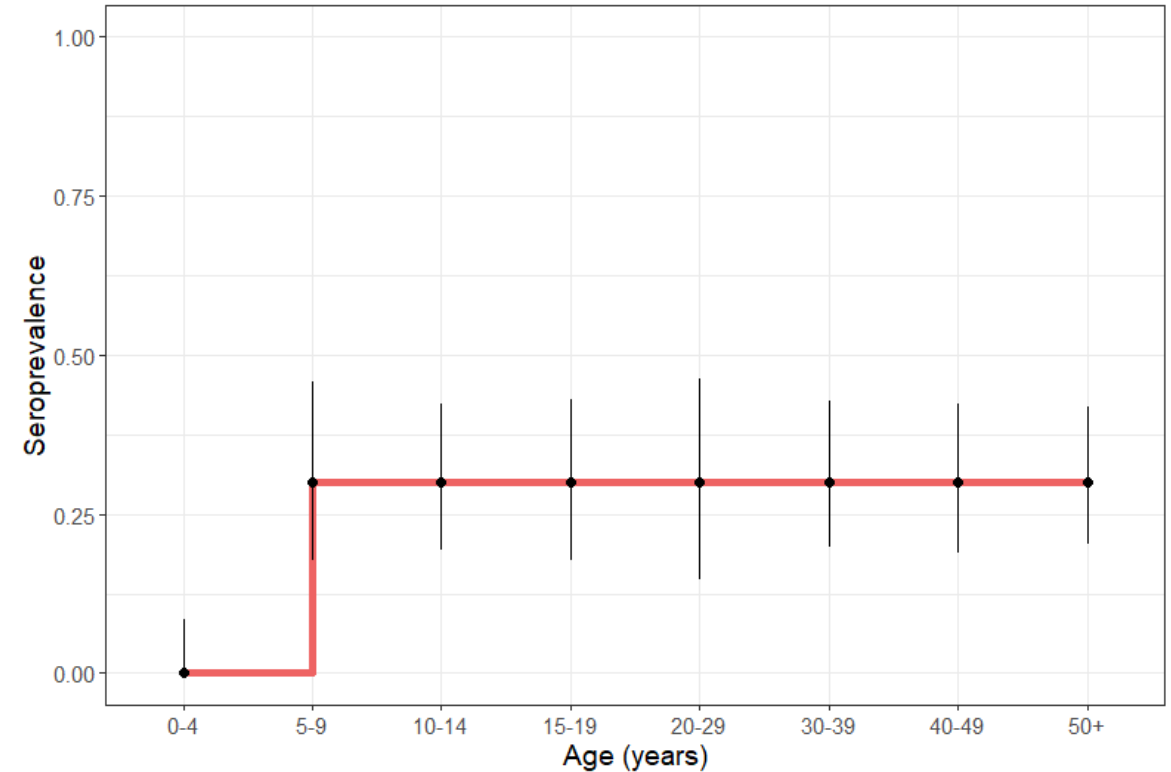
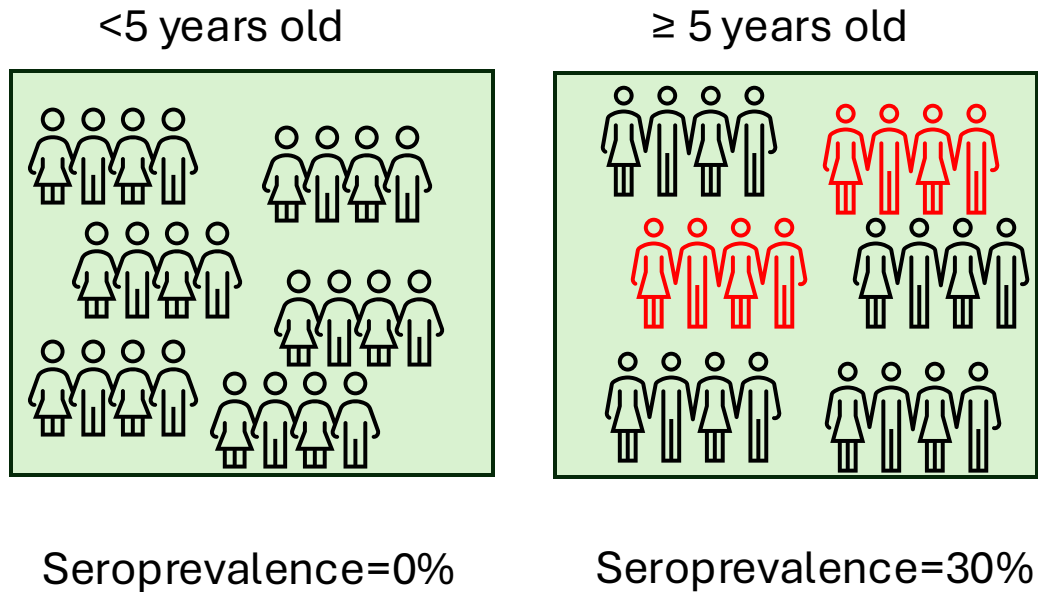
Seroprevalence=0%

$\geq 5$  years old



Seroprevalence=30%

# Example

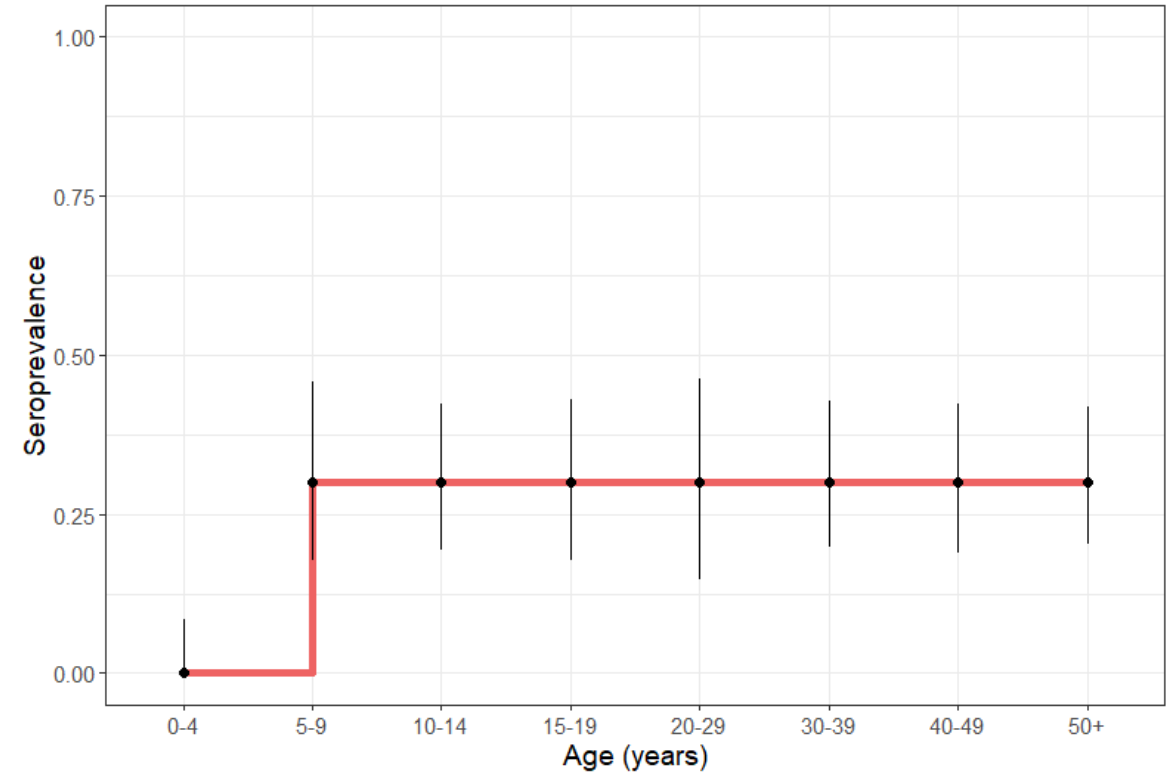


What kind of transmission  
has happened here?

# Example

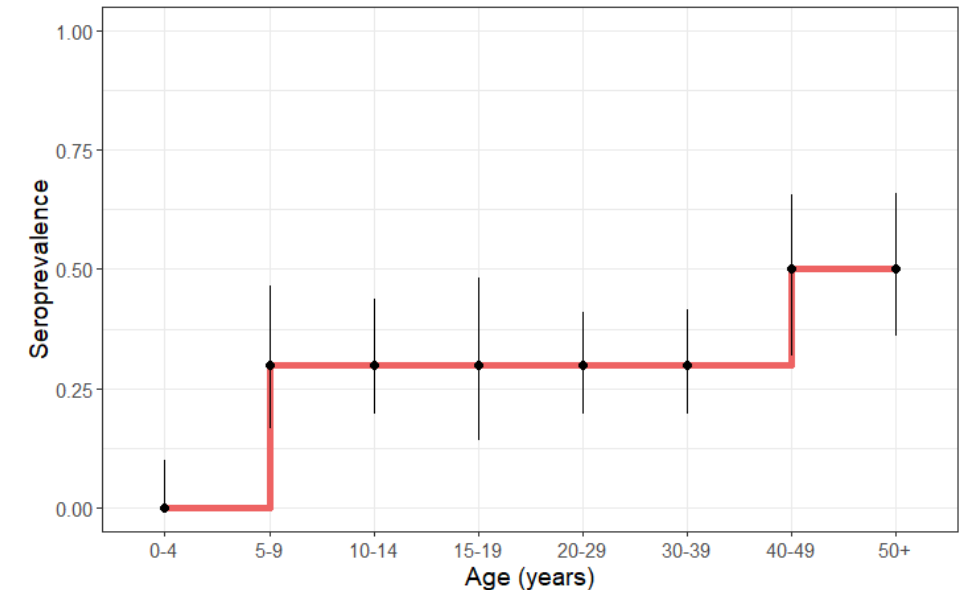
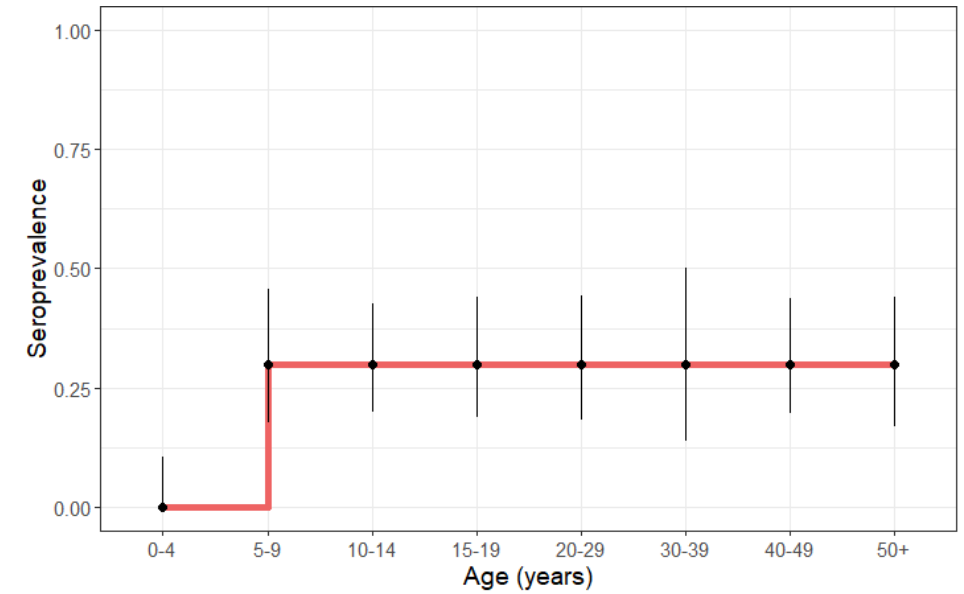
## Non-endemic transmission

- 0% seroprevalence in children aged 0-4 means the pathogen has not transmitted in the past 4 years
- An equal infection attack rate among those  $\geq 5$  years suggests:
  - An outbreak occurred  $\sim 5$  years ago
  - 30% infection attack rate

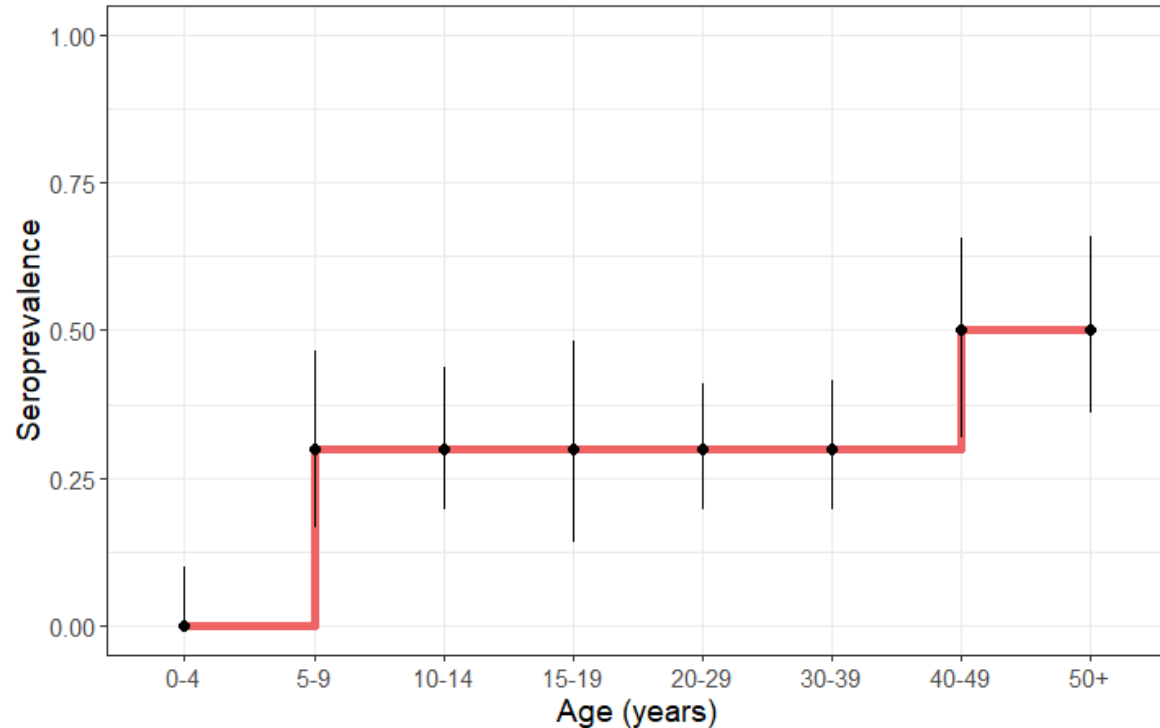


# Non-endemic transmission

- Flat age-specific seroprevalence profiles
- Everyone alive during an epidemic has approximately the same infection risk
- The more epidemics an age-group has lived through, the higher the chance of infection



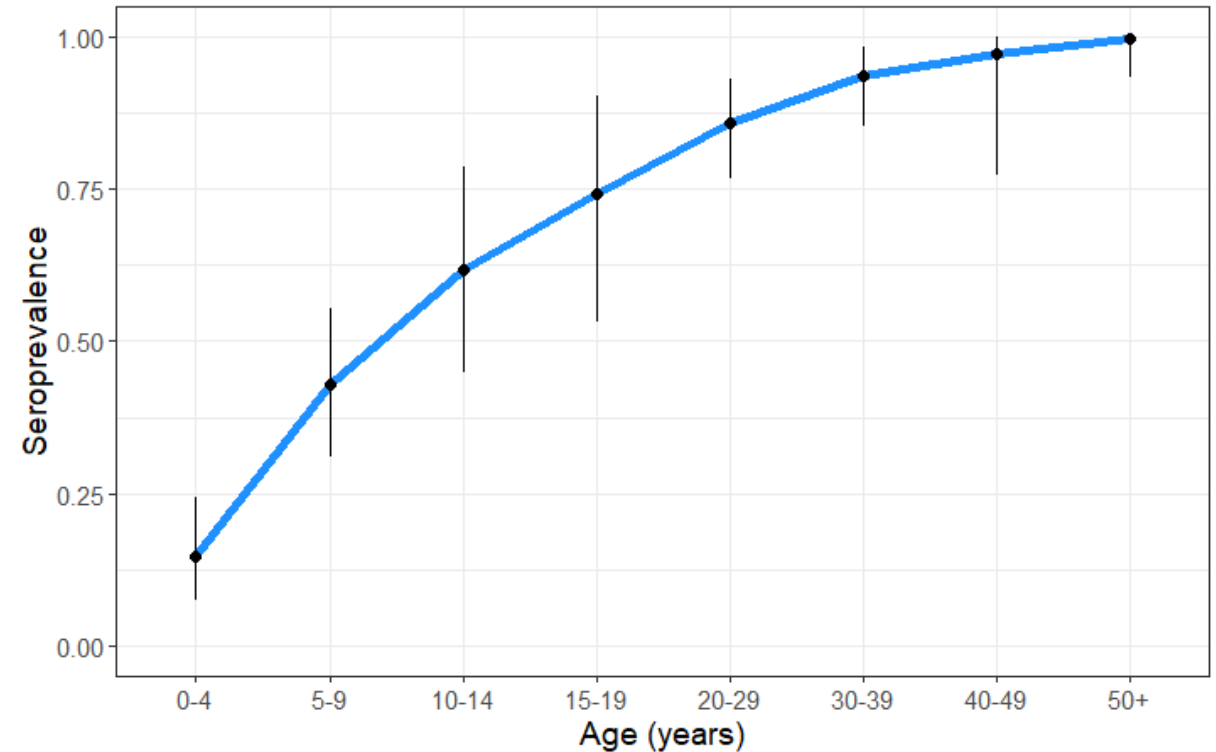
# Non-endemic transmission



- Pathogen has been absent for past 4 years (0% seroprevalence in children <5)
- Participants aged 5-39 have equal attack rates
  - -> outbreak occurred ~ 5 years ago
  - -> 30% attack rate
- Participants aged  $\geq 40$  have equal attack rates
  - -> outbreak occurred ~40 years ago
  - -> 20% attack rate
  - These participants were alive for 2 outbreaks (20% + 30% attack rates = 50% seroprevalence)

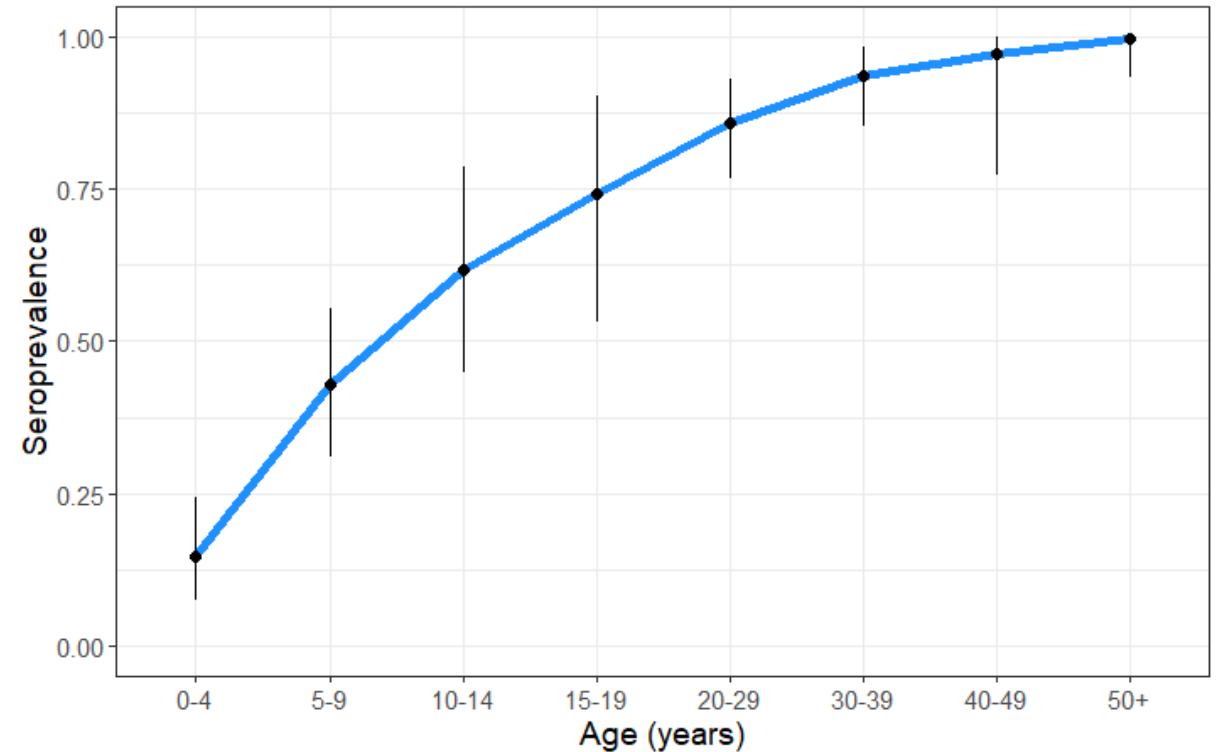
# Endemic transmission

- Increasing seroprevalence with increasing age
- When a pathogen continuously transmits in a population, age is a direct measure of the time spent at risk of infection
- Valuable to quantify the force of infection (FOI)



# Endemic transmission: FOI

- Force of infection (FOI) is also often called transmission intensity
- Defined as: “Rate at which susceptible individuals become infected”
- Can be estimated using a serocatalytic model
  - Fit to age-specific seroprevalence data

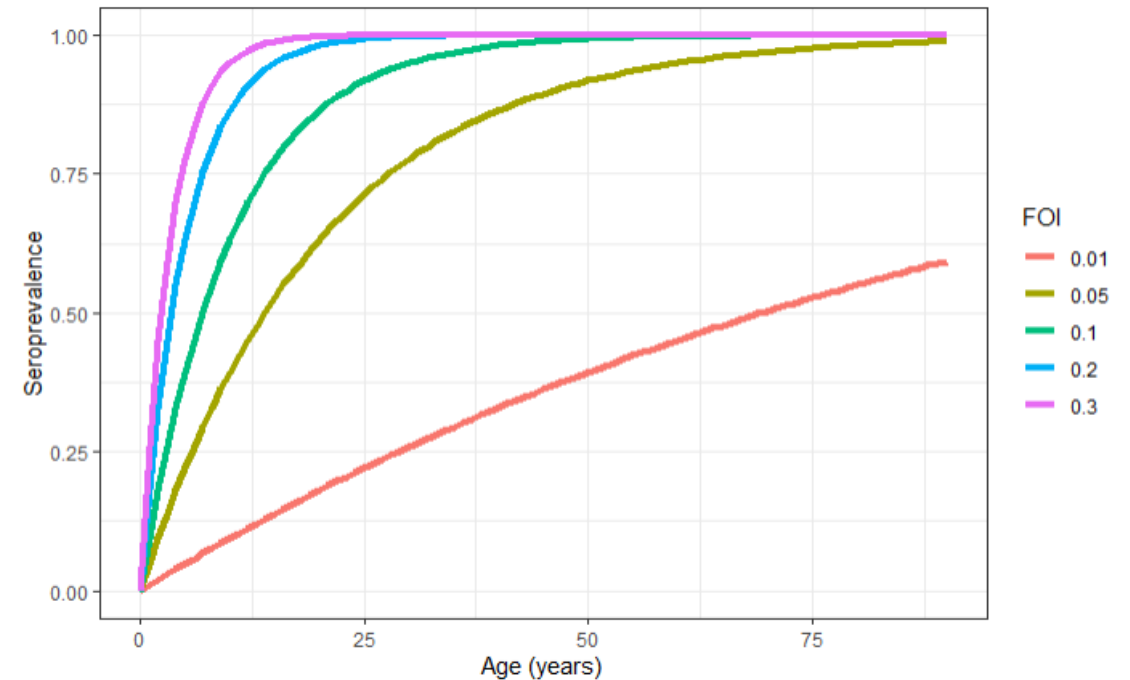




# Serocatalytic model

$$\pi_a = 1 - \exp(-\lambda * a)$$

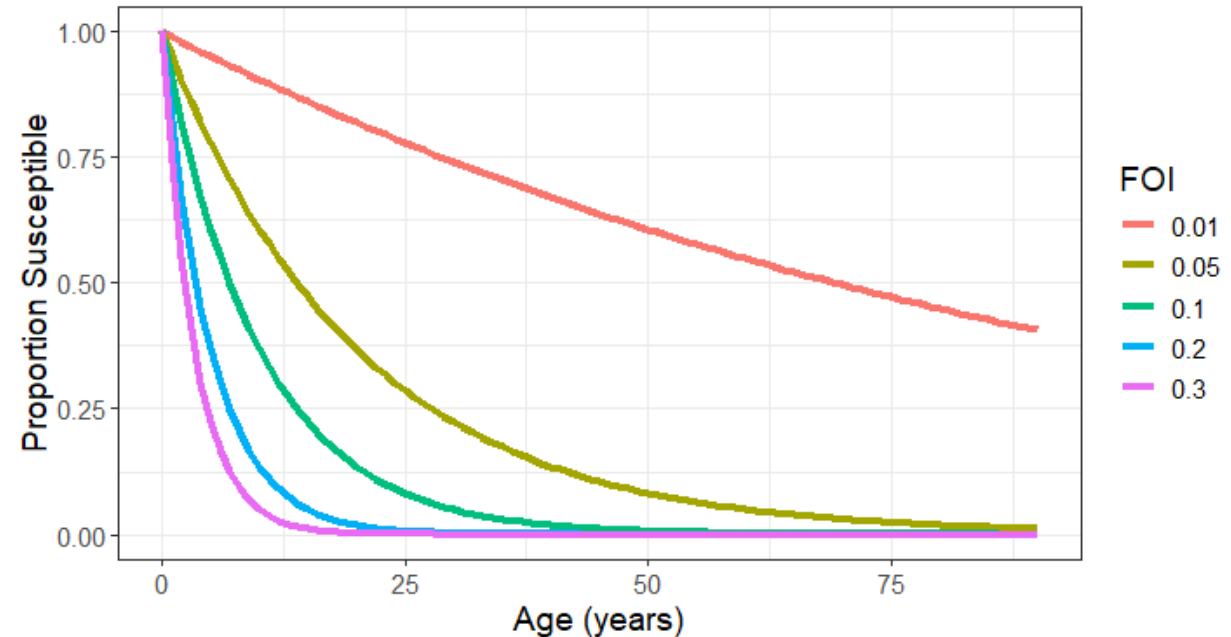
- $\lambda$  = FOI
- $\pi_a$  = proportion positive at age  $a$
- Assumptions:
  - Transmission is constant over time
  - Infection risk is independent of age
- The cumulative risk of ever having been infected accumulates with age



# Serocatalytic model

$$\pi_a = 1 - \exp(-\lambda * a)$$

- $\lambda = \text{FOI}$
- $\pi_a$  = proportion positive at age  $a$
- $\text{Susceptible}_a = 1 - \pi_a$
- Assumptions:
  - Transmission is constant over time
  - Infection risk is independent of age
- We will implement this using a simple regression model
  - glm function
  - complementary log-log link



# Value of FOI

- Allows us to quantify the level of transmission
  - number of annual infections
- Prioritization of vaccines and other control strategies

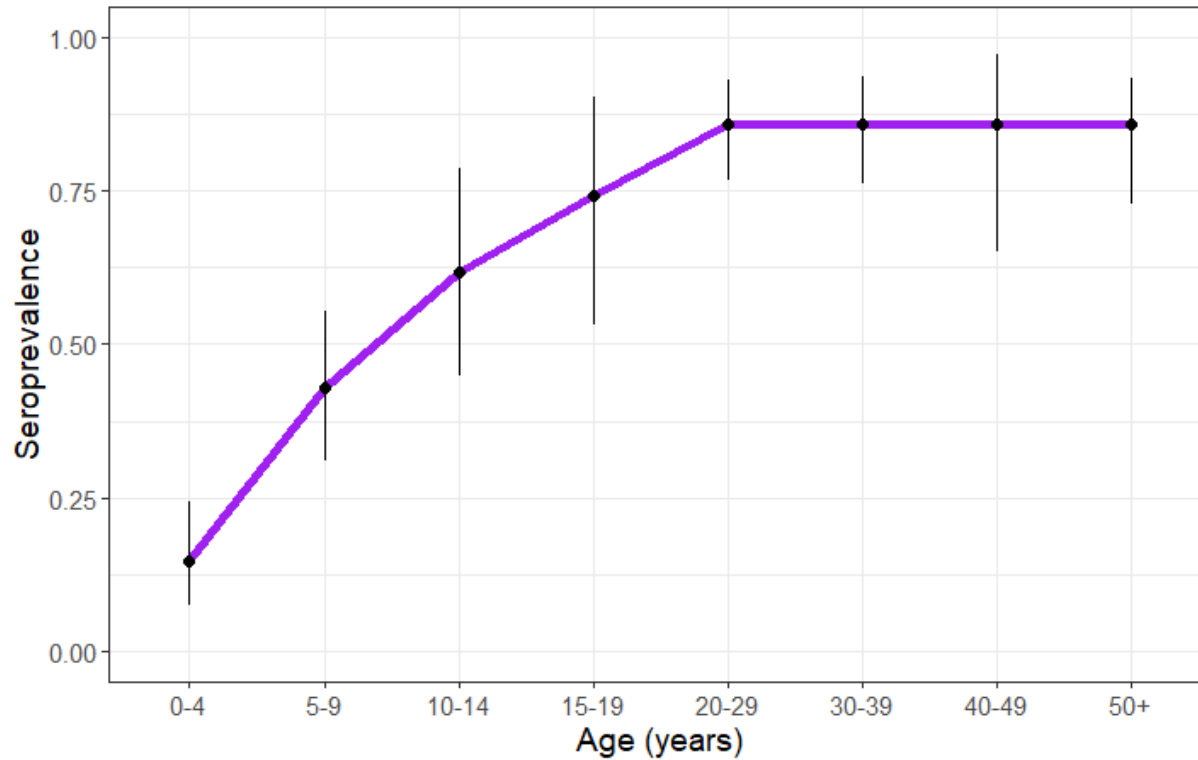
SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE



**Fig. 1. Geographic location of FOI data.** A total of 382 data points are shown comprising the national administrative division of all countries and the second national administrative division (admin 2) of Mexico, Colombia, Venezuela, Brazil, India, and Australia. Color scale shows FOI value (average per-serotype).

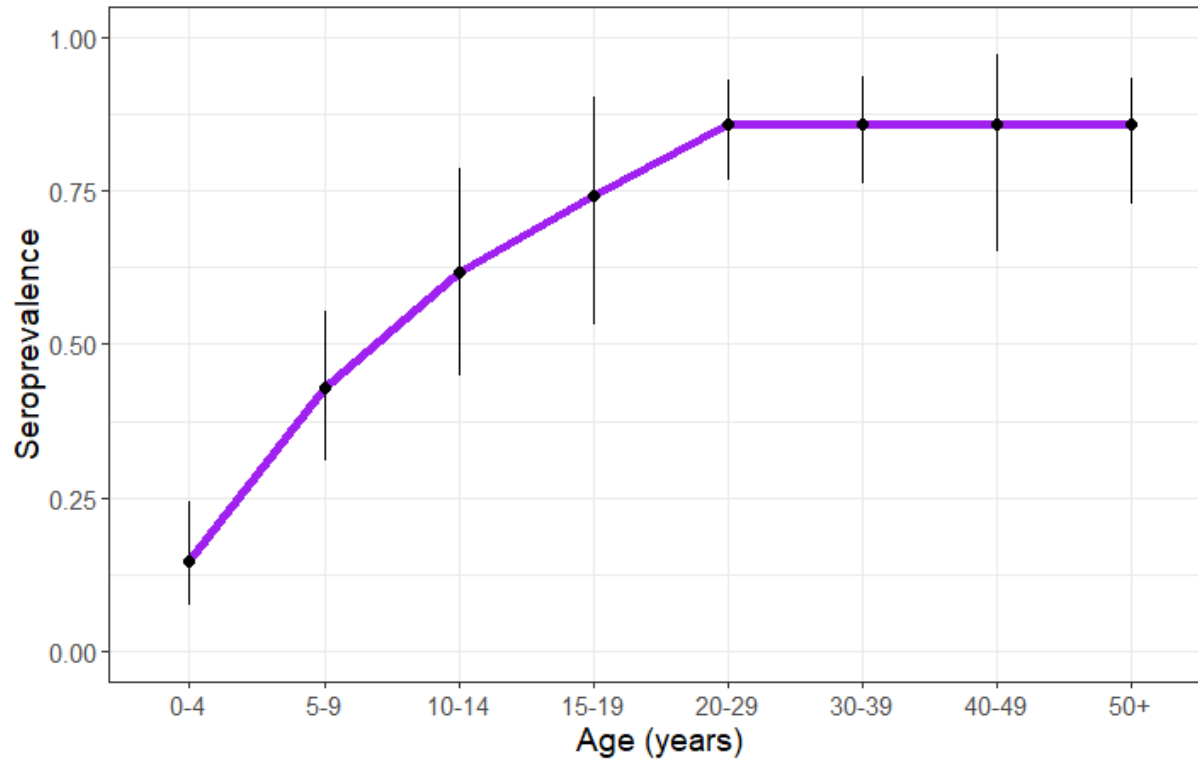
Catterino et al., Science Translational Medicine, 2020

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What kind of transmission  
has happened here?

# Recently established endemic transmission

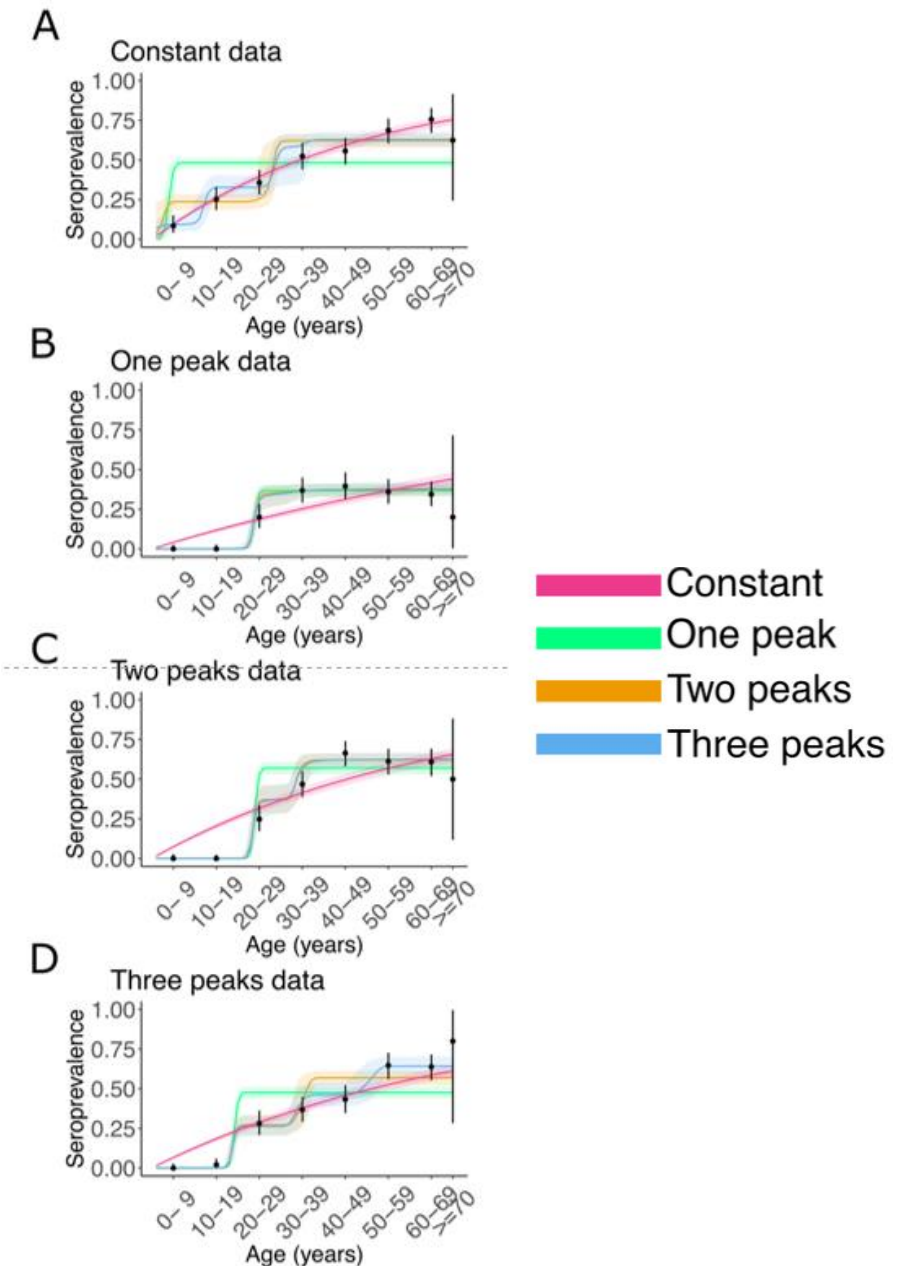


- Pathogen began circulating ~20 years ago
  - Everyone >20 years has same attack rate
- Increasing seroprevalence with increasing age in younger age groups
  - -> recent endemic transmission

# RSero: R package

## RSero: A user-friendly R package to reconstruct pathogen circulation history from seroprevalence studies

Nathanaël Hozé , Margarita Pons-Salort, C. Jessica E. Metcalf, Michael White, Henrik Salje, Simon Cauchemez



# Additional resources

- RSero package for reconstructing past transmission
  - <https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1012777>
- Seroincidence estimation (pathogens that induce only short-lived antibody responses)
  - Cholera: <https://pmc.ncbi.nlm.nih.gov/articles/PMC7738617/>
  - Typhoid: <https://pubmed.ncbi.nlm.nih.gov/35750069/>
- Reversible catalytic model (when antibody responses wane significantly over time)
  - Malaria: <https://www.pnas.org/doi/10.1073/pnas.0408725102>
  - Enteropathogens: <https://elifesciences.org/articles/45594#s4>
- Joint fitting of mixture and catalytic models
  - <https://journals.sagepub.com/doi/10.1177/1471082X12457495>
  - <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0010592>

# Conclusions

- Age-specific seroprevalence data can help us reconstruct past transmission dynamics
  - Seroprevalence that continuously increases with age indicates endemicity
  - Staggered, step-wise increases in seroprevalence indicate sporadic epidemics
- Understanding if a pathogen is endemic or not has important public health implications
- Past infection rates can be quantified
  - Non-endemic settings: frequency & magnitude of outbreaks
  - Endemic settings: force of infection

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# Lab 6

- Calculate age-specific seroprevalence
- Investigate the transmission dynamics of two pathogens
- Fit a serocatalytic model to estimate FOI