Week 2: Using Serology Data & Modeling Interventions

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Week 2 Overview

- ~~Monday, August 2:~~
  - ~~Relating SIR models to epidemic parameters~~
  - ~~Estimating parameters in R~~
- ~~Tuesday, August 3:~~
  - ~~Guest lecture by Caroline Trotter~~
  - ~~Modeling meningitis~~
  - ~~Guided practice in R~~
- Thursday, August 5:
  - Using serological data for modeling
  - Guided practice in R

Workshop Schedule

Time	Topics
2:00–2:05 pm	~~Greetings~~
2:05–2:50 pm	Using Serology Data
2:50–3:00 pm	Break
3:00–3:40 pm	Modeling Interventions
3:40–3:50 pm	Break
3:50–5:00 pm	R Session

Data for Parameters

- How do we know what values to enter for our model parameters?
- How do we know what to use for starting values?
- Models (depending on the structure) need a lot of inputs, such as:
  - birth rates
  - death rates
  - transmission rate
  - latency rate
  - recovery rate
  - number in each compartment
  - Where might we find these numbers?

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Potential Data Sources

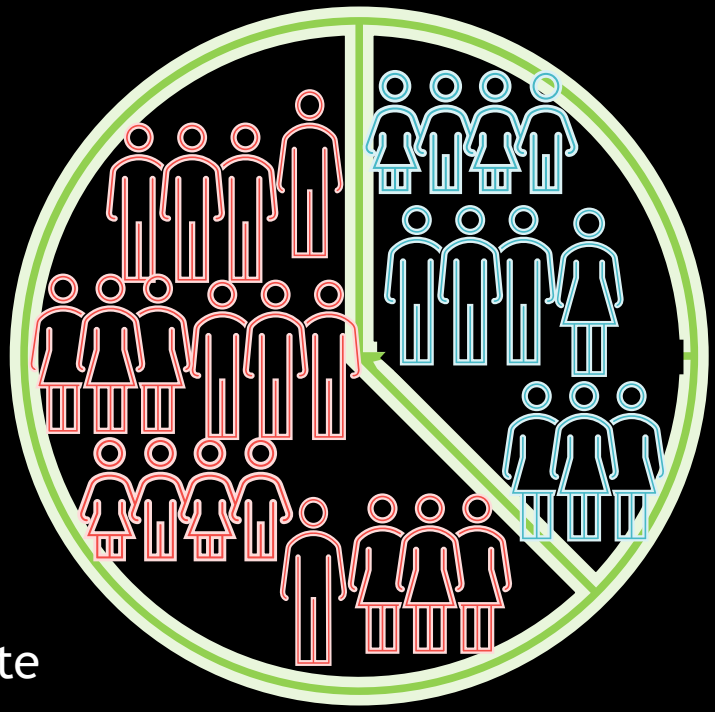
- Prevalence
  - age-specific prevalence
- Seroprevalence
  - age-specific seroprevalence

How Could We Use Prevalence?

- Prevalence data would be great to have and would represent the number in our I compartment
  - value for I*
  - letters with an * indicate the number of people in the compartment
- For an endemic disease (when R0>1), the number of people in each compartment can be calculated if we know the natural history of the disease:
  - (when we have values for natural history parameters)

How Could We Use Prevalence?

- Recall that:
  - $N = S^* + E^* + I^* + R^*$
- When R0>1:
  - $I^* = \frac{\mu N}{\mu+\gamma}\left(1 - \frac{1}{R_0}\right)\left(\frac{\sigma}{\mu+\sigma}\right)$

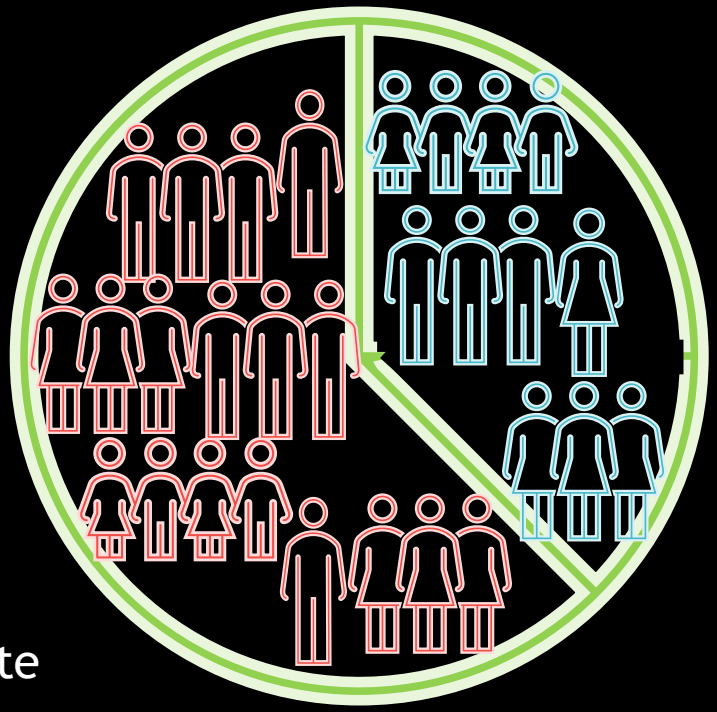


This equation can be rearranged

μ: birth/death rate
γ: recovery rate
σ: latency rate
ß: transmission coefficient

How Could We Use Prevalence?

- Rearrange this:
  - $I^* = \frac{\mu N}{\mu+\gamma}\left(1-\frac{1}{R_0}\right)\left(\frac{\sigma}{\mu+\sigma}\right)$
- To this:
  - $R_0 = \left[1 - I^* \frac{\mu+\gamma}{\mu N}\frac{\mu+\sigma}{\sigma}\right]^{-1}$



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  - important for our policy decisions!

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- For any disease, we have a range of values for R0, but this would allow us to estimate R0 for our specific population/epidemic
  - important for our policy decisions!
  - we just need the natural history parameters and the prevalence

How Easily Can We Get Accurate Prevalence Data?

- … not very easily
- Difficult to collect prevalence data!
  - partial observation: acute infections are short and hard to observe/capture
  - expense: pathogen isolation, laboratory confirmations
  - biased sampling: isolated populations may have lower/higher disease burden

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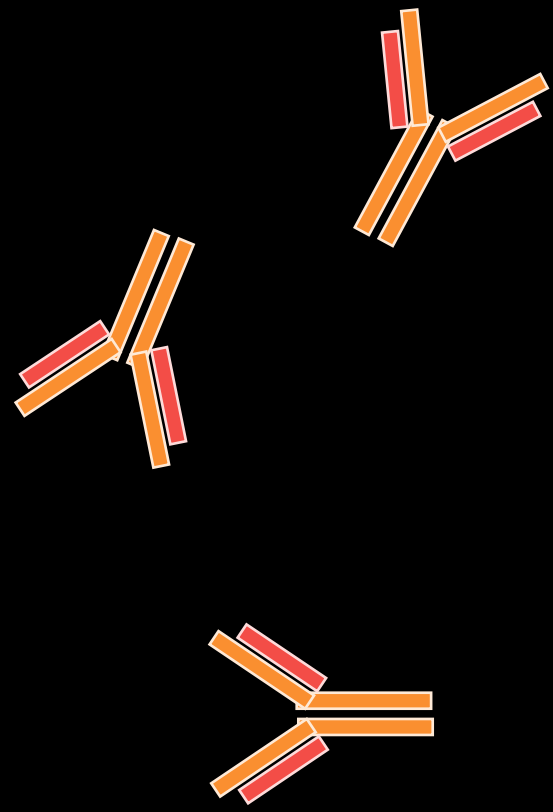
  - partial observation: acute infections are short and hard to observe/capture
  - expense: pathogen isolation, laboratory confirmations
  - biased sampling: isolated populations may have lower/higher disease burden
- Disease prevalence may vary by year
  - Example: annual dengue prevalence in low versus high dengue year

What's seroprevalence data?

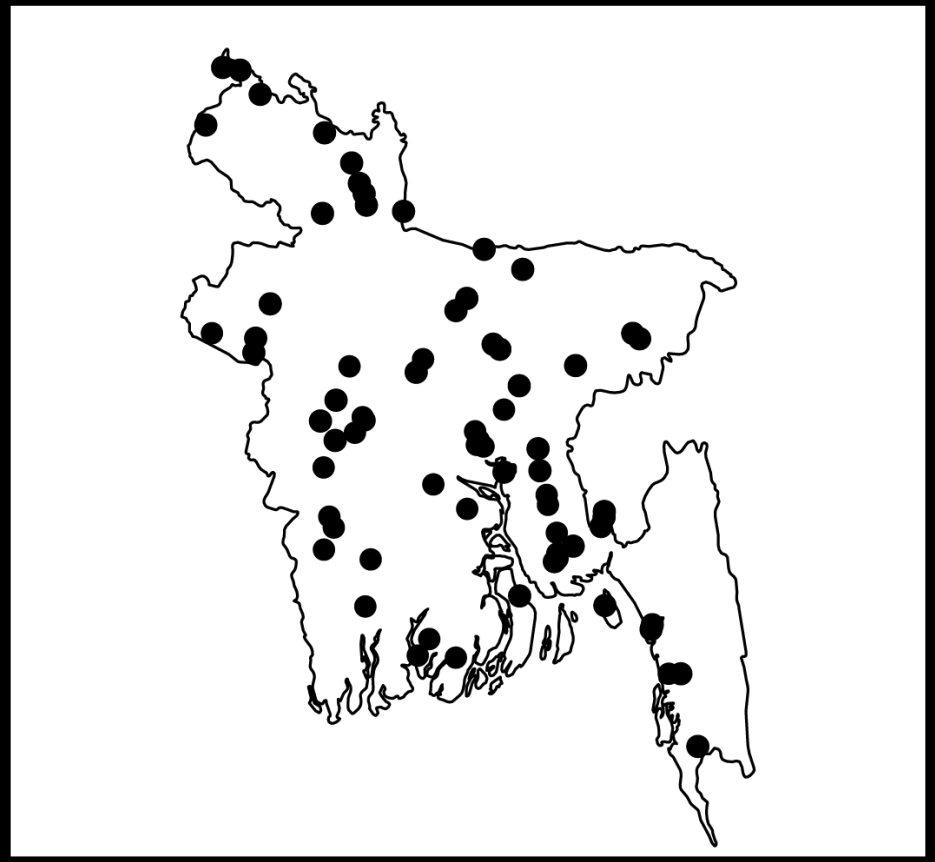
- Post infection, individuals develop antibodies
- These can be detected by specific assays

What About Seroprevalence Data?

- Seroprevalence will often include all currently and formerly infected
  - depends on the disease and the duration of antibodies
- Good approximation: 1 – proportion susceptible
  - 1 – (S*/N)
- Can this help us estimate epidemic parameters?
  - Yes, but we'll need to use a different equation

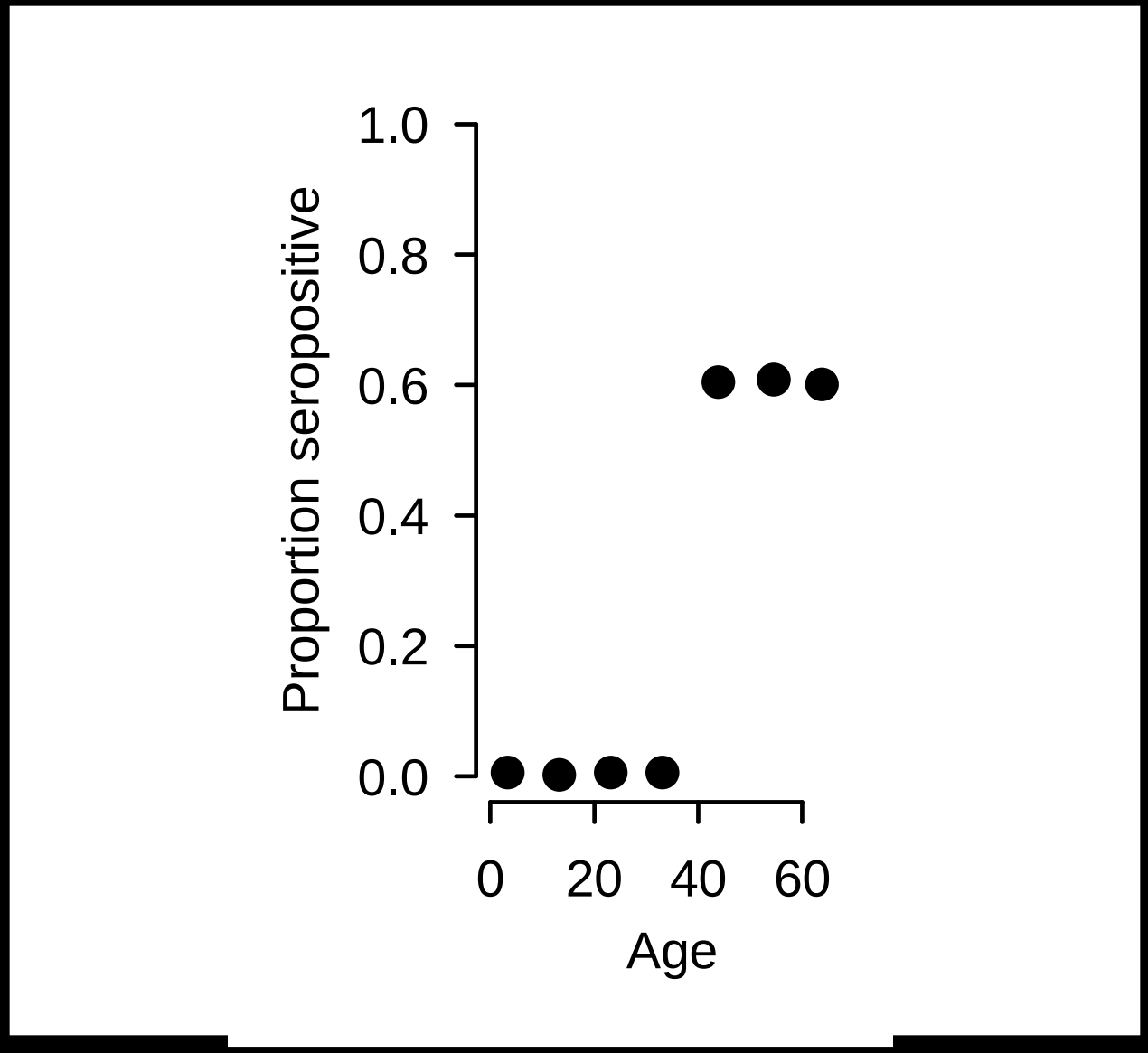


Seroprevalence studies

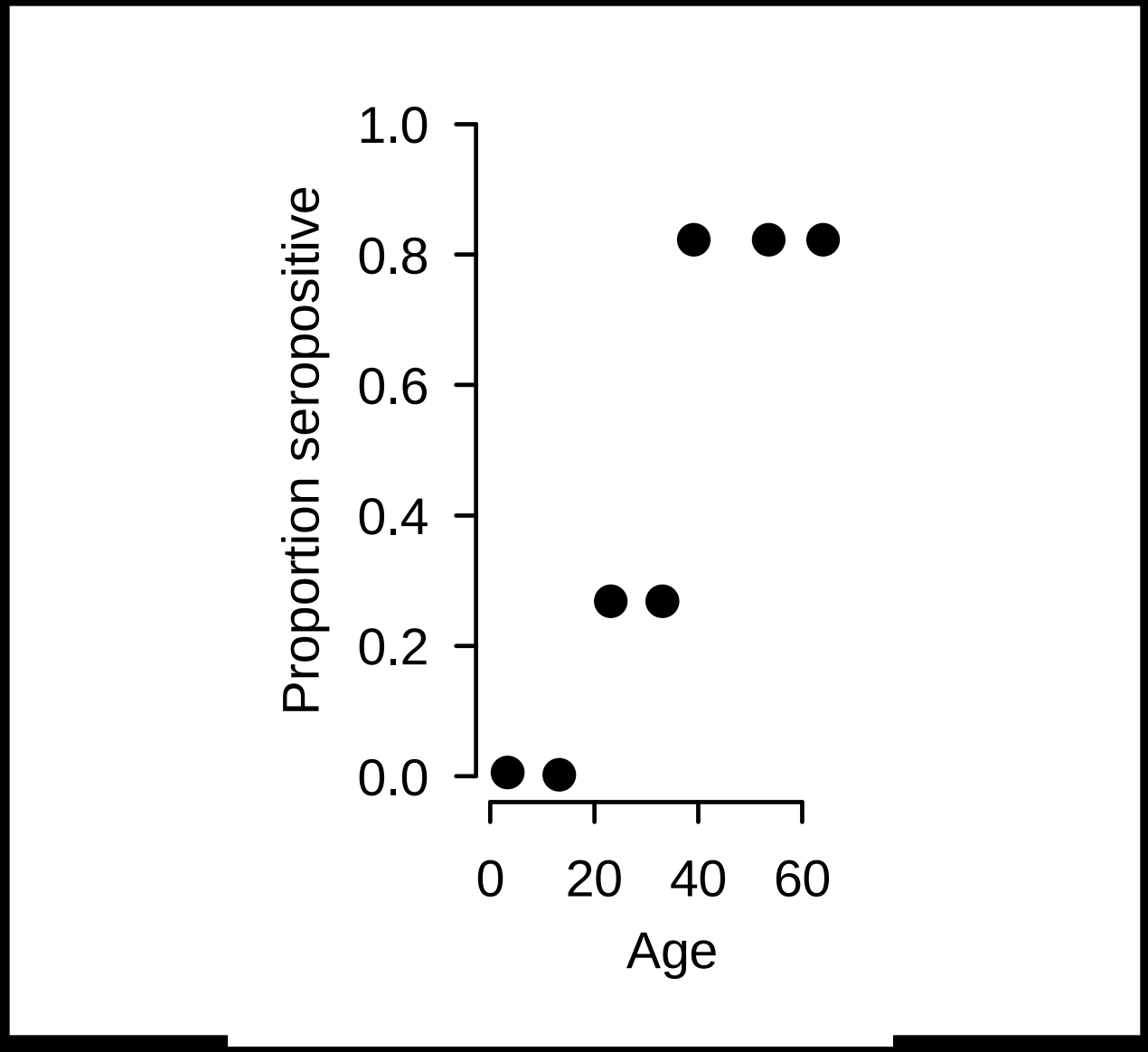


- Select random communities and random members of population
- Blood draw
- Look in blood for antibodies specific to your pathogen
- We conducted one in Bangladesh in 2016 for dengue virus and found a seropositivity of ~25%

Incorporating age



What would this mean?



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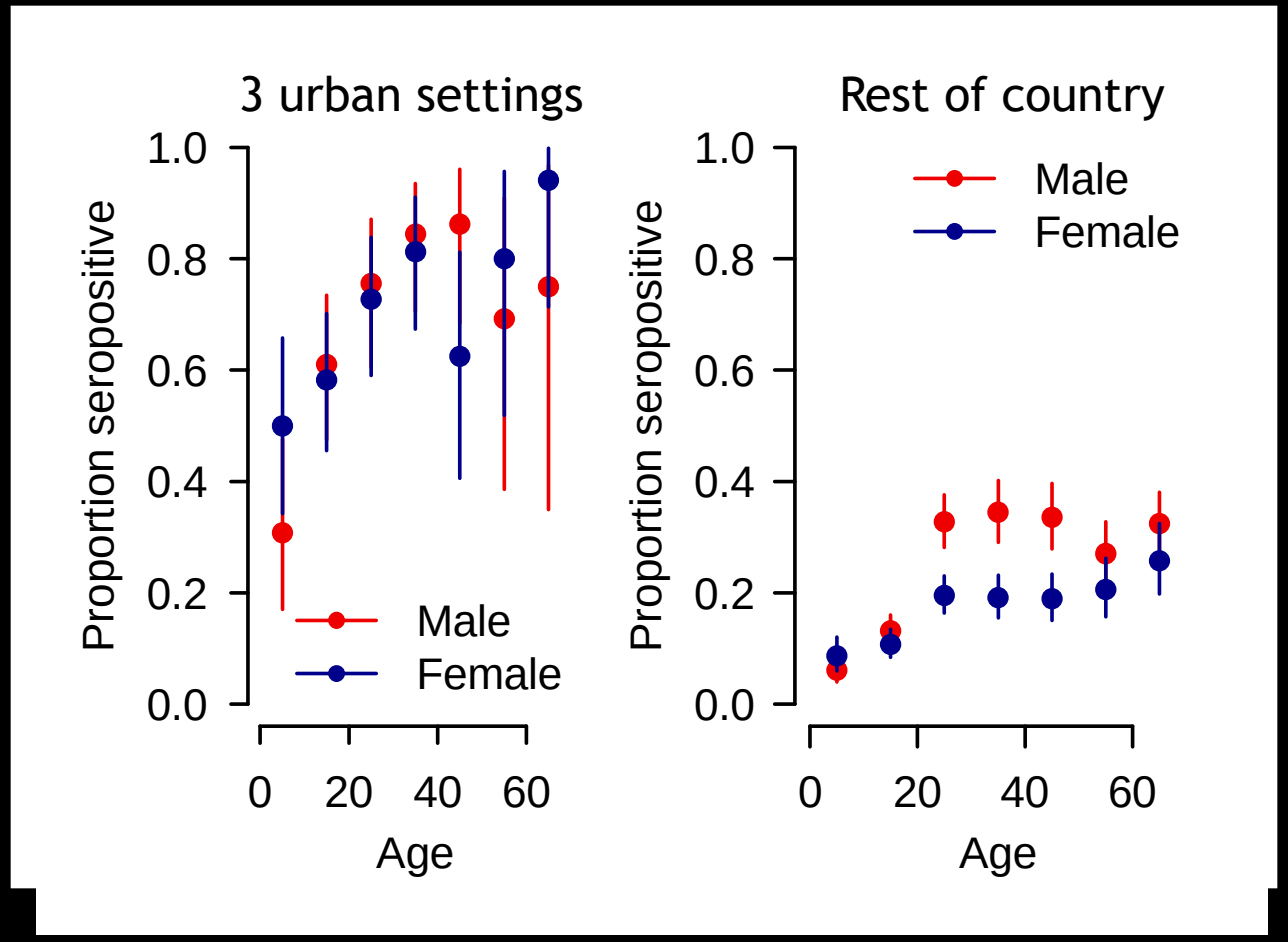
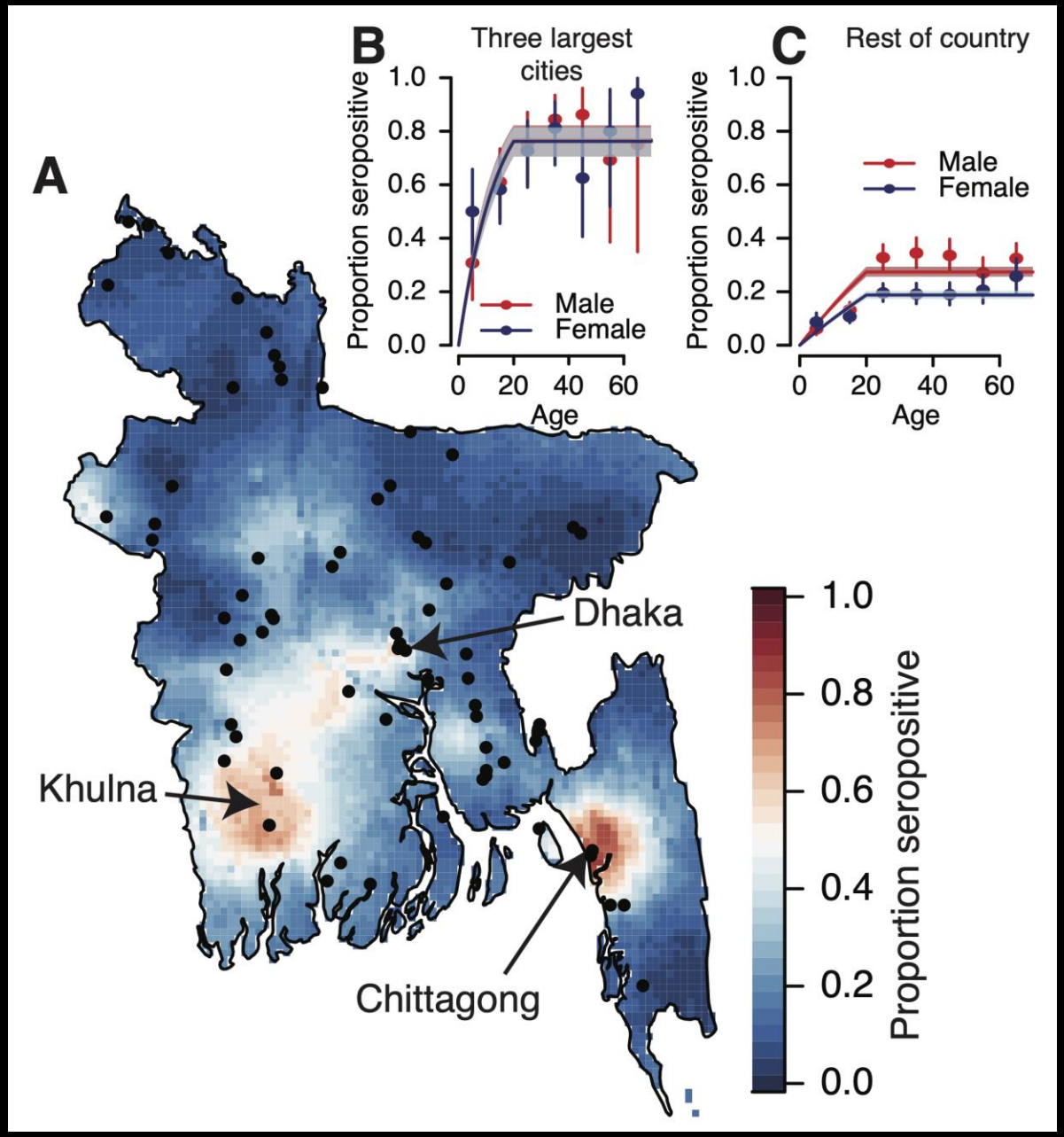


What's going on here?


A
B
Three largest cities
Proportion seropositive
1.0
0.8
0.6
0.4
0.2
0.0
0
20
40
60
Age
Male
Female
C
Rest of country
Proportion seropositive
1.0
0.8
0.6
0.4
0.2
0.0
0
20
40
60
Age
Male
Female
Dhaka
Khulna
Chittagong
1.0
0.8
0.6
0.4
0.2
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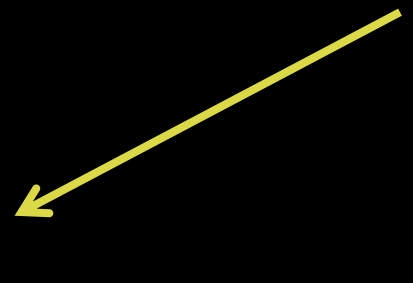
Proportion seropositive

Age & Seroprevalence

- For an endemic pathogen, the average amount of time in S before becoming infected is the average age of infection (A)
  - $A = \frac{1}{\mu(1-R_0)}$
  - $R_0 = 1 + \frac{1}{\mu A}$

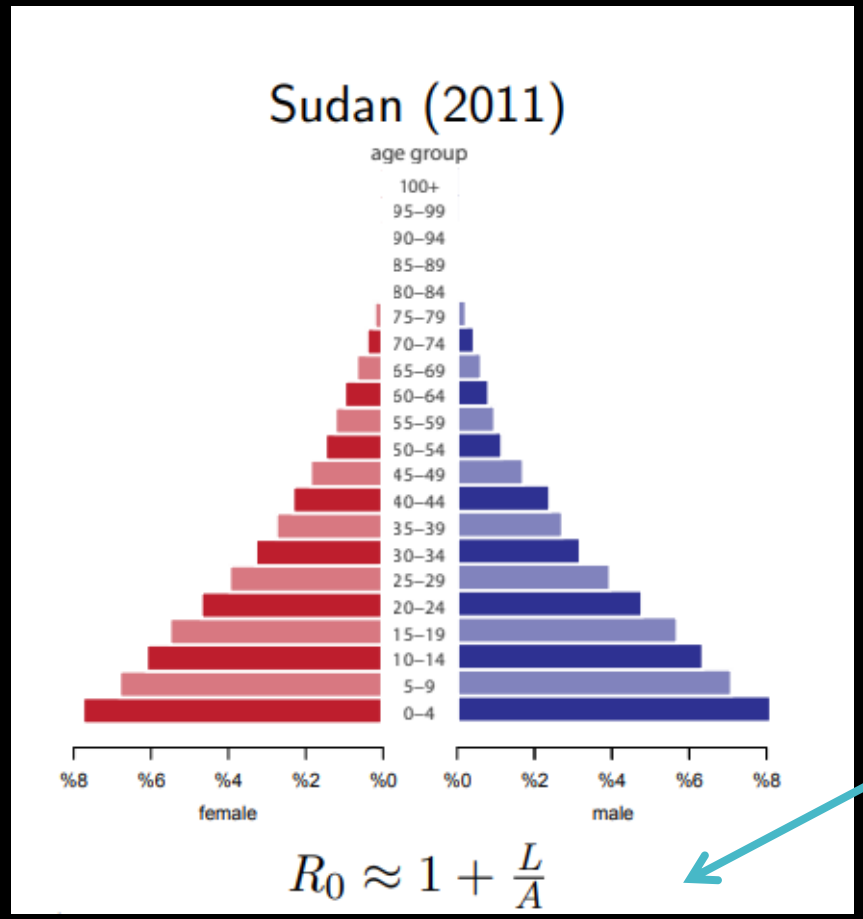
Age & Seroprevalence

- The average amount of time in S before becoming infected is the average age of infection (A)
  - $A = \frac{1}{\mu(1-R_0)}$
  - $R_0 = 1 + \frac{1}{\mu A}$
- Because 1/μ is the life expectancy for people in the population, this equation could also be written as:
  - $R_0 = 1 + \frac{L}{A}$



- μ: birth rate

Age & Seroprevalence



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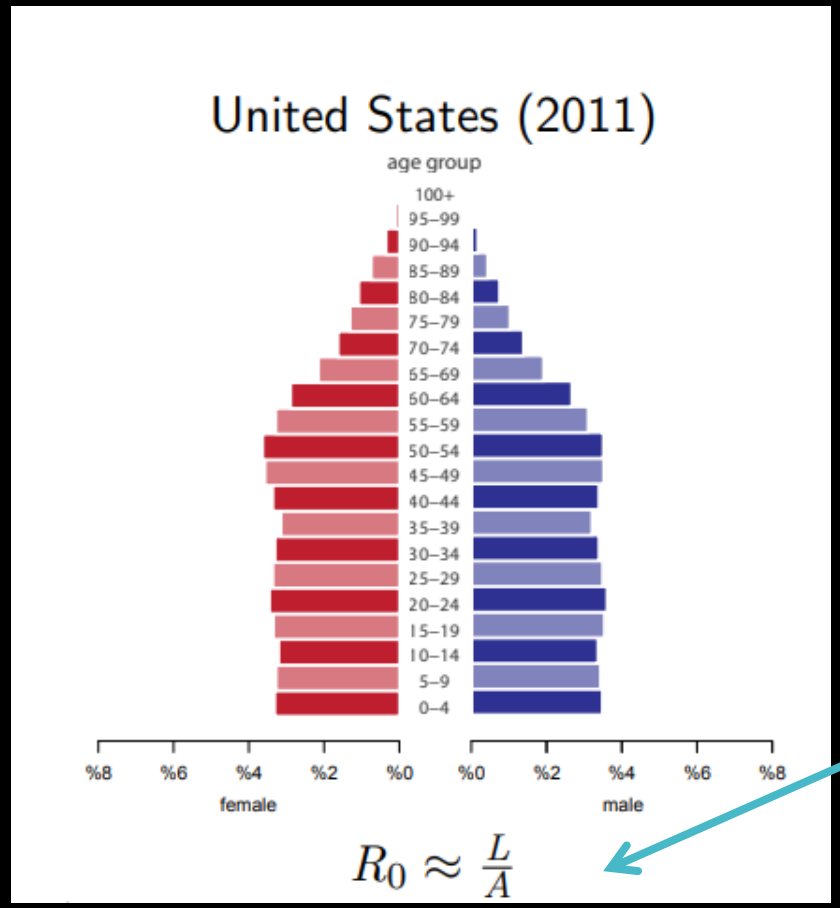
- However, this relationship depends on the overall structure of the population
  - For a pyramidal population, people are dying at a constant rate

Age & Seroprevalence



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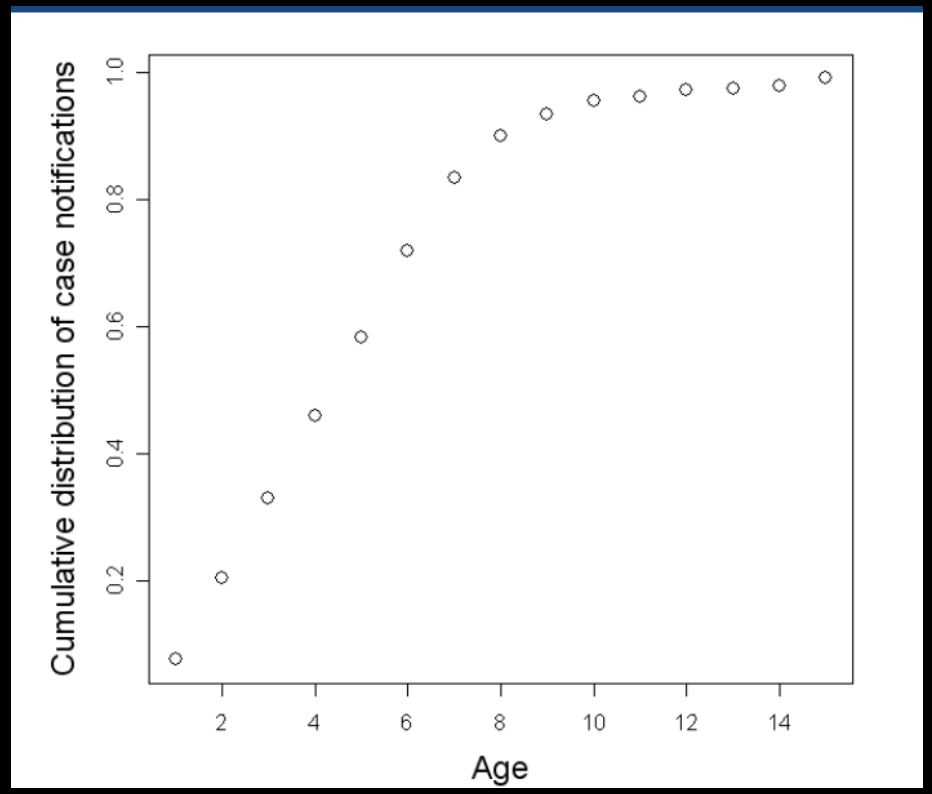
  - For a square population, people die at older ages

Age-specific Seroprevalence

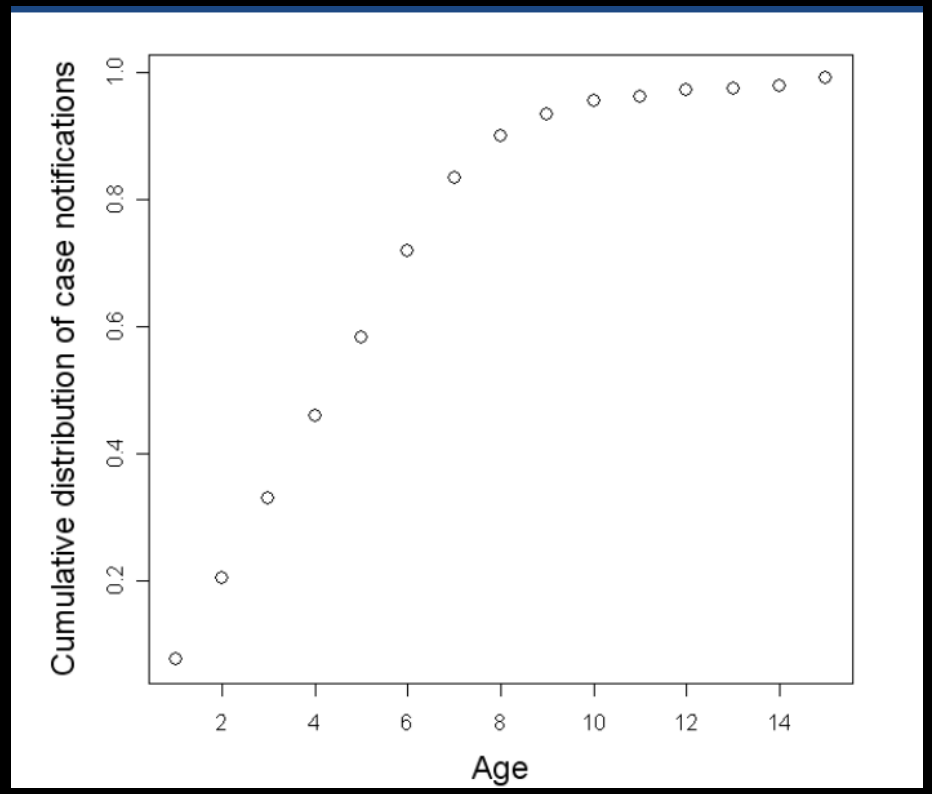


- Seroprevalence of measles in Aberdeen, UK
  - age-specific seroprevalence
  - this can be used to learn additional details about the disease dynamics
- What is the force of infection for this group?

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



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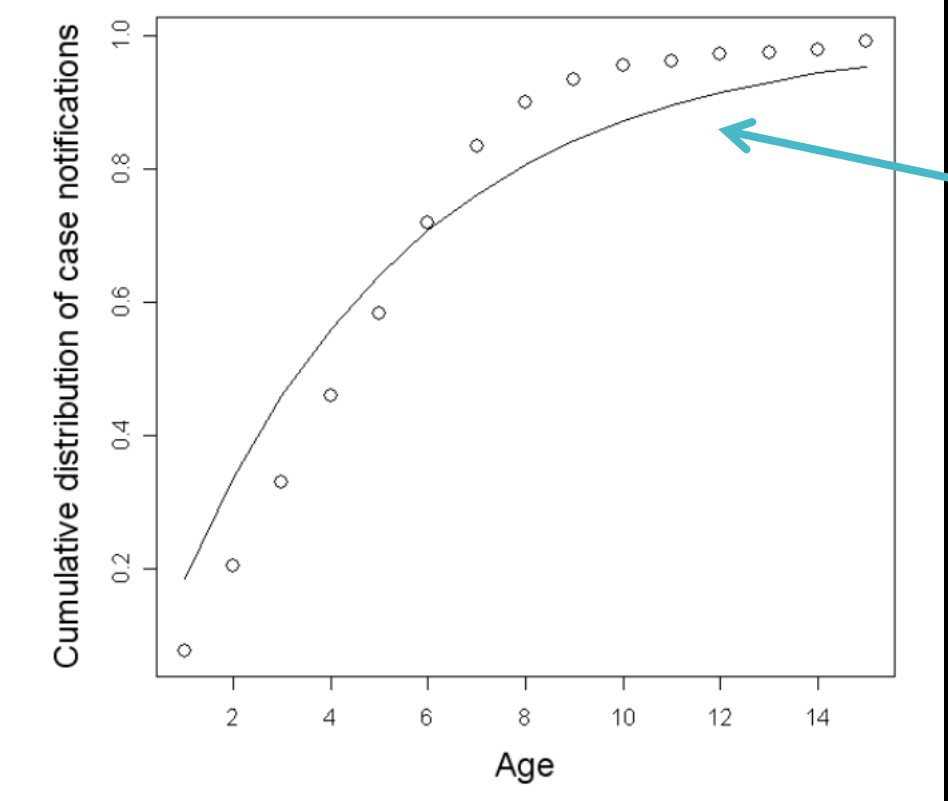

- What is the force of infection for this group?
- If we fit a constant force of infection, we see the fit is not very good
  - $\lambda=0.21$
  - 21% chance of becoming infected each year

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

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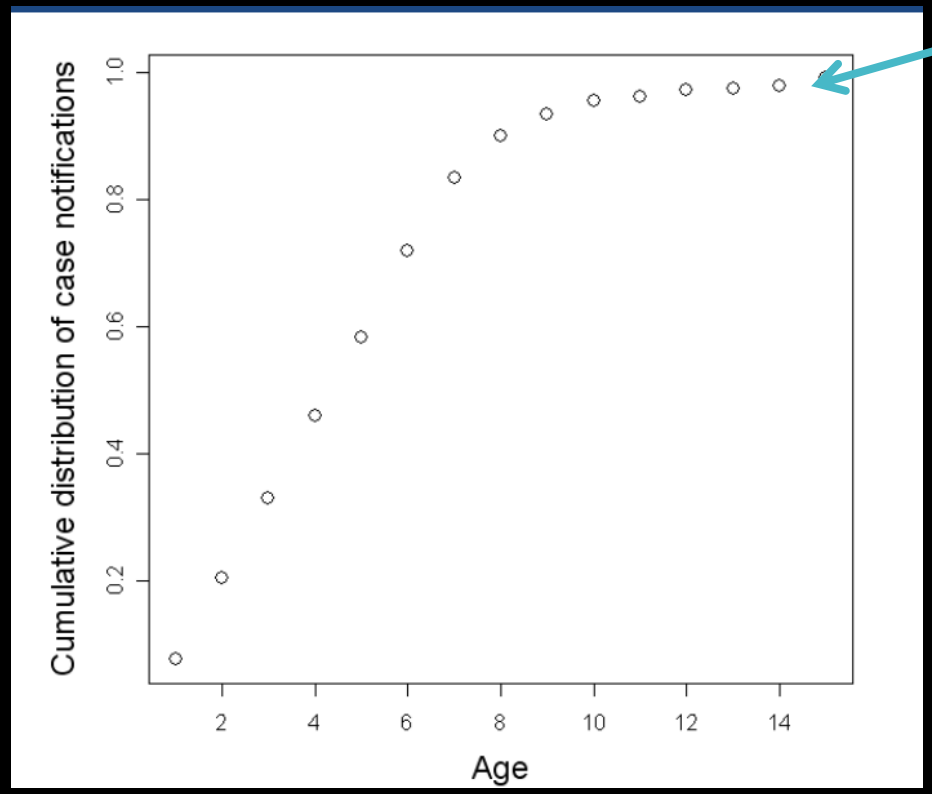
- These factors indicate that constant FOI is a poor assumption
- Age-specific FOI would be much better and age-specific seroprevalence can help estimate this!

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

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    - $x(a) = e^{-\lambda a}$
  - 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
  - $F(a) = 1 - e^{-\lambda a} \approx y(a)$

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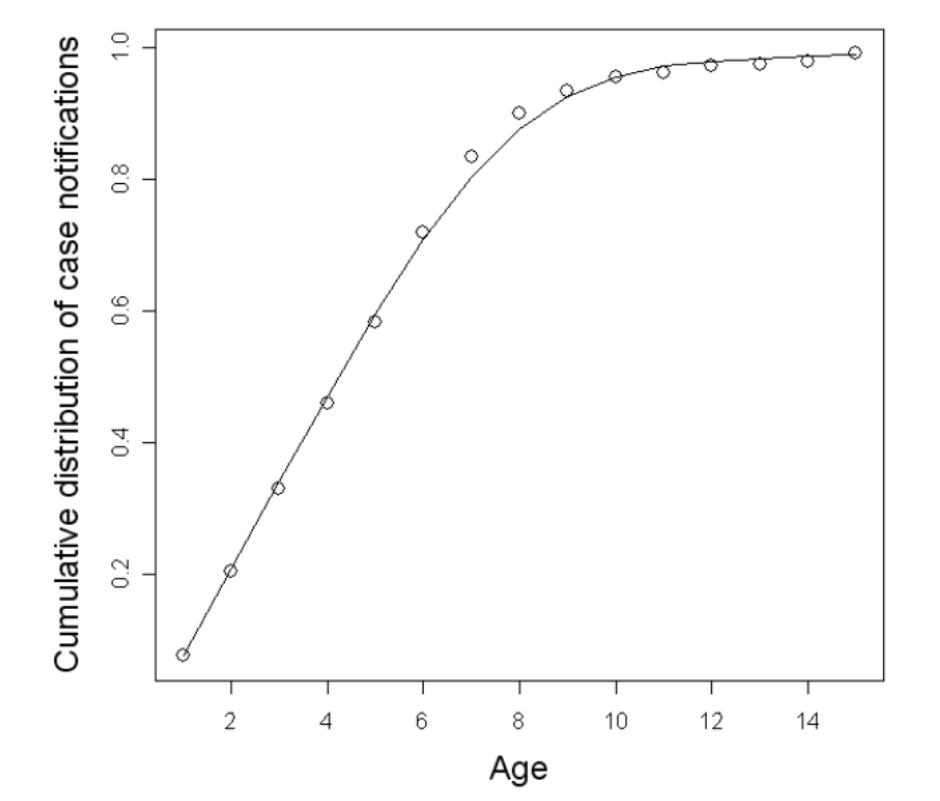
Force of Infection

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

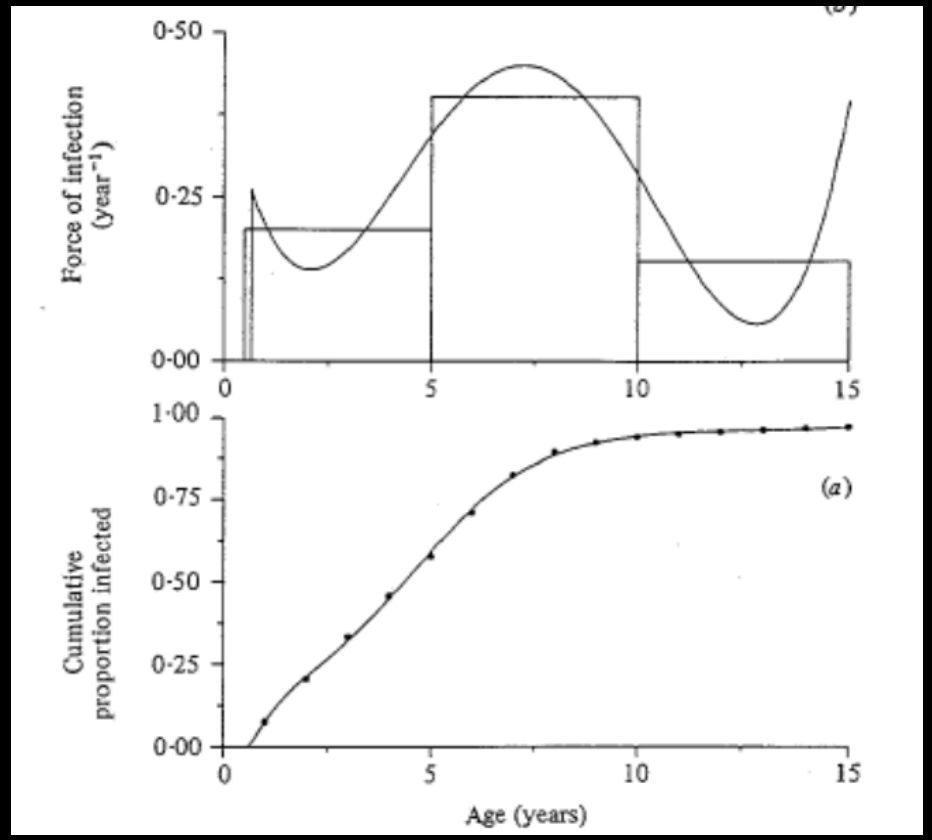
- We can use a binomial (statistical) framework to relate the seroprevalence to force of infection
- we are estimating a joint likelihood
- by using this statistical method, we can:
  - account for the different sample sizes among age groups
  - calculate confidence intervals for our estimate of FOI

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



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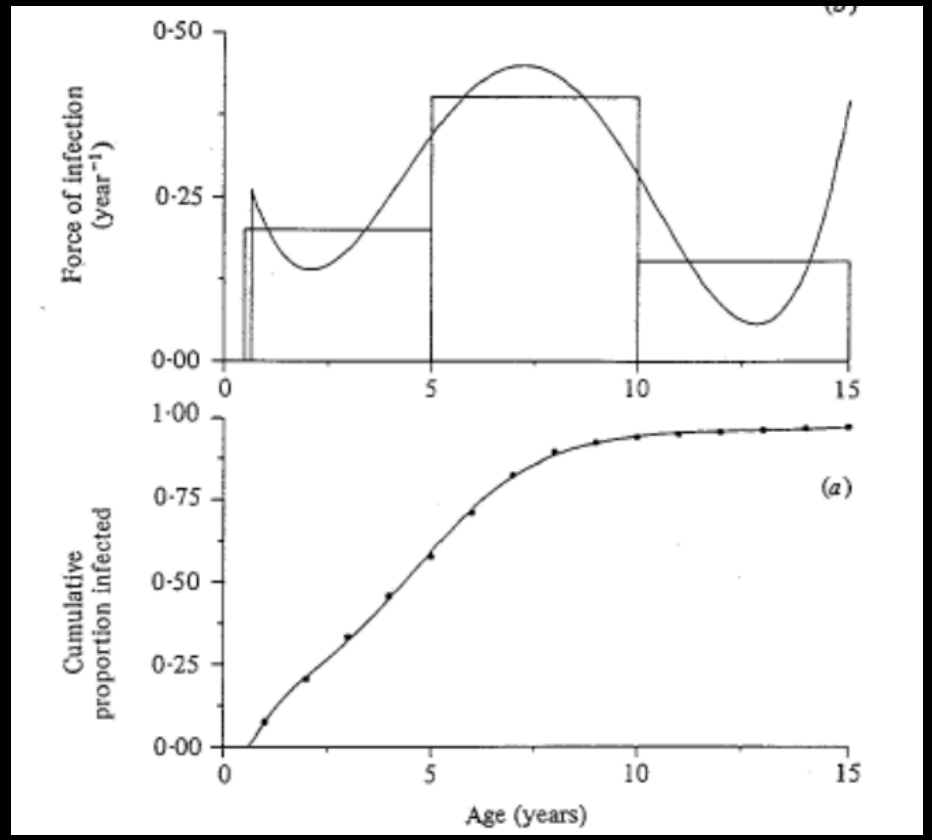
  - pre-school (<5 years old): 0.18
  - early school (5-10 years old): >0.3
  - late school (10-15 years old): <0.18

FOI for Measles in Aberdeen



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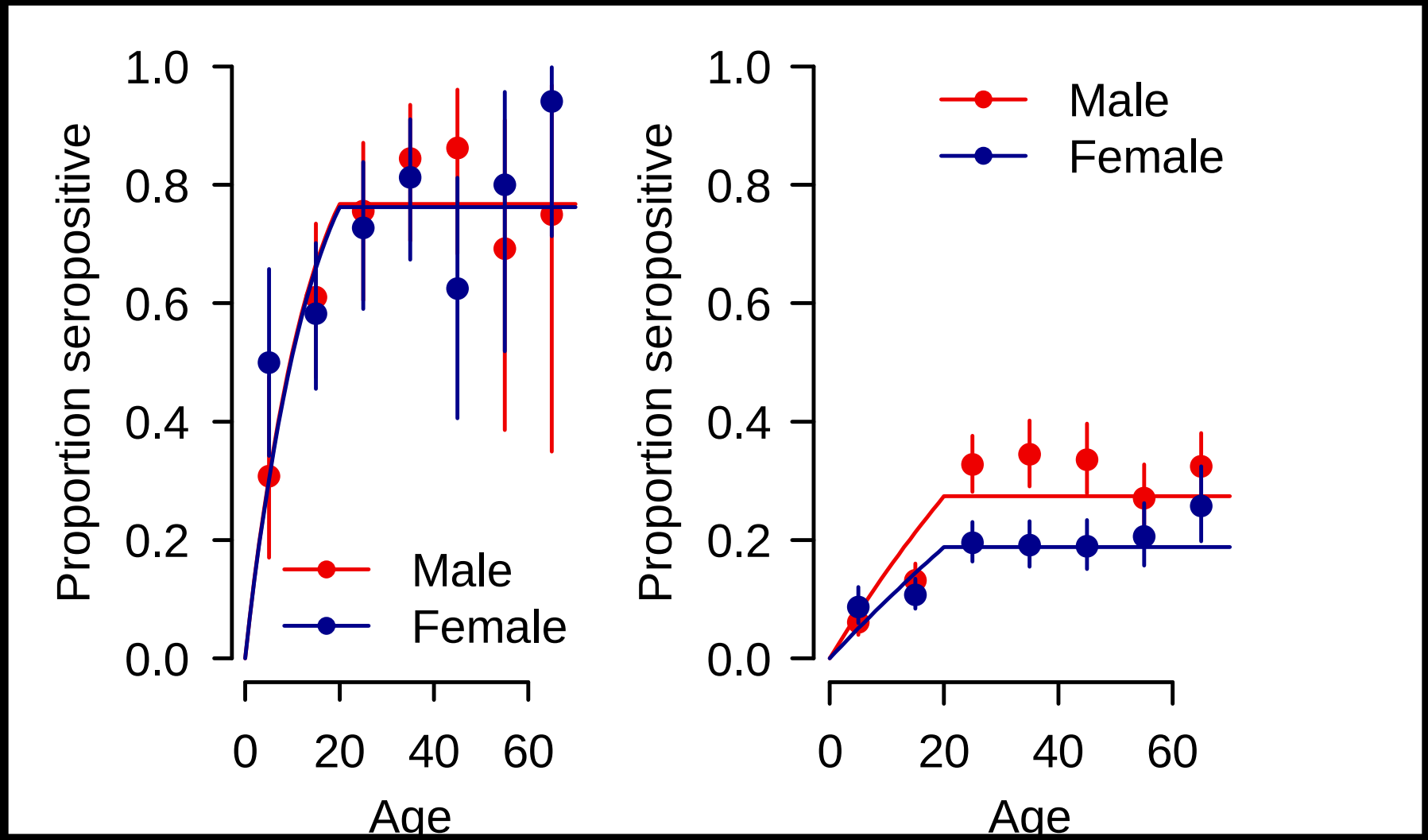
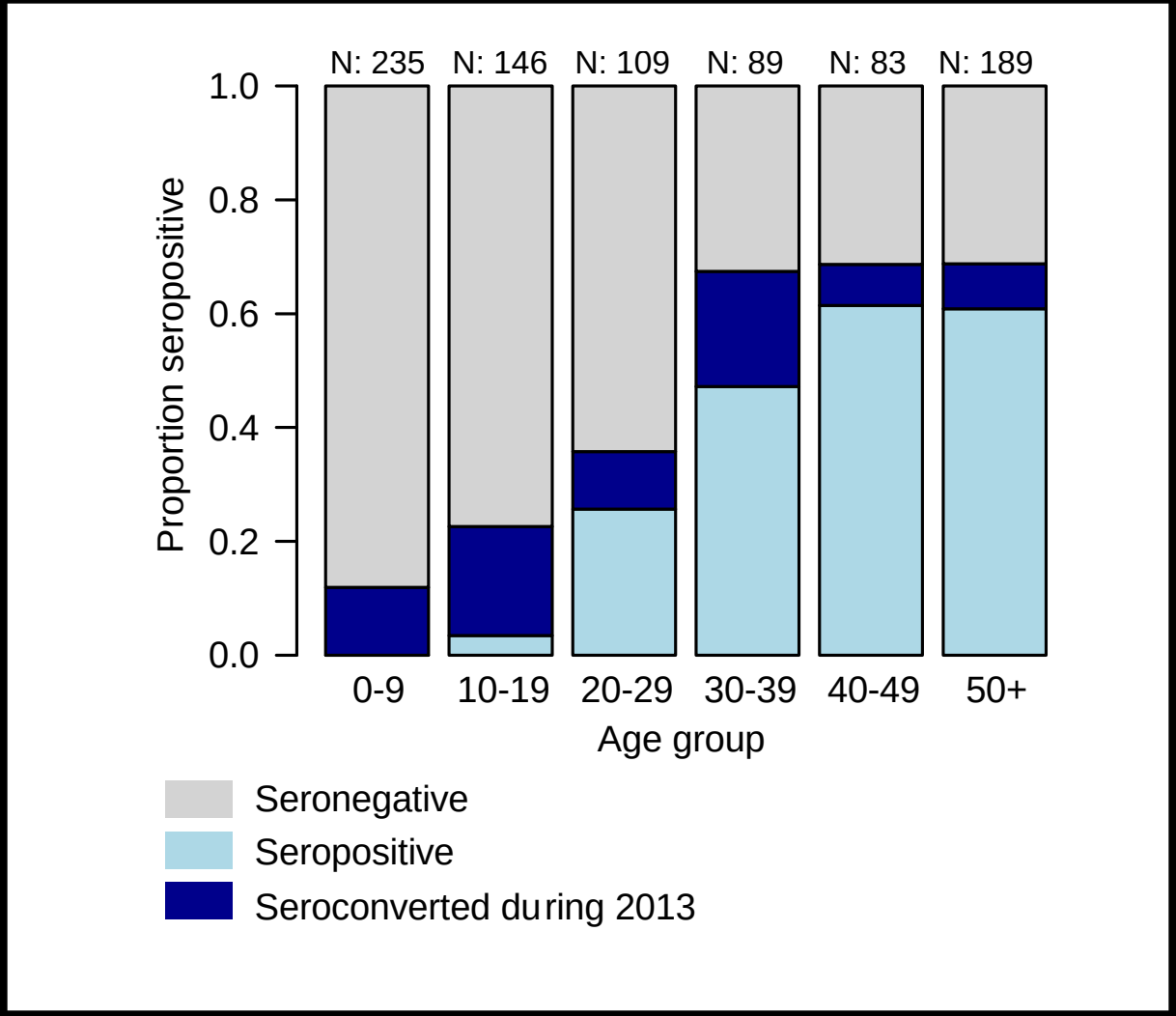
  - three FOIs for three age groups
  - pre-school (<5 years old): 0.18
  - early school (5-10 years old): >0.3
  - late school (10-15 years old): <0.18
- This is the fraction of each group that will become infected per year

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

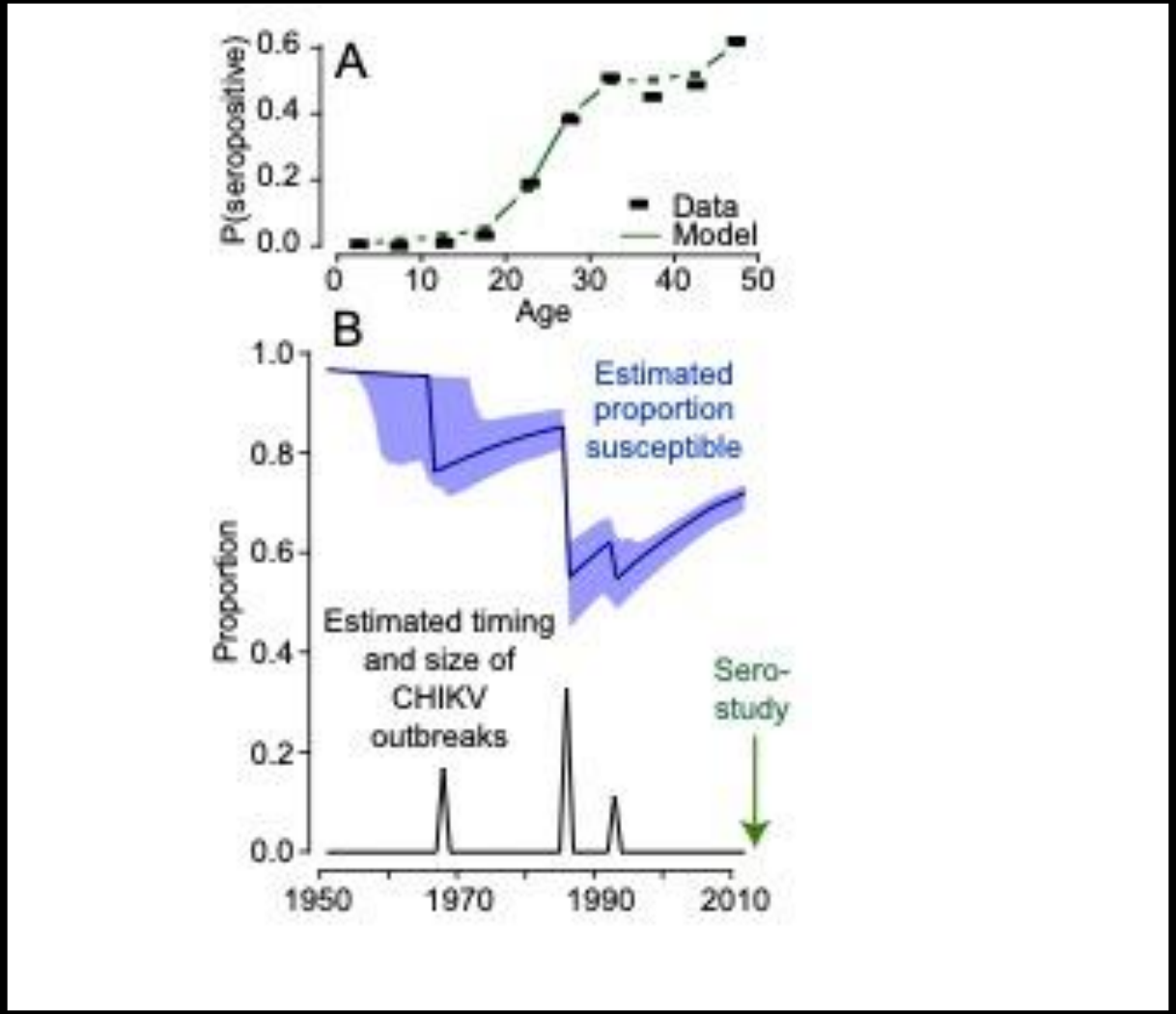


We can also identify more complex past infection histories – example with chikungunya



- 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.

Questions?

10 minute break

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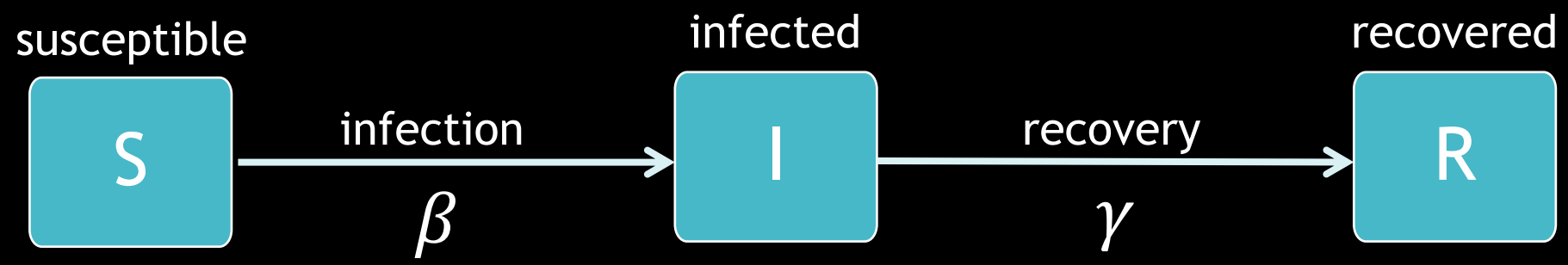
SIR Model



$$\frac{dS(t)}{dt} = -\beta S(t) I(t)$$

$$\frac{dI(t)}{dt} = \beta S(t) I(t) - \gamma I(t)$$

$$\frac{dR(t)}{dt} = \gamma I(t)$$

SIR Model Modifications

- We may want to investigate a new scenario
- Let’s say we have a bacterial infection where people start as susceptible, become infected, then recover
- But also we have a treatment that helps people recover more quickly
  - but the treatment still takes a little time to work (2 days)
  - everyone remains on the treatment until they recover

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- How does using this treatment affect the total number of people who get infected?

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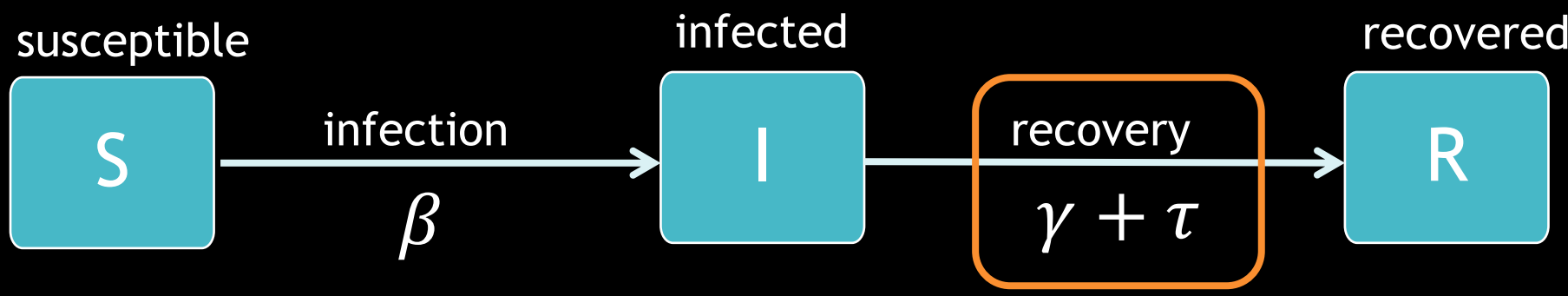

- β: transmission coefficient
- γ: recovery rate
- τ: treatment rate (1/2 days)

Treatment to Reduce Infectious Period

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- γ: recovery rate
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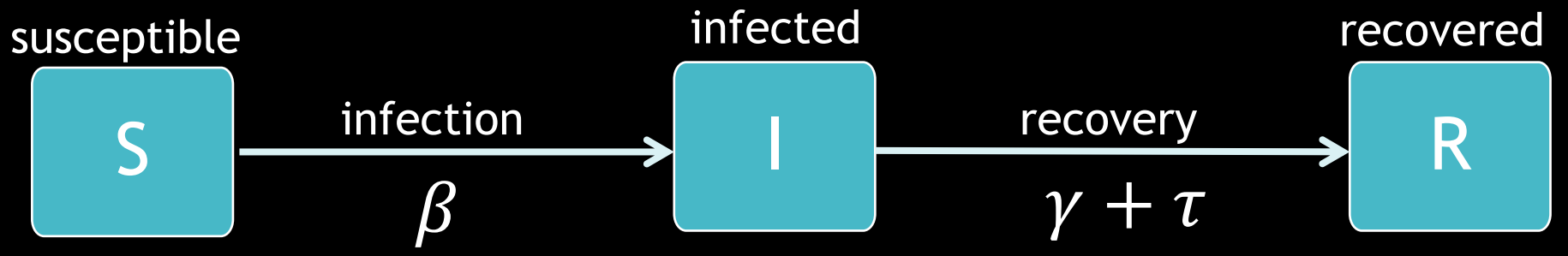


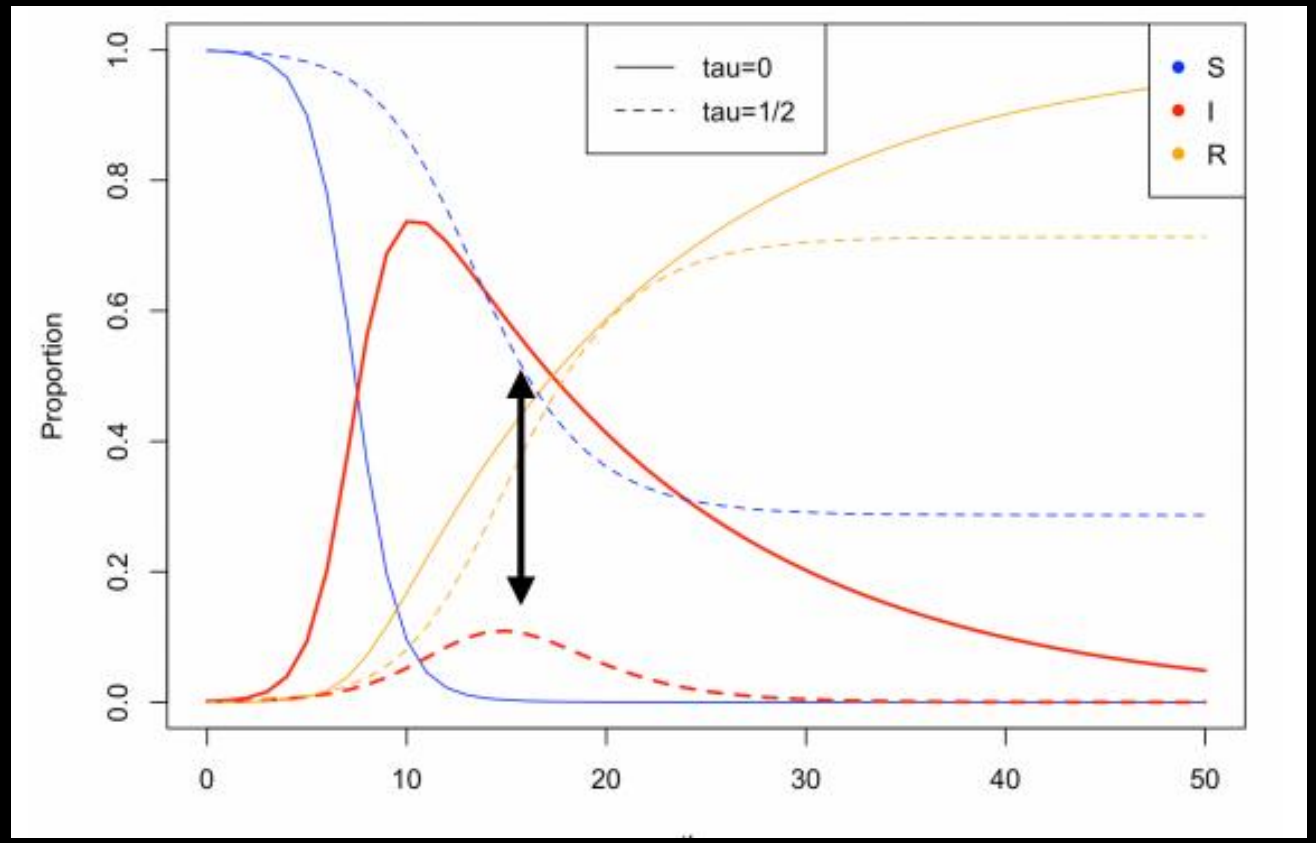
$$\frac{dS(t)}{dt} = -\beta S(t)I(t)$$

$$\frac{dI(t)}{dt} = \beta S(t)I(t) - (\gamma + \tau)I(t)$$

$$\frac{dR(t)}{dt} = (\gamma + \tau)I(t)$$

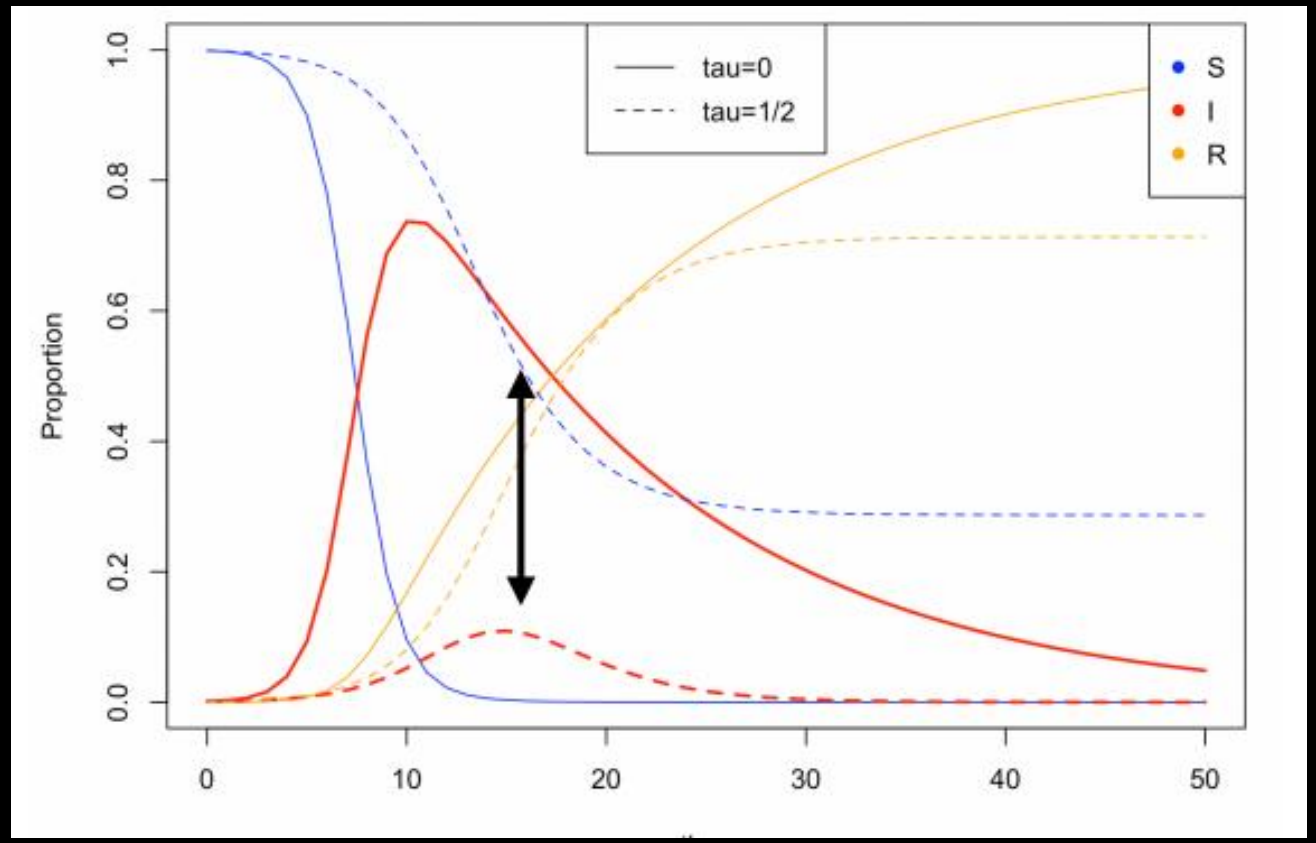
- Treatment makes people recover more quickly

Treatment to Reduce Infectious Period



- compare epidemic dynamics:
  - without treatment (τ=0)
  - with treatment (τ=1/2)

Treatment to Reduce Infectious Period

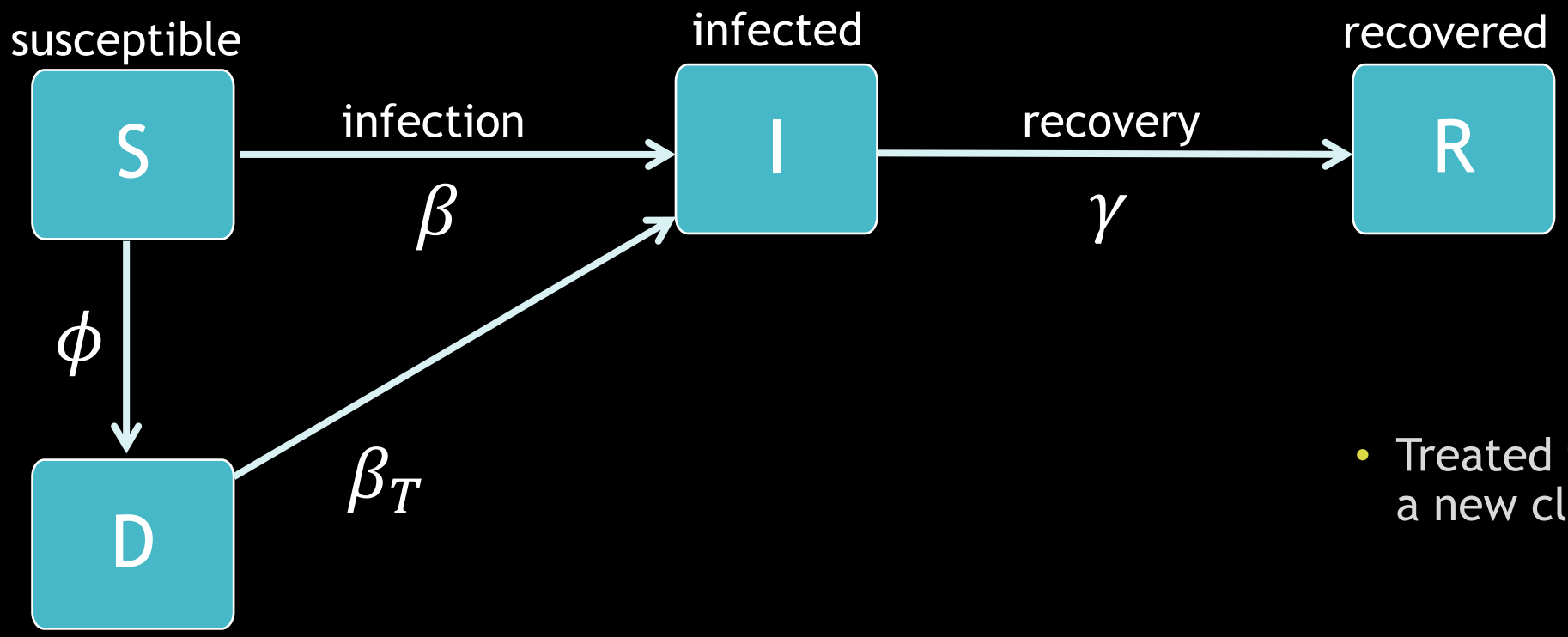


- compare epidemic dynamics:
  - without treatment (τ=0)
  - with treatment (τ=1/2)
- How does using this treatment affect the total number of people who get infected?
  - without treatment: 99% infected
  - with treatment: 71% infected

Treatment Provides Partial Protection

- Let’s say we have a viral infection where people start as susceptible, become infected, then recover
- But we have a drug treatment that helps decrease transmission in infected people
  - transmission is reduced by half
  - treatment occurs at a specific rate
  - everyone remains on the treatment until they recover

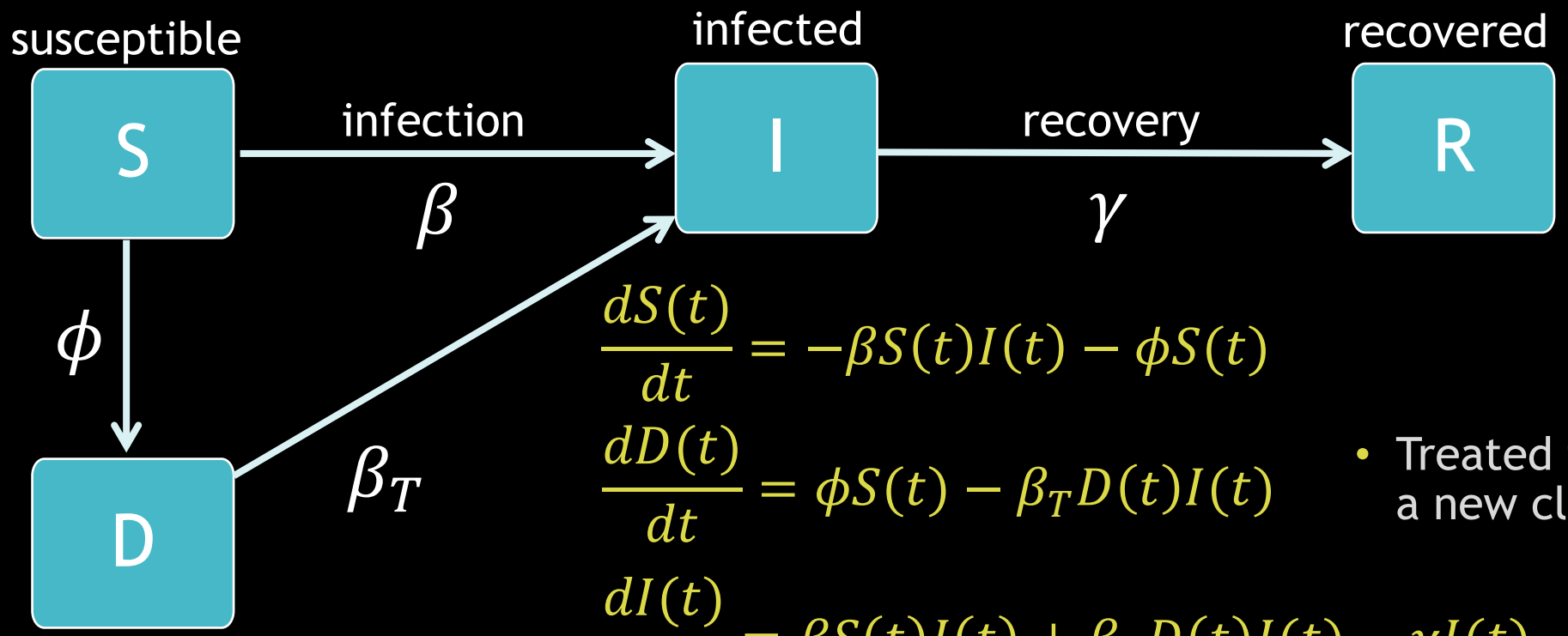
Treatment Provides Partial Protection



- β: transmission coefficient
- γ: recovery rate
- ϕ: rate of providing treatment
- β_T: transmission coefficient for treated individuals

- Treated individuals are in a new class

Treatment Provides Partial Protection



$$\frac{dS(t)}{dt} = -\beta S(t)I(t) - \phi S(t)$$

$$\frac{dD(t)}{dt} = \phi S(t) - \beta_T D(t)I(t)$$

$$\frac{dI(t)}{dt} = \beta S(t)I(t) + \beta_T D(t)I(t) - \gamma I(t)$$

$$\frac{dR(t)}{dt} = \gamma I(t)$$

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- γ: recovery rate
- ϕ: rate of providing treatment
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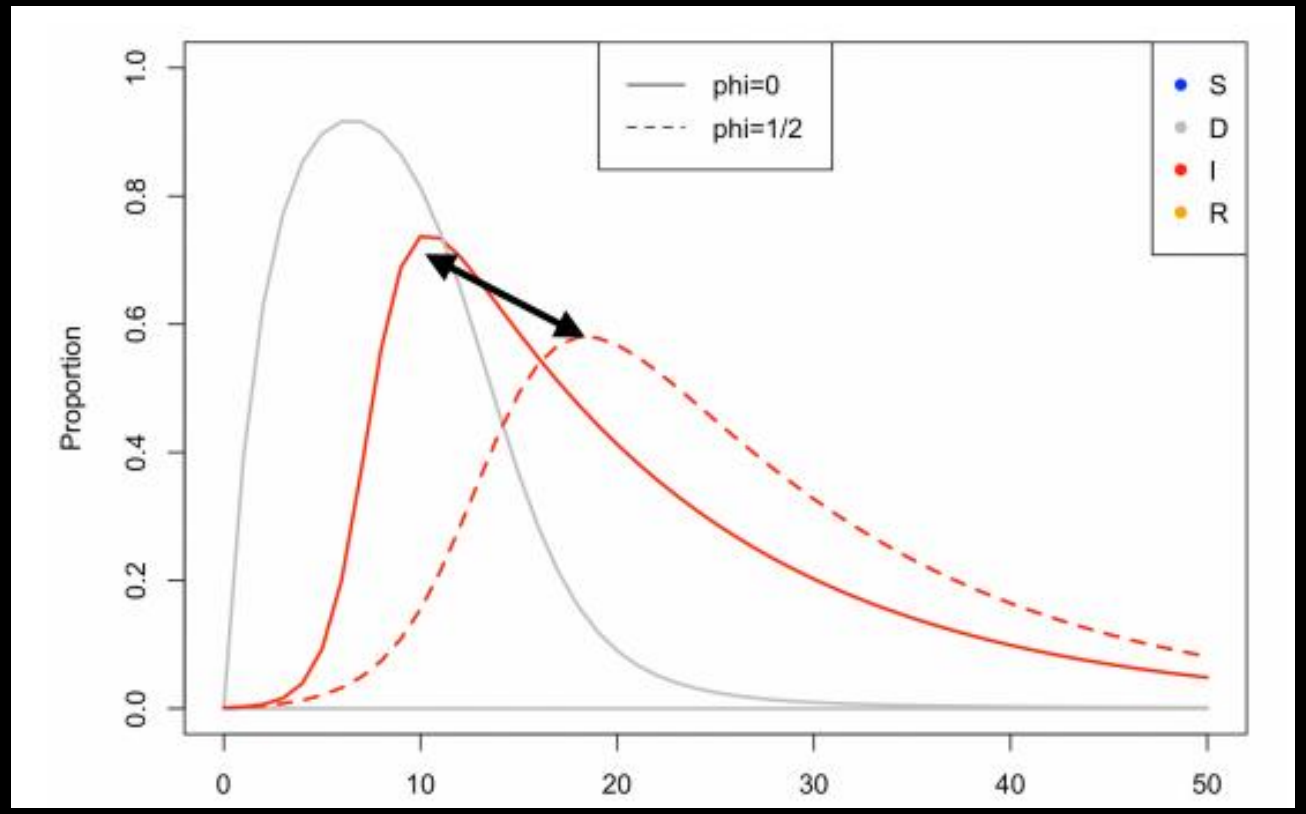
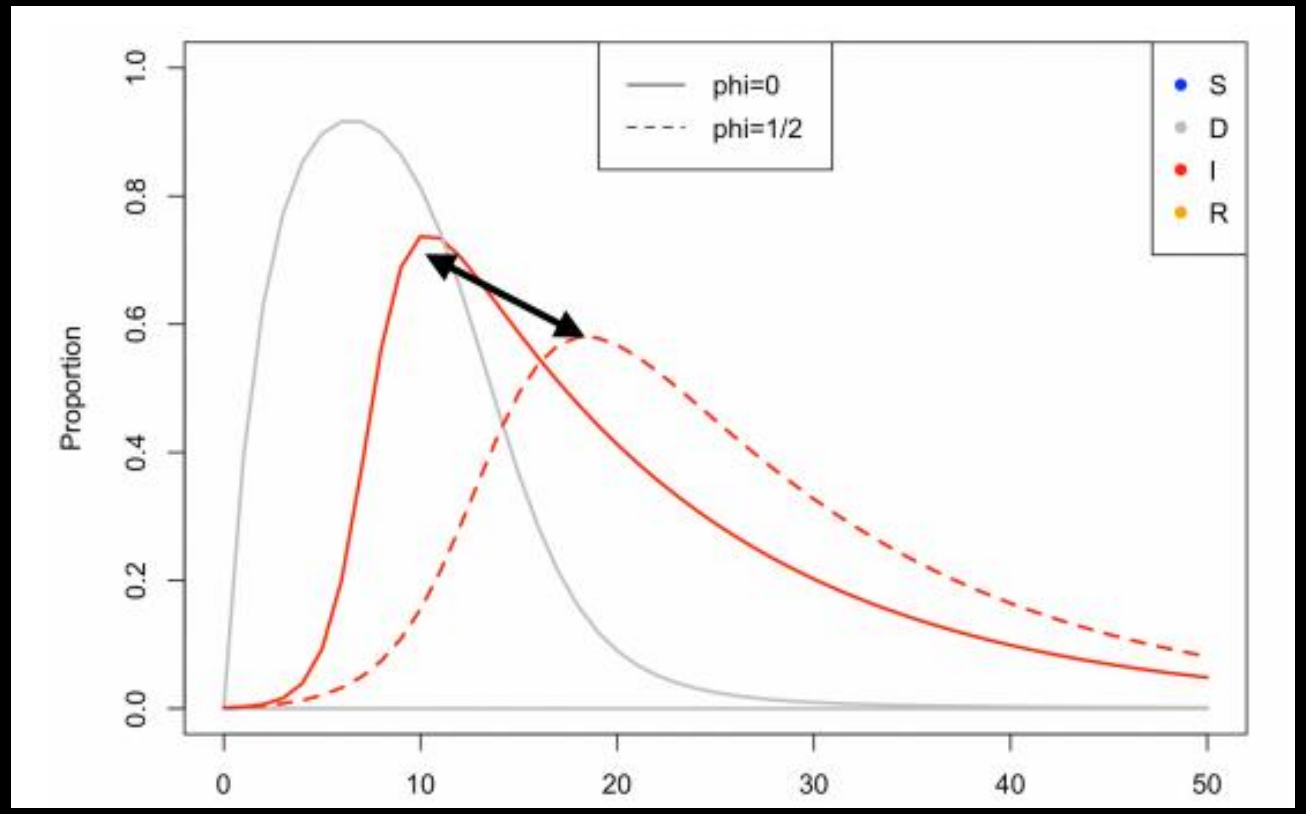
Treatment Provides Partial Protection



- compare epidemic dynamics:
  - without treatment (ϕ =0)
  - with treatment (ϕ =1/2)

Treatment Provides Partial Protection

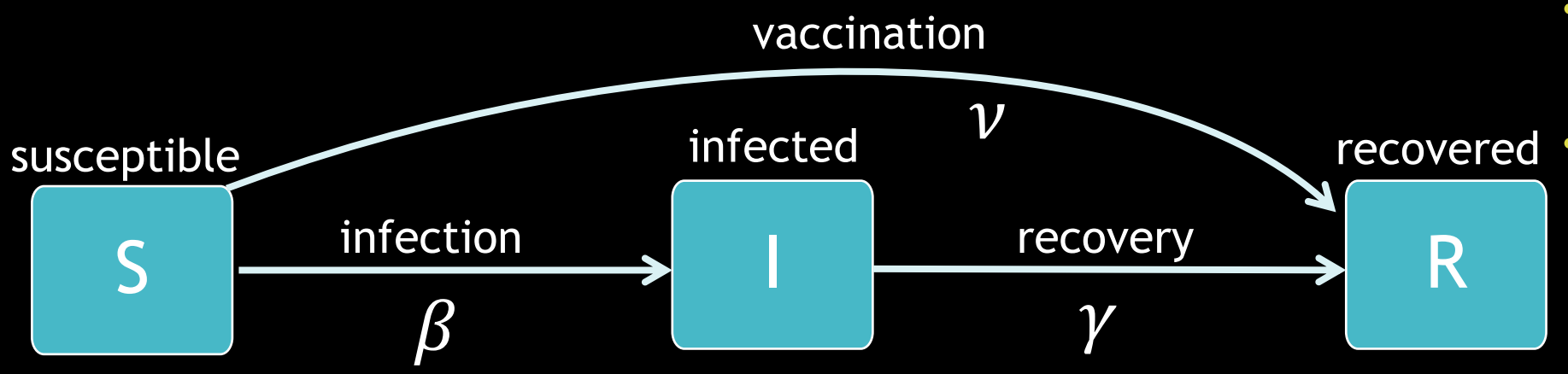


- compare epidemic dynamics:
  - without treatment (ϕ =0)
  - with treatment (ϕ =1/2)
- How does using this treatment affect the total number of people who get infected?
  - without treatment: 99% infected
  - with treatment: 99% infected

Perfect Vaccination

- No waning immunity, no partial protections
- Susceptible individuals are vaccinated at a specific rate

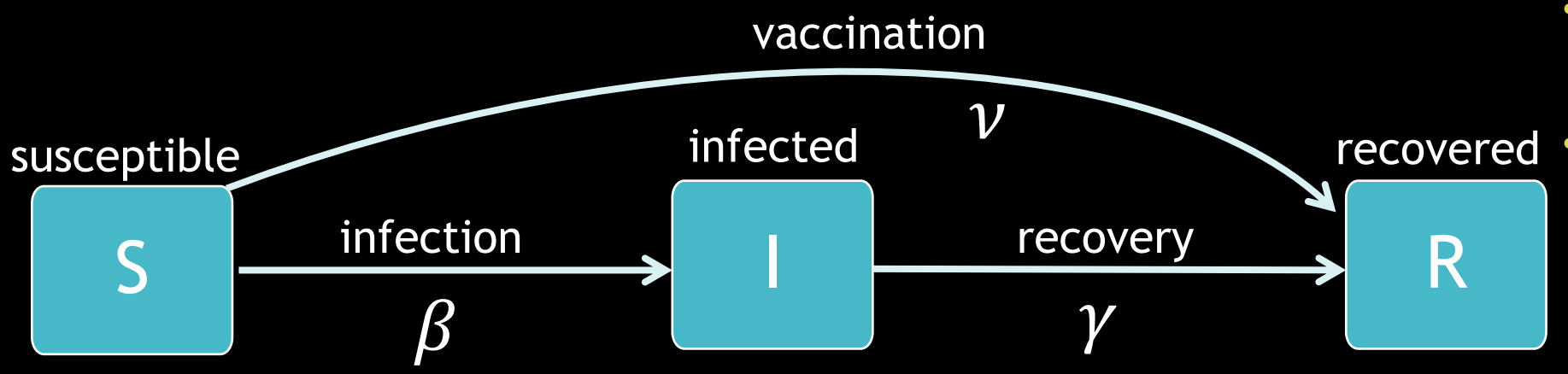
Perfect Vaccination



- ß: transmission coefficient
- γ: recovery rate
- v: vaccination rate (1/3 days)

- Vaccination moves susceptible people to the recovered compartment

Perfect Vaccination



- ß: transmission coefficient
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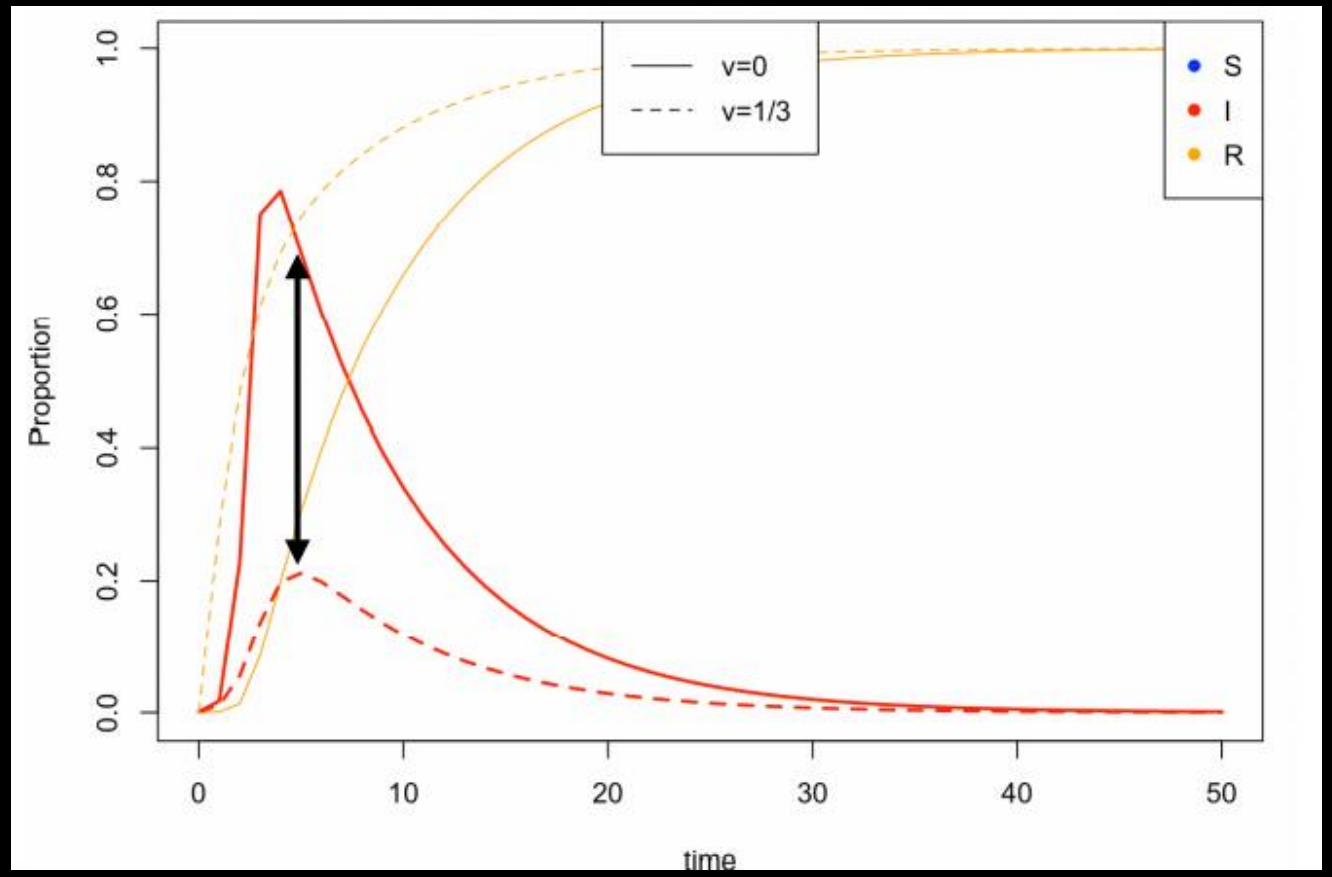
$$\frac{dS(t)}{dt} = -\beta S(t)I(t) - \nu S(t)$$

$$\frac{dI(t)}{dt} = \beta S(t)I(t) - \gamma I(t)$$

$$\frac{dR(t)}{dt} = \gamma I(t) + \nu S(t)$$

- Vaccination moves susceptible people to the recovered compartment

Perfect Vaccination



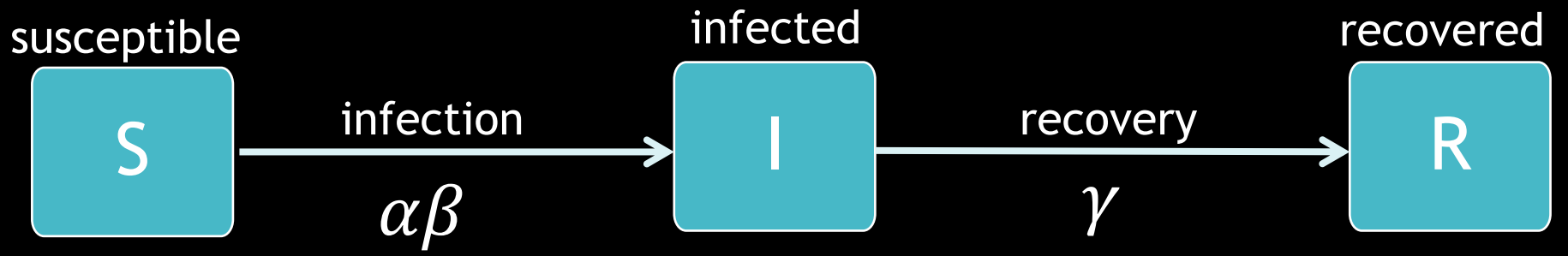
- compare epidemic dynamics:
  - without vaccine (v=0)
  - with vaccine (v =1/3)
- Enormous decrease in total number infected!

Social Distancing

- When there is no treatment available, non-pharmaceutical interventions are a good option
- Social distancing reduces the number of contacts at a set rate

Social Distancing

- β: transmission coefficient
- γ: recovery rate
- α: reduction coefficient



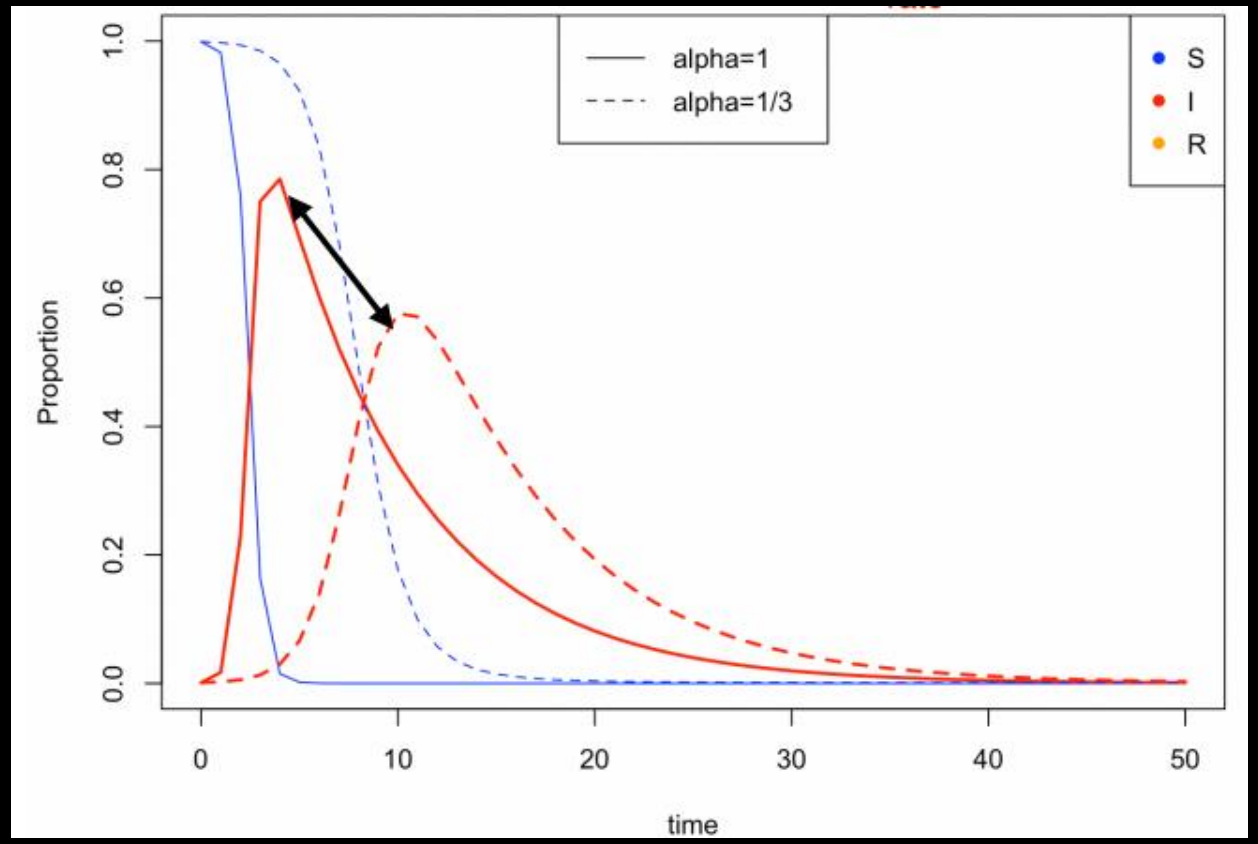
$$\frac{dS(t)}{dt} = -\alpha\beta S(t)I(t)$$

$$\frac{dI(t)}{dt} = \alpha\beta S(t)I(t) - \gamma I(t)$$

$$\frac{dR(t)}{dt} = \gamma I(t)$$

- Transmission is reduced because contact is reduced

Perfect Vaccination



- compare epidemic dynamics:
  - without distancing (α=0)
  - with distancing (α =1/3)

Thought Process for Building Models

- The basic SIR model can be adapted for many situations
- For any new model, consider:
  - What is changing?
  - Do I need a new compartment? Fewer compartments?
  - Do I need to change rates?
  - Do I need additional transitions?

Thought Process for Building Models

- The basic SIR model can be adapted for many situations
- For any new model, consider:
  - What is changing?
  - Do I need a new compartment? Fewer compartments?
  - Do I need to change rates?
  - Do I need additional transitions?
- Translate this to your differential equations
  - represent the flow of individuals between compartments
  - update your equations to reflect any new transitions

Questions?

10 minute break

Workshop Schedule

Time	Topics
2:00–2:05 pm	~~Greetings~~
2:05–2:50 pm	~~Using Serology Data~~
2:50–3:00 pm	~~Break~~
3:00–3:40 pm	~~Modeling Interventions~~
3:40–3:50 pm	Break
3:50–5:00 pm	R Session