Week 2: SIR Models & Epidemic Parameters

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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

Objectives

- Understand how SIR models can be used to estimate epidemic determinants
- Learn new methods to estimate R0

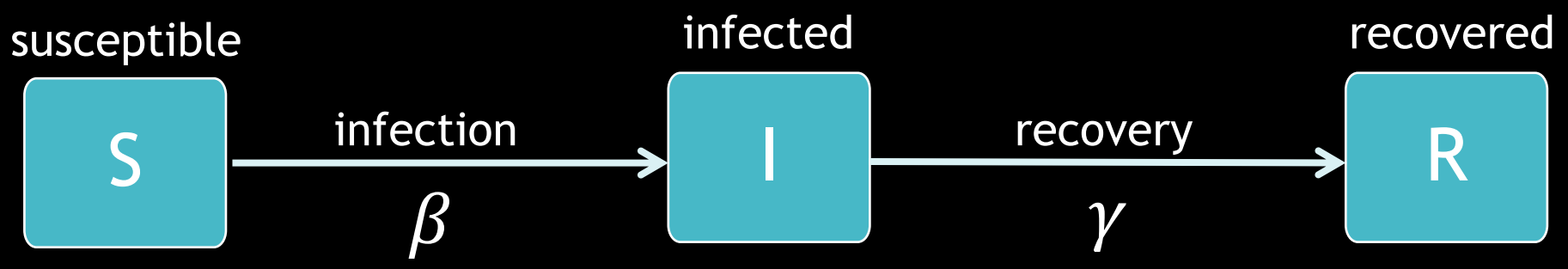
Post Questions in the Chat!

(or ask over microphone)

Workshop Schedule

Time	Topics
2:00—2:10 pm	~~Greetings~~
2:10—2:40 pm	SIR & R0 Relationship
2:40—2:50 pm	Break
2:50—3:15 pm	R0 & Final Epidemic Size
3:15—3:30 pm	R0 & Initial Growth
3:30—3:40 pm	Break
3:40—5:00 pm	R Session

SIR Model: Kermack & McKendrick



- β is a transmission coefficient
  - it is the probability of a susceptible becoming infected if they contact an infected person

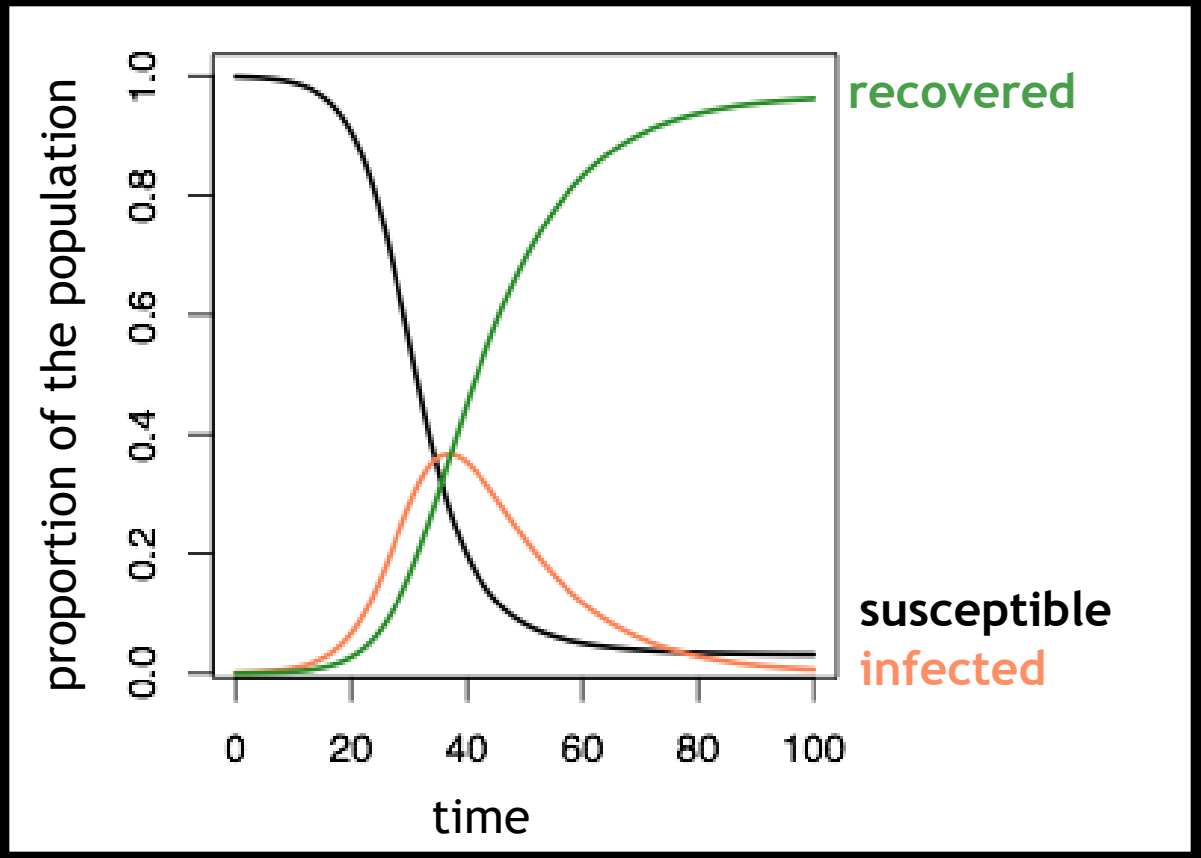
$$\frac{dS(t)}{dt} = -\beta S(t)I(t)$$

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

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

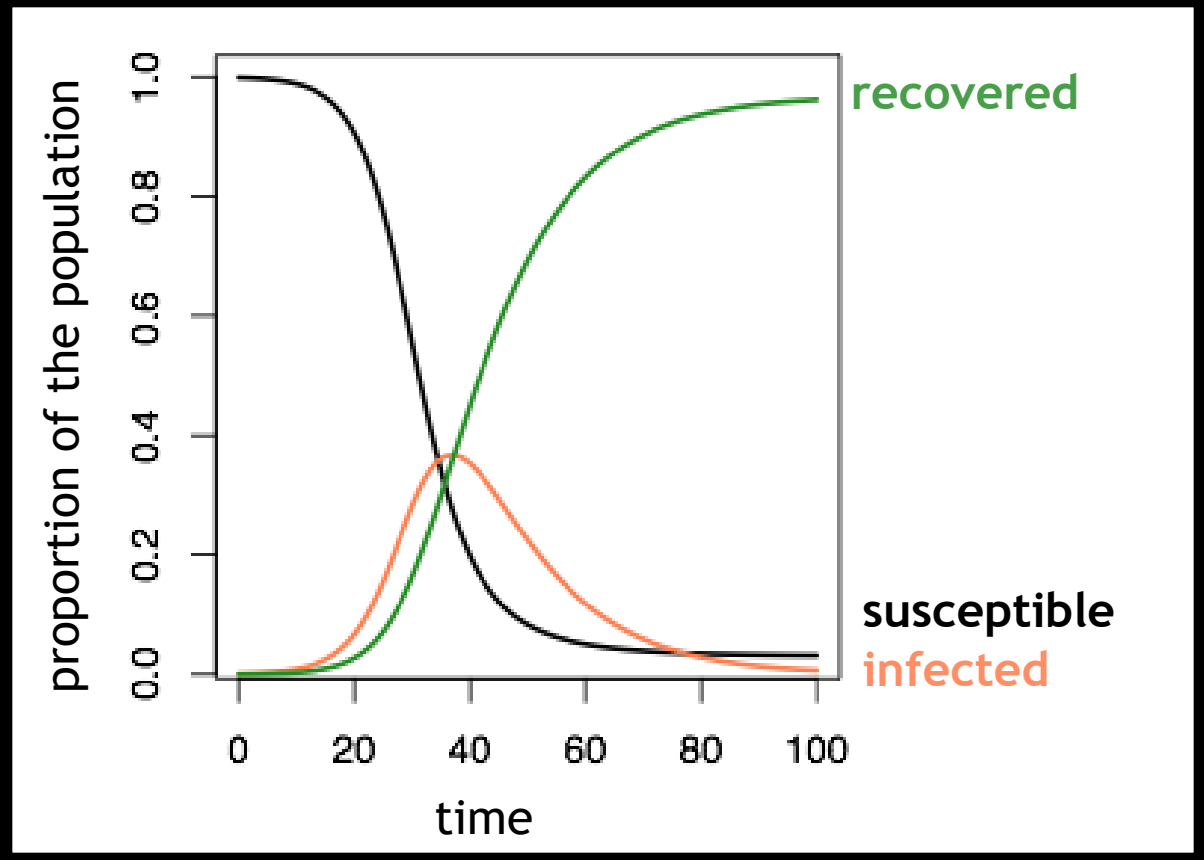
- γ is the recovery rate
  - 1/ γ is the duration of infectiousness

SIR Model Output



- We can examine the epidemic dynamics
- We will have values for S(t), I(t), and R(t) for each time step t
  - these can be expressed as population proportions and plotted
  - we can also find totals for each compartment at the end of the epidemic

SIR Model Output



- In our first examples last week, we input parameter values and starting values

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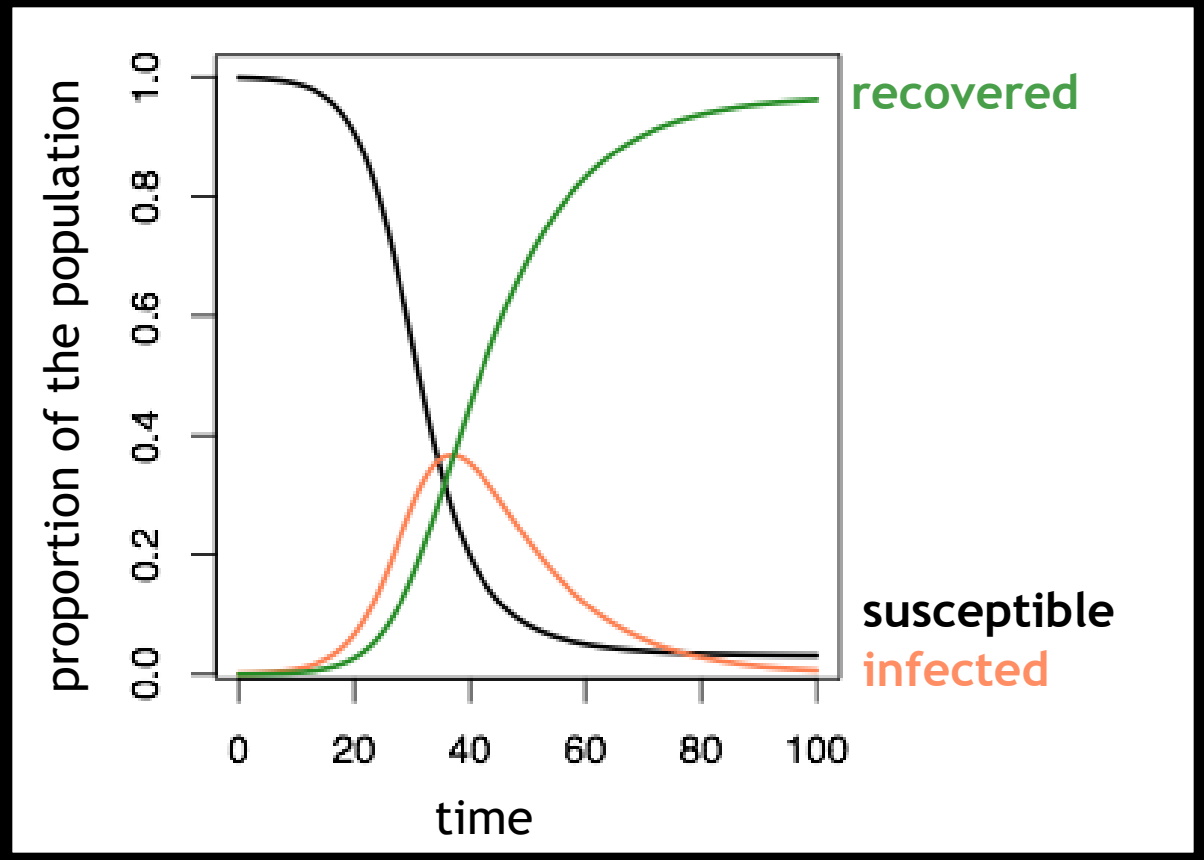

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  - parameter values for beta and gamma
  - starting values for number of people in each compartment S, I, R

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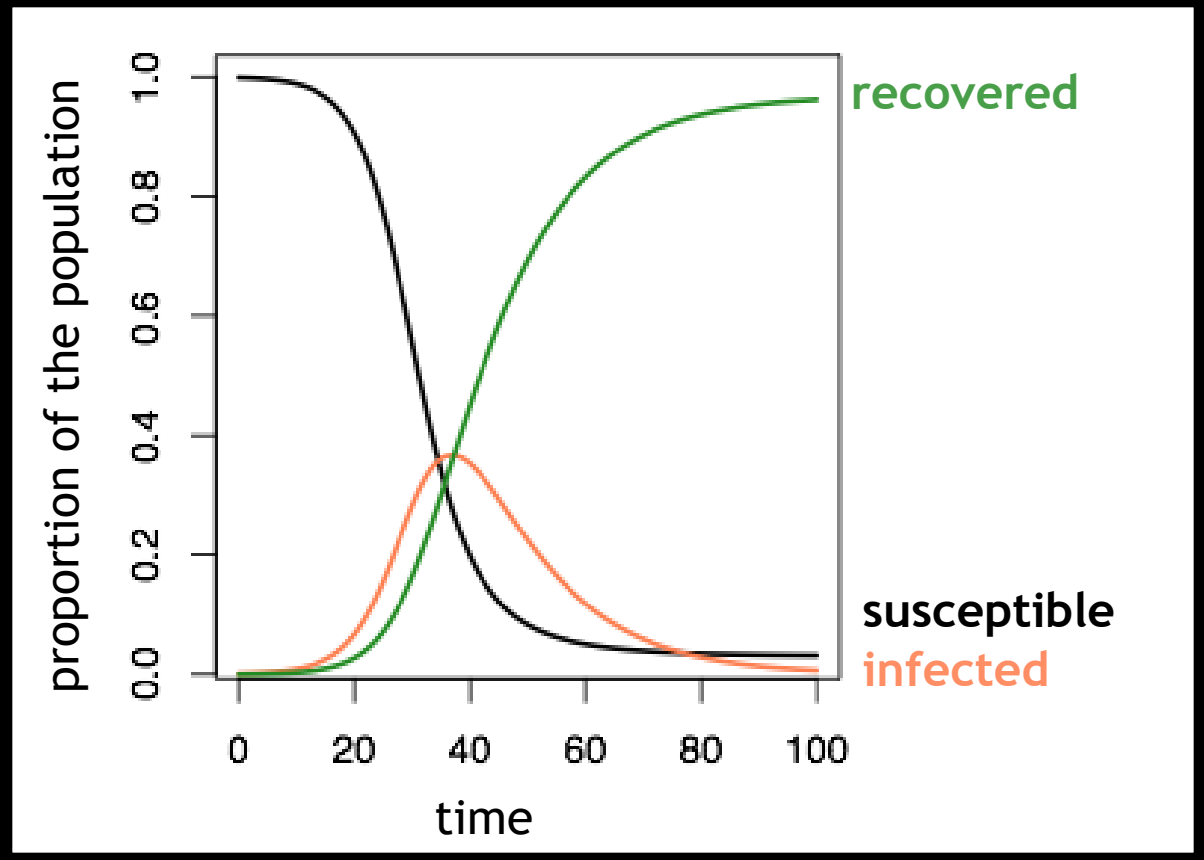
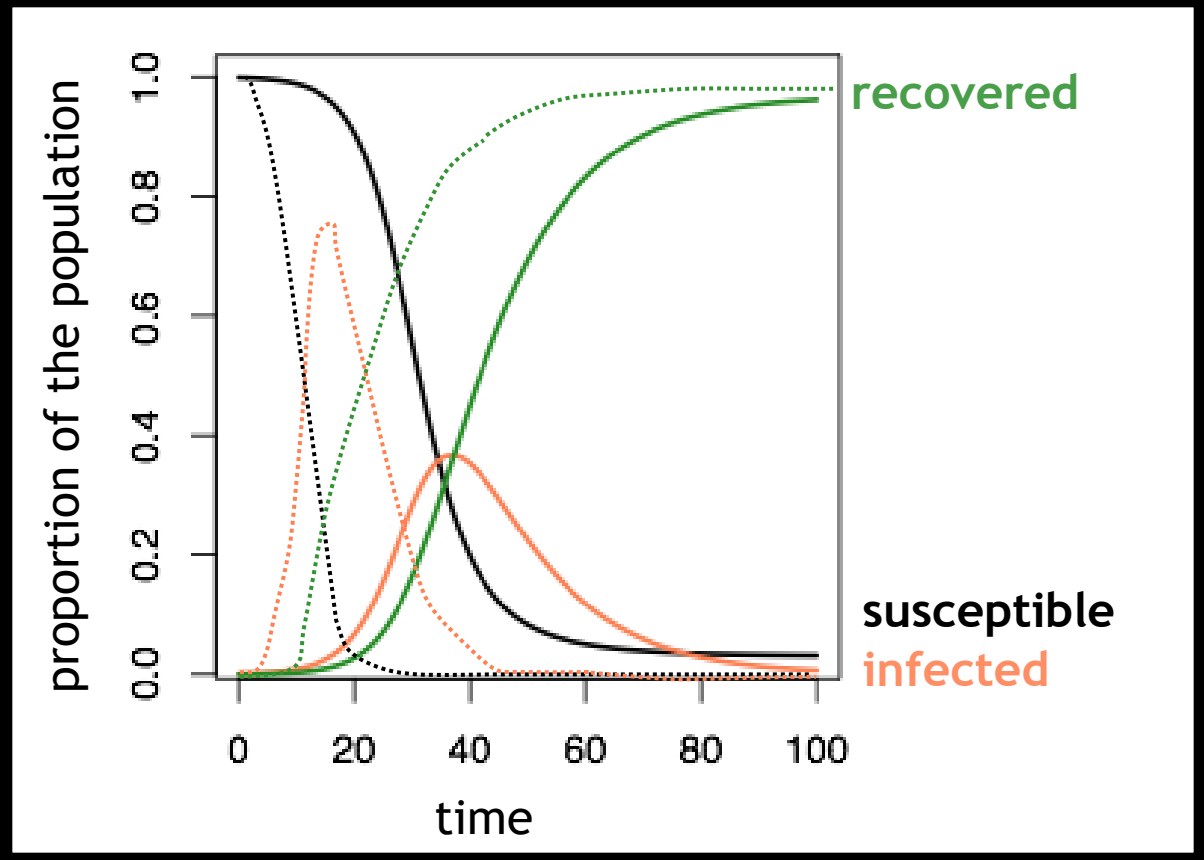


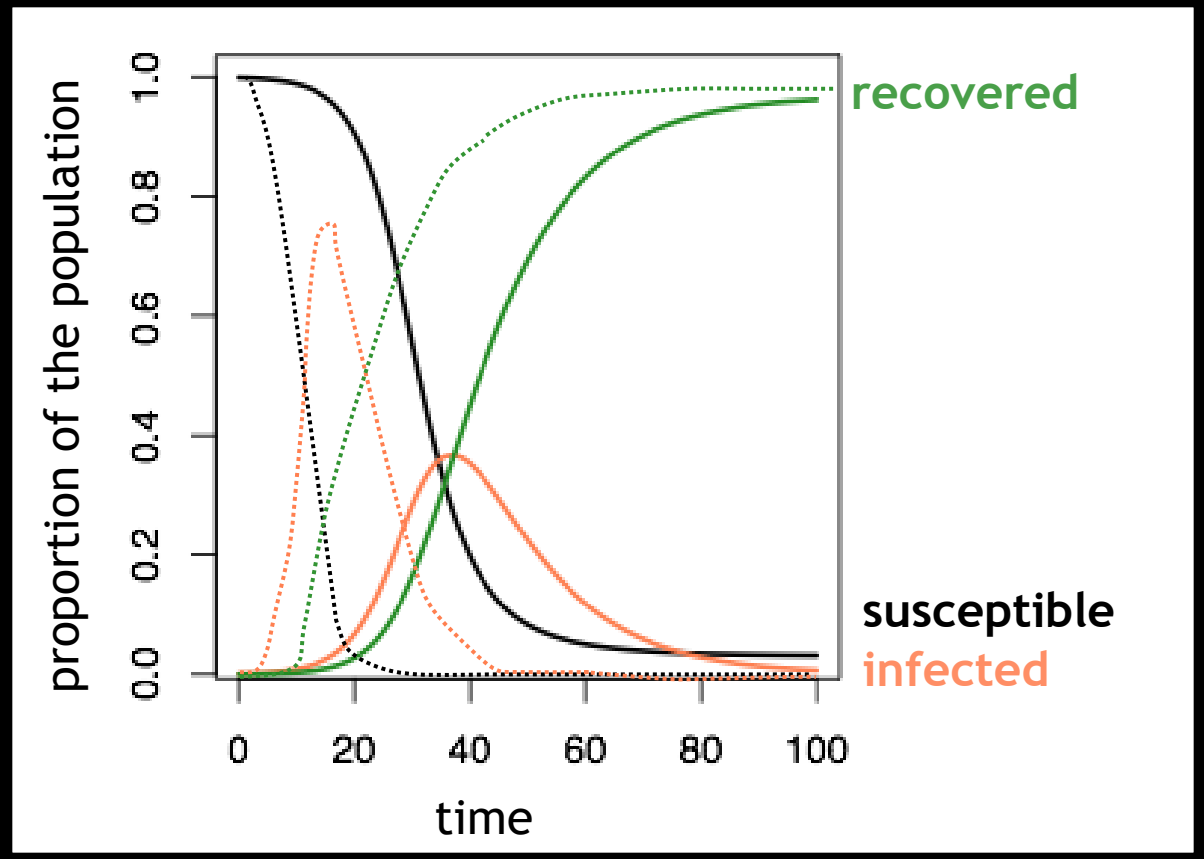
- In our first examples last week, we input parameter values and starting values
  - parameter values for beta and gamma
  - starting values for number of people in each compartment S, I, R
- What about our other epidemic determinants?

SIR Model Output



- Shape of curves will depend on epidemic determinants
  - solid lines → $R_0 = 3.6$
  - dotted lines → $R_0 = 13.2$

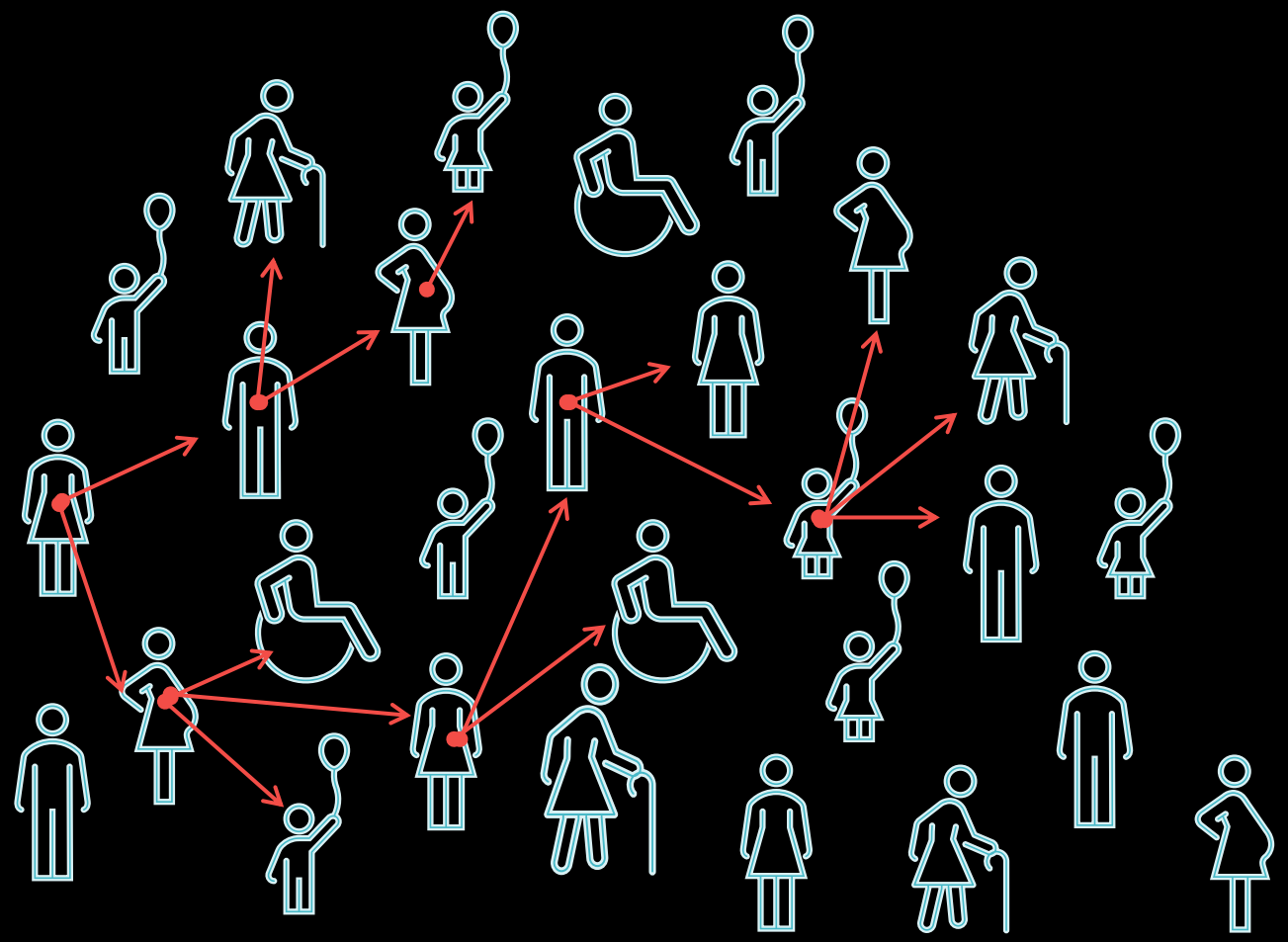
SIR Model Output



- Shape of curves will depend on epidemic determinants
  - solid lines → $R_0 = 3.6$
  - dotted lines → $R_0 = 13.2$
- What differences can we note about these two epidemics with two different basic reproductive numbers?

R_0 & SIR Models

- The calculation of R0 depends on the structure of the model being used
  - for our SIR model:
  - $R_0 = \frac{\beta N}{\gamma}$
  - β = the transmission coefficient
  - γ = the recovery rate
  - N = the total population



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- Recall that our model assumes:
  - closed SIR structure
  - steady values for beta and gamma
  - random mixing

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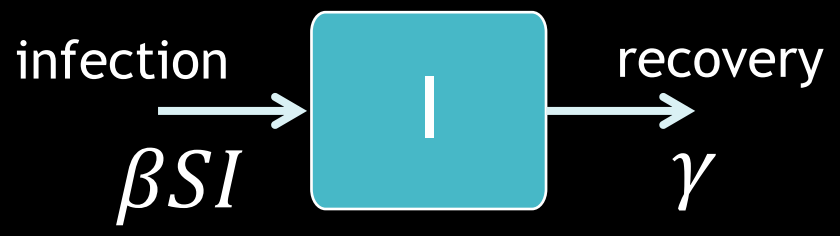
- Recall that our model assumes:
  - closed SIR structure
  - steady values for beta and gamma
  - random mixing
- We may want to consider non-random mixing and add a contact rate *c* to the model
  - c=probability of contact
  - In this case:
  - $R_0 = \frac{\beta_c N c}{\gamma}$

R_0 & SIR Models

- What is R0 doing in our SIR model?
- Think about the beginning of the epidemic
  - R0 is appropriate because it is the start of the epidemic
  - R0 drives the number of people going into the infected compartment
  - everyone is susceptible
  - no one is infected



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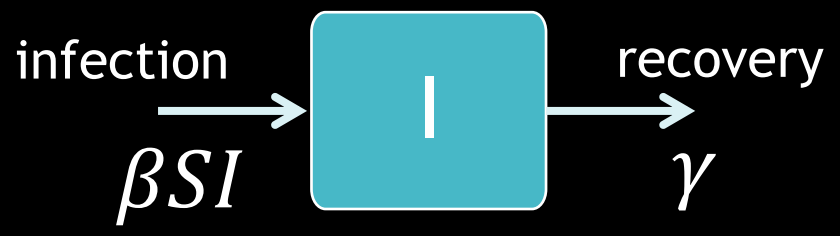
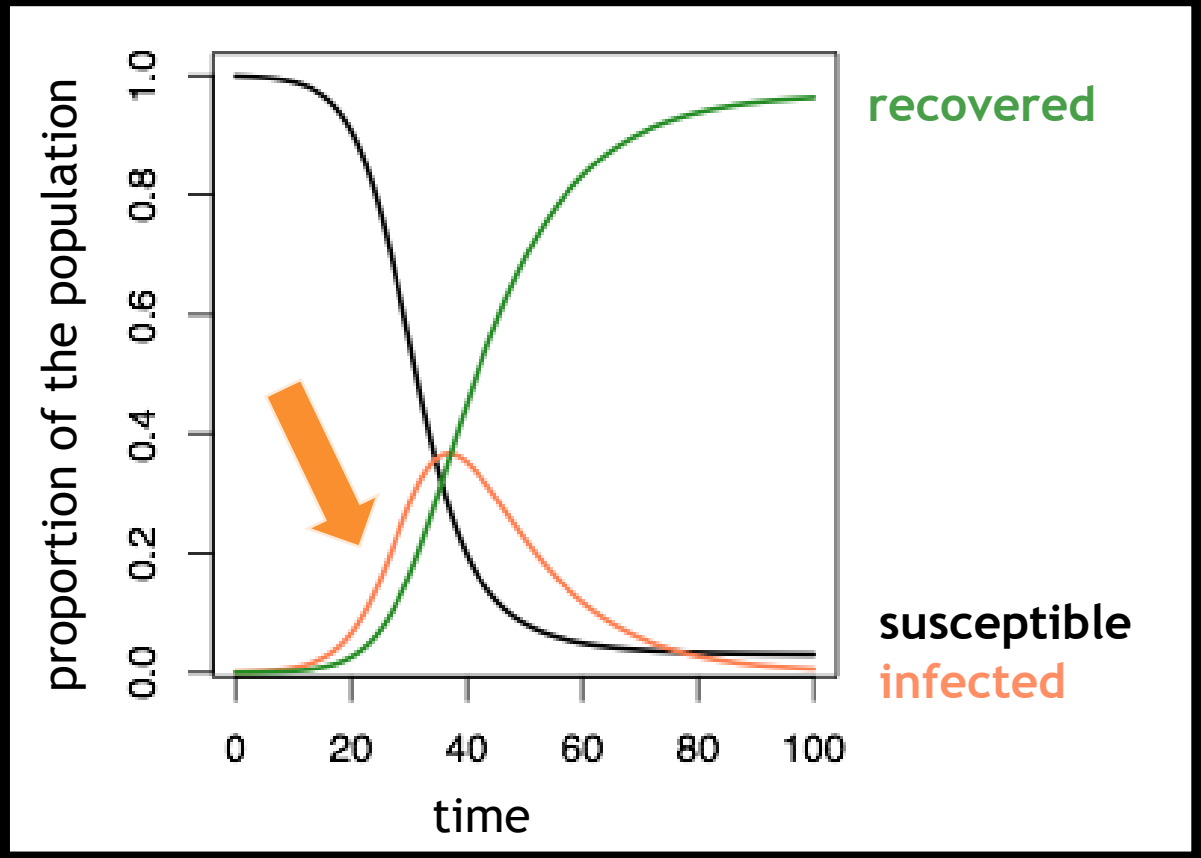


$$\boxed{\beta S \approx \beta N}$$

at the start of an epidemic, contact with anyone could result in an infection

$$R_0 = \frac{\beta N}{\gamma}$$

R_0 & Transmission Dynamics



- Early in the epidemic, the number infected is increasing
  - the rate of change is greater than 0

$$0 < \frac{dI(t)}{dt} = \beta S(t) I(t) - \gamma I(t)$$

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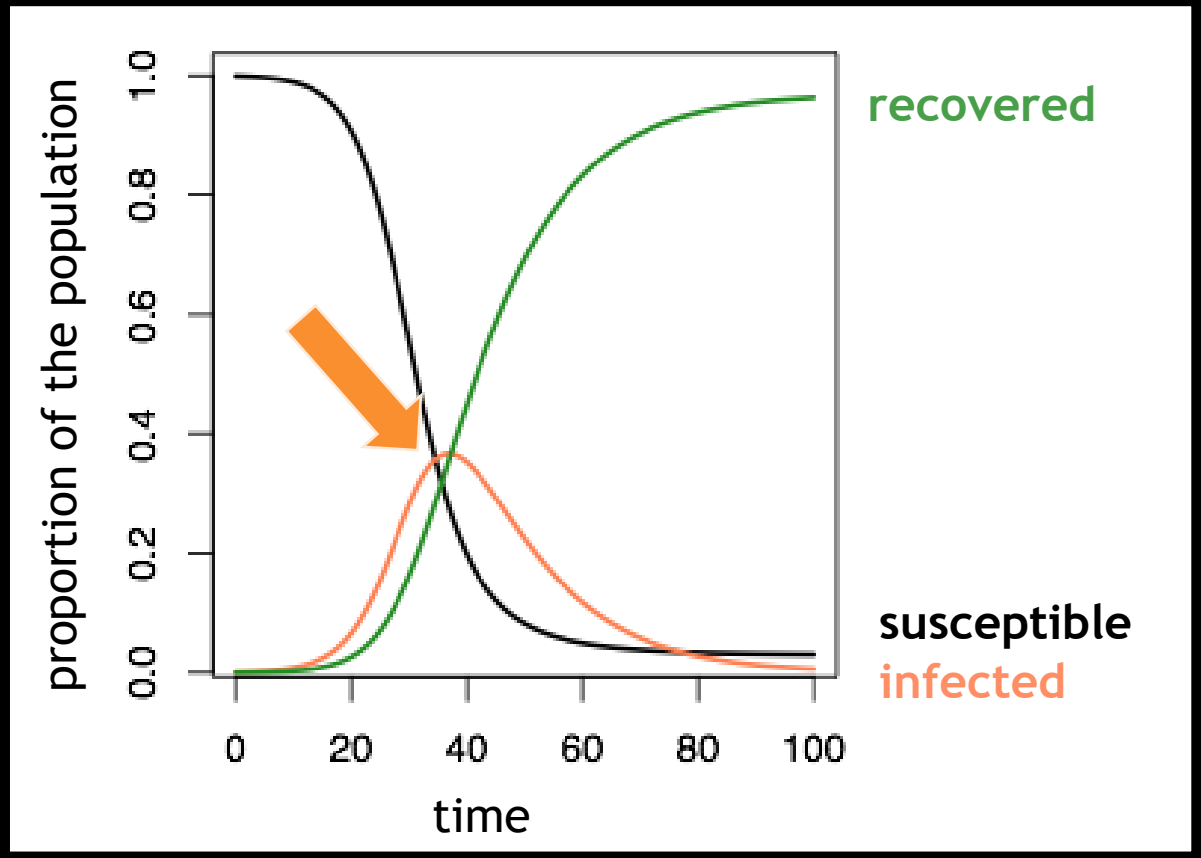

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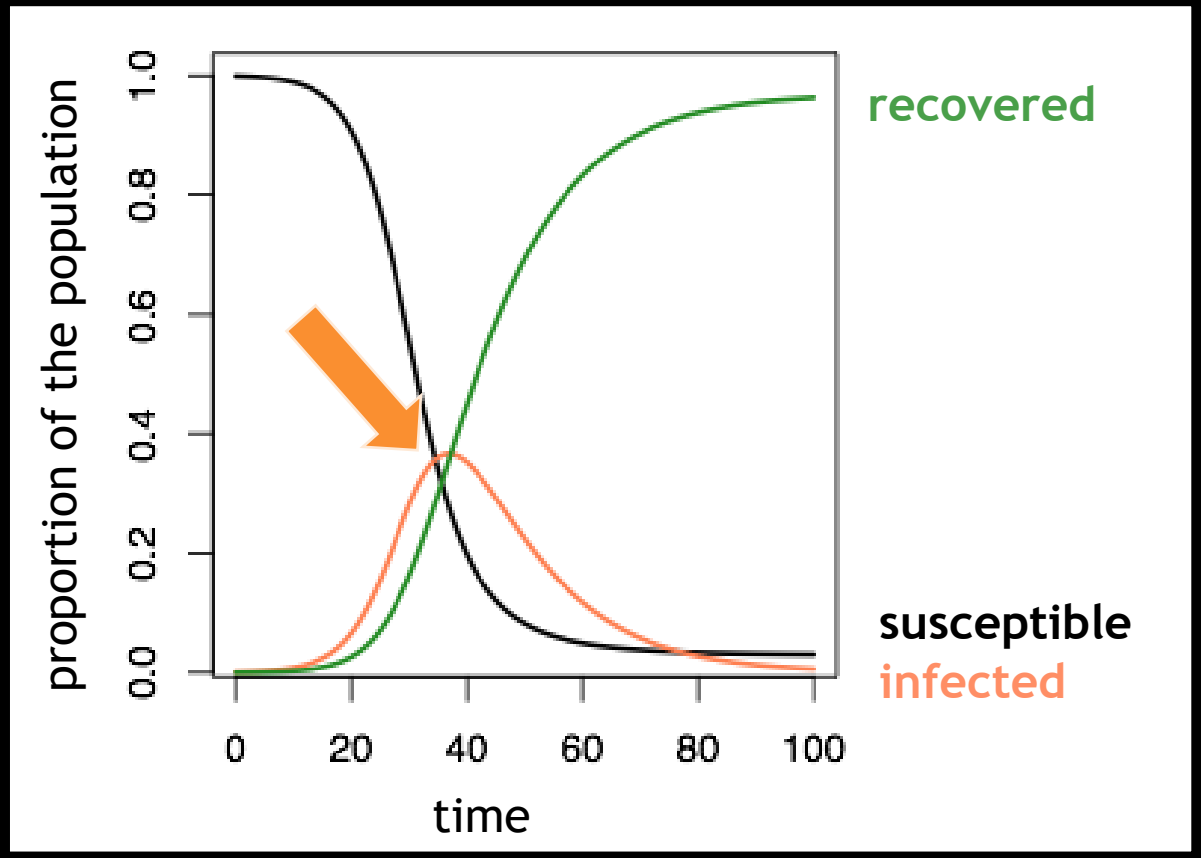

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$$\beta S(t)I(t) = \gamma I(t)$$

$$\frac{\beta S(t)}{\gamma} = 1$$

Reproductive Number during Epidemic

R_0

- If population is fully susceptible:

$$R_0 = \frac{\beta N}{\gamma}$$

R

- If only a fraction of the population is susceptible (later in the epidemic)
  - only contacts that are susceptible (S/N) could lead to infection

$$R = \frac{\beta N}{\gamma}\frac{S}{N} = \frac{\beta S}{\gamma}$$

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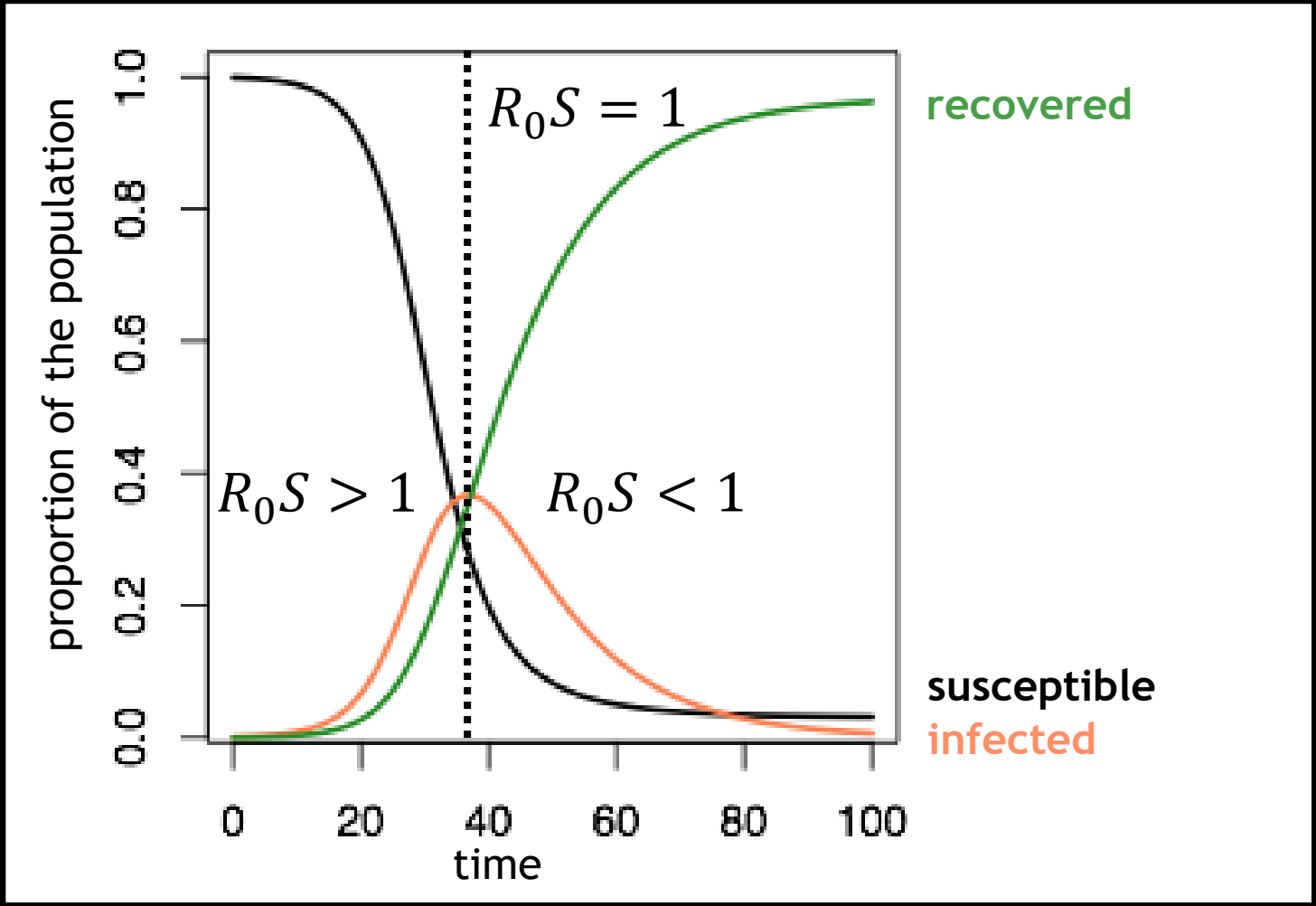
- Remember, on the previous slide we showed when this expression equals 1, the infection rate of change is 0

Reproductive Number during Epidemic



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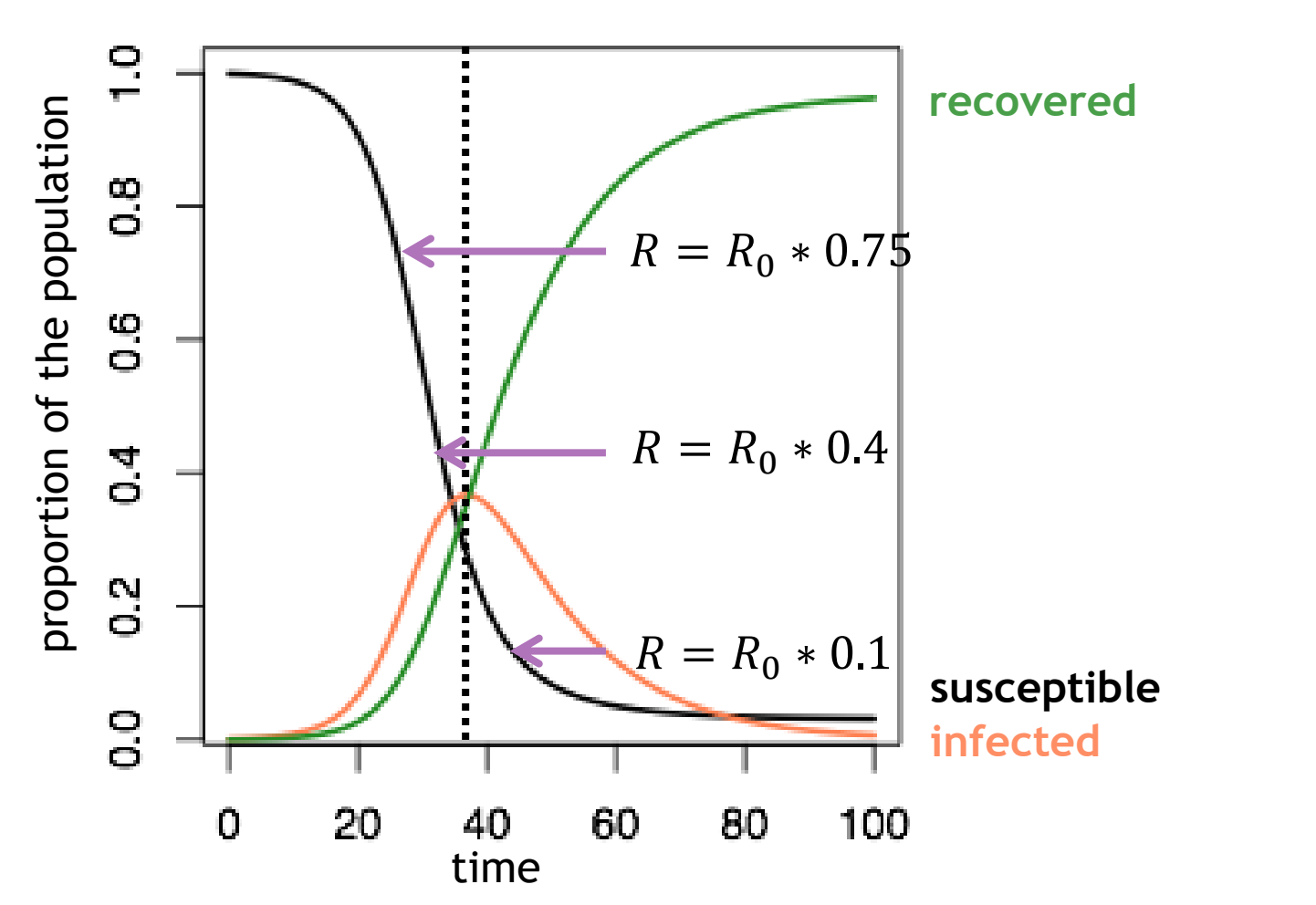
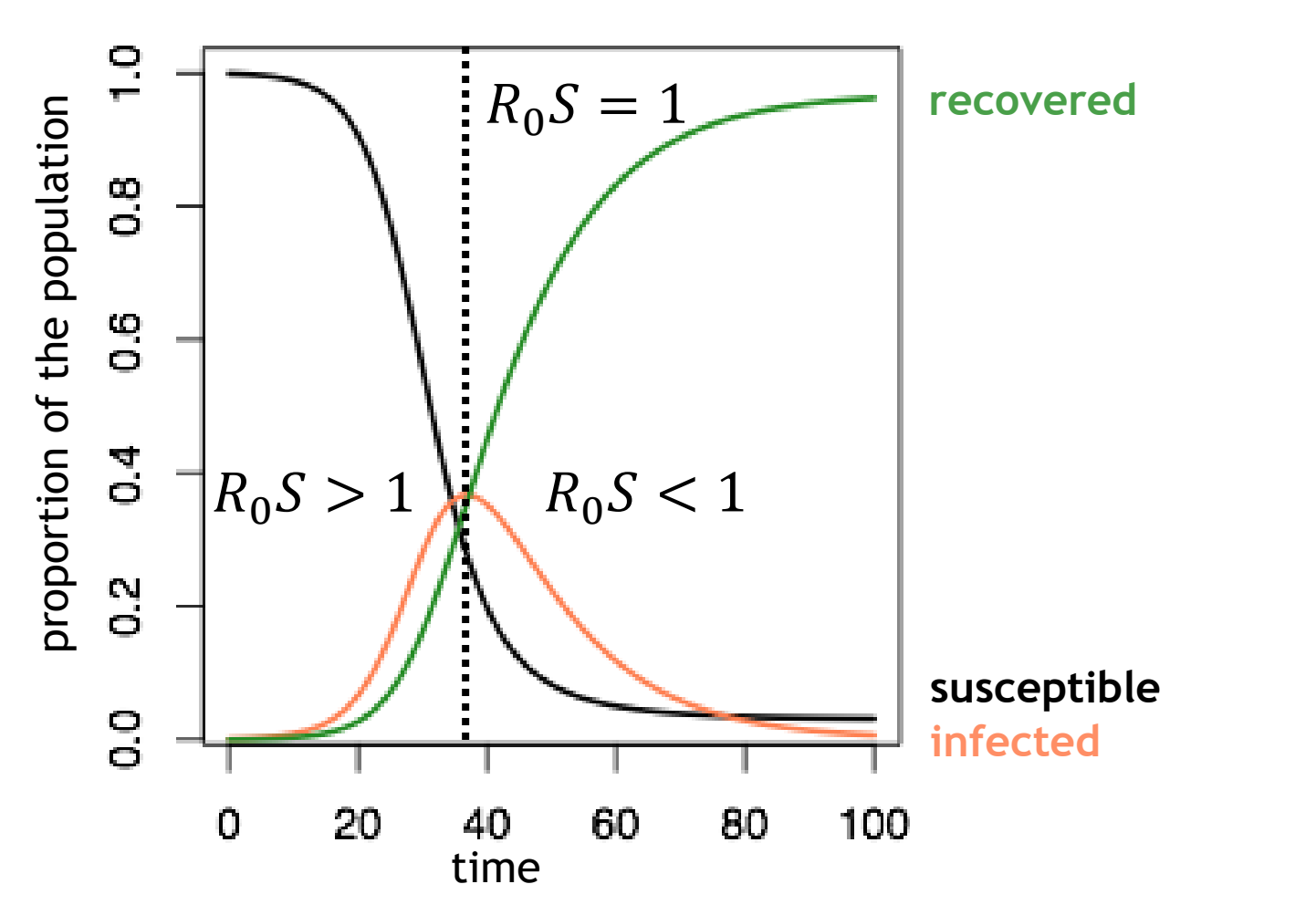


- Can translate R0 to R based on proportion of susceptibles at specific time points

Reproductive Number during Epidemic



- The basic reproductive number is driving the behavior of the epidemic
  - how we calculate R0 depends on the type of model
- During the epidemic, we can use the relationship between R0*S and 1 to see when the epidemic will increase, stabilize, or decrease

Questions?

10 minute break

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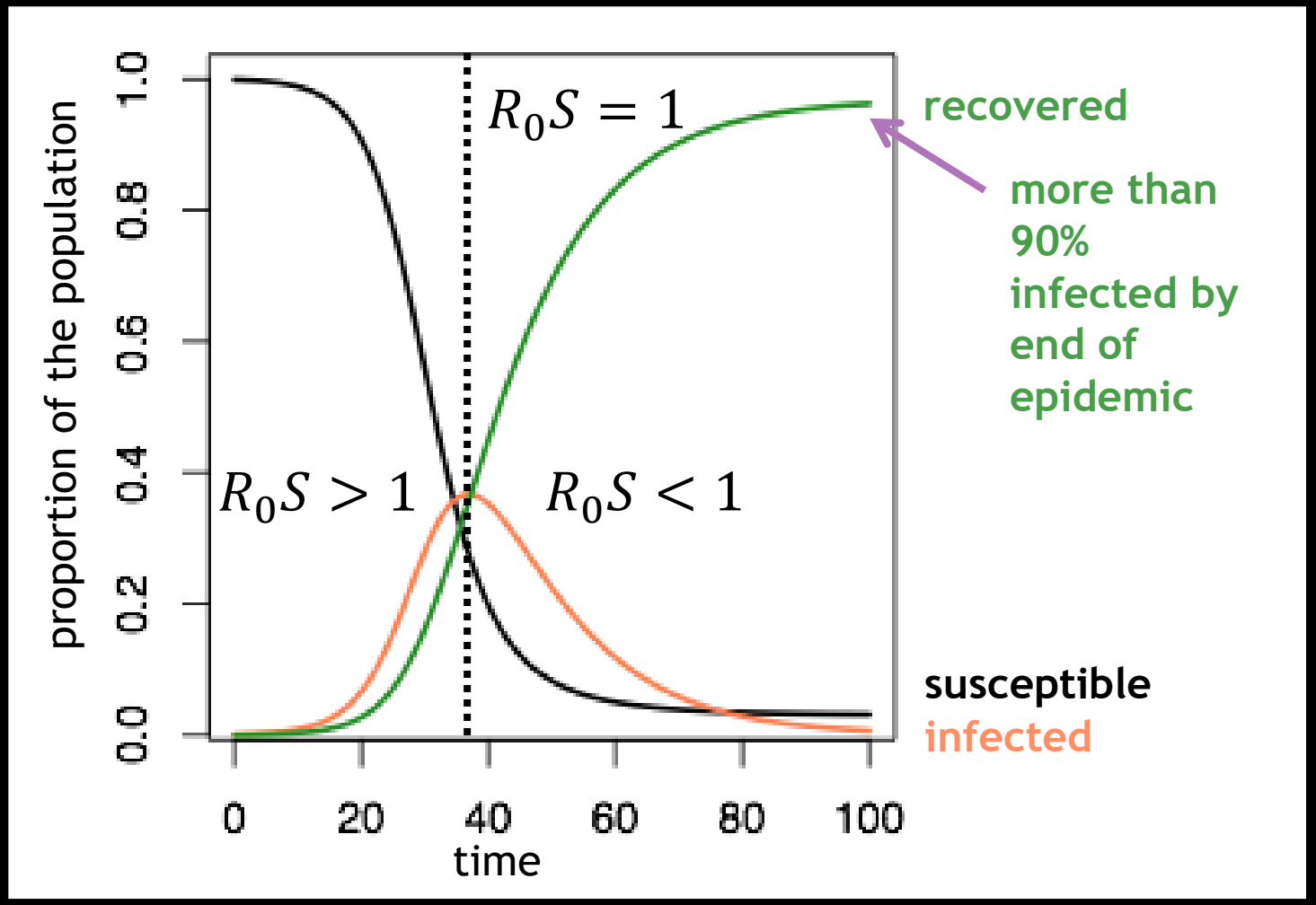
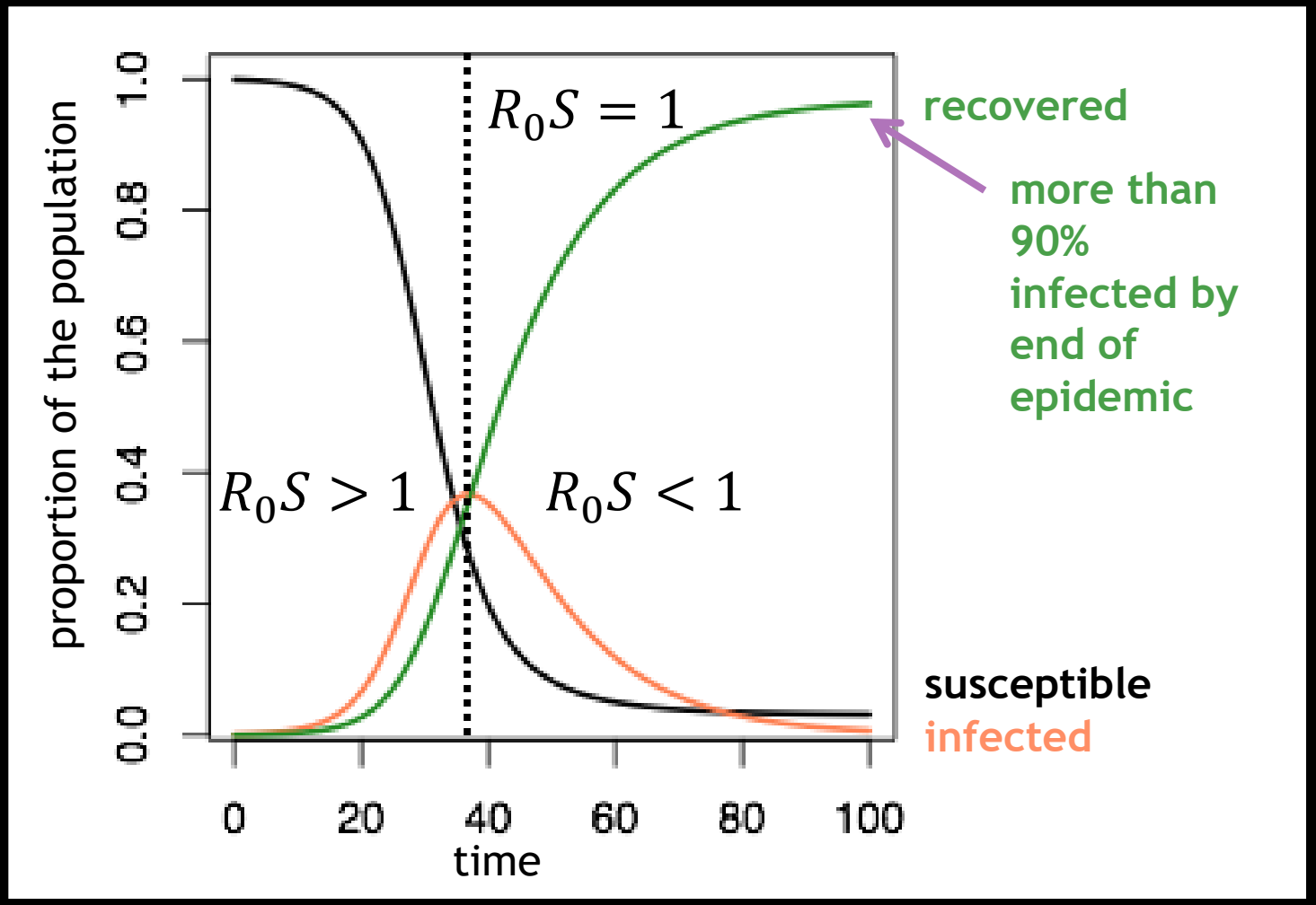
Reproductive Number & Final Size



- We also know the total proportion who got infected
  - whoever is in the "recovered" compartment at the end of the epidemic is someone who was infected
  - this can also be translated into an R0 value

Reproductive Number & Final Size



- But can we estimate the total number infected just using our modeling parameters?
  - yes we can!

Reproductive Number & Final Size

- Importantly:
  - $N = S(t) + I(t) + R(t)$
  - $1 = s(t) + i(t) + r(t)$

- N is our total population
- capitol S, I, R refers to the absolute number of people in the compartment
- lower-case s, i, r refers to the proportion in each compartment

Reproductive Number & Final Size

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- N is our total population
- capitol S, I, R refers to the absolute number of people in the compartment
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- we are interested in calculating $r(\infty)$, which is the final epidemic size
- we need to rearrange some equations first

Reproductive Number & Final Size

- $\frac{ds/dt}{di/dt} = \frac{-\beta si}{\beta si - \gamma i}$

- Don’t worry about memorizing these derivations…

Reproductive Number & Final Size

- $\frac{ds/\cancel{dt}}{di/\cancel{dt}} = \frac{-\beta si}{\beta si - \gamma i}$
- $\frac{ds}{di} = \frac{-1}{1 - \frac{\gamma}{\beta s}}$

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- this is possible because:
  - $R_0 = \frac{\beta N}{\gamma}$ and
  - $R = R_0 * s$

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- $\left(1 - \frac{1}{R_{0s}}\right) ds = -1 di$
- this gets integrated to:
- $s - \frac{1}{R_0} \ln s + i = c$

- Don't worry about memorizing these derivations…
- this is possible because:
  - $R_0 = \frac{\beta N}{\gamma}$ and
  - $R = R_0 * s$
- c is a constant

Reproductive Number & Final Size

- let’s use this equation

- since c is a constant, it is conserved; it is the same throughout the epidemic

Reproductive Number & Final Size

- let's use this equation
  - $s - \frac{1}{R_0} \ln s + i = c$
- since c is a constant, it is conserved; it is the same throughout the epidemic
  - remember everyone is susceptible at the start of the epidemic, and $t = \infty$ is the end of the epidemic
  - $\underbrace{1 - \frac{1}{R_0} \ln 1 + i(0)}_{\text{early epidemic}} = \underbrace{s(\infty) - \frac{1}{R_0} \ln s(\infty) + i(\infty)}_{\text{late epidemic}}$

Reproductive Number & Final Size

- let's use this equation
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- since c is a constant, it is conserved; it is the same throughout the epidemic
  - remember everyone is susceptible at the start of the epidemic, and $t = \infty$ is the end of the epidemic
  - $1 - \cancel{\frac{1}{R_0}\ln 1} + \cancel{i(0)} = s(\infty) - \frac{1}{R_0}\ln s(\infty) + \cancel{i(\infty)}$
  - $1 = (1 - r(\infty)) - \frac{1}{R_0}\ln(1 - r(\infty))$

- remember at the end of the epidemic, when $t = \infty$:

$$1 = s(\infty) + r(\infty)$$
$$0 = i(\infty)$$

Reproductive Number & Final Size

- $1 = (1 - r(\infty)) - \frac{1}{R_0}\ln(1 - r(\infty))$
- $-R_0 r(\infty) = \ln(1 - r(\infty))$
- $r(\infty) = e^{-R_0 r(\infty)}$

Reproductive Number & Final Size

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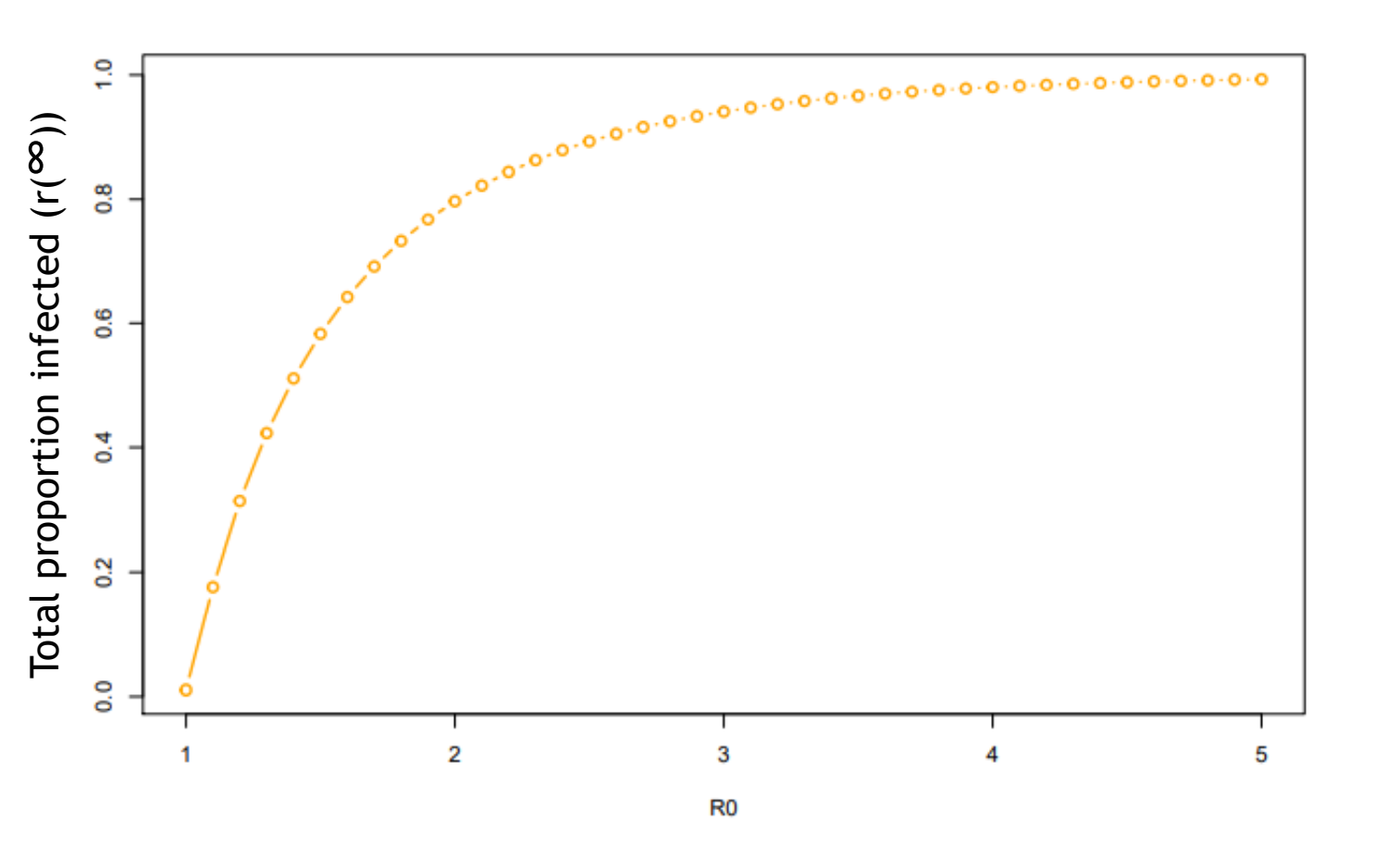
- the same term is on both sides
  - special type of equation that needs to be solved with a numeric solver
  - keeps trying values until one that works is discovered

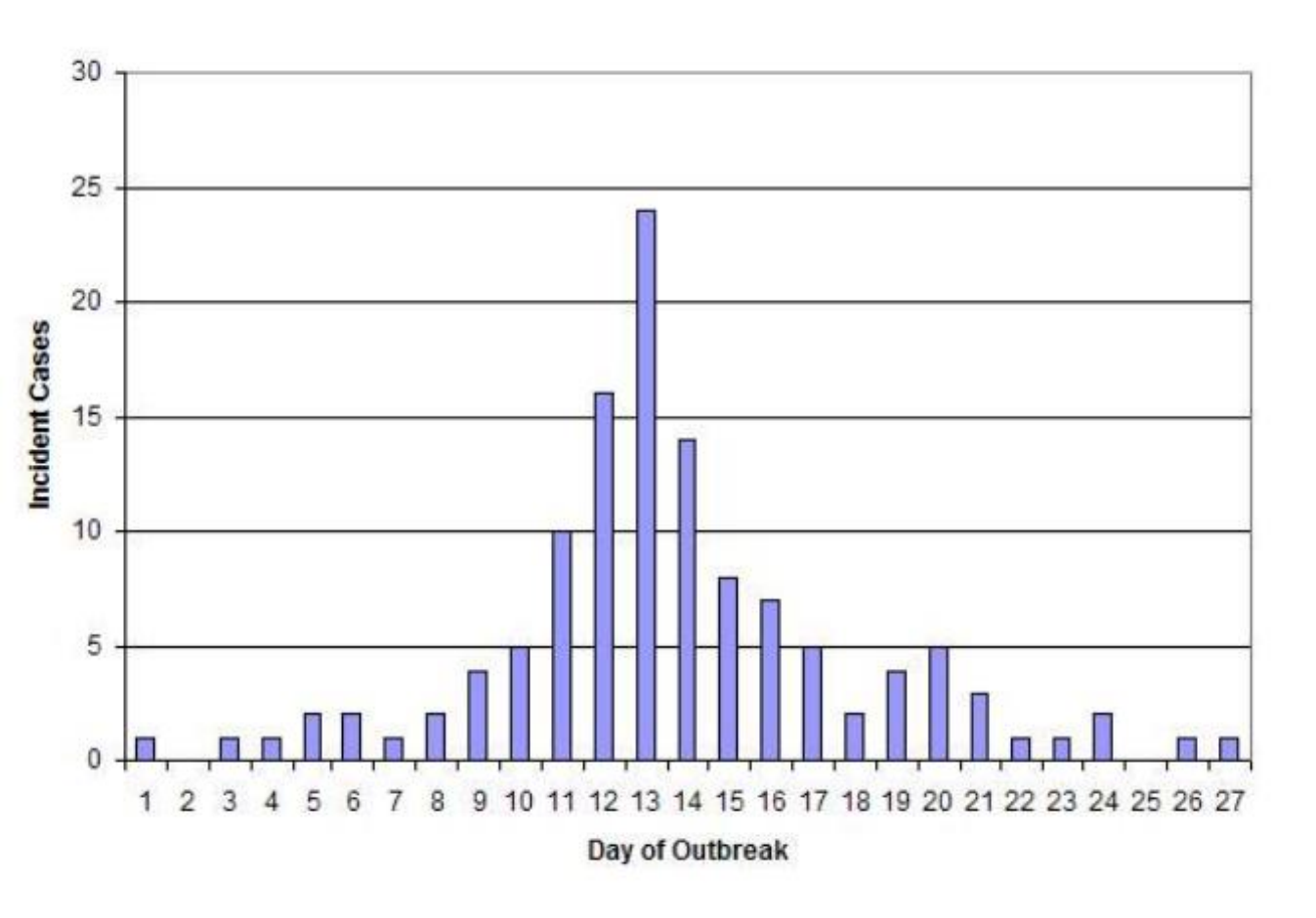


Reproductive Number & Final Size

- For R0>3, nearly everyone will get infected

Reproductive Number & Final Size

- When does this equation work?
  - $r(\infty) = e^{-R_0 r(\infty)}$
- We need to know:
  - s(0): we've assumed it is everyone
  - i(0): we assume this is so small we can ignore it
  - transmission conditions are stable
    - no controls introduced
    - no major changes in behavior
- there are more complex versions of this equation that don't require the first two assumptions



- $r(\infty) = e^{-R_0 r(\infty)}$

Reproductive Number & Final Size

- Influenza B outbreak in a long-term care facility
- R0=1.5—2
- theoretical estimates:
  - $r(\infty) = 0.58 - 0.8$
  - $s(\infty) = 0.2 - 0.42$

Reproductive Number & Final Size

- We have this equation:
  - $r(\infty) = e^{-R_0 r(\infty)}$
- Which can be arranged as:
  - $R_0 = -\frac{\ln(1-r(\infty))}{r(\infty)}$
- final epidemic size and basic reproductive number can be used to calculate each other if we already know one

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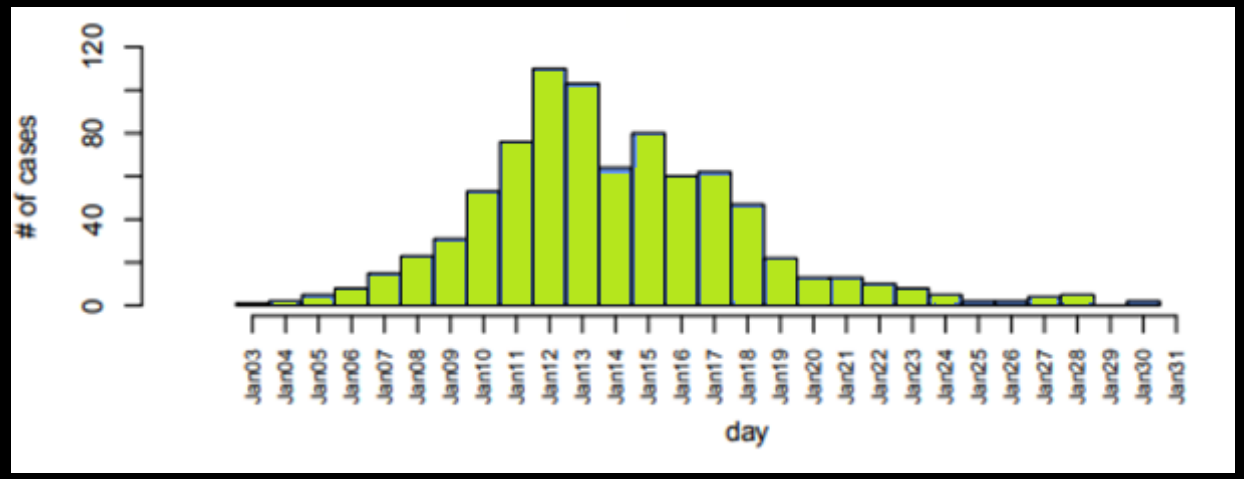
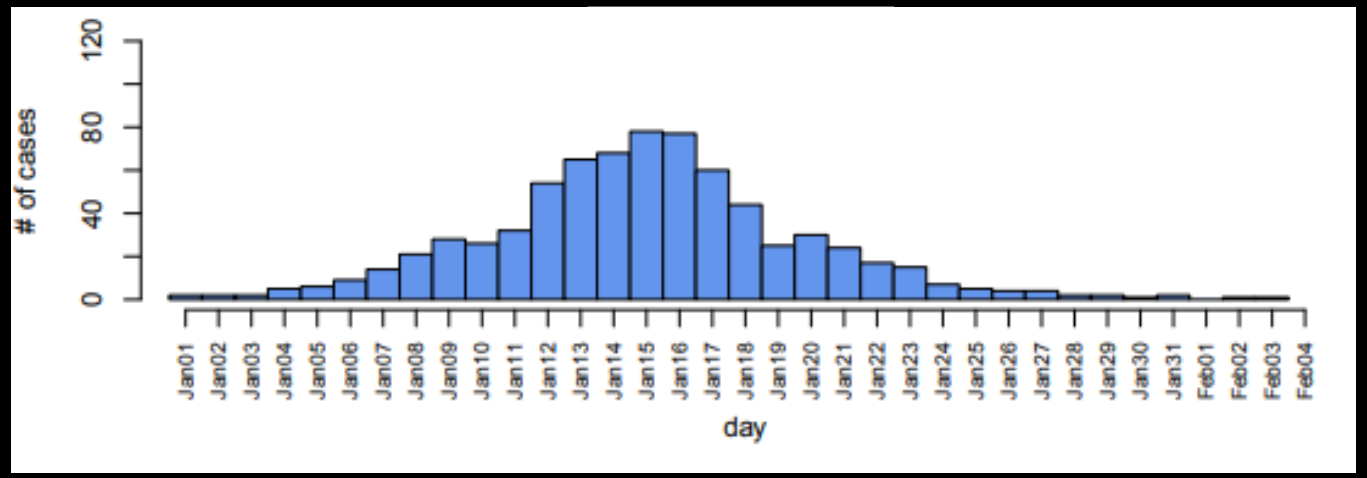
- final epidemic size and basic reproductive number can be used to calculate each other if we already know one
- Without going through the derivation, there is another equation for calculating R0 from final size
  - $R_0 = \frac{N}{N-S(0)-R(\infty)} ln \frac{\mathrm{N}-R(\infty)}{S(0)}$

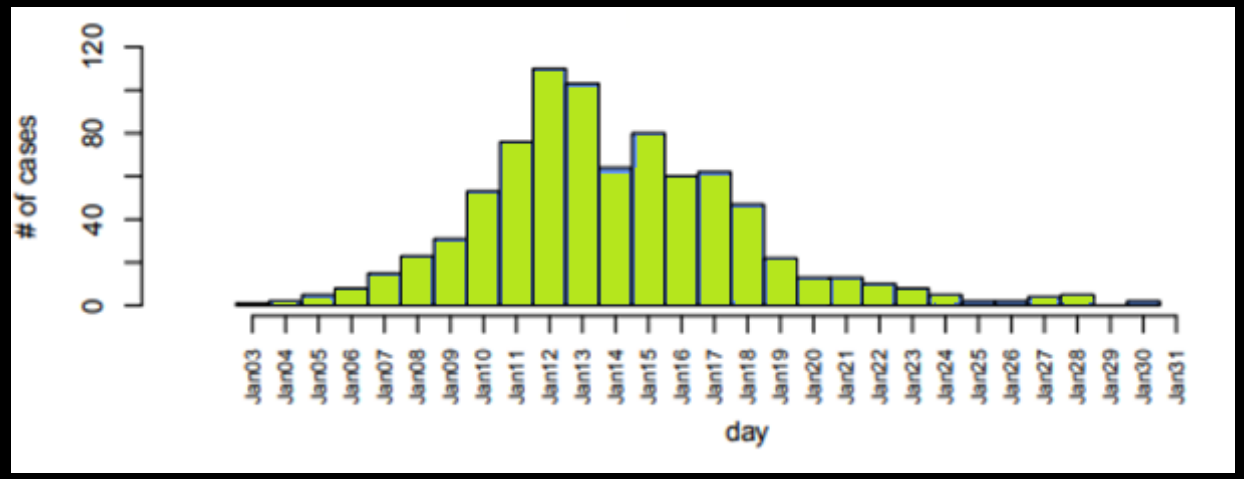


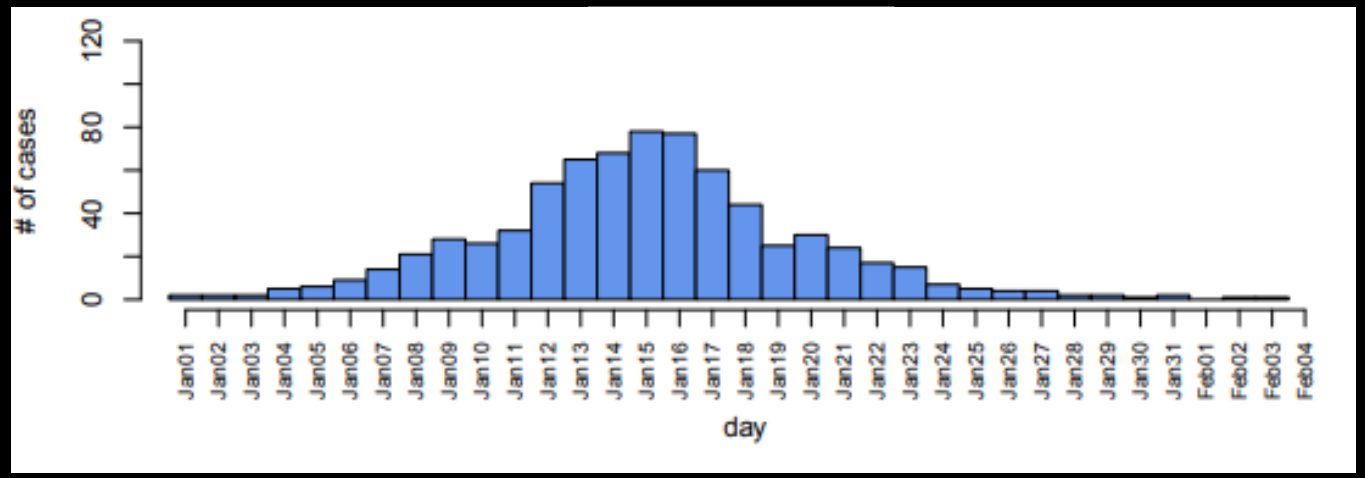


- $R_0 = \frac{N}{N-S(0)-R(\infty)} ln \frac{N-R(\infty)}{S(0)}$

Reproductive Number & Final Size

- Epidemic A
  - population=1.024
  - cases=826
- Epidemic B
  - population=952
  - cases=733





- $R_0 = \frac{N}{N-S(0)-R(\infty)} ln \frac{N-R(\infty)}{S(0)}$
- $R_0 = \frac{1024}{1024-1023-826} ln \frac{1024-826}{1023} = 2.04$

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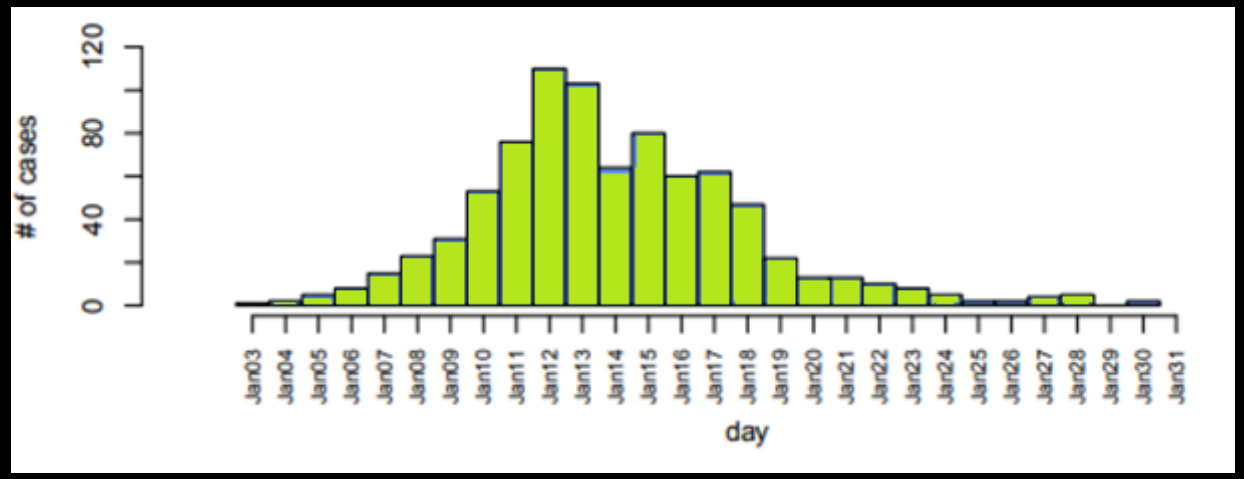
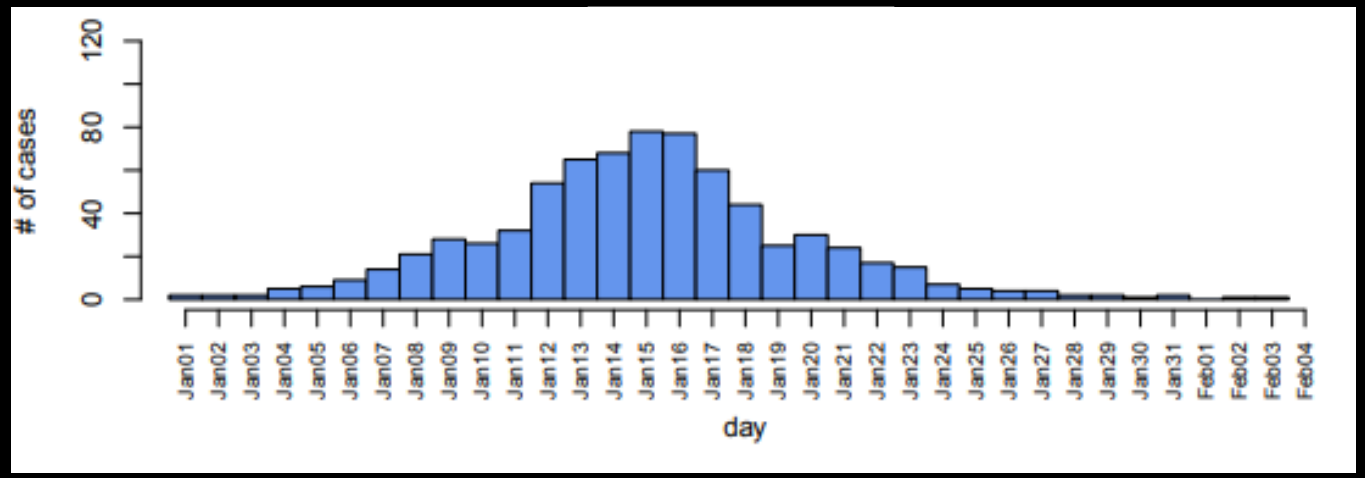
  - cases=733

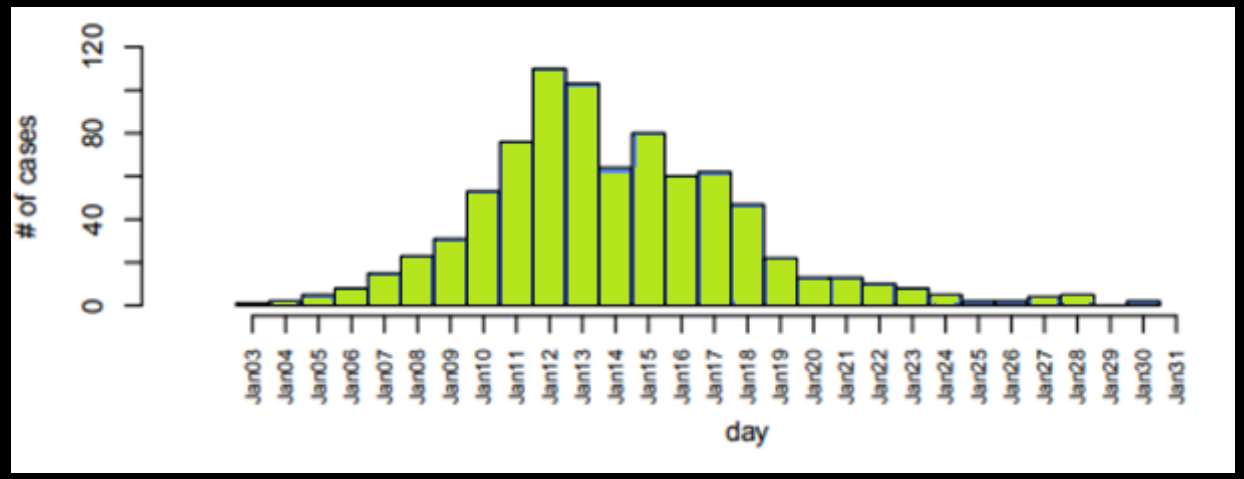


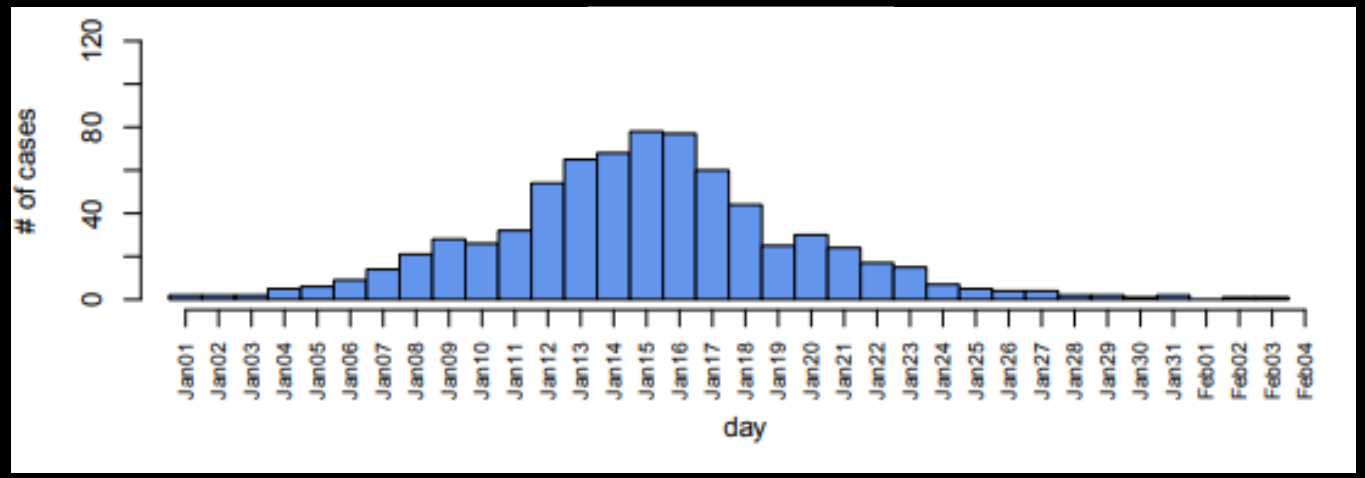


- $R_0 = \frac{N}{N-S(0)-R(\infty)} ln \frac{N-R(\infty)}{S(0)}$
- $R_0 = \frac{1024}{1024-1023-826} ln \frac{1024-826}{1023} = 2.04$

Reproductive Number & Final Size

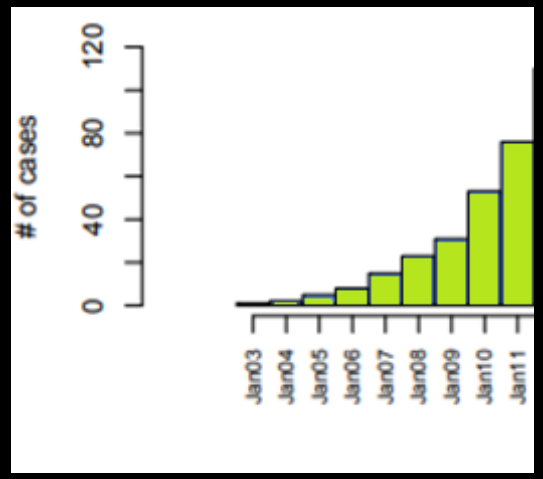
- Epidemic A
  - population=1.024
  - cases=826
  - R0=2.04
- Epidemic B
  - population=952
  - cases=733
  - R0=1.91



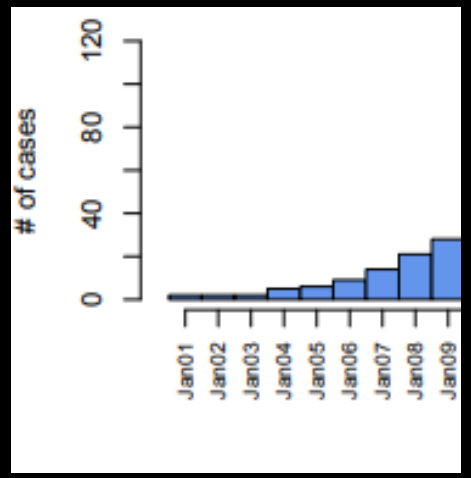


Reproductive Number & Early Size

- We can also use the cumulative number of cases early in an epidemic by fitting an exponential curve to the outbreak
- $R_0 = 1 + \frac{\ln(Y(t))/t}{\gamma}$
- Y(t)=cumulative number of cases at time t



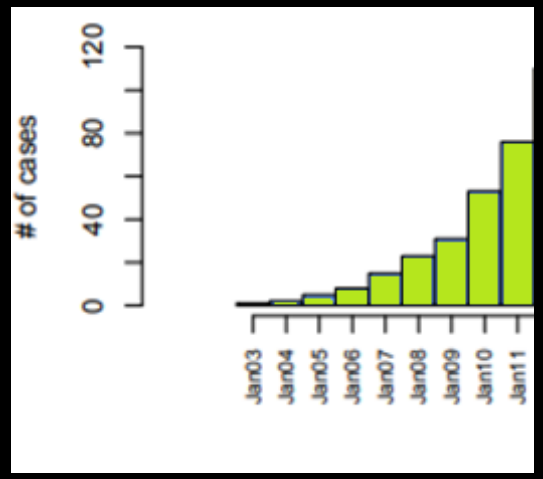
- Epidemic A
  - Y(t)=218
  - t=8
  - γ=1.5



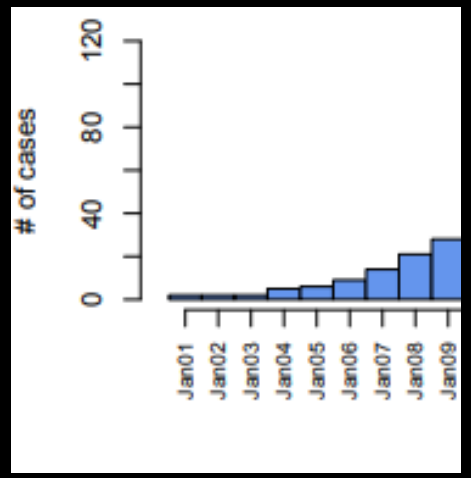
- Epidemic B
  - Y(t)=89
  - t=8
  - γ=1.5

Reproductive Number & Early Size

- We can also use the cumulative number of cases early in an epidemic by fitting an exponential curve to the outbreak
- $R_0 = 1 + \frac{\ln(Y(t))/t}{\gamma}$
- Y(t)=cumulative number of cases at time t



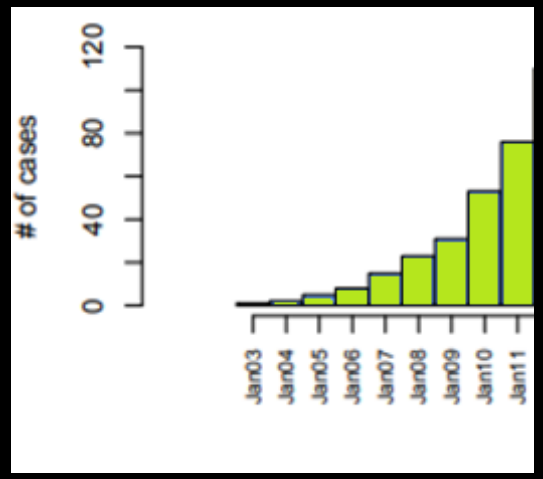
- Epidemic A
  - Y(t)=218
  - t=8
  - γ=1.5
  - R0=2.01



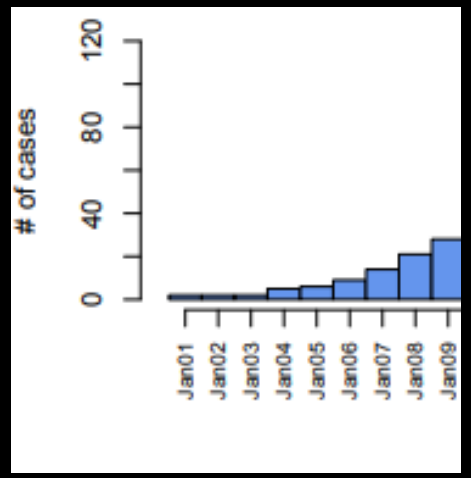
- Epidemic B
  - Y(t)=89
  - t=8
  - γ=1.5
  - R0=1.84

Reproductive Number & Early Size

- We can also use the cumulative number of cases early in an epidemic by fitting an exponential curve to the outbreak
- $R_0 = 1 + \frac{\ln(Y(t))/t}{\gamma}$
- Y(t)=cumulative number of cases at time t



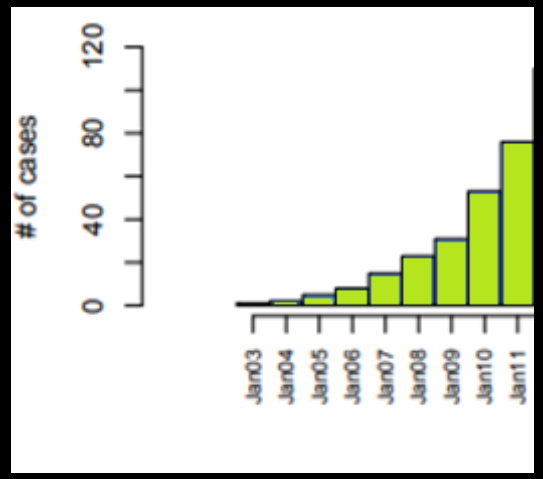
- Epidemic A
  - Y(t)=218
  - t=8
  - γ=1.5
  - R0=2.01
  - Y(t)=31
  - t=4
  - γ=1.5
  - R0=2.29



- Epidemic B
  - Y(t)=89
  - t=8
  - γ=1.5
  - R0=1.84
  - Y(t)=17
  - t=4
  - γ=1.5
  - R0=2.06

Reproductive Number & Early Size

- We can also use the cumulative number of cases early in an epidemic by fitting an exponential curve to the outbreak
- $R_0 = 1 + \frac{\ln(Y(t))/t}{\gamma}$
- Y(t)=cumulative number of cases at time t



- Epidemic A
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  - t=4
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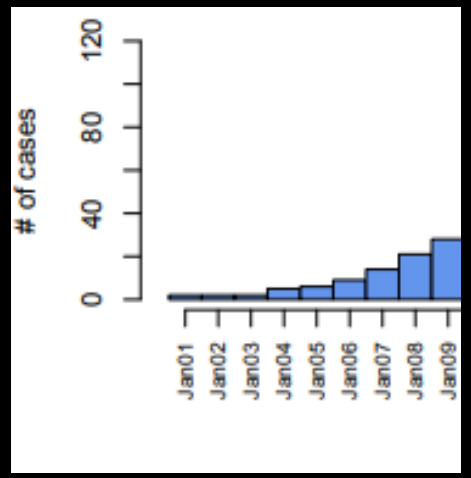
  - R0=2.29



- Epidemic B
  - Y(t)=89
  - t=8
  - γ=1.5
  - R0=1.84
  - Y(t)=17
  - t=4
  - γ=1.5
  - R0=2.06

Method	Epidemic A R0	Epidemic B R0
Final epidemic size	2.04	1.91
Exponential at t=8	2.01	1.84
Exponential at t=4	2.29	2.06

Reproductive Number & Early Size

- We can also use the cumulative number of cases early in an epidemic by fitting an exponential curve to the outbreak
- $R_0 = 1 + \frac{\ln(Y(t))/t}{\gamma}$
- Y(t)=cumulative number of cases at time t

Workshop Schedule

Time	Topics
2:00—2:10 pm	~~Greetings~~
2:10—2:40 pm	~~SIR & R0 Relationship~~
2:40—2:50 pm	~~Break~~
2:50—3:15 pm	~~R0 & Final Epidemic Size~~
3:15—3:30 pm	~~R0 & Initial Growth~~
3:30—3:40 pm	Break
3:40—5:00 pm	R Session

Week 2: Compartmental Models & Expanded

Dr. Rachel Sippy
University of Cambridge

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

Objectives

- Learn how to include births and deaths in an SIR model
- Modify model structure to create an SEIR model

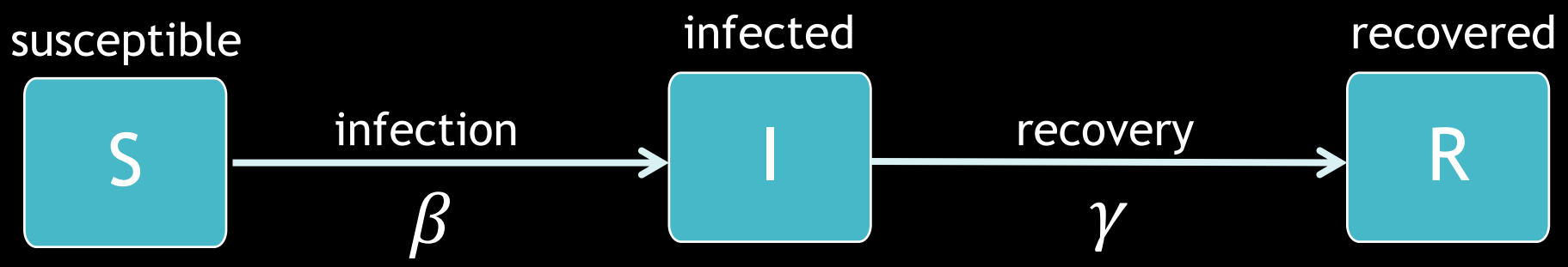
Post Questions in the Chat!

(or ask over microphone)

Workshop Schedule

Time	Topics
2:00—2:10 pm	~~Greetings~~
2:10—2:50 pm	Other Compartmental Models
2:50—3:00 pm	Break
3:00—3:50 pm	Guest Lecture: Modeling meningitis
3:50—4:00 pm	Break
4:00—5:00 pm	R Session

SIR Model



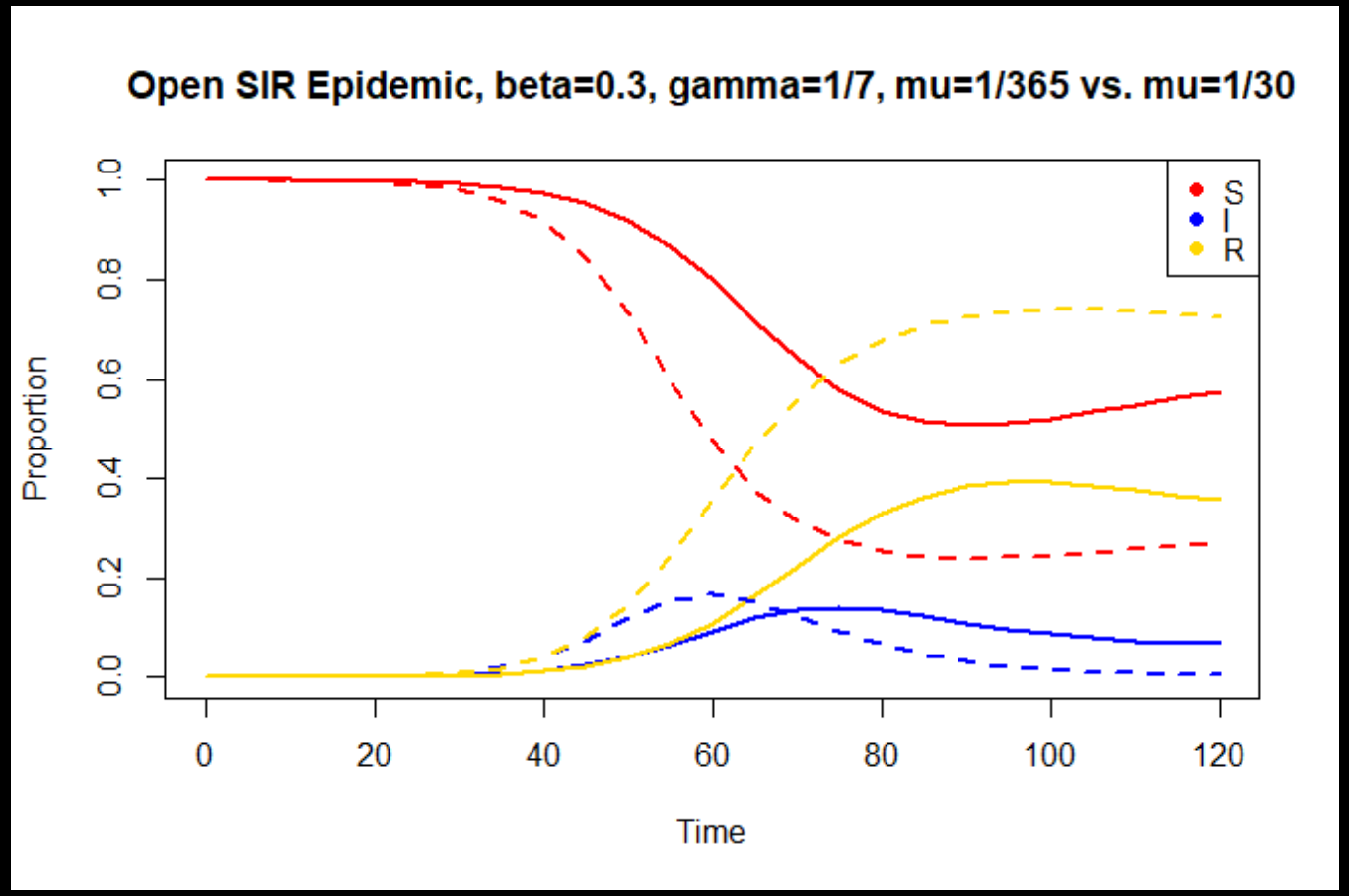
- this is a closed model
  - β is a transmission coefficient
  - γ is the recovery rate

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

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

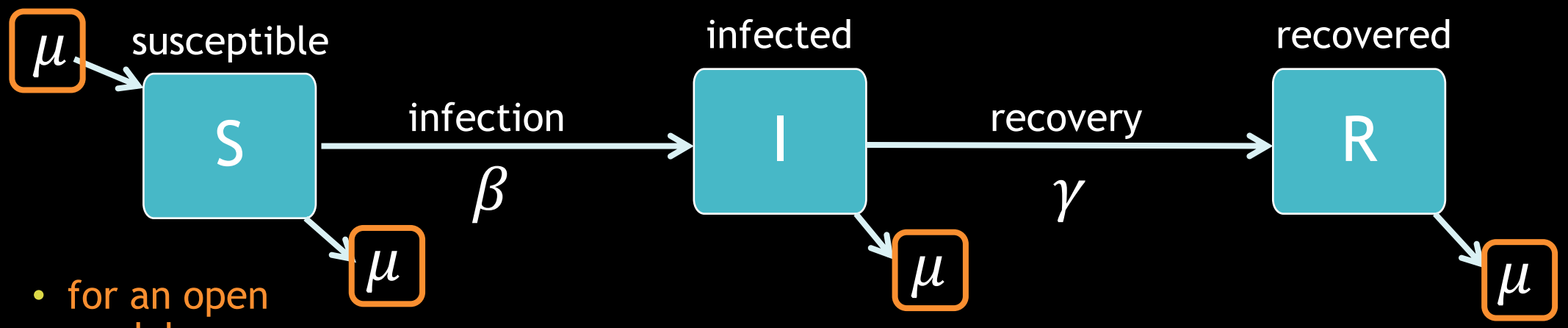
$$\frac{dR(t)}{dt} = \gamma I(t)$$

SIR Model Output



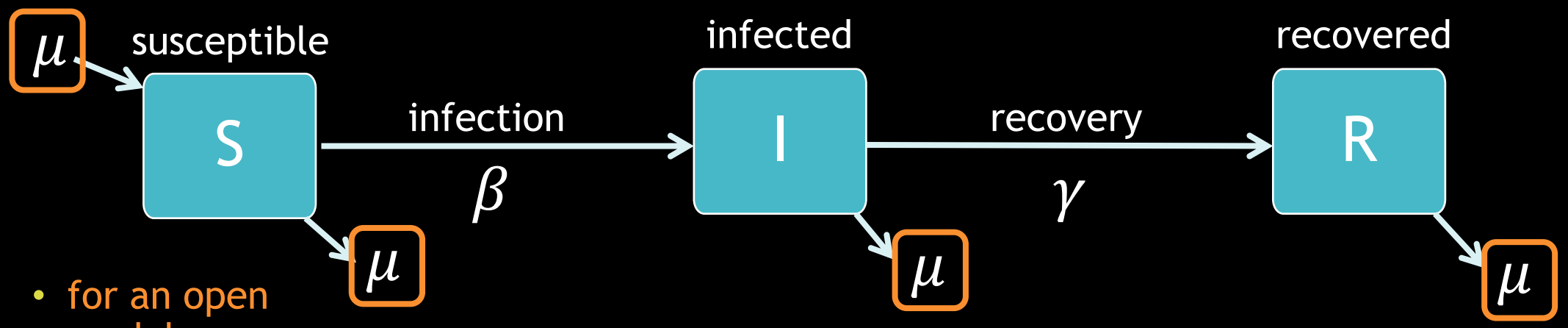
- Having an open population can greatly impact the epidemic dynamics!

SIR Model



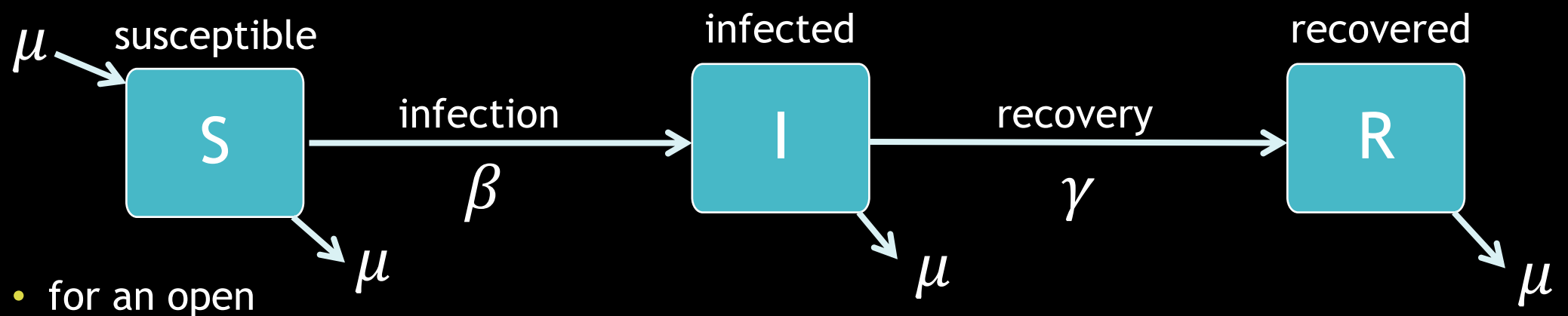
- for an open model:
  - μ is our birth/death rate
- What are our assumptions?

SIR Model



- for an open model:
  - μ is our birth/death rate
  - births are all susceptible
  - anyone can die

SIR Model



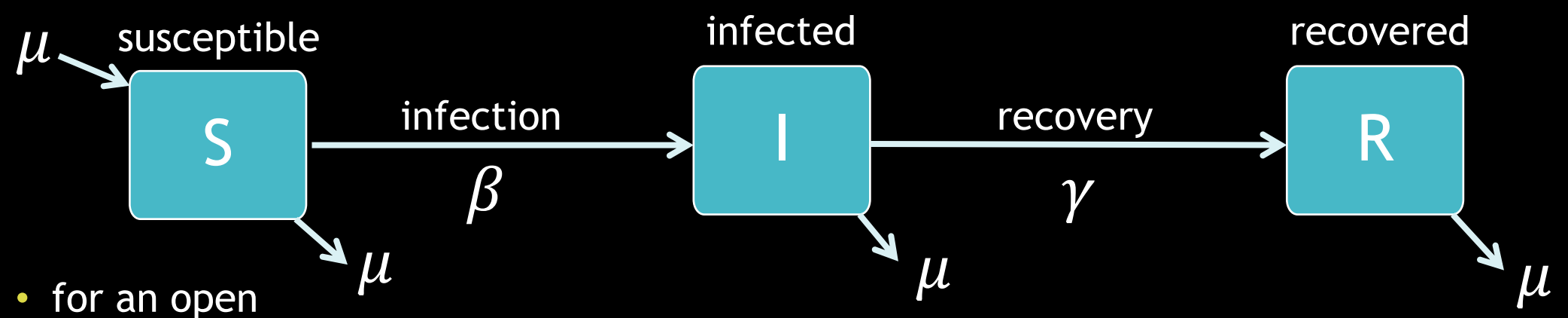
- for an open model:
  - μ is our birth/death rate
  - births are all susceptible but anyone can give birth
  - anyone can die

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

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

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

SIR Model



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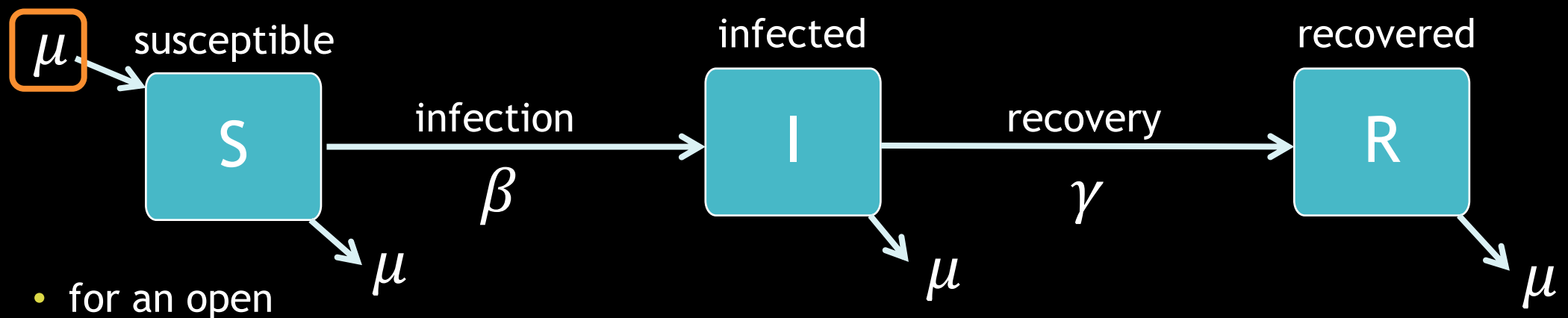
$$\frac{dI(t)}{dt} = \underline{\beta S(t) I(t) - \gamma I(t)} - \mu I(t)$$

$$\frac{dR(t)}{dt} = \underline{\gamma I(t)} - \mu R(t)$$

- we still have the same parts from the closed model

SIR Model



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  - μ is our birth/death rate
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  - anyone can die

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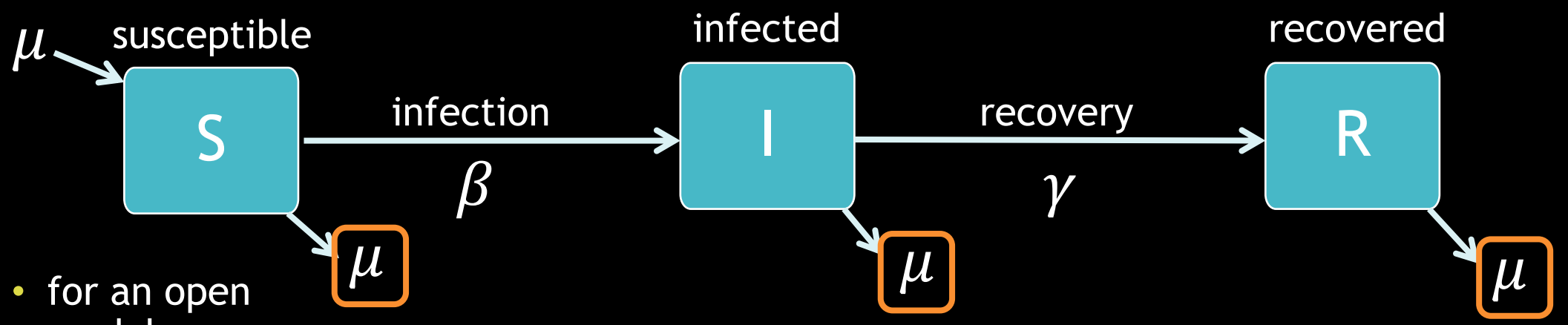
$$\frac{dI(t)}{dt} = \beta S(t)I(t) - \gamma I(t) - \mu I(t)$$

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

SIR Model



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  - births are all susceptible but anyone can give birth
  - anyone can die

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

$$\frac{dR(t)}{dt} = \gamma I(t) \boxed{- \mu R(t)}$$

R_0 & Model Structure

- The calculation of R0 depends on the structure of the model being used

- for our closed SIR model:
  - $R_0 = \frac{\beta}{\gamma}$

- for an open SIR model:
  - $R_0 = \frac{\beta}{\gamma+\mu}$

R_0 & Model Structure

- The calculation of R0 depends on the structure of the model being used

- for our closed SIR model:
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- for duration of infection:
  - $\frac{1}{\gamma}$

- for an open SIR model:
  - $R_0 = \frac{\beta}{\gamma+\mu}$
- for duration of infection:
  - $\frac{1}{\gamma+\mu}$

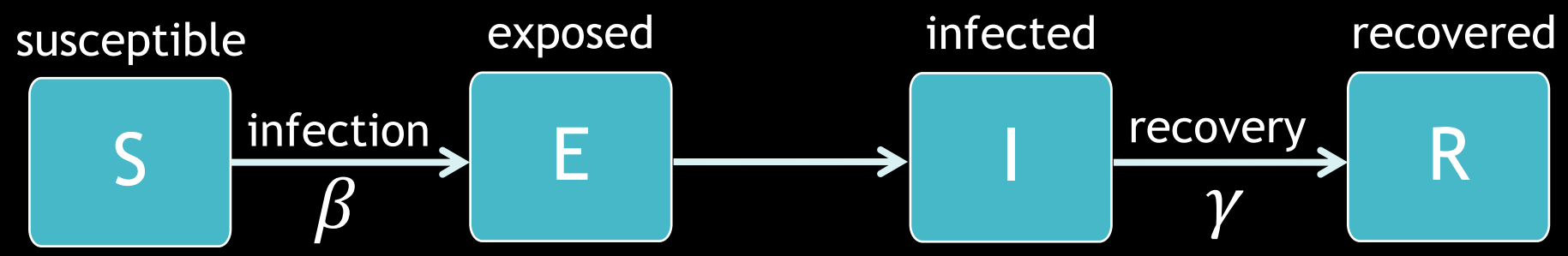
R_0 & Model Structure

- The calculation of R0 depends on the structure of the model being used

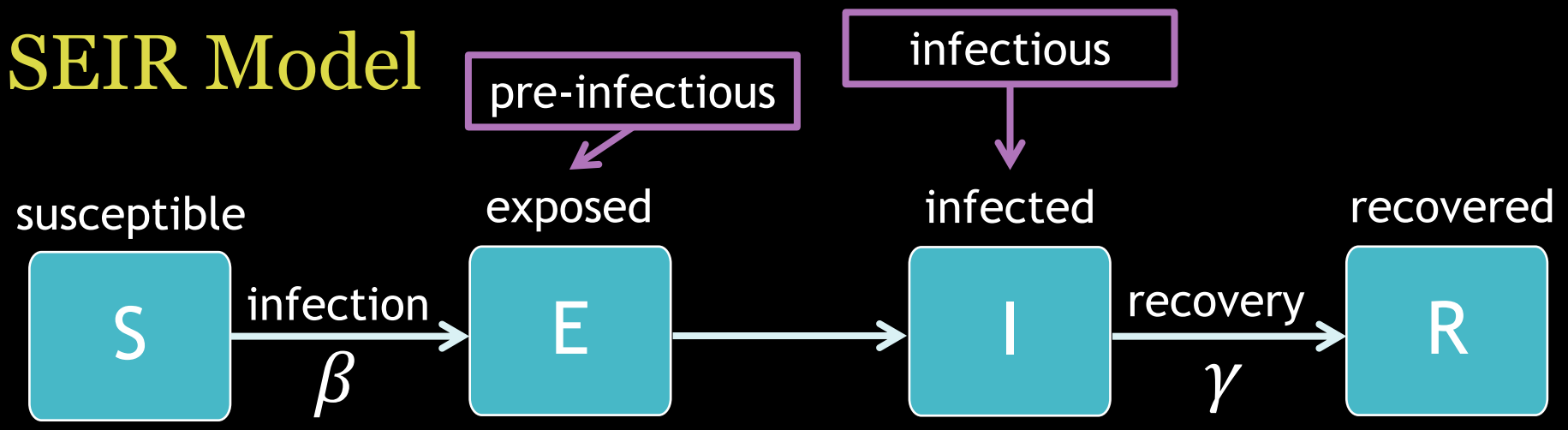
- for our closed SIR model:
  - $R_0 = \frac{\beta}{\gamma}$
- for duration of infection:
  - $\frac{1}{\gamma}$
- But usually $\gamma \gg \mu$ so:
  - $R_0 = \frac{\beta}{\gamma} \approx R_0 = \frac{\beta}{\gamma+\mu}$

- for an open SIR model:
  - $R_0 = \frac{\beta}{\gamma+\mu}$
- for duration of infection:
  - $\frac{1}{\gamma+\mu}$

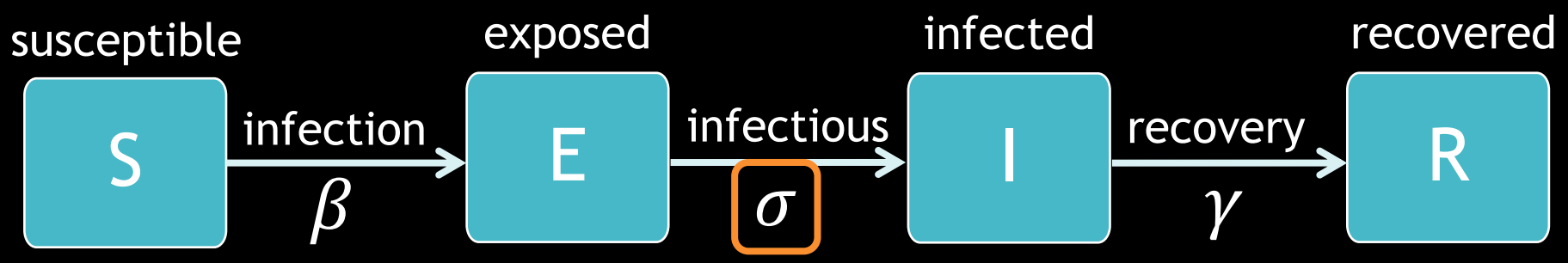
SEIR Model


susceptible
S
infection
β
exposed
E
infected
I
recovery
γ
recovered
R

SEIR Model

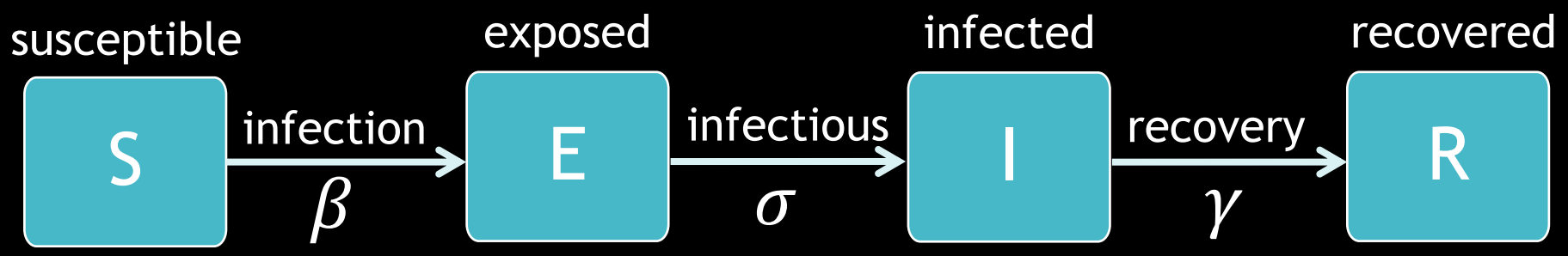

pre-infectious
infectious
susceptible
exposed
infected
recovered
S
infection
β
E
I
recovery
γ
R

SEIR Model



- for an SEIR model:
  - σ is the rate at which people change from exposed to infectious
  - 1/σ is the latent period

SEIR Model



- for an SEIR model:
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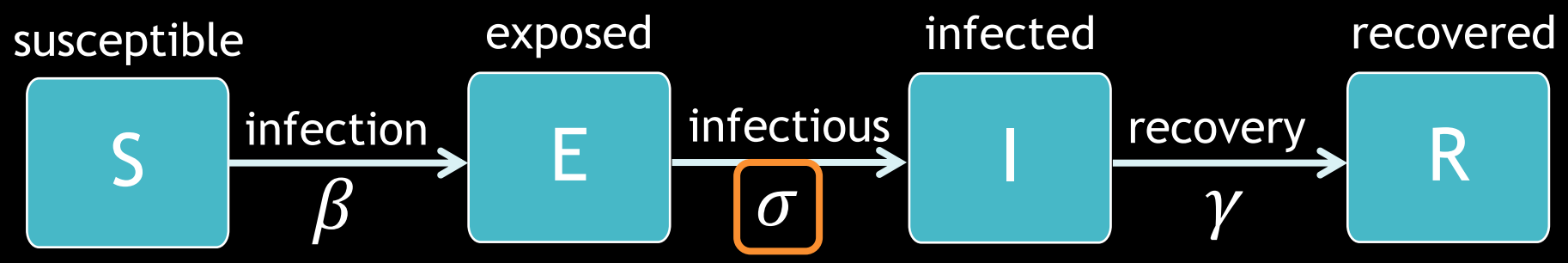
  - 1/σ is the latent period

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

- the first equation is exactly the same

SEIR Model



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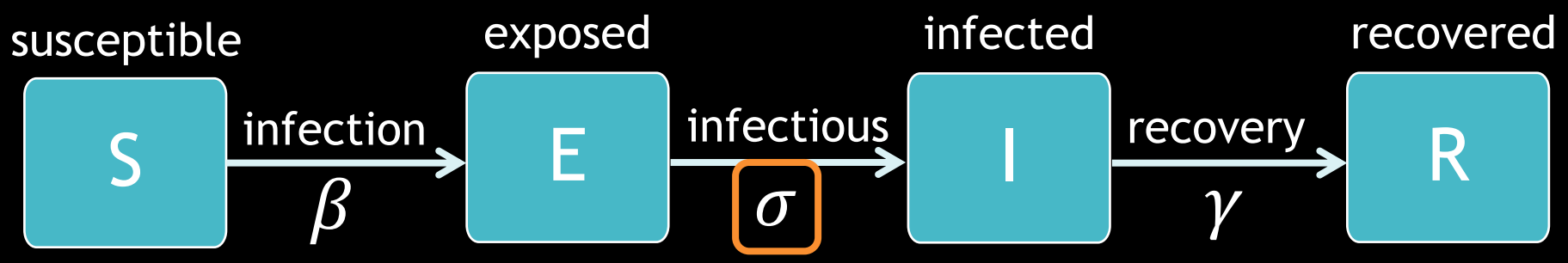
$$\frac{dE(t)}{dt} = \beta S(t)I(t) \boxed{- \sigma E(t)}$$

SEIR Model



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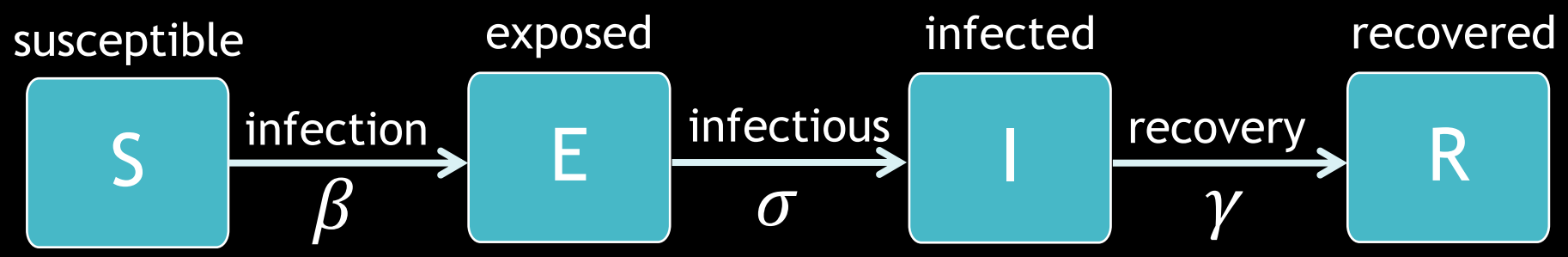
SEIR Model



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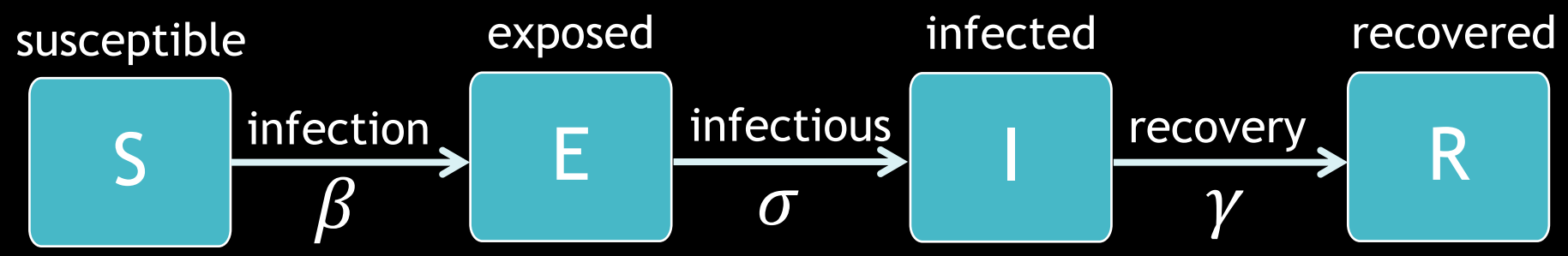
$$\frac{dI(t)}{dt} = \sigma E(t) - \gamma I(t)$$

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

- the last equation is exactly the same

SEIR Model



- We could also make the SEIR (or a model with any other structure) be open (include birth/death/migration)
  - we can also make different death rates for each compartment
  - models are extremely flexible!

Questions?

10 minute break

Workshop Schedule

Time	Topics
2:00—2:10 pm	~~Greetings~~
2:10—2:50 pm	~~Other Compartmental Models~~
2:50—3:00 pm	Break
3:00—3:50 pm	Guest Lecture: Modeling meningitis
3:50—4:00 pm	Break
4:00—5:00 pm	R Session

MODELLING THE IMPACT OF MENINGOCOCCAL VACCINES IN THE AFRICAN MENINGITIS BELT

Caroline Trotter
clt56@cam.ac.uk
UNIVERSITY OF CAMBRIDGE

OVERVIEW

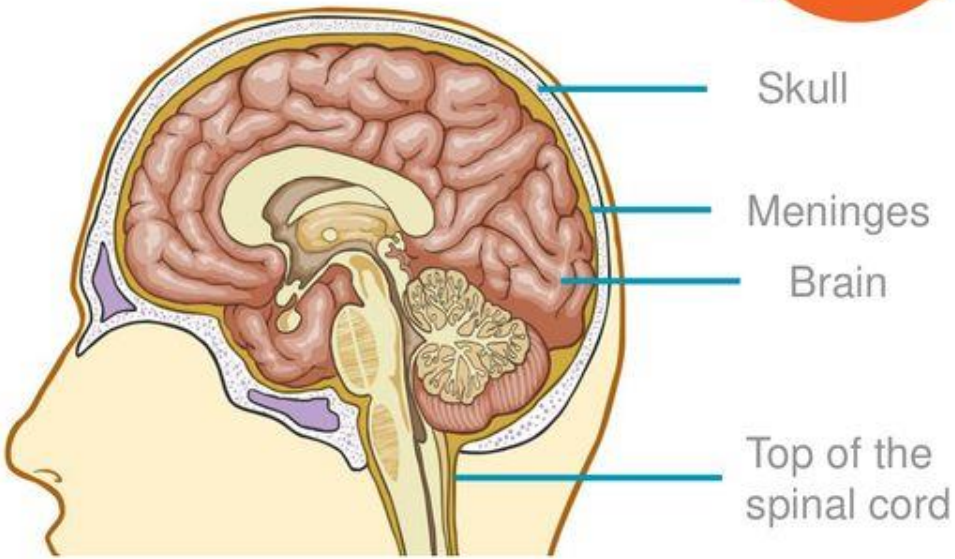
- Description of meningitis and the African meningitis belt
- Models to investigate epidemiology
- Meningitis Vaccine Project, vaccine implementation and evaluation
- Models to support policy for MenAfriVac
- Other model applications
- Future challenges

AIM

To illustrate how modelling can be used as an integrated part of public health strategy

What is meningitis?

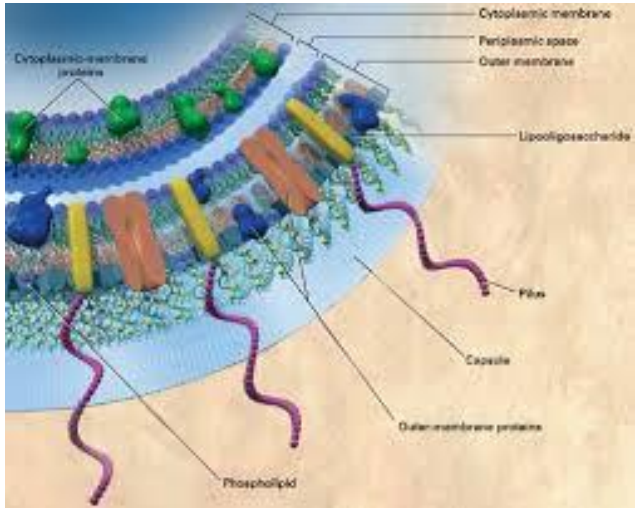
Inflammation of the protective layers (meninges) that surround the brain and part of the spinal cord



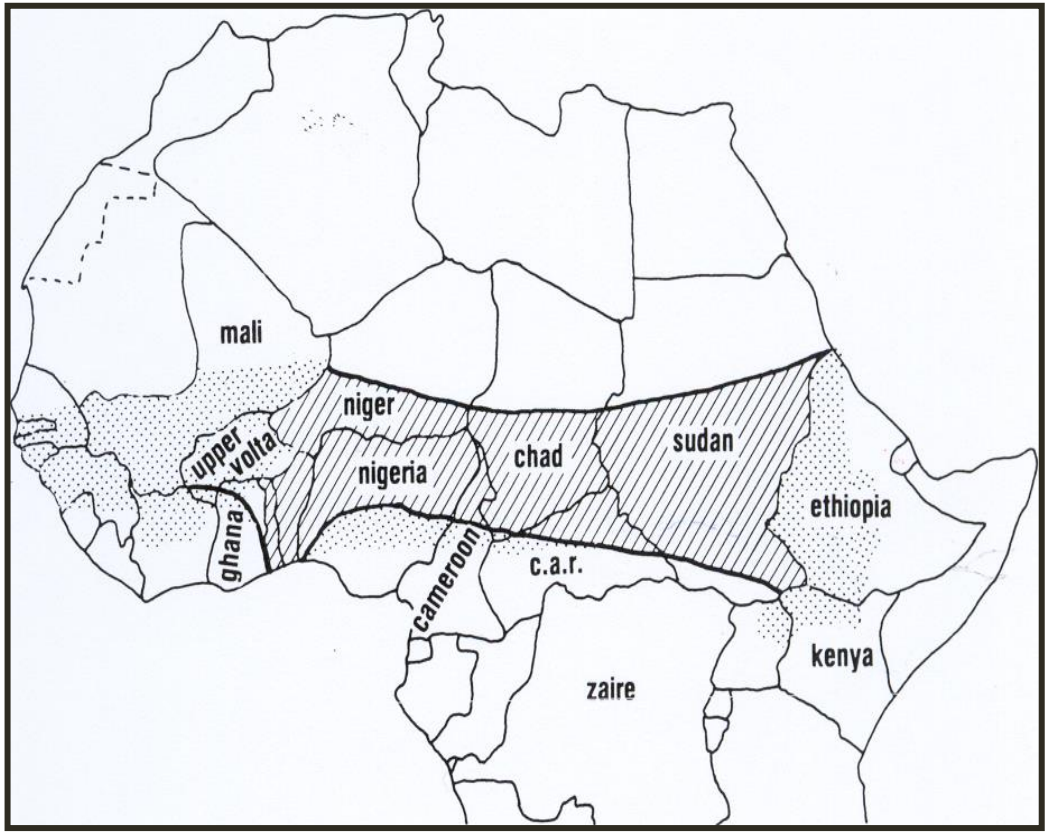
THE MENINGOCOCCUS

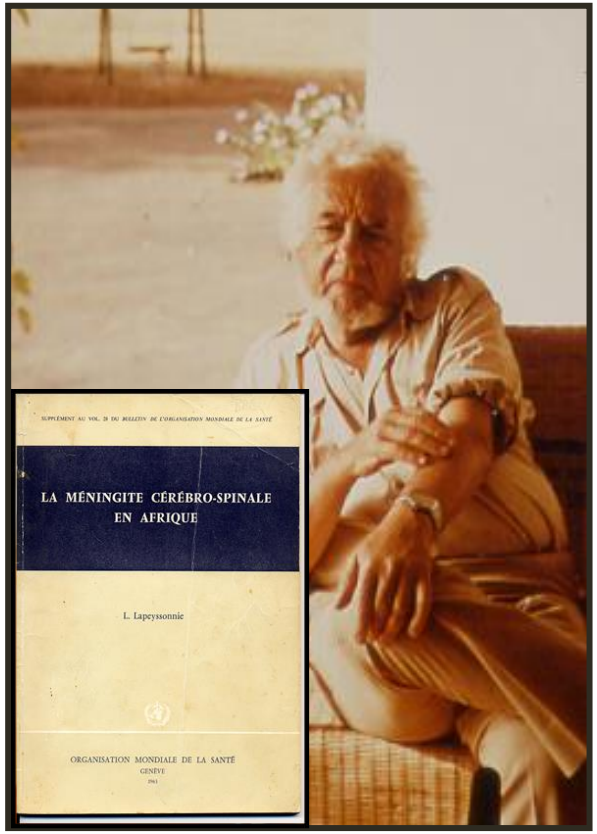
- *Neisseria meningitidis*
- specific to human nasopharynx
- spread through respiratory droplets
- fragile organism
- acquisition followed by asymptomatic carriage

  or
- more rarely by invasive disease
  - meningitis and sepsis
  - high case fatality (3-10%)
  - disabling sequelae (up to 25%)



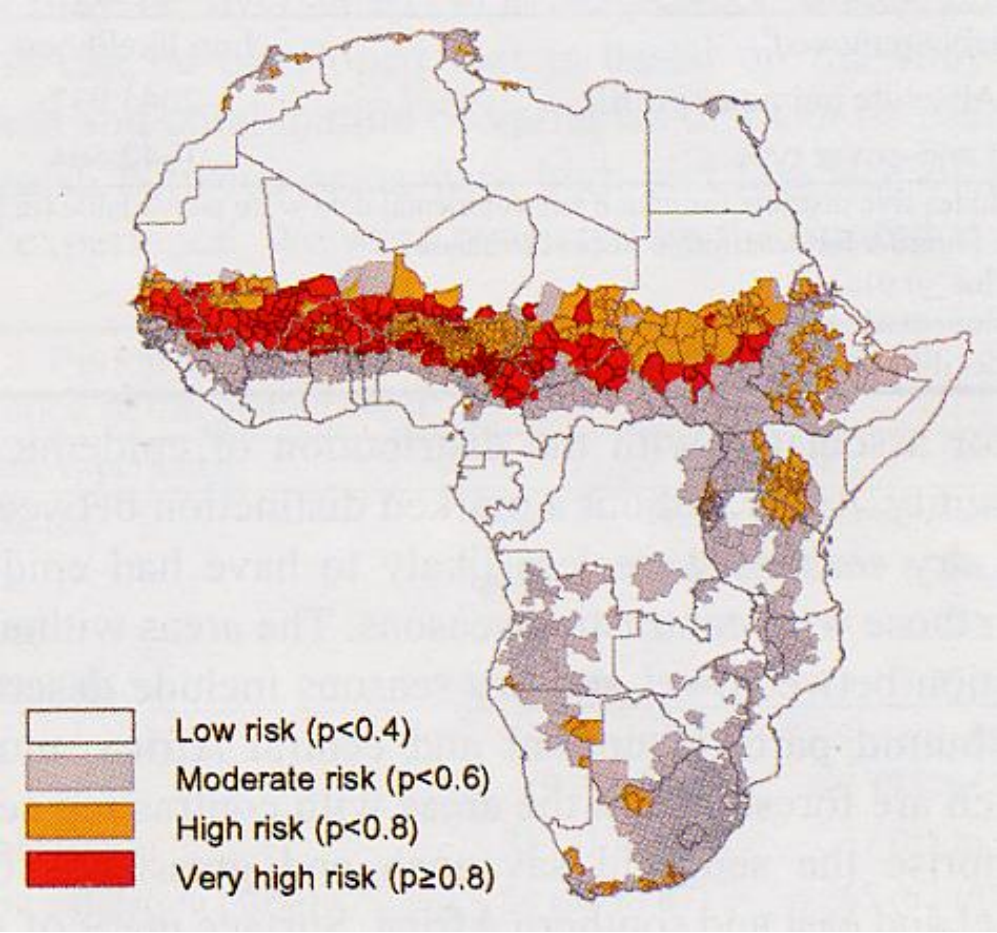
AFRICAN MENINGITIS BELT





Lapeyssonnie, Bull WHO 1963;28 suppl:3-114

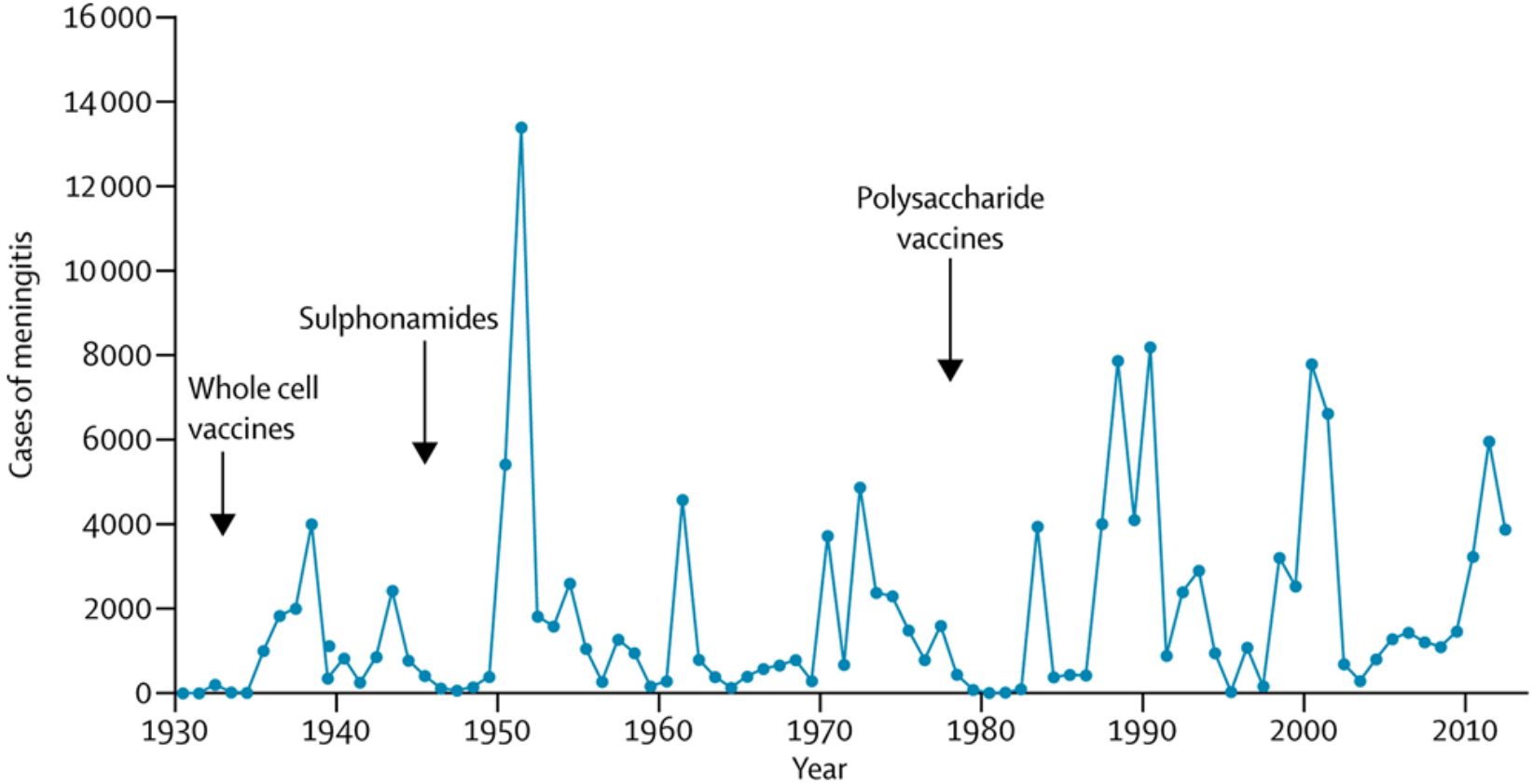
QUANTIFYING EPIDEMIC RISK



Topography
Humidity
Dust
Population density

Molesworth *et al*. Emerg Infect Dis 2003

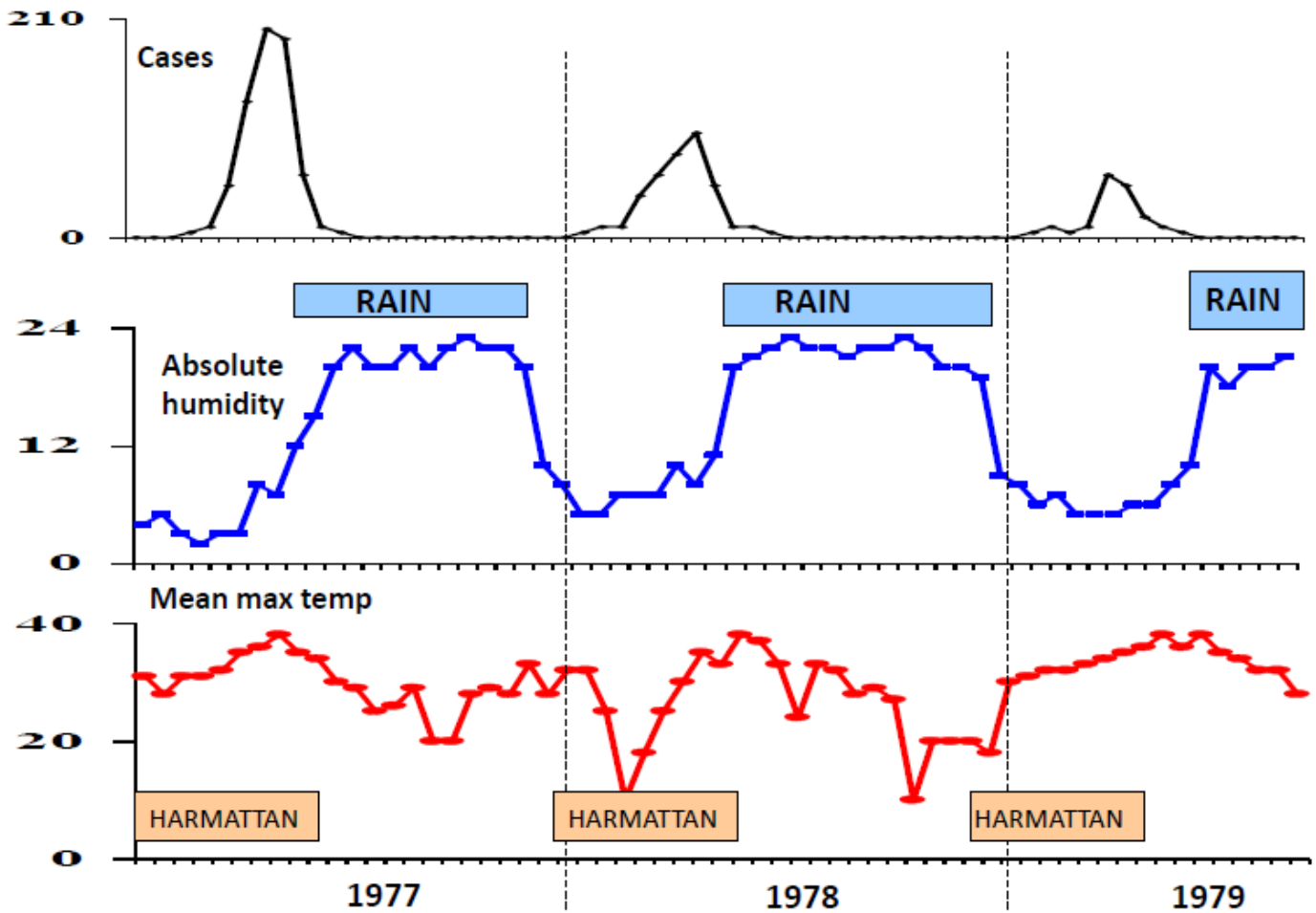
PERIODIC AND IRREGULAR EPIDEMICS



Daugla et al, Lancet 2014

SEASONALITY

Greenwood et al. Lancet 1979

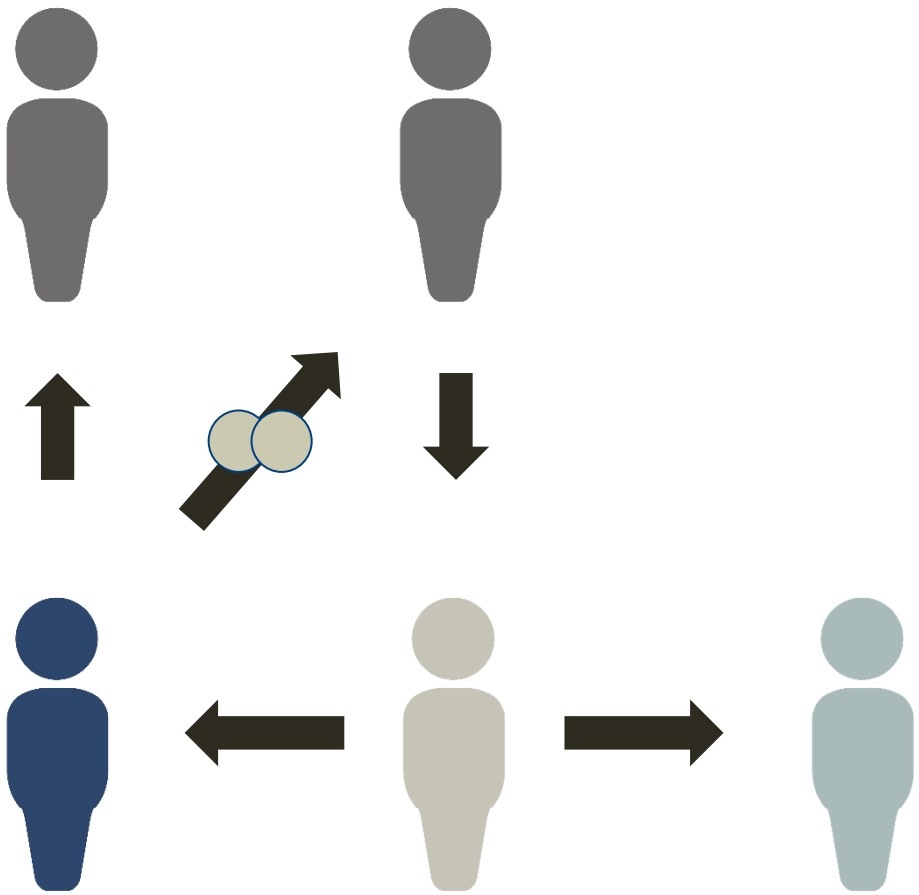


CARRIAGE

'Cases of meningitis alone cannot serve as an adequate index for estimating the extent of dissemination of the meningococcus through a population.'

(Schoenbach and Phair Am J Hyg 1948:47:271-281)

TRANSMISSION OF *N. MENINGITIDIS*



Adapted from Trotter & Maiden 2009

MODELLING TO UNDERSTAND DISEASE DYNAMICS

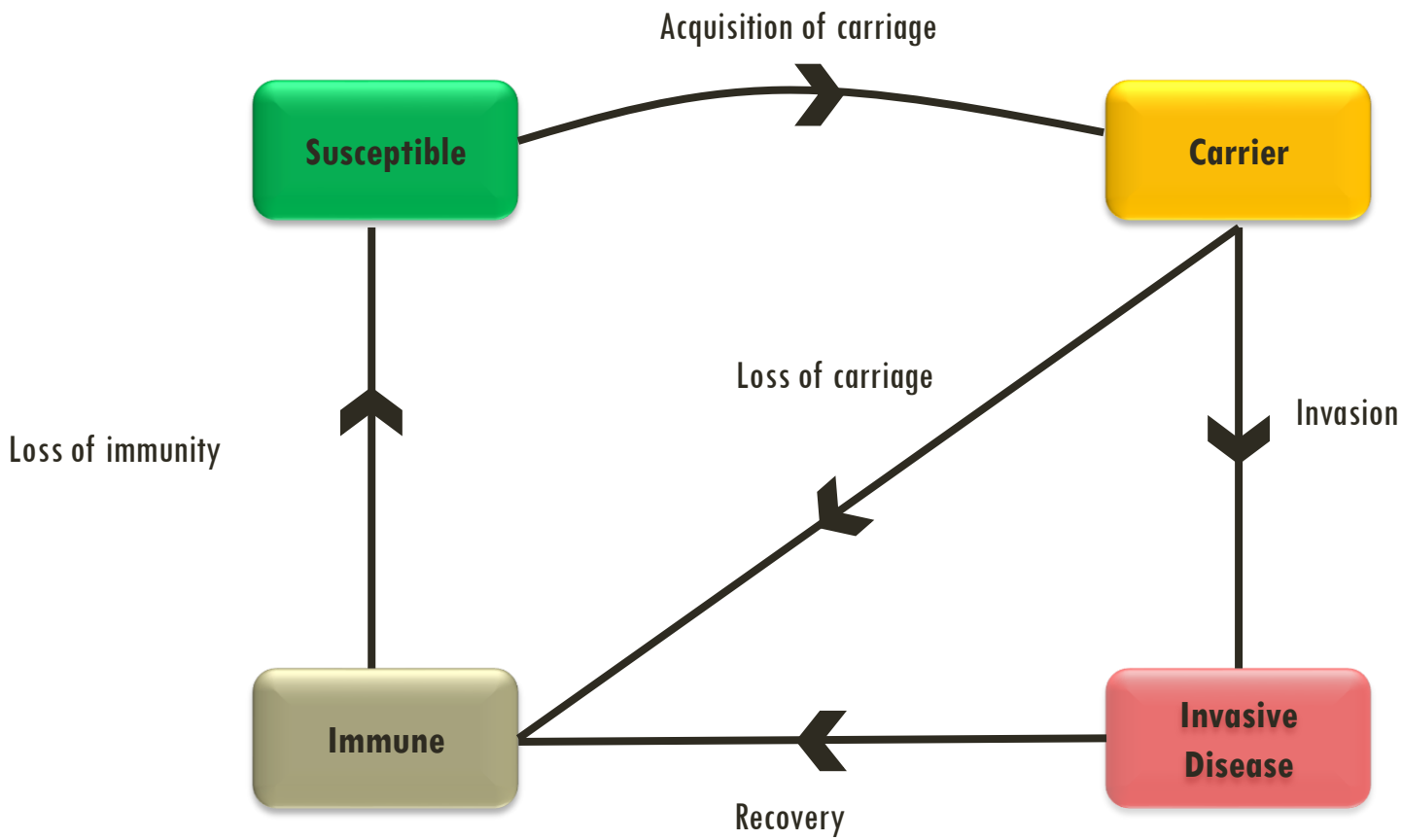
Is it possible to capture these complex patterns in a simple model?

- Seasonality
- Irregular but periodic epidemics
- Immunity?
  - SIS vs SIRS
- Relative importance of seasonal changes in:
  - Risk of disease given infection
  - Changes in transmission rate

Dr Tom Irving

University of BRISTOL

MODEL STRUCTURE



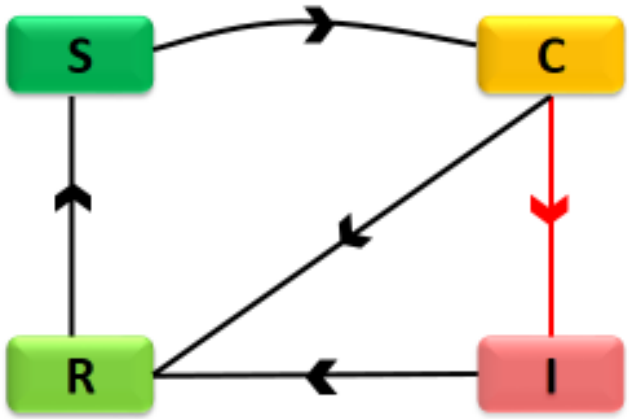
FORCING INVASION RATE

$$\frac{dS}{dt} = b - \frac{\beta S(C+I)}{N} + \phi R - \mu S$$

$$\frac{dC}{dt} = \frac{\beta S(C+I)}{N} - (a + \alpha + \mu)C$$

$$\frac{dI}{dt} = aC - (\gamma + \rho I + \mu)I$$

$$\frac{dR}{dt} = \rho I + \alpha C - (\phi R + \mu R)$$



$$a_0\left(1 + \epsilon_a \cos(2\pi t)\right)$$

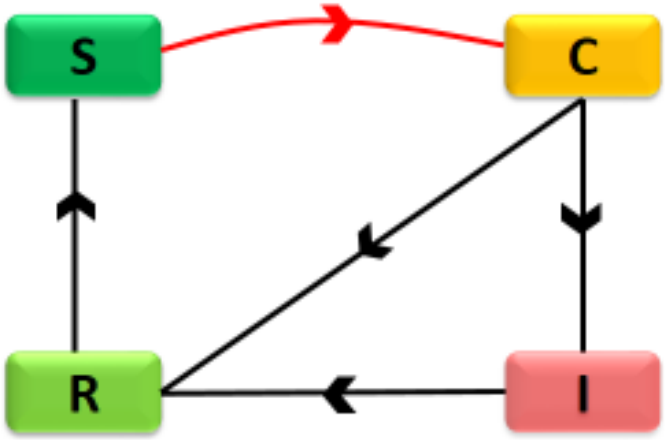
FORCING TRANSMISSION RATE

$$\frac{dS}{dt} = b - \frac{\beta S(C+I)}{N} + \phi R - \mu S$$

$$\frac{dC}{dt} = \frac{\beta S(C+I)}{N} - (a + \alpha + \mu)C$$

$$\frac{dI}{dt} = aC - (\gamma + \rho I + \mu)I$$

$$\frac{dR}{dt} = \rho I + \alpha C - (\phi R + \mu R)$$



$$\beta_0 \left(1 + \epsilon_\beta \cos(2\pi t)\right)$$

FORCING TRANSMISSION OR INVASION?

Only regular annual peaks possible if forcing invasion rate alone

Dynamics become more interesting by forcing transmission rate

VARYING IMMUNITY

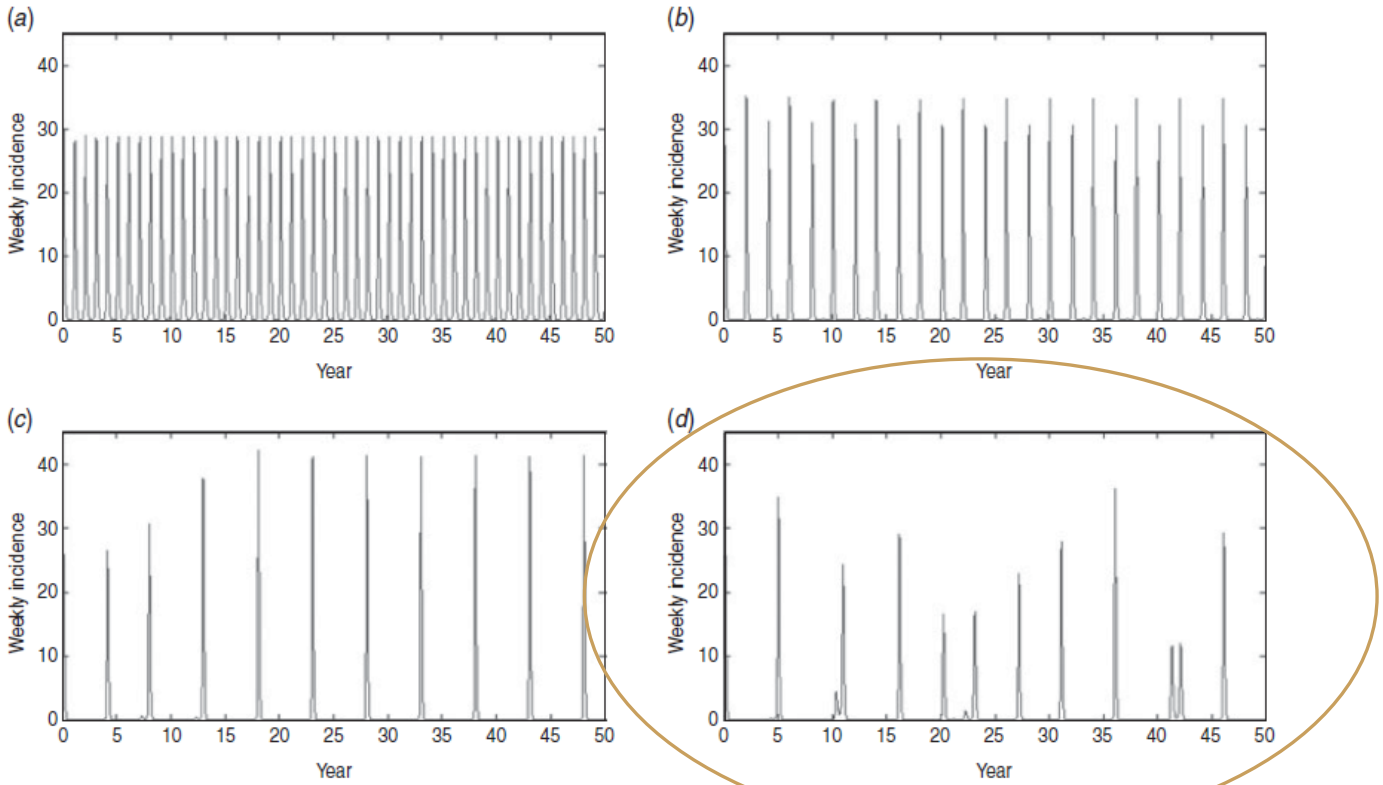


Fig. 4. Weekly incidence of meningitis per 100 000 population in the $SCIRS^{CI}$ model for different lengths of immunity, forcing only β. Calculated from time-series by weekly incidence $= \int_{t_0}^{t_0+1/52} aC\,\mathrm{d}t$. (*a*) Annual epidemics. (*b*) Biennial epidemics. (*c*) Epidemics every 5 years. (*d*) Epidemics of unpredictable magnitudes and occurring in unpredictable years. Parameters: $a_0 = 0{\cdot}2$, $\alpha = 26$, $\varepsilon_a = 0$, $\beta_0 = 90$, $\varepsilon_\beta = 0{\cdot}5$. (*a*) $\varphi = 0{\cdot}5$; (*b*) $\varphi = 0{\cdot}25$; (*c*) $\varphi = 0{\cdot}1$; (*d*) $\varphi = 0{\cdot}085$.

Irving *et al*. Epidemiology & Infection 2012

FINDINGS FROM SIMPLE MODEL

When carriage doesn't lead to immunity, with realistic parameter values only annual dynamics are possible

- Build up of susceptibles required before an epidemic is possible

When carriage does lead to immunity

- If invasion rate is forced, only annual dynamics are possible.
- If transmission rate is forced, "realistic" patterns of epidemics can be reproduced
- Not mutually exclusive both could occur, but transmission> invasion

Carriage low outside of epidemics

- Carriage and disease increase together

Other factors do not need to be invoked

- Delay caused by immune period resonates with seasonality, giving frequent and irregular epidemics

Epidemic meningitis: impact on families

PATH/Monique Berlier

- More than 10 percent of patients die, typically within 24-48 hours of the onset of symptoms
- 25% of survivors have long-term aftereffects
- Expenditures of 3 to 4 months of disposable income

Source: WHO, Colombini A, Barliano F, Zongo, S, et al. *Costs for households and community perception of meningitis epidemics in Burkina Faso.* Clinical Infectious Diseases 2009;49:1520-1525.

Slide courtesy of Dr Marie-Pierre Preziosi

Epidemic meningitis: impact on public health

- Marked seasonality with periodic devastating epidemics
- Overwhelms health infrastructures and disrupts routine programs
- Greater than 80% serogroup A

WHO/Kader Konde

Confidential & Proprietary Information

Slide courtesy of Dr Marie-Pierre Preziosi

TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE (2000) 94, 265–270

A severe epidemic of meningococcal meningitis in Nigeria, 1996

Idris Mohammed[1]*, Abdussalam Nasidi[3], A. S. Alkali[1], M. A. Garbati[1], E. K. Ajayi-Obe[1], Kudi A. Audu[2], Abdulmumini Usman[4] and Suleiman Abdullahi[5] *Departments of [1]Medicine and [2]Microbiology, University of Maiduguri, P.M.B. 1069, Bama Road, Maiduguri, Nigeria; [3]Department of Disease Control and International Health, Federal Ministry of Health, Abuja, Nigeria; [4]Epidemiological Unit, Kano State Ministry of Health, Kano, Nigeria; [5]Infectious Diseases Hospital, Sabon Gari, Kano, Nigeria*

Abstract

A particularly severe epidemic of meningococcal meningitis (cerebrospinal meningitis, CSM) occurred in Nigeria between January and June 1996. There were 109 580 recorded cases and 11 717 deaths, giving a case fatality rate of 10·7% overall. This is the most serious epidemic of CSM ever recorded in Nigeria, and may be the largest in Africa this century. It took over 3 months and the combined efforts of a National Task Force set up by the Federal Ministry of Health, the WHO, UNICEF, UNDP, Médecins Sans Frontières, the International Red Cross and several other non-governmental organizations to bring the epidemic under control. The main control measures centred on active treatment of infected persons, mass vaccination and health education. The exact number of persons treated cannot be ascertained, but there were treatment centres in almost every Local Government Area in the affected States. A study of 1577 patients admitted at the Infectious Diseases Hospital, Kano, showed that 84% of those infected were aged ≤20 years and that, for the first time, infants aged ≤2 months were affected. Despite intervention, the case fatality rate of 9·1% among this group of patients was similar to the nationwide figure of 10·7%. Long-acting oily chloramphenicol proved highly effective in the treatment of patients, and its routine use in epidemic CSM is

250,000 cases
25,000 deaths

Intro

STEIN *et al.*, 1970; WAHDAN *et al.*, 1973; ETTORI *et al.*, 1977; GREENWOOD & WALL, 1980; MOHAMMED & ZARUBA, 1981). Sulphonamides, penicillin, chloramphenicol and rifampicin have been used to good effect in reducing meningococcal carriage in the nasopharynx, a factor in preventing outbreaks, although the potential costs would militate against their use in controlling epidemics of CSM (GREENWOOD, 1999). Vaccination appears to hold the best promise for ultimate control of epidemic meningococcal disease. Earlier trials of meningococcal vaccines produced inconclusive or disappointing results, either because the trials were not properly conducted or because the vaccines used were poorly immunogenic (DAVIS, 1931; RIDING & CORKHILL, 1932). Groups A & C polysaccharide vaccines developed later were more immunogenic in adults (GOLDSCHNEIDER *et al.*, 1969; GREENWOOD *et al.*, 1980), but less so in infants and young children (MONTO *et al.*, 1973; PELTOLA *et al.*, 1977; MOHAMMED & DAMISAH, 1982). In recent years mass vaccination using groups A & C meningococcal polysaccharide vaccines has been carried out in several States in northern Nigeria with fairly good results (MOHAMMED & ZARUBA, 1981; MOHAMMED *et al.*, 1984a, 1984b). Sustained routine mass vaccination with currently available bivalent vaccines, backed up by

and Saudi Arabia in 1987 (MOORE, 1992), and may have been introduced to Africa by pilgrims returning home from that country. There is some evidence that this strain of meningococcus was introduced to Nigeria from Niger Republic through Jibia, the border town in Katsina State which is some 30 kilometers from Maradi.

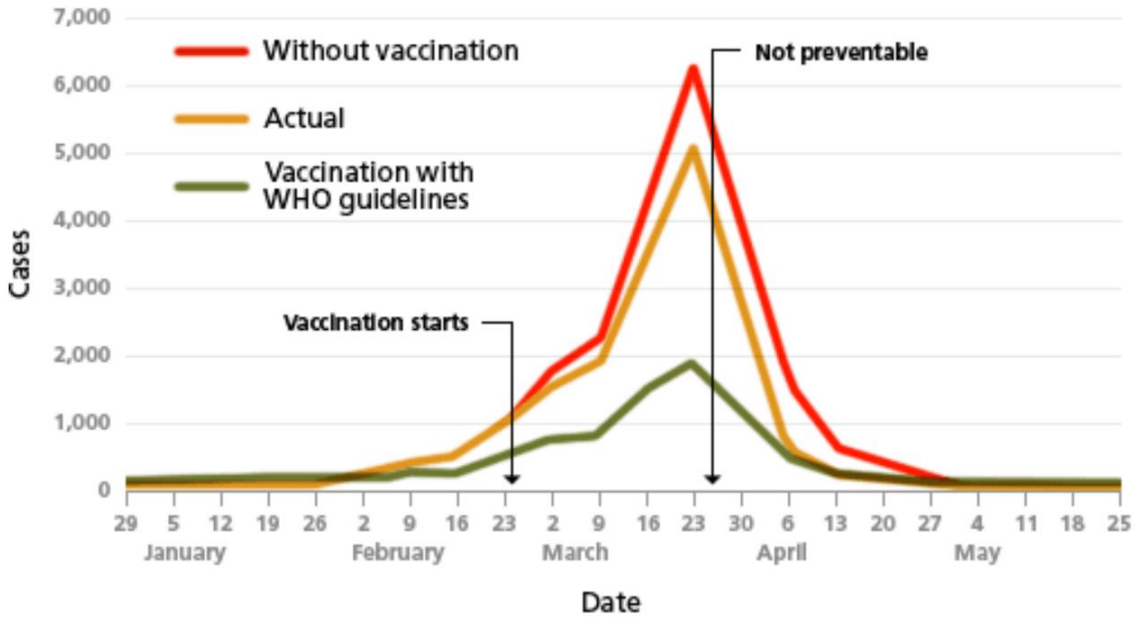
The factors responsible for the severity of this epidemic are not clearly known, but the outbreak occurred in the hot, dry and dusty season when the absolute humidity was also low. Herd immunity in the general population was probably low since vaccination coverage in the preceding 2 years had been low (Federal Epidemiological Unit, personal communication). Poor environmental conditions facilitated the rapid spread of the epidemic, as the majority of those infected were of low socio-economic status living in over-crowded, poorly ventilated and dirty dwellings. The strain of meningococcus responsible for the epidemic was new to the region, and its virulence may have been due in part to an inability to mount an effective immune response.

Features of the epidemic

A formal report of the outbreak was made to the Epidemiological Unit of the Federal Ministry of Health at the end of February 1996. However, the record books of several Local Government health units show that cases of meningitis had been diagnosed with increasing frequency as far back as October 1995. In a rural health centre at Jibia, a town in north-western Nigeria bordering Niger Republic, the epidemic threshold (15 cases per

*Author for correspondence:
e-mail maiduguri-lab@who.nigeria.org

REACTIVE VACCINATION



Emergency vaccination with polysaccharide vaccine**.** Source: Woods et al. 2000.

1. Woods CW, Armstrong G, Sackey SO, et al. Emergency vaccination against epidemic meningitis in Ghana: implications for the control of meningococcal disease in West Africa. *The Lancet*. 2000;355(9197):30–33.

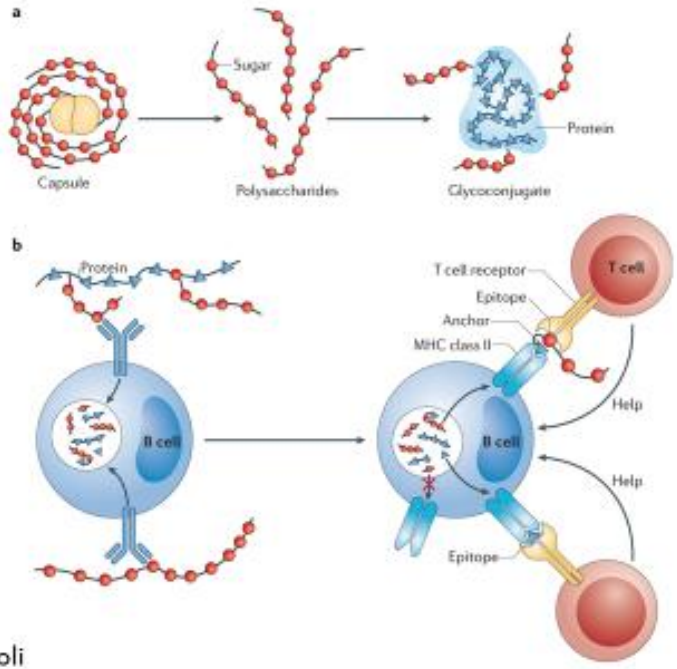
CALL FROM AFRICAN MINISTERS

In 1997, after the catastrophic epidemic, a meeting of 26 ministries of health tool place in Ougadougou and issued a plea to the global health community to “do something”

Initial efforts led by WHO convened a group of experts, which culminated in a funding application to the, then relatively new, Bill and Melinda Gates Foundation.

In 2001, the Meningitis Vaccine Project was launched with a grant of $70m to create an effective **conjugate** meningococcal vaccine for Africa

CONJUGATE VACCINES



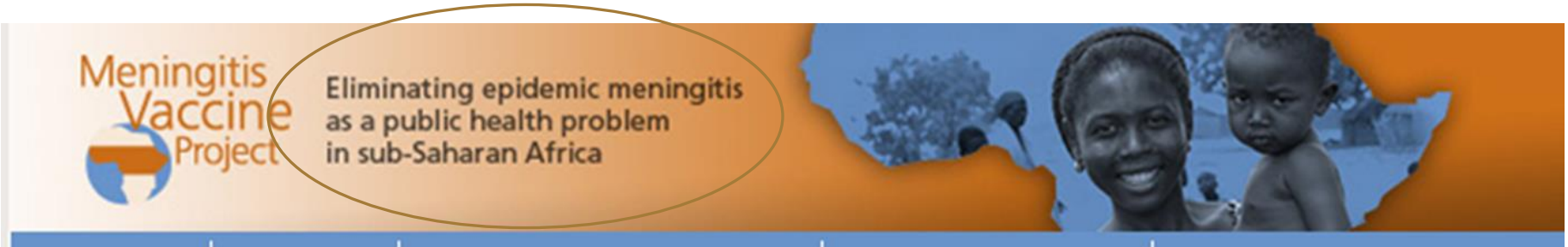
De Gregorio & Rappuoli
Nature Reviews Immunology 14, 505–514 (2014)
doi:10.1038/nri3694

a | Polysaccharides that are present on the surface of capsulated bacteria are composed of many identical repeating units of simple sugars (represented by red circles).
b | When purified, the polysaccharides are poorly immunogenic, as they are unable to enter the cavity of MHC molecules and therefore they fail to be presented to T cells. In conjugate vaccines, such as those against Haemophilus influenzae type b, pneumococcus, meningococcus and group B streptococcus, polysaccharides are covalently linked to proteins. The peptides that are derived from the proteins (represented by blue triangles) enter the cavity of the MHC molecule and engage the T cell receptor directly (bottom right) or function as an anchor for a sugar epitope (top right).

MENINGITIS VACCINE PROJECT

Established in 2001 as a partnership between WHO and PATH

Single goal of developing, licensing and introducing at public health scale a group A meningococcal conjugate vaccine for sub-Saharan Africa



VACCINE DEVELOPMENT PROGRAMME

It soon became clear to MVP that large pharmaceutical companies already producing group C conjugate vaccines would not produce an affordable group A vaccine

MVP thus became a *virtual vaccine company*, drawing together different partners.

Conjugation, process development, process optimisation, quality control, batch size scale up at Serum Institute of India Limited assisted by experienced technical consultants

Clinical trials from 2005 to 2010 for use in individuals 1-29 years, 2008-2013 for children <1 year

- First in India, then sub-Saharan Africa
- Well tolerate, robustly immunogenic in approx. 7000 subjects accross 7 clinical trials

Yaoundé Declaration (2008) – African health ministers commit to vaccinated 320 million individuals across 26 countries by 2015

LICENSURE OF MENAFRIVAC®

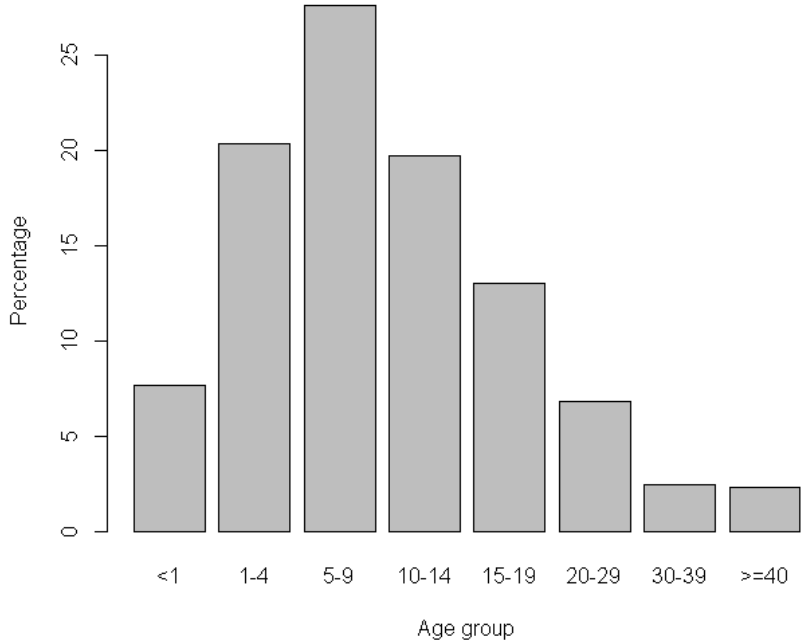
Marketing Authorisation India, January 2010

WHO Prequalification, June 2010

SIIL manufacturing capacity of ~50 million doses/ year

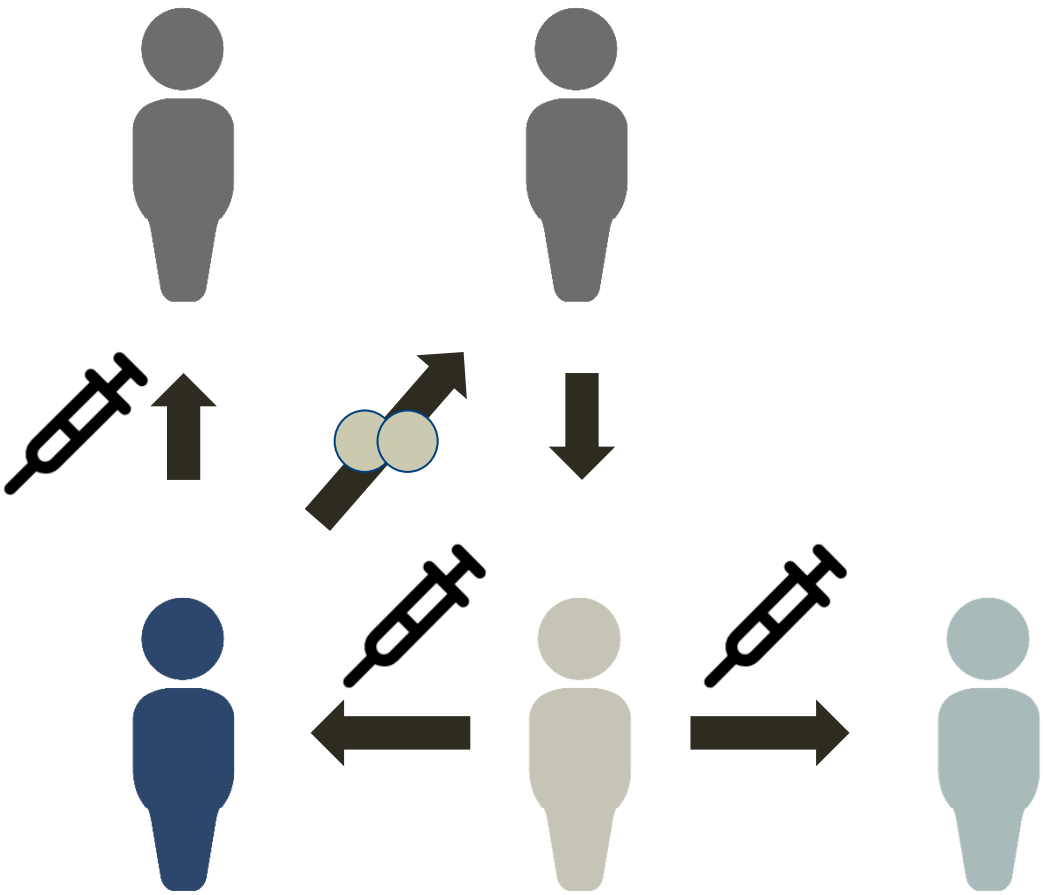
Price of $0.40

RATIONALE FOR MASS VACCINATION OF 1-29 YEAR OLDS – DISEASE BURDEN



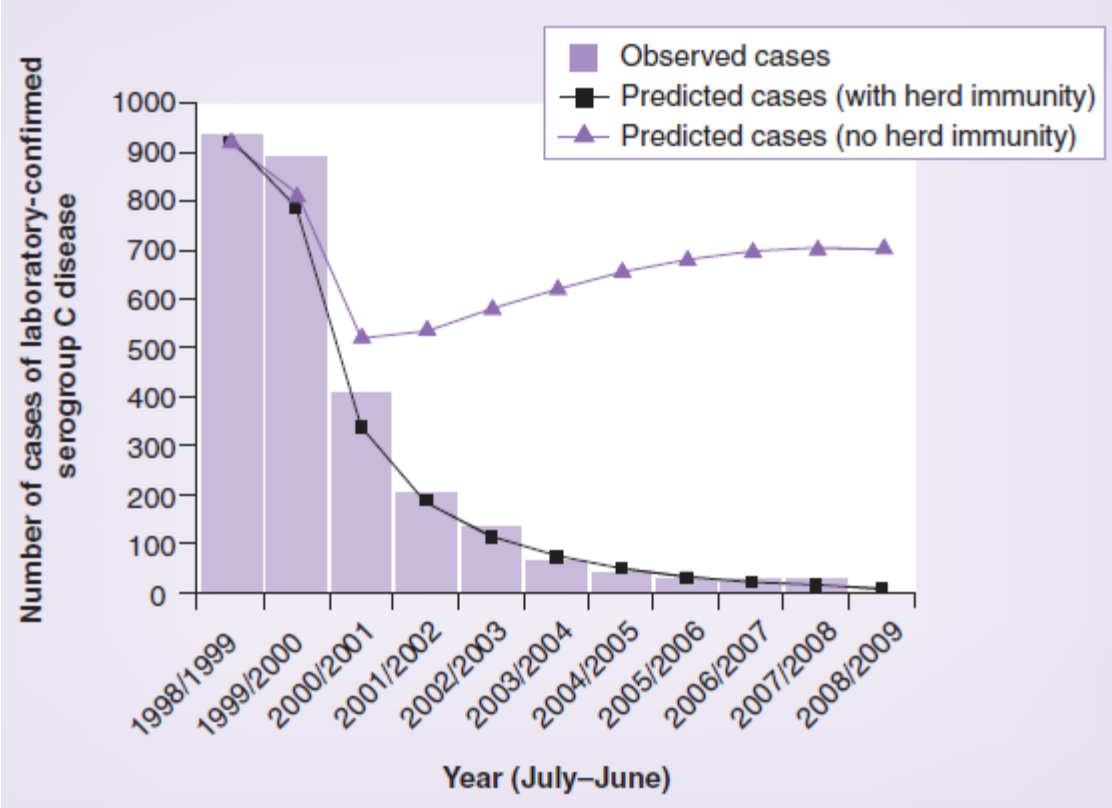
Age distribution of Nm disease in Niger, Campagne et al, Bull WHO1999

TRANSMISSION OF *N. MENINGITIDIS*



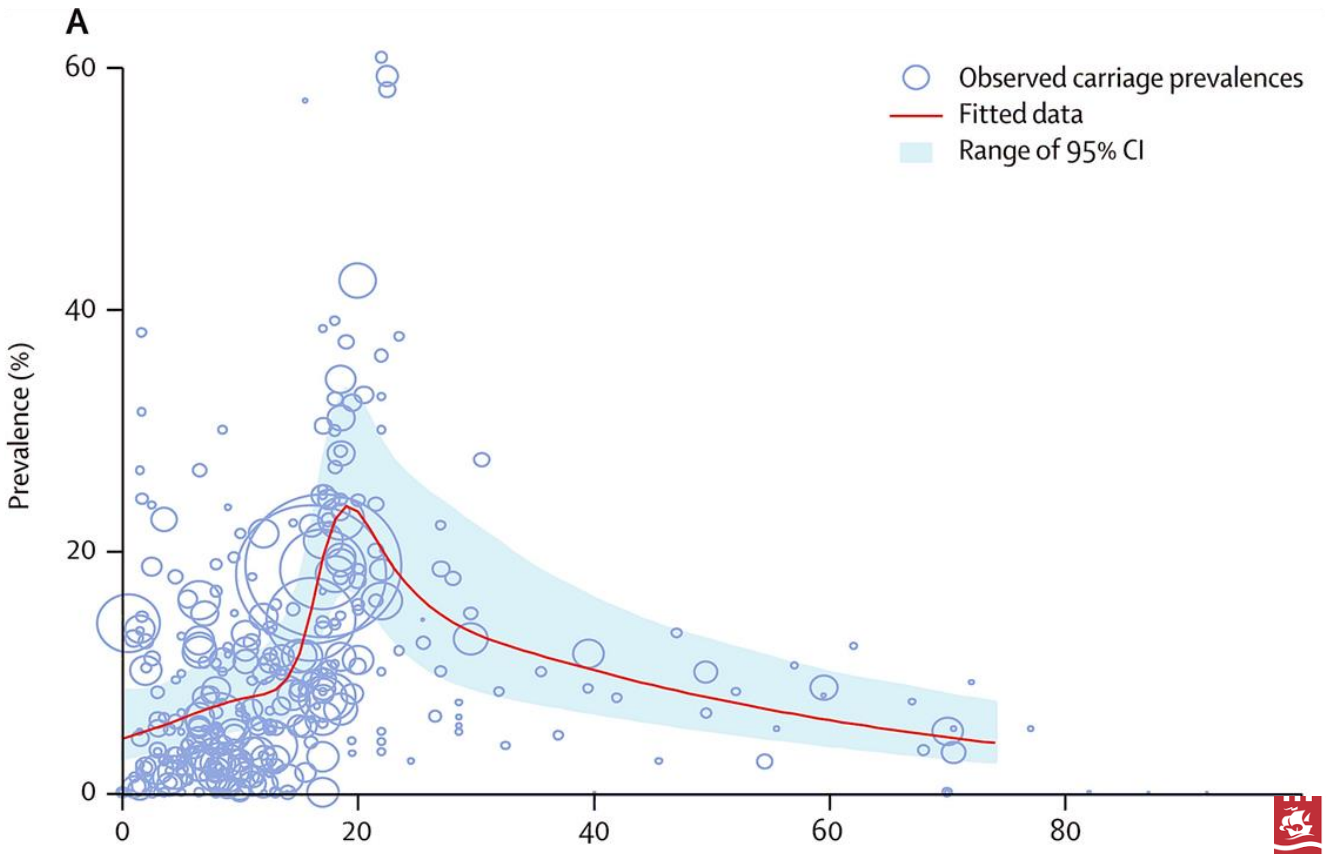
Adapted from Trotter & Maiden 2009

RATIONALE FOR MASS VACCINATION OF 1-29 YEAR OLDS - DYNAMICS



Mass campaign (1-18years) with NmC vaccine resulted in large herd effects
Trotter & Maiden, Expert Rev Vaccines 2009

MENC CAMPAIGN INCLUDED PEAK OF TRANSMISSION

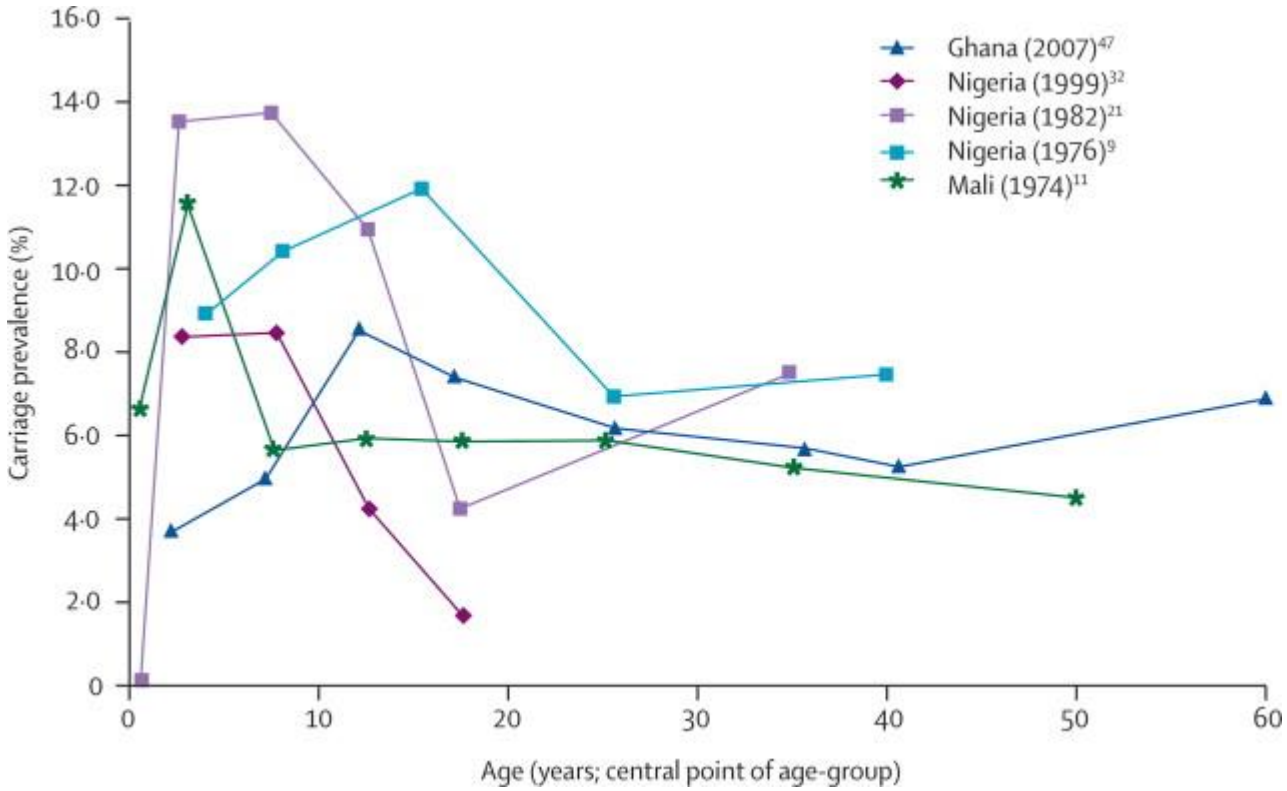


Christensen et al, 2010

Dr Hannah Christensen

University of BRISTOL

AGE DISTRIBUTION IN AFRICAN STUDIES



Trotter & Greenwood, Lancet ID 2007

VACCINE INTRODUCTION 2010-2019 CAMPAIGNS

Meningitis Vaccine Project

The 2010 MenAfriVac® vaccine launch in Burkina Faso was a cause for celebration—it marked a turning point in Africa's history with meningococcal meningitis. Photo: PATH/Gabe Bienczycki

MENAFRICAR

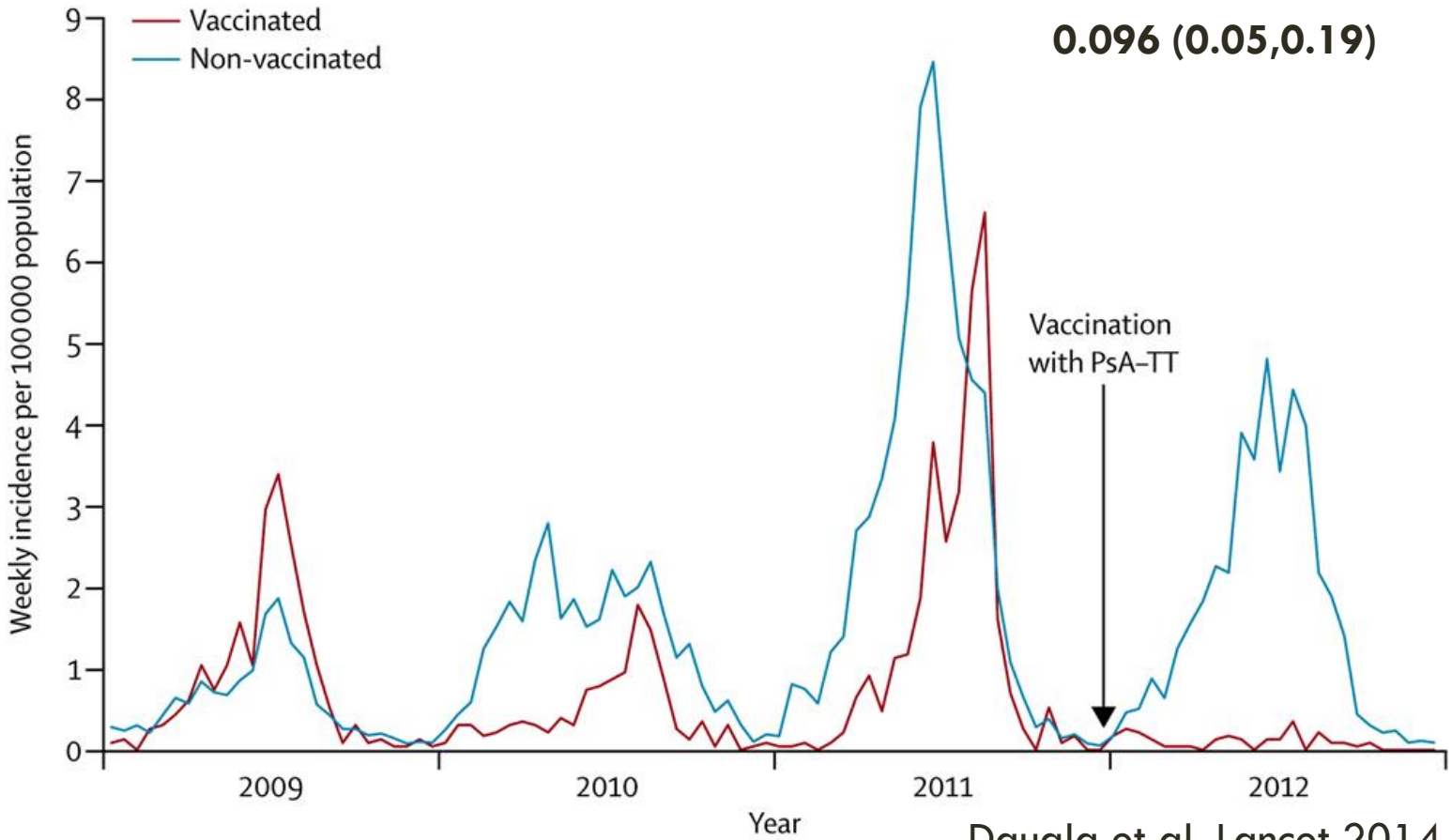
menafricar African Meningococcal Carriage Consortium

IRD Senegal; CVD-Mali; CERMES Niger; Navrongo Health Research Centre, Ghana; University of Maidugiri, Nigeria; CSSI Chad; AHRI Ethiopia; LSHTM and other northern partners

IMPACT ON MENINGITIS

menafricar African Meningococcal Carriage Consortium

Incidence rate ratio
0.096 (0.05,0.19)



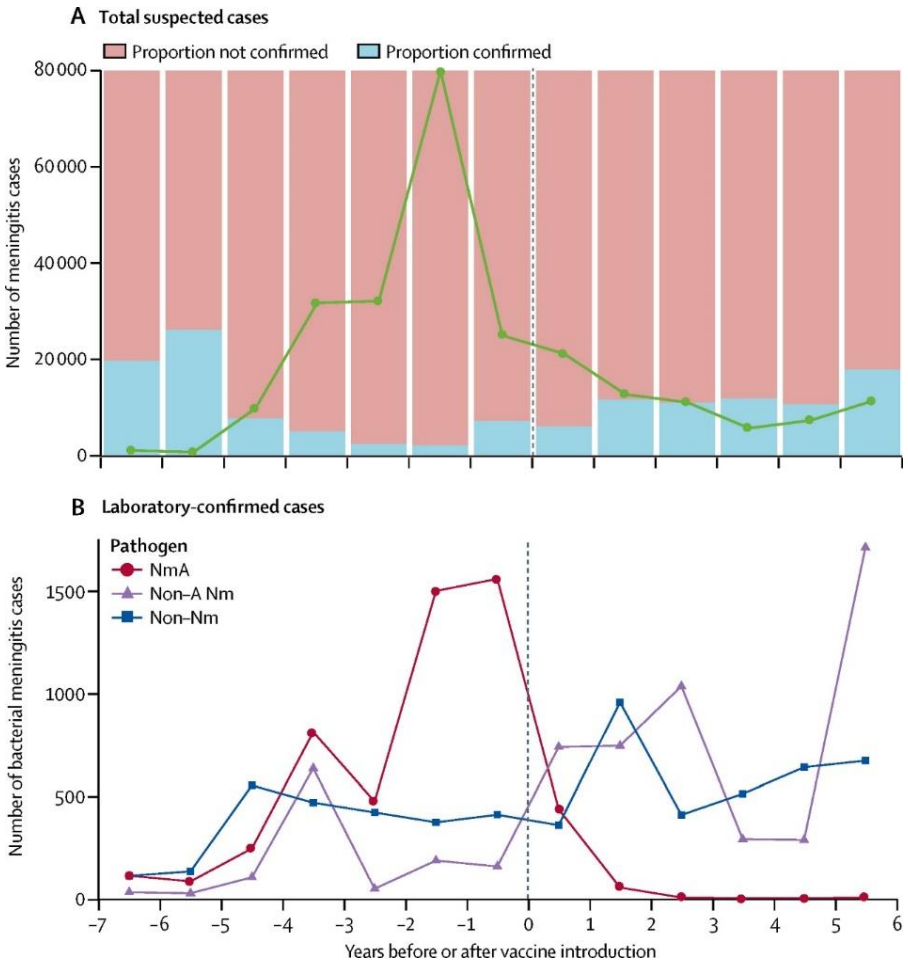
Daugla et al, Lancet 2014

IMPACT ON CARRIAGE

- 32/4278 group A carriers in 2011 pre-vaccine survey
- Only 1/5001 group A carrier post-vaccination
- 98% difference in group A carriage prevalence
- Adjusted Odds Ratio 0.019, 95% CI 0.002, 0.14

Daugla et al, Lancet 2014

VACCINE IMPACT IN 9 CORE COUNTRIES



World Health Organization

Trotter et al, Lancet Infect Dis 2017

MODELLING TO INFORM VACCINE STRATEGY

Aim:

To develop and apply mathematical models of *Neisseria meningitidis* group A (NmA) transmission and disease to investigate the optimal use of MenAfriVac® in the long term

Andromachi Karachaliou

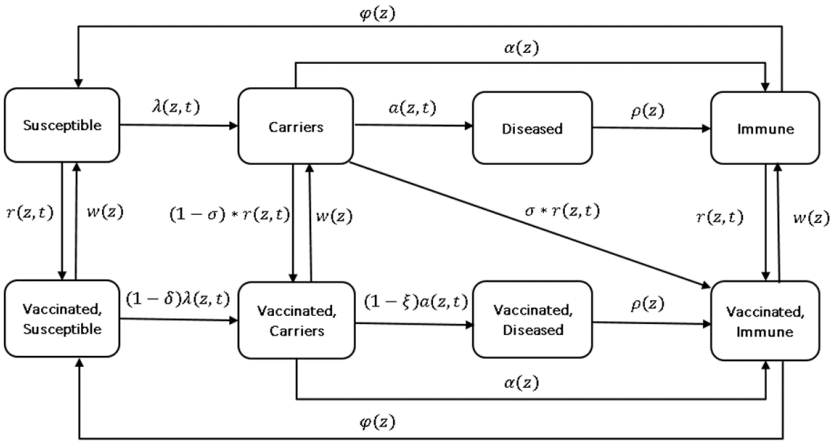
UNIVERSITY OF CAMBRIDGE

In partnership with Meningitis Vaccine Project / WHO

MODEL DESCRIPTION

We used an **age-structured transmission dynamic** model that was able to capture these key epidemiological features of MenA in the African meningitis belt

- Periodic but irregular epidemics
- Seasonality
- Epidemics of varying size
- Stochasticity included (transmission rate)
- Variable risk of disease by age
- Variable prevalence of carriage by age
- Transmission between asymptomatic carriers
- Temporary immunity from carriage
- Susceptible- Infected- Recovered (SIRS) structure
- African specific parameters



MODEL PARAMETERS

Some data are readily available

- Demographic parameters
- Duration of carriage and disease
- Vaccine coverage

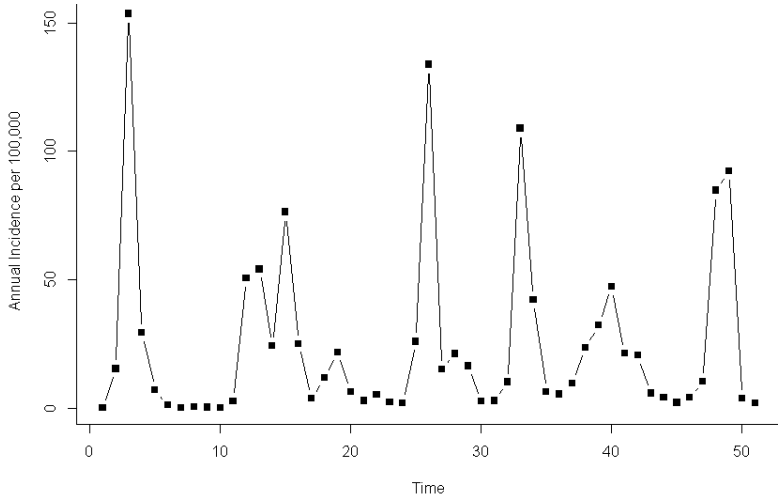
Some data are available by proxy

- Vaccine effectiveness against meningitis
- Reduction in carriage prevalence following vaccination
- Case counts of clinically diagnosed meningitis over time
- Case: carrier ratio
- Duration of vaccine protection

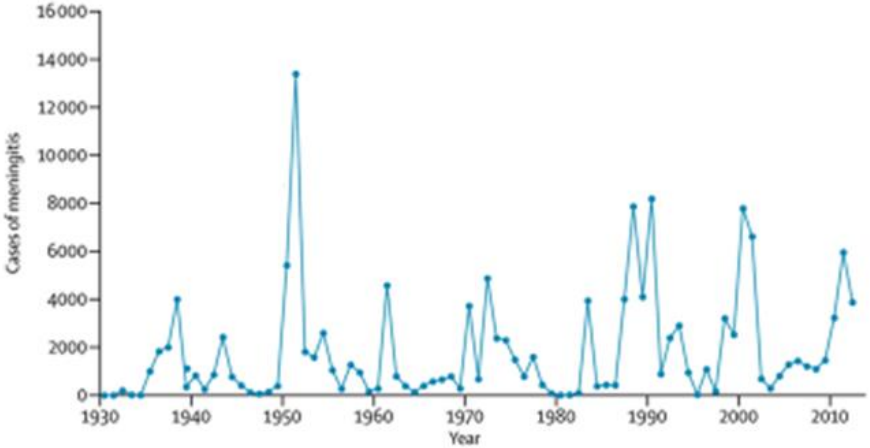
Others are not known!

- Contact patterns/ WAIFW ➔ try a range, fit to disease/ carriage data
- Immunity following carriage ➔ range defined by study of infection dynamics

DISEASE DYNAMICS



Example model run (no vaccination) showing incidence of meningitis over 50 year period



Cases of meningitis in Chad 1930-2012, Daugla et al, Lancet 2014

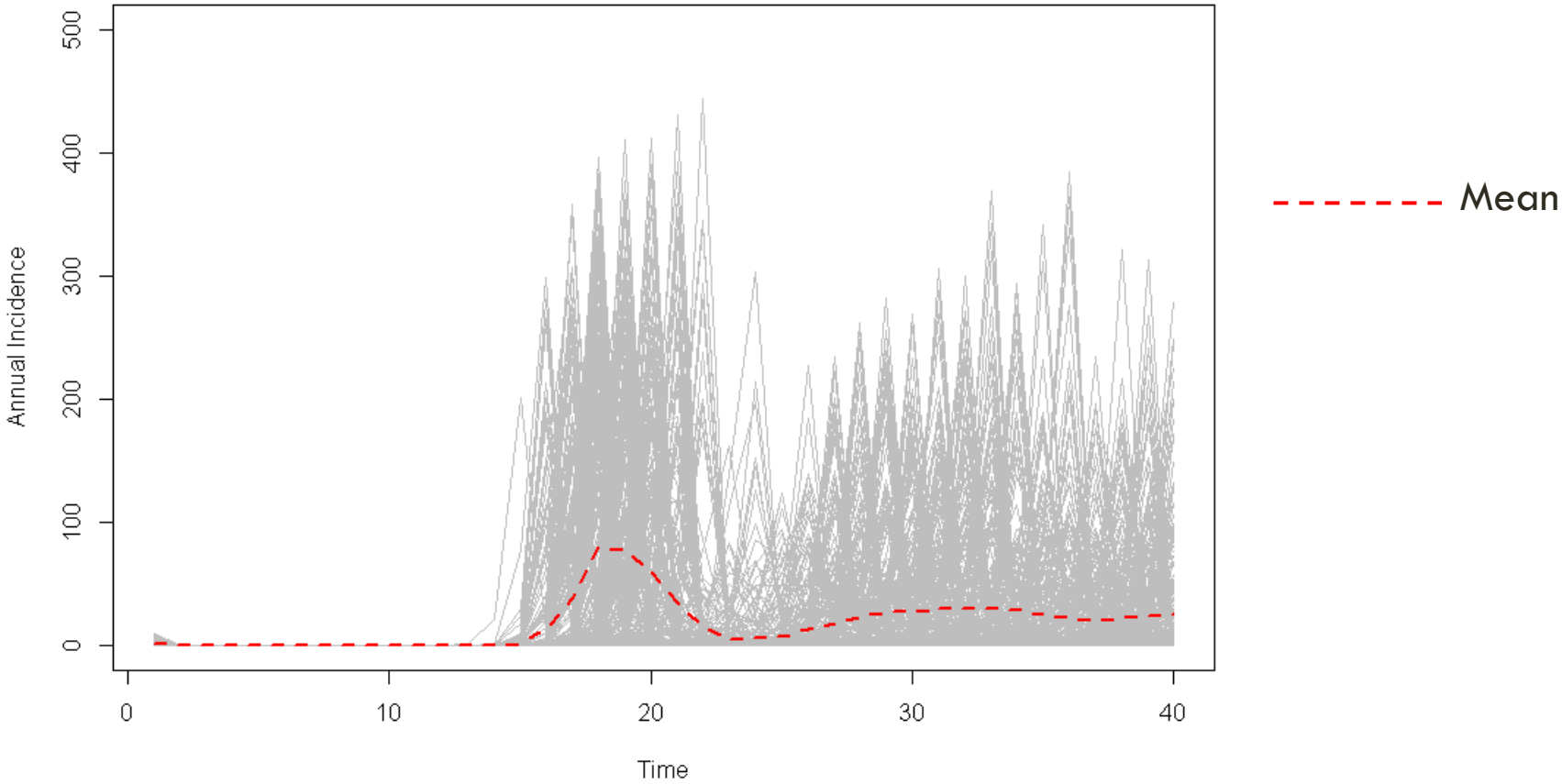
VACCINE STRATEGIES

Vaccine strategy	Introduction	Long-term
A. Initial campaign only	Mass immunisation of 1-29 year olds	Nothing
B. Periodic campaigns	Mass immunisation of 1-29 year olds	Periodic mass immunisation of 1-4 year olds
C. Routine EPI	Mass immunisation of 1-29 year olds	Routine EPI @ 9 months, 5 years after introduction
D. Combination	Mass immunisation of 1-29 year olds	Routine EPI @ 9 months, 5 years after introduction plus 1-4 year old catch-up

Vaccinated individuals assumed to have some protection against carriage and disease resulting in direct and indirect (herd immunity) protection

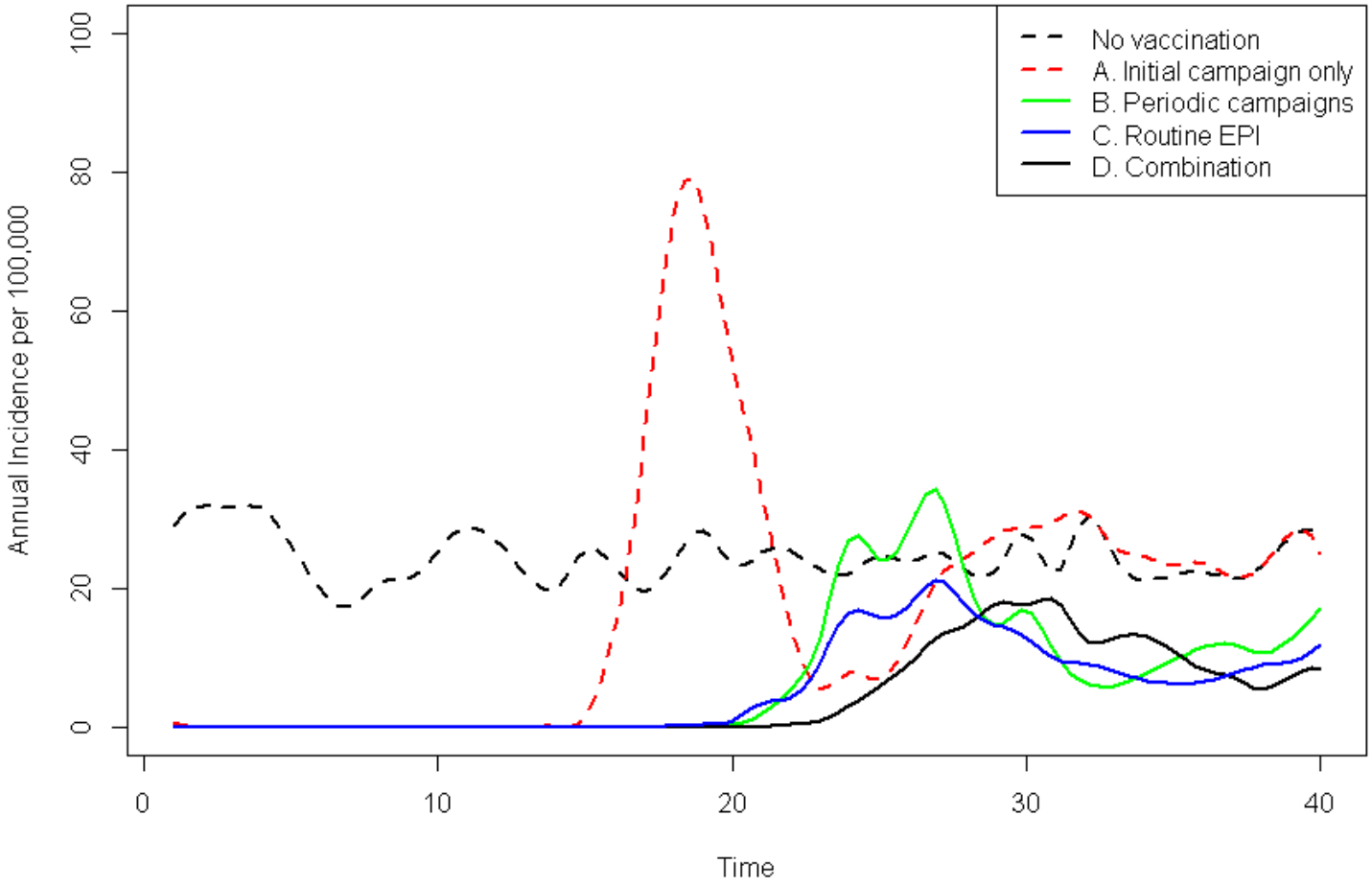
A. MASS 1-29 YEAR OLDS ONLY*

Because of stochastic variation each scenario was simulated 300 times.

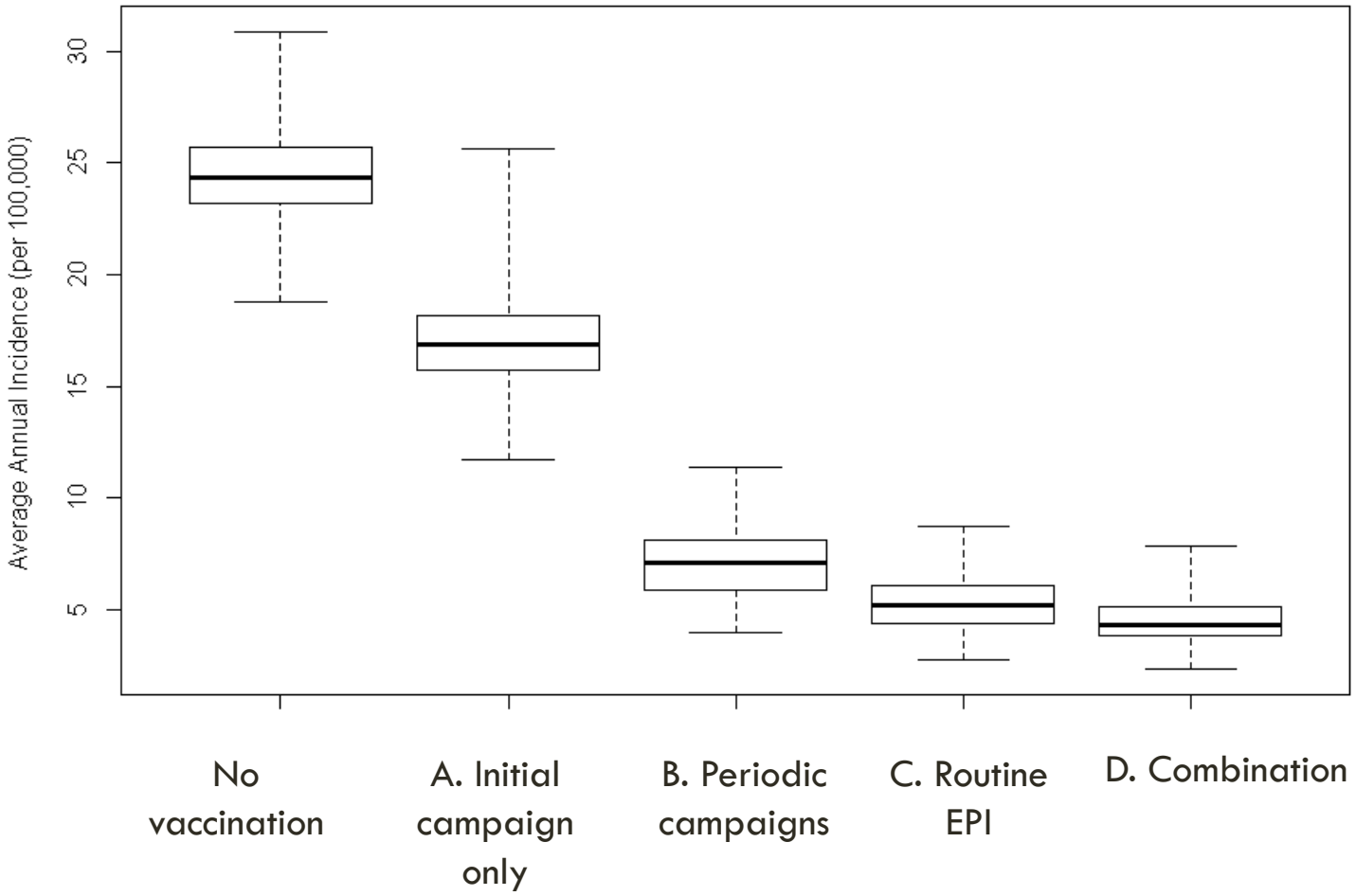


*Assumes 10 years average vaccine protection

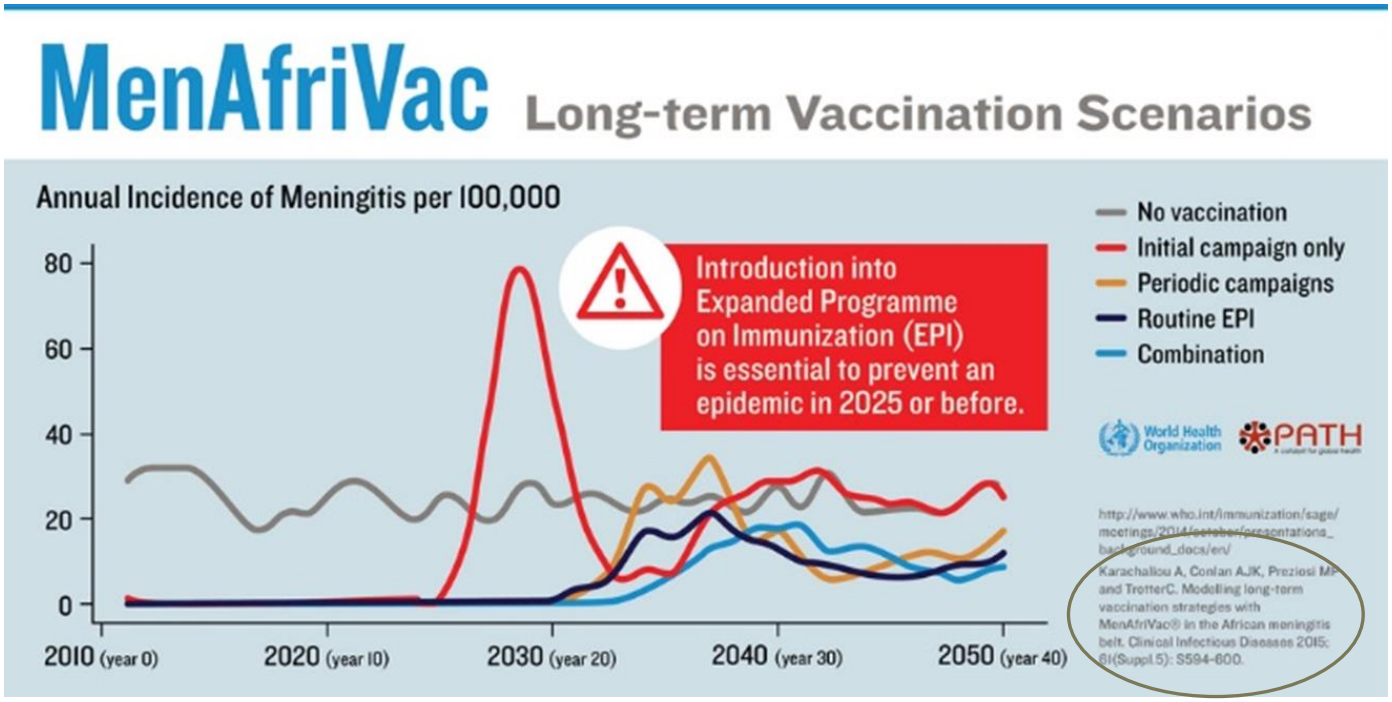
COMPARISON OF STRATEGIES A-D



COMPARISON OF STRATEGIES A-D



LONG TERM VACCINATION IS ESSENTIAL



ROUTINE IMMUNISATION

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Meningitis A vaccine now recommended in routine immunization schedules

Brazzaville, 20 January 2015 – The World Health Organization (WHO) now recommends the conjugate meningitis A vaccine MenAfriVac® to be introduced in routine immunization schedules in sub-Saharan Africa. This recommendation ensures that infants are protected against meningitis and population-wide immunity is maintained.

The use of the MenAfriVac® vaccine to prevent meningitis A epidemics is one of the greatest vaccination success stories in public health history and highlights what partners can accomplish when unified by a compelling cause. In 2014, the MenAfriVac® campaigns reached more than 63 million people with remarkable success.

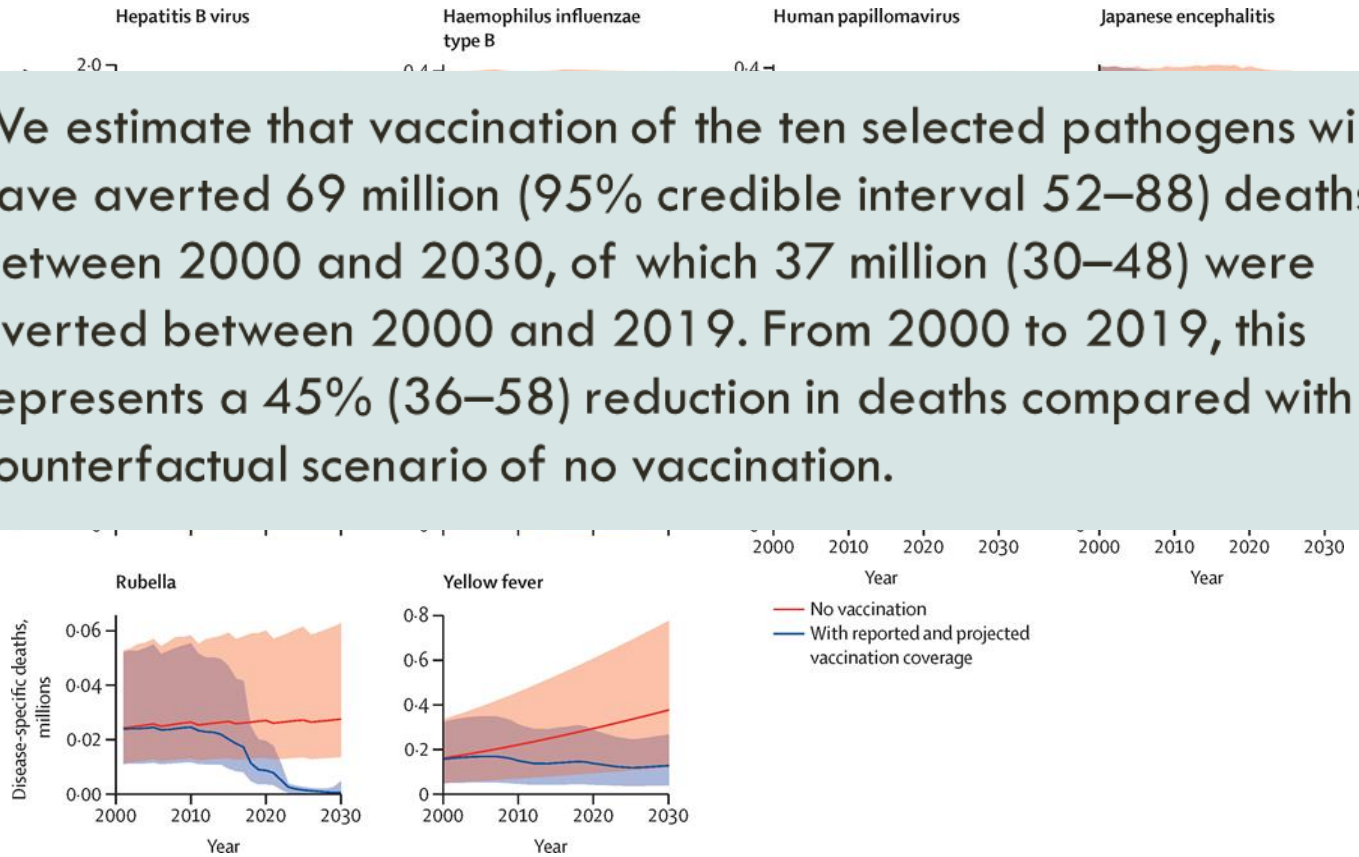
In all, over 217 million people between one and 29 years of age have benefited from the vaccine since 2010.

This unprecedented achievement is due to the overall availability, safety and effectiveness of the vaccine. MenAfriVac® is incredibly stable – being the first vaccine to be used with the controlled temperature chain (CTC) approach. This has allowed its transport and storage for as long as four days in ambient temperatures up to 40°C. This shattered preexisting cold chain limitations and paved the way to effectively deliver the vaccine to the hardest to reach people in need.

In October 2014, the WHO Strategic Advisory Group of Experts (SAGE) on immunization concluded that a one-dose schedule at nine months of age or older is recommended. At least six countries (Burkina Faso, Chad, Ghana, Mali, Niger, and Nigeria) are planning to introduce MenAfriVac® into their routine immunization programmes by late 2015.

VACCINE IMPACT MODELLING CONSORTIUM

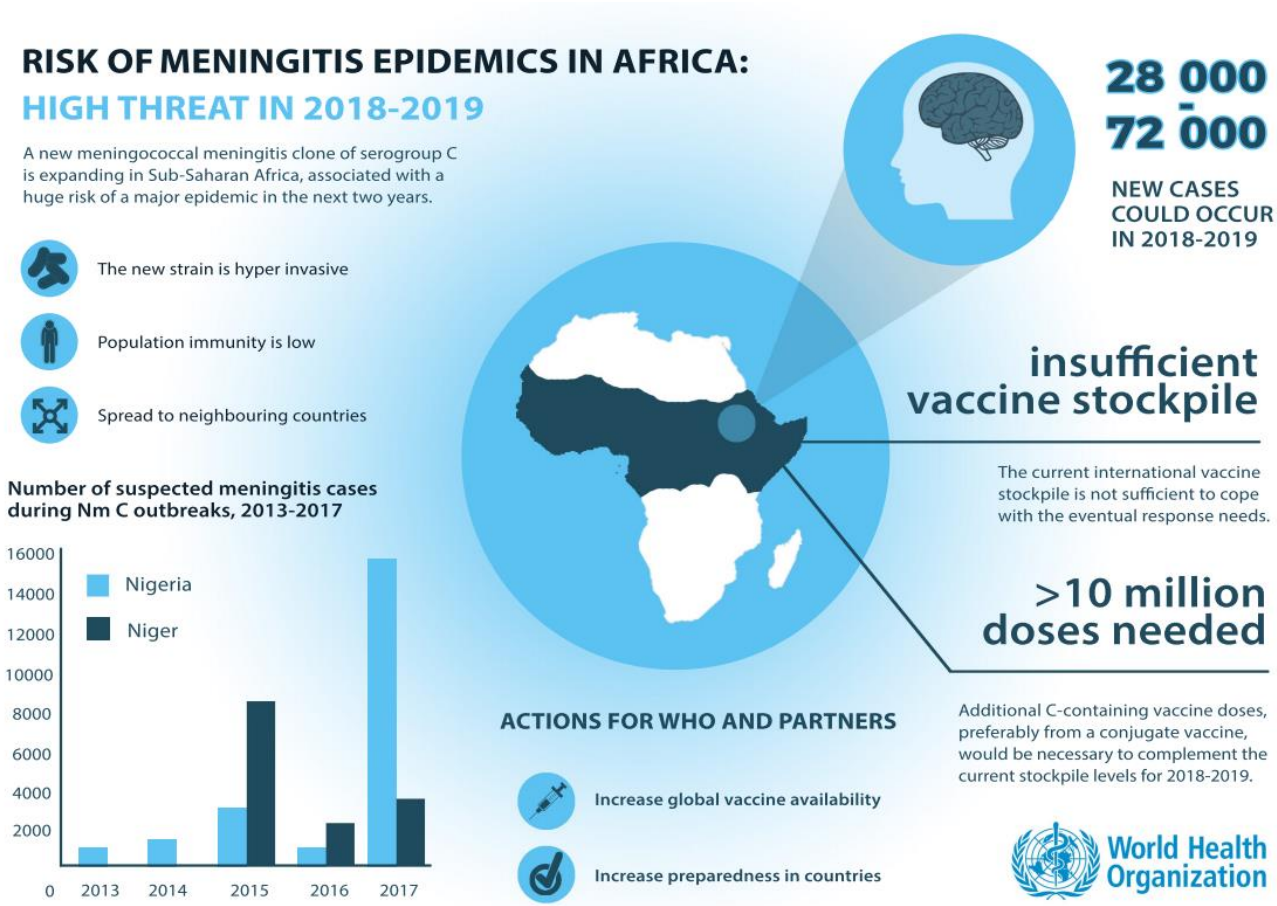
We estimate that vaccination of the ten selected pathogens will have averted 69 million (95% credible interval 52–88) deaths between 2000 and 2030, of which 37 million (30–48) were averted between 2000 and 2019. From 2000 to 2019, this represents a 45% (36–58) reduction in deaths compared with the counterfactual scenario of no vaccination.



Li et al, *Lancet 2021*

The Lancet 2021 397398-408DOI: (10.1016/S0140-6736(20)32657-X)

THE END OF THE STORY?



PENTAVALENT CONJUGATE VACCINES

SERUM INSTITUTE OF INDIA PVT. LTD.

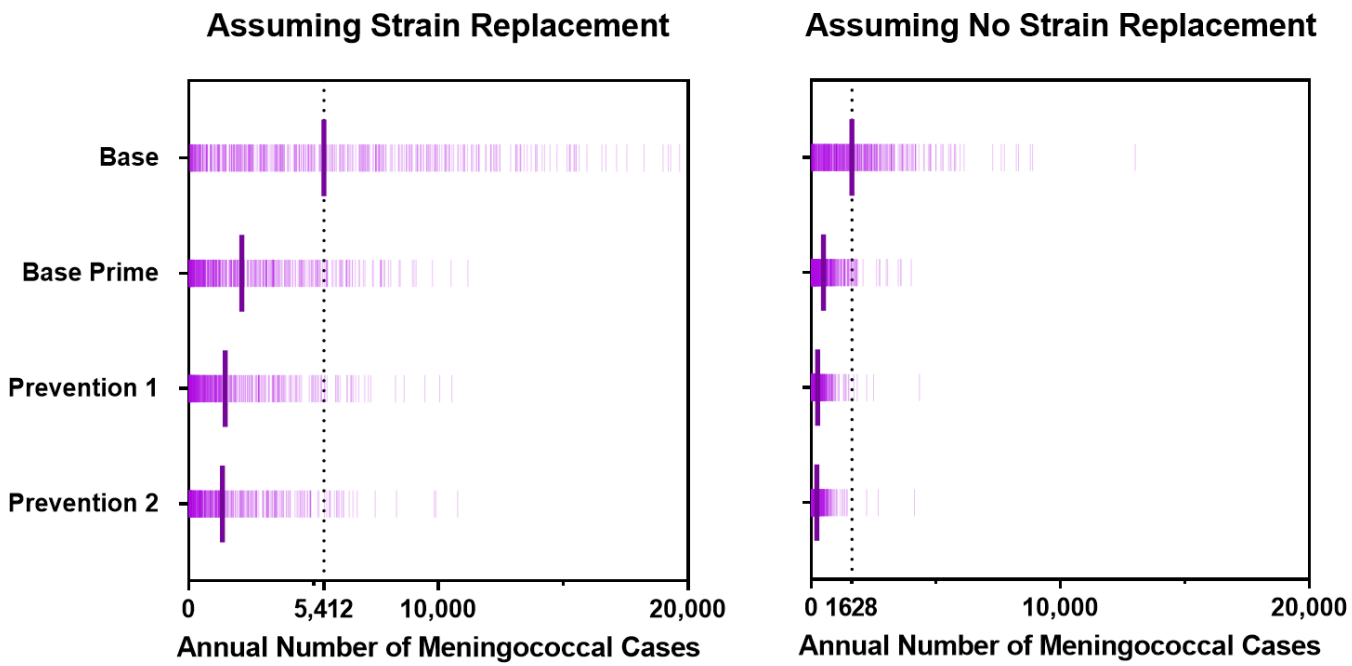
PATH

Goal:

To eliminate epidemic meningitis from sub-Saharan Africa through the development, testing, licensure, and introduction of a pentavalent (A, C, W, X, Y), heat-stable meningococcal conjugate vaccine.

Marc LaForce.
https://www.meningitis.org/healthcare-professionals/conferences-and-symposia/mrf-conference-2019

MODELLING COST-EFFECTIVENESS



Strategies using pentavalent conjugate vaccine would be cost-saving or cost-effective at $4 per dose in Burkina Faso

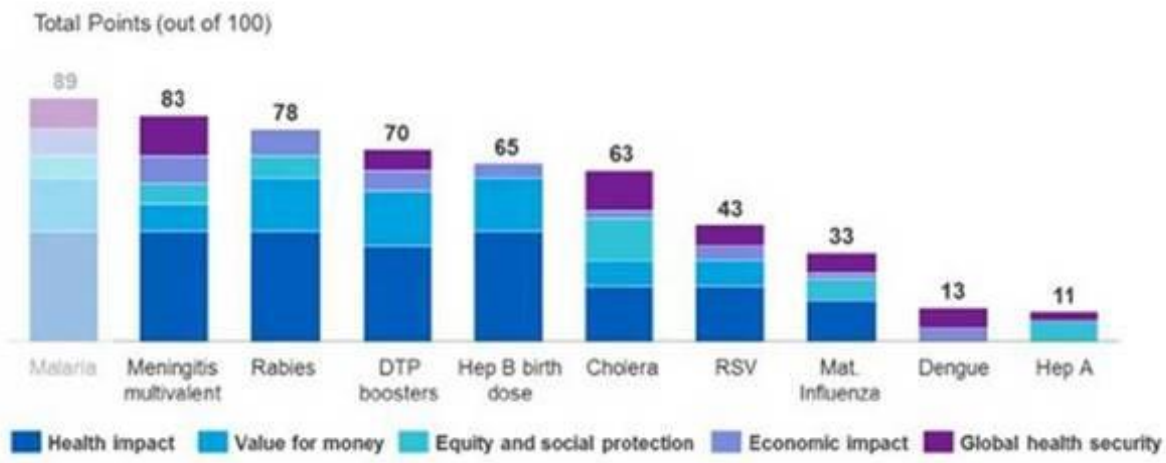
Yaesoubi et al, PLOS Med 2018

GAVI 2018 INVESTMENT STRATEGY

VACCINE IMPACT MODELLING CONSORTIUM

We modelled potential impact of 4 different vaccine strategies in 26 countries over 30 years

Figure 1: Vaccine scores based on assessment against ranking criteria[5]



MULTIVALENT VACCINE SUPPORTED IN VIS

Gavi Board starts framing Alliance's approach to 2021-2025 period

[French]

Gavi Board approves in principle a set of new and expanded vaccine programmes.

Geneva, 29 November 2018 – The Gavi Board has made a series of decisions that will help shape the Alliance's approach for the period 2021-2025 during a two-day meeting in Geneva's Global Health Campus. The Board will adopt the 2021-2025 strategic goals at its next meeting in June 2019.

"The Board had extensive discussions on Gavi's future direction which will lead to intense work over the coming months to develop a strategy for the 2021-2025 period – the fifth in Gavi's existence," said Dr Ngozi Okonjo-Iweala, Gavi Board Chair. "The global landscape has changed fundamentally since Gavi was created in 2000 and the Alliance is changing with it. While for Gavi the core focus remains on its current mission of accelerating access to vaccines and increasing equitable coverage in the world's poorest countries, Gavi is also adapting to meet the challenges of the future."

LATEST PRESS RELEASES

Typhoid vaccination campaign to tackle outbreak in Zimbabwe

Coalition for Epidemic Preparedness Innovation turns to IFFIm to accelerate funding for new vaccine development

Global health leaders hail immunisation as shortest path to healthy lives

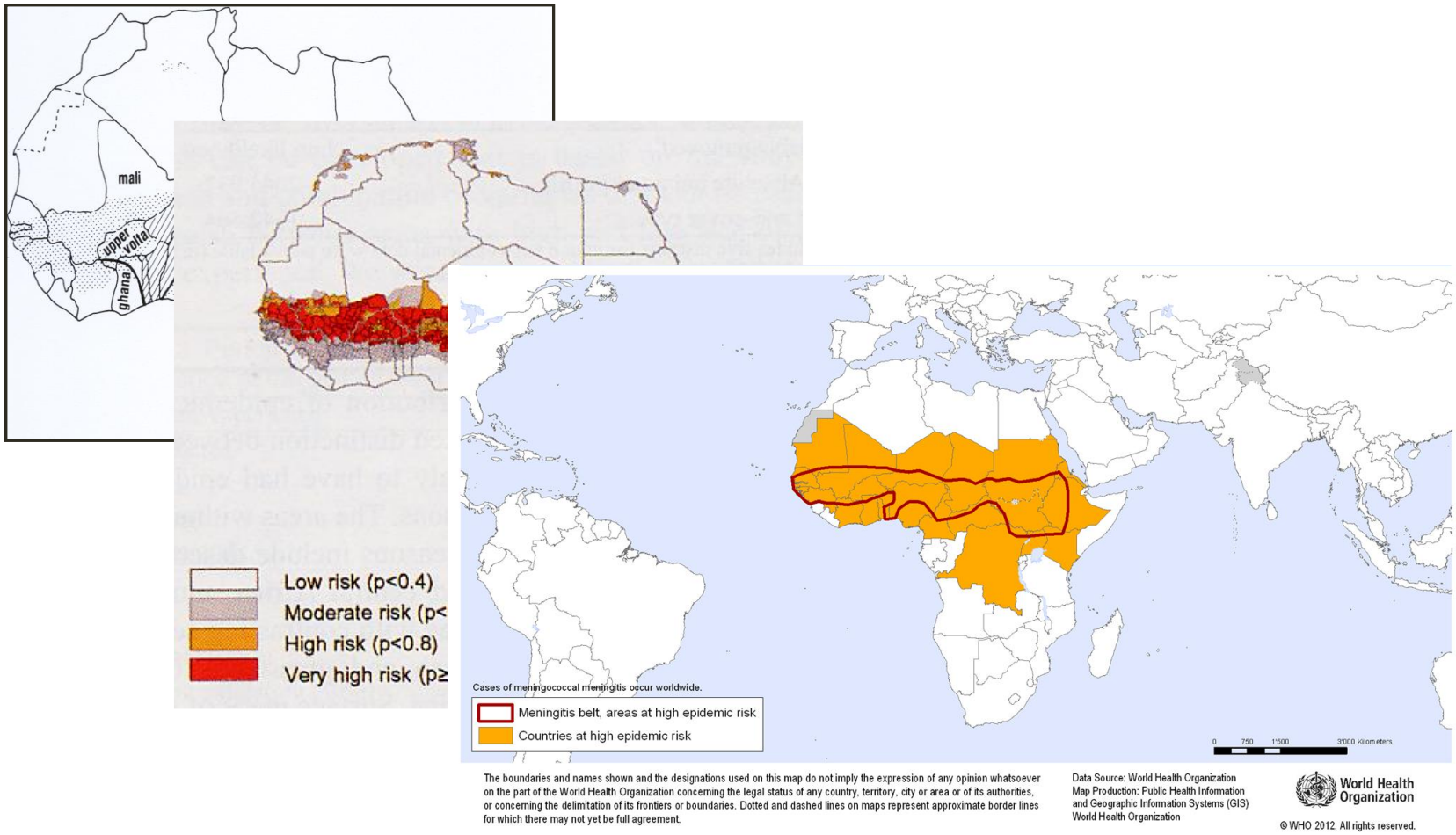
Gavi and Mastercard join forces to reach more children with lifesaving vaccines

HOW CAN A PENTAVALENT VACCINE BE BEST USED?

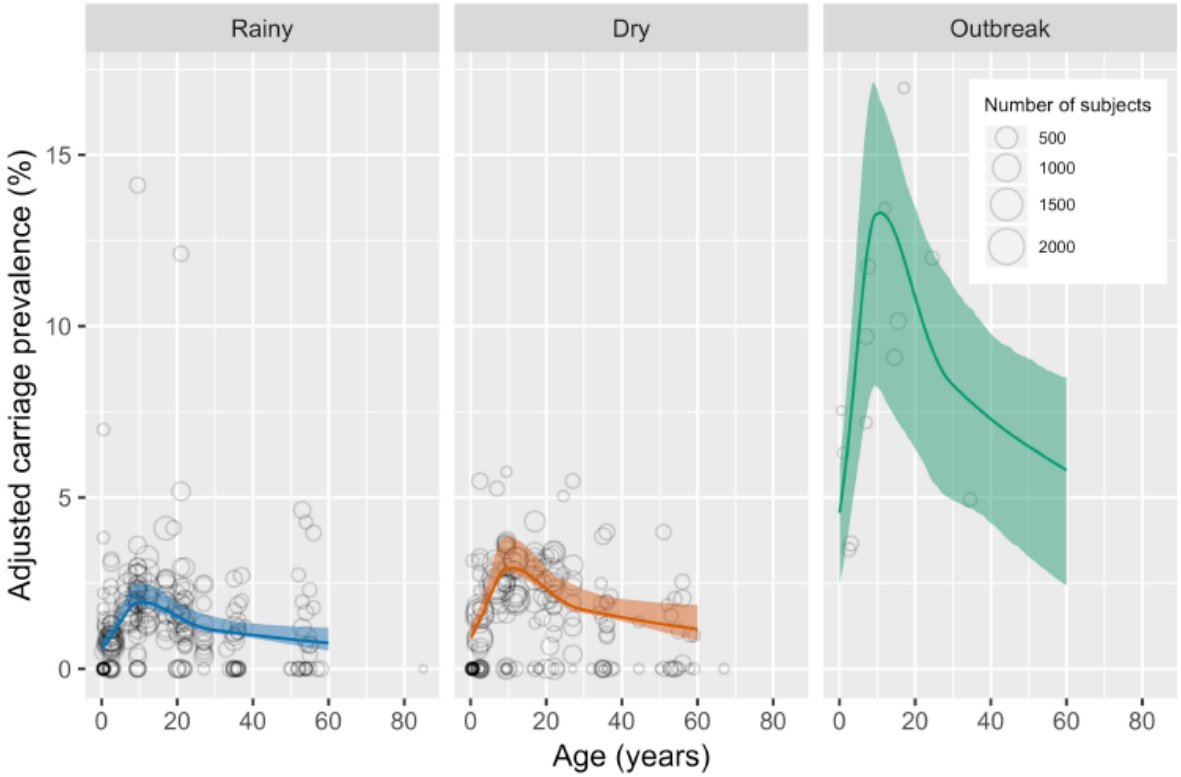
- Reactive vaccination is generally a poor public health response
- Preventive campaigns (plus routine) demonstrated to work
- The new pentavalent vaccine will be more expensive
- Burden of CWYX disease is lower than A
- Donors do not have appetite for mass campaigns targeting 300 million people

  ➔ evidence needed to define populations at (highest) risk

WHERE IS THE MENINGITIS BELT NOW?



CAN WE TARGET A NARROWER AGE RANGE?

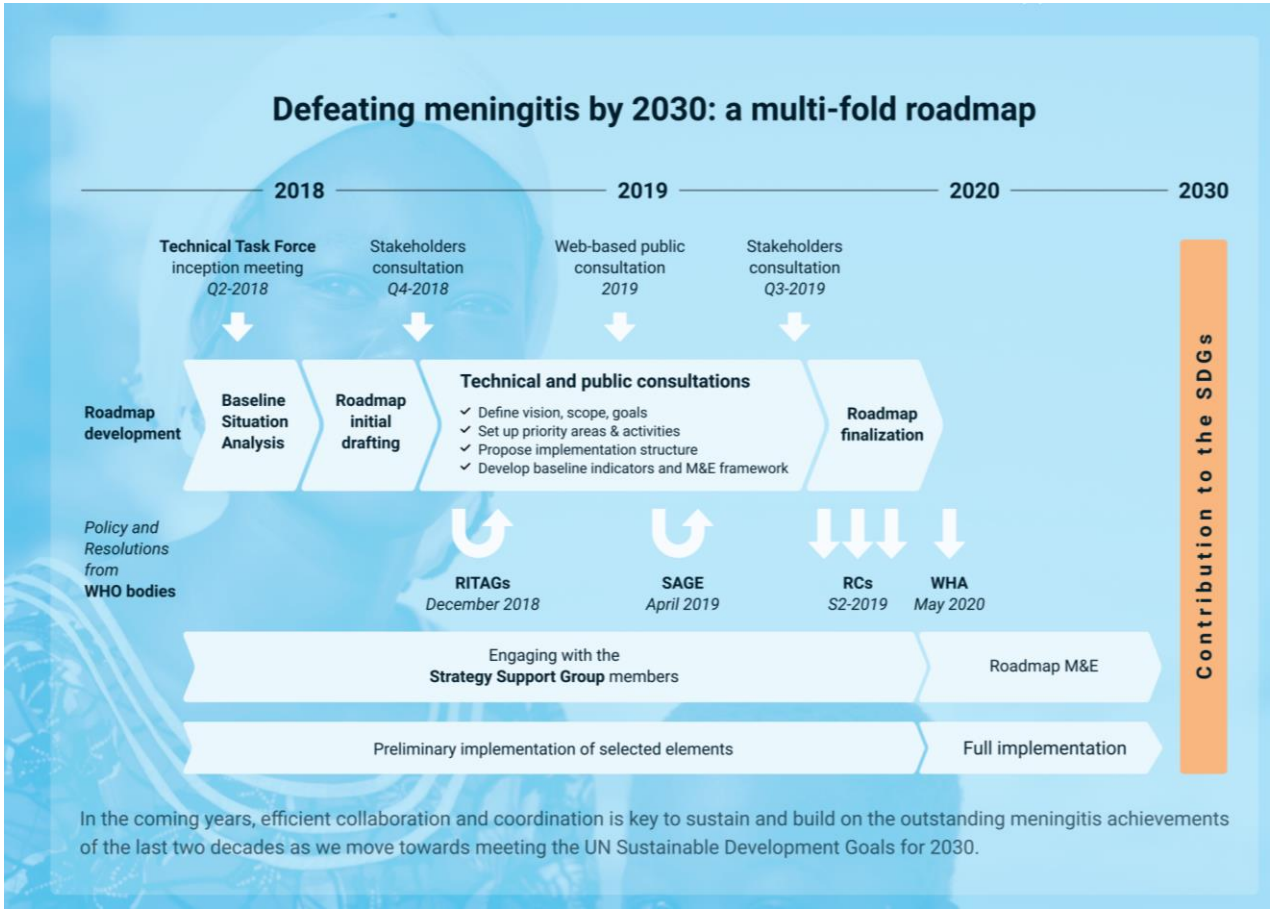


Laura Cooper

UNIVERSITY OF CAMBRIDGE

Cooper et al, Epi & Infect 2019

A NEW ROADMAP



https://www.who.int/emergencies/diseases/meningitis/meningitis-2030.pdf

CONCLUSIONS

MenAfriVac has been a major public health success and demonstrates the power of public-private partnerships

Research efforts have helped to understand vaccine effectiveness, vaccine action and guide policy

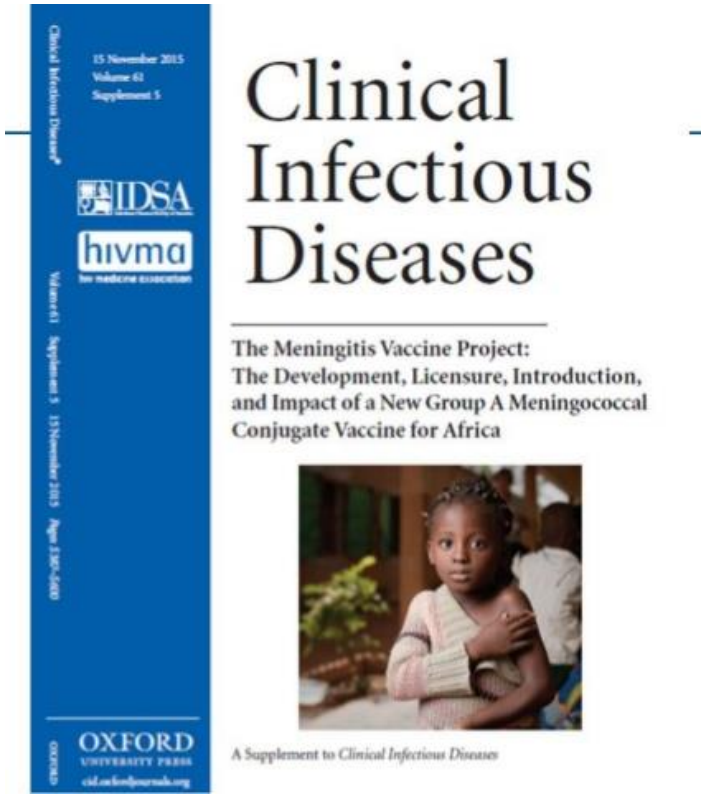
Remaining threat from other serogroups and other bacteria

Roadmap to defeating meningitis by 2030 is being developed

ACKNOWLEDGEMENTS

Tom Irving, Hannah Christensen, Andromachi Karachaliou, Laura Cooper

James Stuart, Brian Greenwood, Marie-Pierre Preziosi, Clement Lingani, Katya Fernandez, Olivier Ronveaux



World Health Organization

Meningitis Vaccine Project

menafricar African Meningococcal Carriage Consortium

Gavi The Vaccine Alliance

VACCINE IMPACT MODELLING CONSORTIUM

MenAfriNet

Week 2: Using Serology Data & Modeling Interventions

Dr. Henrik Salje
University of Cambridge

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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natural history parameters

(important term)

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?

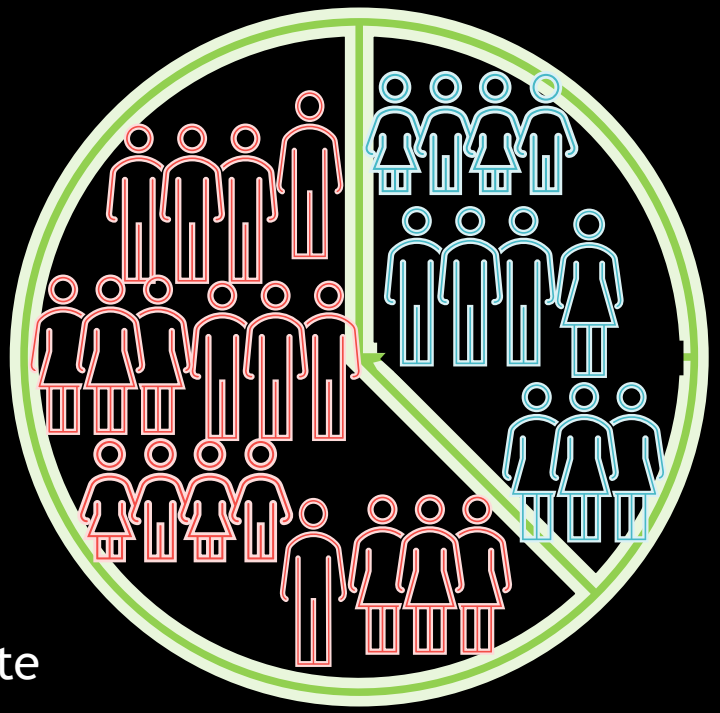
- Recall that:
  - $N = S^* + E^* + I^* + R^*$
- When R0>1:
  - $I^* = \frac{\mu N}{\mu+\gamma}\left(1 - \frac{1}{R_0}\right)\left(\frac{\sigma}{\mu+\sigma}\right)$

This equation can be rearranged

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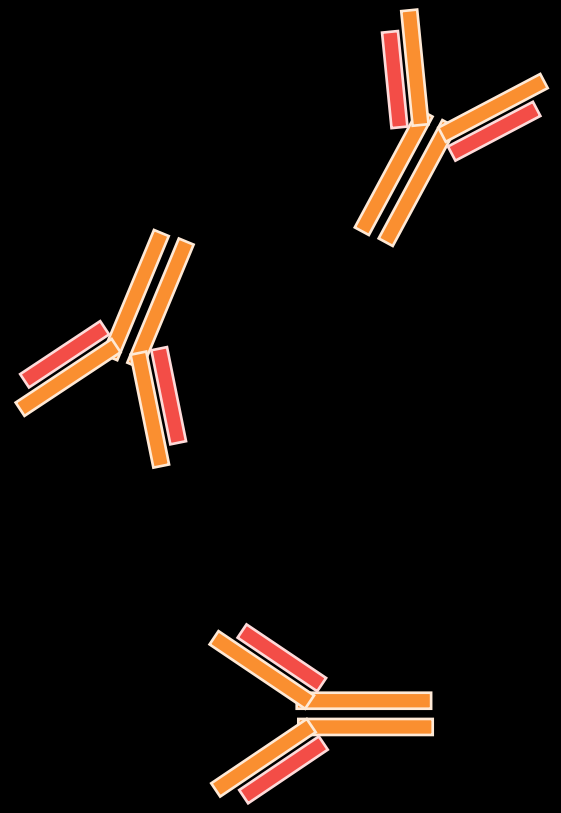
  - partial observation: acute infections are short and hard to observe/capture
  - expense: pathogen isolation, laboratory confirmations
  - biased sampling: isolated populations may have lower/higher disease burden
- Disease prevalence may vary by year
  - Example: annual dengue prevalence in low versus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

What’s seroprevalence data?

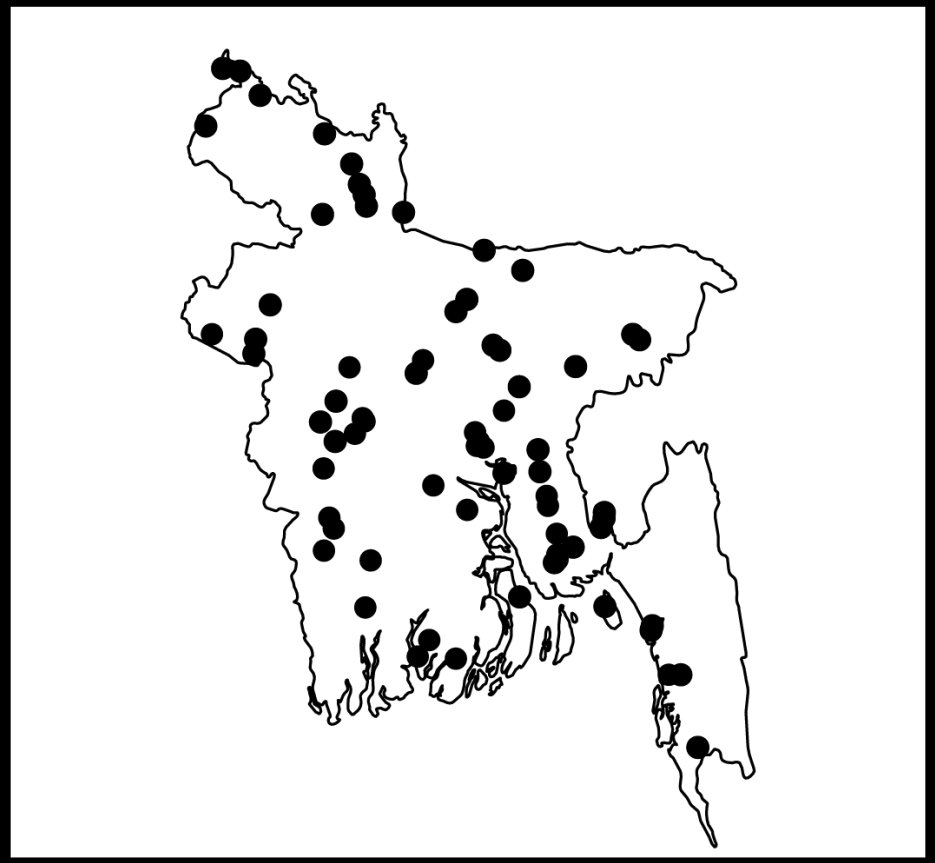
- Post infection, individuals develop antibodies
- These can be detected by specific assays

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

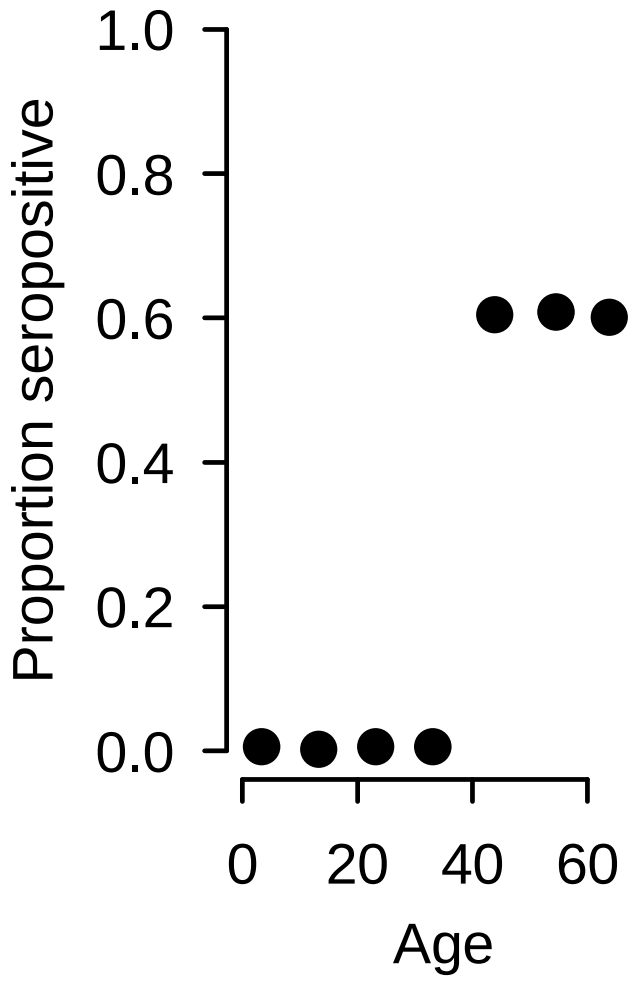


Seroprevalence studies

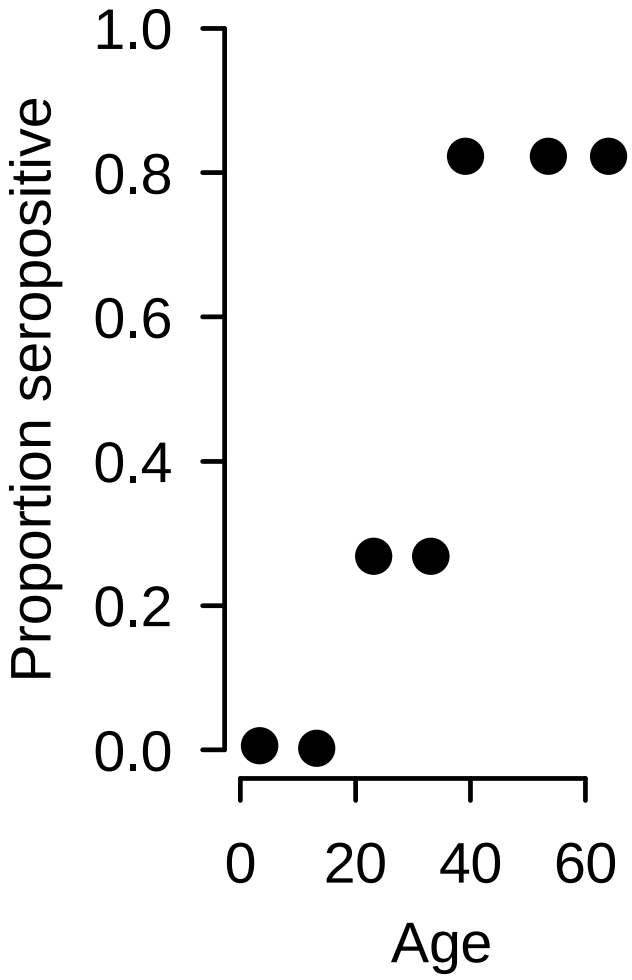


- Select random communities and random members of population
- Blood draw
- Look in blood for antibodies specific to your pathogen
- We conducted one in Bangladesh in 2016 for dengue virus and found a seropositivity of ~25%

Incorporating age



What would this mean?



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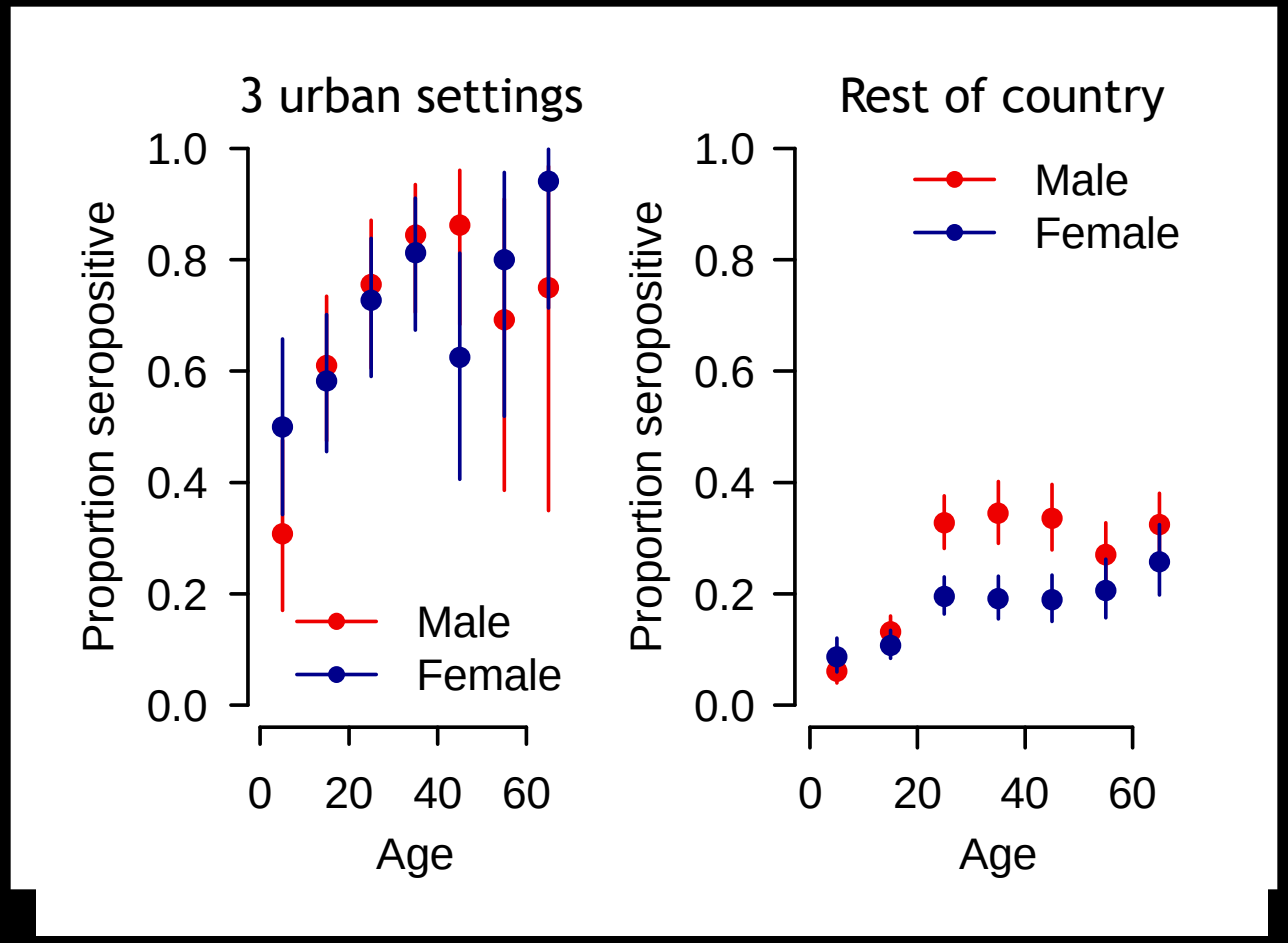
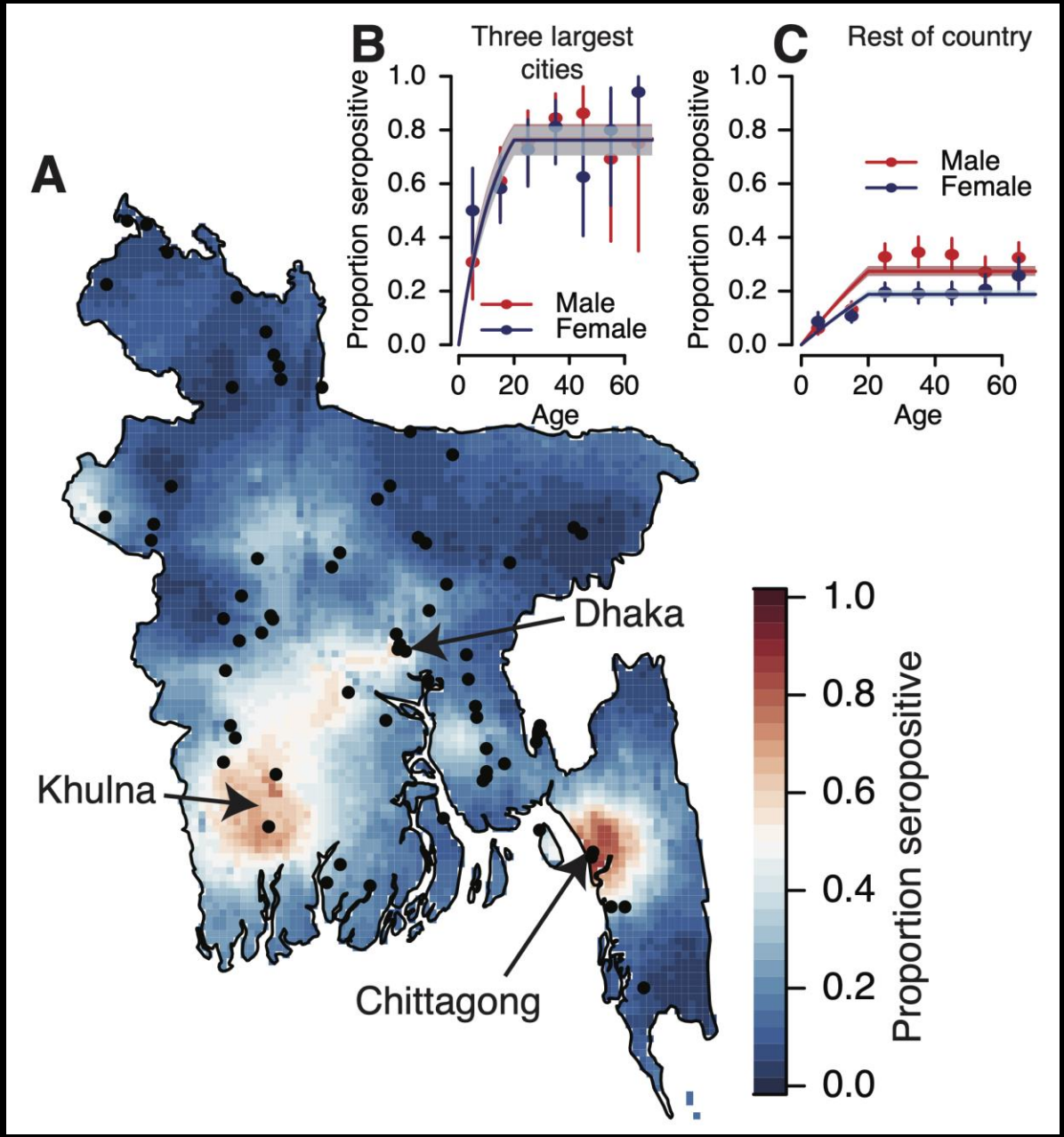


What's going on here?


A
B
Three largest cities
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
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

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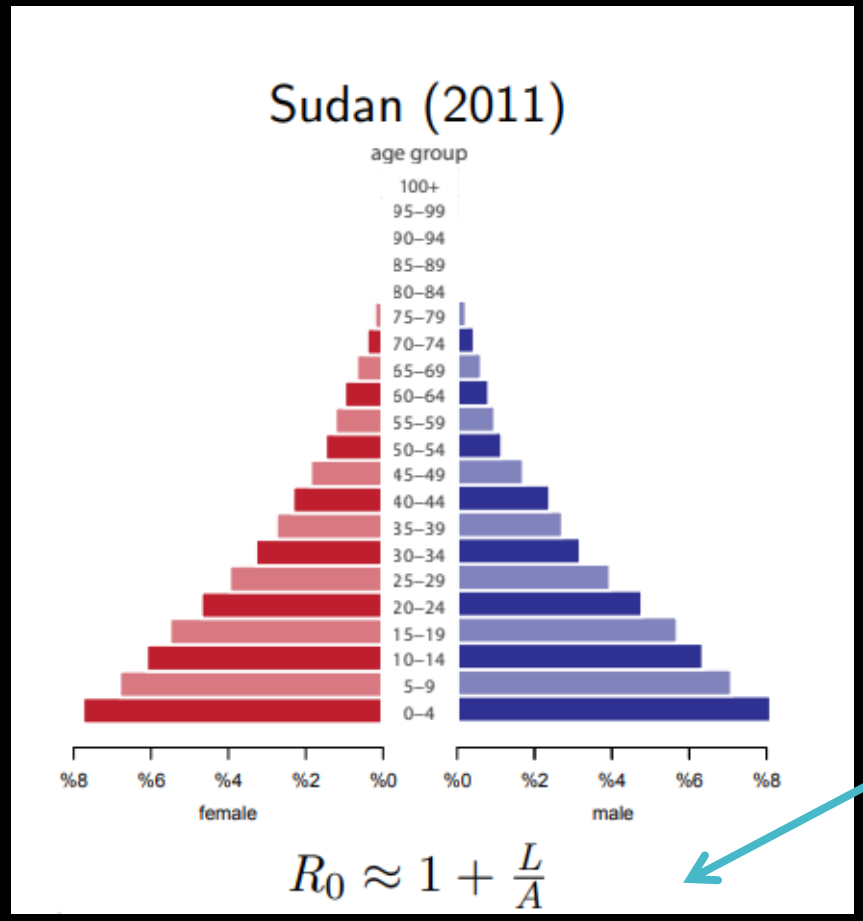
  - $A = \frac{1}{\mu(1-R_0)}$
  - $R_0 = 1 + \frac{1}{\mu A}$
  - μ: birth rate

- Because 1/μ is the life expectancy for people in the population, this equation could also be written as:
  - $R_0 = 1 + \frac{L}{A}$

Age & Seroprevalence



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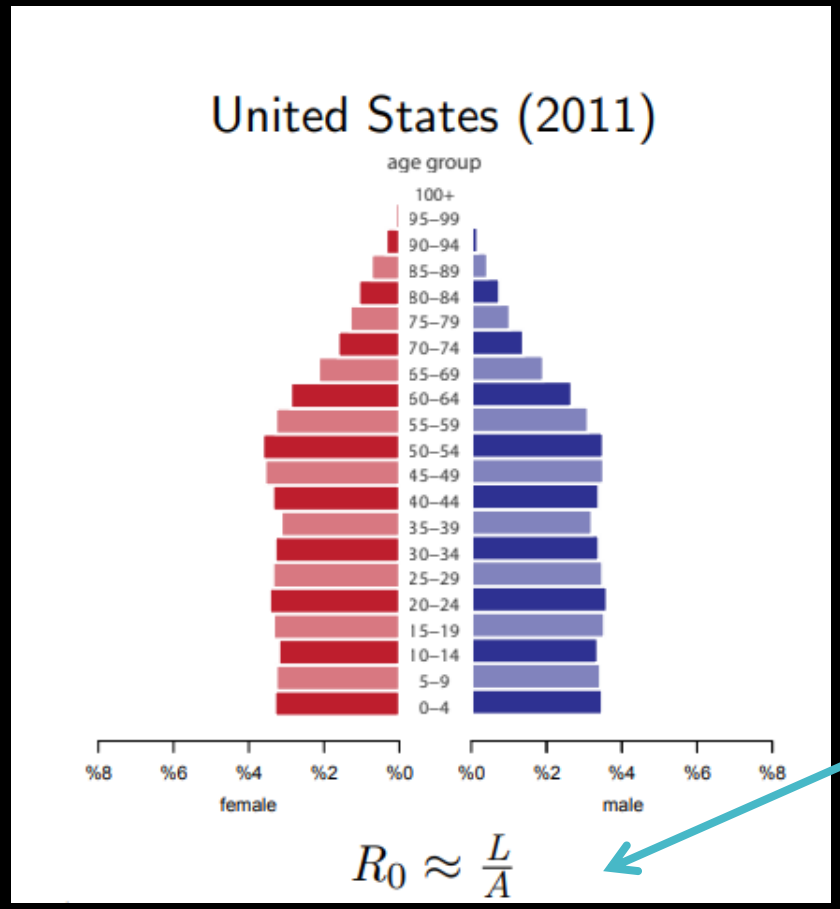
- However, this relationship depends on the overall structure of the population
  - For a pyramidal population, people are dying at a constant rate

Age & Seroprevalence



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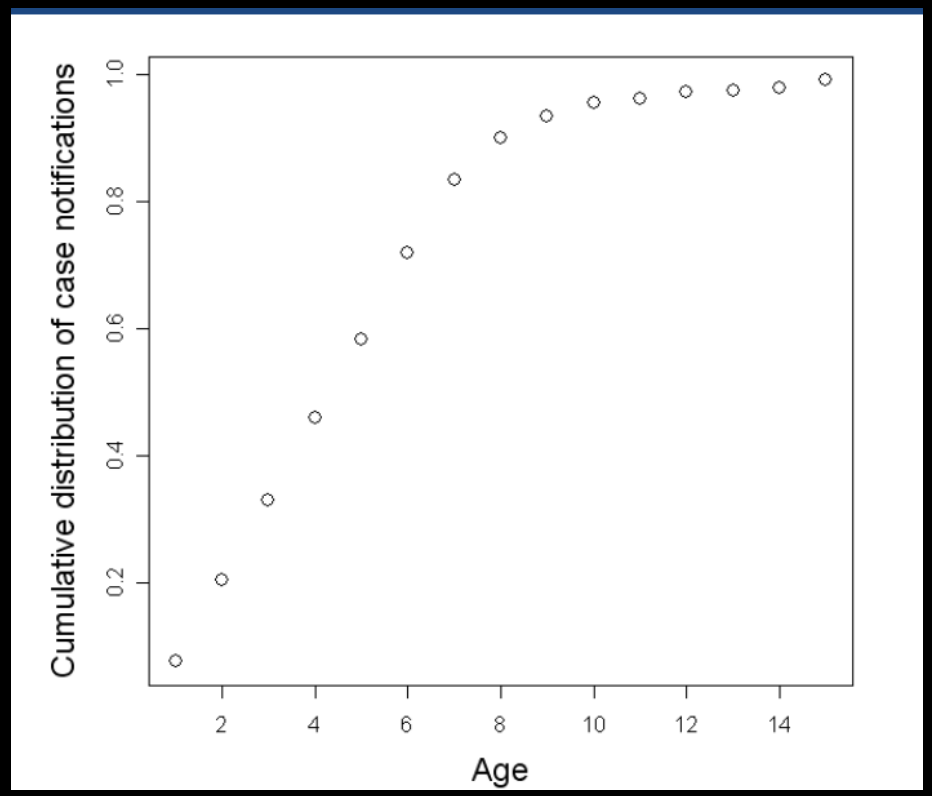
Age-specific Seroprevalence

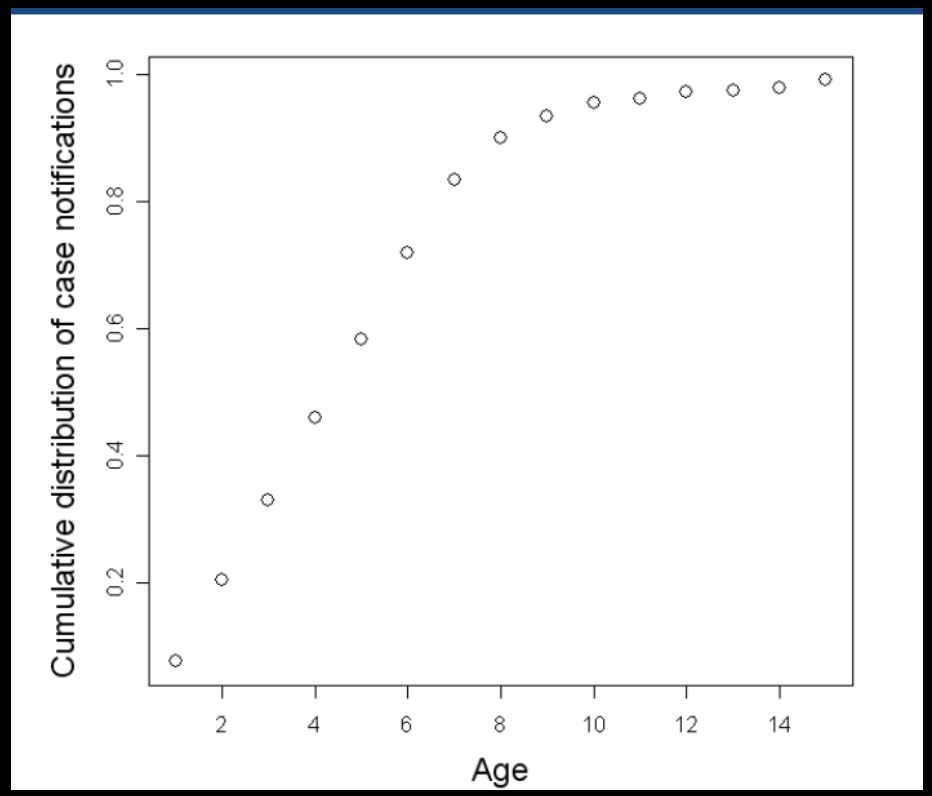


- Seroprevalence of measles in Aberdeen, UK
  - age-specific seroprevalence
  - this can be used to learn additional details about the disease dynamics
- What is the force of infection for this group?

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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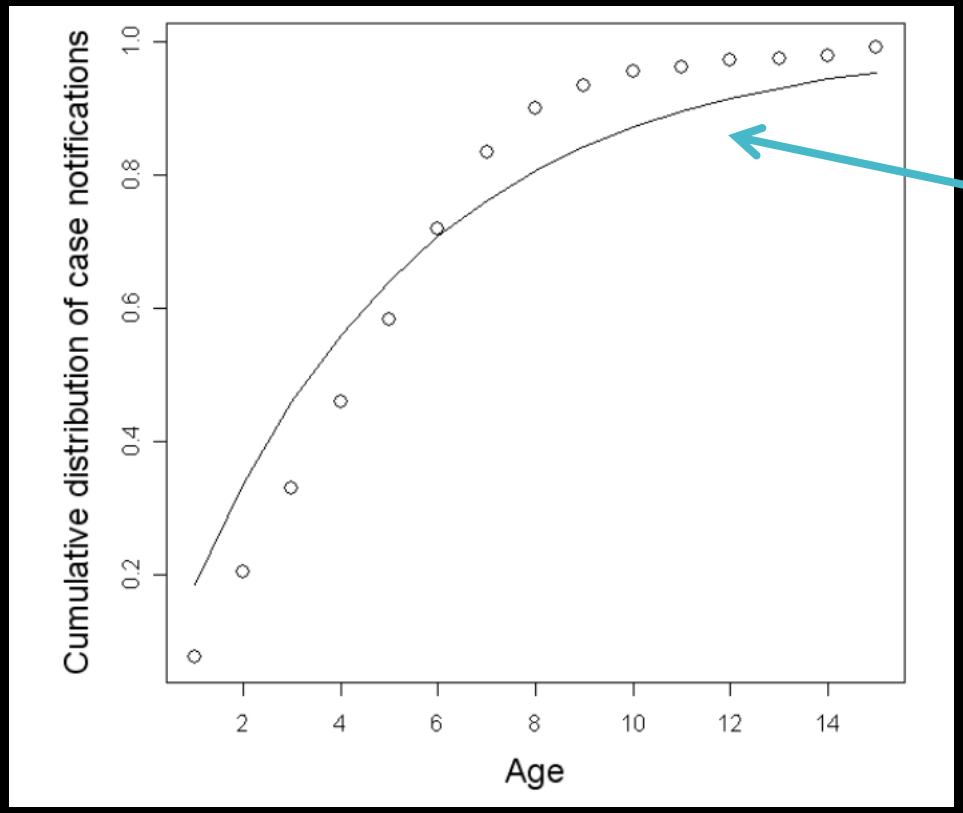


- What is the force of infection for this group?
- If we fit a constant force of infection, we see the fit is not very good
  - λ=0.21
  - 21% chance of becoming infected each year

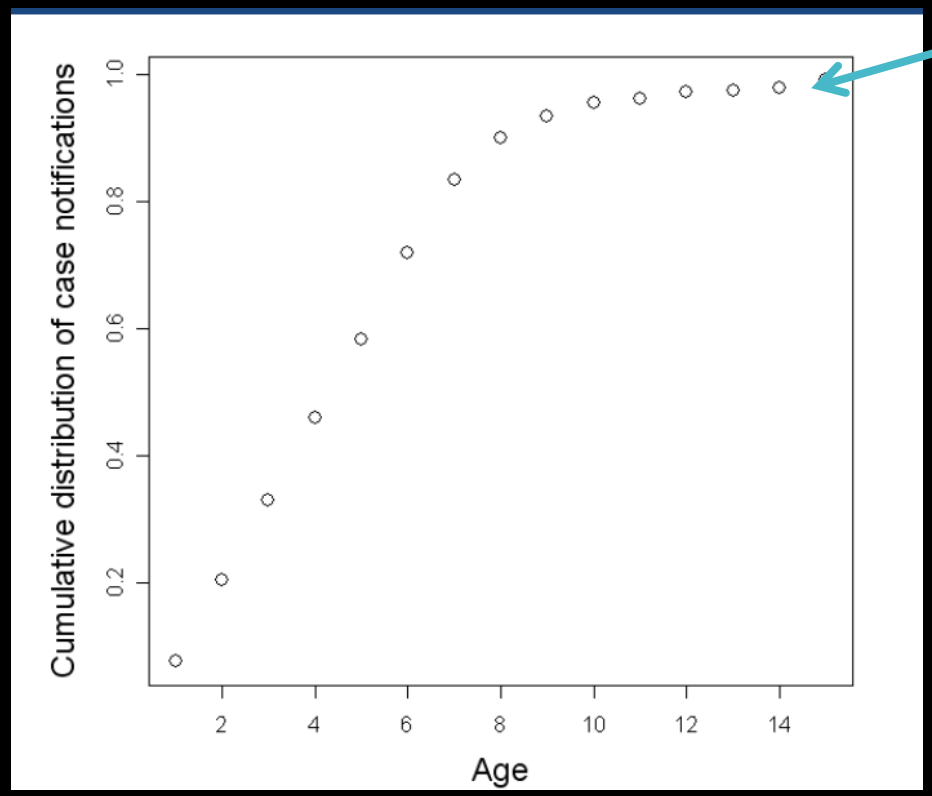
Force of Infection

- 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

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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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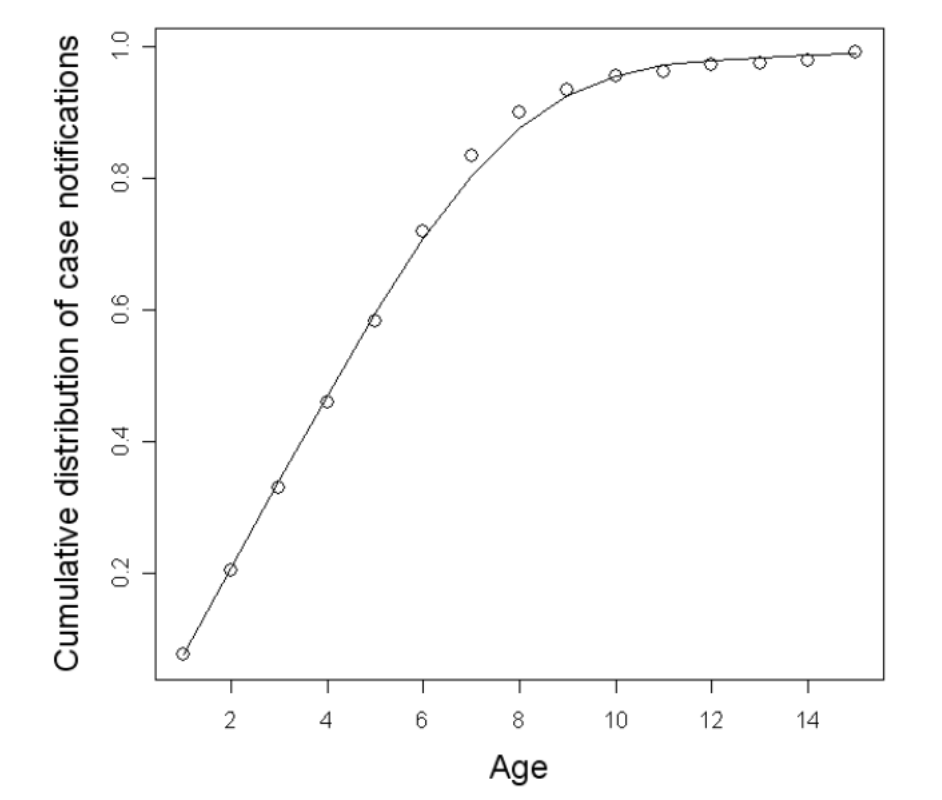
Force of Infection

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

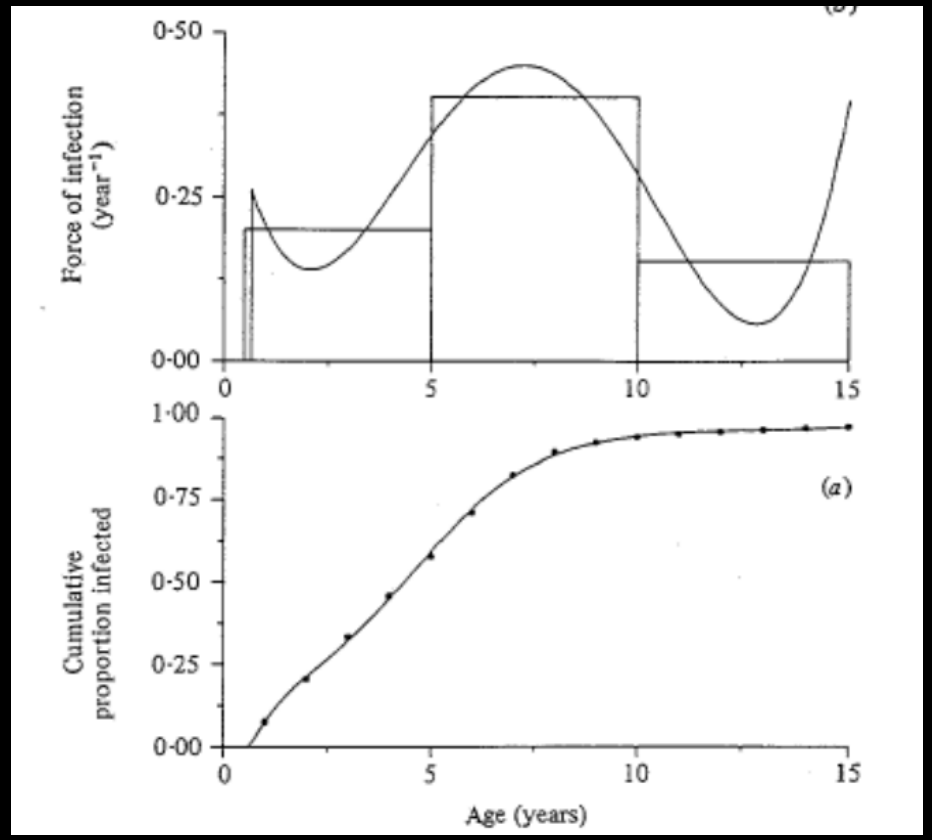
- We can use a binomial (statistical) framework to relate the seroprevalence to force of infection
- we are estimating a joint likelihood
- by using this statistical method, we can:
  - account for the different sample sizes among age groups
  - calculate confidence intervals for our estimate of FOI

FOI for Measles in Aberdeen



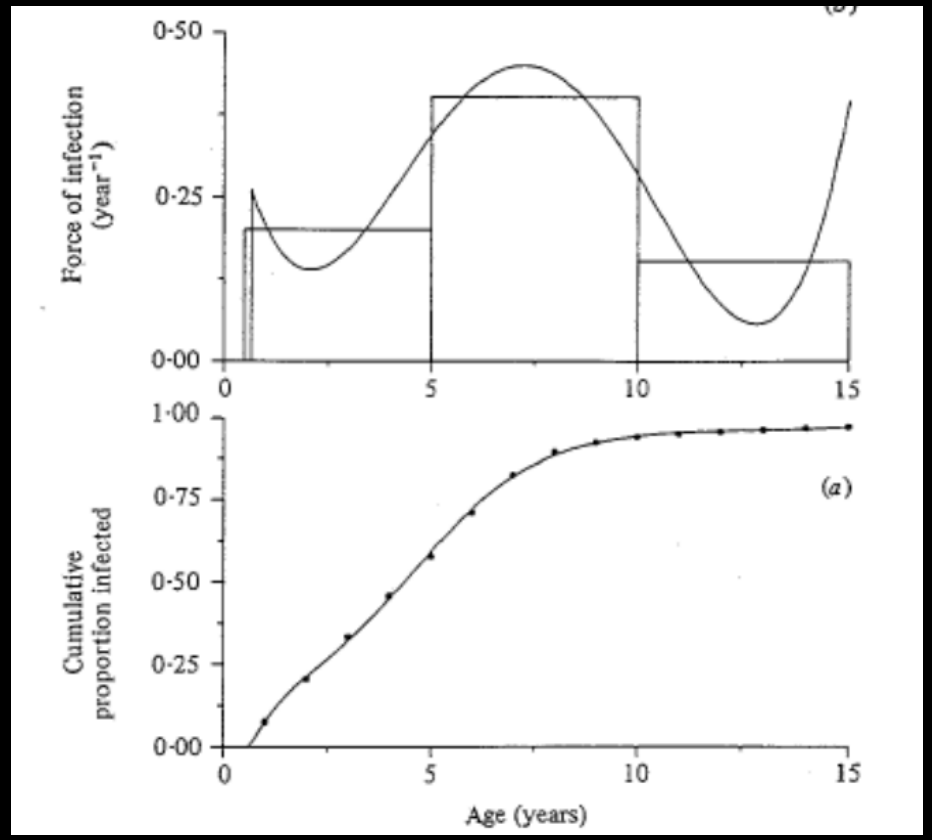
- What is the force of infection for this group?
- If we fit age-specific force of infection, we see the fit is excellent
  - three separate FOIs for three age groups

FOI for Measles in Aberdeen



- 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

FOI for Measles in Aberdeen



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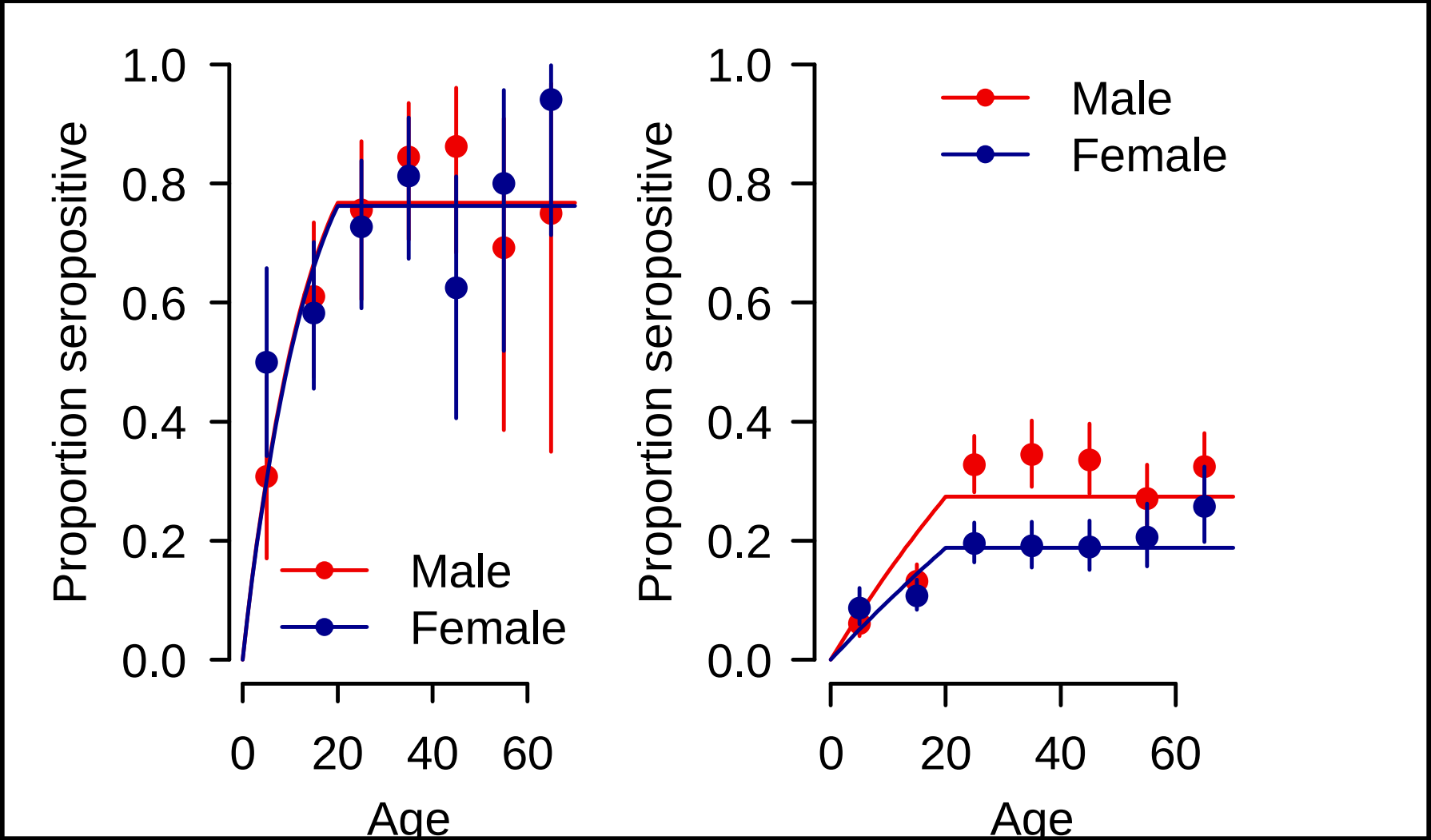
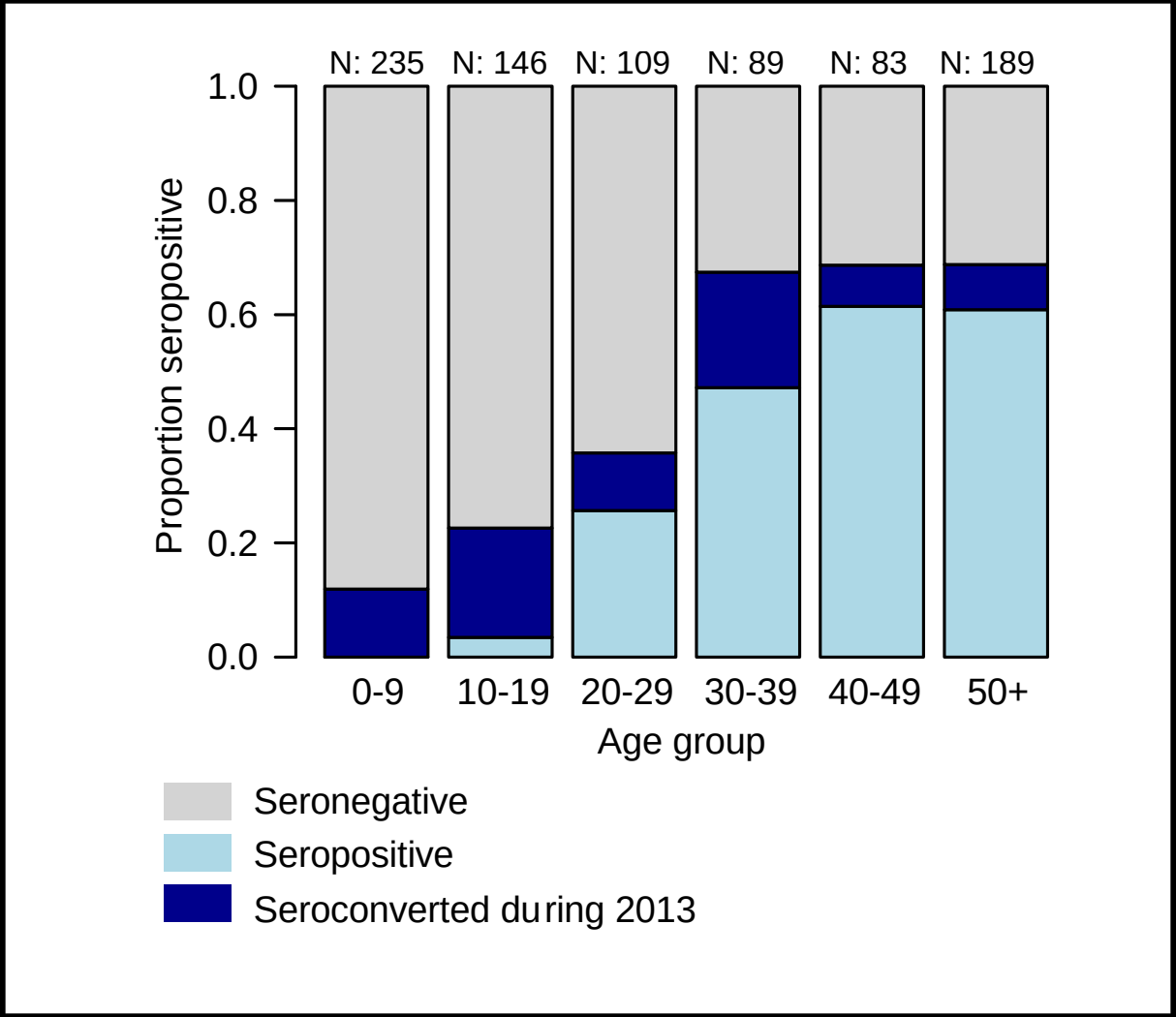
  - three FOIs for three age groups
  - pre-school (<5 years old): 0.18
  - early school (5-10 years old): >0.3
  - late school (10-15 years old): <0.18
- This is the fraction of each group that will become infected per year

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

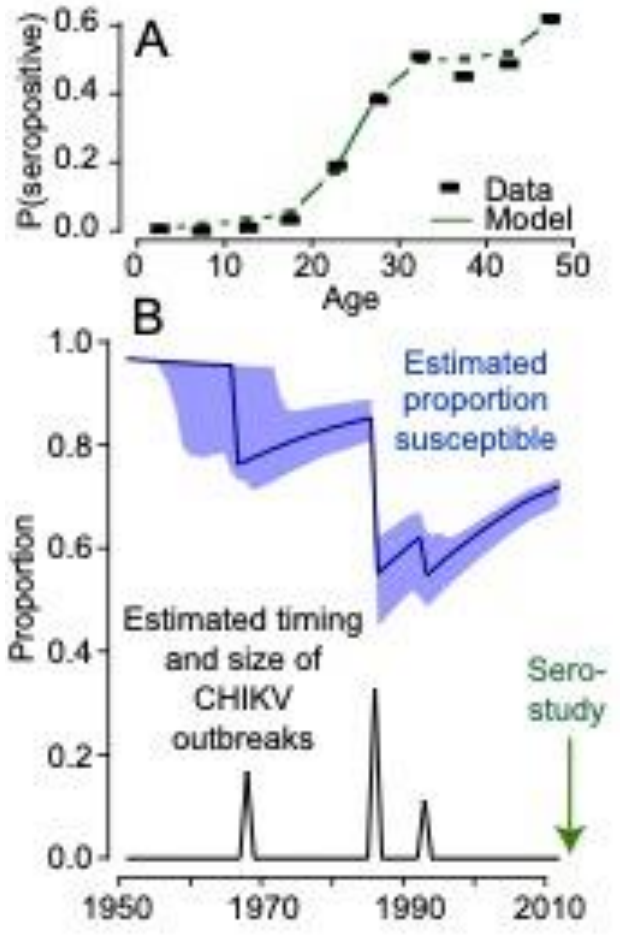


We can also identify more complex past infection histories – example with chikungunya



- 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.

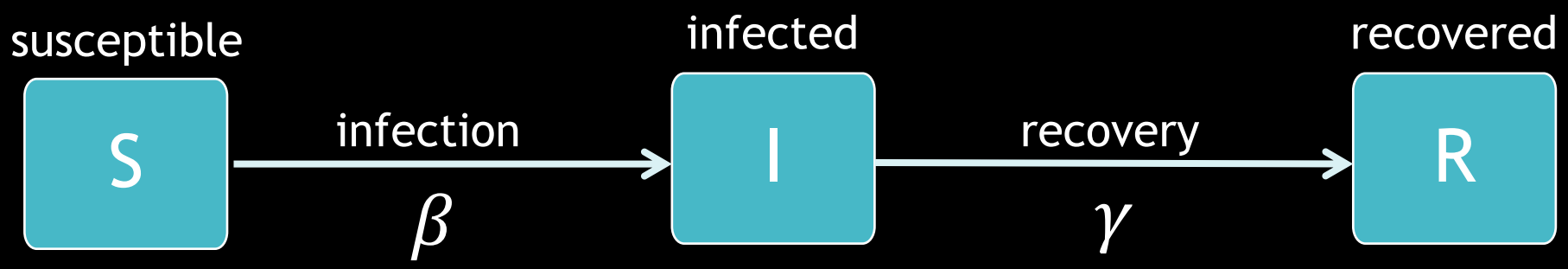
Questions?

10 minute break

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

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

SIR Model Modifications

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

SIR Model Modifications

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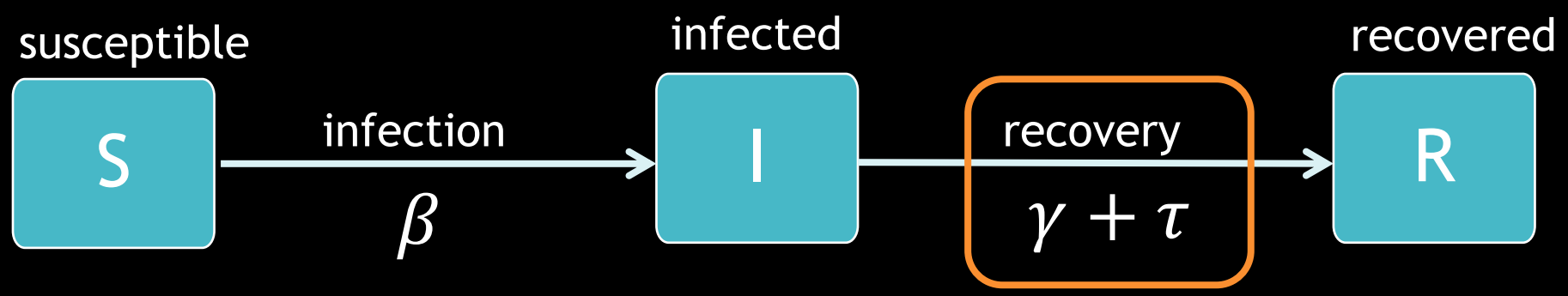
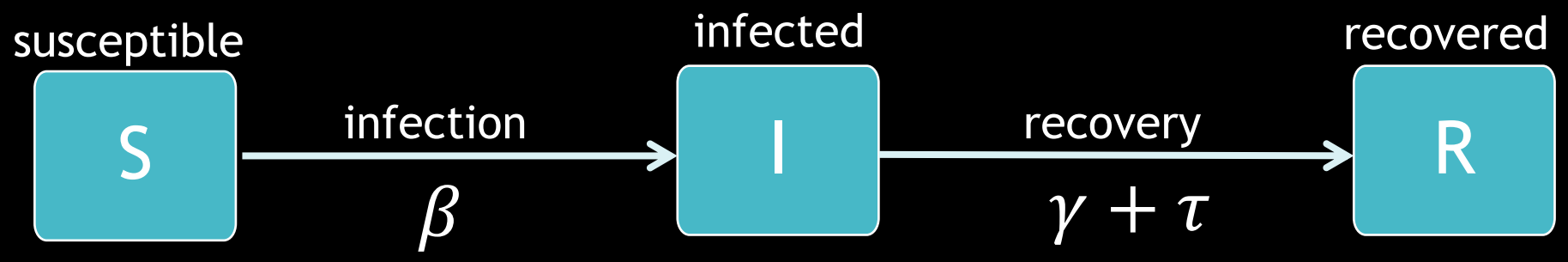


- β: transmission coefficient
- γ: recovery rate
- τ: treatment rate (1/2 days)

Treatment to Reduce Infectious Period

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



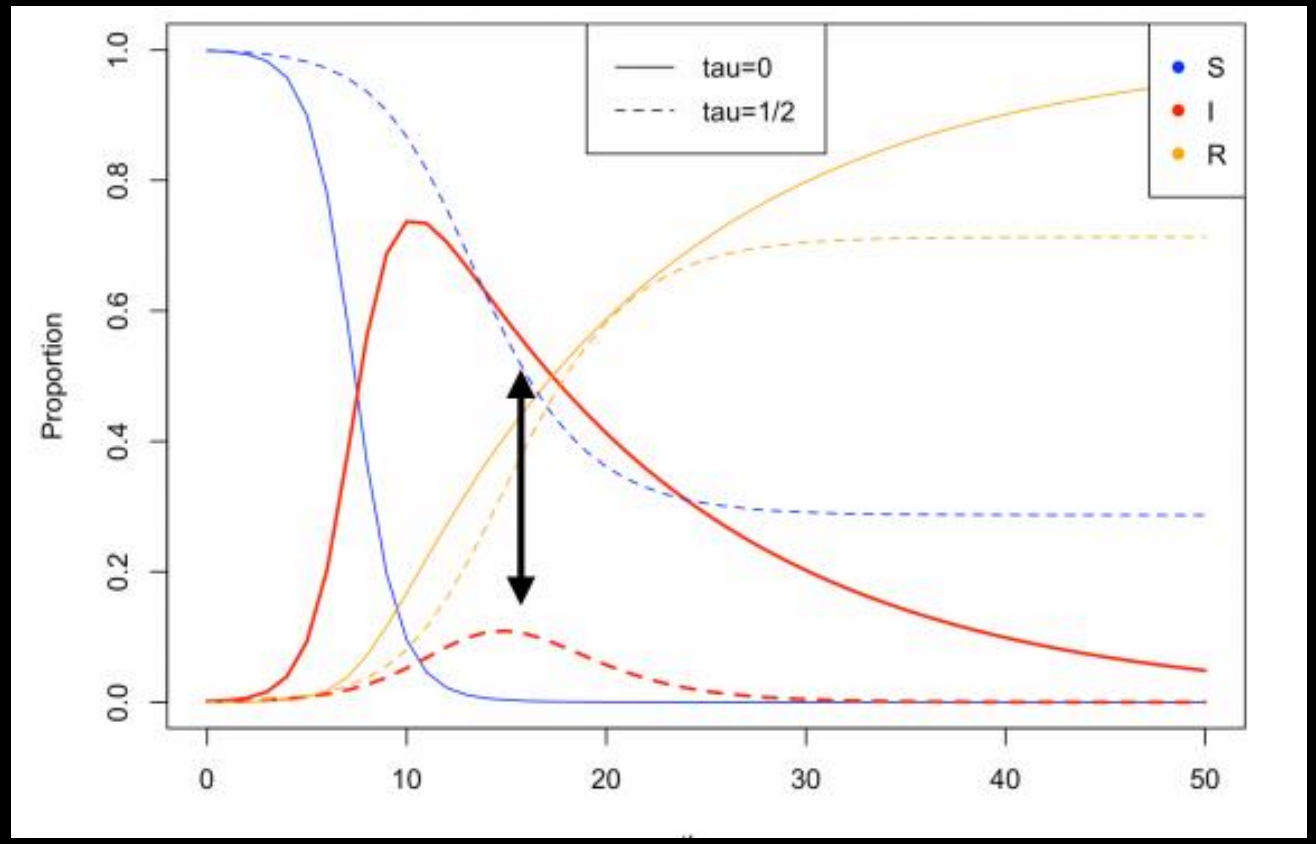
$$\frac{dS(t)}{dt} = -\beta S(t)I(t)$$

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

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

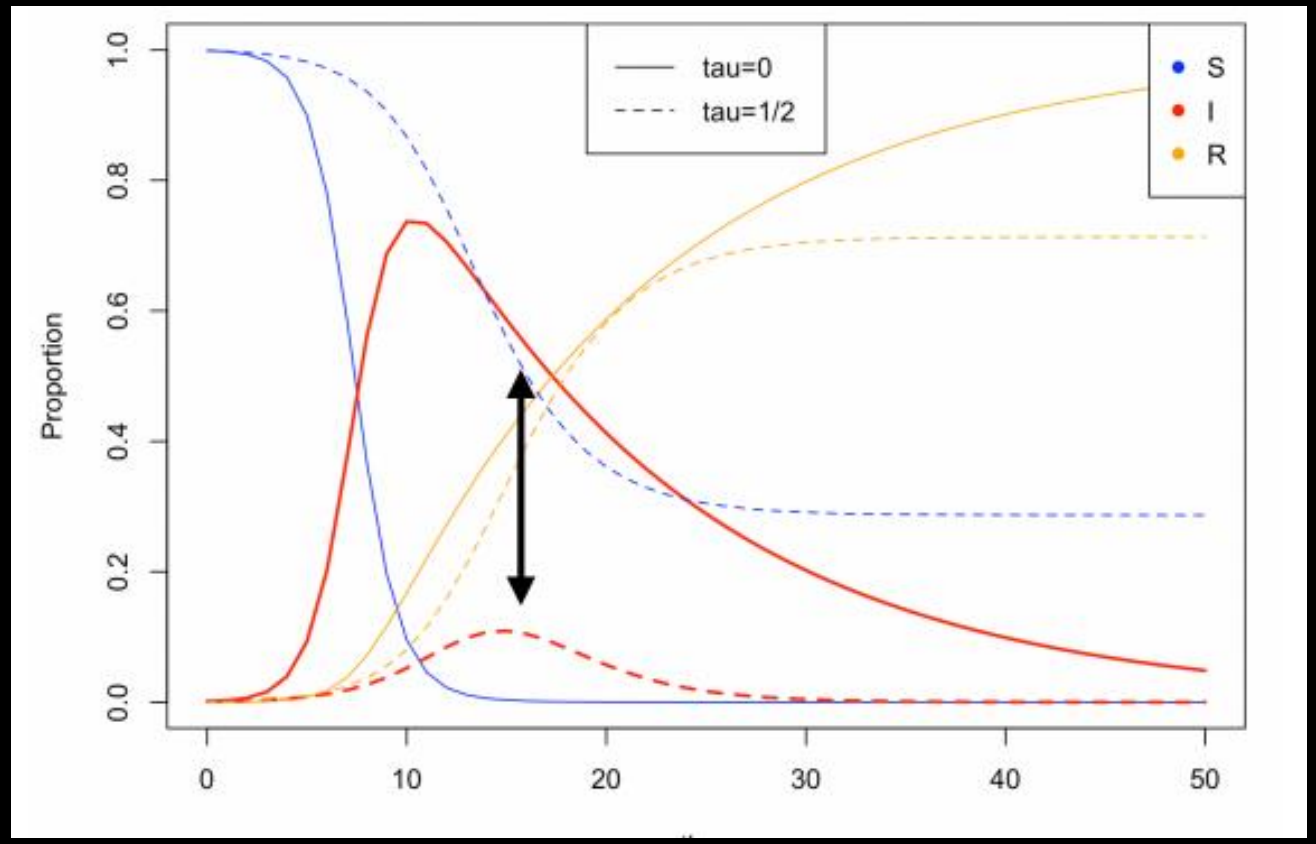
- Treatment makes people recover more quickly

Treatment to Reduce Infectious Period



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

Treatment to Reduce Infectious Period

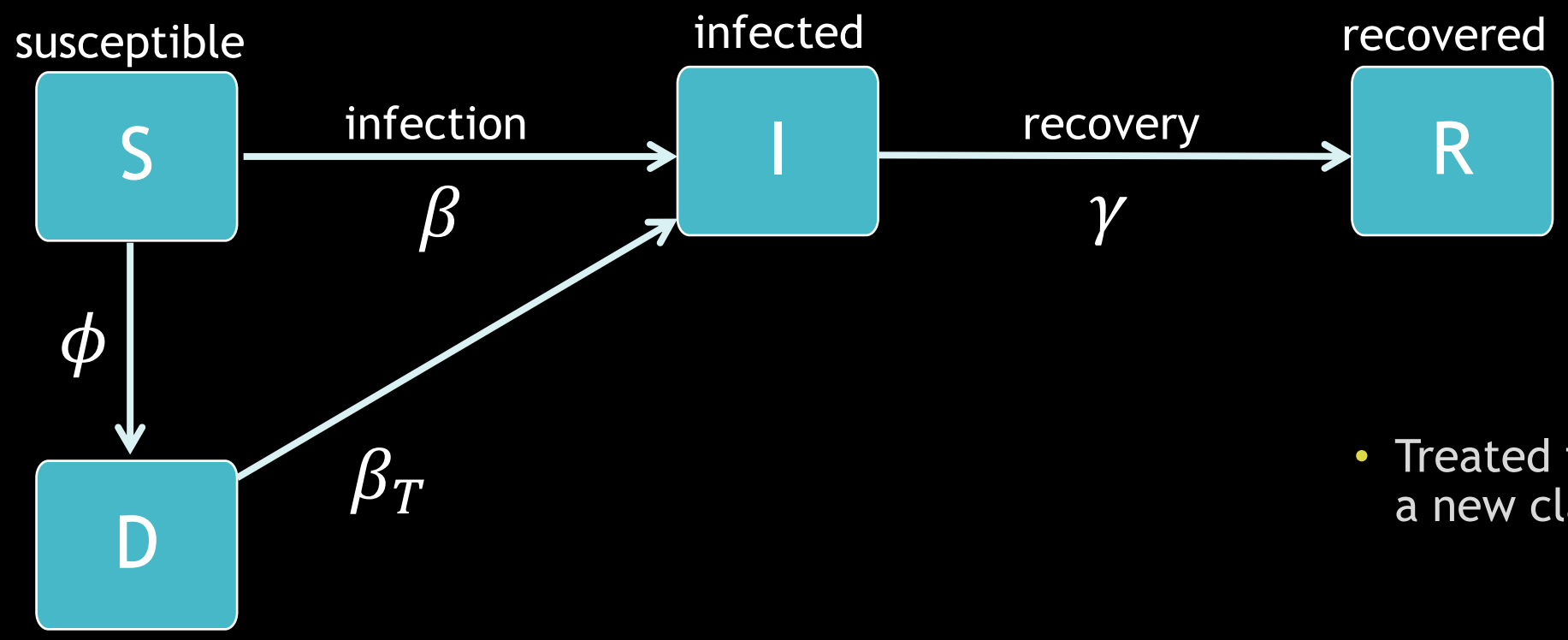


- compare epidemic dynamics:
  - without treatment (τ=0)
  - with treatment (τ=1/2)
- How does using this treatment affect the total number of people who get infected?
  - without treatment: 99% infected
  - with treatment: 71% infected

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

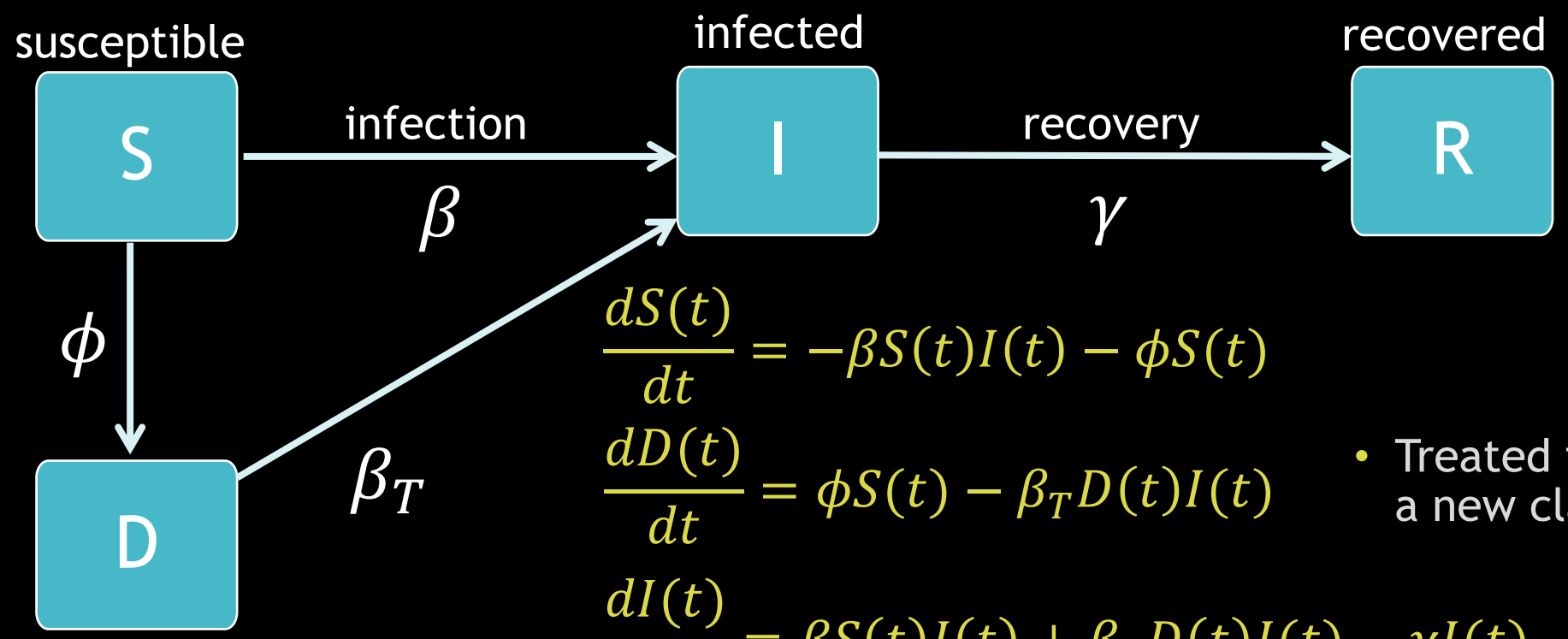
Treatment Provides Partial Protection



- 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



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

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

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

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

- β: transmission coefficient
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- β_T: transmission coefficient for treated individuals

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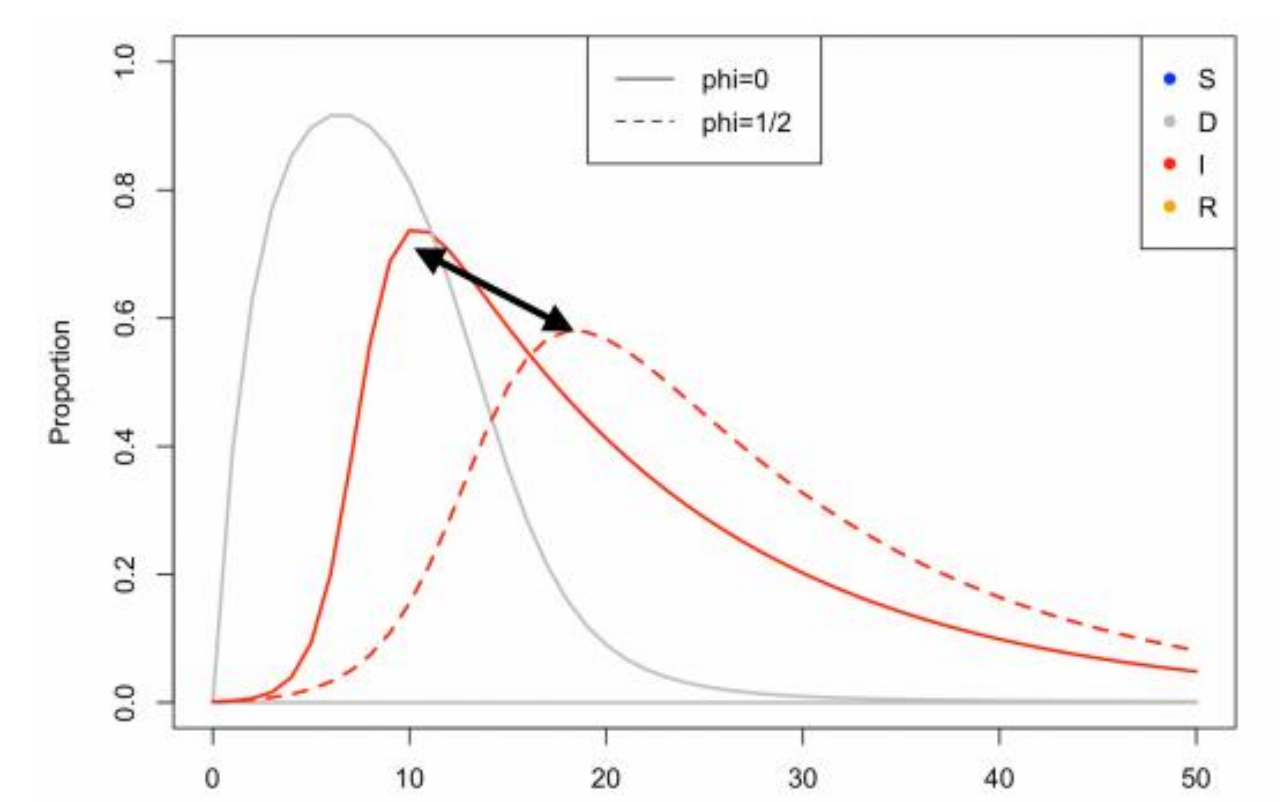
Treatment Provides Partial Protection



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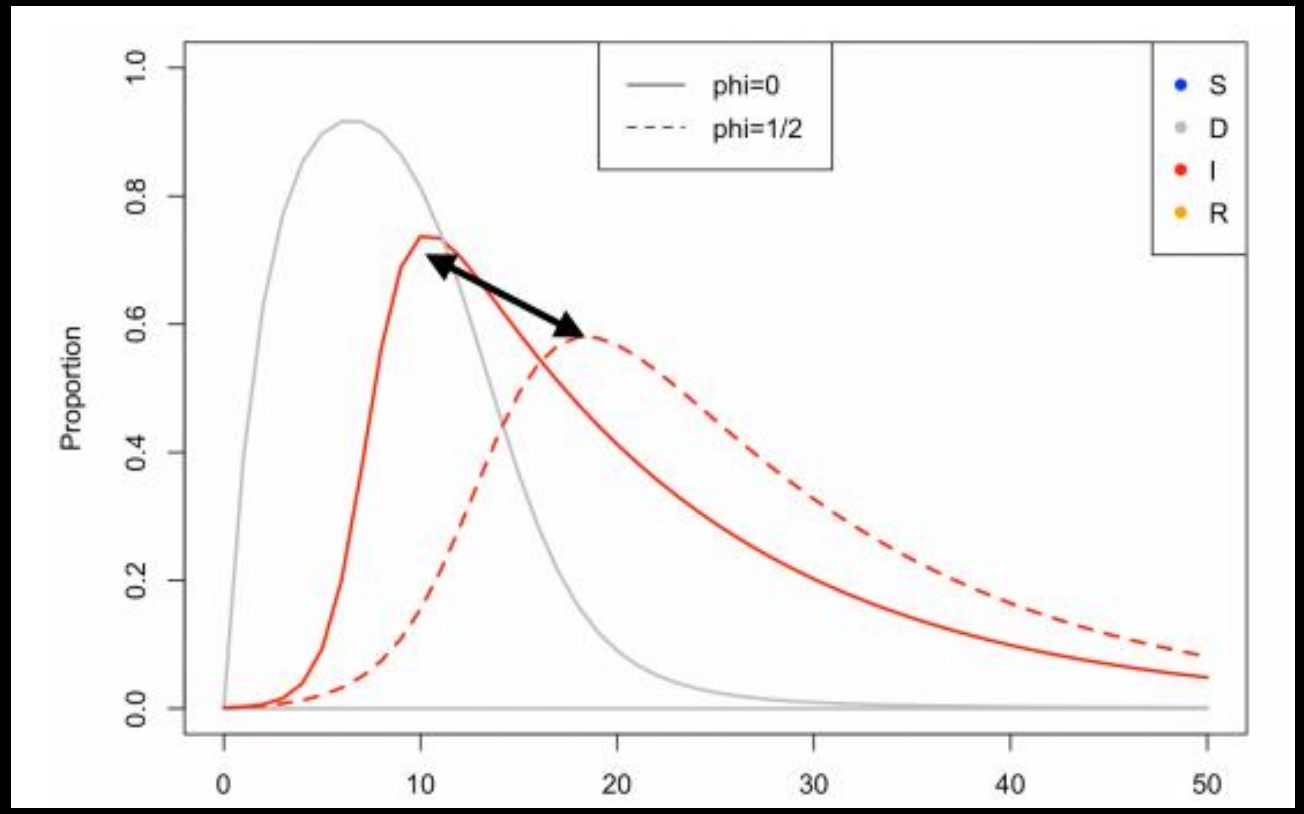
Treatment Provides Partial Protection

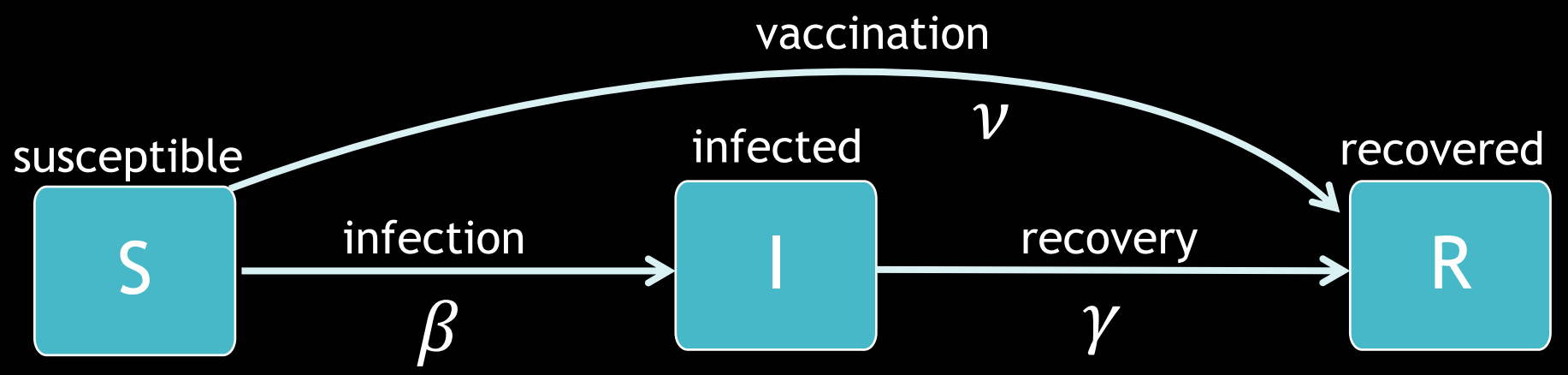


- compare epidemic dynamics:
  - without treatment (ϕ =0)
  - with treatment (ϕ =1/2)
- How does using this treatment affect the total number of people who get infected?
  - without treatment: 99% infected
  - with treatment: 99% infected

Perfect Vaccination

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

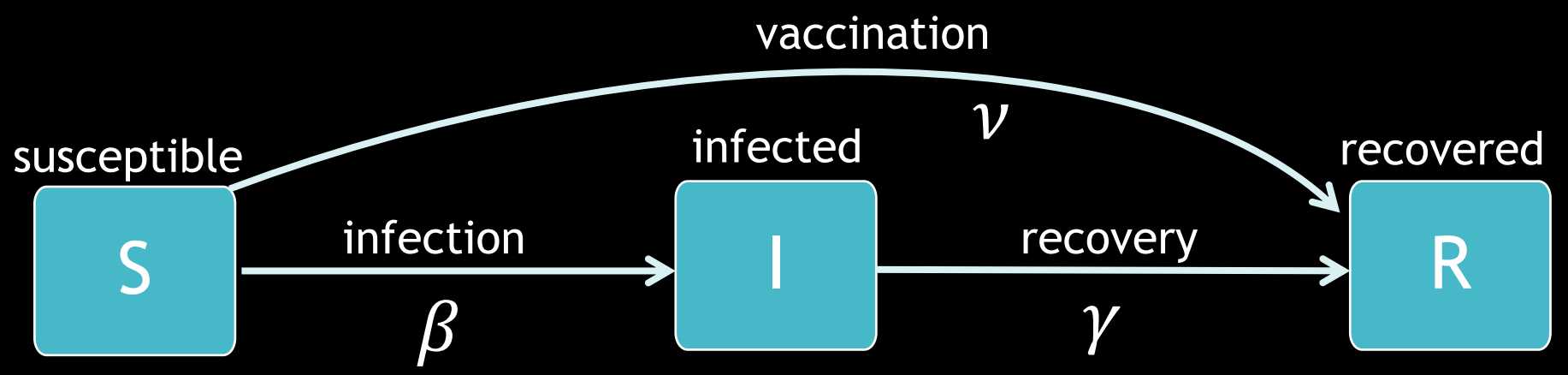
Perfect Vaccination



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

- Vaccination moves susceptible people to the recovered compartment

Perfect Vaccination



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

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

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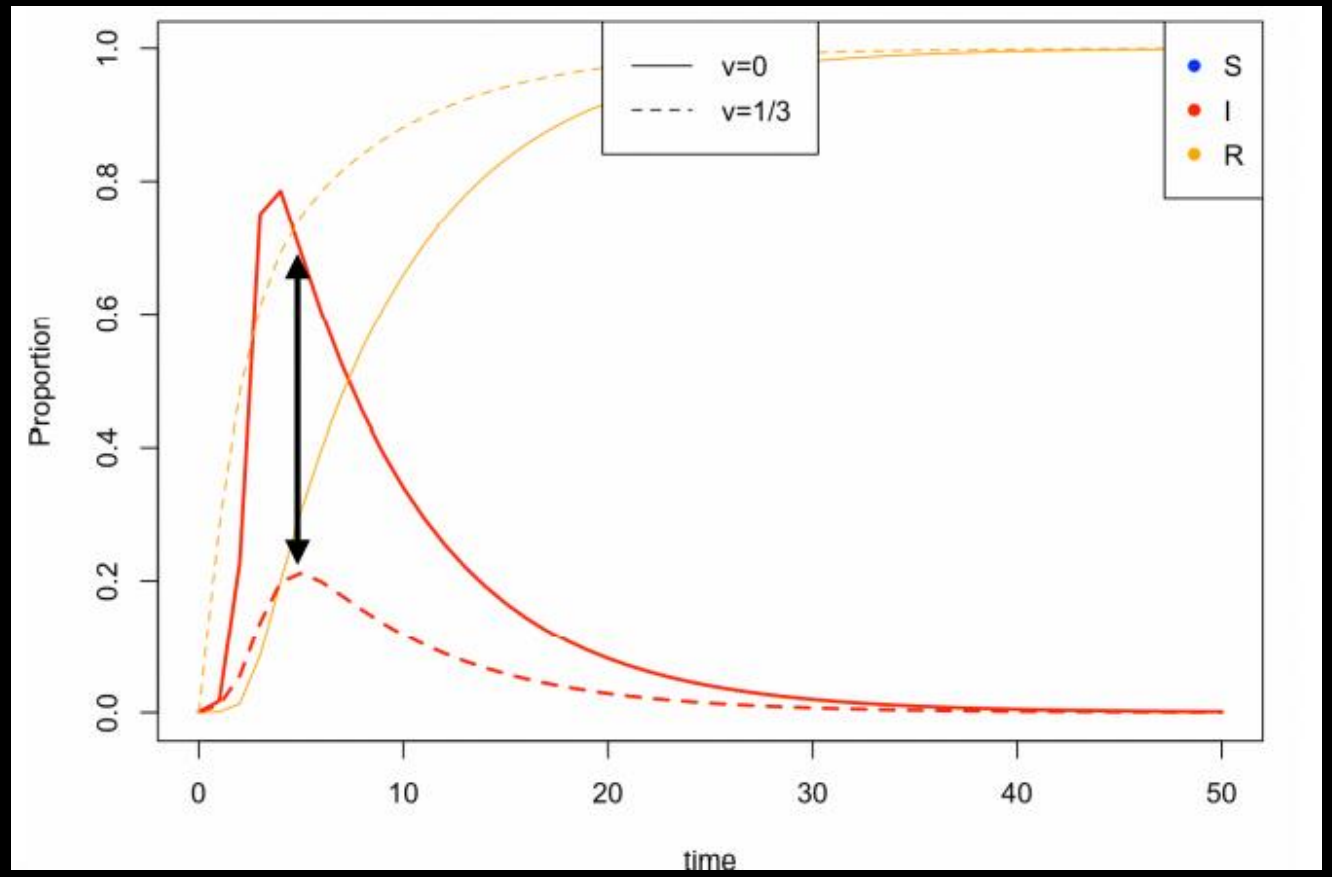
Perfect Vaccination



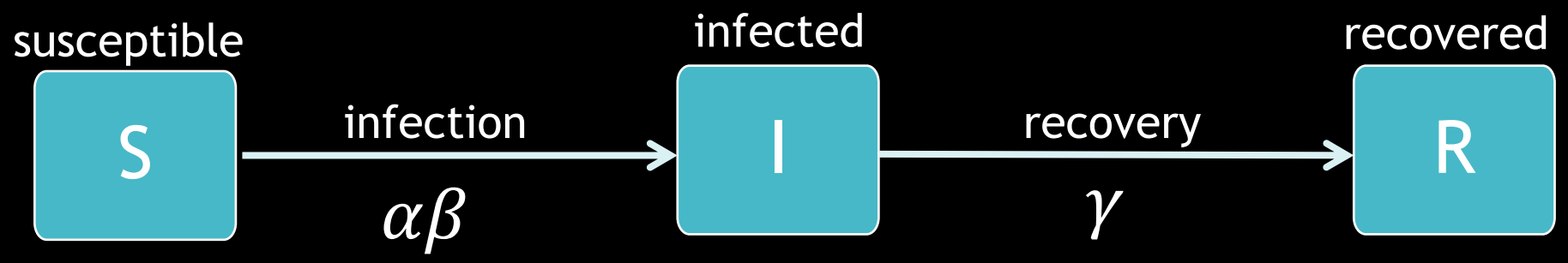
- compare epidemic dynamics:
  - without vaccine (v=0)
  - with vaccine (v =1/3)
- Enormous decrease in total number infected!

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



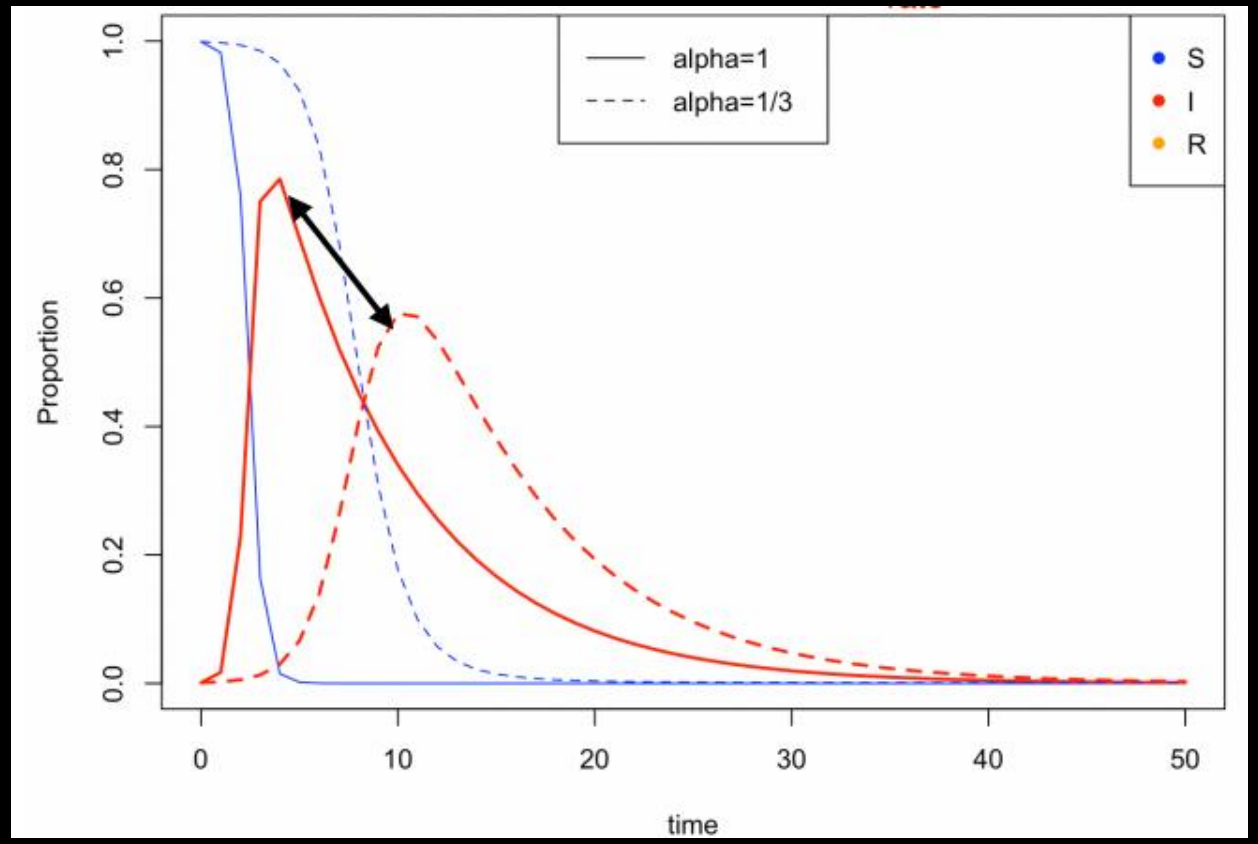
$$\frac{dS(t)}{dt} = -\alpha\beta S(t)I(t)$$

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

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

- 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

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