Introduction to Infectious Disease Modelling

Clinic on the Meaningful Modeling of Epidemiological Data, 2016

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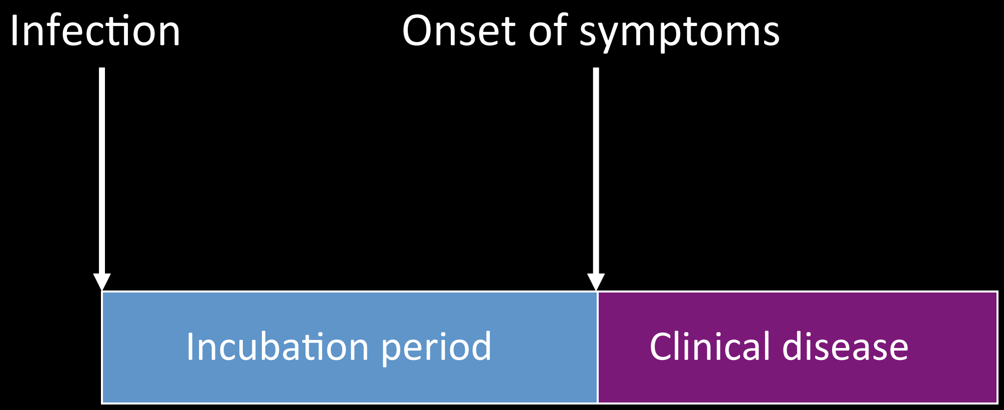
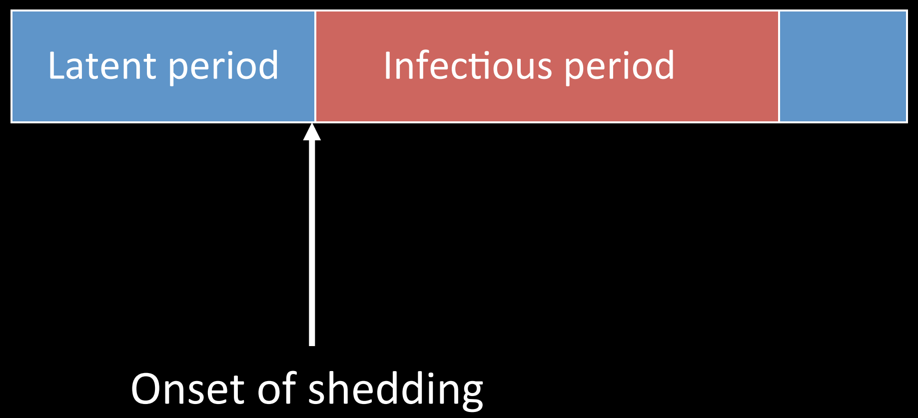
Natural History of Infection

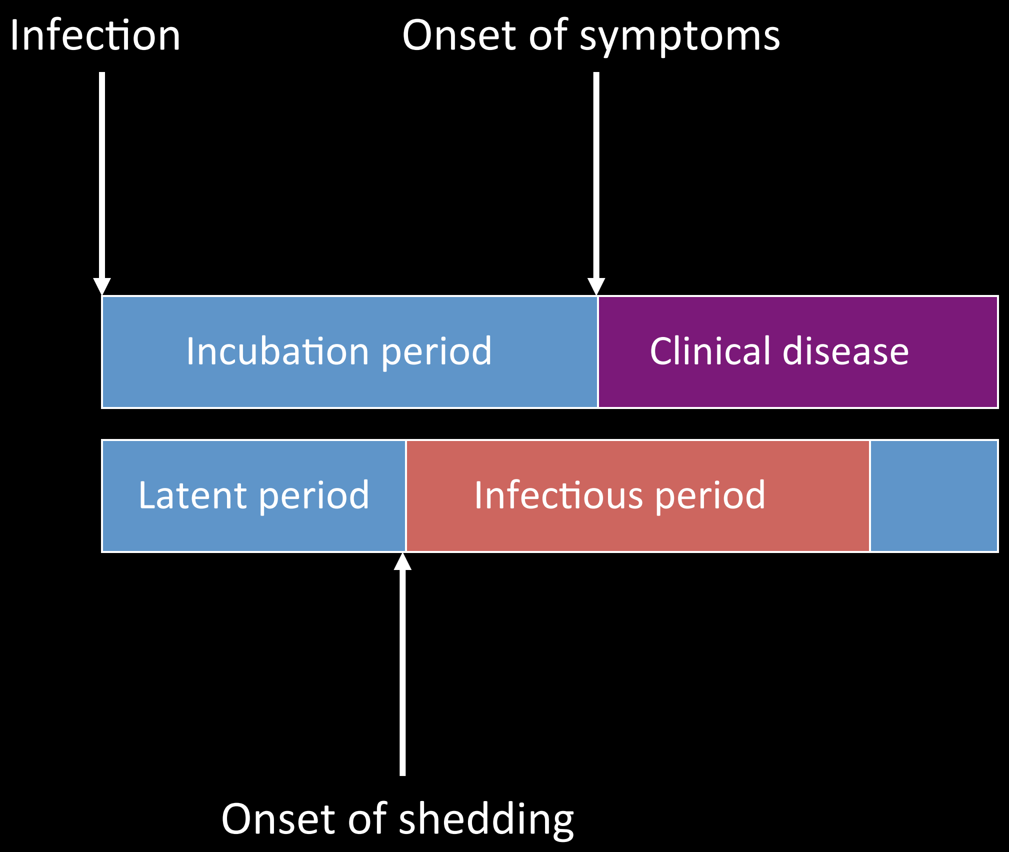


Natural History of Infection



Natural History of Infection

Let's start by talking about acute, immunizing diseases



<u>Acute</u>

Infection time course
<<
host lifespan

<u>Immunizing</u>

infection ➔ antibody production

prevents future infection

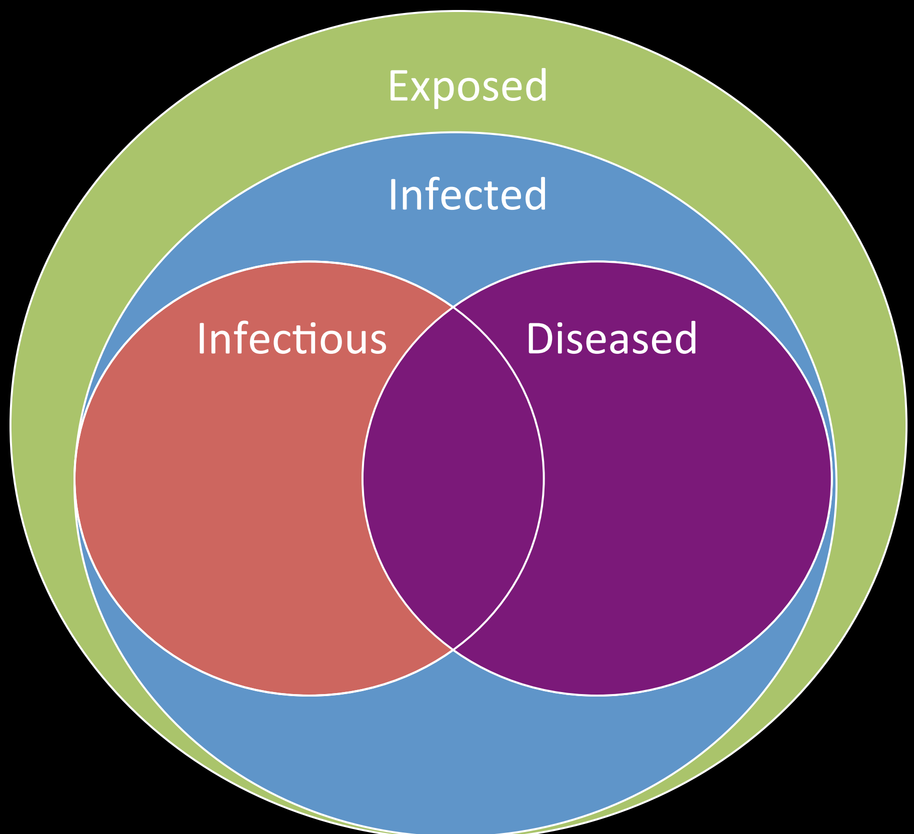
Examples

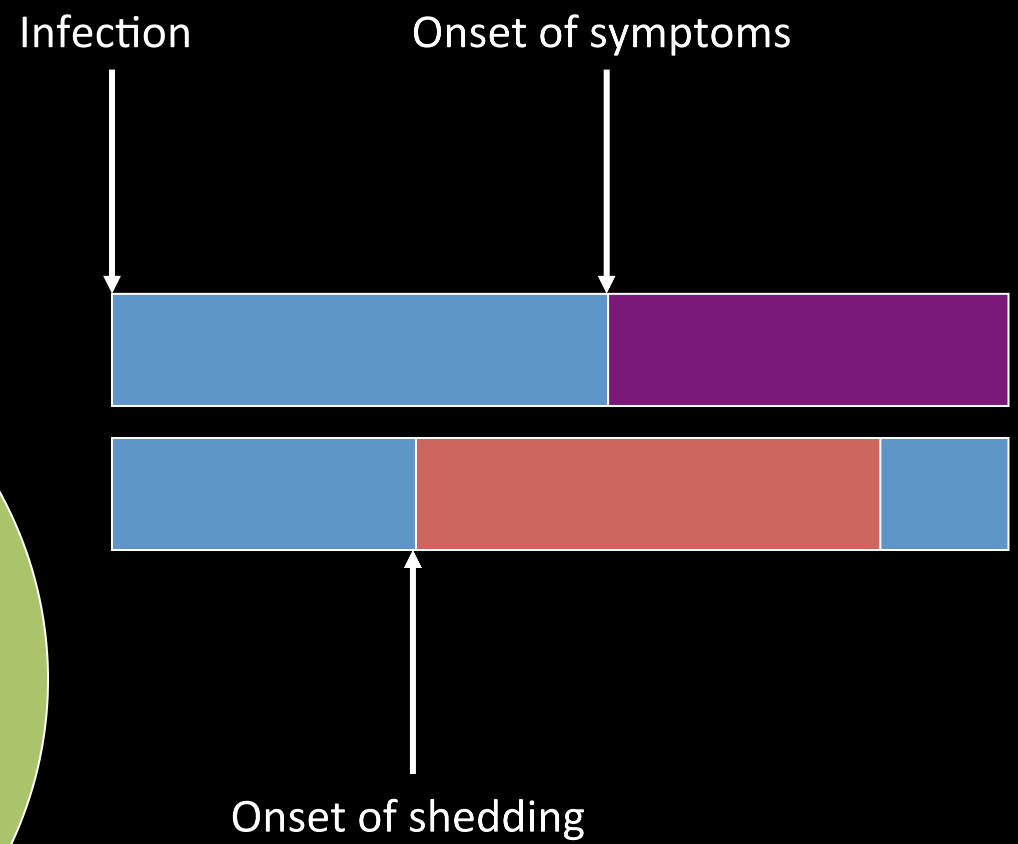
Natural History of Infection

Table 3.1 Incubation, latent and infectious periods (in days) for a variety of viral and bacterial infections. Data from Fenner and White (1970), Christie (1974), and Benenson (1975)

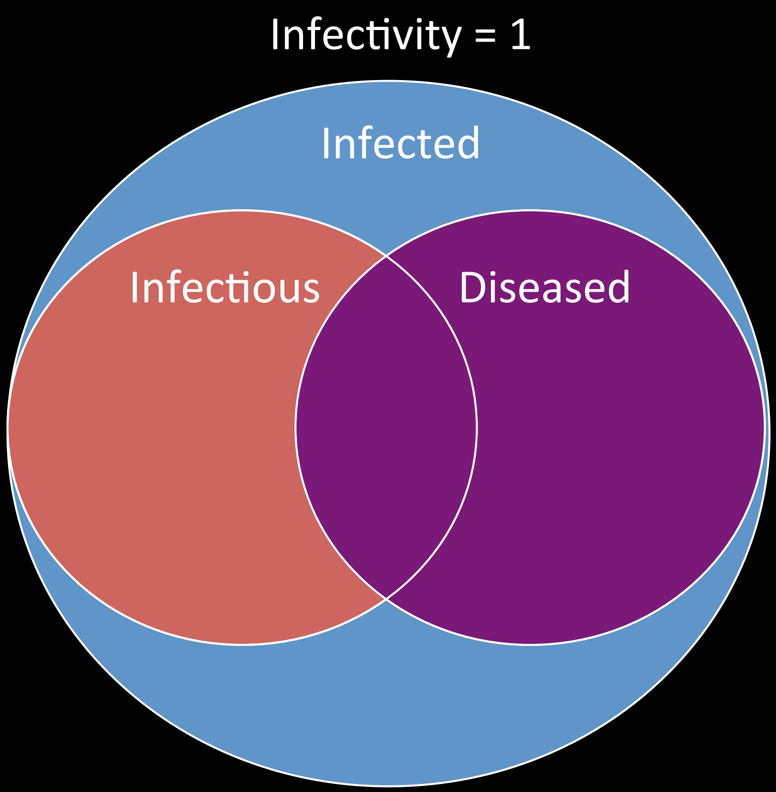
Infectious disease	Incubation period	Latent period	Infectious period
Measles	8–13	6–9	6–7
Mumps	12–26	12–18	4–8
Whooping cough (pertussis)	6–10	21–23	7–10
Rubella	14–21	7–14	11–12
Diphtheria	2–5	14–21	2–5
Chicken pox	13–17	8–12	10–11
Hepatitis B	30–80	13–17	19–22
Poliomyelitis	7–12	1–3	14–20
Influenza	1–3	1–3	2–3
Smallpox	10–15	8–11	2–3
Scarlet fever	2–3	1–2	14–21

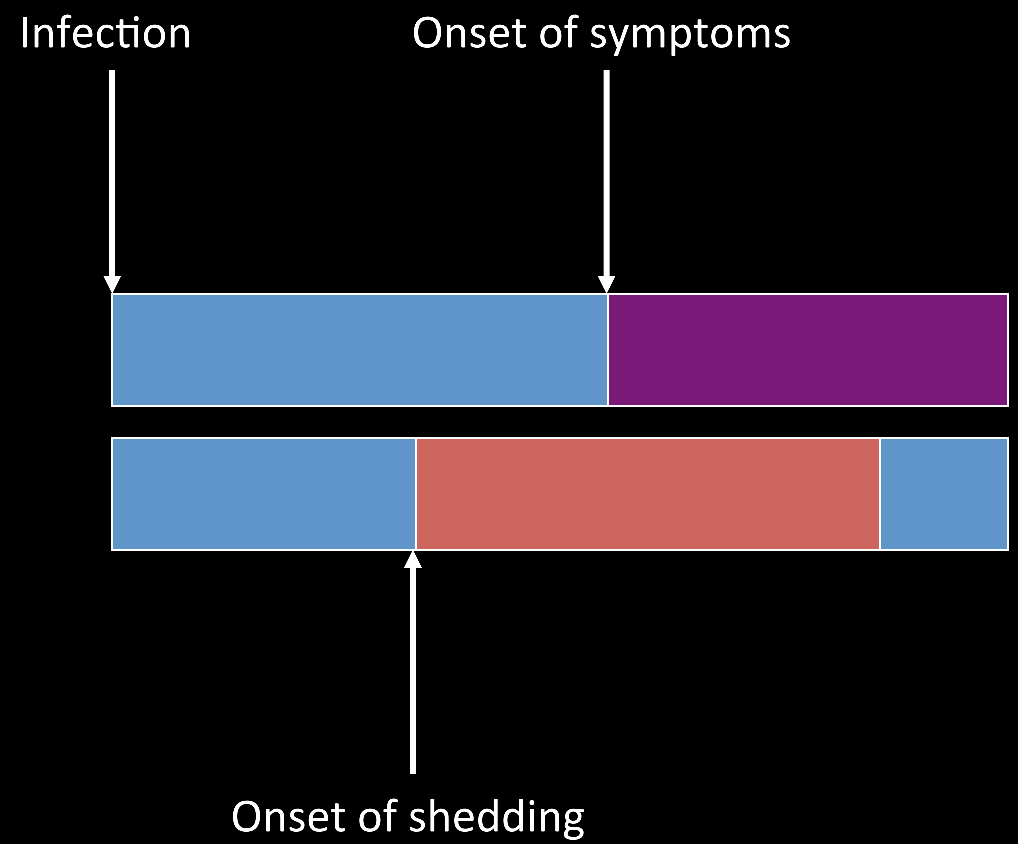
Terminology





A simple view of the world

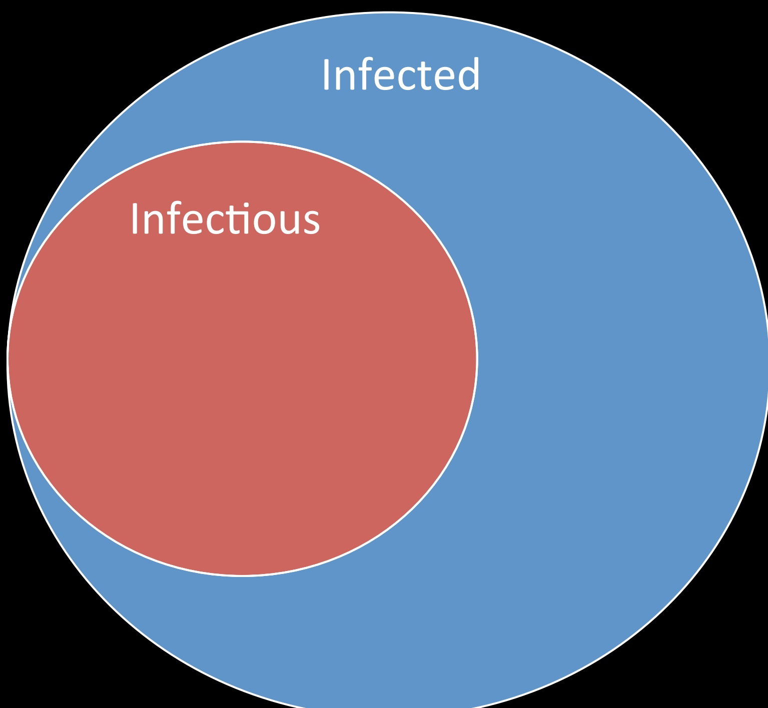


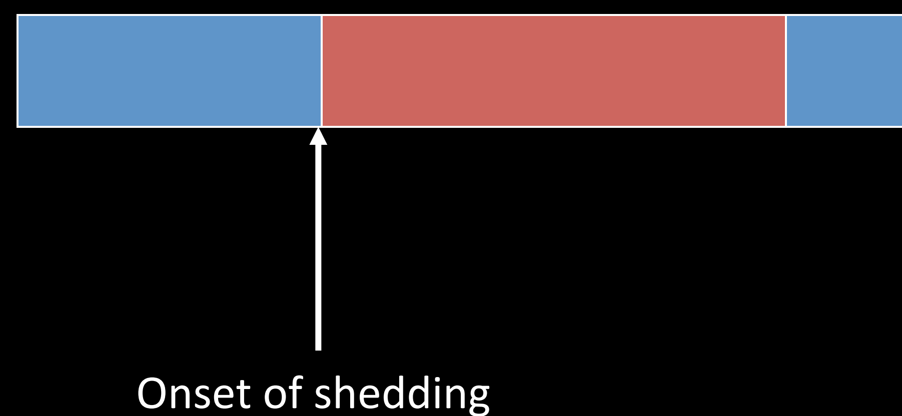


A simpler view of the world

Don’t worry about
symptoms and disease!

Infectivity = 1

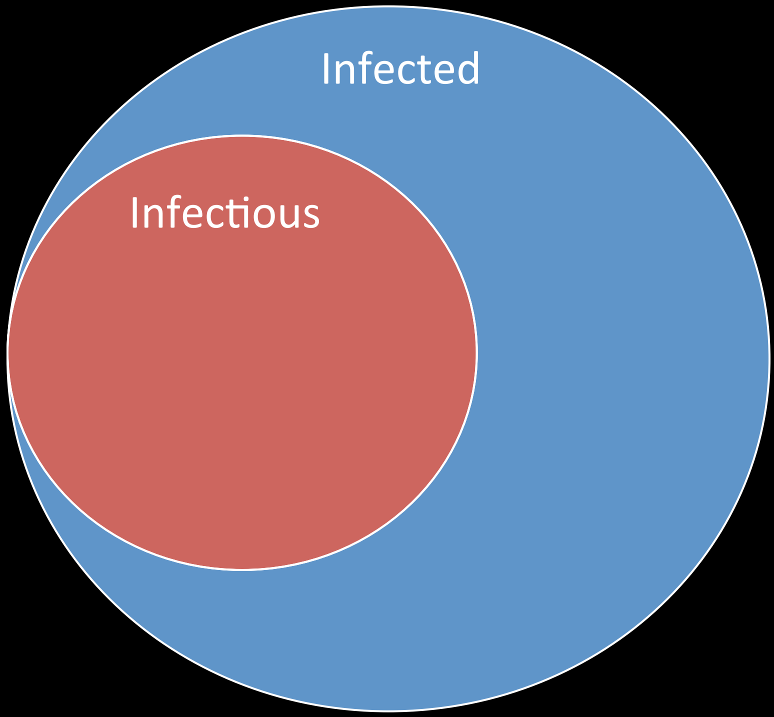


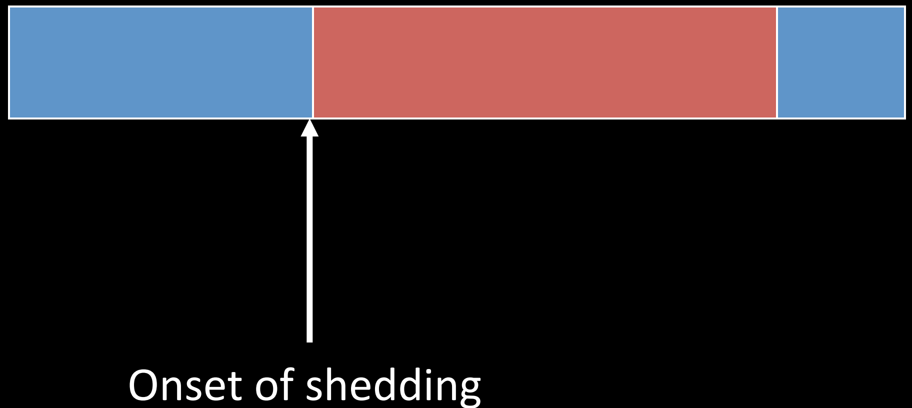


An even simpler view of the world

Don't worry about symptoms and disease!

Infectivity = 1

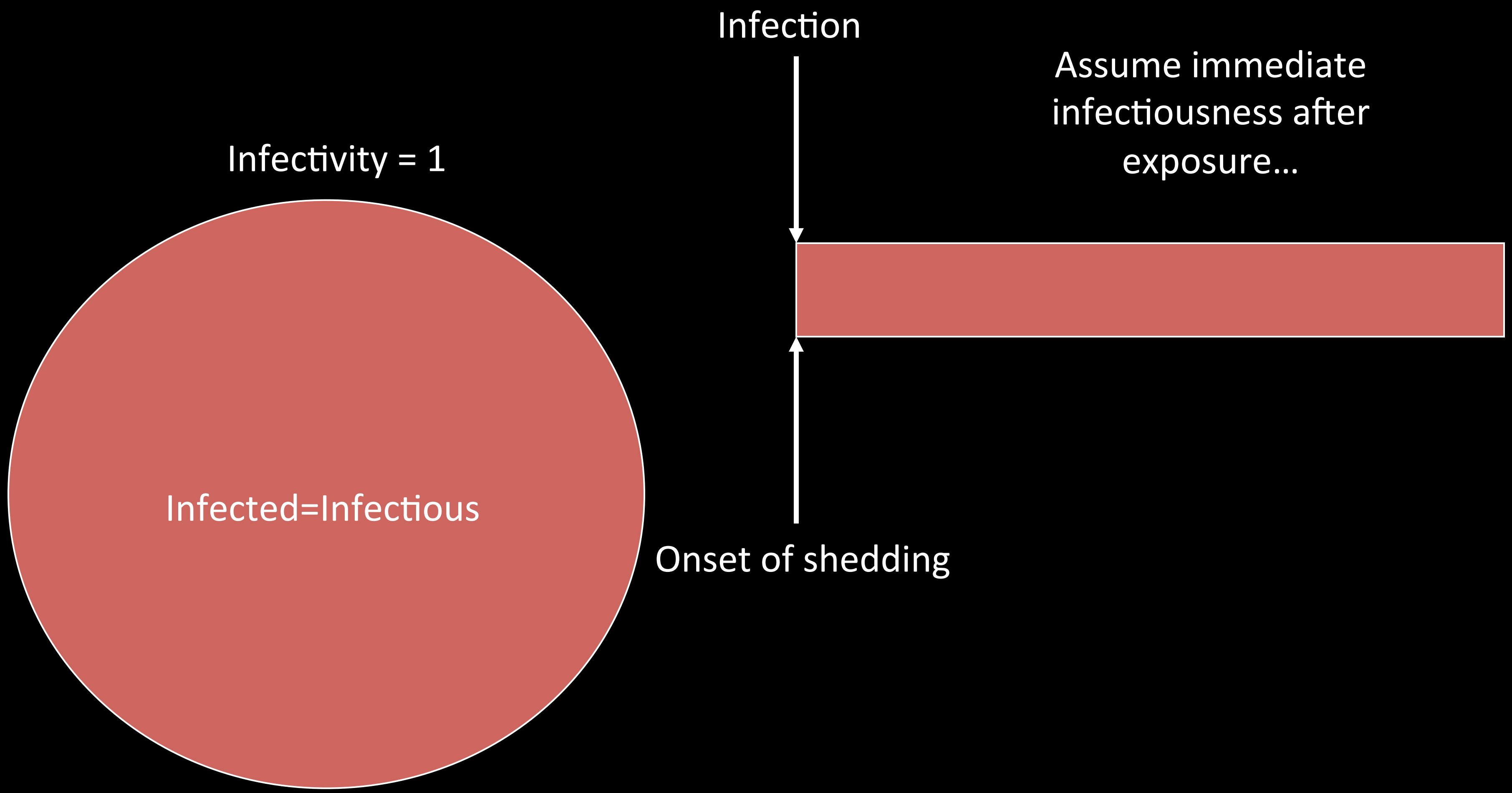




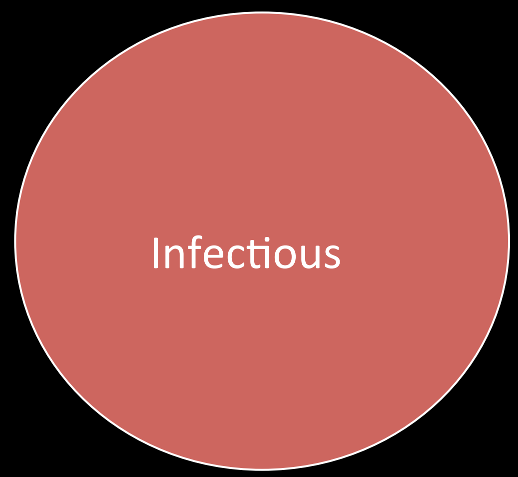
An extremely simple view of the world

Don't worry about symptoms and disease!

Assume immediate infectiousness after exposure…



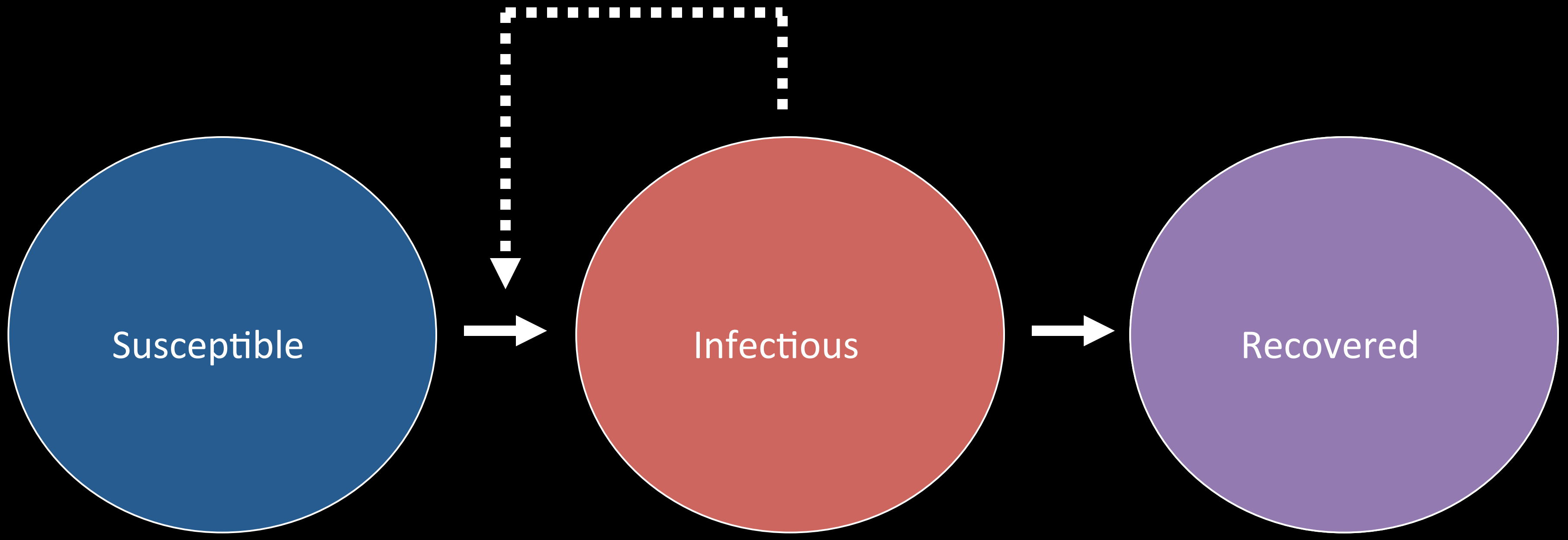
An extremely simple view of the world



An extremely simple view of the world

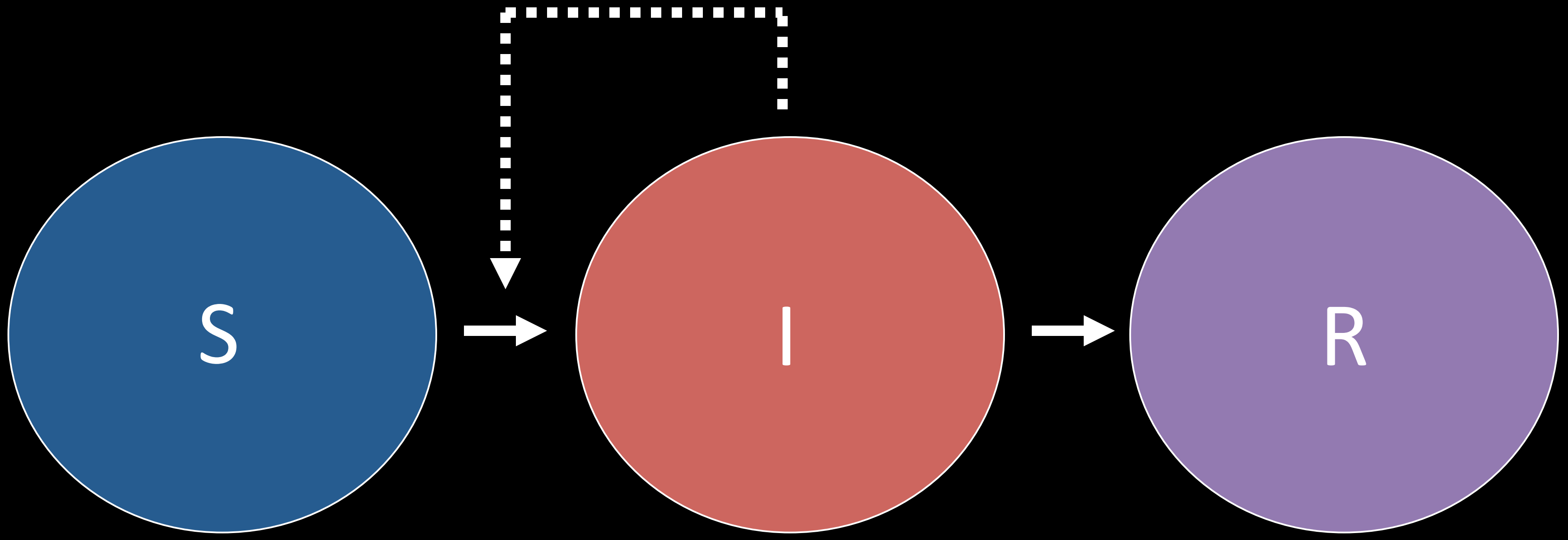
An extremely simple view of the world

Health-related States

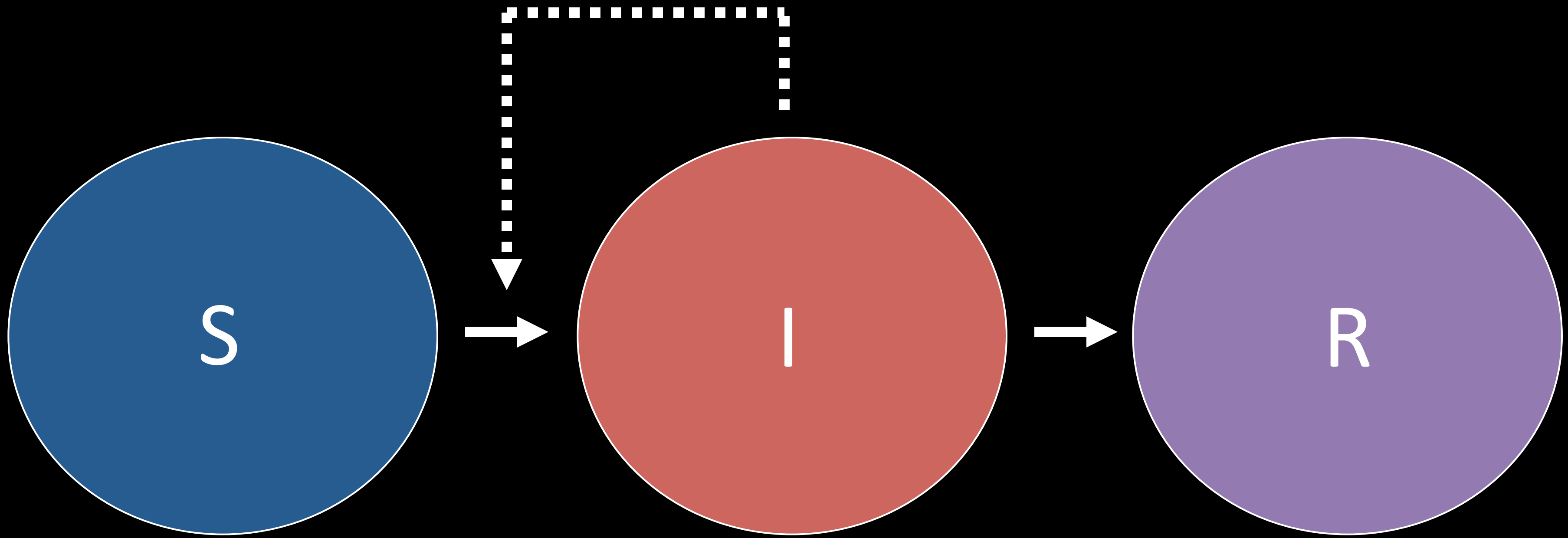


The rate at which susceptible individuals become infected depends on how many infectious people are in the population

State variables

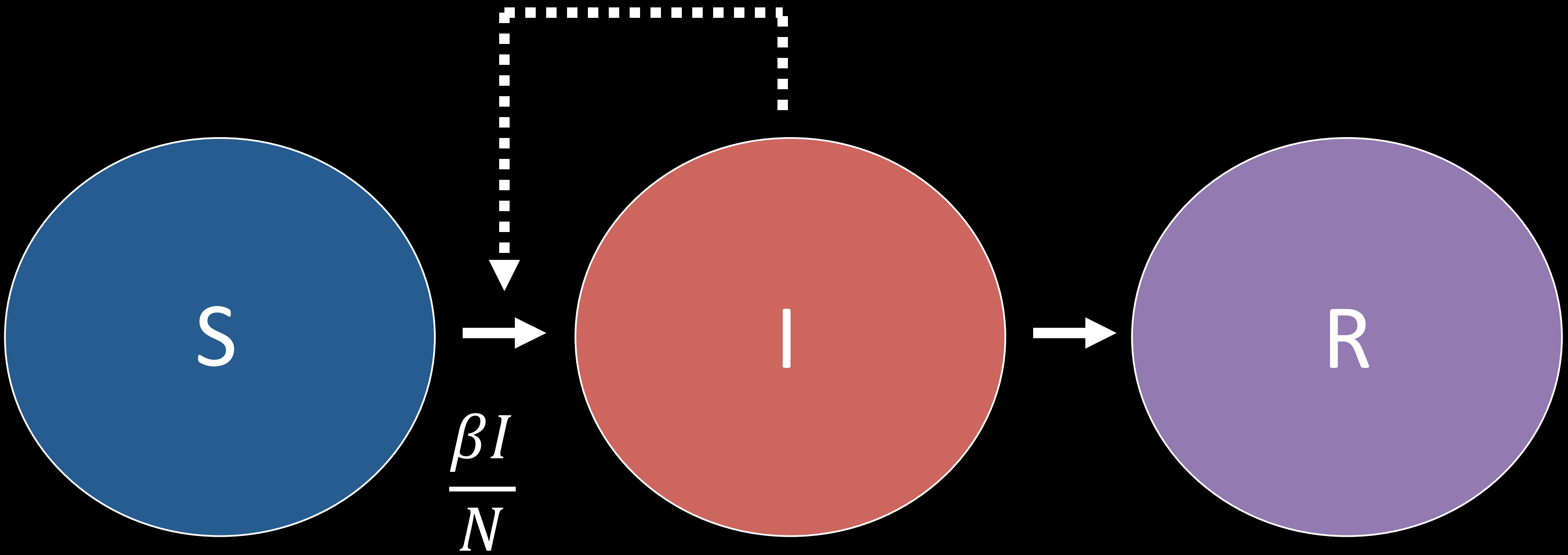


State variables



We can use ordinary differential equations to describe the rate at which individuals flow between states

SIR Model



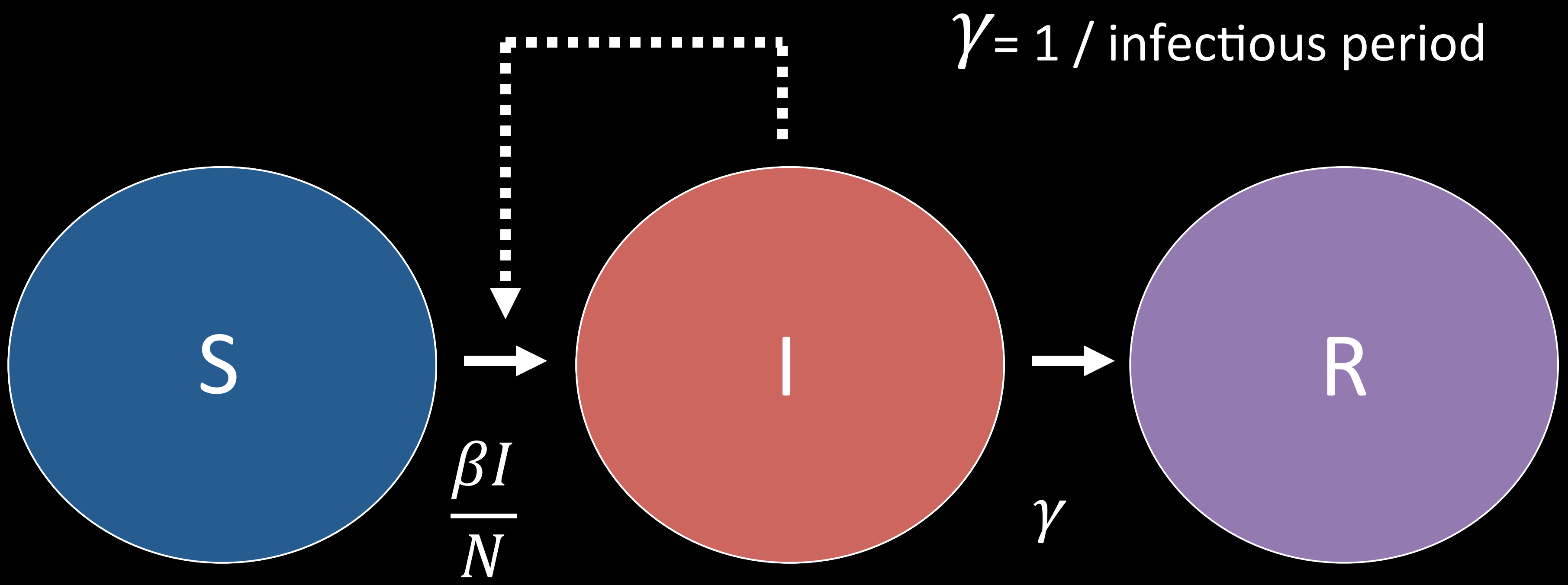
β = transmission coefficient

= per capita contact rate * infectivity

= per capita contact rate (infectivity = 1)

$\frac{I}{N}$ proportion of contacts that are with an infectious individual

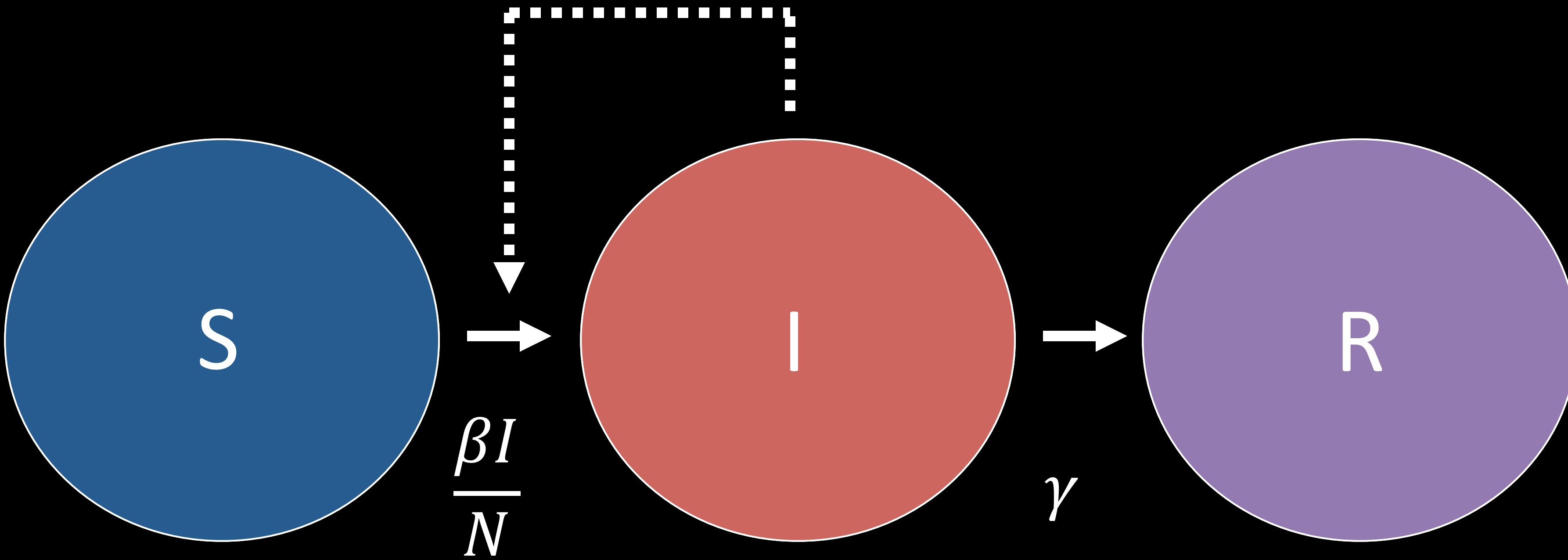
SIR Model



If infectious people recover at a rate of 0.2 / day,

the average time they spend infectious is 1 / 0.2 = 5 days

SIR Model



$$\frac{dS}{dt} = -\frac{\beta S I}{N}$$

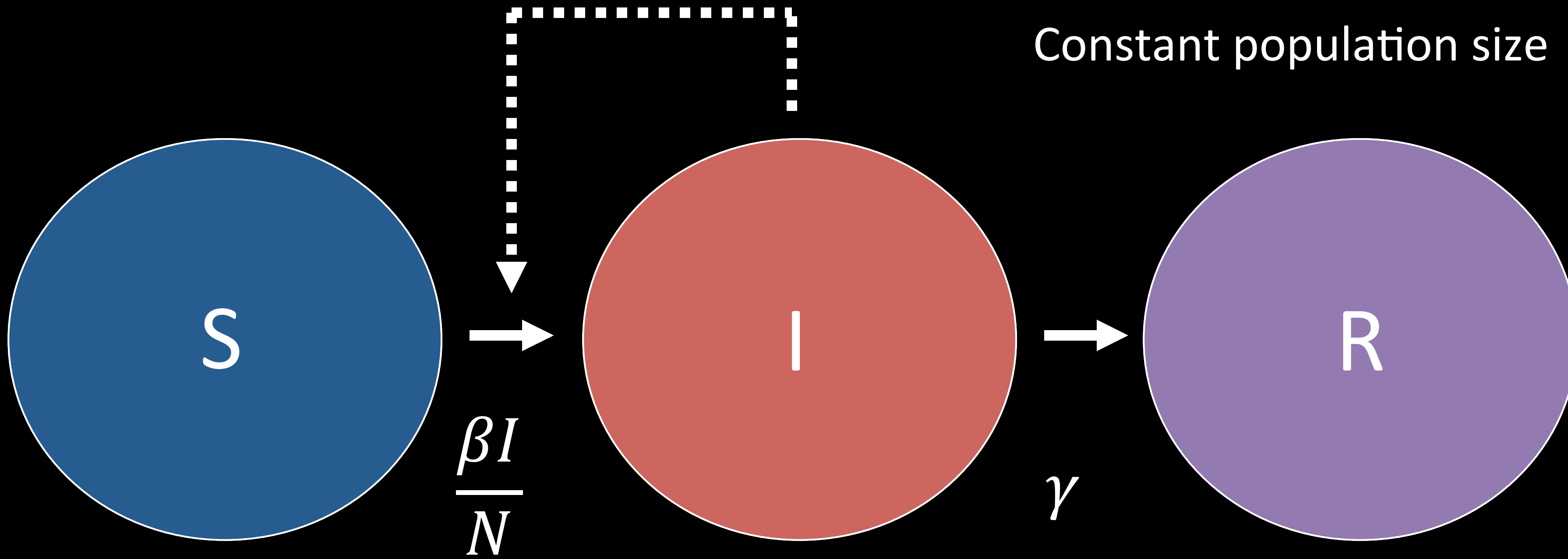
$$\frac{dI}{dt} = \frac{\beta S I}{N} - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

SIR Model

$$N = S + I + R$$

Constant population size



$$\frac{dS}{dt} = -\frac{\beta SI}{N} \qquad \frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I \qquad \frac{dR}{dt} = \gamma I$$

SIR Model

$$\frac{dS}{dt} = -\frac{\beta SI}{N}$$

$$\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

N	population size
γ	recovery rate
β	transmission coefficient

SIR Model

$$\frac{dS}{dt} = -\frac{\beta SI}{N}$$

$$\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

$R_0 =$

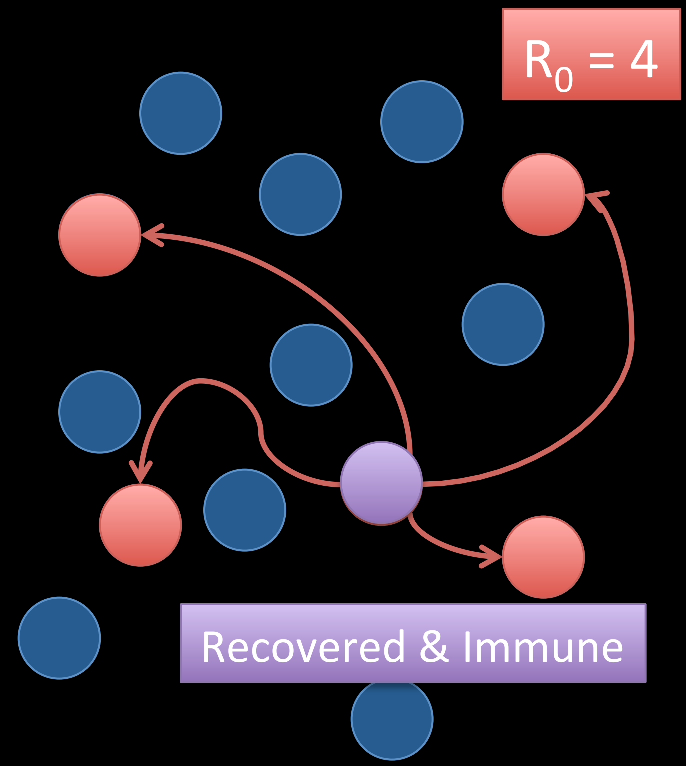
infections produced by

1 infectious individual

in a fully susceptible population.

R_0: The Basic Reproductive Number

- Average # of secondary infections an infected host produces in a susceptible population.



SIR Model

$$R_0 =$$

$$\frac{\beta S I}{N} \xrightarrow{N \text{ large}} \beta$$

Rate at which an infected individual produces new infections in a naïve population

X

$$1$$

Proportion of new infections that become infectious

X

$$1/\gamma$$

Average duration of infectiousness

SIR Model

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

$R_0 =$

Rate at which an infected individual produces new infections in a naïve population

X

Proportion of new infections that become infectious

X

Average duration of infectiousness

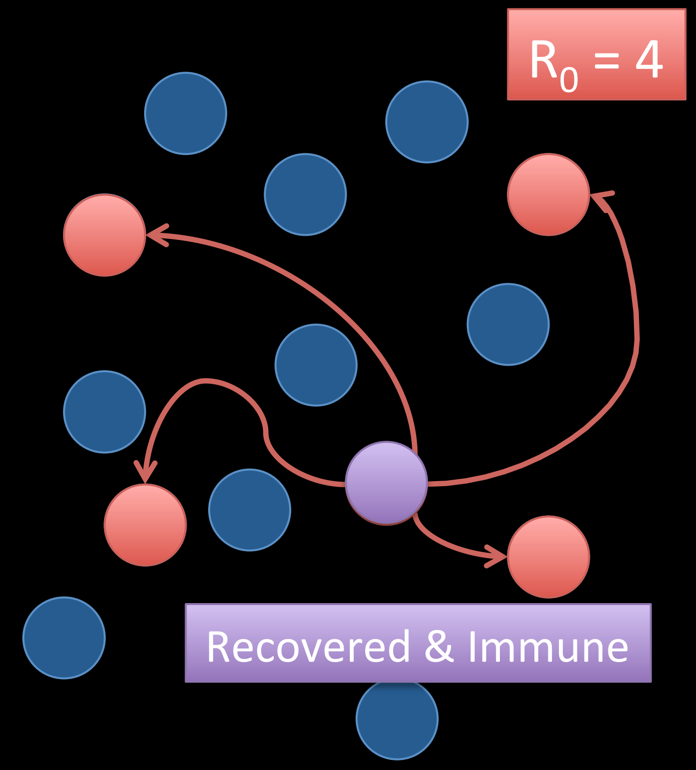
R_0: The Basic Reproductive Number

- Average # of secondary infections an infected host produces in a susceptible population.

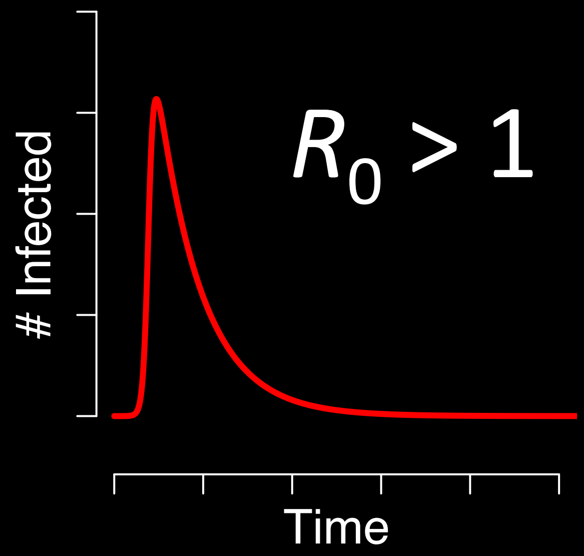
- Threshold criteria:

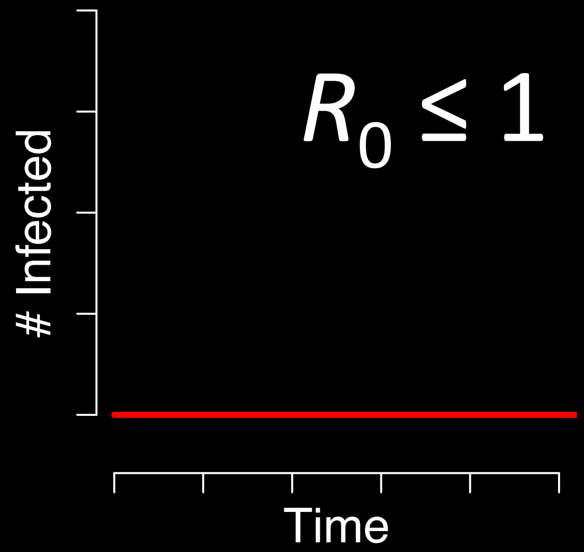
  If $R_0 < 1$, no epidemic

  If $R_0 > 1$, epidemic



SIR Model: R_0 as a Threshold





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

Disease Introduction:

Epidemic occurs if $R_0 > 1$.

R_{eff}: Effective Reproductive Number

$\frac{\beta S}{N}$ Rate at which an infected individual produces new infections in a non-fully susceptible population

X

1 Proportion of new infections that become infectious

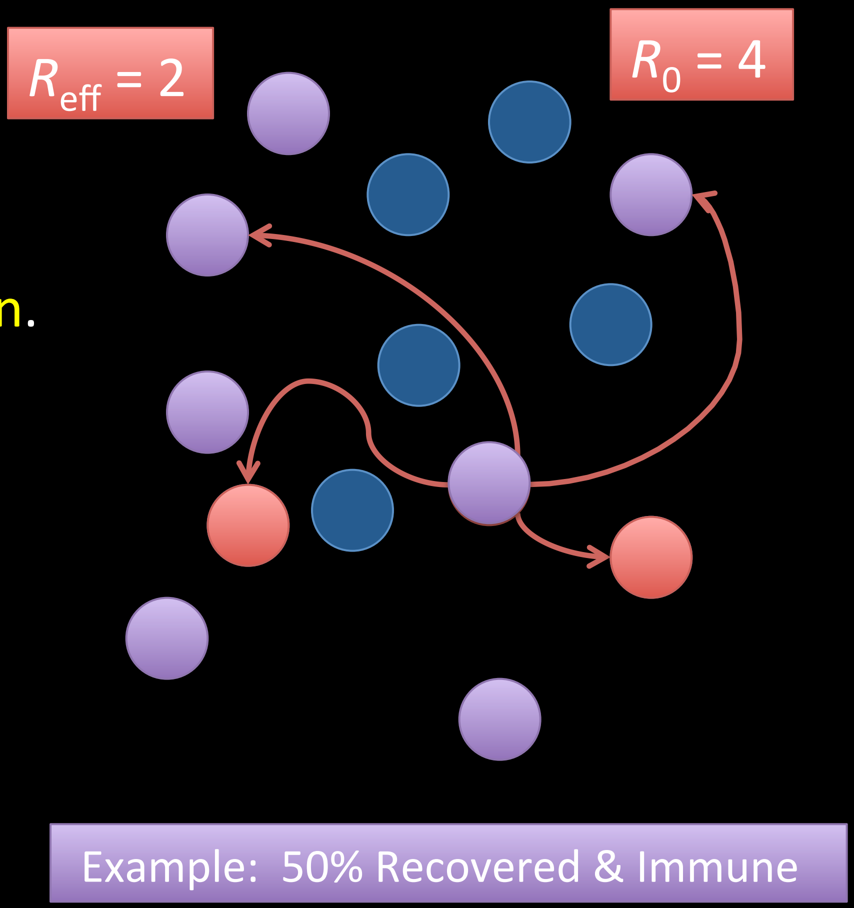
X

$1/\gamma$ Average duration of infectiousness

$$R_{eff} = R_0 \frac{S}{N}$$

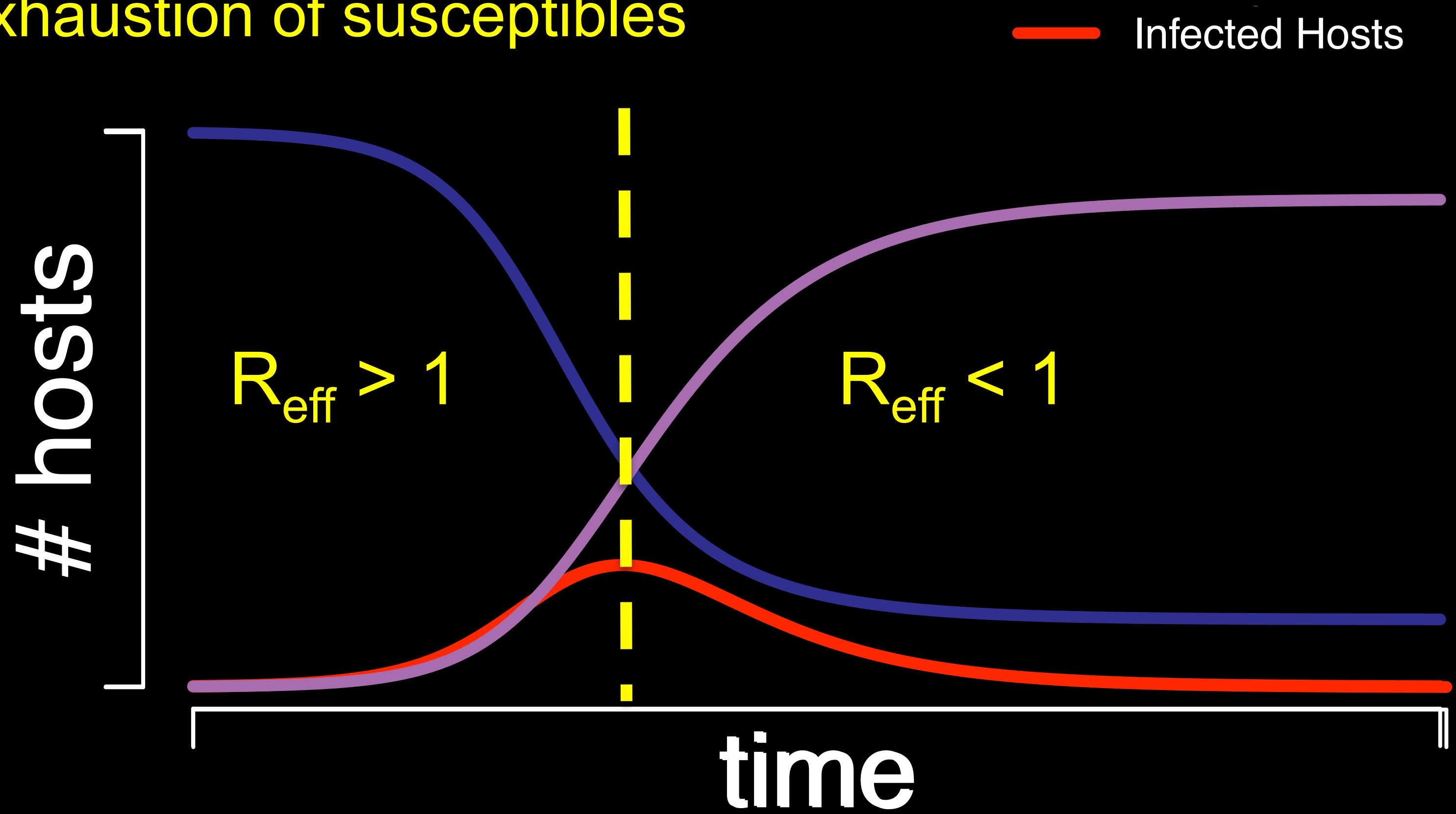
R_{eff}: The Effective Reproductive Number

- The average # of secondary infections that an infected host produces in an only partially susceptible population.

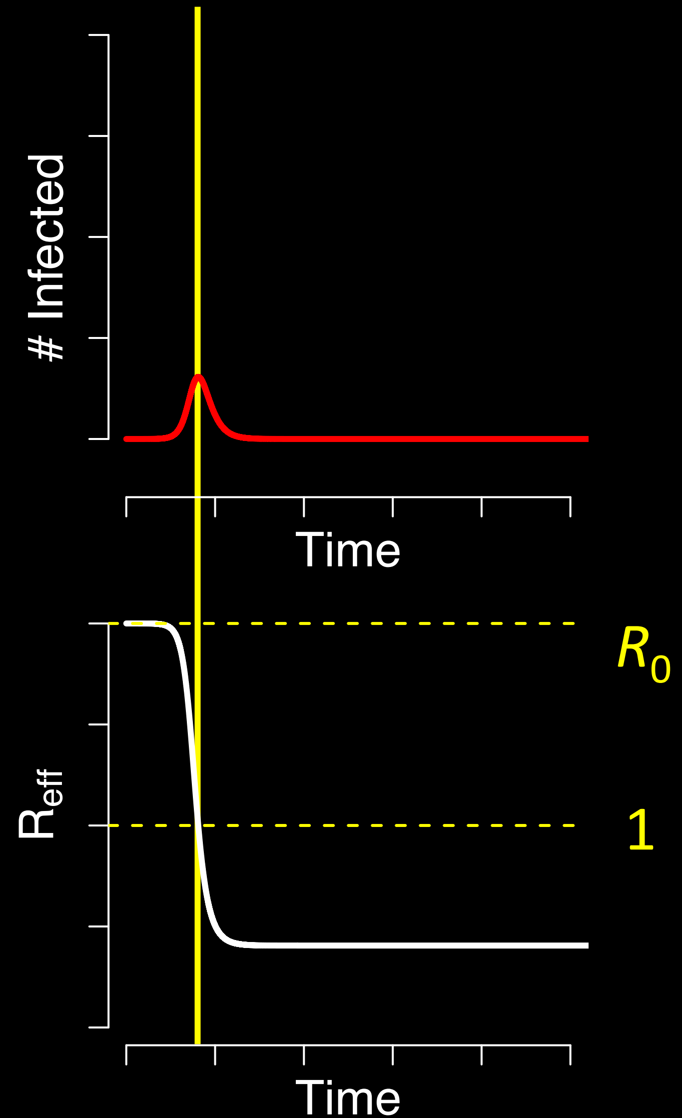


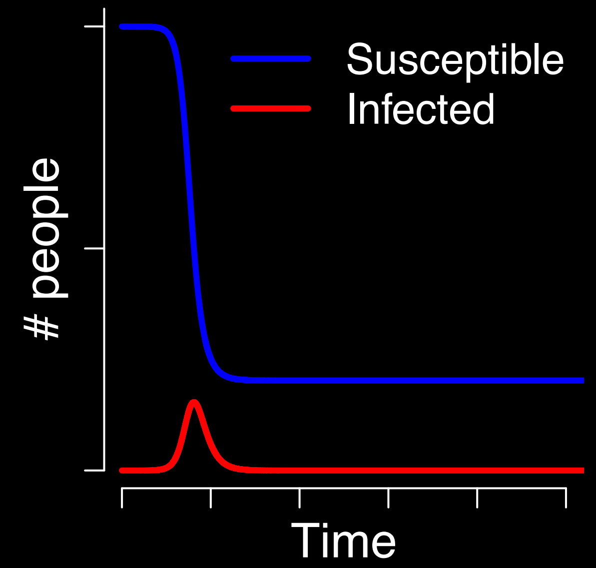
Why do epidemics peak?

Death or long-term immunity leads to exhaustion of susceptibles



R_{eff}: The Effective Reproductive Number



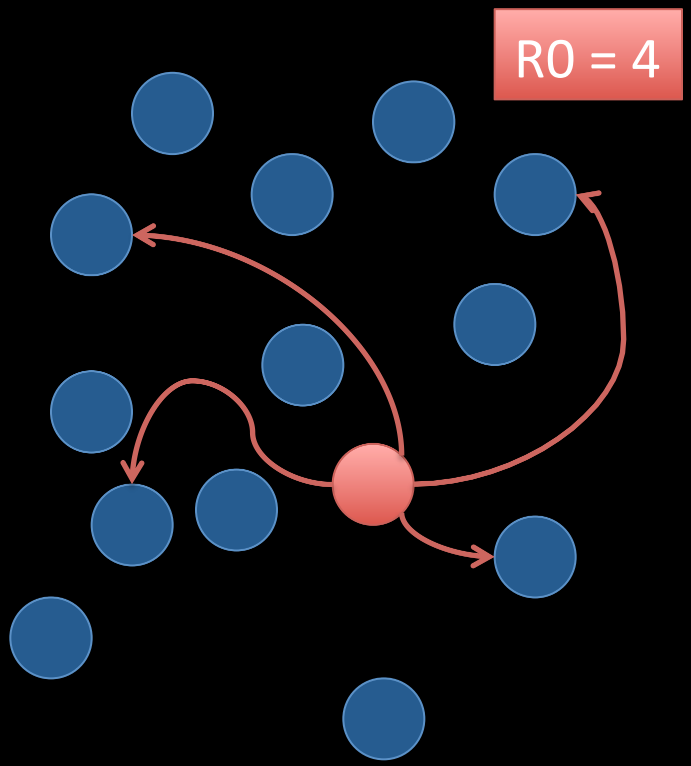


$$R_{eff}(t) = R_0 \frac{S(t)}{N}$$

$$R_{eff}(t) = \frac{\beta S(t)}{\gamma N}$$

Proportion to Vaccinate

- So what % of the population must be vaccinated to eliminate transmission in a population?



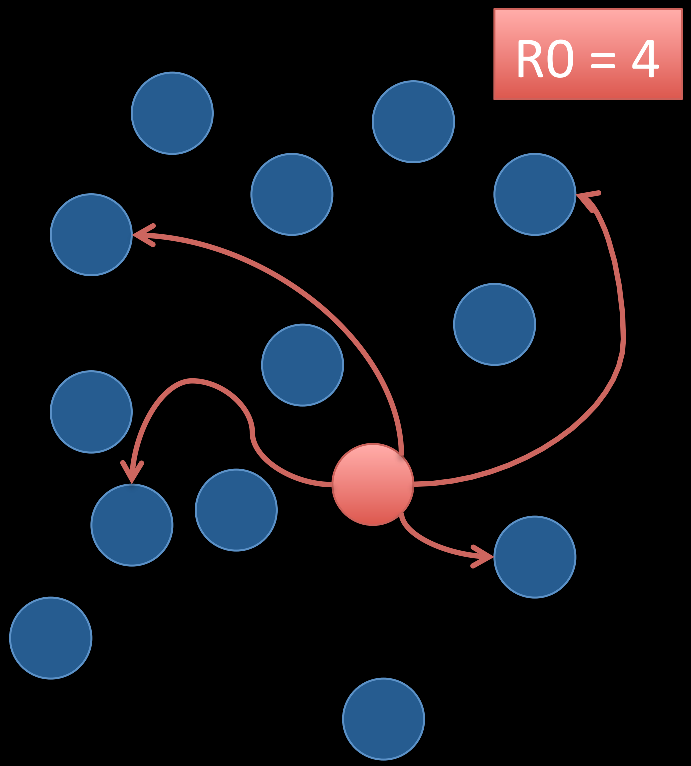
Proportion to Vaccinate

$$R_{eff} = R_0 \frac{S}{N}$$

For a disease to die out, $R_{eff} \leq 1$

$$R_0 \frac{S}{N} \leq 1$$

$$\frac{S}{N} \leq \frac{1}{R_0}$$



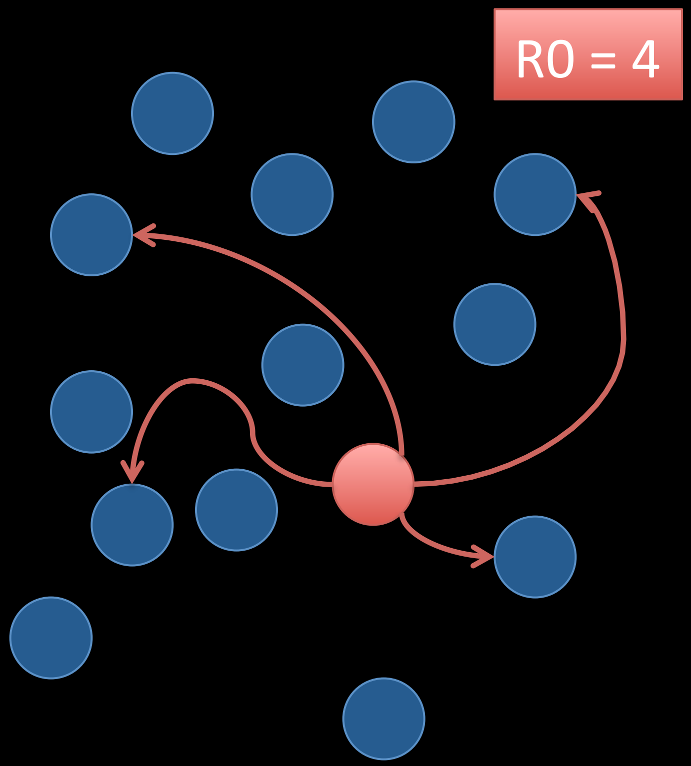
Proportion to Vaccinate

$$\frac{S}{N} \leq \frac{1}{R_0}$$

Proportion immune = P_V =
1 – proportion susceptible

$$P_V \geq 1 - \frac{1}{R_0}$$

$$P_V \geq \frac{R_0 - 1}{R_0}$$



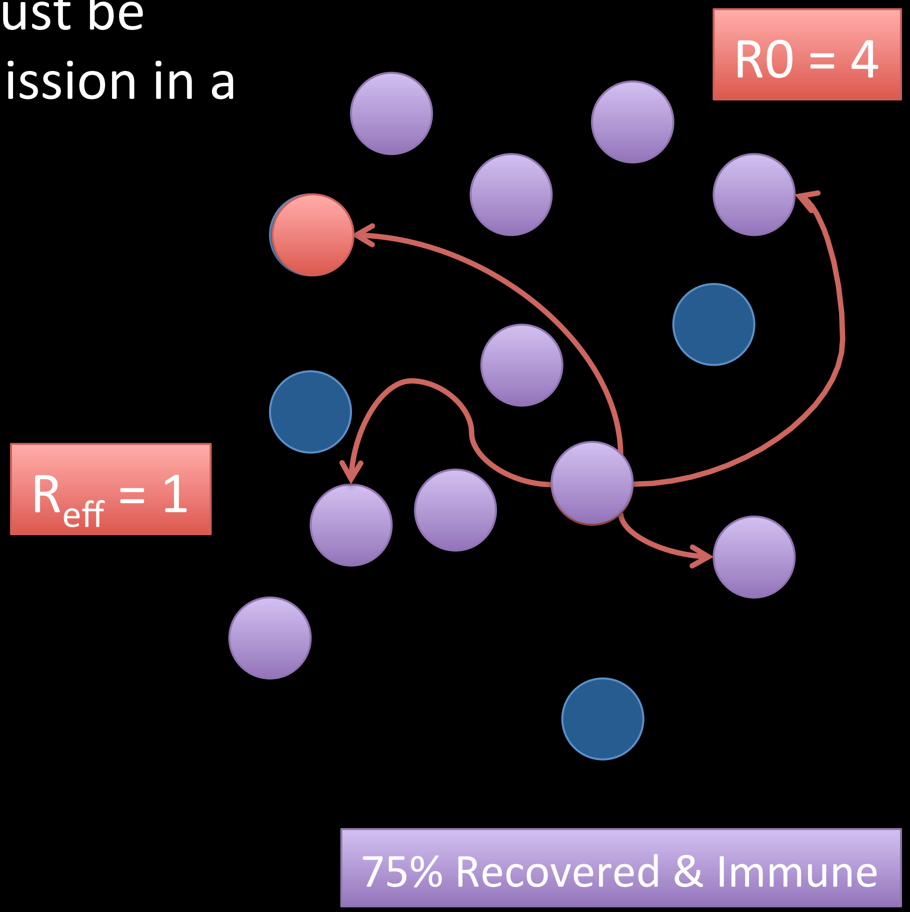
You don't have to vaccinate everyone to eliminate transmission!!!

Proportion to Vaccinate

- So what % of the population must be vaccinated to eliminate transmission in a population?

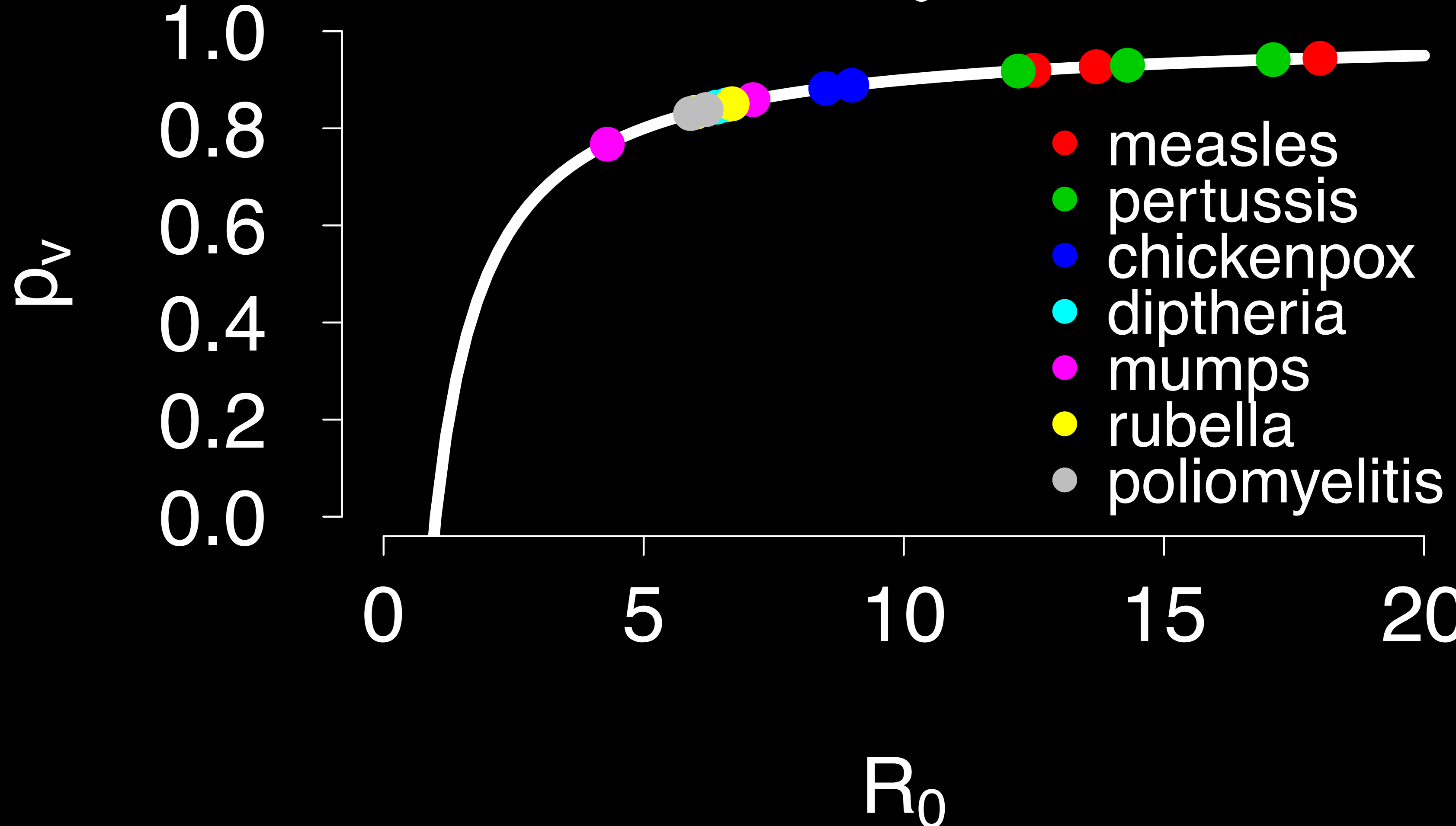
$$P_V \geq \frac{R_0 - 1}{R_0}$$

$$P_V \geq \frac{4 - 1}{4} = \frac{3}{4}$$

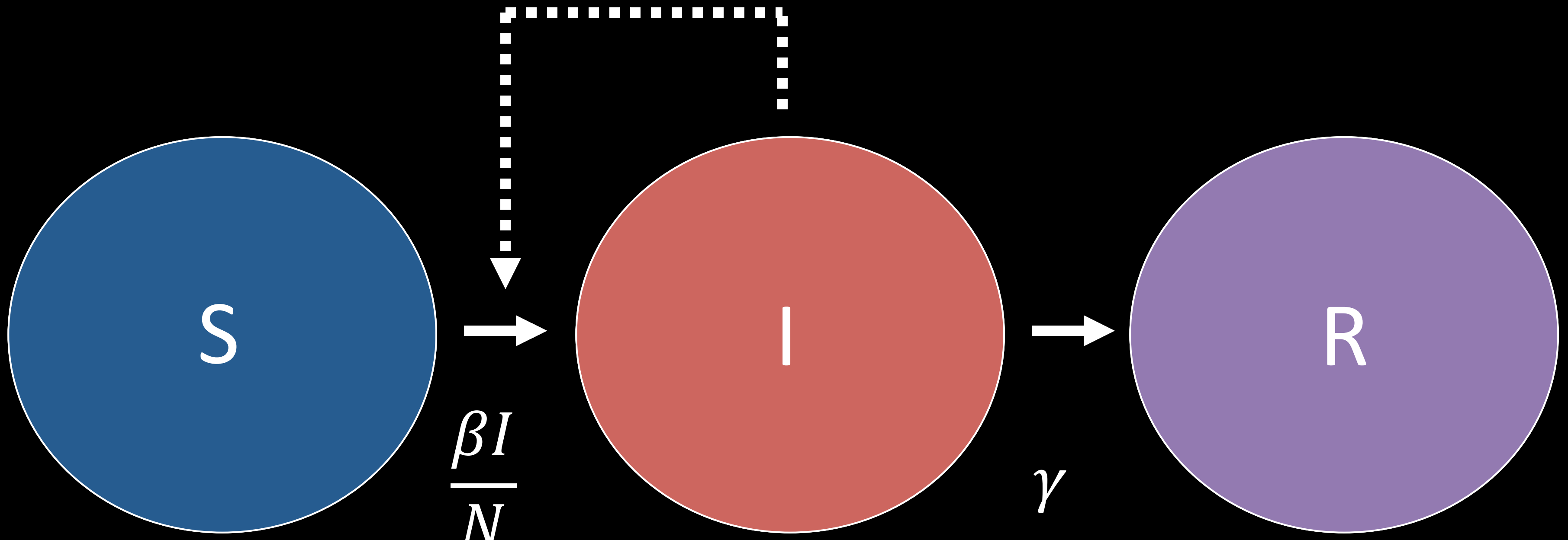


Elimination Thresholds

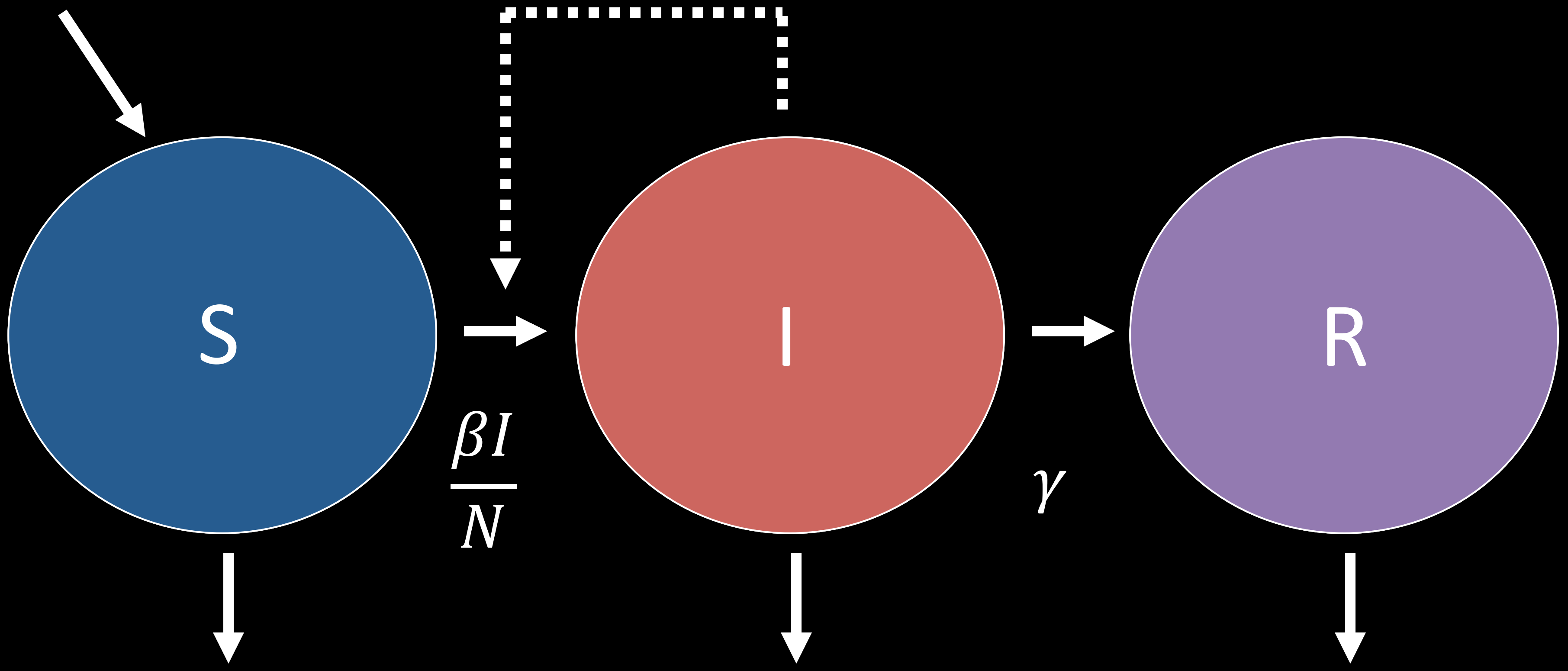
$$P_V = \frac{R_0 - 1}{R_0}$$



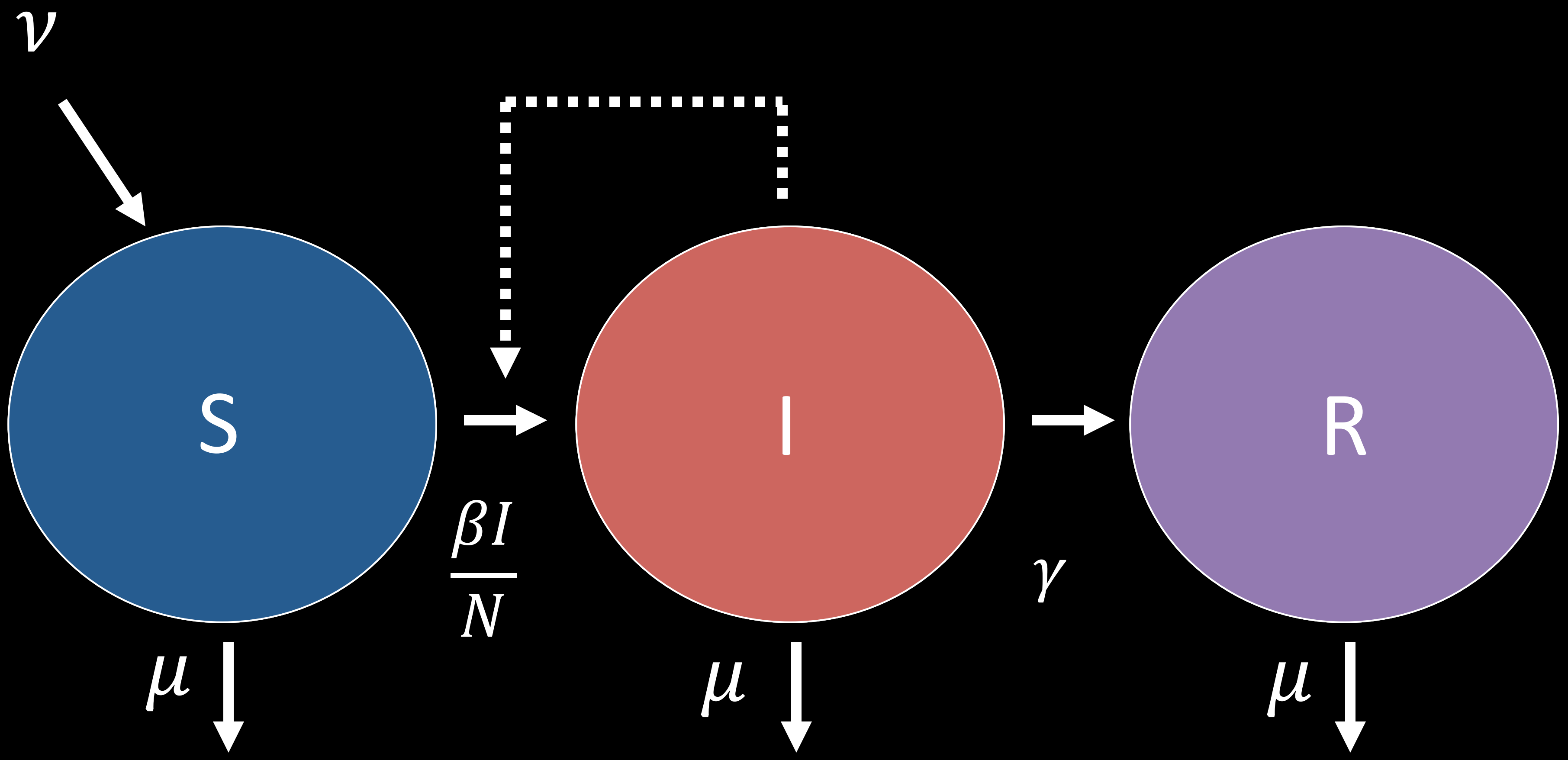
SIR Model



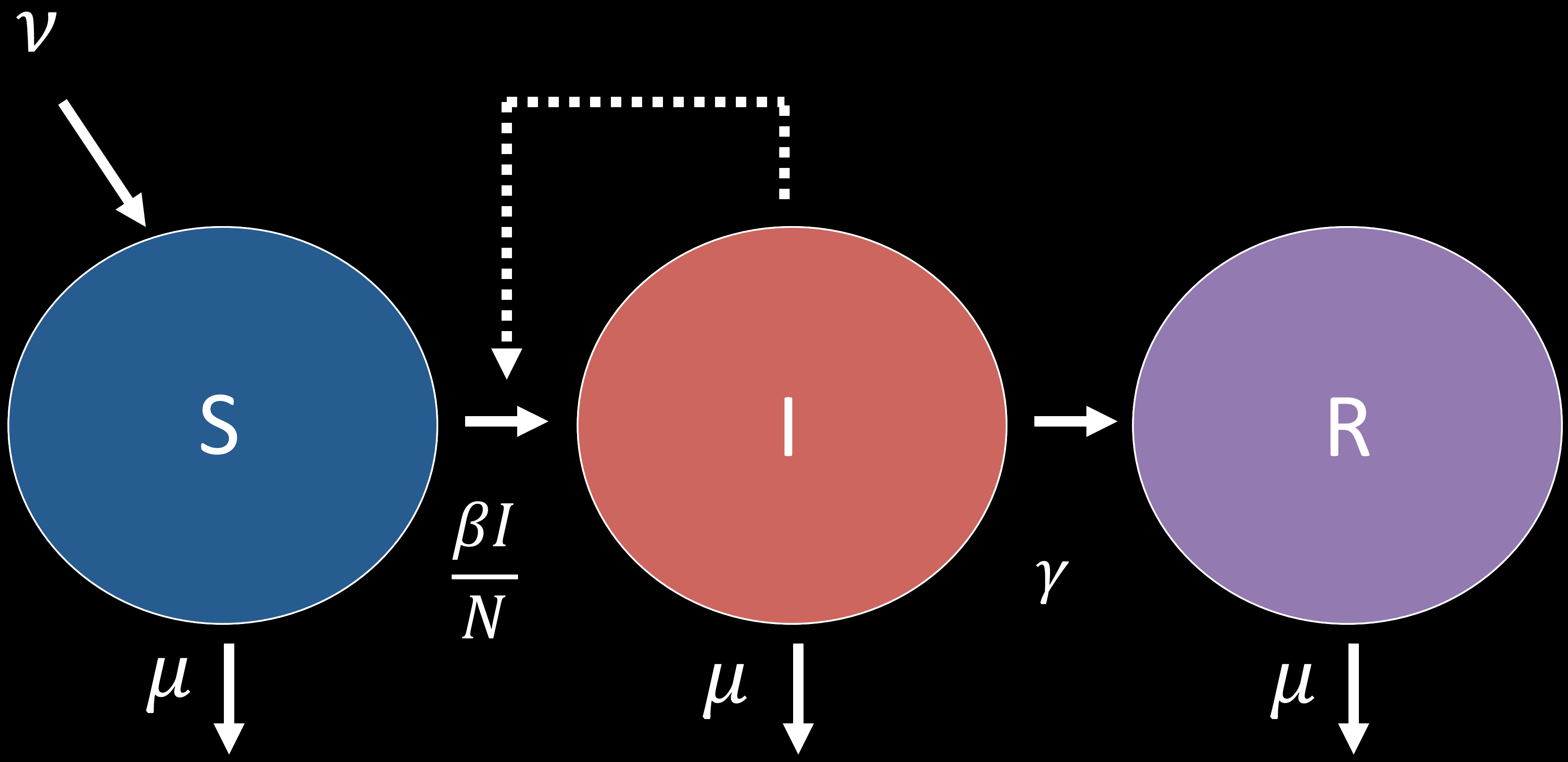
SIR Model with Birth & Death



SIR Model with Birth & Death



SIR Model with Birth & Death



$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

$$\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I - \mu I$$

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

SIR Model with Birth & Death

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

$$\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I - \mu I$$

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

$$N = S + I + R$$

so

$$\frac{dN}{dt} = \nu - \mu N$$

SIR Model with Birth & Death

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

$$\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I - \mu I$$

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

$$N = S + I + R$$

so

$$\frac{dN}{dt} = \nu - \mu N$$

To assume constant population size, births = deaths:

$$\nu = \mu N$$

SIR Model with Birth & Death

$$R_0 =$$

$$\frac{\beta S I}{N} \xrightarrow{N \text{ large}} \beta$$

Rate at which an infected individual produces new infections in a naïve population

X

$$1$$

Proportion of new infections that become infectious

X

$$\frac{1}{\gamma + \mu}$$

Average duration of infectiousness

SIR Model with Birth & Death

$$R_0 = \frac{\beta}{\gamma + \mu}$$

$R_0 =$

Rate at which an infected individual produces new infections in a naïve population

X

Proportion of new infections that become infectious

X

Average duration of infectiousness

SIR Model with Birth & Death

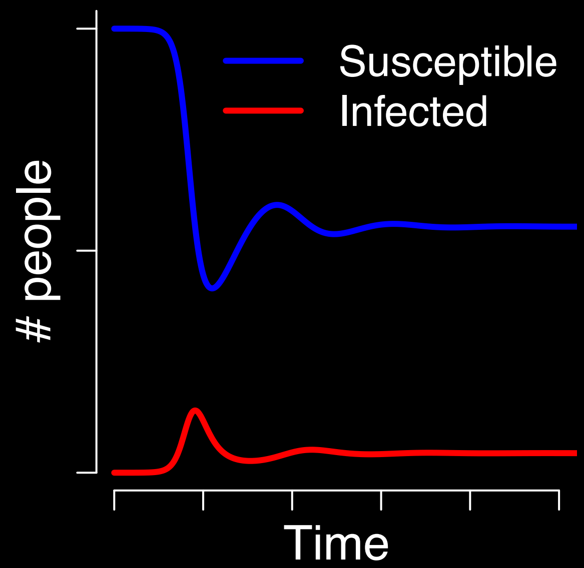
Dynamics upon introduction:

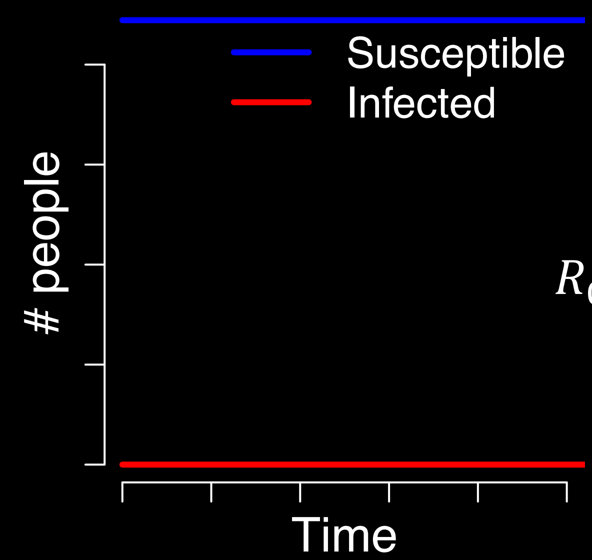
Epidemic if $R_0 > 1$

No epidemic if $R_0 \leq 1$

Endemic state

No endemic state





$$R_0 = \frac{\beta}{\gamma + \mu}$$

R_{eff}: Effective Reproductive Number

$$\frac{\beta S}{N}$$

Rate at which an infected individual produces new infections in a non-fully susceptible population

X

$$1$$

Proportion of new infections that become infectious

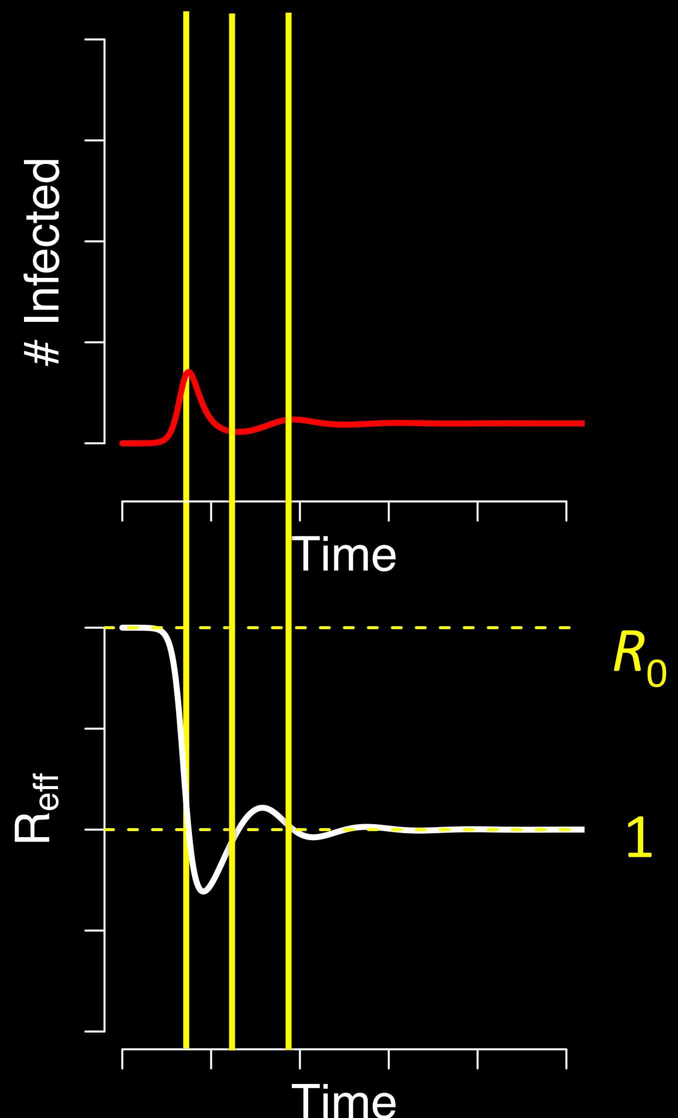
X

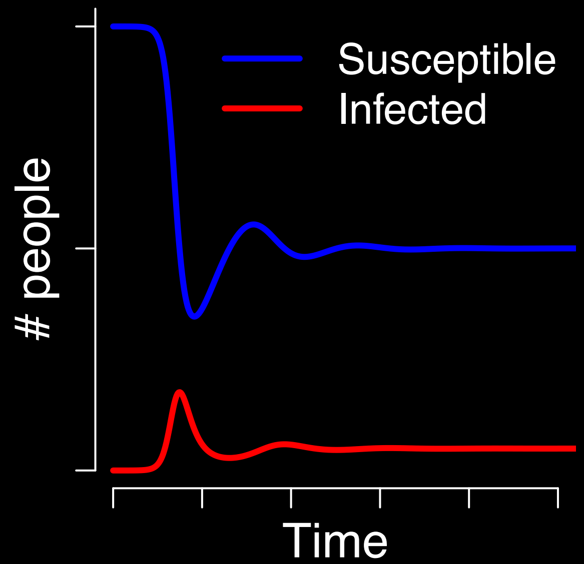
$$\frac{1}{\gamma + \mu}$$

Average duration of infectiousness

$$R_{eff} = R_0 \frac{S}{N}$$

R_{eff}: The Effective Reproductive Number



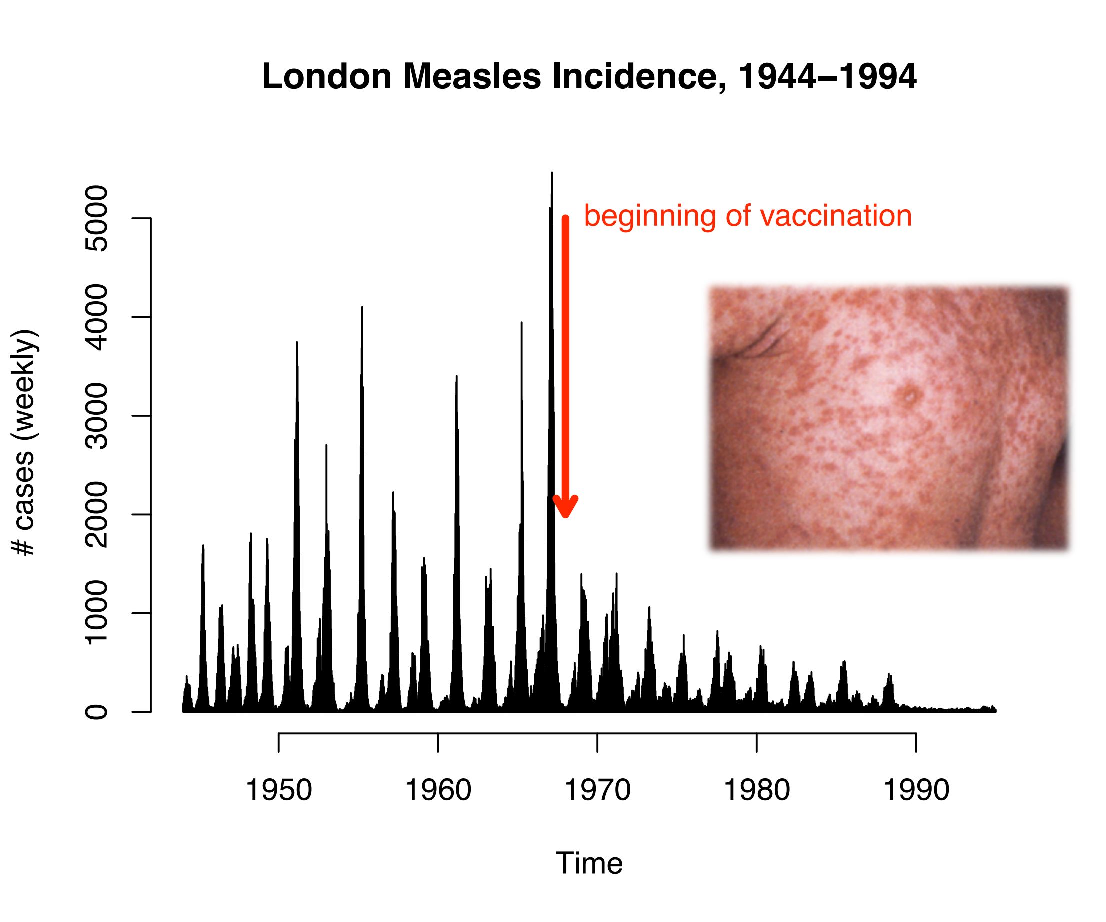


$$R_{eff}(t) = R_0 \frac{S(t)}{N}$$

$$R_{eff}(t) = \frac{\beta S(t)}{(\gamma + \mu)N}$$

Why do recurrent epidemics happen?

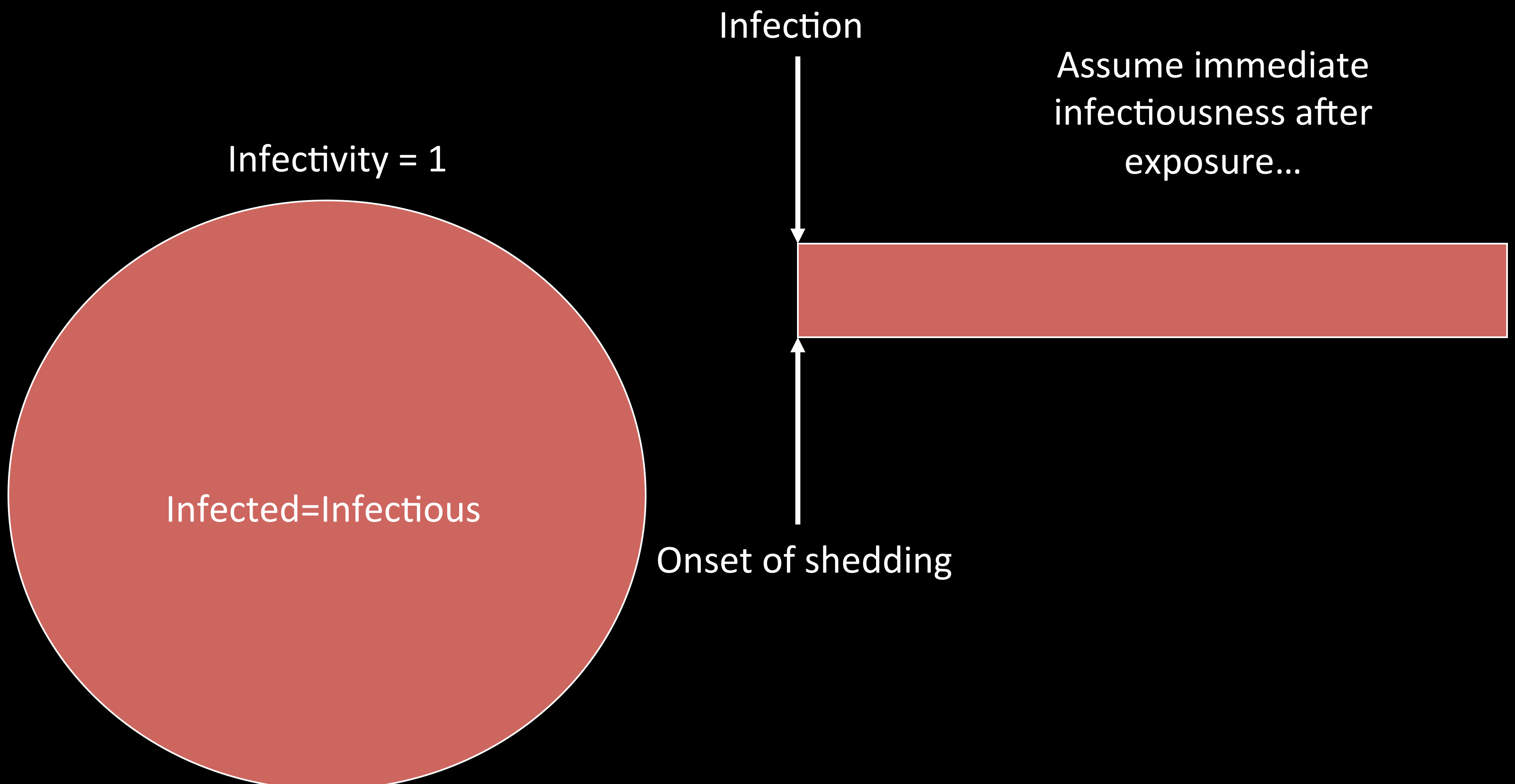
- Susceptibles exhausted from an epidemic
- Disease does not completely die out (or is reintroduced).
- Susceptibles replenished through birth or loss of immunity, epidemic occurs.



An extremely simple view of the world

Don't worry about symptoms and disease!

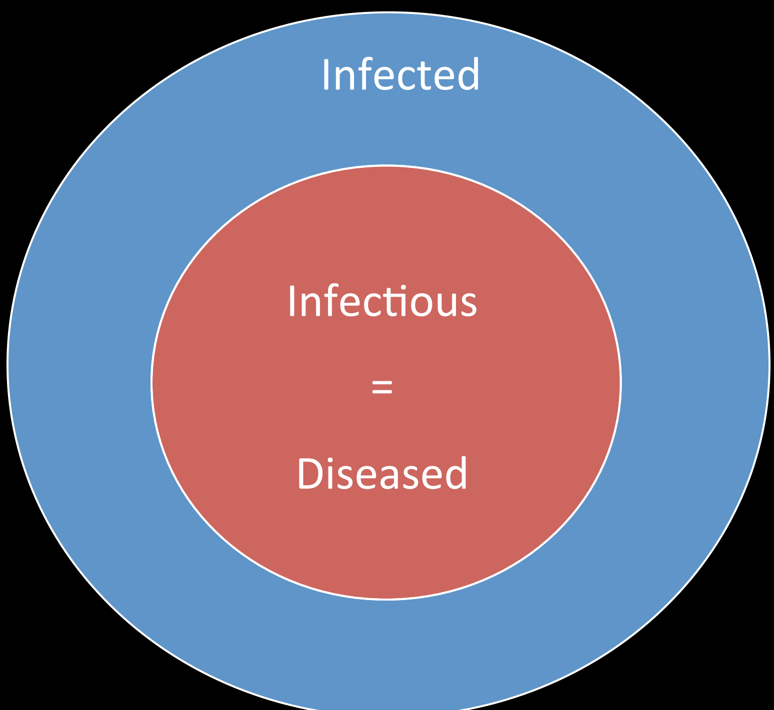
Assume immediate infectiousness after exposure…

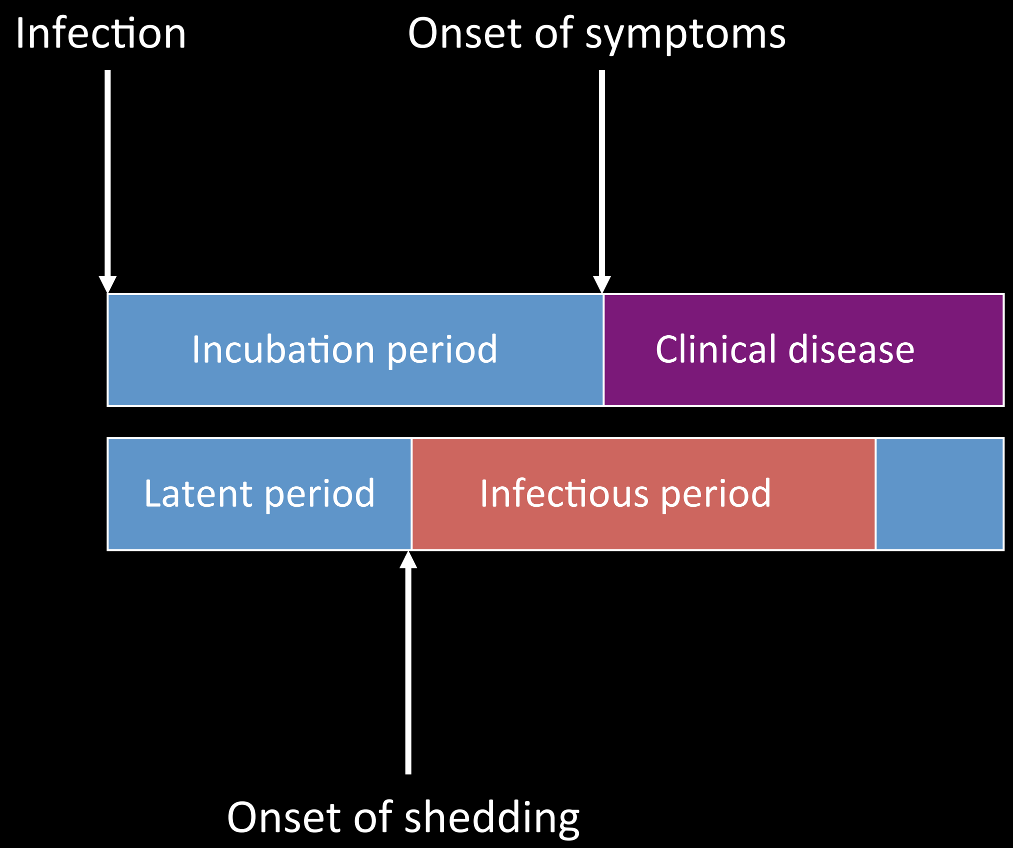


A slightly more realistic model

Infectivity = 1

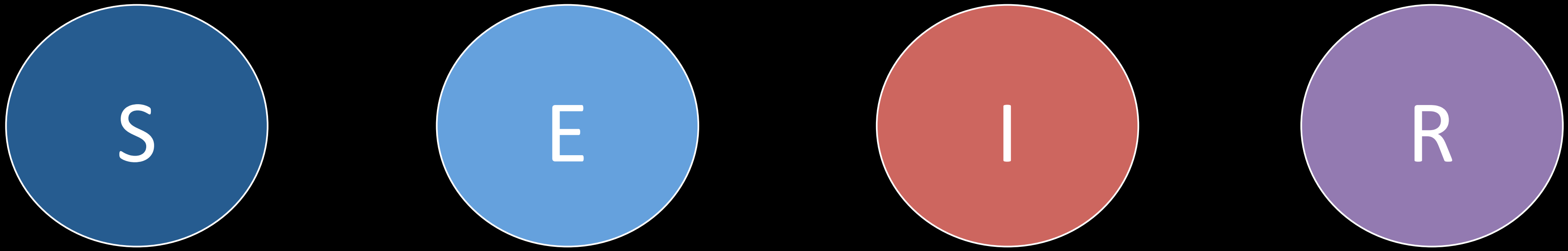
(everyone exposed becomes infected)



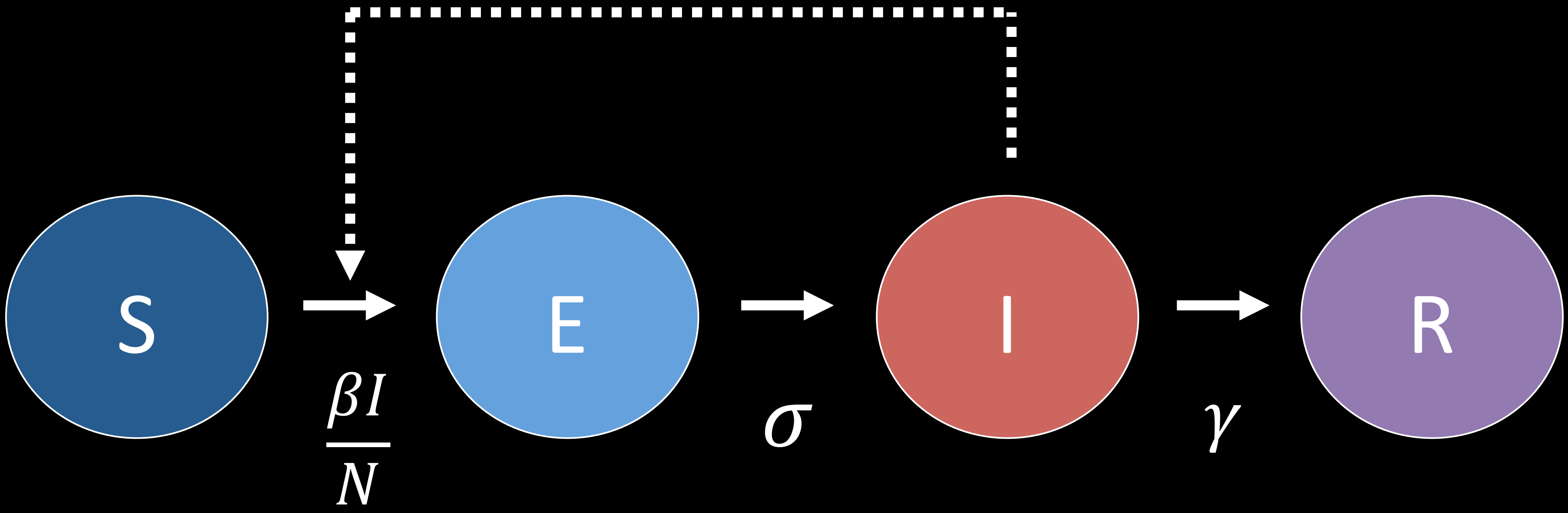


A slightly more realistic model

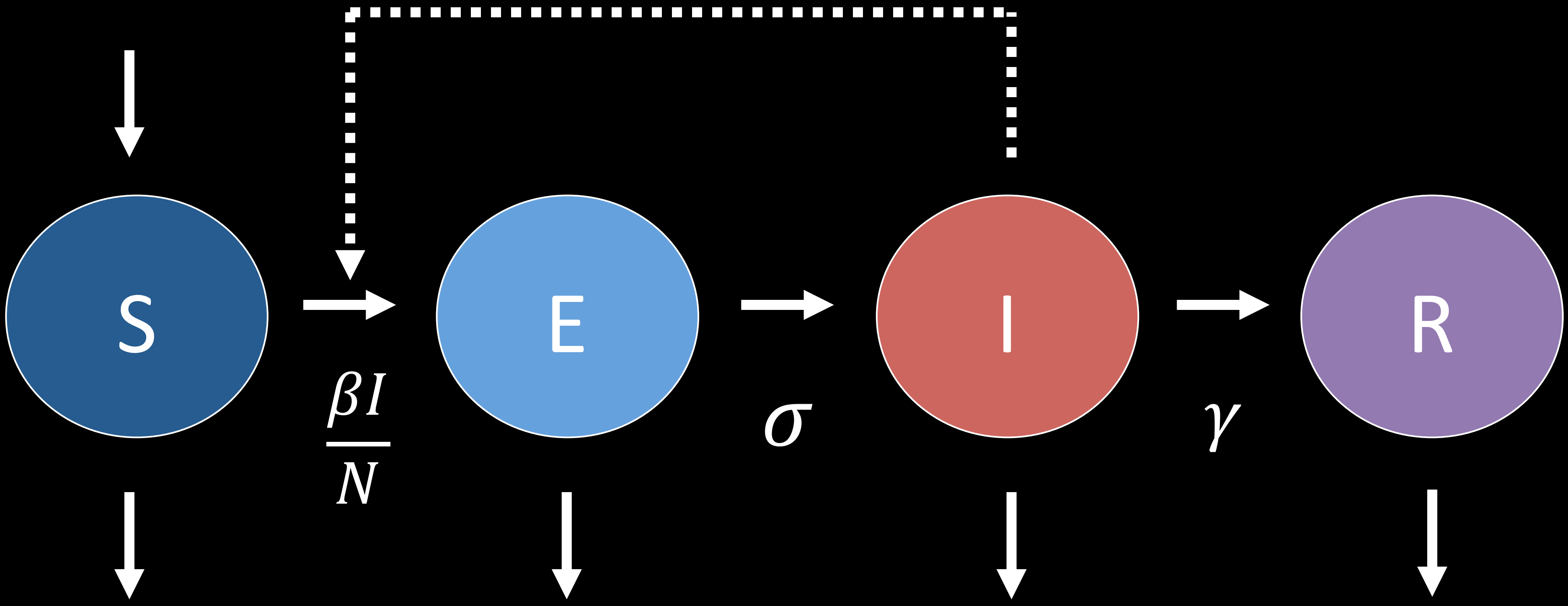
SEIR Model



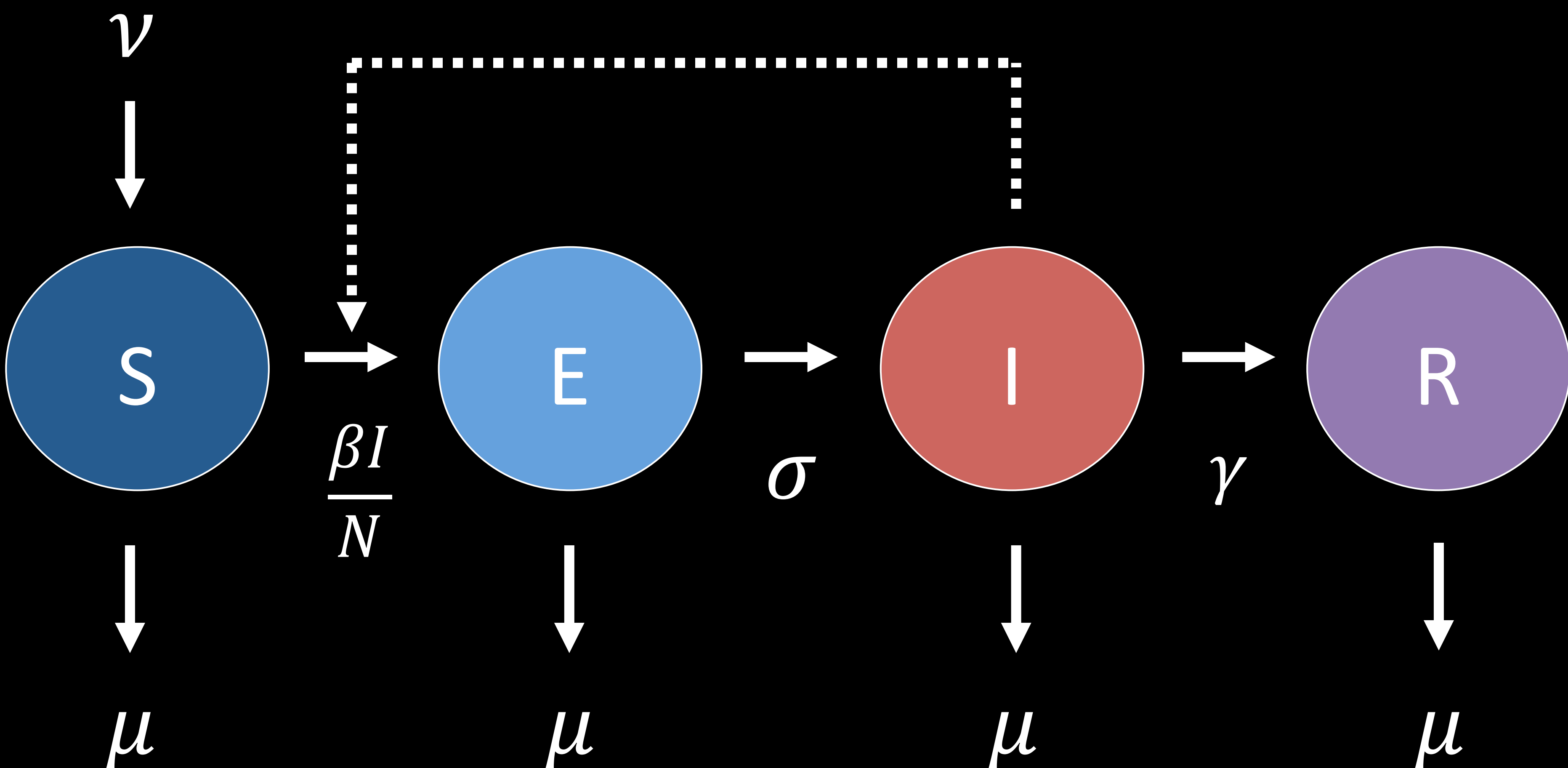
SEIR Model



SEIR Model



SEIR Model



SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

$$\frac{dE}{dt} = \frac{\beta SI}{N} - \sigma E - \mu E$$

$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I$$

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

ν	birth rate
μ	mortality rate
σ	1 / latent period
γ	1 / infectious period
β	transmission coefficient

SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

Assume constant population size

$$\frac{dE}{dt} = \frac{\beta SI}{N} - \sigma E - \mu E$$

$$\nu = \mu N$$

$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I$$

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

SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

$$\frac{dE}{dt} = \frac{\beta SI}{N} - \sigma E - \mu E$$

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

$R_0 =$

Rate at which an infected individual produces new infections in a naïve population

X

Proportion of new infections that become infectious

X

Average duration of infectiousness

SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

$$\frac{dE}{dt} = \frac{\beta SI}{N} - \sigma E - \mu E$$

$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I$$

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

$$R_0 = \beta \left(\frac{\sigma}{\mu + \sigma}\right)\left(\frac{1}{\mu + \gamma}\right)$$

SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

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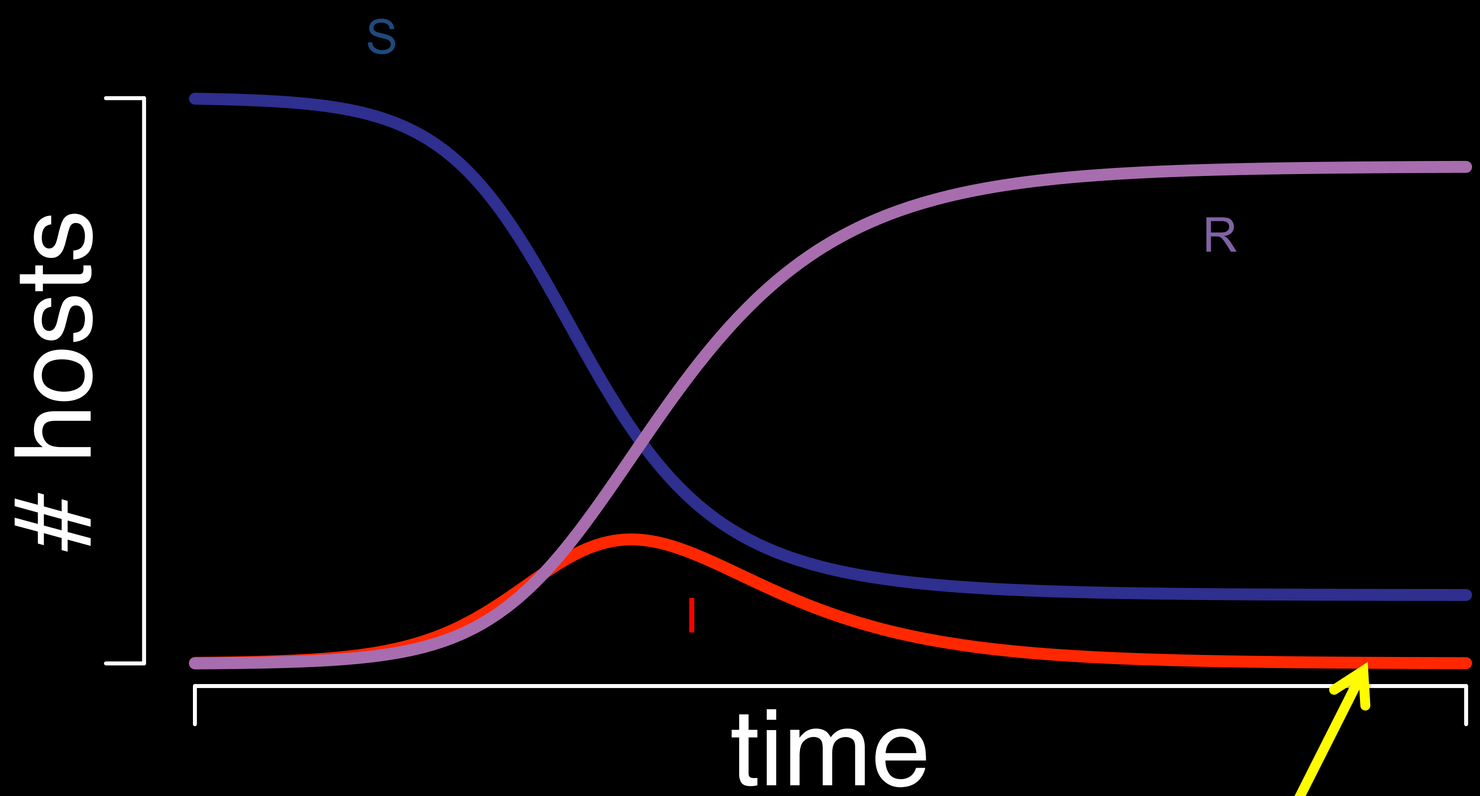
$$\frac{dR}{dt} = \gamma I - \mu R$$

Equilibria…

Disease free equilibrium

Endemic equilibrium

Back to the SIR:
When does a disease fade out?



In simple "SIR" models of epidemics, # of infected hosts never goes to zero… What allows a fadeout?

Fadeouts do occur!

- Critical Community Size
  The (≈) threshold population size at which a disease can persist.

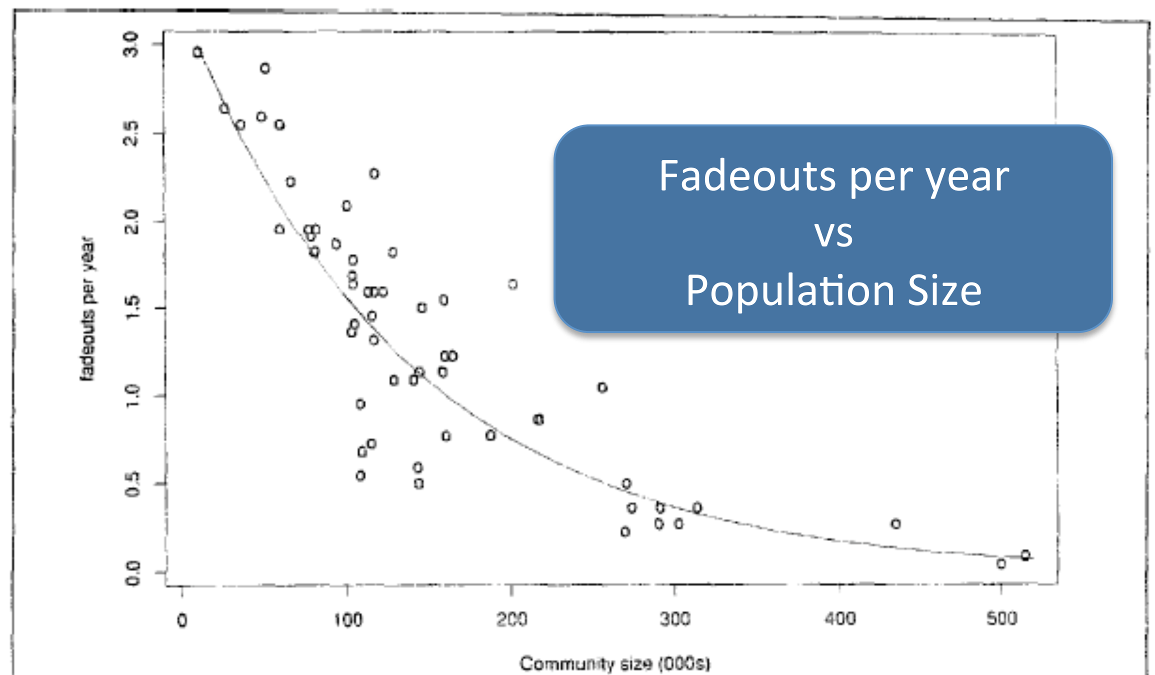
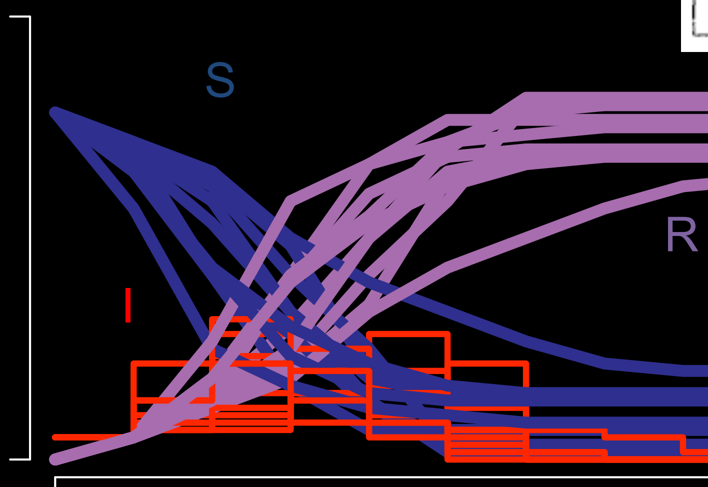


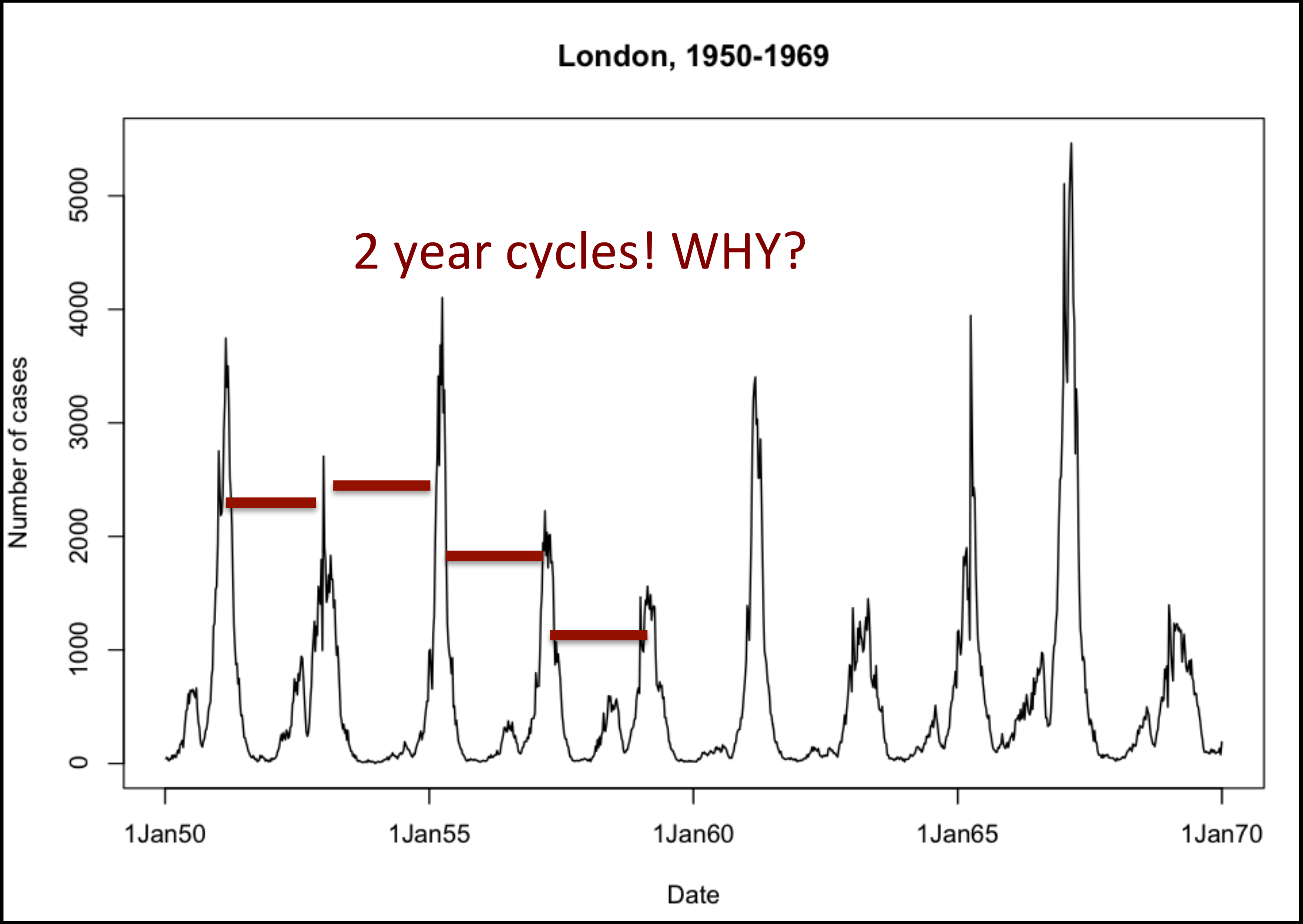
Fig. 1. Persistence of measles in 60 towns and cities in England and Wales in the pre-vaccination era (1944–67), as a function of population size in 1960. Persistence is measured inversely by the proportion of weeks with 'fade-outs' (three or more weeks without infection, to allow for under-notification of cases[34]). The curve is a simple least squares exponential fit. The figure clearly shows the CCS – a population threshold of 300–500 000 – above which measles persists.

Grenfell and Harwood, 1997



- Stochasticity in epidemic troughs causes disease fadeout in small populations.

What accounts for epidemic cycles?



Earn et al. 2000 *Science*

Seasonal SEIR Model

$$\frac{dS}{dt} = \nu - \frac{\beta SI}{N} - \mu S$$

$$\frac{dE}{dt} = \frac{\beta SI}{N} - \sigma E - \mu E$$

$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I$$

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

$\nu = \mu N$ individuals/year

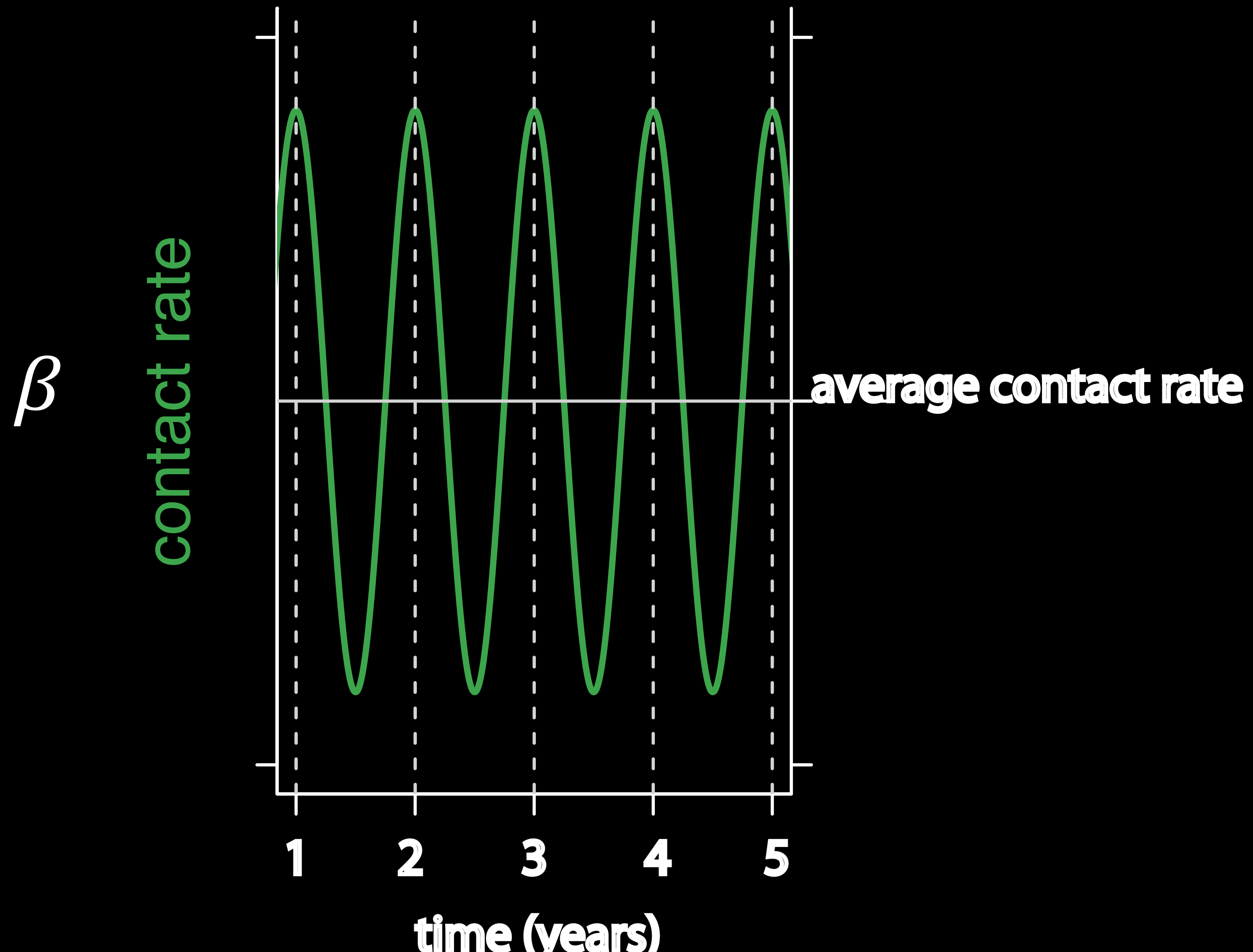
$\mu = 0.02$ years^{-1}

$\sigma = 1/8$ days^{-1}

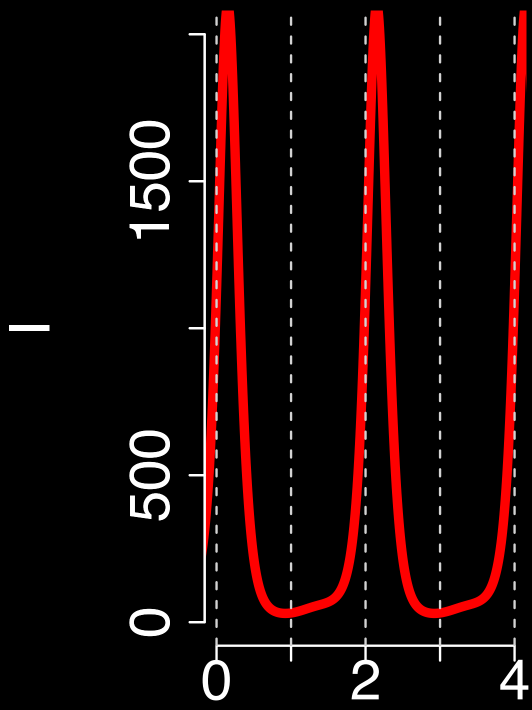
$\gamma = 1/5$ days^{-1}

β seasonal (school terms)

Seasonal SEIR Model

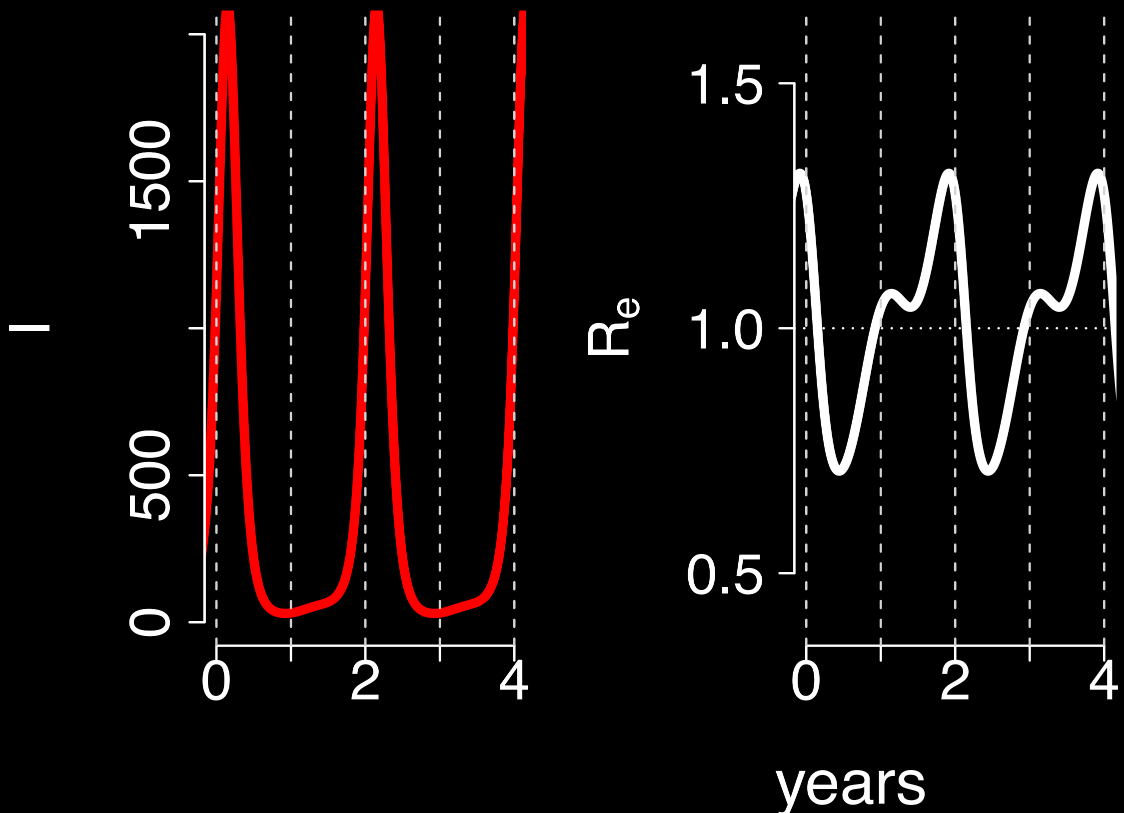


Susceptible Replenishment & Periodicity



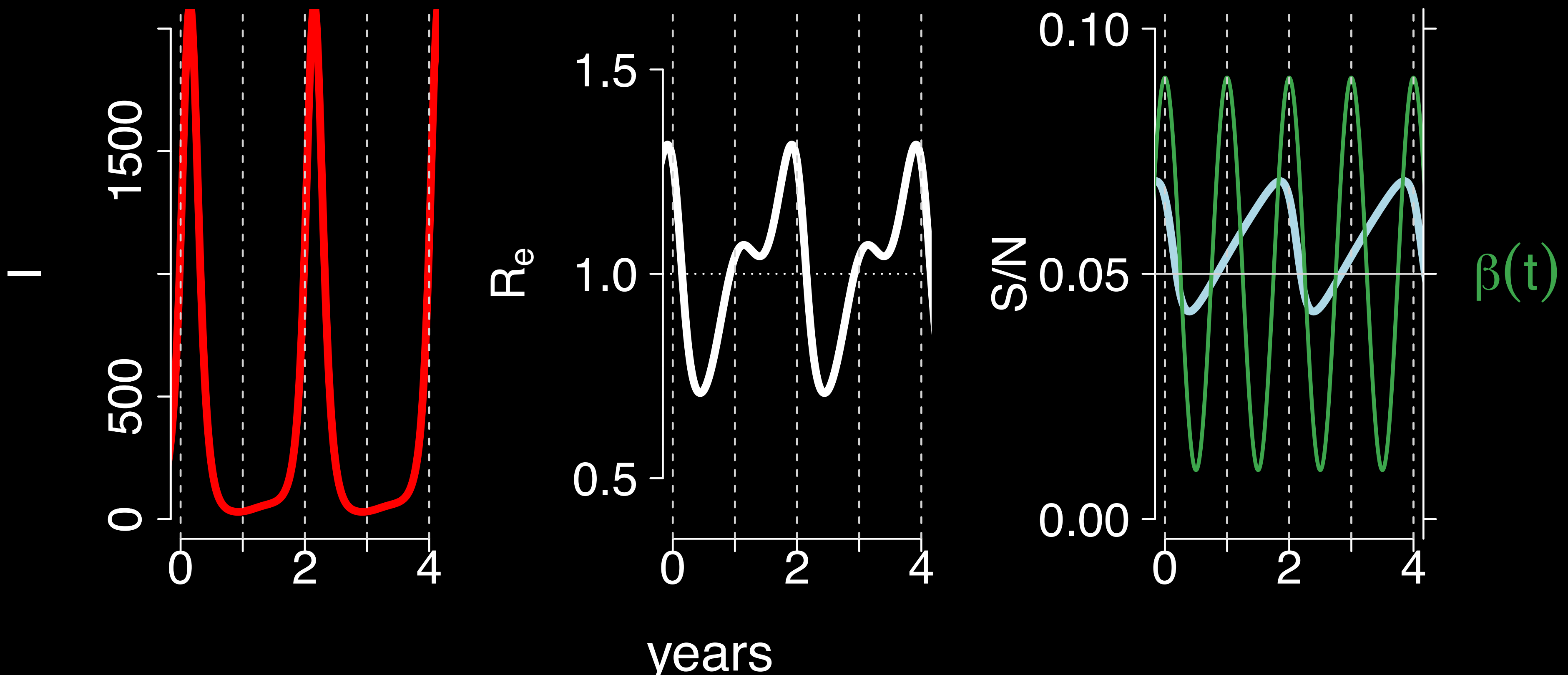
Life Expectancy of 40 years

Susceptible Replenishment & Periodicity



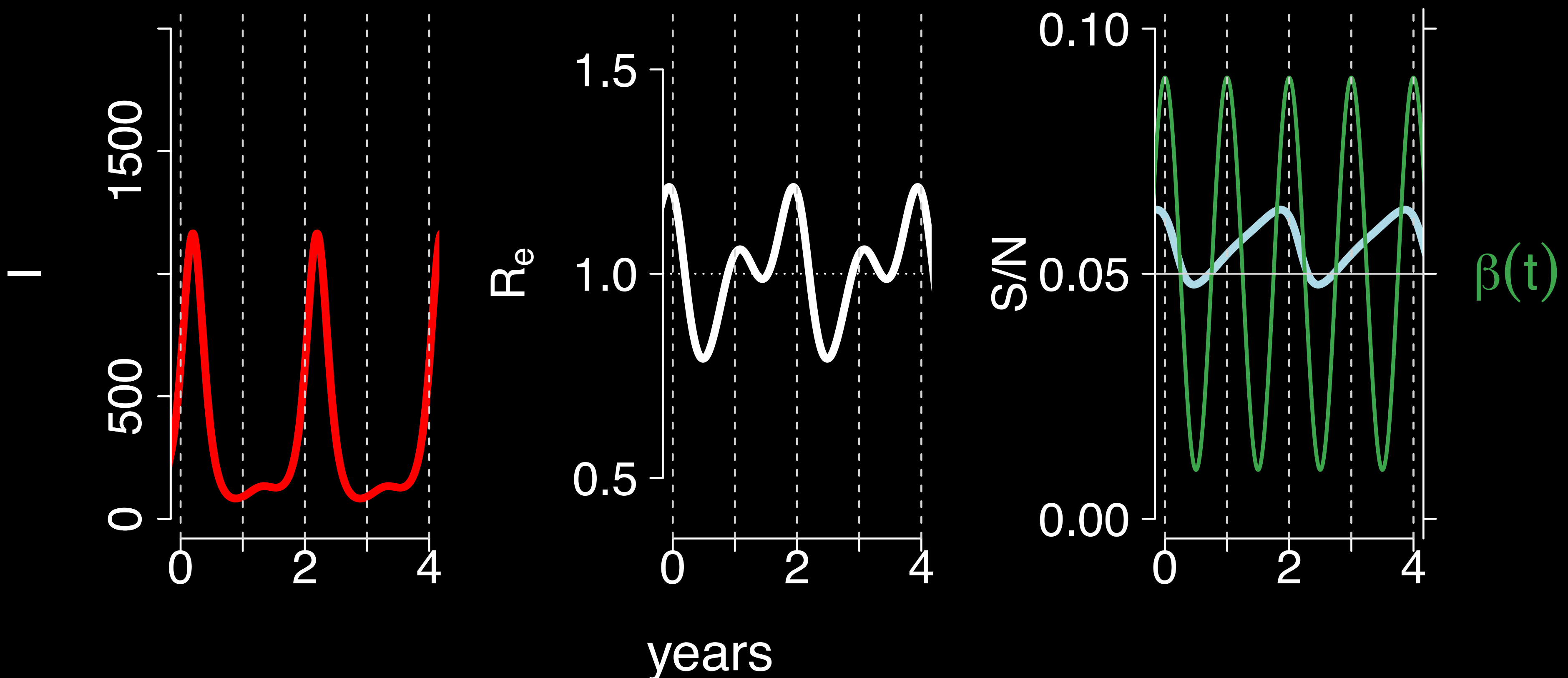
Life Expectancy of 40 years

Susceptible Replenishment & Periodicity



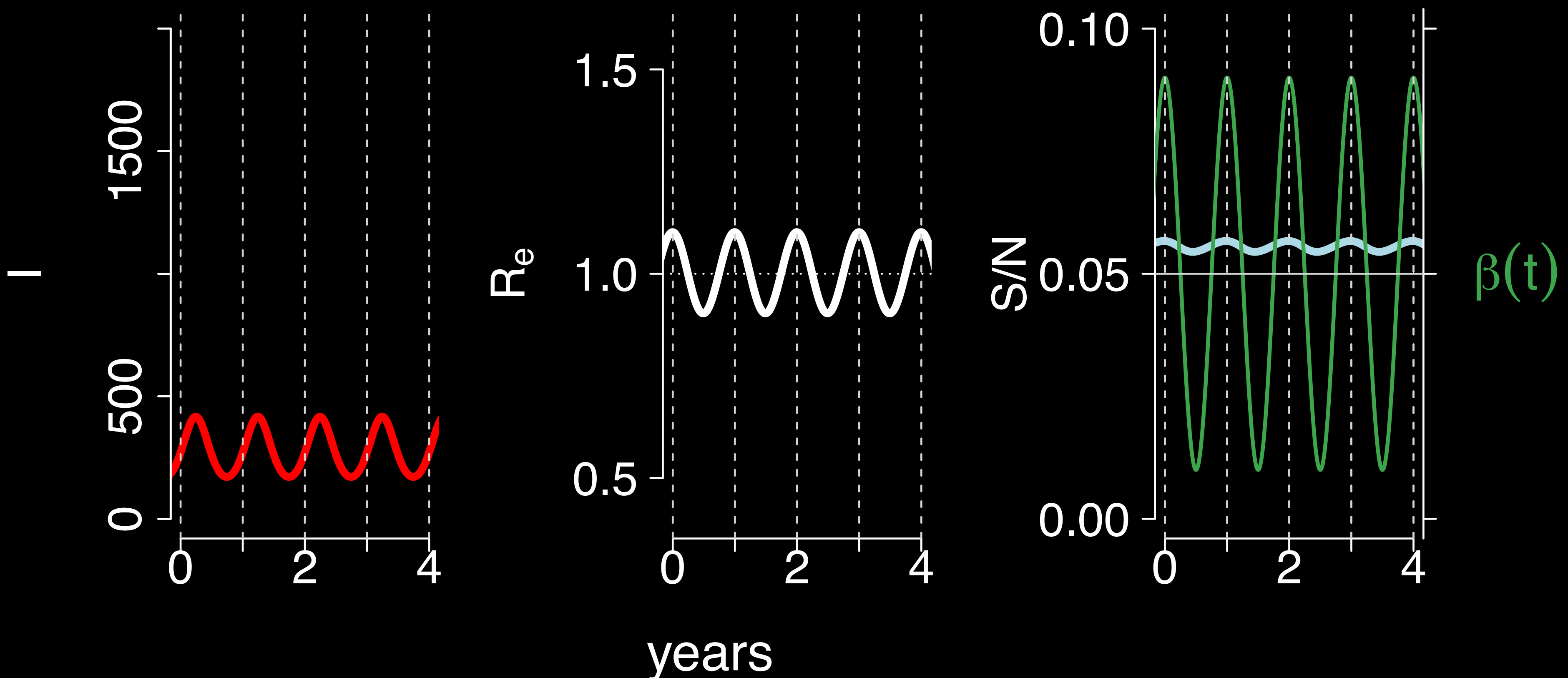
Life Expectancy of 40 years

Susceptible Replenishment & Periodicity



Life Expectancy of 50 years

Susceptible Replenishment & Periodicity



Life Expectancy of 60 years