with thanks to Dr. Steve Bellan and the Alachua County Control Flu Program.

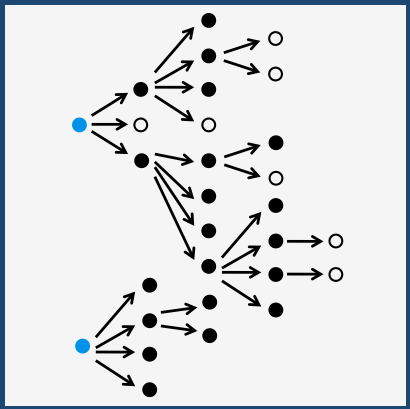
Title: Simplification for generalization 1 – Intuitive aspects of dynamics and introduction to model worlds

Attribution: Dr. Juliet Pulliam

For further information please contact Dr. Juliet Pulliam (pulliam@ufl.edu).

Simplification for Generalization 1:

intuitive aspects of dynamics and introduction to model worlds



Clinic on Dynamical Approaches to Infectious Disease Data

December 15, 2014

Juliet R.C. Pulliam, PhD

Department of Biology and Emerging Pathogens Institute

University of Florida

School-located Influenza Vaccination

<u>Alachua County Control Flu Program</u>

- Community-supported
- 2006/07; 2009-Present
- K-8th; Pre-K to 12th
- Live-attenuated vaccine at school
- Inactivated vaccine at provider
- 300 volunteers, 27 community partners
- Recognized by AMA/CDC & IOM

Slide courtesy of CH Tran

Alachua County Control Flu Program

Coverage

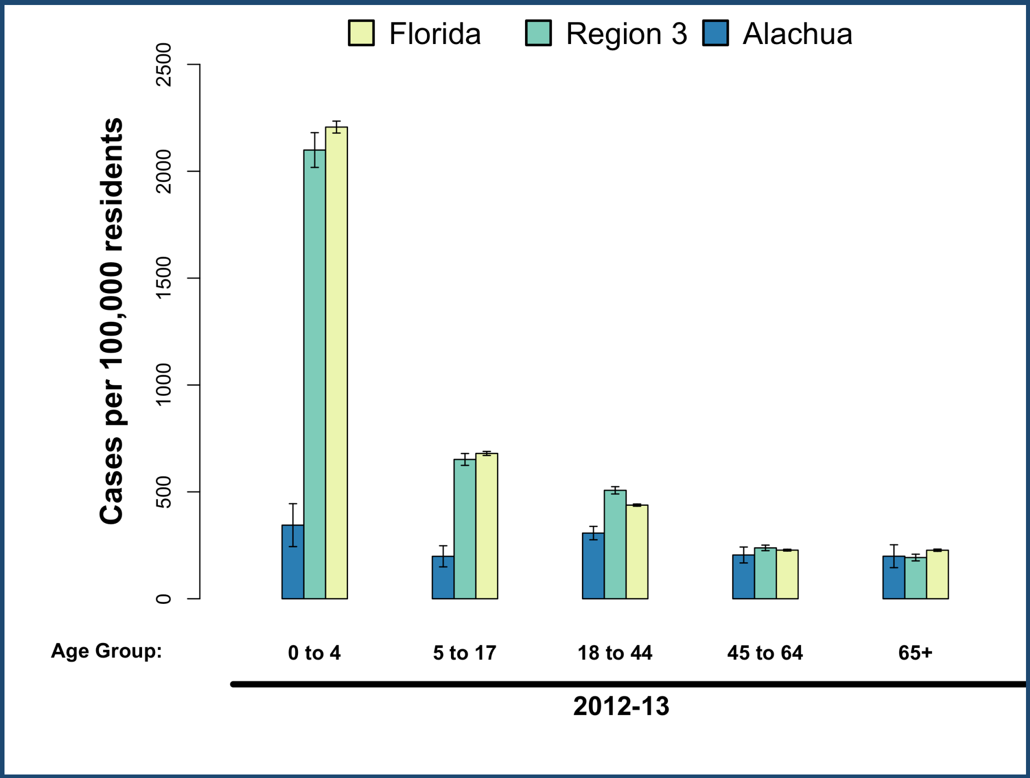
	8 States Averaged+	Alachua County						
	08/09	06/07	07/08	08/09	09/10	10/11	11/12	12/13
Preschool	~26%	-	-	-	12%	16%	16%	16%
Elementary	16%	>25%	-	-	67%	67%	63%	65%
Middle	13%	>24%	-	-	43%	41%	43%	49%
High	9%	-	-	-	6%	23%	24%	30%
School-Aged	-	>25%	-	-	42%	48%	47%	50% *(13,579)*

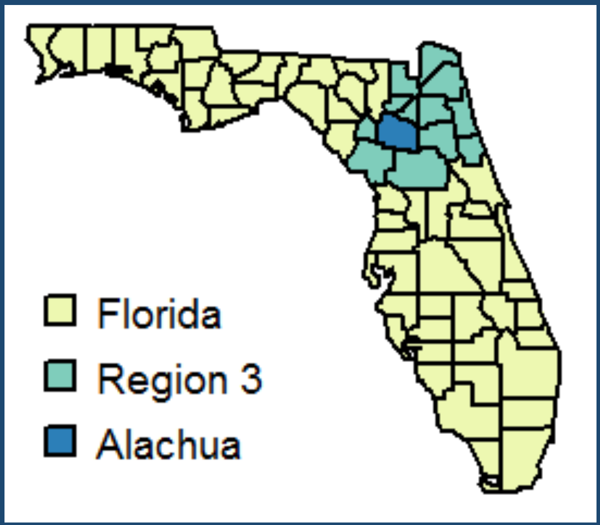
Slide courtesy of CH Tran

Alachua County Control Flu Program

Impact

2011-2012 season





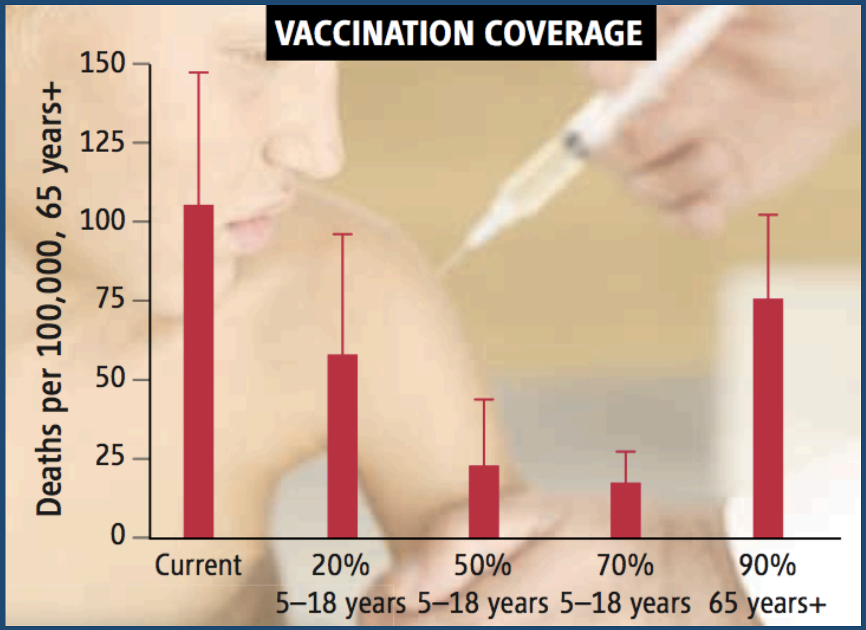
Tran *et al*. 2014

Alachua County Control Flu Program

Why did they think it would work?

Alachua County Control Flu Program

Why did they think it would work?

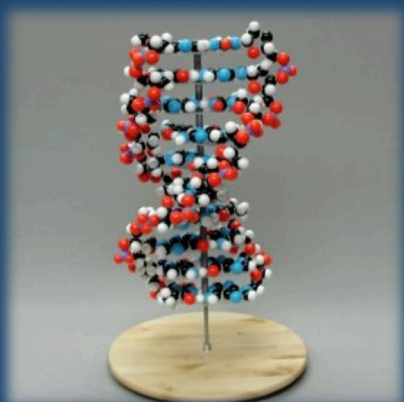


Halloran & Longini 2006 Science

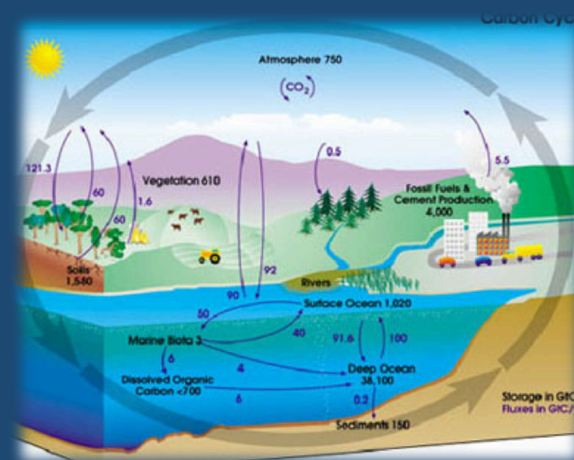
Model-based prediction…

What are models?

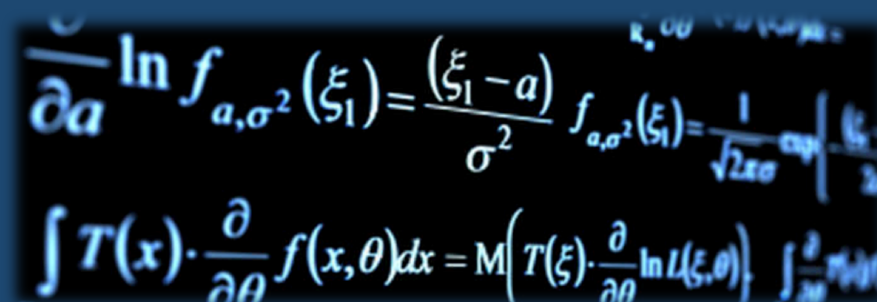
- Physical



- Conceptual



- Mathematical



What are dynamical models?

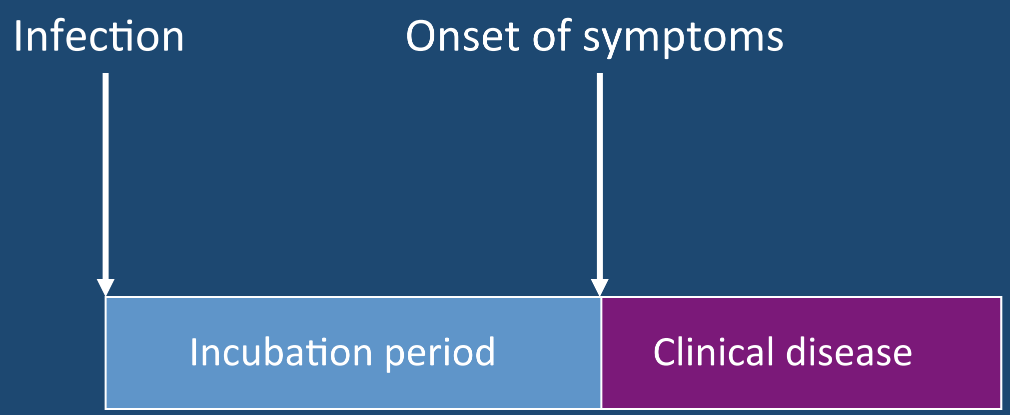
Statistical Models	Dynamical Models
• Account for bias and random error to find correlations that may imply causality.	• Systems Approach: Explicitly model multiple mechanisms to understand their interactions.
• Often the first step to assessing relationships.	• Link observed relationships at different scales.
• Assume independence of individuals (at some scale).	• Explicitly focus on dependence between individuals

Dynamical models

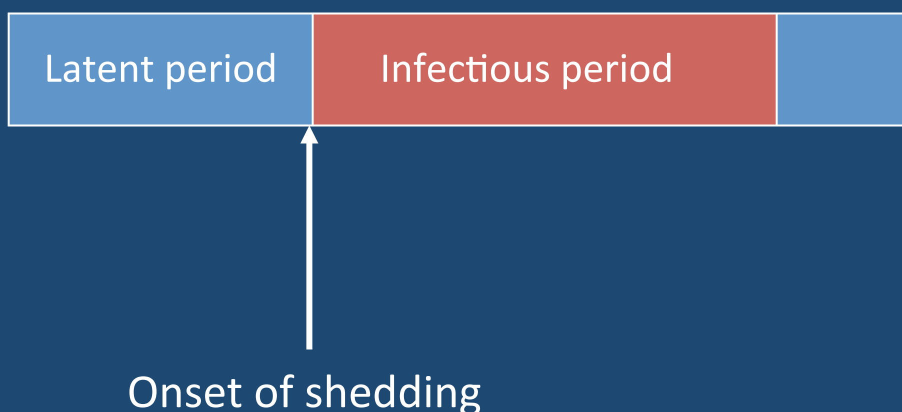
Explicitly account for the dependence between individual outcomes that is inherent in the transmission process for communicable diseases

Can be used to describe the evolution of a system through time – such as changes in disease incidence that result from the interaction between transmission and immunity

Natural History of Infection

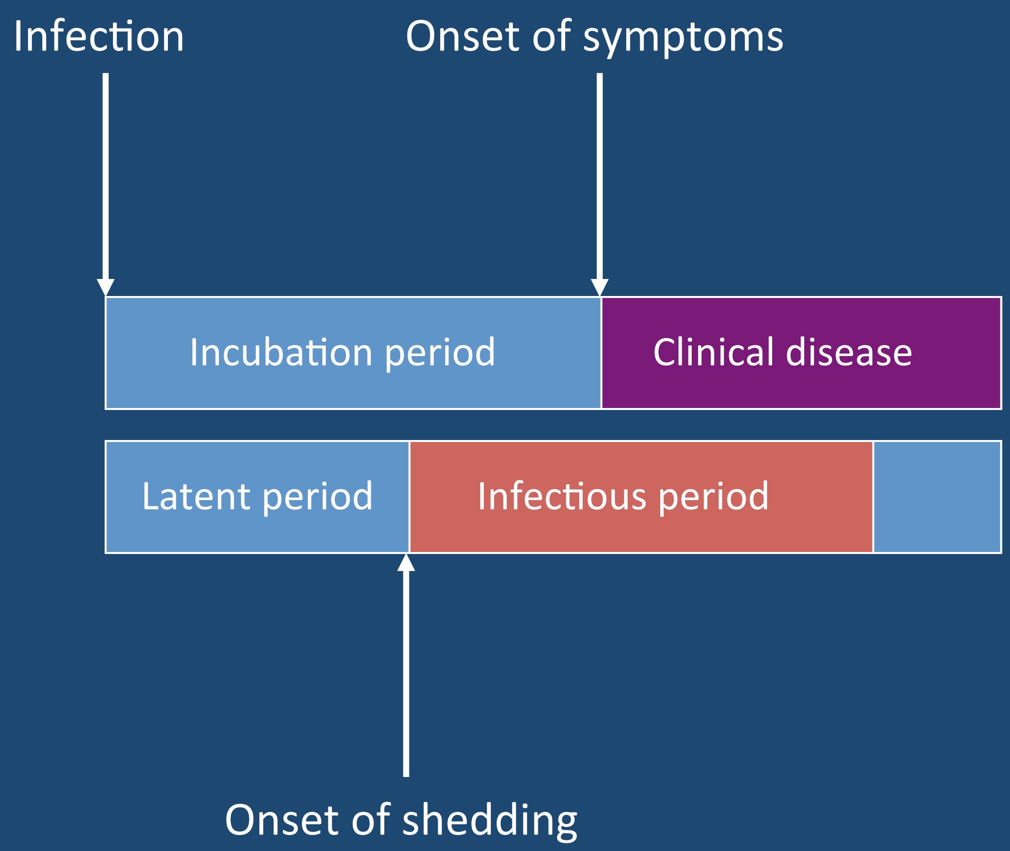


Natural History of Infection



Natural History of Infection

Acute, immunizing infections



<u>Acute</u>

Infection time course
<<<
host lifespan

<u>Immunizing</u>

infection → antibody production

prevents future infection

Examples

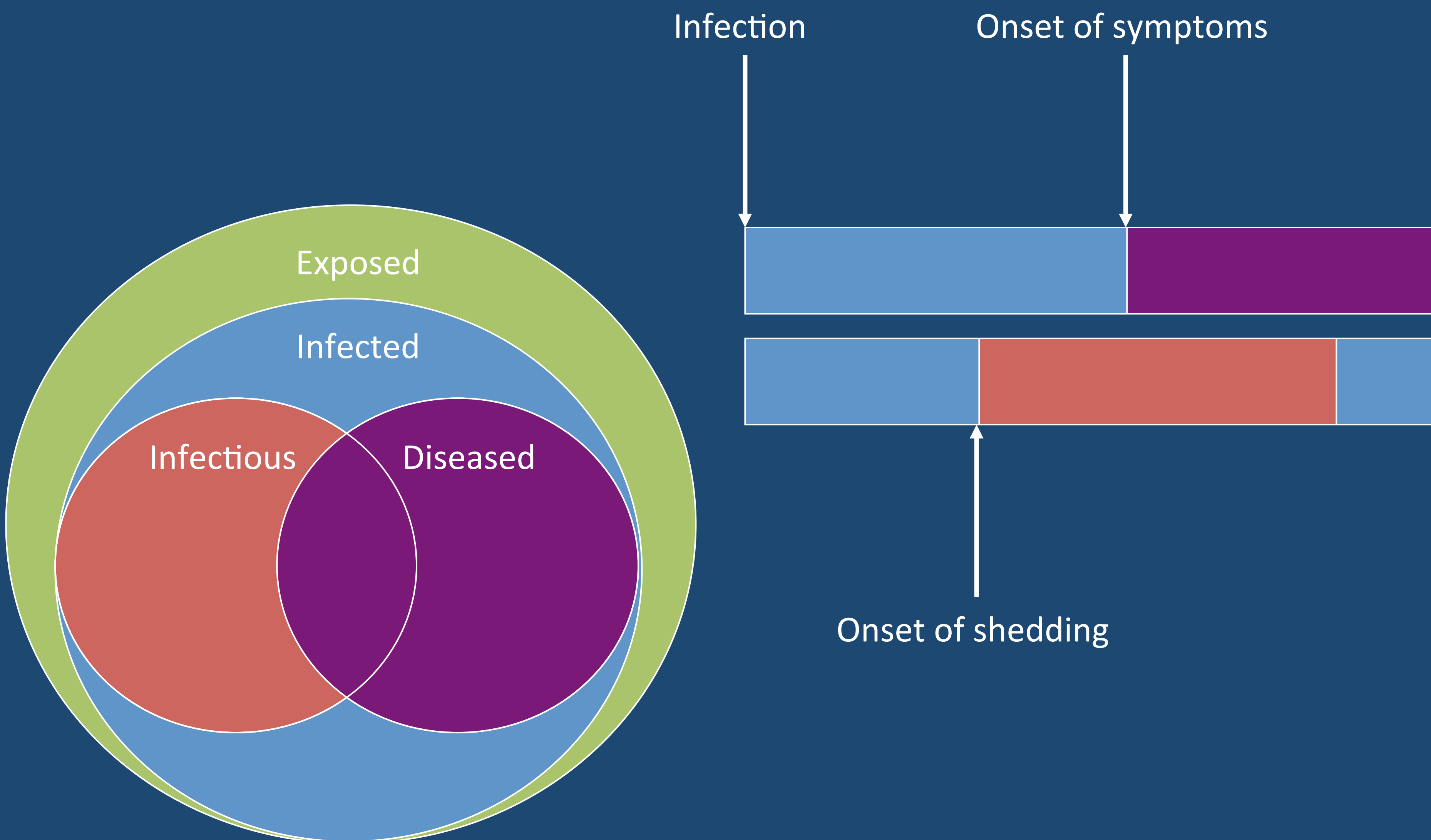
Natural History of Infection

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)

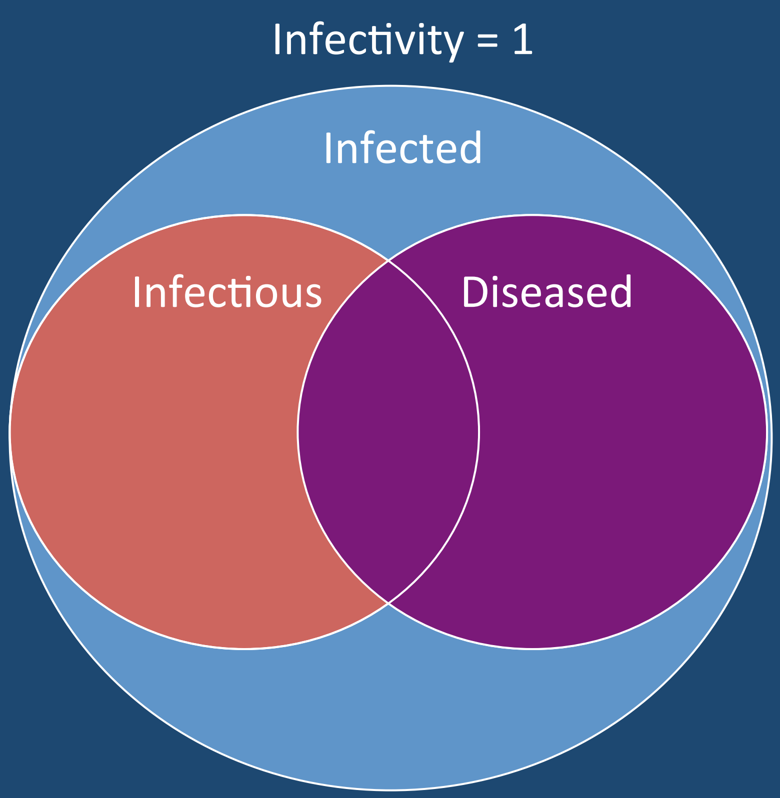
Infectious disease	Incubation period	Latent period	Infectious period
Measles	8–13	6–9	6–7
Mumps	12–26	12–18	4–8
Whooping cough (pertussis)	6–10	21–23	7–10
Rubella	14–21	7–14	11–12
Diphtheria	2–5	14–21	2–5
Chicken pox	13–17	8–12	10–11
Hepatitis B	30–80	13–17	19–22
Poliomyelitis	7–12	1–3	14–20
Influenza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

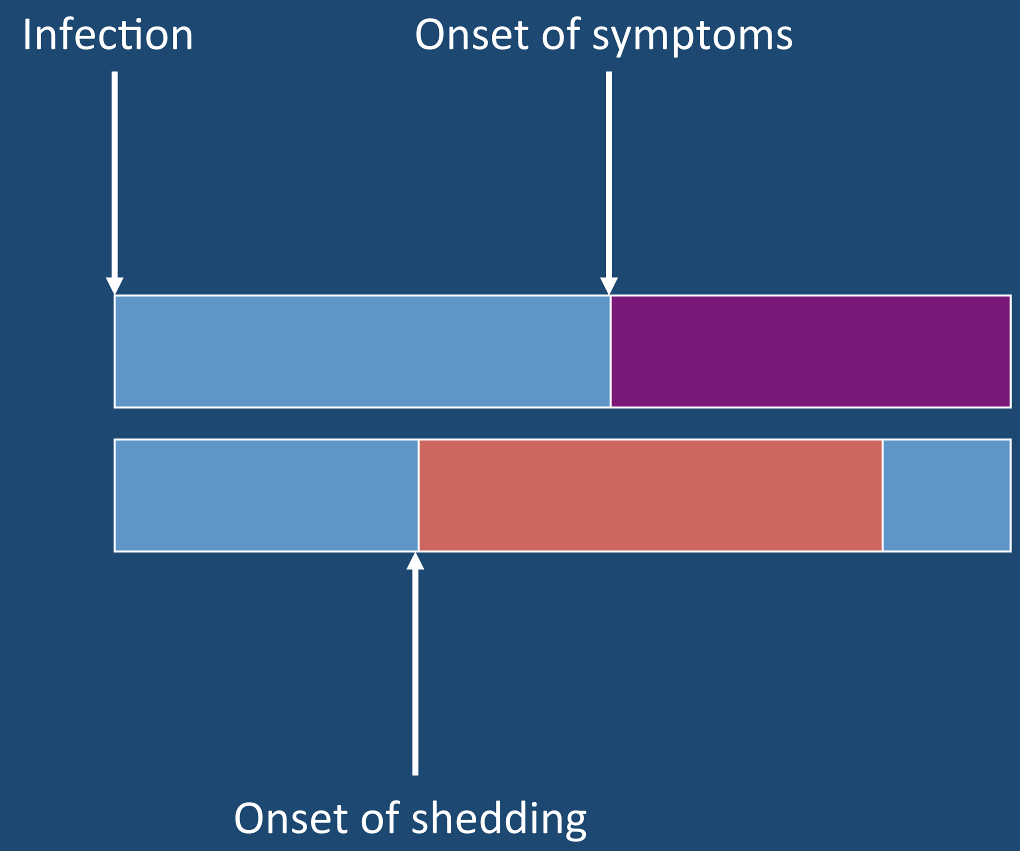
Anderson and May 1982 Science

Terminology



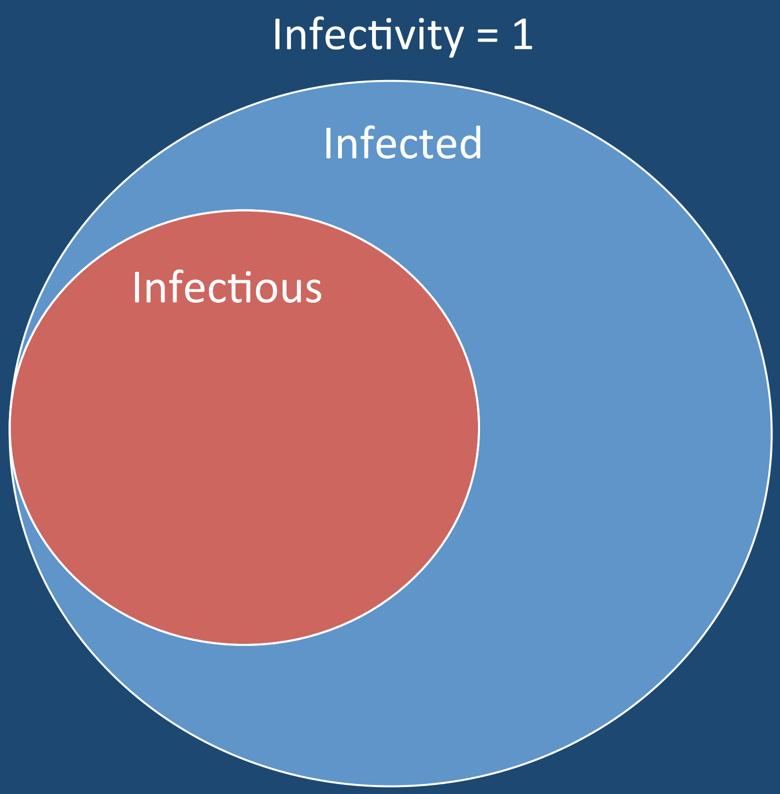
A simple view of the world

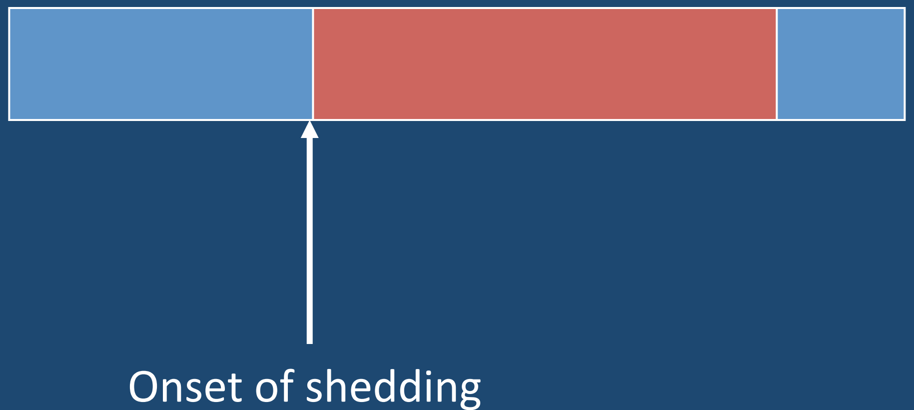




A simpler view of the world

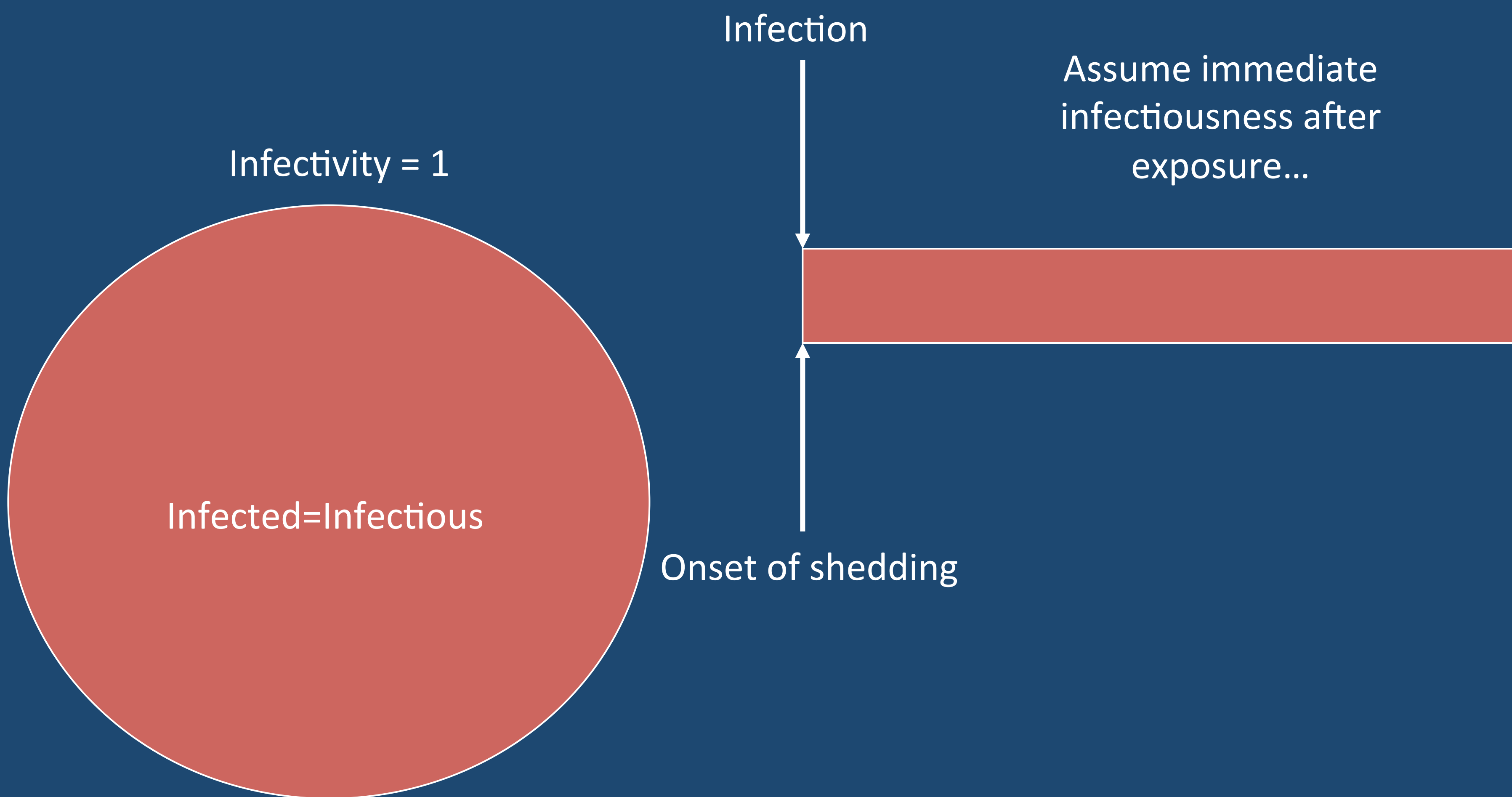
Don't worry about symptoms and disease!



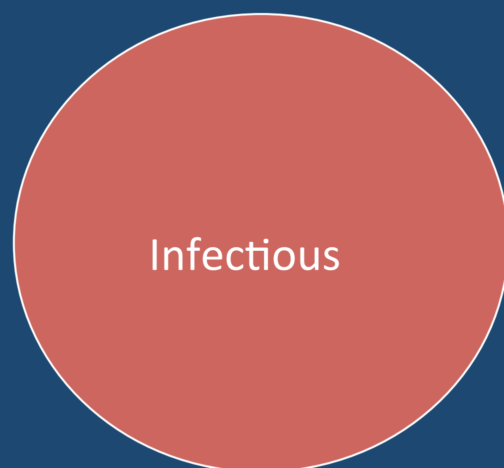


An extremely simple view of the world

Don't worry about symptoms and disease!



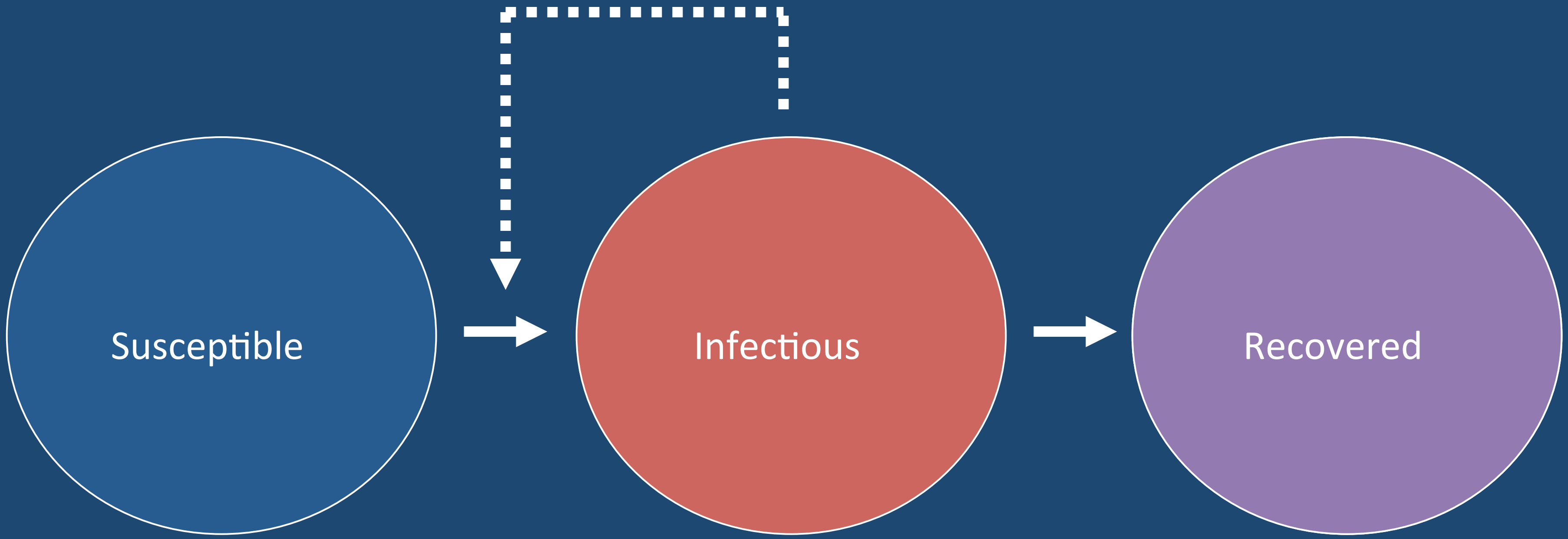
An extremely simple view of the world



An extremely simple view of the world

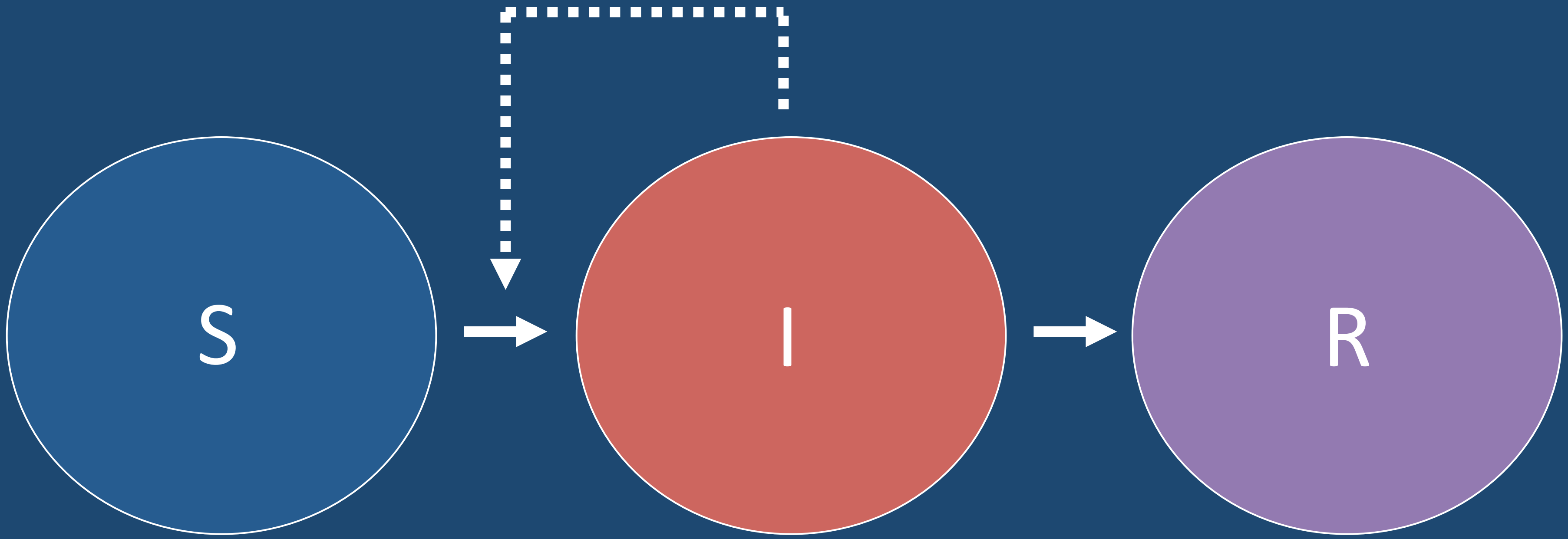
An extremely simple view of the world

Health-related States

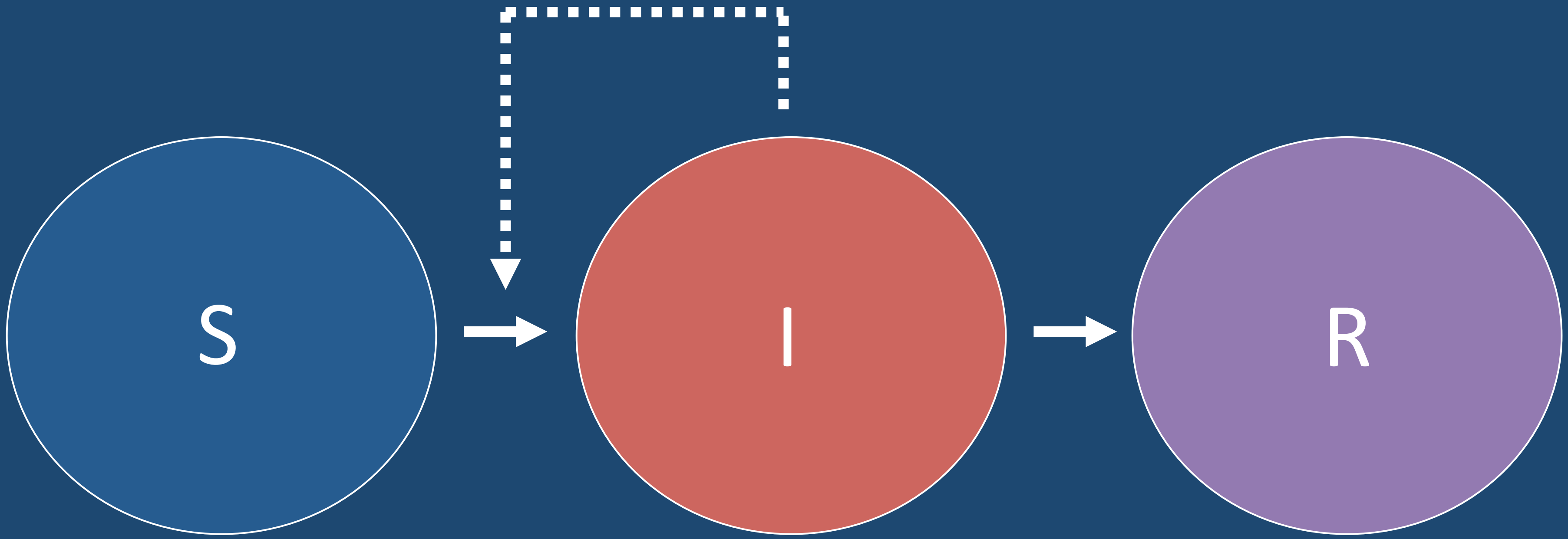


The rate at which susceptible individuals become infected depends on how many infectious people are in the population

State variables

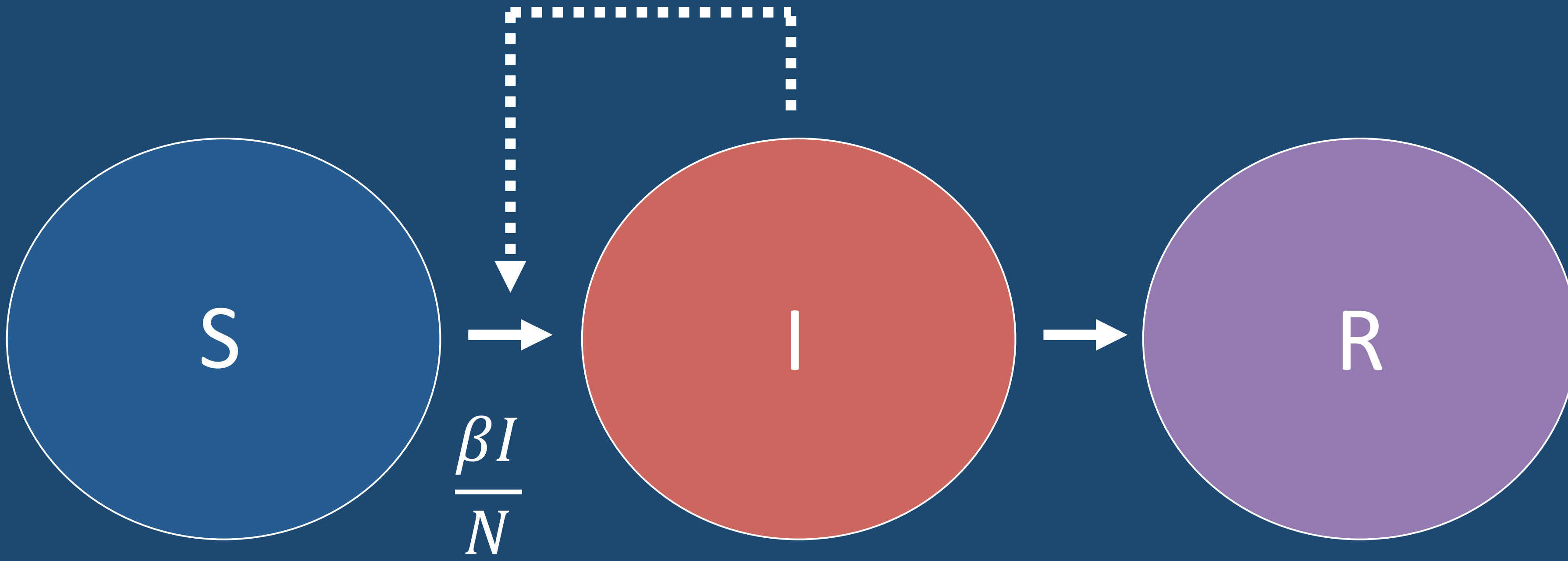


State variables



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

SIR Model



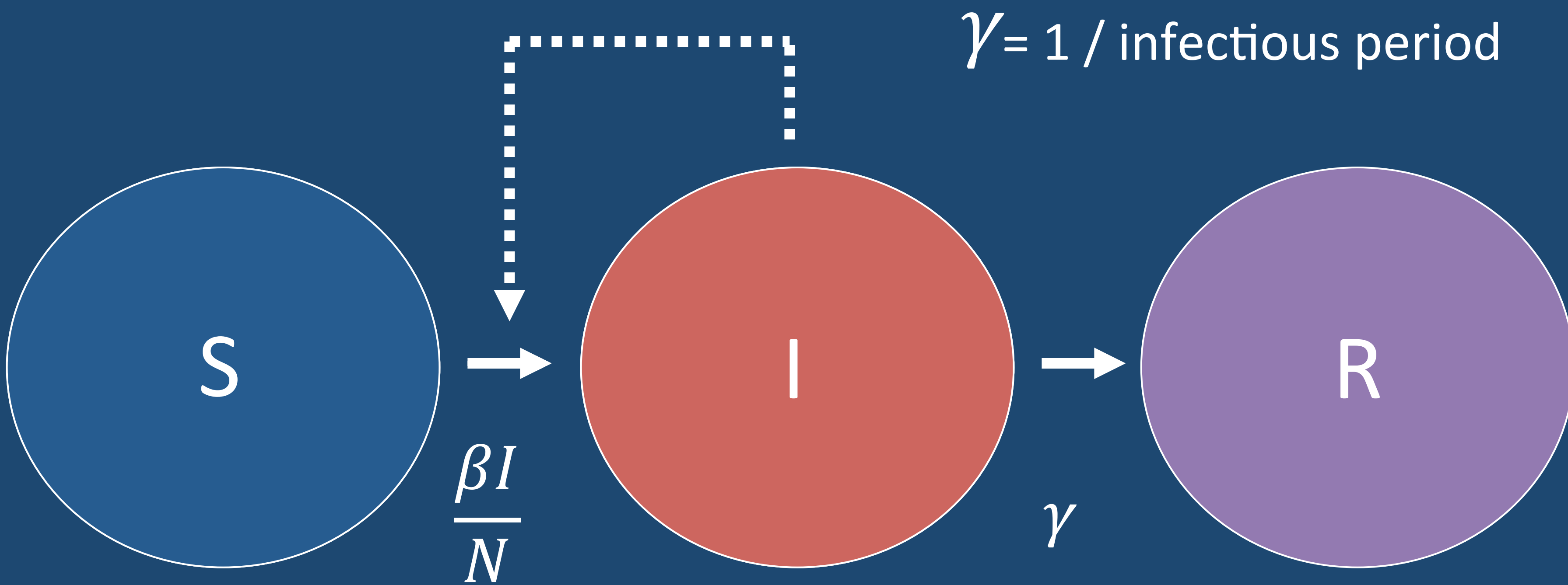
β = transmission coefficient

= per capita contact rate * infectivity

= per capita contact rate (infectivity = 1)

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

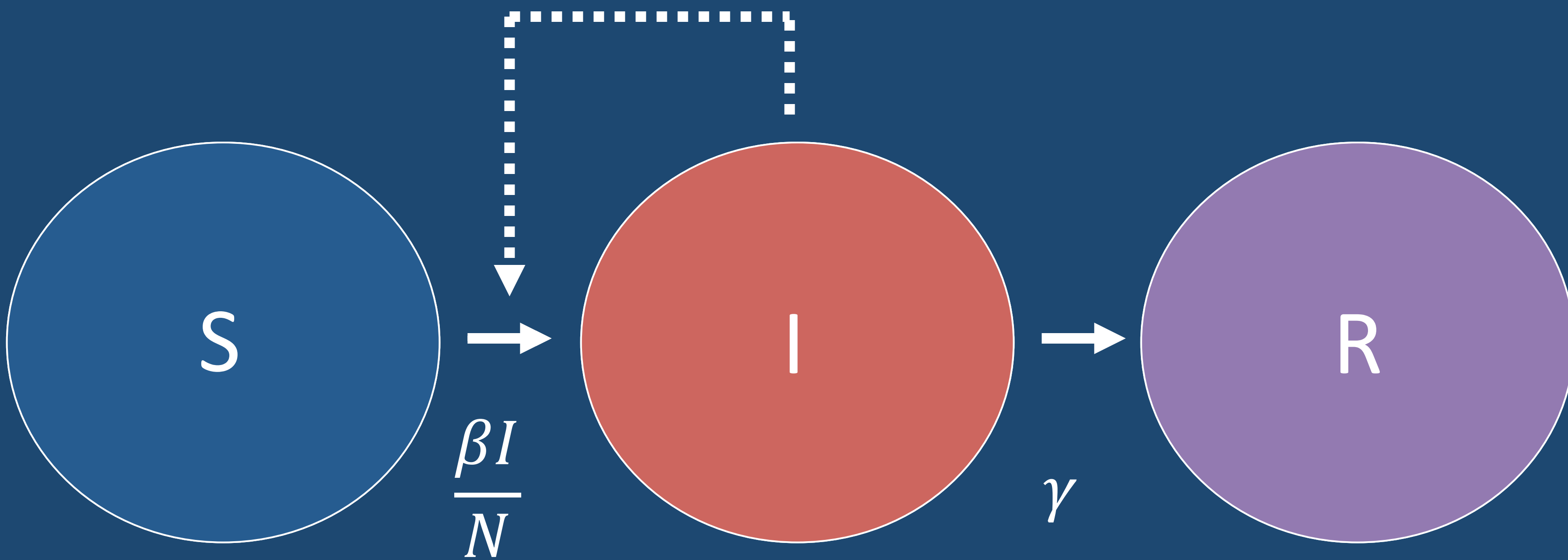
SIR Model



If infectious people recover at a rate of 0.5 / day,

the average time they spend infectious is 1 / 0.5 = 2 days

SIR Model

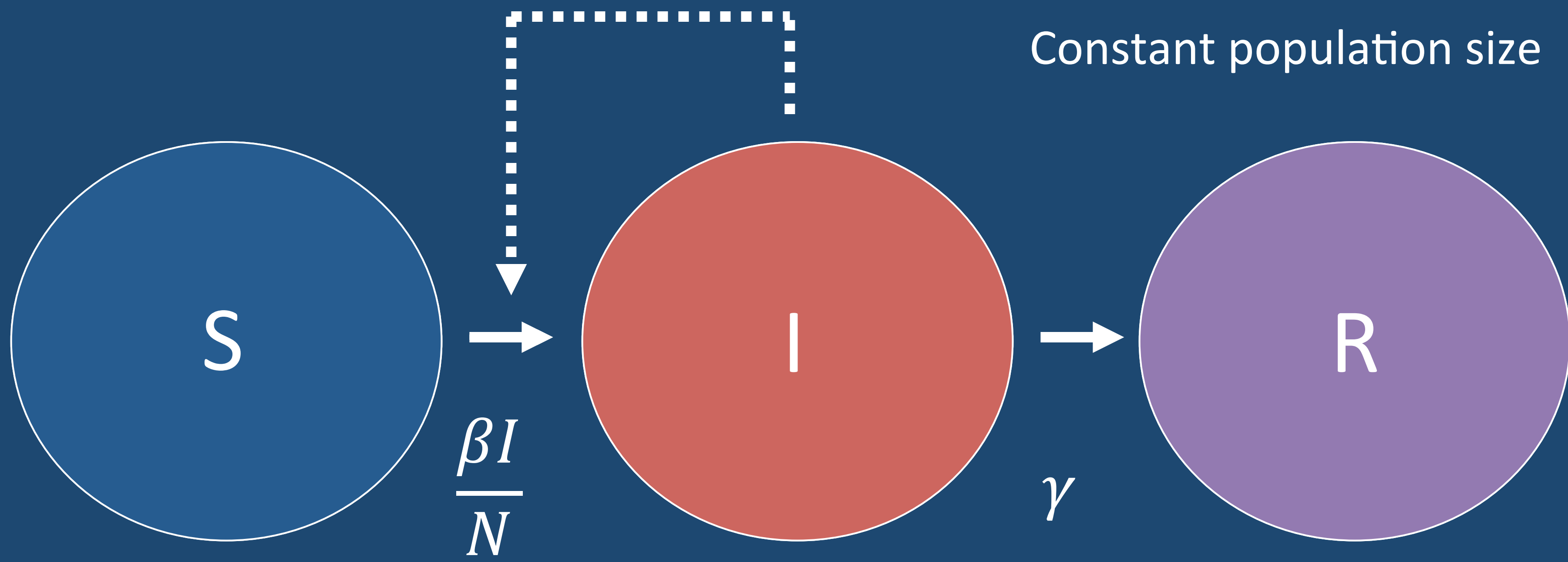


$$\frac{dS}{dt} = -\frac{\beta SI}{N} \qquad \frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I \qquad \frac{dR}{dt} = \gamma I$$

SIR Model

$$N = S + I + R$$

Constant population size



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

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

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

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

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

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

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

$R_0 =$

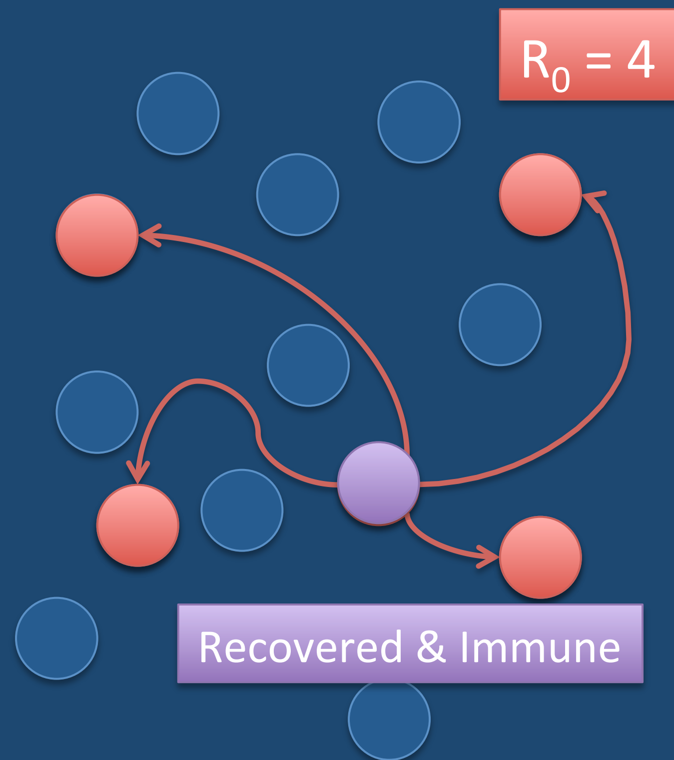
infections produced by

1 infectious individual

in a fully susceptible population.

R_0: The Basic Reproductive Number

Average # of secondary infections an infected host produces in a population with no pre-existing immunity



SIR Model

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

$$1$$

$$1/\gamma$$

$R_0 =$

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

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

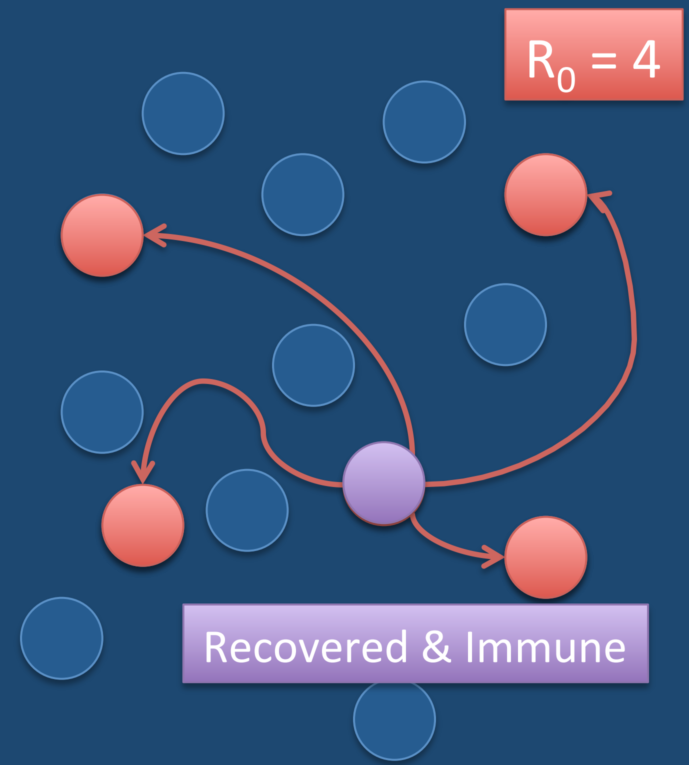
R_0: The Basic Reproductive Number

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

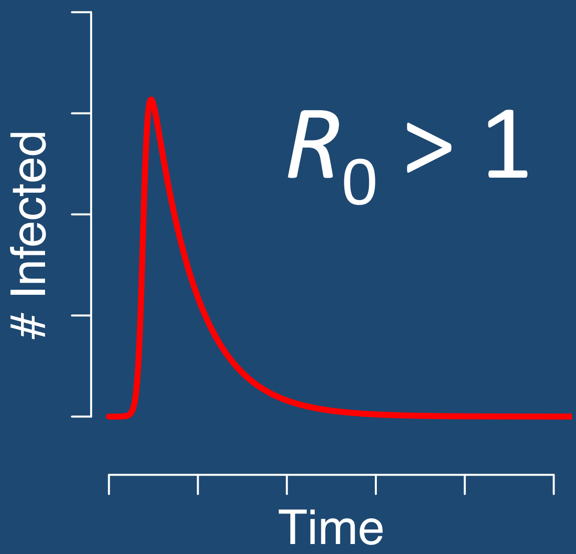
- Threshold criteria:

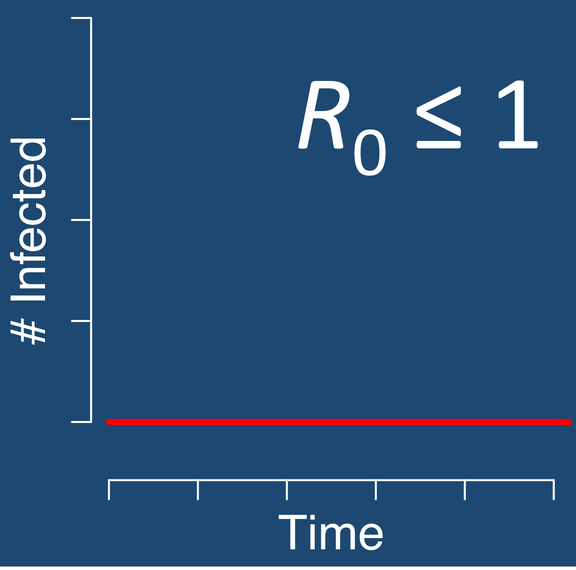
  If $R_0 < 1$, disease dies out

  If $R_0 > 1$, disease persists



SIR Model: R_0 as a Threshold





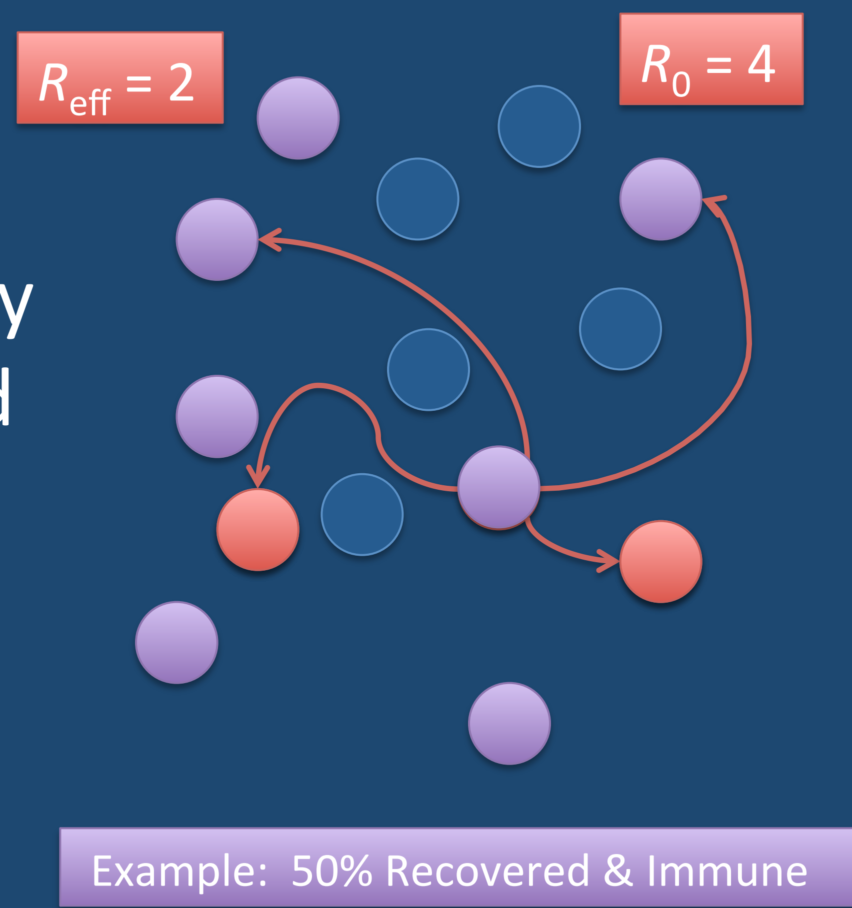
$$R_0 = \frac{\beta}{\gamma}$$

Disease Introduction:

Epidemic occurs if $R_0 > 1$.

R_{eff}: The Effective Reproductive Number

The average # of secondary infections that an infected host produces in a population



R_{eff}: Effective Reproductive Number

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

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

X

$$1$$

Proportion of new infections that become infectious

X

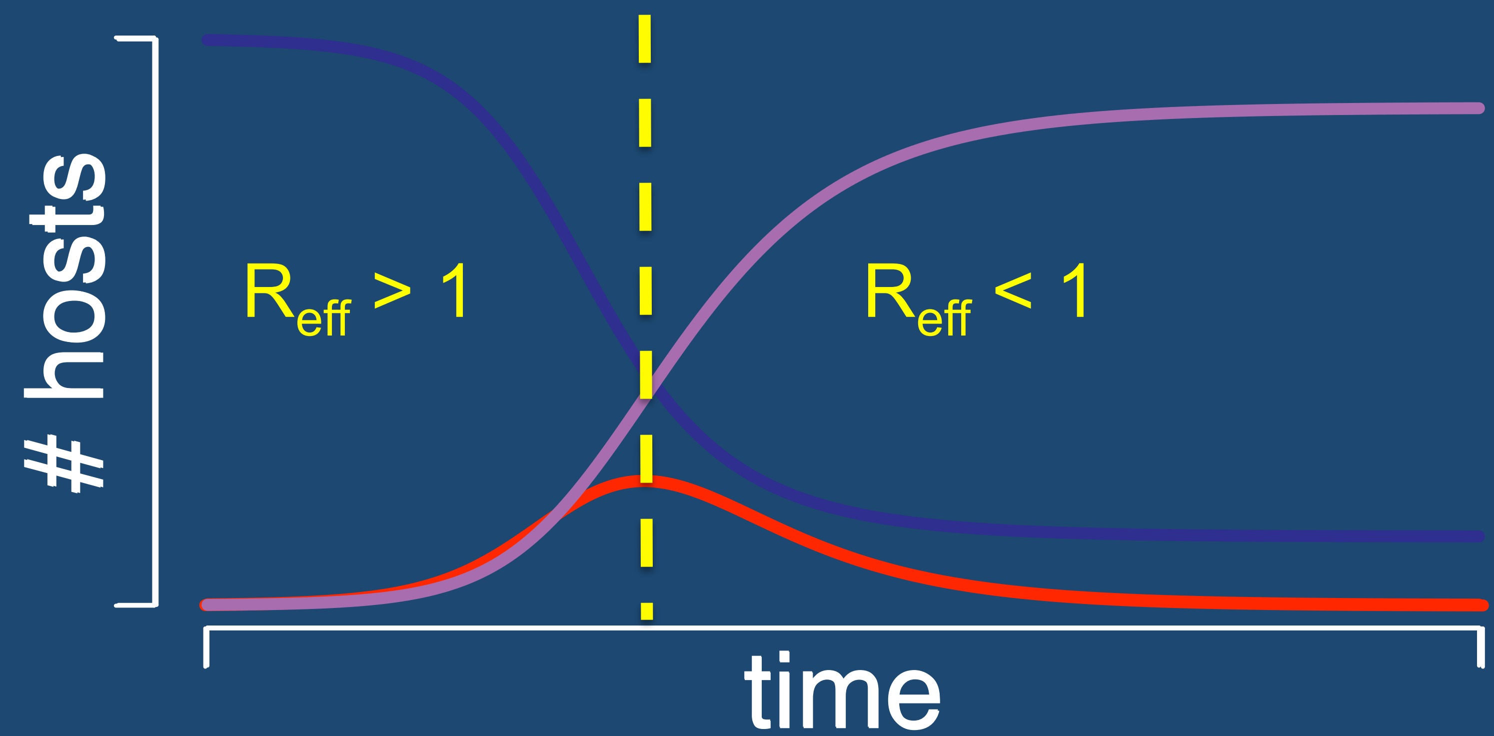
$$1/\gamma$$

Average duration of infectiousness

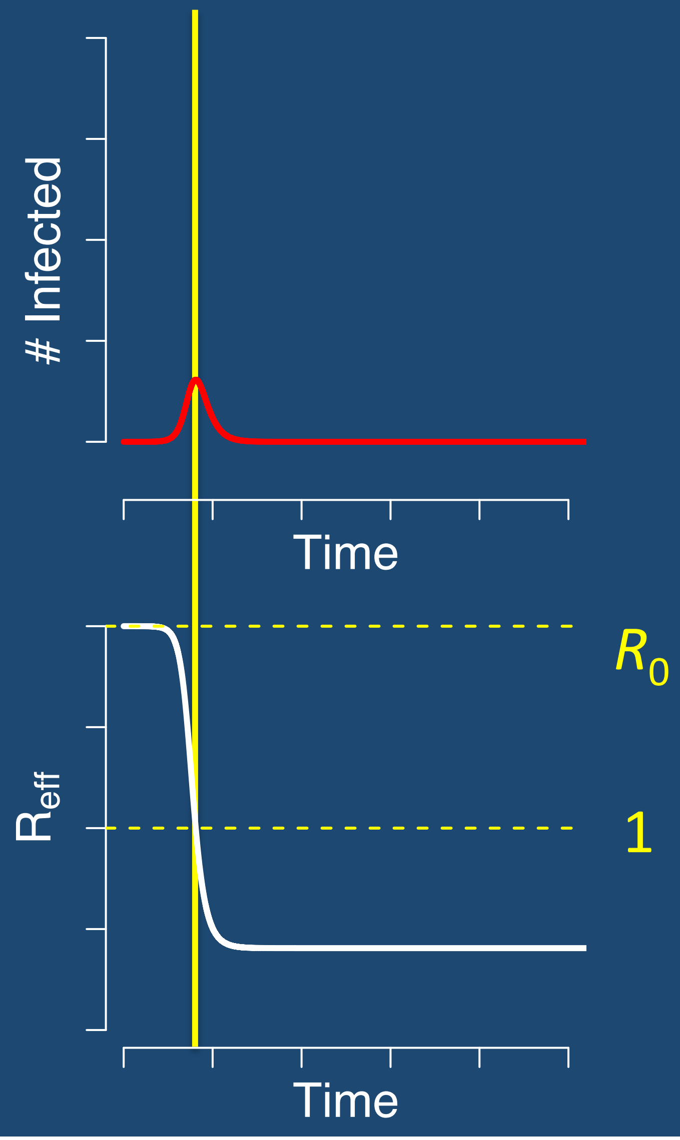
$$R_{eff} = R_0 \frac{S}{N}$$

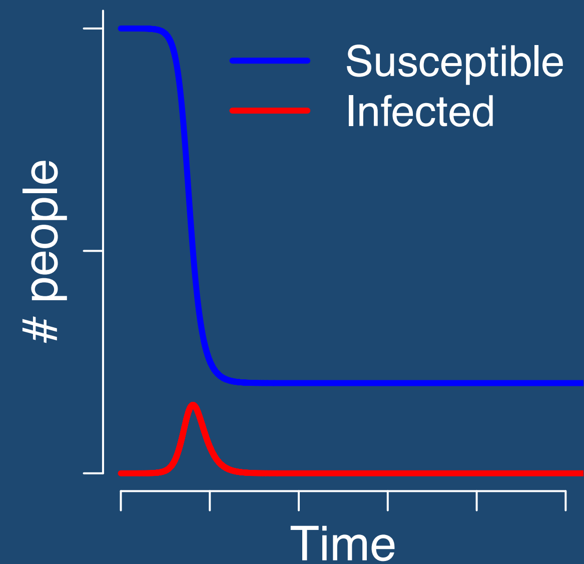
Why do epidemics peak?

Death or long-term immunity leads to exhaustion of susceptibles



R_{eff}: The Effective Reproductive Number

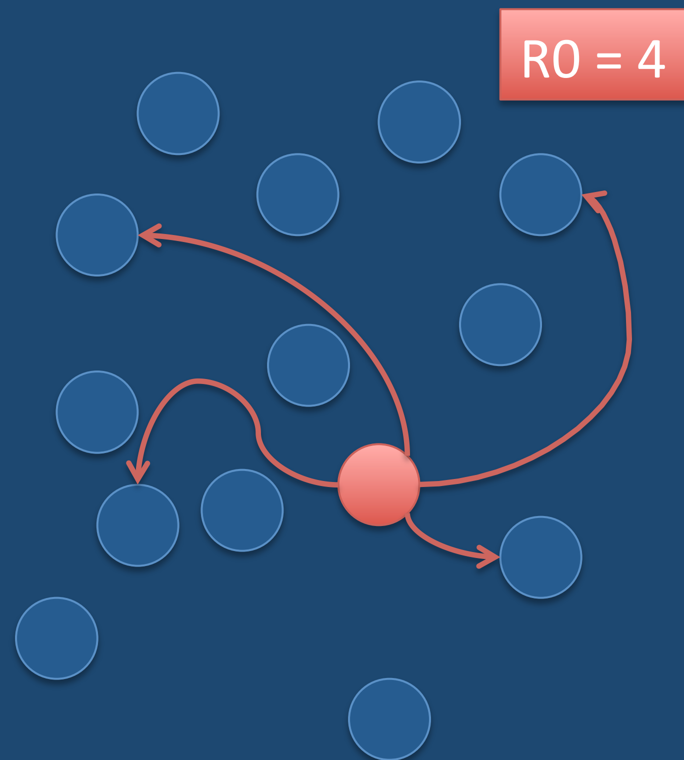




$$R_{eff}(t) = R_0 \frac{S(t)}{N}$$

Proportion to Vaccinate

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



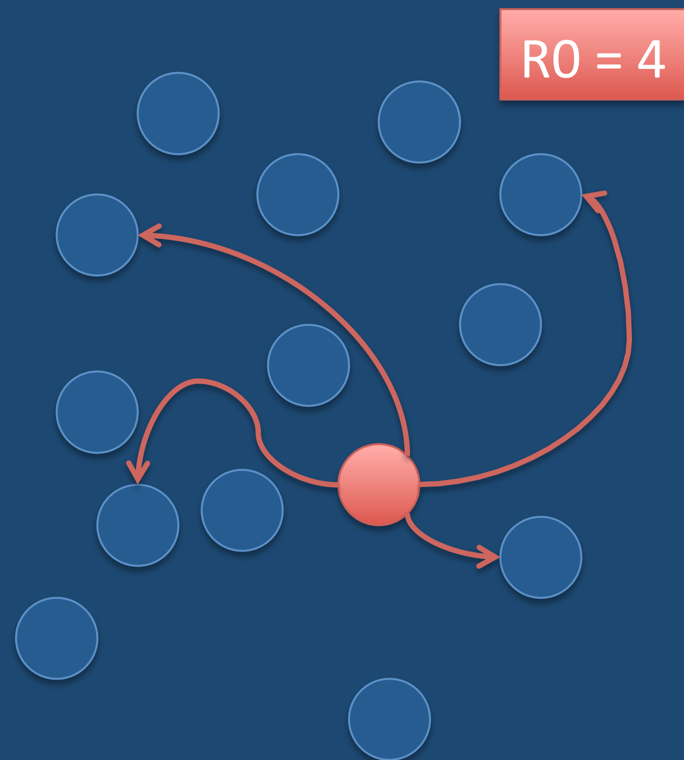
Proportion to Vaccinate

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

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

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

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



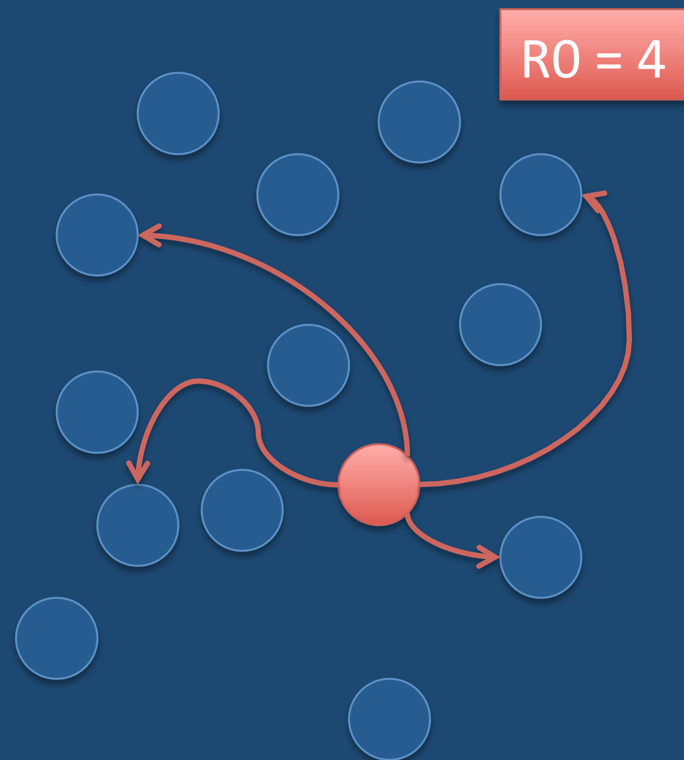
Proportion to Vaccinate

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

Proportion immune = P_V =
1 – proportion susceptible

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

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



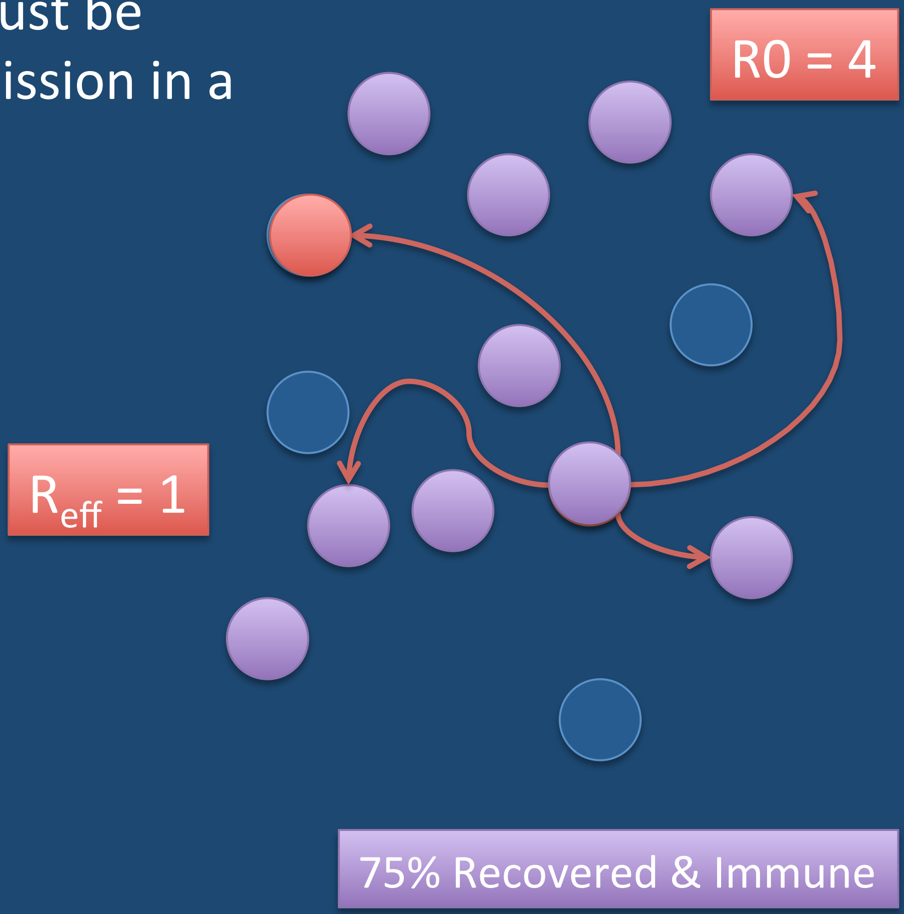
You don't have to vaccinate everyone to eliminate transmission!!!

Proportion to Vaccinate

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

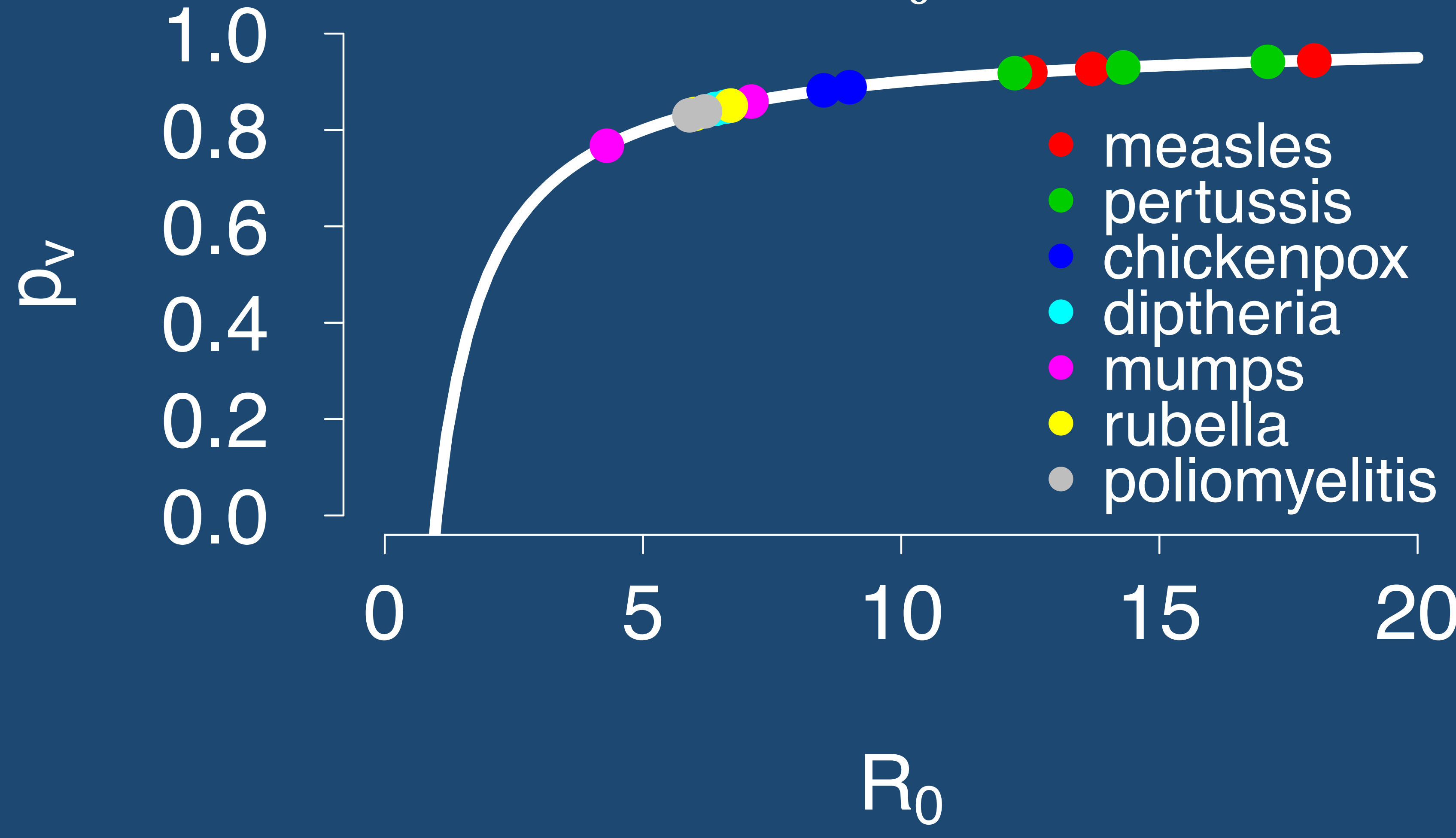
$$P_V \geq \frac{R_0 - 1}{R_0}$$

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



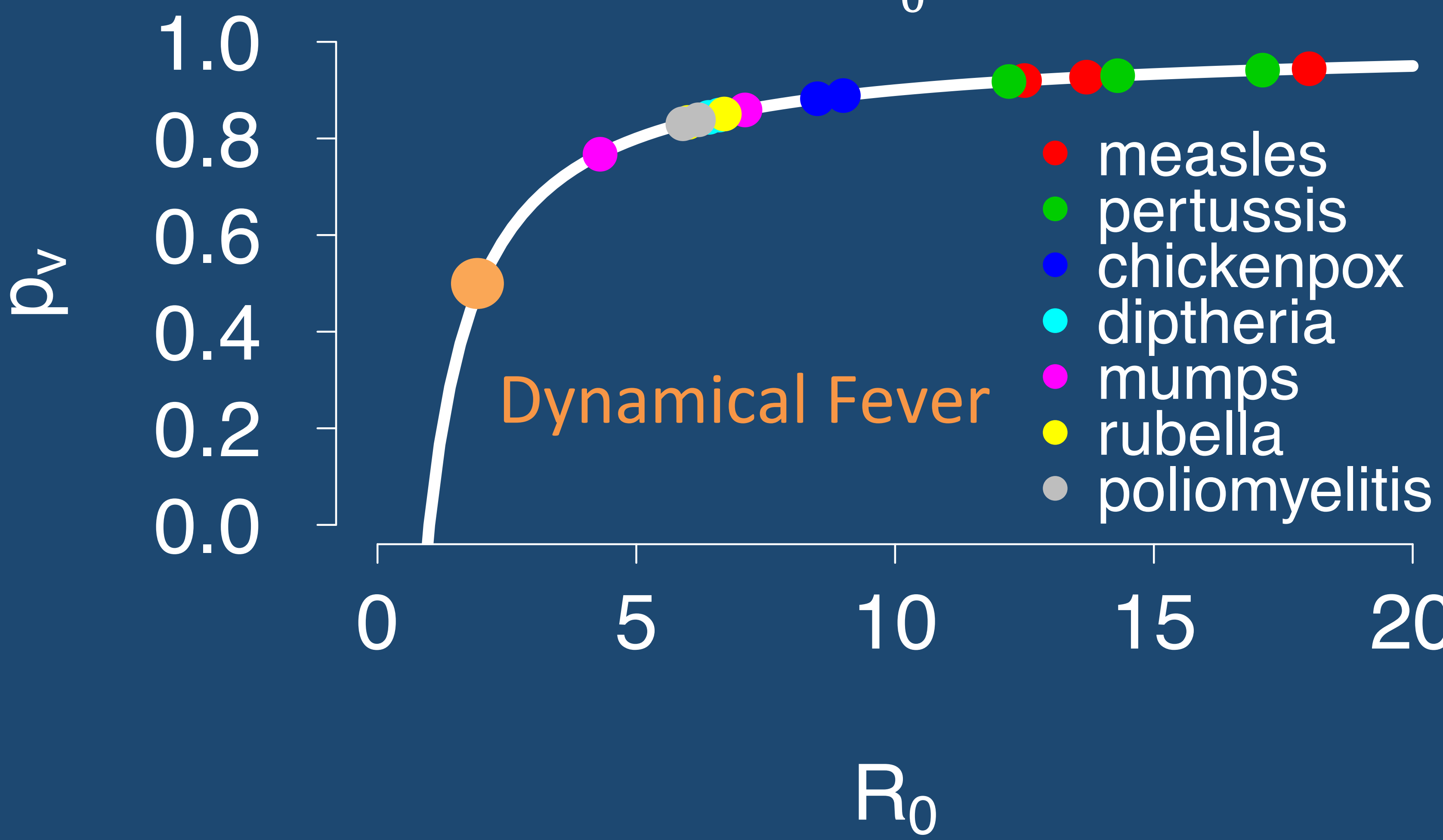
Elimination Thresholds

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

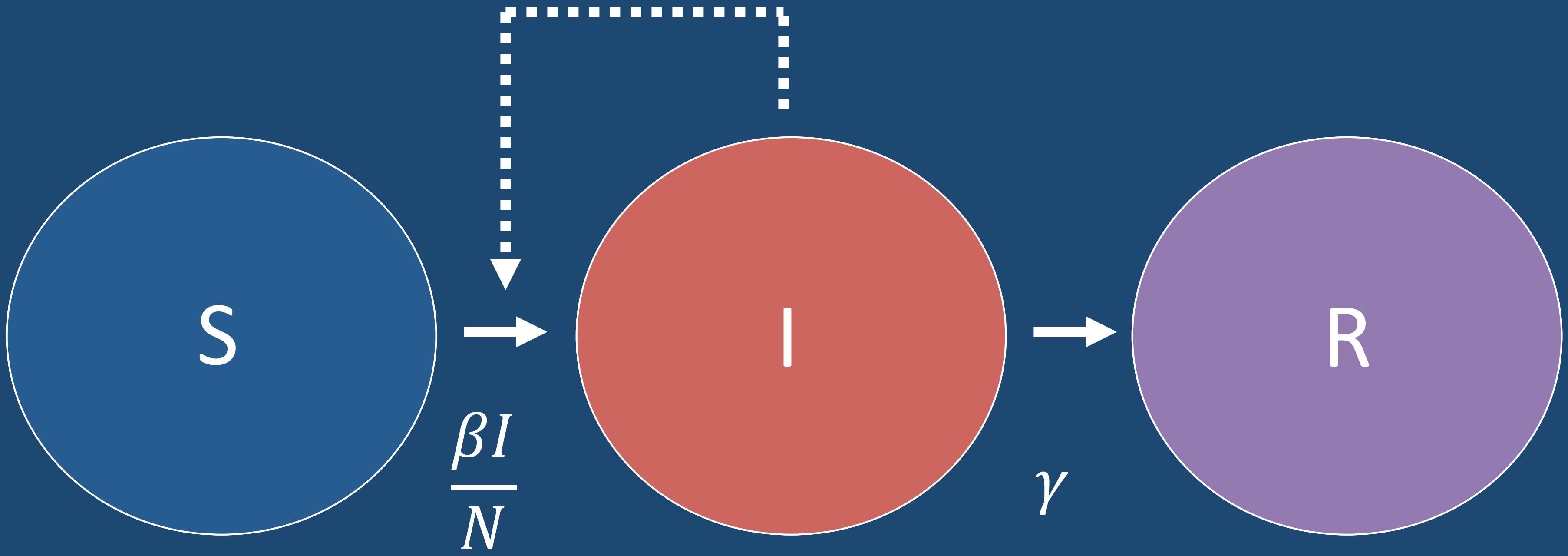


Elimination Thresholds

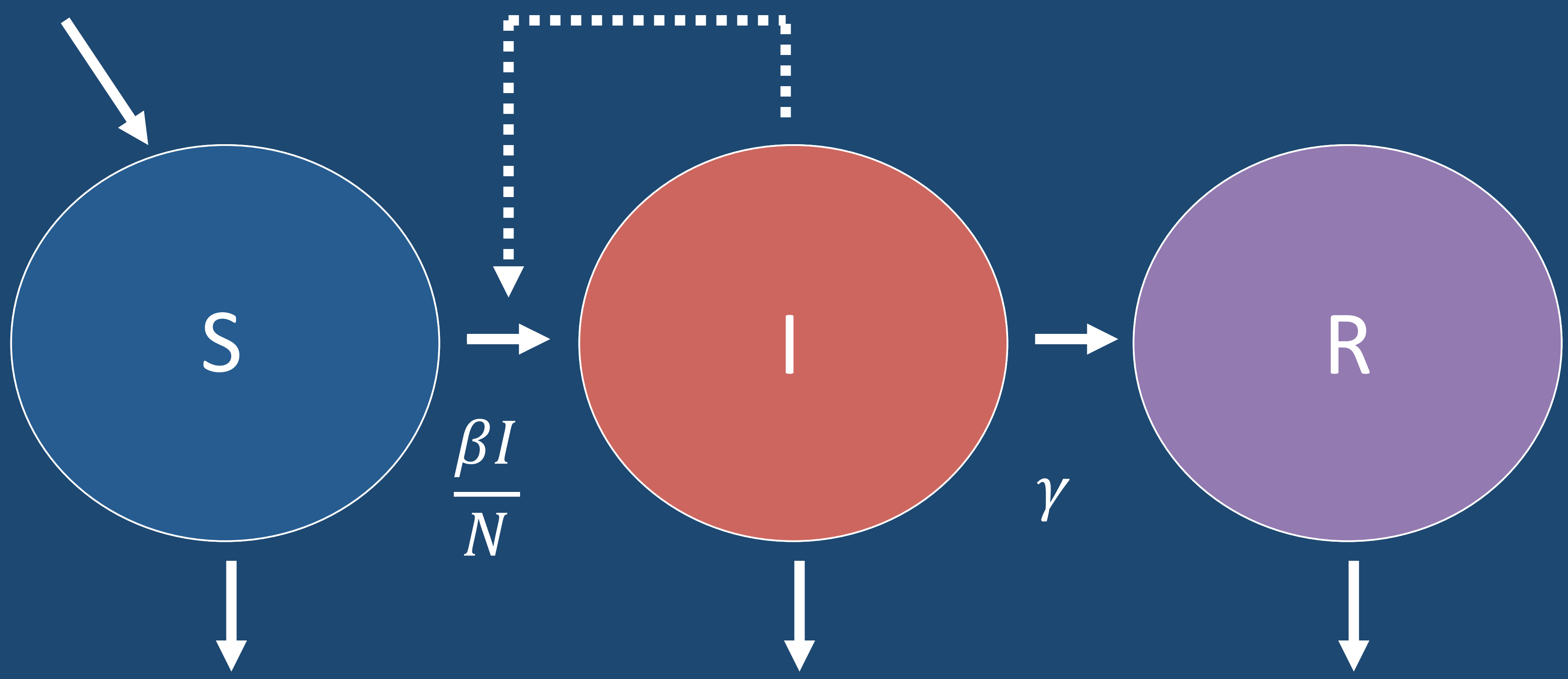
$$P_V = \frac{R_0 - 1}{R_0}$$



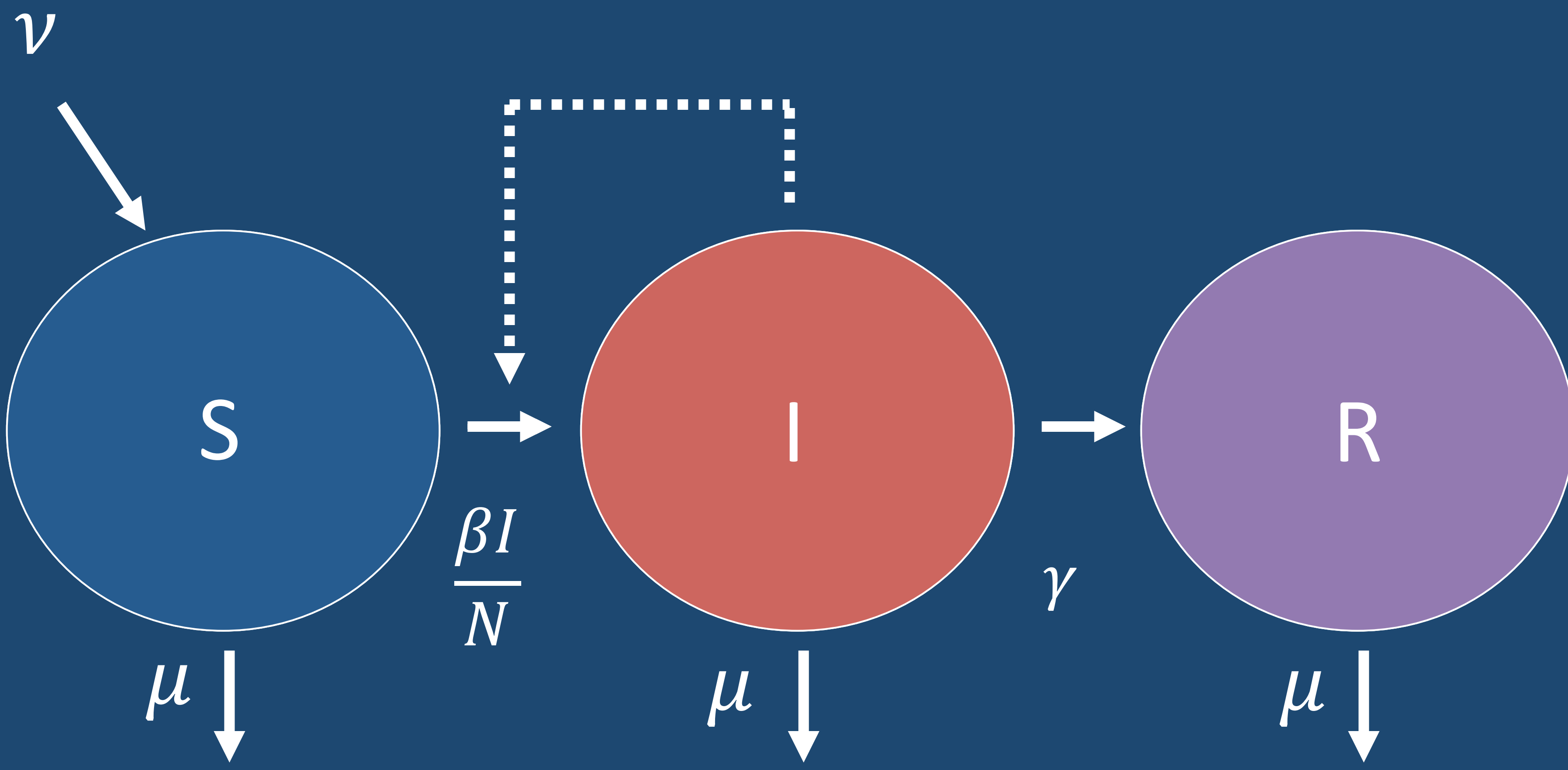
SIR Model



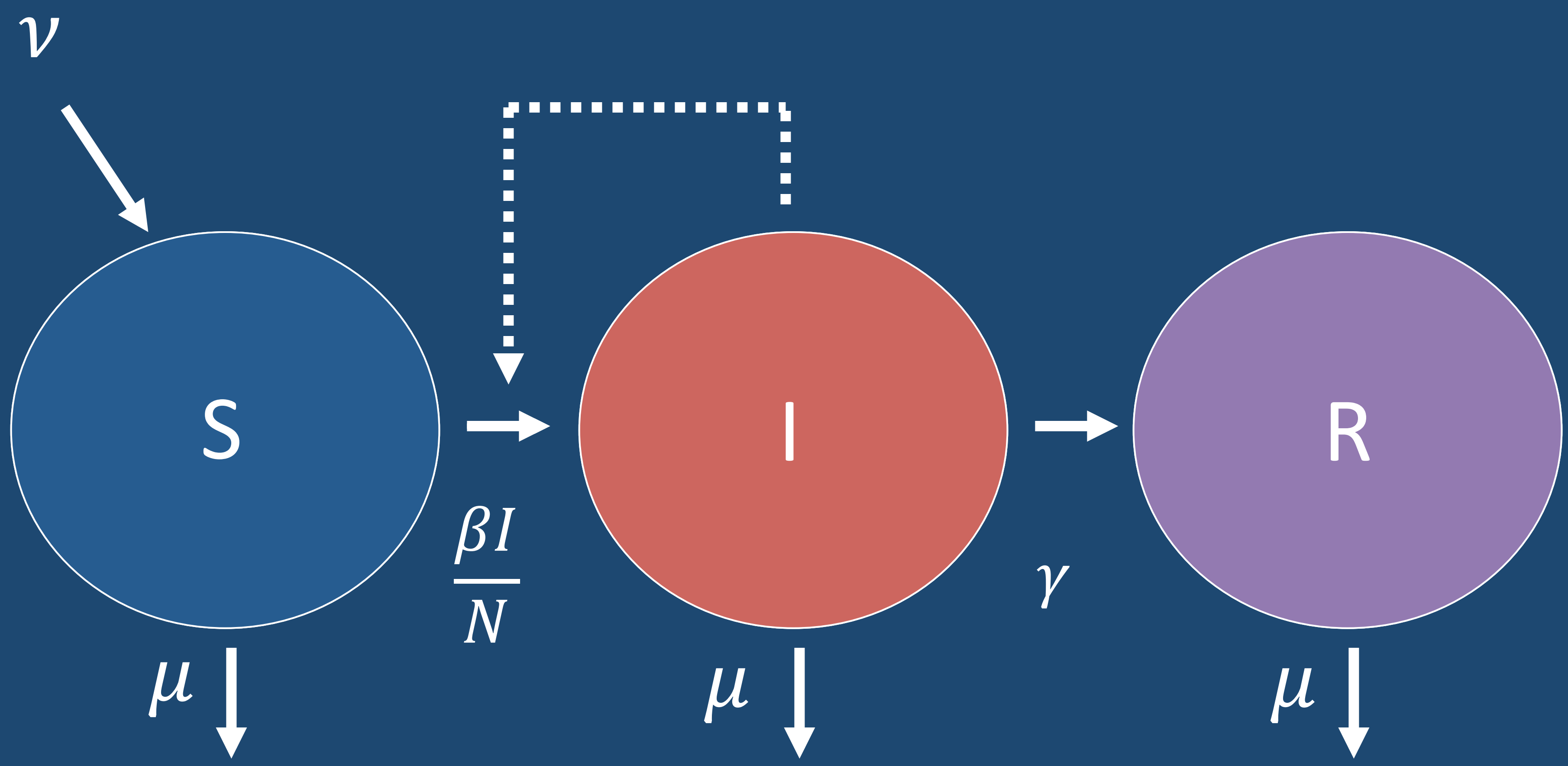
SIR Model with Birth & Death



SIR Model with Birth & Death



SIR Model with Birth & Death



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

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

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

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

$$R_0 =$$

$$\frac{\beta SI}{N} \xrightarrow{N \text{ large}} \beta$$

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

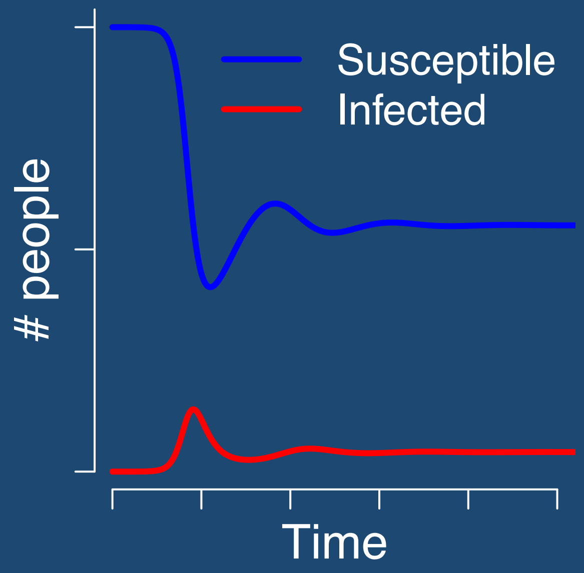
Average duration of infectiousness

SIR Model with Birth & Death

Dynamics upon introduction:

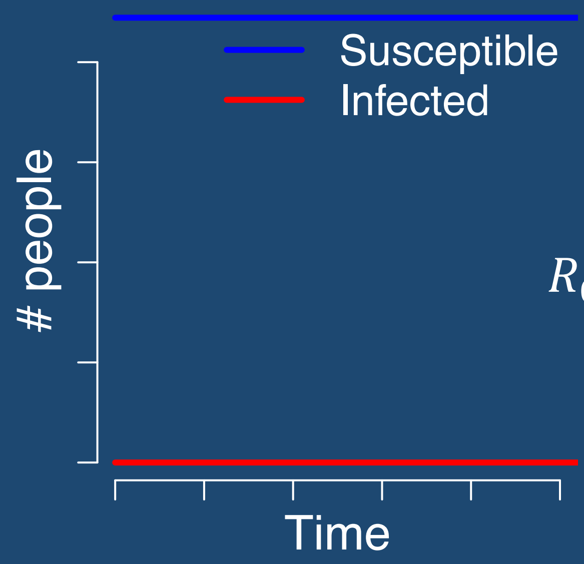
Epidemic if $R_0 > 1$

Endemic state



No epidemic if $R_0 \leq 1$

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

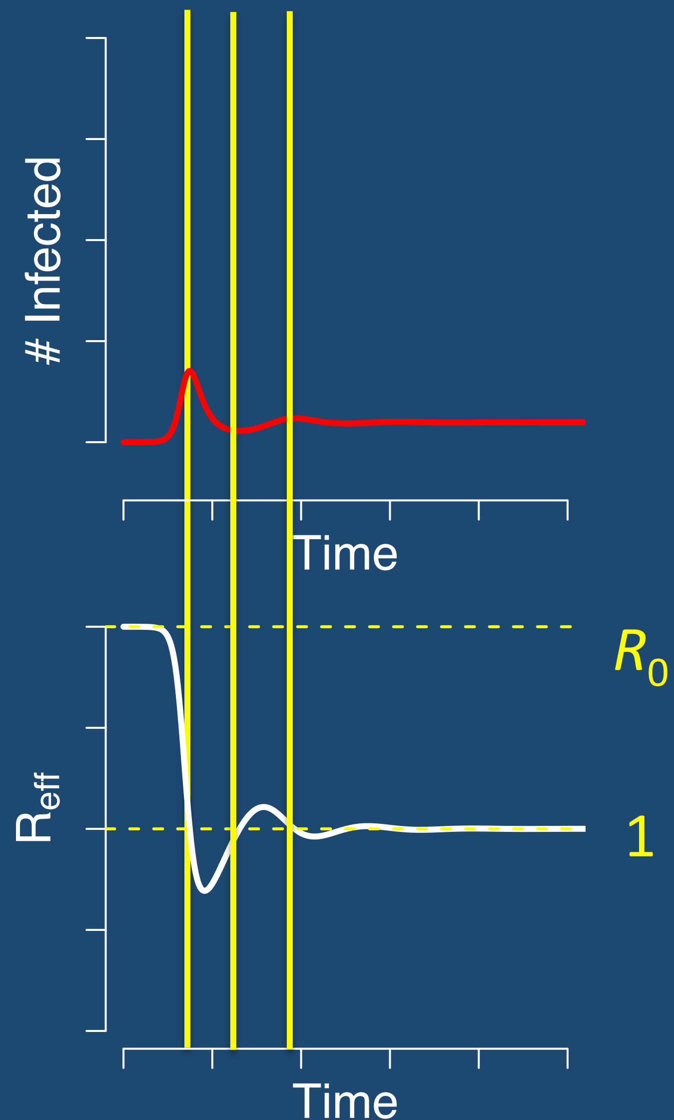
X

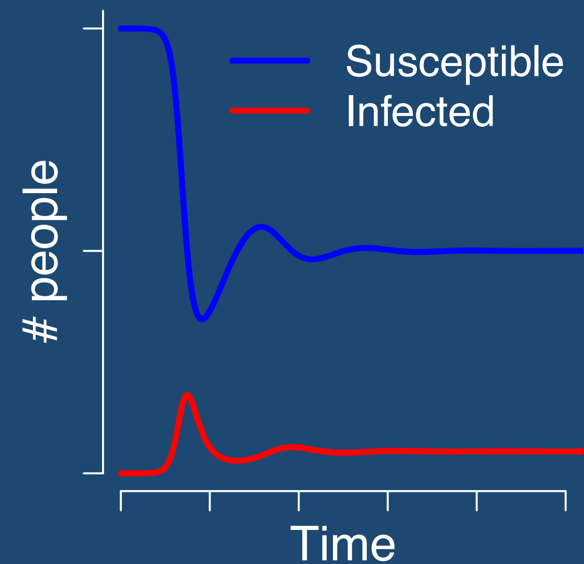
$$\frac{1}{\gamma + \mu}$$

Average duration of infectiousness

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

R_{eff}: The Effective Reproductive Number



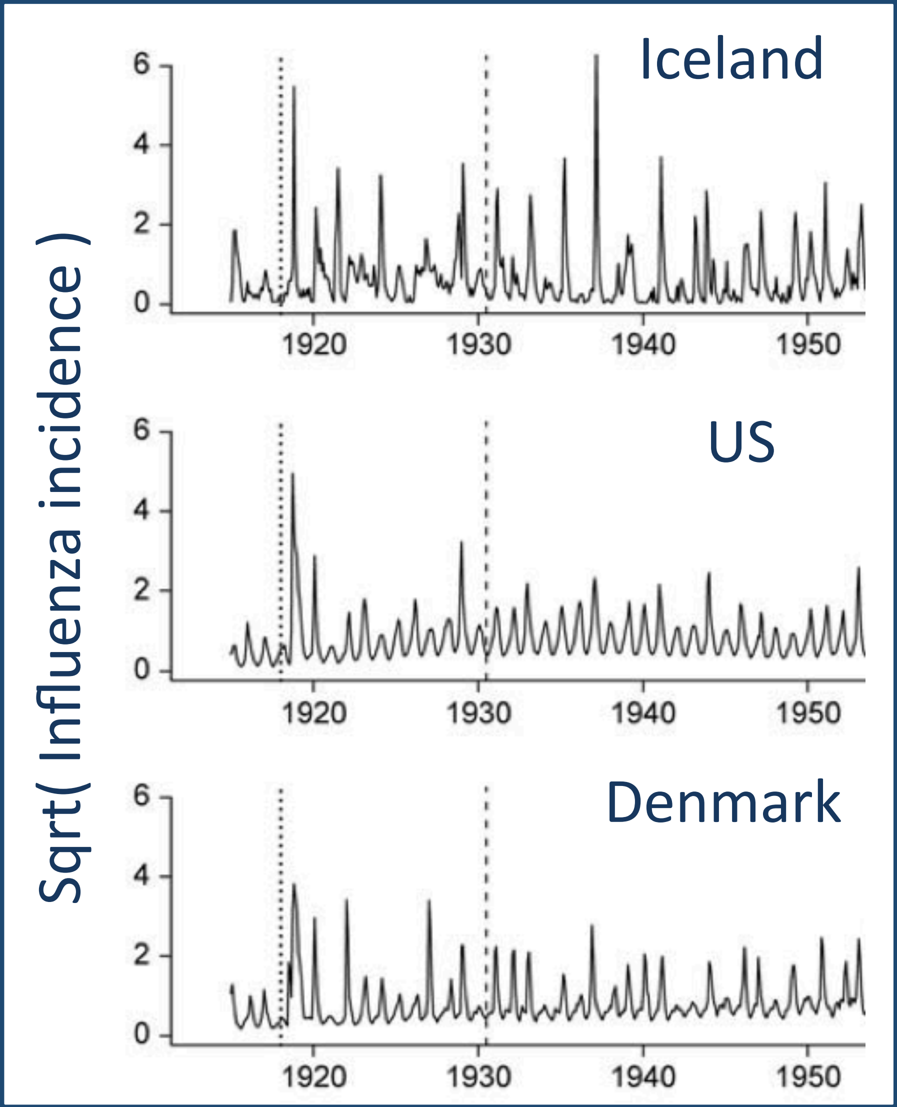


$$R_{eff}(t) = R_0 \frac{S(t)}{N}$$

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

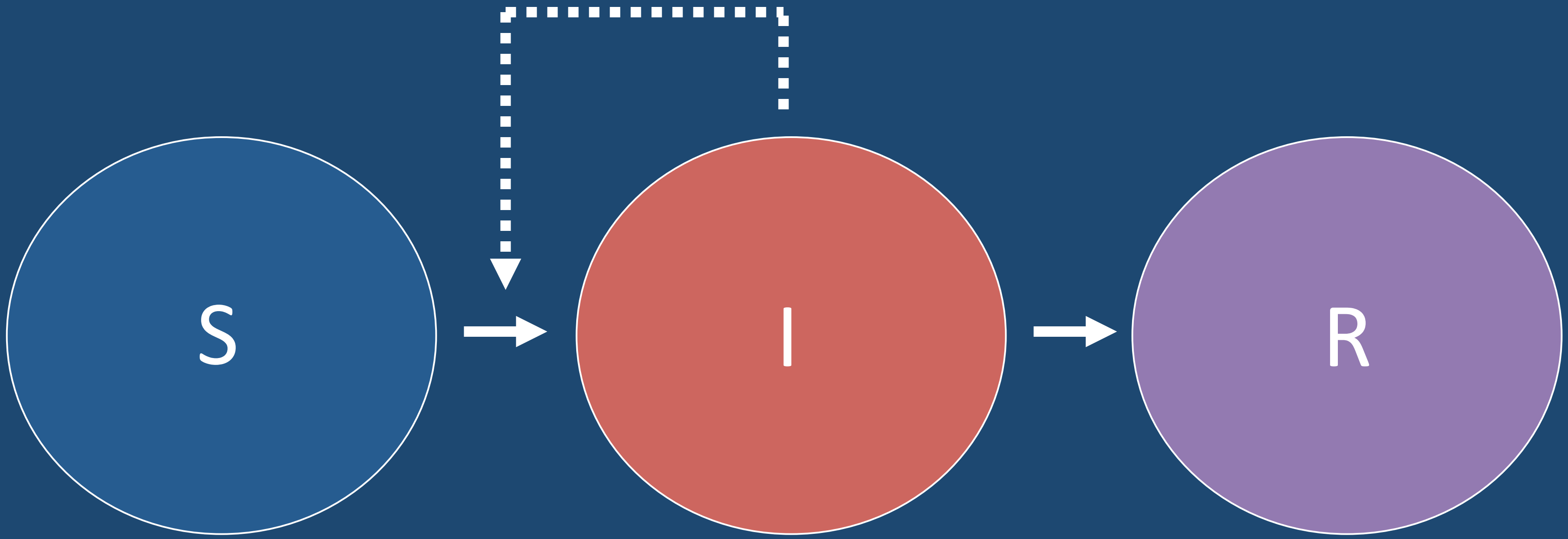
Why do recurrent epidemics happen?

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



Weinberger *et al*. 2012 Am J Epidemiol

State variables



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

Features of models discussed so far:

Ordinary differential equations

- Deterministic
- Well-mixed
- All individuals are identical (except in disease status)
- Continuous time with exponential waiting times
- State variables are continuous quantities

Extremely simple models…

- Important insights
  - Why and when epidemics peak
  - What determines the endemic level of infection in a population
  - The level of effort needed to eliminate transmission
- Lots of assumptions

Extremely simple models…

- Important insights
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  - What determines the endemic level of infection in a population
  - The level of effort needed to eliminate transmission
- Lots of assumptions

These assumptions rarely hold in the real world…

So, what did the influenza transmission model that motivated the Alachua County SLIV program look like?

- Stochastic
- Contacts based on population structure
  - households
  - neighborhoods
  - work/school groups
- Each individual is a discrete entity with identifying features
- Discrete time

So, what did the influenza transmission model that motivated the Alachua County SLIV program look like?

- Synthetic population
- Influenza outcomes
- Transmission patterns
- Vaccination options

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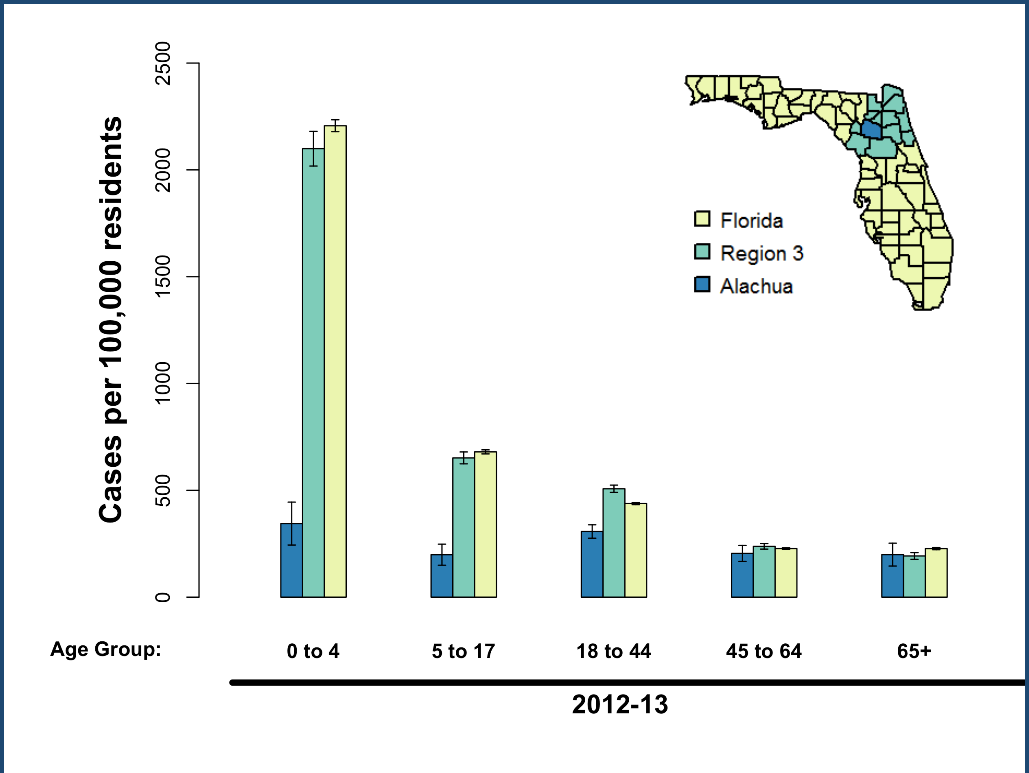
Details:

Weycker *et al.* 2005 *Vaccine*; Halloran *et al*. 2006 *Science*; Germann *et al.* 2006 *PNAS*; Basta *et al*. 2009 *AJE*; Longini 2012 *Pediatrics*

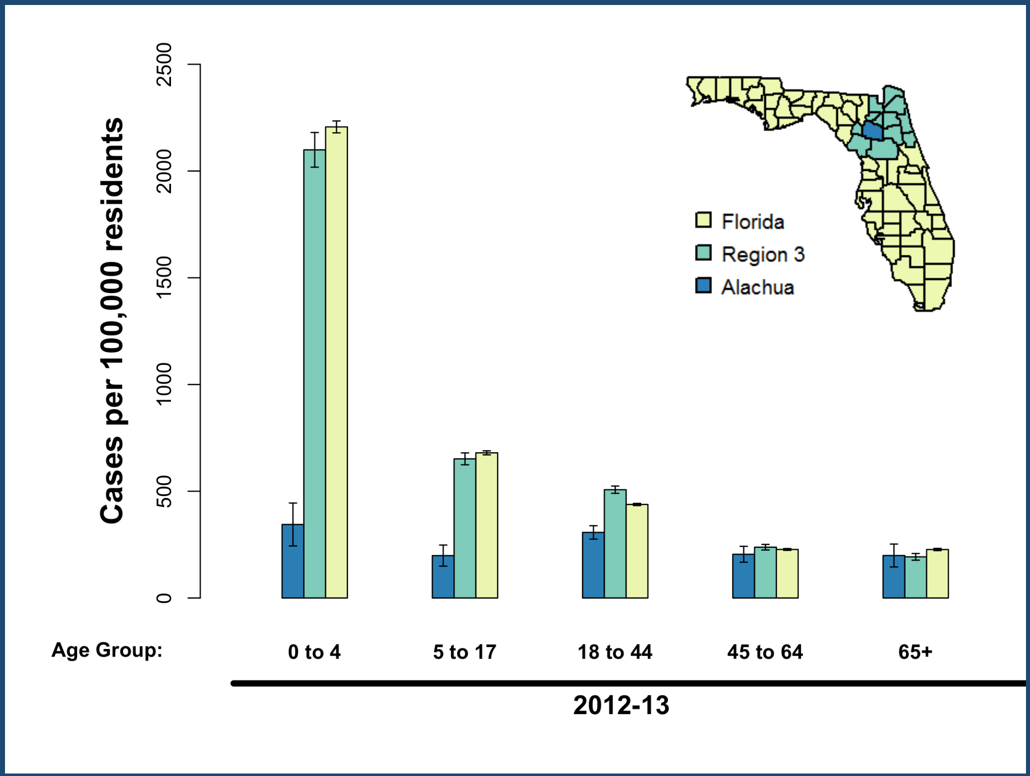
Were the predictions borne out?



Tran *et al*. Submitted

- Not entirely

Were the predictions borne out?



Tran *et al*. Submitted

- Not entirely
- Is the model still valuable?

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