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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

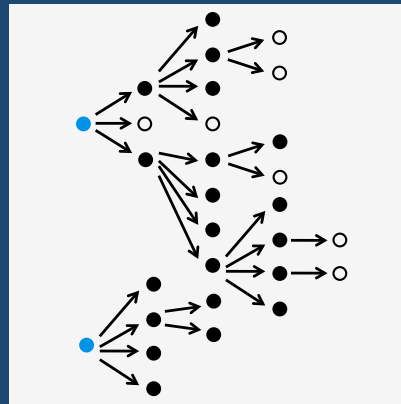
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For further information please contact Dr. Juliet Pulliam (pulliam@ufl.edu).

Simplification for Generalization 1:

intuitive aspects of dynamics and introduction to model worlds



Clinic on Dynamical Approaches to Infectious Disease Data

December 13, 2015

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Department of Biology and Emerging Pathogens Institute

University of Florida

School-located Influenza Vaccination

Alachua County Control Flu Program



- 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



Alachua County Control Flu Program

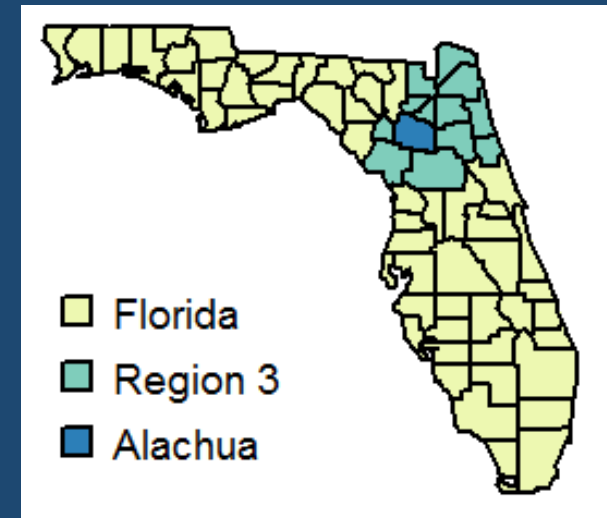
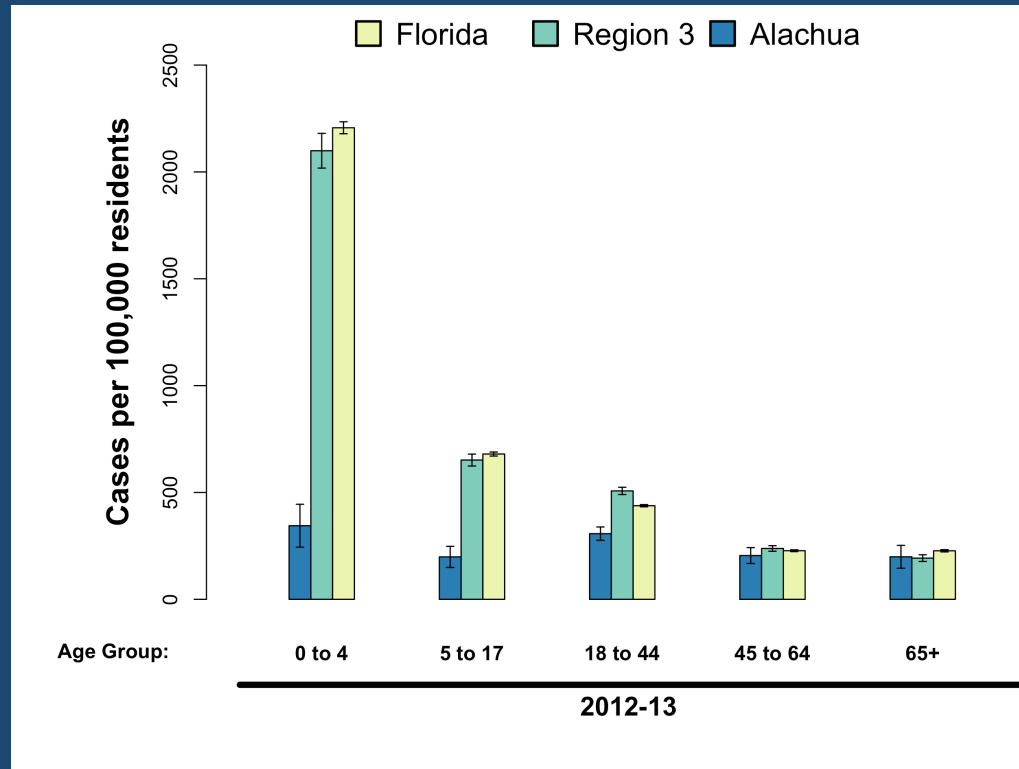
Coverage

	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)

Alachua County Control Flu Program

Impact

2011-2012 season

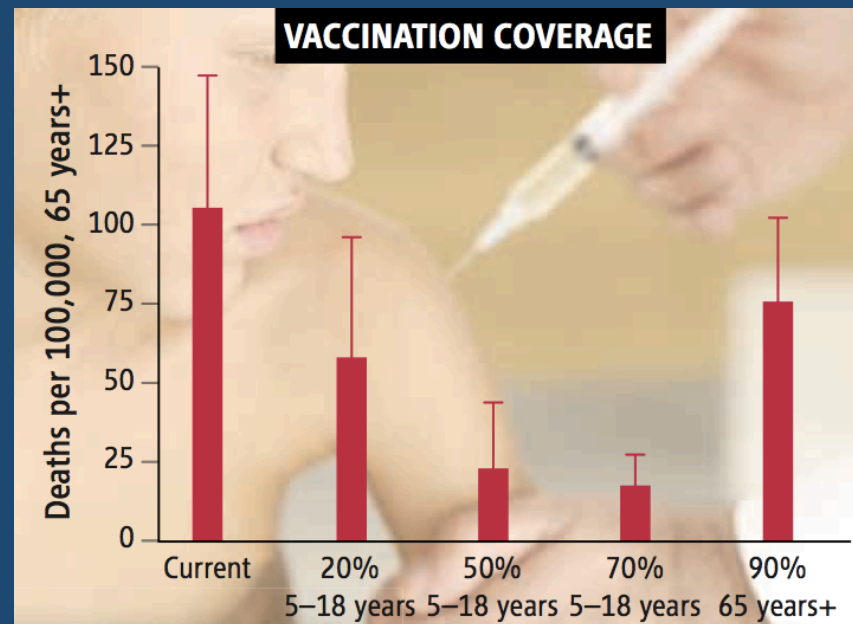


Alachua County Control Flu Program

Why did they think it would work?

Alachua County Control Flu Program

Why did they think it would work?

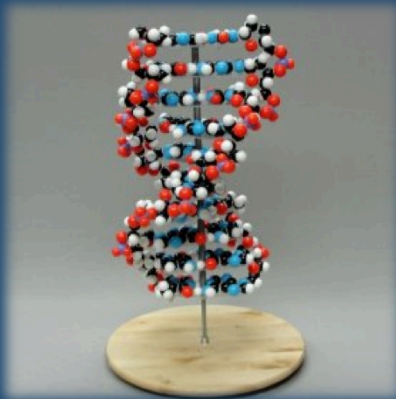


Halloran & Longini 2006 Science

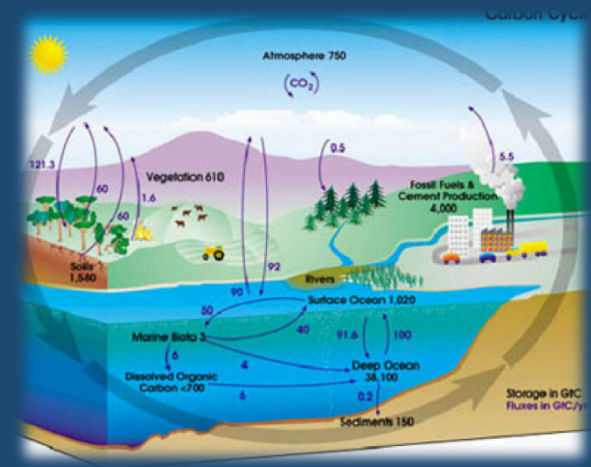
Model-based prediction...

What are models?

- Physical



- Conceptual



- Mathematical

$$\frac{\partial}{\partial a} \ln f_{a, \sigma^2}(\xi_1) = \frac{(\xi_1 - a)}{\sigma^2} f_{a, \sigma^2}(\xi_1) = \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left\{-\frac{(\xi_1 - a)^2}{2\sigma^2}\right\}$$

$$\int T(x) \cdot \frac{\partial}{\partial \theta} f(x, \theta) dx = M\left(T(\xi) \cdot \frac{\partial}{\partial \theta} \ln L(\xi, \theta)\right) \int_{-\infty}^{\infty} T(x) f(x, \theta) dx$$

What are **dynamical** models?

Statistical Models

- Account for bias and random error to find correlations that may imply causality.
- Often the first step to assessing relationships.
- Assume independence of individuals (at some scale).

Dynamical Models

- Systems Approach: Explicitly model multiple mechanisms to understand their interactions.
- Link observed relationships at different scales.
- 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

Model World

an **abstraction** of the world that is **simple and fully specified**, which we construct to help us understand particular aspects of the real world

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sometimes they reflect reality and sometimes they do not

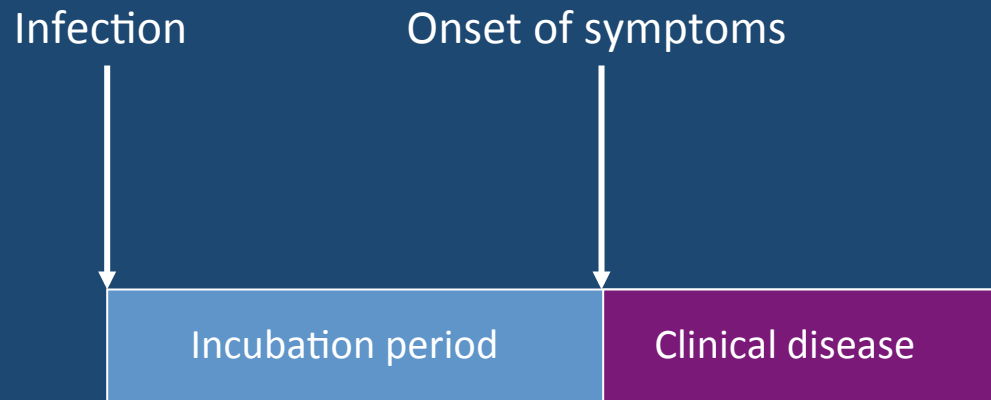
Model World

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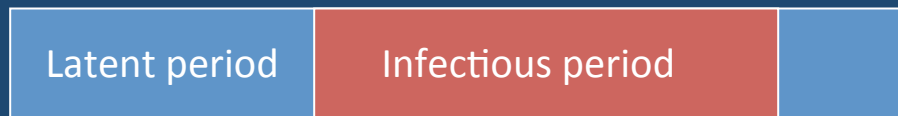
model worlds have **their own rules**

sometimes they reflect reality and sometimes they do not
but if you specify all of your assumptions, you can figure out
what things are possible given your assumptions

Natural History of Infection



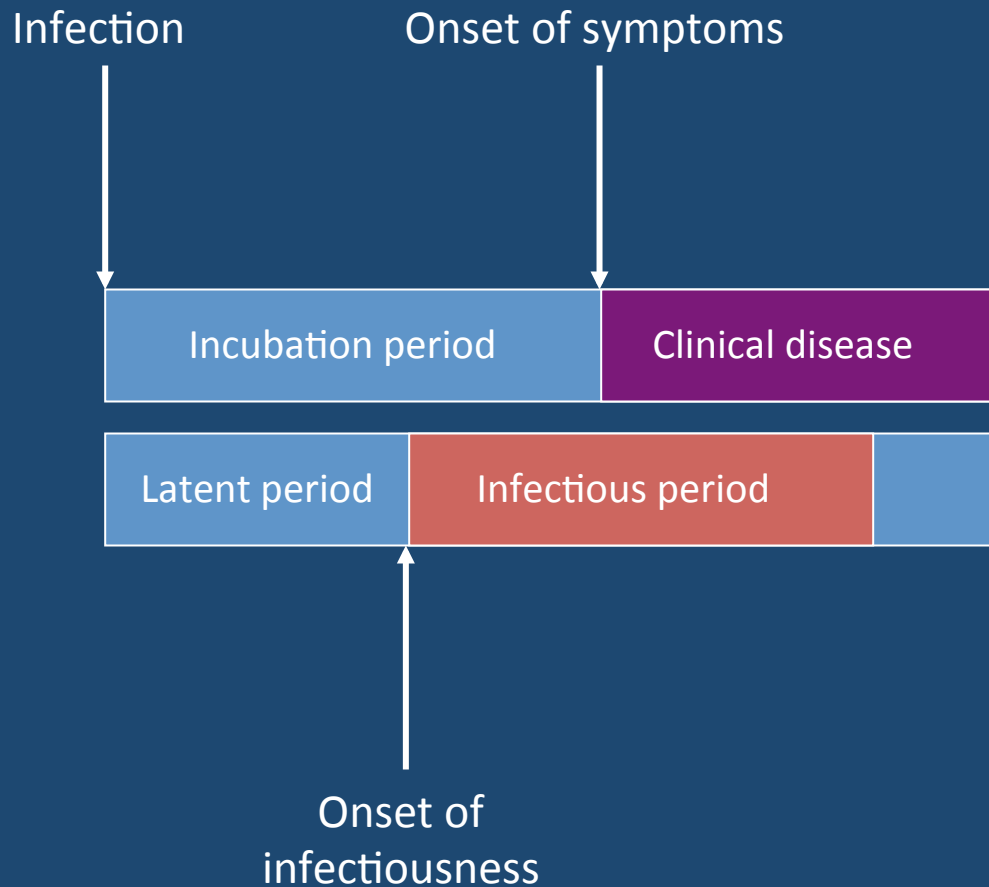
Natural History of Infection



Onset of
infectiousness

Natural History of Infection

Acute, immunizing infections



Acute

Infection time course
<<<
host lifespan

Immunizing

infection → antibody production
prevents future infection

Examples

Whooping cough



Foodborne



Chicken pox



Measles



Smallpox

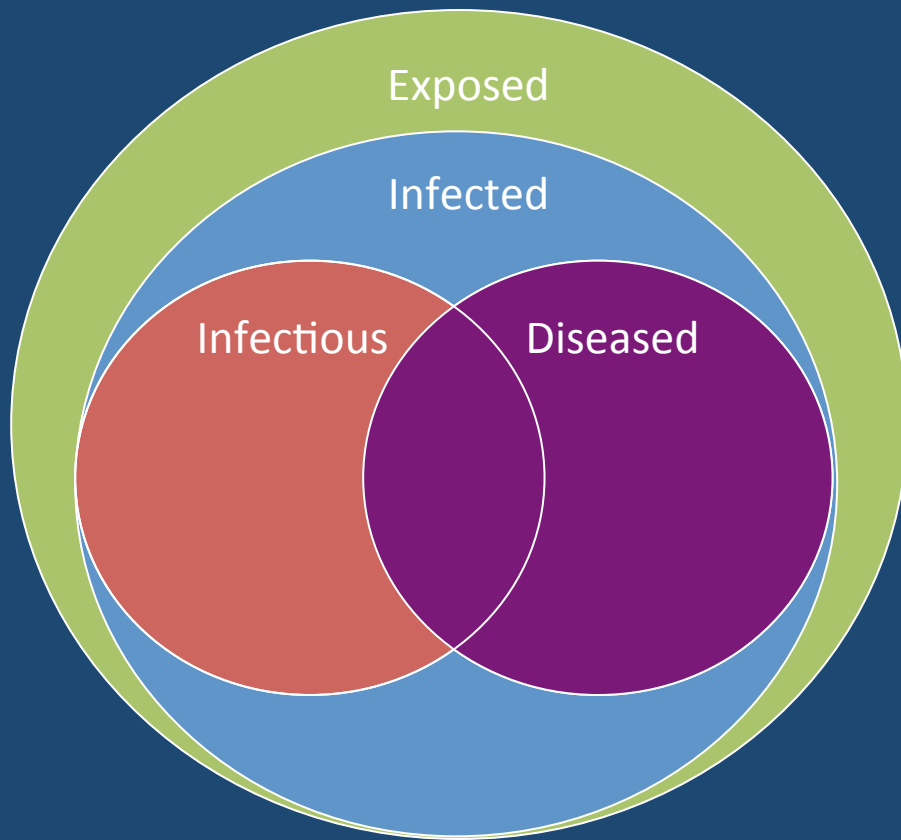


Natural History of Infection

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)

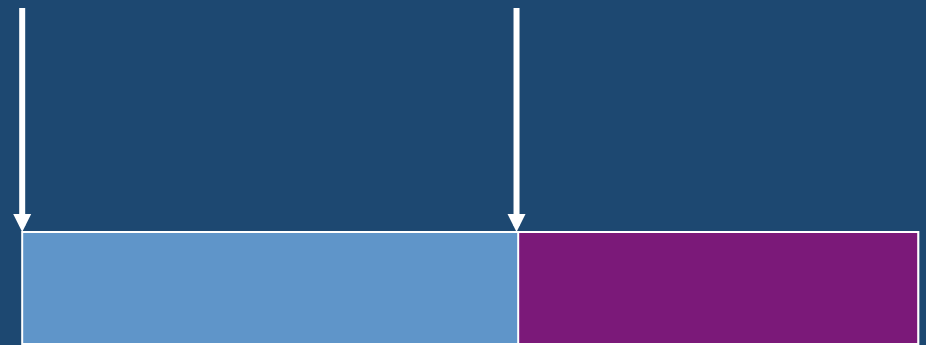
Infectious disease	Incubation period	Latent period	Infectious period
Measles	8–13	6–9	6–7
Mumps	12–26	12–18	4–8
Whooping cough (pertussis)	6–10	21–23	7–10
Rubella	14–21	7–14	11–12
Diphtheria	2–5	14–21	2–5
Chicken pox	13–17	8–12	10–11
Hepatitis B	30–80	13–17	19–22
Poliomyelitis	7–12	1–3	14–20
Influenza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

Terminology



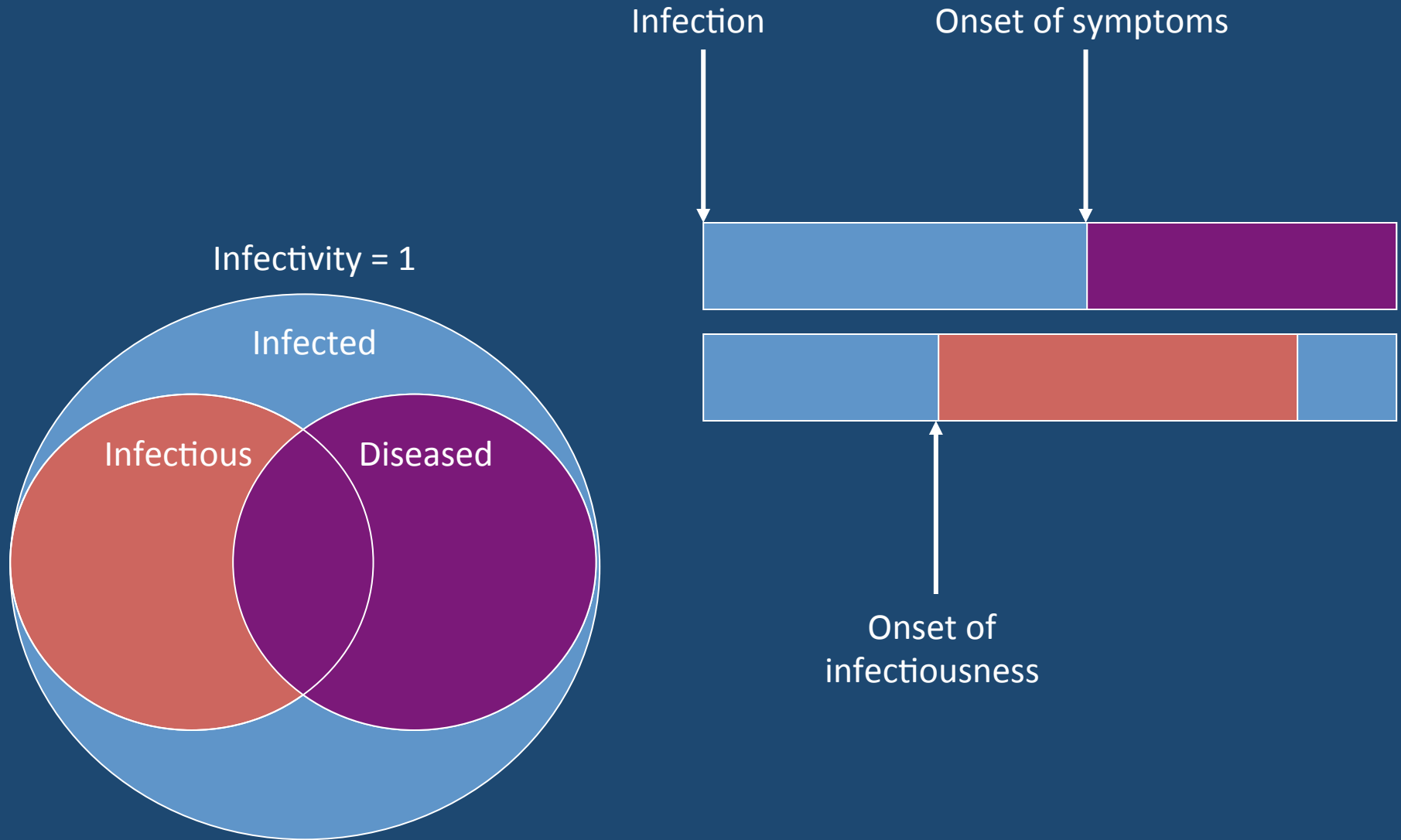
Infection

Onset of symptoms



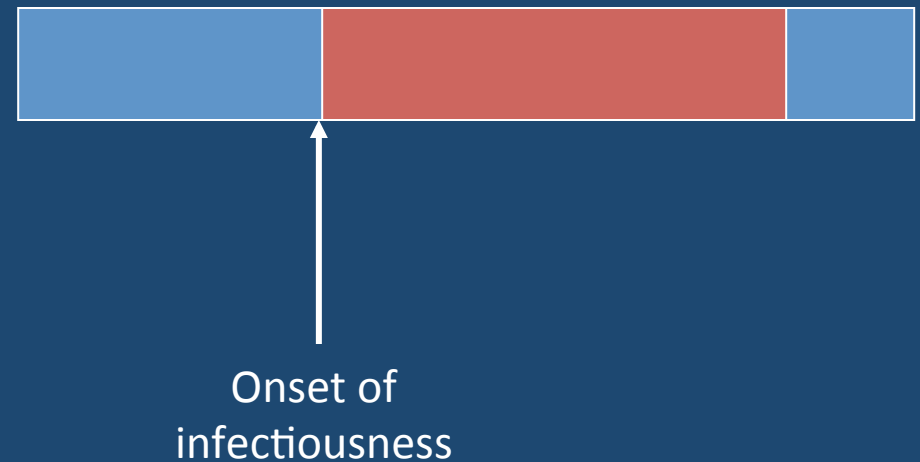
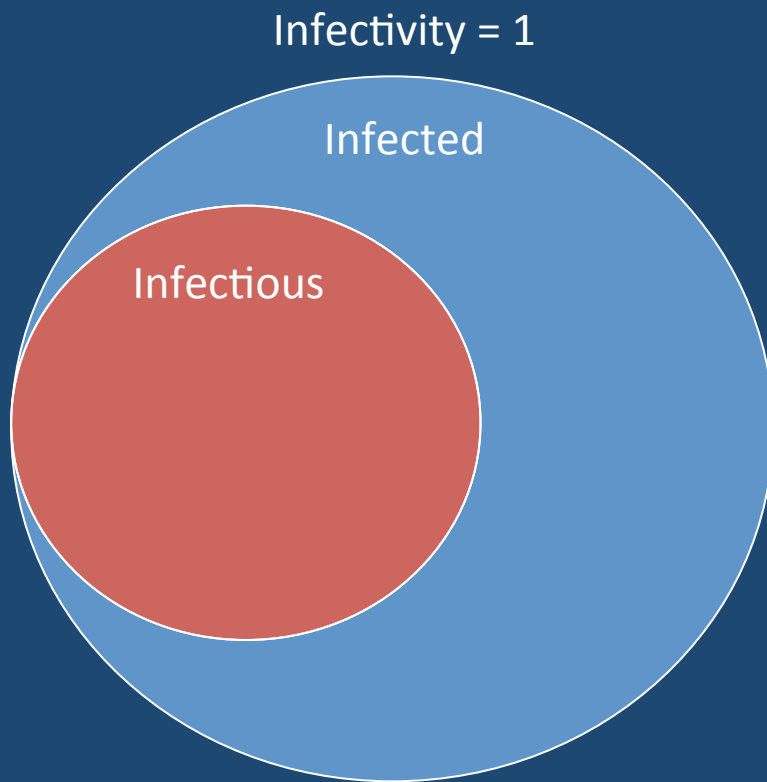
Onset of infectiousness

A **simple** view of the world



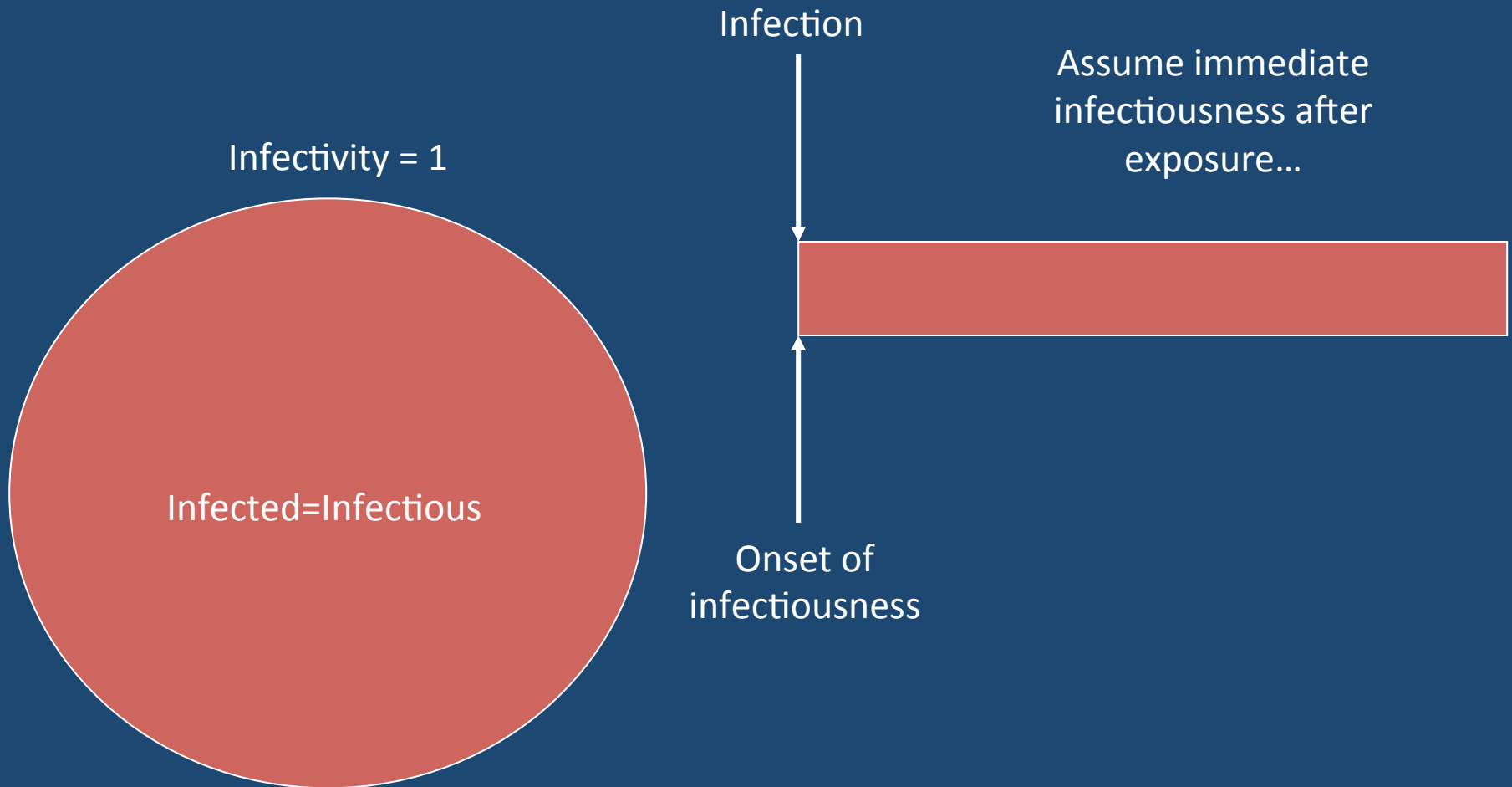
A simpler view of the world

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



Susceptible

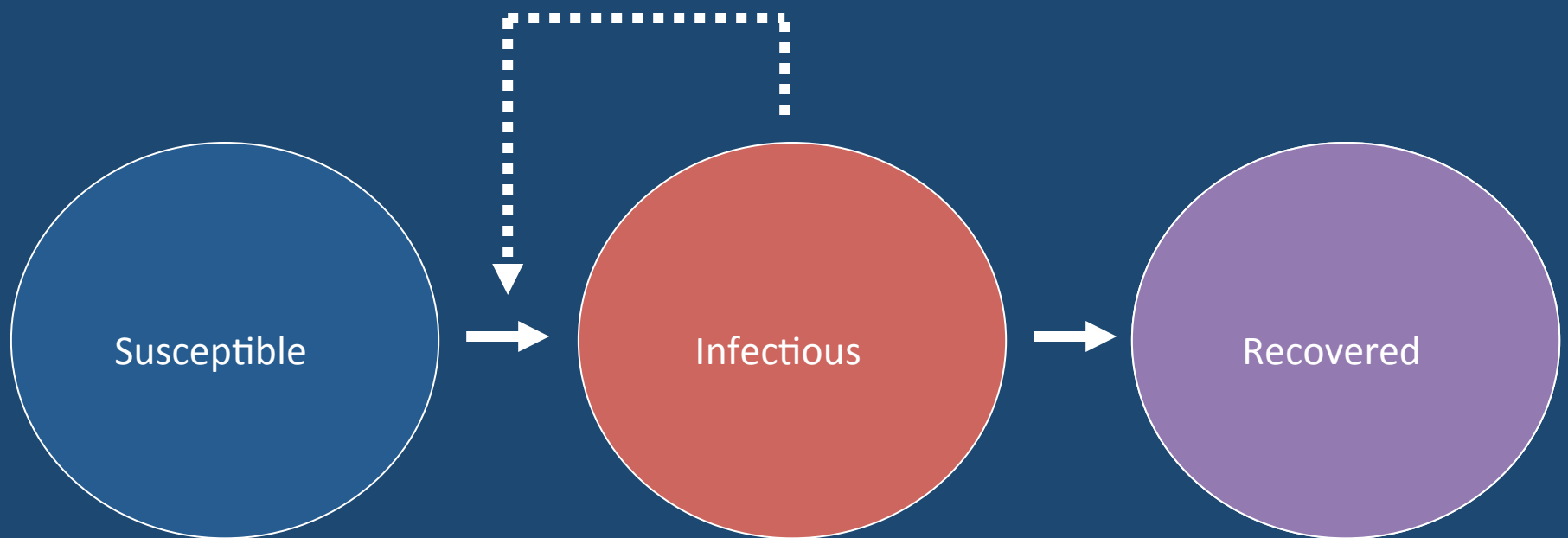
Infectious

Recovered

An **extremely simple** view of the world

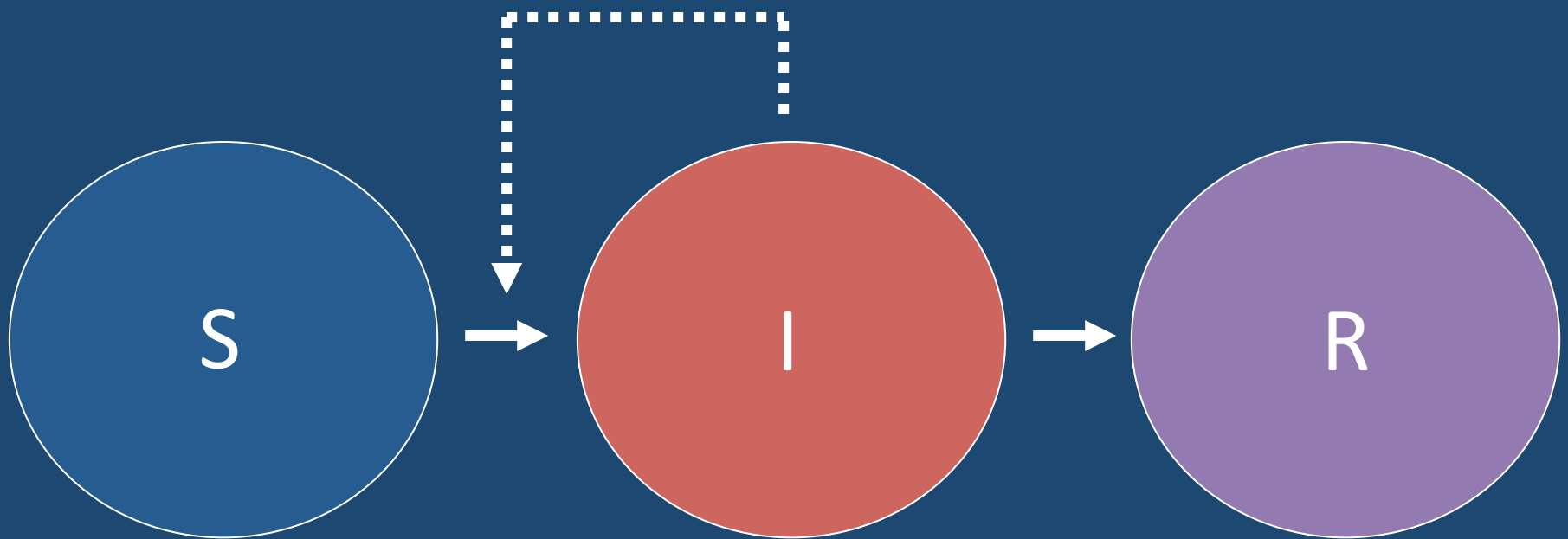


Health-related States

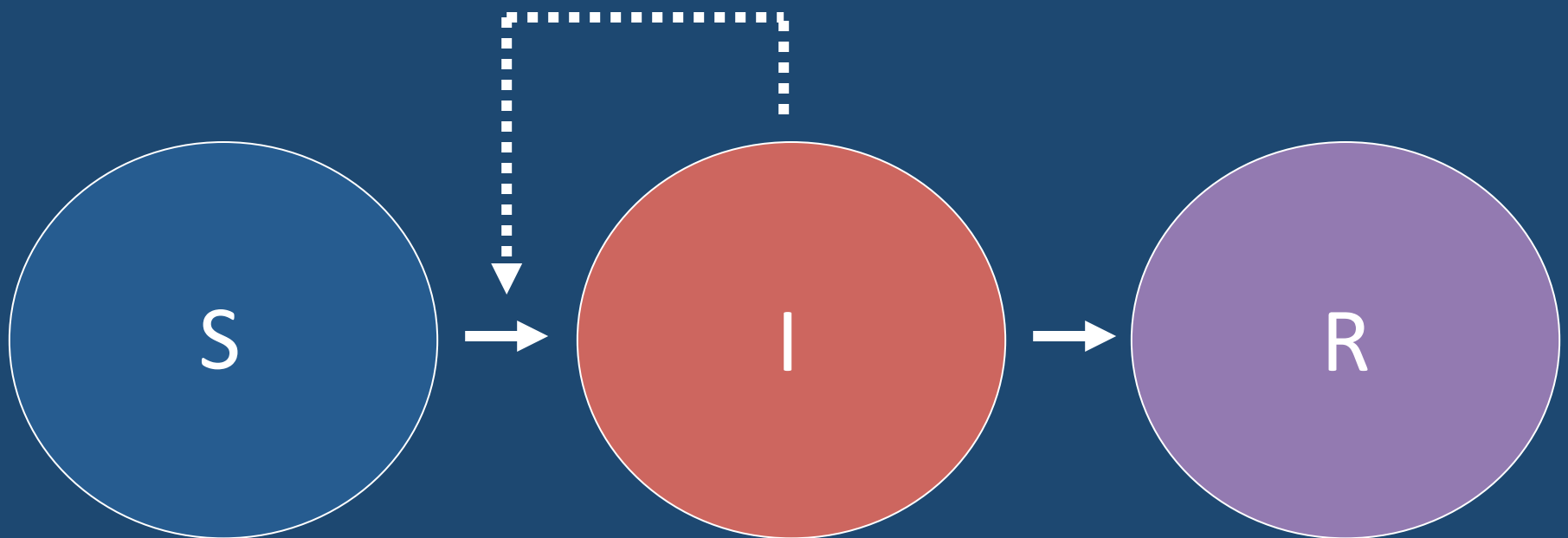


The rate at which susceptible individuals become infected depends on how many infectious people are in the population

State variables

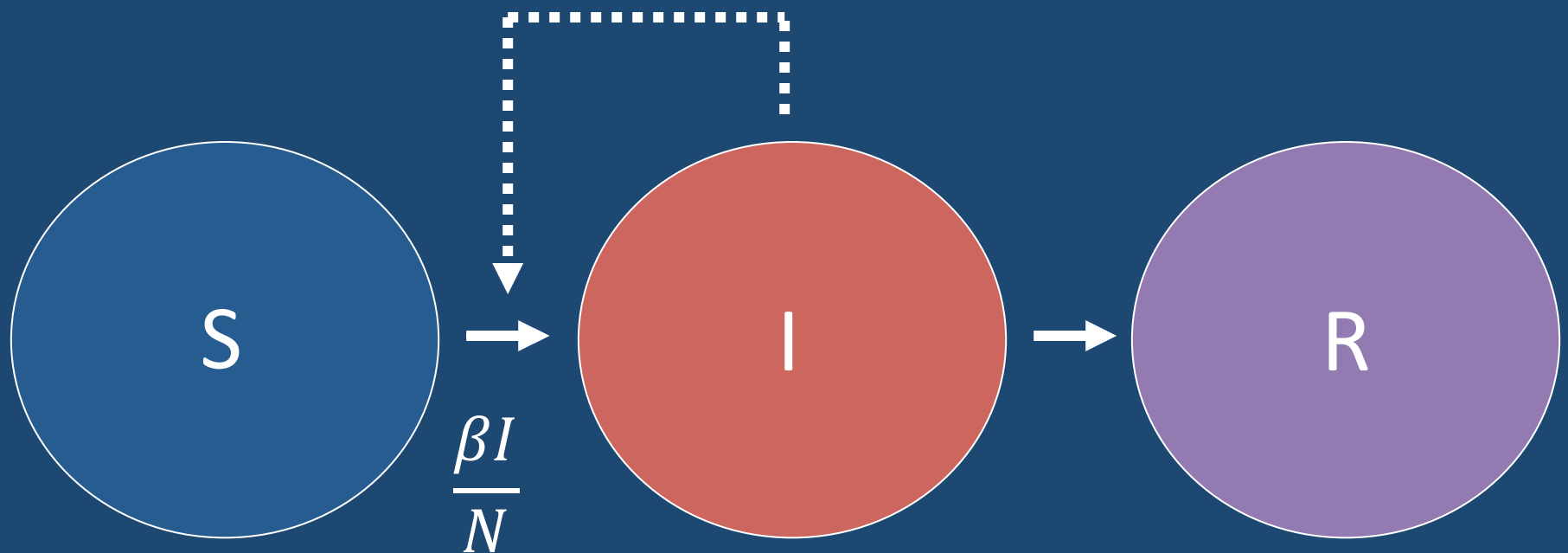


State variables



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

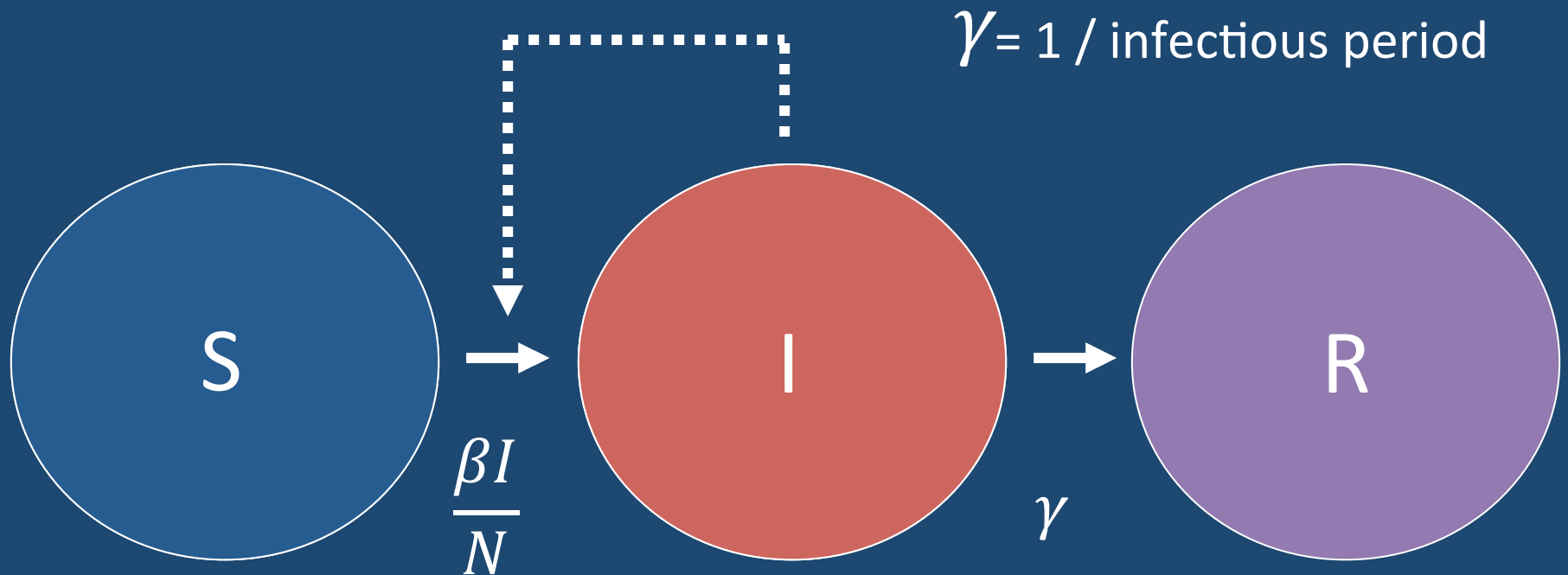
SIR Model



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

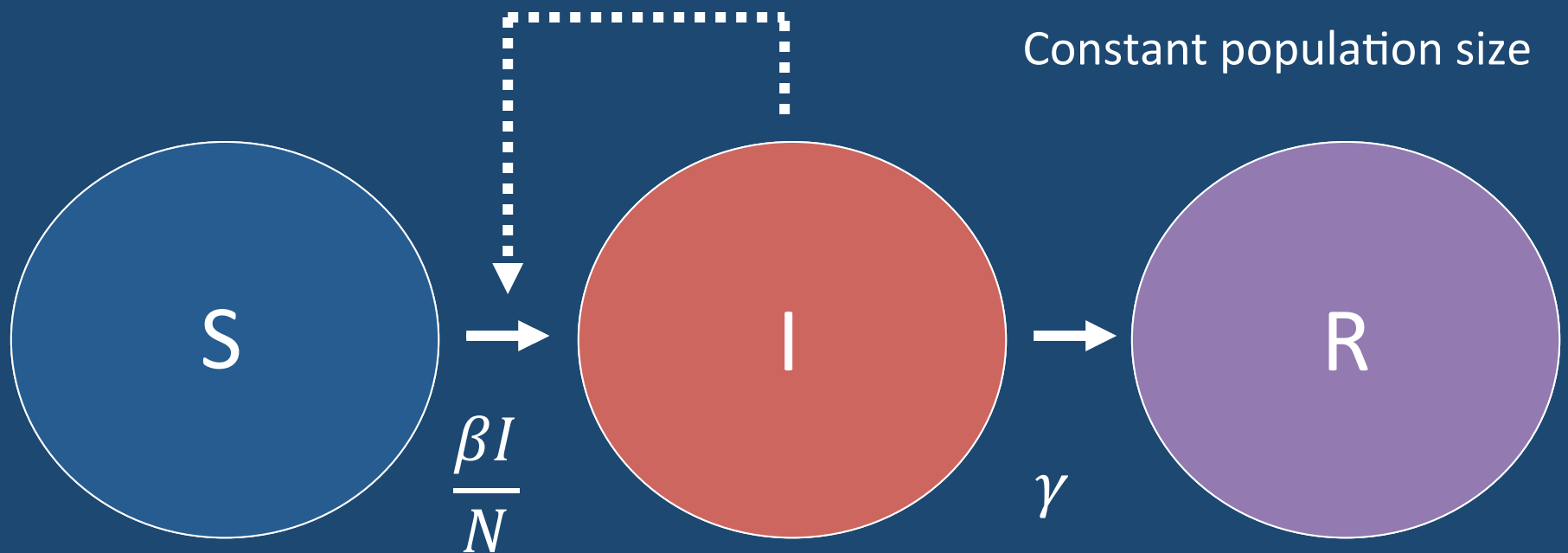


If infectious people recover at a rate of 0.5 / day,
the average time they spend infectious is $1 / 0.5 = 2$ days

SIR Model

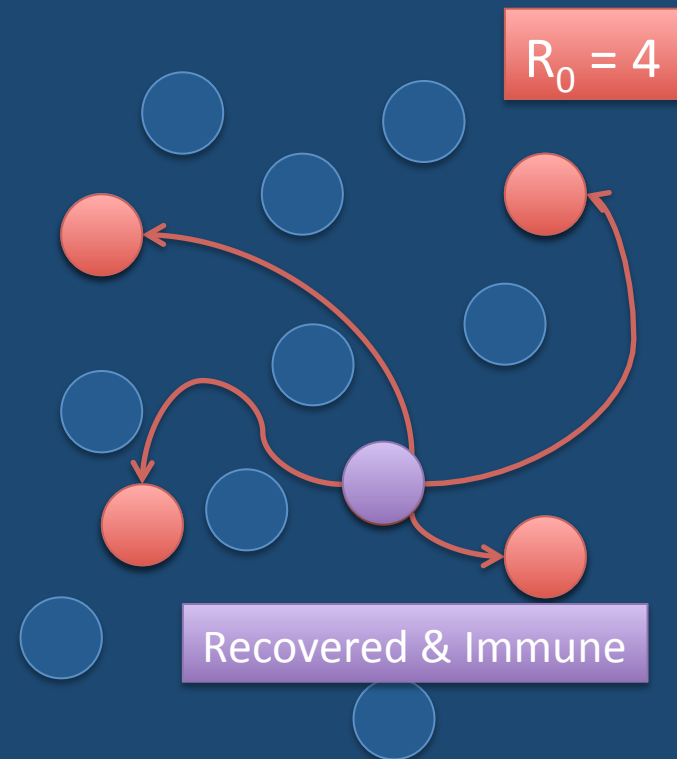
$$N = S + I + R$$

Constant population size



R_0 : The Basic Reproductive Number

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



SIR Model

$$R_0 =$$

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

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

X

1

Proportion of new infections that become infectious

X

$1/\gamma$

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

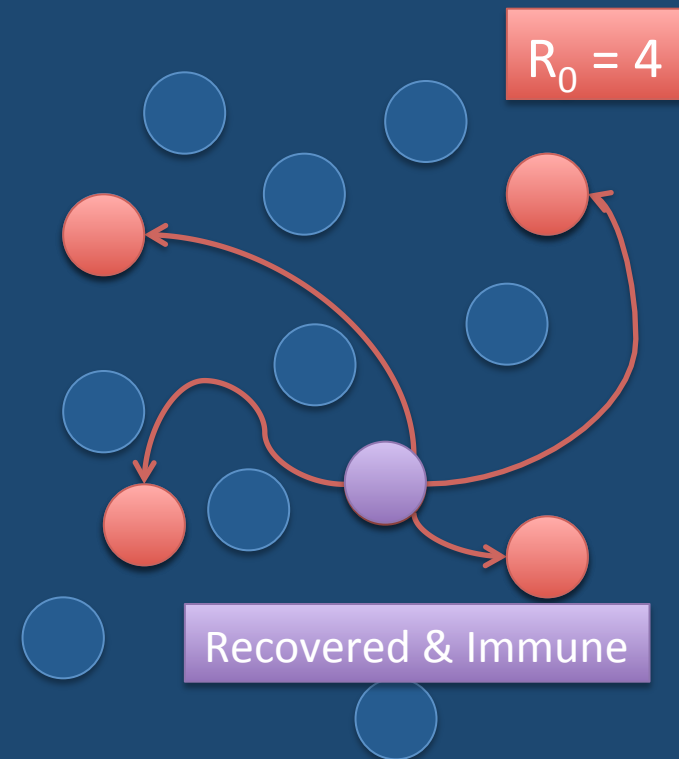
Proportion of new infections that become infectious

X

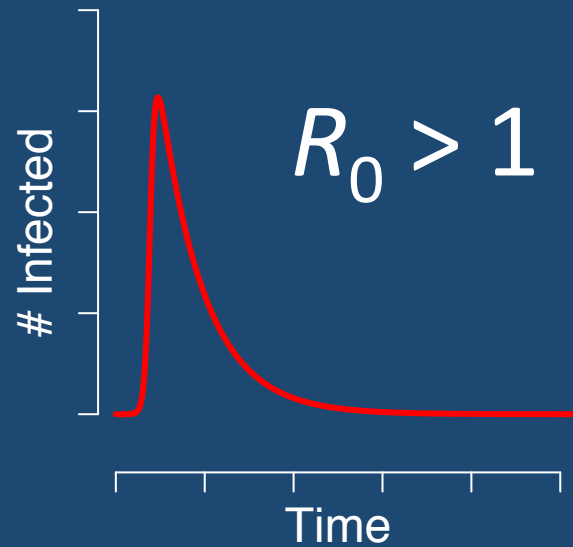
Average duration of infectiousness

R_0 : The Basic Reproductive Number

- Average # of secondary infections an infected host produces in a susceptible population.
- Threshold criteria:
 - If $R_0 < 1$, disease dies out
 - If $R_0 > 1$, disease persists



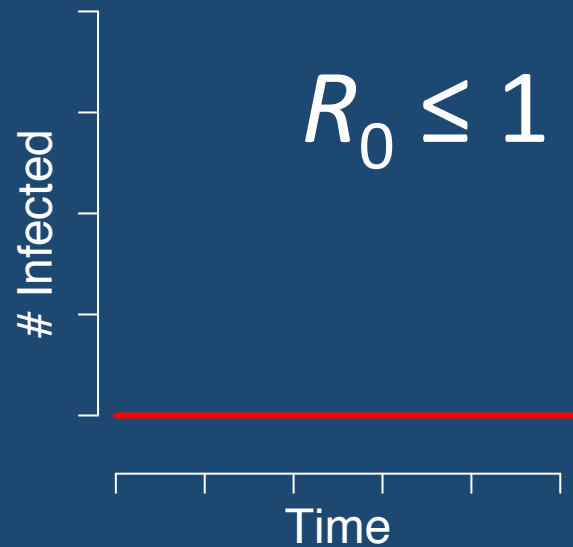
SIR Model: R_0 as a Threshold



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

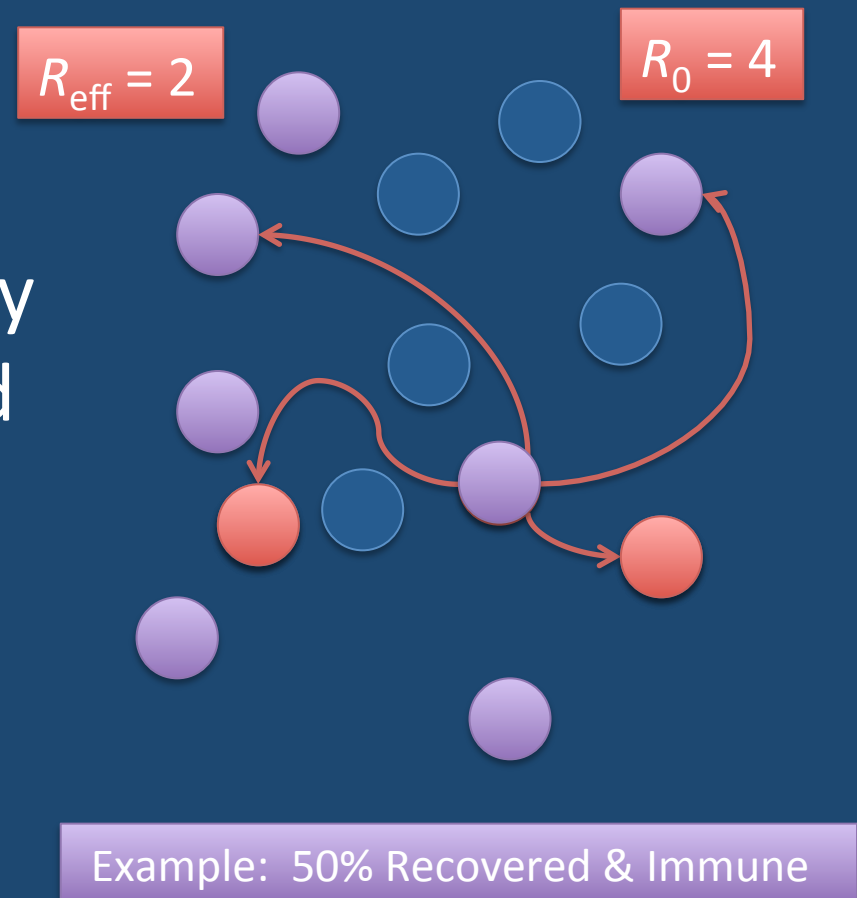
Disease Introduction:

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

$$1/\gamma$$

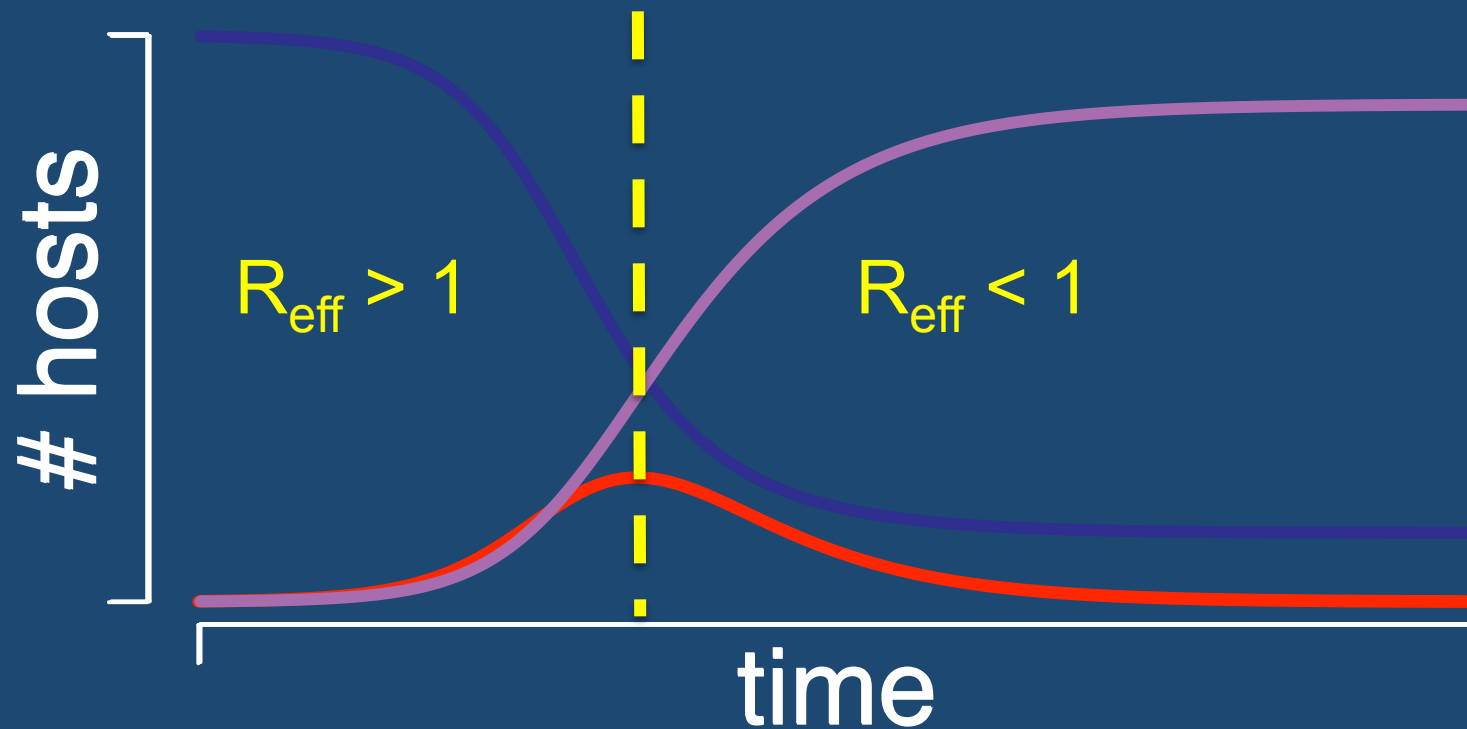
Average duration of infectiousness

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

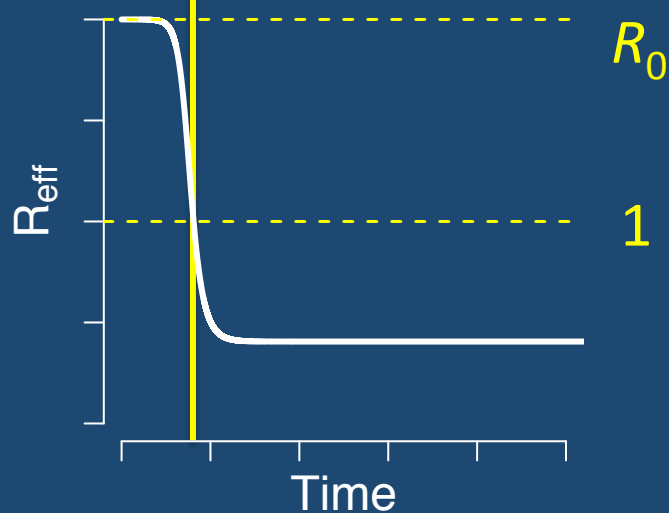
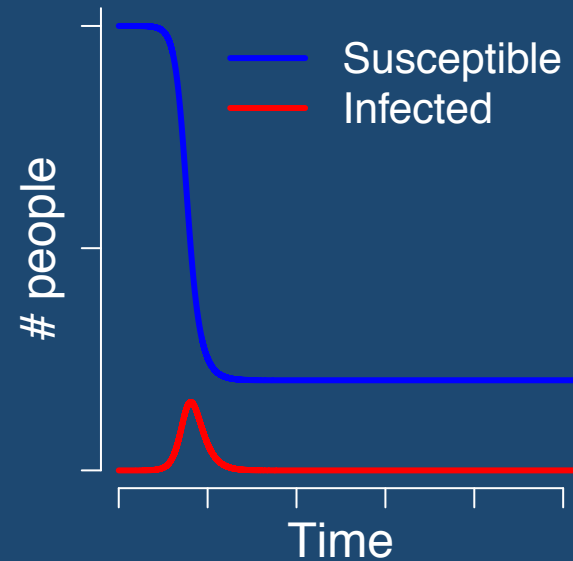
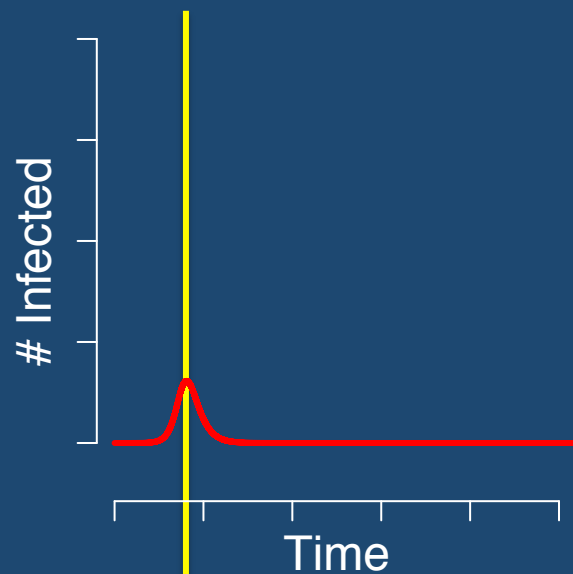
Why do epidemics peak?

Death or long-term immunity leads to exhaustion of susceptibles

— Infected Hosts



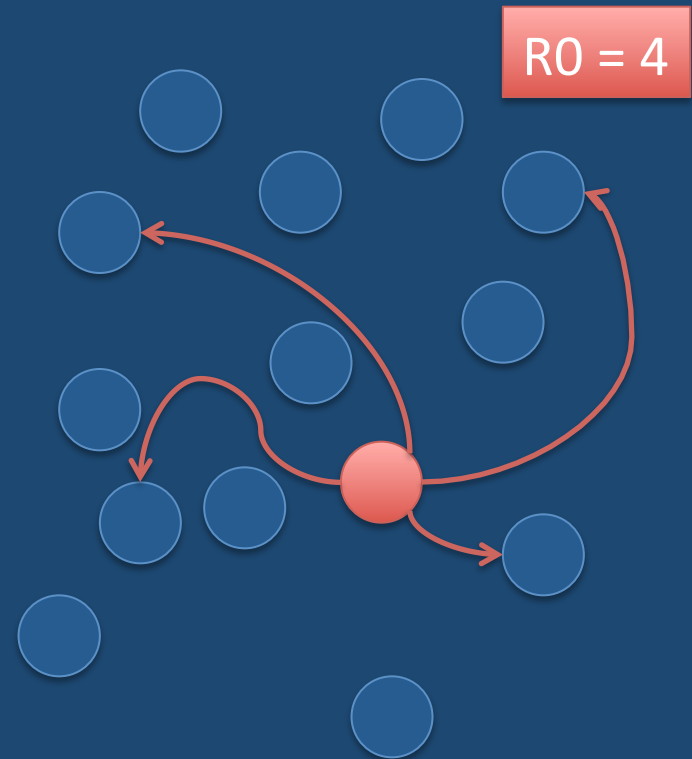
R_{eff} : The Effective Reproductive Number



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

Proportion to Vaccinate

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



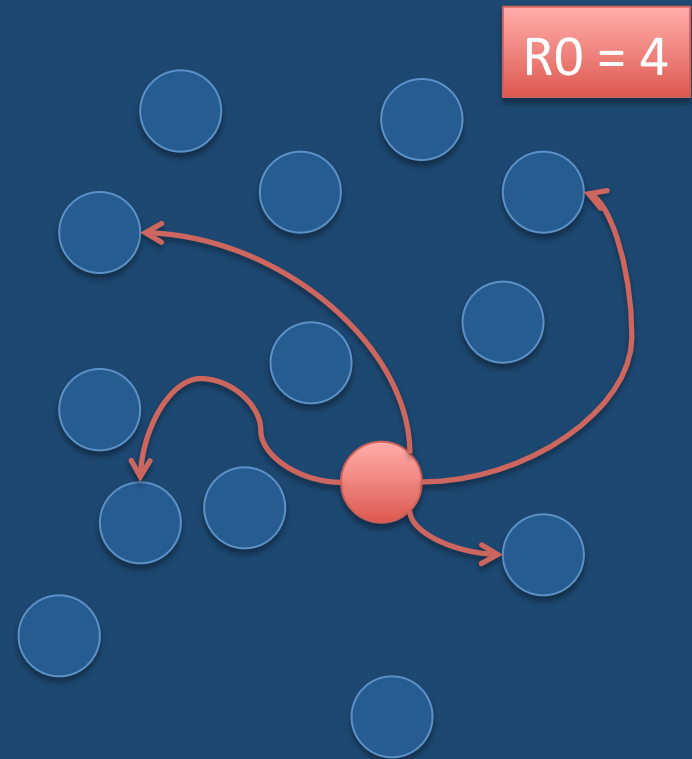
Proportion to Vaccinate

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

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

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

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



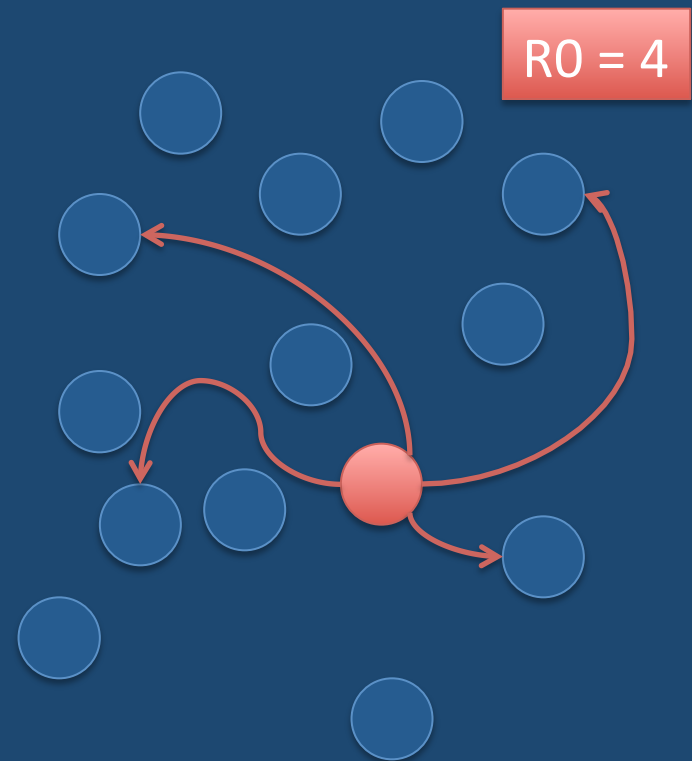
Proportion to Vaccinate

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

Proportion immune = $P_V =$
1 – proportion susceptible

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

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



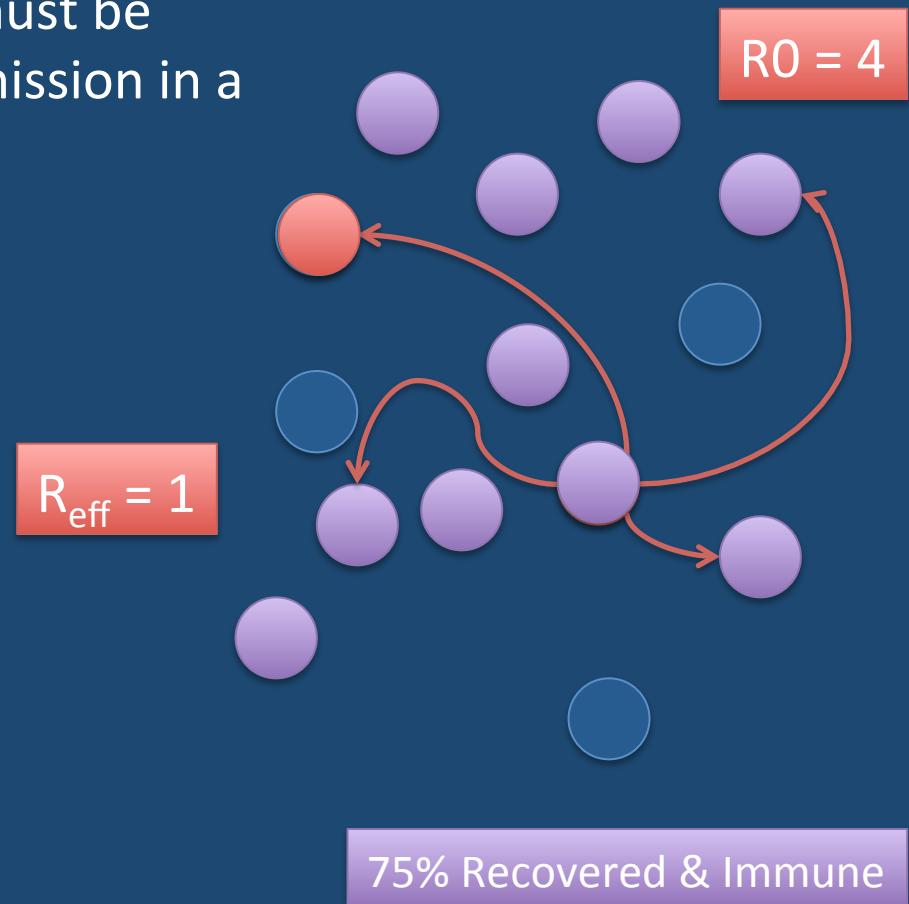
You don't have to vaccinate everyone to eliminate transmission!!!

Proportion to Vaccinate

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

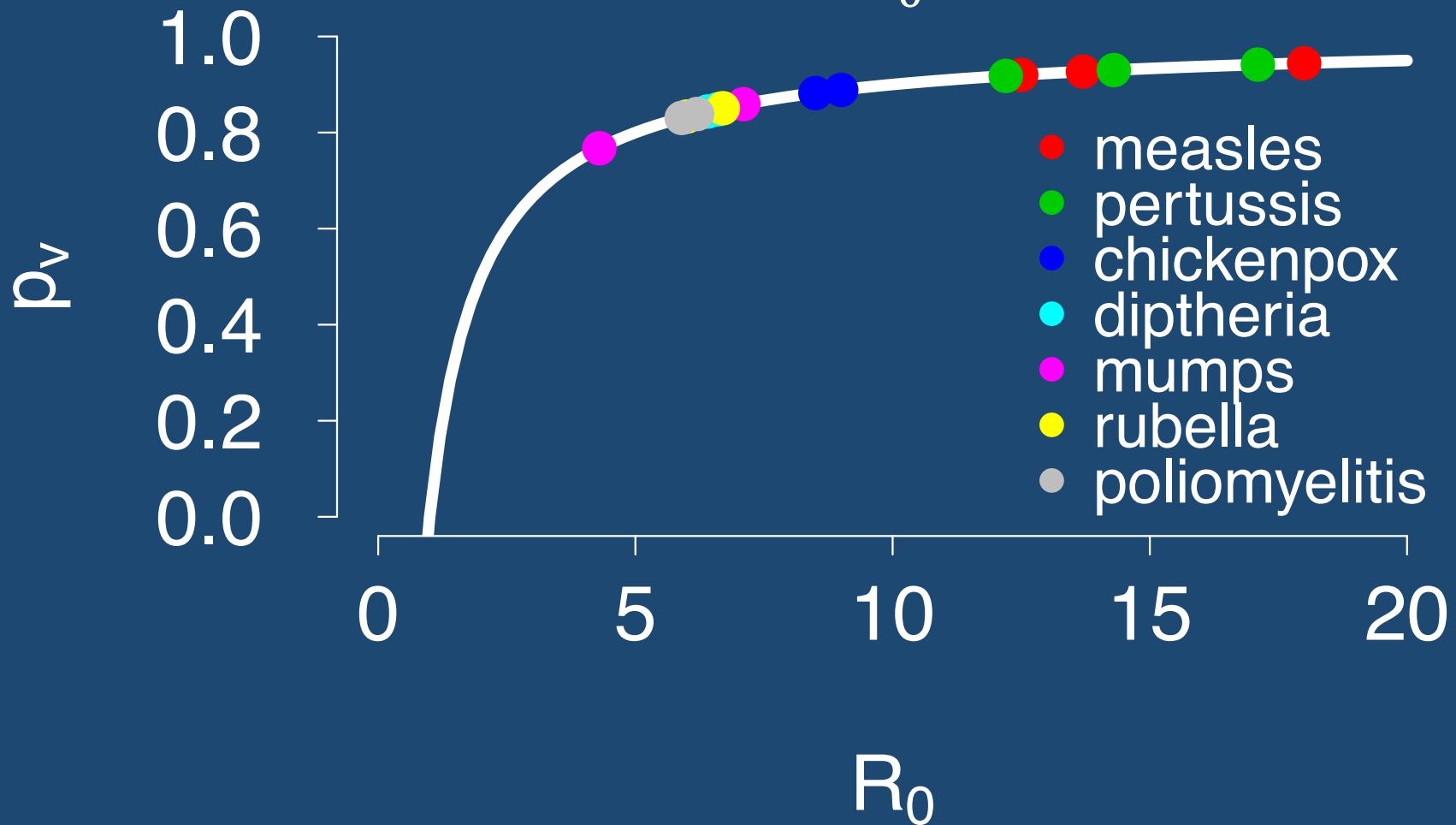
$$P_V \geq \frac{R_0 - 1}{R_0}$$

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

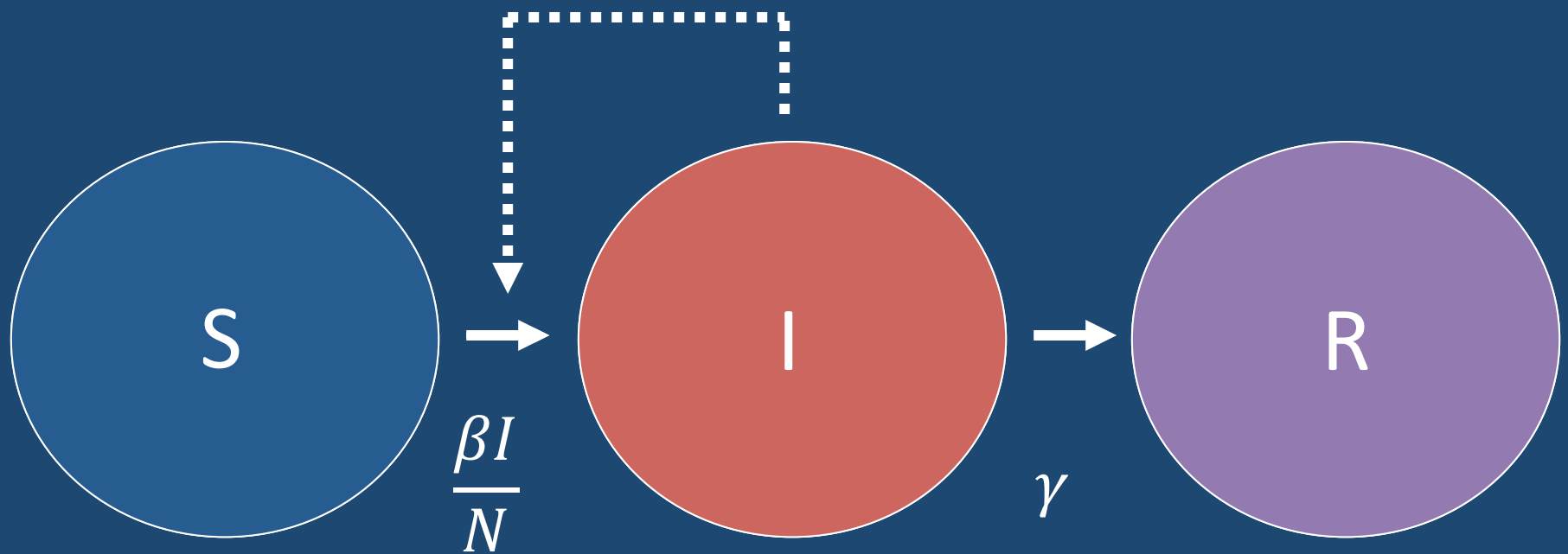


Elimination Thresholds

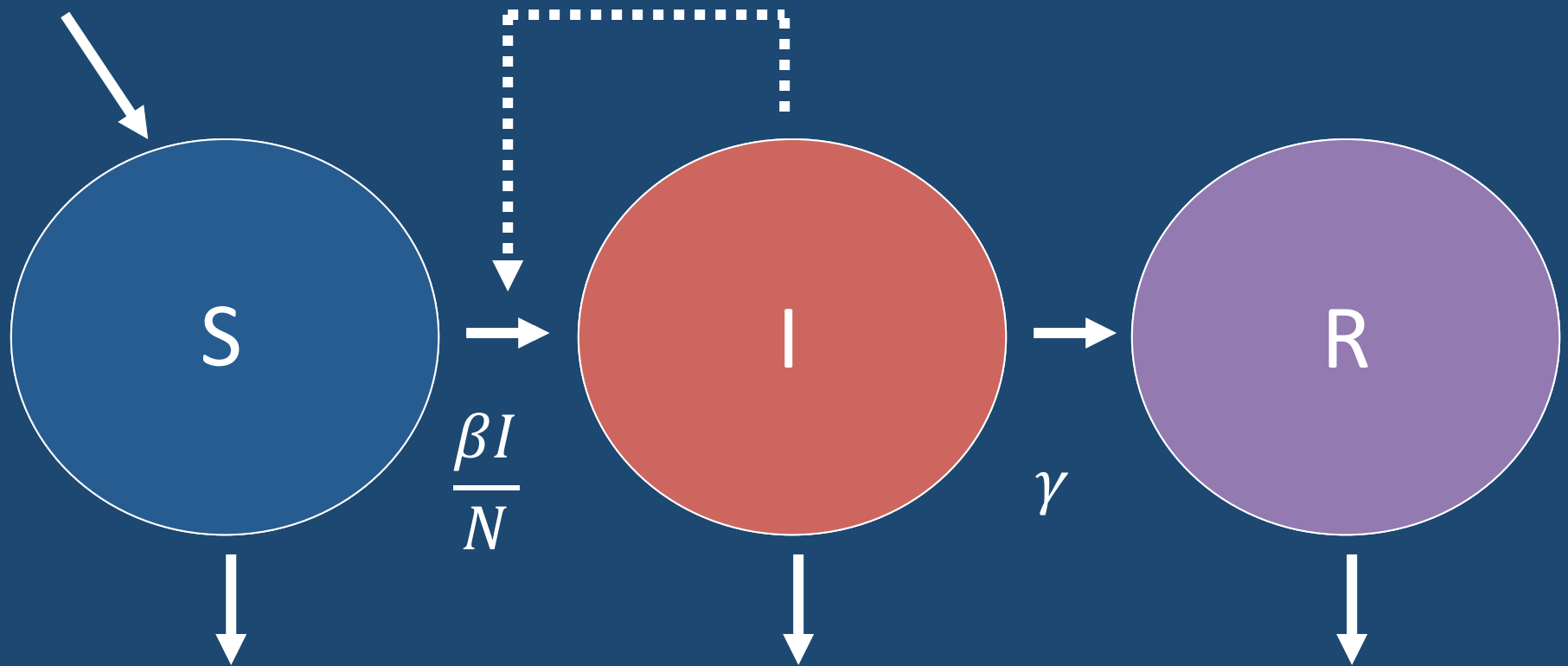
$$P_V = \frac{R_0 - 1}{R_0}$$



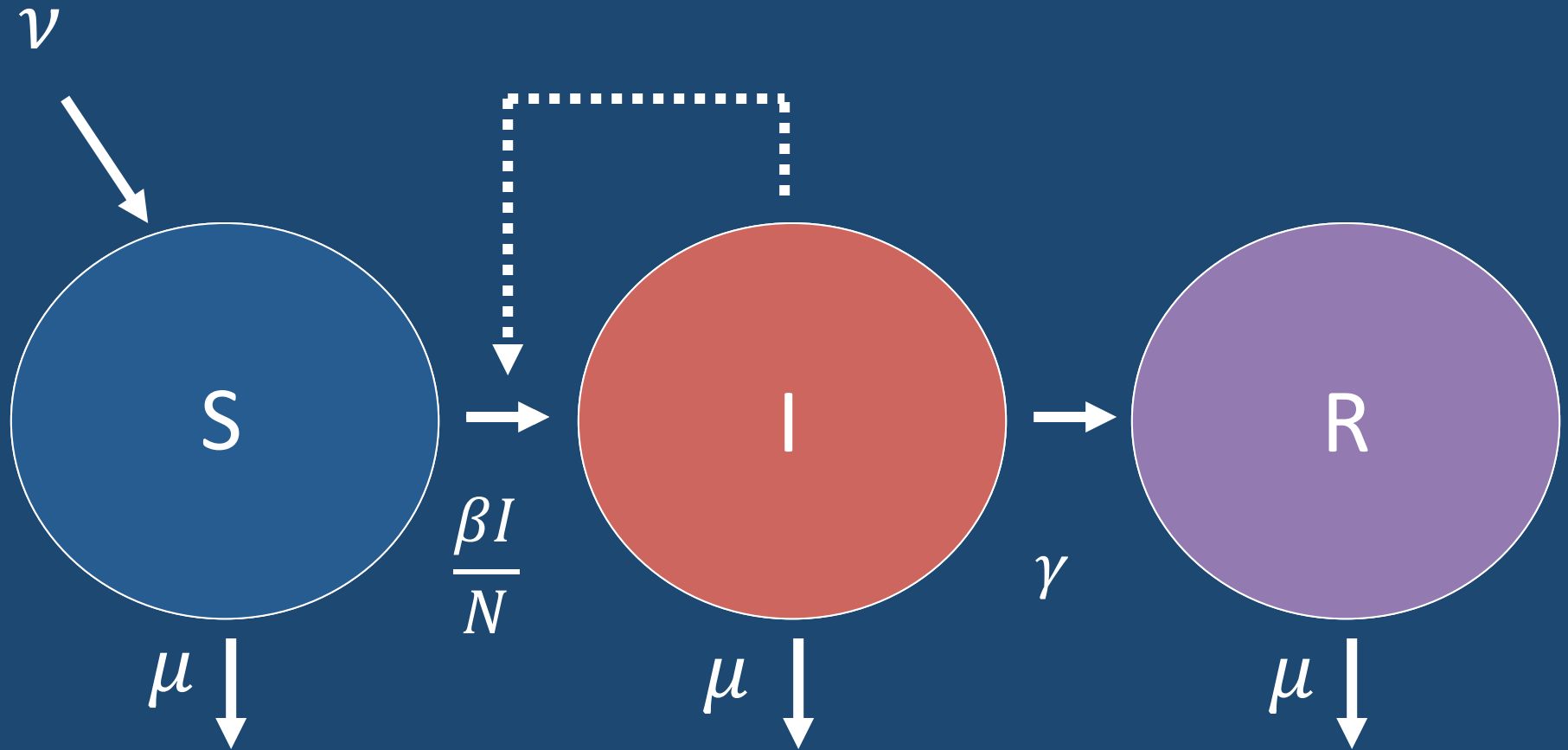
SIR Model



SIR Model with Birth & Death



SIR Model with Birth & Death



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

1

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

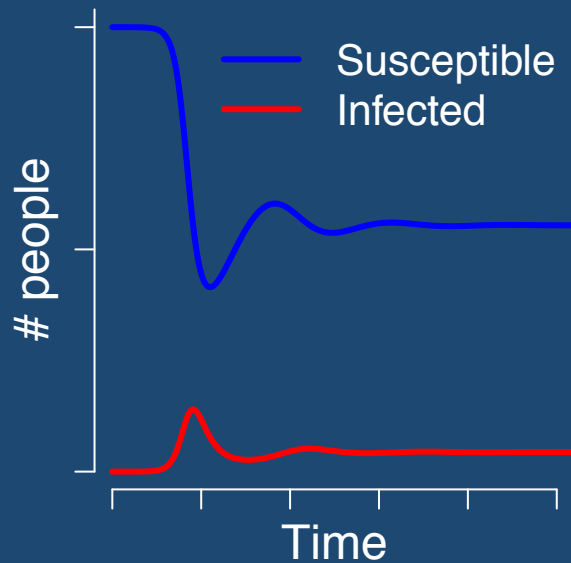
SIR Model with Birth & Death

Dynamics upon introduction:

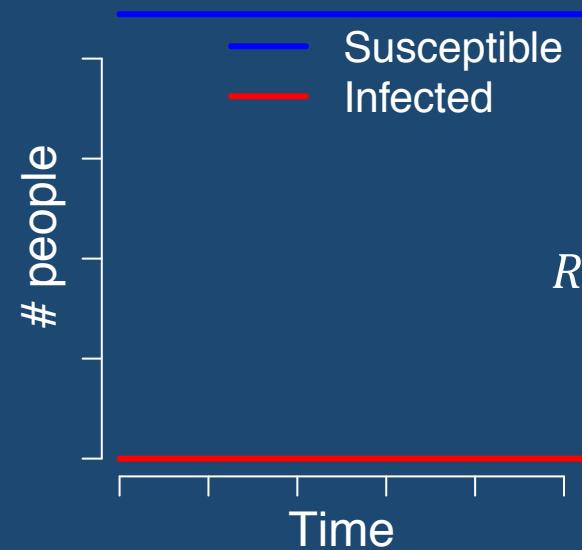
Epidemic if $R_0 > 1$

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

$$1$$

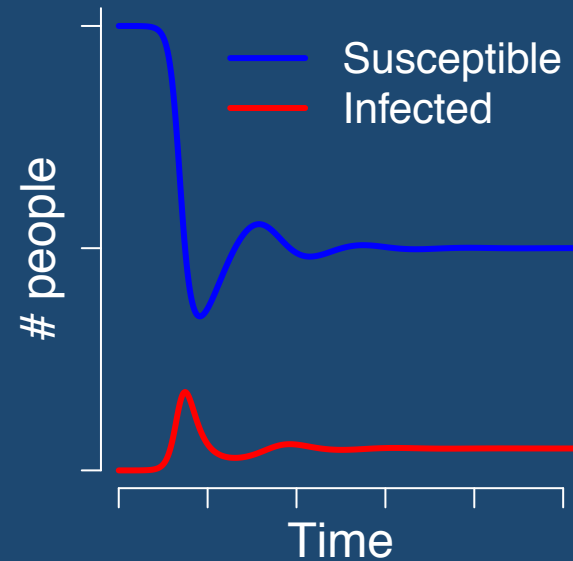
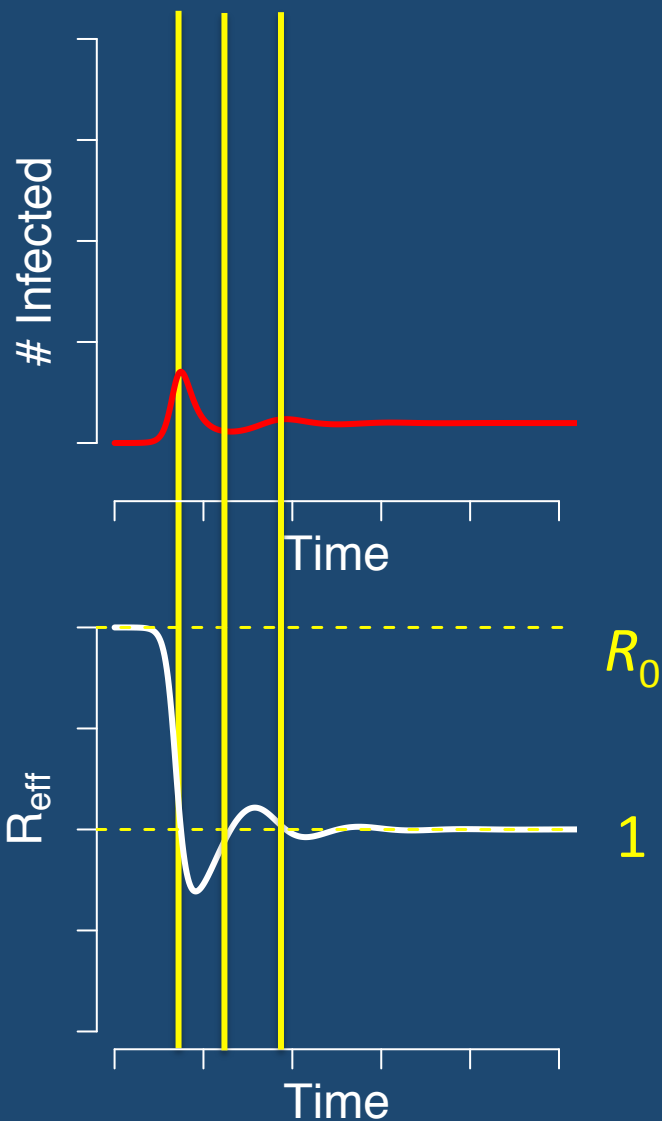
x

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

Average duration of infectiousness

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

R_{eff} : The Effective Reproductive Number

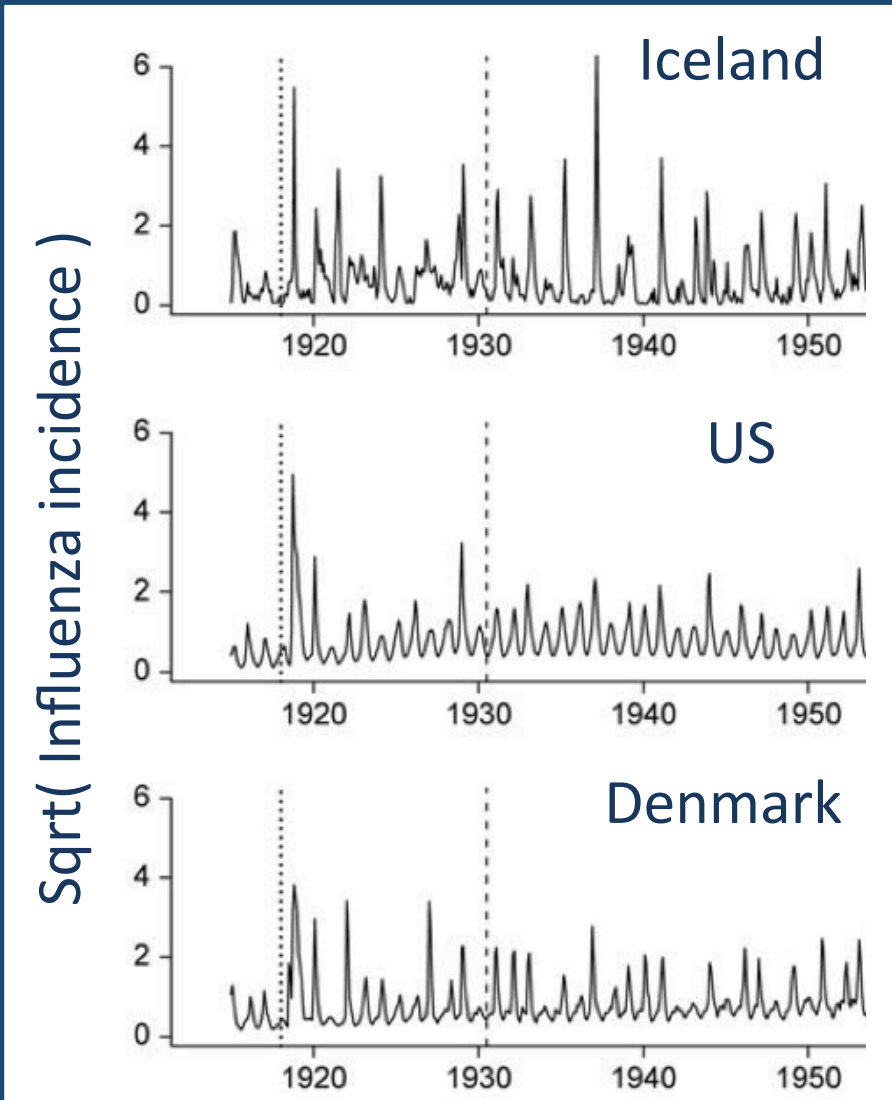


$$R_{\text{eff}}(t) = R_0 \frac{S(t)}{N}$$

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

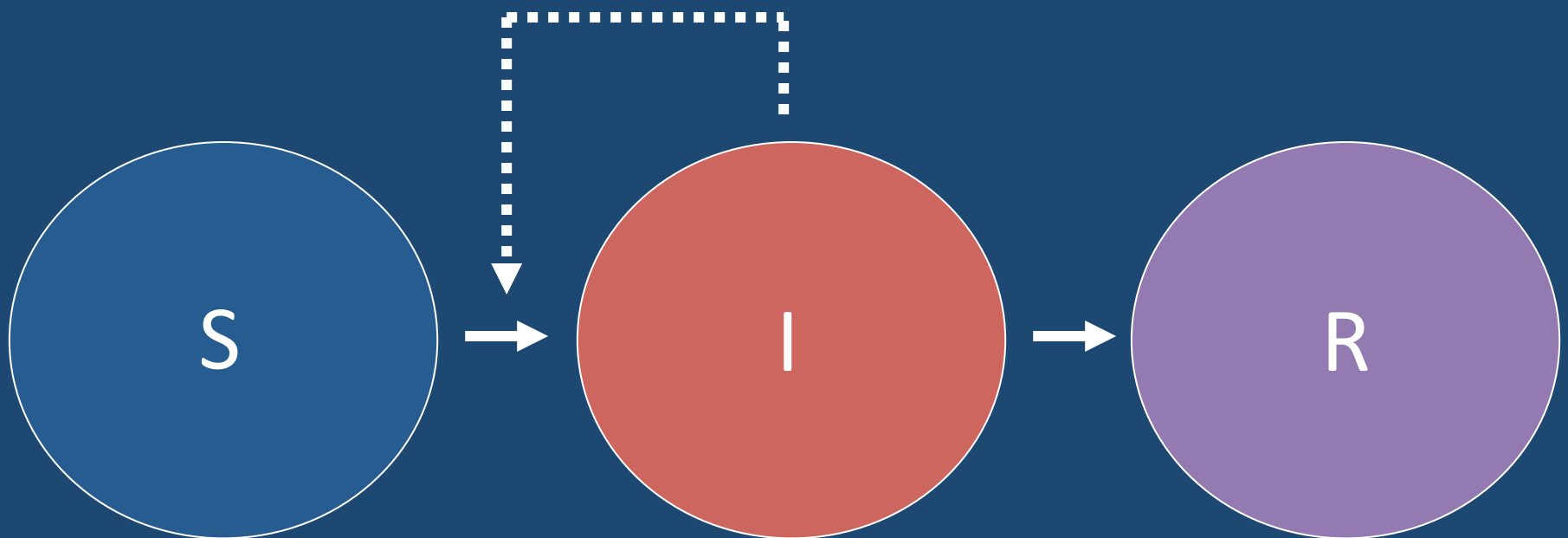
Why do recurrent epidemics happen?

- 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
 - 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

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

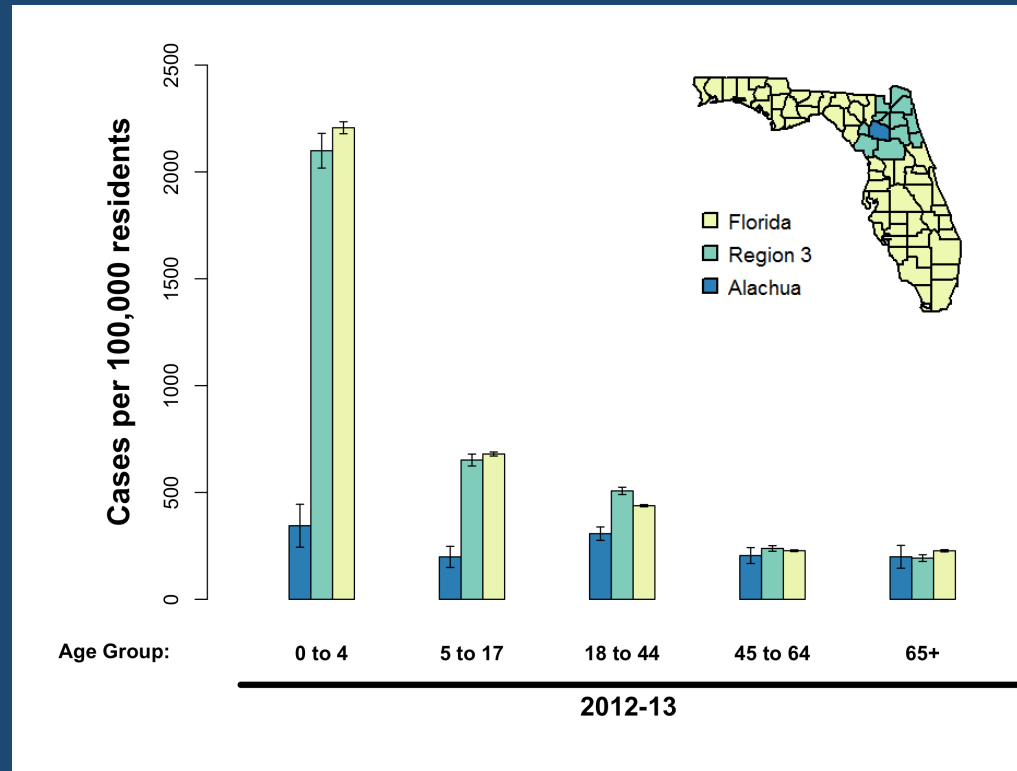
So, what did the influenza transmission model that motivated the Alachua County SLIV program look like?

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

Details:

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

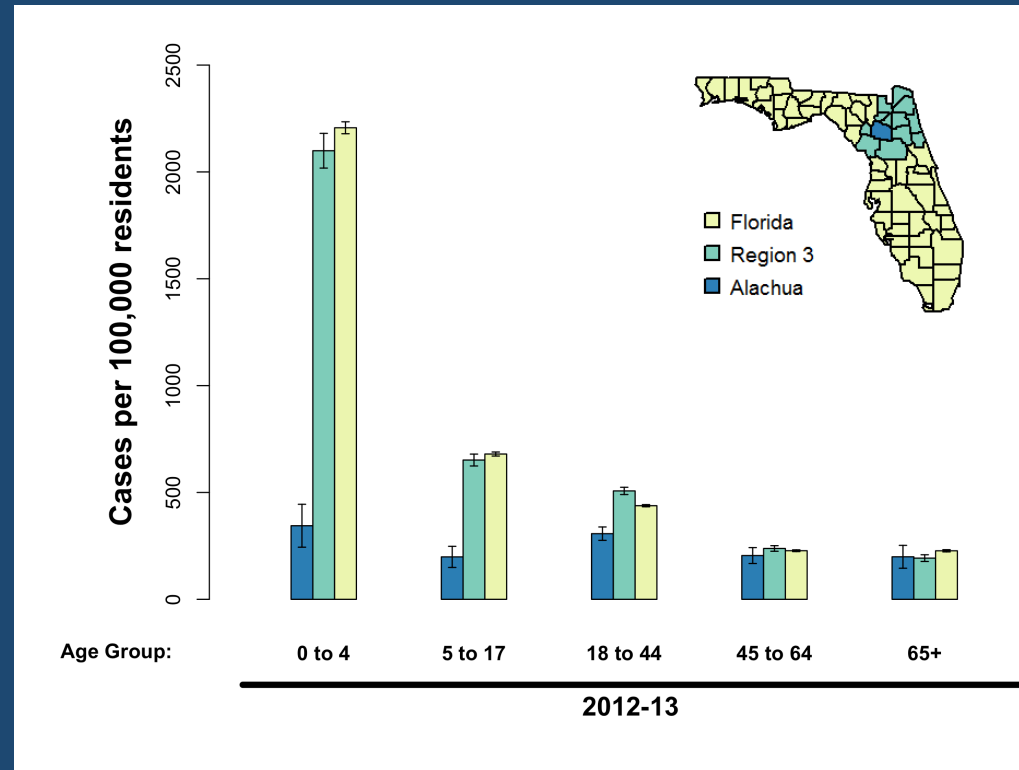
Were the predictions borne out?



Tran *et al.* Submitted

- Not entirely

Were the predictions borne out?



Tran *et al.* Submitted

- Not entirely
- Is the model still valuable?

Dynamical Fever Tutorial - goals

- develop an intuition for how transmission patterns influence the outcome of interventions
- practice making arguments based on indirect evidence, and
- internalize the concept of a “model world”
 - an abstraction of the world that is simple and fully specified, which we construct to help us understand particular aspects of the real world

Acknowledgements

Alachua County Control Flu Program

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- Cuc Tran & Parker Small

For sharing materials used in this presentation

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FOGARTY



NIGMS, National Institutes of Health
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UF Emerging Pathogens Institute

