



**HARVARD
T.H. CHAN**

SCHOOL OF PUBLIC HEALTH

Introduction to SIR Modeling

12th Annual Workshop to Increase Diversity in Mathematical
Modeling and Public Health



CENTER *for*
COMMUNICABLE
DISEASE DYNAMICS

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Acknowledgments



Previous version of this lecture by:

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University of Colorado Boulder

<https://kisslerlab.github.io/>

Infectious disease burden

Economic burden

US\$ 8 trillion

Health burden

**168 million
disability-adjusted
life years lost**

* of just 8 infectious diseases in a single year (HIV/AIDS, malaria, measles, hepatitis, dengue fever, rabies, tuberculosis and yellow fever)

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GDP of Germany:
\$4.1 trillion



Net worth of the 735 billionaires in the
United States: **\$4.5 trillion**



Forbes

Infectious disease burden

Economic burden

US\$ 8 trillion

Health burden

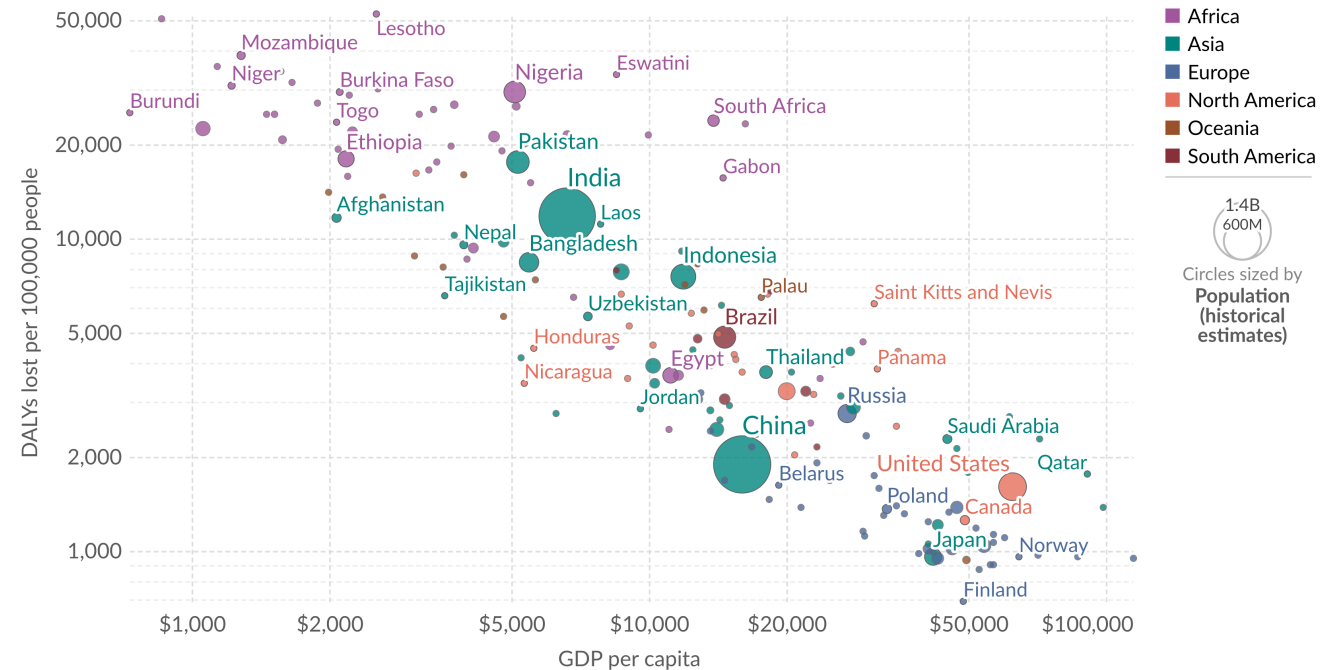
168 million
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life years lost

* of just 8 infectious diseases in a single year (HIV/AIDS, malaria, measles, hepatitis, dengue fever, rabies, tuberculosis and yellow fever)

Disease burden due to communicable diseases vs. GDP per capita, 2019

Our World in Data

Disease burden to communicable, maternal, neonatal and nutritional diseases, measured in DALYs (Disability-Adjusted Life Years) per 100,000 individuals versus gross domestic product (GDP) per capita, measured in constant international-\$.
Circles sized by Population (historical estimates)

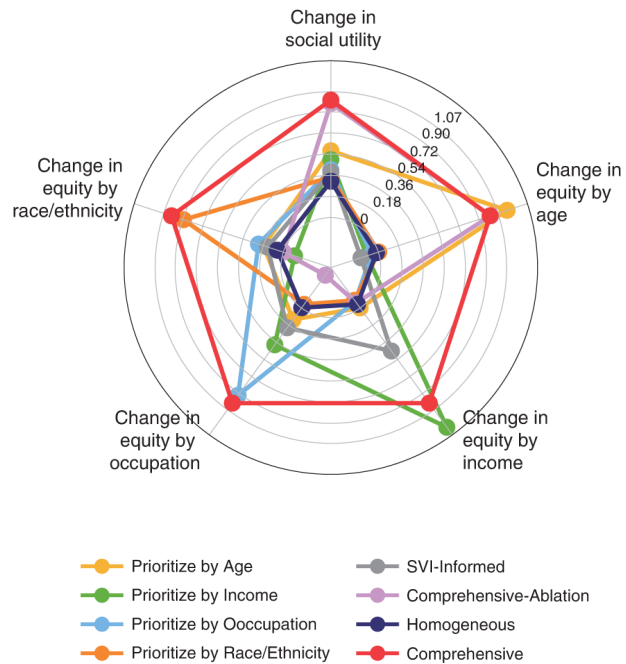


Data source: IHME, Global Burden of Disease (2019); Data compiled from multiple sources by World Bank
OurWorldInData.org/burden-of-disease | CC BY

Mathematical models to achieve public health goals

Prevention

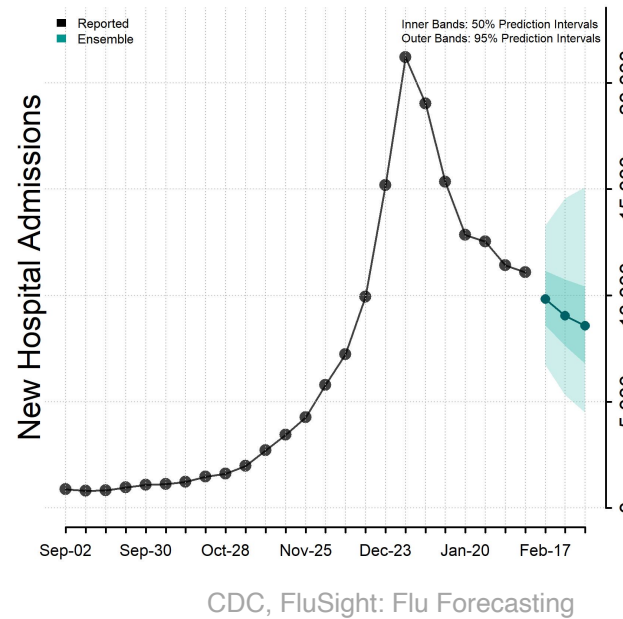
Which vaccine allocation strategy is most equitable?



Chen et al. (2022)

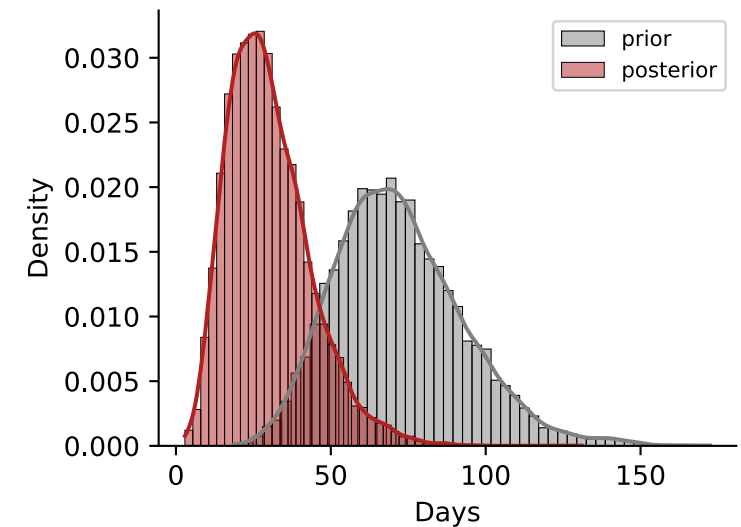
Prediction

How many hospitalizations?

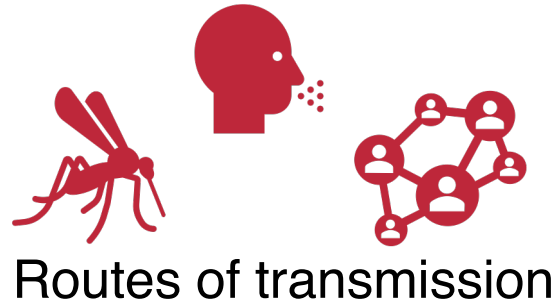
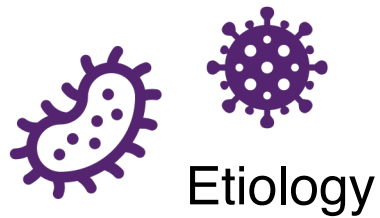


Understanding

How long is the latent period?



Characterizing infectious diseases



Malaria

Anopheles



Image: Wikipedia

- Active between sunset and sunrise
- Breed in natural bodies of water
- Multiple hosts

Insecticide treated bed nets



Image: USAID

Malaria

Anopheles



Image: Wikipedia

- Active between sunset and sunrise
- Breed in natural bodies of water
- Multiple hosts

Insecticide treated bed nets



Image: USAID

Dengue Fever

Aedes



Image: Wikipedia

- Daytime feeders
- Highly domesticated
- Human is preferred host

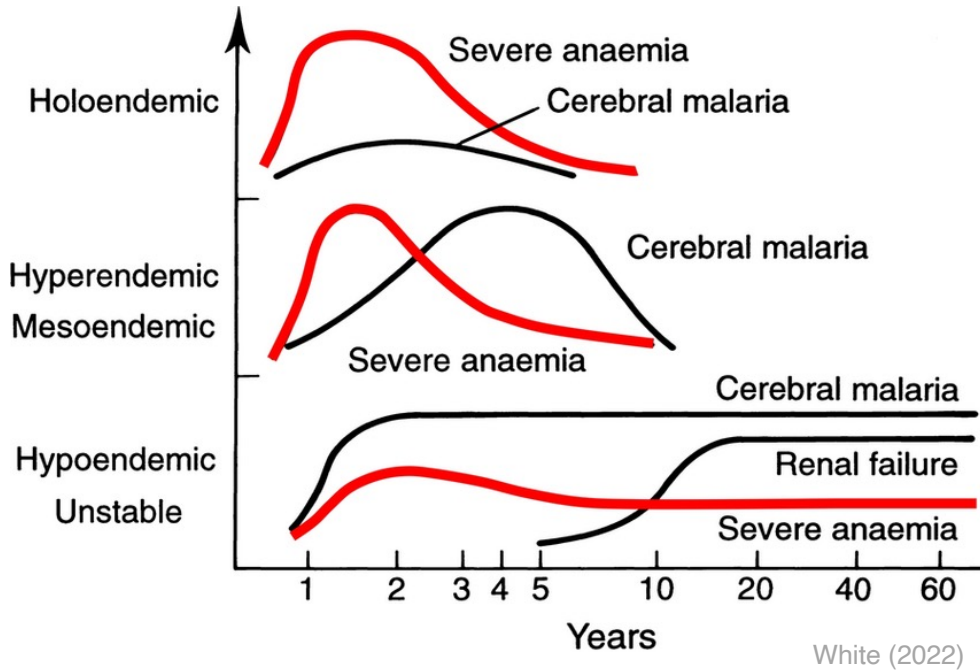
Removal of open water containers



Images: Municipal Government of Acerburgo, BR; FAPTO

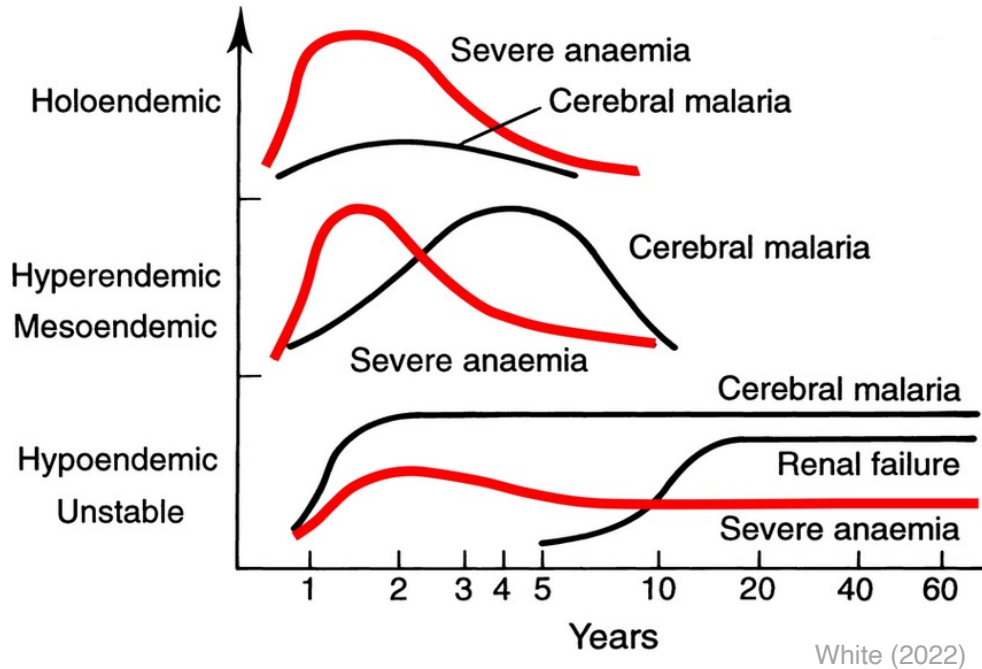
Malaria

Prior infection conveys some protection against reinfection and severe outcomes



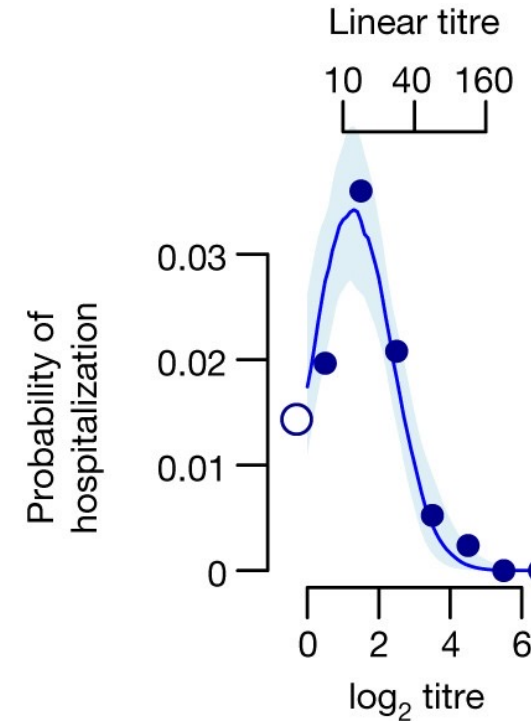
Malaria

Prior infection conveys some protection against reinfection and severe outcomes



Dengue Fever

Prior infection increases the risk of severe dengue

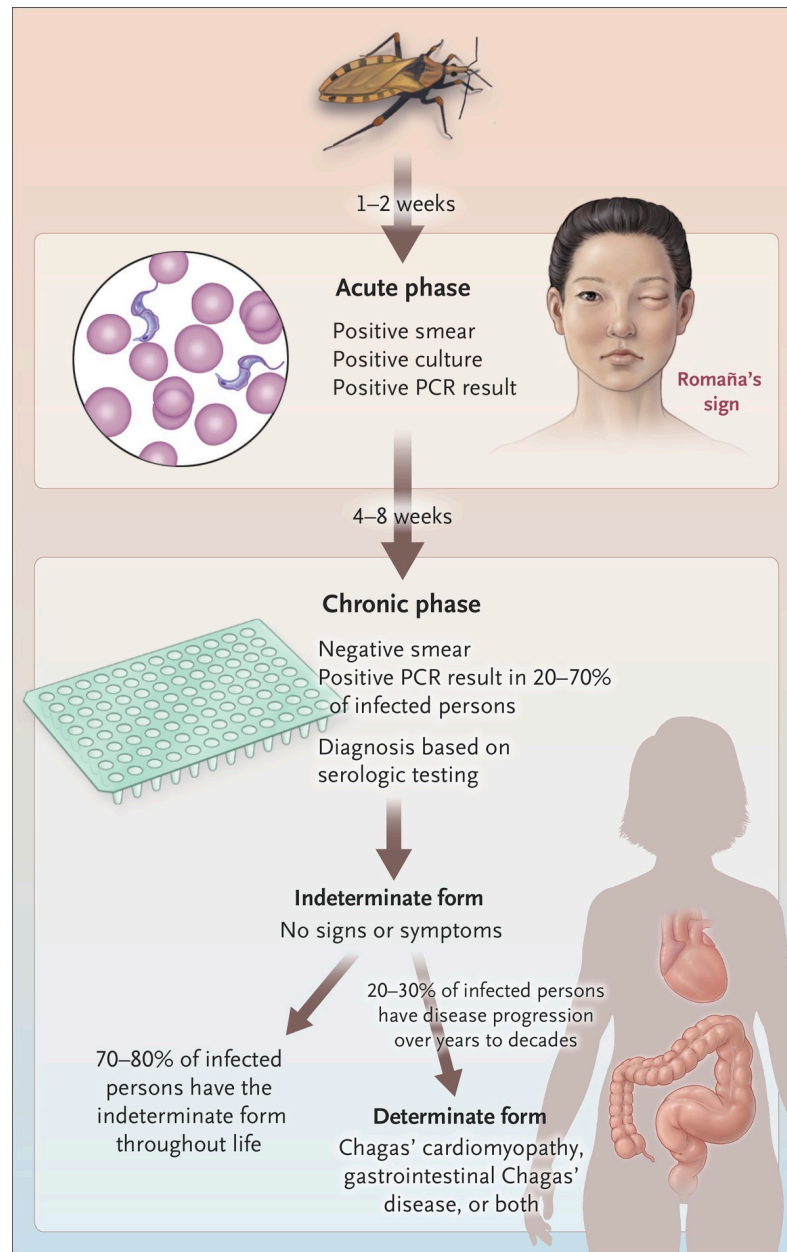


Chagas Disease

Carlos Chagas (1879 – 1934)



Image: Casa de Oswaldo Cruz

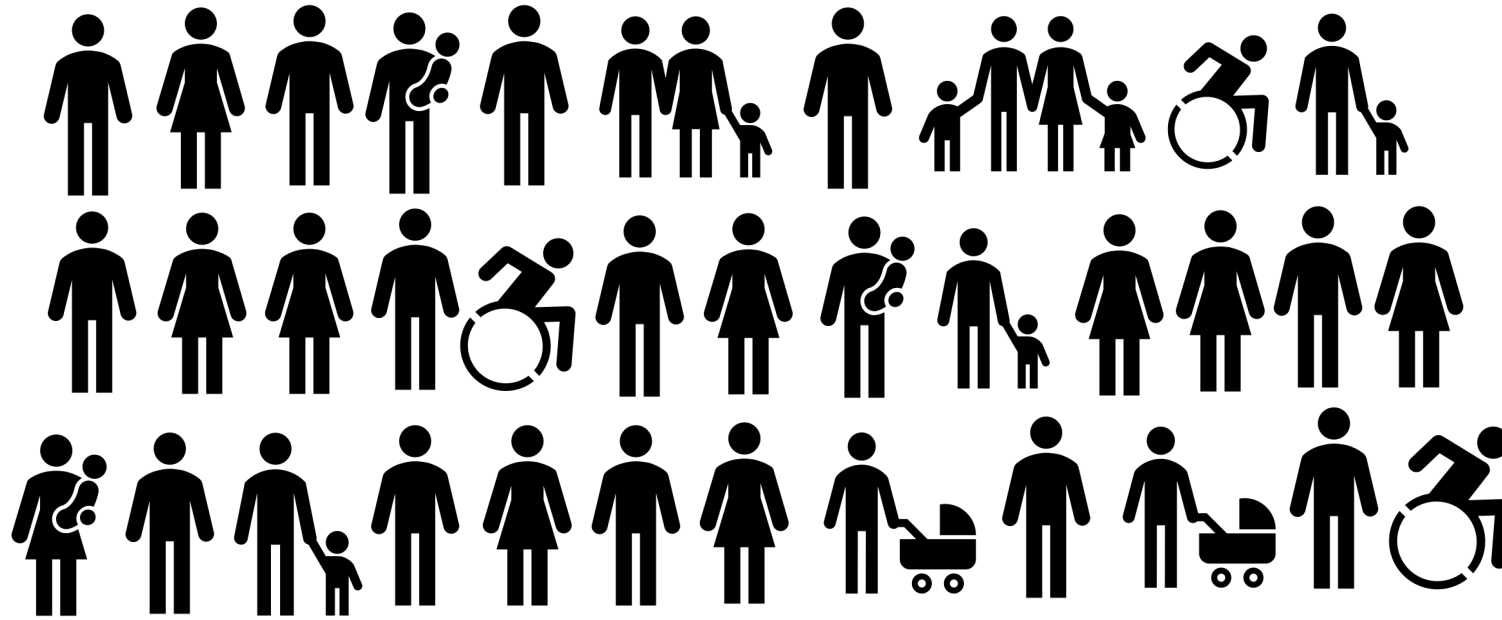
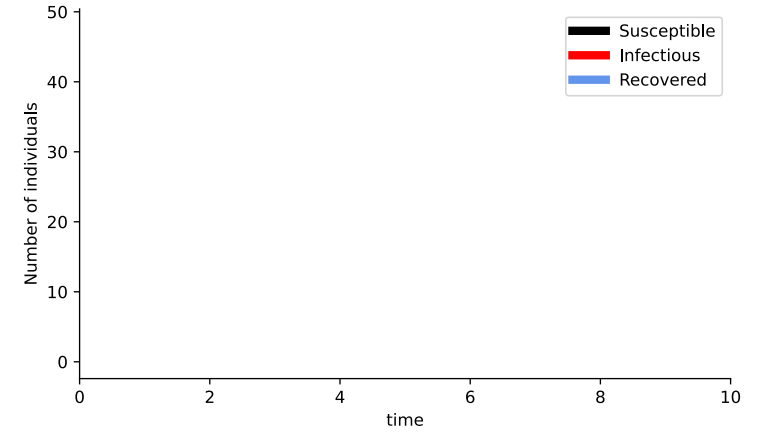
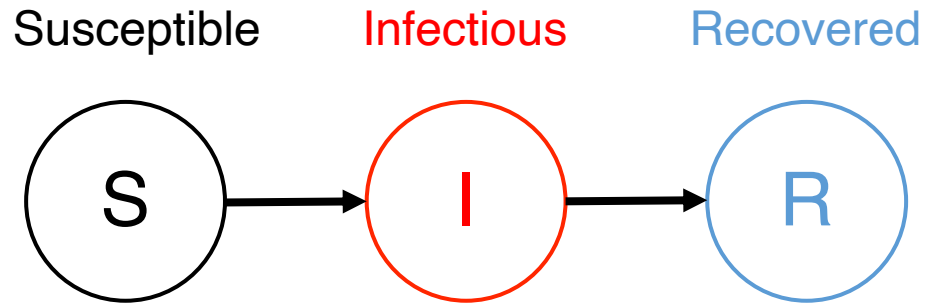


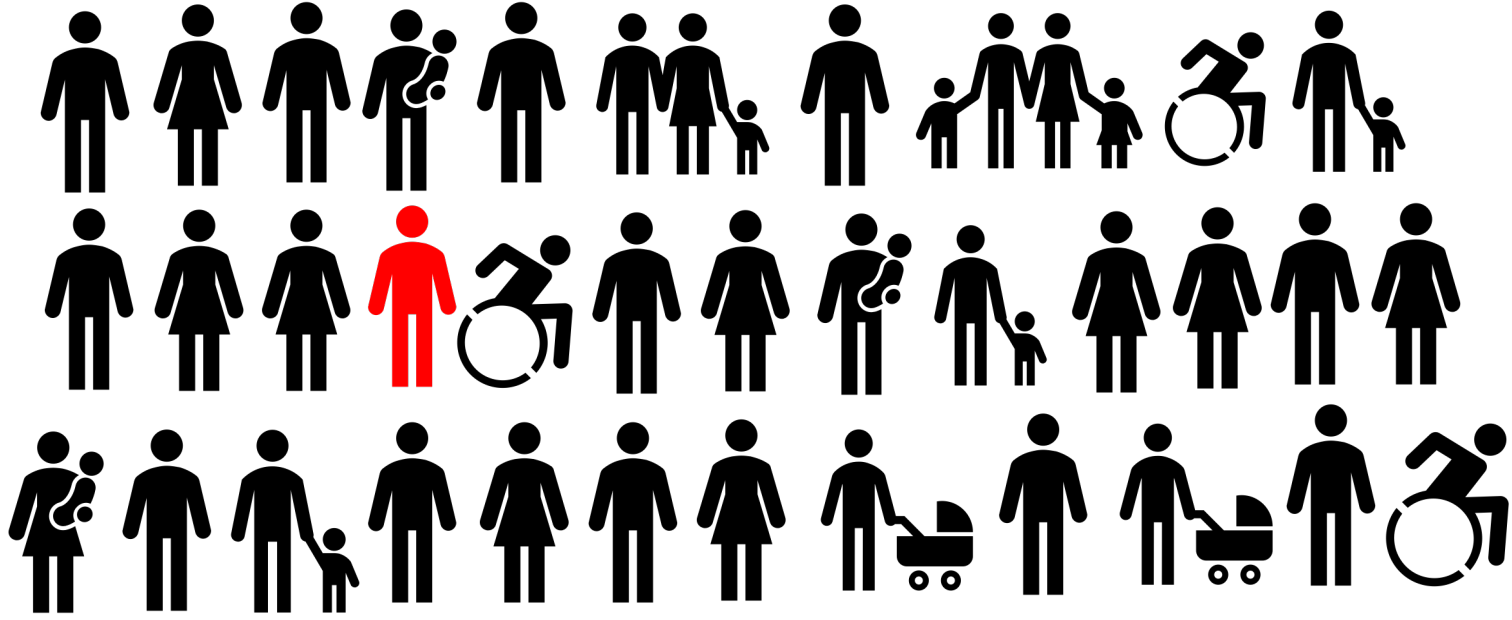
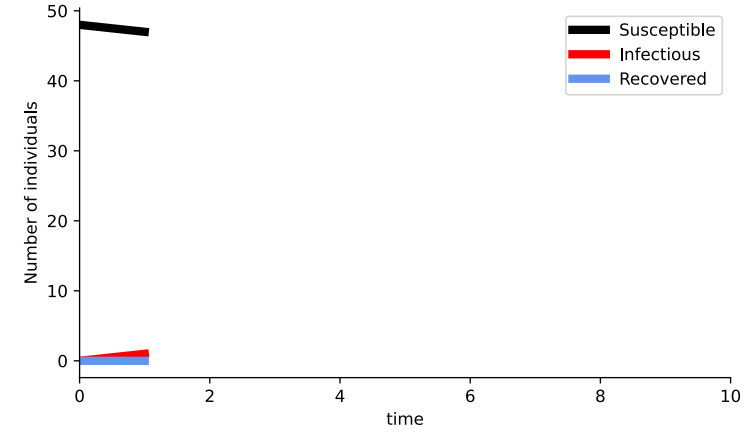
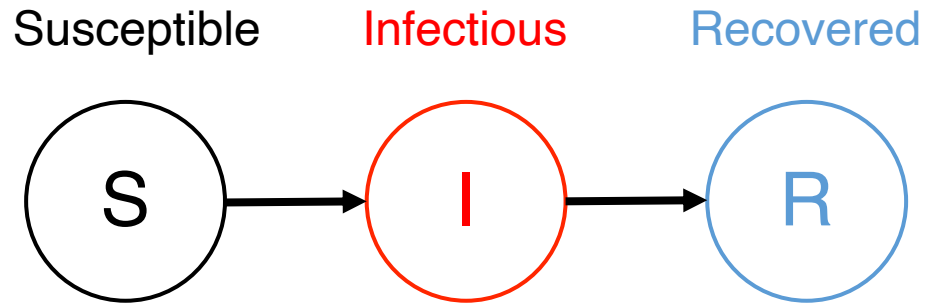
Vector control

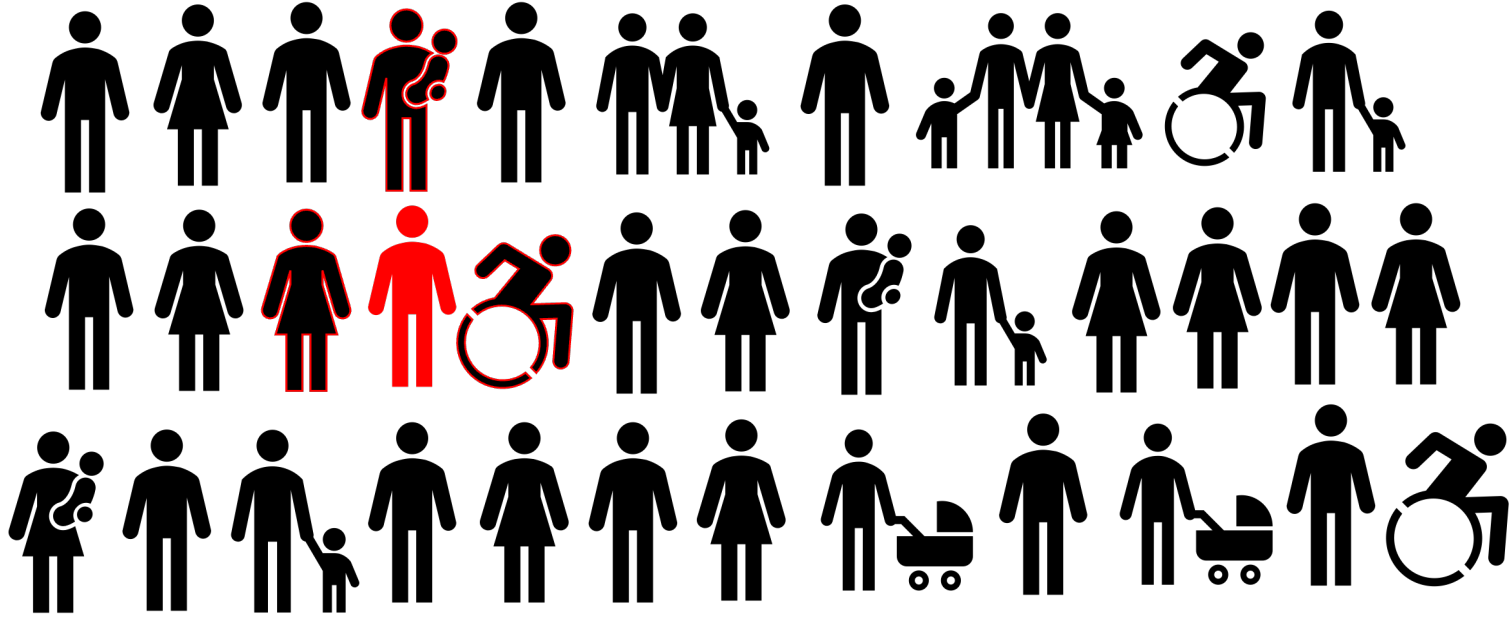
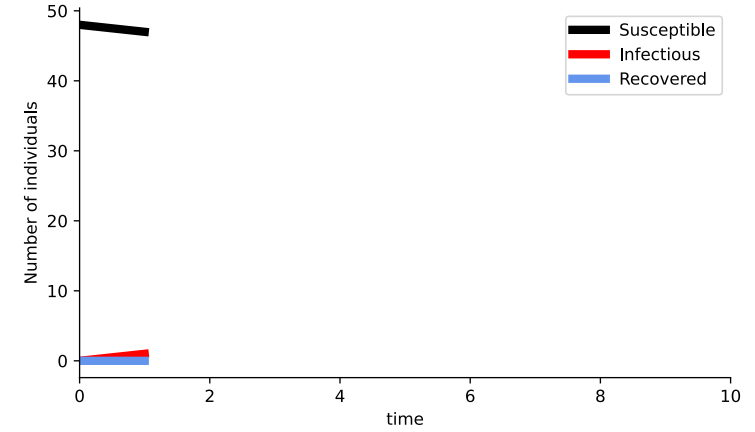
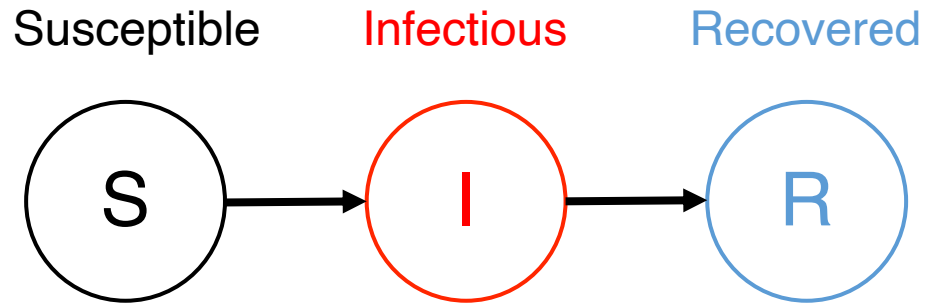


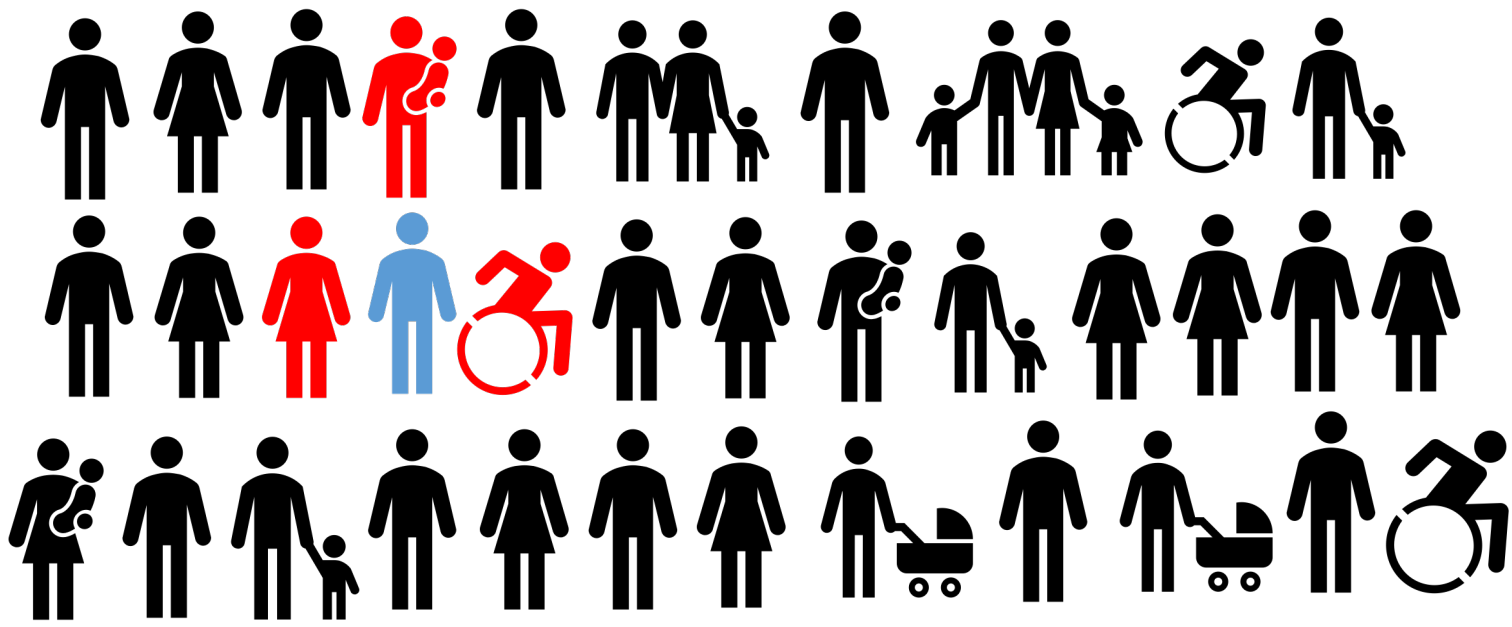
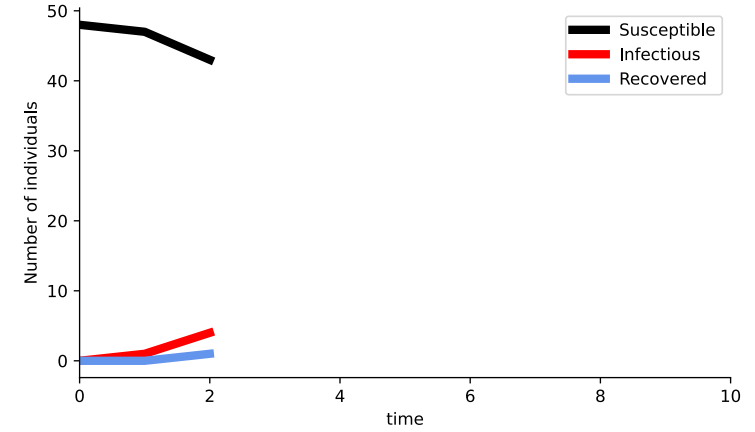
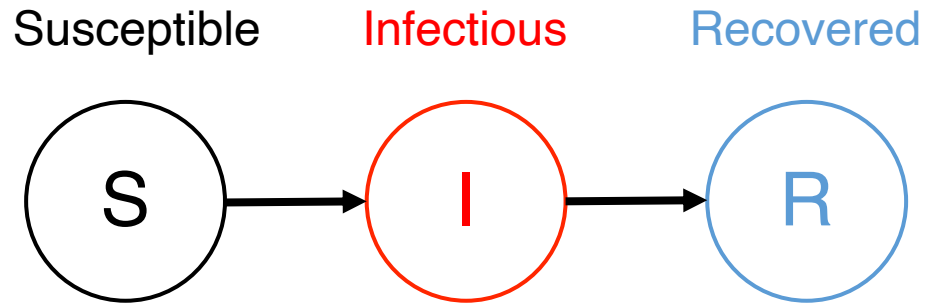
Image: PAHO

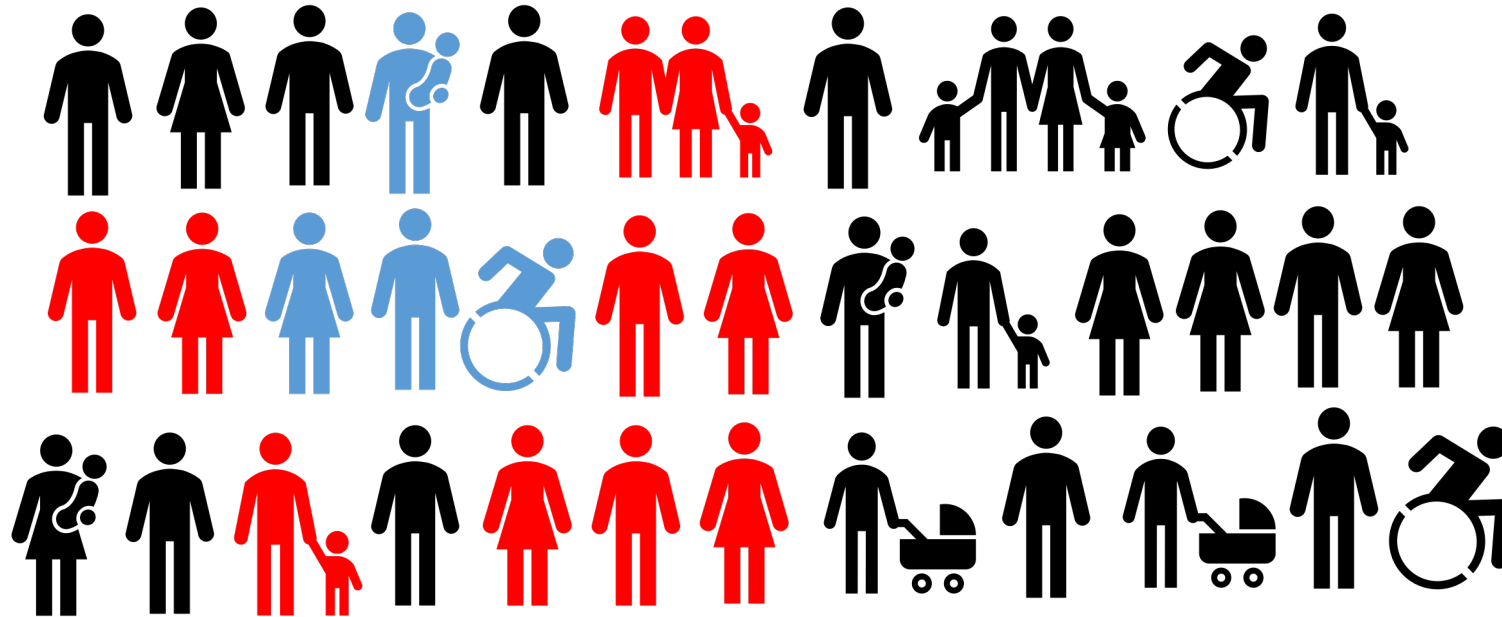
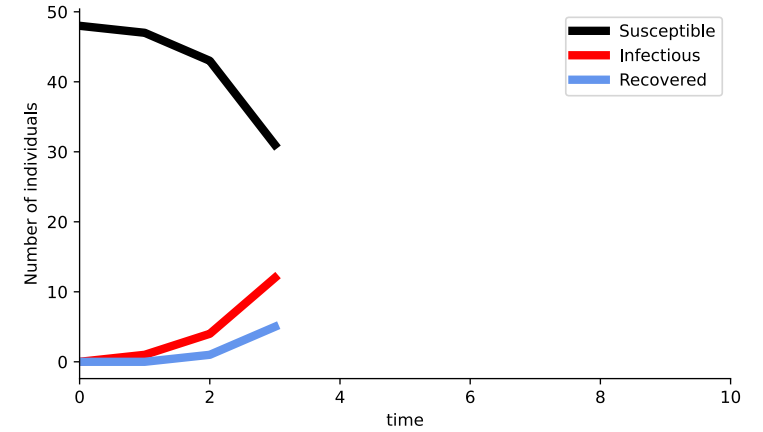
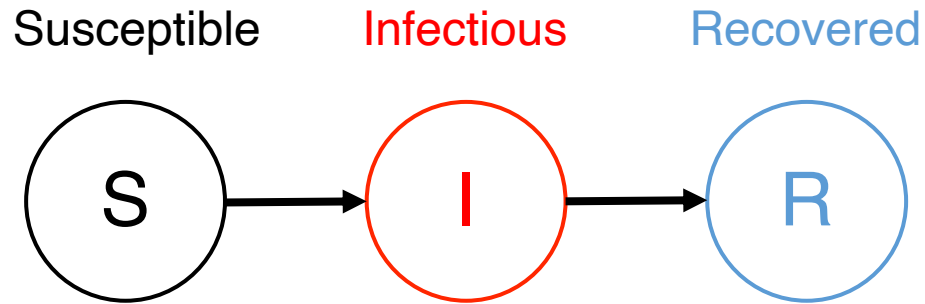
Translating a disease process into a mathematical model

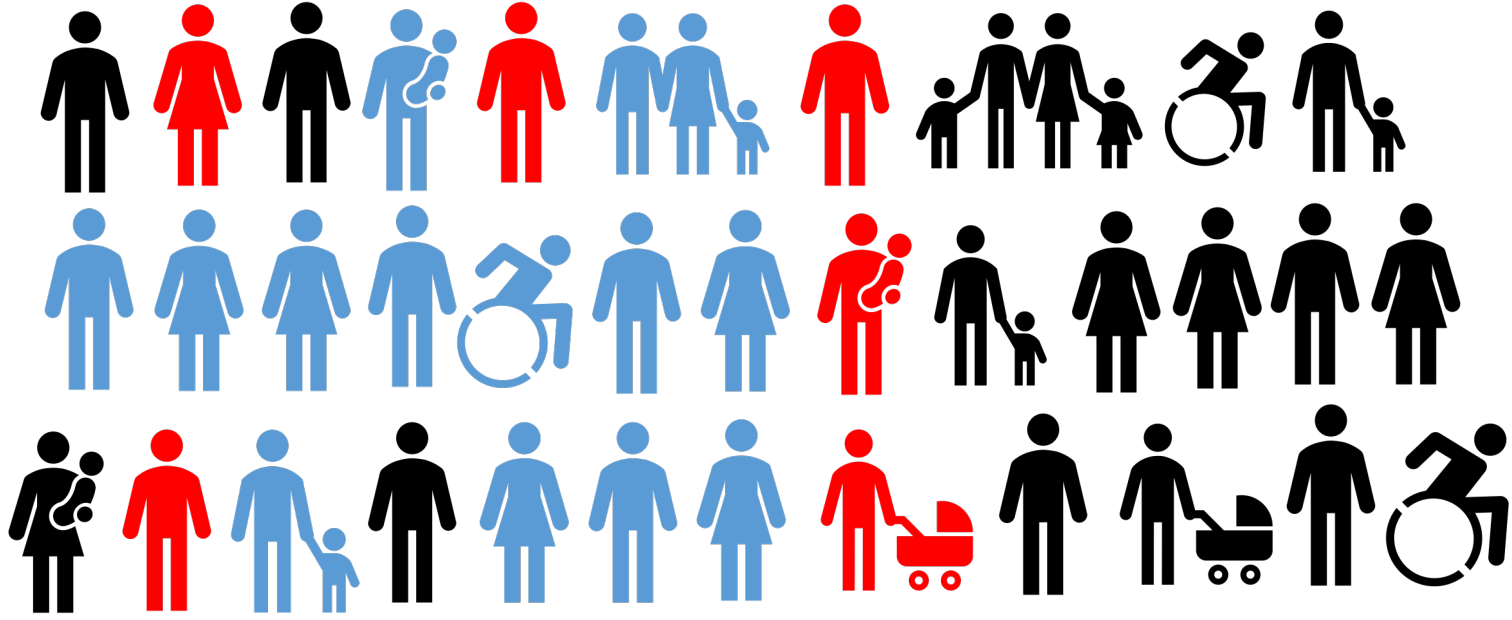
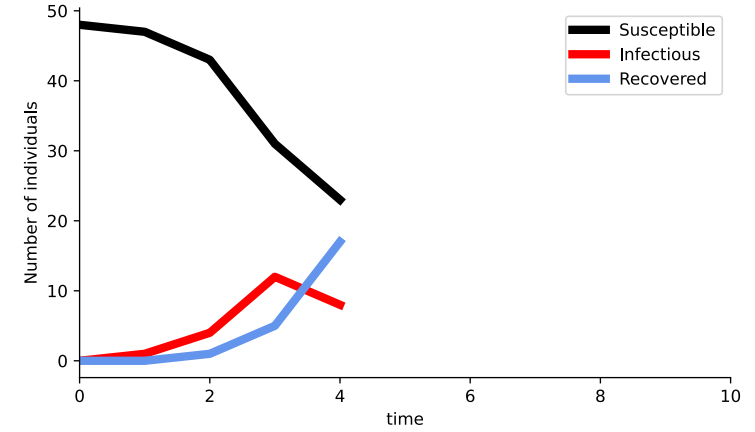
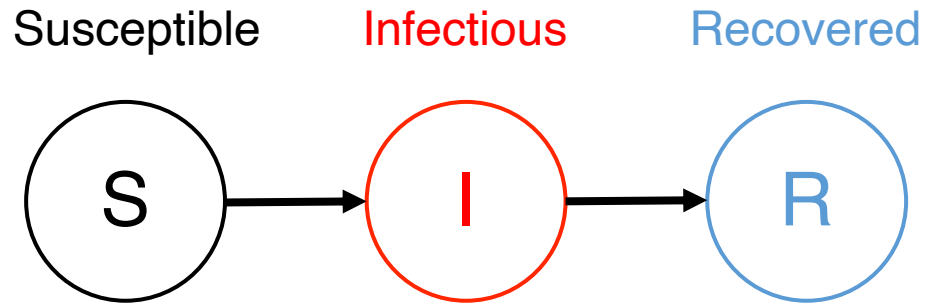


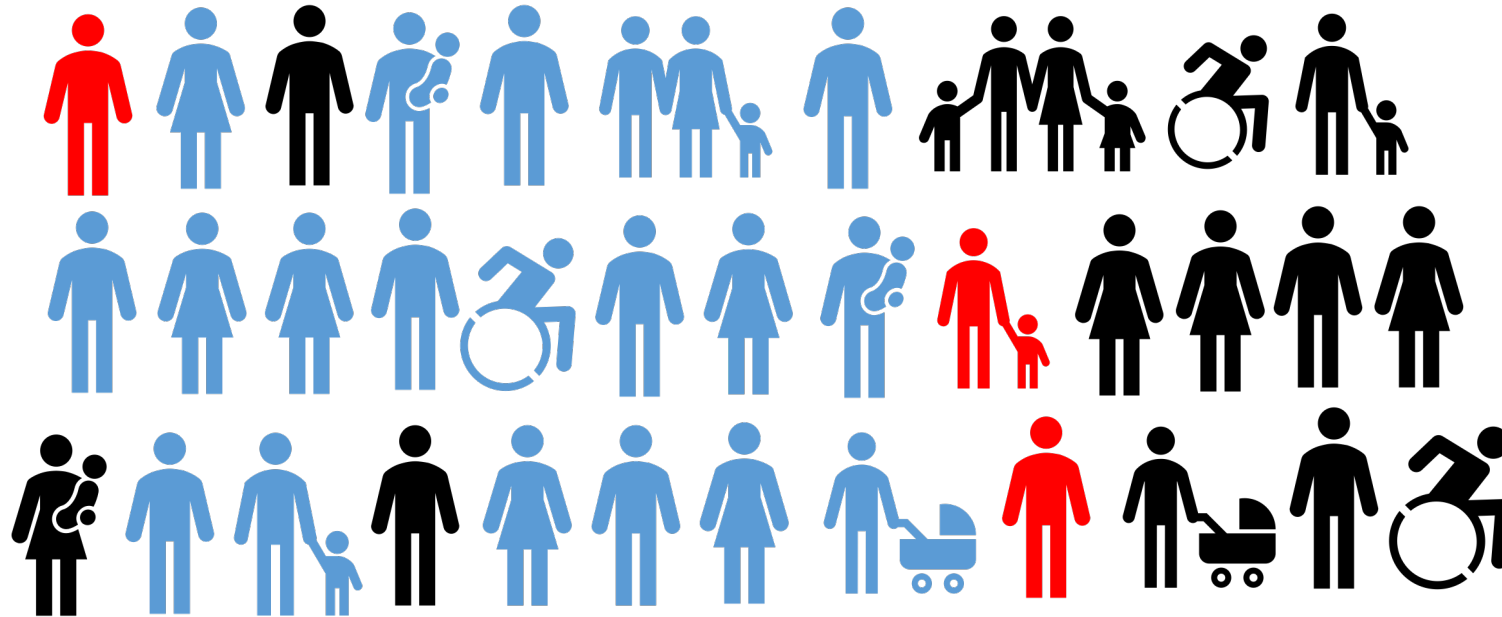
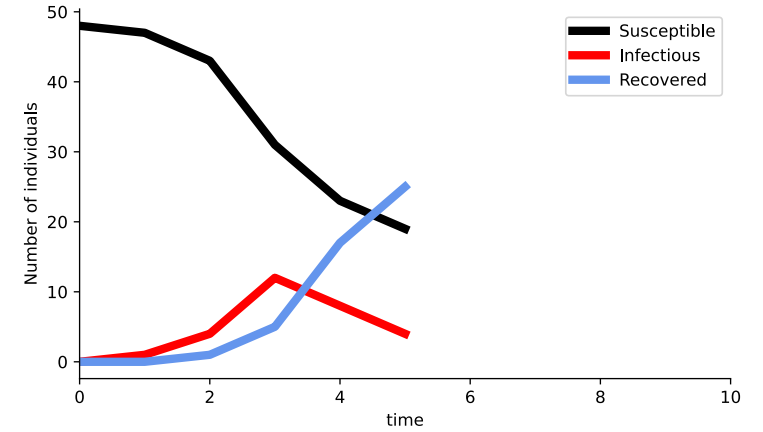
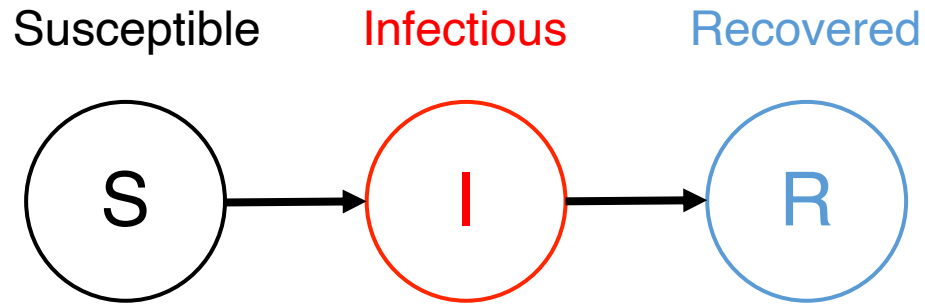


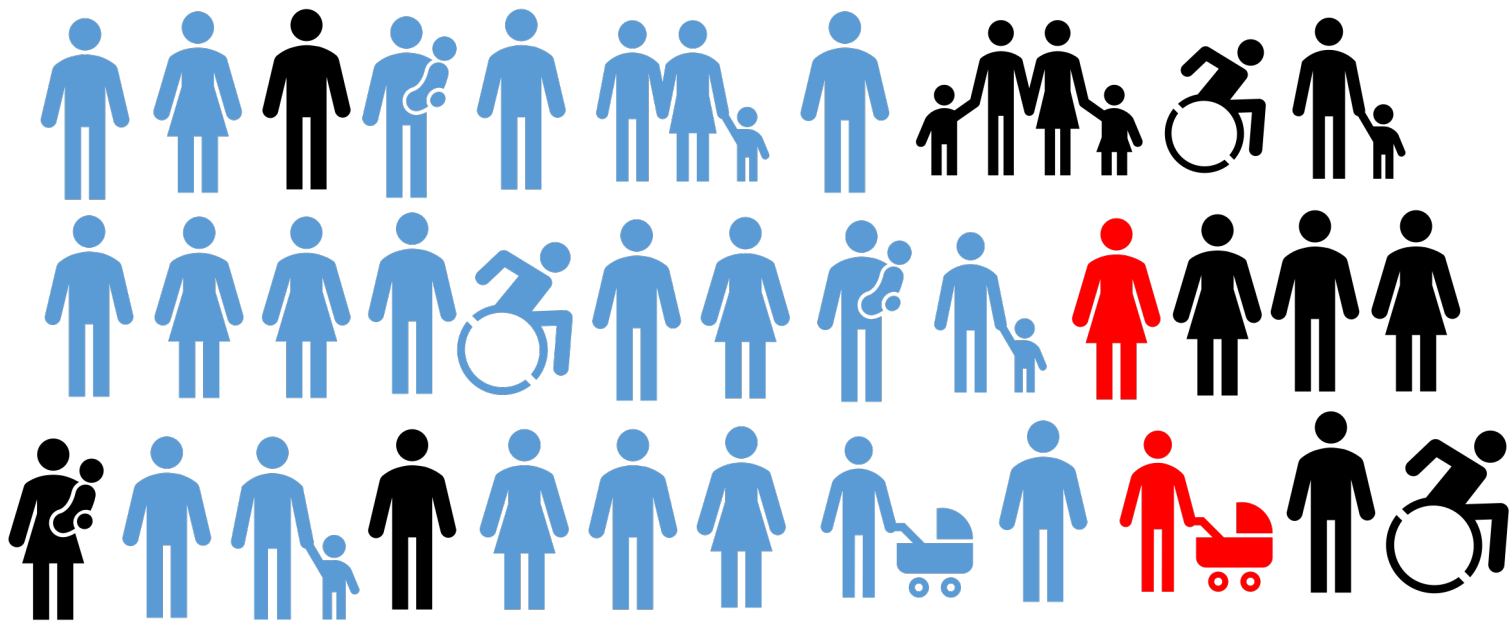
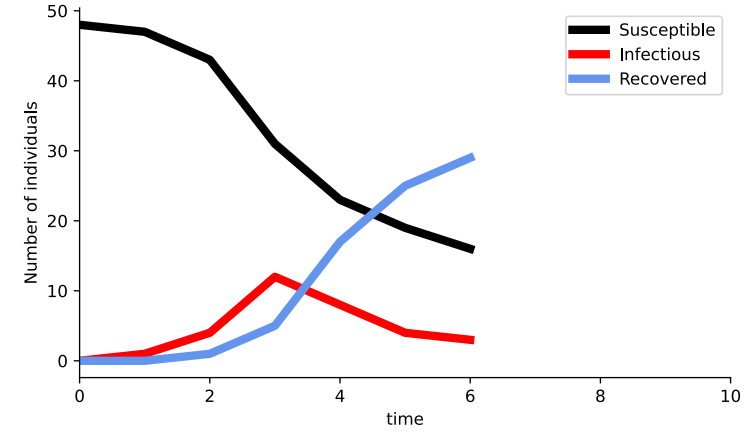
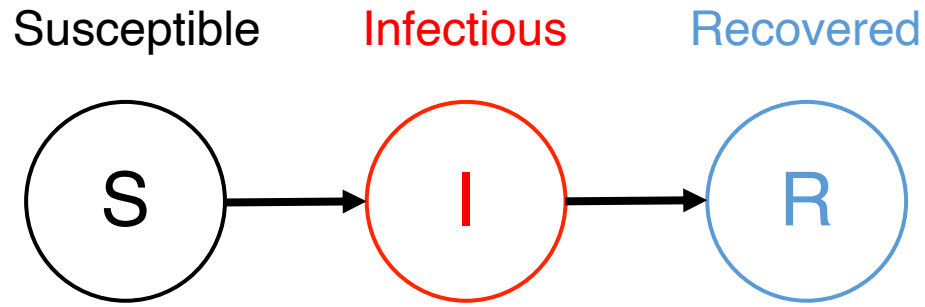


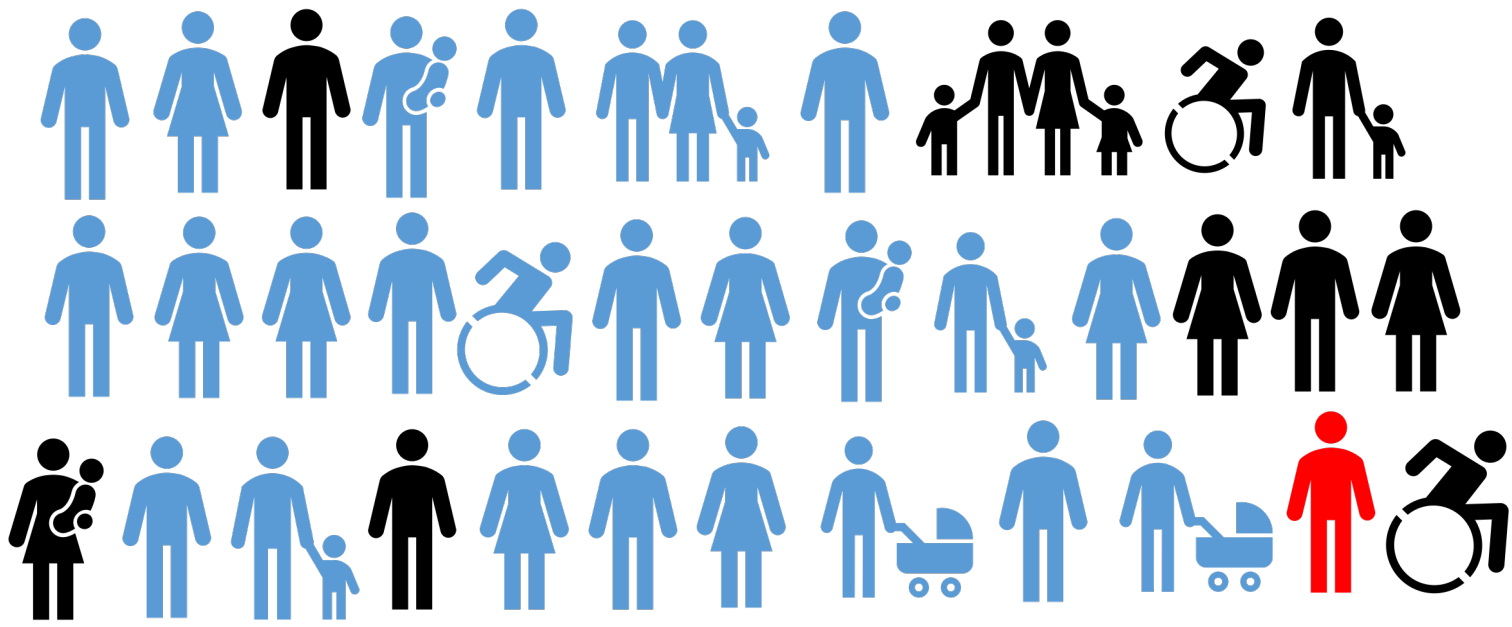
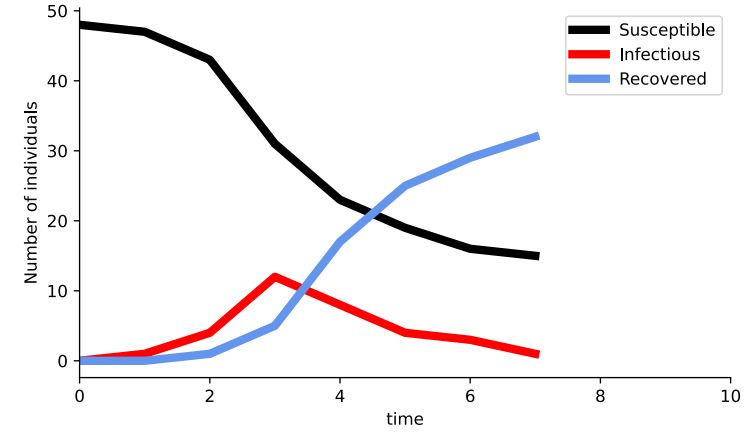
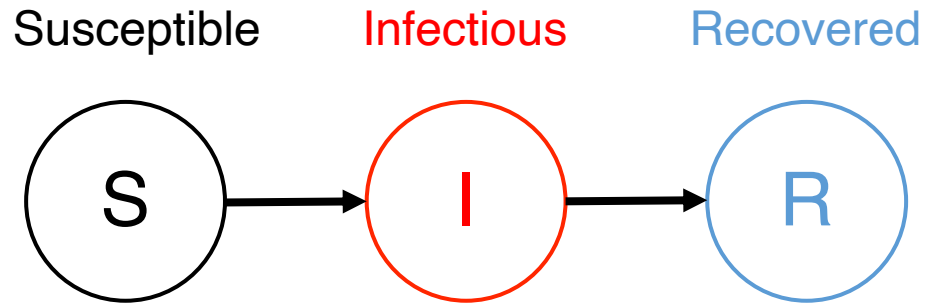


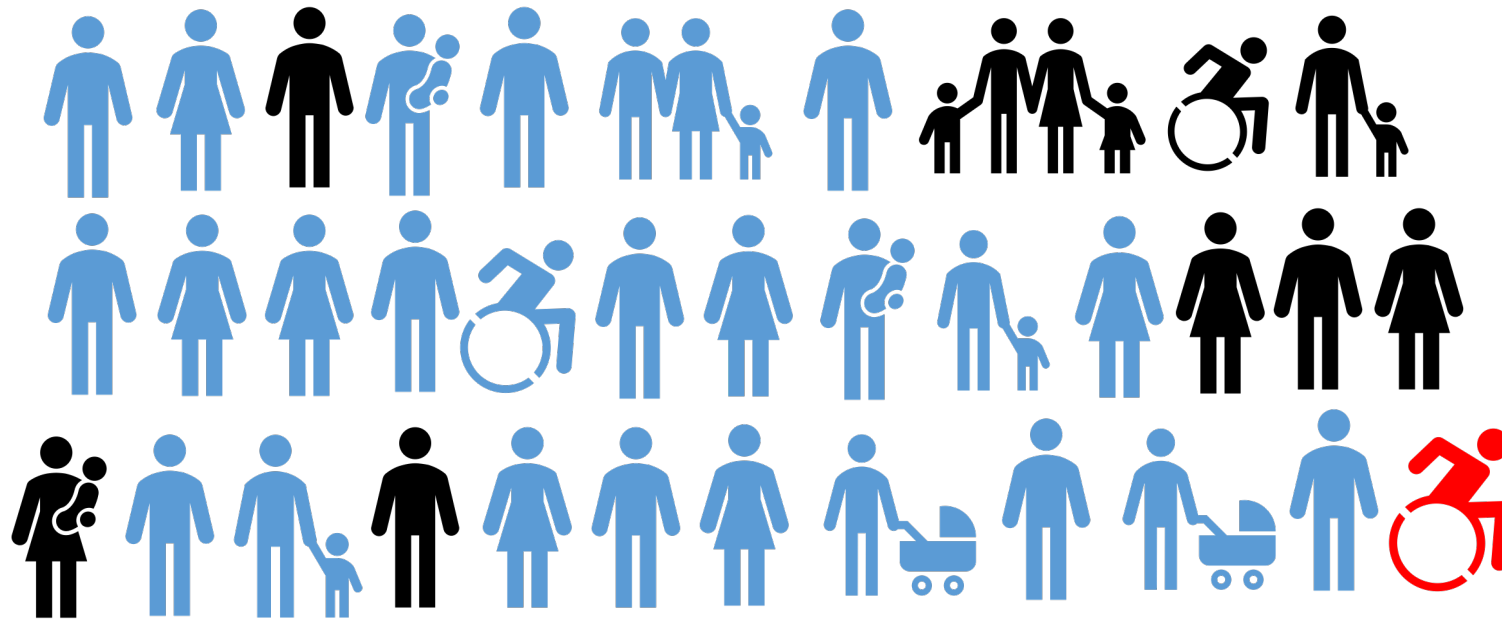
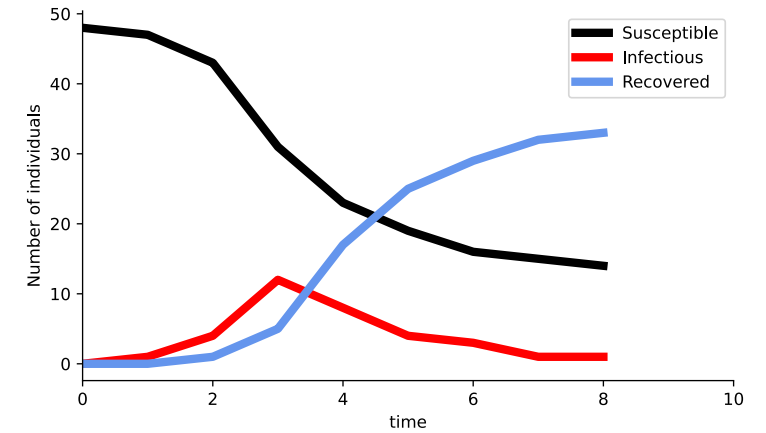
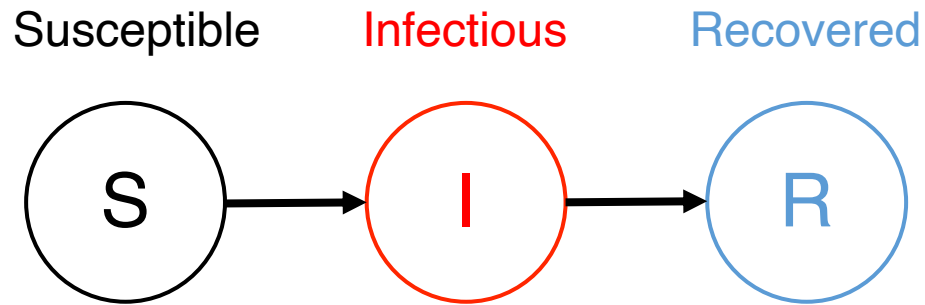


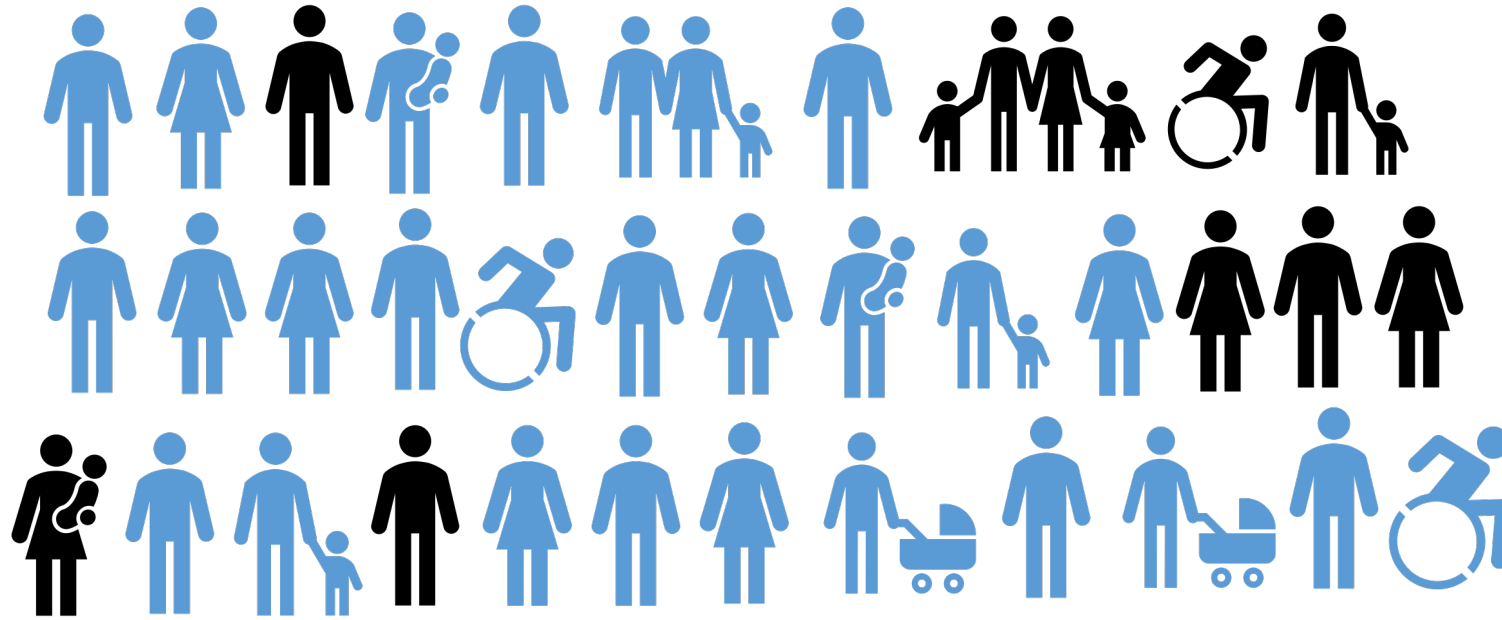
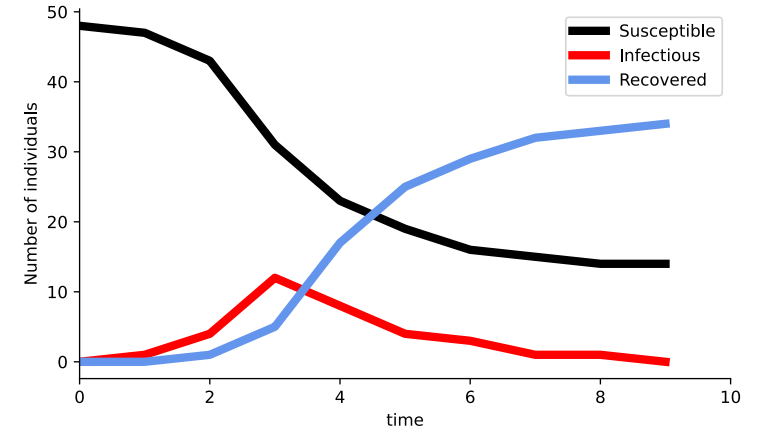
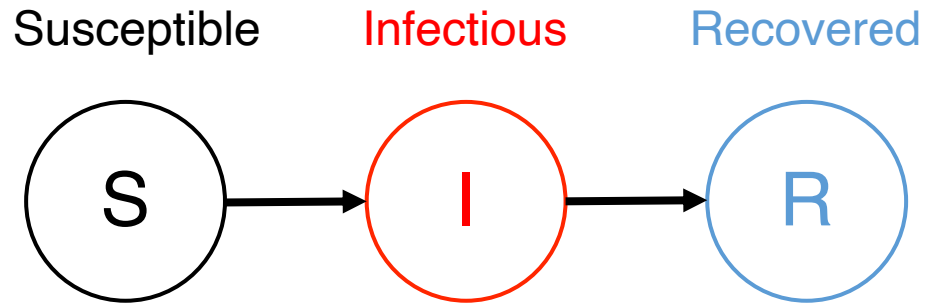




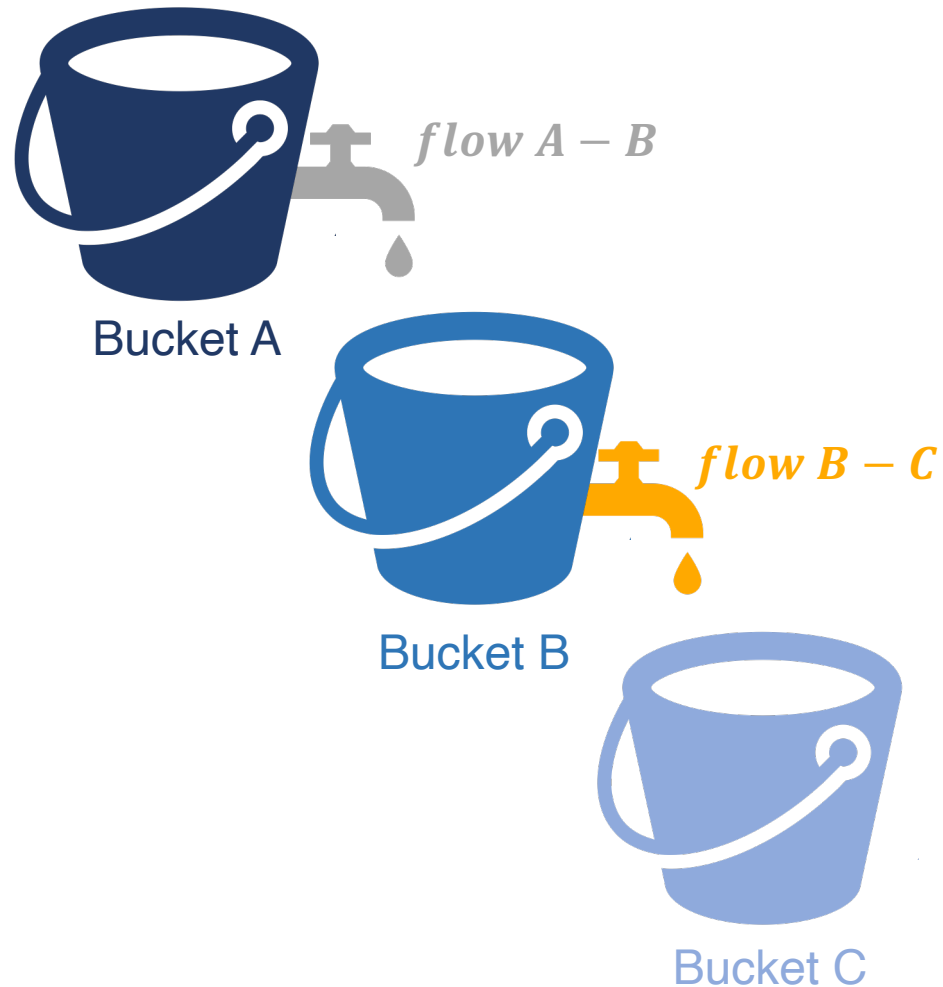








Compartmental models



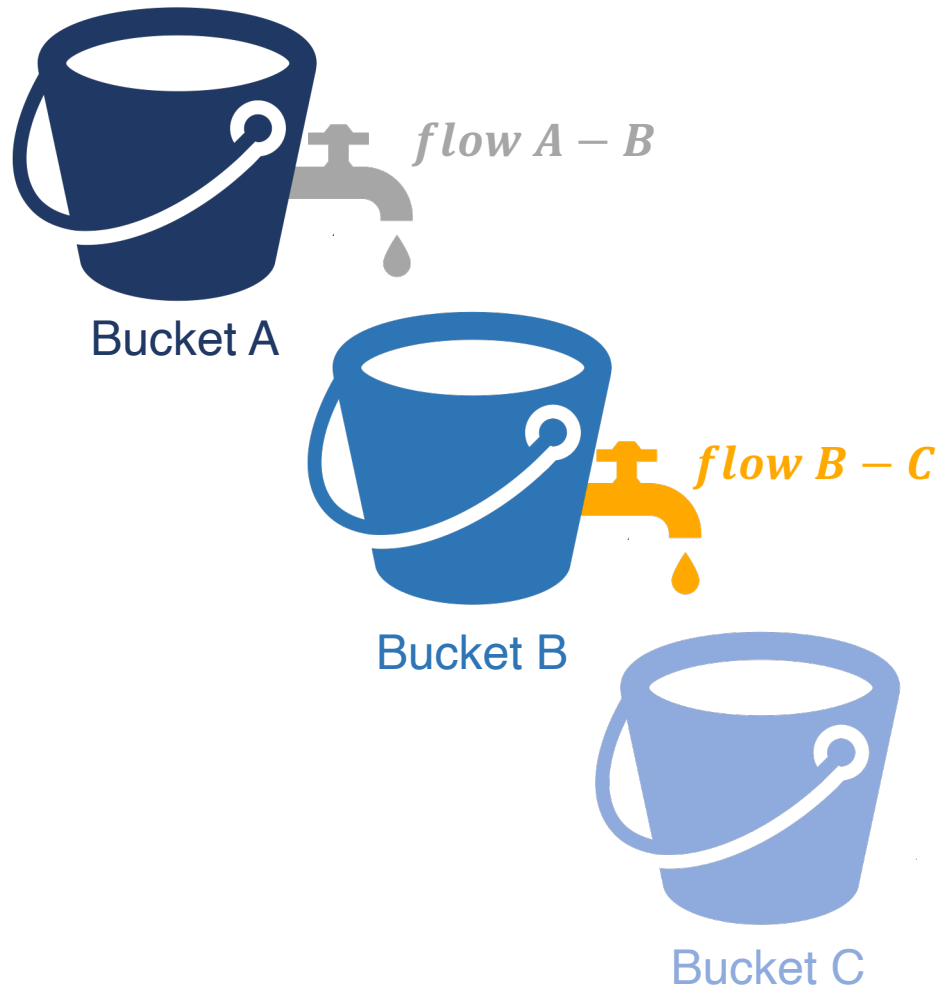
Difference equations

$$\text{Bucket A (t+1)} = \text{Bucket A (t)} - \text{flow A-B}$$

$$\text{Bucket B (t+1)} = \text{Bucket B (t)} + \text{flow A-B} - \text{flow B-C}$$

$$\text{Bucket C (t+1)} = \text{Bucket C (t)} + \text{flow B-C}$$

Compartmental models



Difference equations

$$\text{Bucket A (t+1)} = \text{Bucket A (t)} - \text{flow A-B}$$

$$\text{Bucket B (t+1)} = \text{Bucket B (t)} + \text{flow A-B} - \text{flow B-C}$$

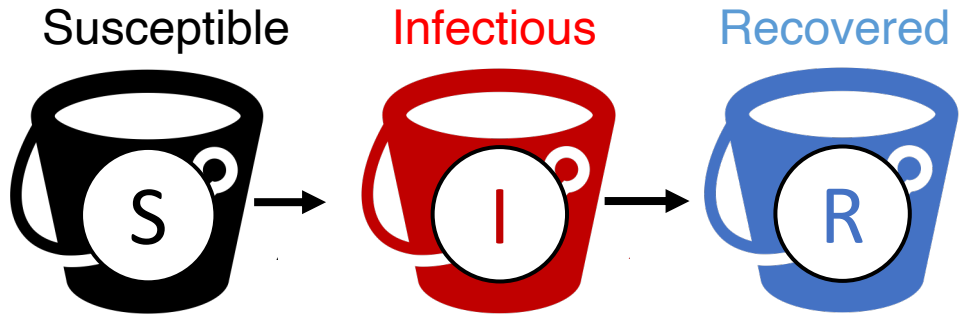
$$\text{Bucket C (t+1)} = \text{Bucket C (t)} + \text{flow B-C}$$

Differential equations

$$\frac{dA}{dt} = -a A$$

$$\frac{dB}{dt} = a A - b B$$

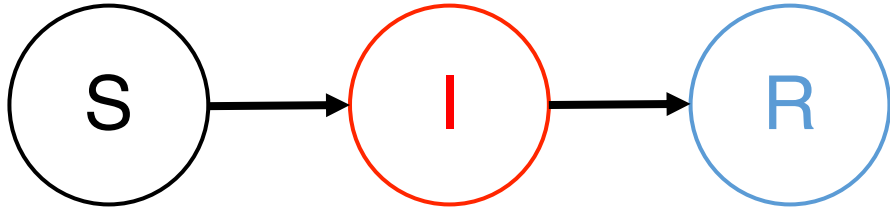
$$\frac{dC}{dt} = b B$$



$$\frac{dS}{dt} = -(\text{rate out})S$$

$$\frac{dI}{dt} = (\text{rate in})S - (\text{rate out})I$$

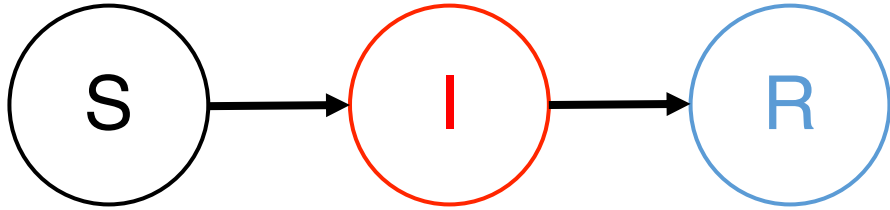
$$\frac{dR}{dt} = (\text{rate in})I$$



$$\frac{dS}{dt} = -(\text{rate out})S - (\text{infectiousness} * P(\text{contact with infectious person}))S$$

$$\frac{dI}{dt} = (\text{rate in})S - (\text{rate out})I$$

$$\frac{dR}{dt} = (\text{rate in})I$$



–(rate out) S

–(infectiousness * P (contact with infectious person)) S

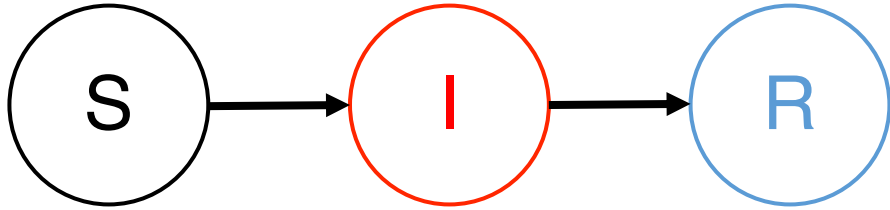
$$\frac{dS}{dt} = -\beta \frac{I}{N} S$$

β : *infectiousness*

N : *population size* $\rightarrow N = S+I+R$

$$\frac{dI}{dt} = (\text{rate in})S - (\text{rate out})I$$

$$\frac{dR}{dt} = (\text{rate in})I$$



$-(\text{rate out})S$
 $-(\text{infectiousness} * P(\text{contact with infectious person}))S$

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

β : *infectiousness*

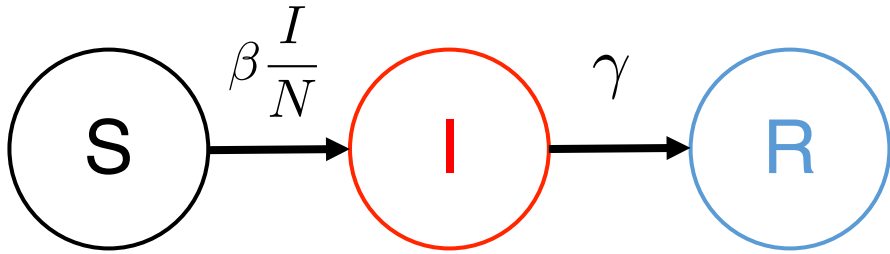
$$\frac{dI}{dt} = \beta \frac{I}{N} S - \gamma I$$

(rate in)S - (rate out)I

N : *population size* $\rightarrow N = S+I+R$

γ : *recovery*

$$\frac{dR}{dt} = (\text{rate in})I$$



-(rate out)S

-(infectiousness * P(contact with infectious person))S

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

(rate in)S - (rate out)I

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

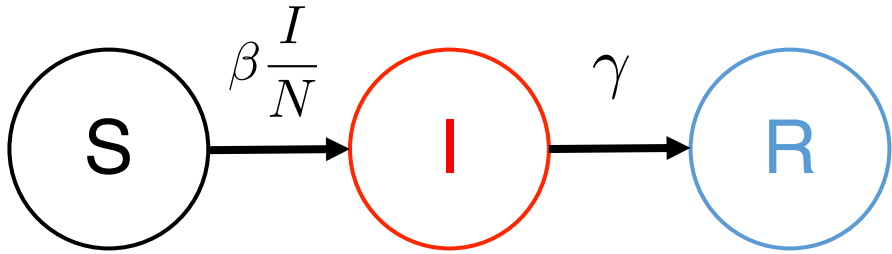
(rate in)I

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

β : infectiousness

N : population size $\rightarrow N = S+I+R$

γ : recovery

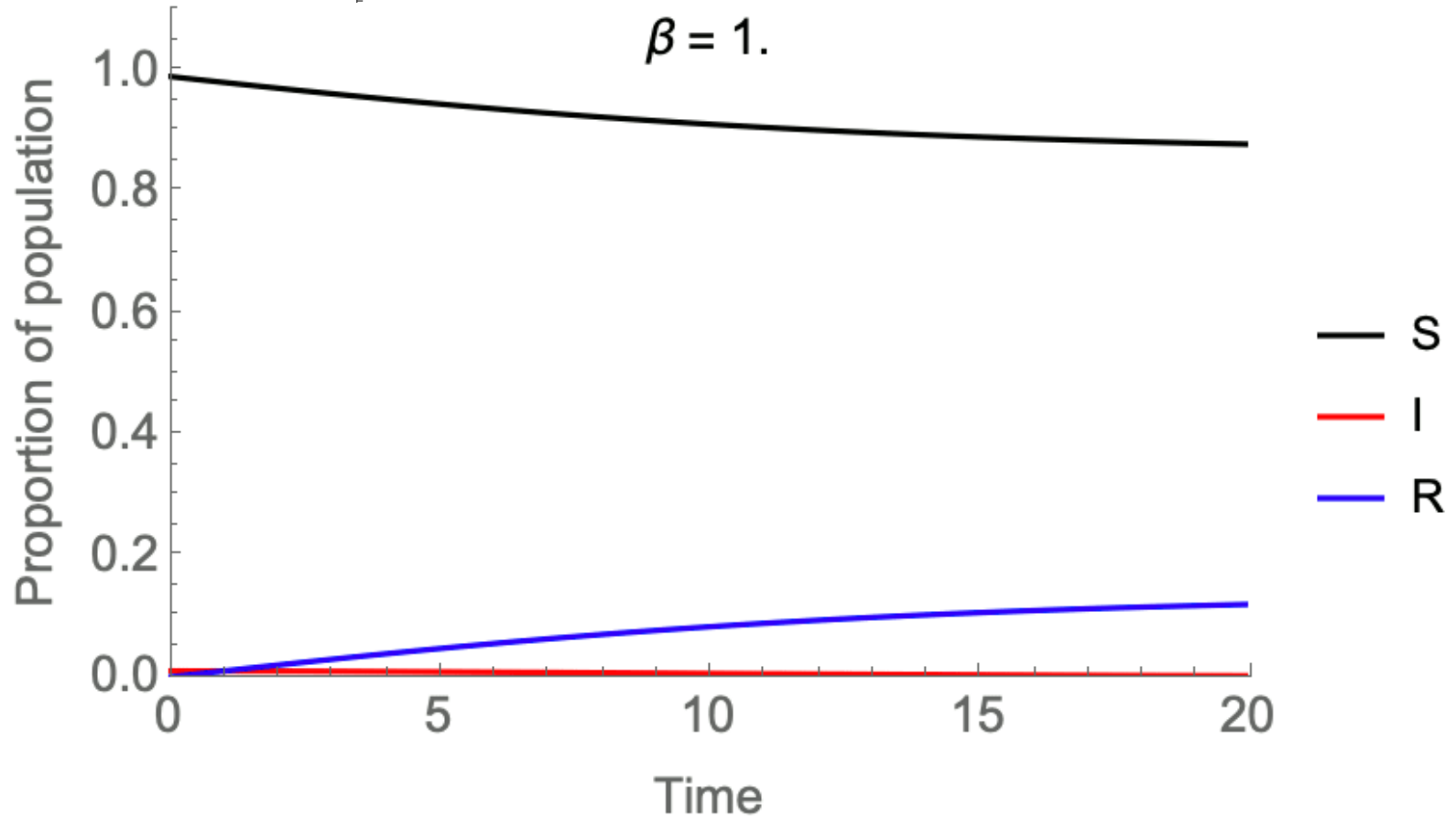


$\gamma = 1$
 $\beta = 1.$

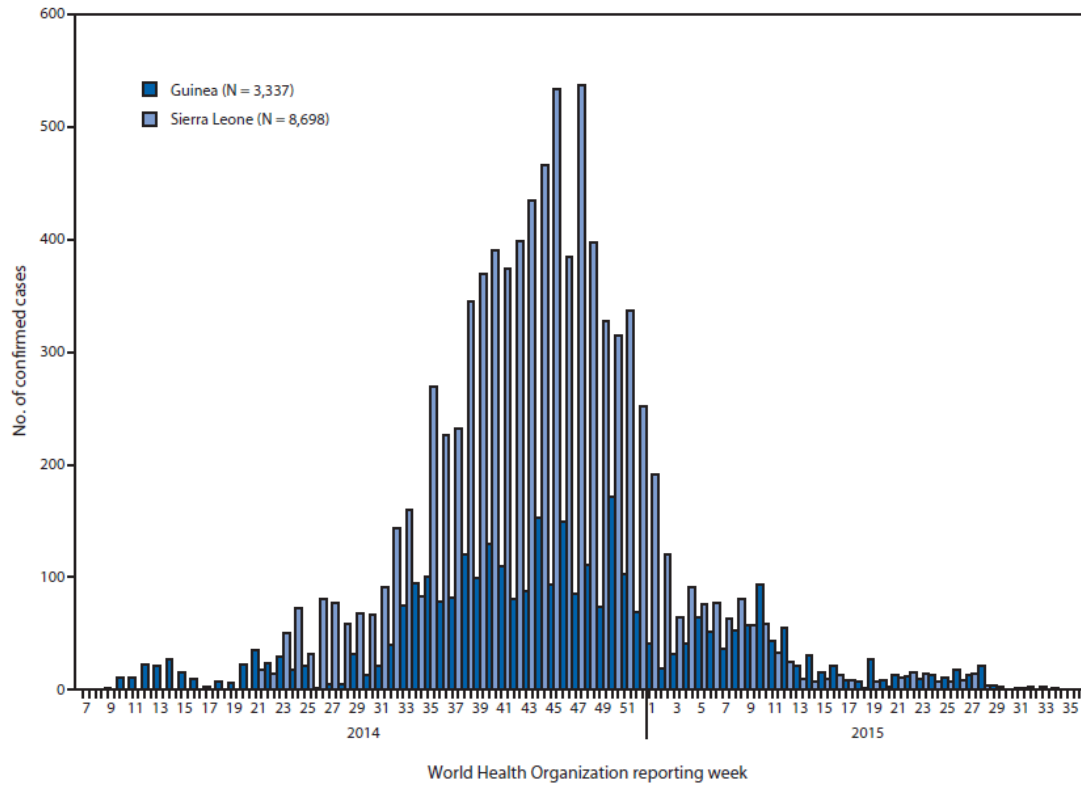
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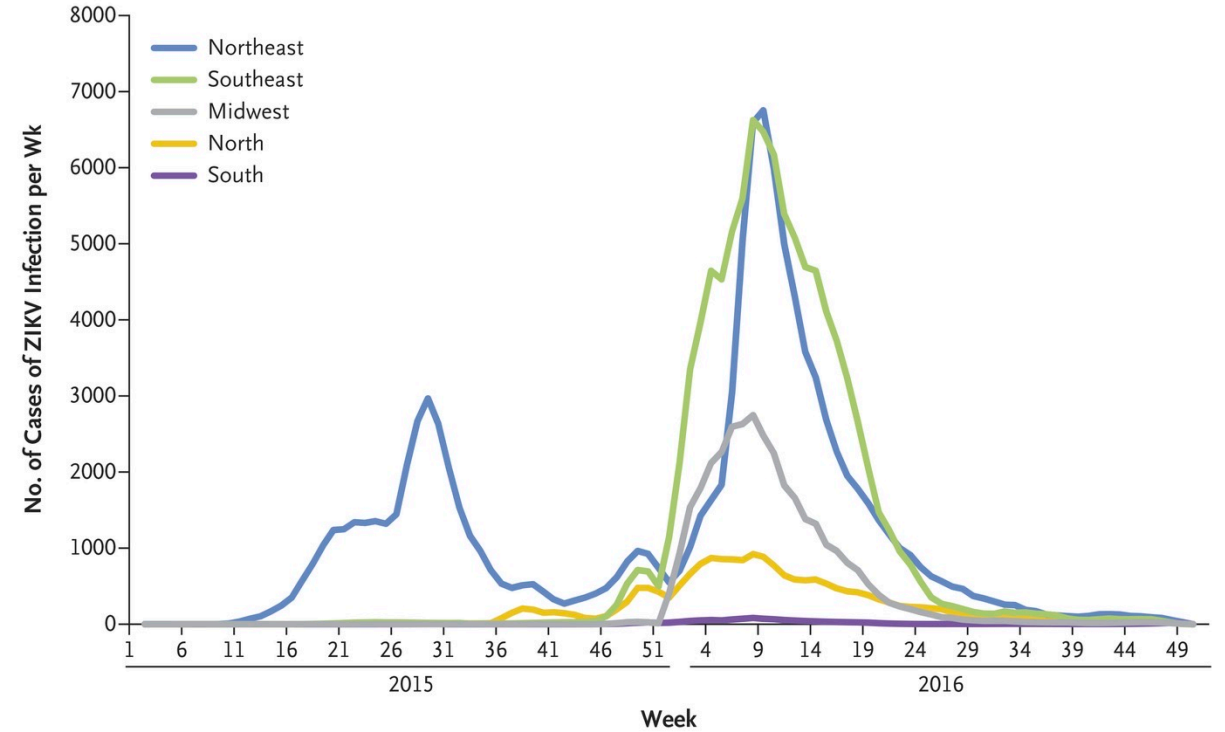
$$\frac{dR}{dt} = \gamma I$$



Ebola: weekly confirmed cases in Guinea and Sierra Leone in 2014-15



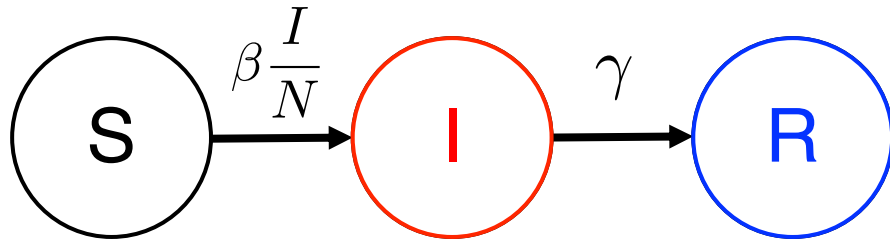
Zika: weekly suspected cases in different regions of Brazil in 2015-16





Will there be an outbreak?

Will an outbreak happen?



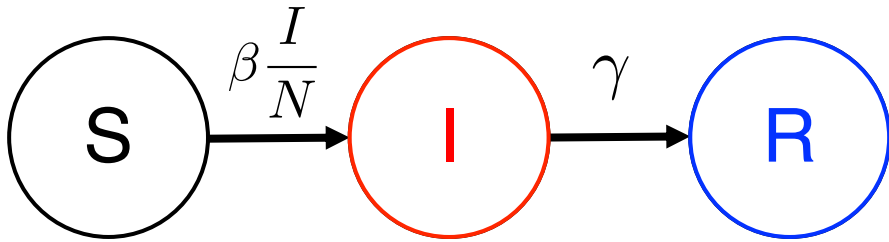
“The number infected must increase”

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

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

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

Will an outbreak happen?



“The number infected must increase”

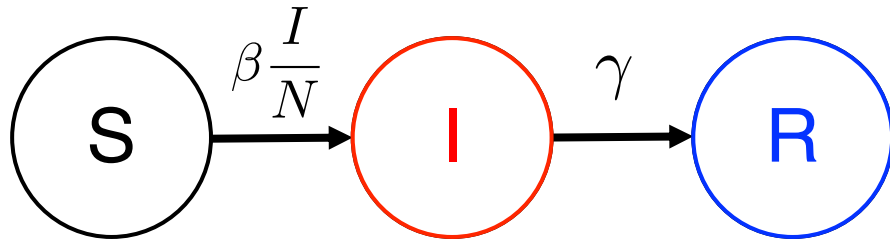
$$\frac{dI}{dt} > 0$$

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

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

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

Will an outbreak happen?



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

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

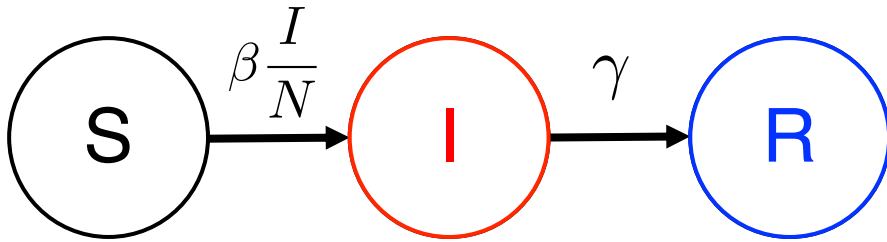
$$\frac{dR}{dt} = \gamma I$$

“The number infected must increase”

$$\frac{dI}{dt} > 0$$

$$\beta \frac{I}{N} S - \gamma I > 0$$

Will an outbreak happen?



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

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

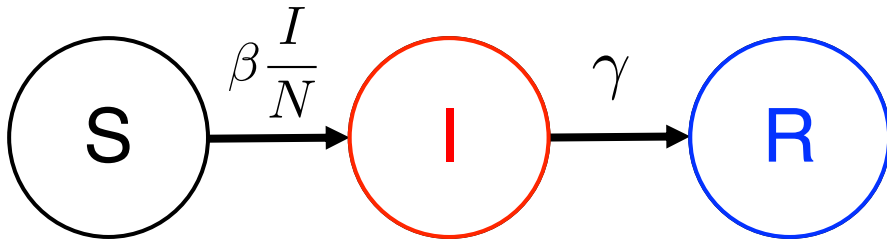
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Will an outbreak happen?



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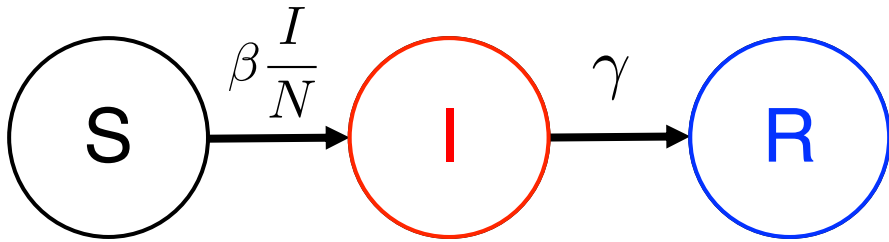
“The number infected must increase”

$$\frac{dI}{dt} > 0$$

$$\beta \frac{I}{N} S - \gamma I > 0$$

$$\beta \frac{I}{N} S > \gamma I \quad (S_0 \approx N)$$

Will an outbreak happen?



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

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

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

“The number infected must increase”

$$\frac{dI}{dt} > 0$$

$$\beta \frac{I}{N} S - \gamma I > 0$$

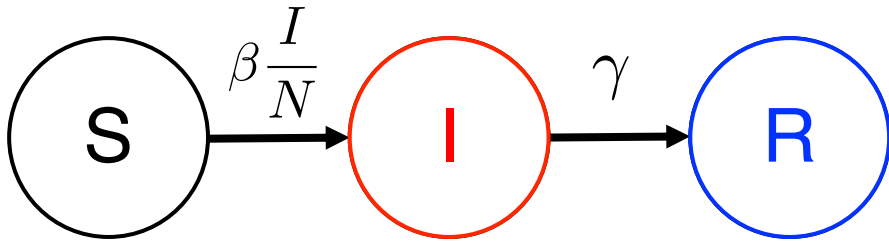
$$\beta \frac{I}{N} S > \gamma I \quad (S_0 \approx N)$$

infectiousness

$$\beta > \gamma$$

recovery

Will an outbreak happen?



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

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

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

“The number infected must increase”

$$\frac{dI}{dt} > 0$$

$$\beta \frac{I}{N} S - \gamma I > 0$$

$$\beta \frac{I}{N} S > \gamma I \quad (S_0 \approx N)$$

infectiousness

$$\beta > \gamma$$

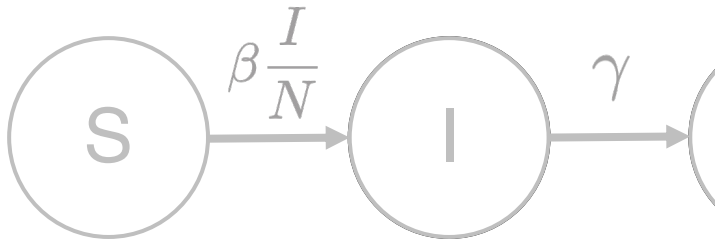
recovery

Basic reproduction number

$$R_0 = \frac{\beta}{\gamma} > 1$$

$\frac{\beta}{\gamma}$: average number of infections caused by one infectious person

Will an outbreak happen?



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

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

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

Values of R_0 of well-known infectious diseases^[1]

Disease	Transmission	R_0
Measles	Airborne	12–18
Diphtheria	Saliva	6-7
Smallpox	Airborne droplet	5–7
Polio	Fecal-oral route	5–7
Rubella	Airborne droplet	5–7
Mumps	Airborne droplet	4–7
HIV/AIDS	Sexual contact	2–5
Pertussis	Airborne droplet	5.5 ^[2]
SARS	Airborne droplet	2–5 ^[3]
Influenza (1918 pandemic strain)	Airborne droplet	2–3 ^[4]
Ebola (2014 Ebola outbreak)	Bodily fluids	1.5-2.5 ^[5]

Source: Wikipedia

infected must increase”

$$I > 0$$

$$I < \dots \quad (S_0 \approx N)$$

β : infectiousness

γ : rate of recovery

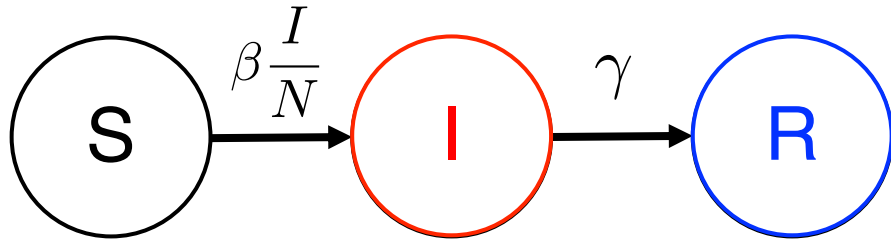
$\frac{\beta}{\gamma}$: average number of infections caused by one infectious person



Can we prevent the outbreak?

Can we prevent it?

What proportion, p , should we vaccinate?

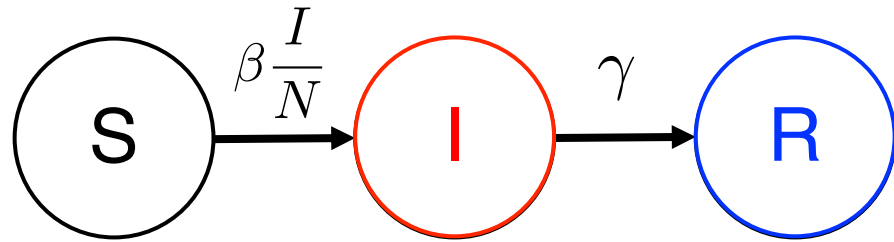


$$\frac{dS}{dt} = -\beta \frac{I}{N} S$$

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

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

Can we prevent it?



What proportion, p , should we vaccinate?

$$\frac{dI}{dt} < 0$$

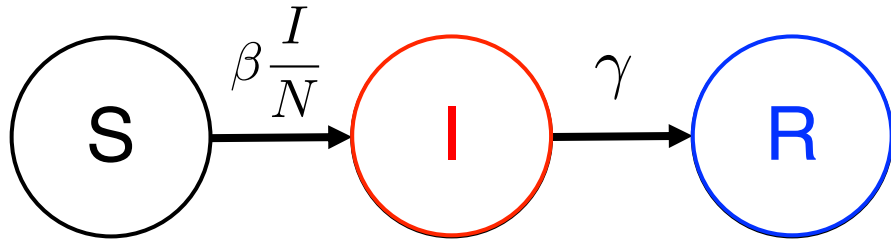
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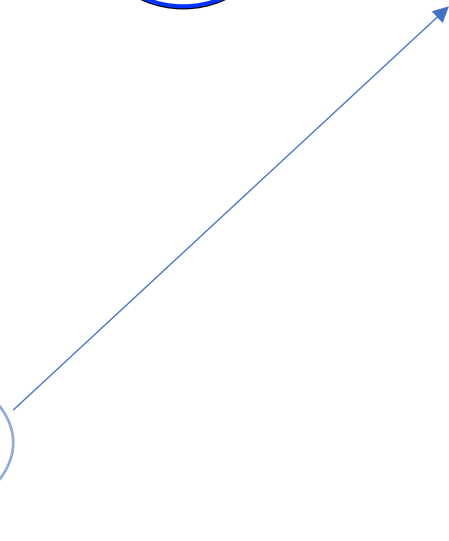
$$\frac{dI}{dt} < 0$$

$$\beta \frac{I}{N} S - \gamma I < 0$$

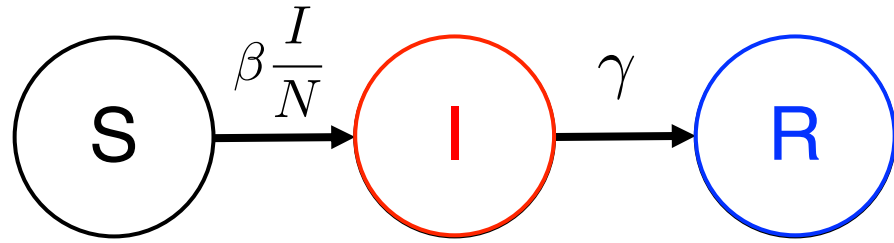
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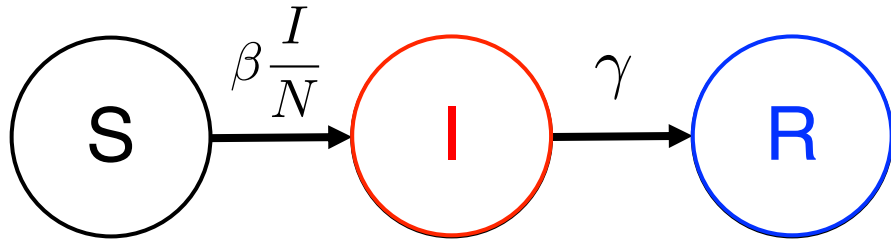
$$\beta \frac{I}{N} S < \gamma I$$

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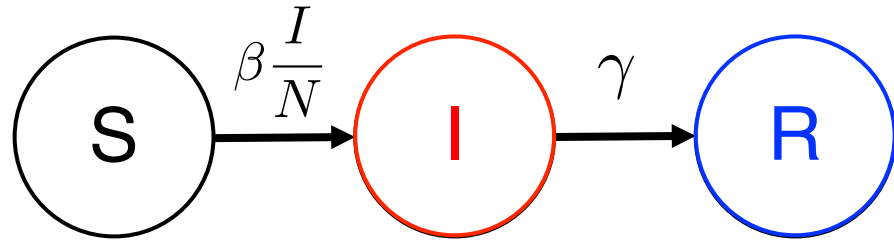
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$$\beta \frac{I}{N} S < \gamma I$$

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Can we prevent it?



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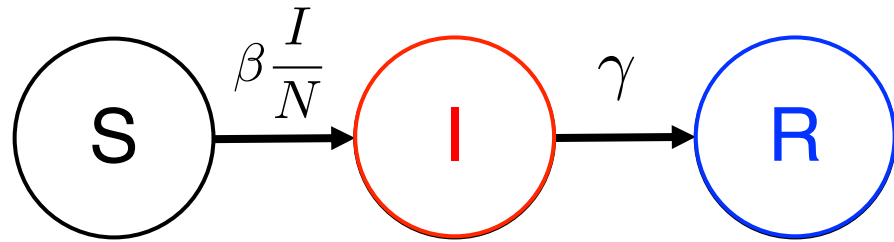
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$$\beta(1 - p) < \gamma$$

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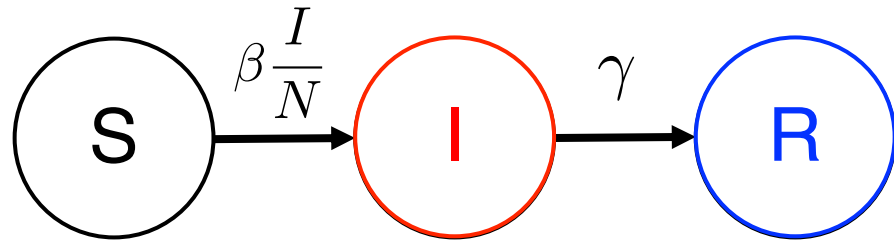
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$$\frac{\beta}{\gamma} < \frac{1}{(1 - p)}$$

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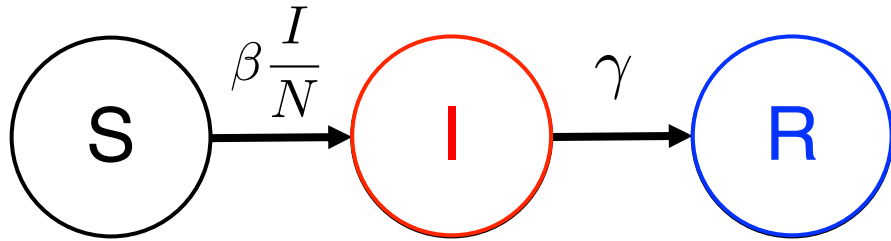
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$$\frac{\beta}{\gamma} < \frac{1}{(1-p)}$$

$$R_0 < \frac{1}{(1-p)}$$

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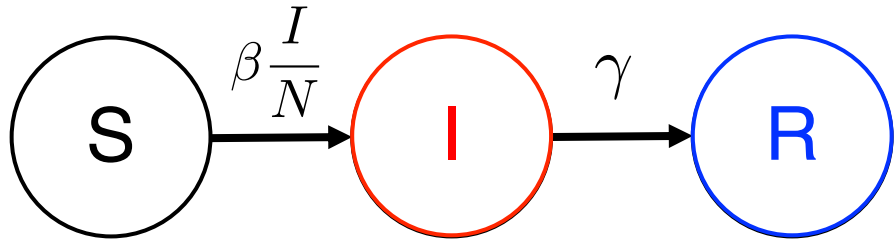
$$\frac{\beta}{\gamma} < \frac{1}{(1-p)}$$

$$R_0 < \frac{1}{(1-p)}$$

$$p > 1 - \frac{1}{R_0}$$

Critical vaccination threshold

Can we prevent it?



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

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

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

What proportion, p , should we vaccinate?

$$\frac{dI}{dt} < 0$$

$$\beta \frac{I}{N} S - \gamma I < 0$$

$$\beta \frac{I}{N} S < \gamma I$$

$$\beta \frac{I}{N} (1-p)N < \gamma I$$

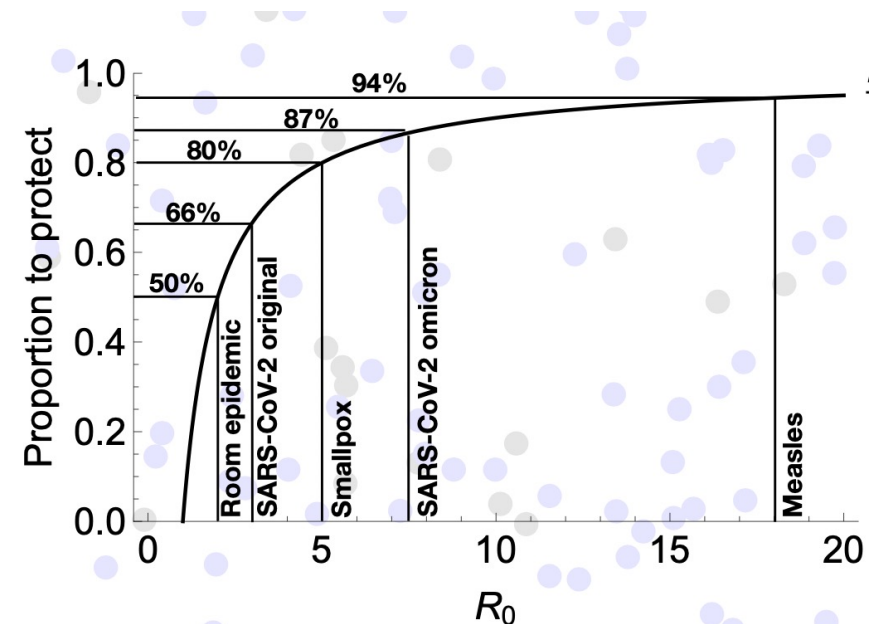
$$(S_0 \approx (1-p)N)$$

$$\beta(1-p) < \gamma$$

$$\frac{\beta}{\gamma} < \frac{1}{(1-p)}$$

$$R_0 < \frac{1}{(1-p)}$$

$$p > 1 - \frac{1}{R_0}$$



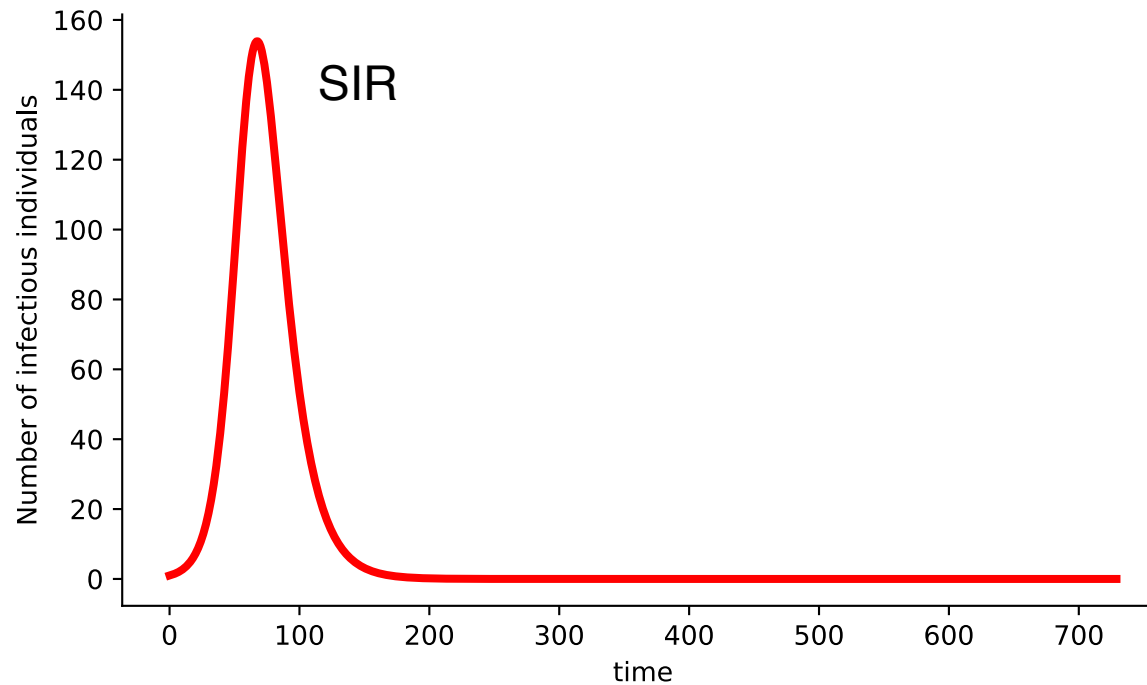
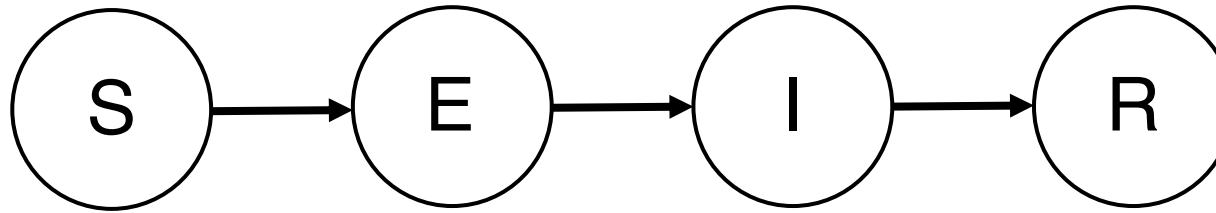
Extensions of the SIR model

We can increase model complexity and realism by:

- adding **disease states** (compartments)
- changing **transitions** (flows), or
- splitting compartments to account for **population heterogeneity**

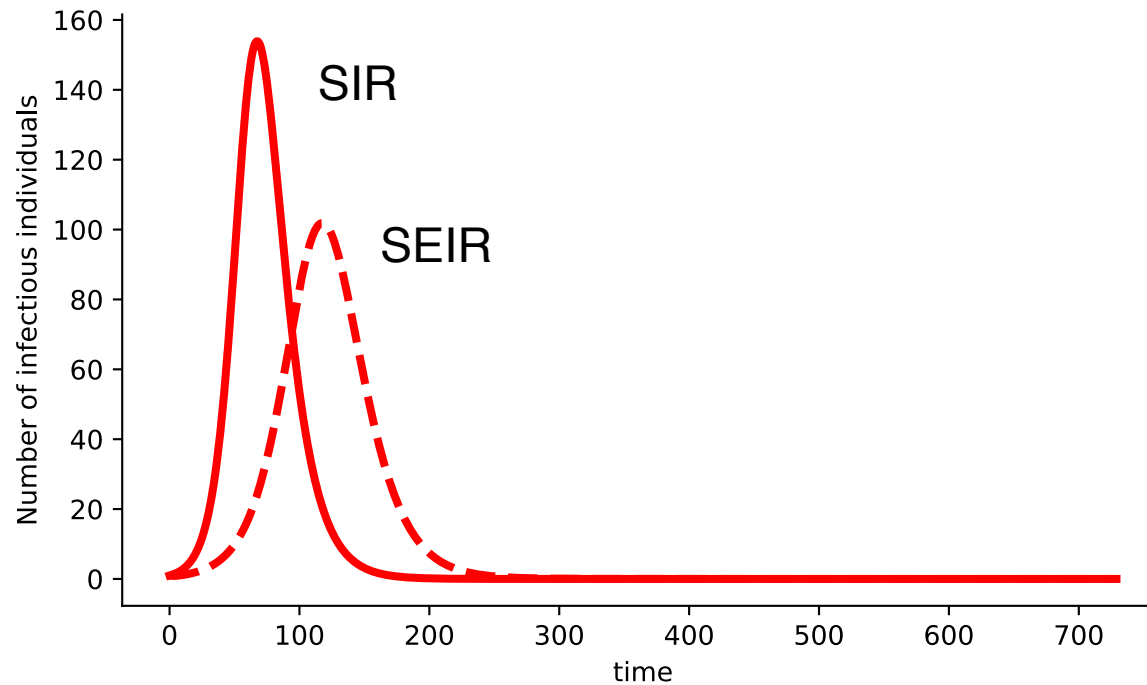
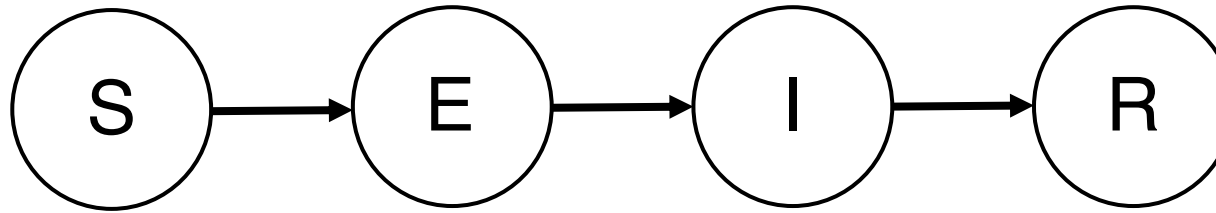
Making compartmental models (a bit) more realistic

What happens if there's an incubation period?



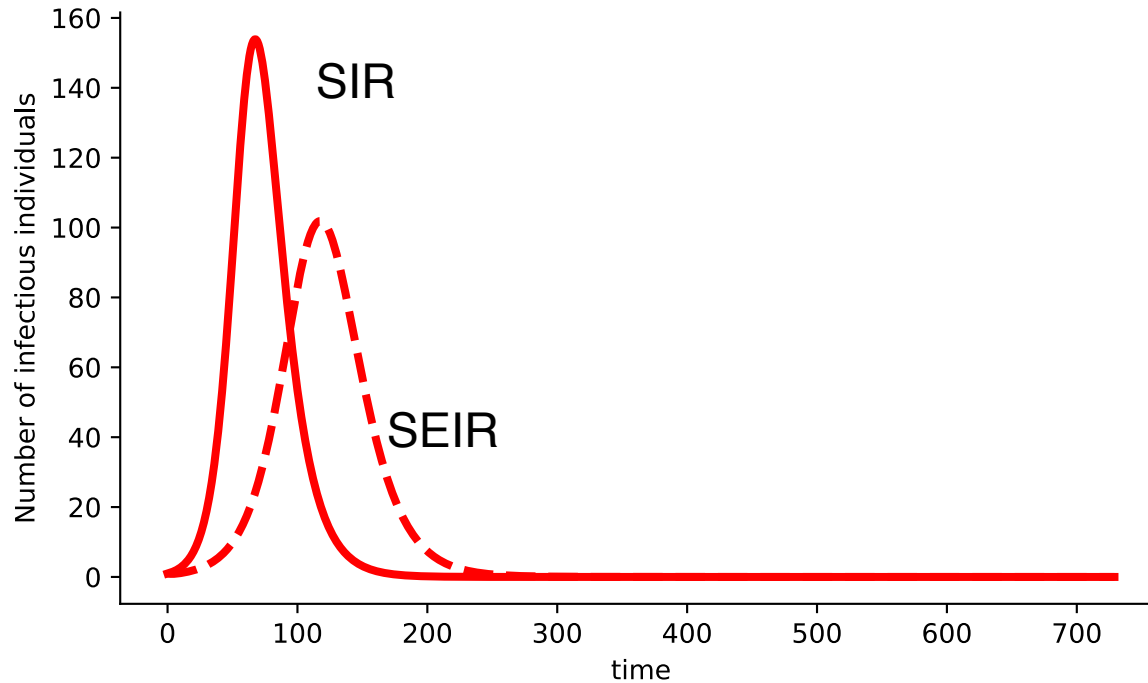
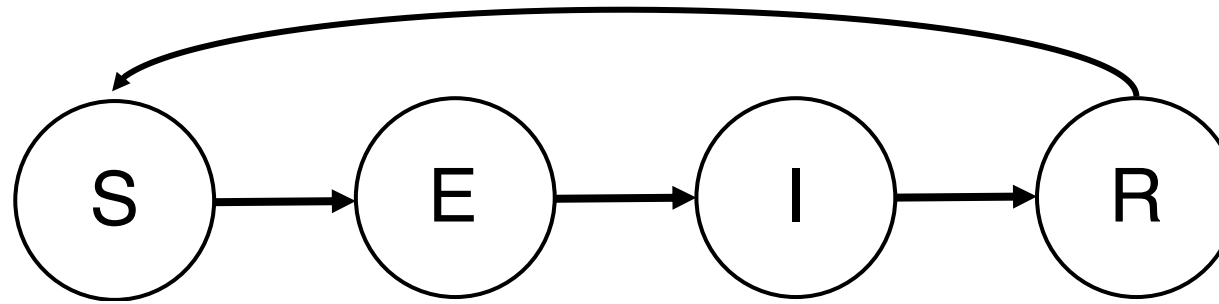
Making compartmental models (a bit) more realistic

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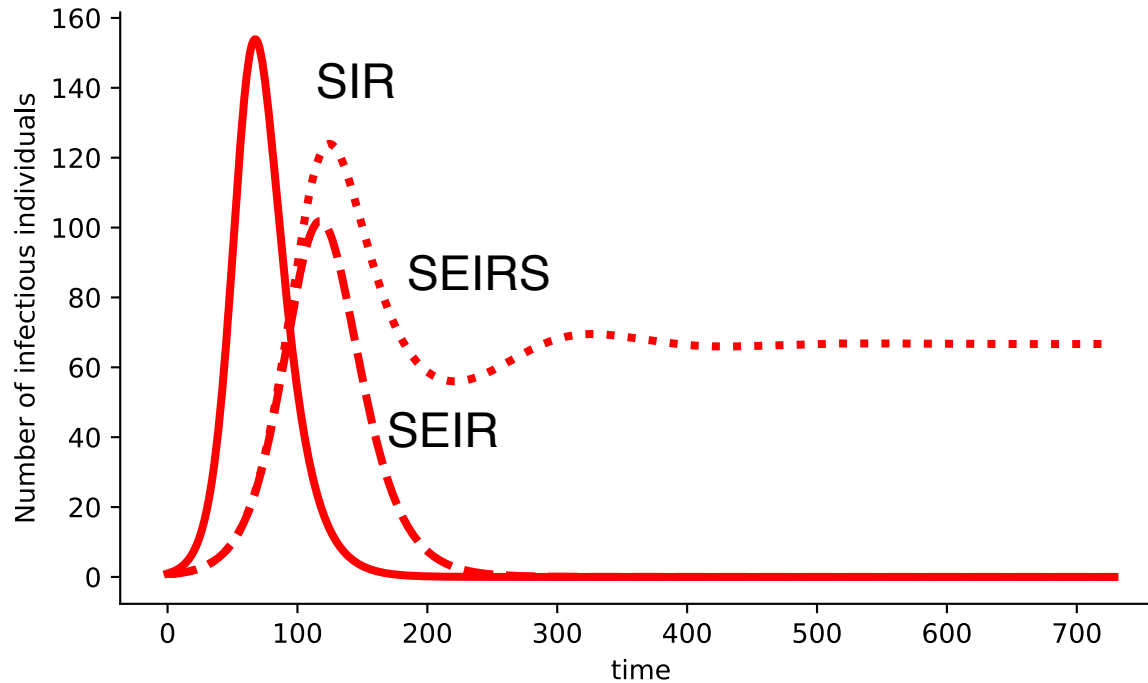
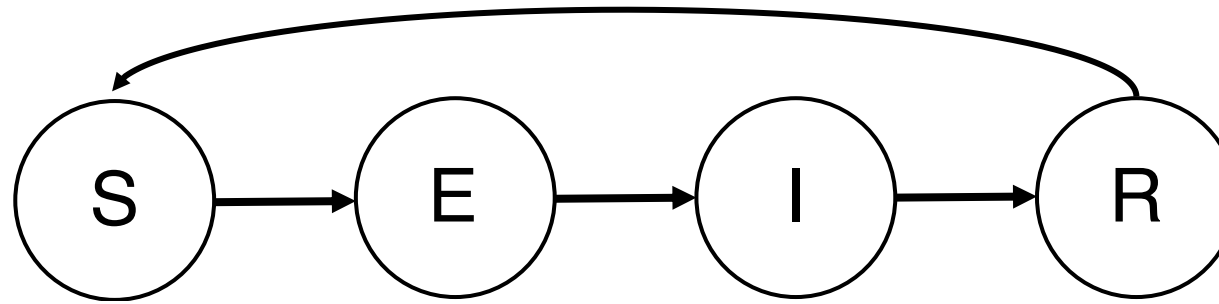
Making compartmental models (a bit) more realistic

What happens if you lose immunity?



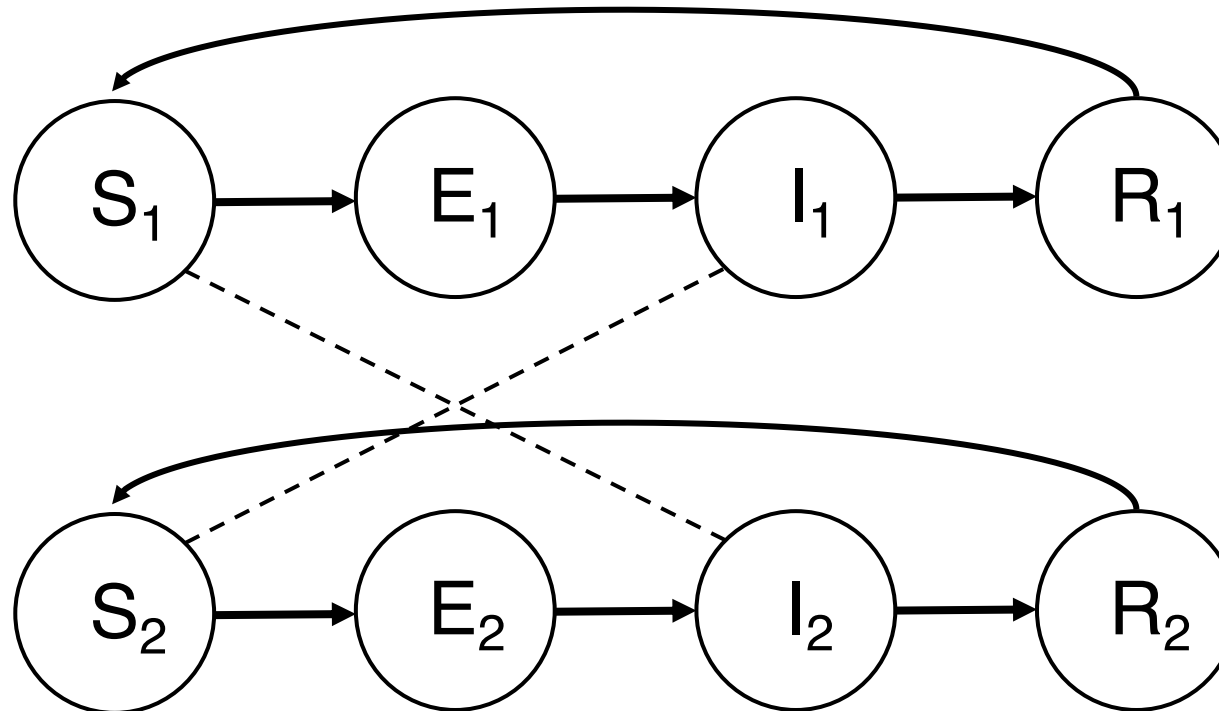
Making compartmental models (a bit) more realistic

What happens if you lose immunity?



Making compartmental models (a bit) more realistic

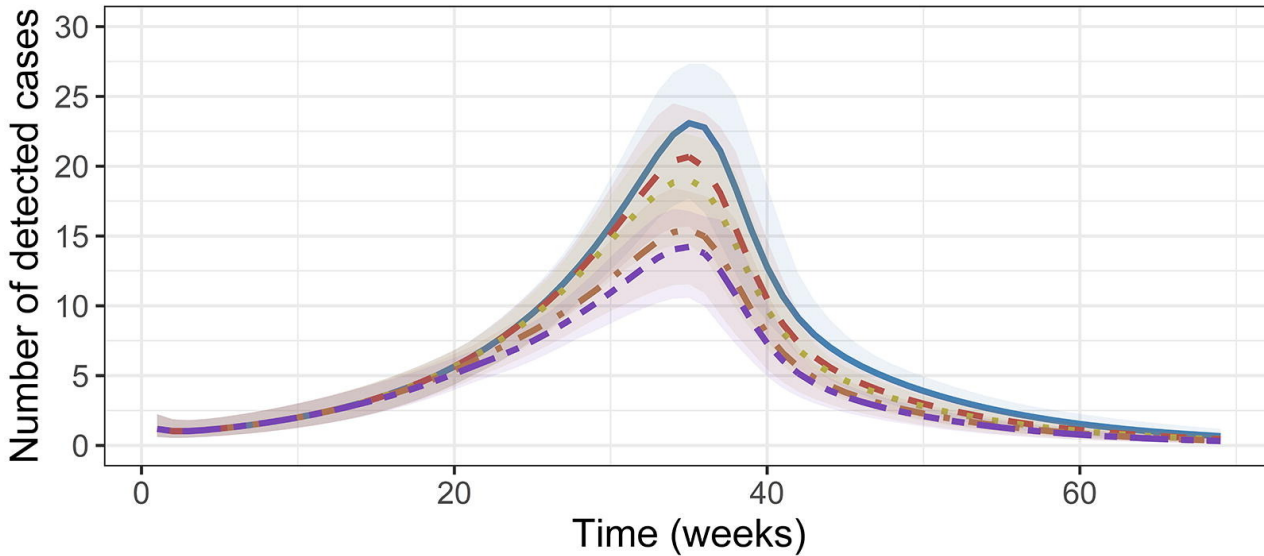
What if age structure matters?



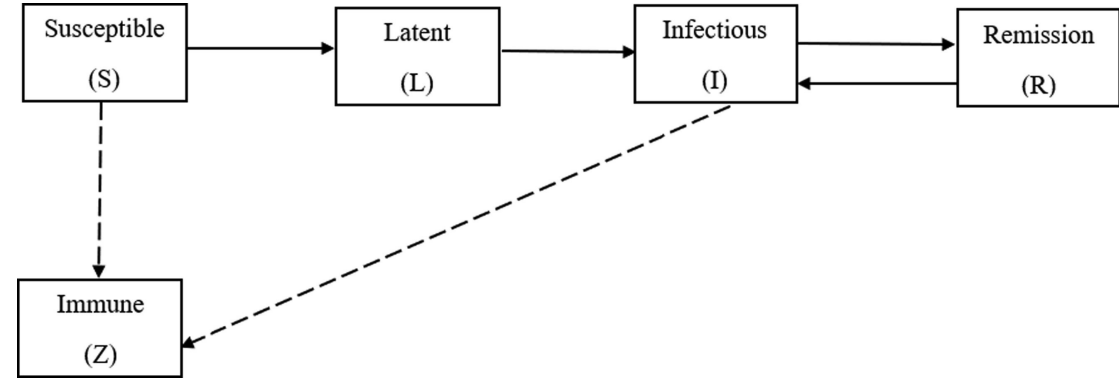
We do really use this stuff...

Comparing timing and coverage of Hepatitis A vaccine

B

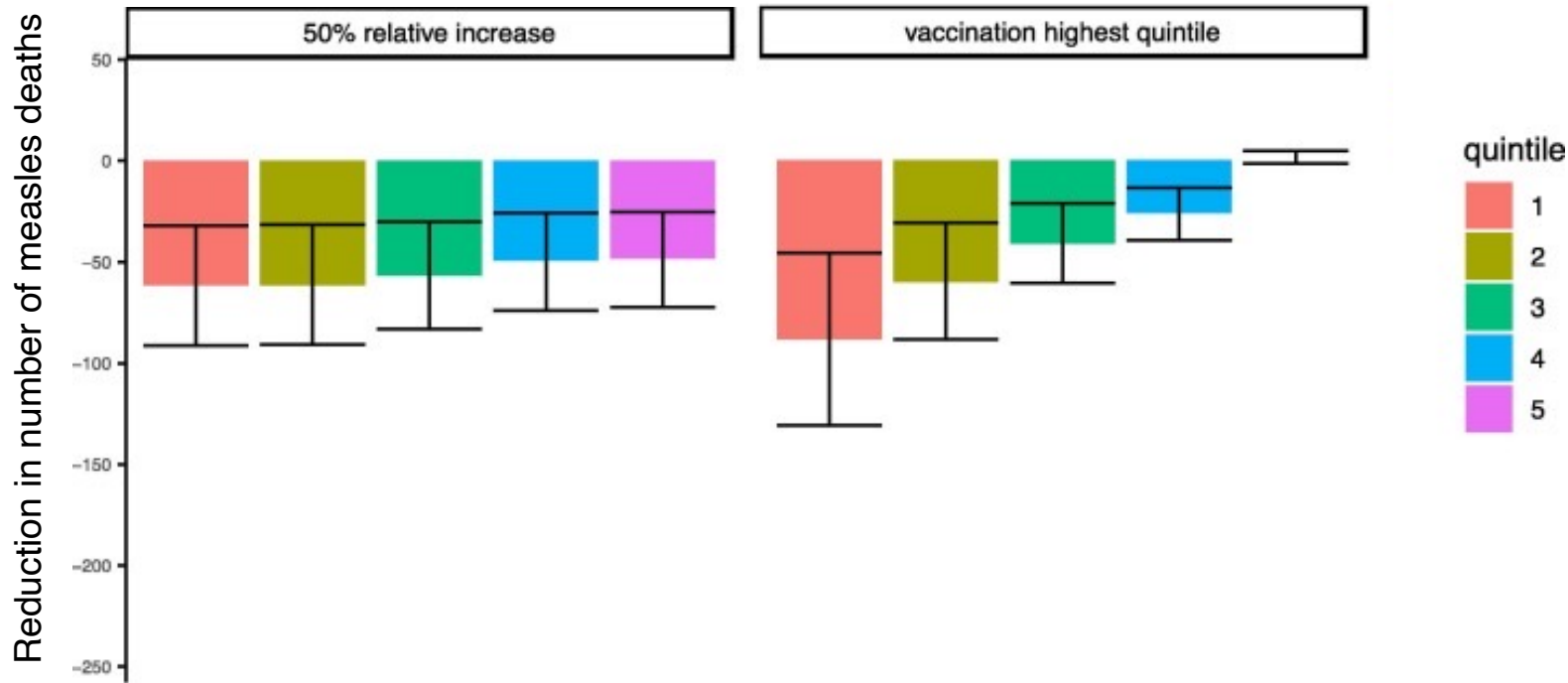


- No vaccination
- Week 10
- Week 21
- Week 18
- Week 10, rate doubled

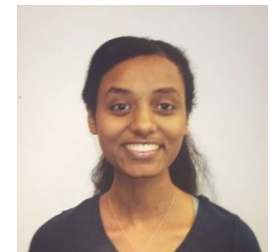


Dankwa, et al. (2021)

Incorporating equity in infectious disease modeling and vaccination decisions



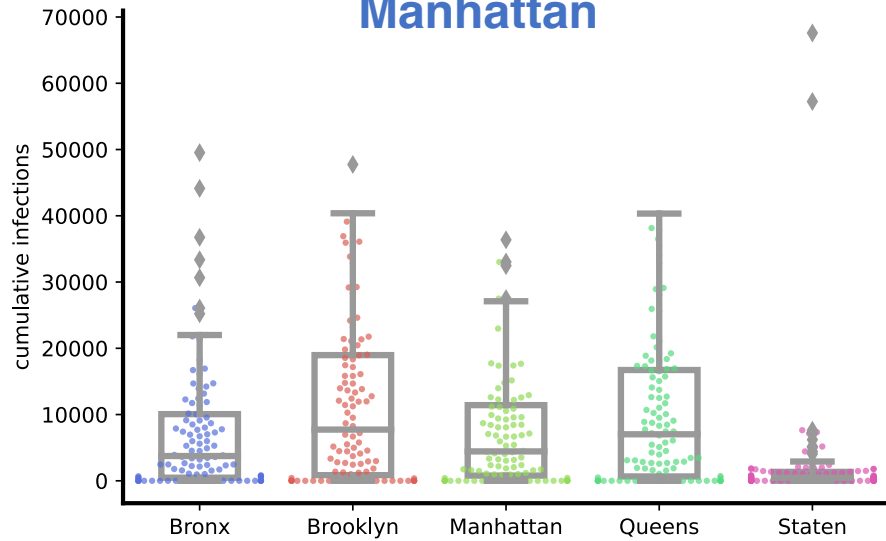
<https://pubmed.ncbi.nlm.nih.gov/33863575/>



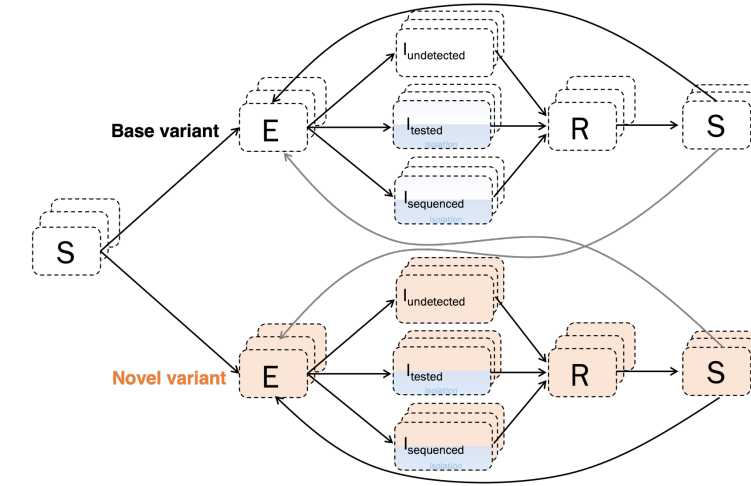
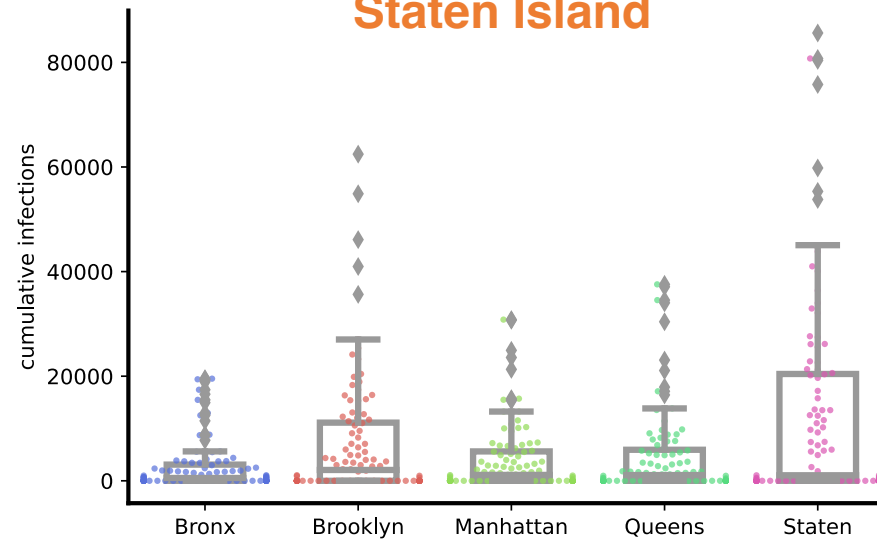
Menkir *et al.* (2021)

Where do we see the greatest number of infections if new SARS-CoV-2 variants emerge in different places across the city?

Variant emerges in **Manhattan**



Variant emerges in **Staten Island**



Final thoughts

- Compartmental models are *simple* but *powerful*
- Start by understanding the disease process
- Identify the public health goal
- Translate the disease process into a model
- Start with a simple model, add complexity as needed, but no more!
- Return to the disease process & public health impact

Thank you!

Textbooks & Academic Articles

Modeling Infectious Diseases in Humans and Animals

(Matt J. Keeling and Pejman Rohani)

An Introduction to Infectious Disease Modelling

(Emilia Vynnycky and Richard White)

Mathematical Modelling of Zombies

(Robert Smith?)

<https://people.maths.ox.ac.uk/maini/PKM%20publications/384.pdf>

An introduction to compartmental modeling for the budding infectious disease modeler

(Lauren Childs)

<https://vtechworks.lib.vt.edu/items/61e9ca00-ef21-4356-bcd7-a9294a1d2f17>

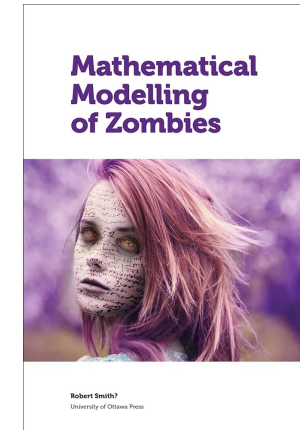
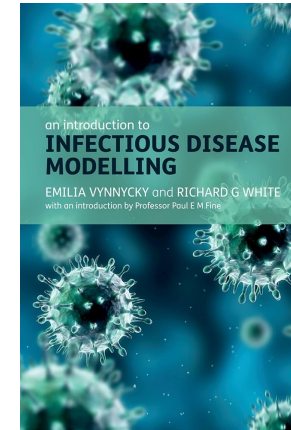
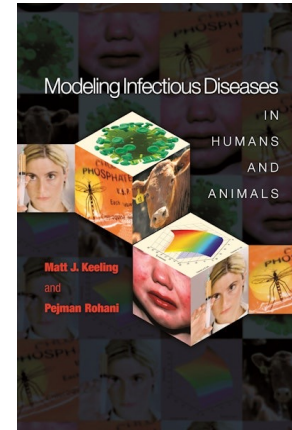
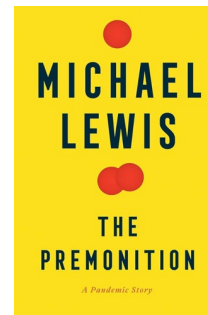
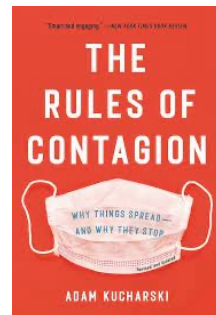
Popular Science

The Rules of Contagion: Why Things Spread and Why They Stop

(Adam Kucharski)

The Premonition: A Pandemic Story

(Michael Lewis)



Online Courses

Introduction to Infectious Disease Modelling

(Caroline Buckee, Inga Holmdahl, Ayesha Mahmud)

<https://ccdd.hsph.harvard.edu/introduction-to-infectious-disease-modeling/>

Coursera: Infectious Disease Modelling Specialization

(Nimalan Arinaminpathy)

<https://www.coursera.org/specializations/infectious-disease-modelling#courses>

Contagious Maths

(Julia Gog)

<https://plus.maths.org/content/contagious-maths>