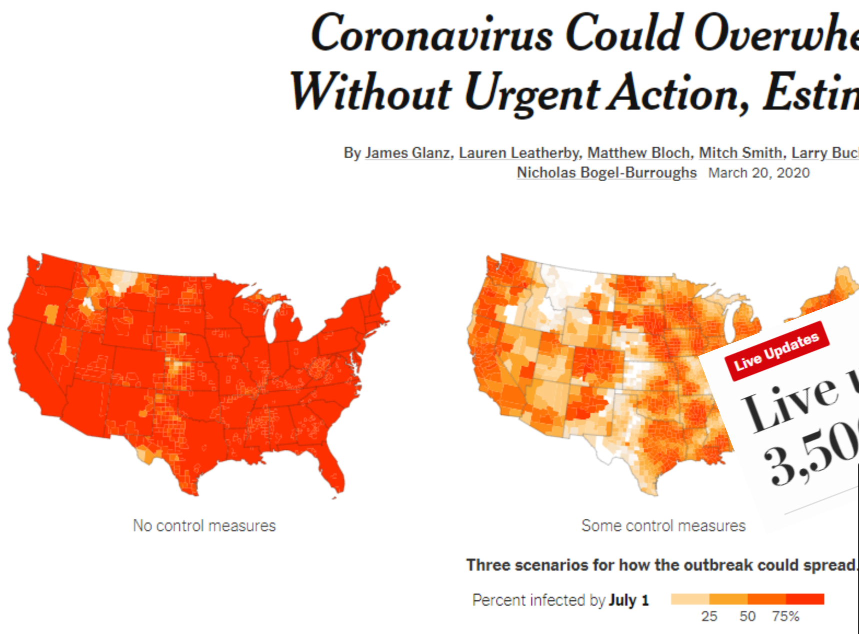
Module 1:

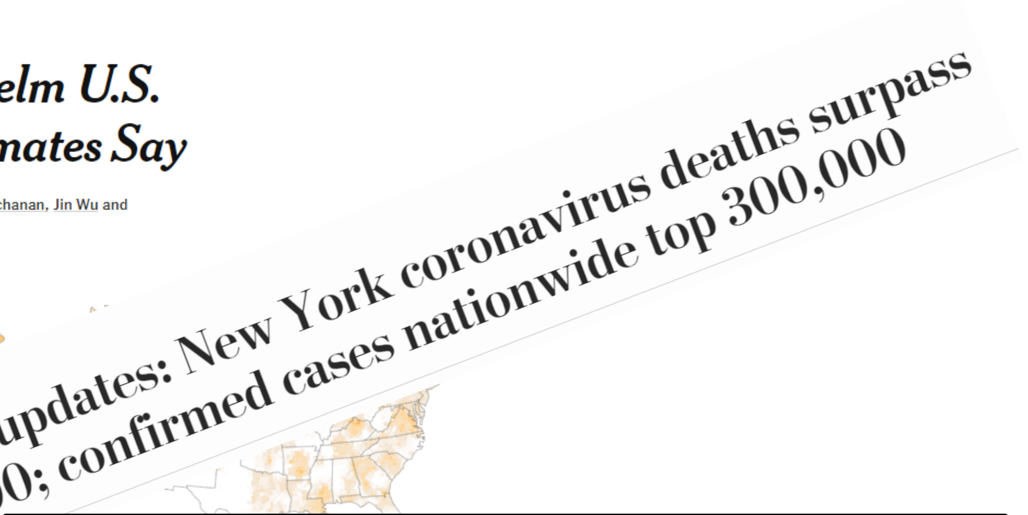
Quantitative Approaches for Modeling COVID-19 and Other Pandemics



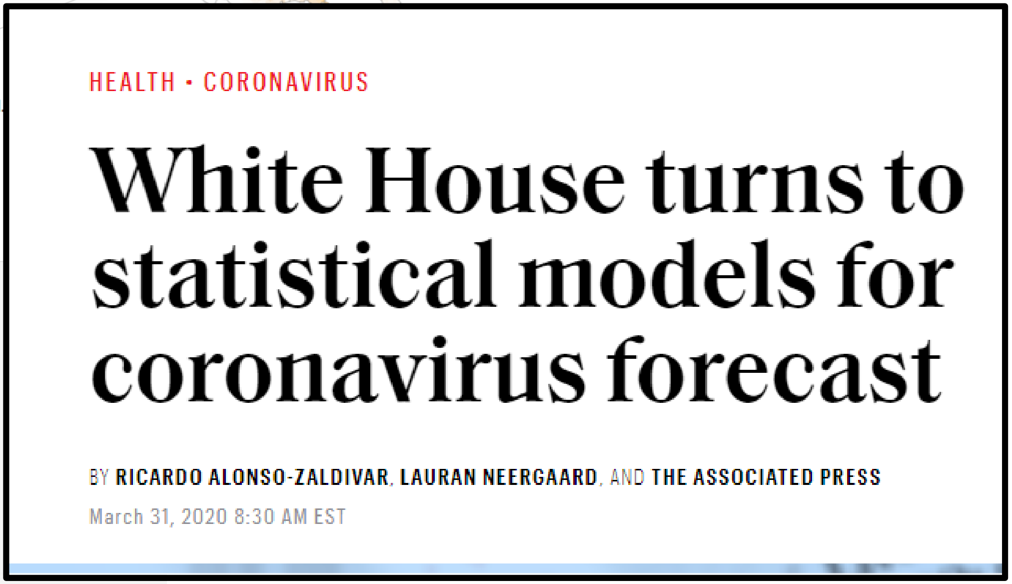
Coronavirus Could Overwhelm U.S. Without Urgent Action, Estimates Say

By James Glanz, Lauren Leatherby, Matthew Bloch, Mitch Smith, Larry Buchanan, Jin Wu and Nicholas Bogel-Burroughs March 20, 2020

Three scenarios for how the outbreak could spread.



Live updates: New York coronavirus deaths surpass 3,500; confirmed cases nationwide top 300,000

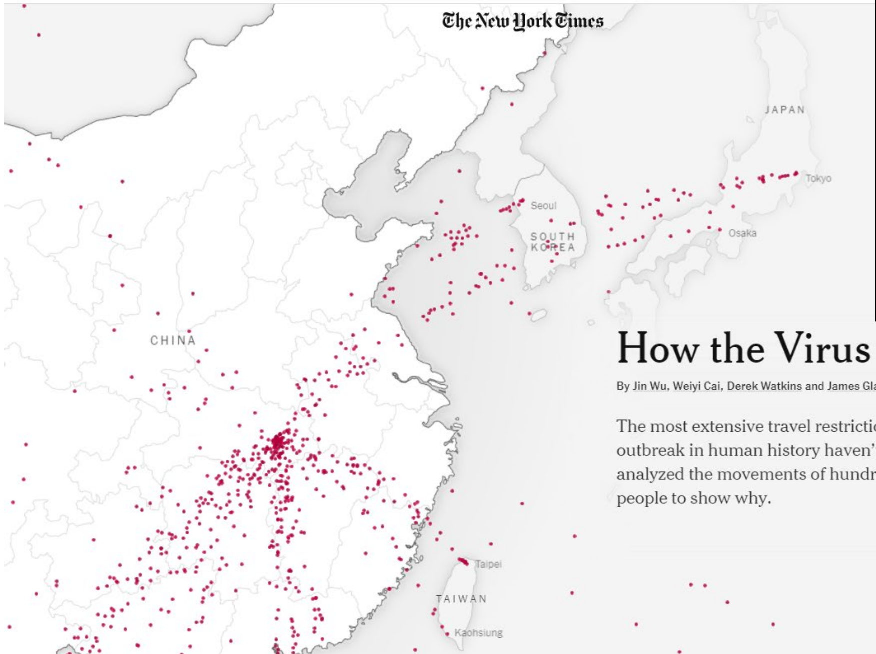


HEALTH • CORONAVIRUS

White House turns to statistical models for coronavirus forecast

BY **RICARDO ALONSO-ZALDIVAR**, **LAURAN NEERGAARD**, AND **THE ASSOCIATED PRESS**

March 31, 2020 8:30 AM EST



How the Virus Got Out

By Jin Wu, Weiyi Cai, Derek Watkins and James Glanz March 22, 2020

The most extensive travel restrictions to stop an outbreak in human history haven't been enough. We analyzed the movements of hundreds of millions of people to show why.

Suppression

Statistical models

R0

Flatten the Curve

Asymptomatic cases

Vaccination

Rebound

Peak bed capacity

Centralized Quarantine

Travel restrictions

Social Distancing

Control measures

Outline

1) Some universal dynamical features of outbreaks
2) What is the basic reproduction number R0
   and why is it so important?
3) What stops disease outbreaks?
4) Essential core of models of disease dynamics:
   the Susceptible-Infectious-Recovered (SIR) model

Pandemics in History

Plague of Athens, 430-427 BC

- Killed ~1/4 of the city's population

Black Plague, 1347-1351

- Killed 30-60% of Europe's population
- Fleas acted as the vector

Native American epidemics, 1518-1830's

- Smallpox and other diseases
- May have killed 90% of native Americans

Spanish flu (H1N1), 1918-1920

- Infected 1/3 of world population

Recent outbreaks

- Ebola, Zika, SARS, MERS

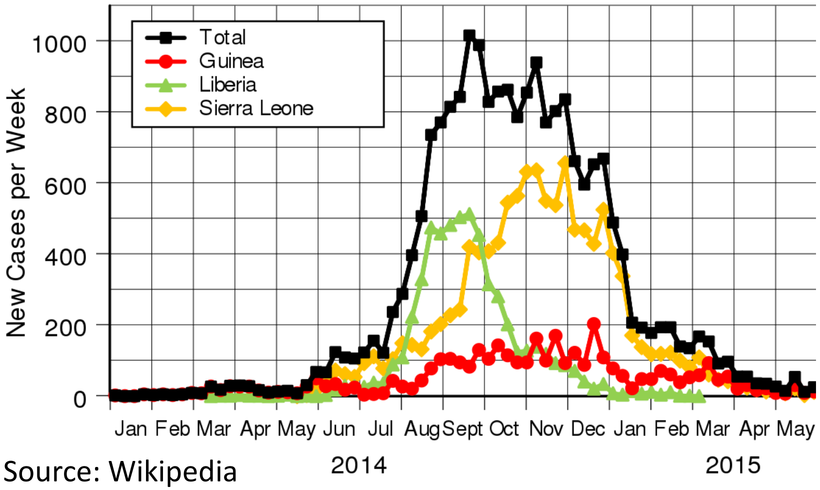
Without strong control measures, can affect large fractions of population

Pandemics differ in many ways…

- *Transmission rates*: fast or slow
- *Transmission routes*: human vs. non-human carrier, airborne vs. contact
- *Mortality & recovery rates*

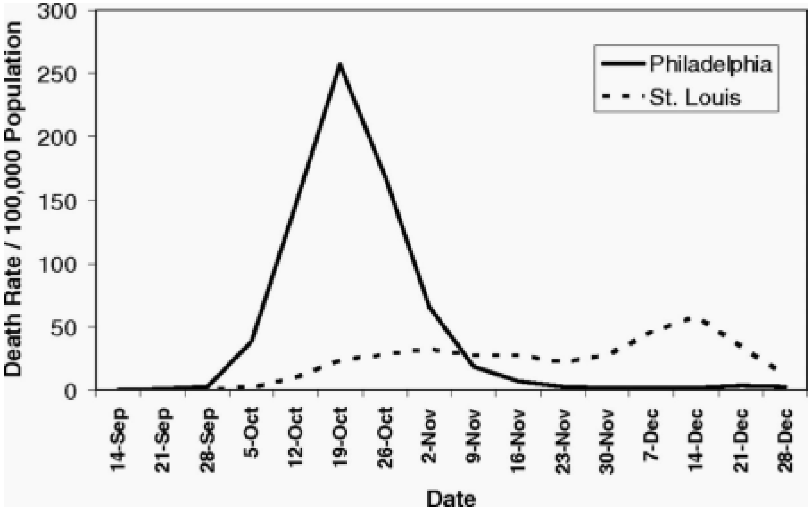
But also share many core features…

2014 West Africa Ebola Epidemic



Source: Wikipedia

1918 Spanish flu



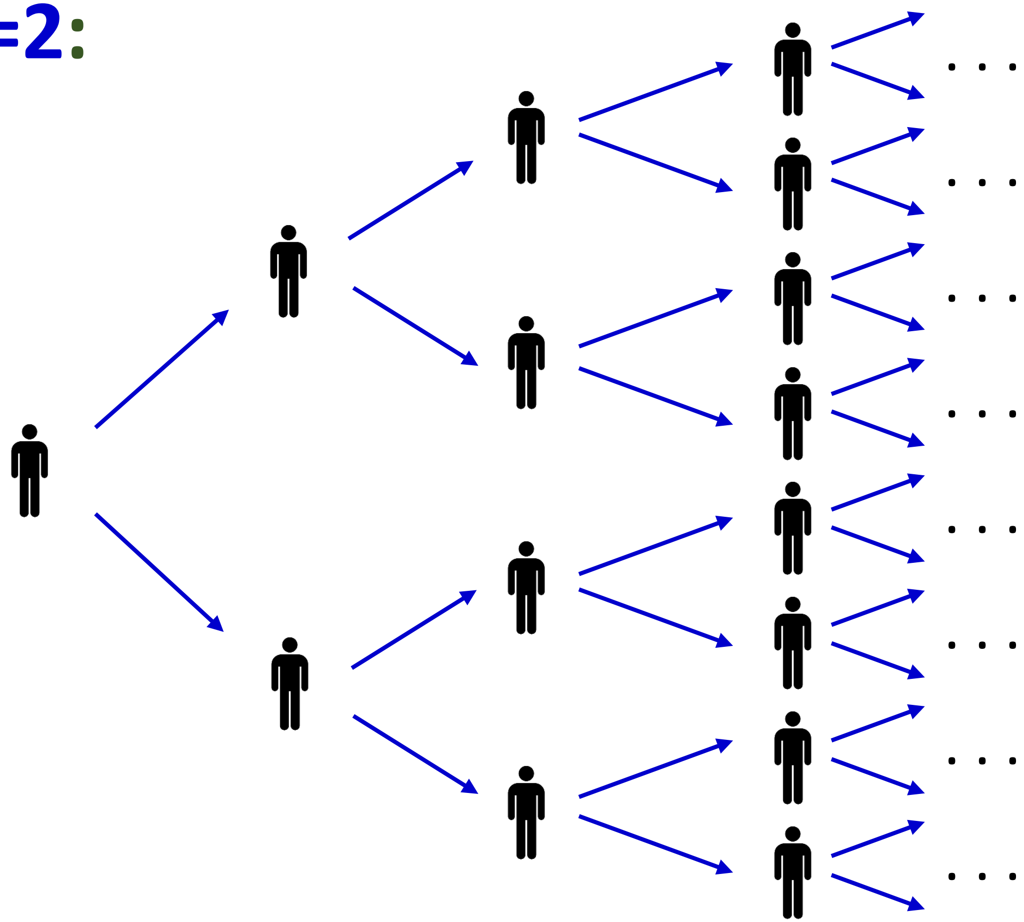
These core shared features have allowed models of previous pandemics to be re-purposed for predicting the course of COVID-19

Key Concept:
The “basic reproduction number” R0

R0 = average # of people that each infected person infects, **in a nearly entirely susceptible population**

Why is this number so important?

Consider R0=2:



Initially 1 infected person (I_0)

generation: (n)

0

1

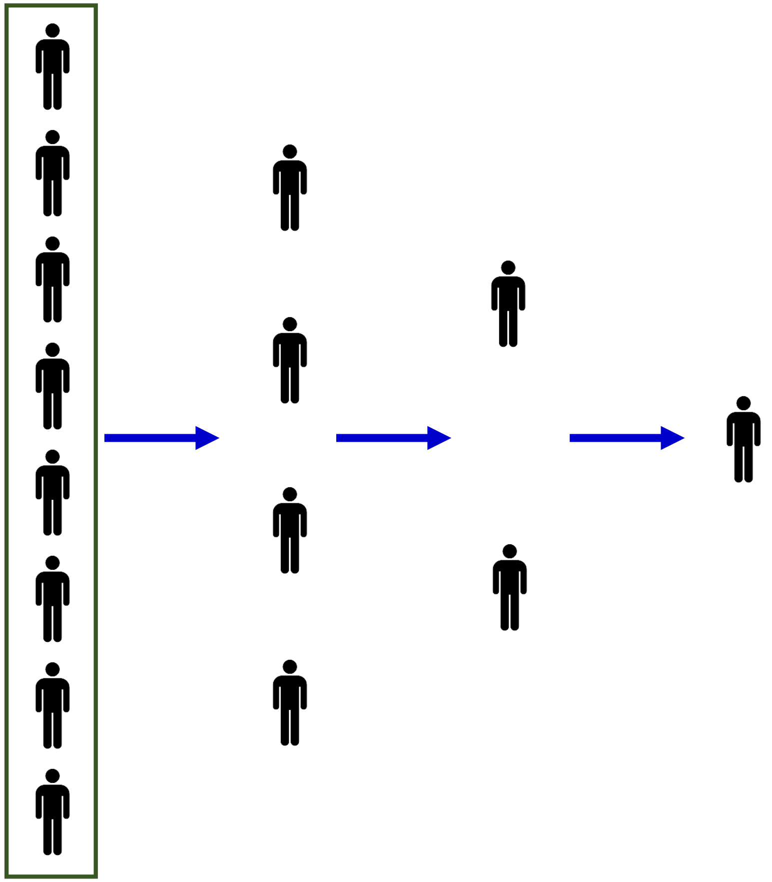
2

3

$$I(n)=(\#\text{ new infections in generation } n) = (1)(2)^n = I_0 R0^n$$

Grows exponentially fast – outbreak!!!

Consider R0=½:



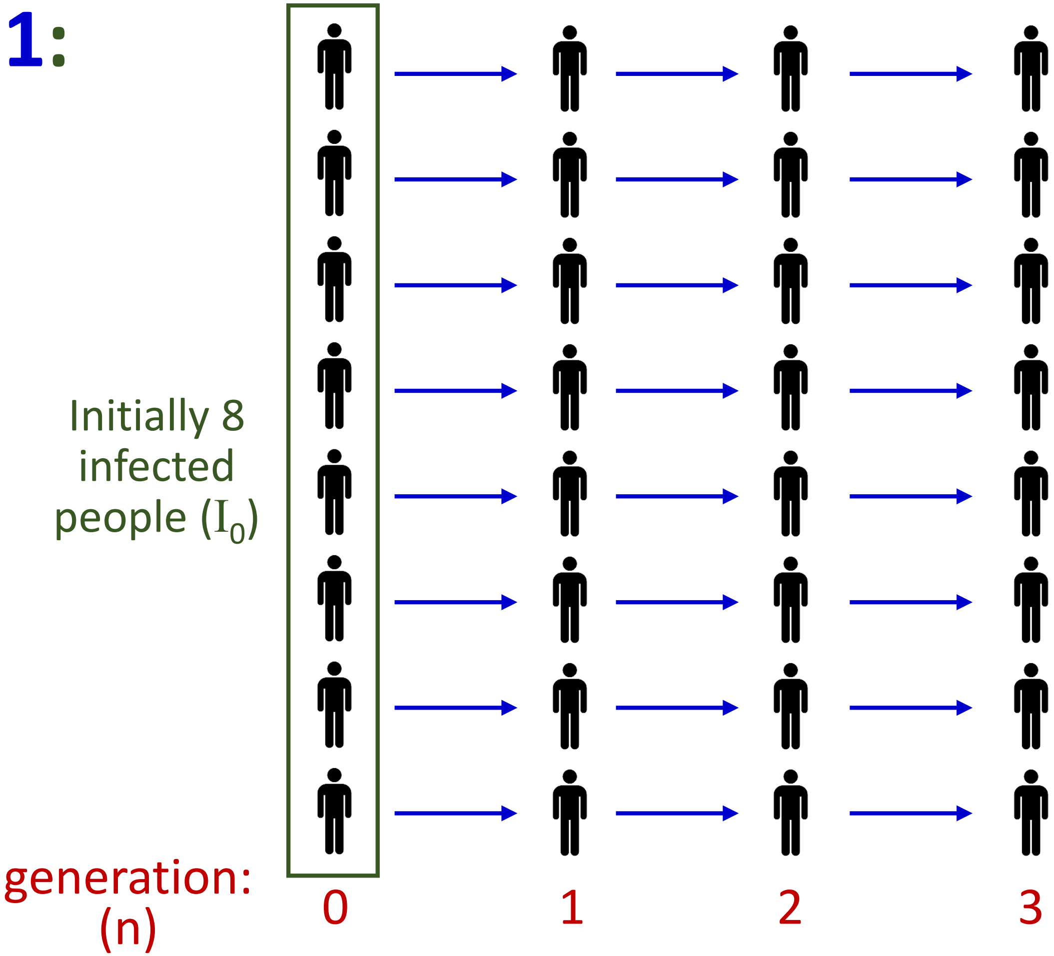
Initially 8 infected people (I_0)

generation: (n) 0 1 2 3

$I(n)$=(# new infections in n^{th} generation) = $(8)(½)^n = I_0 R0^n$

Decays exponentially fast – rapid recovery!

Consider R0=1:



Initially 8 infected people (I_0)

generation: (n)

0

1

2

3

$$I(n) = (\#\text{ new infections in } n^{th} \text{ generation}) = (8)(1)^n = I_0 R0^n$$

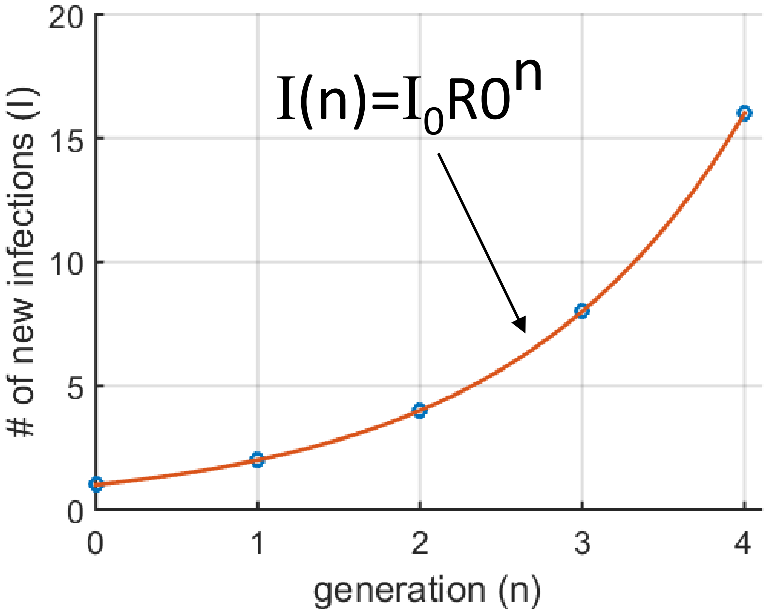
No change: borderline between growth and decay

R0: Summary So Far

R0 = average # of people that each infected person infects,
in a nearly entirely susceptible population

R0 > 1: exponential growth (outbreak)

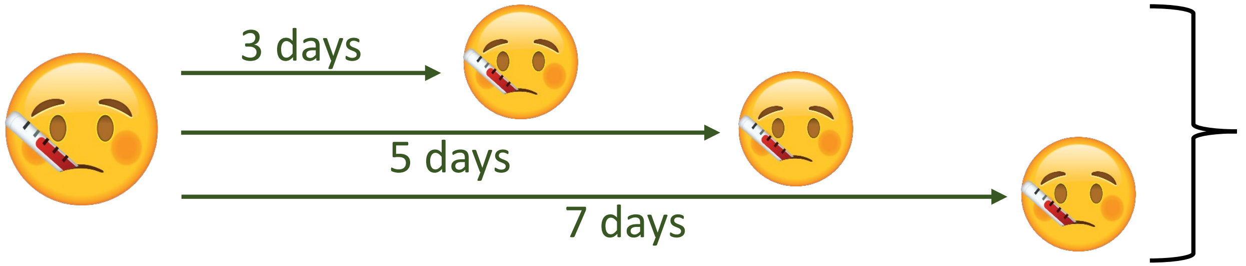
R0 < 1: no outbreak



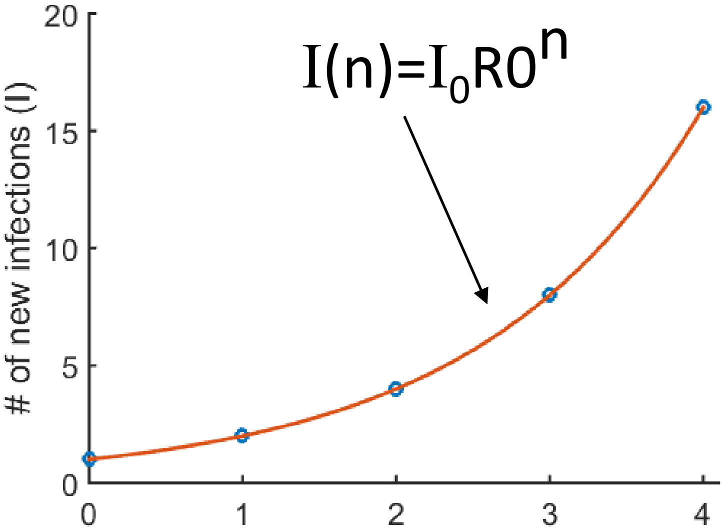
Issue: Real data is plotted versus *time*, not generation

Generation Time

Generation time **g**: mean time interval between infection of one person, and infections of the people that this person infects



g = 5 days



$I(n)=I_0 R0^n$

0 5 10 15 20

← # of *generations* (n)

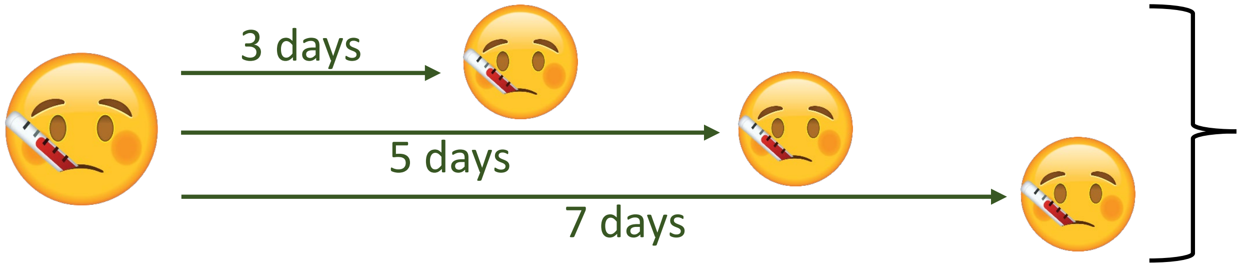
← time in *days* (t)

time in days = (# of generations) * (time per generation)

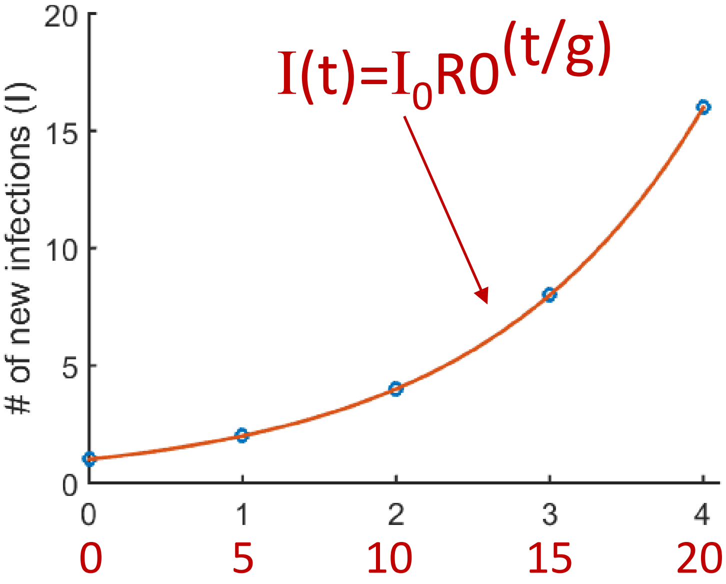
$\boxed{t = n*g}$ or $\boxed{n = t/g}$

Generation Time

Generation time g: mean time interval between infection of one person, and infections of the people that this person infects



g = 5 days



$I(t)=I_0R0^{(t/g)}$

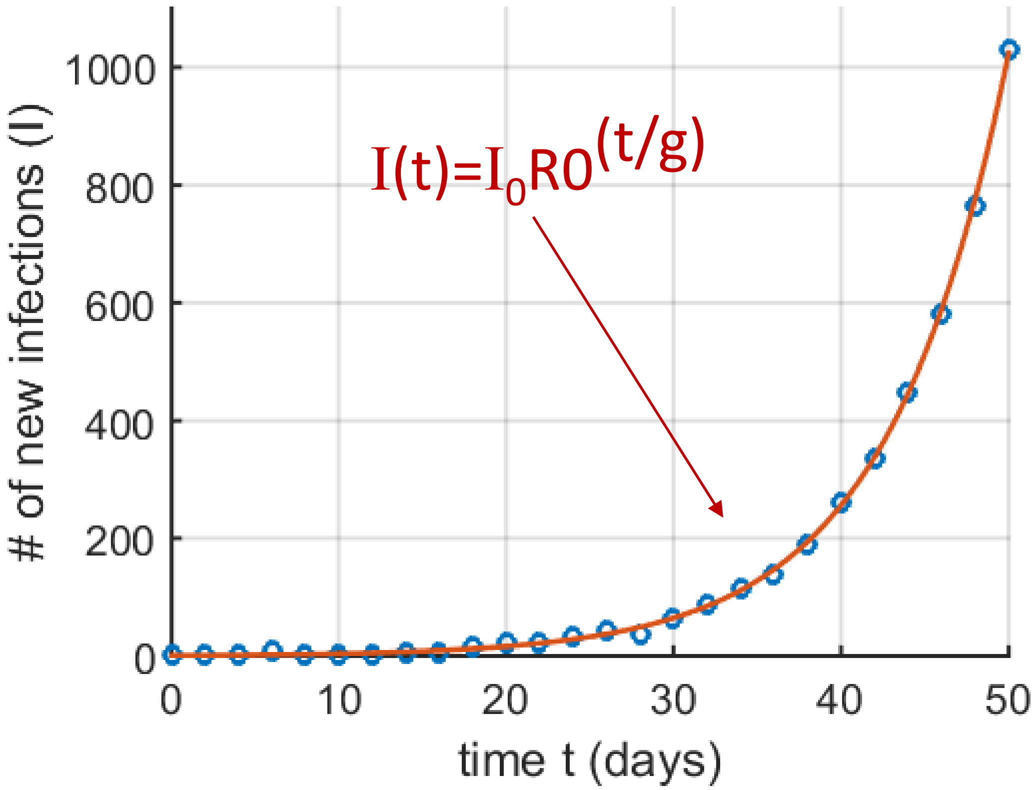
← # of *generations* (n)

← time in *days* (t)

time in days = (# of generations) * (time per generation)

$\boxed{t = n*g}$ or $\boxed{n = t/g}$

Question: How do we determine R0 from real data?

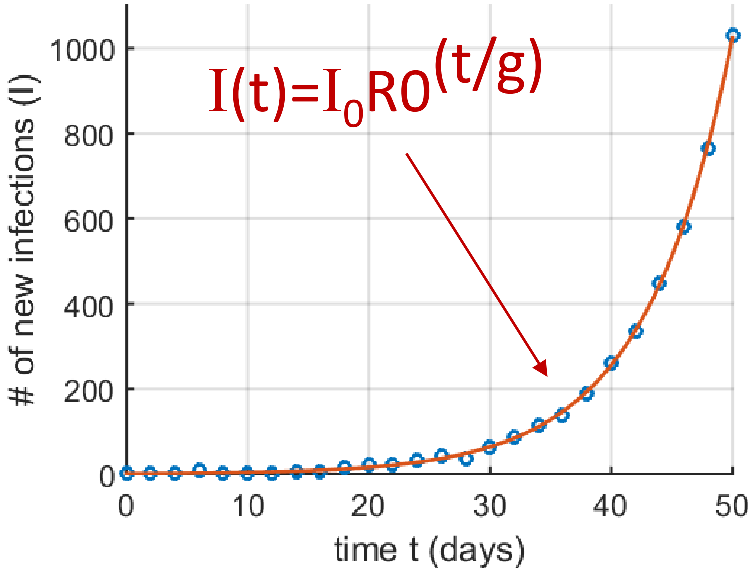


$I(t)=I_0 R0^{(t/g)}$

Issue: Even if we know g = 5 days, still <u>very</u> hard to see what R0 is from this graph

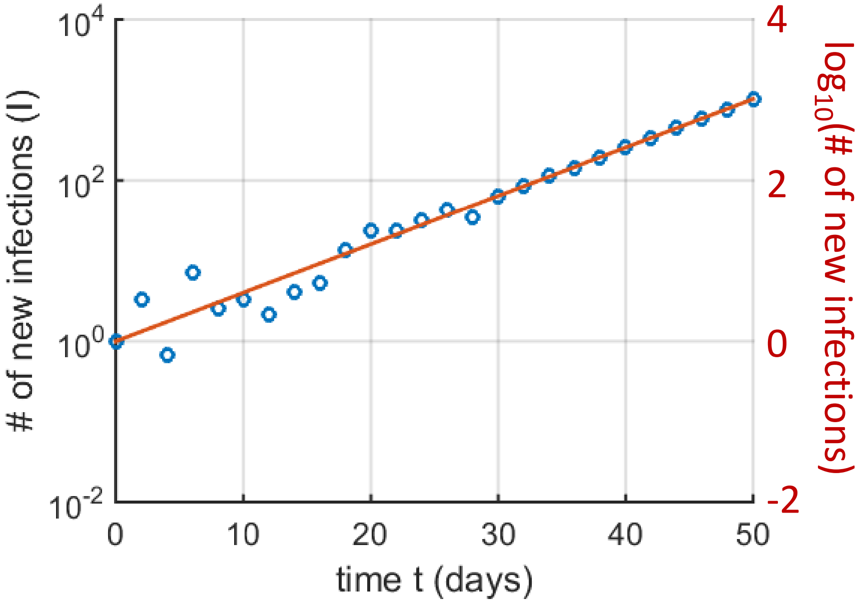
Answer: Instead plot on semi-log plot!

Original plot (linear y-axis)



$I(t)=I_0 R0^{(t/g)}$

Semi-log plot (logarithmic y-axis)

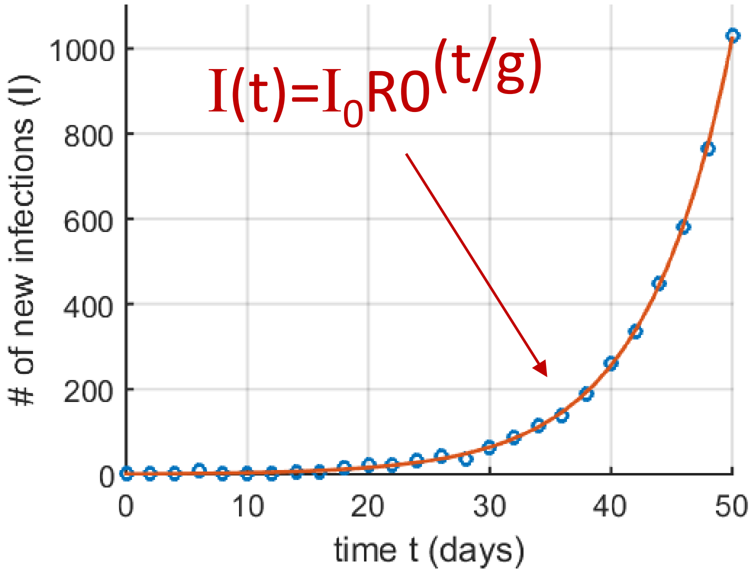


Math:

$$I(t)=I_0 R0^{(t/g)}$$

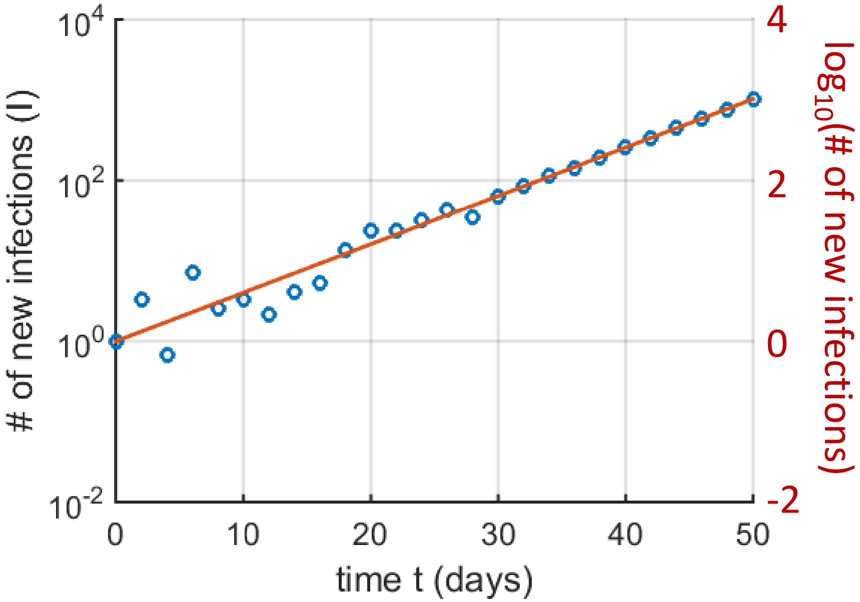
Answer: Instead plot on semi-log plot!

Original plot (linear y-axis)



$I(t)=I_0 R0^{(t/g)}$

Semi-log plot (logarithmic y-axis)



Math:

$$\log_{10}(I(t))=\log_{10}(I_0\, R0^{(t/g)})$$

$$\log_{10}(I(t))=\log_{10}(R0^{(t/g)}) + \log_{10}(I_0)$$

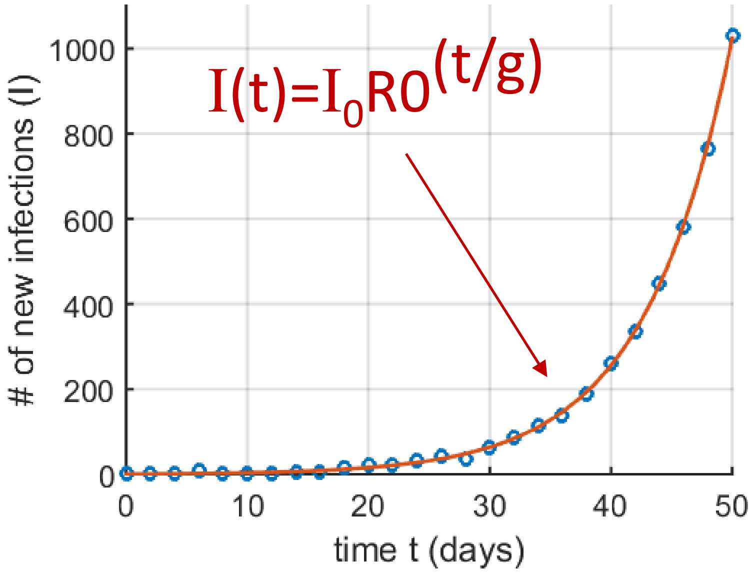
Recall:

$\log(a*b) = \log(a) + \log(b)$

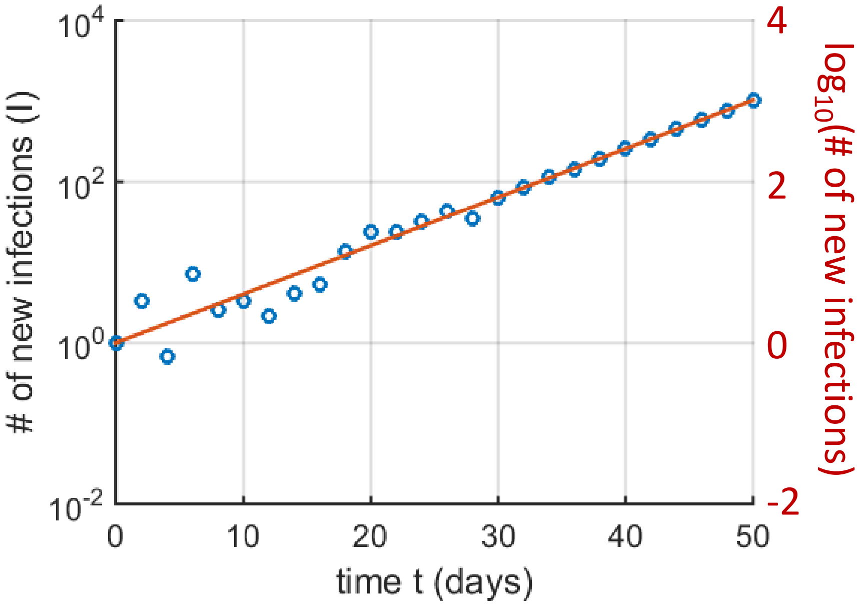
$\log(a^t) = t*\log(a)$

Answer: Instead plot on semi-log plot!

Original plot (linear y-axis)



Semi-log plot (logarithmic y-axis)



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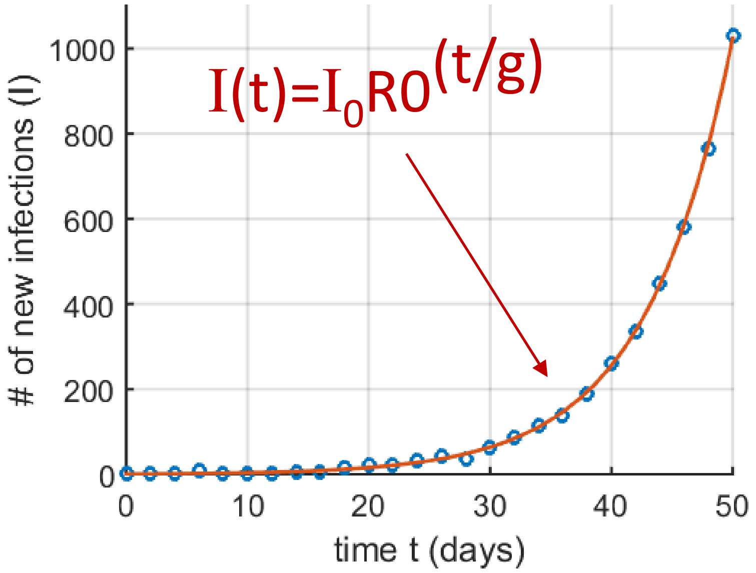
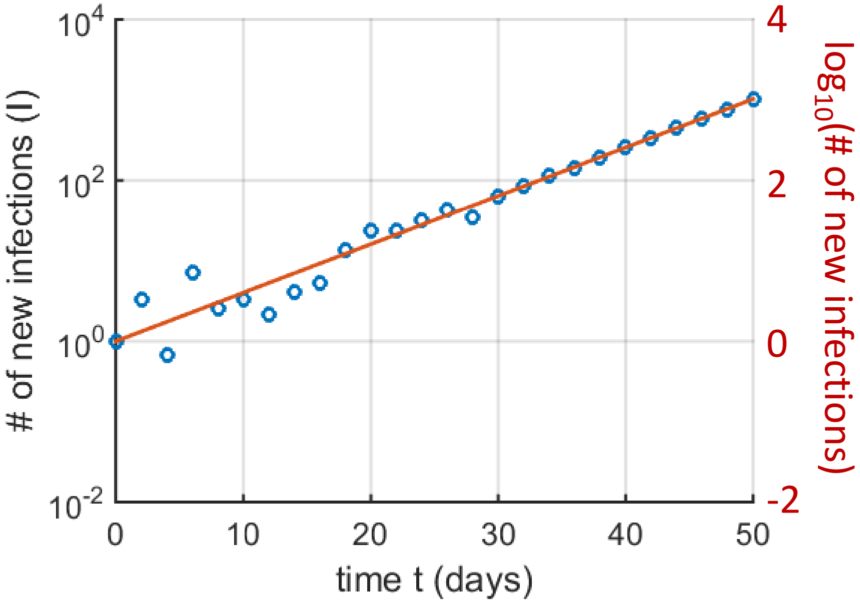


$I(t)=I_0R0^{(t/g)}$

Semi-log plot (logarithmic y-axis)



Math:

$$\log_{10}(I(t))=\log_{10}(I_0\,R0^{(t/g)})$$

$$\log_{10}(I(t))=(t/g)\log_{10}(R0^{\cancel{(t/g)}})+\log_{10}(I_0)$$

$$\log_{10}(I(t))=(1/g)\log_{10}(R0)t+\log_{10}(I_0)$$

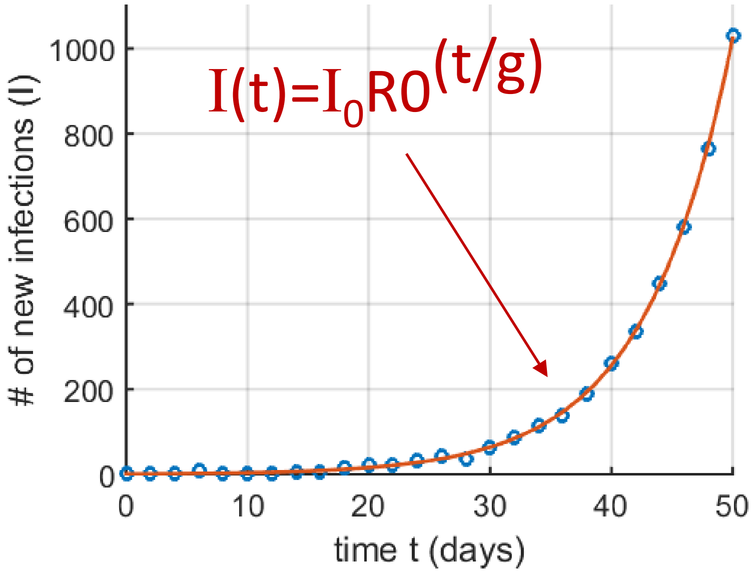
Recall:

$\log(a*b) = \log(a) + \log(b)$

$\log(a^t) = t*\log(a)$

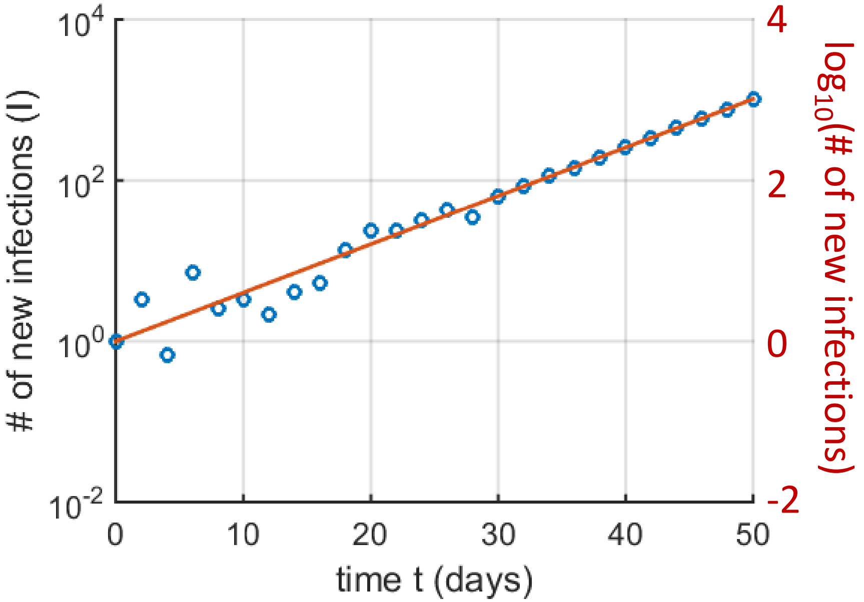
Answer: Instead plot on semi-log plot!

Original plot (linear y-axis)



$I(t)=I_0 R0^{(t/g)}$

Semi-log plot (logarithmic y-axis)



Math: $\log_{10}(I(t))=\log_{10}(I_0\, R0^{(t/g)})$

$\log_{10}(I(t))= (t/g)\log_{10}(R0^{\cancel{(t/g)}}) + \log_{10}(I_0)$

$\log_{10}(I(t))=(1/g)\log_{10}(R0)t + \log_{10}(I_0)$

"y" = "m x" + "b"

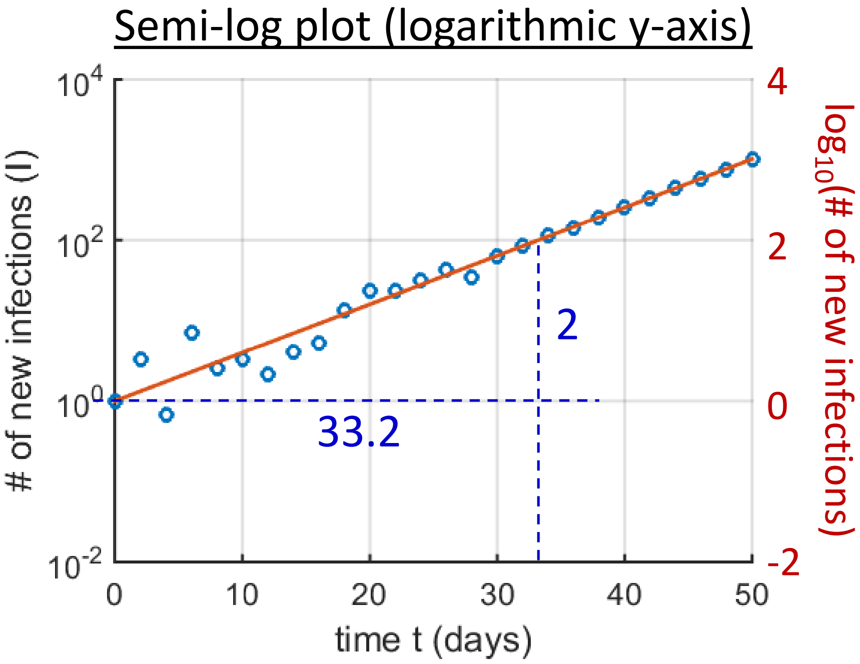
slope intercept

Recall:

$\log(a*b) = \log(a) + \log(b)$

$\log(a^t) = t*\log(a)$

Determine R0 from slope of semi-log plot!



Math:

$$\log_{10}(I(t)) = \underbrace{(1/g)\log_{10}(R0)}\,t + \log_{10}(I_0)$$

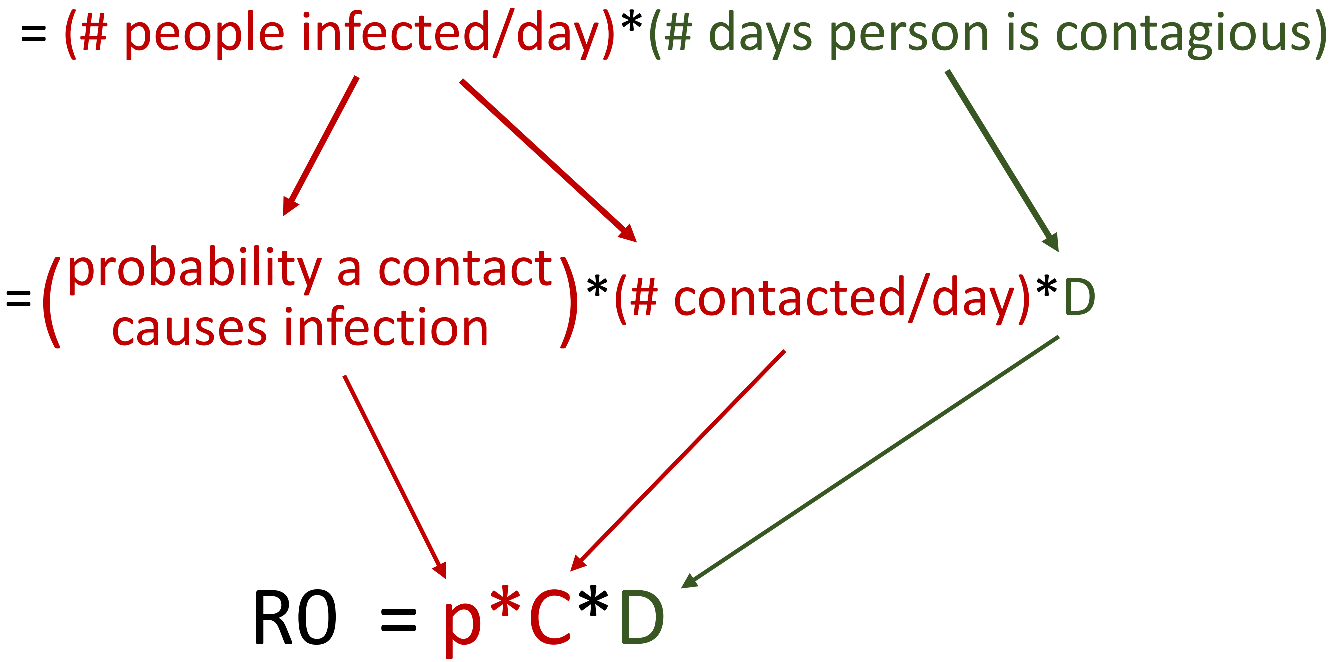
$$\cancel{(1/g)}\log_{10}(R0) = \text{slope} * g$$

$$\boxed{R0 = 10^{(\text{slope} * g)}} = 10^{(2/33.2\text{ days})*(5\text{ days})} = 2$$

Next Question:
What mechanistic factors influence R0?

R0 = average # of people that each infected person infects,
in a nearly entirely susceptible population

R0 = (# people infected)



= (# people infected/day)*(# days person is contagious)

= (probability a contact causes infection)*(# contacted/day)*D

R0 = p*C*D

Thought Question:
Which factor does *social distancing* affect?

1) Probability of transmission p
2) # of contacts C
3) # of days infected D
4) All of the above

Answer: (2) # of contacts C

Explanation:

By keeping people away from each other, it reduces the # of contacts we make each day. It does not reduce the # of days we are infected. If you make a contact, it does not reduce the probability p of transmitting the disease.

R0 vs. Effective R

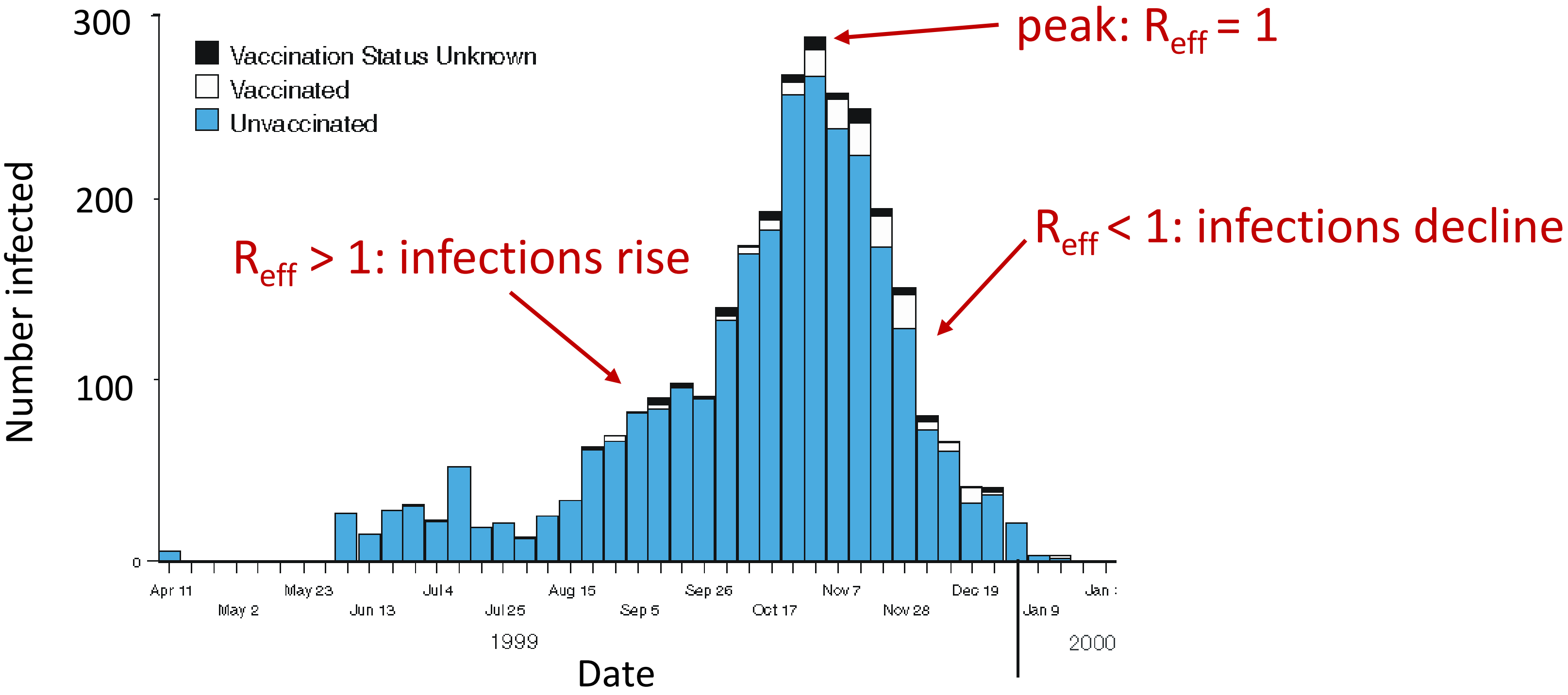
Basic reproduction number R0:

R0 = average # of people that each infected person infects, in a nearly entirely susceptible population

Effective reproduction number R_{eff}:

R_{eff} = average # of people that each infected person infects, when some of the population is immune (=R0 at start of epidemic)

1999 Measles outbreak in the Netherlands



peak: $R_{eff} = 1$

$R_{eff} > 1$: infections rise

$R_{eff} < 1$: infections decline

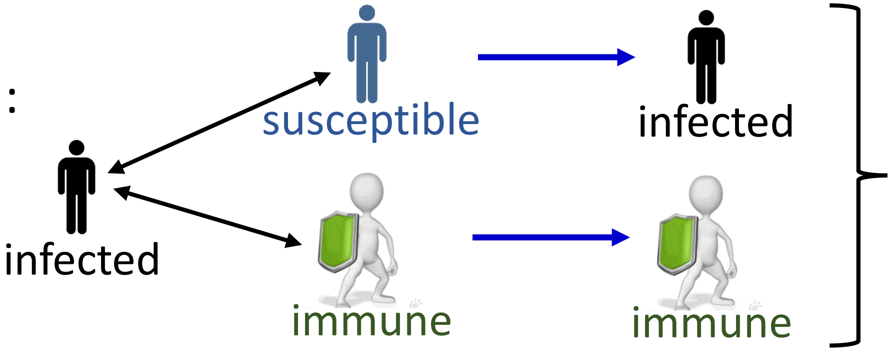
Effect of Vaccination

Question: What fraction of the population must be vaccinated to avoid outbreaks for a disease with basic reproduction number R0?

Answer: Let v = fraction of people vaccinated

1-v = fraction of susceptible people

e.g. R0=2, v = ½:



infected

susceptible

infected

immune

immune

No increase in
# of infected!
$R_{eff} = 1$

<u>Math</u>: To avoid an outbreak, need $R_{eff} < 1$:

R_{eff} = (# of infections if all susceptible)*(fraction susceptible) < 1

$$R0 * (1-v) < 1$$

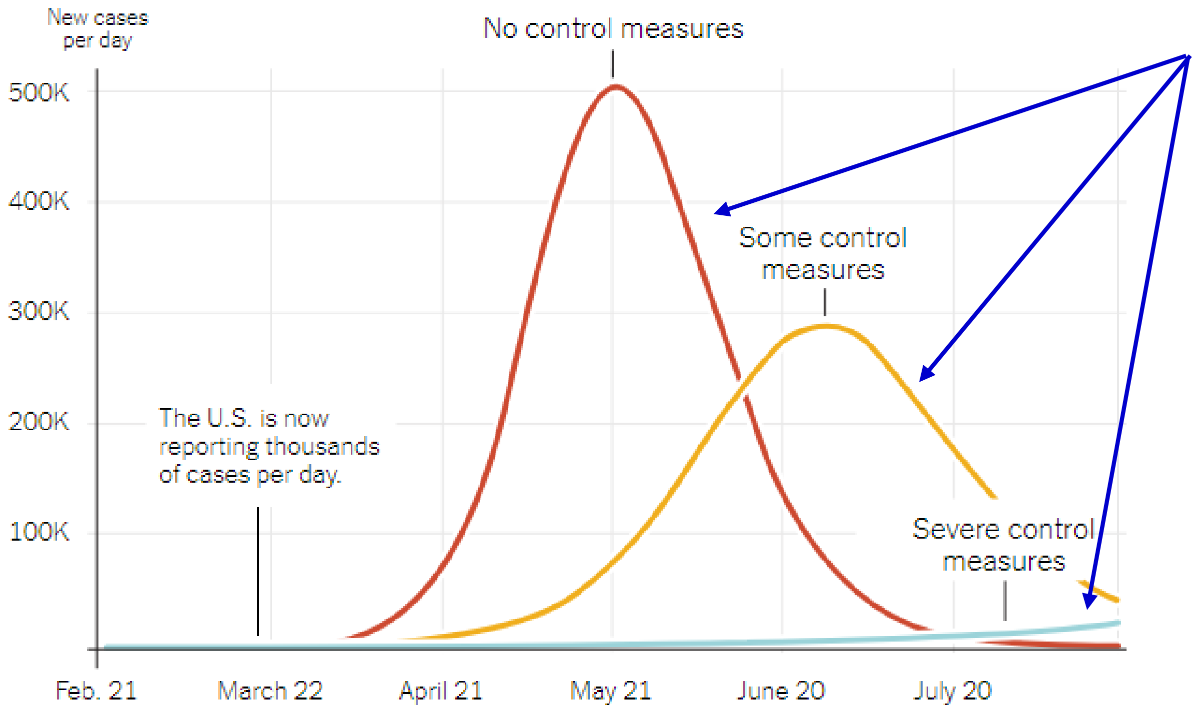
$$(1-v) < 1/R0$$

$$\boxed{v > 1 - 1/R0}$$

"Herd immunity": Only need to vaccinate a fraction of the herd (i.e. population) to eradicate a disease

Part 2: Disease Dynamics & the SIR Model

Flattening the curve:



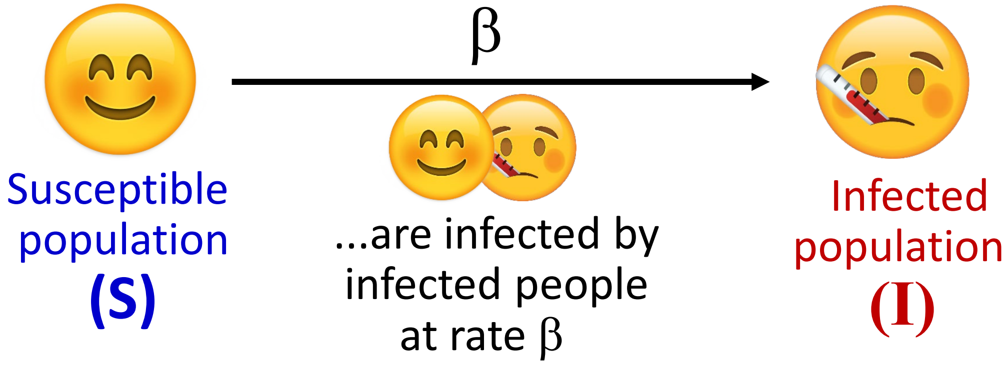
How Control Measures Could Slow the Outbreak

By The New York Times · Source: Sen Pei and Jeffrey Shaman, Columbia University

***Key Question*:**
How can we understand where the shapes of these curves come from?

The SIR Model:
Susceptible-Infected-(Recovered or Removed)

Rule 1:



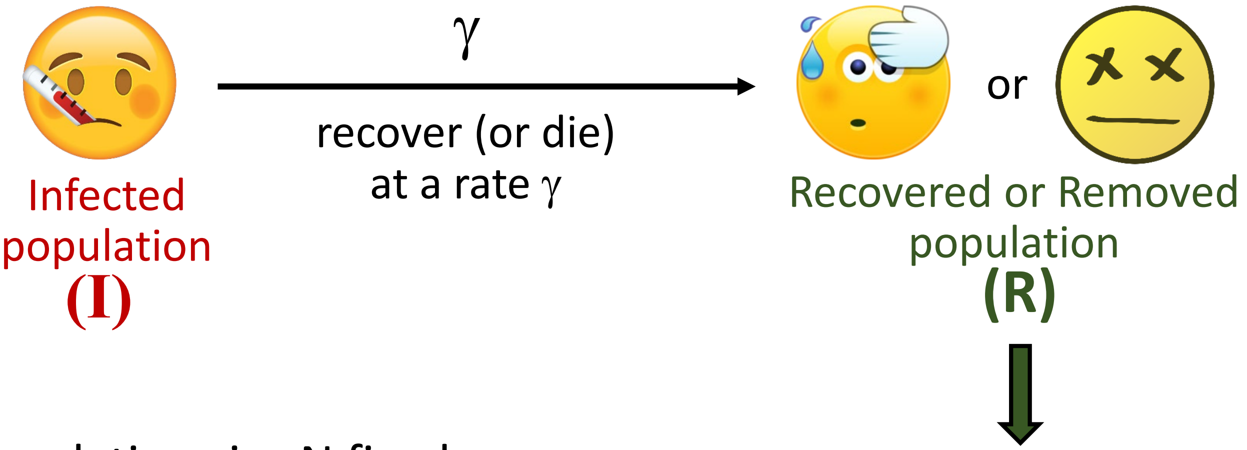
β

Susceptible population **(S)**

...are infected by infected people at rate β

Infected population **(I)**

Rule 2:



γ

Infected population **(I)**

recover (or die) at a rate γ

or

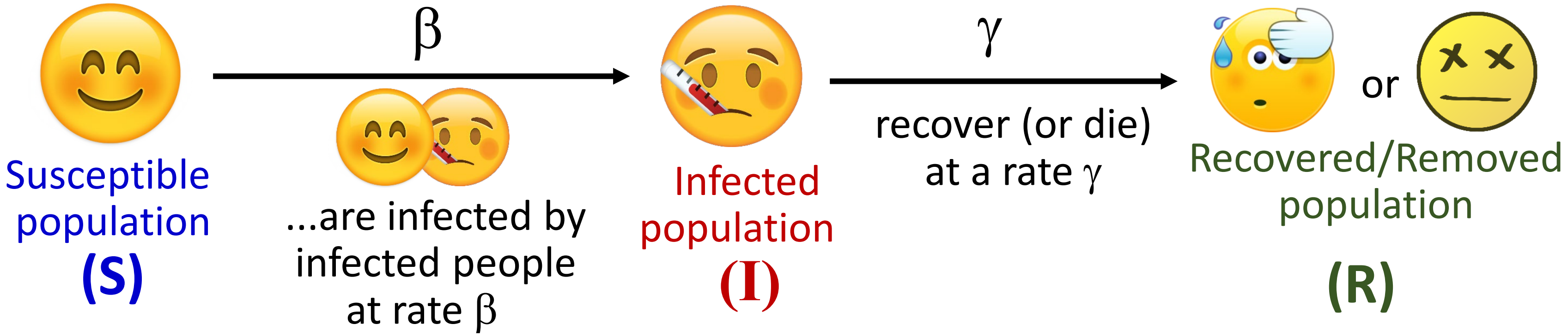
Recovered or Removed population **(R)**

Assumed to be immune (includes vaccinated as well)

Assume total population size N fixed:

S + I + R = N

Let’s turn this into a quantitative model:



β

γ

Susceptible population **(S)**

...are infected by infected people at rate β

Infected population **(I)**

recover (or die) at a rate γ

or

Recovered/Removed population

(R)

In a time interval Δt:

ΔS = Change in # susceptibles = - (# who get infected) = $-\beta S I \Delta t$

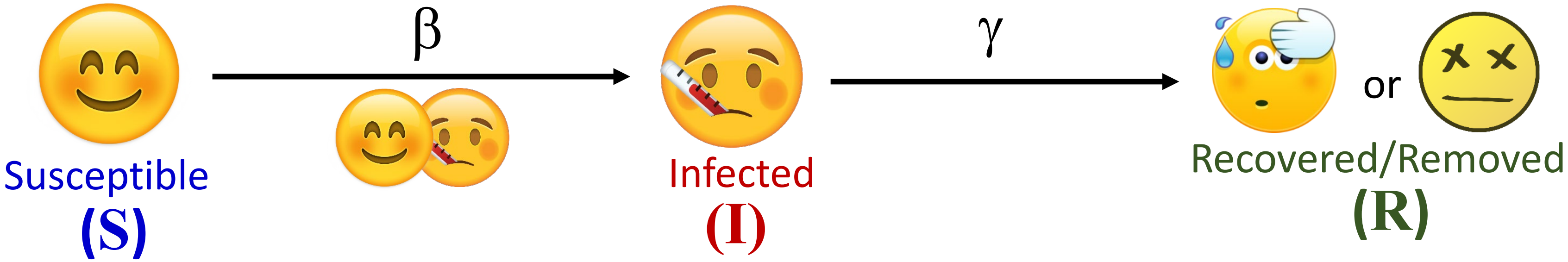
ΔR = Change in # recovered/removed = # infected who recover = $\gamma I \Delta t$

ΔI = Change in # infected = (# who get infected) – (# who recover)

$$\Delta I = \beta S I \Delta t - \gamma I \Delta t$$

For small Δt, we divide by Δt and write: $\frac{dS}{dt} = -\beta S I$

SIR model summary



β

γ

Susceptible
(S)

Infected
(I)

or

Recovered/Removed
(R)

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

(Susceptibles get infected by infected)

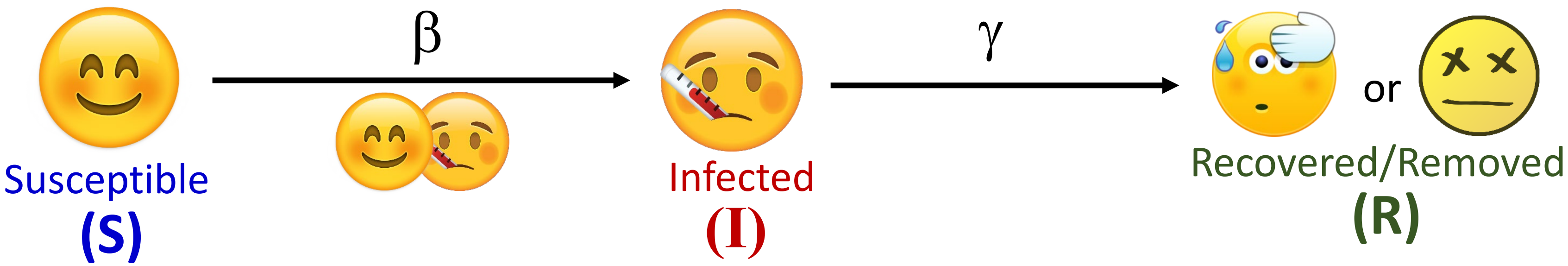
$$\frac{dI}{dt} = \beta SI - \gamma I$$

(Susceptibles get infected &
infecteds recover/get removed)

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

(Infecteds recover or are removed)

When Does an Outbreak Occur?



Outbreak occurs when # of infected grows:

dI/dt = (new infection rate) – (recovery/removal rate) > 0

$$\beta S\cancel{I} > \gamma\cancel{I}$$

$$\underbrace{\beta S(1/\gamma)}_{\text{this is } R_{eff} \text{ for the SIR model!}} > 1$$

When whole population is susceptible, S=N → $\boxed{R0=\beta N(1/\gamma)}$ for the SIR model

Comparison between our 2 formulas for R0 formula

Simple model: no dynamics

SIR dynamical model

$$R0=(pC)D \longleftrightarrow R0=\beta N(1/\gamma)$$

$$D = \text{mean \# of days contagious} \xleftrightarrow{\text{relation 1}} 1/\gamma = D$$

γ = recovery rate = 1/D
= 1/(mean # days contagious)

$$pC = \text{\# people infected/day by 1 infected person} \xleftrightarrow{\text{relation 2}} \beta N = pC$$

$$\beta = \frac{pC}{N} = \frac{\text{\# people infect/day}}{\text{total \# of people}}$$

β = fraction of population infected per day by each infected person

Extensions of the SIR Model

The SIR model contains the essence of nearly all disease dynamics models.

There are many possible extensions, including...

...more states & connections between states:

- A **latent** period after Exposure but before becoming infectious ('SEIR model')
- An **asymptomatic** period after becoming infectious, but before showing symptoms.
- Recovered people losing their immunity & returning to susceptible (e.g. flu)
- Different susceptible or infected populations (e.g. young vs. old)

...spatial dynamics:

- Travel, spatial spread between different regions
- Different people contact more or fewer other people

...randomness + time-varying parameters (e.g. seasonal changes):

You will have a chance to play with a few of these in this week's and next week's laboratories...and can play with more on your own!