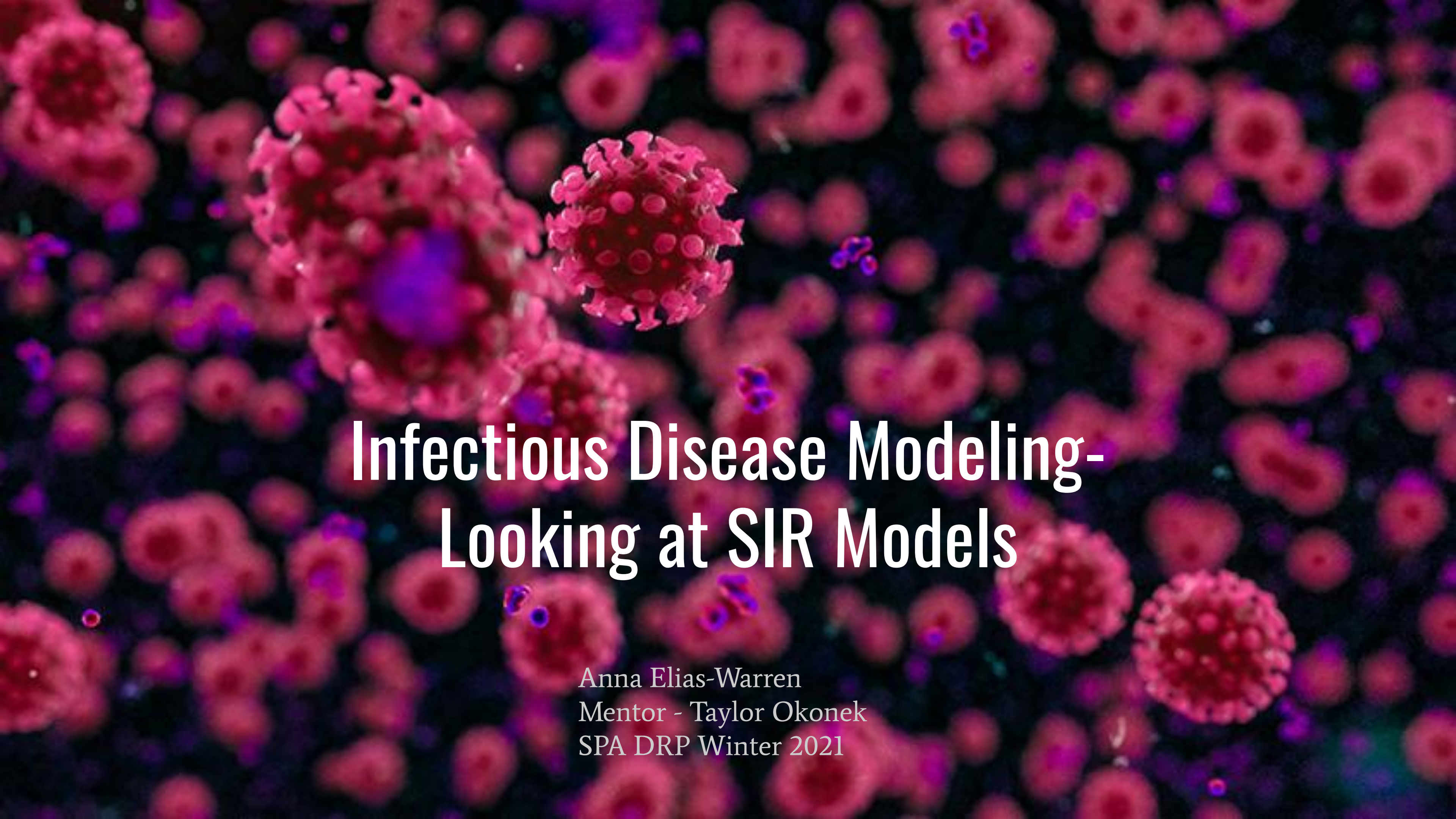

Infectious Disease Modeling- Looking at SIR Models

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SPA DRP Winter 2021

First a brief look at some main Biostatistics topics we discussed

Clinical Trials

Phase I - Trying to figure out an appropriate dosage

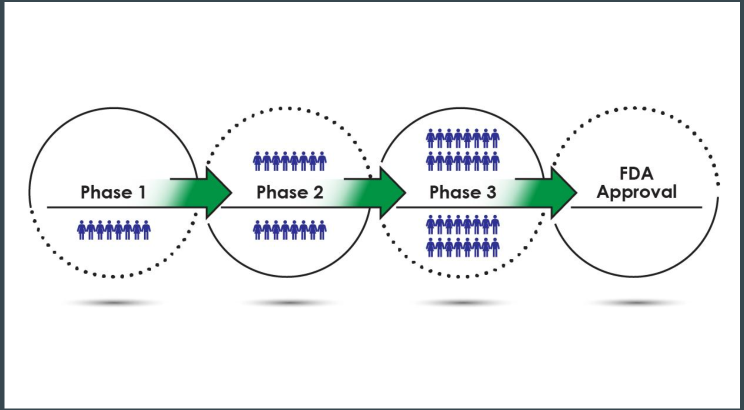
Phase II - Looking for immediate side effects and efficacy

Phases III - Looking at efficacy and adverse reactions

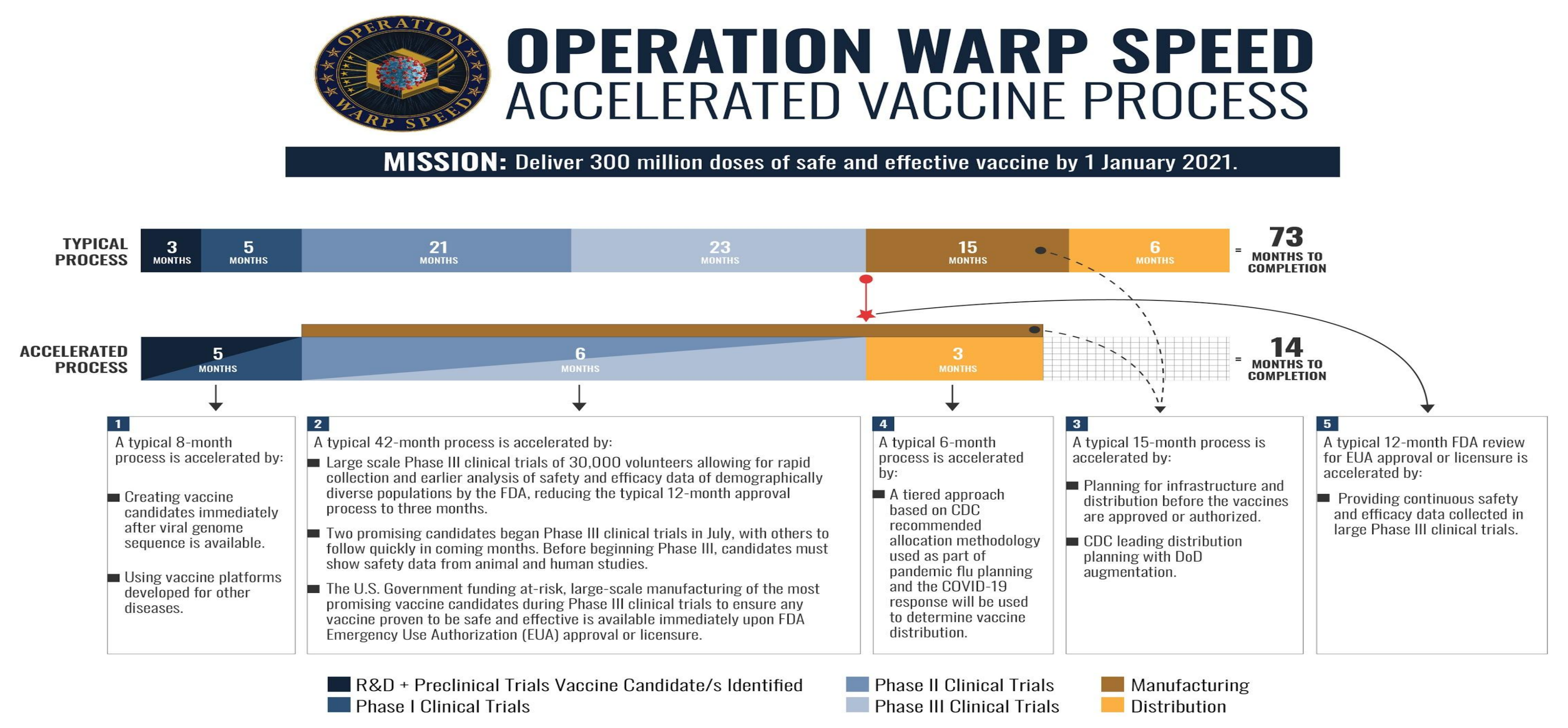
Phase IV - Long term side effects and efficacy

Efficacy vs effectiveness

Ethical considerations: clinical equipoise



Clinical Trials for COVID-19 Vaccine



OPERATION WARP SPEED
ACCELERATED VACCINE PROCESS

MISSION: Deliver 300 million doses of safe and effective vaccine by 1 January 2021.

1

A typical 8-month process is accelerated by:

- Creating vaccine candidates immediately after viral genome sequence is available.
- Using vaccine platforms developed for other diseases.

2

A typical 42-month process is accelerated by:

- Large scale Phase III clinical trials of 30,000 volunteers allowing for rapid collection and earlier analysis of safety and efficacy data of demographically diverse populations by the FDA, reducing the typical 12-month approval process to three months.
- Two promising candidates began Phase III clinical trials in July, with others to follow quickly in coming months. Before beginning Phase III, candidates must show safety data from animal and human studies.
- The U.S. Government funding at-risk, large-scale manufacturing of the most promising vaccine candidates during Phase III clinical trials to ensure any vaccine proven to be safe and effective is available immediately upon FDA Emergency Use Authorization (EUA) approval or licensure.

4

A typical 6-month process is accelerated by:

- A tiered approach based on CDC recommended allocation methodology used as part of pandemic flu planning and the COVID-19 response will be used to determine vaccine distribution.

3

A typical 15-month process is accelerated by:

- Planning for infrastructure and distribution before the vaccines are approved or authorized.
- CDC leading distribution planning with DoD augmentation.

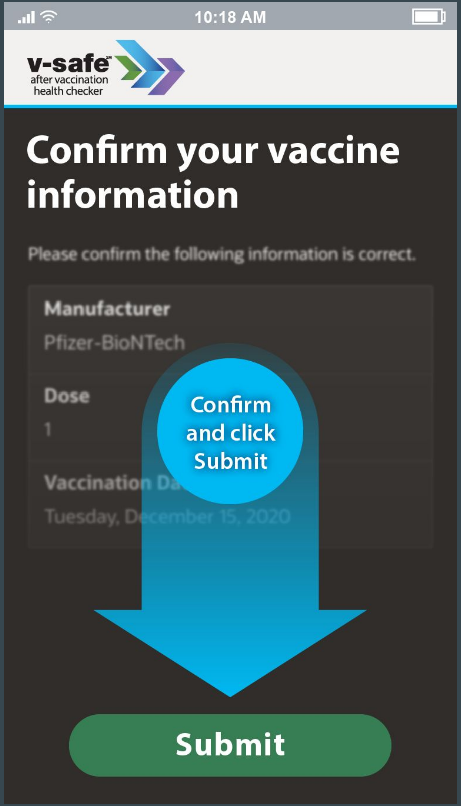
5

A typical 12-month FDA review for EUA approval or licensure is accelerated by:

- Providing continuous safety and efficacy data collected in large Phase III clinical trials.

Source: https://www.defense.gov/Explore/Spotlight/Coronavirus/Operation-Warp-Speed/

Phase IV for COVID-19 Vaccines



Confirm your vaccine information

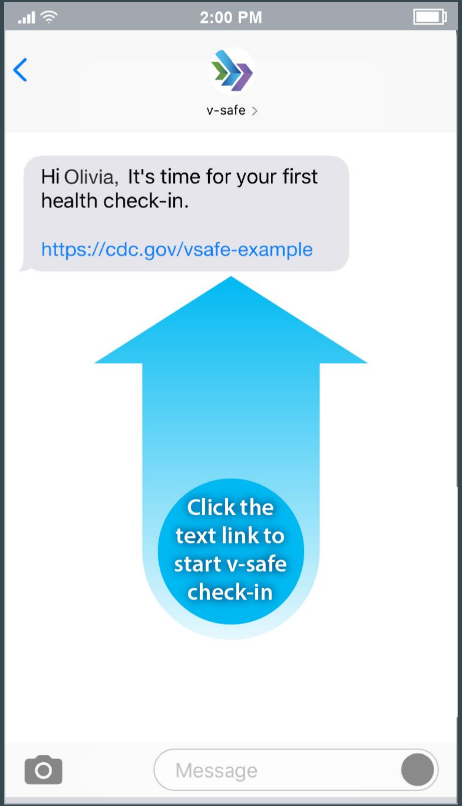
Please confirm the following information is correct.

Manufacturer
Pfizer-BioNTech

Dose
1

Vaccination Da
Tuesday, December 15, 2020

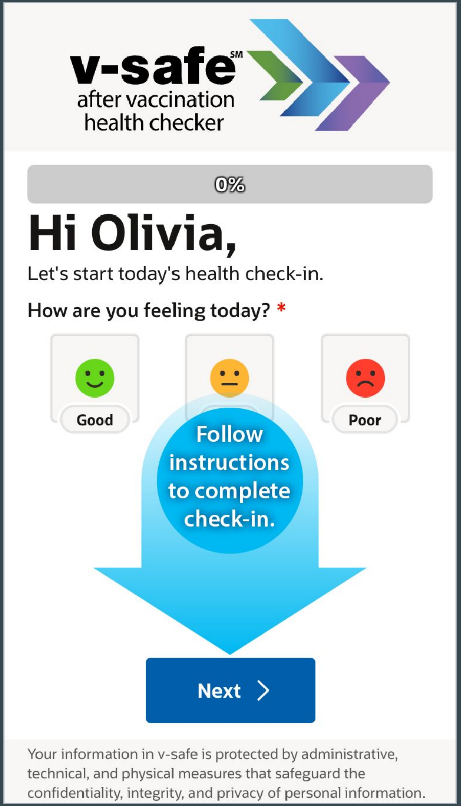
Confirm and click Submit



Hi Olivia, It's time for your first health check-in.

https://cdc.gov/vsafe-example

Click the text link to start v-safe check-in



Hi Olivia,

Let's start today's health check-in.

How are you feeling today? *

Follow instructions to complete check-in.

Your information in v-safe is protected by administrative, technical, and physical measures that safeguard the confidentiality, integrity, and privacy of personal information.

- Voluntary
- Could lead to response bias
- Is it also biased towards young tech-savvy people?

Source: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafe.html

Survival Analysis

Time to event data, calculating risk of a certain outcome

- Event of interest is usually death
- Given that you’ve survived until time x, what is the probability that you survive until time y

Censoring - when a participant is lost to follow-up, drops out

Competing risk - when a different event (that conflicts someway) occurs before event of interest

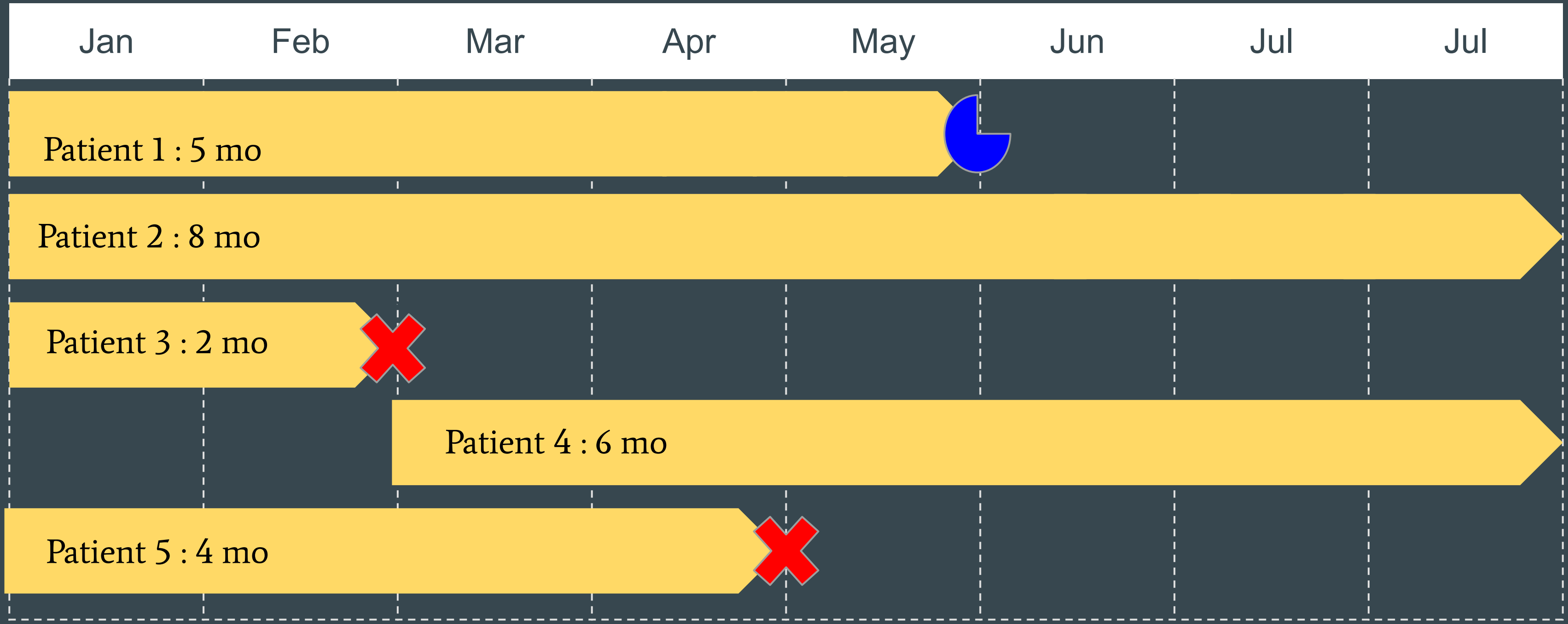
- ex| death due to cancer vs death due to heart disease

Traditional survival methods assume that competing risks are independent/absent, but this is not always the case

Survival Analysis Example

● = censored

✗ = event of interest (death)



Jan Feb Mar Apr May Jun Jul Jul

Patient 1 : 5 mo

Patient 2 : 8 mo

Patient 3 : 2 mo

Patient 4 : 6 mo

Patient 5 : 4 mo

Can be complicated due to censoring (i.e. patient dropping out of study), people enrolling at different times, competing risks and some people not having the event of interest at all

Infectious Disease Models That We Discussed

- Wanting to play out the different courses disease spread could take
- Some main models
  - SIR Model*
  - Traveling Wave Solution
  - SIR Incubation Model

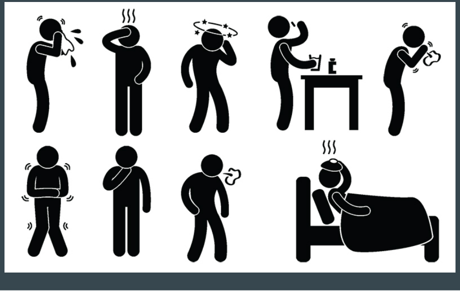
What does SIR stand for?

Susceptibles

Those in the population who are at risk of contracting the disease

Infectious

Those who have the disease and are actively contagious



Removed/Recovered

People who have already had the disease (or have been vaccinated) and cannot get it again

Could be due to antibodies or death

sometimes removed can go back to susceptible

Assumptions of an SIR Model

- The population of interest remains constant
- The rate of infection is proportional to the number of contacts
- There is a constant rate of death or recovery
    - Infectives recover/die at a constant rate

Key variables in SIR Model

R_0 - basic reproductive ratio

Looking at the number of secondary infections from a primary infection

Anything above 1 is considered an epidemic

R_0 for some diseases
Flu: 1.9-2
COVID-19: 3-4
Measles: 12-18

q

Contact ratio

Proportion of population that comes into contact with an infectious individual, while the individual is infectious

Reducing q in the equations involved in SIR model is key to controlling the spread of a disease

Project objective:

Create an SIR model in R to simulate different viral outbreaks

Some parameters to consider in our model

So what affects the transmission of a disease throughout a population?

- Are people wearing masks?
  - Those infected vs not infected wearing masks
- How far can the virus travel?
- What is the number of days someone is infected for?
- What is the general infection probability?
  - How inherently infectious is a virus?
- How many people are starting with the disease?

We had to code up our model...

Obstacle 1

When we randomly move our 100 “people” we needed them to stay within the bounds of the graph (0, 1)

Obstacle 2

After moving the people, we had to create a new way to store that information without overriding the original information

Obstacle 3

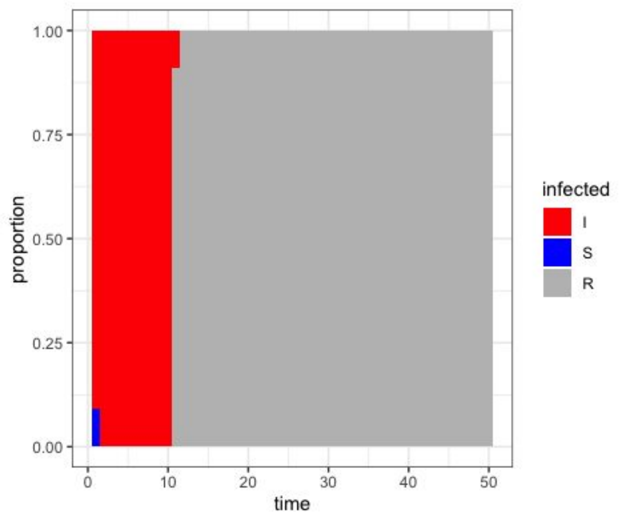
Including probability of transmission/infection based on mask usage

If sick but wearing a mask, probability of transmission reduced by 70%

If not sick and wearing a mask probability of infection is reduced by 80%

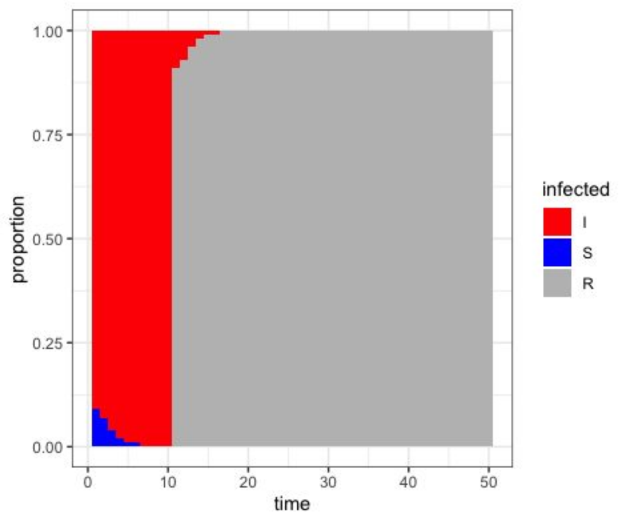
Trying to make the worst possible scenario

First let's compare mask usage



Mask usage - 5%, Starting # infected - 15, Number of days infected - 10, Infect probability - 0.95, Virus can travel a distance of 0.1 units

Red = infected
Blue = susceptible
Gray = removed



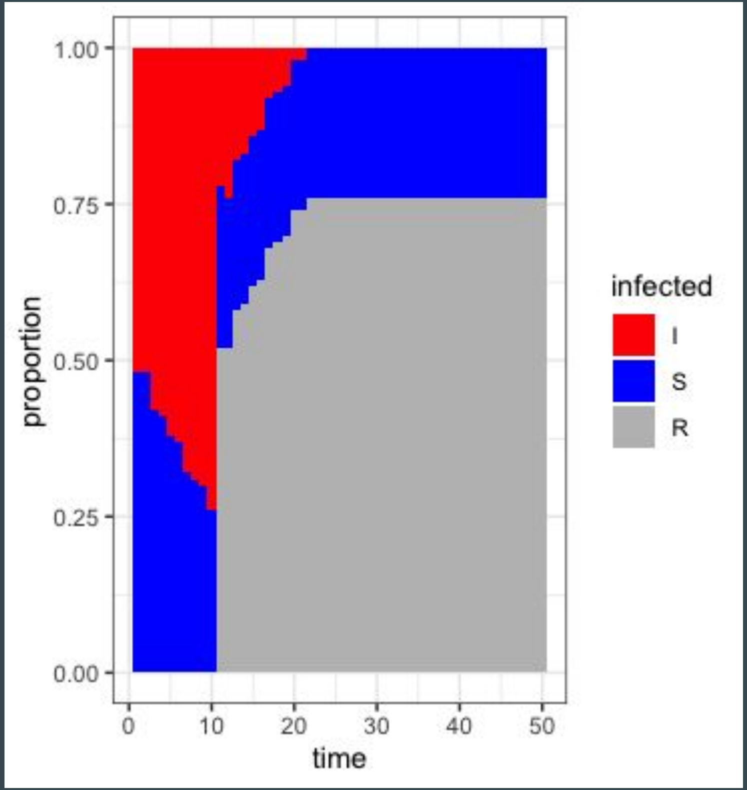
Mask usage - 50%, Starting # infected - 15, Number of days infected - 10, Infect probability - 0.95, Virus can travel a distance of 0.1 units

Masks seem to help slow the spread... slightly

Takeaway: Very infectious virus is difficult to contain, even with strong mitigation practices in place

Trying to make the best possible scenario

Trying to create better scenarios



Mask usage - 95%

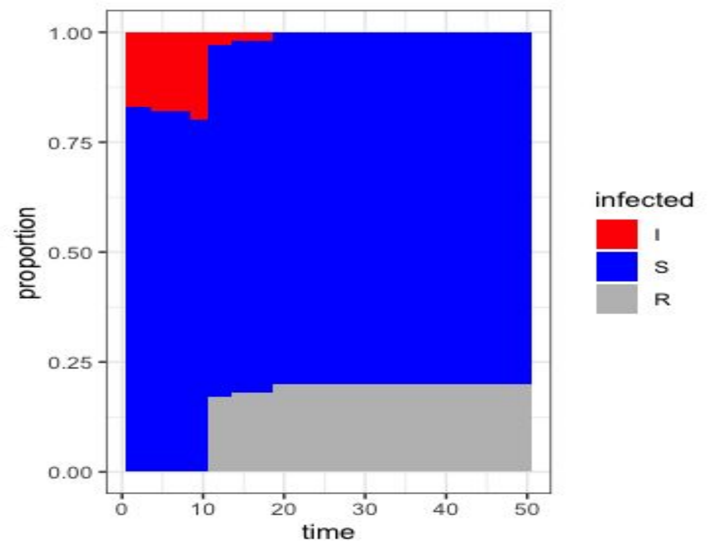
Starting # infected - 15

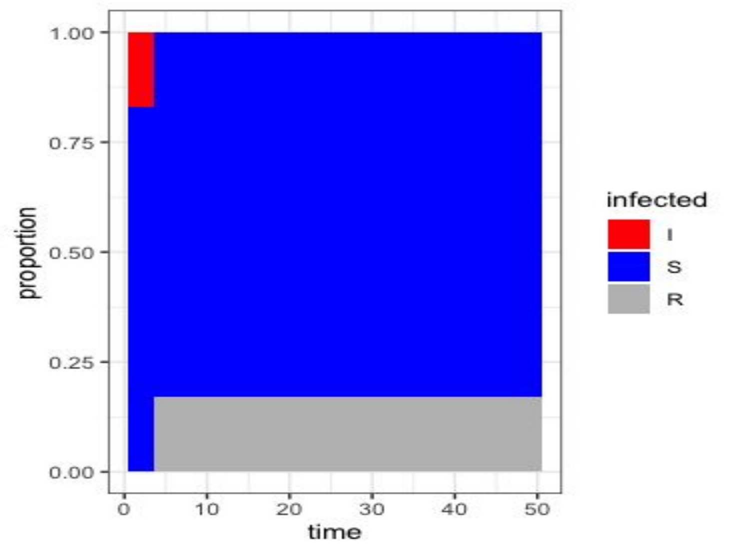
Number of days infected - 10

Infect probability - 0.50

Virus can travel a distance of 0.1 units

Changing a few parameters....





Mask usage - 95%

Starting # infected - 15

Number of days infected - 10

Infect probability - 0.10

Mask usage - 95%

Starting # infected - 15

Number of days infected - 3

Infect probability - 0.10

Takeaway: Decreasing number of days infected helps to control the number of people infected

What we learned

For a worse case scenario:

- Increasing the distance a virus can travel
- Low mask usage
- High infection probability

Leads to the most infections in the population

For a best case scenario:

- High mask usage
- Low infection probability
- Small number of days infected
    - i.e. quarantining = less people infected

Leads to a more controlled outbreak, less total infections in the population

Questions?

Shoutout to Taylor for all the help and guidance along the way :)