MODULE 2: Epidemiology Principles

Student Authors: Jakub Glowala; Kiryung Kim; Katherine McDaniel, MSc; Katherine Nabel; Deborah Plana; Emily Rencsok.
External Reviewers: Rebecca Kahn, MS; James Hay, PhD.
Faculty Reviewers: Wolfram Goessling, MD, PhD; Andrea Wershof Schwartz, MD, MPH; William Hanage, PhD.

In this module, we move from the biology and pathophysiology of SARS-CoV-2 to its implications at a population level. We start with an introduction to epidemiological **terms**. To understand where the epidemic is **now**, we link a curated set of continuously updating resources. Current estimates for the U.S. indicate a caseload of 10-50x what is currently recognized, **with asymptomatic and mildly symptomatic people as a major contributor to transmission.** Next, we give an overview of the factors used to **predict** where the epidemic is going in the U.S., focusing on the concept of exponential growth. Mathematically and empirically, small modifications to the parameters of this growth can "flatten the curve", which lengthens the time over which severely ill people present, providing the healthcare system more time to prepare to treat patients and scientists time to test and optimize new treatment strategies to reduce mortality. At this phase, the U.S. is primarily attempting to flatten the curve by "social distancing". Modeling from the UK indicates social distancing may be required for months.

We end with two **case studies** to contextualize these epidemiology principles. The influenza pandemic of 1918 prompted different responses from three U.S. cities, with three dramatically different outcomes for morbidity and mortality. South Korea presents a contemporary example of a country that rapidly scaled up testing, contact tracing, and social distancing without nationwide lockdown, and has brought new cases to a minimum.

OVERARCHING LEARNING GOAL:

Introduce epidemiological principles used to describe the spread of COVID-19, and evaluate the potential impact of public health interventions via modeling and historical and contemporary examples.

LEARNING OBJECTIVES:

By the end of this module, medical students should be able to:

- Define **R0**, **Re**, **incubation period**, **serial interval**, **epidemic curve**, **community transmission**, **social distancing**, and **flattening the curve** as they pertain to COVID-19
- Identify and access a reliable source of the latest epidemiologic information about COVID-19
- Describe how changing epidemiological parameters changes disease dynamics
- Contrast two cases that illustrate how flattening the curve saves lives in a pandemic

CORE MATERIALS:

- Pueyo, T. Coronavirus: Why You Must Act Now. Medium, 3.10.20
- Sanderson, G. Exponential Growth and Epidemics. Youtube, 3.8.20

- Stevens, H. Why outbreaks like coronavirus spread exponentially, and how to "flatten the curve". Washington Post, 3.14.20.
- Bitton, A. Social Distancing: This Is Not a Snow Day. Ariadne Labs, 3.20.20
- Barry, J. The Single Most Important Lesson From the 1918 Influenza. New York Times, 3.17.20.

INTRODUCTION TO EPIDEMIOLOGICAL TERMS

Attack Rate/Ratio: Refers to the (number of new cases of disease)/(population at risk) during a specified time interval. Generally, the time interval here is defined as "the duration of the outbreak". (CDC)

R0 (basic reproduction number or "R naught"): Refers to the estimated contagiousness of an infectious agent and is affected by its biological features as well as human behaviors. Generally, it refers to the average number of people an infectious person is expected to infect in an entirely susceptible population (i.e., no immunity or vaccination). For this reason, R0 is by definition unaffected by vaccination but it can change over time and place and is not a constant of the disease (i.e., an outbreak of a disease can have a different R0 the second time there is an outbreak in the same place if population density is higher.). R0 can also be defined as R0= probability of transmission per contact * contact rate * duration of infectiousness. (CDC)

Re (effective reproduction number): The same as R0 without the assumption that everyone is susceptible. Re = R0*X, where X is the proportion of the population susceptible. Therefore, vaccination would decrease X and correspondingly the Re value. Additionally, as more people are infected with a virus, more individuals become immune to reinfection from the virus, and X decreases . When Re <1, the total number of infected persons declines, and the outbreak dies out. Re=1 would keep numbers stable, and Re>1 would lead to continued growth in the numbers of infected persons. Re gives an idea of transmission over time and is useful for monitoring *during* an outbreak, as compared to R0, which is most useful in forecasting potential severity and spread at the *start* of an outbreak. (CDC)

Epidemic curve: A graph of cases vs. time. Most graphs being used in articles are examples of this type of curve. Epidemic curves may be presented as the cumulative number of cases or number of new cases over time, the latter being more commonly used. It can be used to make predictions about how well interventions are working and compare across different communities. Like any graph or curve, it is only as reliable as the data it is based on. (CDC)

Incubation period: The period of time between exposure to a pathogen and onset of first symptoms. (CDC)

Latent period: The period of time between exposure to a pathogen and onset of infectiousness. Note that the latent period can be shorter than the incubation period, leaving a window of pre-symptomatic infectiousness. In addition, virus transmission can happen even with a person that ultimately does not develop symptoms, known as asymptomatic infectiousness.

Serial interval: The period of time between symptom onsets in an infector-infectee pair. This period is often used as a proxy for **generation interval**, which is the period of time between infection of an infector-infectee pair. The serial interval helps determine the speed with which an outbreak spreads, and along with Re is a key parameter for how "steep" or "flat" an epidemic curve will appear.

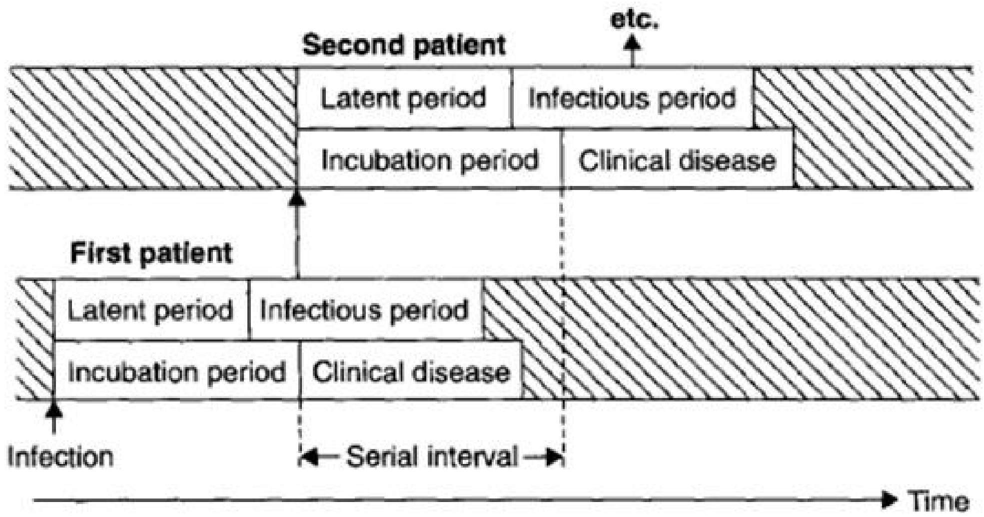


Figure 2.2 The relationships of some important time periods. The patient at the bottom is infected first, and transmits the infection to a second patient.

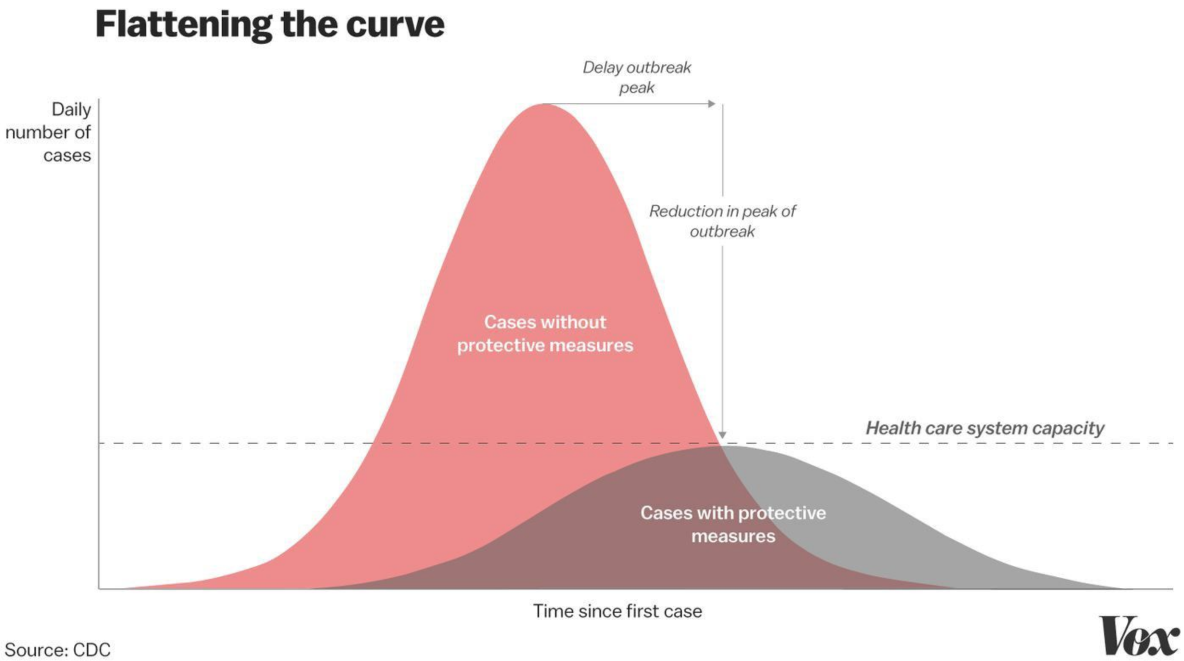
Adapted from Giesecke, J. Modern Infectious Disease Epidemiology. 2002.

Community transmission: Refers to transmission occurring between people within the same community. This phenomenon is separate from people acquiring the infection while traveling or due to close contact with someone who visited an area with the infection as it implies that there are unknown cases spreading the infection locally. (CDC)

Social distancing: A public health practice that aims to prevent sick people from coming in close physical contact with healthy people in order to reduce opportunities for disease transmission. It can include large-scale measures like canceling group events or closing public spaces, as well as individual decisions, such as avoiding crowds. The goal of these interventions is to avoid infecting high-risk populations and "flatten the curve".

Flattening the curve: The concept is based on the reality that the healthcare system can only handle a limited number of sick patients at one time. Measures to "flatten the curve" attempt to slow the spread so that there are fewer cases at any one time (however, cases are spread out over a longer period of time) and the healthcare system is capable of providing appropriate care without being overwhelmed. Failing to do so increases the spread of the infection and the case fatality rate as the healthcare system is unable to provide appropriate care to every patient. Should improvements in treatment occur, a larger proportion of the infected population will have access to appropriate treatment. Should a vaccine be developed, more people will gain immunity that way rather than by getting sick.

*Note: flattening the curve does not necessarily mean that fewer people will become infected and require medical care in total - the area under the curve is not necessarily reduced (even though many graphs on the Internet might suggest otherwise)



WHERE ARE WE NOW?

The following is a set of basic figures about the epidemic as a snapshot, which will be updated in this document as we receive new information.

Continuously Updated Resources

- Simple map of the US
- More complete global map and associated publication from Johns Hopkins, featuring data from a variety of sources.
- Additional maps and resources.

Reported cases **underestimate** the total number of cases due to the incubation period, asymptomatic carriers, limited testing availability, and delays in receiving testing results after the initial onset of symptoms. The following resource is an excellent explanation of this phenomenon working from data publicly available in early March.

CORE TEXT: Pueyo - Coronavirus: Why You Must Act Now. 3/10/20. Medium.

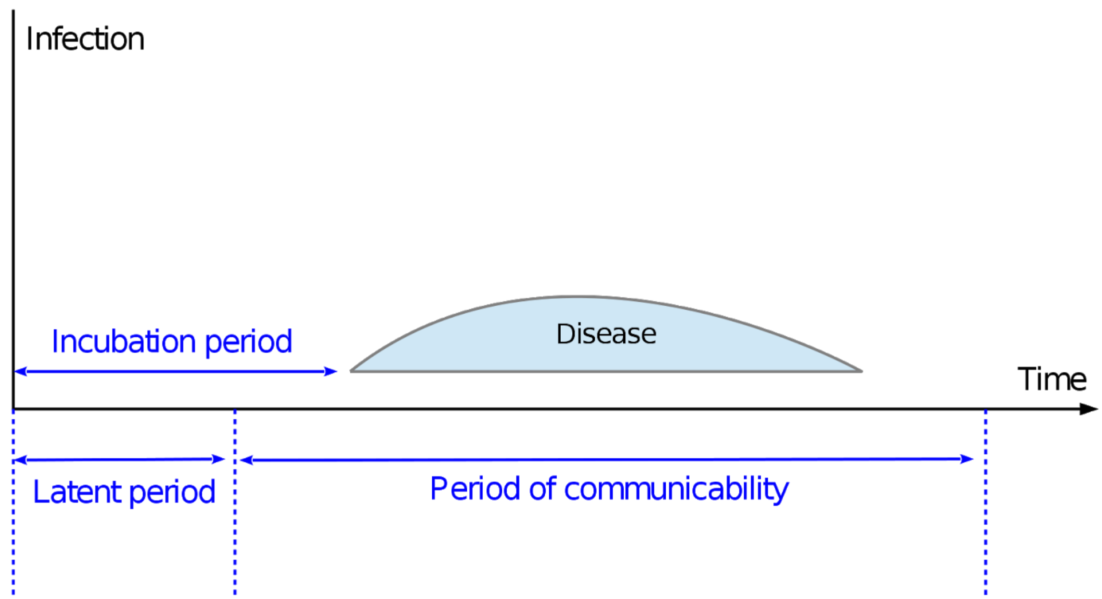
It is estimated that for every 1 case that is reported, there are at least 10-50 other cases that we don't know about. So when you hear "confirmed cases", mentally multiply that number by 10 to have an idea of the disease incidence (NYTimes U.S. Coronavirus Map, Lipsitch M. Presentation 3.16.20).

Supplementary video on how to accurately estimate actual COVID-19 cases based on reported data

Overall, it seems like patients infected with SARS-CoV-2 have a 1-2% chance of dying (as of 3/16/2020). This case fatality rate rate increases substantially with age (see Module 1 for more information). It is important to note that since it takes 1-2 weeks for newly infected patients to develop symptoms, there is a corresponding 1-2 week delay to see the effect of new interventions on disease infection and mortality rates. (Fauci et. al. 2.28.2020; Lipsitch M. Presentation 3.16.20).

Asymptomatic Transmission

Recall that the **latent period**, or time from exposure to transmissibility, can differ from the **incubation period,** or time from exposure to first symptoms (see Fig. II.1). Several sources of evidence suggest SARS-CoV-2 has a shorter latent period than incubation period, **opening the door for presymptomatic transmission**. Current estimates of the SARS-CoV-2 incubation period, from initial exposure to symptom onset, range from 1-14 days with a **median of 5-7.5 days (** Bi et al. 03.03.2020; Tapiwa et al. 03.05.2020) and 95th percentile of 12 days (Lauer et al., Ann Intern Med 2020; Li et al., NEJM 2020). Meanwhile, analyses of infector-infectee pairs show a mean serial interval of 4.0 days [95% CI 3.1, 4.9] (Nishiura et al, Int J Infect Dis., 3.4.20) or 3.96 days [95% CI 3.53-4.39], widely distributed with SD of 4.75 days. Put together, these estimates imply a period of presymptomatic transmissibility. Patients may be able to transmit the virus for a prolonged period of time, , as SARS-CoV-2 RNA has been detected in patients for an average of20 days, lasting as long as 37 days (Zhou et al., Lancet 2020). However, detection of RNA does not necessarily indicate the presence of live virus, and it is still unclear for how many days patients remain infectious.



A difference between latent period and incubation period can lead to a period of asymptomatic communicability. The period of communicability may also extend beyond the duration of symptoms. Figure from Wikimedia, contributor Patilsaurabhr.

It is becoming increasingly clear that **most new confirmed COVID-19 cases (an estimated 79%, from models based on data from Wuhan) are likely spread by people that show mild or no symptoms of the disease** (Ruiyan et al. Science 3.16.20). Social isolation, especially of young, healthy, asymptomatic people, will be critical to controlling disease spread.

Thought Question:
How would you talk with **Brian** about the importance of speedy social distancing, including with peers? (For a more extensive dive into this task, stay tuned for Module 4.)

WHERE WILL WE BE NEXT? - APPROACHES TO PREDICTION

Many models for the expected impact and spread of the virus are being shared on social media and reported in popular news. Below, we hope to point you to a couple of such models, and provide a basic introduction to the assumptions that they use and their key conclusions about what we can do to slow the spread of the virus.

Common Assumptions about Virus Spread

- Almost everyone in a population is **susceptible** to be ill because our immune systems have not recognized an organism like this before.
- Current estimates for **R0** vary, considered to be somewhere between 2-4. This means each infected person will transmit the virus to 2-4 other people during the course of their illness. Most models assume a value of around 2.3 (Tuite et al. 2.5.20), which is higher than the estimated R0 for the seasonal flu (~1-2) (Callaway et al. 3.18.20).
- We can quantify how quickly a virus spreads by the virus **doubling time** (the time it takes for the number of cases to double). Currently, the doubling time for the virus is estimated to be 5-7 days (Lin, M. Lin Lab Presentation 3.13.20)
- We are assuming patients cannot be **re-infected** with the virus in the short-term (months-years). As discussed in Module 1, this is an open question, and will only be answered with data gathered over the coming weeks or months. It is important to note that some apparent reinfections reported in case studies may reflect deficiencies in test sensitivity.

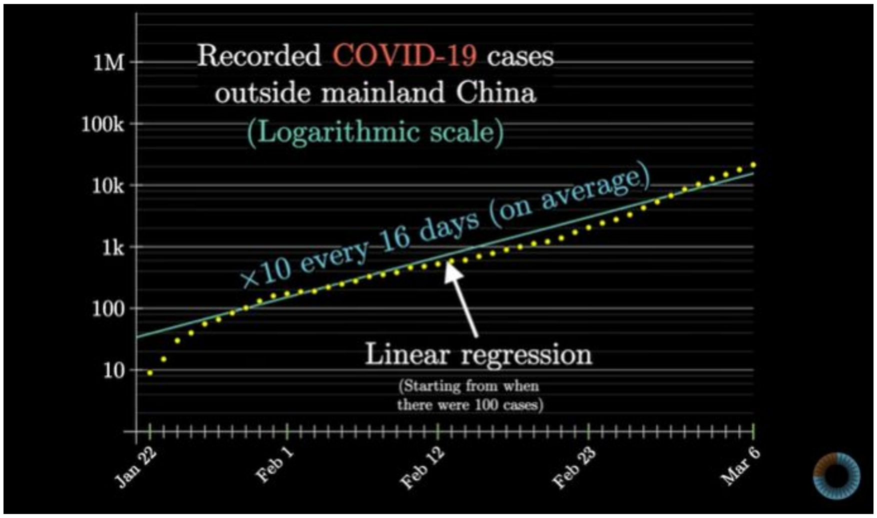
Models of Virus Spread

Creating a complete, accurate model for the spread of SARS-CoV-2 will require the expertise of multiple highly trained scientists and complex computational tools. We will not present such a model here. Instead, we hope to introduce an intuitive, simple model that helps explain the spread of the virus based on current data. Such a model is being used to make estimates about how many people will get sick from SARS-CoV-2.

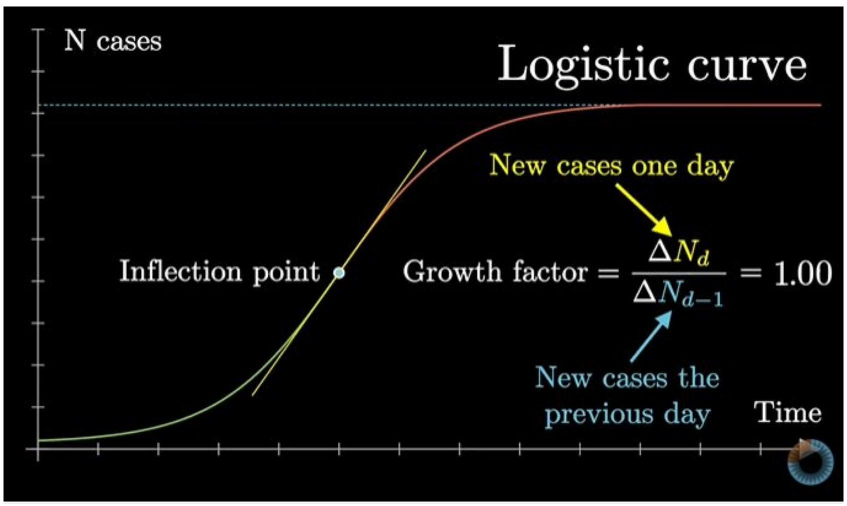
This video describes what we can expect from the simplest model of virus spread, using real data. **If there is only one thing that you click on in this section, it should be this video**. It's only 9 minutes long (4.5 if you watch at 2X speed). We will emphasize some key take-aways from the video below:

CORE VIDEO: Exponential Growth and Epidemics

The epidemic spread is modeled by an exponential curve at the beginning, because most people have not been infected by the virus yet and are therefore susceptible to become infected. This is what the spread of the virus looks like right now based on existing data; the scale on the y-axis is a log scale, so cases grow a lot quicker as time goes on in the x axis. (Note: a limitation of an exponential growth model is that it assumes homogeneous mixing of individuals in the population, which is not true, especially in the latter stages of an epidemic).



As more people are infected, the spread of an epidemic slows down because there are fewer people who can still get sick from the virus. The spread of virus will eventually slow down and look logistic:



Without a vaccine, the majority of people in the entire world will eventually become infected by SARS-CoV-2. This is why the curve flattens out: because there will be no one left to infect. Our goal is for the spread of the virus to slow down, so that our healthcare system can provide the best possible clinical care for the critical cases of SARS-CoV-2 coming in every day, along with the routine clinical cases that you would expect irrespective of the pandemic (heart attacks, cancer treatments, hip replacements, car accidents).

In the worst case scenario, if we do nothing to change the disease doubling rate, the CDC estimates up to 214 million cumulative infections (⅔ of the American population), and 1.7 million deaths (assuming 1-2% chance of dying if infected) in the United States in the coming months (NYTimes 3.13.20).

How Social Distancing Could Impact Spread

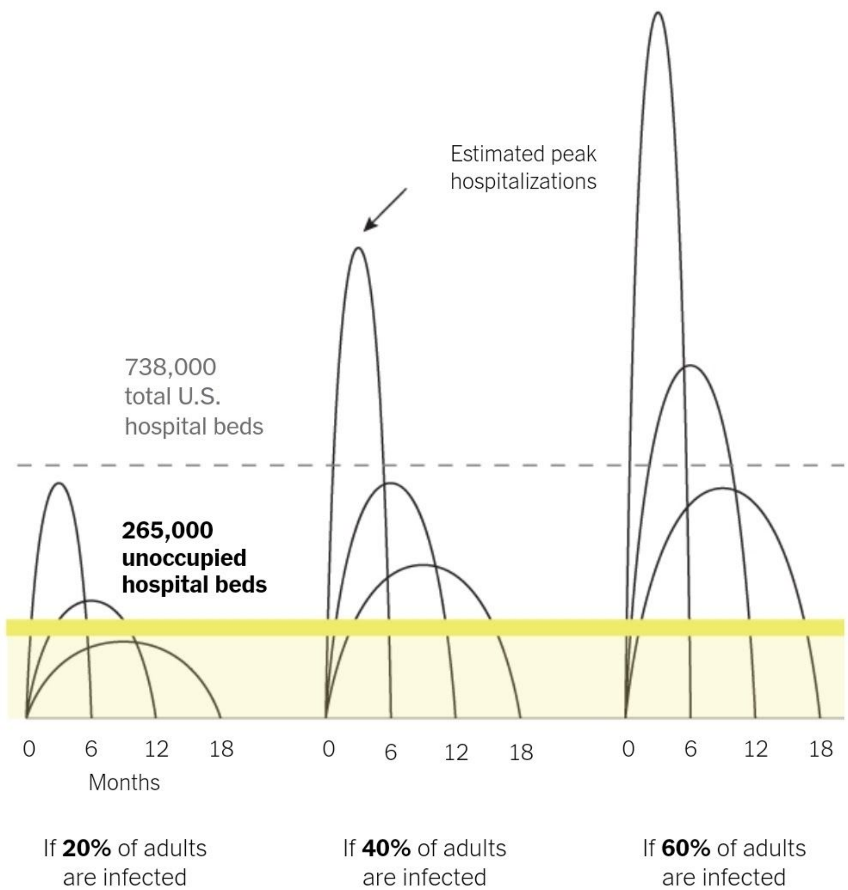
Our main strategy to stop these outcomes is **mitigation**: we cannot stop transmission completely, but we can reduce the pandemic's impact on the healthcare system.

> **CORE TEXT (simple model to illustrate concept): Stevens, H. Why outbreaks like coronavirus spread exponentially, and how to "flatten the curve". Washington Post, March 14th, 2020.**
>
> Supplementary material: a tunable model that allows the user to change model parameters to visualize how they could affect virus spread.

There is a lot to be hopeful for. If we implement these mitigating interventions, which use social distancing to slow down the spread of the virus, and reduce the Re by half (from 2-3 new cases per infected person to ~1.2 per case), then the doubling time will be **4 times longer.**

The key take-away is that social distancing measures will have a profound effect in delaying the "peak" in the number of critical COVID-19 cases in the US. **We buy the healthcare system valuable time to get ready for this crisis by increasing the protective equipment, beds, ventilators, and healthcare workers available to care for those critically ill from the virus and from causes other than the virus, decreasing overall mortality. This is why social distancing is critical.**

Simulations show that slowing disease spread by a couple of months will dramatically affect the number of critically ill COVID-19 patients who can get hospital beds:



Source: Harvard Global Health Institute estimates of hospital bed capacity and Covid-19 infections

In the figure above, each line describes the number of simulated COVID-19 cases under different assumptions about the total number of infected cases needed to establish herd immunity (20, 40, or 60%) and about the success of social distancing. Successful social distancing is simulated, "flattening the curve", such that the spread of the virus lasts 6, 12, or 18 months respectively. Full simulation linked here.

Actually implementing social distancing requires fundamentally changing our habits and daily routines. Though many households across the country have adopted social distancing measures, many are not yet there**. The brief article below makes these recommendations concrete and clear, including reducing all public gatherings of *any* size, ceasing visits to others' homes, and limiting trips. We recommend reading it if you haven't already, and sharing it with friends and family.**

CORE TEXT: Bitton, A. Social Distancing: This Is Not a Snow Day, Ariadne Labs, 3.13.20

Social Distancing is a Long-Term Intervention

Many governors and mayors around the country have implemented policies in recent weeks promoting social distancing for their states/cities (closing bars and restaurants, moving schooling online, banning public gatherings, etc). As of March 16th, the CDC and the White House recommended canceling events expected to host at least 10 people. Some cities, such as San Francisco, have already implemented or are strongly considering shelter-in-place precautions for their citizens, meaning that individuals must stay home except to conduct essential activities related to health, work, food and exercise. These initiatives help to flatten the curve, decreasing the peak number of COVID cases and increasing the length of the pandemic. Yet they come at a substantial economic and social cost, including increased rates of unemployment, which will likely in themselves impact population health in the long-term.

When considering social distancing and lockdowns as measures of disease control, it is important to acknowledge that these are long-term solutions that will require many months of continual participation to be effective. An Imperial College report (analysis specific to the U.S. is found on page 19) suggests that social distancing needs to be maintained "until a vaccine becomes available (potentially 18 months or more)" in order to actually decrease deaths from COVID in the long run. Furthermore, mortality rates will certainly be worsened if the healthcare system is overwhelmed and unable to provide appropriate care to all who need it. Lifting lockdowns and social distancing restrictions immediately once the curve is flattened will essentially release the virus back into a population without immunity; creative methods, such as stratified lockdowns, to increase herd immunity are necessary to ensure prevention of a second viral outbreak (Hernán, 3.15.20).

It is important to note that models, such as those in the Imperial College report, do not take into account the implementation of new therapeutic and vaccine options (such as remdesivir and other antivirals, viral proteins and mRNA vaccine approaches described in Module 1) that might become widely available to treat COVID-19 in the coming months. Nor do they account for expansion of health care facilities, for instance allowing time to make more ventilators to manage the surge. Mortality will also increase in an overwhelmed health care system.

As we have discussed, social distancing buys the healthcare system time to adapt to the outbreak. Importantly, social distancing also buys physicians and scientists time to test and optimize the efficacy of new therapies to treat COVID-19 patients, thereby reducing the percent of those patients requiring critical care and the disease mortality.

Thought Questions:

1. Current models estimate that social distancing measures might need to be implemented for months, not weeks, to slow the spread of the virus and its impact on our healthcare system. How will our society need to adapt to these long-term changes?
2. How do we make sure vulnerable populations (including families dependent on jobs unable to be adapted to remote work) are adequately supported during this time?

CASE STUDY: 1918 INFLUENZA PANDEMIC AND LESSONS FROM 3 US CITIES

(Image from Arnett, 03.14.2020)

Prior to COVID-19, the 1918 influenza pandemic was the most severe pandemic in recent history. First identified in military personnel in the spring of 1918, the influenza was an H1N1 virus of avian origin. It is commonly referred to by scientists and historians as "the Mother of all Pandemics." This pandemic is often referred to as the "Spanish Flu" in the lay press, though this name is a misnomer and the virus likely originated elsewhere. Contemporary reporting focused heavily on Spain as it was one of few places at the time that did not have restrictions on the press during World War I.

Fast Facts about the 1918 Flu:

- Infectivity: 500 million people or ⅓ of the world's population. Note that this is smaller than estimates for SARS-CoV-2, as the population had some pre-existing immunity from prior influenza exposure.
- Death rates: at least 50 million people worldwide with 675,000 deaths in the United States
- Mortality: highest in people age <5, 20-40, and 65+ years. It is thought that this unusual age-distribution of cases may be due to differences in prior influenza exposure across different age groups.
- More soldiers died from the 1918 flu pandemic than were killed in battle during World War I in 1918
- In 1918, there were no flu vaccines, antiviral drugs, antibiotics, or mechanical ventilators. Treatment options were limited to supportive care and unproven remedies.
- There were 3 waves of the epidemic, which lasted from January 1918 - December 1920 (CDC)
    - First wave: March 1918 - Summer 1918
    - Second wave: Fall 1918 (peak of epidemic)
    - Third wave: Winter 1918 - Spring 1919

- According to a 2007 study in the *Internal Journal of Epidemiology* (Vynnycky et al.), the **R** for the 1918 influenza virus was in the range of 1.2-3.0 for community-based settings.
    - The study estimates that in a totally susceptible population, a single infectious case could have led to 2.4-4.3 cases in a community-based setting.
- Link out: CDC's 1918 Pandemic Influenza Historic Timeline

How 3 US Cities Tried to Stop the Spread of the 1918 Flu

Philadelphia held a parade

By mid-September 1918, the second wave of the flu epidemic was in full effect, spreading from Boston to New York and Philadelphia before traveling west to St. Louis and San Francisco. Without a vaccine or known cause for the outbreak, mayors and city health officials were grappling with how to implement **social distancing** and reduce **community transmission**. They asked themselves the following questions:

- Should they close schools and ban all public gatherings?
- Should they require all citizens to wear a gauze face mask?
- Would shutting down financial centers during a time of war be unpatriotic?

Wilmer Krusen, Philadelphia's public health director, advised citizens they could lower their risk for flu by: staying warm, keeping their feet dry, and "loosening their bowels." Krusen refused to cancel the Liberty Loan parade on September 28, 1918, even as cases steadily increased up to this point. Infectious disease experts warned Krusen that the parade (likely to attract several hundred thousand people) would be a "ready-made inflammable mass for a conflagration." Krusen kept the parade on because it would raise millions of dollars in war bonds. The parade took place: soldiers, Boy Scouts, marching bands, and local dignitaries processed two miles through downtown Philadelphia past sidewalks teeming with spectators. **Just 72 hours after the parade, all 31 of Philadelphia's hospitals were full. By the end of the week, 2,600 people were dead.**

St. Louis flattened the epidemic curve

Before the first case of 1918 flu appeared in the city, health commissioner Dr. Max Starkloff wrote an editorial about the importance of avoiding crowds in the *St. Louis Post-Dispatch*, putting local physicians on high alert. When a flu outbreak from nearby military barracks spread to St. Louis, Starkloff closed schools, closed movie theaters and pool halls, and banned public gatherings. When infections surged, thousands of sick residents were treated at home by a network of volunteer nurses. George Dehner, author of *Global Flu and You: A History of Influenza*, writes that because of these precautions, St. Louis public officials **flattened the curve** and prevented the flu epidemic from exploding overnight like in Philadelphia. According to a 2007 NIH analysis in *PNAS* of 1918 flu death records (Hatchett *et al.*), the **peak mortality rate in St. Louis was only ⅛ of Philadelphia's death rate** at its worst.

San Francisco required face masks

California governor William Stephens declared it the "patriotic duty of every American citizen" to wear a gauze face mask and eventually made it the law. Citizens found in public without a face mask or wearing it improperly were arrested, charged with disturbing the peace, and fined $5. San Francisco's low infection rates were likely not due to the face masks, but instead due to:

- Well-organized campaigns to quarantine all naval institutions before the flu arrived
- Early efforts to close schools
- Bans on social gatherings
- Closing all places of "public amusement"

San Francisco did well in the second wave of the epidemic through the fall of 1918. When the third wave struck in January 1919, businesses and theater owners fought back against closings, as they believed masks were what saved them the first time. The 2007 NIH analysis found that **if San Francisco had kept up the same flu protections in the third wave as it did in the second wave, it could have reduced deaths by 90%.**

CORE TEXT: Barry, J. The Single Most Important Lesson From the 1918 Influenza. New York Times, (March 17, 2020)

Supplementary reading:

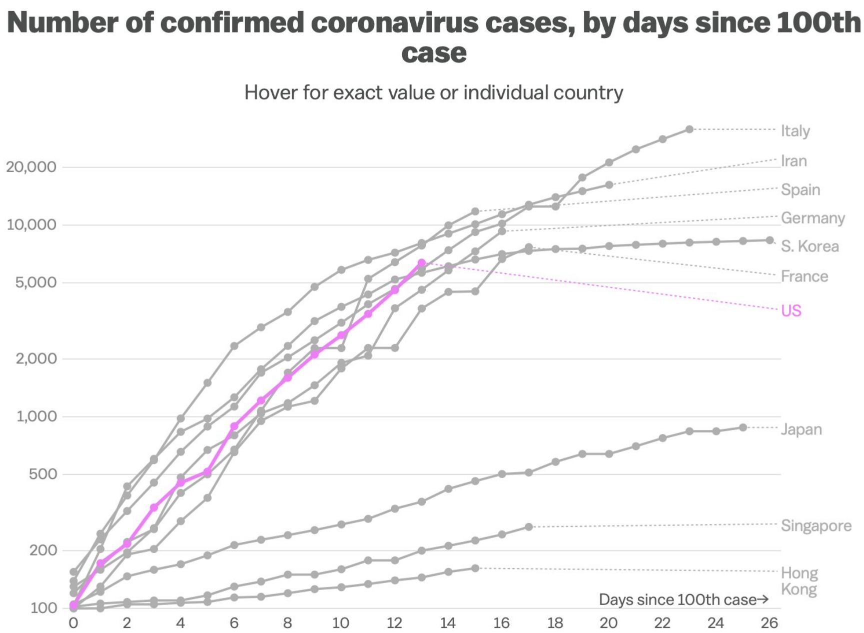
- "How U.S. Cities Tried to Halt the Spread of the 1918 Spanish Flu," Dave Roos. History.com (March 11, 2020)
- "The effect of public health measures on the 1918 influenza pandemic in U.S. cities," M. C. J. Bootsma and N. M. Ferguson. PNAS (May 1, 2007).
- *The Great Influenza: The Story of the Deadliest Pandemic in History*, John Barry (2004).
- *Global Flu and You: A History of Influenza,* George Dehner (2012).

Thought Questions:

1. If you were a public health official in the early 1900s trying to determine what the cause of the outbreak was, what methods would you use to find the answer? (Assume you can only use resources available from the early 1900s)
2. How could public health officials in San Francisco have probed deeper into whether it was gauze face masks that reduced transmission or closing of public spaces?
3. What are the challenges for trying to determine R0 and Re values for the 1918 flu epidemic? What assumptions can be made in modeling? What challenges do these assumptions bring?

CASE STUDY: SOUTH KOREA, 2020

As COVID-19 cases in the US continue to rise, we can look to other countries that are farther ahead in their epidemics as sources of instruction. Of particular interest is the case of South Korea. SK is a democratic country, with largely privatized healthcare and strong corporate research presence, much like the US. Cases in SK initially grew exponentially but have flattened in recent days with extensive efforts to scale up testing, perform contact tracing, and promote social distancing, without nationwide lockdown. Here we present an overview of SK's interventions.



Total confirmed cases of SARS-CoV-2 starting from 100th case (data through 3/18)
Italy and SK had initially shown similar trajectory in the rise of cases, however, SK in recent days has plateaued**.** The US is about 1-2 weeks behind SK and Italy.

Testing Strategies in South Korea
Both US and SK detected their first case of COVID-19 on Jan 20. In response, the SK government urged SK medical companies to immediately develop a testing kit. By Feb 4th, SK approved the first testing kit, when only 16 cases had been confirmed in SK. Rapid approval was possible because of the emergency use authorization policy enacted after the MERS outbreak in 2015. This cooperation between the private biotechnology sector and government led to efficient roll out of its extensive testing capacity. Currently, four biotech companies are producing testing kits around the clock to meet the demand, distributed to over 600 testing centers. All labs upload their results to the shared database and are reported to KCDC, which then releases daily reports detailing the epidemiologic data to the public. SK's maximal testing capacity is ~22,000 tests per day, currently administering close to 20,000 tests per day. **Why is extensive testing so important? It means that infected individuals, and contacts of those individuals can be isolated and/or treated with minimal delay. This drastically reduces opportunity for transmission, thereby decreasing Re.**

In addition to scaling up testing capacity, SK has come up with creative testing strategies to *reduce risk of contamination, reduce risk of cross transmission, increase efficiency and prioritize safety of healthcare workers.*

- **Automatic testing:** Done by a diagnostic machine, rather than by a lab technician. This decreases risk of contamination, risk of transmission to healthcare workers, and allows for faster turnaround of results.
- **Drive-through testing:** Patient stays in their vehicle with recirculating air turned on, to minimize risk of transmission to healthcare workers. (Think of it as a makeshift negative pressure vehicle.) This method is much faster than point of care testing, because time is not wasted in disinfecting the facility and

reduces risk of cross transmission. The results are texted to patients the next day. Currently, SK has 43 drive-through testing centers, part of more than 600 testing sites.

- **Telephone booth testing**: For those without access to vehicles. Nasopharynx and oropharynx swabs are collected while the patient is in a negative-pressure telephone booth sized room, which takes only 2 minutes to disinfect. Same advantages as drive-through testing. Link to a video.

Image Source: AFP

Reducing Barriers for Quarantine and Treatment

With a large capacity to test individuals, SK can offer testing to individuals who have been in contact with a confirmed case, even if asymptomatic. When an individual tests positive, thorough contact and location tracing is done, and locations where possible transmission might have occured are sent as text alerts, alerting the public. This has allowed for detection of mildly symptomatic to asymptomatic cases, which have contributed to a low case fatality rate of 0.7% in SK in comparison to 3.4% global average. Determining asymptomatic carriers and isolating those individuals may be of great importance as increasing evidence [1,2,3] suggests that asymptomatic carriers may be a significant vector for transmission.

In addition, the government bears the cost of testing and medical care received for COVID-19. It is free regardless of immigration status, for anyone with doctor's referral or with contact with an infected person. Those required to quarantine are provided food and other essentials via package deliveries, paid for by the government. This decreases barriers for those in low socioeconomic status, helps curb the panic and allows for individuals to adhere to strict quarantine.

Thought questions:

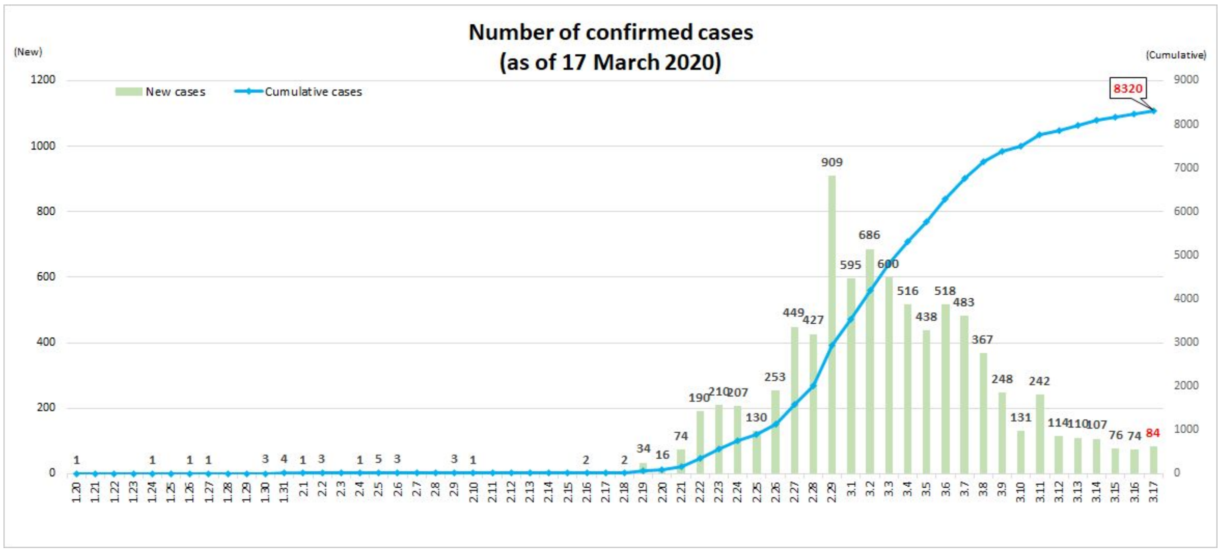
1. What factor(s) may contribute to differences in case fatality rates between countries?

Social Distancing

Using aggressive testing and contact tracing measures, SK had been controlling COVID-19 cases since their first reported case on 1/20/2020 until patient 31 who tested positive on 2/18/2020, deemed "super spreader." As shown in **the figure below** South Korean cases spiked after the 31st patient who had attended mass religious gatherings, coming into contact with more than a thousand people. This cluster now accounts for 60% of the confirmed cases in SK. Large mass gatherings in closed confined space have led to massive increase in cases. This stresses that **public participation in engaging in social distancing is critical for reducing Re, lengthening doubling time, and thereby flattening the curve.**

Unlike China, SK has not implemented domestic travel bans, and did not immediately ban travel from China at the beginning of the outbreak. Instead of a lockdown, South Korea has focused on engaging the public to practice social distancing in addition to cancelling large events, school openings and religious gatherings. While the number of new cases have decreased consistently, there are still clusters of new cases reported. These clusters have been attributed to large gatherings in confined rooms such as churches, call-centers (where large groups of people work in close proximity without wearing masks so they can speak clearly on the phone), internet cafes, hospitals, and gym facilities.

Current Situation in South Korea



As of March 17, 2020 (source: KCDC):
Green bars: number of new cases per day
Blue curve: cumulative cases

As evidenced by the figure above, numbers of new cases per day have been consistently declining and stabilizing. The slope of the cumulative curve has been decreasing, no longer showing exponential growth pattern, suggesting that SK may have been successful in reducing Re. While SK's health minister has said he is hopeful that SK has passed the 'peak' of the outbreak, it remains to be seen whether this depression is temporary. As stated earlier, the majority of the population has not been infected and therefore remains susceptible. This is particularly challenging given differences in intervention across countries responding to this pandemic, such that the risk of reintroduction from different locations persist. How SK adapts its control measures to respond to new infections will be a useful case study for other countries.

Summary

South Korea and other Asian countries experienced the MERS outbreak in 2015, which contributed to increased preparedness for this pandemic. Although more time and monitoring is needed to determine whether SK has been able to suppress the COVID-19 outbreak, current trends suggest that their strategies of public transparency, civic awareness and responsibility, cooperation of the private sector and the government, decreasing barriers, and widespread testing has led to slowing the outbreak.

Thought questions:

1. What strategies to reduce disease spreading and case fatality rates can we implement here in the US?
2. How could we advocate to increase preparedness for the next pandemic as future physicians?

Supplementary Reading:

- **Effective reproduction number**, transmission dynamics in South Korea from 1/20/2020 to 2/26/2020
- CDC daily COVID-19 updates
- Interview of SK Foreign Minister - Coronavirus: South Korea Seeing a ‘stabilizing’ trend

---

We hope this module introduced you to epidemiological principles underlying the current public health interventions regarding COVID-19, and helped you evaluate how these interventions could influence the impact of the pandemic.

To continue in our COVID-19 curriculum, please click here: Module 3: Current Situation and Healthcare Response, in Massachusetts and Beyond. Click here to return to our Overview.

We welcome your feedback on this module and on the curriculum overall. Please share it here.