COVID-19 Vaccine Development and Herd Immunity

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What is a vaccine?

- Vaccines help the body's immune system recognize and respond to severe diseases
  - To do this, a vaccine must trigger an immune response, usually through the use of an invader's (virus, bacteria, pathogen) surface proteins, weakened or killed variants of an invader, or a byproduct of a disease
  - When a vaccinated individual is exposed to the disease, the body can more readily and quickly respond and neutralize the disease
- **Vaccines can prevent and/or reduce the severity of diseases and are one public health's most effective disease prevention methods**

The push for COVID-19 vaccines

- Given the benefits of vaccines, global efforts for a vaccine for COVID-19 have been massive
- Vaccines could not only protect individuals, but if large enough populations received them, a COVID-19 vaccine could protect those who were ineligible to receive a vaccine through **herd immunity** or **community immunity**

The push for COVID-19 vaccines

- **However:**
  - Vaccines need to show **efficacy** and **effectiveness** during testing; in other words, COVID-19 vaccines need to prove themselves effective at preventing COVID-19 infections
    - **Vaccine Efficacy:** How good a vaccine is at preventing a disease in a controlled experiment.
    - **Vaccine Effectiveness:** How good a vaccine is at preventing a disease among the general population
  - Vaccine testing must be **thorough** and **transparent** to ensure the risk of receiving a vaccine does not put individuals at unnecessary risk
  - Vaccines need **high uptake** to be effective; if nobody agrees to receive a vaccine, it is useless

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What does vaccine development normally look like?

- Vaccine development is very similar to the development of pharmaceuticals
- Extensive testing is completed through multiple phases to determine **efficacy** (how well the vaccine protects against disease) and **safety** (whether the benefits of the vaccine outweigh their potential side effects)
- Normally, a vaccine can take **10-15 years to develop**.

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Pre-human stages of vaccine development

- **Exploratory Stage:** during this phase, all testing is done in labs; intention is to find antigens that could prevent/treat disease
- **Pre-clinical stage:** Candidate vaccines from the exploratory stage used on animal subjects to assess response; idea is to get a good picture of how living things will react to the vaccine
- Assuming candidate vaccine makes it through the pre-clinical stage, the company must apply for an Investigational New Drug (IND) application to the FDA; approval allows clinical trials in human subjects

Clinical Trials

- **Phase I:** Very few human subjects are given the candidate vaccine, with an emphasis on determining safety
- **Phase II:** At this stage, more subjects are brought in to test the vaccine's safety and immunogenicity (ability to trigger an immune response – good!); may also look at potential schedules, dosing, and delivery methods
- **Phase III:** Generally, the final stage of a vaccine trial; involve thousands of individuals and assesses safety and efficacy
- If vaccines can make it through Phase III trials, developers get apply for approval and licensure through the FDA; if approved can distribute vaccine to general population
- **Among all drug trials that make it to Phase I, less than 10% are approved.**

What happens once a COVID-19 vaccine is developed?

- Production, distribution, and storage are key.
  - Manufacturers must be ready to develop the vaccines
  - Facilities must have the means to storing the vaccines
- Vaccines would likely not be distributed to the general public until several months after development
  - High risk individuals (i.e. health care, incarcerated, older adults) would be prioritized because vaccinations in these populations would offer the highest benefit
- Even if logistic challenges are handled, individuals can opt out of receiving the vaccine
  - **Herd immunity and community immunity are only possible if a large portion of the population is vaccinated!**

The pandemic does not immediately end just because a vaccine is developed!

Vaccine efficacy is determined in an experimental setting. Therefore, it does not account for logistical challenges, risk of reinfection, etc.

Vaccine efficacy and herd immunity

What do we know from other vaccines?

- The measles vaccine is 98% effective. And in order to achieve herd immunity, approximately a +70% vaccination rate is needed.
- The seasonal flu vaccine efficacy varies between 40-60%.

What about for COVID-19?

- The number of people who would need to be immunized depends on the efficacy of the vaccine in the general population and among particular sectors
  - Will the vaccine be as effective for the very young and old
  - Will conditions like obesity effect efficacity

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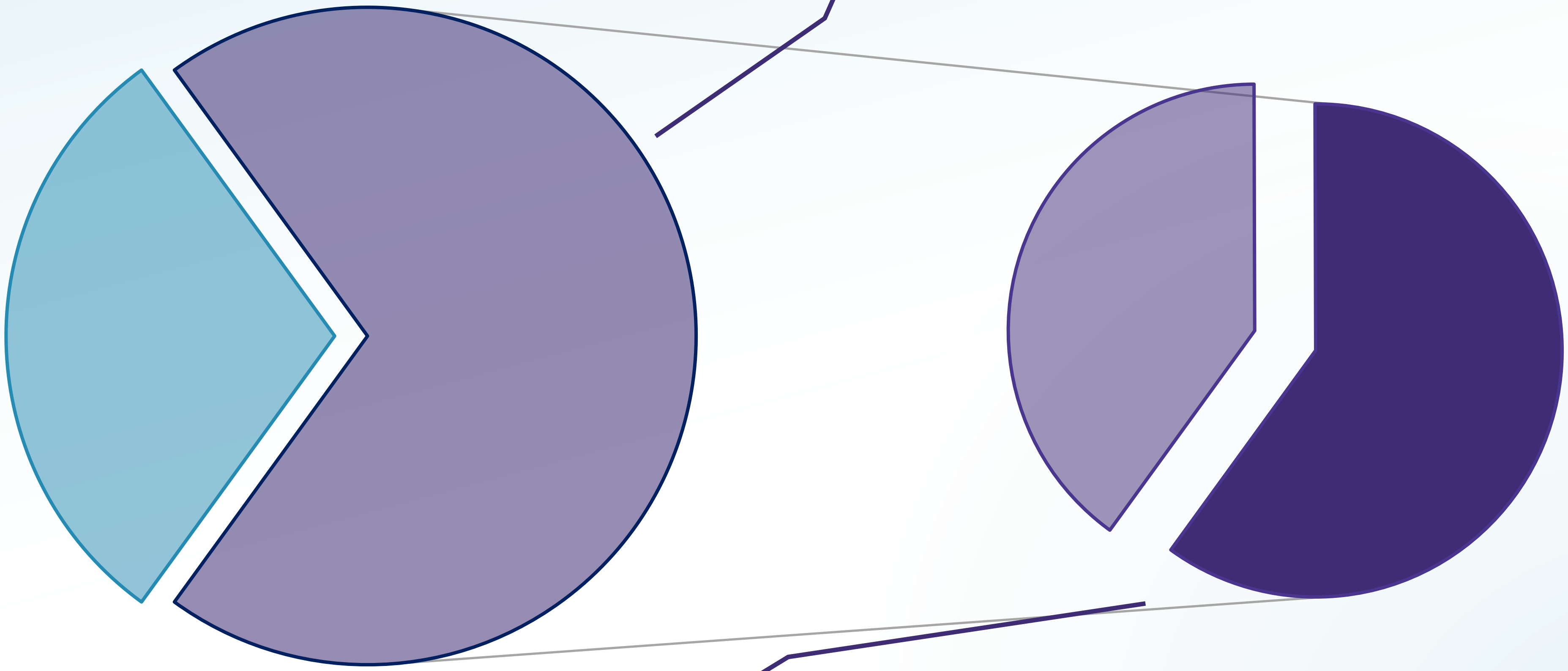
Out of the ~325 million people that live in the US, it is estimated that 70% will need to either be immune to COVID-19 (either through infection or vaccination) to achieve herd immunity



At this point in time, approximately 136.6 million people would be immune due vaccination. We would still need to wait until 90.9 million more people become immune through infection or vaccination to reach herd immunity overall in the US.

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Factors that might affect an individual's response to a vaccine

- It is unclear how individuals will respond to COVID-19 vaccines, but health conditions and other factors may influence your immune system's reaction to the vaccination. *The important point to remember though, is that these factors have historically influenced reactions to other vaccines as well and are not novel to vaccines for COVID-19*. Below are just a few examples of such factors:
  - **Obesity:** among individuals vaccinated to influenza, obese individuals saw a nearly 2x increase in risk of influenza compared to those who were normal BMI
  - **Age:** age of vaccination may result in differing responses
    - Older individuals have been observed with diminished responses to vaccines for diphtheria, hepatitis A, hepatitis, etc.
  - **Comorbidities:** comorbidities such as diabetes, celiac disease, and renal failure in children have seen lower responses to various vaccines
  - **Other behavioral factors:** stress, smoking, and sedentary lifestyles may result in poorer vaccine responses

What makes COVID-19 vaccines different?

- **Vaccine sponsors are attempting to safely condense the usual vaccine development process (10-15 years) into 1-2 years**
  - **Phases II and III clinical trials (which normally take place separately) now overlap**
- COVID-19 vaccine development is being fast-tracked via ***Operation Warp Speed (OWS)***
  - Huge amounts of resources from the federal government (CDC, National Institutes of Health, Biomedical Advanced Research and Development Authority, and Department of Defense) have been funneled to pharmaceutical companies and researchers looking to create a safe and effective COVID-19 vaccine

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Is Operation Warp Speed (OWS) safe?

- The short answer: **Yes!**
- **This sped-up development process presents as financial risk to pharmaceutical companies** rather than a decrease in safety of the vaccine.
  - Most candidate drugs and vaccines are eliminated through the multi-phasal development process
    - The further a vaccine makes it through the multiphase process, the more expensive it becomes to develop and test it
    - E.g. Stopping a vaccine candidate at Phase I clinical trials saves huge amounts of money compared to stopping a vaccine at Phase III
  - Because in ***OWS*** these phases overlap, an ineffective vaccine might be stopped at Phase III when under normal circumstances, it might be stopped in Phase I/II
- Long-term safety of the vaccine will be continually assessed over time (Phase IV clinical trials)

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The primary and secondary purpose of the initial COVID vaccine(s), as quoted by Dr. Fauci

- **The goal of the initial COVID-19 vaccines will be to prevent symptoms in those who become infected with the coronavirus rather preventing the infection entirely.**
  - Preventing symptoms is a **"primary endpoint"** in the vaccine development process
  - Preventing the infection altogether is considered a **"secondary endpoint."**
- "What I would settle for, and all of my colleagues would settle for, is the primary endpoint to prevent clinically recognizable disease … And that's what we hope happens, and if we do, that will go a long way to diffusing this very difficult crisis"
  - Even if a vaccine isn't able to prevent someone from getting infection, if the vaccine reduces their chance of experiencing symptoms, you will have ultimately prevented them from getting seriously ill or dying.
  - With less people experiencing severe symptoms, the coronavirus would pose a lower threat to communities and prevent healthcare systems from becoming overloaded
- **So just like with the seasonal flu, getting a vaccination may not prevent the illness in all cases, but render it less serious**

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Vaccine delivery to reach herd immunity

- Dr. Fauci, estimates that 80 to 85 percent of Americans need to be vaccinated to reach herd immunity.
- Both the Pfizer and Moderna vaccines require two doses. Eighty percent of the American population is around 264 million people, so we need to administer 528 million doses to achieve herd immunity.
- The Centers for Disease Control and Prevention reported on December 29, 2020 that 2.1 million doses of coronavirus vaccines have been administered in the last two weeks.
  - At this rate, it will take, approximately 10 years to reach the level of inoculation needed for herd immunity
  - This is why vaccination roll out has been stepped up in 2021
- In order for every American to be able to receive the vaccine by the end of June 2021, 3.5 million vaccinations will need to be administered ***per day.***
  - The issue is not just supply (production is ramping up to meet the challenge) , but distribution and administration.

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