

COVID Vaccine Primer

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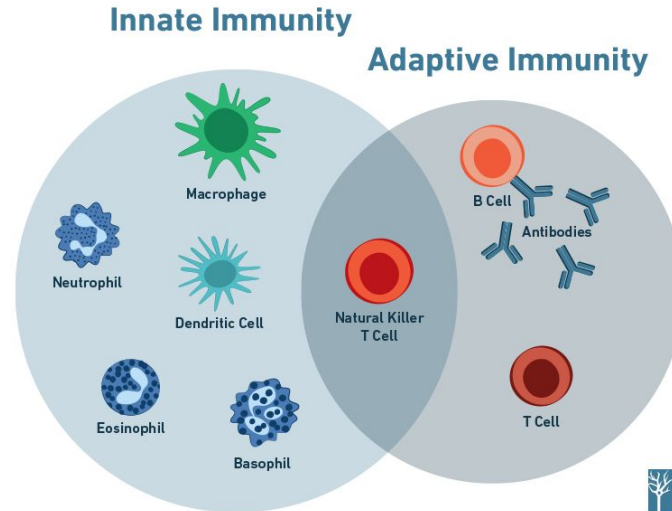
Slowly he would cruise the neighborhood, waiting for that occasional careless child who confused him with another vendor.

Outline

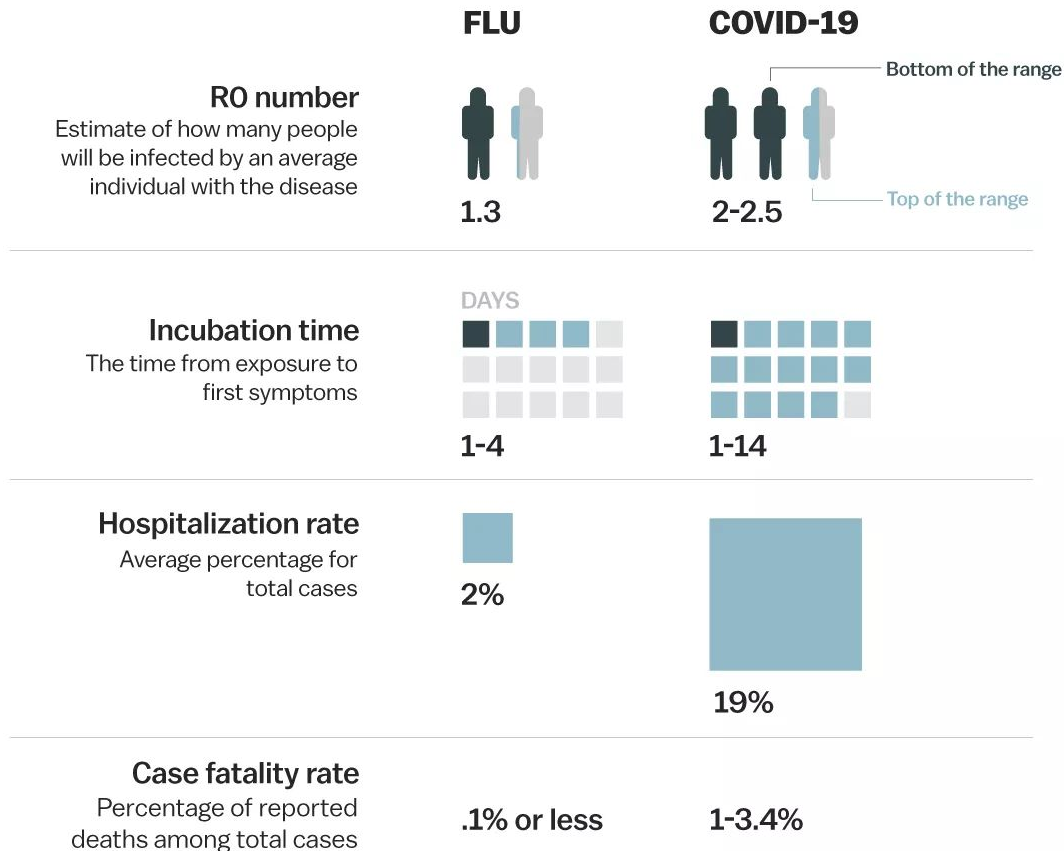
- Vaccine development
- How do the Pfizer, and Moderna vaccines work?
- What do we know about efficacy and safety at this point?
- What are the side effects of the Pfizer and Moderna vaccines

How do vaccines help with our immunity?

Vaccination is the process of boosting protective adaptive immune responses against microbes by exposure to dead microbes or parts of dead microbes or parts that look like dead microbes.



How seasonal flu and Covid-19 compare



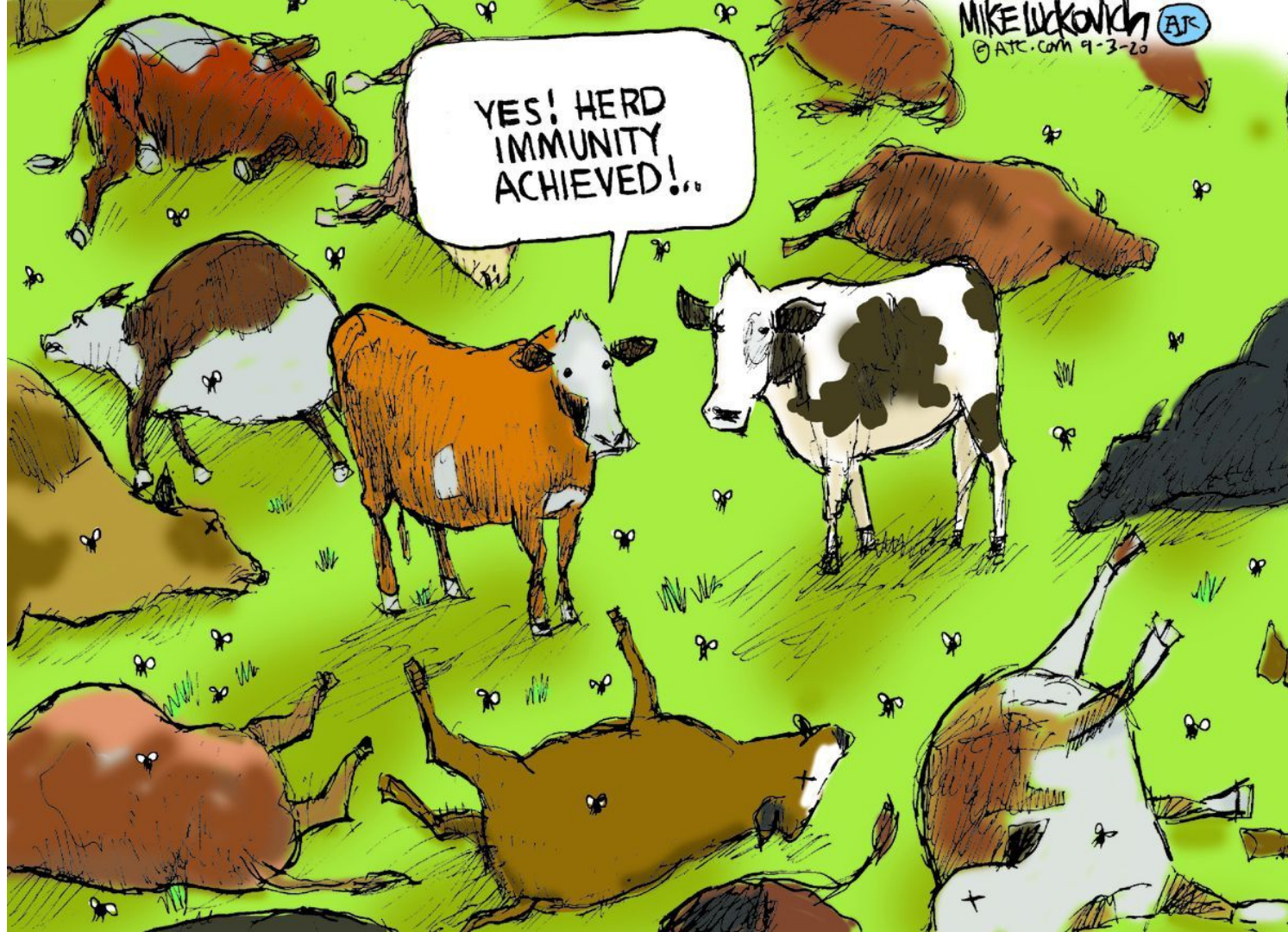
Sources: CDC, WHO, NCBI

Vox

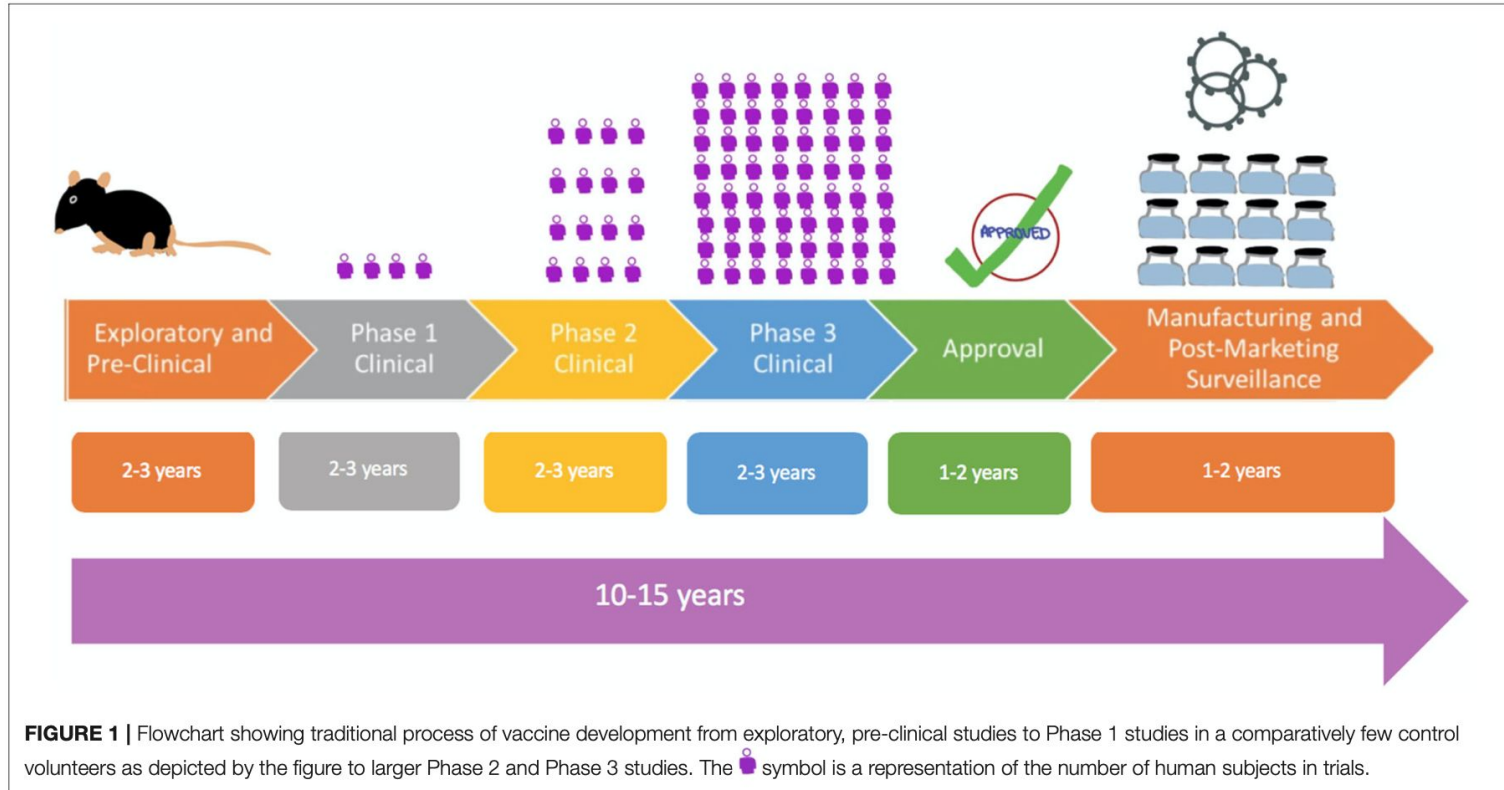
What happens if we do not have or use a vaccine?

- Eventually most of the population will get infected
- 10-20% will be without symptoms
- 10-20% will be hospitalized
- 1-3% may die - (3-9 million)
- An unknown # of people will develop long term sequelae (heart, lungs, neurological complications) that could result in disability

YES! HERD
IMMUNITY
ACHIEVED!..



Vaccine development usually takes 10-15 years



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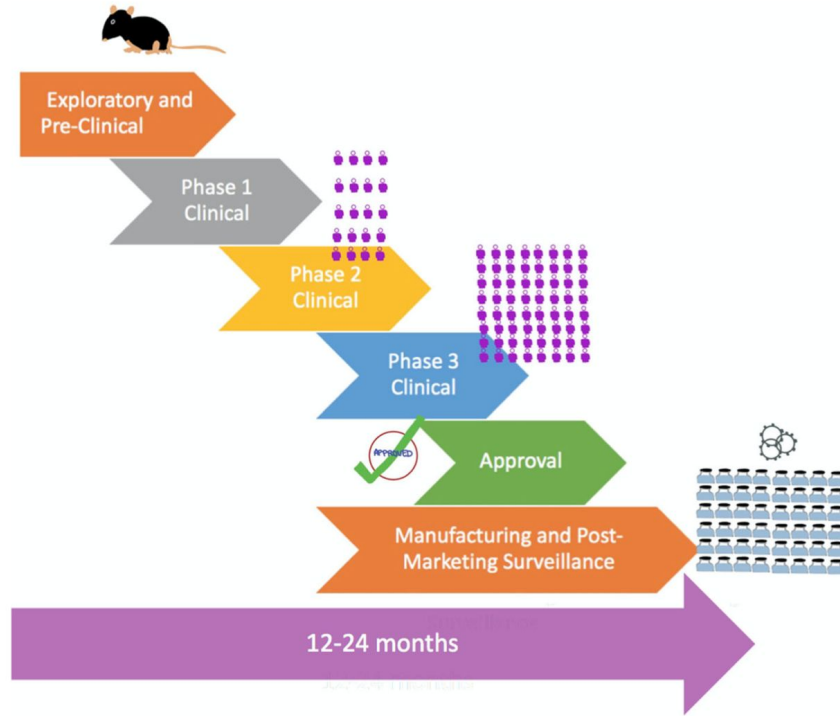



FIGURE 2 | Flowchart showing accelerated process of vaccine development in a pandemic with combined phases, pre-approval, and rapid large-scale manufacturing. The  symbol is a representation of the number of human subjects in trials.



MIRACLE



How was the COVID vaccine developed so fast?

The world was able to develop COVID-19 vaccines so quickly because of years of previous research on related viruses and faster ways to manufacture vaccines, **enormous funding** that allowed firms to run multiple trials in parallel, and regulators moving more quickly than normal.

[SARS-CoV-2](#), is a virus that mutates relatively slowly and that happens to belong to a well-studied family. Within weeks of identifying the virus scientists had mapped out its complete gene sequence. That information was shared immediately all over the world to vaccine researchers and developers.

With large sums given to vaccine firms by public funders and private philanthropists, they could do preclinical and phase I, II and III trials, as well as manufacturing, in parallel instead of sequentially.

In the final stages of trials, it helped that COVID-19 was everywhere because firms need infections to show that vaccines work. It's hard to run efficacy trials when the diseases themselves aren't prevalent.

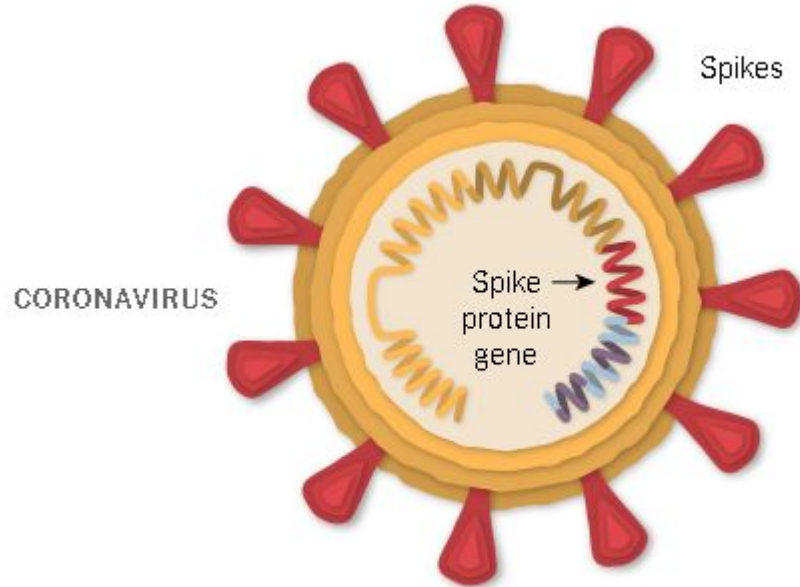
30 years of painstaking research allowed several groups of scientists — including a group at Pfizer working with a German company called BioNTech, and a young company in Massachusetts called Moderna — to bring mRNA vaccine technology to the threshold of actually working. The companies had built platforms that, theoretically, could be used to create a vaccine for any infectious disease simply by inserting the right mRNA sequence for that disease.

Within weeks of identifying the responsible virus, scientists in China had determined the structure of all of its genes, including the genes that make the spike protein, and published this information on the Internet.

Within minutes, scientists 10,000 miles away began working on the design of an mRNA vaccine. Within weeks, they had made enough vaccine to test it in animals, and then in people. Just 11 months after the discovery of the SARS-CoV-2 virus, regulators in the United Kingdom and the US confirmed that an mRNA vaccine for COVID-19 is effective and safely tolerated, paving the path to widespread immunization. Previously, no new vaccine had been developed in less than four years.

Vaccines generally target the “spike protein”

- Spike Protein - is a protein on the surface of the virus.
- A latch/target for the immune system
- The whole virus “gene” can make a whole new virus
- The Spike protein gene can only make the spike protein
NOT the VIRUS

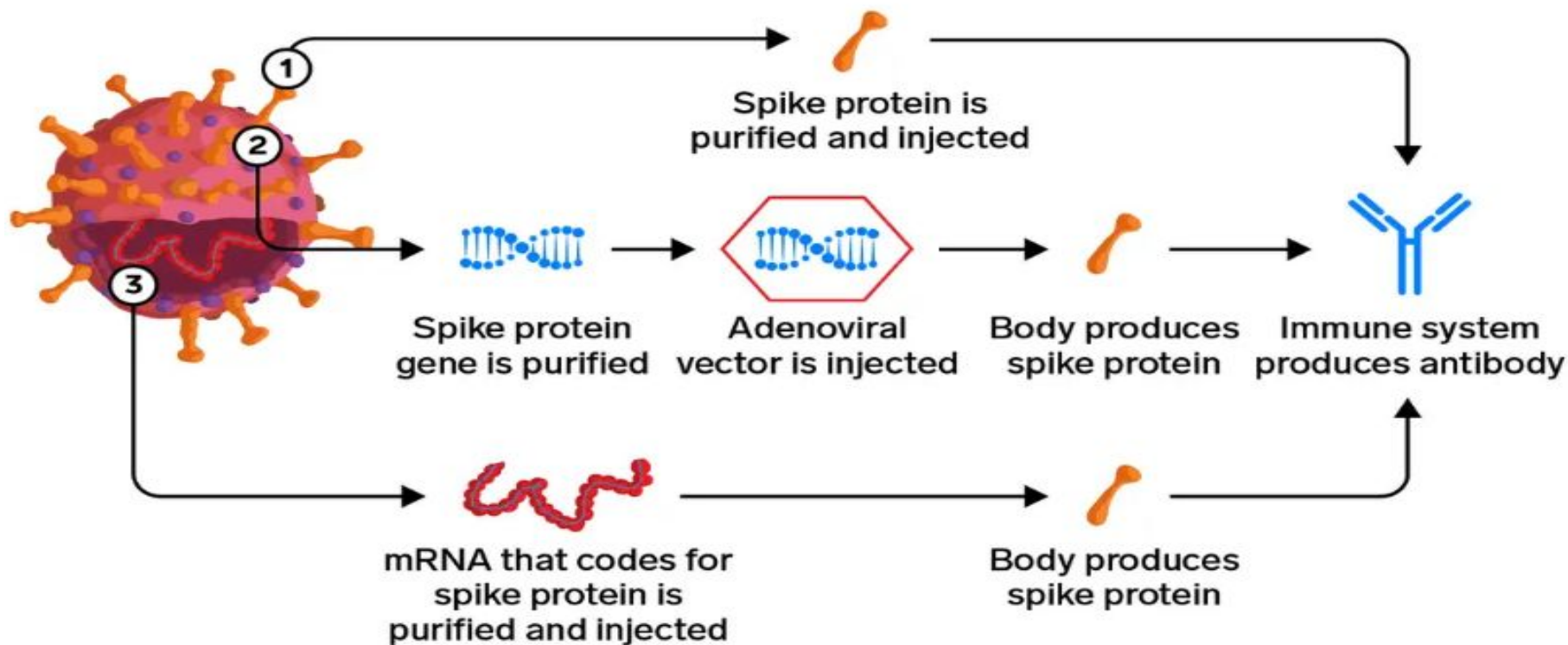


Spike protein is like
A flag in front of a house.
It's a way for the immune
system to identify viruses



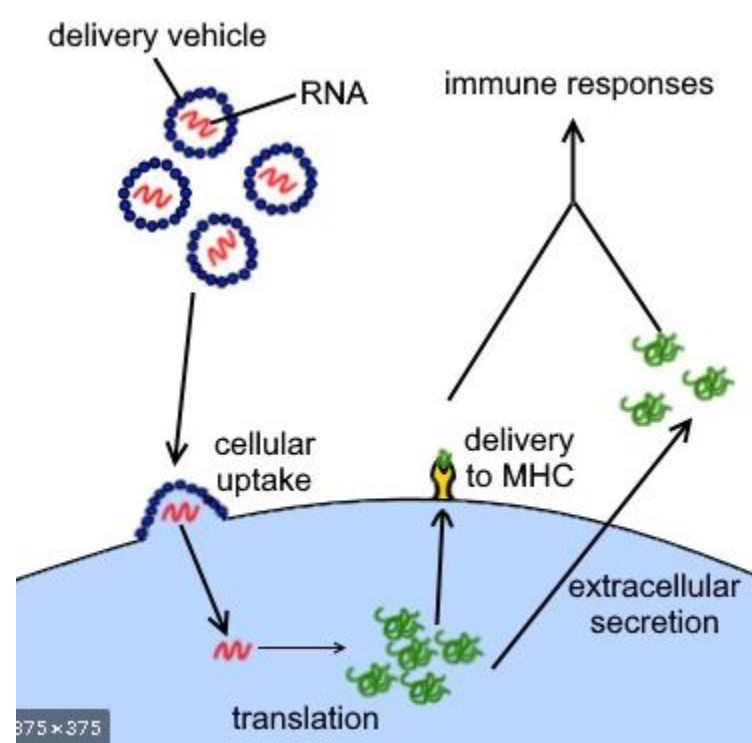
Three types of coronavirus vaccines in development

- ① Protein-based ② Viral vector ③ mRNA



Pfizer and Moderna vaccines use mRNA

- How do they work?
 - A snippet of mRNA is coated in a synthetic lipid shell.
 - It enters cells near injection site and cell machinery creates the spike protein and sticks it on the outside of cells, generating an immune response



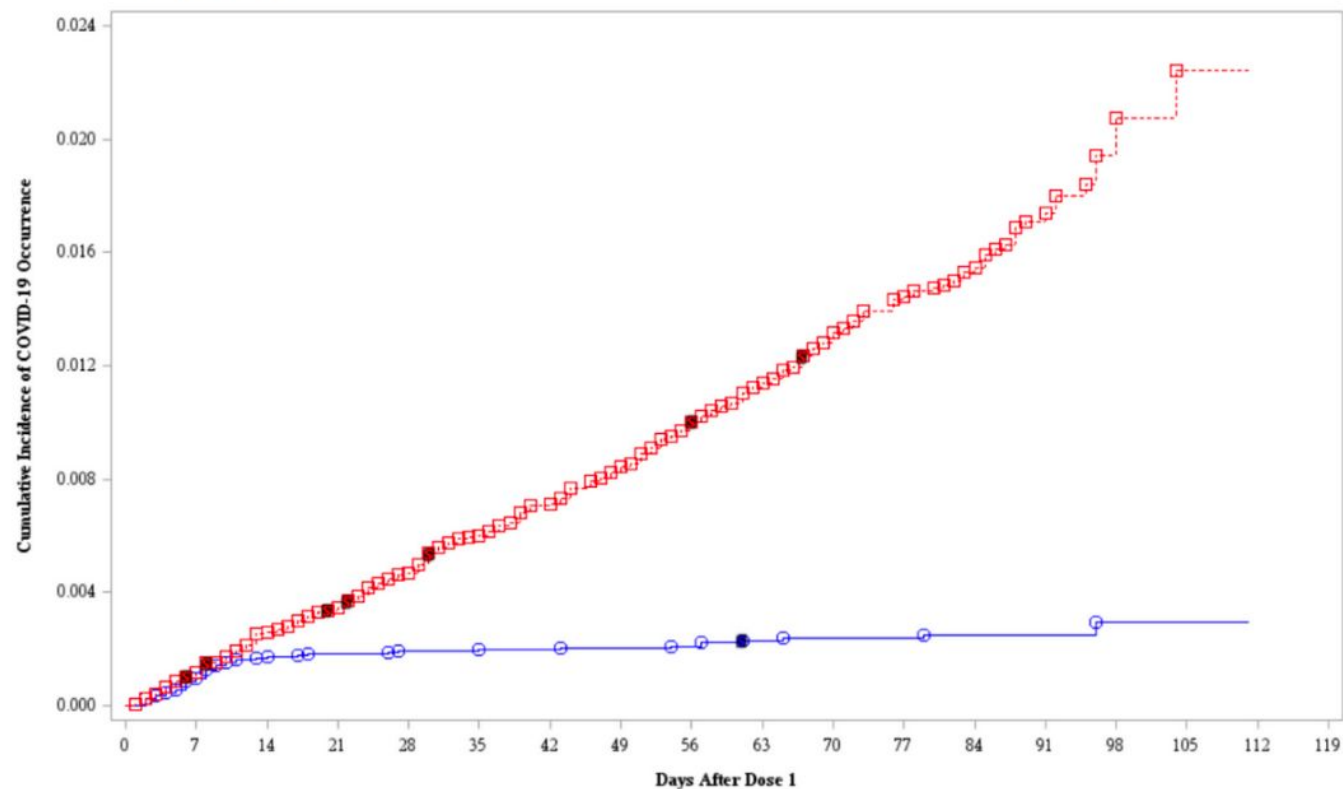
mRNA vaccines are new but have great potential

- Are they safe?
 - Despite being a new technology, safety is actually a big advantage of mRNA vaccines
 - Content of vaccine is simple - it does not contain any live virus.
 - It does not go to the nucleus or interact with host genome
 - A number of mRNA vaccines have been shown to be safe in human trials since 2008 (mainly cancer vaccines, none effective enough to be approved)
- Advantages
 - Easy to rapidly develop new vaccines
 - Safety
 - Generates strong immune response (no need for adjuvants)
- Disadvantages
 - Highly unstable; needs to be kept cold, so a challenge for distribution
 - Expensive

Pfizer/BioNTech

- ❖ 2-dose mRNA vaccine
- ❖ Phase 2/3 trial with 43,000 participants, first trial to include children 12+
- ❖ Preliminary analysis:
 - Out of **170** cases of COVID-19, **162** were in the placebo group
 - Out of **10** severe cases, **9** were in the placebo group
 - Efficacy rate estimated at **95%** (94% in adults 65+)
 - No serious side effects detected
- ❖ UK, Canada and US approved emergency use

Figure 13 Cumulative Incidence Curves for the First COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population



No. with events/No. at risk

A:	0/21314	21/21230	37/21054	39/20481	41/19314	42/18377	42/17702	43/17186	44/15464	47/14038	48/12169	48/9591	49/6403	49/3374	50/1463	50/398	50/0
B:	0/21258	25/21170	55/20970	73/20366	97/19209	123/18218	143/17578	166/17025	192/15290	212/13876	235/11994	249/9471	257/6294	267/3301	274/1449	275/398	275/0

—○— A: BNT162b2 (30 µg) - - - □ - - - B: Placebo

Moderna

- ❖ 2-dose mRNA vaccine
- ❖ Phase 3 testing with 30,000 participants
- ❖ Preliminary data:
 - Out of **196** cases of COVID-19, **185** were in the placebo group
 - All of the **30** cases of severe disease were in the placebo group
 - Efficacy rate estimated at **94.1%**
- ❖ Approved by FDA for Emergency Use

Reactogenicity Side Effects within 7 days of vaccine Solicited Via E-Diary

Most common reactogenicity

symptoms	Pfizer	Moderna
Pain at injection site	84.1%	91.6%
Fatigue	62.9%	68.5%
Headache	55.1%	63.0%
Muscle Pain	38.3%	59.6%
Joint Pain	23.6%	44.8%
Chills	31.9%	43.4%
Fever	14.2%	14.8%

Nausea and Vomiting:

-Moderna(**nausea and** vomiting): highest rate was in age < 64, after second dose: 21%

-Pfizer (vomiting): < 1%

Lymphadenopathy:

-Moderna: 10.2% after first dose, 14% after second dose

-Pfizer: < 5%

Systemic reactogenicity symptoms

- More common after second dose than first
- More common in younger age groups d/t more robust immune systems
- Generally occur on day 1 or day 2 and resolved within 2-3 days
- Most often mild or moderate in intensity
- More common in Moderna Phase 3 Trial than Pfizer Phase 3 Trial
- Should prompt staggering vaccines for hospital staff on same unit

Reactogenicity Symptoms Are More Common in Younger Age Group

Pfizer Vaccine

	Age 16-55	Age > 55
Pain at Injection Site	83% after first shot 78% after second shot	71% after first shot 66% after second shot
Fatigue	59% after second dose	51% after second dose
Headache	52% after second dose	39% after second dose
Fever	16% after second dose	11% after second dose
Muscle Aches	37% after second dose	29% after second dose
Chills	35% after second dose	23% after second dose
Joint Pain	22% after second dose	19% after second dose

Vaccine Side Effects Compared

(<55 yr, after Dose 2 – highest side effect group found)



Shingrix



COVID-19
mRNA-1273



COVID-19
BNT 162b2



Flu

Local Pain	88.4%	90.1%	77.8%	45.4%
Redness	38.7%	9.0%	5.9%	13.4%
Swelling	30.5%	12.6%	6.3%	11.6%
Myalgia	56.9%	61.3%	37.3%	15.4%
Fatigue	57%	67.6%	59.4%	17.8%
Headache	50.6%	62.8%	51.7%	18.7%
Chills	35.8%	48.3%	35.1%	6.2%
Fever	27.8%	17.4%	15.8%	0.8%
Overall Grade 3%	5.2%	4.1%	1.5%	0.5%
Overall SE %	48%	46%	36%	15%
	1	2	3	4

What do we know about severe allergic reactions? **Emerging Story**

Pfizer Clinical Trial

- No cases of anaphylaxis related following administration of the vaccine in the clinical trial
BUT people with a history of anaphylaxis to vaccines were excluded from Pfizer clinical trial

Week 1 of Pfizer roll out :

- 2 cases of anaphylaxis in UK, 5 cases of anaphylaxis or severe allergic reaction in US (2 were in Alaska)
 - 2 individuals in UK both had history of anaphylaxis to food, needed epinephrine to treat vaccine induced anaphylaxis and recovered
- What is causing the anaphylaxis: not known, could be PEG (polyethylene glycol) which is an ingredient in both vaccines “but in different formulations”
- PEG is ubiquitous (ultrasound gel, miralax, injectable steroids) and allergy is rare

Moderna Clinical Trial

- People with a history of anaphylaxis were included
- No cases of anaphylaxis following administration of the vaccine

Pregnant Women

- Clinical trials did not include pregnant women (d/t fear of injuring fetus or threatening pregnancy)
- Not enough data to gauge whether they are safe for pregnant or lactating people
- DART animal studies
 - Moderna has completed animal studies the FDA demanded of manufacturers; these studies look for evidence that the vaccine might harm the pregnancy or the developing fetus. The company said it saw no such signals.
 - Pfizer has only interim data from its animal studies, but said it saw no concerning signs either.
- CDC has said pregnant women should be offered the chance to get the Pfizer vaccine
- (Great Britain advised against giving Pfizer vaccine to pregnant women)
- Pregnant women should discuss risks and benefits of vaccine with obstetrician taking into account
 - Pregnancy seems to increase risk of severe COVID course
 - Level of community transmission
 - Personal risk of exposure
- Post-vaccine fever should be treated with acetaminophen

Vaccine triggered anaphylaxis Non Covid vaccine 1.31/million doses
Pfizer/Moderna 2.6/million doses.

Summary

Early Data show that both Pfizer and Moderna vaccines are very effective and safe

The Pfizer and Moderna vaccines often causes both local and systemic reactions. Most are minor and resolve within 24 hours.

Do the benefits of vaccination outweigh the risks?



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