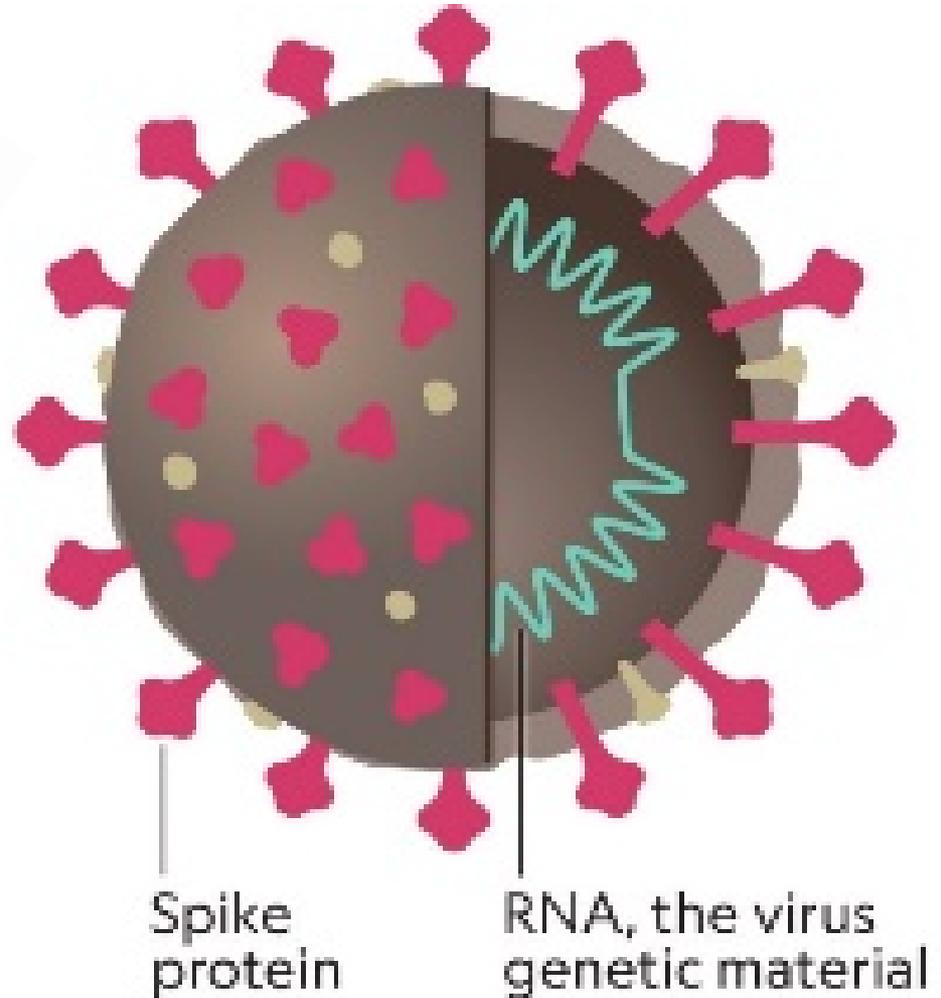


COVID vaccination

Peggy L. Carver



Anatomy of a coronavirus

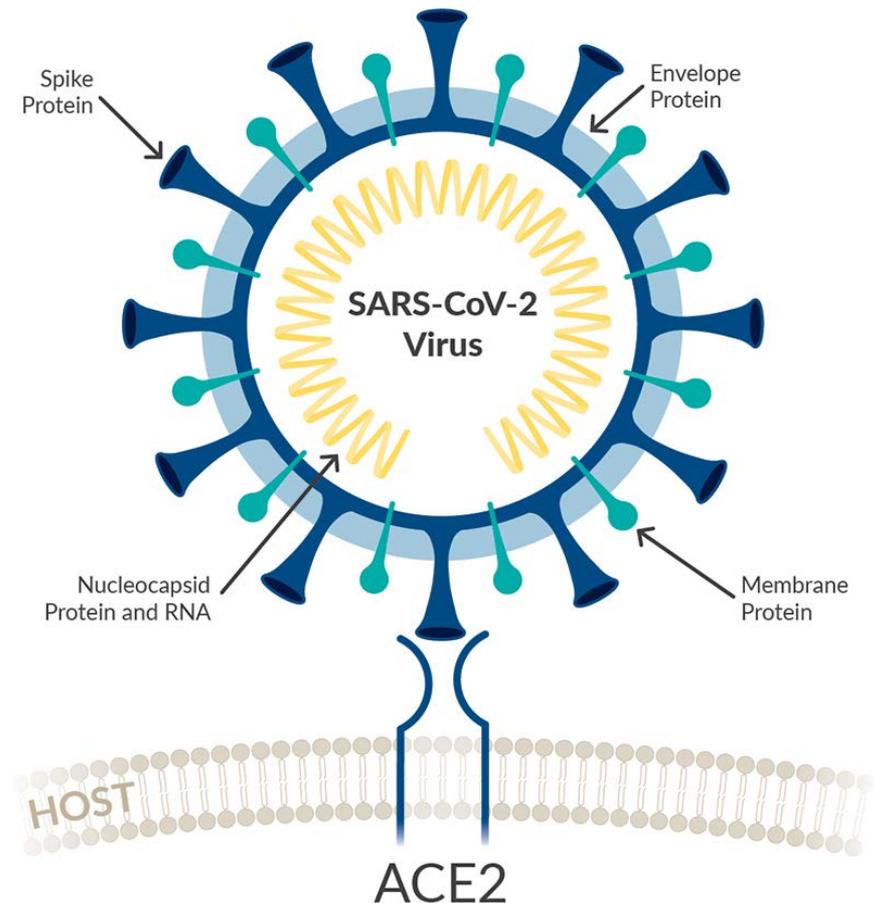
■ The 'spike protein'

- Allows attachment to host cell
- Alerts host immune system to fight against it (make antibodies)
- Target of vaccines !

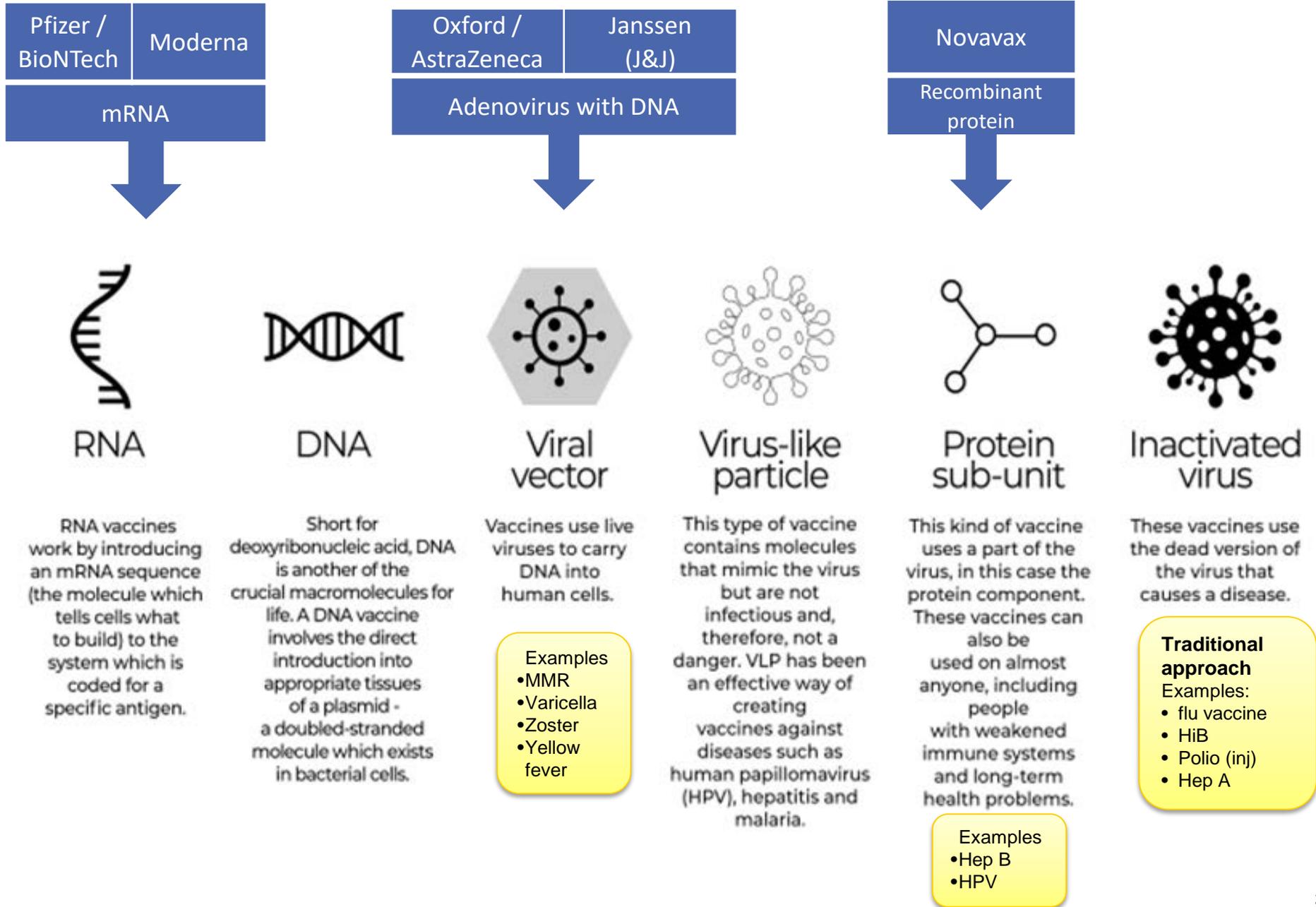
■ Virus mutations (AKA variants)

- ❖ UK (B.1.1.7 variant)
- ❖ S. Africa (B.1.351 variant)
- ❖ Brazil (P.1 variant)
- Often due to spike protein mutations
→ more tight binding of spike protein to ACE2 receptor?
- Have ↑ 'transmissibility' (ie can be spread more easily)
- Have ↑ mortality?
- Currently covered by vaccines?

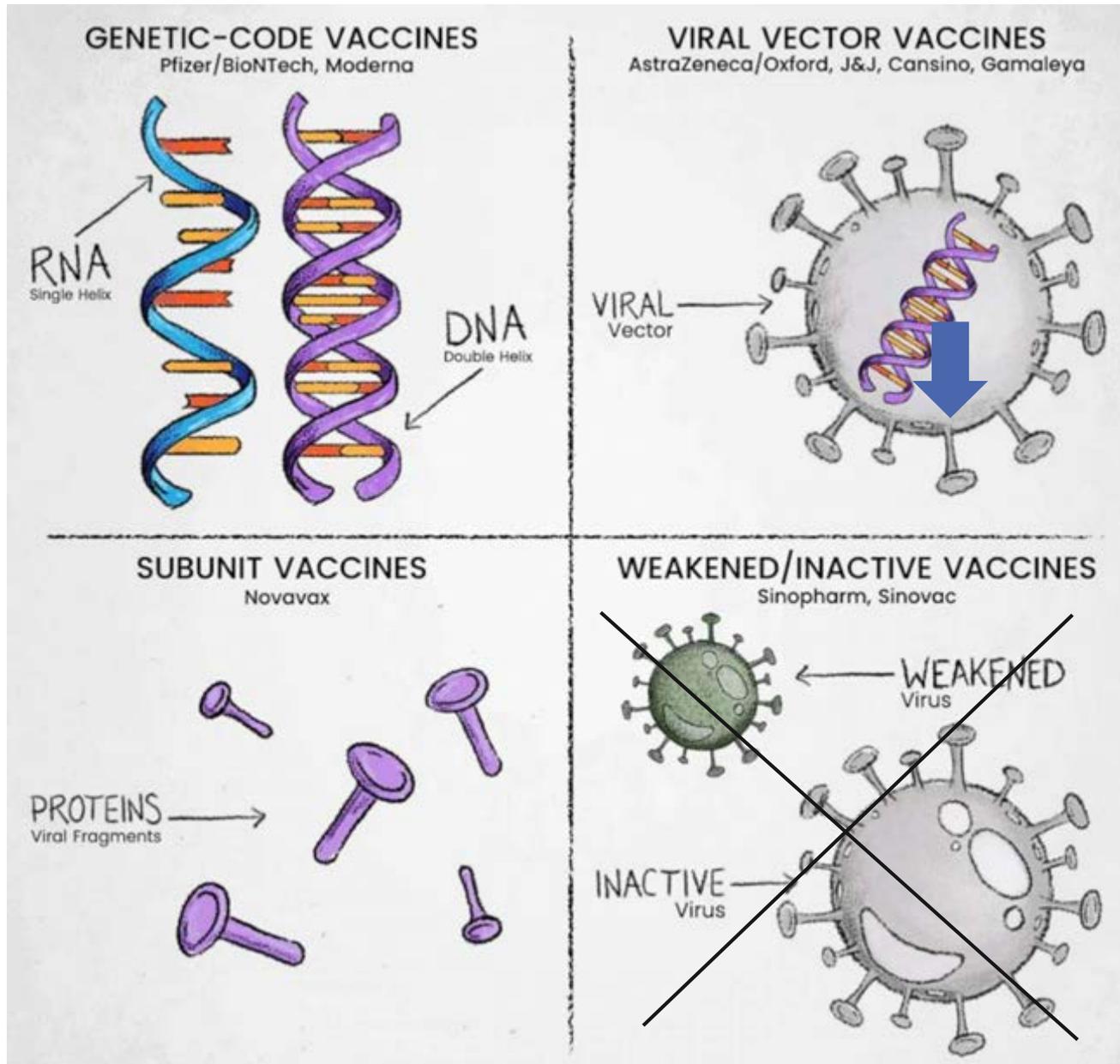
ALL viruses MUTATE !!!



What are the different ways to make vaccines ?



4 main approaches to COVID vaccine development



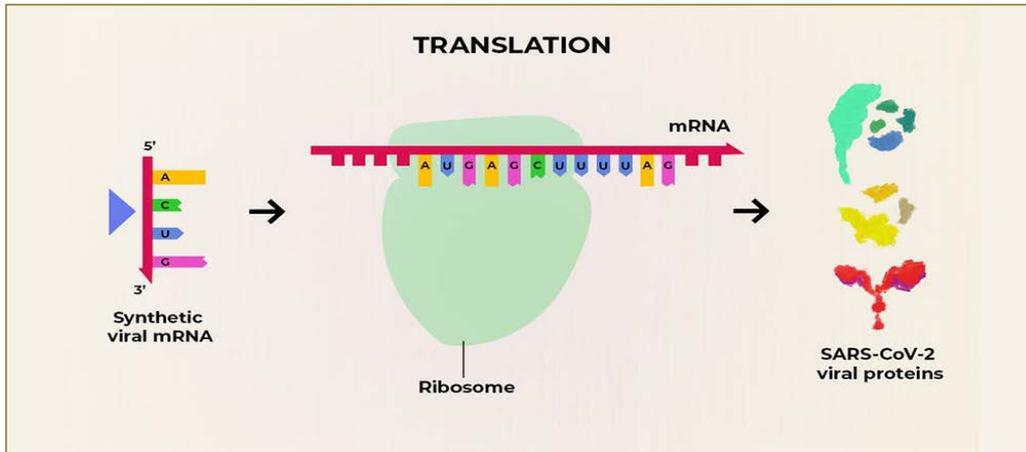
uses inactive virus (adenovirus) as a 'Trojan horse' to deliver genetic material from the COVID-19 virus
(AstraZeneca/Oxford, J & J, CanSino, Gamaleya)

traditional approach - uses real weakened or killed virus stimulate an immune reaction

genetic material instruct cells to start making spike proteins normally found on the outside of the virus.
(Pfizer/BioNTec, Moderna)

uses little pieces of the virus' surface, rather than a whole dead virus
(Novavax)

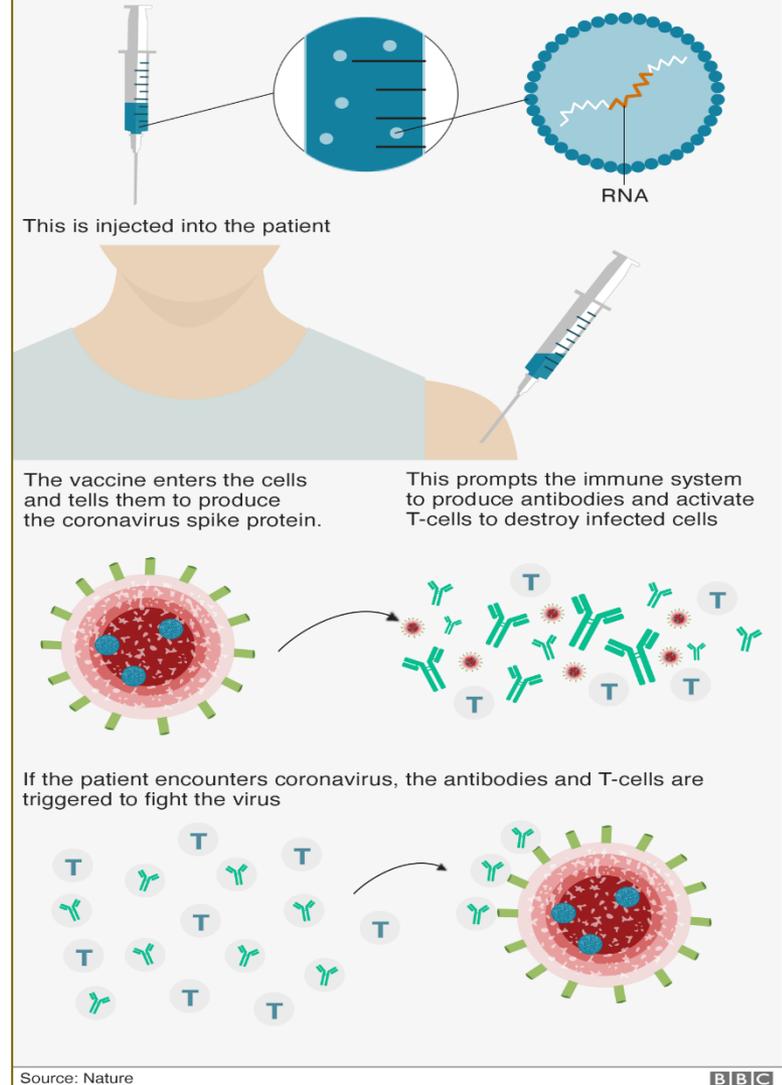
What happens when you get the mRNA (Pfizer or Moderna) vaccine ?



- In our bodies, our naturally created mRNA (messenger RNA) acts like a 'recipe' to tell our cells how to make specific proteins.
- The COVID-19 vaccine **will not alter your DNA**, nor does it enter the nucleus of your cells.
- The mRNA COVID-19 vaccine (Pfizer or Moderna)
 - delivers a 'recipe' (lab-developed mRNA) to your cells on how to make the **spike protein**, telling your body to be on the lookout for the spike protein and to develop an immune response to defeat it. Then, your natural cell processes take over.
 - Within days, the mRNA from the vaccine is destroyed by our cells, leaving no permanent mark on our bodies
 - After receiving both doses of the vaccine, your body will be prepared to identify and attack the SARS-CoV-2 virus, if it ever enters your system..

How an RNA vaccine would work

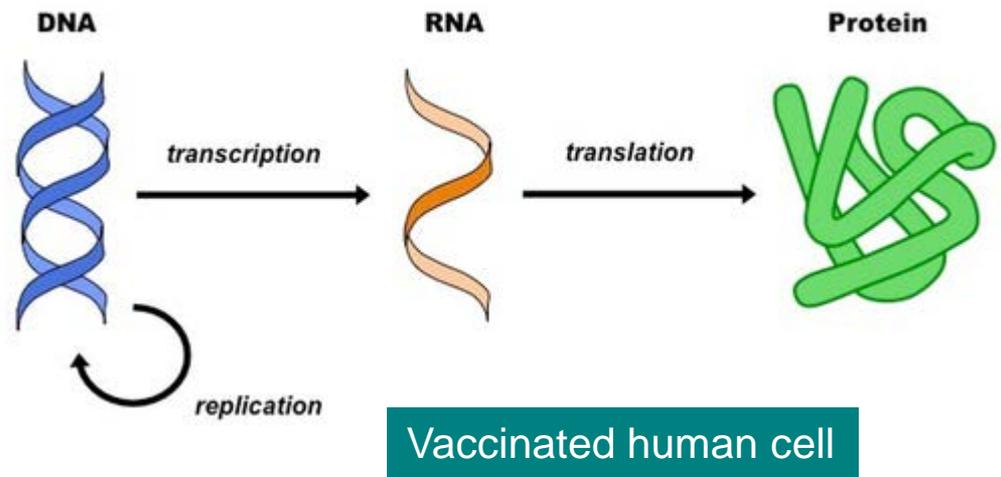
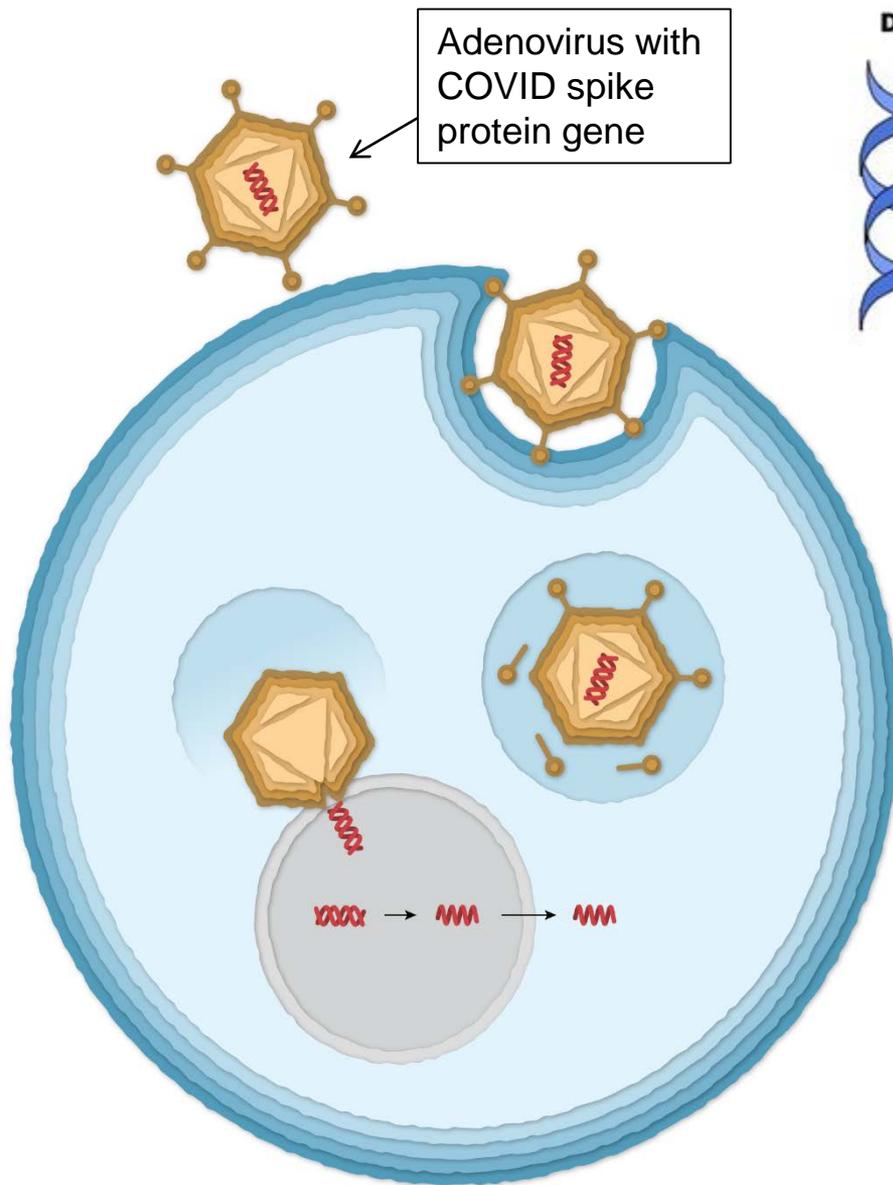
Scientists take part of the virus genetic code that tells cells what to build and coat it in a lipid so it can enter the body's cells



Source: Nature

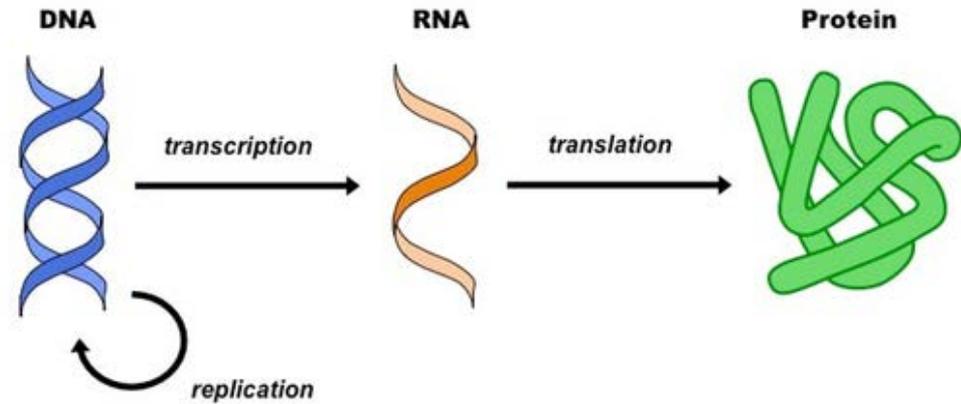
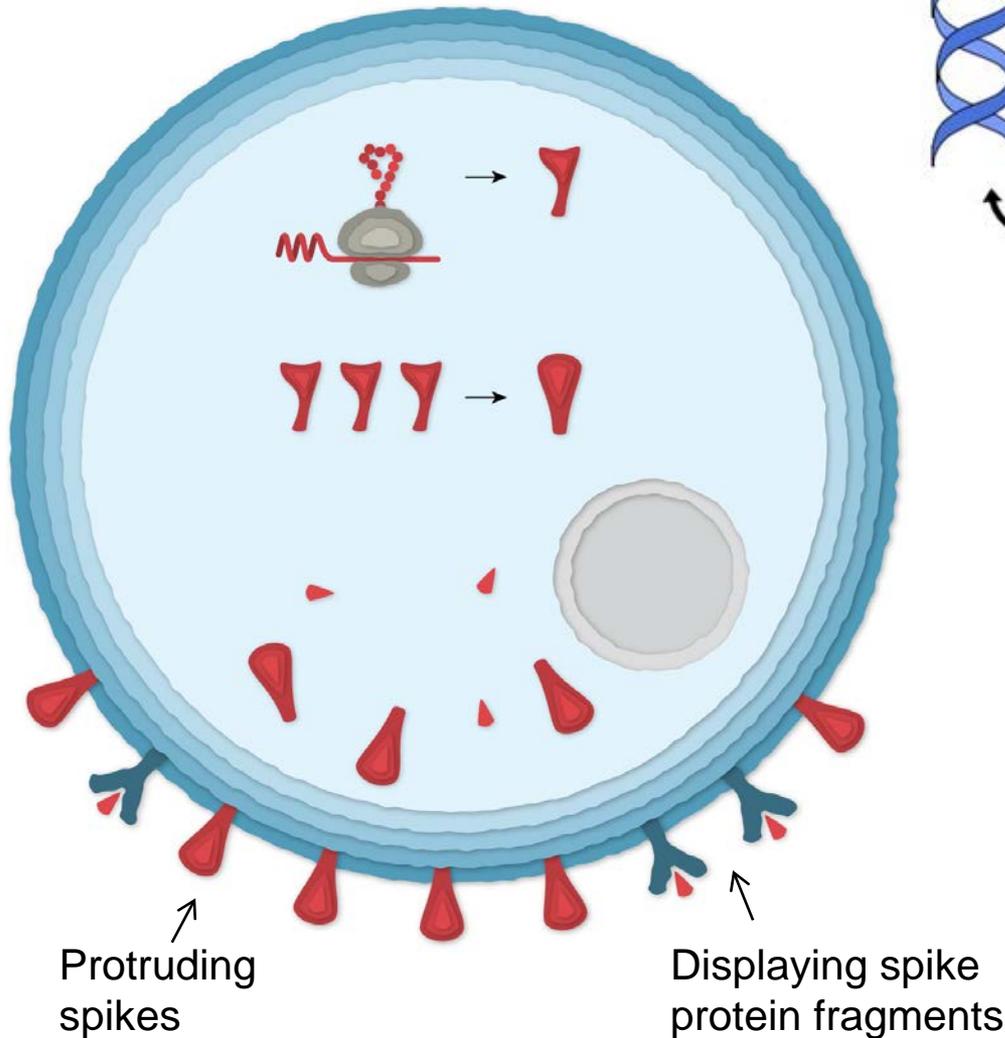


What happens when you get the adenovirus (J&J) vaccine



- The adenovirus pushes its **DNA** into the nucleus of cell
- the DNA (gene) for the **coronavirus spike protein** can be read by the cell and copied into mRNA.
- mRNA leaves the nucleus & the cell reads the mRNA sequence to begin making & assembling viral spike proteins

What happens when you get the adenovirus (J&J) vaccine



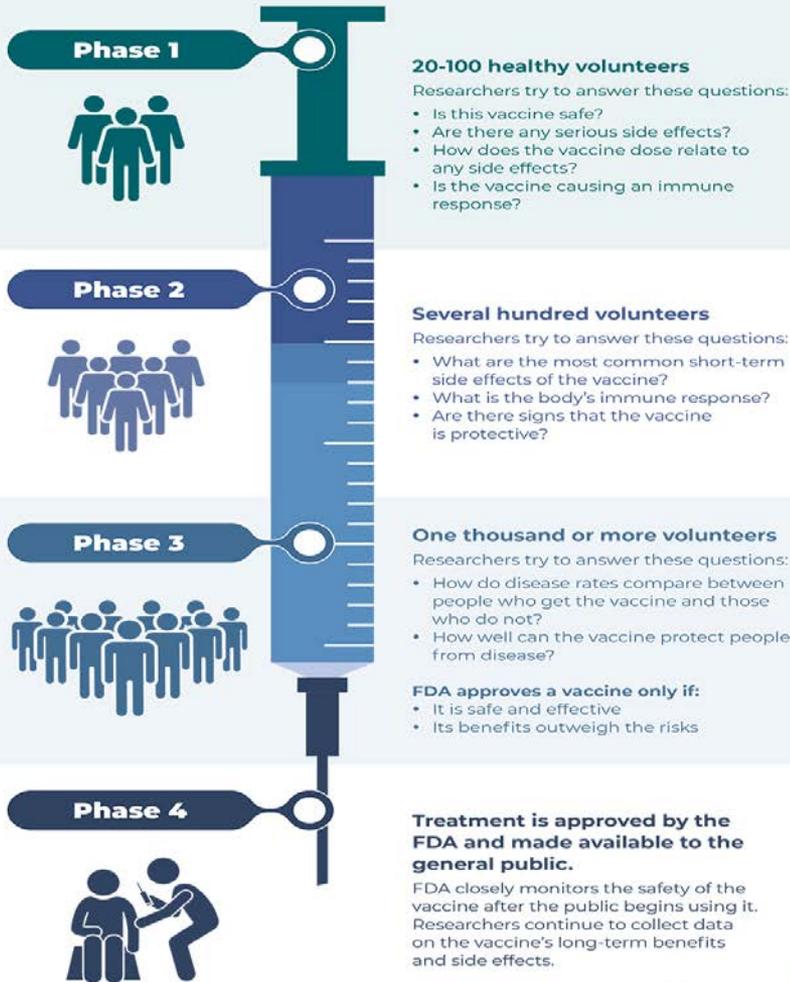
Vaccinated human cell

- mRNA leaves the nucleus
- cell's molecules read mRNA sequence & begin assembling spike proteins
- Spike proteins, & fragments, go to the cell surface
- The host immune system is alerted by spike proteins to activate immune cells to make antibodies

The Journey of a Vaccine

How a new vaccine is developed, approved, and manufactured

The U.S. Food and Drug Administration (FDA) sets rules for the four phases of clinical research so that researchers can learn about the effects of new therapies while keeping volunteers safe. This includes trials of new vaccines to protect against infection; researchers always test vaccines with adults first.



Emergency use approval (EUA)

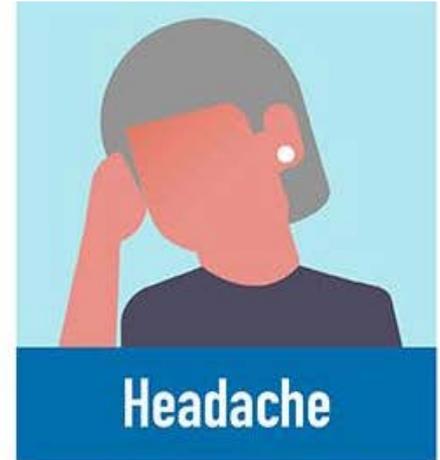
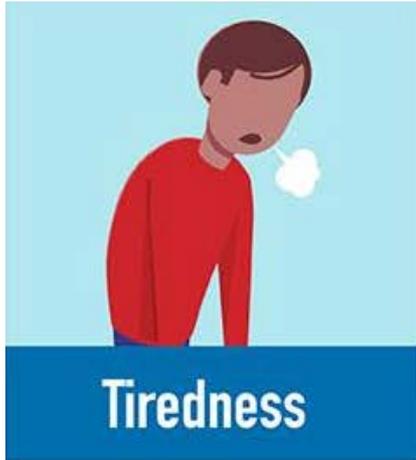
COVID vaccines

		Pfizer / BioNTech	Moderna	Oxford / AstraZeneca	Janssen (J&J)	Novavax	
		Biotechnology	mRNA	mRNA	Adenovirus	Adenovirus	Recombinant protein
Symptomatic COVID	Efficacy	original strain	<ul style="list-style-type: none"> 95% 85% 15-28 days after 1st dose 	<ul style="list-style-type: none"> 94.1% 	<ul style="list-style-type: none"> 62 % (SD/SD) 90 % (LD/SD) 	<ul style="list-style-type: none"> 72% 	<ul style="list-style-type: none"> 95.6%
		B1.1.7 variant (UK)	<ul style="list-style-type: none"> No impact on efficacy 	<ul style="list-style-type: none"> Predicted to have no impact 	<ul style="list-style-type: none"> Predicted to have no impact 		<ul style="list-style-type: none"> 85.6% efficacy
		B.1.351 variant (S. Africa)	<ul style="list-style-type: none"> 0.8-1.46-fold ↓ in neutralizing antibodies 	<ul style="list-style-type: none"> 6-fold ↓ in neutralizing antibodies 	<ul style="list-style-type: none"> ~10% efficacy minimal protection vs mild & moderate COVID) 	<ul style="list-style-type: none"> 57% efficacy 	<ul style="list-style-type: none"> 60% efficacy among HIV- study subjects; 49.5% efficacy vs HI+ & HIV- subjects
Severe COVID		Effectiveness	<ul style="list-style-type: none"> 90% 	<ul style="list-style-type: none"> 100% 	<ul style="list-style-type: none"> 100% 	<ul style="list-style-type: none"> 85% after 28 days; 100% after 49 days 	<ul style="list-style-type: none"> 100%
	# doses 	2 (3 weeks apart)	2 (4 weeks apart)	2 (4 weeks apart)	1 or 2 (depending on study trial)	2 (3 weeks apart)	
	storage	-70°C (-25 to -15°C not yet FDA approved)	-20°C x 6 months (-25 to -15°C not yet FDA approved)	Regular frig	1-2°C	2-8°C	
	USA approval status	Emergency use approval (EUA) in Dec 2020	Emergency use approval (EUA) in Dec 2020	In middle of Phase III trial in USA	Meeting for FDA approval Feb 26th	In middle of Phase III trial in USA	
	Pregnancy	USA/global enrollment in 18+ y/o ongoing					
	Pediatric	USA Enrollment complete Dec '20 (2000 12-15 y/o)	USA Enrollment open (3000 12-17 y/o)	UK Enrollment open (300 age 12+ and 6-12 y/o)			

Adapted from 'Your local epidemiologist'
<https://yourlocalepidemiologist.com/>

LD=low dose;
 SD=standard dose

Side effects of COVID vaccines



■ Rare: anaphylaxis

- Usually seen with pre-existing PEG (polyethylene glycol) or polysorbate allergy
- Occurs very quickly after vaccination (so, we monitor for 15-30 minutes after giving vaccine)

Common side effects

On the arm where you got the shot:



- Pain
- Swelling

Throughout the rest of your body



- Fever
- Chills
- Tiredness
- Headache

After vaccination:

What to expect, and what to do...

Helpful tips

If you have pain or discomfort, talk to your doctor about taking over-the-counter medicine, such as ibuprofen, aspirin, antihistamines, or acetaminophen, for any pain and discomfort you may experience after getting vaccinated. You can take these medications to relieve post-vaccination side effects if you have no other medical reasons that prevent you from taking these medications normally. It is not recommended you take these medicines before vaccination for the purpose of trying to prevent side effects, because it is not known how these medications may impact how well the vaccine works.

To reduce pain and discomfort where you got the shot



- Apply a clean, cool, wet washcloth over the area.
- Use or exercise your arm.

To reduce discomfort from fever



- Drink plenty of fluids.
- Dress lightly.

When to call the doctor

In most cases, discomfort from fever or pain is normal. Contact your doctor or healthcare provider:

- If the redness or tenderness where you got the shot increases after 24 hours
- If your side effects are worrying you or do not seem to be going away after a few days



Taking pain relievers (Tylenol, ibuprofen, etc) before / after vaccination



- It is recommended **not to take pain relievers PRIOR to vaccination**. Having said that, the minimum data we have is in kids with other vaccines, and the immune response with COVID is different (which, could be good or bad).
- Given the common incidence of fever and/or pain after the COVID vaccine, a lot of study patients likely took it (even if told not to in the protocol...) and they had great responses.
- **After** vaccination it is thought to be OK to take pain relievers, but there is little data on timing. (For that matter, we have little data on this even with regular (nonCOVID) vaccines.)

Symptomatic pregnant women with COVID-19 have an ↑ risk of more severe illness



- Pregnant women are at ↑ risk:
 - ICU admission
 - need for mechanical ventilation
 - death
- COVID-19 (infection or vaccine) does not cause infertility or miscarriages
 - Antibodies to COVID-19 spike protein (from getting the virus or from getting vaccinated) have not been linked to infertility
 - No ↑ risk of miscarriage with COVID-19 during pregnancy
 - The virus' spike protein does **not** attach to the placenta and cause miscarriage.

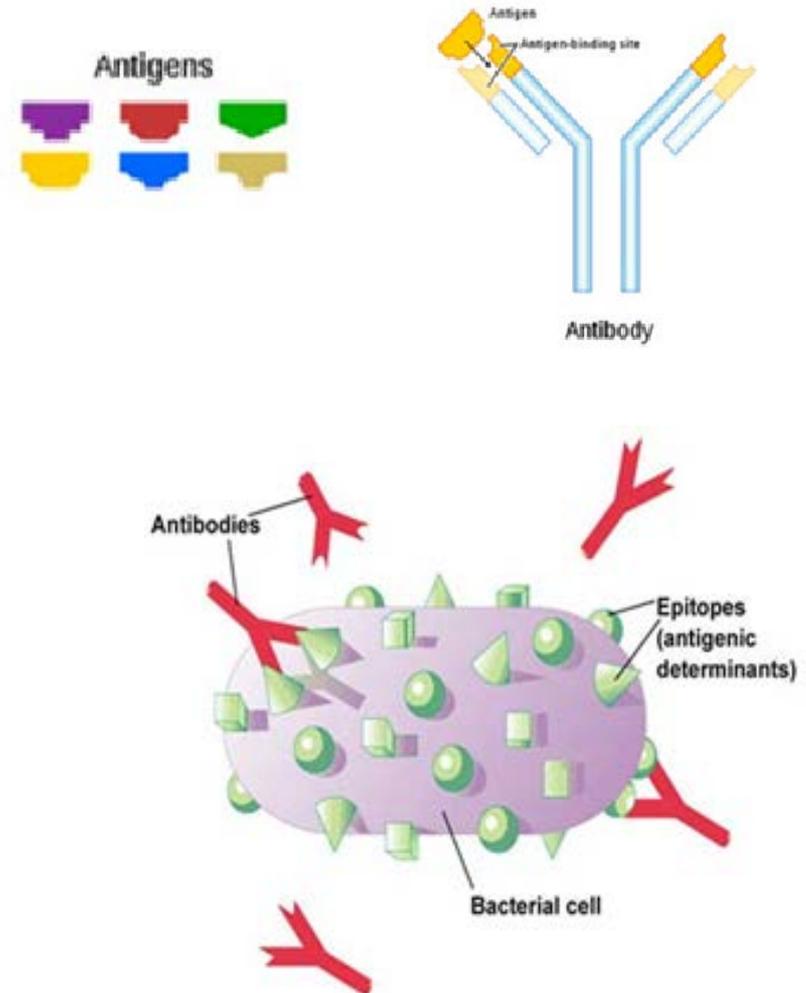
Vaccination during pregnancy or breastfeeding

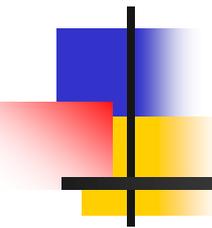
- The mRNA vaccines do not contain virus particles.
 - Within hours or days our bodies eliminate mRNA particles used in the vaccine, so these particles are unlikely to reach or cross the placenta.
 - The immunity that a pregnant individual generates from vaccination can cross the placenta, and may help to keep the baby safe after birth.
- Vaccines currently available under EUA
 - vaccine trials did not deliberately include pregnant or breastfeeding individuals
 - a trial is ongoing.
 - There are no safety data specific to use in pregnancy
- Should pregnant / breastfeeding women get vaccinated?
 - The CDC recommends vaccination
 - Several professional societies have advocated vaccination.
 - Pregnancy testing should **not** be a requirement prior to receiving any EUA-approved COVID-19 vaccine.



Would the vaccine cause you to test positive for COVID-19?

- Vaccines currently in clinical trials in the United States won't cause you to test positive on **viral tests**, which are used to see if you have a current infection.
- 'false positive' results can occur with **antigen** tests, esp if users do not follow the instructions for use.
- If your body develops an immune response, which is the goal of vaccination, there is a possibility you may test positive on some **antibody** tests.
 - Antibody tests indicate you had a previous infection and that you may have some level of protection against the virus.
 - Experts are currently looking at how COVID-19 vaccination may affect **antibody** testing results.





Why are there usually 2 doses?

- For those without prior COVID
 - Dose # 1 'primes' the immune system
 - Dose # 2 induces a vigorous immune response and production of **antibodies**
 - Dose # 2 adverse reactions > dose # 1
- Better immune response
 - Dose # 1 ↓ risk of symptomatic infection ~50% (Pfizer vaccine) to 80 % (Moderna vaccine).
 - Dose # 2 (either vaccine) ↓ risk ~95 %
- For those with prior COVID, dose #1 usually has more adverse reactions than dose 2
- What about missing the 2nd dose?
 - A delay of 3-7 days for 2nd dose is probably ok
 - CDC: up to 42 days between Pfizer or Moderna doses
 - UK: spacing of 12 weeks best for AstraZeneca
 - Concern that partial immunization could help new coronavirus variants to develop

Michigan vaccination priority groups

		Estimated schedule for first doses administered												
Phase	People covered	Dec	Jan	Feb	March	April	May	June	July	Aug	Sept	Oct	Nov	Dec
1A	Healthcare workers	[Green bar]												
	Long term care residents and staff	[White]	[Green bar]											
1B	75 years and over not covered in Phase 1a	[White]	[Green bar]											
	Prioritized Frontline Responders	[White]	[Green bar]											
	School and child care staff	[White]	[Green bar]											
	Corrections staff	[White]	[Green bar]											
	Agriculture and food processing workers	[White]	[White]	[Green bar]										
1C	Other essential frontline workers	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]
	65-74 years old	[White]	[Green bar]											
	18-64 with COVID-19 risk factors/pre-existing conditions	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]
2	All remaining essential workers	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]
	16 to 64 years not covered above	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]	[White]

Preexisting conditions = COPD, hypertension, chronic kidney disease, heart disease, diabetes, obesity, & other high risk conditions
 As of Feb 15: https://www.michigan.gov/documents/coronavirus/MI_COVID-19_Vaccination_Prioritization_Guidance_710349_7.pdf