

The COVID-19 Pandemic

Development of Vaccines

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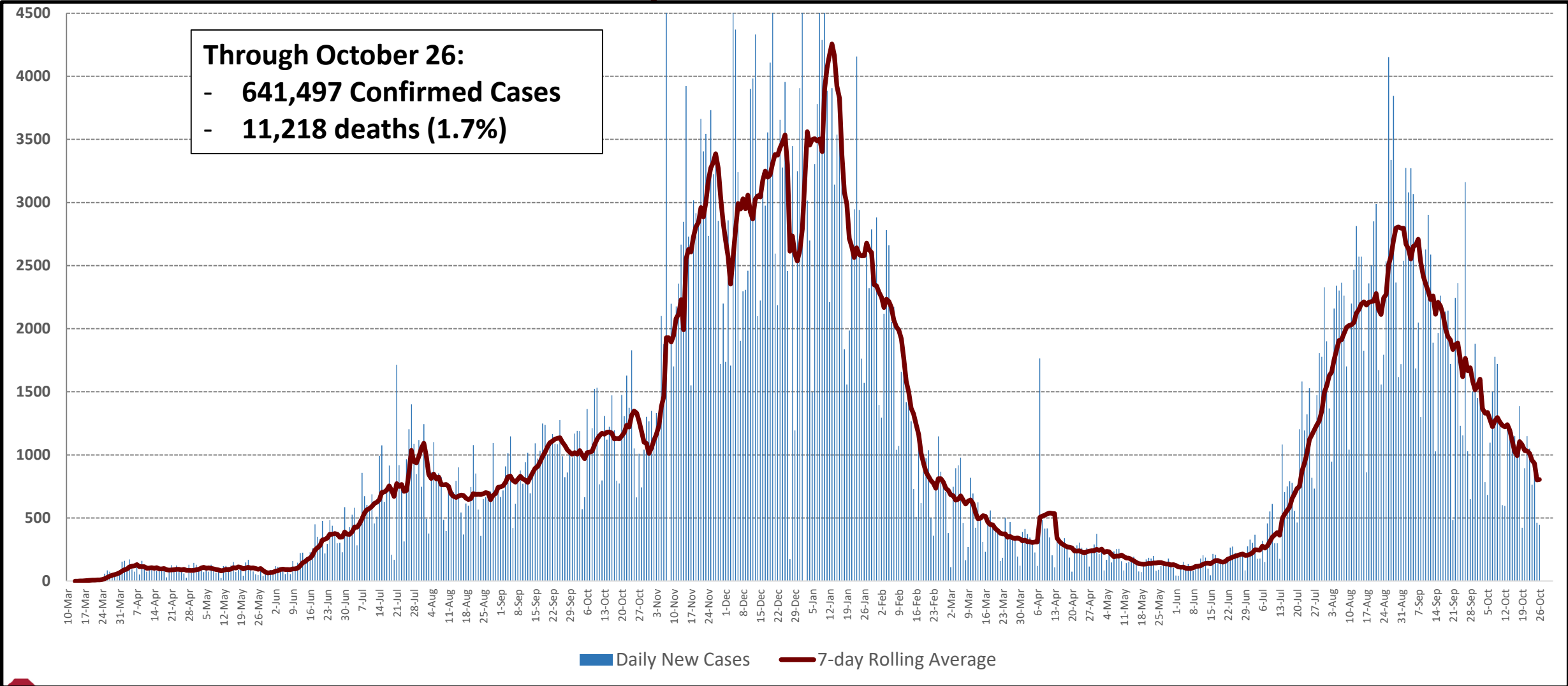
Presentation Outline

- Protecting our most vulnerable.
- Development of the COVID vaccines.
- How do the COVID vaccines work?
- Debunking some of the misconceptions.

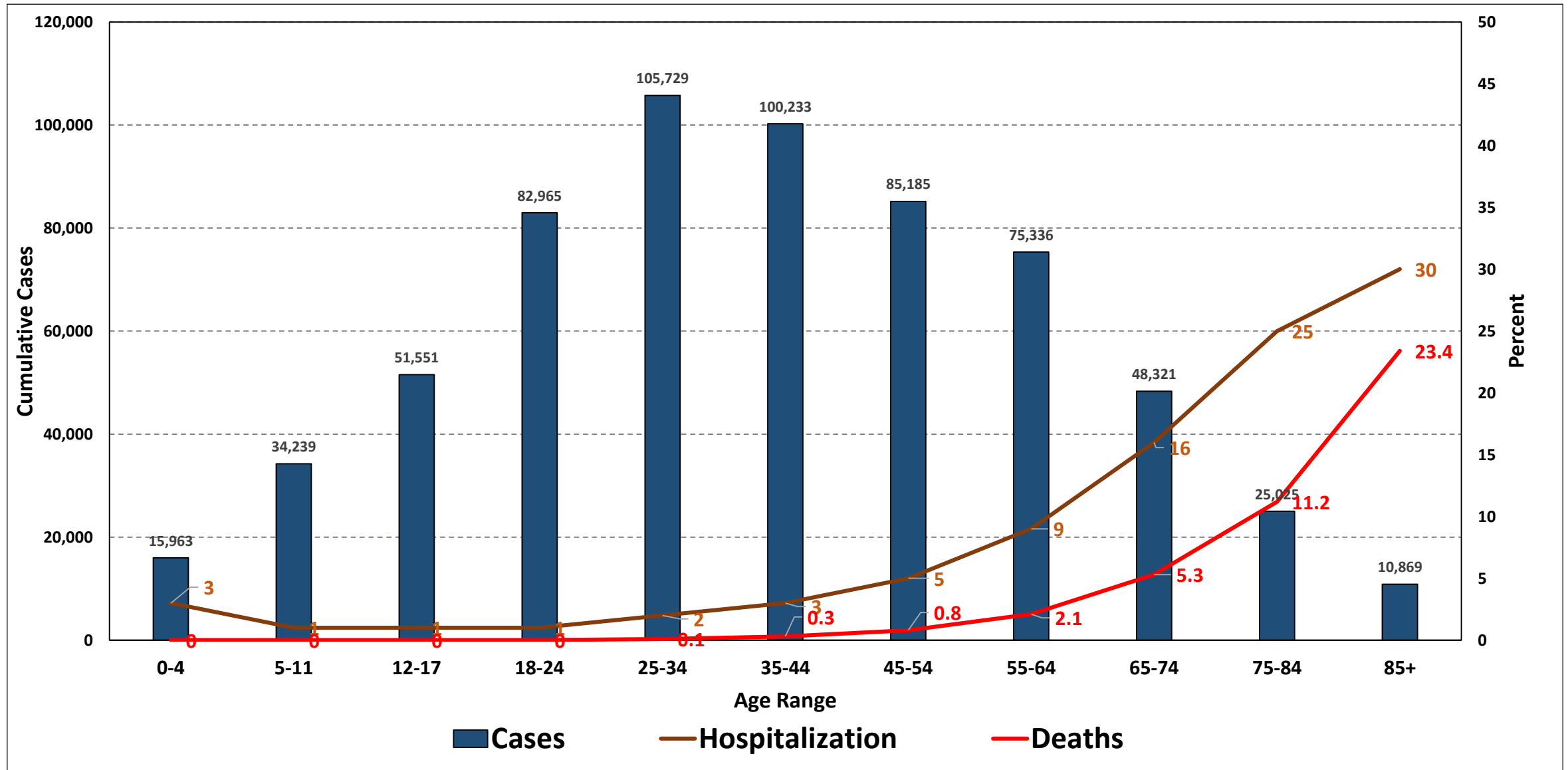
Daily New Cases with 7-day Rolling Average

Oklahoma – We're in a better place now!

Through October 26:
- 641,497 Confirmed Cases
- 11,218 deaths (1.7%)



Age and COVID – Our elderly are at the greatest risk!



DISTRIBUTION OF RECENT COVID-19 HOSPITAL ADMISSIONS BY VACCINATION STATUS AND AGE GROUP AS OF OCTOBER 4, 2021

Vaccination Status	Age Group	Hospital Admissions in the last 30 days***	Percentage within Vaccination Status Category	Percentage of Total Hospitalizations
Non-Vaccinated	Under 1- 4	44	2.2%	1.9%
	5-17	37	1.9%	1.6%
	18-35	249	12.6%	10.9%
	36-49	367	18.5%	16.0%
	50-64	580	29.3%	25.3%
	65+	703	35.5%	30.7%
	Unknown	1	0.1%	0.0%
	Total	1,981	100.0%	86.6%
Fully Vaccinated*	5-17	1	0.4%	0.0%
	18-35	2	0.9%	0.1%
	36-49	9	3.9%	0.4%
	50-64	48	20.7%	2.1%
	65+	172	74.1%	7.5%
	Total	232	100.0%	10.1%
Partially Vaccinated**	5-17	2	2.7%	0.1%
	18-35	6	8.0%	0.3%
	36-49	7	9.3%	0.3%
	50-64	22	29.3%	1.0%
	65+	38	50.7%	1.7%
	Total	75	100.0%	3.3%
Total Hospitalizations	2,288			

94.8% of hospitalizations in fully vaccinated individuals were in people 50 years of age and older.

How did we get vaccines for COVID so fast?

The history of mRNA vaccines

*“In late 1987, Robert Malone performed a landmark experiment. He mixed strands of messenger RNA with droplets of fat, to create a kind of molecular stew. Human cells bathed in this genetic gumbo absorbed the mRNA, and began producing proteins from it.”**

Proc. Natl. Acad. Sci. USA
Vol. 86, pp. 6077–6081, August 1989
Biochemistry

Cationic liposome-mediated RNA transfection

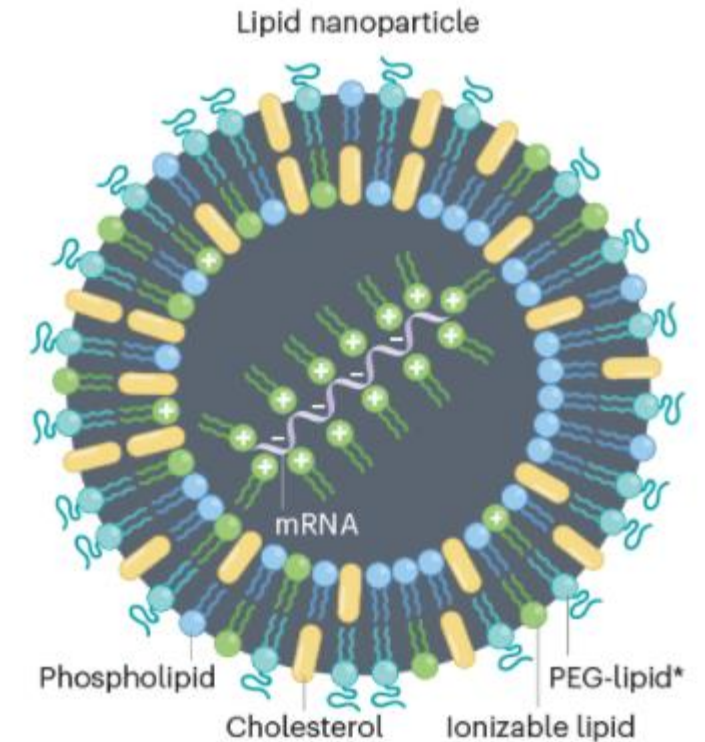
[cationic lipid vesicles/*N*-[1-(2,3-dioleoyloxy)propyl]-*N,N,N*-trimethylammonium chloride (DOTMA)/translation]

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Development of the COVID vaccines

Culmination of years of research on both sequencing and stabilizing mRNA for injection and development of the “fatty nanoparticle” technology that surrounds the mRNA and makes the vaccine viable.



How did it happen so fast?

A long story short.....

- mRNA vaccine technology already existed – in trials for other diseases
- The genetic sequence for SARS-CoV-2 was published on January 10, 2020
- Vaccine developed and injected into mice by February 4
- Phase 1 clinical trial initiated in humans on March 14
- Phase 3 clinical trials began enrolling in July 2020
- Results of Moderna and Pfizer clinical trials presented to the FDA
- First EUA issued on December 11

Multiple steps done in parallel rather than serial steps. No steps skipped.



OPERATION WARP SPEED VACCINE DISTRIBUTION PROCESS

IN SUPPORTING THE DISTRIBUTION & ADMINISTRATION OF COVID-19 VACCINES, OWS HAS FOUR KEY GOALS, TENETS, AND ARCHITECTURE

Advanced purchase agreement for EUA/Licensed vaccine

Companies were paid by the federal government to start producing stockpiles of the vaccines before they knew if they would work!

Efficacy Results - starting Nov 2020



Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine

FP Polack et al. for the C4591001 Clinical Trial Group

- 2-dose regimen of BNT162b2
- 43,548 participants randomized
- **95% Ve** (95% CI 90.3; 97.6)
- **EUA issued December 11, 2020**
- FDA approval August 23, 2021



Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

LR Baden et al. for the COVE Study Group

- 2-dose regimen of mRNA-1273
- 30,420 participants randomized
- **94.1% Ve** (95% CI 89.3; 96.8)
- **EUA issued Dec 18, 2020**



Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19

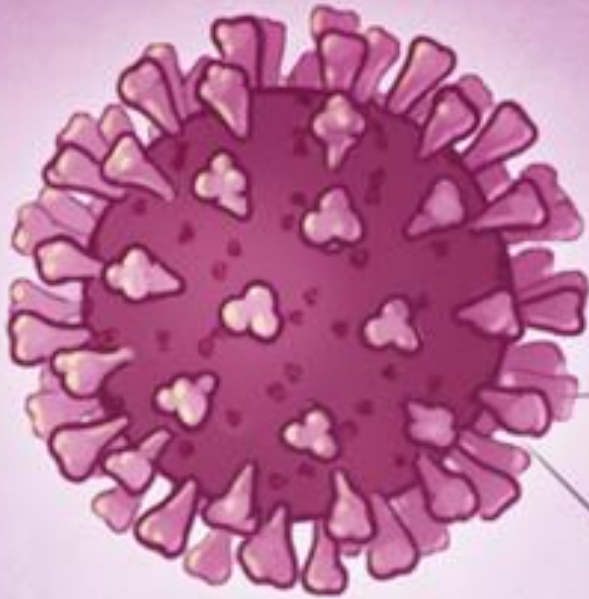
J Sadoff et al. for the ENSEMBLE Study Group

- 1-dose regimen of Ad26.COV2.S
- 44,325 participants randomized
- **66.1% Ve** (95% CI 55.0; 74.8) overall
- **US: 72% Ve** (95% CI 58.2; 81.7)
- **EUA issued Feb 27, 2021**



How do the COVID vaccines work?

SARS-CoV-2



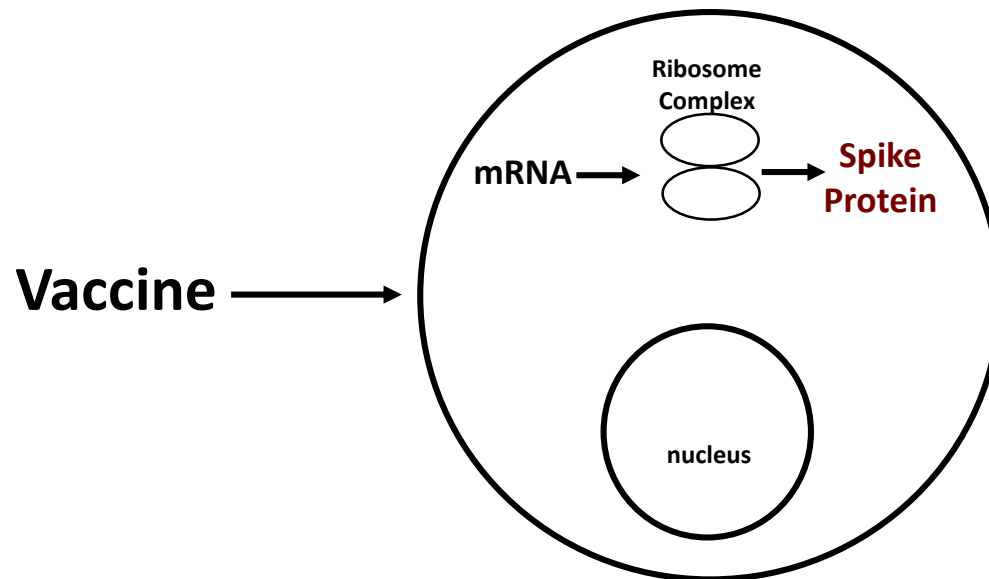
The surface of **SARS-CoV-2**, the virus that causes COVID-19, is covered in spike proteins that help the virus enter human cells. The spike protein is the target for COVID-19 vaccines.



Spike protein

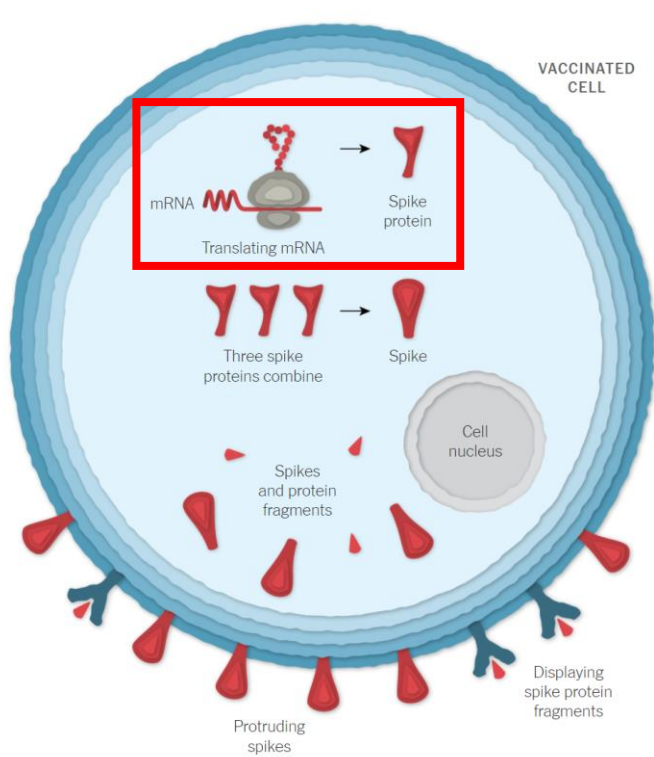
How do the vaccines work?

- The end result for all three approved vaccines (Pfizer, Moderna, and Janssen) is the same:
 - Ultimately all of the vaccines get mRNA into the cytoplasm of the cell that will encode the production of the spike protein of the SARS-CoV-2 virus
 - The spike protein is expressed on the surface of those cells and also released into the circulation to stimulate an immune response

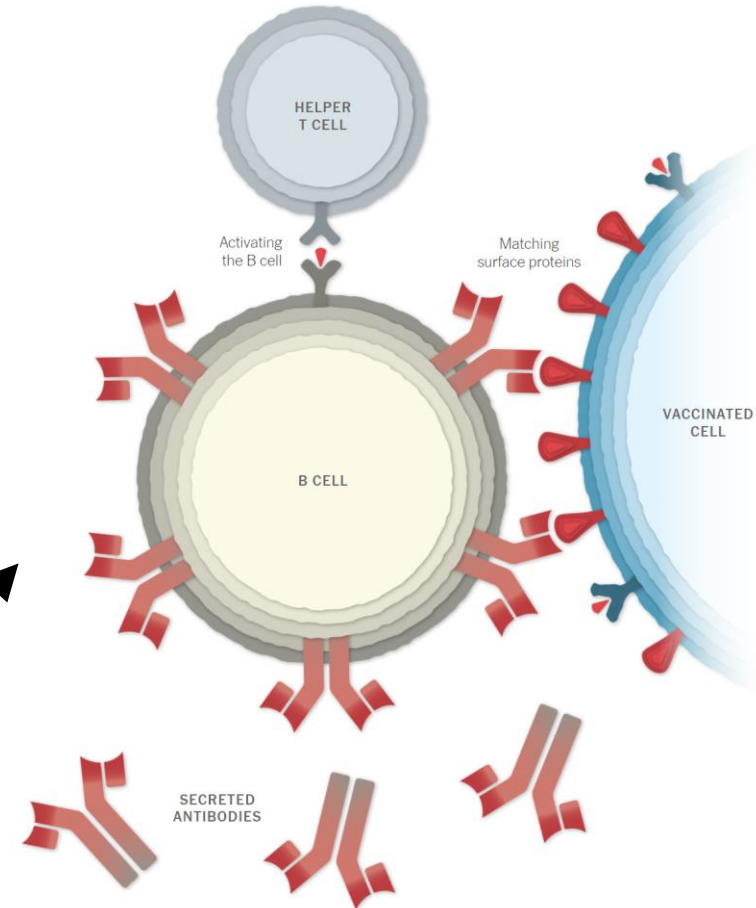
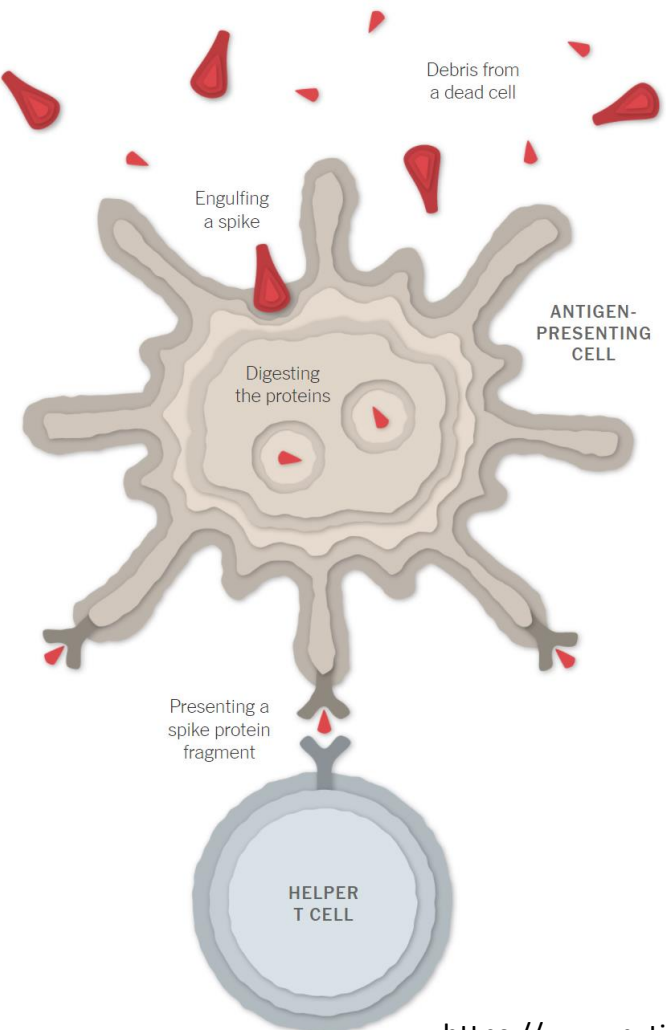


Spike protein expressed on the surface of the cell and released into the circulation.

Recognized as “foreign” generating an immune response.



The spike protein is recognized as “foreign” by the immune system



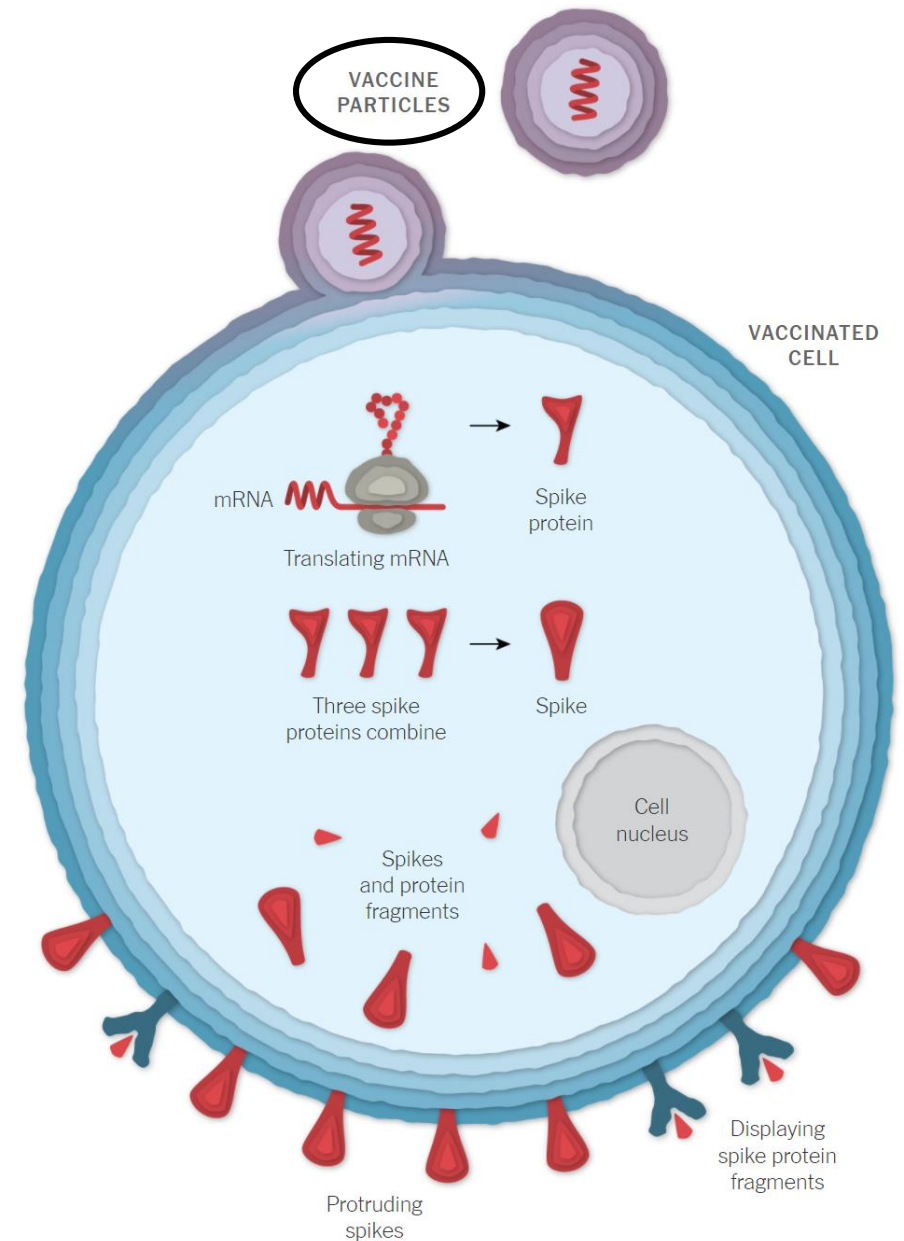
mRNA is translated by the ribosomes to produce the spike protein that is expressed on the surface of the cell and released into the circulation

End result – production of **anti-spike antibodies** and activated killer T-cells

How do the mRNA and Janssen vaccines differ to stimulate the production of spike protein?

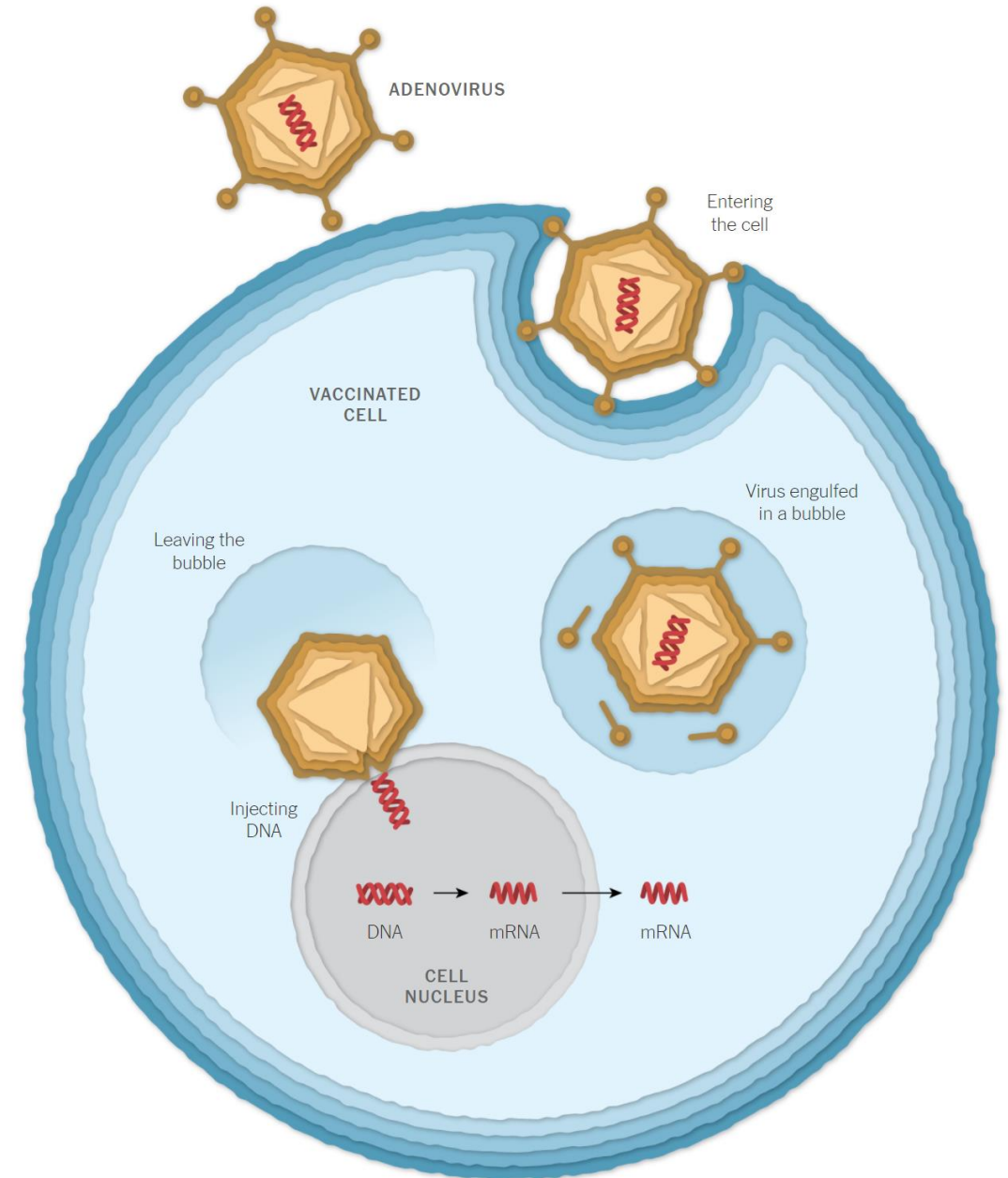
mRNA Vaccines (Pfizer and Moderna)

- The vaccine that is injected contains mRNA that will encode for the spike protein. That mRNA is surrounded with a lipid nanoparticle that prevents immediate breakdown of the mRNA on injection.
- The mRNA from the vaccine is taken up by the cells to enter the ribosome complex to produce spike protein.



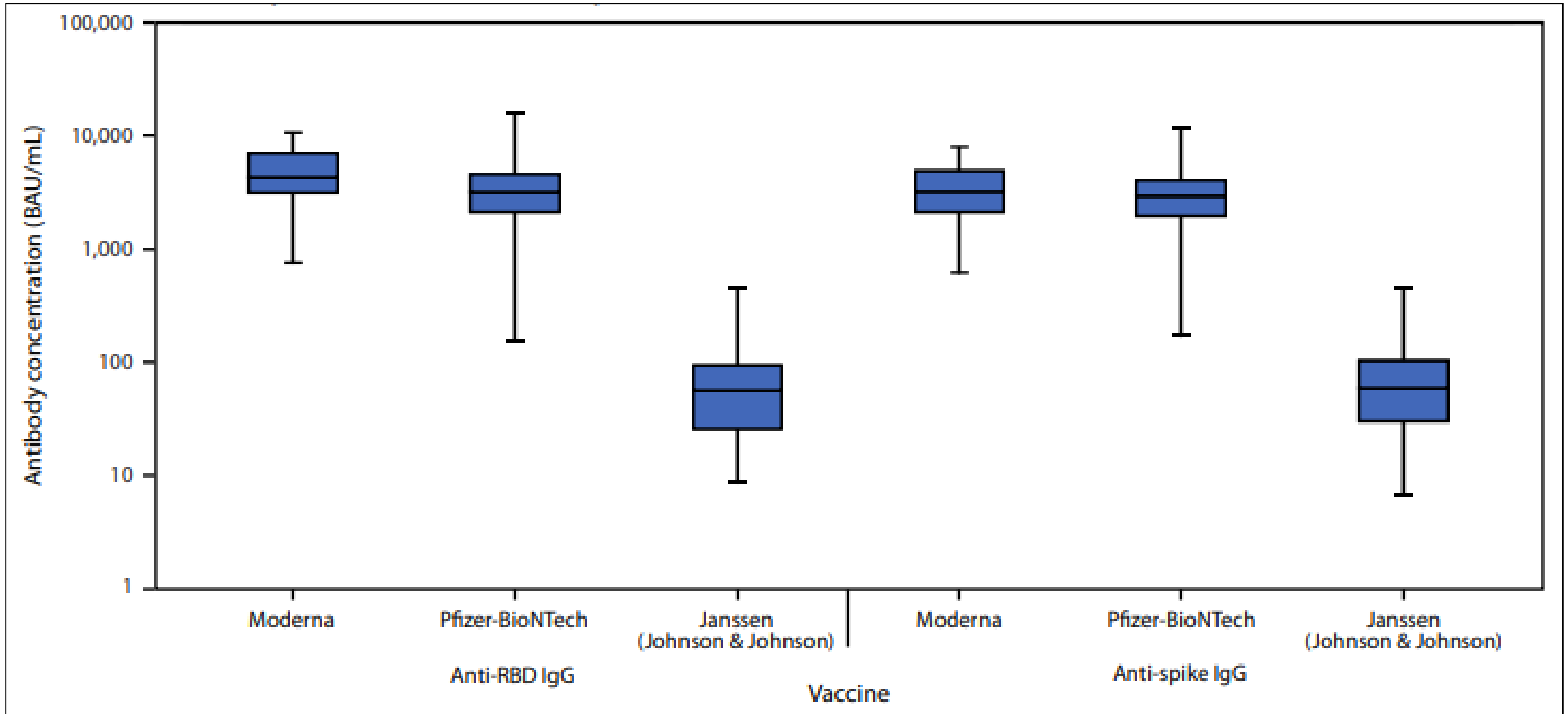
Janssen (J&J) Vaccine

- A small piece of DNA from the adenovirus is modified with the spike protein gene that encodes for production of the mRNA. The adenovirus cannot replicate.
- The adenovirus enters the cell and injects the DNA into the cell nucleus where it is transcribed to mRNA.
- The mRNA enters the cytoplasm of the cell to be translated by ribosomes to produce spike protein.



How effective are the vaccines?

Antibody Levels after Full Vaccination



Effectiveness to prevent hospitalization

Subgroup	No. of Patients	Positive for SARS-CoV-2 <i>no. (%)</i>	Vaccine Effectiveness (95% CI) %
Effectiveness against hospitalization			
BNT162b2 vaccine Pfizer			
Unvaccinated (referent)	20,406	3695 (18.1)	
Partially vaccinated			
Dose 1	1,444	140 (9.7)	33 (18–46)
Dose 2	1,348	57 (4.2)	73 (63–81)
Fully vaccinated — 2 doses	8,500	163 (1.9)	87 (85–90)
mRNA-1273 vaccine Moderna			
Unvaccinated (referent)	20,406	3695 (18.1)	
Partially vaccinated			
Dose 1	1,639	91 (5.6)	68 (59–75)
Dose 2	1,134	50 (4.4)	74 (64–82)
Fully vaccinated — 2 doses	6,374	95 (1.5)	91 (89–93)
Ad26.COVS vaccine Janssen			
Unvaccinated (referent)	10,761	2006 (18.6)	
Fully vaccinated — 1 dose	707	30 (4.2)	68 (50–79)

Who can't take the COVID vaccines

(Hint: Medical Contraindications are Rare)

- CDC considers a history of the following to be a contraindication to vaccination with COVID-19 vaccines:
 - **Severe allergic reaction** (e.g., anaphylaxis) after a previous dose or to a component of the COVID-19 vaccine (2.5 cases per 10,000 doses)
 - Immediate allergic reaction of any severity to a previous dose or known (diagnosed) allergy to a component of the COVID-19 vaccine

Very uncommon:

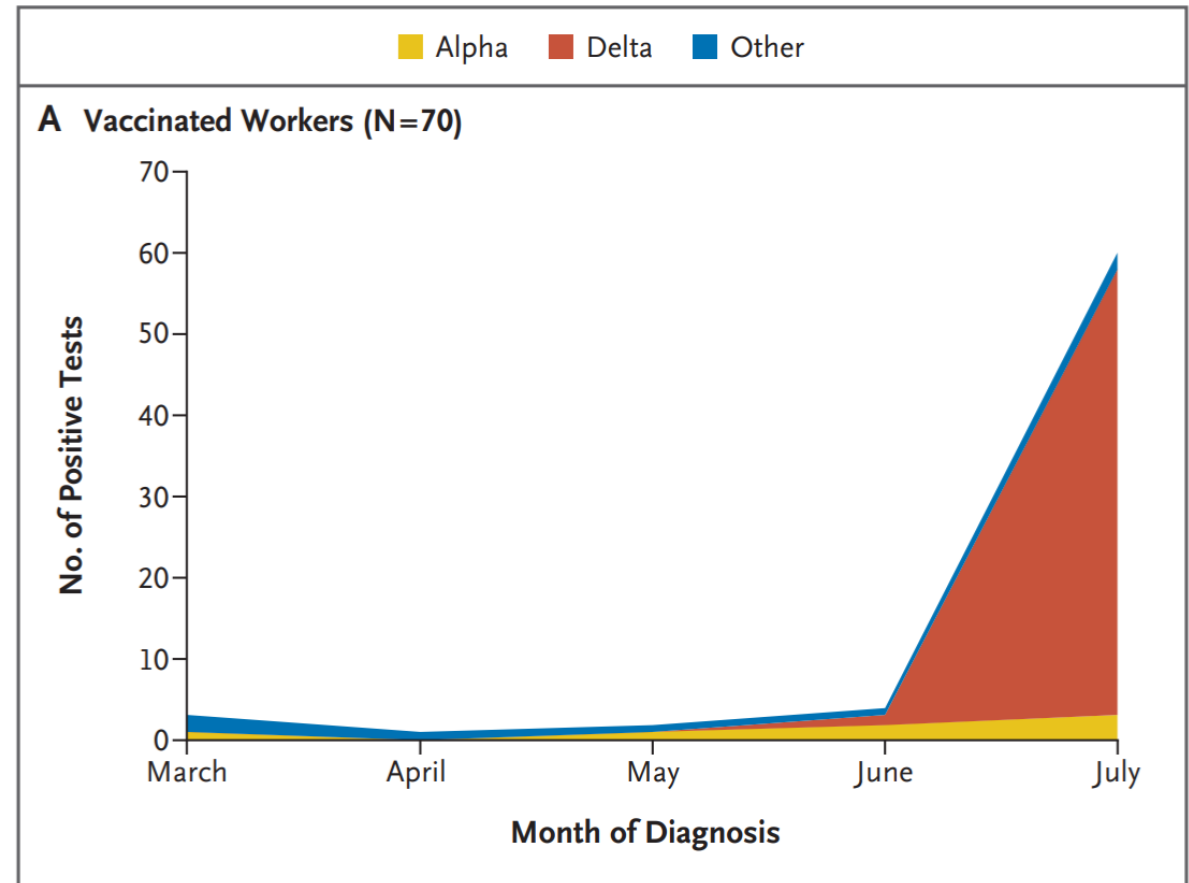
- mRNA vaccine – polyethylene glycol allergy (PEG)
- J&J vaccine – Polysorbate 80 allergy

Too many people are being told that they shouldn't take the vaccine!

What about boosters?

Healthcare Workers and the Delta Variant

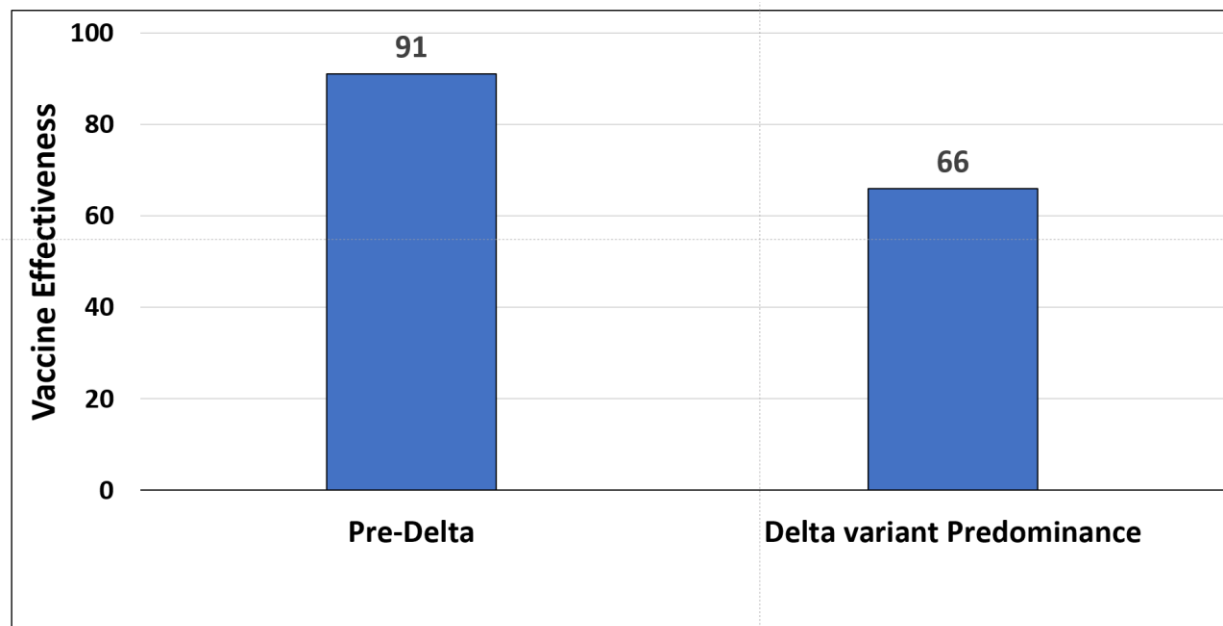
- Study from the University of California San Diego
- 87% of the workforce was fully vaccinated against SARS-CoV-2
- **Vaccine effectiveness pre-delta variant was 93.9% but fell to 65.5% by July 2021**



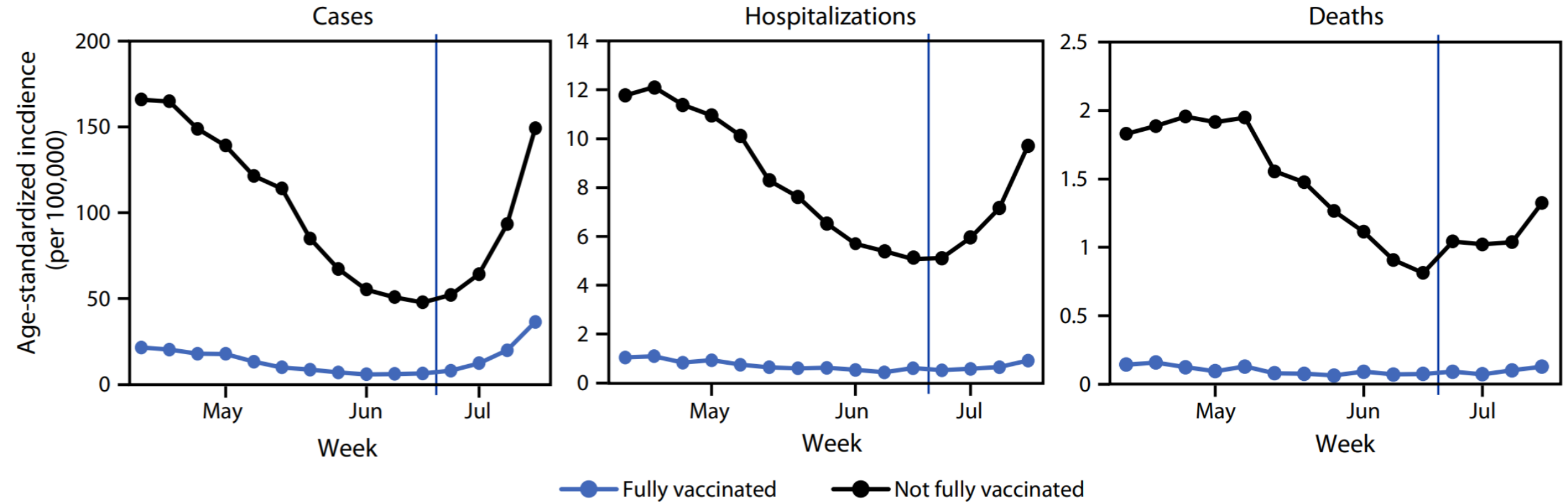
Effectiveness of COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Frontline Workers Before and During B.1.617.2 (Delta) Variant Predominance — Eight U.S. Locations, December 2020–August 2021

Ashley Fowlkes, ScD¹; Manjusha Gaglani, MBBS²; Kimberly Groover, PhD³; Matthew S. Thiese, PhD⁴; Harmony Tyner, MD⁵; Katherine Ellingson, PhD⁶; HEROES-RECOVER Cohorts

Vaccine effectiveness declined from 91% before predominance of the delta variant to 66% since delta variant became predominant at these eight U.S. locations.



Monitoring Incidence of COVID-19 Cases, Hospitalizations, and Deaths, by Vaccination Status — 13 U.S. Jurisdictions, April 4–July 17, 2021



Booster doses should be no surprise for COVID vaccines (many other vaccines require a series of shots)

- **Pfizer primary series** – two 30 mcg doses three weeks apart; 30 mcg booster dose after 6 months
- **Moderna primary series** – two 100 mcg doses four weeks apart; applied for a booster dose of 50 mcg after 6 months
- **Johnson & Johnson** – vector vaccine (0.5 mL dose)
 - Everyone should get a booster dose!
 - Booster shot at 2 months provided a four- to six-fold increase in antibodies
 - Booster shot at six months provided 12-fold increase in antibodies

Who should get a booster?

- Anyone 65 years of age and older
- Anyone 18-64 years of age who are at risk of COVID complications
- Anyone 18-64 who works in a high-risk occupation (healthcare workers, first responders, teachers, etc) and in certain settings such as nursing homes, assisted living, prisons
- Anyone who got one dose of the Johnson & Johnson vaccine (regardless of age or underlying conditions)

Mix and Match COVID Vaccines

- FDA: “A single booster dose of any of the available COVID-19 vaccines may be administered as a heterologous booster dose following completion of primary vaccination with a different available COVID-19 vaccine.”
- Antibody levels in people who were originally vaccinated with Johnson & Johnson’s single shot were about five times higher after they received matching Johnson & Johnson boosters. Those who originally received Johnson & Johnson’s vaccine but were given the Moderna vaccine had antibody levels that were more than 50 times higher.

Other falsehoods.....

COVID Vaccines and Pregnancy

- American College of Obstetricians and Gynecologists and now the CDC strongly recommend COVID vaccination for pregnant patients.
- Study of 869,079 from 499 US academic medical centers.
- *This retrospective cohort study found that women with COVID-19 giving birth had higher rates of mortality (15.4X), intubation (14.3X), ICU admission (5.8X), and preterm birth than women without COVID-19.*

JAMA
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Original Investigation | Obstetrics and Gynecology

Characteristics and Outcomes of Women With COVID-19 Giving Birth at US Academic Centers During the COVID-19 Pandemic

Justine Chinn, BS; Shaina Sedighim, MD; Katharine A. Kirby, MS; Samuel Hohmann, PhD; Afshan B. Hameed, MD; Jennifer Jolley, MD; Ninh T. Nguyen, MD

The vaccines affect fertility or pregnancy

- CDC recommends:
 - COVID-19 vaccination is recommended for everyone 12 years of age and older, including people who are trying to get pregnant now or might become pregnant in the future, as well as their partners.
 - Currently no evidence shows that any vaccines, including COVID-19 vaccines, cause fertility problems (problems trying to get pregnant) in women or men.

“Remember, the vaccines do not affect your DNA. They do not affect a pregnant woman’s placenta. They do not interact with anything in your body that could cause fertility problems.”

Many misconceptions.....

- I've already had COVID-19 – I don't need the vaccine (you should)
- The vaccines were rushed (I already explained)
- I don't need to wear a mask or take precautions since I am vaccinated (wrong)
- I can get COVID from the vaccine (You can't)
- The side effects of the COVID vaccines are common (Exceedingly rare)
- The vaccine changes your DNA (It does not touch your DNA)
- There are controversial substances in the vaccine (very "clean" vaccines)
- Vaccines make you magnetic (Nope)
- The government is microchipping us (You already did that with your cell phone)
- Vaccine will cause long term complications (RNA vaccines have been studied for years – no long term complications)

The vaccines are very safe and very effective – particularly at preventing severe complications of COVID-19, including death.

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