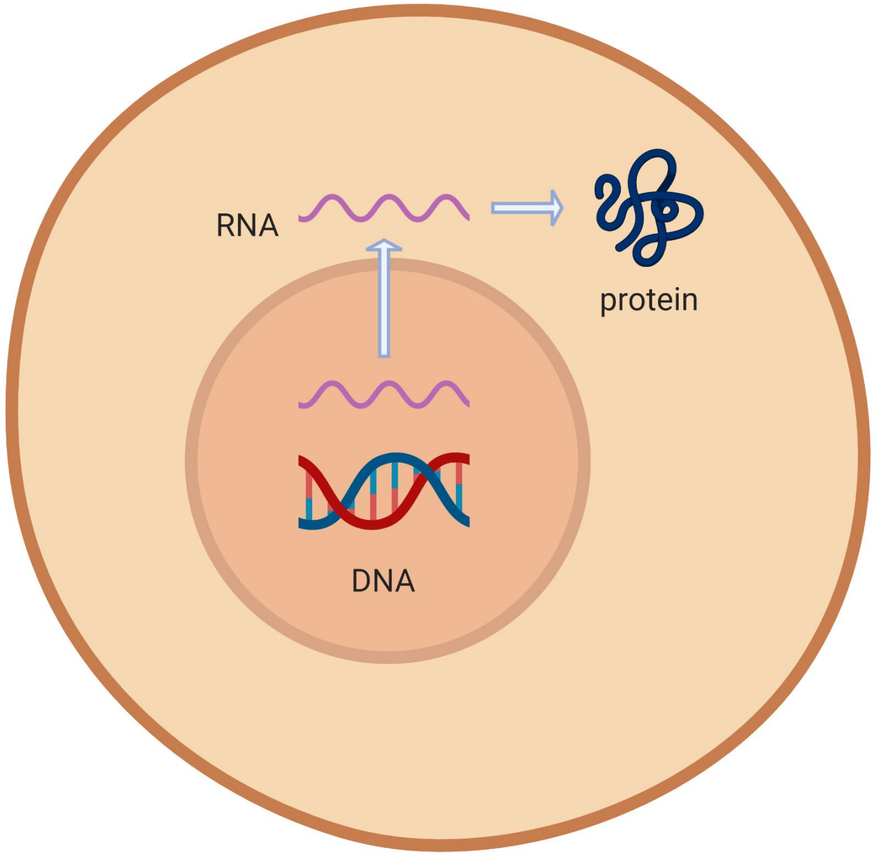
The Central Dogma: DNA->RNA->protein



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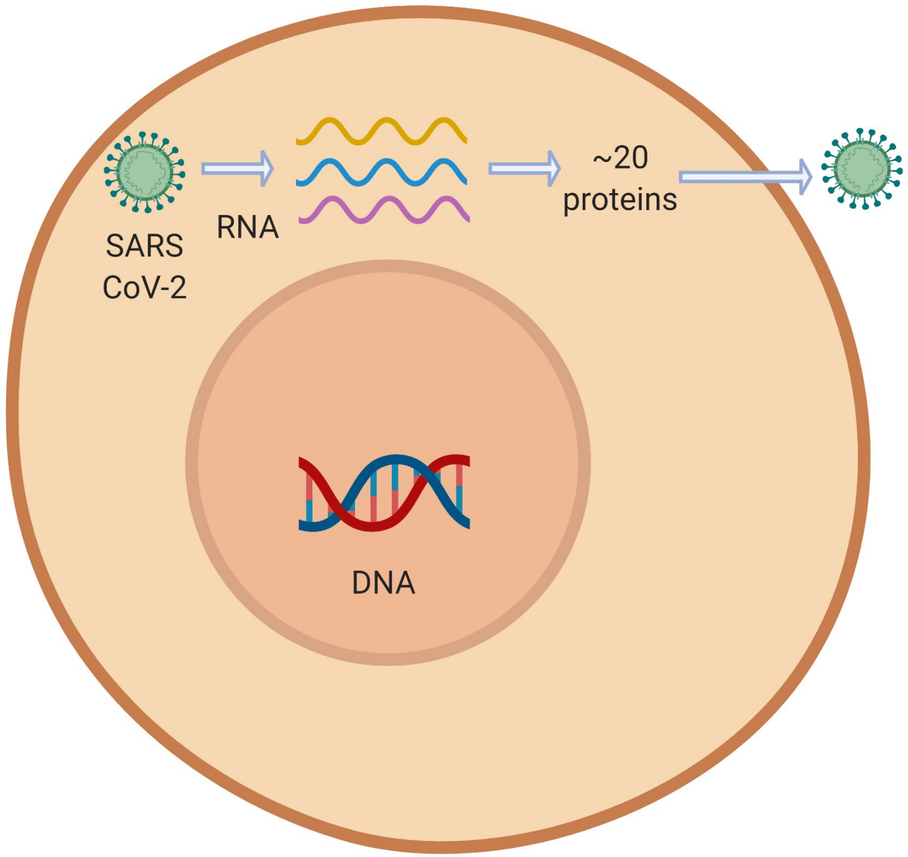
Life Cycle of SARS-CoV-2, the virus that causes COVID-19



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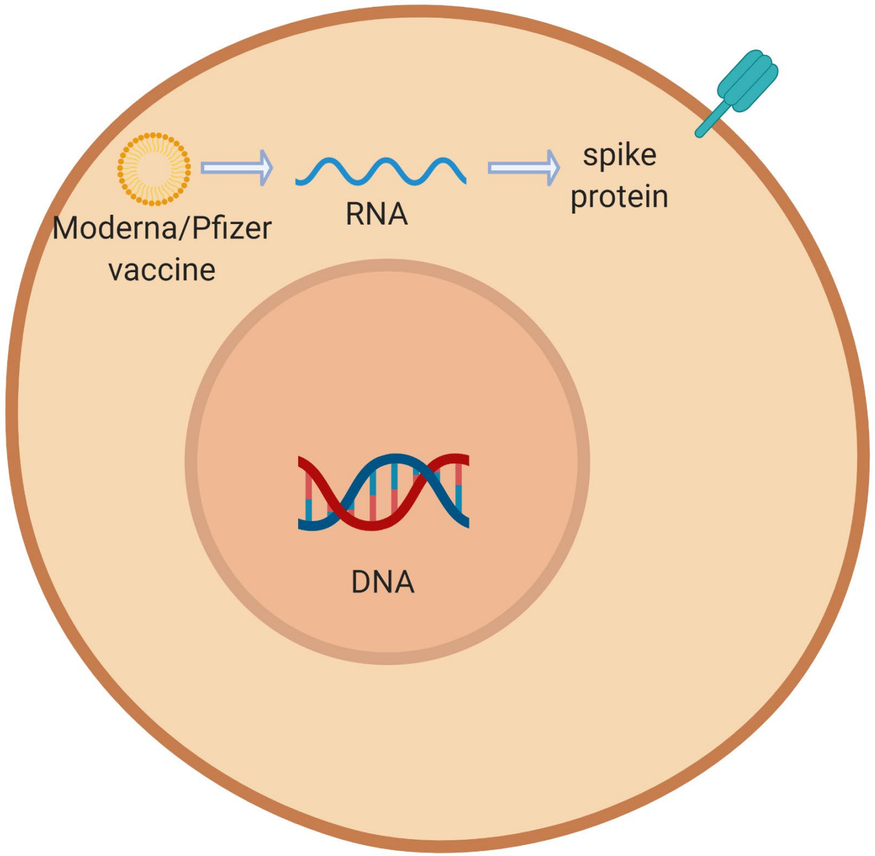
The Moderna and Pfizer/BioNTech vaccines contain just 1 type of RNA



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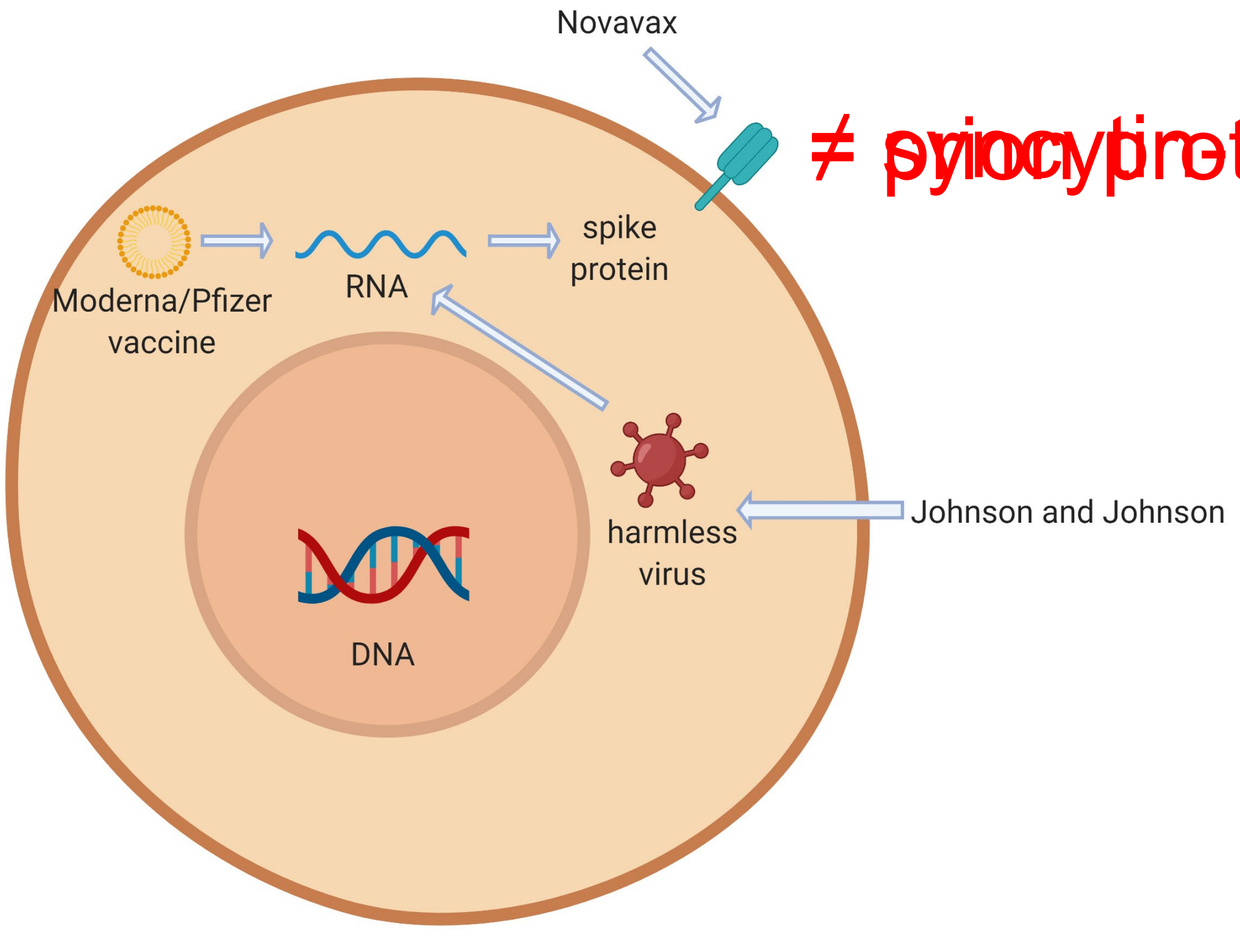
All advanced vaccine candidates produce only the spike protein of the virus



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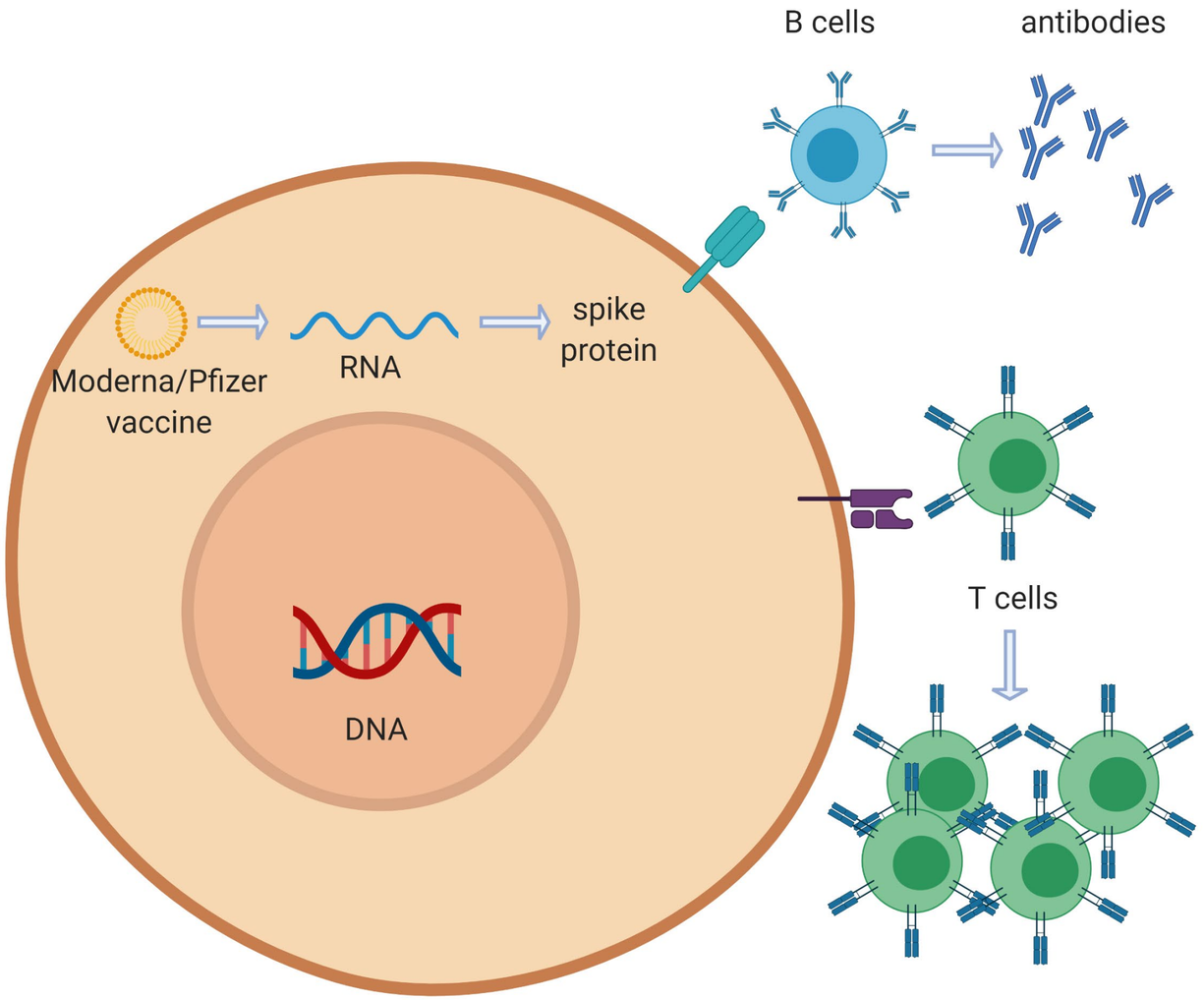
The immune system recognizes spike protein and responds



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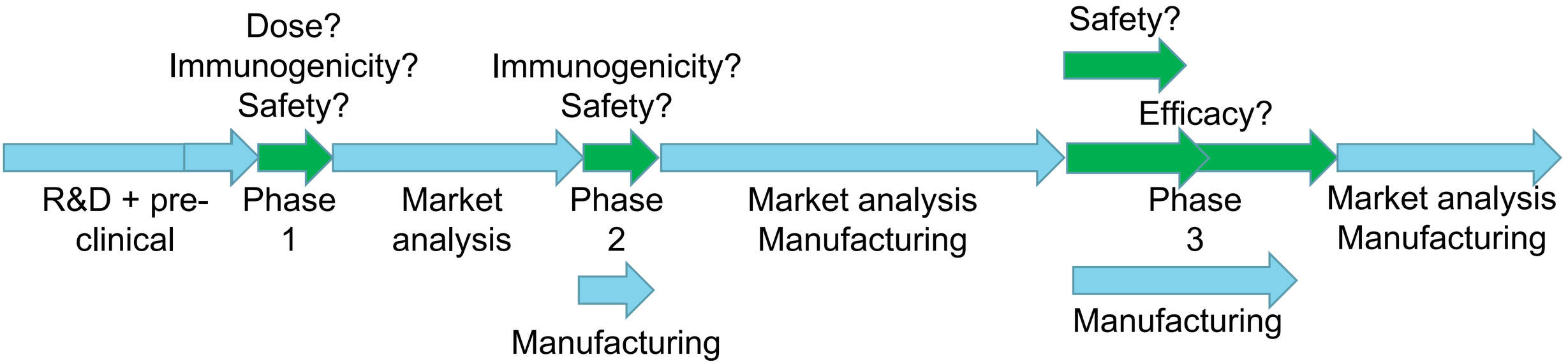
Operation Warp Speed: What was accelerated?



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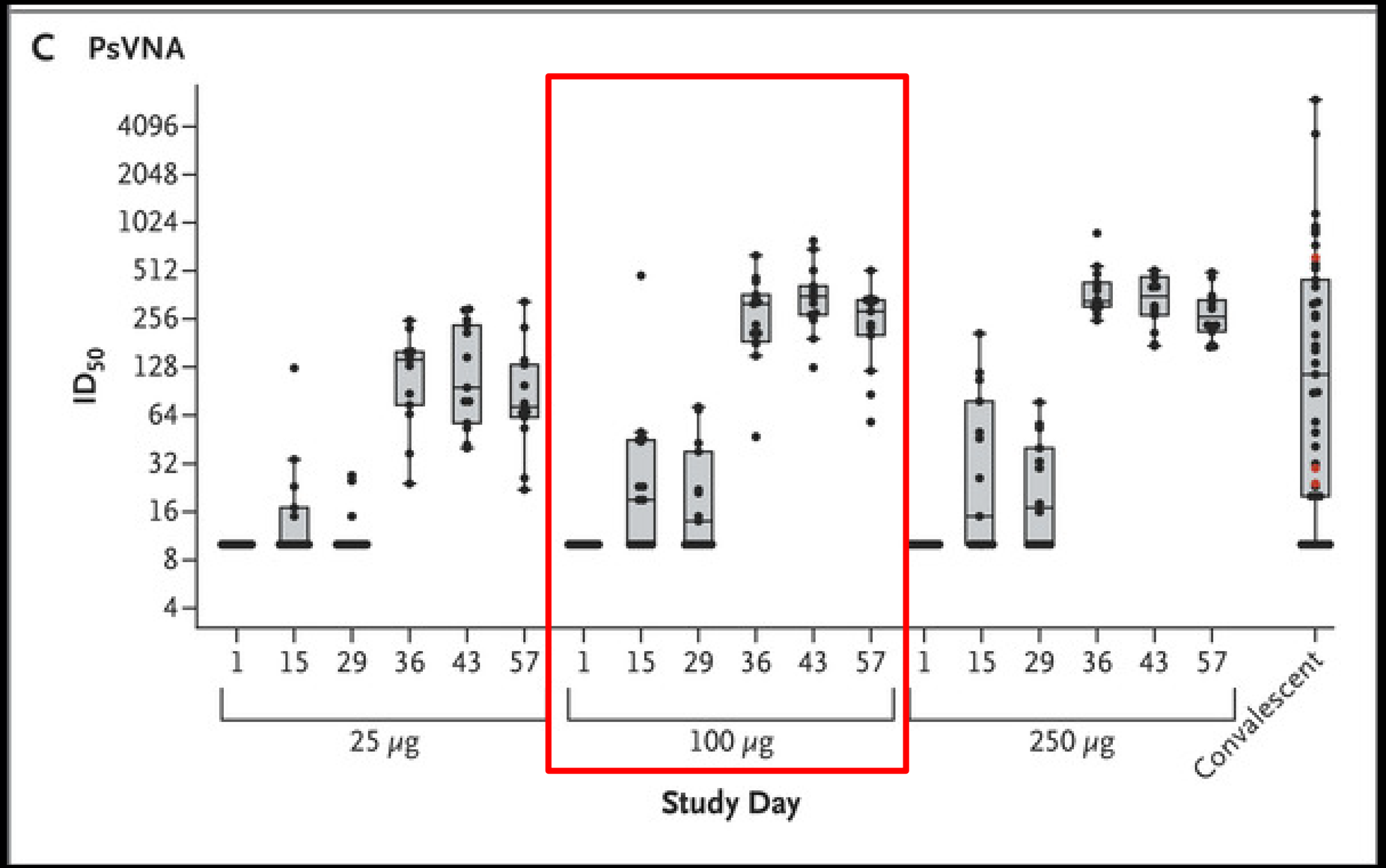
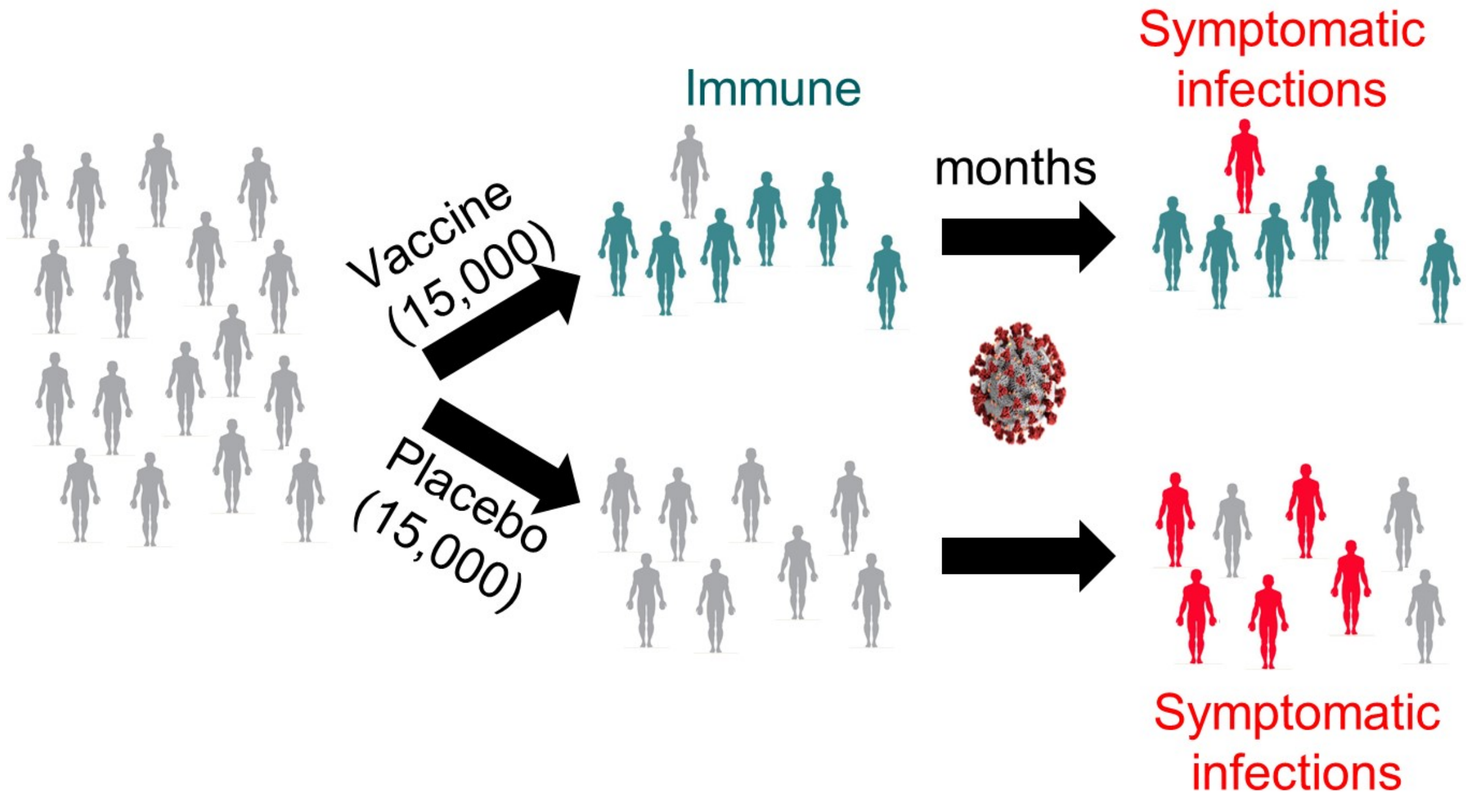
Antibody levels after the Moderna vaccine



LA Jackson et al. N Engl J Med 2020;383:1920-1931.

The NEW ENGLAND JOURNAL of MEDICINE

How are safety and efficacy assessed in a Phase 3 trial?



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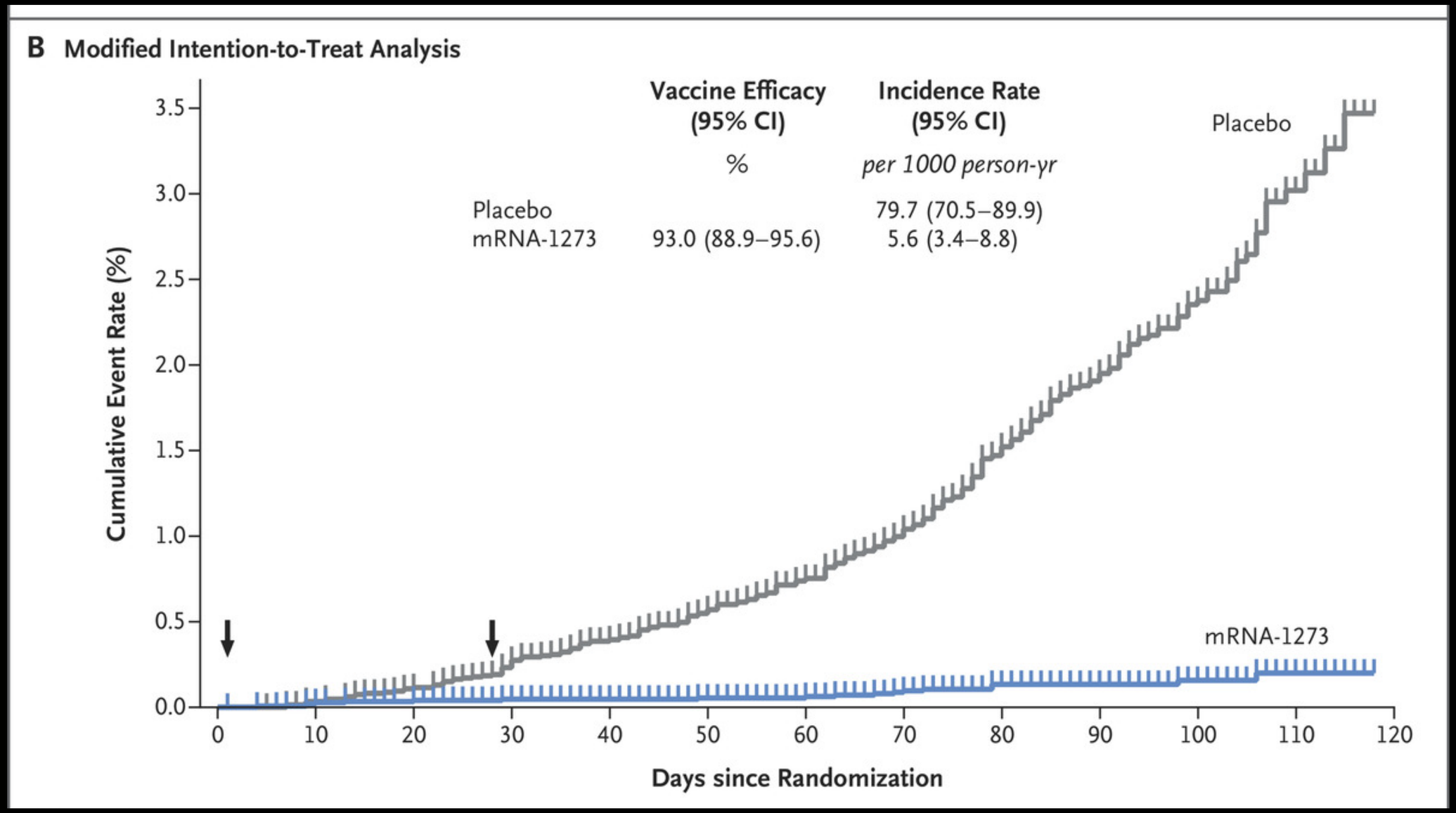
Efficacy of the Moderna vaccine



LR Baden et al. N Engl J Med 2020. DOI: 10.1056/NEJMoa2035389

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Phase 3 COVID-19 Vaccines

	Pfizer/BioNTech	Moderna	AstraZeneca/Oxford
Efficacy:	95% (162 vs. 8)	94% (185 vs. 11)	?? (68-90%)
Adverse events:	mild/moderate	mild/moderate	mild/moderate

Not yet authorized
by the FDA

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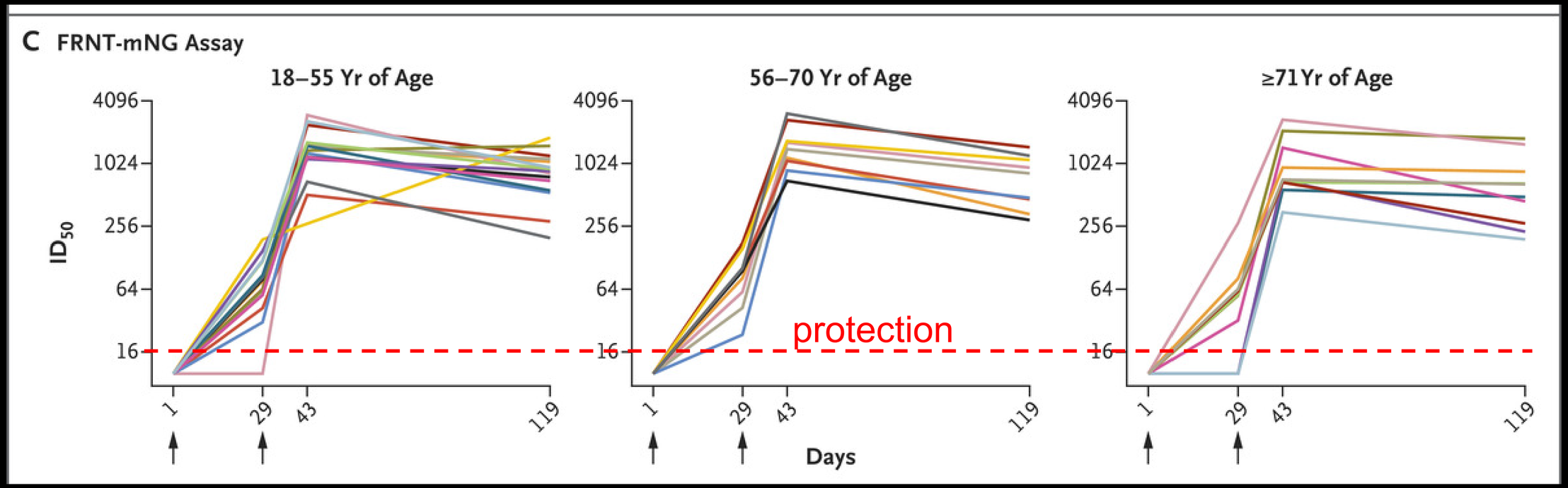
Protective antibody levels are stable over time after vaccination.



AT Widge et al. N Engl J Med 2021;384:80-82.

The NEW ENGLAND JOURNAL of MEDICINE

How is it possible that the vaccines were developed so quickly?

- The groundwork had been laid for SARS and MERS vaccines.
- Operation Warp Speed/governmental investment eliminated financial risk.
- Unlike other problem viruses like HIV, the virus can be cleared and generates immunity.
- The pandemic is widespread. Infections occurred quickly in the trials.

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Key Takeaways

- Both the Pfizer/BioNTech and Moderna vaccines are highly efficacious for preventing symptomatic infections
- Overall infections are reduced in early data post-vaccine, likely meaning substantial reductions in overall transmission

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Ready for the COVID-19 Vaccine?

Karl Krupp, PhD, MSc

University of Arizona, Tucson
January 28, 2021

Vaccinating America

- According to the CDC, 18.5 million people have received one dose of a Covid-19 vaccine, and 3.2 million people have been fully vaccinated (01-25-21)[1]
- To date, Alaska, West Virginia, Connecticut, North and South Dakota have vaccinated the highest percentage of their populations.
- Arizona has administered approximately 400,000 doses.
- It is estimated that between 166 and 265 million Americans will have to be vaccinated to end the pandemic[2]

1. CDC. https://covid.cdc.gov/covid-data-tracker/#vaccinations; 2. Cleveland Clinic: https://health.clevelandclinic.org/how-much-of-the-population-will-need-to-be-vaccinated-until-the-pandemic-is-over/

Confidence in the COVID-19 Vaccination

Kaiser Family Foundation survey published 12/15/2020:

- COVID-19 Vaccine Confidence is increasing (63% Sep ➡ 71% Dec)
- 27% say they probably or definitely would not get a COVID-19 vaccine, with highest rates in minority groups (Blacks 35%; Hispanics 29%)
- General population vaccine hesitancy is highest among Republicans (42%), ages 30-49 (36%), and rural residents (35%).

1. Liz Hamel: @lizhamel on Twitter; Ashley Kirzinger @AshleyKirzinger on Twitter; C Muñana & M Brodie. KFF COVID-19 Vaccine Monitor: December 2020; 2. Khubchandani J, Sharma S, Price JH *et al*. COVID-19 Vaccination Hesitancy in the United States: A Rapid National Assessment. *J Community Health,* 2021.

Vaccines A Public Health Success Story

THEN

Annual U.S. disease cases in the 1900s

(JAMA 2007)

NOW

U.S. disease cases in 2016

(CDC 2017)

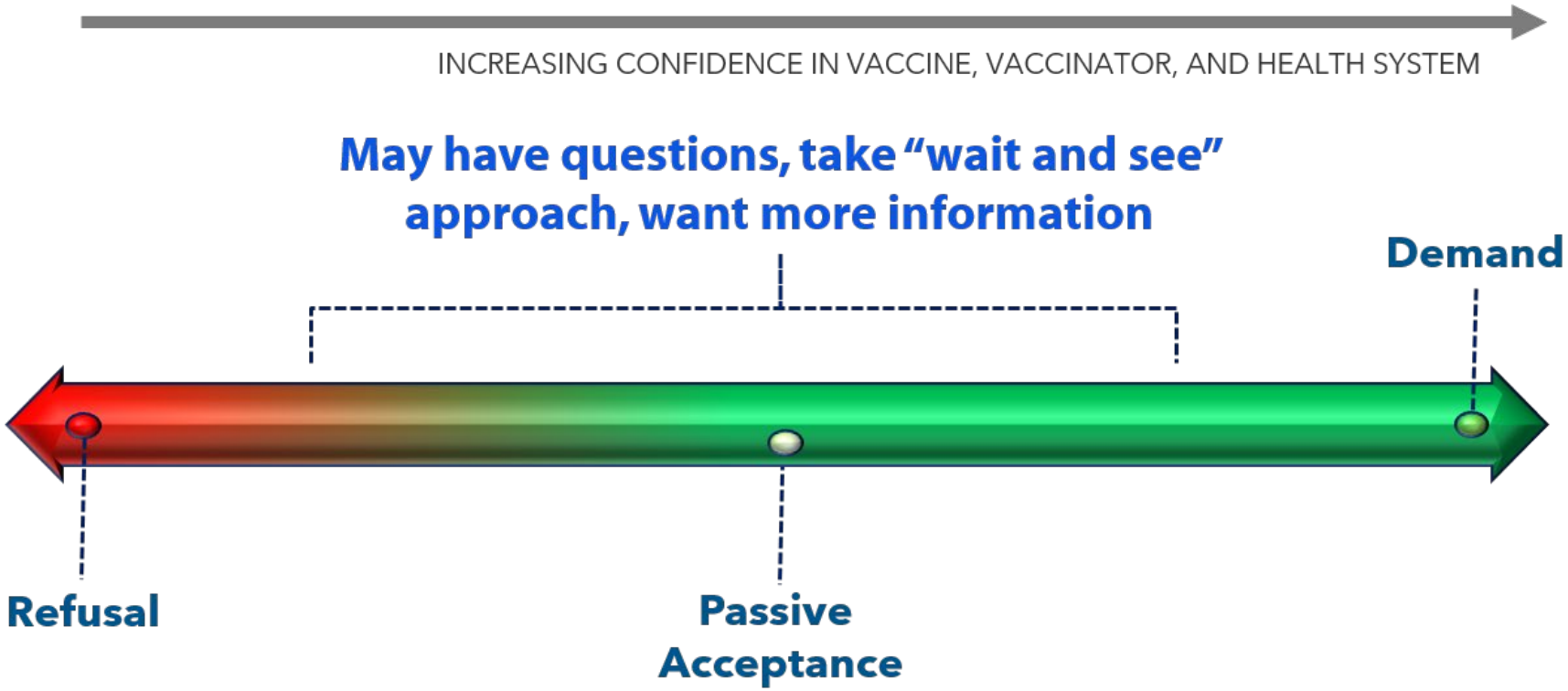
SMALLPOX		MUMPS	
THEN	29,005	THEN	162,344
NOW	0	NOW	2,039
DIPHTHERIA		RUBELLA	
THEN	21,053	THEN	47,745
NOW	0	NOW	1
PERTUSSIS		HEPATITIS A	
THEN	200,752	THEN	117,333
NOW	10,585	NOW	1,222
POLIO (PARALYTIC)		HEPATITIS B	
THEN	16,316	THEN	66,232
NOW	0	NOW	2,040
MEASLES		PNEUMOCOCCUS	
THEN	530,217	THEN	63,067
NOW	85	NOW	11,553

Victims of Our Own Success: U.S. Adults saying Vaccines 'Very Important' to Health of Society is Declining

Thinking about the common vaccines available today such as polio, tetanus, measles and flu, how important do you believe vaccines are to the health of our society today?

Source: Research! America surveys of US adults conducted in partnership with Zogby Analytics in Jan 2020 and with Charlton Research Company in Nov 2008

Willingness to accept a vaccine falls on a continuum



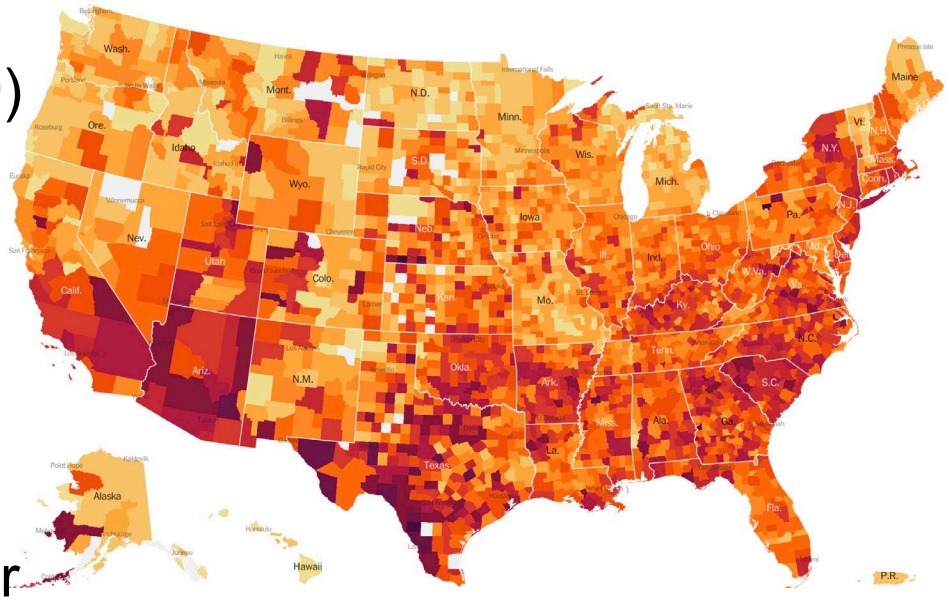
Why are People Hesitant to Vaccinate?

- *Illnesses are rare*
- *Illnesses aren't all that bad*
- *Vaccines cause autism*
- *Vaccines have side effects*
- *The preservatives in vaccines are dangerous*
- *Vaccines aren't tested in my community so they many not be safe*
- *I trust my family, friends and community more than my doctor.*

Source: C McCarthy, Pediatrician at Boston Children's Hospital, Assistant Professor, Pediatrics, Harvard Medical School

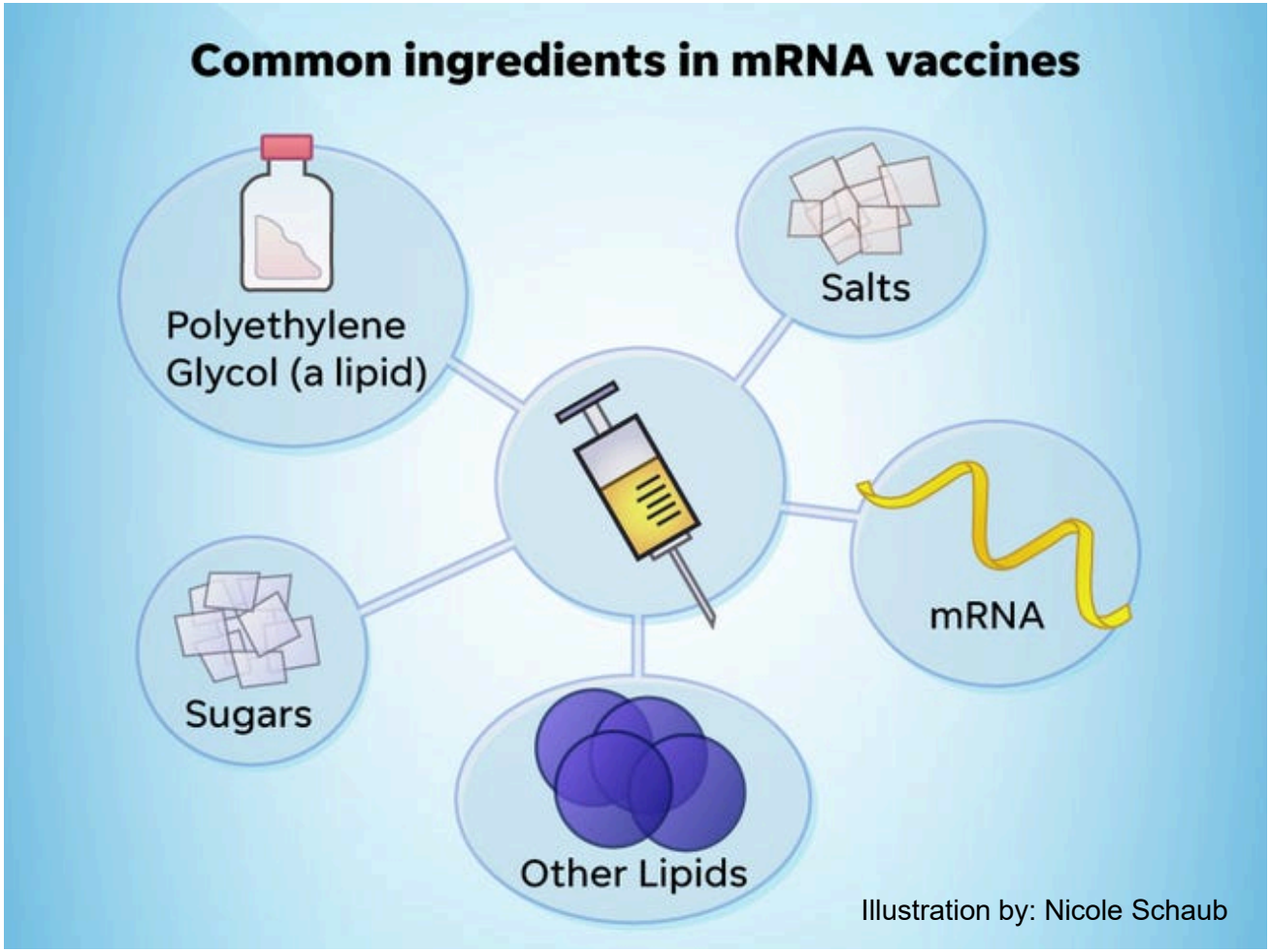
COVID-19 Disease is Widespread and Serious

- 25,439,570 cases[1](1 in 13 Americans have had COVID-19)
- 425,119 deaths[1] (Almost as many people as Atlanta, Georgia)
- 1.7% case fatality rate[1] (Compared with influenza average case fatality of 0.1% for 2018-2019)[2]



1. John Hopkins. Mortality Analysis. https://coronavirus.jhu.edu/data/mortality; 2. Fox, J. Bloomberg Opinion. https://www.bloomberg.com/opinion/articles/2020-08-06/revisiting-how-covid-19-ranks-with-seasonal-flu-and-1918-pandemic

Vaccine ingredients are safe and are modeled on fats, salts, and sugars found in living cells



Pfizer-BioNTech COVID-19 Vaccine

1. mRNA
2. Lipids (modeled on phospholipids and glycophospholipids found in cell walls and membranes)
   - (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis (2-hexyldecanoate), 2 [(polyethylene glycol)-2000]-N,N-ditetradecylacetamide
   - 1,2-Distearoyl-snglycero-3- phosphocholine
   - cholesterol
3. Salts that help balance the acidity in your body:
   - potassium chloride
   - monobasic potassium phosphate
   - sodium chloride
   - dibasic sodium phosphate dihydrate
4. Sugar: sucrose helps the molecules maintain their shape during freezing

Moderna COVID-19 Vaccine

1. mRNA
2. Lipids (Fats) – Protect mRNA as they make their way into your cells.
   - SM-102
   - 1,2-dimyristoyl-rac-glycero3-methoxypolyethylene glycol-2000
   - Cholesterol
   - 1,2-distearoyl-snglycero-3-phosphocholine
3. Acids
   - Acetic acid
4. Acid Stabilizers
   - Tromethamine
   - Tromethamine hydrochloride
5. Salt
   - Sodium acetate
6. Sugar
   - Sucrose

COVID-19 Vaccines Do Have Side-Effects!

- The most common are injection site pain, fatigue, headache, muscle pain, and joint pain.
  - A small number of people have reported fever.
- In the Pfizer vaccine trial, the only two side effects exceeding 2% of the vaccinated population were fatigue (3.8%) and headache (2.0%)
- Side effects are more common after the 2nd dose; younger adults, who have robust immune systems are more likely to experience any side effect compared to older adults.

Side Effects Mean the Vaccine is Working!

Allergic Reactions and COVID-19 Vaccine

- Anaphylaxis associated with COVID-19 vaccines (COVID-19 Task Force 012721)
  - Moderna Vaccine: 2.1 per million doses
  - Pfizer Vaccine: 6.2 per million doses
- All cases were treatable with no fatalities
- Comparisons
  - Varicella Vaccine: 2.1 per million doses[1]
  - Any Vaccine: 1.3 cases per million doses[2]

1. JR Su, PL Moro, CS Ng, *et al*. Anaphylaxis after vaccination reported to the Vaccine Adverse Event Reporting System, 1990-2016. *J Allergy Clin Immunol* 2019; 2. McNeil MM, Weintraub ES, Duffy J, *et al.* Risk of anaphylaxis after vaccination in children and adults. J Allergy Clin Immunol 2016.

Have Current Vaccines been Tested in My Community?

Pfizer/BioNTech

- **43,931** enrolled
- **150** clinical sites
  - 39 U.S. states
- Racial/ethnic distribution
  - **13% -** Hispanic
  - **10% -** African American
  - **6% -** Asian
  - **1% -** Native American
- **45%** ages 56-85

Moderna

- **30,000** enrolled
- **89** clinical sites
  - 32 U.S. states
- Racial/ethnic distribution
  - **63% -** White
  - **20% -** Hispanic
  - **10% -** African American/Black
  - **4% -** Asian
  - **3% -** All others
- **64%** ages 45 and older
  - 39% ages 45-64
  - 25% ages 65+

Sources: https://www.pfizer.com/science/coronavirus/vaccine; https://www.modernatx.com/cove-study ; www.clinicaltrials.gov

mRNA Vaccines are not new

RNA vaccine trials in humans
(not including a large number of cancer vaccines and therapeutic approaches based on mRNA)

Target	Started in	Individuals enrolled[2]	Company	Status	Phase	Registration numbe
CMV	2017	181	Moderna	Fully enrolled	Phase 1	NCT03382405
hMPV/PIV3	2019	114	Moderna	Recruiting	Phase 1	NCT04144348
Zika	2019	120	Moderna	Fully enrolled	Phase 1	NCT04064905
Influenza	2017	156	Moderna	Fully enrolled	Phase 1	NCT03345043
Rabies	2018	53	Curevac	Fully enrolled	Phase 1	NCT03713086
Rabies	2013	101	Curevac	Completed	Phase 1	NCT02241135
Rabies	2014	72	Curevac	Completed	Phase 1	NCT02238756
CMV	2020	452	Moderna	Recruiting	Phase 2	NCT04232280
Chikungunya[1]	2019	39	Moderna	Fully enrolled	Phase 1	NCT03829384

[1]Passive immunity based on *in vivo* mAb expression

[2]Includes individuals who received placebo, some trials are still recruiting

Credit: Florian Krammer, Mt. Sinai

Are the mRNA Vaccines Safe in Pregnancy?

- Moderna animal studies detected no signals of teratogenic effects—effects that would endanger a fetus.
- Pfizer has only interim data from its animal studies, but to date has found no concerning signs for women that are pregnant.

Overcoming Distrust of Healthcare

- Only 6 of 10 Black adults said they trust doctors to do what is right most of the time, compared with 72% of Hispanics and 80% White Americans[1].
- One in 5 Black adults say they were treated unfairly because of their race in the past year when getting health care for themselves or a family member[1].
- Only 56% of Blacks and 62% of Hispanics trust their local hospital compared with 70% of Whites[1].

How You Can Help

- Trusted Messengers[2]
- Trusted Institutions[3]
- Community Champions
- Reversing the rule (A dissatisfied customer will tell between 9-15 people about their experience)
- Reframing Vaccine Side Effects

1. KFF. https://www.kff.org/racial-equity-and-health-policy/press-release/new-nationwide-poll-by-the-kaiser-family-foundation-and-the-undefeated-reveals-distrust-of-the-health-care-system-among-black-americans/; 2, SM Eldred. Trusted Messengers May Help Disenfranchised Communities Overcome Vaccine Hesitancy. https://khn.org/news/article/trusted-messengers-may-help-disenfranchised-communities-overcome-vaccine-hesitancy/; 3. Bonner et al. Trust Building Recruitment Strategies for Researchers Conducting Studies in African American (AA) Churches: Lessons Learned. https://doi.org/10.1177/1049909116666799