ALBANY COLLEGE OF PHARMACY
AND HEALTH SCIENCES

Keeping Eyes on the Shot Clock: Timely Updates on the COVID-19 Pandemic and Vaccination

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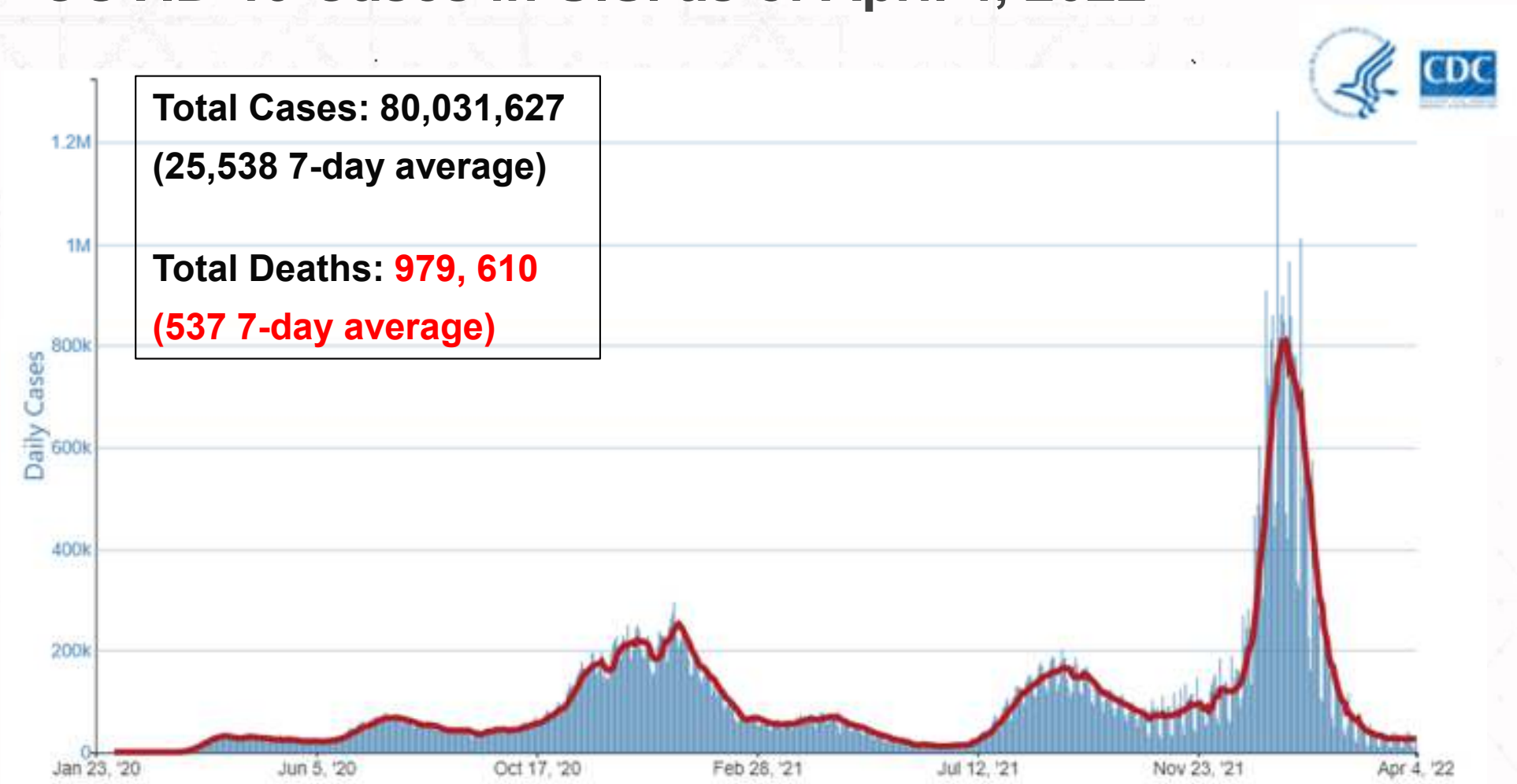
Disclaimers

- This presentation is intended to provide current and accurate information. Its content is not intended to be a substitute for professional medical advice, diagnosis, or treatment.
- Information on COVID-19 and the SARS-CoV-2 virus is rapidly changing, at times daily.
- Dr. Yager has no financial, commercial or promotional interest to declare.

Topics to be covered:

1. Review the latest COVID-19 vaccine products and available data on their respective safety and efficacy.
2. Discuss clinical considerations that guide the use of COVID-19 vaccines and boosters in children and adolescents.
3. Explain how emerging SARS-CoV-2 variants may impact vaccine efficacy and future vaccine development.
4. Identify barriers to COVID-19 vaccine confidence and create effective communication strategies when conversing with patients about COVID-19 vaccination, particularly in children and adolescents.

COVID-19 Cases in U.S. as of April 4, 2022

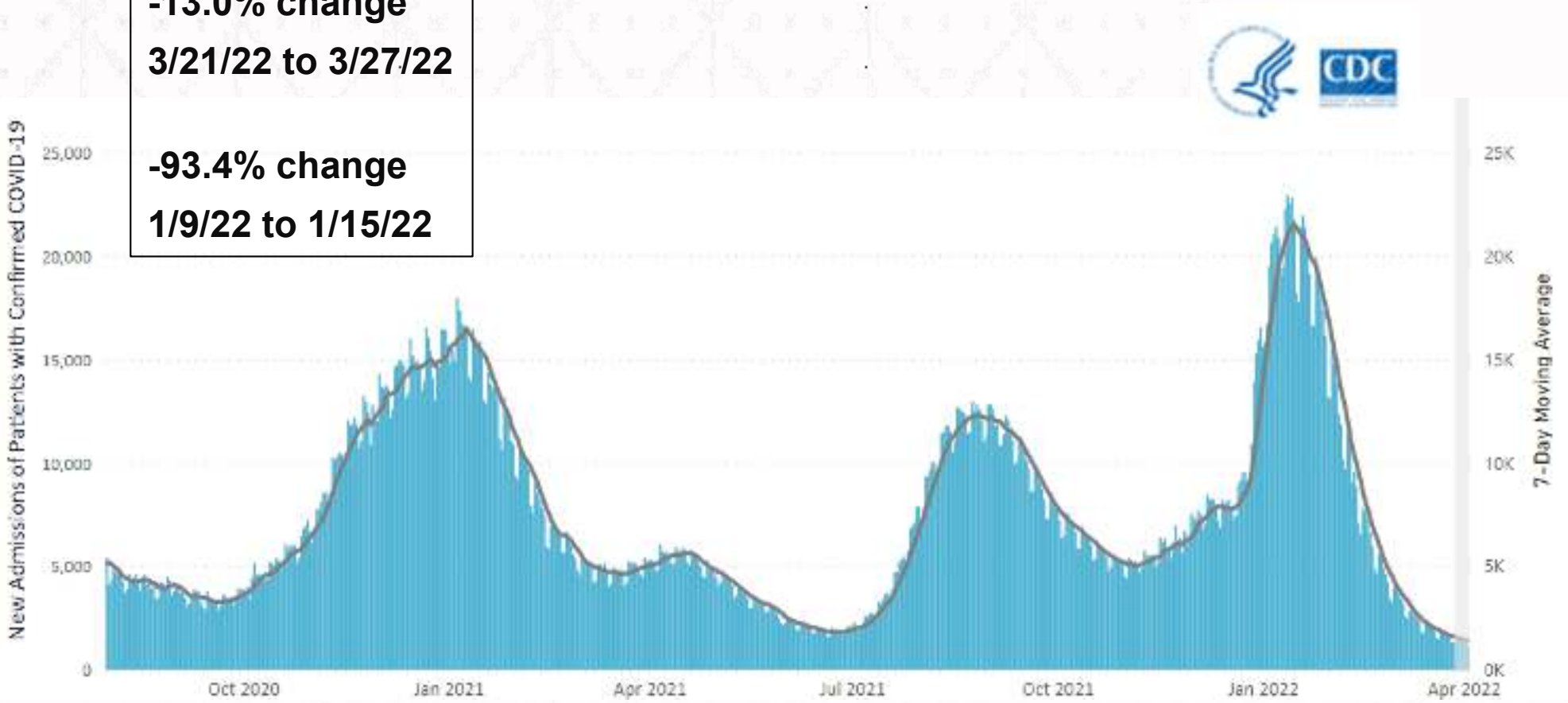


References: **CDC**. "COVID-19 Cases in the US Reported to the CDC, by State/Territory". https://covid.cdc.gov/covid-data-tracker/#cases_casesper100klast7days

Hospital Admissions with COVID-19 as of April 3, 2022

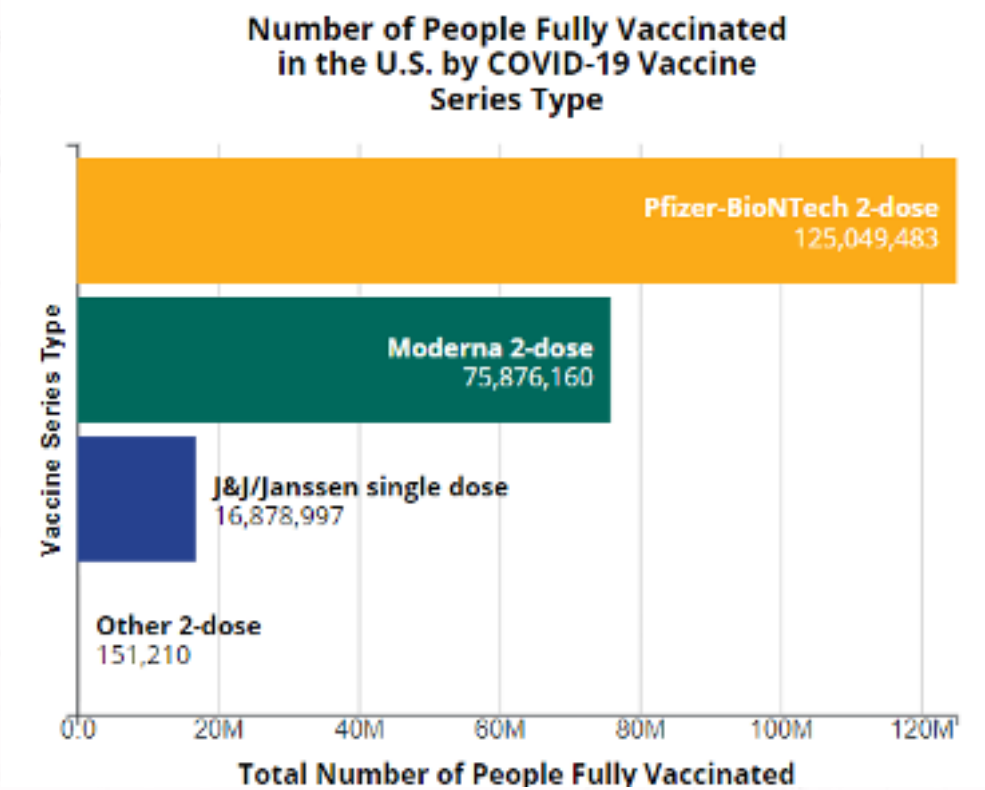
-13.0% change
3/21/22 to 3/27/22

-93.4% change
1/9/22 to 1/15/22



References: **CDC**. "New admission of patients with confirmed COVID-19, Unites States". https://covid.cdc.gov/covid-data-tracker/#new-hospital-admissions

COVID-19 Vaccines Administered



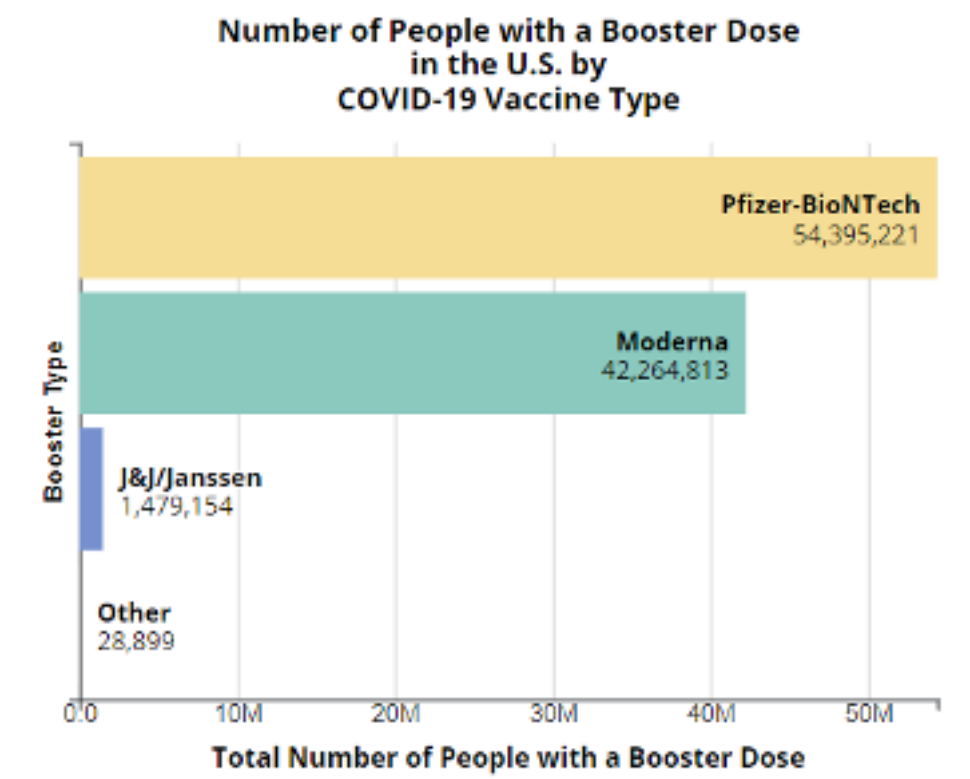
% US population

Total	**65.6%**
≥5 years of age	**69.8%**
≥12 years of age	**74%**
≥ 18 years of age	**75.5%**
≥ 65 years of age	**89.2%**

Reference. CDC. https://covid.cdc.gov/covid-data-tracker

**Data as of April 5,2022*

COVID-19 Booster Doses Administered



% fully vaccinated

Total **45%**

≥12 years of age **46.8%**

≥ 18 years of age **48.5%**

≥ 65 years of age **67.5%**

Reference. CDC. https://covid.cdc.gov/covid-data-tracker

**Data as of April 5, 2022*

Available COVID-19 Vaccines

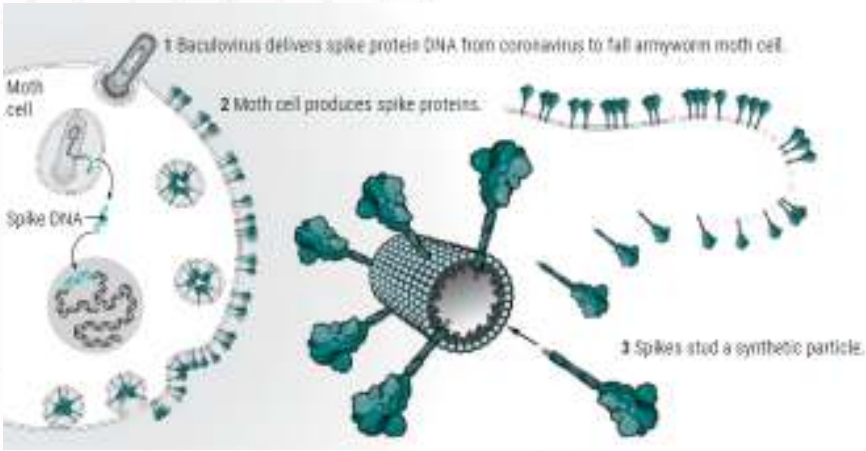
	Pfizer-BioNTech	Moderna	J&J/Janssen
Brand name	Comirnaty	Spikevax	-
Platform	BNT162b2; mRNA in lipid nanoparticle	mRNA-1273; mRNA in lipid nanoparticle	Ad26.COV2.S; non-replicating human adenovirus/DNA
Primary Series	Two doses; 21 days	Two doses; 28 days	One dose
Ages recommended	5+ years old	18+ years old	18+ years old
US Approval Status	FDA (16+ yo)	FDA (18+ yo)	EUA (≥18 yo)
Fully vaccinated	2 weeks after 2nd dose	2 weeks after 2nd dose	2 weeks after 1st dose
VE (ancestral)	95% severe disease, 86% infection	97% severe disease, 92% infection	86% severe disease, 72% infection
VE (Omicron)	72% severe disease, 44% infection	73% severe disease, 48% infection	57% severe disease, 33% infection
Booster eligible	5 months after last dose	5 months after last dose	2 months after last dose
Booster types	18+: Pfizer or Moderna 12-17: Pfizer	18+: Pfizer or Moderna	18+: Pfizer or Moderna

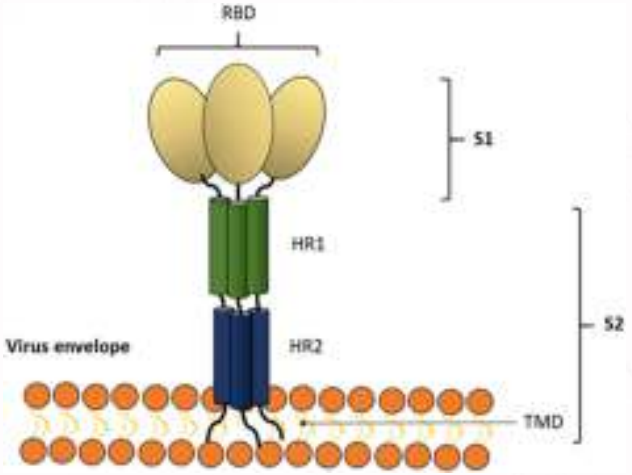
Reference. CDC. Different COVID-19 Vaccines; IHME. COVID-19 vaccine efficacy summary

NVX-CoV2373

NOVAVAX

- Protein subunit vaccine
  - Baculovirus produced Spike protein nanoparticles (same tech as FluBlok flu vaccine)
  - rSARS-CoV-2 spike generated in prefusion confirmation and protease resistant
  - Matrix M adjuvant (saponin-based)
  - Stored and stable at 2° to 8° C
- Immunogenic and protective in pre-clinical NHP studies
- Phase I-2: May 2020; 131 individuals
  - Safe and well-tolerated: injection site pain; fatigue, headache, muscle pain
  - Two-dose 5-μg adjuvanted regimen induced titers of anti-Spike antibodies exceeding convalescent serum





References: Guebre-Xabier M et al. 2020. NVX-CoV2373 vaccine protects cynomolgus macaque upper and lower airways against SARS-CoV-2 challenge. Vaccine. DOI: 10.1016/j.vaccine.2020.10.064 ; Keech C et al. 2020. Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine. NEJM. DOI: 10.1056/NEJMoa2026920

NVX-CoV2373: Phase III Studies

ORIGINAL ARTICLE

Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine

Paul T. Heath, F.R.C.P.C.H., Eva P. Galiza, M.B., B.S., David N. Baxter, M.D., Ph.D., Marta Boffito, M.D., Ph.D., Duncan Browne, M.D., Fiona Burns, Ph.D., David R. Chadwick, Ph.D., Rebecca Clark, M.B., Ch.B., Catherine Cosgrove, Ph.D., James Galloway, Ph.D., Anna L. Goodman, D.Phil., Amardeep Heer, M.B., Ch.B., et al., for the 2019nCoV-302 Study Group*

- 15,187 individuals over 33 sites in the UK; enrolled between September 28 to November 28, 2020
- Participants were randomly assigned in a 1:1 ratio to receive two 5-µg doses of NVX-CoV2373 or placebo (normal saline) administered 21 days.
- Safety was assessed in all the participants who had received at least one dose of NVX-CoV2373 or placebo. Solicited local and systemic adverse events were summarized according to the toxicity grading criteria of the Food and Drug Administration (FDA).
- Primary end point was the vaccine efficacy against the first occurrence of virologically confirmed symptomatic mild, moderate, or severe Covid-19 with onset at least 7 days after the second dose

Reference: Heath PT et al. 2019nCoV-302 Study Group. Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine. *N Engl J Med*. 2021 Sep 23;385(13):1172-1183

NVX-CoV2373: Phase III Studies

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Table 1. Demographic and Clinical Characteristics of the Participants at Baseline (Per-Protocol Efficacy Population).

Characteristic	NVX-CoV2373 (N=7020)	Placebo (N=7019)	All Participants (N=14,039)
Median age (range) — yr	56 (18–84)	56 (18–84)	56 (18–84)
Age group — no. (%)			
18–64 yr	5067 (72.2)	5062 (72.1)	10,129 (72.1)
≥65 yr	1953 (27.8)	1957 (27.9)	3910 (27.9)
Sex — no. (%)			
Male	3609 (51.4)	3629 (51.7)	7238 (51.6)
Female	3411 (48.6)	3390 (48.3)	6801 (48.4)
Race or ethnic group — no. (%)*			
White	6625 (94.4)	6635 (94.5)	13,260 (94.5)
Black	26 (0.4)	26 (0.4)	52 (0.4)
Asian	201 (2.9)	212 (3.0)	413 (2.9)
Hispanic or Latinx	63 (0.9)	51 (0.7)	114 (0.8)
Multiple races	70 (1.0)	59 (0.8)	129 (0.9)
Other	4 (0.1)	6 (0.1)	10 (0.1)
Not reported or missing data	89 (1.3)	81 (1.2)	170 (1.2)
Body-mass index ≥30 — no. (%)†	1784 (25.4)	1863 (26.5)	3647 (26.0)
Coexisting condition — no. (%)‡			
Yes	3117 (44.4)	3143 (44.8)	6260 (44.6)
No	3903 (55.6)	3876 (55.2)	7779 (55.4)

* Race or ethnic group was reported by the participants, who could have listed more than one category.
† The body-mass index is the weight in kilograms divided by the square of the height in meters. A value of more than 30 is considered to indicate obesity.
‡ Coexisting conditions that were classified by the Centers for Disease Control and Prevention as risk factors for severe Covid-19 included chronic respiratory, cardiac, renal, neurologic, hepatic, and immunocompromising conditions as well as obesity.

- Study included diversity of racial/ethnic groups
- Older median age (56 yrs)
- Included individuals with health conditions know to be risk factors for severe COVID-19

Reference: Heath PT et al. 2019nCoV-302 Study Group. Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine. *N Engl J Med*. 2021 Sep 23;385(13):1172-1183

NVX-CoV2373: Phase III Studies

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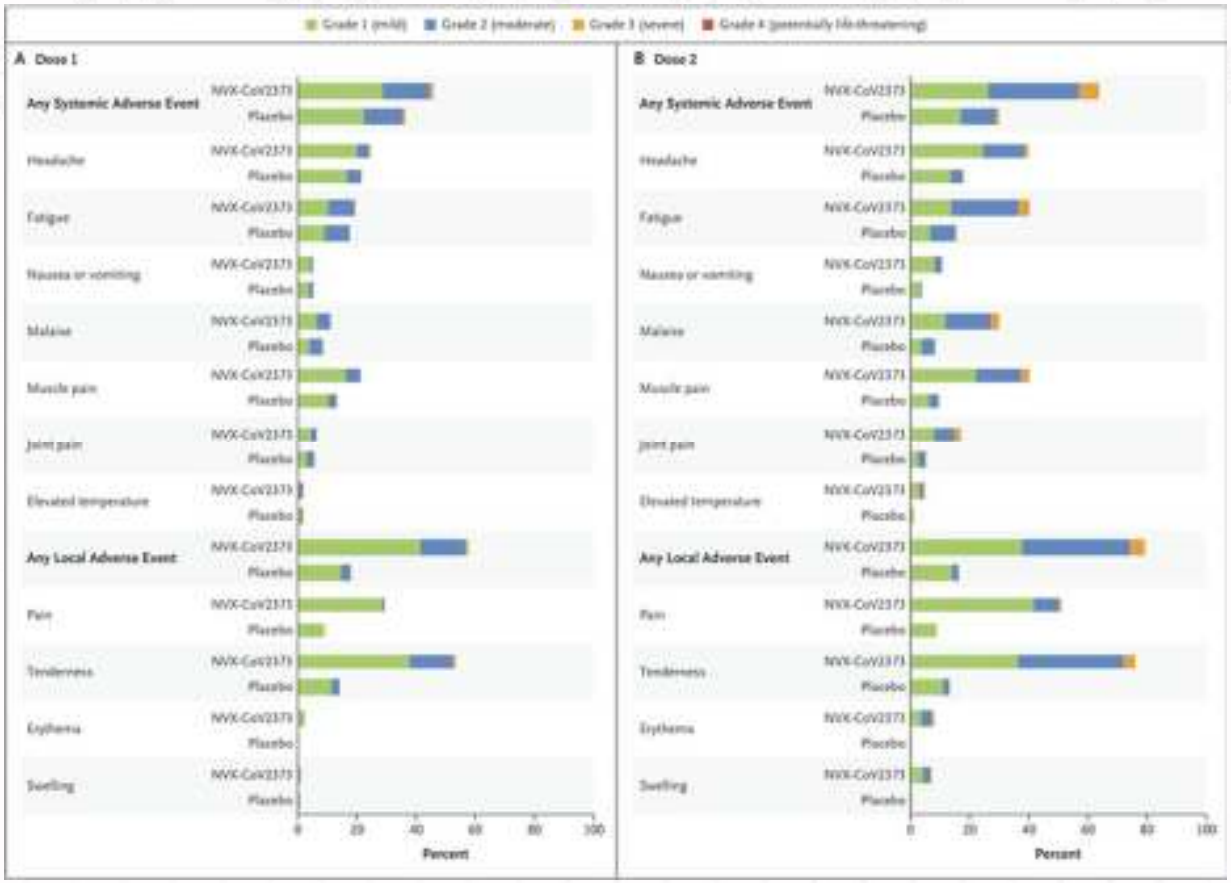

- Systemic adverse events were reported more often by younger vaccine recipients than by older vaccine recipients
- More often after the second dose
- Myocarditis reported in 1 vaccine recipient

Reference: Heath PT et al. 2019nCoV-302 Study Group. Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine. *N Engl J Med*. 2021 Sep 23;385(13):1172-1183

NVX-CoV2373: Phase III Studies

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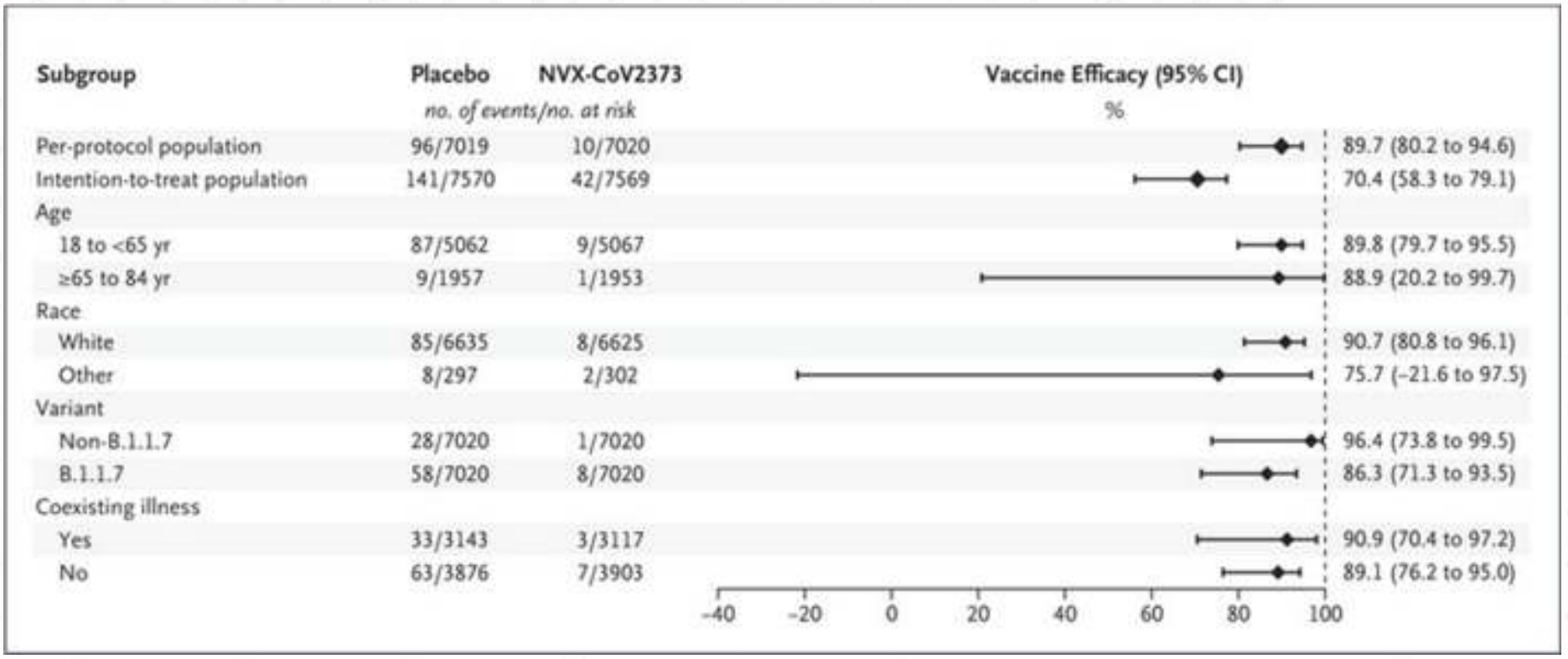

Subgroup	Placebo	NVX-CoV2373	Vaccine Efficacy (95% CI)
	no. of events/no. at risk		%
Per-protocol population	96/7019	10/7020	89.7 (80.2 to 94.6)
Intention-to-treat population	141/7570	42/7569	70.4 (58.3 to 79.1)
Age			
18 to <65 yr	87/5062	9/5067	89.8 (79.7 to 95.5)
≥65 to 84 yr	9/1957	1/1953	88.9 (20.2 to 99.7)
Race			
White	85/6635	8/6625	90.7 (80.8 to 96.1)
Other	8/297	2/302	75.7 (−21.6 to 97.5)
Variant			
Non-B.1.1.7	28/7020	1/7020	96.4 (73.8 to 99.5)
B.1.1.7	58/7020	8/7020	86.3 (71.3 to 93.5)
Coexisting illness			
Yes	33/3143	3/3117	90.9 (70.4 to 97.2)
No	63/3876	7/3903	89.1 (76.2 to 95.0)

- 89.7% effective against symptomatic Covid-19 caused by both B.1.1.7 and non-B.1.1.7 variants (pre-Delta and Omicron).
- No hospitalizations or deaths were reported among the cases of infection in the vaccine group.

Reference: Heath PT et al. 2019nCoV-302 Study Group. Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine. *N Engl J Med*. 2021 Sep 23;385(13):1172-1183

NVX-CoV2373: Phase III Studies

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ORIGINAL ARTICLE

Efficacy and Safety of NVX-CoV2373 in Adults in the United States and Mexico

Lisa M. Dunkle, M.D., Karen L. Kotloff, M.D., Cynthia L. Gay, M.D., M.P.H., Germán Áñez, M.D., Jeffrey M. Adelglass, M.D., Alejandro Q. Barrat Hernández, M.D., Wayne L. Harper, M.D., Daniel M. Duncanson, M.D., Monica A. McArthur, M.D., Ph.D., Diana F. Florescu, M.D., R. Scott McClelland, M.D., M.P.H., Veronica Garcia-Fragoso, M.D., et al., for the 2019nCoV-301 Study Group*

- PREVENT-19: 29,949 individuals over 119 sites in US and Mexico; enrolled between December 27, 2020 and February 18, 2021
- Participants were randomly assigned in a 2:1 ratio to receive two 5-µg doses of NVX-CoV2373 or placebo (normal saline) administered 21 days apart.
- Safety was assessed in all the participants who had received at least one dose of NVX-CoV2373 or placebo. Solicited local and systemic adverse events were summarized according to the toxicity grading criteria of the Food and Drug Administration (FDA).
- Primary objective was to determine vaccine efficacy against RT-PCR–confirmed Covid-19 occurring at least 7 days after the second dose

Reference: Dunkle LM, Kotloff KL, Gay CL, et al. Efficacy and Safety of NVX-CoV2373 in Adults in the United States and Mexico. N Engl J Med. 2022;386(6):531-543. doi:10.1056/NEJMoa2116185

NVX-CoV2373: Phase III Studies

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Table 1. Demographic and Clinical Characteristics of the Participants at Baseline (Per-Protocol Efficacy Analysis Population).*

Characteristic	NVX-CoV2373 (N=17,312)	Placebo (N=8140)	Total (N=25,452)
Median age (range) — yr	47.0 (18–95)	47.0 (18–90)	47.0 (18–95)
Age group — no. (%)			
18 to 64 yr	15,264 (88.2)	7,194 (88.4)	22,458 (88.2)
≥65 yr	2,048 (11.8)	946 (11.6)	2,994 (11.8)
Sex — no. (%)			
Male	9,050 (52.3)	4,131 (50.7)	13,181 (51.8)
Female	8,262 (47.7)	4,009 (49.3)	12,271 (48.2)
Race or ethnic group — no. (%)†			
White	13,140 (75.9)	6,184 (76.0)	19,324 (75.9)
Black or African American	1,893 (10.9)	900 (11.1)	2,798 (11.0)
American Indian or Alaska Native, including Mexican Natives	1,074 (6.2)	498 (6.1)	1,572 (6.2)
Asian	761 (4.4)	366 (4.5)	1,127 (4.4)
Multiple	293 (1.7)	132 (1.6)	425 (1.7)
Native Hawaiian or other Pacific Islander	47 (0.3)	10 (0.1)	57 (0.2)
Not reported	104 (0.6)	45 (0.6)	149 (0.6)
Hispanic or Latino			
No	13,538 (78.2)	6,379 (78.4)	19,917 (78.3)
Yes	3,733 (21.6)	1,751 (21.5)	5,484 (21.5)
Not reported	22 (0.1)	9 (0.1)	31 (0.1)
Unknown	19 (0.1)	1 (<0.1)	20 (0.1)
Overall high risk of Covid-19 — no. (%)‡			
Yes	16,493 (95.3)	7,737 (95.0)	24,230 (95.2)
No	819 (4.7)	403 (5.0)	1,222 (4.8)
High risk of severe Covid-19 — no. (%)‖			
Yes	9,046 (52.3)	4,294 (52.8)	13,340 (52.4)
No	8,266 (47.7)	3,846 (47.2)	12,112 (47.6)
Coexisting conditions — no. (%)			
Any	8,117 (46.9)	3,910 (48.0)	12,027 (47.3)
Obesity	6,406 (37.0)	3,070 (37.7)	9,470 (37.2)
Chronic lung disease	2,442 (14.1)	1,218 (15.0)	3,660 (14.4)
Diabetes mellitus type 2	1,303 (7.5)	677 (8.3)	1,980 (7.8)
Cardiovascular disease	191 (1.1)	91 (1.1)	282 (1.1)
Chronic kidney disease	109 (0.6)	50 (0.6)	159 (0.6)
HIV infection — no. (%)	128 (0.7)	38 (0.5)	166 (0.7)
Country — no. (%)			
United States	16,294 (94.1)	7,638 (93.8)	23,932 (94.0)
Mexico	1,018 (5.9)	502 (6.2)	1,520 (6.0)

- High risk: ≥ 65 years of age, those with chronic health condition, or risk due to work/living conditions
- Risk for severe COVID: BMI ≥ 30, chronic lung disease, diabetes, cardiovascular disease, or chronic kidney disease

Reference: Dunkle LM, Kotloff KL, Gay CL, et al. Efficacy and Safety of NVX-CoV2373 in Adults in the United States and Mexico. N Engl J Med. 2022;386(6):531-543. doi:10.1056/NEJMoa2116185

NVX-CoV2373: Phase III Studies

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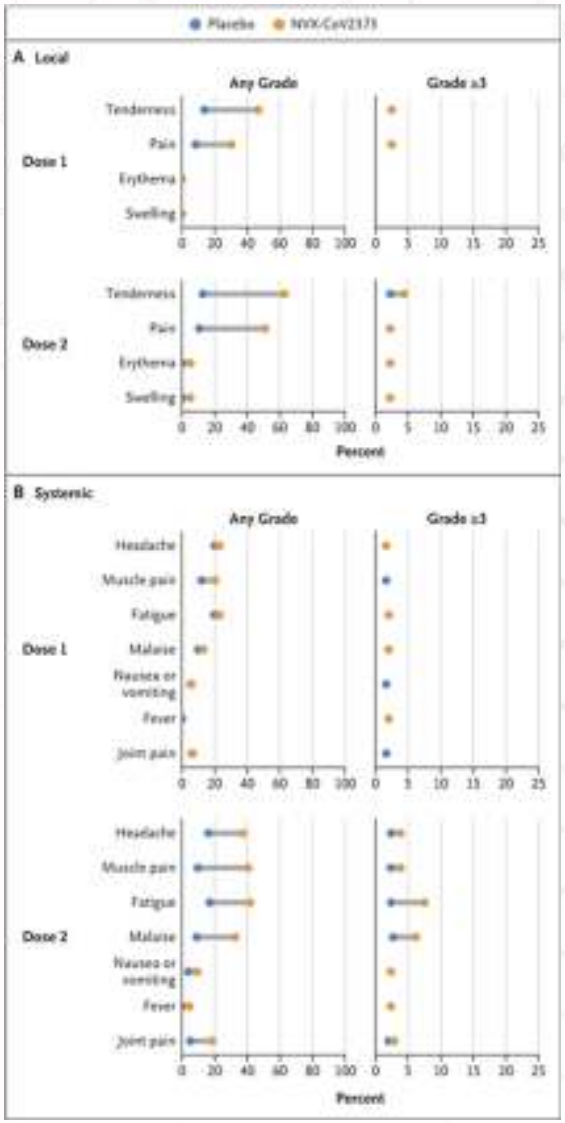

- Solicited local and systemic adverse events were predominantly mild to moderate and transient.
- More frequent in vaccine group and more reported after dose 2
- Local: tenderness and injection-site pain; lasted 2 days or less
- Systemic: headache, myalgia, fatigue, and malaise; lasted 1 day or less
- Fever was rare
- No evidence of anaphylaxis, GBS, myocarditis, pericarditis, or thrombosis with thrombocytopenia

Reference: Dunkle LM, Kotloff KL, Gay CL, et al. Efficacy and Safety of NVX-CoV2373 in Adults in the United States and Mexico. N Engl J Med. 2022;386(6):531-543. doi:10.1056/NEJMoa2116185

NVX-CoV2373: Phase III Studies

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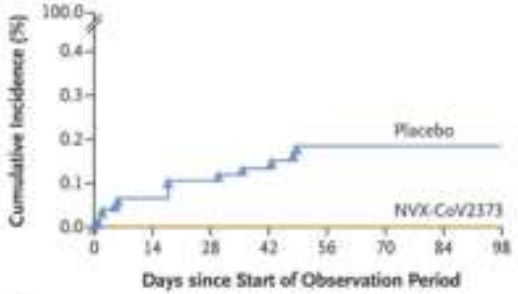
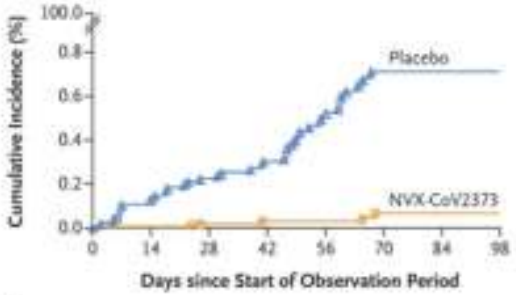
D Analysis of Covid-19 Due to Non-VOC and Non-VOI SARS-CoV-2 (Per-Protocol Efficacy Analysis Population)



No. at Risk								
Placebo	8,140	7,619	6,989	6,349	4,627	2803	1055	220
NVX-CoV2373	17,312	16,782	16,166	15,330	11,458	6951	2447	379

No. of Events								
Placebo	0	5	8	10	13	13	13	13
NVX-CoV2373	0	0	0	0	0	0	0	0

E Analysis of Covid-19 Due to VOC or VOI (Per-Protocol Efficacy Analysis Population)



No. at Risk								
Placebo	8,140	7,619	6,989	6,349	4,627	2803	1055	220
NVX-CoV2373	17,312	16,782	16,166	15,330	11,458	6951	2447	379

No. of Events								
Placebo	0	10	17	22	34	41	41	41
NVX-CoV2373	0	0	2	4	4	7	7	7

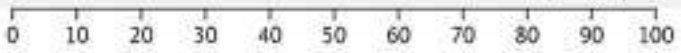
- **VOI**: posses markers associated with changes to binding, transmission, or neutralization
- **VOC**: evidence of increased transmissibility, disease severity, or reduced neutralization
- Alpha variant was dominant VOC
- VE against alpha= 93.6% (95% CI, 81.7 to 97.8)
- VE against VOC/VOI= 92.6% (95% CI, 83.6 to 96.7)

Reference: Heath PT et al. 2019nCoV-302 Study Group. Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine. *N Engl J Med*. 2021 Sep 23;385(13):1172-1183

NVX-CoV2373: Phase III Studies

The NEW ENGLAND JOURNAL of MEDICINE

Analysis Group	NVX-CoV2373	Placebo	Vaccine Efficacy (95% CI)
	no. of events/no. at risk (%)		
Per-protocol efficacy analysis population	14/17,312 (0.1)	63/8140 (0.8)	90.4 (82.9–94.6)
Full analysis population	16/18,584 (0.1)	69/9144 (0.8)	89.3 (81.6–93.8)
Subgroups			
Age of 18–64 yr	12/15,264 (0.1)	61/7194 (0.8)	91.5 (84.2–95.4)
Sex			
Male	5/9050 (0.1)	23/4131 (0.6)	90.9 (76.0–96.5)
Female	9/8262 (0.1)	40/4009 (1.0)	90.0 (79.3–95.1)
Race			
White	12/13,140 (0.1)	48/6184 (0.8)	89.4 (80.0–94.4)
Black	0/1893 (0.0)	7/905 (0.8)	100.0 (67.9–100.0)
Non-White	2/4068 (<0.1)	14/1911 (0.7)	93.6 (71.7–98.5)
Ethnic group			
Hispanic or Latino	8/3733 (0.2)	11/1751 (0.6)	67.3 (18.7–86.8)
Not Hispanic or Latino	6/13,538 (<0.1)	52/6379 (0.8)	95.1 (88.5–97.9)
Country: United States	14/16,294 (0.1)	62/7638 (0.8)	90.4 (82.8–94.6)
Coexisting conditions			
Yes	7/8109 (0.1)	34/3910 (0.9)	90.8 (79.2–95.9)
No	7/9203 (0.1)	29/4230 (0.7)	89.9 (77.1–95.6)
At high risk for Covid-19	13/16,493 (0.1)	62/7737 (0.8)	91.0 (83.6–95.0)

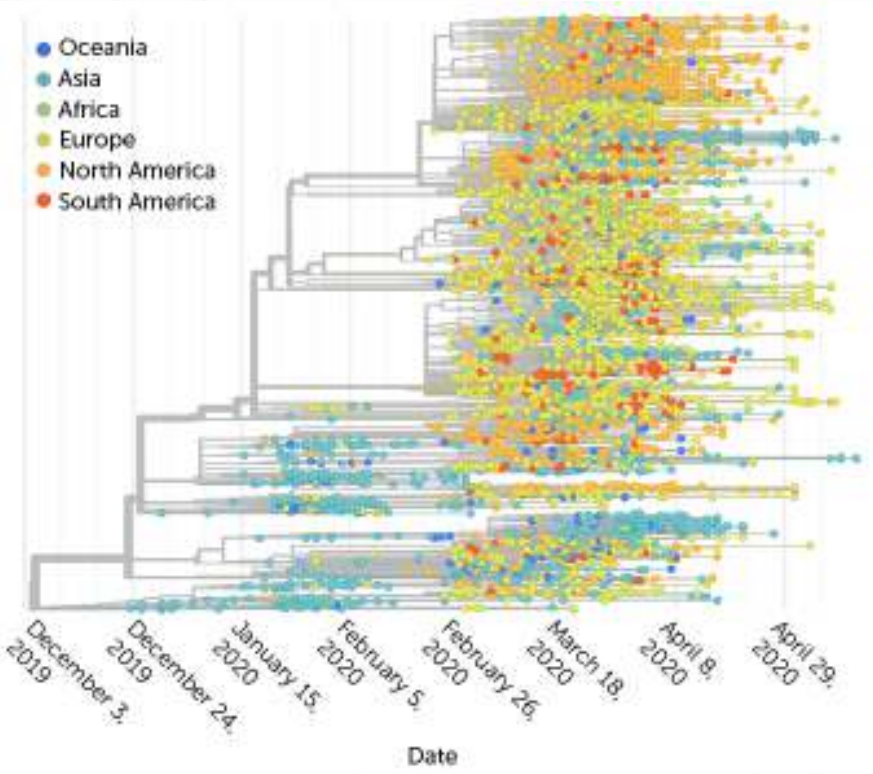


- Evidence of high short-term vaccine efficacy of NVX-CoV2373 for the prevention of Covid-19 (>90%) and for the prevention of moderate-to-severe disease (100%).
- Vaccine efficacy of greater than 90% against variants circulating during study in the US and Mexico

Reference: Heath PT et al. 2019nCoV-302 Study Group. Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine. *N Engl J Med*. 2021 Sep 23;385(13):1172-1183

Flashback: Is SARS-CoV-2 Mutating?

- Every virus mutates- part of the viral life cycle
  - Shifts and changes don't always equal bad news
  - Some mutations lead to a weaker virus
- SARS-CoV-2 is mutating, but at a very slow pace
  - Much slower than influenza
- Dominant strains have been detected
  - **D614G** mutation
  - No change in rates of illness and hospitalization
- Genetic changes have been used to reveal the movement of a virus through a population
- Current data suggest that mutations likely won't interfere with the effectiveness of the COVID-19 vaccine

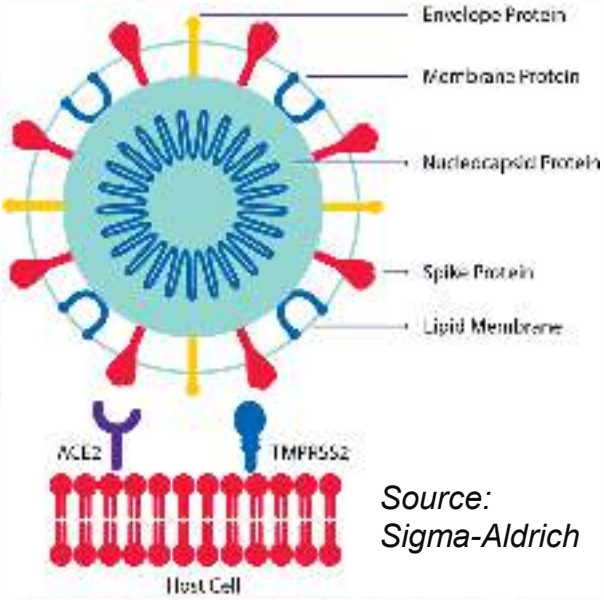


Source: Nextstrain.org

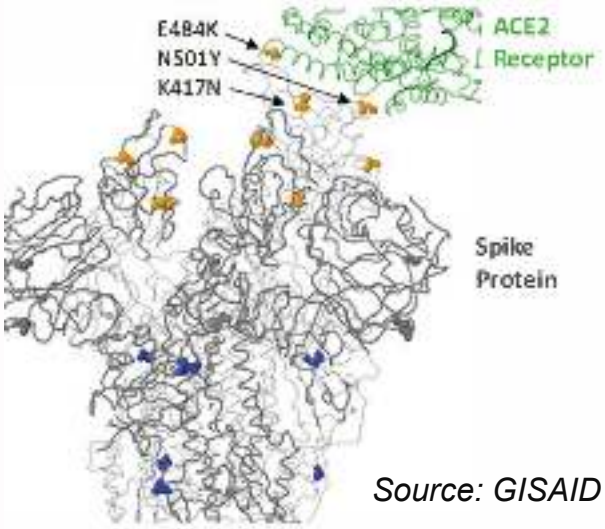
References: **Science News**. "Coronavirus's genetic fingerprints are used to rapidly map its spread". https://www.sciencenews.org/article/coronavirus-genetic-fingerprints-are-used-to-rapidly-map-spread

Viral Variants

- Key mutations in have emerged (most in S protein):
  - D614G, N501Y: increased binding to ACE2
  - E484K: evasion of antibody immunity
- Variant of interest (VOI)
  - Caused discrete clusters of infection or driving a surge
  - Genetic changes suggest increased transmissibility or ability to evade
- Variant of concern (VOC): Alpha, Beta, Gamma, Delta
  - Scientific data has revealed increased transmissibility and/or potential reductions in the efficacy of therapeutics and vaccines
- Variant of high consequence (VOHC)
  - Cause more severe disease and defeats therapeutics and/or vaccines



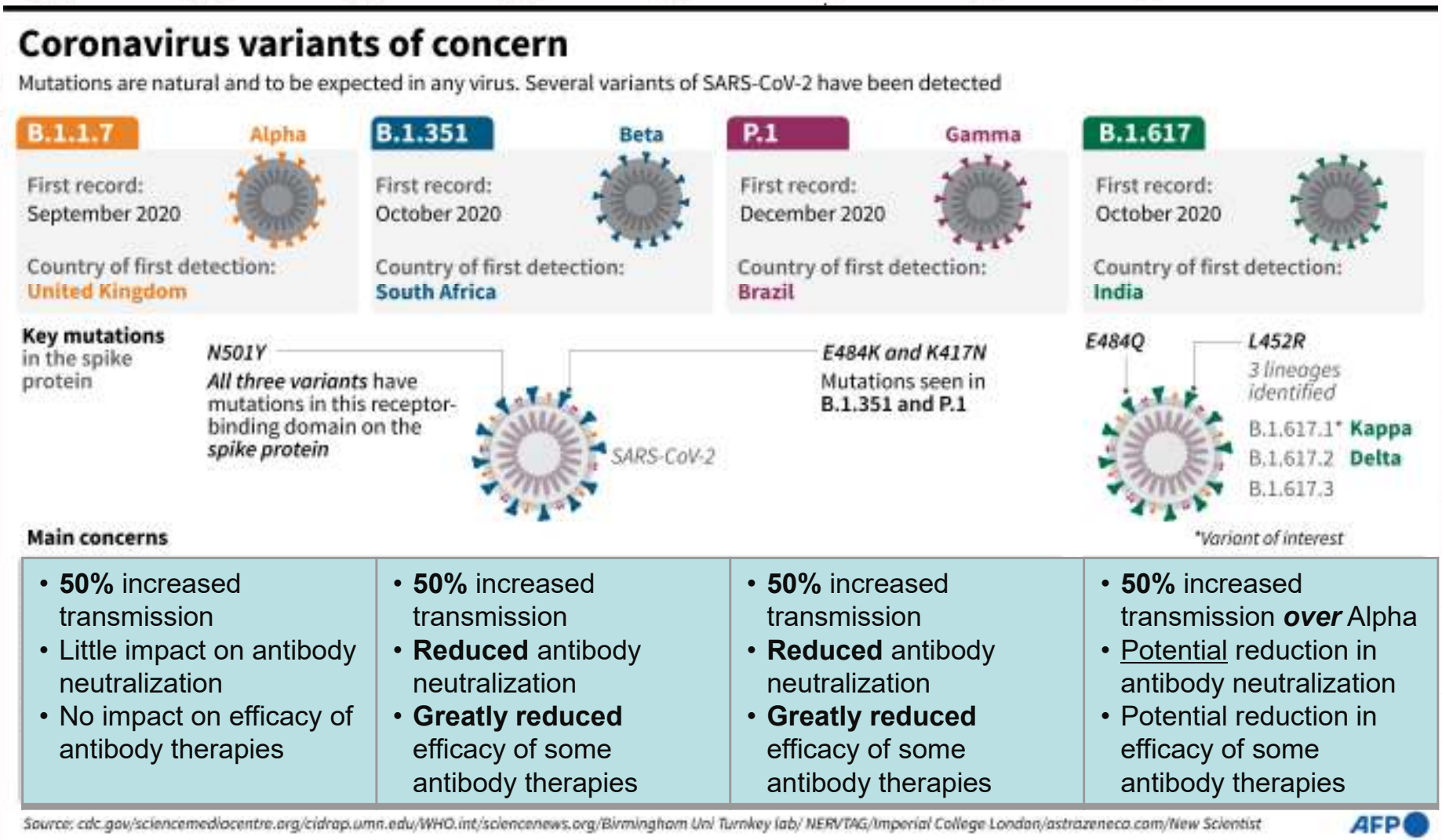
Source: Sigma-Aldrich



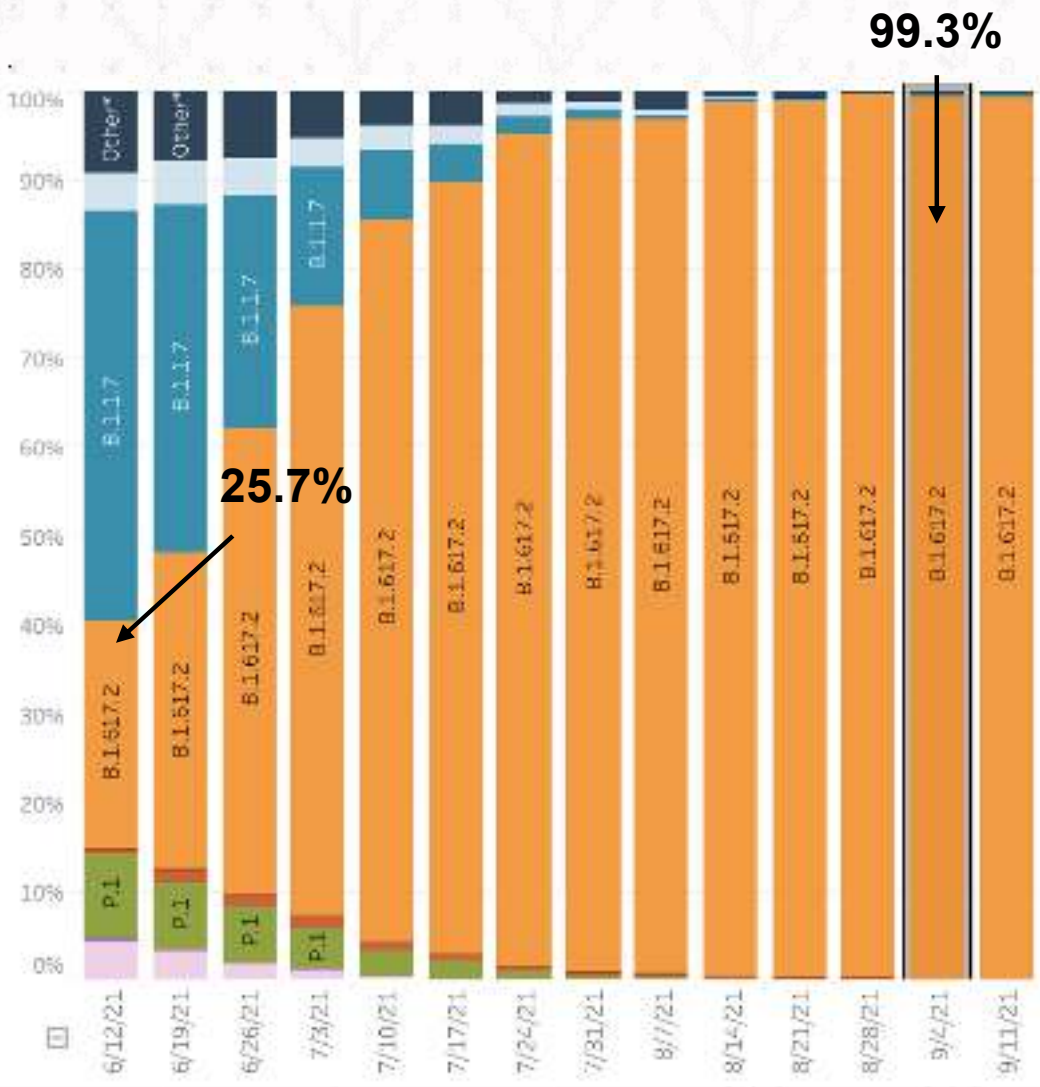
Source: GISAID

Reference: Hackethal, V. Tracking the Evolution of SARS-CoV-2. Medpage Today, May 6, 2021; Wang J et al. Antibody Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7. bioRxiv 2021.01.25.428137. https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-info.html

Viral Variants



Variant Proportion in the US (June-Sept)



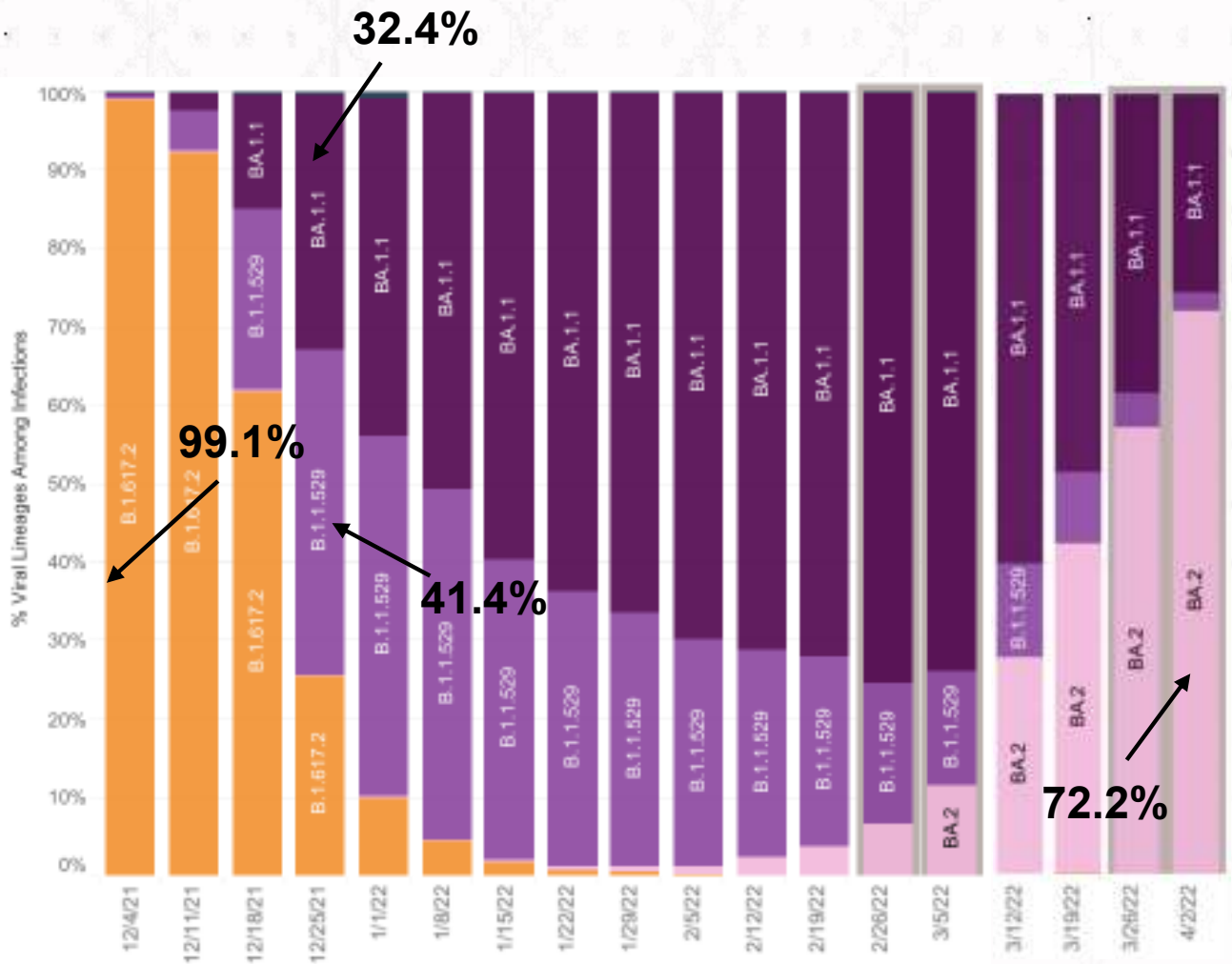
USA

WHO label	Lineage #	Type	%Total	95%PI
Alpha	B.1.1.7	VOC	0.0%	0.0-0.2%
Beta	B.1.351	VOC	0.0%	0.0-0.2%
Gamma	P.1	VOC	0.0%	0.0-0.2%
Delta	B.1.617.2	VOC	99.3%	98.3-100.0%
	AY.1	VOC	0.2%	0.0-0.7%
	AY.2	VOC	0.1%	0.0-0.5%
Eta	B.1.525	VOI	0.0%	0.0-0.2%
Iota	B.1.526	VOI	0.0%	0.0-0.2%
Kappa	B.1.617.1	VOI	0.0%	0.0-0.2%
Mu	B.1.621		0.1%	0.0-0.5%
N/A	B.1.617.3	VOI	0.0%	0.0-0.2%
Other	Other*		0.3%	0.0-0.7%

Each infection = chance to mutate

Source: https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Variant Proportion in the US (Nov-Apr)



USA

WHO label	Lineage #	US Class	% total	95%PI
Omicron	BA.1.1	VOC	73.7%	70.1-77.0%
	B.1.1.529	VOC	14.7%	12.4-17.4%
	BA.2	VOC	11.6%	9.8-13.6%
Delta	B.1.617.2	VOC	0.0%	0.0-0.0%
Other	Other*		0.0%	0.0-0.0%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed

Source: https://covid.cdc.gov/covid-data-tracker/#variant-proportions

**Data as of April 2, 2022*

Omicron & Efficacy of Antiviral Agents

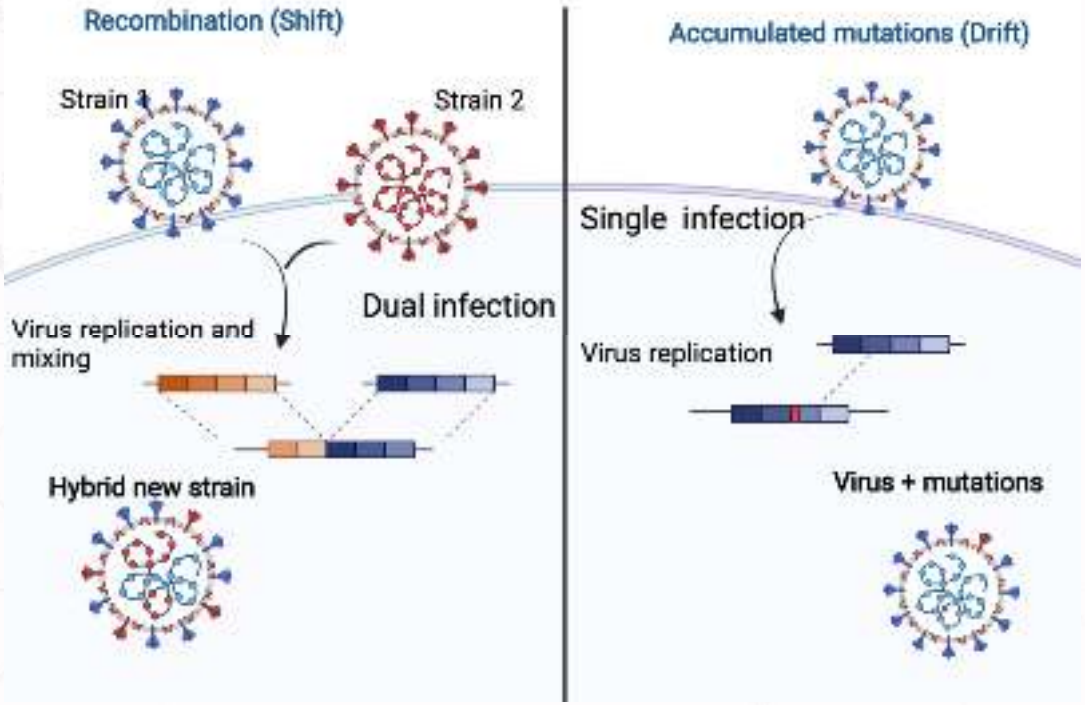
Table 1. Efficacy of Monoclonal Antibodies and Antiviral Drugs against the Omicron/BA.2 Subvariant in Vitro.*

Monoclonal Antibody or Antiviral Drug	hCoV-19/Japan/UT-NCD1288-2N/2022 (Omicron/BA.2)	
	Tested Value	Factor Increase as Compared with the Ancestral Strain
Neutralization activity of monoclonal antibody†		
LY-CoV016, etesevimab	>50,000 ng/ml	>2749
LY-CoV555, bamlanivimab	>50,000 ng/ml	>10,661
REGN10987, imdevimab	68.65±8.84 ng/ml	22.5
REGN10933, casirivimab	1666.19±771.77 ng/ml	597.2
COV2-2196, tixagevimab	395.78±62.37 ng/ml	206.1
COV2-2130, cilgavimab	4.44±2.72 ng/ml	0.6
S309, sotrovimab precursor	1359.05±269.23 ng/ml	49.7
LY-CoV016 plus LY-CoV555	>10,000 ng/ml	>794
REGN10987 plus REGN10933	222.59±64.47 ng/ml	63.1
COV2-2196 plus COV2-2130	14.48±2.04 ng/ml	4.2
Viral susceptibility to drug‡		
GS-441524§	2.85±0.31 μM	2.7
EIDD-1931¶	0.67±0.22 μM	1.3
PF-07321332‖	6.76±0.69 μM	1.9

Reference: Takashita E, Kinoshita N, Yamayoshi S, et al. Efficacy of antiviral agents against the SARS-CoV-2 Omicron subvariant BA.2. N Engl J Med. 2022 Mar 9.

"Deltacron"

- Variant containing genes from both Delta and Omicron
  - Recombination during co-infection of the same cell
- Small number of cases detected in US, UK, France, Denmark, Netherlands
  - 17 patients
- No changes in epidemiology or disease severity observed yet
  - Not yet a variant of concern



Source: The Scientist; created by Lara Herrero using BioRender

Reference: Philippe Colson, Pierre-Edouard Fournier, Jeremy Delerce, et al. Culture and identification of a "Deltamicron" SARS-CoV-2 in a three cases cluster in southern France. medRxiv 2022.03.03.22271812.

Continuing Viral Surveillance

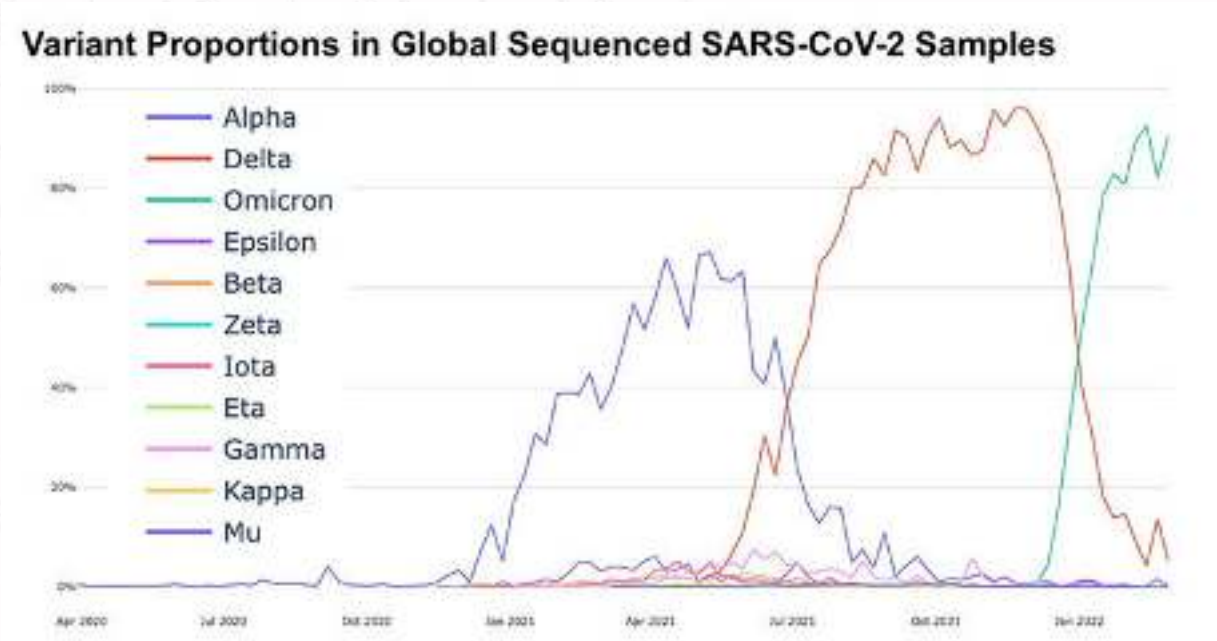
- At home rapid antigen tests now widely available
  - 70-90%; depends on timing and presence of symptoms
  - Many infections are likely never reported
- Data from wastewater can spot a rise in infections before COVID cases show up in tests
  - Wastewater samples can't tell how many people have Covid-19

Source: Shutterstock.com

Source: CDC; data are for Feb 25-Mar 11

Continuing Viral Surveillance

- Genome sequencing key for:
  - Characterize the virus
  - Estimate a particular variant's prevalence in a population
  - Design of mitigation efforts
- 200,000 SARS-CoV-2 sequences every week
- Efforts vary by country and state
  - UK 12%, US 3.6%, Germany 2.6%, South Africa 0.9%
  - NYC and Los Angeles



Source: Johns Hopkins. Pandemic Data Initiative

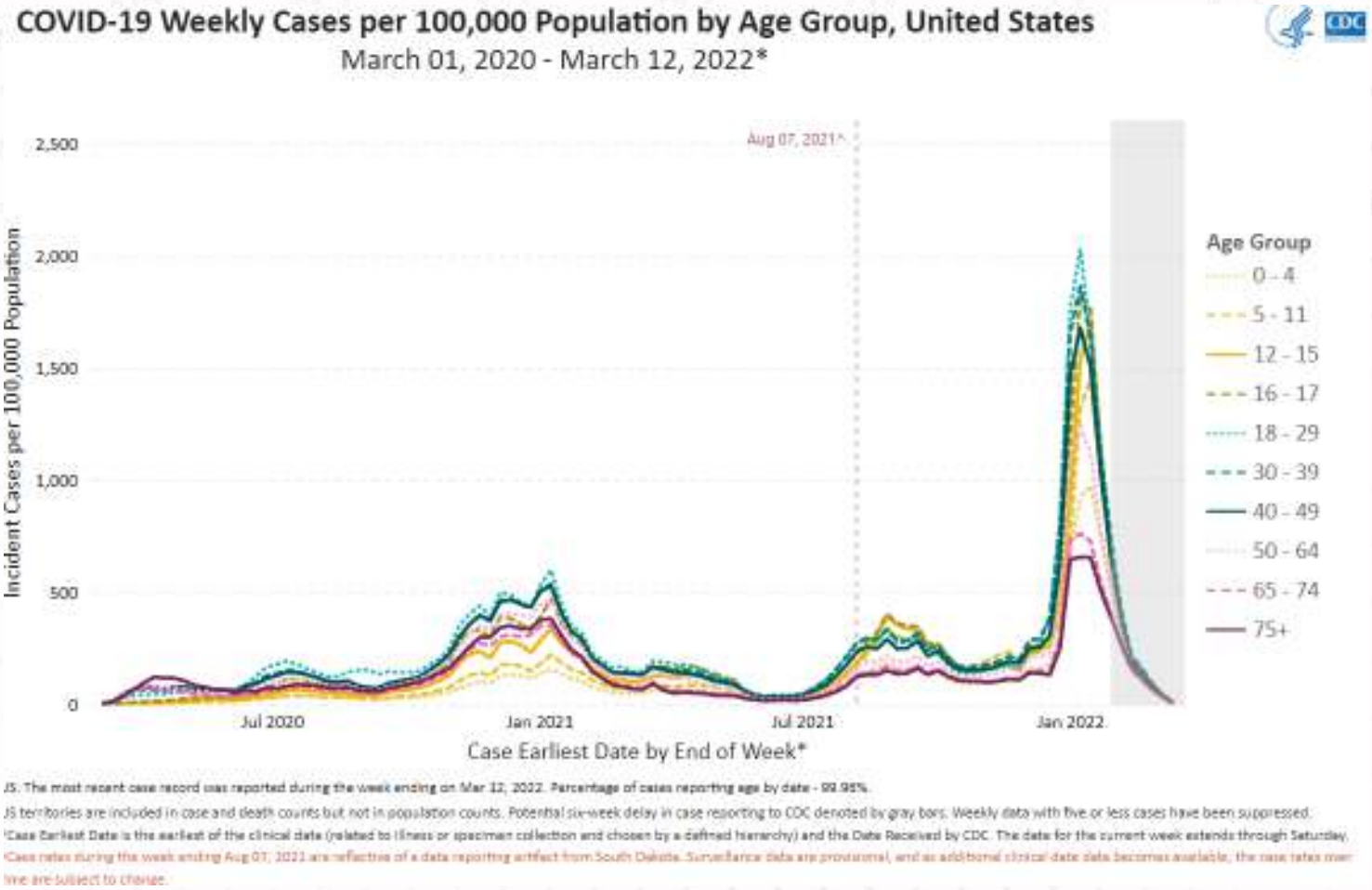
Flashback: Children and COVID-19

- Children infected with SARS-CoV-2 are less likely to develop severe illness
  - Significantly lower hospitalization rates compared to adults
- Children likely have the same or higher viral loads in their nasopharynx compared with adults
- Some evidence for an age gradient in infectiousness
  - Young children (>10 years) less likely to be a source of infection in households and other settings
  - Older children may transmit at levels similar to adults
- Impact of reopening schools on community transmission?

Source: Halfpoint/iStock

Reference: **CDC**. "COVID-19: Information for Pediatric Healthcare Providers". https://www.cdc.gov/coronavirus/2019-ncov/hcp/pediatric-hcp.html

Children and COVID-19



- ~12.7 million children have tested positive for COVID-19 since pandemic onset
- 4.8 million child cases were reported since the beginning of January 2022
- w.e. March 3: 20.2% of US weekly caseload
- Children under 18: 22.2% of US population

References: CDC. COVID Data Tracker. Accessed 3/11/2022. American Academy of Pediatrics. Children and COVID-19: State-Level Data Report. Accessed 3/11/22.

Children and COVID-19

Week ending January 9, 2021

Age Group	Cases per 100,000
0-4 yrs.	154.71
5-11 yrs.	220.66
12-15 yrs.	336.45
16-17 yrs.	467.51
18-29 yrs.	599.06
30-39 yrs.	535.11
40-49 yrs.	527.34
50-64 yrs.	463.59
65-74 yrs.	353.90
75+ yrs.	381.40

Week ending January 8, 2022

Age Group	Cases per 100,000
0-4 yrs.	924.34
5-11 yrs.	1326.10
12-15 yrs.	1540.05
16-17 yrs.	1824.93
18-29 yrs.	2030.44
30-39 yrs.	1863.76
40-49 yrs.	1678.08
50-64 yrs.	1238.65
65-74 yrs.	760.83
75+ yrs.	656.51

References: **CDC**. “Demographic Trends of COVID-19 cases and deaths in the US reported to CDC”. https://covid.cdc.gov/covid-data-tracker/#demographicsovertime

Children and COVID-19: Hospital Admissions

Data collected January 9, 2021

Age Group	New Admissions per 100,000
0-17 yrs.	0.28
18-29 yrs.	1.13
30-39 yrs.	2.00
40-49 yrs.	3.14
50-59 yrs.	5.46
60-69 yrs.	8.91
70+ yrs.	19.51
All ages	4.97

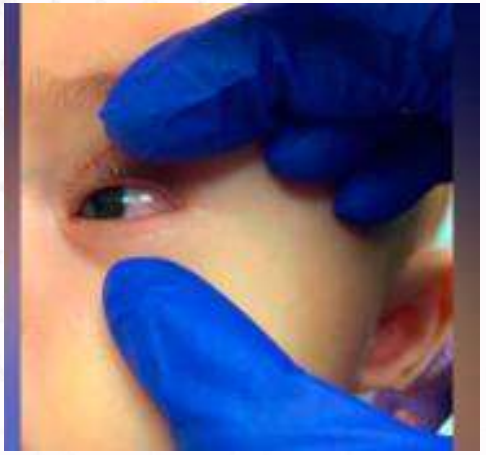
Data collected January 9, 2022

Age Group	New Admissions per 100,000
0-17 yrs.	1.19
18-29 yrs.	3.07
30-39 yrs.	4.06
40-49 yrs.	4.22
50-59 yrs.	6.45
60-69 yrs.	9.69
70+ yrs.	18.99
All ages	6.02

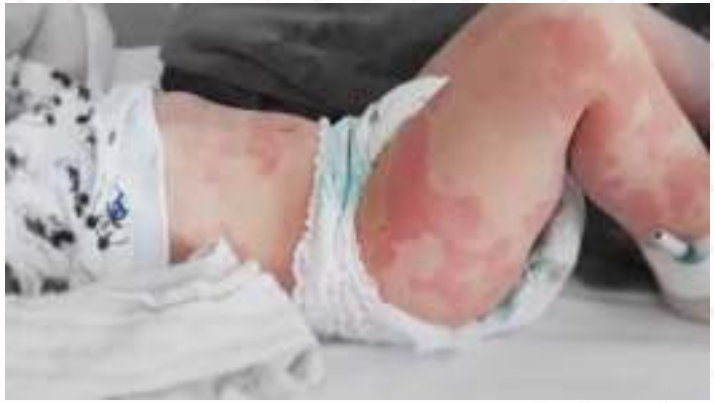
References: **CDC**. “Demographic Trends of COVID-19 cases and deaths in the US reported to CDC”. https://covid.cdc.gov/covid-data-tracker/#demographicsovertime

Multisystem inflammatory syndrome in children (MIS-C)

- First identified in the UK and US in April 2020
- 7,459 cases in US; 63 deaths
  - Median age is 9 years
  - 60% of patients are male
- Inflammation of various tissues and organs
  - Heart, blood vessels, kidneys, digestive system, brain, skin or eyes
- Shares some signs and symptoms with Kawasaki disease
  - Fever, vomiting, diarrhea, skin rash, red eyes, fatigue, swelling of lips and tongue
  - Shock, which affects blood pressure and heart function



Source: CNN

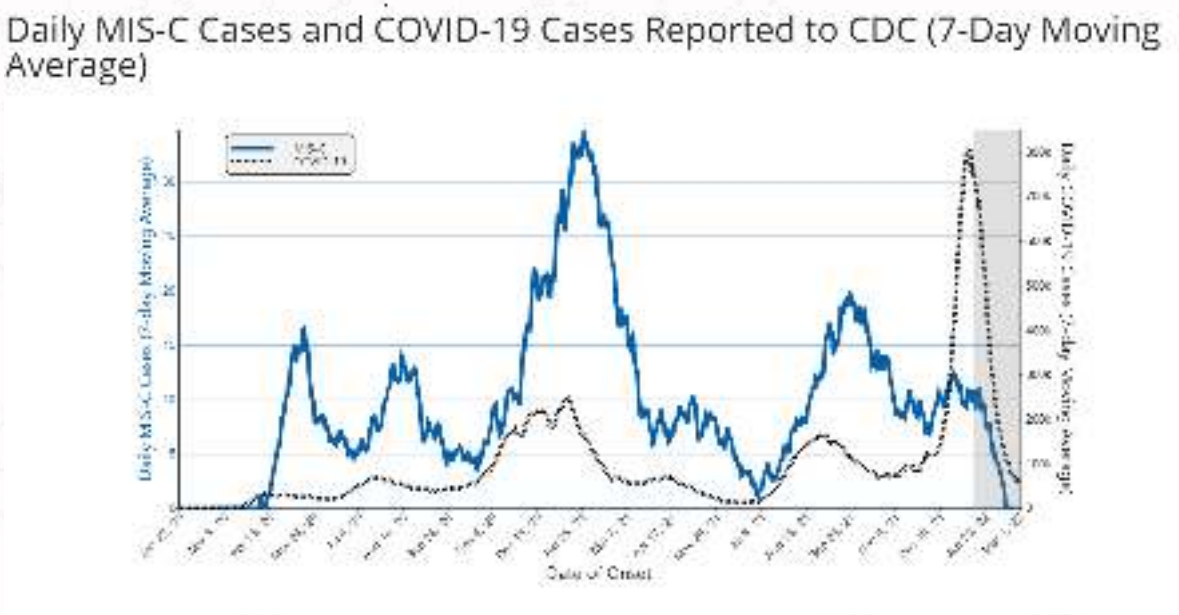


Source: NBC news

References: Dufort EM et al. 2020. Multisystem Inflammatory Syndrome in Children in New York State. *N Engl J Med*. 383(4):347-358. doi:10.1056/NEJMoa2021756; Feldstein LR et al. 2020/ Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. *N Engl J Med*. 383(4):334-346. doi:10.1056/NEJMoa2021680

Multisystem inflammatory syndrome in children (MIS-C)

- Emergence coincides with widespread SARS-CoV-2 transmission
- 98% of patients had a positive test result for SARS CoV-2
- ~80% of the children require intensive care and ~ 20% required mechanical ventilation
- Treatments:
  - Intravenous immunoglobin (IVIG)
  - Anti-inflammatory drugs (steroids, anti-IL-1 or IL-6)
  - Aspirin to reduce clots
  - Meds to normalize low BP

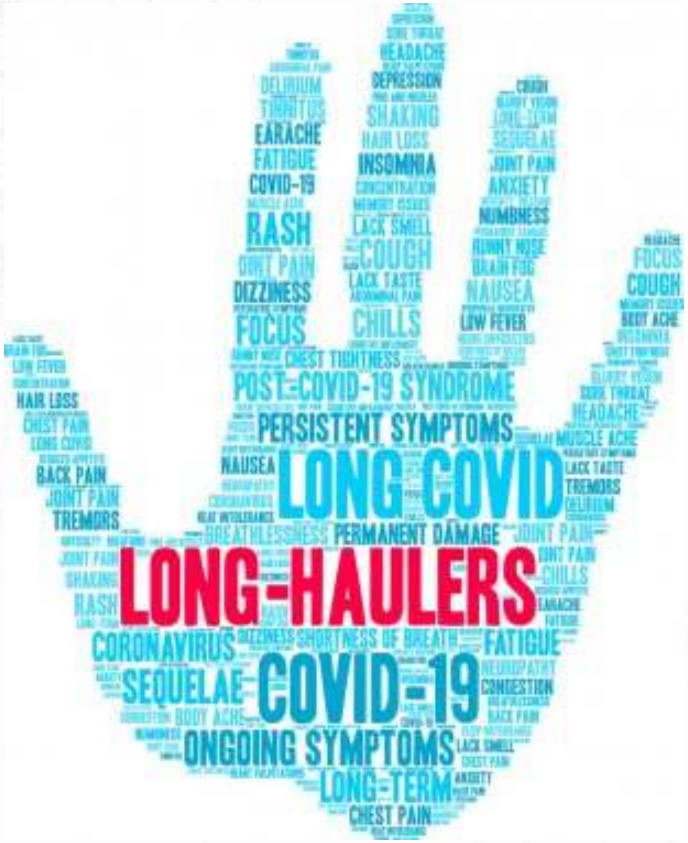


Source: CDC

References: Dufort EM et al. 2020. Multisystem Inflammatory Syndrome in Children in New York State. *N Engl J Med*. 383(4):347-358. doi:10.1056/NEJMoa2021756; Feldstein LR et al. 2020/ Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. *N Engl J Med*. 383(4):334-346. doi:10.1056/NEJMoa2021680

Long-term complications of COVID

- COVID-19 seen as a respiratory disease, but it can damage other organ systems as well
- Some COVID-19 patients exhibit persistent or new symptoms **>4 weeks** after diagnosis
  - Long-haul COVID, long COVID, post-acute sequelae of COVID (PASC)
- FAIR Health: repository of private healthcare claims data to study 1,959,982 COVID-19 patients
  - **23.2%** of all patients had at least one post-COVID symptom (19% asymptomatic, 50% hospitalized)
  - Women were more likely to report than men
  - Most common: pain, breathing difficulties, hyperlipidemia, malaise and fatigue, & hypertension
  - Others: brain fog, loss of taste and smell, joint pain, sleep disturbance
  - Mental health conditions: anxiety and depression
  - Higher risk of death after the first 30 days of illness



Source: WDRFree.com

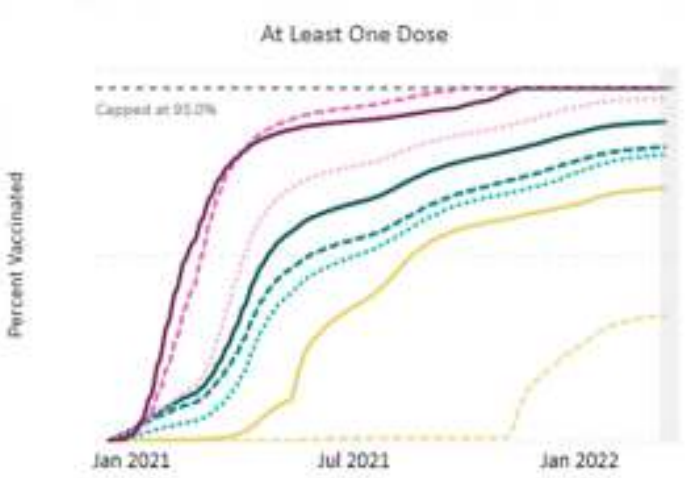
Source: FAIR Health. A Detailed Study of Patients with Long-Haul COVID: An Analysis of Private Healthcare Claims

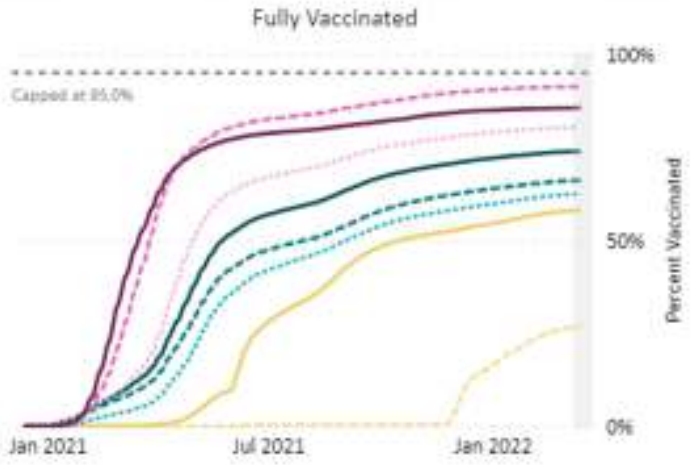
Formulation and Dosing for Pfizer-BioNTech COVID-19 Vaccines

	Formulation for ≥12-year-olds (purple cap)	Formulation for 5–11-year-olds (orange cap)
Age group	12 years and older	5-11 years
Vial cap color		
Dose (mRNA concentration)	30 ug	10 ug
Injection volume	0.3 mL	0.2 mL
Fill Volume (before dilution)	0.45 mL	1.3 mL
Amount of Diluent* Needed per vial	1.8 mL	1.3 mL
Doses per Vial	6 (after dilution)	10 (after dilution)
Storage conditions		
Ultralow temperature freezer (-90°C to -60°C)	9 months	6 months
Freezer (-25°C to -15°C)	2 weeks	N/A
Refrigerator (2°C to 8°C)	1 month	10 weeks

References: CDC. K.Woodworth. Interim Clinical Considerations for COVID-19 Vaccine in Children Ages 5–11 Years. ACIP February 4, 2022 Meeting

Children and COVID-19 Vaccination Trends





12/12/20: FDA EUA for ≥16 years
5/11/21: FDA EUA for 12-15 years
10/29/21: FDA EUA for 5-11 years

Ages 5-11

- 9.4 million (33%) received at least one dose
- 7.4 million (26%) completed 2-dose series

Ages 12-17

- 16.8 million (67%) received at least one dose
- 14.4 million (57%) completed 2-dose series

References: CDC. COVID Data Tracker. Accessed 3/11/2022. American Academy of Pediatrics. Children and COVID-19: State-Level Data Report. Accessed 3/11/22.

BNT162b2 mRNA Vaccine Effectiveness Against Omicron in Children & Adolescents

- 852,384 newly fully vaccinated children aged 12 to 17 years and 365,502 children aged 5 to 11 years between Dec. 13, 2021, and Jan. 31, 2022
- Against hospitalization
  - 12 to 17 yo: declined **85%** (95% CI: 63%,95%) to **73%** (95% CI: 53%,87%
  - 5-11 yo: declined **100%** (95% CI:-189%,100%) to **48%** (95% CI: -12%,75%)
- Against infection
  - 12 to 17 yo: declined **66%** (95% CI: 64%,67%) to **51%(**95% CI: 48%,54%)
  - 5-11 yo: declined **68%** (95% CI: 63%,72%) to **12%** (95% CI: 6%,16%)
  - Jan 30 data: 67% for 12 yo and 11% for 11 yo

Reference: Vajeera Dorabawila, Dina Hoefer, Ursula E. Bauer, Mary T. Bassett, Emily Lutterloh, Eli S. Rosenberg. Effectiveness of the BNT162b2 vaccine among children 5-11 and 12-17 years in New York after the Emergence of the Omicron Variant. medRxiv 2022.02.25.22271454

BNT162b2 mRNA Vaccine Effectiveness Against Omicron in Children & Adolescents

TABLE 3. COVID-19 Pfizer-BioNTech vaccine effectiveness against asymptomatic or symptomatic SARS-CoV-2 infection among children and adolescents aged 5–15 years, by time since receipt of second vaccine dose and variant — PROTECT* cohort study, four states, July 2021–February 2022

Age group and COVID-19 vaccination status (no. of days since receipt of most recent dose)	No. of contributing participants†	Total person-days	Median no. of days (IQR)	No. of SARS-CoV-2 infections§	VE, % (95% CI)	
					Unadjusted	Adjusted¶
Children aged 5–11 yrs						
Omicron variant infections						
Unvaccinated (referent)	336	13,801	41 (28 to 62)	137	—	—
2 doses (14–82 days)	640	29,996	53 (34 to 61)	184	47 (32 to 59)	31 (9 to 48)
Adolescents aged 12–15 yrs						
Delta variant infections						
Unvaccinated (referent)	139	9,786	65 (25 to 107)	23	—	—
2 doses (≥14 days)	193	23,575	142 (91 to 156)	7	87 (70 to 95)	81 (51 to 93)
2 doses (14–149 days)	188	16,517	97 (75 to 105)	3	93 (76 to 98)	87 (49 to 97)
2 doses (≥150 days)	138	7,058	57 (49 to 63)	4	67 (0 to 89)	60 (−35 to 88)
Omicron variant infections						
Unvaccinated (referent)	76	3,001	37 (24 to 62)	38	—	—
2 doses (≥14 days)	192	5,432	22 (22 to 31)	18	64 (37 to 80)	59 (24 to 78)
2 doses (14–149 days)	65	2,623	42 (28 to 56)	14	62 (30 to 79)	59 (22 to 79)
2 doses (≥150 days)	134	2,809	22 (22 to 22)	4	74 (16 to 92)	62 (−28 to 89)

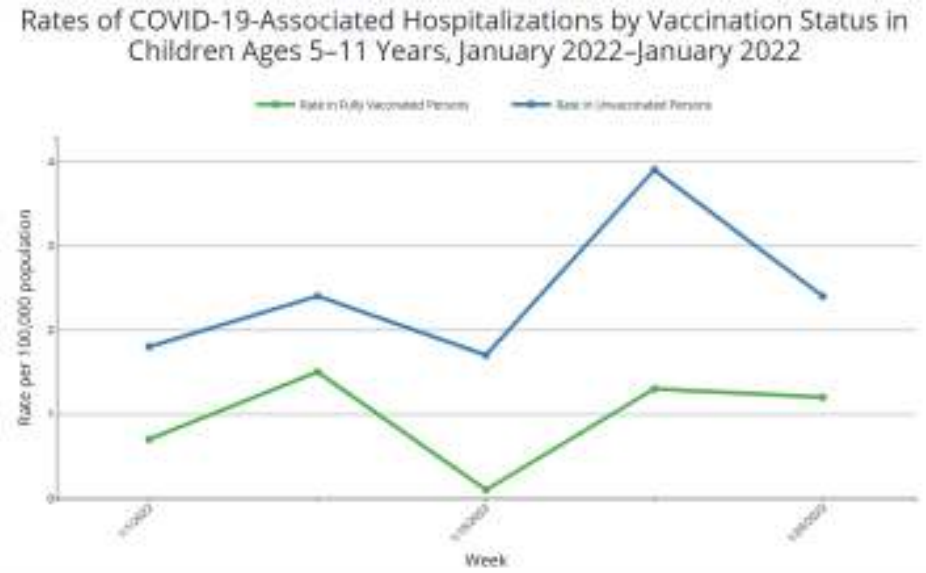
Abbreviations: SMD = standard mean difference; VE = vaccine effectiveness.

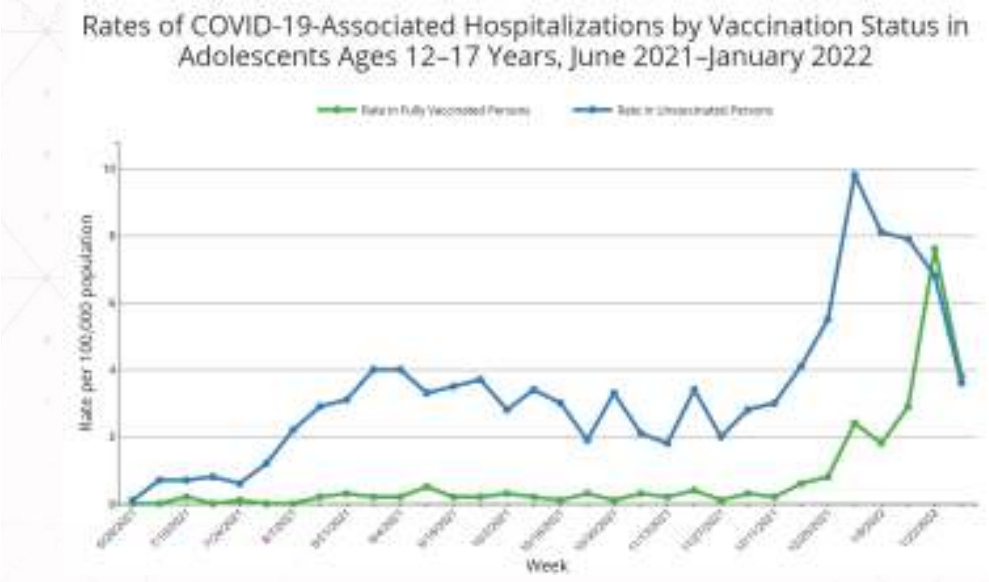
* PROTECT (Pediatric Research Observing Trends and Exposures in COVID-19 Timelines) is conducted in Phoenix and Tucson, Arizona; Miami, Florida; Temple, Texas; and Salt Lake City, Utah.

Reference: Fowlkes AL, Yoon SK, Lutrick K, et al. Effectiveness of 2-Dose BNT162b2 (Pfizer BioNTech) mRNA Vaccine in Preventing SARS-CoV-2 Infection Among Children Aged 5–11 Years and Adolescents Aged 12–15 Years — PROTECT Cohort, July 2021–February 2022. MMWR Morb Mortal Wkly Rep. ePub: 11 March 2022

6x Higher in Unvaccinated Adults Ages 18 Years and Older

3x Higher	2x Higher	5x Higher	5x Higher	8x Higher
in Unvaccinated Children Ages 5-11 Years	in Unvaccinated Adolescents Ages 12-17 Years	in Unvaccinated Adults Ages 18-49 years	in Unvaccinated Adults Ages 50-64 years	in Unvaccinated Adults Ages 65 Years and Older





Source: CDC. Age-Adjusted Rates of COVID-19-Associated Hospitalizations by Vaccination Status in Adults Ages ≥18 Years, January 2021–January 2022

CDC Vaccine Safety Monitoring

VAERS- Vaccine Adverse Event Reporting System

- Rapidly detect potential safety problems as well as rare adverse events
- Passive surveillance system- relies on individuals to send in reports of their experiences; reporting biases exist
  - Anyone can submit a report to VAERS- patients, providers, vaccine manufacturers

VSD- Vaccine Safety Datalink

- Collaborative project between CDC and 9 integrated healthcare organizations
- Monitor safety of vaccines and conduct vaccine safety studies based on questions or concerns raised from the medical literature and VAERS

CISA- national network of vaccine safety experts from the CDC's Immunization Safety Office and 7 medical research centers

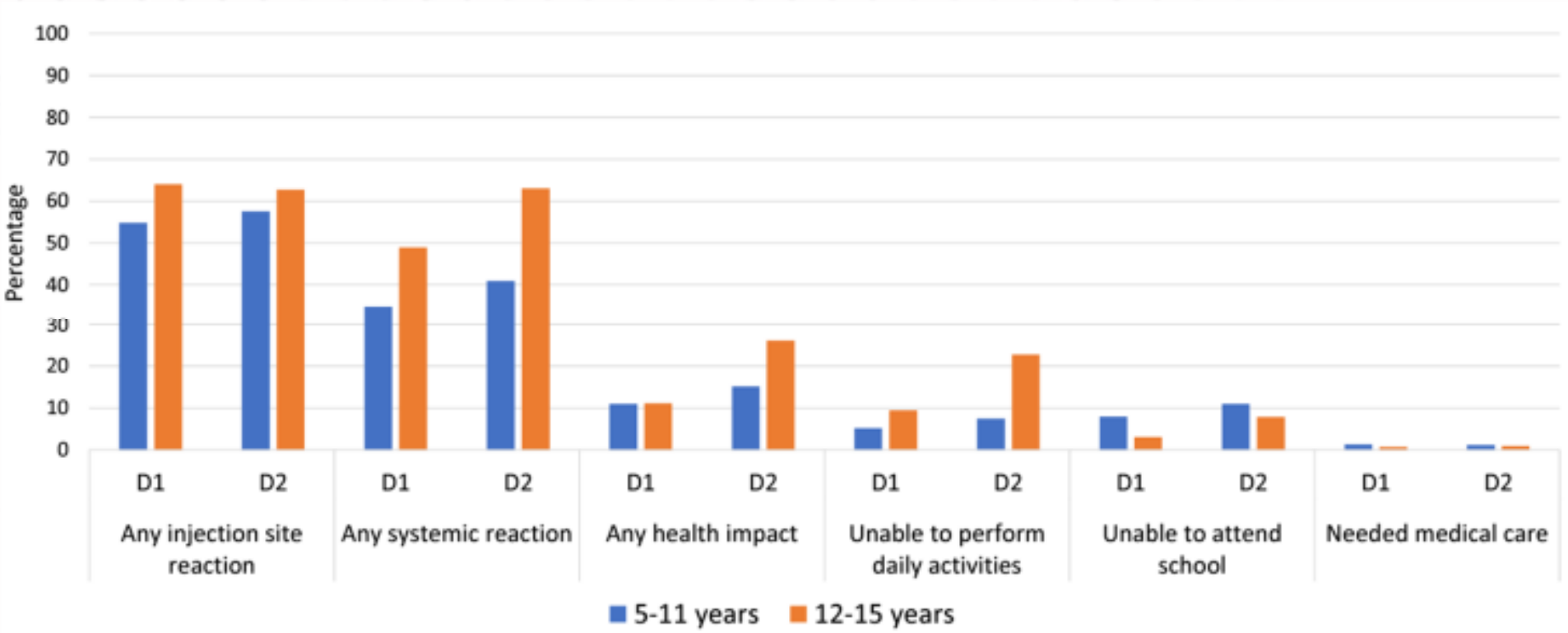
Reference: A. Hause. Early safety monitoring for additional COVID-19 vaccine doses: Reports to VAERS and v-safe. October 21, 2021, Meeting.

CDC Vaccine Safety Monitoring

V-safe- smart phone-based monitoring program for COVID-19 vaccine safety in the U.S.

- Solicits participants' reports on how they feel after COVID-19 vaccination
- Active outreach, provides longitudinal data
- Voluntary enrollment
- Requires a smartphone

V-safe: Events reported at least once in days 0-7 after Pfizer-BioNTech vaccination for children and adolescents ages 5-11 and 12-15 years, by dose



- 115,208 participants ages 5-15 years
- 63% 12-15 years; 78% not Hispanic/Latino; 68% white
- Top reactions: injection site pain, fatigue, headache, myalgia, and chills

Reference: A. Hause. Safety monitoring of COVID-19 vaccine among children and young adults in v-safe. January 5, 2022, Meeting.

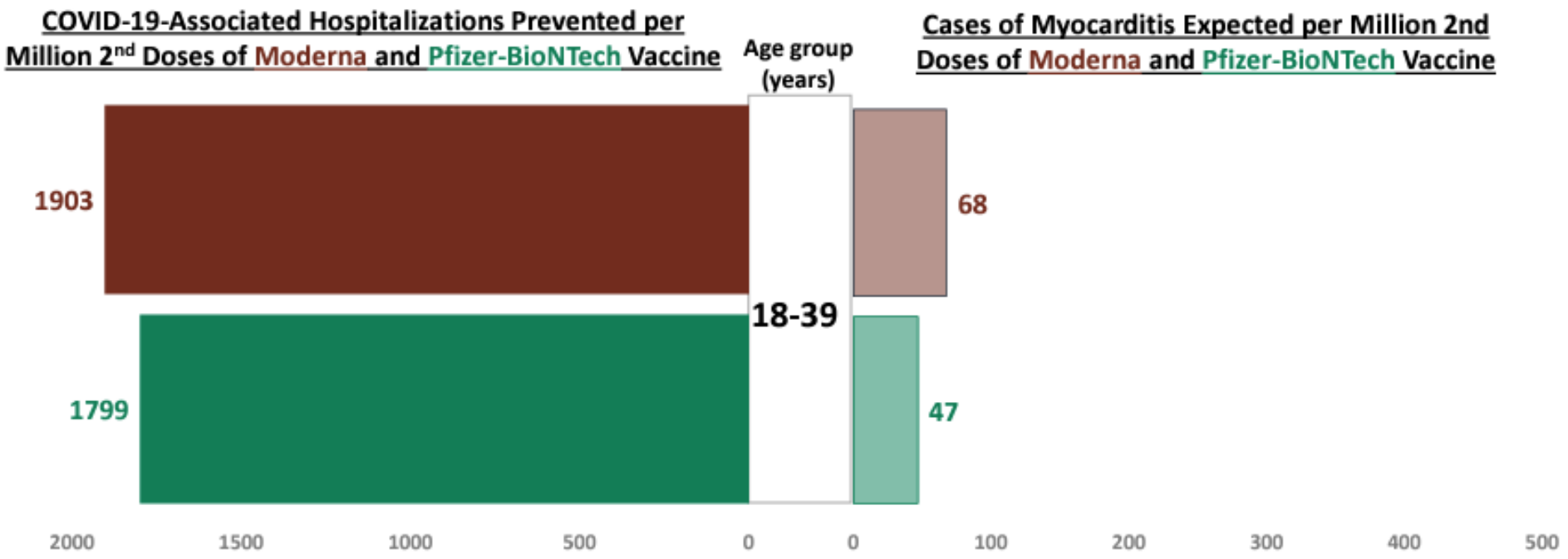
Myocarditis outcomes following vaccination

- **May 31**: myocarditis/pericarditis reports to VAERS following mRNA vaccination in teens
- **June 10**: FDA VRBPAC Meeting
  - Chest pain, Dyspnea, wave change, elevated cardiac enzymes, abnormal echocardiography
  - 475 cases under review (≤ 30 years of age)
  - Predominance of male patients in younger age groups, especially after dose 2
  - Observed reports > expected cases after dose 2 (16–24 years of age)
  - Limited outcome data suggested most patients (at least 81%) had full recovery of symptoms
- ACIP continuously evaluating data

Vaccine	Sex	Rate per 1M 2nd Doses in 7-day risk period among persons ages 18–39 years[2]
Moderna	Males	67.5
	All	33.0
Pfizer-BioNTech	Males	46.8
	All	24.1

Reference: VRBPAC June 10, 2021, Meeting. T. Shimabukuro. COVID-19 Vaccine Safety Updates; CDC. S. Oliver. Summary and Work Group Interpretation: Extended intervals for mRNA COVID-19 vaccines. ACIP February 4, 2022, Meeting.

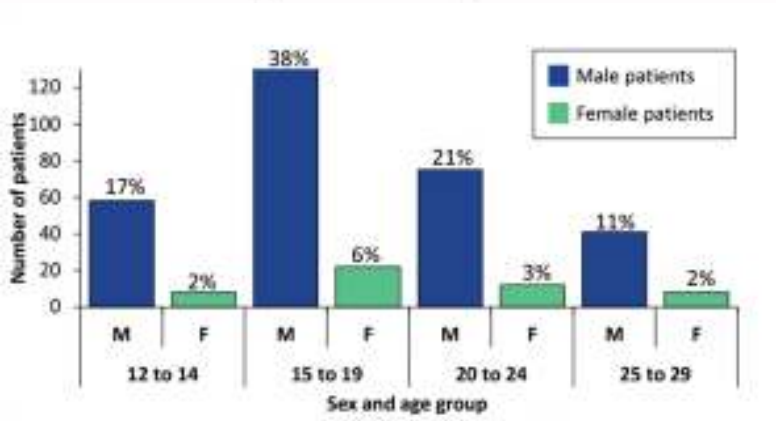
Benefits and Risks After mRNA COVID-19 Vaccination: Males 18-39 years

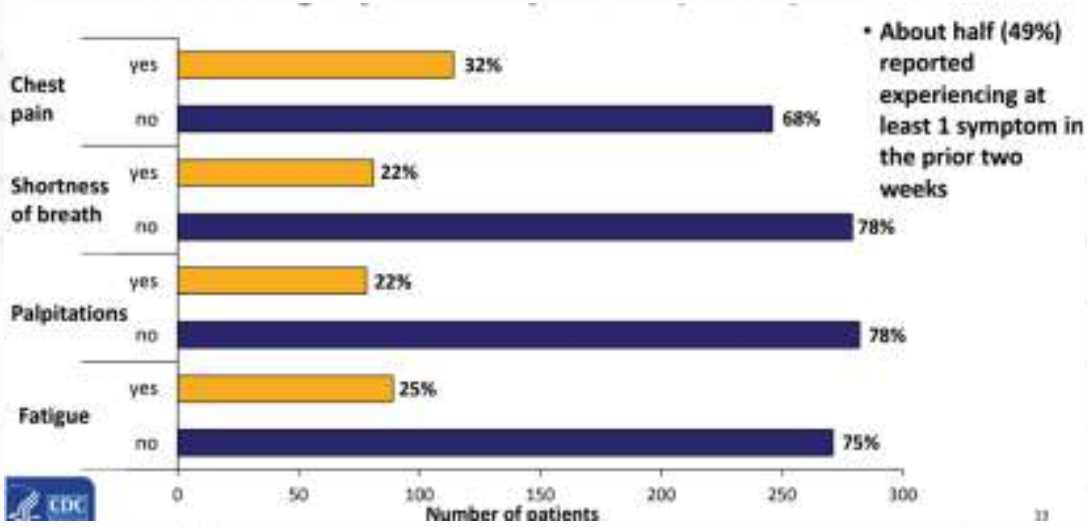


Reference: CDC. S. Oliver. Summary and Work Group Interpretation: Extended intervals for mRNA COVID-19 vaccines. ACIP February 4, 2022, Meeting.

Myocarditis Outcomes Following Vaccination: 12-29 years

- 360/850 patients ages 12-29 with reports of myocarditis or myopericarditis
- Most reported no impact on quality of life, and most did not report missing school or work
- Only (13%) were re-admitted to the hospital
- Most (81%) HCP indicated patient was probably fully or fully recovered
- Risk of myocarditis **6-34 times** higher with SARS-Cov-2 infection



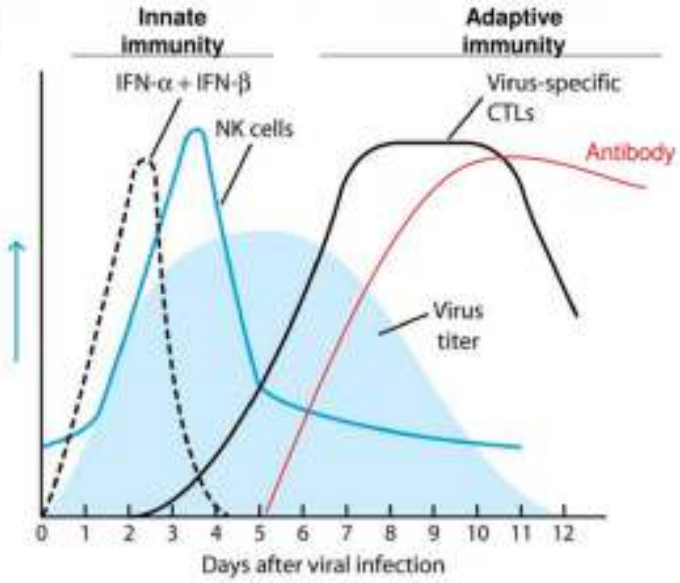


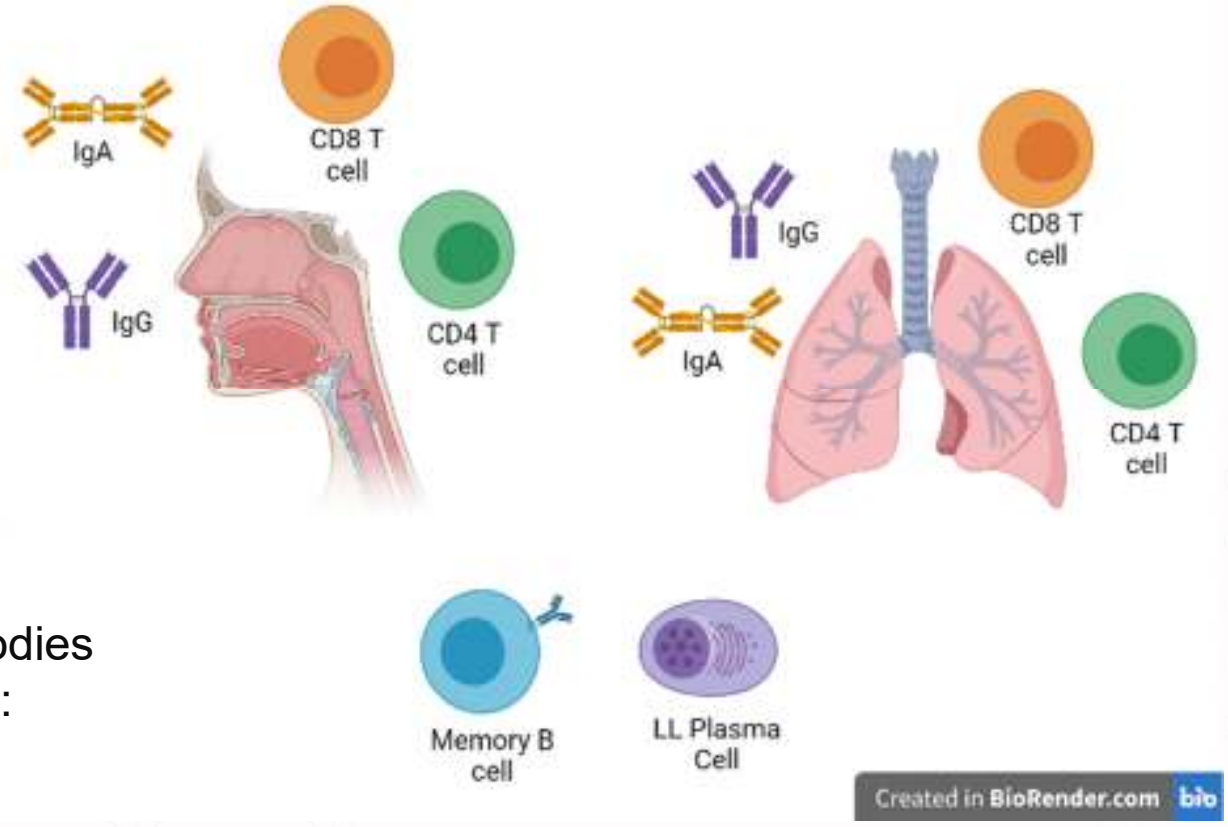
Reference: I. Kracalik. Mycocarditis outcomes following mRNA COVID-19 vaccination. ACIP February 4, 2022, Meeting.

Status on COVID-19 Vaccines for Children Under 5

- 18 million children under the age of 5
  - Less likely to develop severe disease than adults, but same risk of infection
  - Concerns about lingering symptoms
- Moderna (approved for 18+ years)
  - Under 6: 2-shot regimen; 25 μg dose
  - 6 to 11 years: 50 μg dose & 12 to 17 years: 100 μg dose
  - **March 23 data**: 43.7% VE in children 6 months to 2 years old, and 37.5% VE in children from 2 to under 6
- Pfizer-BioNTech (approved for 5+ years)
  - 2-shot regimen, 3 μg dose failed to elicit protective titers in children 2-4 years of age
  - Testing 3-shot regimen
  - Also testing 3-shot regimen for 5-11-year-olds (10 μg)
- Different timing between doses?
- Expected that companies will seek approval in April

Adaptive Immunity to SARS-CoV-2





Protection from Infection: Antibodies
Protection from Severe Disease:
Antibodies, T cell, Memory B cells

Reference: Abbas AK et al. Cellular and Molecular Immunology, 8th ed. Elsevier Saunders.2015

Immunity from Childhood to Adulthood

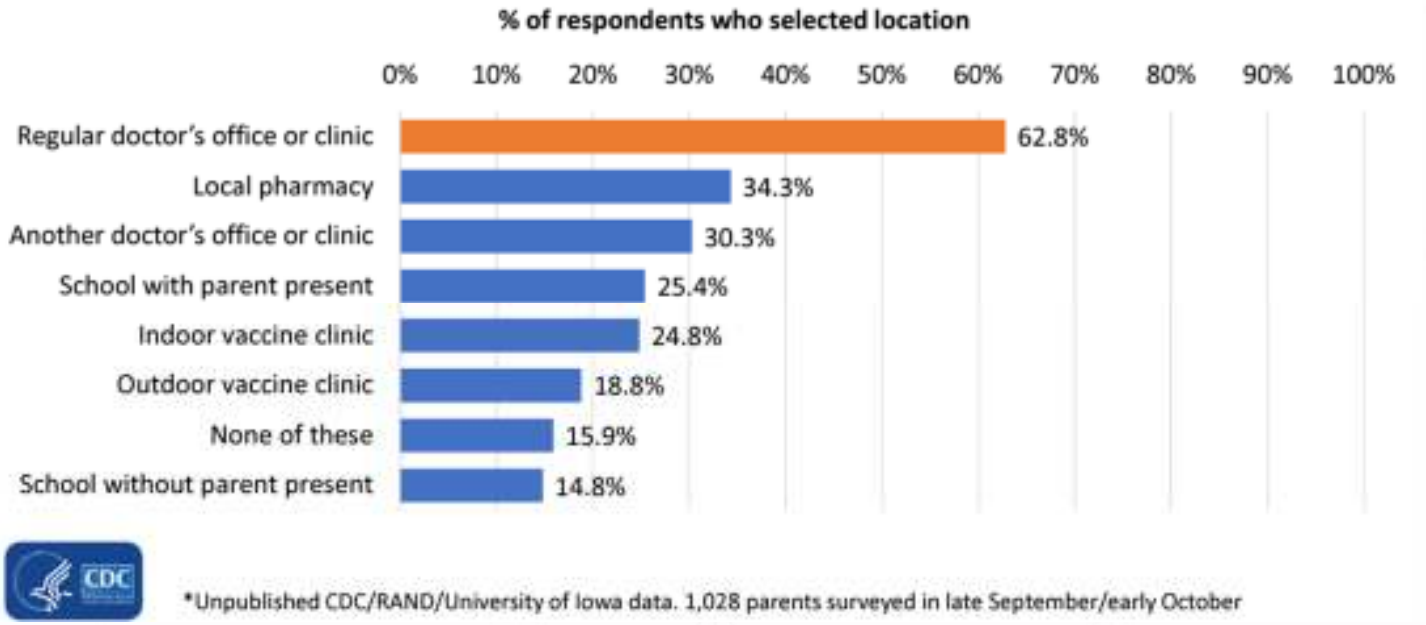
Childhood
- Highly functional innate immunity
- Developing T and B cells
- Natural antibody (IgM)
- At risk from many pathogenic microbes
- Dependence on maternal IgG transplacentally & breast milk

Into Adulthood
- Functional innate immunity
- Developed adaptive responses
- Expanding repertoire of memory T and B cells triggered by previous infections and vaccinations

Old Age
- Profound remodeling and decline
- Major impact on health and survival

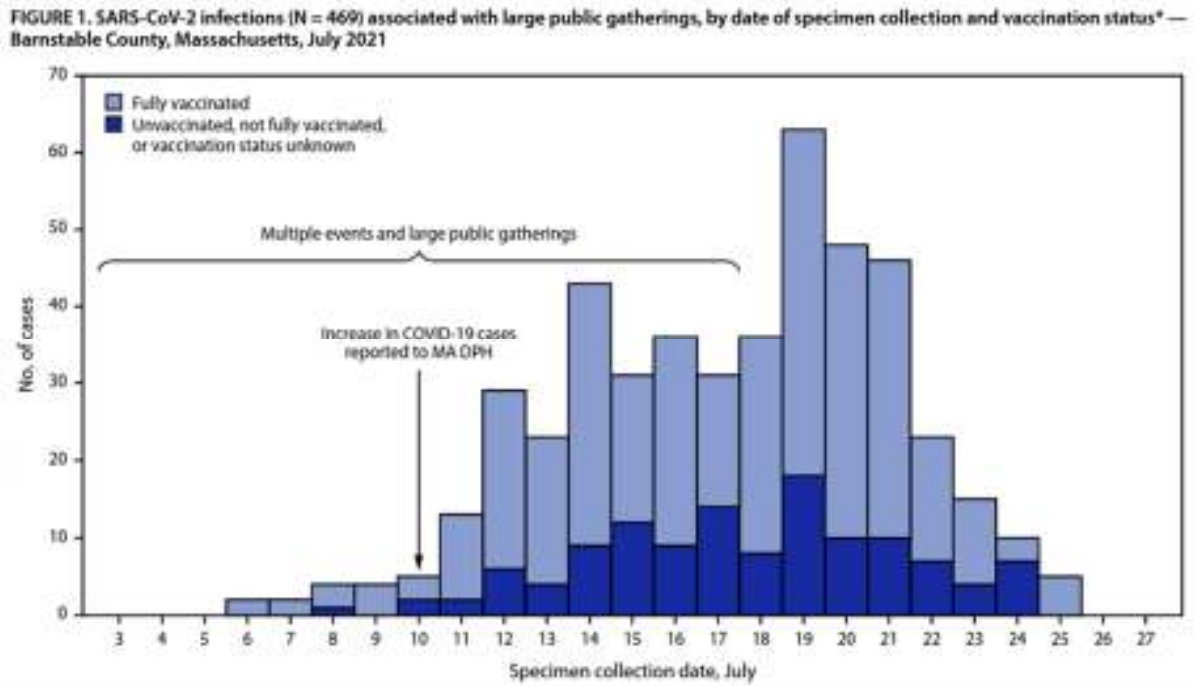
References: Simon A.K. et al. 2015. Evolution of the immune system in humans from infancy to old age. https://royalsocietypublishing.org/doi/10.1098/rspb.2014.3085

Pediatric COVID-19 Vaccine Planning



Reference: Kevin Chatham-Stephens. Implementation of COVID-19 vaccine pediatric program. ACIP November 2, 2021 Meeting

Summer of Breakthroughs & Boosters



- **July 2021**: 469 cases of COVID-19 associated with multiple summer events and large public gatherings
  - 89% specimens positive for Delta variant
  - 74% of case occurred in fully vaccinated individuals; 4 hospitalizations, no deaths
- Viral load same among fully vaccinated people as those who were not vaccinated or partially vaccinated
- Resulted in CDC mask recommendation

Reference. Brown CM, Vostok J, Johnson H, et al. Outbreak of SARS-CoV-2 Infections, Including COVID-19 Vaccine Breakthrough Infections, Associated with Large Public Gatherings — Barnstable County, Massachusetts, July 2021. MMWR 2021;70:1059-1062.

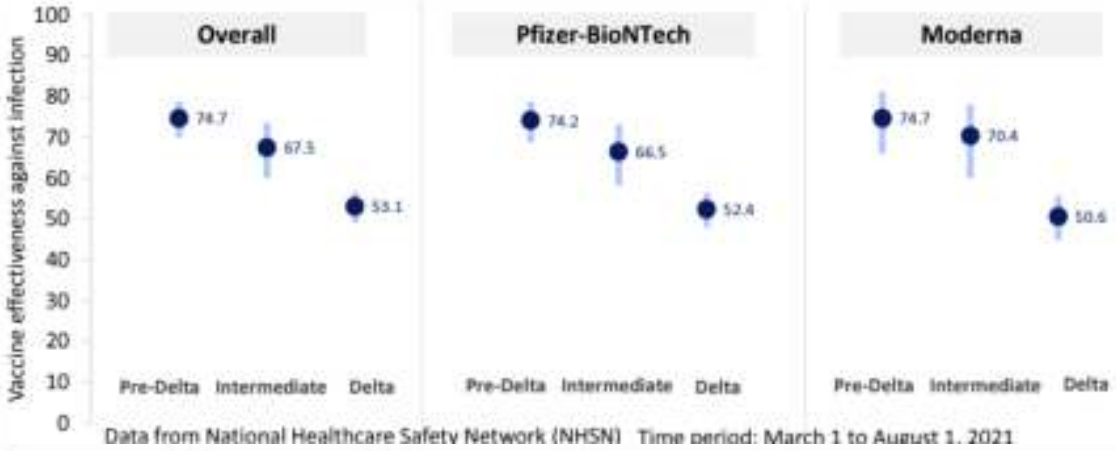
Booster Vaccinations: Early Considerations & Data

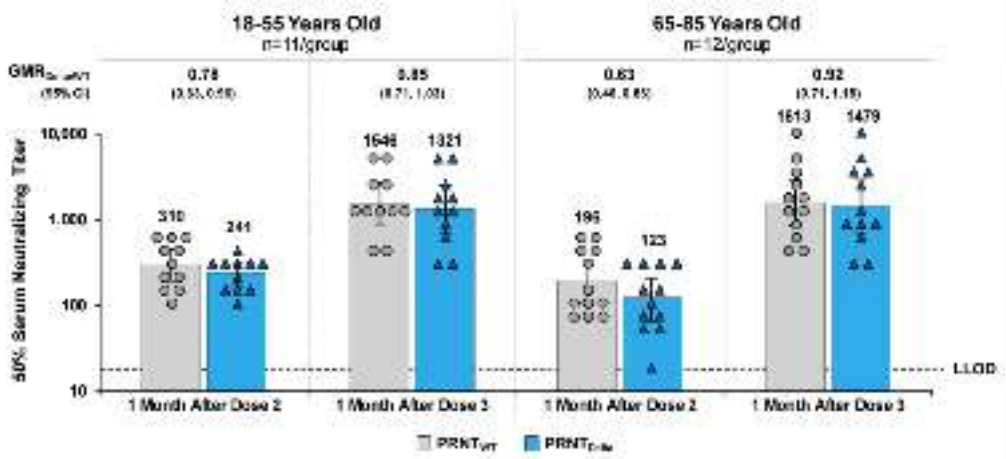
- Israeli Ministry of Health performed analyses of Pfizer vaccine efficacy (retrospective cohort studies)
- Surge in Delta cases despite widespread vaccination (>60%)
- **2.3-fold** increased risk for breakthrough infection among persons vaccinated in January vs. April 2021
- Higher breakthrough infection rate among those who received two doses ≥5 months ago (**2.4%**) compared to <5 months ago (1.1%)
- **July 30:** boosters administered to people > ≥60 years of age; extended to all adults in August
  - 4-fold greater protection against infection from 10 days after booster
  - 5-6-fold greater protection against severe disease and hospitalization from 10 days after booster

Booster Vaccinations: Early Considerations & Data

- Protection against infection (asymptomatic or mild) waned; noticeable in ≥ 60 years of age
- 3rd dose substantially boosted neutralizing antibody titers
- Safety and reactogenicity similar to that observed after dose #2

Long-term care residents





Reference. Oliver S. Updates to COVID-19 Epidemiology and COVID-19 Vaccines. VBRPAC Meeting, September 17, 2021; Pfizer/BioNTech. BNT162b2 [COMIRNATY® (COVID-19 Vaccine, mRNA)] Booster (Third) Dose. VRBPAC Meeting. September 17, 2021.

Booster Vaccinations: Current Status

- **September 17**: VRBPAC voted on booster recommendations
  - For individuals 16 years of age and older: 2 Yes **16 No**
  - For individuals 65 years of age and older: **18 Yes** 0 No
  - Not enough safety data and lack of clarity on whether VE has declined substantially (risk vs. benefit)
- **October 21:** CDC expanded booster eligibility to those aged 18+ years
- **January 5**: CDC expanded booster eligibility to those aged 12-17 years
- Largest public health impact realized by vaccinating the unvaccinated
- Critical to ensure global vaccine availability- reduce appearances of new variants (WHO)

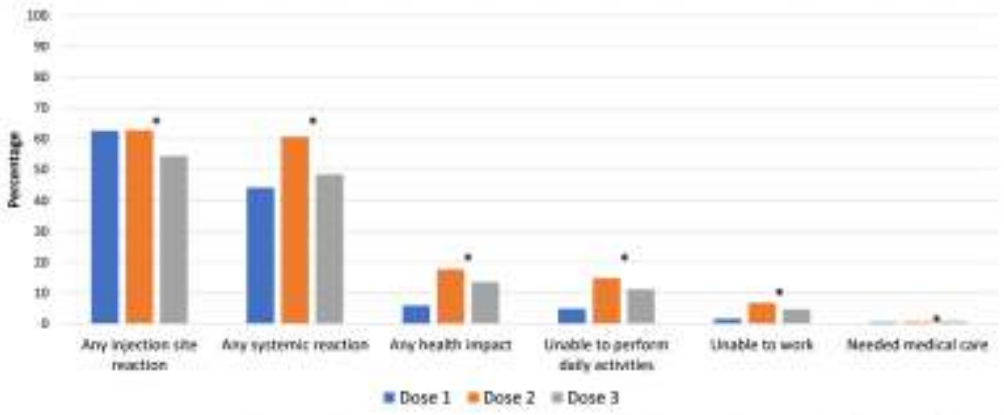
Booster for Adolescents Aged 12-15 Years

- CDC working group recommended boosters for individuals aged 12-15 at least 5 months after completion of primary series of Pfizer-BioNTech vaccination based on individual benefit-risk
  - Waning immunity following primary vaccine series and rise of Omicron variant
  - Minimize disruption to school attendance
- Data do not suggest safety concerns regarding a Pfizer-BioNTech COVID-19 vaccine booster dose for 12–15-year-olds, beyond those previously identified in older age groups
  - Lower risk for myocarditis in this age group
  - Data suggest low risk following booster
- Emphasis on the importance of clear and consistent recommendations for all adolescents (12–17 years of age)
- Vaccine recommendations can be updated as needed, especially in rapidly evolving pandemic

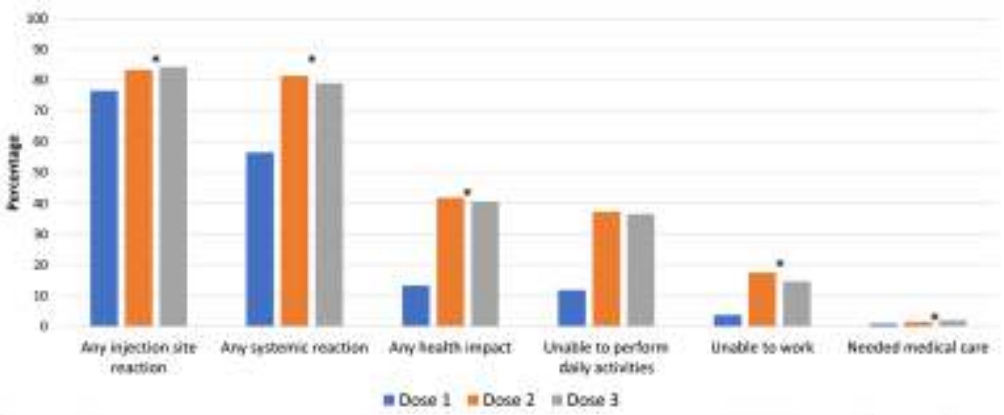
References: CDC. S. Oliver. Updates to the Evidence to Recommendation Framework: Pfizer-BioNTech vaccine booster doses in 12–15 year olds. ACIP January 5, 2022 Meeting

V-safe: Reactions and health impact events reported at least once in days 0-7 after vaccination, by dose

Pfizer-BioNTech



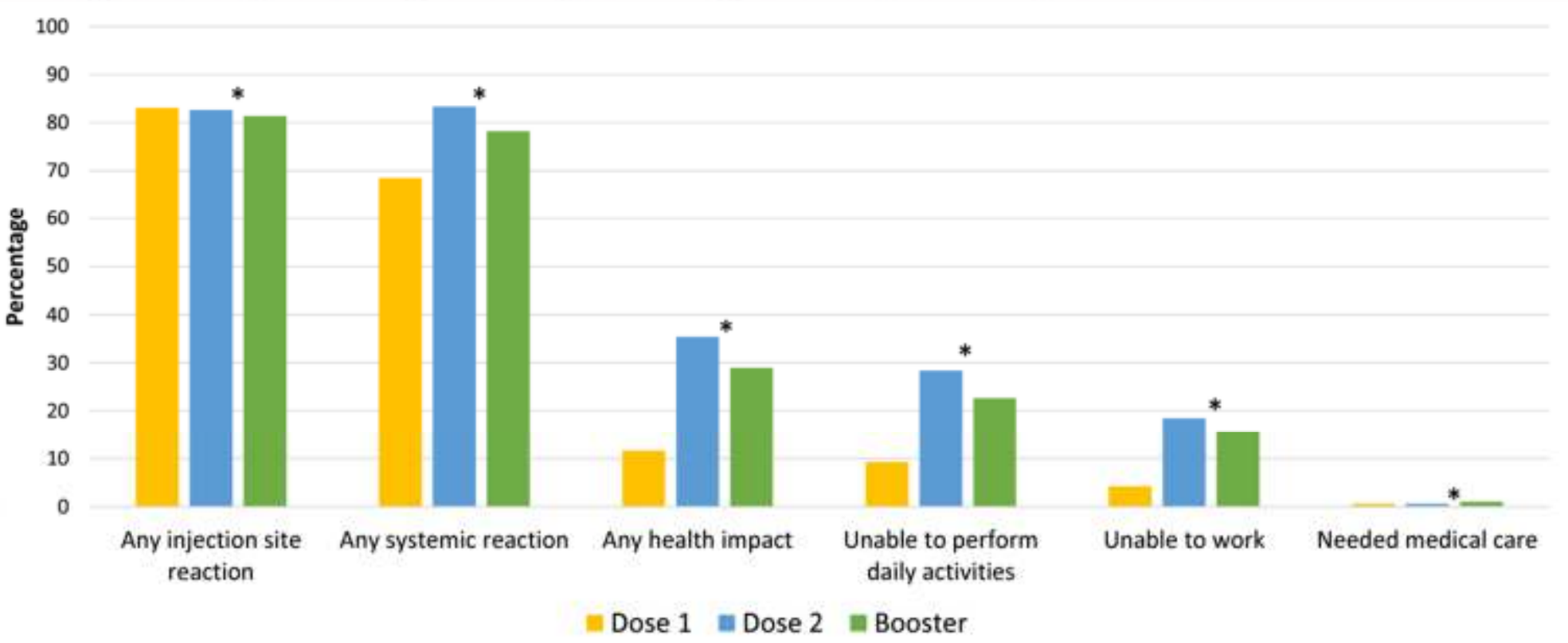
Moderna



- 274,167 participants who reported an additional dose
- 62% female; 37% male
- 27% 18-24 years; 23% 50-64; 39% 65-74
- 90% not Hispanic/Latino; 84% white
- Most reported a dose 3 from the same manufacturer
- Systemic reactions slightly less frequently following dose 3 than dose 2

Reference: A. Hause. Early safety monitoring for additional COVID-19 vaccine doses: Reports to VAERS and v-safe. October 21, 2021, Meeting.

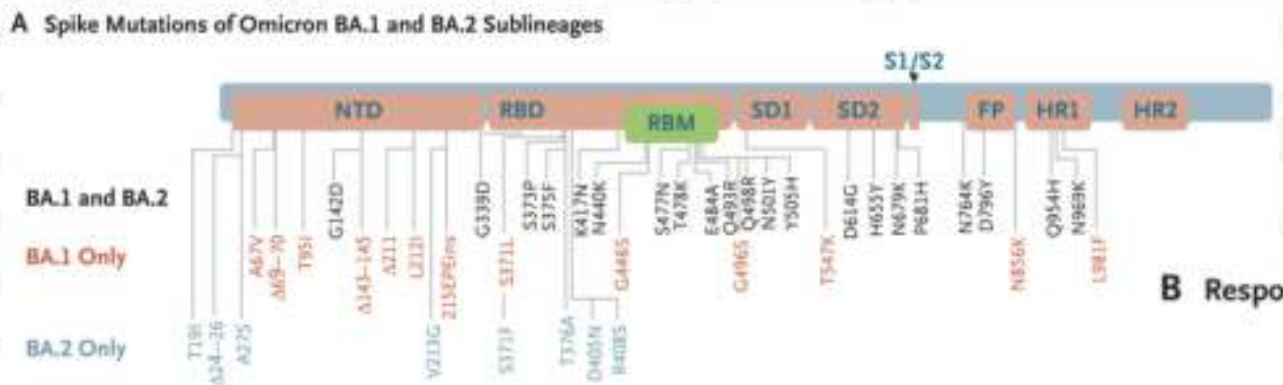
V-safe: Events reported by participants ages 16-24 years at least once in days 0-7 after Pfizer-BioNTech vaccination, by dose

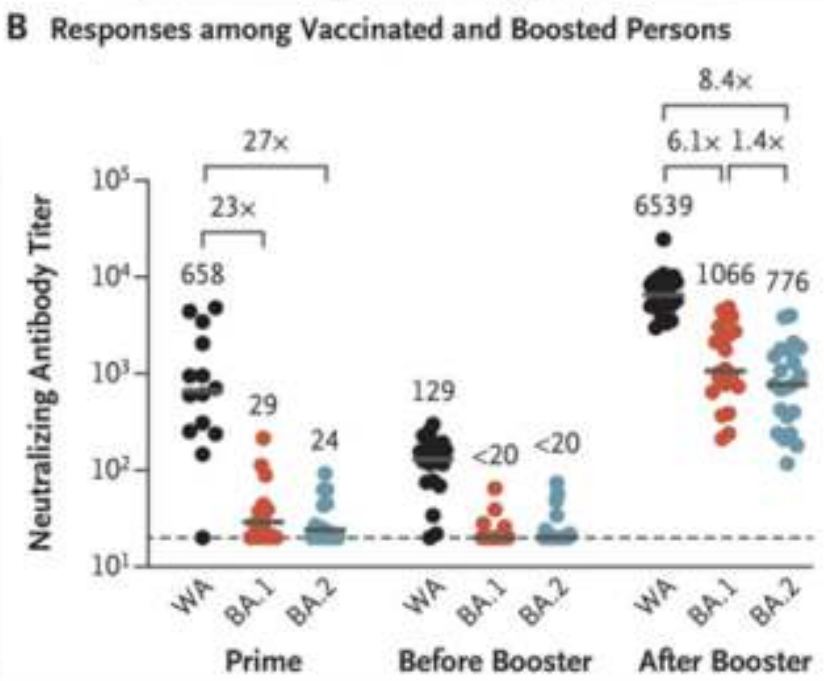


- 7,088 participants ages 16-24 years
- 72% female; 93% 18-24 years; 84% not Hispanic/Latino; 74% white
- Top reactions: injection site pain, fatigue, headache, myalgia, and chills

Reference: A. Hause. Safety monitoring of COVID-19 vaccine among children and young adults in v-safe. January 5, 2022, Meeting.

Booster Vaccinations: Immunogenicity





- Omicron sub-lineages BA.1 and BA.2
- n=24 individuals vaccinated and boosted with BNT162b2 mRNA vaccine
- Titers measured 2 wks after prime, 6 m after full series, and 2 wks after boost

Reference: Yu J, Collier AY, Rowe M, et al. Neutralization of the SARS-CoV-2 Omicron BA.1 and BA.2 Variants. N Engl J Med. 2022 Mar 16.

Booster Vaccinations: Effectiveness

	Vaccinated with 2 doses (≥ 5 months after receipt)			Vaccinated with 3 doses (≥7 days after receipt))		
	Tests	Events	Risk per 100,000 people	Tests	Events	Risk per 100,000 people
Documented infection	93,566	6,131	3662.3	77,184	1,135	422.9
Symptomatic infection	95,934	3,345	1909.6	78,507	514	178.9
Admission to hospital		231	220.8		29 (93%)	14.4
Severe disease		157	158.9		17 (92%)	12.9
Death		44	31.9		7 (81%)	6.1

Study period: July 30, 2020, to Sept 23, 2021 (Delta predominant)
n=728,321 individuals for both groups; BNT162b2 mRNA vaccine only

Reference: Barda N, Dagan N, Cohen C, et al. Effectiveness of a third dose of the BNT162b2 mRNA COVID-19 vaccine for preventing severe outcomes in Israel: an observational study. Lancet 2021;398:2093–100.

Booster Vaccinations: Durability

- Vaccine effectiveness (VE) against COVID-19–associated emergency department/urgent care (ED/UC) visits and hospitalizations among U.S. adults aged ≥18 years
- Persons categorized as having received 3 doses included those who received a third dose in a primary series or a booster dose after a 2 dose primary series
- 241,204 ED/UC encounters** and 93,408 hospitalizations across 10 states during August 26, 2021–January 22, 2022
  - 77% ED/UC encounters and 89% hospitalizations during Delta-predominant period
  - 23% ED/UC encounters and 11% hospitalizations during Omicron-predominant period

Reference: Ferdinands JM, Rao S, Dixon BE, et al. Waning 2-Dose and 3-Dose Effectiveness of mRNA Vaccines Against COVID-19–Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Adults During Periods of Delta and Omicron Variant Predominance — VISION Network, 10 States, August 2021–January 2022. MMWR Morb Mortal Wkly Rep 2022;71:255–263

Durability of Booster Vaccinations: Delta-predominant period

Time	ED/UC encounters		Hospitalizations	
	2 doses (n=85,371)*	3 doses (n=14,207)*	2 doses (n=38,707)*	3 doses (n=8,124)*
Overall	80 (79-81)	96 (95-96)	85 (84-85)	95 (95-96)
<2 mos	92 (91-94)	97 (96-97)	94 (92-96)	96 (95-97)
2-3 mos	88 (86-89)	93 (92-94)	91 (89-92)	93 (91-95)
4 mos	85 (83-86)	89 (64-97)	90 (89-92)	74 (14-93)
≥5 mos	77 (76-78)		82 (82-83)	

Data shown: VE fully adjusted % (95% CI); * waning trend p <0.001

Reference: Ferdinands JM, Rao S, Dixon BE, et al. Waning 2-Dose and 3-Dose Effectiveness of mRNA Vaccines Against COVID-19–Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Adults During Periods of Delta and Omicron Variant Predominance — VISION Network, 10 States, August 2021–January 2022. MMWR Morb Mortal Wkly Rep 2022;71:255–263

Durability of Booster Vaccinations: Omicron-predominant period

Time	ED/UC encounters		Hospitalizations	
	2 doses (n=19,822)*	3 doses (n=10,931)*	2 doses (n=3,619)	3 doses (n=2,833)*
Overall	41 (38-43)	83 (82-84)	55 (50-60)	88 (86-90)
<2 mos	69 (62-75)	87 (85-88)	71 (51-83)	91 (88-93)
2-3 mos	50 (45-55)	81 (79-82)	65 (53-74)	88 (85-90)
4 mos	48 (41-54)	66 (59-71)	58 (38-71)	78 (67-85)
≥5 mos	37 (34-40)	31 (-50-68)	54 (48-59)	

Data shown: VE fully adjusted % (95% CI); * waning trend p <0.001

Reference: Ferdinands JM, Rao S, Dixon BE, et al. Waning 2-Dose and 3-Dose Effectiveness of mRNA Vaccines Against COVID-19–Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Adults During Periods of Delta and Omicron Variant Predominance — VISION Network, 10 States, August 2021–January 2022. MMWR Morb Mortal Wkly Rep 2022;71:255–263

Need for a 2nd Booster?

- 1,138,681 participants from the Israeli Ministry of Health database
  - Received three doses of BNT162b2 ≥ 4 months before the start of the study period
- Study period: January 15 to January 27, 2022
  - Omicron predominant
- Individuals aged over 60 years who received the fourth dose ≥12 days earlier compared to those receiving a third dose >4 months earlier
  - Confirmed infection lower by a **factor of 2**
  - Rate of severe illness lowered by a **factor of 3**
  - Protection against infection peaks at 4 weeks
  - Protection against severe illness lasted up to 6 weeks

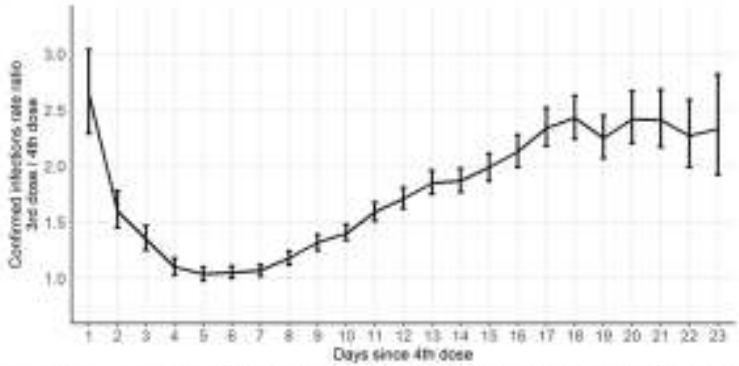
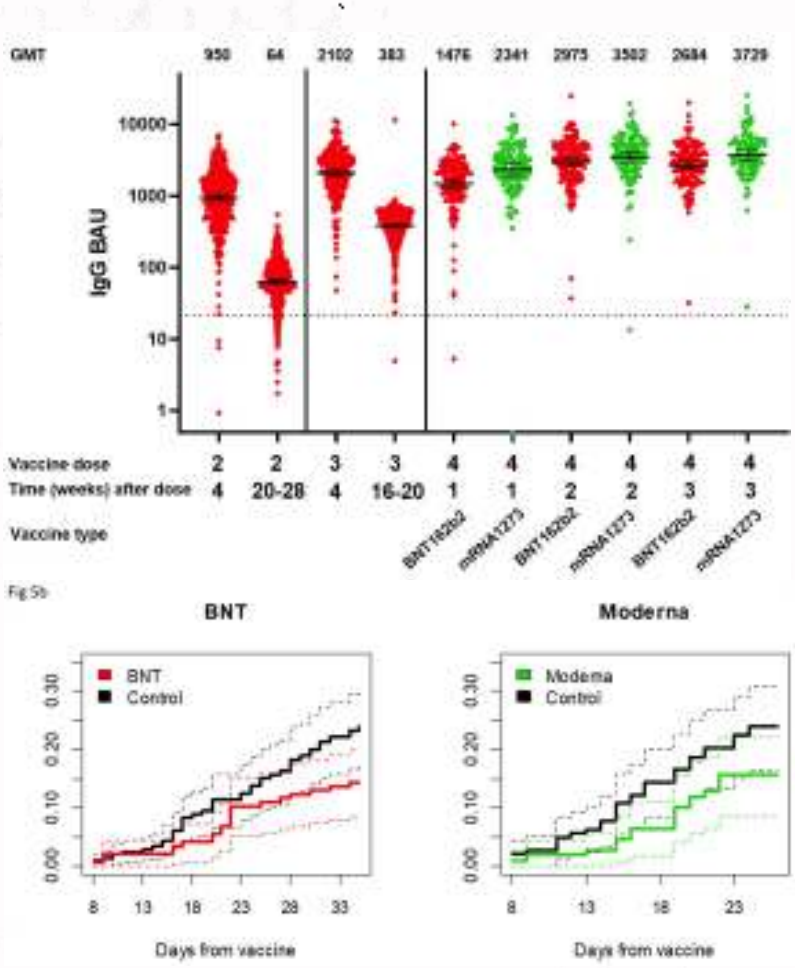


Figure 2. The rate ratio for confirmed infections between the group of people eligible for a fourth dose who had not yet received it to those who had received a fourth dose, as a function of time since the fourth dose.

Reference: Yinon M. Bar-On, Yair Goldberg, Micha Mandel, Omri Bodenheimer, Ofra Amir, Laurence Freedman, Sharon Alroy-Preis, Nachman Ash, Amit Huppert, Ron Milo. Protection by 4th dose of BNT162b2 against Omicron in Israel. N Engl J Med. April 5, 2022

Need for a 2nd Booster?

- Sheba Medical Center: 1,050 eligible HCW ≥18 years of age
  - no known history of SARS-CoV-2 infection
  - received the third dose of BNT162b2 vaccine ≥4 months earlier
- 154 and 120 were enrolled to receive BNT162b2 (30 μg) and mRNA1273 (50 μg), respectively
  - 426 age-matched controls
- Study start: December 27-28, 2021
  - Omicron predominant
- Fourth COVID-19 mRNA dose restored antibody titers to **peak post-third dose titers**
- **Low** vaccine efficacy against infection (11-30%) and symptomatic disease (31-43%); large CIs



Reference: Gili Regev-Yochay, Tal Gonen, Mayan Gilboa, et al. Efficacy of a Fourth Dose of Covid-19 mRNA Vaccine against Omicron. N Engl J Med. March 16, 2022

Need for a 2nd Booster?

- **December 2021** (Israel): individuals aged ≥ 60 years, medical workers, and people with impaired immune systems eligible for a fourth vaccine dose
- **February 2022** (Sweden): individuals aged ≥ 80 years eligible for a fourth vaccine dose
- **March 29, 2022**: FDA authorized second booster dose of the Pfizer-BioNTech or Moderna COVID-19 vaccine for individuals 50 years of age and older at least 4 months after receipt of a first booster dose
  - Second booster dose also authorized for immunocompromised individuals
- **Considerations**
  - Everyone vs. individuals at risk for severe disease and/or hospitalization
  - Timing- now or Fall (if booster protection is short, ~4 months)
  - Wait for changes in vaccine formulation?
- VRBPAC meets on April 6th to discuss nation's booster strategy

Additional Vaccine Dose for Immunocompromised People

- Immunocompromised are more likely to experience severe disease and are at a higher risk for prolonged infection
- Recipients of solid organ-transplantation show weak immune response to 2 doses of COVID-19 vaccines
  - Lower antibody titers and seroconversion
  - High proportion of breakthrough infections occur in immunocompromised people
  - Lower vaccine effectiveness (59-72% versus 90-94%)
- A third dose (***not a booster***) is indicated for immunocompromised patients
  - Organ or stem cell transplant
  - Undergoing active cancer treatment
  - HIV positive with high viral load or low CD4 count
  - Individuals taking high-dose steroids

Reference. Dooling K. Evidence to recommendations framework: additional doses of mRNA COVID-19 vaccines as part of a primary series for immunocompromised. ACIP Meeting, August 13, 2021.

Additional Vaccine Dose for Immunocompromised People

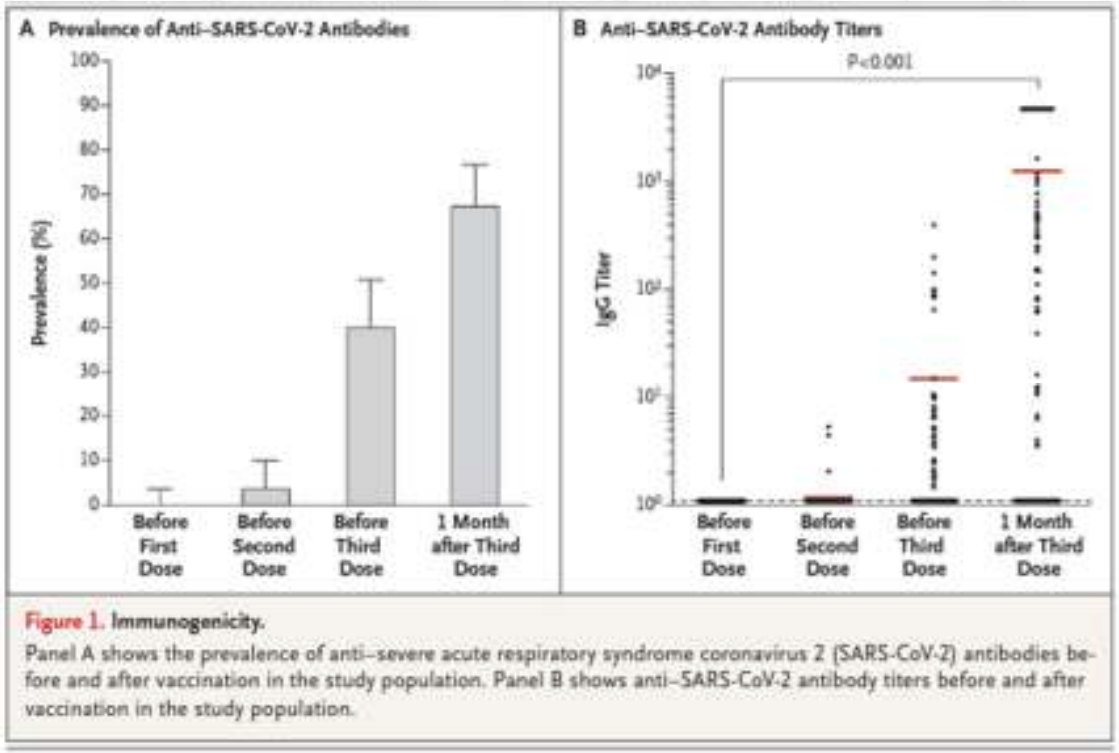


Figure 1. Immunogenicity.
Panel A shows the prevalence of anti–severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies before and after vaccination in the study population. Panel B shows anti–SARS-CoV-2 antibody titers before and after vaccination in the study population.

- 3rd dose of mRNA vaccine increased % seropositivity and anti-Spike antibody titers
- No serious adverse effects reported
- **August 12**: FDA authorized 3rd mRNA vaccine dose (matching) for immunocompromised individuals (*see prior slide*)
- CDC now recommends **four** doses (12 years and older)

References. Kamar et al. (2021) NEJM Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients ; Dooling K. Evidence to recommendations framework: additional doses of mRNA COVID-19 vaccines as part of a primary series for immunocompromised. ACIP Meeting, August 13, 2021.

Prior COVID-19 Vaccination Schedule for People Who Are Moderately or Severely Immunocompromised

Vaccine	Vaccination Schedule			
Pfizer-BioNTech (ages 5 years and older)	1st dose	2nd dose (21 days after 1st dose)	3rd dose (at least 28 days after 2nd dose)	Booster dose* (at least 5 months after 3rd dose)
Moderna (ages 18 years and older)	1st dose	2nd dose (28 days after 1st dose)	3rd dose (at least 28 days after 2nd dose)	Booster dose* (at least 5 months after 3rd dose)
Janssen (ages 18 years and older)	1st dose		Booster dose* (at least 2 months after 1st dose)	

- Concerns about initial immune response and loss of protection over time
- Multiple studies show immunogenicity of a booster as early as 3 months following primary series.

Reference: E. Hall. Updates to Interim Clinical Considerations for Use of COVID19 Vaccines. ACIP February 4, 2022 Meeting

Revised COVID-19 Vaccination Schedule for People Who Are Moderately or Severely Immunocompromised

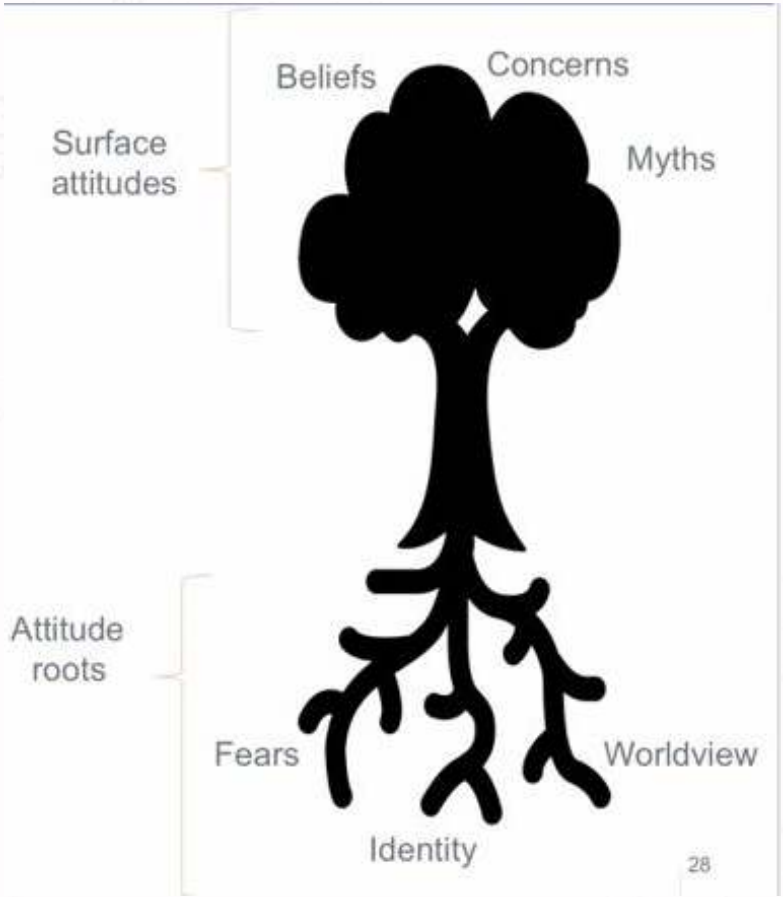
Vaccine	Vaccination Schedule							
Pfizer-BioNTech (ages 5 years and older)	1st dose	2nd dose (21 days after 1st dose)		3rd dose (at least 28 days after 2nd dose)			Booster dose* (at least 3 months after 3rd dose)	
Moderna (ages 18 years and older)	1st dose		2nd dose (28 days after 1st dose)		3rd dose (at least 28 days after 2nd dose)			Booster dose* (at least 3 months after 3rd dose)
Janssen (ages 18 years and older)	1st dose		Additional dose† (at least 28 days after 1st dose)			Booster dose* (at least 2 months after additional dose)		

- Shorter booster interval after an mRNA COVID-19 vaccine primary series
- An additional dose after a Janssen COVID-19 vaccine primary series

References: E. Hall. Updates to Interim Clinical Considerations for Use of COVID19 Vaccines. ACIP February 4, 2022 Meeting; **CDC**. COVID-19 Vaccines for Moderately or Severely Immunocompromised People.

Germinating Trust from Seeds of Doubt

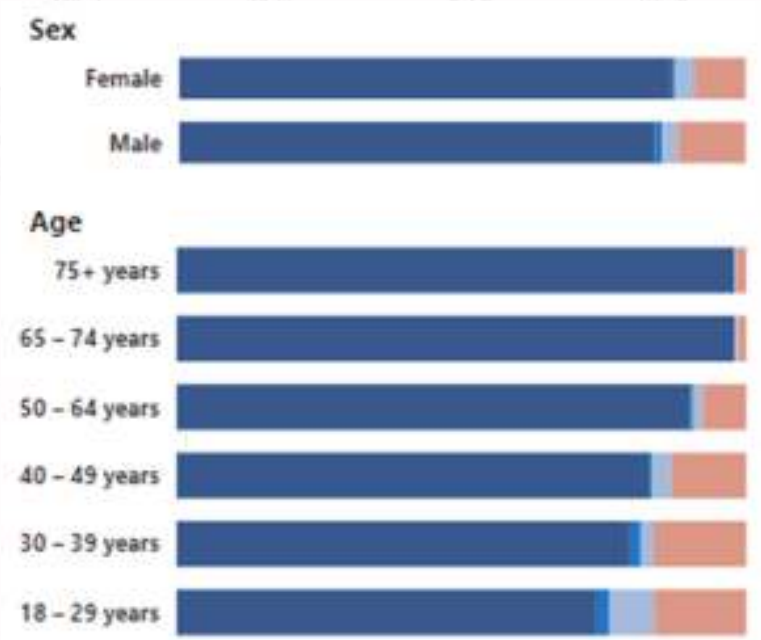
- Much vaccine misinformation & myths persist
  - Exposure to misinformation induced a **6% drop** in intent to vaccinate
- Hesitancy remains highest in groups most impacted by COVID-19
  - Adults aged 18- to 39-years
  - Hispanic and Black adults
- Underlying drivers of hesitancy need to be addressed; more data isn't always the answer
  - Anxiety around new technologies
  - Lack of trust in politicians, public authorities, and medical professionals
  - Negative experiences with healthcare system
- Indecisiveness coupled with the uncertainty of the pandemic ≠ anti-vaccines
- Show empathy and build trust

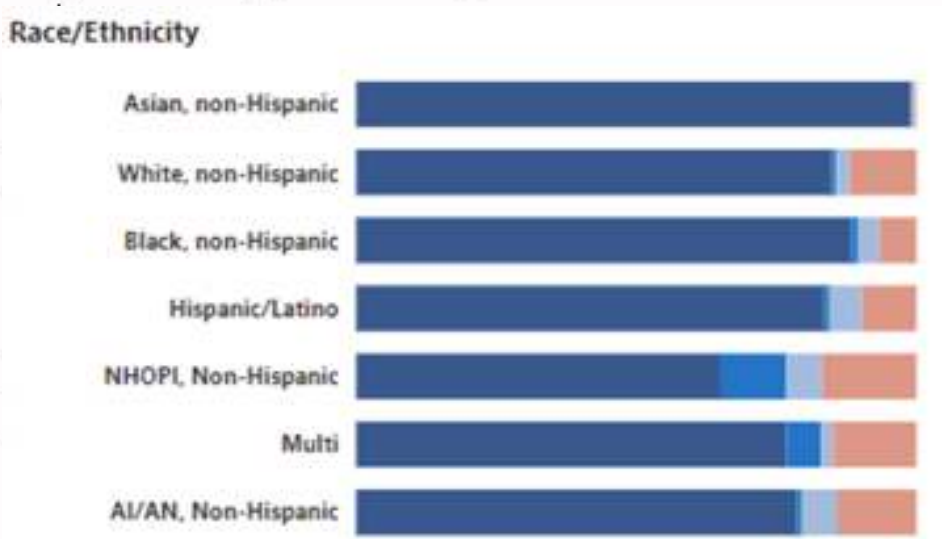


Source: Alla Paskovaty; Sanofi-Pasteur

References: Pertwee, E., Simas, C. & Larson, H.J. An epidemic of uncertainty: rumors, conspiracy theories and vaccine hesitancy. Nat Med (2022).

Vaccination Status & Intent





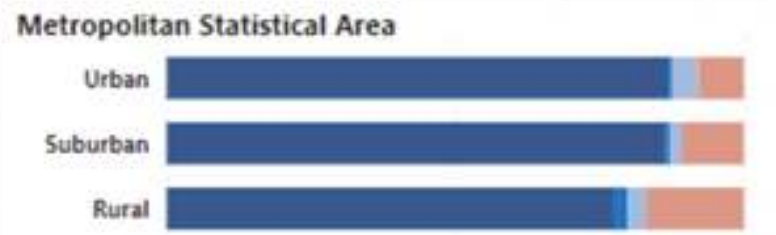
Overall 18+ years

85.4% vaccinated (≥1 dose)

1.0% definitely will get vaccinated

3.1% probably will get vaccinated or unsure

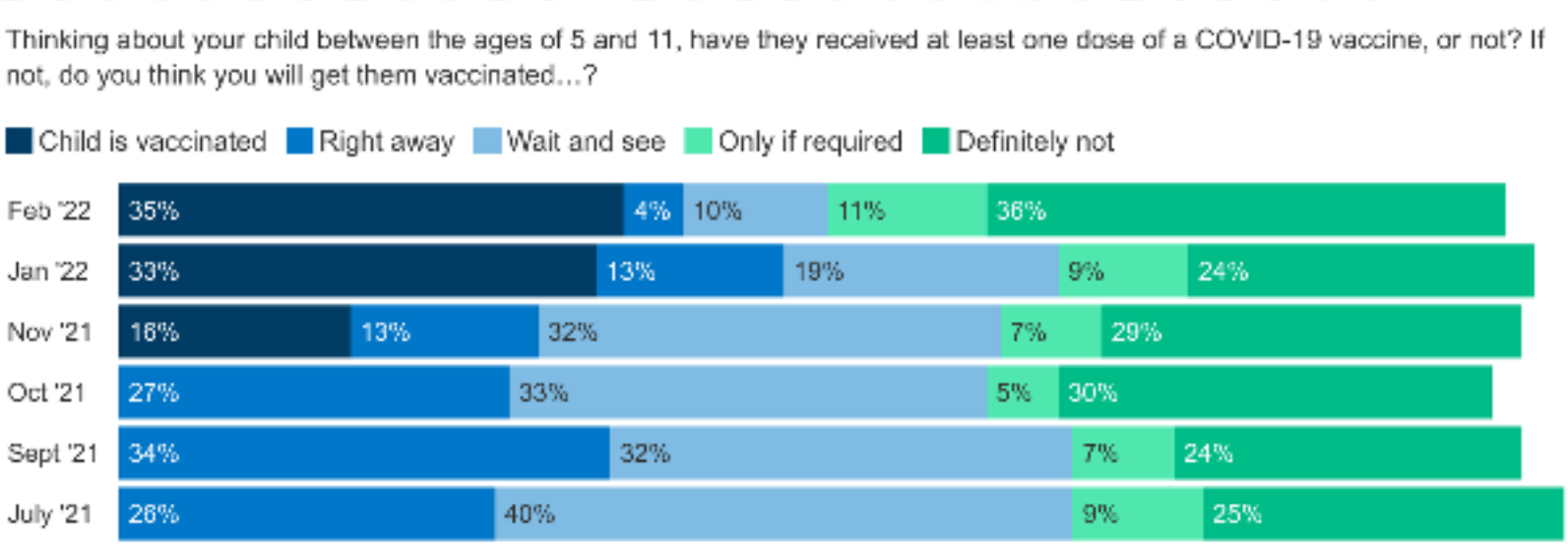
10.5% probably or definitely will not get vaccinated

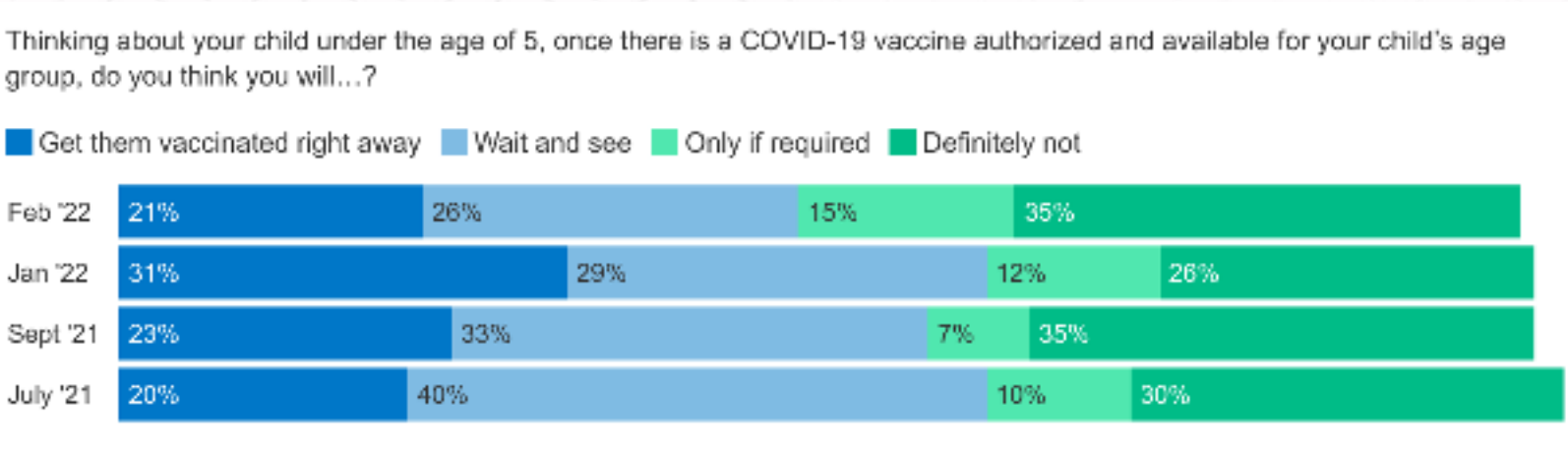


**Data collected Feb 20-26,2022*

Reference. CDC. https://covid.cdc.gov/covid-data-tracker/#vaccine-confidence

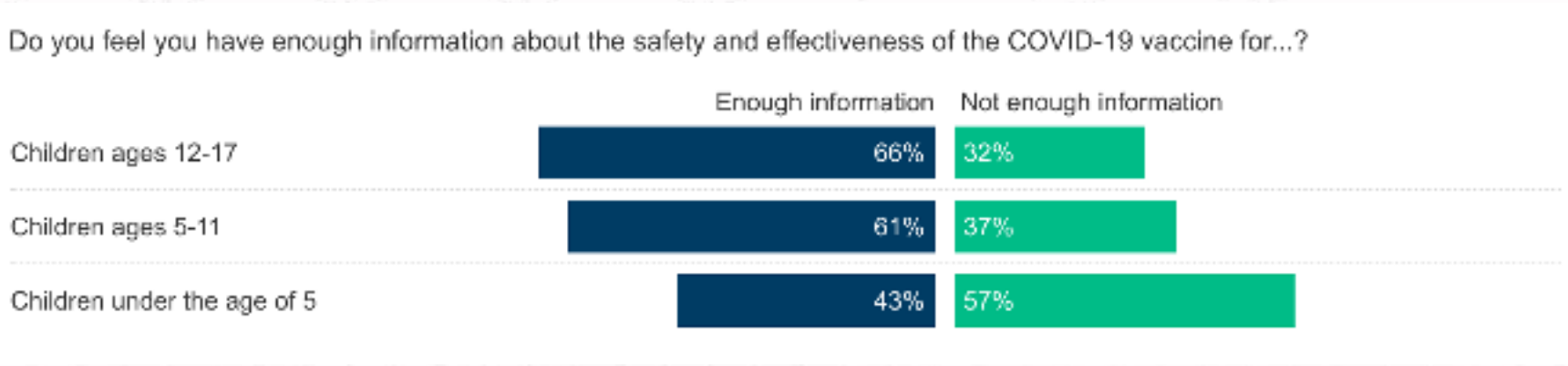
Child Vaccination Status & Intent

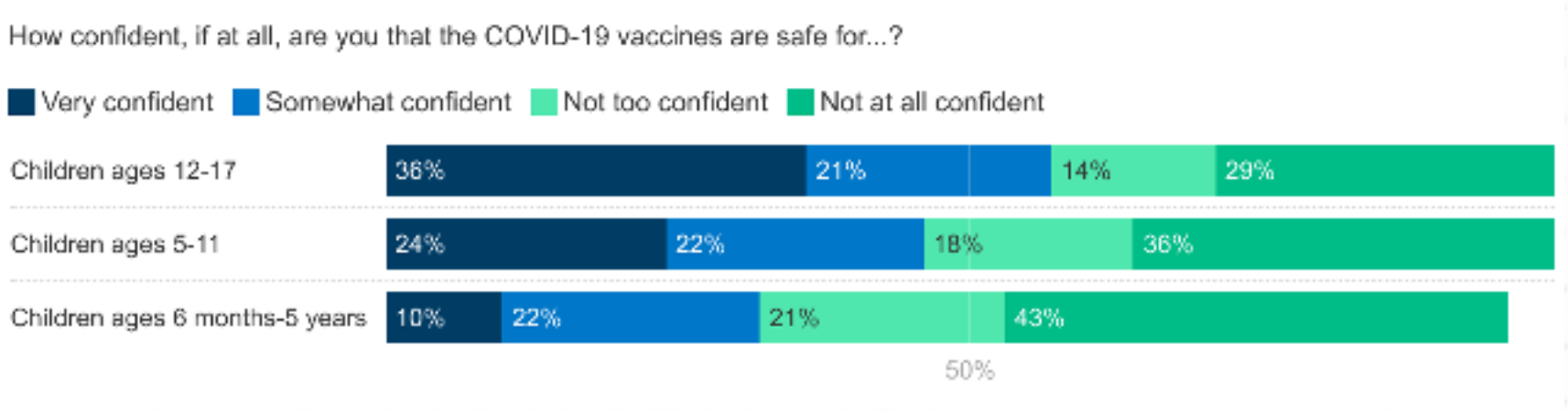




Source. KFF COVID019 Vaccine Monitor

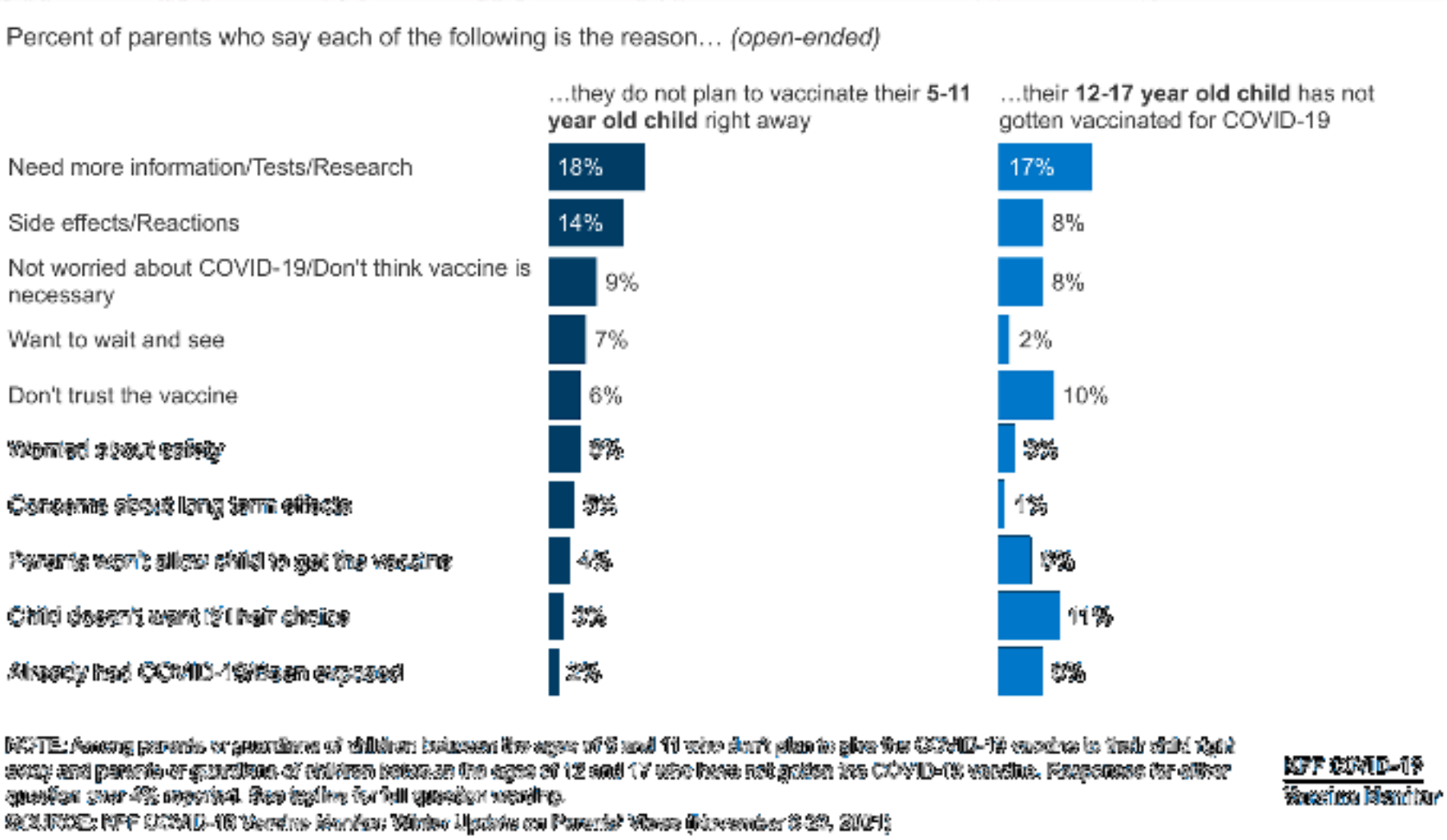
Child Vaccination Status & Intent





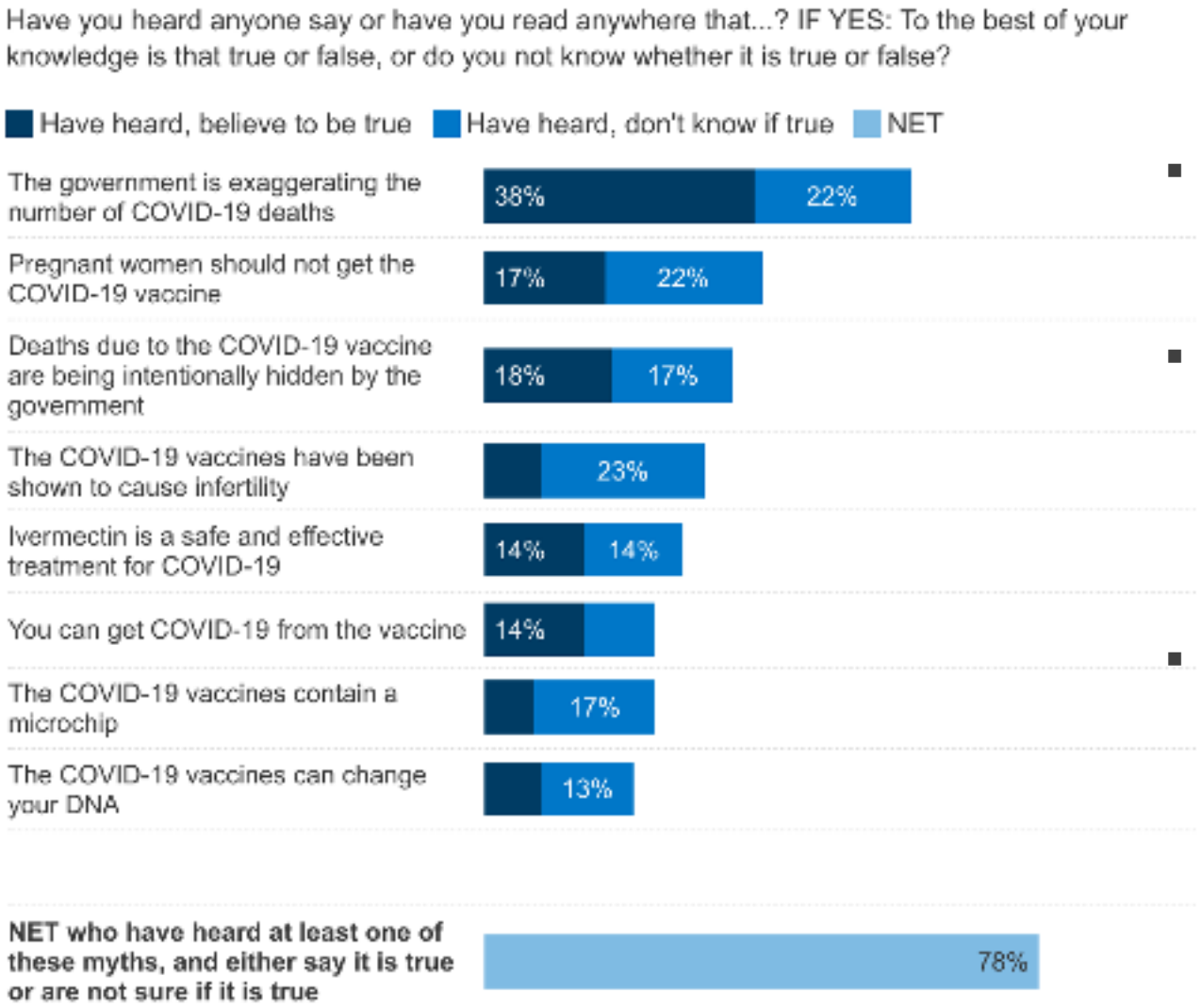
Source. KFF COVID019 Vaccine Monitor (February 9-21, 2022)

Child Vaccination Status & Intent



Source. KFF COVID019 Vaccine Monitor

Combating COVID & Vaccine Misinformation



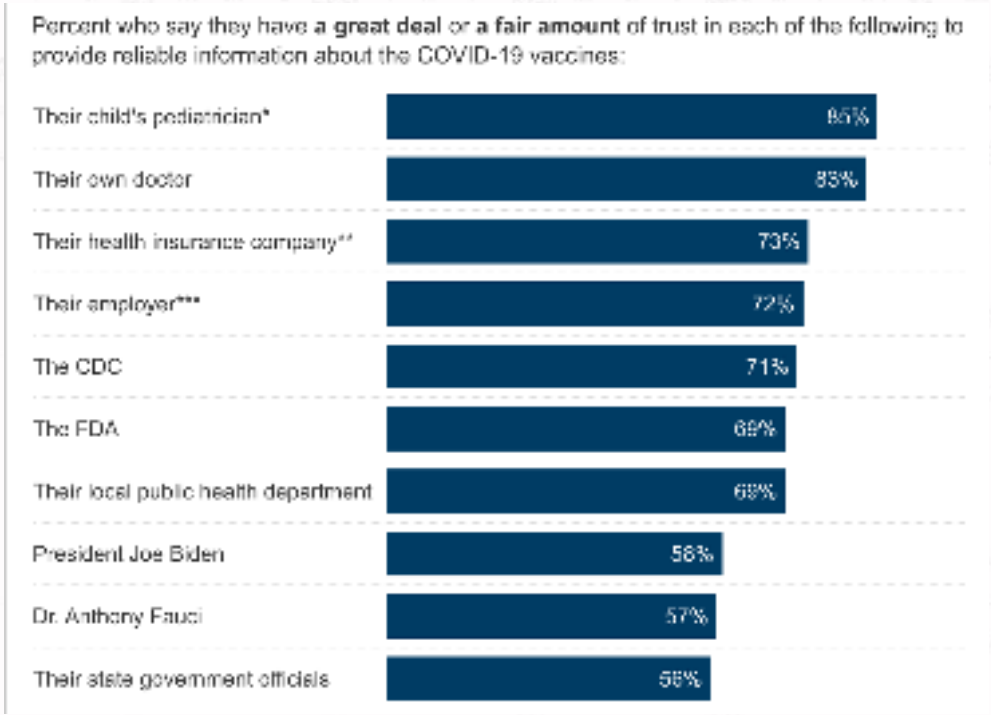
- Belief or uncertainty about COVID-19 misinformation is widespread
- 78 % of adults say they have heard at least four false statements about COVID-19 and believe them to be true or are uncertain
- 32% of adults say they have heard at least four false statements about COVID-19 and believe them to be true or are uncertain

Source. KFF COVID019 Vaccine Monitor

Vaccine Misinformation & Myths

Misinformation/Myth	Response
Vaccines were developed so fast-they are likely to be unsafe.	Vaccines have gone through rigorous trials to meet FDA's high standards for safety, efficacy, and quality
The vaccine will give me COVID-19.	Approved and authorized vaccines do not contain the live virus that causes COVID19.
mRNA-based vaccines will change my DNA	Biologically, mRNA does not enter the cell's nucleus and cannot integrate into DNA. Also, mRNA is short-lived in the body.
The vaccine can cause infertility in women.	Allegations linking vaccines and infertility are "unfounded" and "scientifically disproven". No signs of infertility have been reported among the millions who have received the vaccine.
Vaccines contain unsafe toxins.	Ingredient lists are readily available online for each vaccine
I had COVID19, I don't need the vaccine	Experts do not yet know how long you are protected from getting sick again after recovering from COVID19. Not everyone develops the same level of immunity following infection
Vaccines cause autism	Original study has been debunked and retracted. Over 25 studies and medical records of >700,000 children disprove a connection between autism and the MMR vaccine

Building Vaccine Confidence



A	Assume people want to get vaccinated and be prepared for questions
S	Share key facts and sources of information to counter misinformation
P	Present strong recommendations and stories about vaccination experiences
I	Initiate discussion or address questions about side effects proactively and share credible sources of information
R	Respond to questions and actively listen
E	Empathize and understand concerns

- Pharmacists viewed as trusted sources of health information; cultivated long-term relationships
- Pharmacy locations are within reach of most Americans
- Pharmacies today are hubs for patient services (vaccines)

Source. KFF COVID019 Vaccine Monitor (June 8-21, 2021); Shen AK, Tan ASL. Trust, influence, and community: Why pharmacists and pharmacies are central for addressing vaccine hesitancy. J Am Pharm Assoc (2003). 2022 Jan-Feb;62(1):305-308

Thank You!
Any Questions?