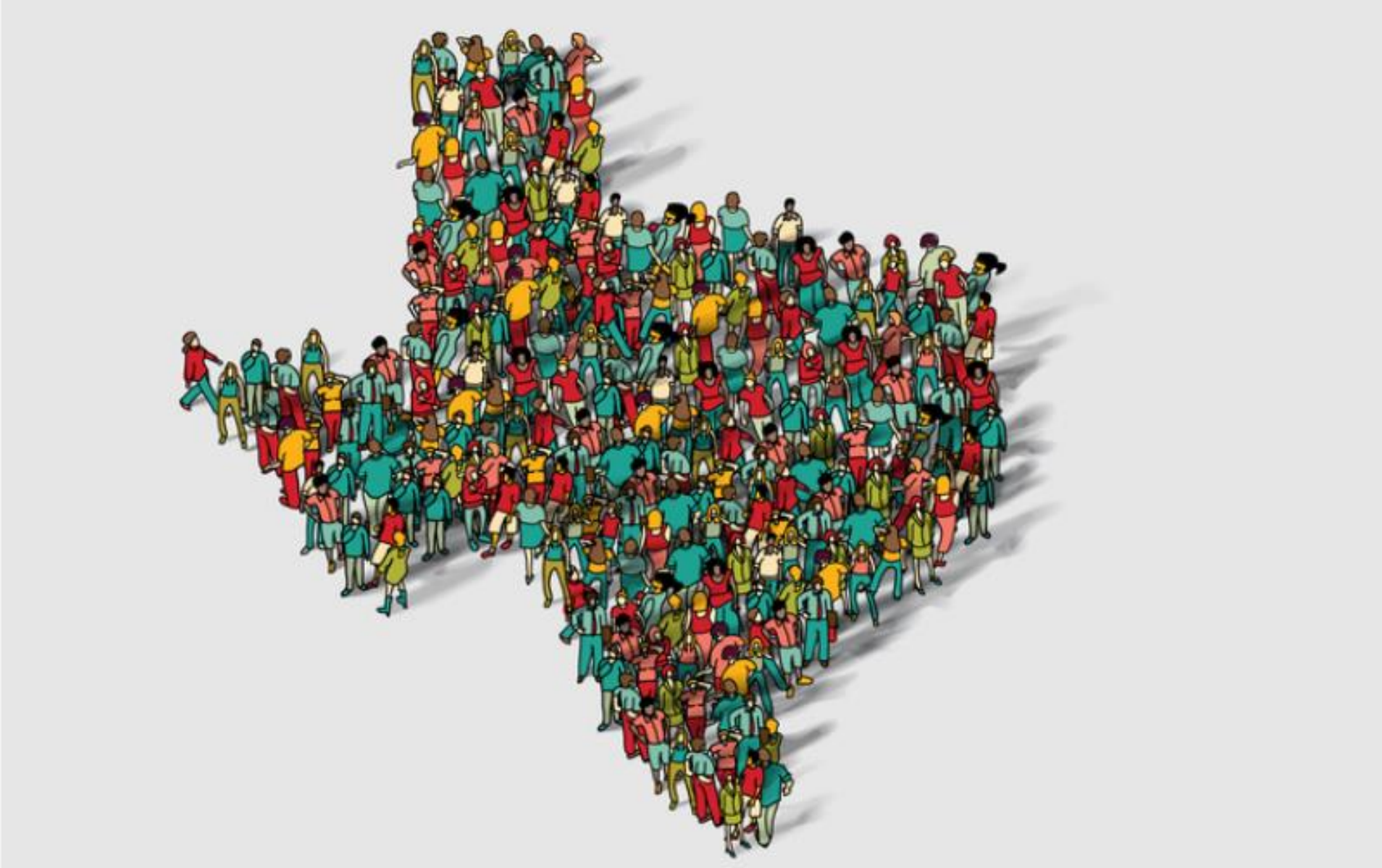


DISCLAIMER

The information presented today is based on CDC's recent guidance and MAY change.

June 29, 2021

COVID-19 Vaccine Updates

Jennifer A. Shuford, MD, MPH

Chief State Epidemiologist| Office of Chief State Epidemiologist

COVID-19 Vaccine	Technology Platform	Storage & Handling	Dose (Intramuscular Injection)	Status
Pfizer	m-RNA	Ultra-low frozen: 6mos Frozen: 2 weeks Refrigerated: 31 days	2 (0, 21 days)	• Authorized for 12 years and older (previously ≥16 yrs). • Minimum order size 450 doses (previously 1,170 doses). • Storage under refrigerated temperatures extended for 31 days (previously 5 days). • Warning on Myocarditis added to the Fact Sheet. • BLA submitted with the FDA.
moderna	m-RNA	Frozen: 6mos Refrigerated: 30 days	2 (0, 28 days)	• Pending authorization from the FDA for 12 years and older (currently ≥18 yrs). • Additional order size of 140 doses (previously only 100 doses). • BLA submitted with the FDA.
janssen	Viral Vector (Non-Replicating)	Frozen: 2 years Refrigerated: 4.5mos	1	• Storage under refrigerated temperatures extended for 4.5 months (previously 3 months). • Warning on Thrombosis with Thrombocytopenia added to the Fact Sheet.
AstraZeneca / University of Oxford	Viral Vector (Non-Replicating)	Refrigerated: 6mos	2 (0, 28 days)	• Phase 3 study completed in the US. • Not yet filed with the FDA.
NOVAVAX	Recombinant Subunit Adjuvant (Matrix M™)	Refrigerated: 3mos	2 (0, 21 days)	• Phase 3 study completed in the US. • Not yet filed with the FDA. • Co-administration with influenza vaccine showed good immunogenicity response in a subset of the UK Phase 3 study participants.

COVID-19 Vaccine & New Variant of Concern: Delta B.1.617.2

Vaccines & New Variant of Concern: Delta B.1.617.2

- Recent study in UK showing resurgence driven by replacement of B.1.1.7 with B.1.617.2, which has higher transmission rate, and infections in unvaccinated children and young adults.

- **B.1.617.2- specific vaccine effectiveness**
  - PCR-confirmed infection: Scotland, 2 doses Pfizer vaccine: 79% (vs. 92% for B.1.1.7)
  - Symptomatic infection: England, 2 doses Pfizer vaccine: 88% (vs. 93% for B.1.1.7)
  - Hospitalization: England, 2 doses Pfizer vaccine: **96%** (similar to B.1.1.7)
- **B.1.617.2 antibody neutralization studies**
  - 4 studies, 2 doses Pfizer vaccine: 1.4, 2.5, 3, and 5.8-fold reduction (vs. wild-type)

Sheikh et al. Lancet (2021): https://doi.org/10.1016/S0140-6736(21)01358-1; Lopez Bernal et al.medRxiv preprint (May 26 2001); https://doi.org/10.1101/2021.05.22.21257658; Stowe et al. PHE preprint: https://khub.net/web/phe-national/public-library/-/document_library/v2WsRK3ZlEig/view/479607266; Planas et al. bioRxiv preprint (May 27 2021) https://doi.org/10.1101/2021.05.26.445838; Wall et al. Lancet (2021) https://doi.org/10.1016/ S0140-6736(21)01290-3; Liu et al. Cell (2021); https://doi.org/10.1016/j.cell.2021.06.020; Riley et al. medRxiv (June 21 2021): https://doi.org/10.1101/2021.06.17.21259103; Liu et al. Nature (2021) https://doi.org/10.1038/s41586-021-03693-y.

Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/06-COVID-Oliver-508.pdf

VE Against Symptomatic Disease for Delta Variant (UK Experience)

Table 2: Vaccine effectiveness against S-gene target negative (B.1.1.7) and S-gene target positive (B.1.617.2)

Vaccination status	Test negative controls	B.1.1.7 or S-gene target negative			B.1.617.2 or S-gene target positive		
		cases	cases:controls	aVE(%)	cases	cases:controls	aVE(%)
Unvaccinated	58253	4891	0.084	base	695	0.012	base
Any vaccine							
Dose 1	32703	1481	0.045	51.1 (47.3 to 54.7)	279	0.009	33.5 (20.6 to 44.3)
Dose 2	8483	74	0.009	86.8 (83.1 to 89.6)	27	0.003	80.9 (70.7 to 87.6)
BNT162b2							
Dose 1	7036	344	0.049	49.2 (42.6 to 55.0)	49	0.007	33.2 (8.3 to 51.4)
Dose 2	6412	28	0.004	93.4 (90.4 to 95.5)	13	0.002	87.9 (78.2 to 93.2)
ChAdOx1							
Dose 1	25667	1137	0.044	51.4 (47.3 to 55.2)	230	0.009	32.9 (19.3 to 44.3)
Dose 2	2071	46	0.022	66.1 (54.0 to 75.0)	14	0.007	59.8 (28.9 to 77.3)

Source: Lopez Bernal et al. https://www.medrxiv.org/content/10.1101/2021.05.22.21257658v1.full.pdf

VE Against Hospitalization for Delta Variant (UK Experience)

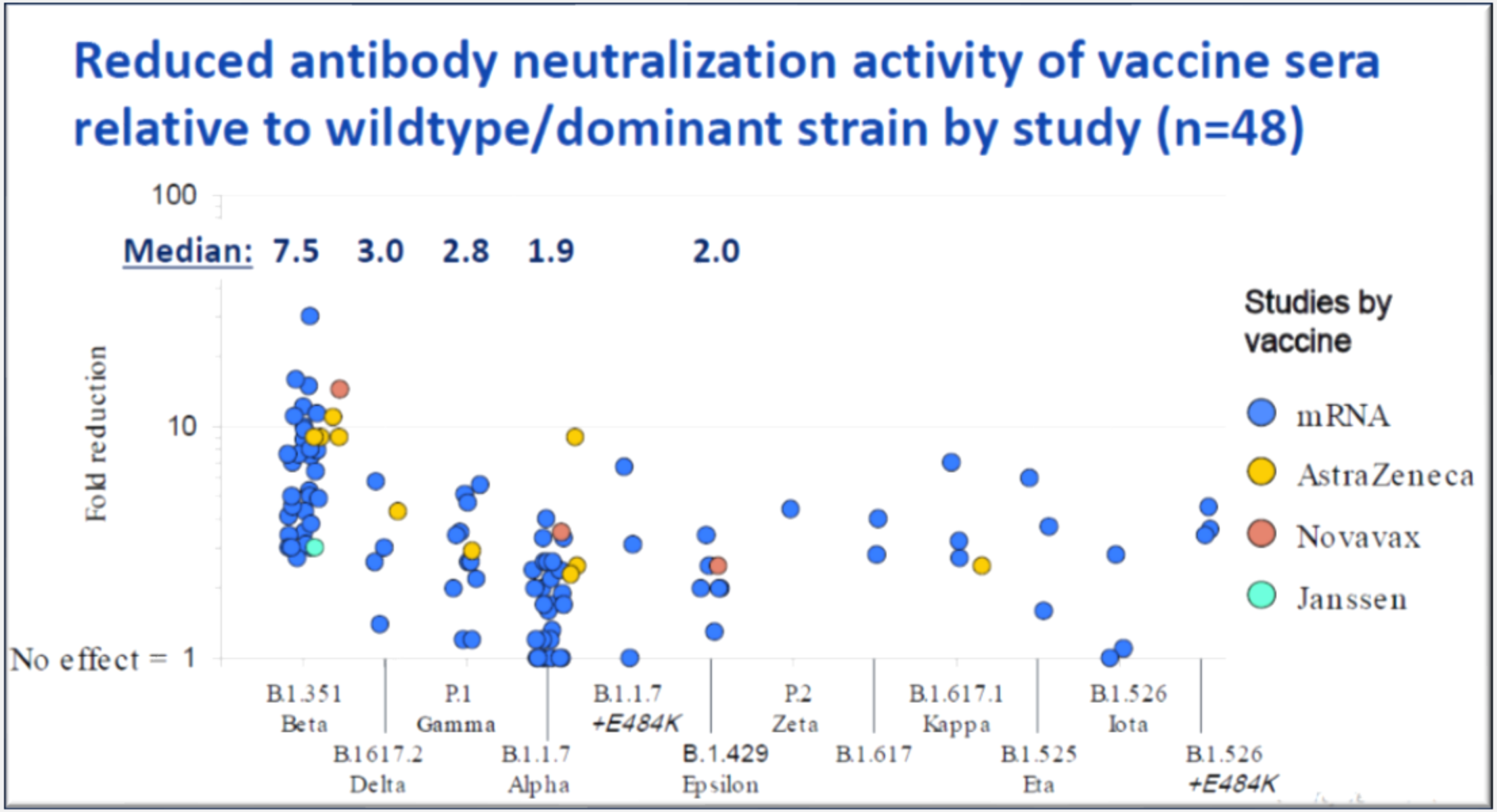
Table 1: Estimated vaccine effectiveness against hospitalisation

		Alpha			Delta		
Vaccination status		OR vs symptomatic disease	HR vs hospitalisation	VE vs hospitalisation	OR vs symptomatic disease	HR vs hospitalisation	VE vs hospitalisation
Any vaccine							
	Dose 1	0.51 (0.48-0.55)	0.44 (0.28-0.70)	78% (65-86)	0.69 (0.64-0.75)	0.37 (0.22-0.63)	75% (57-85)
	Dose 2	0.13 (0.1-0.15)	0.64 (0.24-1.72)	92% (78-97)	0.20 (0.18-0.23)	0.29 (0.11-0.72)	94% (85-98)
Pfizer							
	Dose 1	0.53 (0.47-0.58)	0.32 (0.14-0.73)	83% (62-93)	0.64 (0.54-0.77)	0.10 (0.01-0.76)	94% (46-99)
	Dose 2	0.06 (0.05-0.08)	0.88 (0.21-3.77)	95% (78-99)	0.12 (0.1-0.15)	0.34 (0.10-1.18)	96% (86-99)
Astrazeneca							
	Dose 1	0.51 (0.48-0.55)	0.48 (0.30-0.77)	76% (61-85)	0.70 (0.65-0.76)	0.41 (0.24-0.70)	71% (51-83)
	Dose 2	0.26 (0.21-0.32)	0.53 (0.15-1.80)	86% (53-96)	0.33 (0.28-0.39)	0.25 (0.08-0.78)	92% (75-97)

OR =odds ratio. HR = hazards ratio. VE = vaccine effectiveness. OR vs symptomatic disease as described in (1). HR and VE vs hospitalisation adjusted for age, clinically extremely vulnerable groups, ethnicity and test week

Source: https://media.tghn.org/articles/Effectiveness_of_COVID-19_vaccines_against_hospital_admission_with_the_Delta_B._G6gnnqJ.pdf

Reduced antibody neutralization activity of vaccine sera relative to wildtype/dominant strain by study (n=48)



Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/06-COVID-Oliver-508.pdf

"Real world" vaccine effectiveness:

Studies to inform VE against variants of concern

Country	Vaccine	Dominant strain(s)	Fully vaccinated VE
Israel, Europe & U.K	Pfizer	B.1.1.7 (Alpha)	>85%
Canada	mRNA	B.1.1.7, P.1 (Alpha, Gamma)	79% (65%–88%)
Canada	mRNA	P.1/B.1.351 (Gamma/Beta)	88% (61%–96%)*
Qatar	Pfizer	B.1.1.7 (Alpha)	90% (86%–92%)*
		B.1.351 (Beta)	75% (71%–79%)*
South Africa	Janssen	B.1.351 (Beta)	52% (30%–67%)

* Variant-specific VE

For B.1.351 (Beta), VE shown to be higher for prevention of severe disease

CDC Science Brief: https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html
Abu-Radad and Dutt, NEJM (2021); Sandoff et al. NEJM (2021); Chung et al medRxiv preprint (May 28 2021); Yassi et al medRxiv preprint (May 25 2021))

Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/06-COVID-Oliver-508.pdf

COVID-19 Vaccine - Booster Doses

Booster Doses of COVID-19 Vaccines
Immunogenicity and antibody response

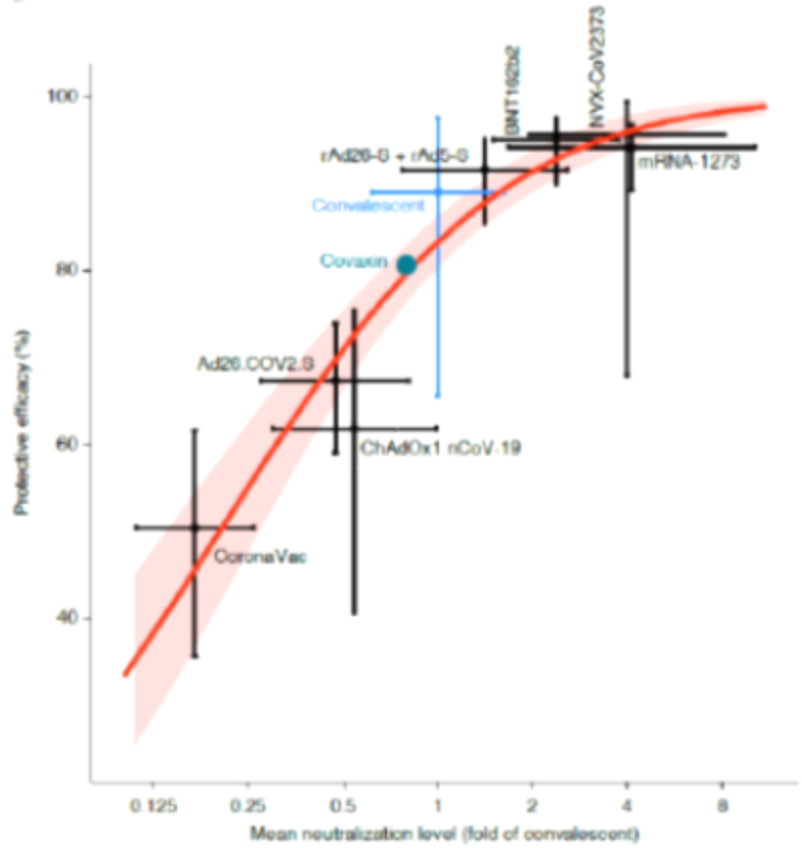
- **Correlates of protection**
  - Immune response that allows prediction of the degree of protection against infection or disease
  - Work ongoing, no correlate established yet

- **Duration of protection**
  - Monitor kinetics of antibody response, efficacy from early phase clinical trials

- **Antibody response to variant-specific boosters**

Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/06-COVID-Oliver-508.pdf

Robust correlation between vaccine efficacy against symptomatic disease and mean neutralizing antibody titer: Two studies



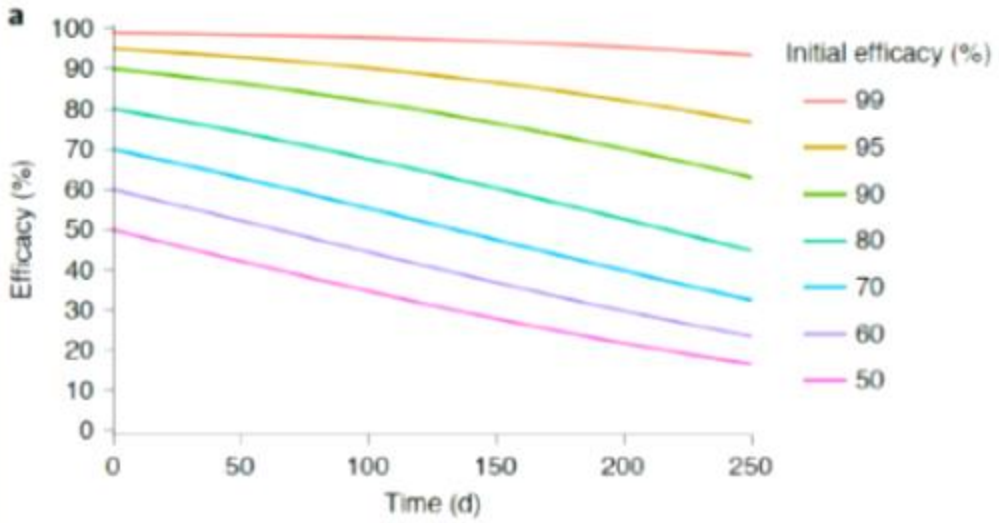
Khoury et al. Nature Medicine (2021)

- Suggests **54** IU/ml as correlate of protection (20% of mean convalescent titer)
- Threshold of protection against **severe disease** is lower (3% of mean convalescent titer), less affected by vaccine differences
- For variants, 5-fold lower neutralizing titer predicted to reduce efficacy from 95% to 77% in high efficacy vaccine, or from 70% to 32% for lower efficacy vaccine

Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/06-COVID-Oliver-508.pdf

Predicted duration of immunity varies with initial vaccine efficacy

- Initial efficacy may be useful in predicting time until boosting may be needed

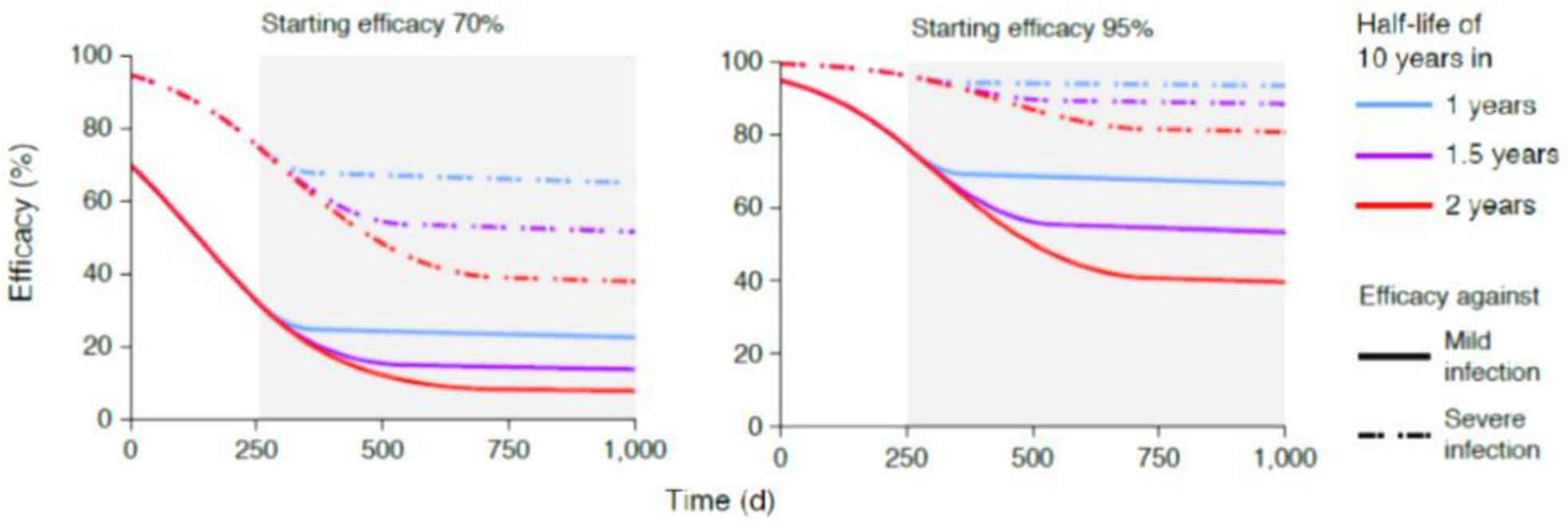


Khoury et al. Nature Medicine (2021)

- Vaccine starting with initial efficacy of 95% expected to maintain high efficacy (77%) after 250 days
- Vaccine starting with initial efficacy of 70% may result in drop to lower efficacy (33%) after 250 days
- Model assumes **neutralization** is major mechanism of protection

Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/06-COVID-Oliver-508.pdf

Protection from severe infection predicted to persist longer than protection against mild infection



- After initial exponential decay, antibody half-lives generally stabilize to ≥10 years (linear decline)
- Depending on when transition occurs, proportion of individuals predicted to be protected against severe disease long-term, even without boosters, but may be susceptible to mild infection

Khoury *et al. Nat Med* (2021). https://doi.org/10.1038/s41591-021-01377-8

Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/06-COVID-Oliver-508.pdf

Booster Doses of COVID-19 Vaccines
Duration of Immunity

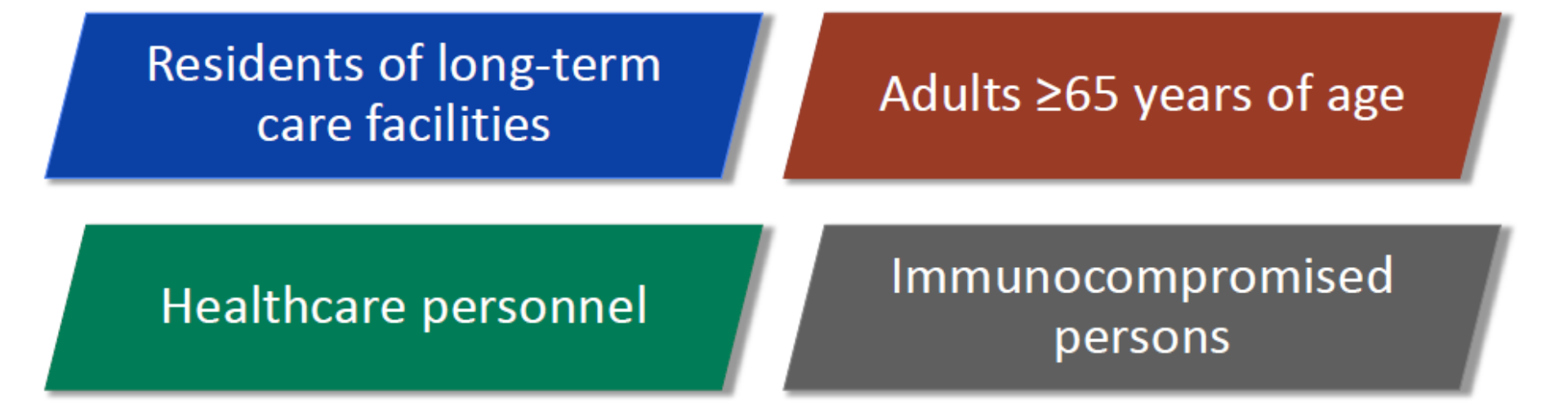
- To date, antibody persistence demonstrated for up to **8 months** after COVID-19 infection and up to **6 months** after the 2nd mRNA vaccine dose
- Two studies, 6 months after receiving Moderna vaccine: Lower neutralizing titers & higher proportions (~50%) with undetectable titers against B.1.351 and P.1, compared with ancestral strain
  - Third modeling study makes similar conclusions
- Many studies have shown larger reduction

Gaebler, C. et al. Evolution of antibody immunity to SARS-CoV-2. Nature 591, 639–644 (2021).
Dan, J. M. et al. Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. Science 371, eabf4063 (2021)
Choe et al. Antibody Responses 8 Months after Asymptomatic or Mild SARS-CoV-2 Infection. Emerg Infect Dis. 2021;27(3):928-931.
Doria-Rose et al. Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for Covid-19. N Engl J Med 2021; 384:2259-226
https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-confirm-high-efficacy-and-no-serious
Khoury*et al.Nat Med*(2021). https://doi.org/10.1038/s41591-021-01377-8; Pegu et al. bioRxiv preprint (May 16 2021): https://doi.org/10.1101/2021.05.13.444010
Wu et al. medRxiv preprint (2021): https://doi.org/10.1101/2021.05.05.21256716Luo, Hu, Letterio, medRxiv preprint (4 2021): medRxiv preprint doi: https://doi.org/10.1101/2021.05.04.21256537

Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/06-COVID-Oliver-508.pdf

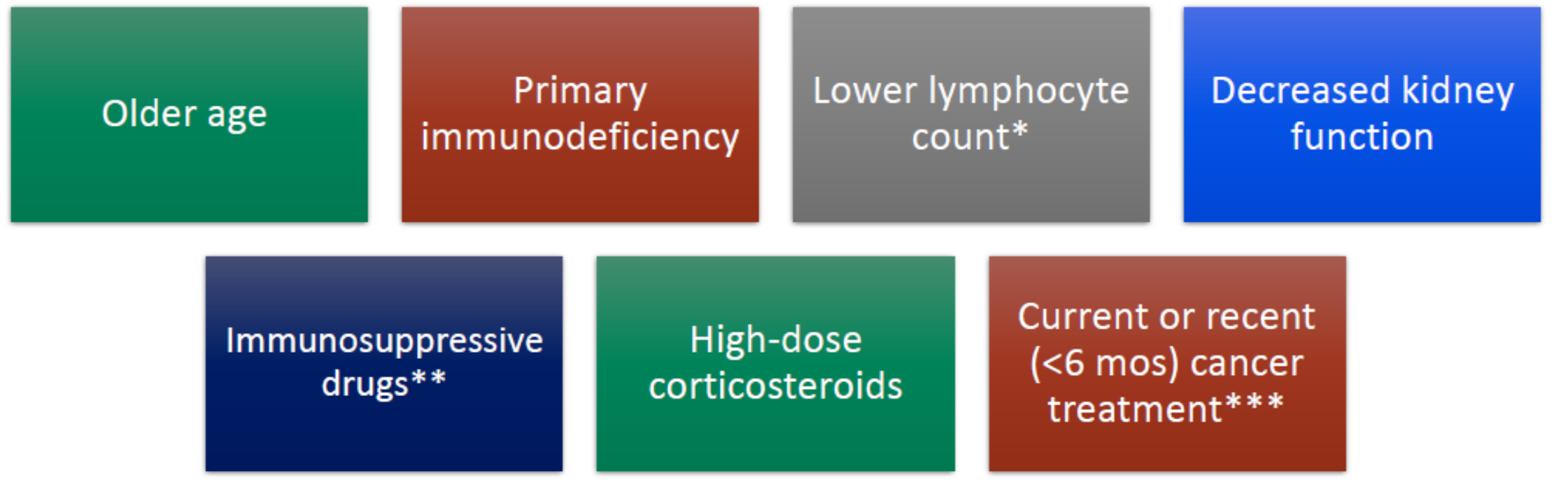
Booster Doses of COVID-19 Vaccines
Specific Populations

- Need for booster doses of COVID-19 vaccines may only be demonstrated in some populations
- Population to closely monitor:



Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/06-COVID-Oliver-508.pdf

Factors that may decrease vaccine response among immunocompromised populations



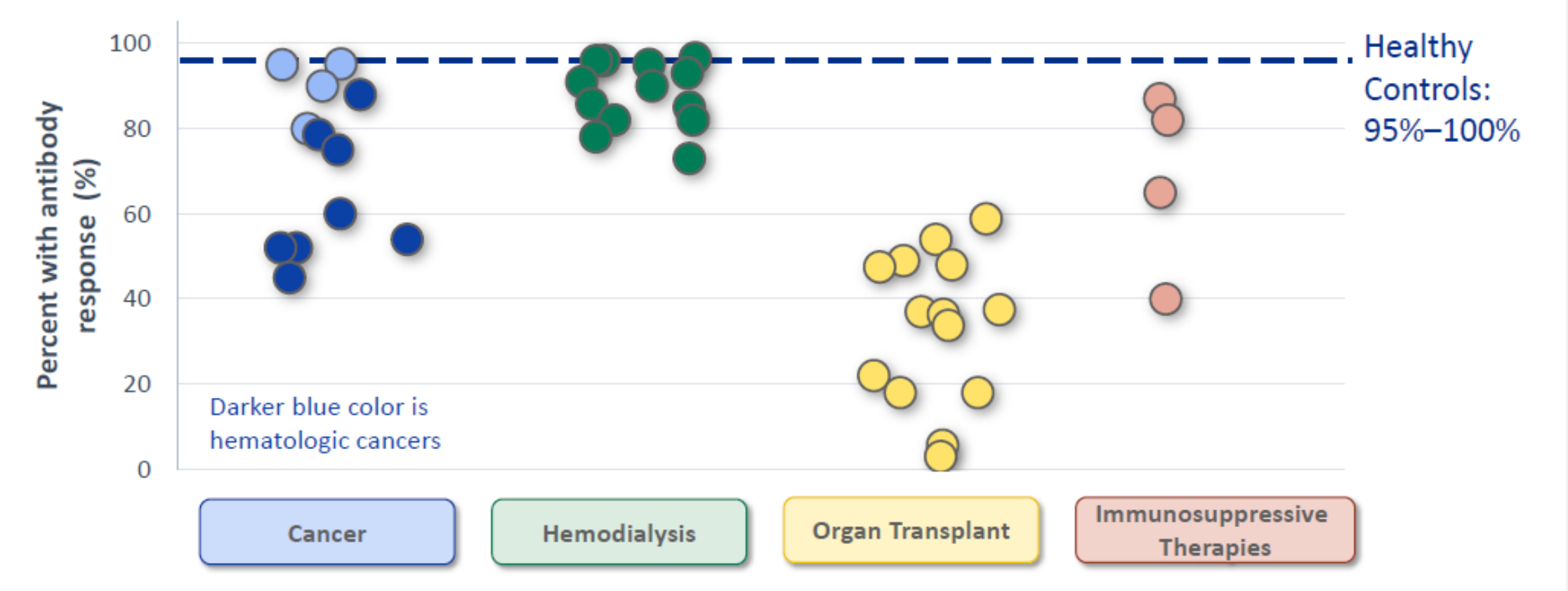
* Including lower CD4 count for people living with HIV

** Immunosuppressive drugs include methotrexate, mycophenolate, rituximab, infliximab, calcineurin-inhibitors

*** BTK inhibitors, anti-CD20 and anti-CD38 therapies, chemotherapy

Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/06-COVID-Oliver-508.pdf

Percent antibody response after two mRNA vaccine doses by immunocompromised condition and study (n=40)



- Studies that compared response after 1st and 2nd dose demonstrated poor response to dose 1
- Antibody measurement and threshold levels vary by study protocol

Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/06-COVID-Oliver-508.pdf

Mix-and-Match

Heterologous Primary Series and Booster Vaccine

- Recent studies from Europe have assessed heterologous primary series with Pfizer and Astra Zeneca with reassuring results
- Evidence is needed regarding the ability to use a different vaccine as a booster than what was used in the primary series
  - Studies specific to U.S. authorized vaccines

Borobia et. Al Reactogenicity and Immunogenicity of BNT162b2 in Subjects Having Received a First Dose of ChAdOx1s: Initial Results of a Randomized, Adaptive, Phase 2 Trial (CombiVacS). Available at SSRN: https://ssrn.com/abstract=3854768

Shaw et. al Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data, ISSN 0140-6736, https://doi.org/10.1016/S0140-6736(21)01115-6.

Hillus D, Schwarz T, Tober-Lau P, et al. Safety, reactogenicity, and immunogenicity of homologous and heterologous prime-boost immunization with ChAdOx1-nCoV19 and BNT162b2: a prospective cohort study. medRxiv; 2021. DOI: 10.1101/2021.05.19.21257334.

Schmidt et al. medRxiv preprint (June 15 2021): https://doi.org/10.1101/2021.06.13.21258859

Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/06-COVID-Oliver-508.pdf

Upcoming Studies and Timing of Additional Data
NIH or Manufacturer Studies

Data from Phase I/II/III trials

- Monitor kinetics of antibody response, efficacy from early phase clinical trials
- BLA submission: Include efficacy for ~6 months

Heterologous boost

- Primary series followed by different boost vaccine
- NIH-sponsored study: 150 individuals, 12-20 weeks following initial series (any series) Results expected late summer 2021

Booster studies

- Moderna: Preliminary results for mRNA-1273 (50µg) published May 2021; Additional data on mRNA-1273 and other variants as boosters expected July-Sept 2021
- Pfizer: Data on BNT162b2 (30µg) and variant booster studies expected July-Sept 2021

https://www.nih.gov/news-events/news-releases/nih-clinical-trial-evaluating-mixed-covid-19-vaccine-schedules-begins

	Adolescents (12 – 17 years)	Pediatric (6 months – 11 years)
Pfizer	• Authorized for 16 years and older • Submitted for EUA expansion for 12 – 15 years	• Phase 1/2/3 Study • Three age cohorts 1. 5 to 11 years 2. 2 to 5 years 3. 6 months to 2 years • N=4,644 in the US and Europe • Two-dose schedule • Begun enrolling
moderna	• Phase 2/3 randomized, placebo-controlled study • N=3,000 • 2-dose schedule • Enrollment completed	• Phase 2/3 Study • N=6,750 in the US and Canada Part 1: 2 to 12 years (either 50ug or 100 ug) Part 1: 6 mos to < 2yrs (25ug, 50ug or 100ug) Part 2: Placebo controlled vs the selected dose • Begun enrolling
janssen	• Expansion of an ongoing Phase 2a study to include adolescents 12 – 17 years of age • Single dose and two-dose regimens • Vaccination schedules at one, two and three-months intervals in two-dose vaccine regimens	
AstraZeneca / University of Oxford	• Phase 2/3 • N=200 • Aged 6 to 17 years • On-hold	
NOVAVAX	None at this time	

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June 29, 2021