



School of Continuous
Professional Development

VACCINES AGAINST SARS-COV-2:

TODAY AND TOMORROW

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Editor-in-Chief, VACCINE



DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INELIGIBLE COMPANIES

- Dr. Poland offers consultative advice on COVID-19 vaccine development to AstraZeneca, Pfizer, Medicargo, Emergent Biosolutions, Johnson&Johnson/Janssen, Novavax, and Moderna.
- Dr. Poland has received grant funding from ICW Ventures for preclinical studies on a peptide-based COVID-19 vaccine for which he holds a patent.

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Nothing to disclose

All relevant financial relationships have been mitigated.



COVID-19 VACCINE EFFICACY AND EFFECTIVENESS

A COMPLEX INTERPLAY

- Host characteristics
 - Age, race, gender
 - Genetics
 - Co-morbidities
- Pathogen (viral) characteristics
 - Variants
 - Inoculum
 - Portal of entry
- Vaccine type
- Time since vaccination (too soon, too late)
- Geography

VACCINE EFFICACY

- *A gradient of protection*
- Disease blocking >>> Infection blocking
- Underlying immune system health
 - Innate, humoral and cellular
- Predominant circulating variant(s)
- Community burden of transmission
- Time since vaccination
- Host genetic factors

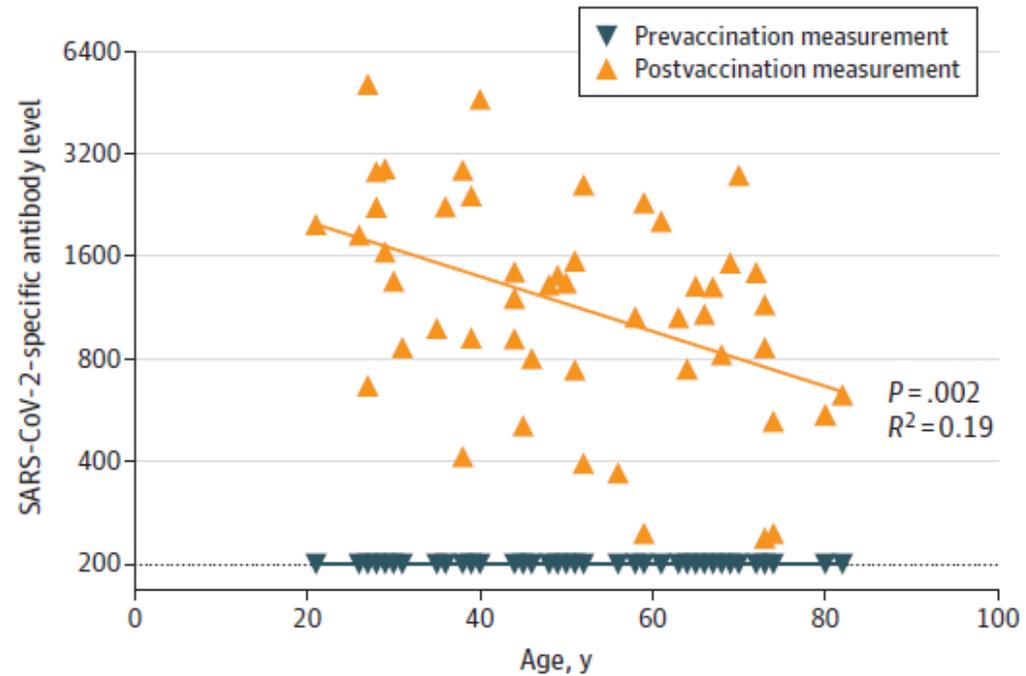
WHAT IS VACCINE EFFICACY?

- A Decreasing Gradient of Protection
 - Prevention of death
 - Prevention of severe disease
 - Prevention of hospitalization
 - Prevention of complications
 - Prevention of mild-moderate disease
 - Prevention of asymptomatic infection
 - Prevention of transmission

THREE ENEMIES

- Age
 - Increasing age, decreasing immunogenicity
 - Comorbidities
- Variant
 - Mutations and recombination events
 - Immune evasion – decreasing ability of neutralizing antibody to bind virus and block attachment to cell receptors
- Time
 - Decreasing levels of antibody over time

Figure 1. SARS-CoV-2-Specific Antibody Levels

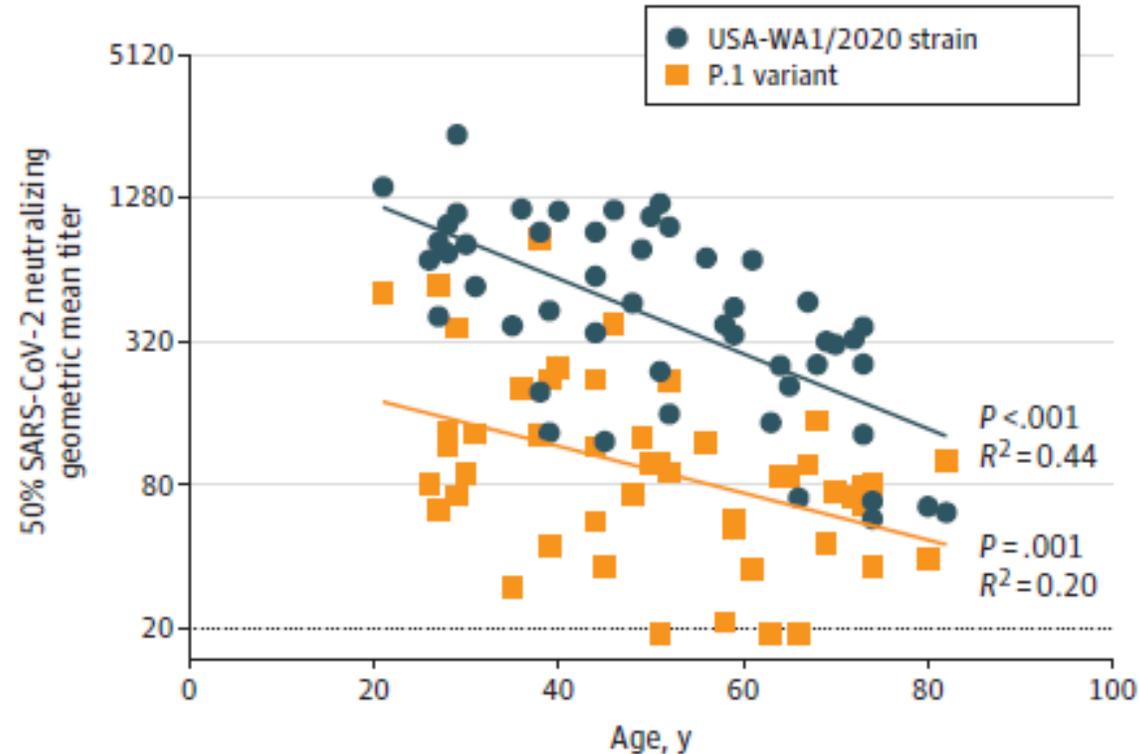


Enzyme-linked immunosorbent assay measurement of SARS-CoV-2 spike receptor-binding domain-specific antibody levels and association with age at time of vaccination for 50 participants 14 days after receiving their second vaccine dose. Prevaccination samples for all participants were below the limit of detection, indicating no prior exposure. Postvaccination samples displayed a significant negative association with age. The dotted line indicates the lower limit of quantification.

Bates, T. A. et al. (2021). Age-Dependent Neutralization of SARS-CoV-2 and P.1 Variant by Vaccine Immune Serum Samples. *JAMA*, e2111656. Advance online publication. <https://doi.org/10.1001/jama.2021.11656>

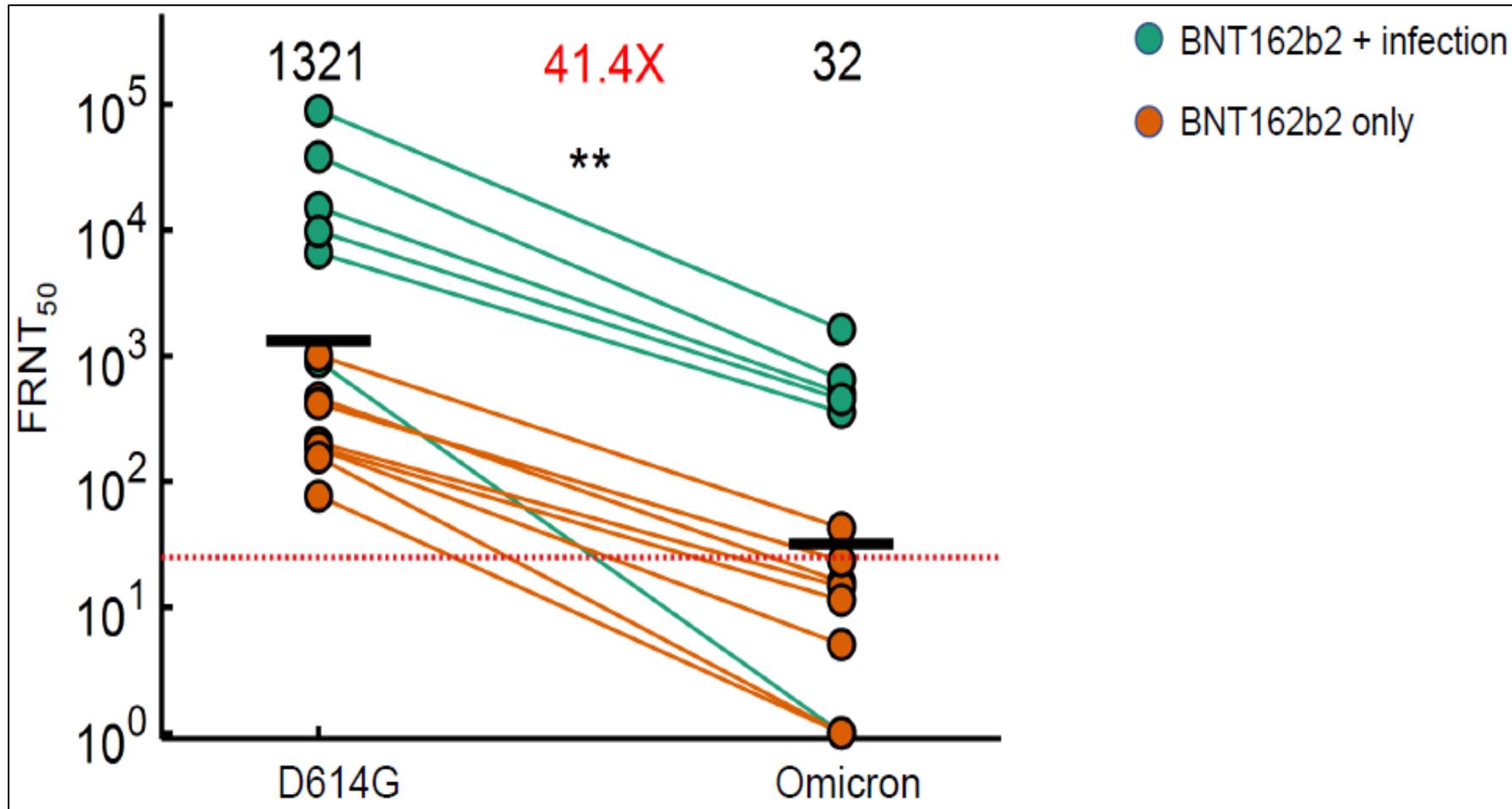
VOC PLUS AGE

Figure 2. Neutralization of Live SARS-CoV-2 Clinical Isolates

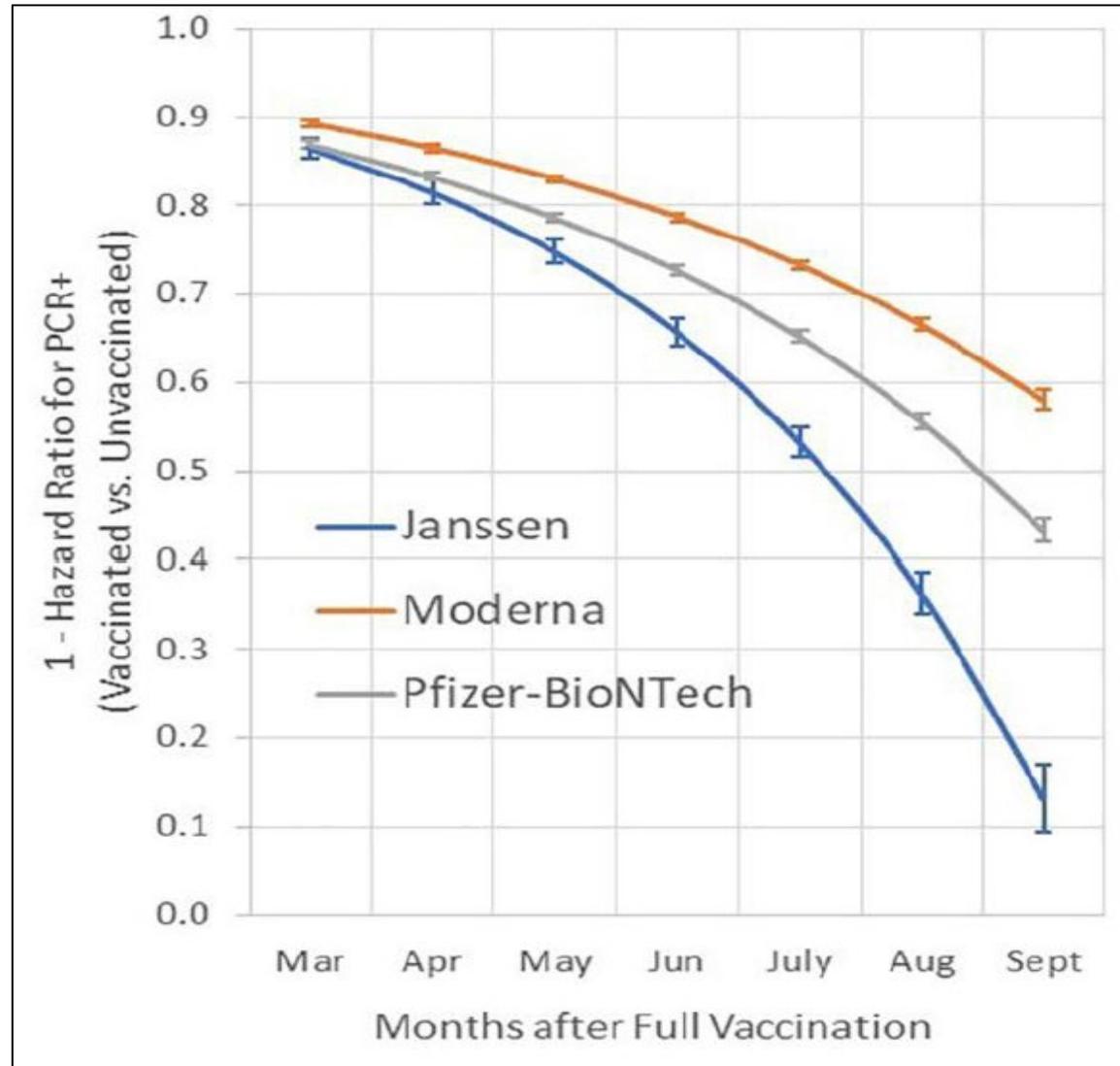


Live virus neutralization of participant serum samples collected 14 days after the second vaccine dose. Neutralization experiments were performed with the USA-WA1/2020 strain and P.1 variant. Both show a significant negative association with participant age. The dotted line indicates the lower limit of quantification.

NEUTRALIZATION OF OMICRON VARIANT BY PFIZER-ELICITED IMMUNITY



TIME DEPENDENT VE AGAINST INFECTION, ADJUSTED FOR AGE, RACE, ETHNICITY, SEX, AND COMORBIDITY



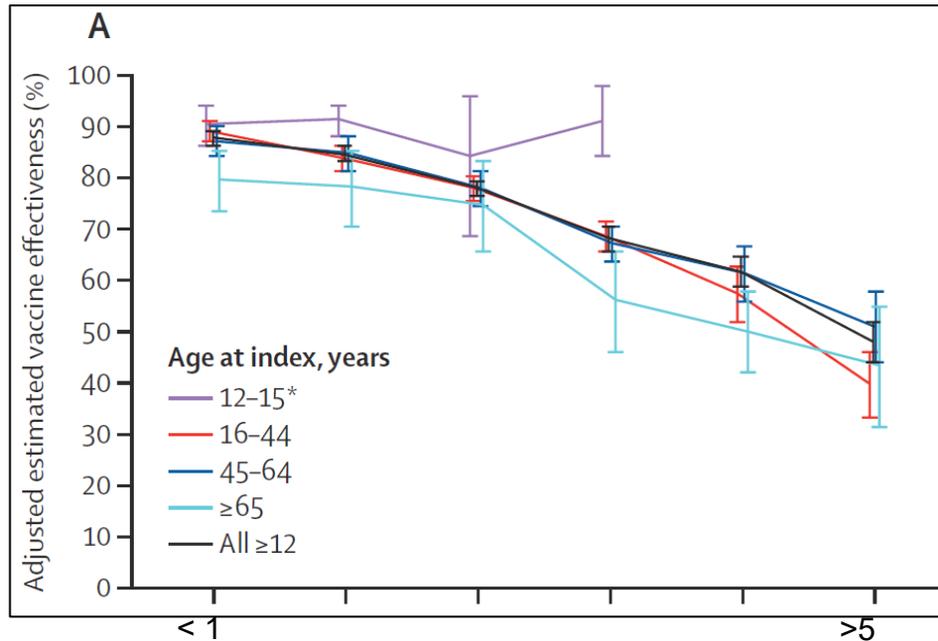
VE - INFECTION OVER TIME US

	3/2021	9/2021	7/2021 – 10/2021***
Moderna	89.2%	58%	81.5% - 75.5%
Pfizer	86.9%	43.3%	84.3% - 70.1%
J&J	86.4%	13%	73% - 52.2%

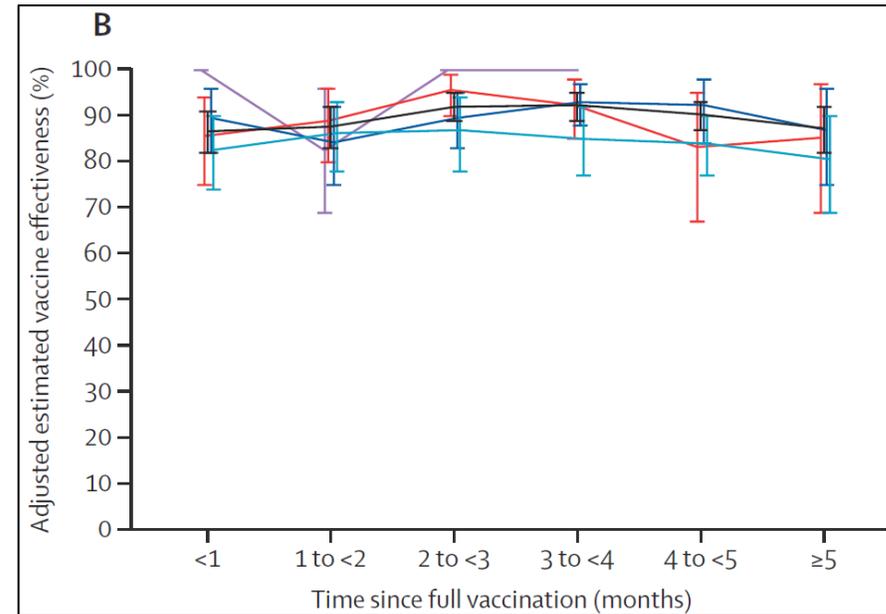
*** VE against death in < 65 y/o and > 65 y/o

B. A. Cohn et al., Science 10.1126/science.abm0620 (2021).

PFIZER VE AGAINST INFECTION AND HOSPITAL ADMISSION (2 DOSES)



VE against infection by age and time since fully vax

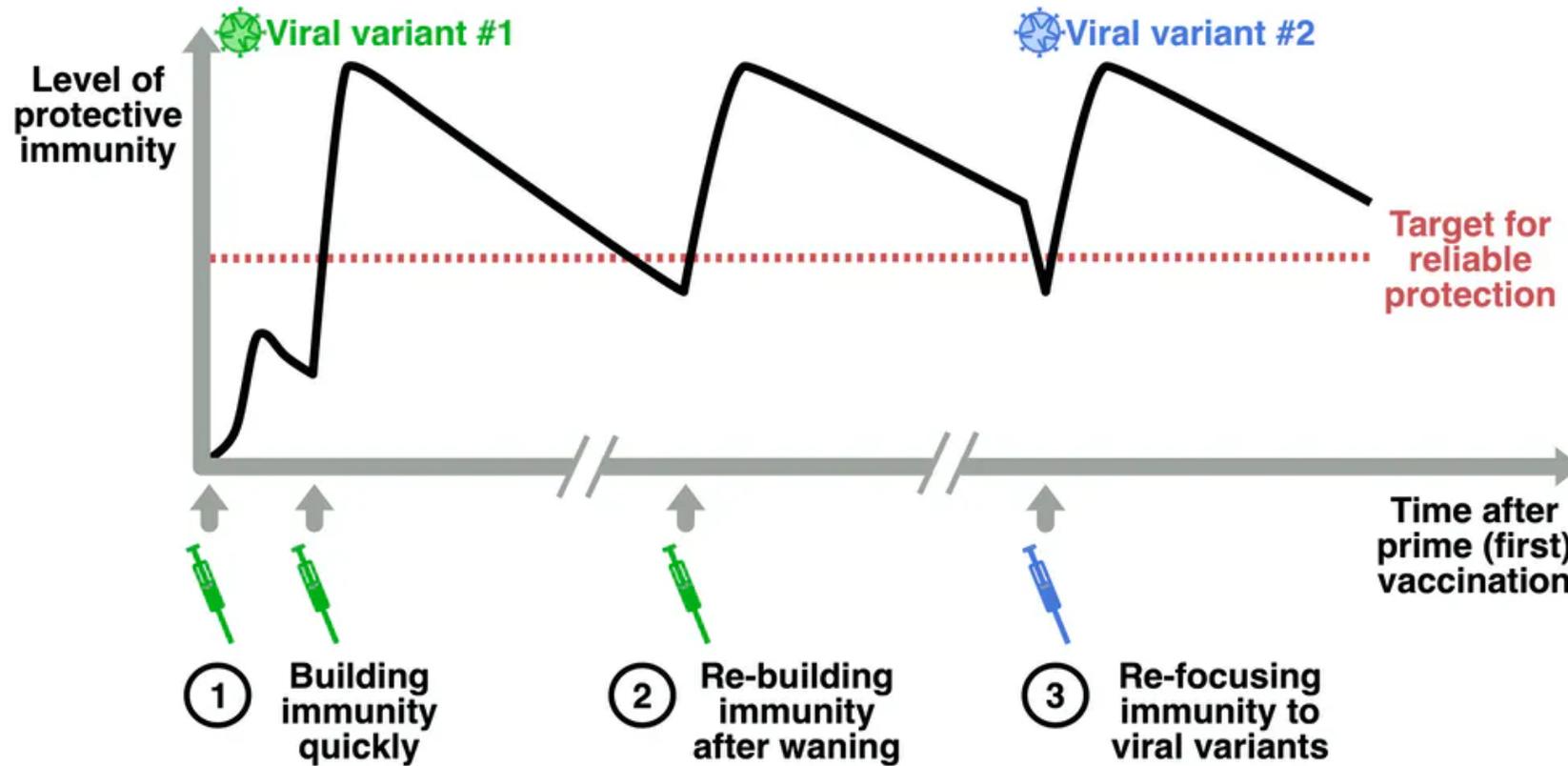


VE against hospitalization by time since fully vax

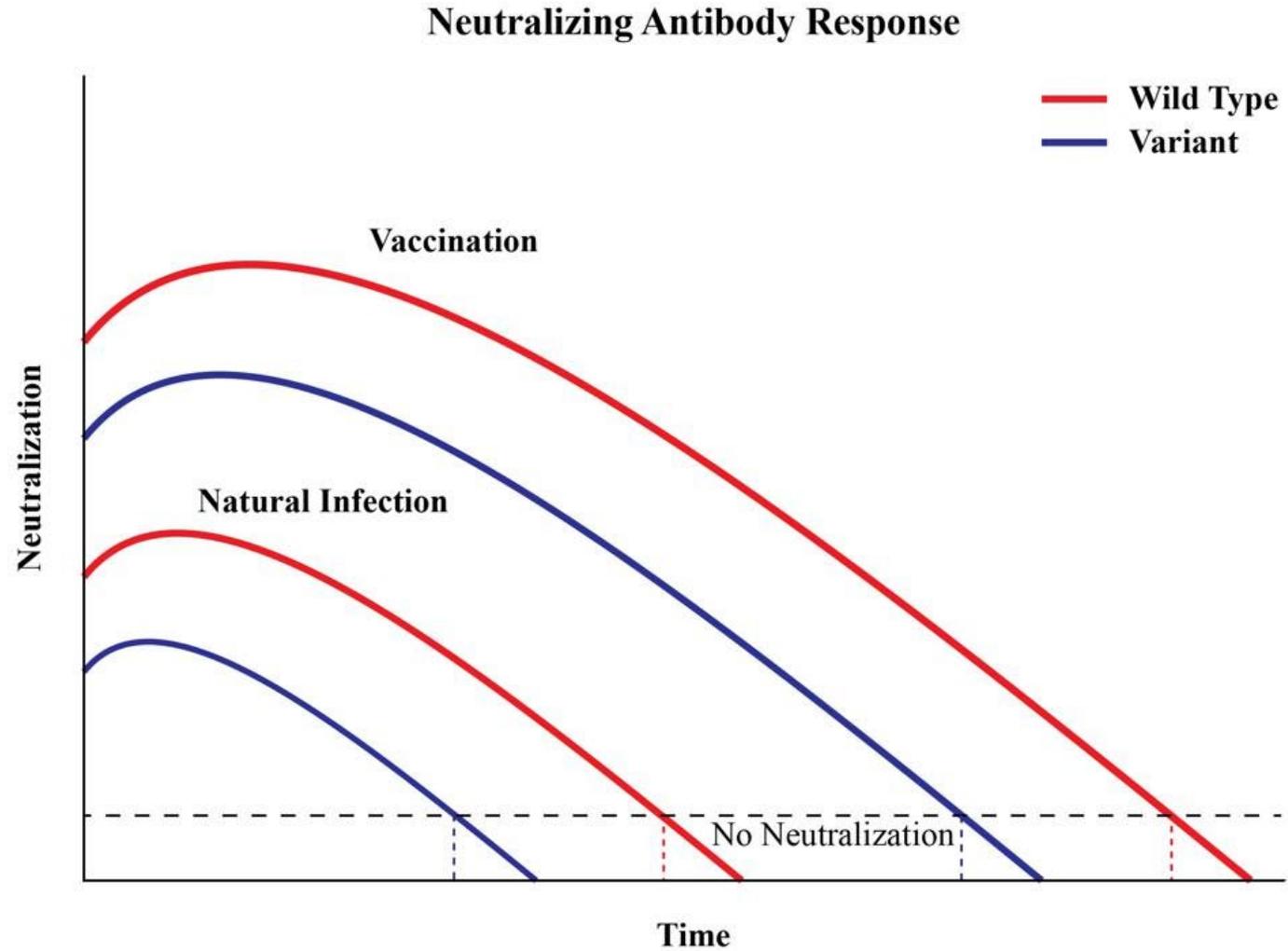


BOOSTER DOSES **ARE THEY OF VALUE?**

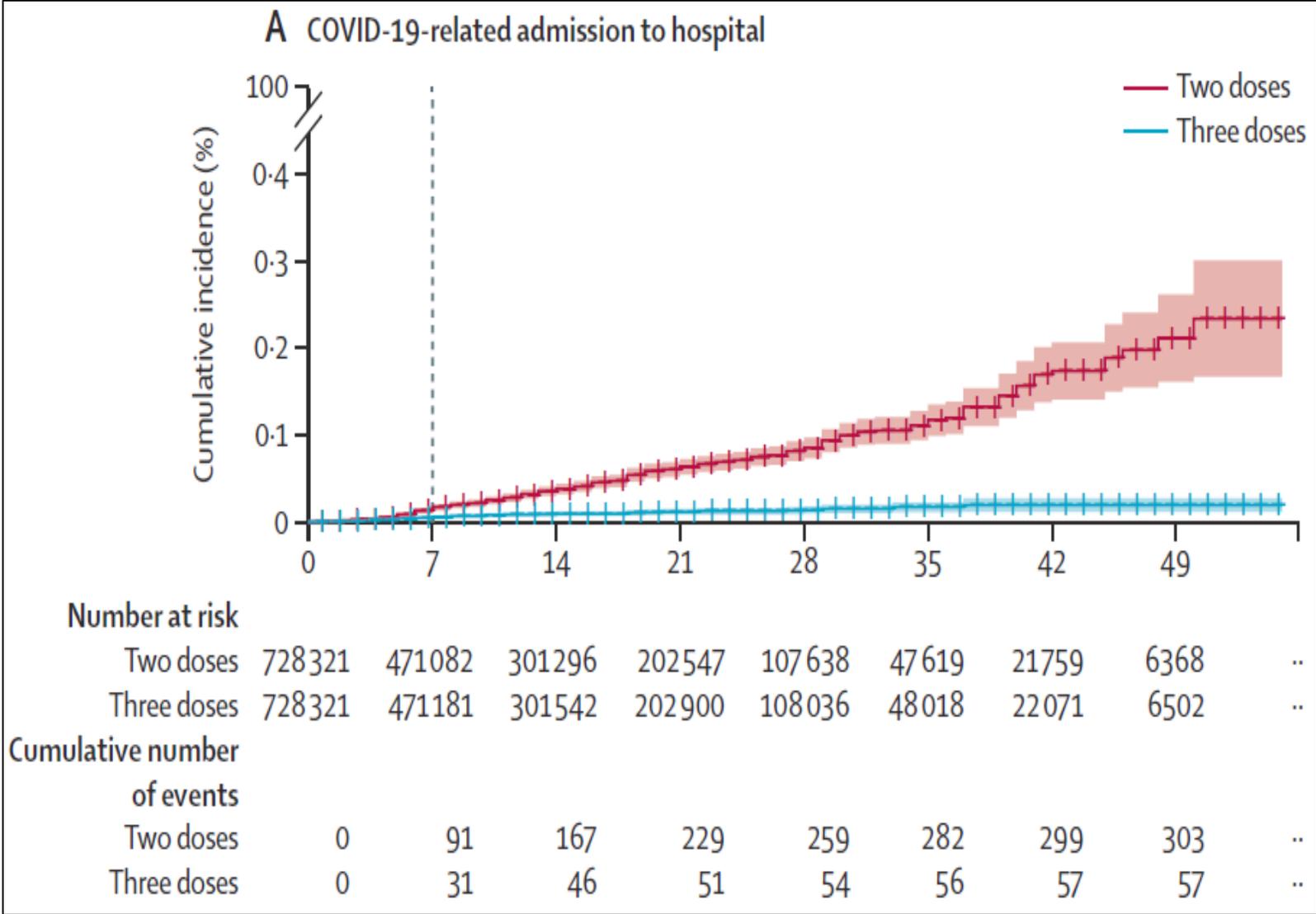
THEORETICAL CONSTRUCT



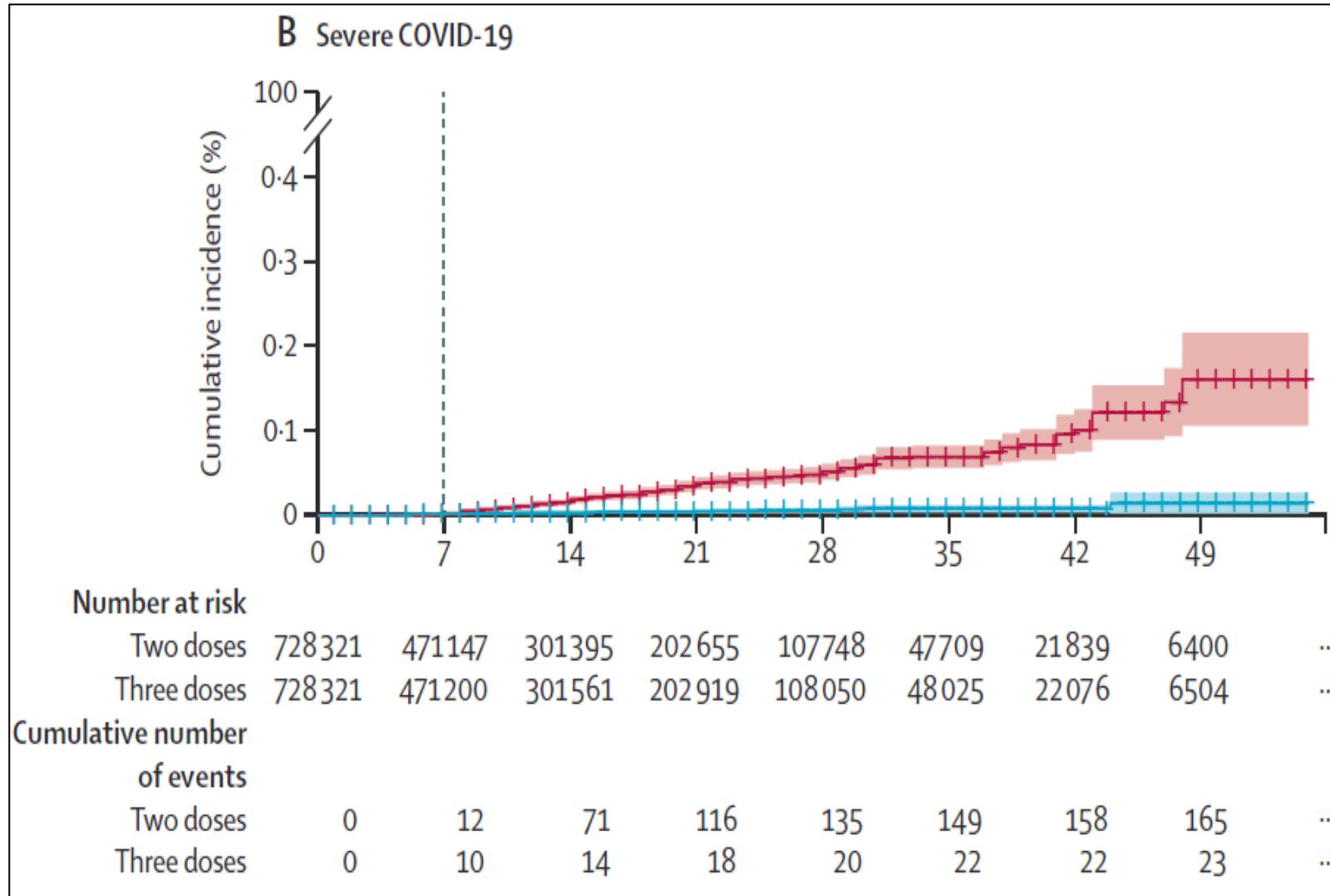
THEORETICAL CONSTRUCT



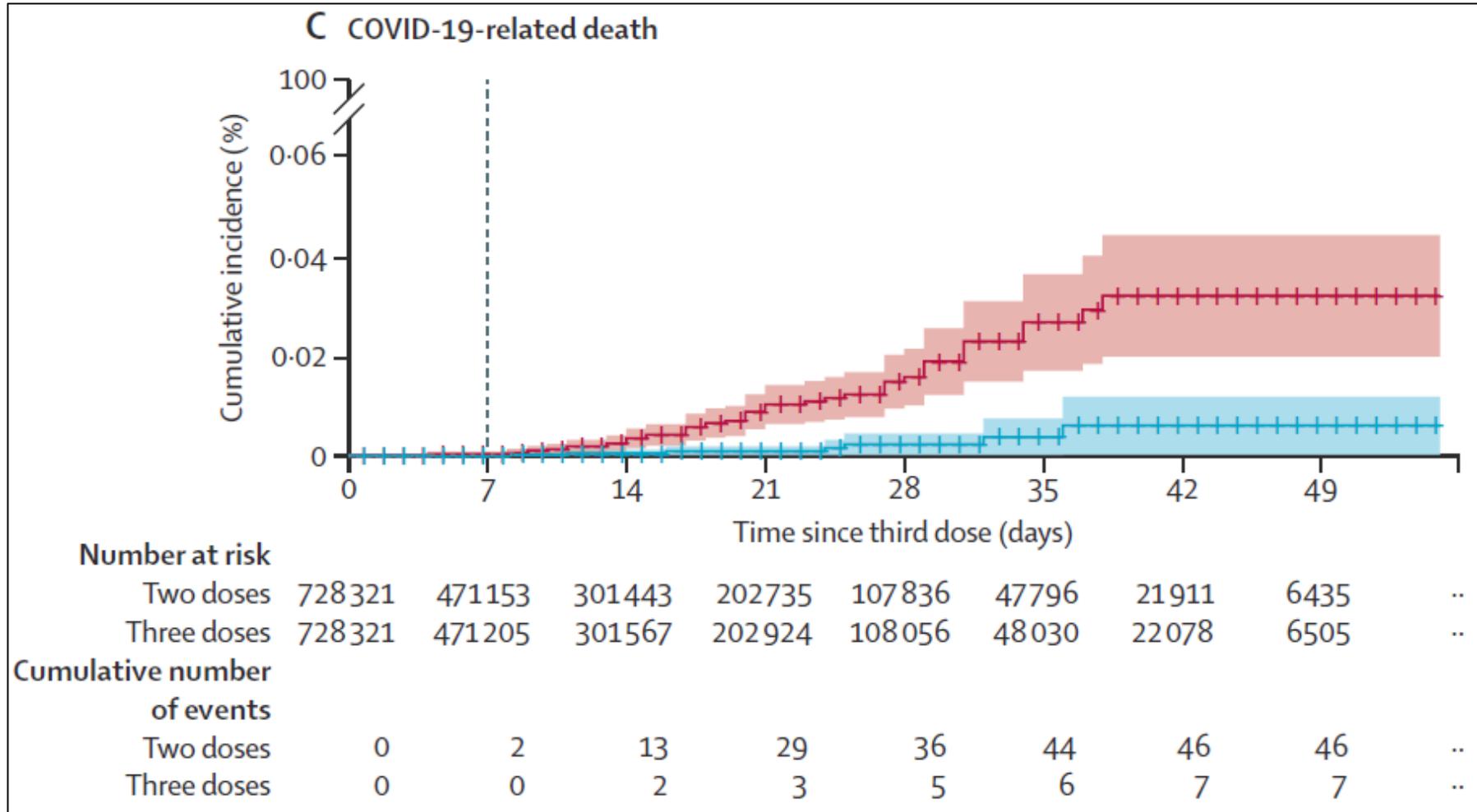
HOSPITALIZATION – 2 VS 3 DOSES PFIZER



SEVERE DISEASE – 2 VS 3 DOSES PFIZER



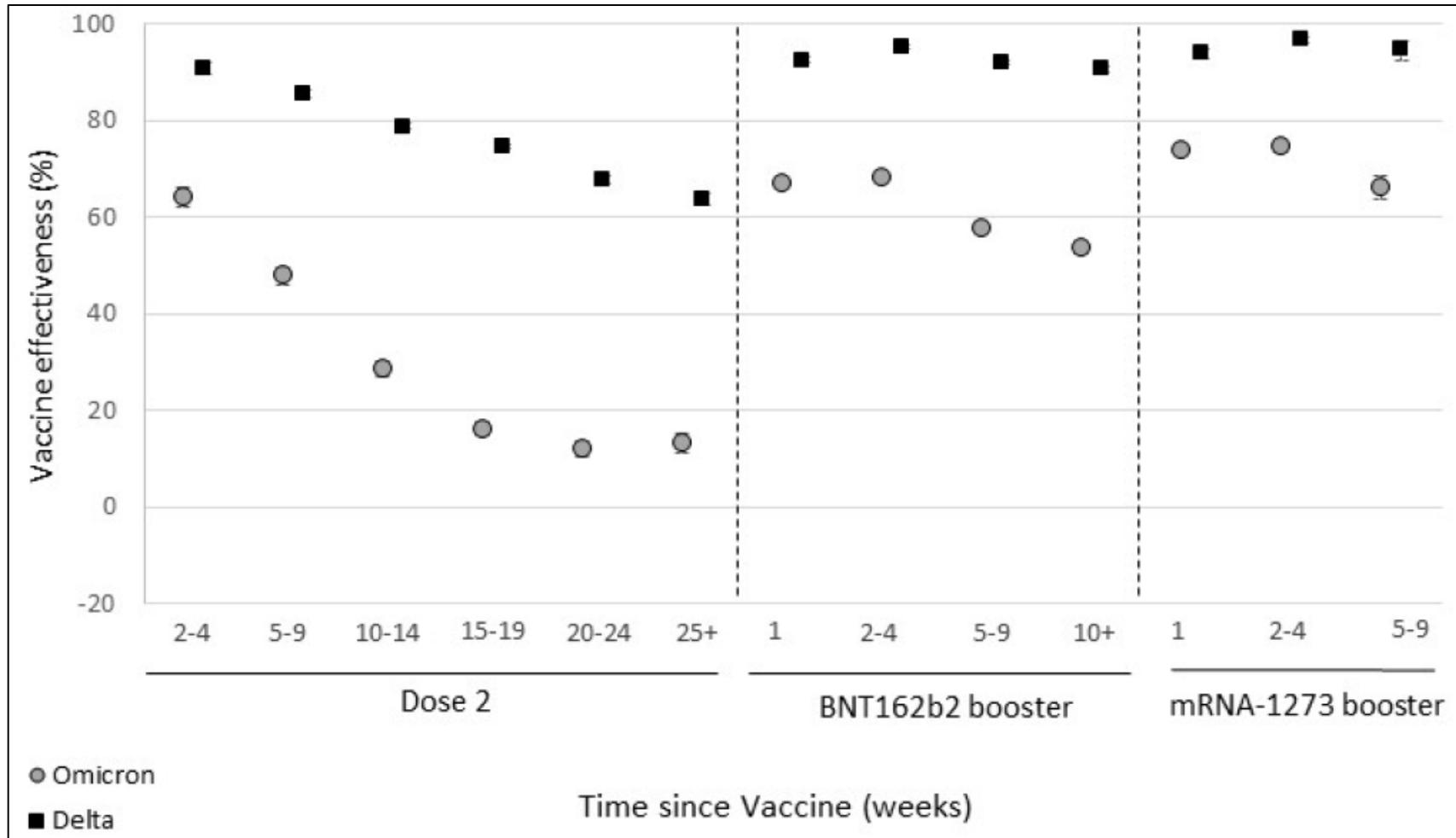
DEATH - 2 VS 3 DOSES PFIZER



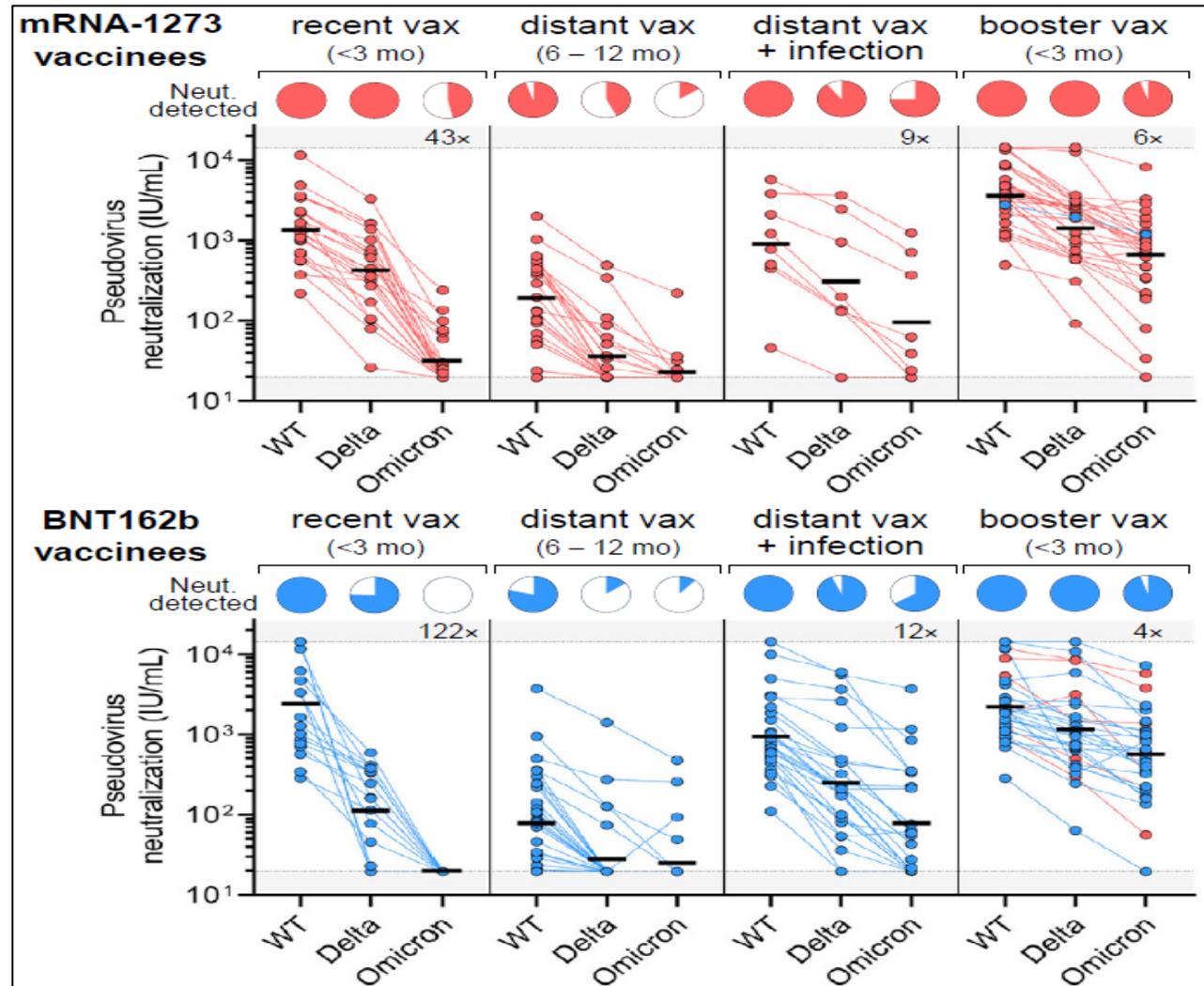
MRNA COVID-19 VE AND HOSPITALIZATIONS AMONG ADULTS AUGUST 2021–JANUARY 2022

Characteristic	Total	SARS-CoV-2 positive test result no. (%)	VE fully adjusted % (95% CI)*	Waning trend p value ^{††}
Any mRNA vaccine, 3 doses	10,957	471 (4)	93 (92–94)	<0.001
<2 mos	7,332	221 (3)	95 (94–95)	
2–3 mos	3,413	211 (6)	91 (89–92)	
≥4 mos	212	39 (18)	81 (72–87)	
Delta-predominant period				
Unvaccinated (Ref)	36,214	14,445 (40)	—	—
Any mRNA vaccine, 2 doses	38,707	3,315 (9)	85 (84–85)	<0.001
<2 mos	1,574	49 (3)	94 (92–96)	
2–3 mos	2,790	154 (6)	91 (89–92)	
4 mos	3,129	192 (6)	90 (89–92)	
≥5 mos	31,214	2,920 (9)	82 (82–83)	
Any mRNA vaccine, 3 doses	8,124	195 (2)	95 (95–96)	<0.001
<2 mos	6,071	118 (2)	96 (95–97)	
2–3 mos	2,030	74 (4)	93 (91–95)	
≥4 mos	23	3 (13)	76 (14–93)	
Omicron-predominant period				
Unvaccinated (Ref)	3,911	1,890 (48)	—	—
Any mRNA vaccine, 2 doses	3,619	979 (27)	55 (50–60)	0.01
<2 mos	88	22 (25)	71 (51–83)	
2–3 mos	294	69 (23)	65 (53–74)	
4 mos	150	42 (28)	58 (38–71)	
≥5 mos	3,087	846 (27)	54 (48–59)	
Any mRNA vaccine, 3 doses	2,833	276 (10)	88 (86–90)	<0.001
<2 mos	1,261	103 (8)	91 (88–93)	
2–3 mos	1,383	137 (10)	88 (85–90)	
≥4 mos	189	36 (19)	78 (67–85)	

TWO DOSES OF BNT162B2 WITH A BNT162B2 OR MRNA-1273 BOOSTER DOSE



MRNA BOOSTER AND NAB AGAINST OMICRON VARIANT



COMING SOON

- **Novavax**
 - Recombinant S protein vaccine with Matrix-M adjuvant
- **Sanofi-GSK**
 - S protein produced in insect cells via baculovirus vector
 - ASO3 adjuvant
- **Medicago**
 - Recombinant S protein produced in tobacco plant – assembles into nanoparticles
 - ASO3 adjuvant

SUMMARY

- Vaccines offer a gradient of protection
 - Extremely efficacious against hospitalization, severe disease, death
 - Reflects B and T cell immunity
- Antibody levels wane with time
 - Disease blocking >> Infection blocking
- The virus will learn to evade vaccine- and illness-induced immunity over time
- Next-generation vaccines
 - Oral/nasal?
 - Peptide-based?
 - Other?

“Each civilization, by its customs, its laws, its principles of thought, creates for itself a pathology appropriate to itself...a society chooses its diseases, and shapes its pathological destiny...”

Marcel Sendrail, 1954



FINI, TERMINE', ACCOMPLI

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OVER THE HORIZON AREAS OF CONCERN

- Cryptic sequences (NYC wastewater)
- White tail deer
 - Evidence of reinfection
 - ? Reverse zoonosis
- Emerging variants
- Emergence of long-term population health effects of COVID-19 infection
 - Long COVID
 - Predisposition to chronic illnesses
 - Behavioral/learning disabilities
 - Other?

VACCINE RECS:

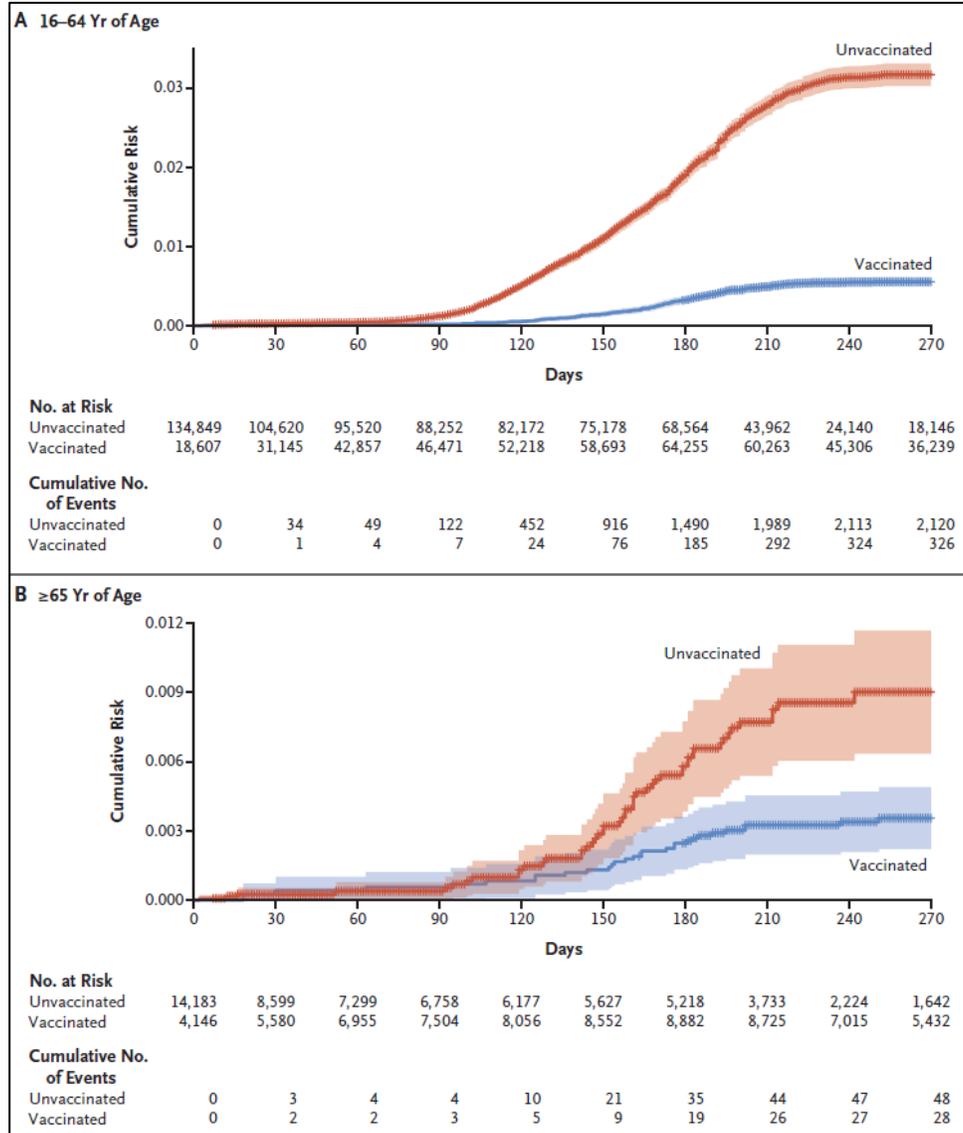
PRIMARY SERIES

Vaccine	Dose and Interval		Booster dose [†]
Pfizer-BioNTech (ages 5 years and older)	1 st dose	2 nd dose (21 days after 1 st dose)	(at least 5 months after 2 nd dose)
Moderna (ages 18 years and older)	1 st dose	2 nd dose (28 days after 1 st dose)	(at least 5 months after 2 nd dose)
Janssen (ages 18 years and older)	1 st dose		Booster dose [†] (at least 2 months after 1 st dose)

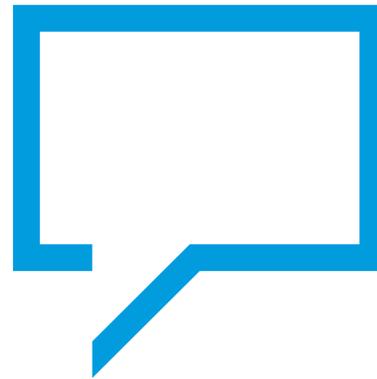
VACCINE RECS: IMMUNOCOMPROMISED

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

CUMULATIVE RISK OF REINFECTION WITH SARS-COV-2, ACCORDING TO AGE AND SUBSEQUENT VACCINATION STATUS



QUESTIONS & DISCUSSION





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THANK YOU FOR JOINING US IN THIS COURSE



Rochester, Minnesota



Phoenix, Arizona



Jacksonville, Florida