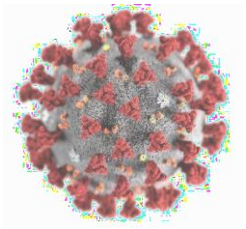
Pediatric Community Forum

"COVID-19 Update: Kids, Omicron and Boosters"

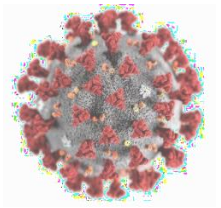
Let's TALK

Presenter:

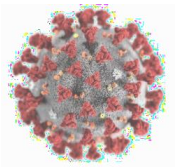
Paul A. Offit, MD, FAAP
Attending Physician, Division of Infectious Diseases
Director, Vaccine Education Center
The Children's Hospital of Philadelphia



Session Learning Objectives:
As a result of participation in this activity, participants will be able to:



- Describe the basic structure and results of the Pfizer COVID vaccine trial involving five- to eleven-year-old children
- Discuss the potential benefits of a third "booster" dose of COVID vaccine for different patient populations
- Describe the risks of myocarditis and other inflammatory syndromes associated with COVID infection, and possibly with COVID vaccines
- Compare the clinical characteristics of the emerging Omicron variant to earlier variants of the SARS-CoV-2 virus



This webinar will begin at 8:00 PM EST

Pennsylvania Chapter
American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®

PENNSYLVANIA IMMUNIZATION COALITION
PAIC

CME/CEU is available for the live webinar. Information on how to obtain credit will be emailed to all participants following the webinar.

COVID-19 Update: Kids, Omicron, and Boosters

Paul A. Offit, MD

Division of Infectious Diseases

Vaccine Education Center

The Children's Hospital of Philadelphia

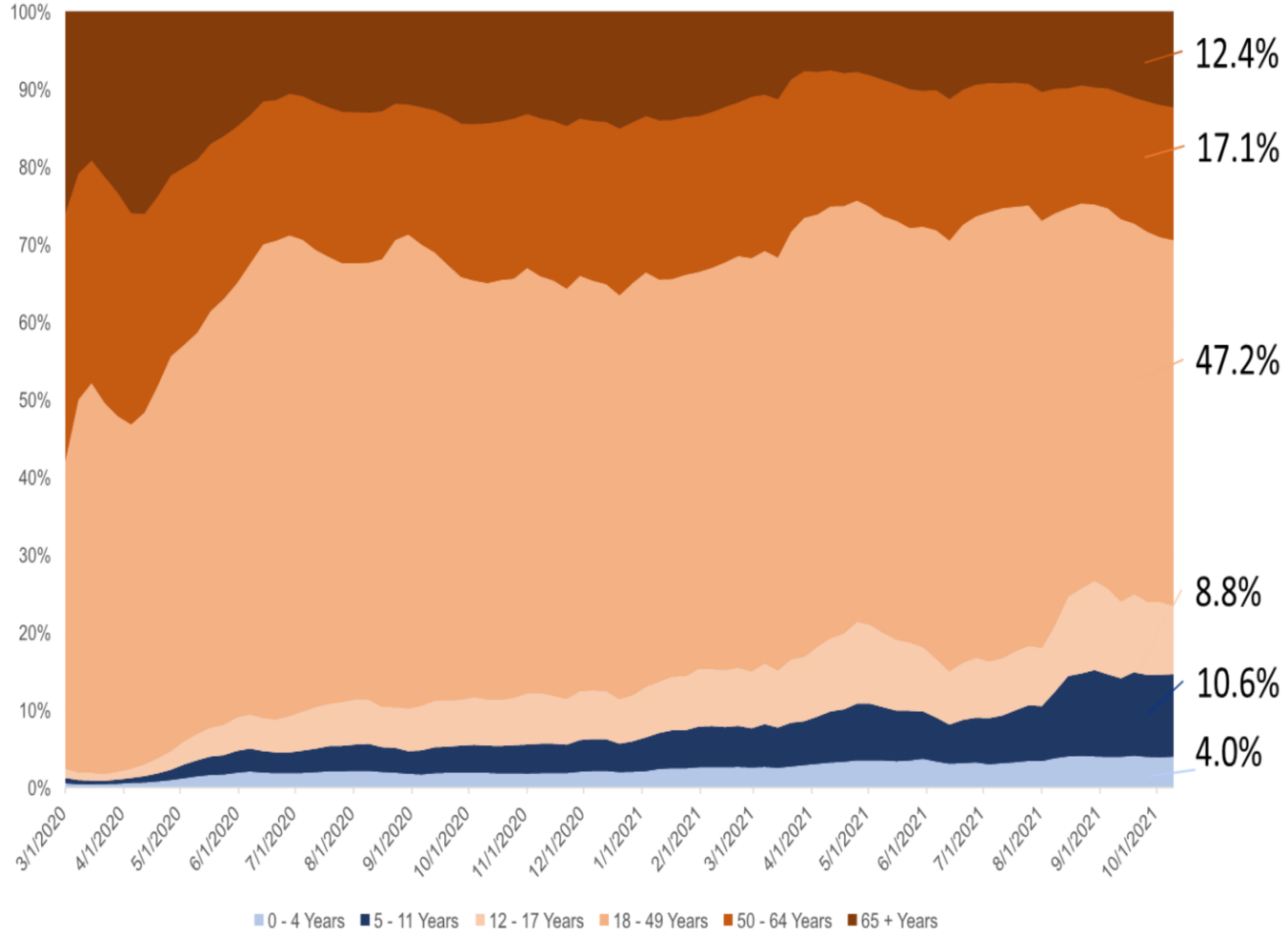
Perelman School of Medicine

The University of Pennsylvania

January 19, 2022

COVID-19 and Young Children

Proportion of Total COVID-19 Cases by Age Group — March 1, 2020–October 10, 2021

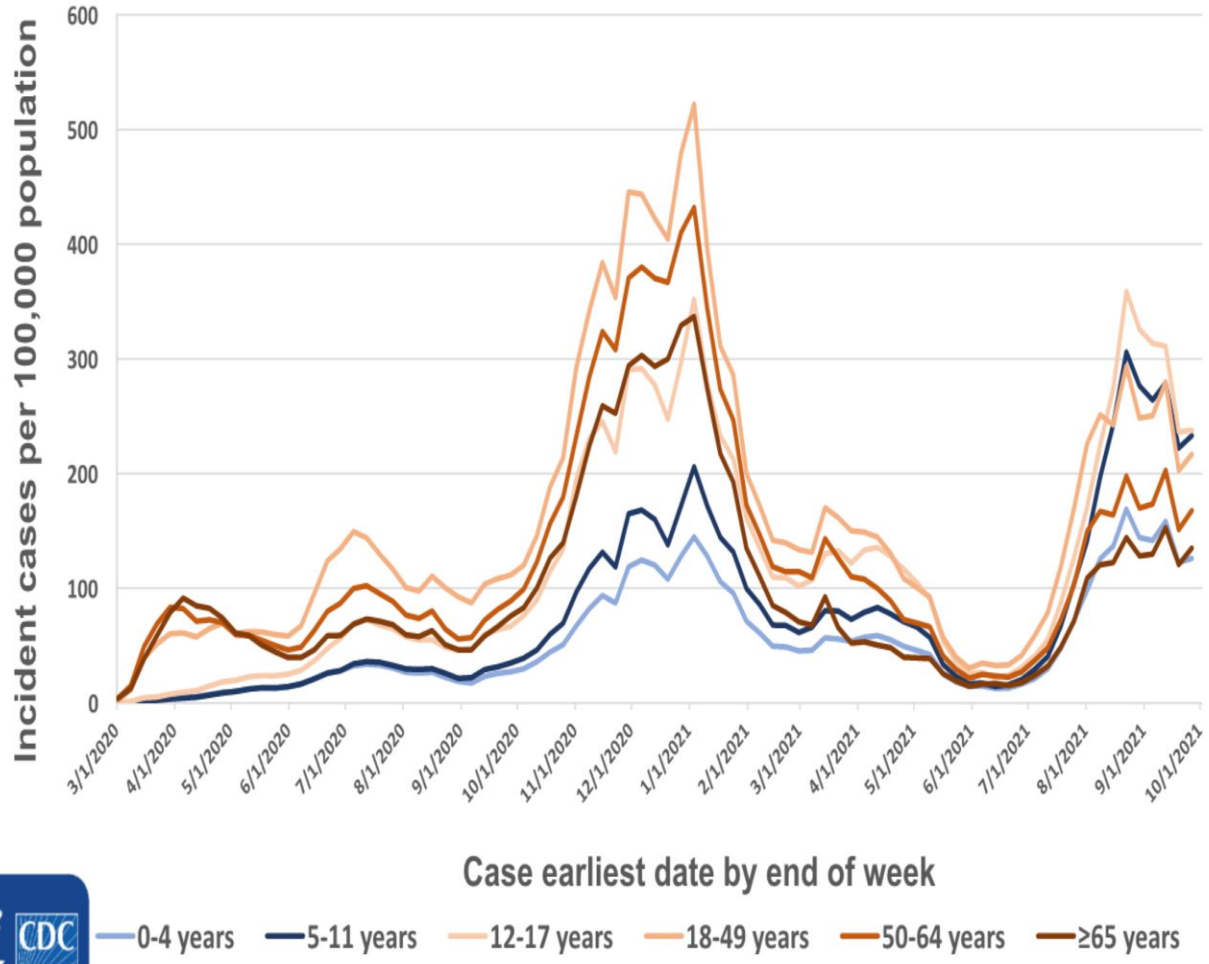


Children 5-11 years are making up a greater proportion of total cases:

10.6% of cases the week of October 10, 2021

https://covid.cdc.gov/covid-data-tracker/#demographicsovertime

COVID-19 Weekly Cases per 100,000 Population by Age — March 1, 2020–October 10, 2021



>1.9 million cases among children 5-11 years of age

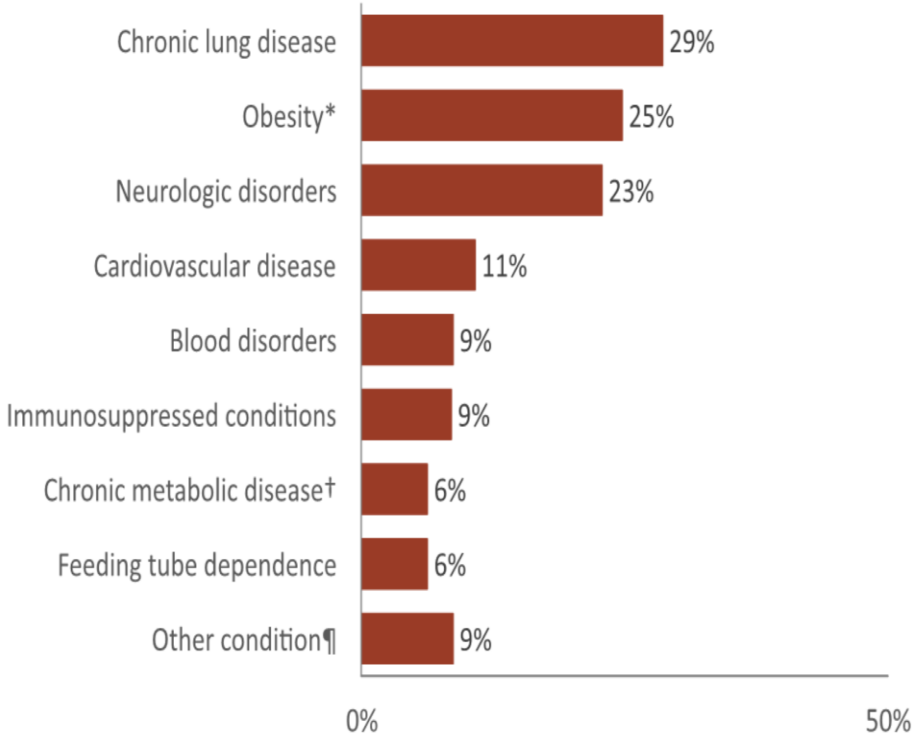
https://covid.cdc.gov/covid-data-tracker/#demographicsovertime

Children Aged 5–11 Years Hospitalized with COVID-19—COVID-NET, March 2020–August 2021

Demographic and clinical characteristics

	N	(%)
Total	562	(100)
Age (yrs) – median (IQR)	8	(6–10)
Sex – Male	320	(57)
Race/ethnicity		
Black, non-Hispanic	207	(37)
Hispanic	177	(31)
White, non-Hispanic	124	(22)
Asian, non-Hispanic	23	(4)
Other, non-Hispanic	31	(6)
Severe disease§	**200**	**(36)**
≥1 underlying condition	**381**	**(68)**

Prevalence of underlying medical conditions



§Requiring intensive care unit admission or mechanical ventilation

*BMI (kg/m^2) ≥95th percentile for age and sex based on CDC growth charts, ICD-10 codes for obesity, or obesity selected on case report form

†Includes type I and type II diabetes mellitus

¶Includes gastrointestinal or liver disease; renal disease; rheumatologic, autoimmune, inflammatory conditions; abnormality of the airway

COVID-NET is a population-based surveillance system that collects data on laboratory-confirmed COVID-19-associated hospitalizations among children and adults through a network of over 250 acute-care hospitals in 14 states. Methods described in: Woodruff RC, et al. Risk factors for Severe COVID-19 in Children. *Pediatrics*. ePub October 2021.

Leading Causes of Death in Children 5-11 Years of Age, NCHS, 2019

Causes of Death	Death (n)	Crude rate per 100,000
Accidents (unintentional injuries)	969	3.4
Malignant neoplasms	525	1.8
Congenital malformations, deformations and chromosomal abnormalities	274	1.0
Assault (homicide)	207	0.7
Diseases of the heart	115	0.4
Chronic lower respiratory diseases	107	0.4
Influenza and pneumonia	84	0.3
Intentional self-harm (suicide)	66	0.2
Cerebrovascular diseases	56	0.2
Septicemia	48	0.2

66 COVID-19 associated deaths in children 5-11 10/3/20-10/2/2021

Total population 5-17 years, 2019: 52,715,248

CDC NCHS WONDER Online Database. Accessed at http://wonder.cdc.gov/ucd-icd10.html on May 6, 2021

Multisystem Inflammatory Syndrome in Children (MIS-C)

- Severe hyperinflammatory syndrome occurring 2-6 weeks after acute SARS-CoV-2 infection, resulting in a wide range of manifestations and complications
  - **60-70%** of patients are admitted to intensive care, 1-2% die[1,2]

- **5,217 MIS-C cases** have been reported to national surveillance as of October 4, 2021[3]
  - Median age of **9 years**, 39% of cases occurred in children 6-11 years
  - **61%** occurred in children who are Hispanic/Latino or Black, Non-Hispanic
  - Adjusted incidence estimates ~100-600 cases per million SARS-Cov-2 infections[4]

1. Feldstein LR, et al. Characteristics and Outcomes of US Children and Adolescents With Multisystem Inflammatory Syndrome in Children (MIS-C) Compared With Severe Acute COVID-19. *JAMA*. 2021;325(11):1074-1087. doi:10.1001/jama.2021.2091
2. Belay ED, et al. Trends in Geographic and Temporal Distribution of US Children With Multisystem Inflammatory Syndrome During the COVID-19 Pandemic [published online ahead of print, 2021 Apr 6]. *JAMA Pediatr*. 2021;e210630. doi:10.1001/jamapediatrics.2021.0630
3. https://covid.cdc.gov/covid-data-tracker/#mis-national-surveillance
4. Payne AB, et al. Incidence of Multisystem Inflammatory Syndrome in Children Among US Persons Infected With SARS-CoV-2. *JAMA Netw Open*. 2021;4(6):e2116420. Published 2021 Jun 1. doi:10.1001/jamanetworkopen.2021.16420

Burden of COVID-19 in children 5-11 years of age

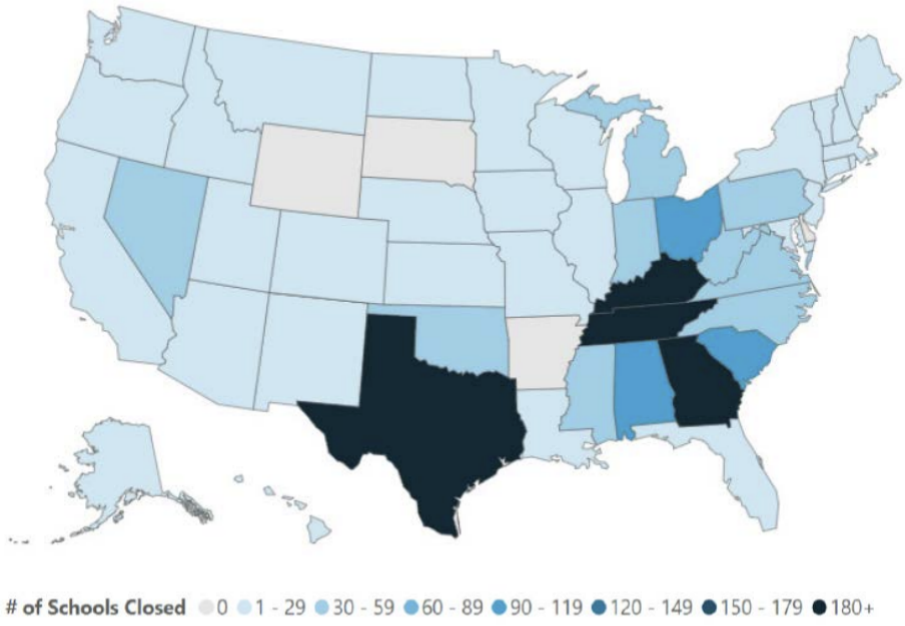
- **1.9 million** cases
- **8,300** hospitalizations
- **2,316** Multisystem Inflammatory Syndrome in Children (MIS-C) cases
- **94** deaths

- Burden extends beyond case counts; school interrupted, lives disrupted

COVID-19 Related K-12 School Closures by State,

August 2, 2021 – October 22, 2021

School districts closed	Total # schools closed*	Estimated # students affected*	Estimated # teachers affected*
313	2,351	**1,217,777**	78,134



Data from the Unplanned School Closure Monitoring Project (DGMQ/CDC), ongoing research that uses systematic daily media searches (methods explained in https://doi.org/10.1371/journal.pone.0248925).

* Number of schools closed in district-wide closures, total number of students, and total number of teachers are estimated by matching the public school district ID or school ID with the district/school data for school year 2019/20 and private school ID with school data for year 2017/18 as obtained from the National Center for Education Statistics (https://nces.ed.gov/ccd/elsi/tableGenerator.aspx, accessed on Apr 20, 2021). Due to missing information in 2019/20 data, the total number of public school teachers in California is estimated using 2018/19 NCES data.

2

Are COVID-19 vaccines effective in young children?

Pfizer-BioNTech Pediatric COVID-19 Vaccine BNT162b2: Study Overview: 5 to <12 Years

Phase 1

48
PARTICIPANTS

5 to <12 yrs

Identification of preferred dose level(s)

10 µg | 20 µg | 30 µg

Phase 2/3

2:1
randomization

~1500 BNT162b2

750 placebo

~Additional 1500 BNT162b2 and 750 placebo recipients most with ≥2 weeks post dose 2 safety data

Non-inferior immune responses have been established to infer vaccine efficacy

Children 5 to <12 years of age — Compared to — 16–25-year-olds from the pivotal Phase 3 study

Although not required for EUA approval, COVID-19 surveillance was conducted permitting evaluation of vaccine efficacy

Pfizer-BioNTech COVID-19 Vaccine Formulations

12 years of age and older:
PBS/Sucrose formulation

- Dilute before use
- Each dose:
  - 0.3 mL
  - 30 μg mRNA
- Must be stored frozen at -80ºC until expiry date or -20°C for up to 2 weeks prior to use

5 through 11 years of age:
Tris/Sucrose formulation

- Dilute before use
- Each dose:
  - 0.2 mL
  - 10 μg mRNA
- Can be stored at refrigerator temperature (2°C to 8°C) for up to 10 weeks prior to use

➢ Tris and PBS are buffering agents that help maintain the pH and stability of the product.

High Efficacy was Observed in 5 to <12 Year Olds Descriptive Analysis of First COVID-19 Occurrence From 7 Days After Dose 2

Subjects WITHOUT Evidence of Infection Prior to 7 Days After Dose 2

	BNT162b2 (10 µg) N=1305		Placebo N=663			
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)
First COVID-19 occurrence ≥7 days after Dose 2	3	0.322 (1273)	16	0.159 (637)	90.7	(67.7, 98.3)

No severe cases of COVID-19 were reported
No cases of MIS-C were reported

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint

Estimated impact of COVID-19 vaccines for young children

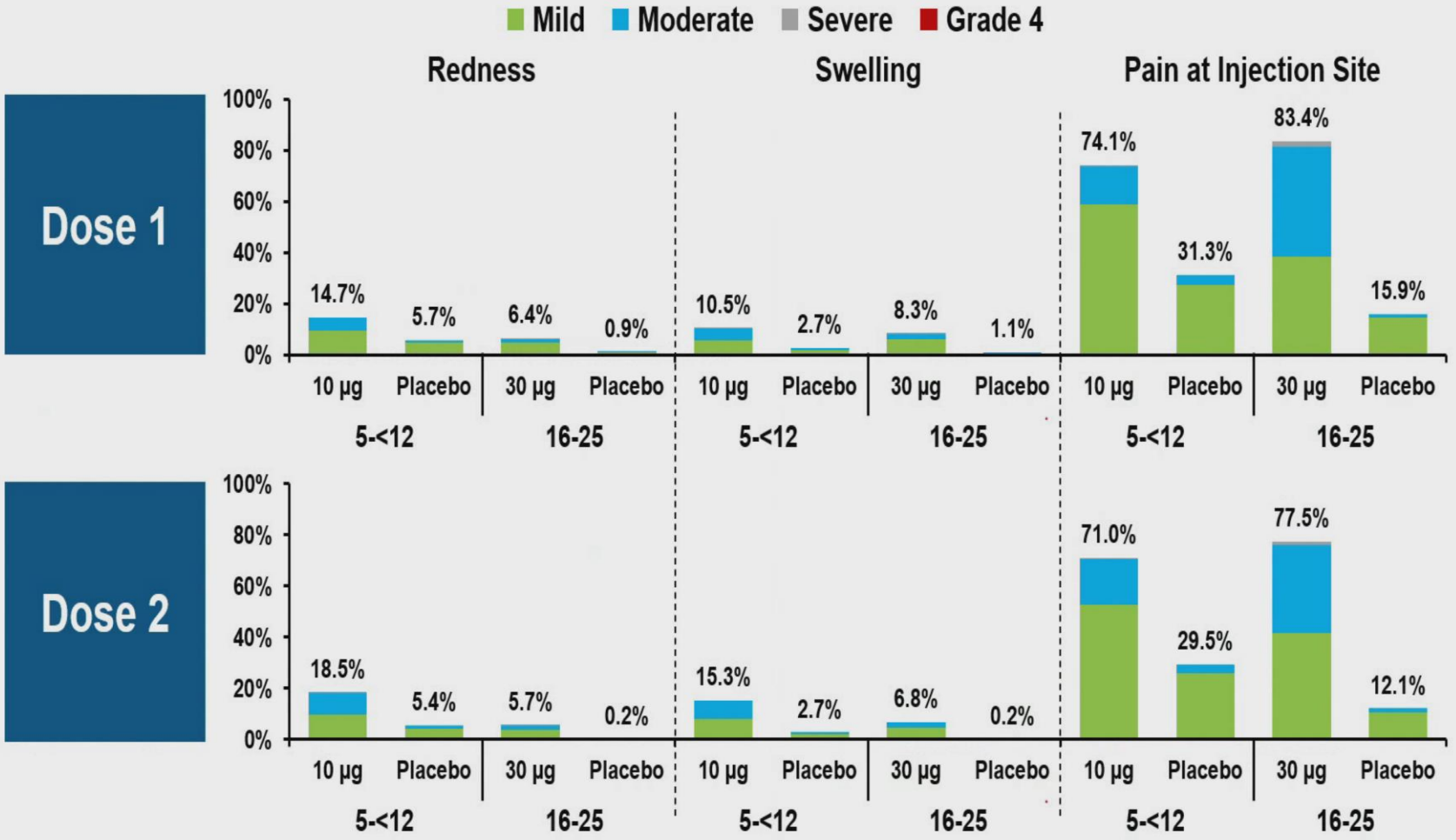
Estimated benefits for every million Pfizer-BioNTech COVID-19 vaccinations in children 5-11 years of age using recent incidence

Females 5-11 years	Males 5-11 years
57,301 COVID-19 cases prevented	**56,954** COVID-19 cases prevented
191 hospitalizations prevented	**226** hospitalizations prevented
130 MIS-C cases prevented	**130** MIS-C cases prevented
60 ICU admissions prevented	**72** ICU admissions prevented

Assumptions: Benefits accrue over **180 days (6 months)**; VE against symptomatic COVID-19: 90%; VE against hospitalization: 95%
Data Sources: COVID Data Tracker. https://covid.cdc.gov/covid-data-tracker/#vaccination-demographic. COVID Data Tracker https://covid.cdc.gov/covid-data-tracker/#trends_dailycases. COVID-Net https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html. All data are from the week ending on **9/11/2021**.

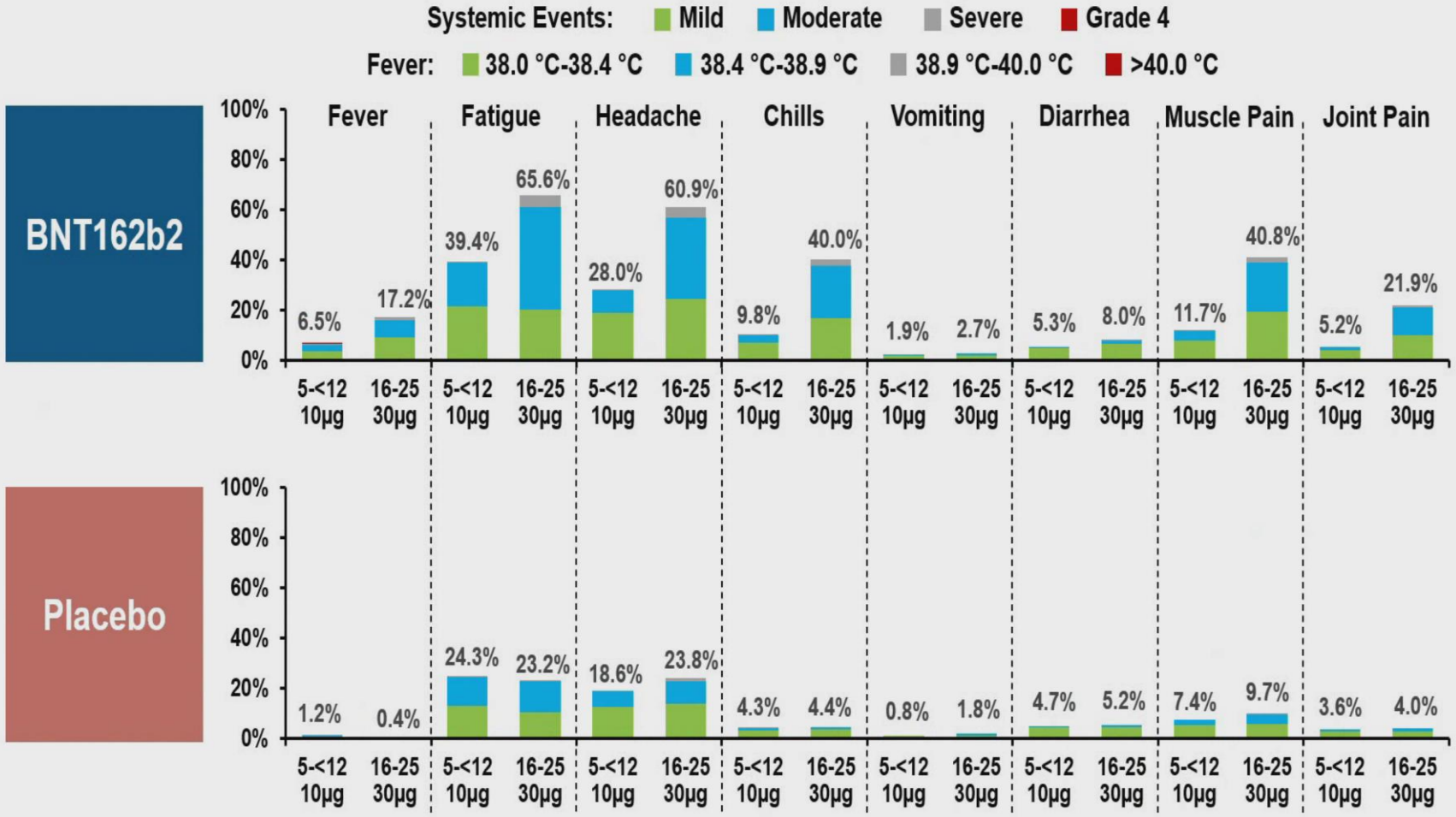
Is the COVID-19 vaccine safe for young children?

Local Reactions, by Maximum Severity, Within 7 Days After Each Dose in 5 to <12 and 16-25 Year Olds



5 to <12 yo: Redness and swelling severity definition: Mild=>0.5-2 cm, Moderate >2-7 cm; Severe >7 cm; Grade 4= necrosis
16-25 yo: Redness and swelling severity definition: Mild=>2-5cm, Moderate= >5-10 cm; Severe= >10 cm; Grade 4= necrosis
Pain at injection site severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Dose 1: 5-<12yrs N=2260; 16-25 yrs N=1064 Dose 2: 5-<12 yrs N=2242 16-25 yrs N=984

Systemic Events, by Maximum Severity, Within 7 Days After Dose 2 in 5 to <12 and 16-25 Year Olds



Fatigue, headache, chills, muscle pain, joint pain severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Vomiting severity definition: Mild=1-2 time in 24h; Moderate=>2times in 24h; Severe=Requires IV hydration; Grade 4=ER visit or hospitalization
Diarrhea severity definition: Mild=2-3 times in 24h; Moderate=4-5 times in 24h; Severe=6 or more times in 24h; Grade 4=ER visit or hospitalization
Dose 2: 5-<12 yrs N=2242 16-25 yrs N=984

Will COVID-19 vaccines cause myocarditis in young children?

Reassuring Fact #1:

Myocarditis is less common in 12-15-year-olds than 16-17-year-olds

Vaccine Adverse Event Reporting System (VAERS): Reporting rates (per 1 million doses administered) of myocarditis among males after mRNA COVID-19 vaccines, 7-day risk period (N=797)*

- **169,740,953** doses of mRNA vaccine administered to males (dose 1 and dose 2) *
- Reporting rates exceed background incidence**

Highest % is among males aged 16-17 years: 0.007%

	Pfizer		Moderna	
	(Males)		(Males)	
Ages	Dose 1	Dose 2	Dose 1	Dose 2
12-15	4.2	39.9		
16-17	5.7	69.1		
18-24	2.3	36.8	6.1	38.5
25-29	1.3	10.8	3.4	17.2
30-39	0.5	5.2	2.3	6.7
40-49	0.3	2.0	0.2	2.9
50-64	0.2	0.3	0.5	0.6
65+	0.2	0.1	0.1	0.3

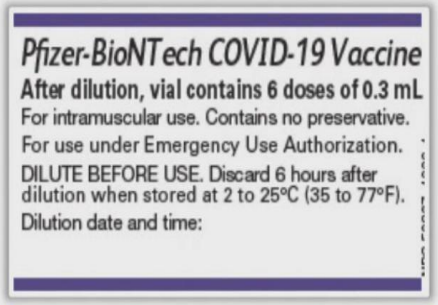
* As of Oct 6, 2021; 797 of 935 reports after doses 1 and 2 of mRNA vaccines occurred during Days 0–6 after vaccination among males; reports verified to meet case definition by provider interview or medical record review

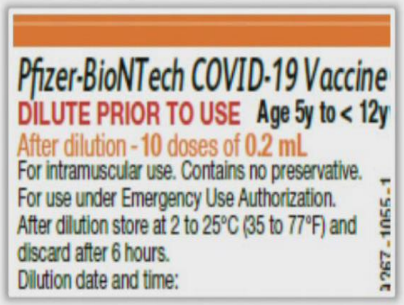
** An estimated 1–10 cases of myocarditis per 100,000 person years occurs among people in the United States, regardless of vaccination status; adjusted for the 7 -day risk period, this estimated background is **0.2 to 1.9 per 1 million person 7-day risk period**

Reassuring Fact #2:

The dose of mRNA for the 5-11-year-old is one-third the dose of the 12-15-year-old

Vial Differentiation



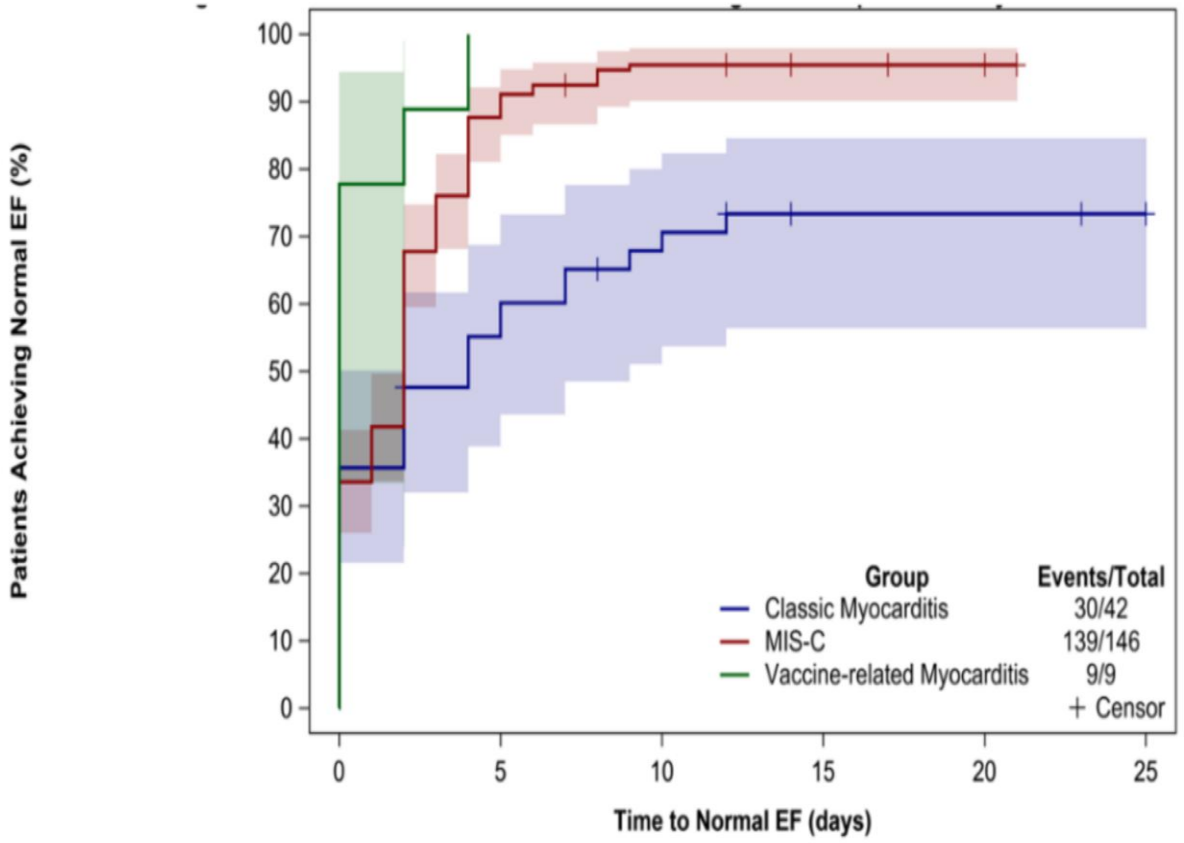


	Current Formulation	
	PURPLE CAP Age: 12+ *Dilute Prior to Use*	ORANGE CAP Age: 5 to <12 *Dilute Prior to Use*
Dose	30 mcg	10 mcg
Injection Volume	0.3 mL	0.2 mL
Fill Volume (before dilution)	0.45mL	1.3 mL
Amount of Diluent Needed per Vial	1.8 mL	1.3 mL
Doses per Vial	6 doses per vial (after dilution)	10 doses per vial (after dilution)

Reassuring Fact #3:

Vaccine-induced myocarditis is generally benign

Comparing Types of Myocarditis: Time to Normal Ejection Fraction (EF) by Echocardiogram



Patel et al. 2021

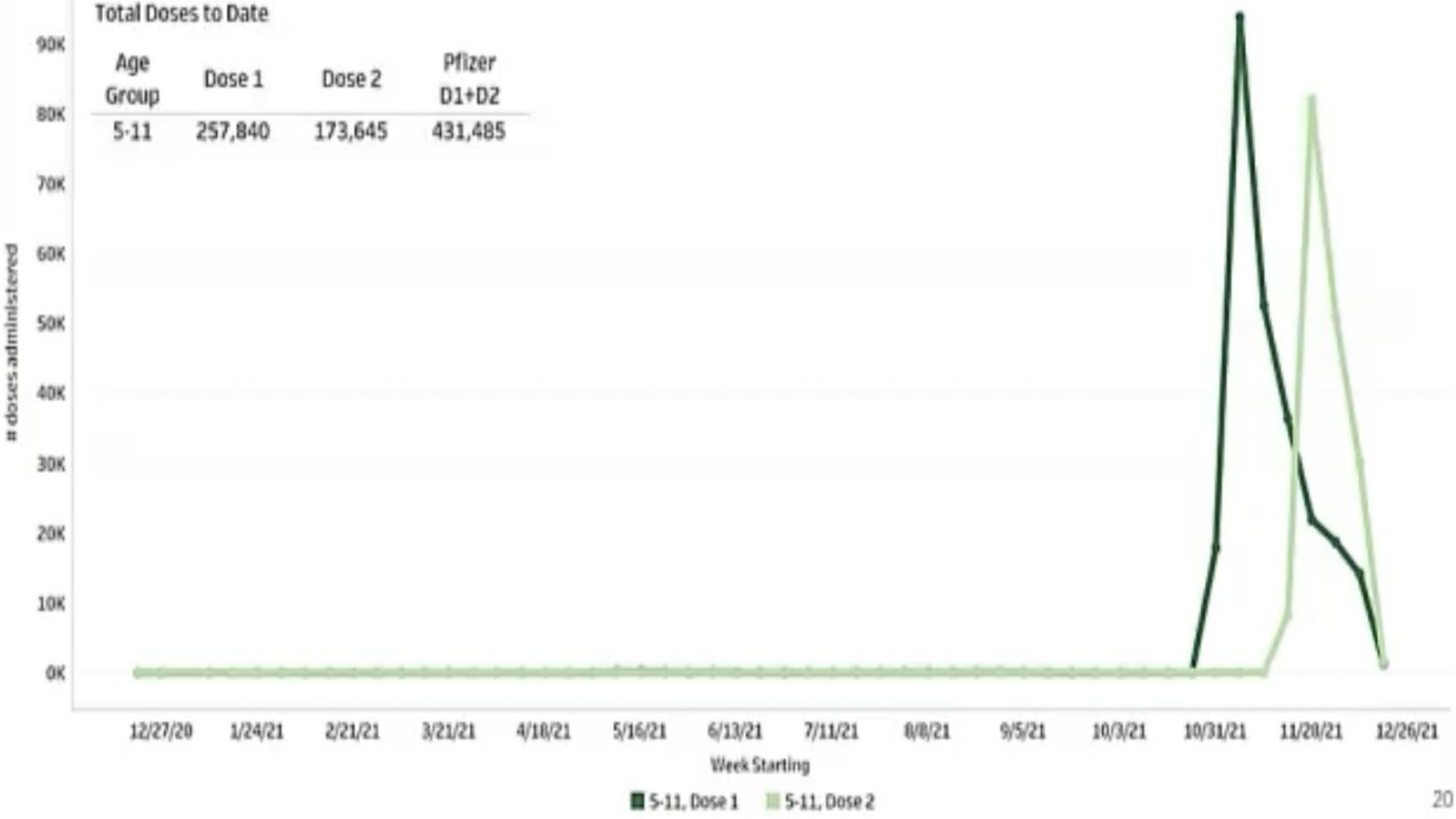
Reassuring Fact #4:

mRNA vaccines safe for young children post-EUA approval

Pfizer Vaccine Totals by Week for Children Aged 5-11 Years

Total Doses to Date

Age Group	Dose 1	Dose 2	Pfizer D1+D2
5-11	257,840	173,645	431,485



Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 70 / No. 51-52
December 31, 2021

COVID-19 Vaccine Safety in Children Aged 5–11 Years — United States, November 3–December 19, 2021

Anne M. Hause, PhD[1]; James Baggs, PhD[1]; Paige Marquez, MSPH[1]; Tanya R. Myers, PhD[1]; Julianne Gee, MPH[1]; John R. Su, MD, PhD[1]; Bicheng Zhang, MS[1]; Deborah Thompson, MD[2]; Tom T. Shimabukuro, MD[1]; David K. Shay, MD[1]

On October 29, 2021, the Food and Drug Administration (FDA) amended the Emergency Use Authorization (EUA) for Pfizer-BioNTech COVID-19 (BNT162b2) mRNA vaccine to expand its use to children aged 5–11 years, administered as 2 doses (10 µg, 0.2mL each) 3 weeks apart (*1*). As of December 19, 2021, only the Pfizer-BioNTech COVID-19 similar to those from preauthorization clinical trials (*4*,*5*). The Advisory Committee on Immunization Practices (ACIP) recommends the Pfizer-BioNTech COVID-19 vaccine for children aged 5–11 years for the prevention of COVID-19 (*6*). Parents and guardians of children aged 5–11 years vaccinated with Pfizer-BioNTech COVID-19 vaccine should be advised that local and

Summary of the Analyses of COVID-19 Vaccine Safety Among 12–17 and 5–11-Year-Olds

- Among 12–17-year-olds, the rate ratio for myocarditis/pericarditis was elevated during days 0-7 after Dose 2.
  - The excess risk was 0.3 cases per million 1st doses.
  - The excess risk was 70 cases per million 2nd doses.
- The VSD has administered 431,485 Pfizer doses to children aged 5-11 years.
- In the VSD, there have been no safety signals among 5–11-year-olds.

Do We Need a Booster Dose?

What is the goal of COVID-19 vaccines?

Goal #1:

Prevent severe illness

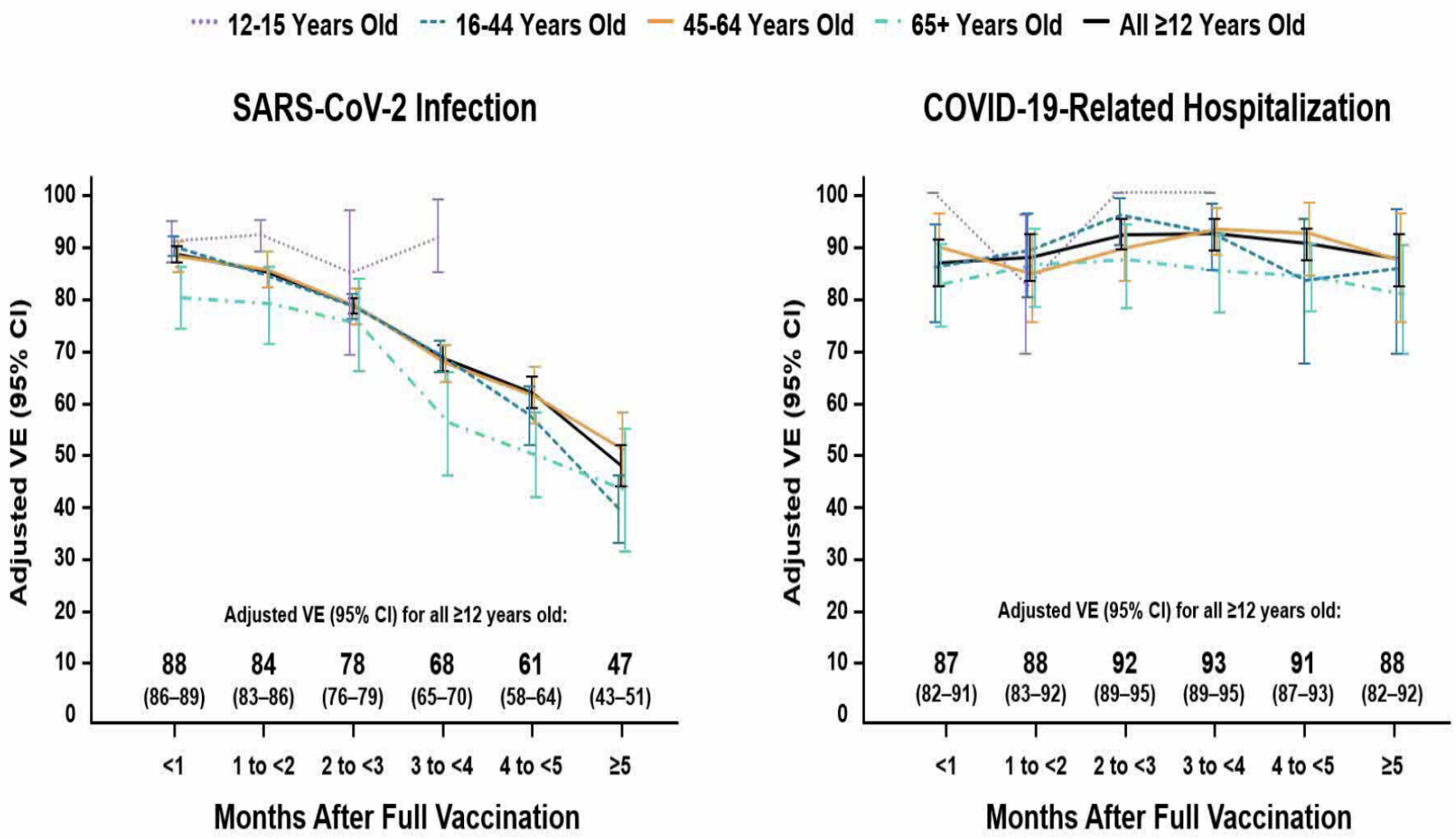
Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study

Sara Y Tartof, Jeff M Slezak, Heidi Fischer, Vennis Hong, Bradley K Ackerson, Omesh N Ranasinghe, Timothy B Frankland, Oluwaseye A Ogun, Joann M Zamparo, Sharon Gray, Srinivas R Valluri, Kaije Pan, Frederick J Angulo, Luis Jodar, John M McLaughlin

Summary

Background Vaccine effectiveness studies have not differentiated the effect of the delta (B.1.617.2) variant and potential waning immunity in observed reductions in effectiveness against SARS-CoV-2 infections. We aimed to evaluate overall and variant-specific effectiveness of BNT162b2 (tozinameran, Pfizer–BioNTech) against SARS-CoV-2 infections and COVID-19-related hospital admissions by time since vaccination among members of a large US health-care system.

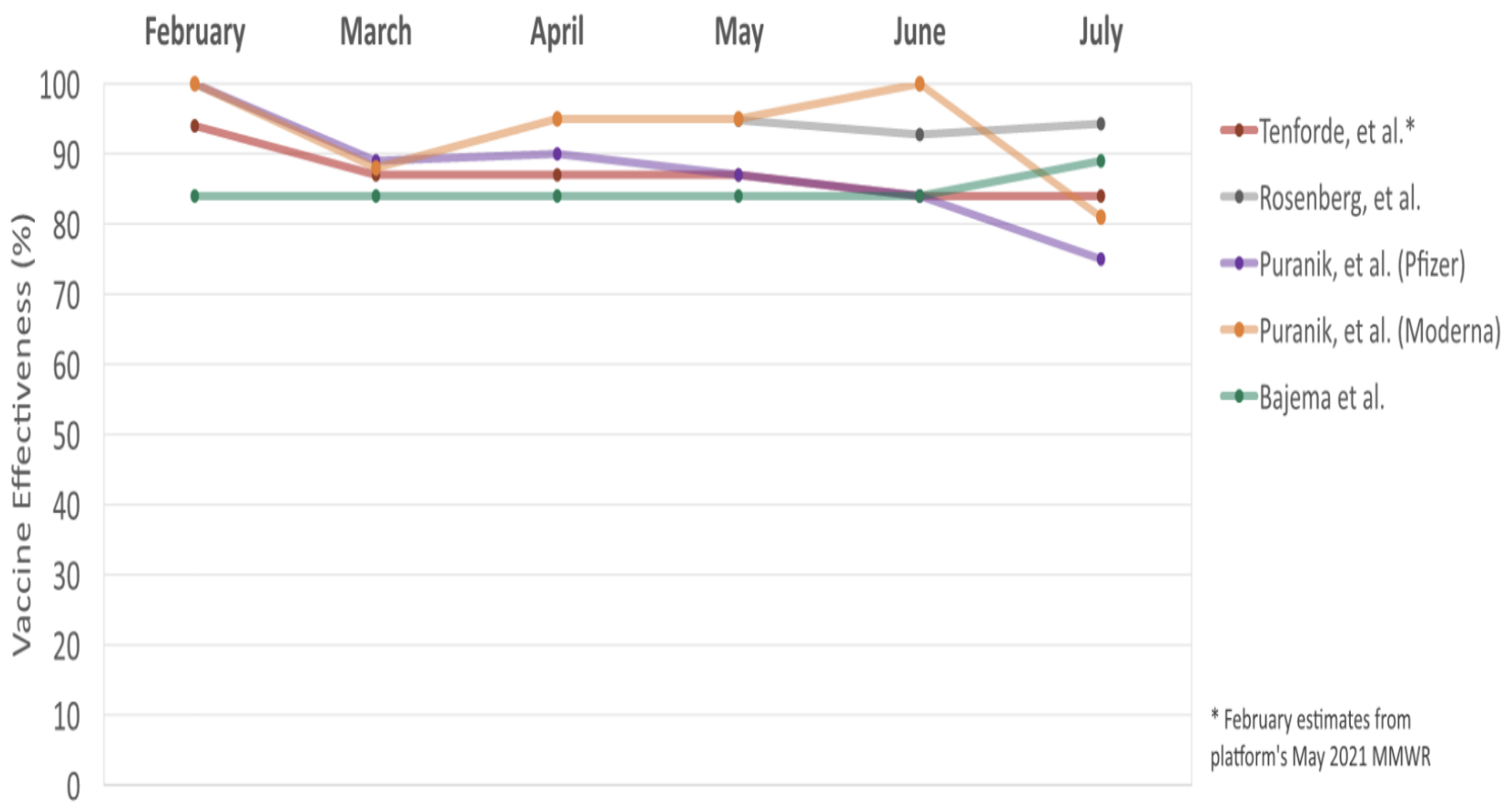
In All Age Groups, Vaccine Effectiveness Wanes Over Time Against Infections but Not Against Hospitalizations



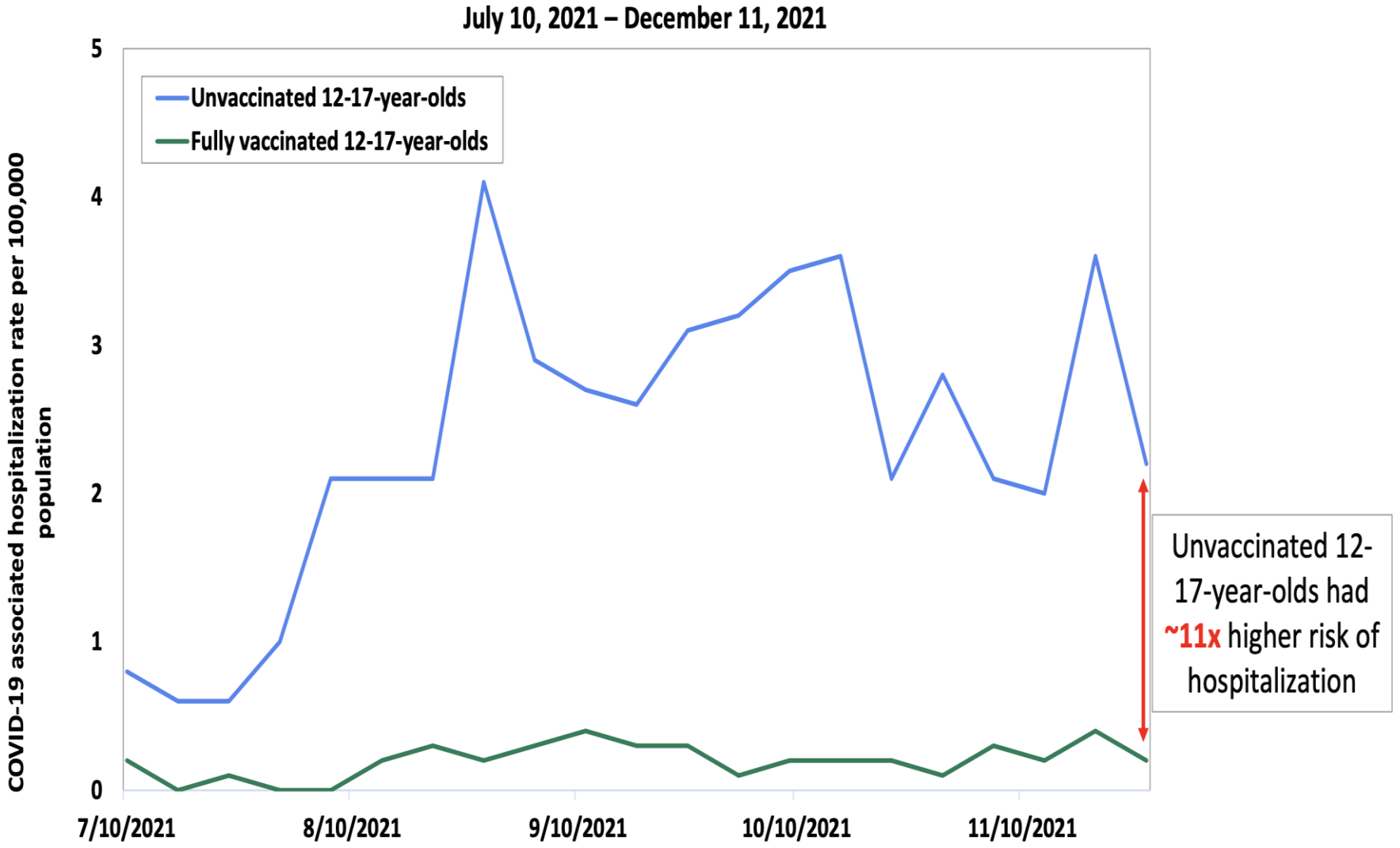
Tartof SY, et al. Six-Month Effectiveness of BNT162B2 mRNA COVID-19 Vaccine in a Large US Integrated Health System: A Retrospective Cohort Study. Available at SSRN: https://dx.doi.org/10.2139/ssrn.3909743

Vaccine effectiveness against **hospitalization** over time

Adults ≥18 years of age



COVID-19-associated hospitalization rates among 12–17-year-olds, by vaccination status



Source: CDC's COVID-NET, https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination

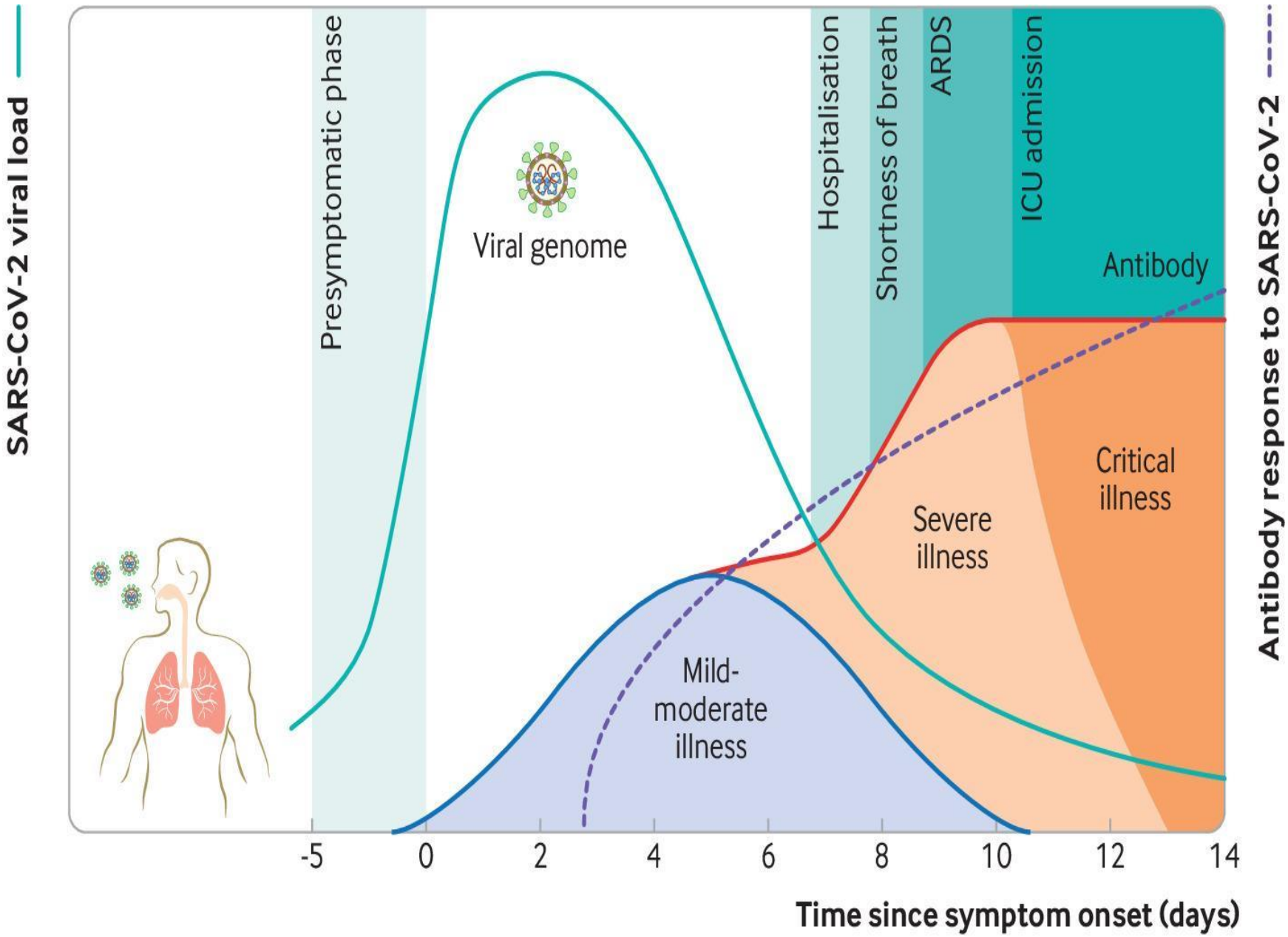
Vaccine effectiveness against COVID-19 hospitalization among patients aged 12–18, 19 pediatric hospitals, 16 states, July – September, 2021

Age group, yrs	No. vaccinated/Total (%)		Vaccine effectiveness, % (95% CI)
	Case-patients	Controls	
All	6/179 (3.4)	93/285 (32.6)	93 (83–97)
12–15	4/106 (3.8)	53/179 (29.6)	91 (74–97)
16–18	2/73 (2.7)	40/106 (37.7)	94 (78–99)

- **Limitation:** VE estimate reflects Delta dominant period

Olson SM, et al. MMWR 2021;70:1483–1488. DOI: http://dx.doi.org/10.15585/mmwr.mm7042e1

Protection against severe illness is mediated by memory B cells and T cells, which are long-lived


SARS-CoV-2 viral load
Antibody response to SARS-CoV-2
Presymptomatic phase
Viral genome
Hospitalisation
Shortness of breath
ARDS
ICU admission
Antibody
Critical illness
Severe illness
Mild-moderate illness
-5
0
2
4
6
8
10
12
14
Time since symptom onset (days)


K

> bioRxiv. 2021 Aug 23;2021.08.23.457229. doi: 10.1101/2021.08.23.457229. Preprint

mRNA Vaccination Induces Durable Immune Memory to SARS-CoV-2 with Continued Evolution to Variants of Concern

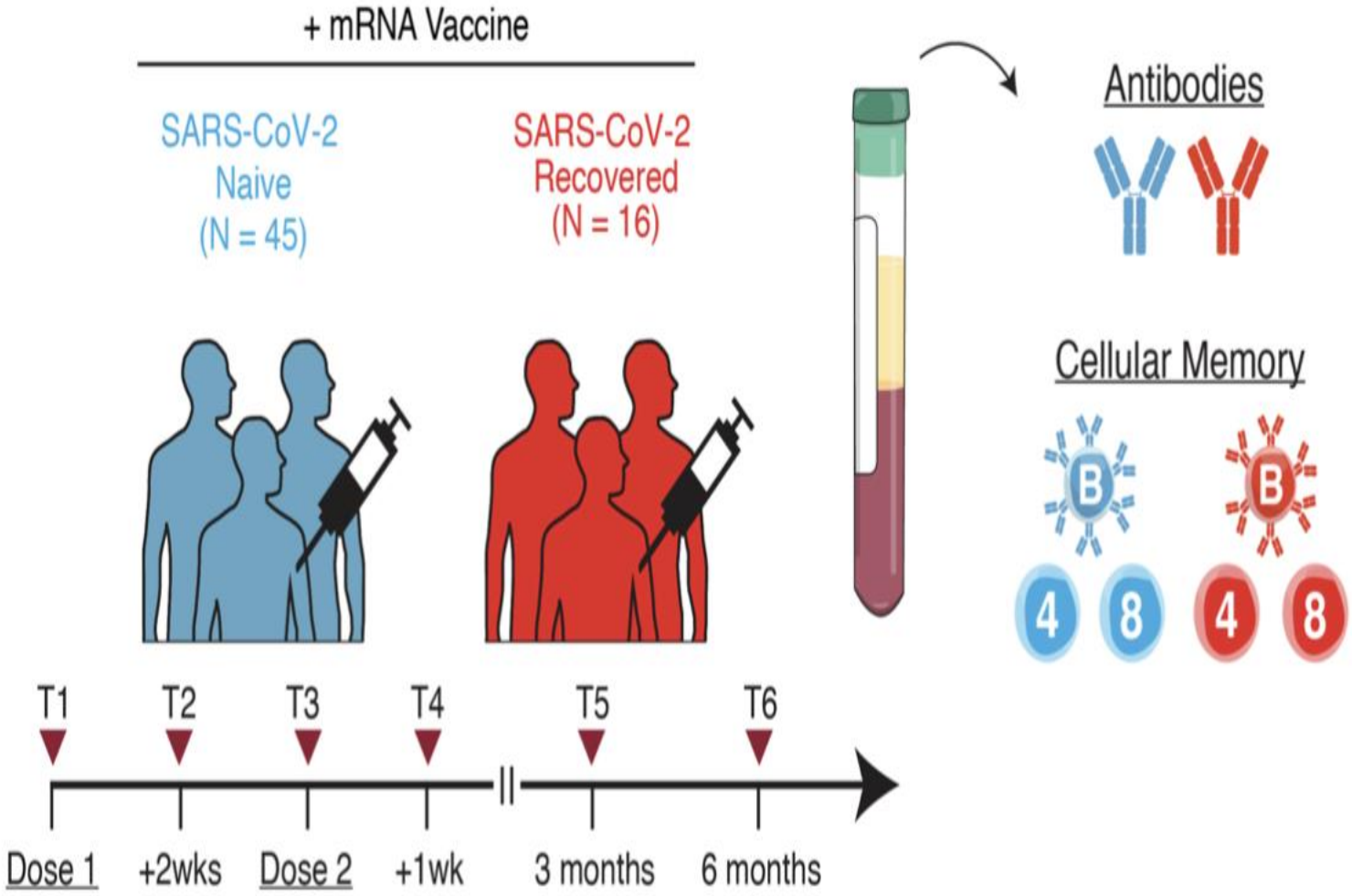
Rishi R Goel, Mark M Painter, Sokratis A Apostolidis, Divij Mathew, Wenzhao Meng, Aaron M Rosenfeld, Kendall A Lundgreen, Arnold Reynaldi, David S Khoury, Ajinkya Pattekar, Sigrid Gouma, Leticia Kuri-Cervantes, Philip Hicks, Sarah Dysinger, Amanda Hicks, Harsh Sharma, Sarah Herring, Scott Korte, Amy E Baxter, Derek A Oldridge, Josephine R Giles, Madison E Weirick, Christopher M McAllister, Moses Awofolaju, Nicole Tanenbaum, Elizabeth M Drapeau, Jeanette Dougherty, Sherea Long, Kurt D'Andrea, Jacob T Hamilton, Maura McLaughlin, Justine C Williams, Sharon Adamski, Oliva Kuthuru, UPenn COVID Processing Unit; Ian Frank, Michael R Betts, Laura A Vella, Alba Grifoni, Daniela Weiskopf, Alessandro Sette, Scott E Hensley, Miles P Davenport, Paul Bates, Eline T Luning Prak, Allison R Greenplate, E John Wherry

PMID: 34462751 PMCID: PMC8404899 DOI: 10.1101/2021.08.23.457229

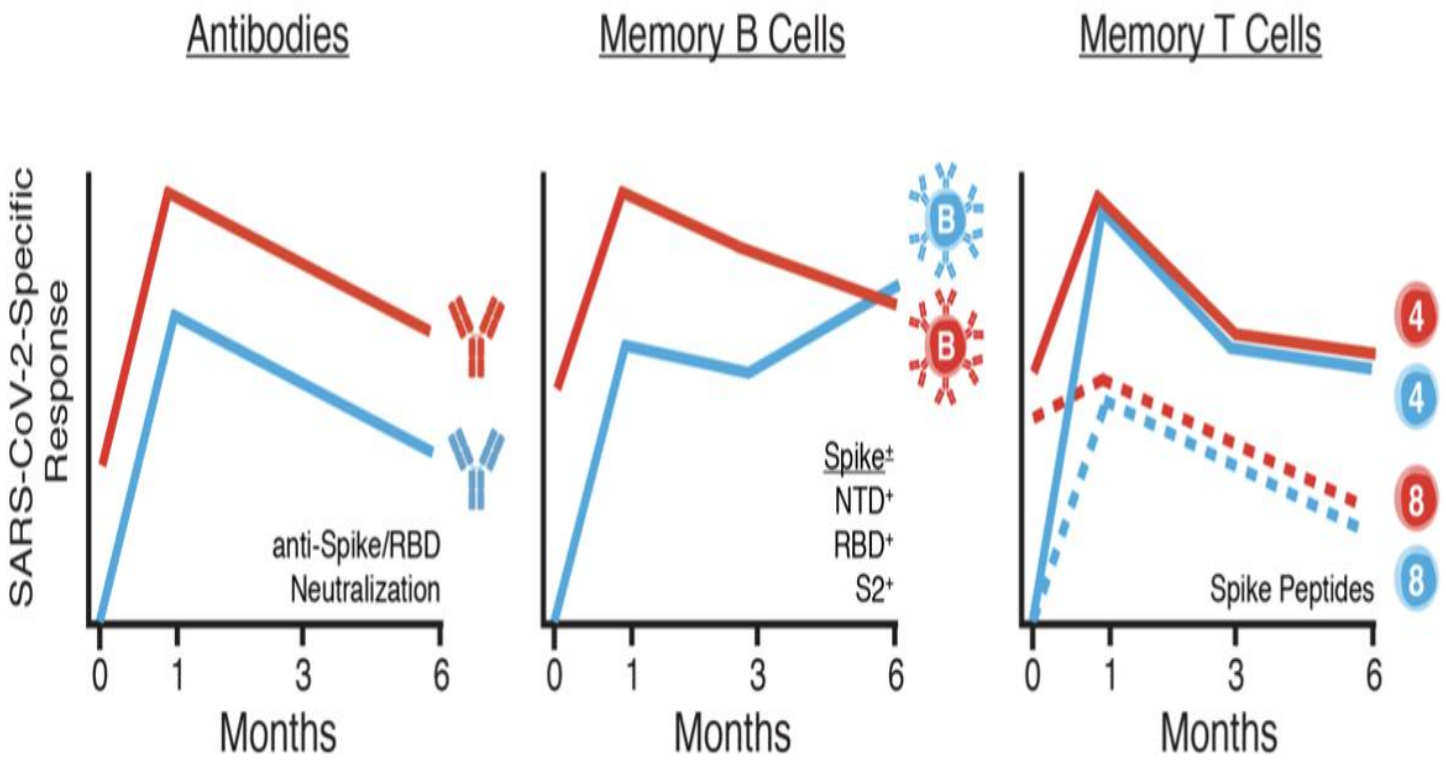
Free PMC article

Abstract

SARS-CoV-2 mRNA vaccines have shown remarkable efficacy, especially in preventing severe illness and hospitalization. However, the emergence of several variants of concern and reports of

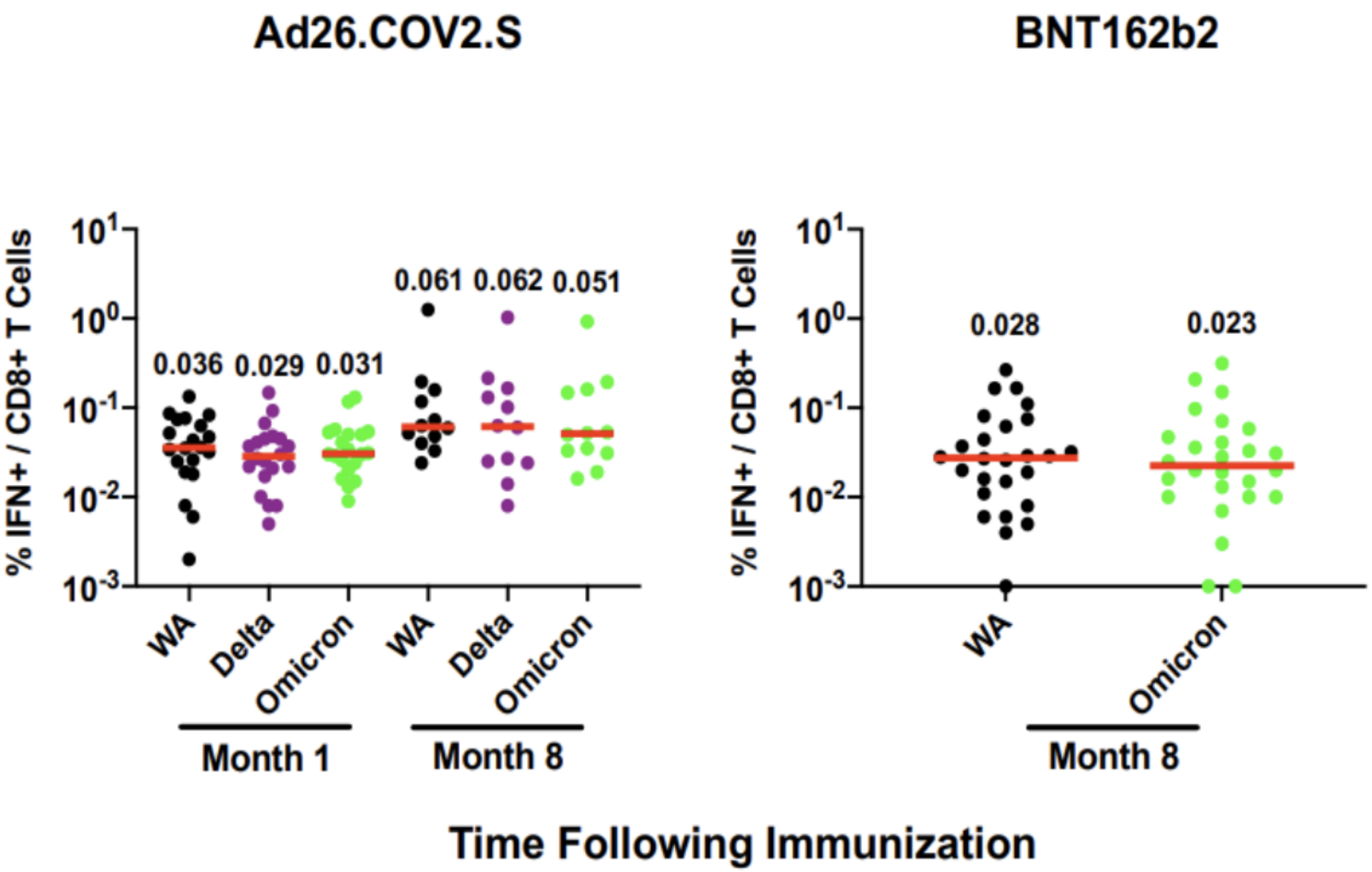

+ mRNA Vaccine
SARS-CoV-2
Naive
(N = 45)
SARS-CoV-2
Recovered
(N = 16)
Antibodies
Cellular Memory
B
B
4
8
4
8
T1
T2
T3
T4
T5
T6
Dose 1
+2wks
Dose 2
+1wk
3 months
6 months

Longitudinal Measurement of Immune Memory

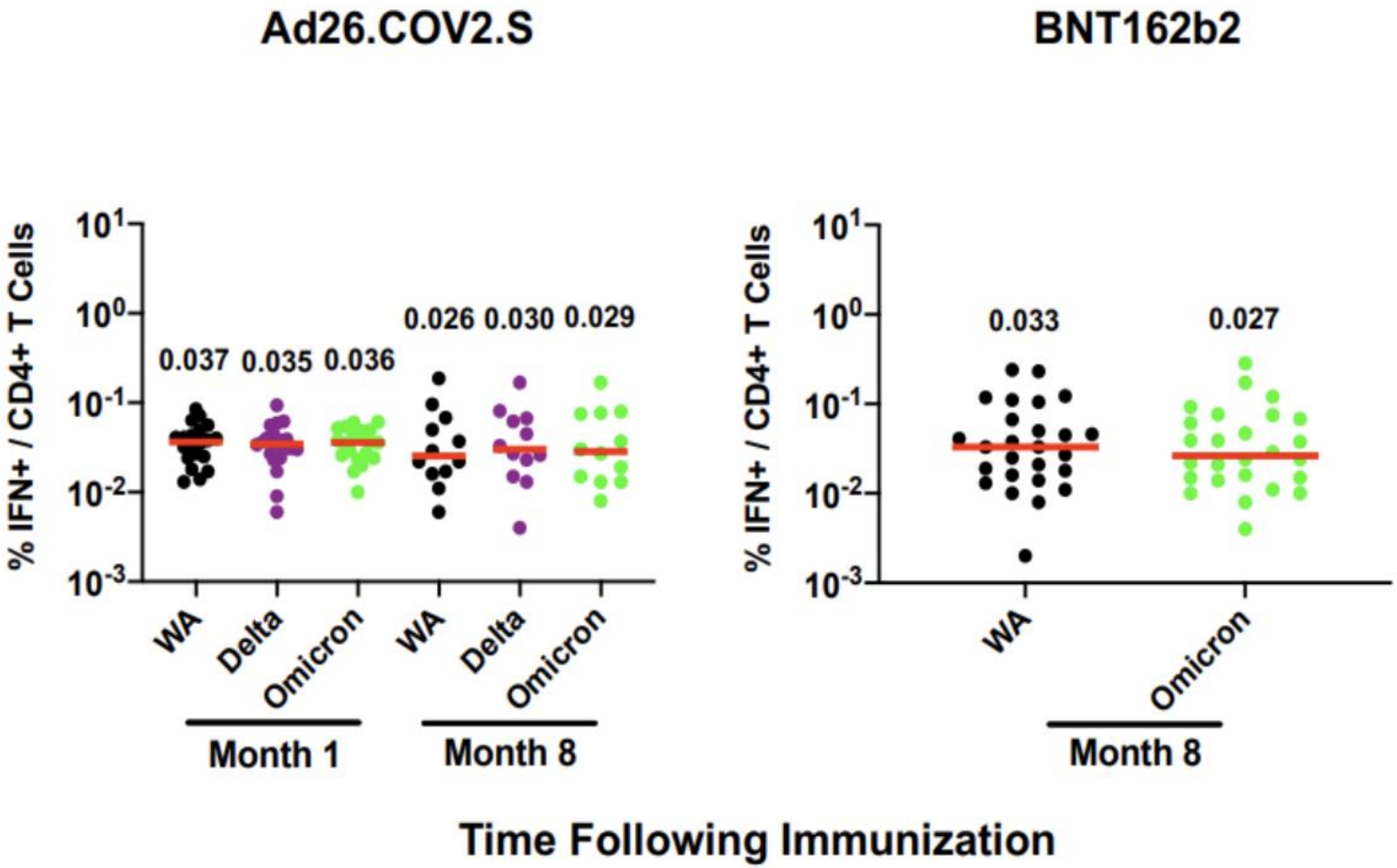


Decay Rate of Boosted Antibodies & T Cells = Decay Rate from Peak 2-dose mRNA

Cytotoxic T cells



Helper T cells



Goal #2:

Prevent all symptomatic illness

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 70
July 30, 2021

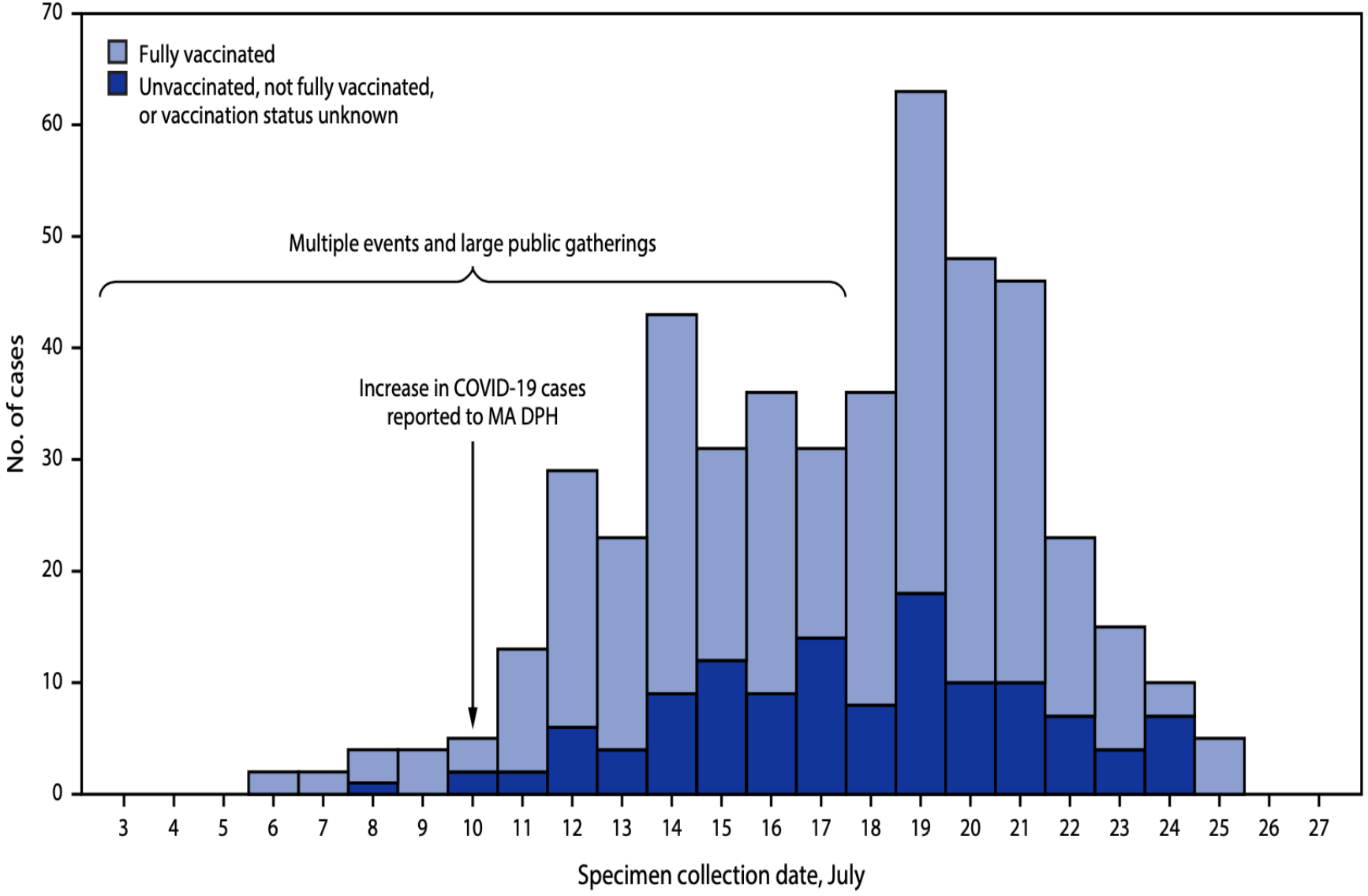
Outbreak of SARS-CoV-2 Infections, Including COVID-19 Vaccine Breakthrough Infections, Associated with Large Public Gatherings — Barnstable County, Massachusetts, July 2021

Catherine M. Brown, DVM[1]; Johanna Vostok, MPH[1]; Hillary Johnson, MHS[1]; Meagan Burns, MPH[1]; Radhika Gharpure, DVM[2]; Samira Sami, DrPH[2]; Rebecca T. Sabo, MPH[2]; Noemi Hall, PhD[2]; Anne Foreman, PhD[2]; Petra L. Schubert, MPH[1]; Glen R. Gallagher PhD[1]; Timelia Fink[1]; Lawrence C. Madoff, MD[1]; Stacey B. Gabriel, PhD[3]; Bronwyn MacInnis, PhD[3]; Daniel J. Park, PhD[3]; Katherine J. Siddle, PhD[3]; Vaira Harik, MS[4]; Deirdre Arvidson, MSN[4]; Taylor Brock-Fisher, MSc[5]; Molly Dunn, DVM[5]; Amanda Kearns[5]; A. Scott Laney, PhD[2]

During July 2021, 469 cases of COVID-19 associated with multiple summer events and large public gatherings in

transmission might consider expanding prevention strategies, including masking in indoor public settings regardless of vac-

FIGURE 1. SARS-CoV-2 infections (N = 469) associated with large public gatherings, by date of specimen collection and vaccination status* — Barnstable County, Massachusetts, July 2021



Phase 3 trials created unrealistic expectations for protection against all symptomatic illness

mRNA vaccines:

Pfizer

First COVID-19 Occurrence From 7 Days After Dose 2

Phase 2/3 Efficacy – Final Analysis

Subjects WITHOUT Evidence of Infection Prior to 7 days after Dose 2

	BNT162b2 (30 µg) N=18,198		Placebo N=18,325				
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)	Pr (VE >30%)
First COVID-19 occurrence ≥7 days after Dose 2	8	2.214 (17,411)	162	2.222 (17,511)	95.0	(90.3, 97.6)	>0.9999

Total surveillance time: 1000 person-years for all subjects within each group at risk for the endpoint..
Pr=Posterior probability

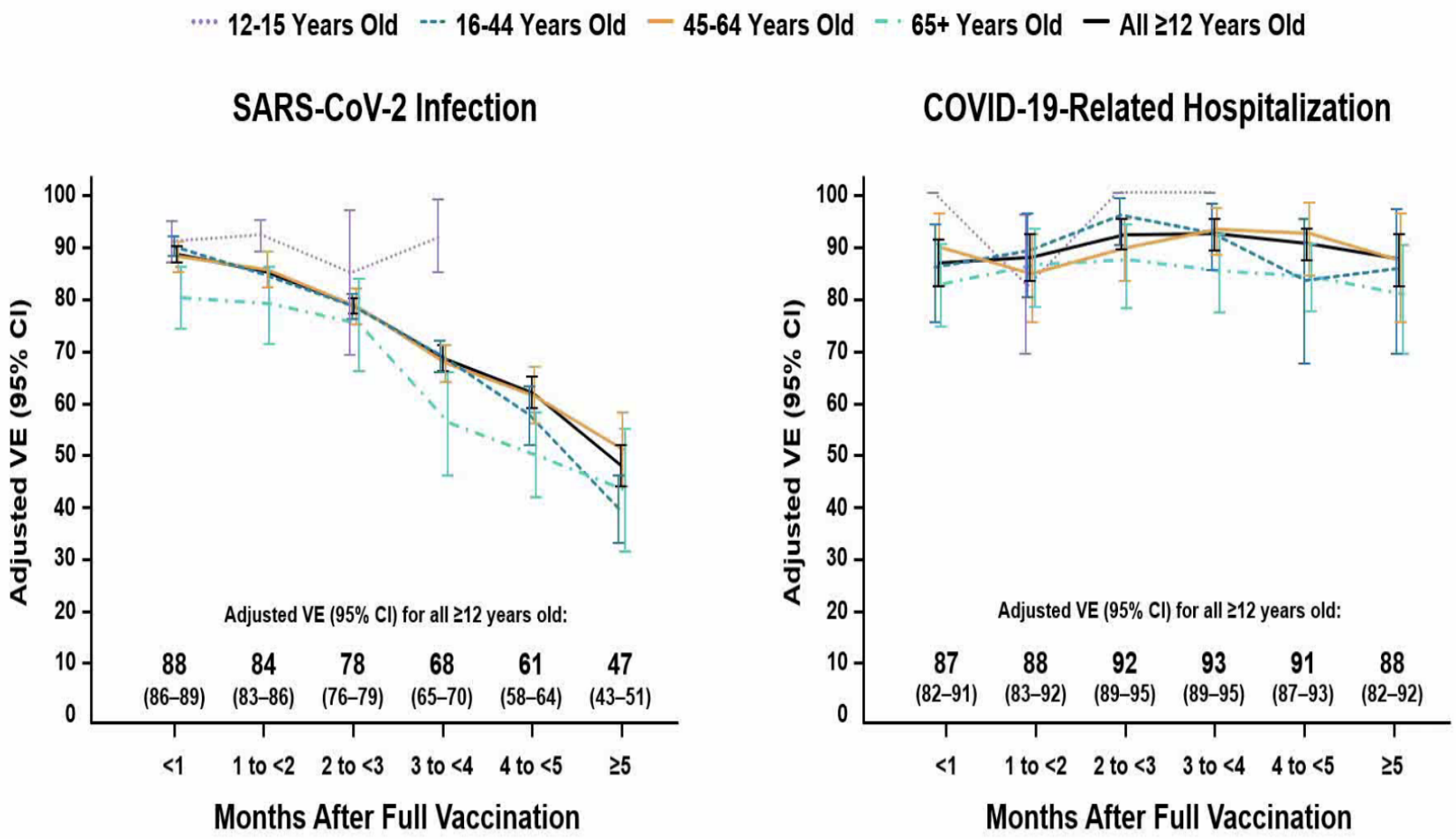
Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study

Sara Y Tartof, Jeff M Slezak, Heidi Fischer, Vennis Hong, Bradley K Ackerson, Omesh N Ranasinghe, Timothy B Frankland, Oluwaseye A Ogun, Joann M Zamparo, Sharon Gray, Srinivas R Valluri, Kaije Pan, Frederick J Angulo, Luis Jodar, John M McLaughlin

Summary

Background Vaccine effectiveness studies have not differentiated the effect of the delta (B.1.617.2) variant and potential waning immunity in observed reductions in effectiveness against SARS-CoV-2 infections. We aimed to evaluate overall and variant-specific effectiveness of BNT162b2 (tozinameran, Pfizer–BioNTech) against SARS-CoV-2 infections and COVID-19-related hospital admissions by time since vaccination among members of a large US health-care system.

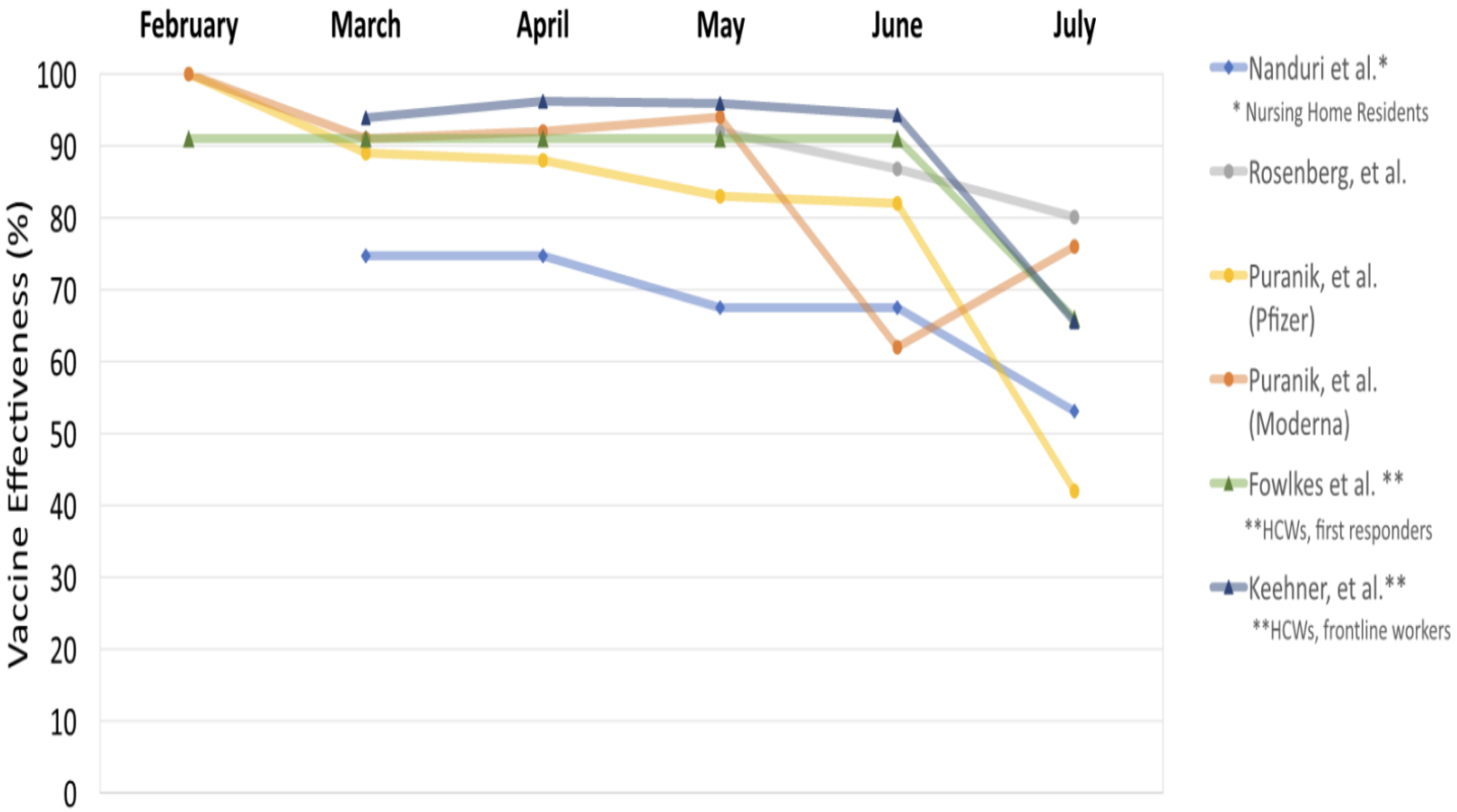
In All Age Groups, Vaccine Effectiveness Wanes Over Time Against Infections but Not Against Hospitalizations



Tartof SY, et al. Six-Month Effectiveness of BNT162B2 mRNA COVID-19 Vaccine in a Large US Integrated Health System: A Retrospective Cohort Study. Available at SSRN: https://dx.doi.org/10.2139/ssrn.3909743

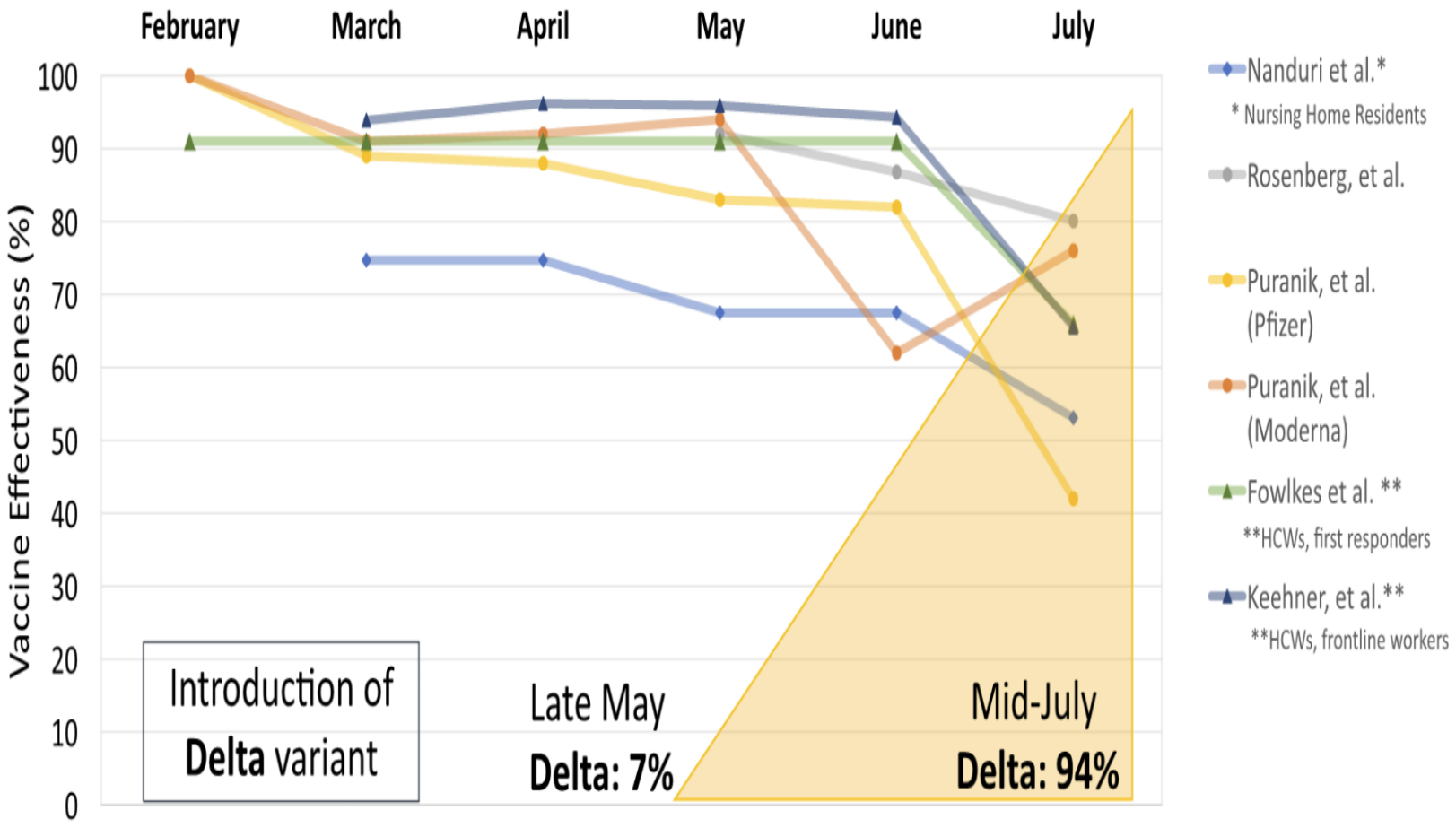
Vaccine effectiveness against **infection** over time

Adults ≥18 years of age



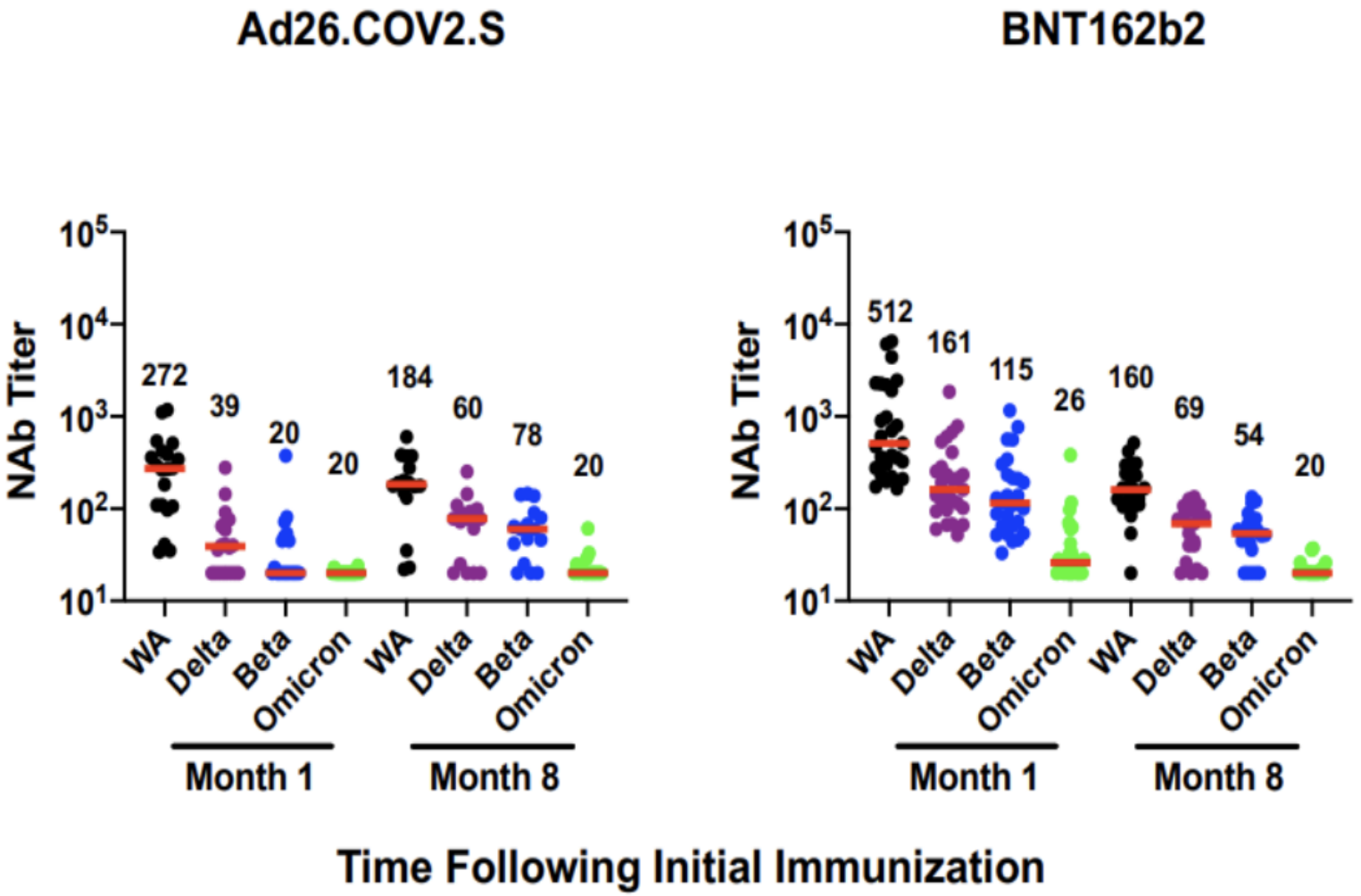
Vaccine effectiveness against **infection** over time

Adults ≥18 years of age



Protection against mild or asymptomatic infection is mediated by high-titers of circulating, virus neutralizing antibodies, which are relatively short-lived

Virus-specific neutralizing antibodies



The Israeli experience:

Erosion in protection against severe disease?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel

Yinon M. Bar-On, M.Sc., Yair Goldberg, Ph.D., Micha Mandel, Ph.D., Omri Bodenheimer, M.Sc., Laurence Freedman, Ph.D., Nir Kalkstein, B.Sc., Barak Mizrahi, M.Sc., Sharon Alroy-Preis, M.D., Nachman Ash, M.D., Ron Milo, Ph.D., and Amit Huppert, Ph.D.

ABSTRACT

BACKGROUND

On July 30, 2021, the administration of a third (booster) dose of the BNT162b2 messenger RNA vaccine (Pfizer–BioNTech) was approved in Israel for persons who

The Israeli Experience

- 75% of participants greater than 70 years old.
- 60-69-year-olds: Incidence of severe illness was 2.8% in the non-booster group and 1.3% in the booster group.
- 70-79-year-olds: Incidence of severe illness was 7.5% in the non-booster group and 1.3% in the booster group.
- >80-years-old: Incidence of severe illness was 18.2% in the non-booster group and 7.9% in the booster group.

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

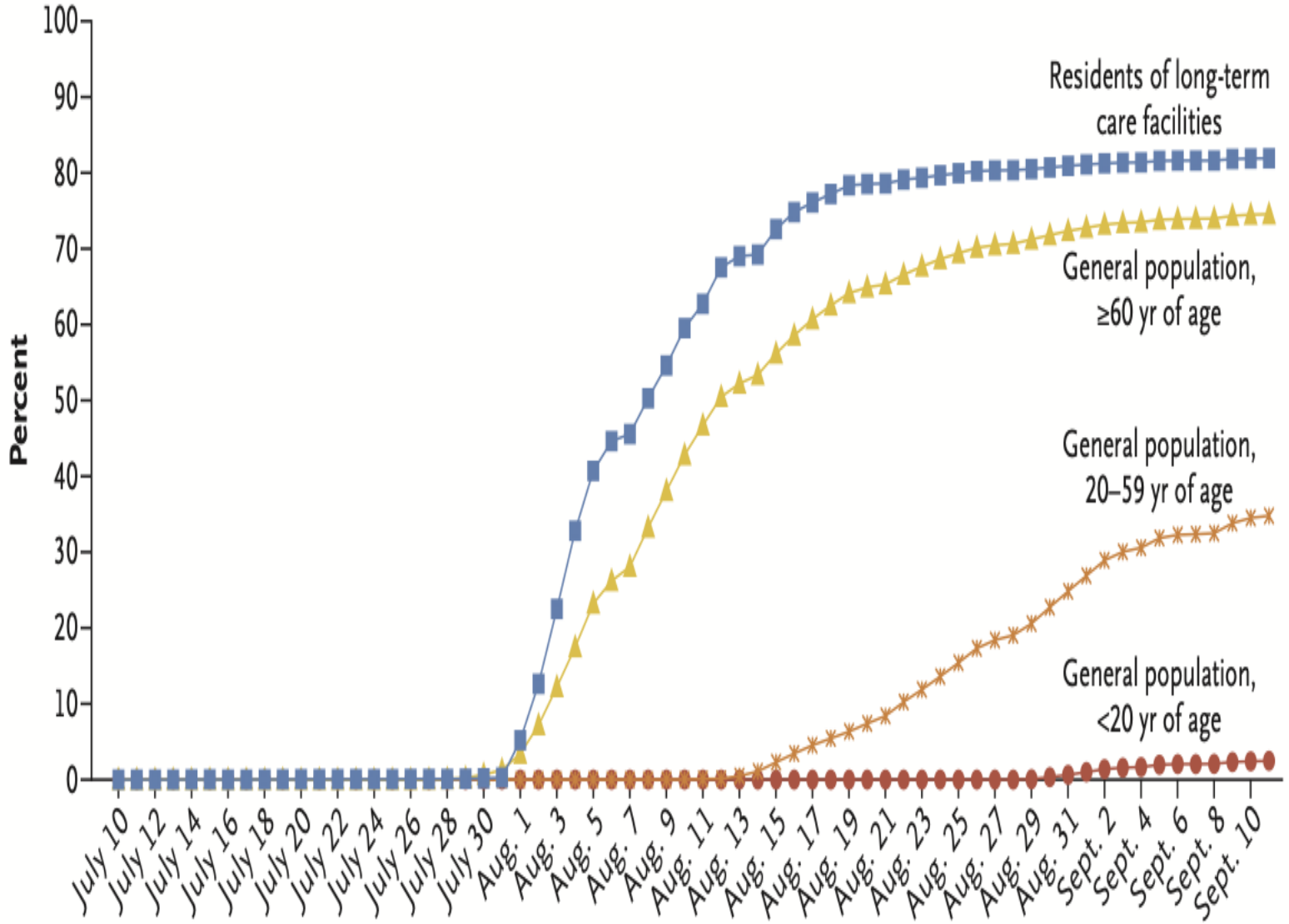
Effects of BNT162b2 Covid-19 Vaccine Booster in Long-Term Care Facilities in Israel

TO THE EDITOR: Residents of long-term care facilities are particularly vulnerable to severe and fatal coronavirus disease 2019 (Covid-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] To protect this population, in April 2020, the Israeli government launched a national-level task force, "Senior Shield," that aimed to support long-term care facilities in managing the Covid-19 crisis. The main efforts included supplying personal protective equipment, initiating

under 20 years of age. In this analysis, we calculated the weekly incidence of PCR-confirmed SARS-CoV-2 infection, hospitalization for severe Covid-19, and Covid-19–related death. Changes in incidence were analyzed with the use of Poisson regression models, as evaluated separately for each group and time period (weeks 26 to 30 before the booster campaign and weeks 31 to 36 after the booster campaign). We compared the rates during a calendar week of interest with the rates

Muhsen, K., et al., "Effects of BNT162b2 Covid-9 Vaccine Booster in Long-Term Care Facilities in Israel," NEJM (2021) DOI: 10.1056/NEJMc2117385.

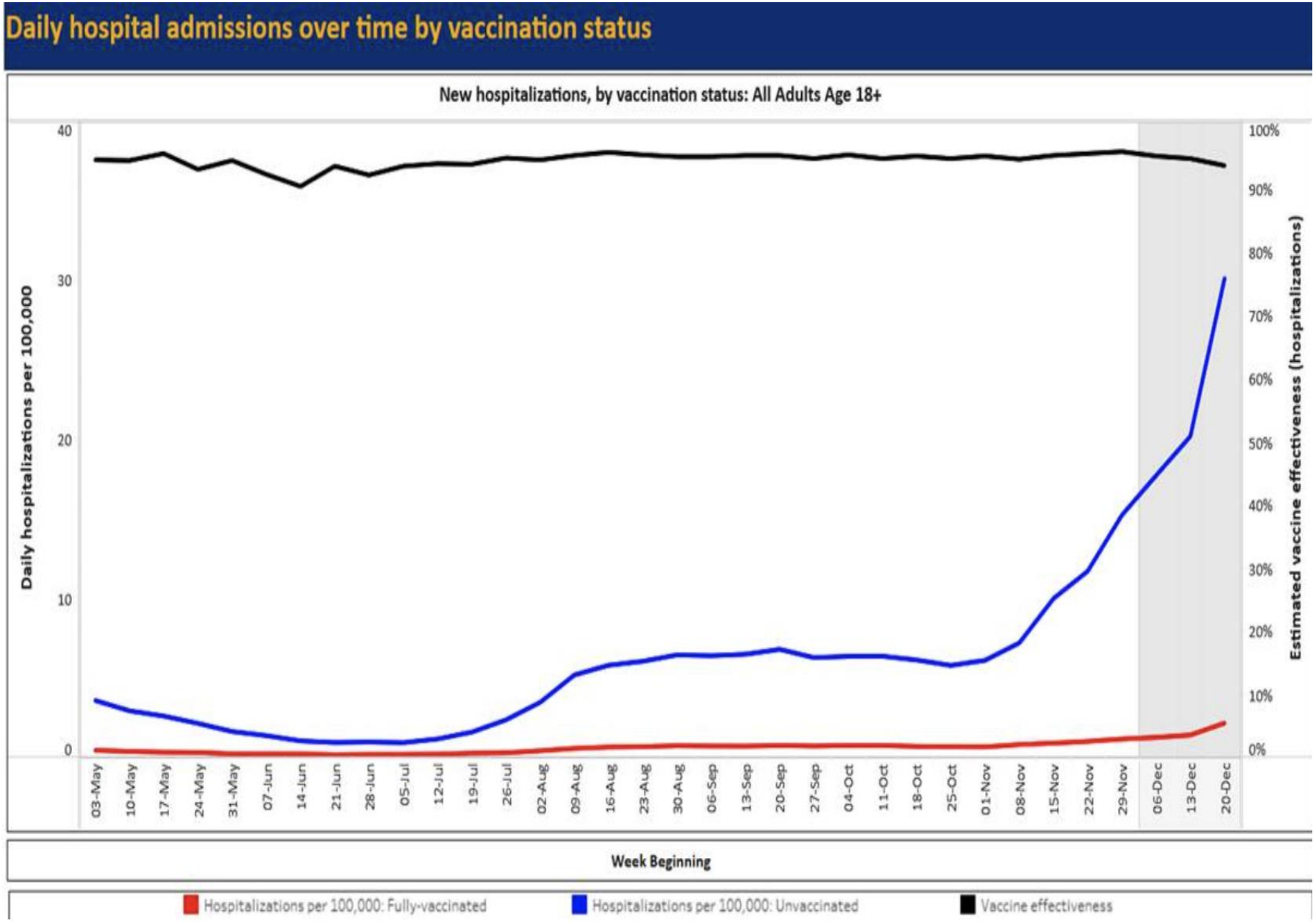
C Uptake of Booster Dose According to Study Group



The Israeli Experience: Part II

- "Among persons who were younger than 60 years of age, no significant decreases [in the booster group] were observed in the incidence of either infection or hospitalization during the study period."
- "In the current study, after the initiation of an extensive booster campaign with high vaccine uptake, we found a significant, rapid, and consistent reduction in COVID-19 burden among persons in the same age group who were living in long-term care facilities."
- "Our results suggest the important real-life effects of the nationwide COVID-19 booster program among residents in long-term care facilities."

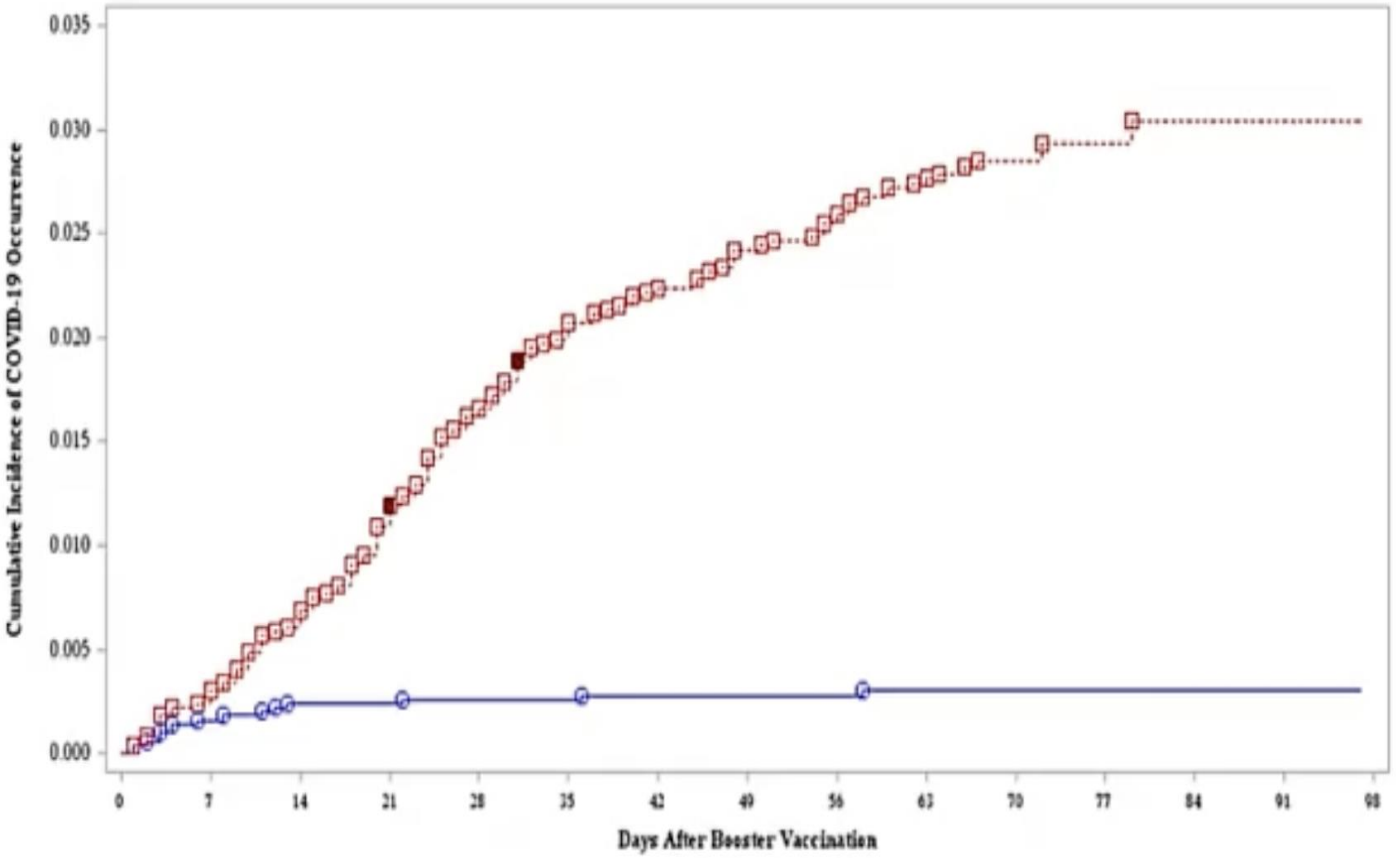
New York State, through December 20, 2021



Pfizer Booster Study

Cumulative Incidence Curve for First COVID-19 Occurrence After Booster Vaccination – All Available Efficacy Population

Curves diverge rapidly, starting even before 7 days after booster



Note the 2 severe cases met the FDA definition only, based only on SpO2 <93%. They were not hospitalized

Relative Vaccine efficacy during blinded follow-up period

Booster dose was highly effective against symptomatic COVID-19

Subjects WITHOUT Evidence of Infection Prior to 7 days after Dose 2

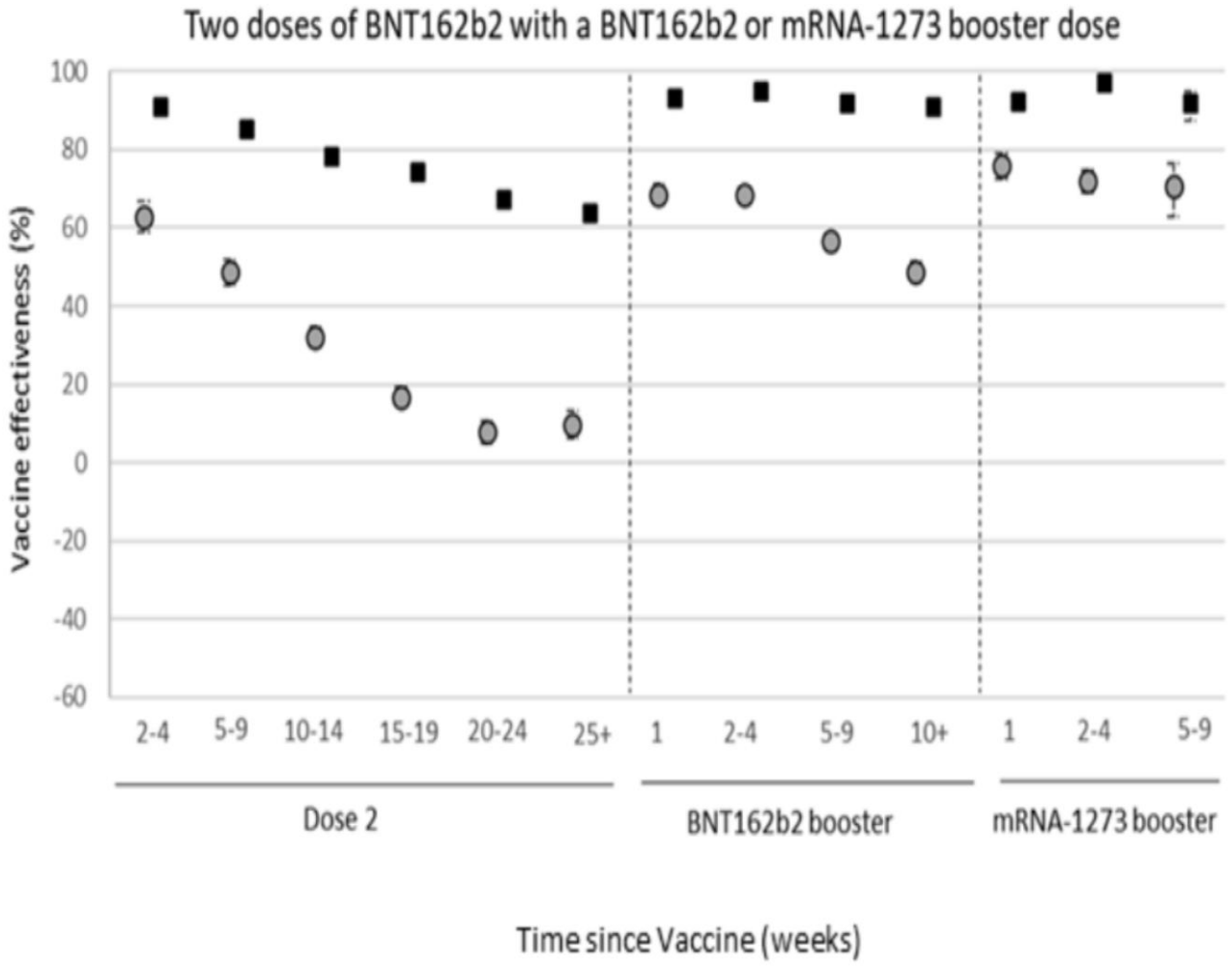
	BNT162b2 (30 µg) N=4695		Placebo N=4671			
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	RVE (%)	(95% CI)
First COVID-19 occurrence from ≥7 days after booster vaccination to <2 months after booster vaccination	6	0.823 (4659)	123	0.792 (4614)	95.3	(89.5,98.3)

Total surveillance time in 1000 person-years for the given endpoint across all participants within each group at risk for the endpoint
RVE = relative vaccine efficacy of the BNT162b2 booster group relative to the placebo group (nonbooster)

Booster dosing

- If the goal of COVID-19 vaccines is to prevent severe disease, which is mediated by immune memory cells, all available epidemiological and immunological evidence in the US supports the fact that protection is holding up.
- If the goal of COVID-19 vaccine is to prevent all symptomatic illness (a high bar), which is mediated by circulating, neutralizing antibodies, then we need to define what level of symptomatic illness is acceptable, because neutralizing antibodies will fade over time, even after a third dose.

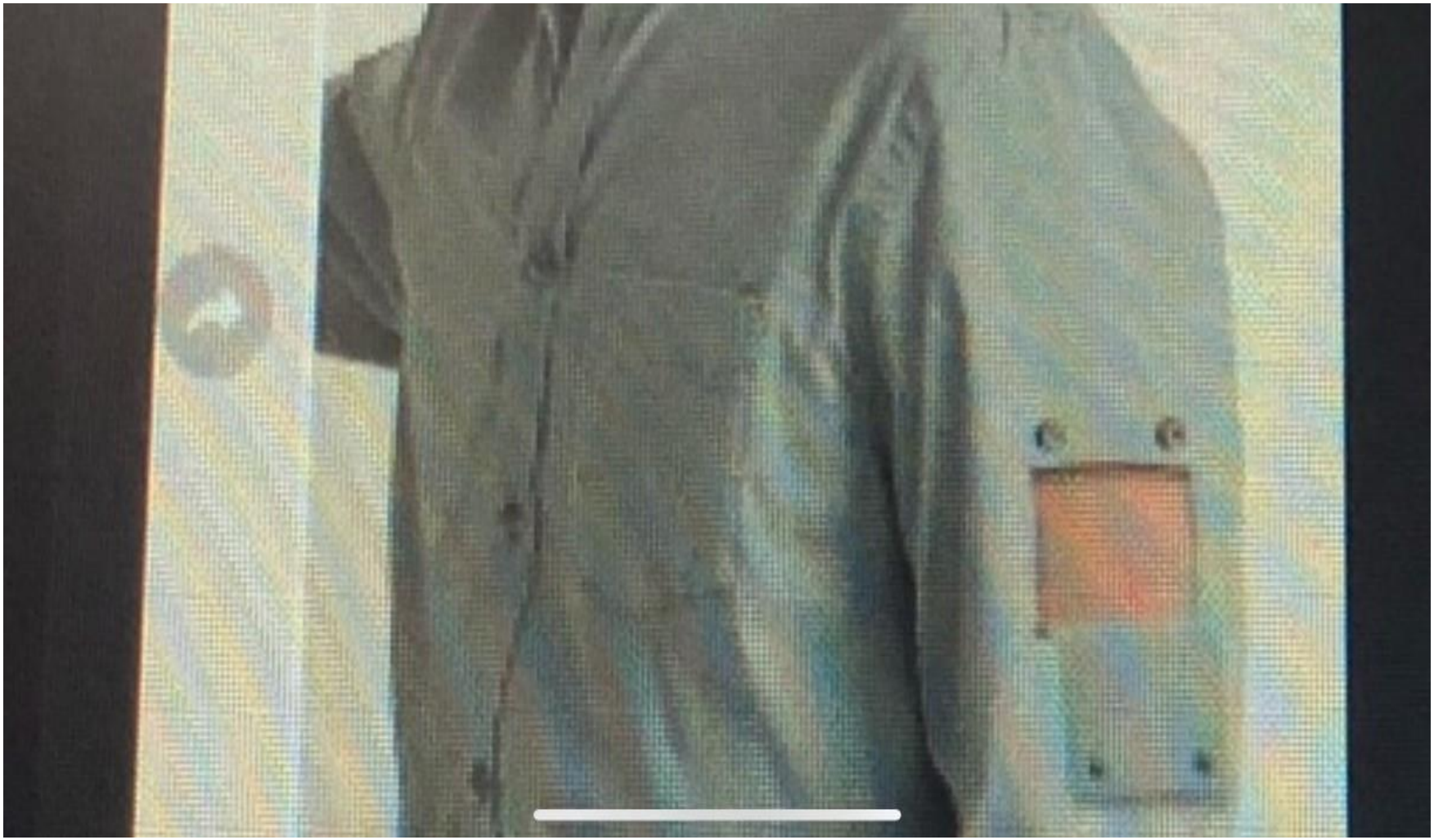
Pfizer mRNA vaccine effectiveness (VE) against infections with Delta and Omicron variants, United Kingdom



- Increased waning immunity for Omicron vs Delta
- mRNA vaccine booster increased VE against Omicron

Andrews et al.. https://khub.net/documents/135939561/430986542/Effectiveness+of+COVID-19+vaccines+against+Omicron+variant+of+concern.pdf/f423c9f4-91cb-0274-c8c5-70e8fad50074

Israeli Meme



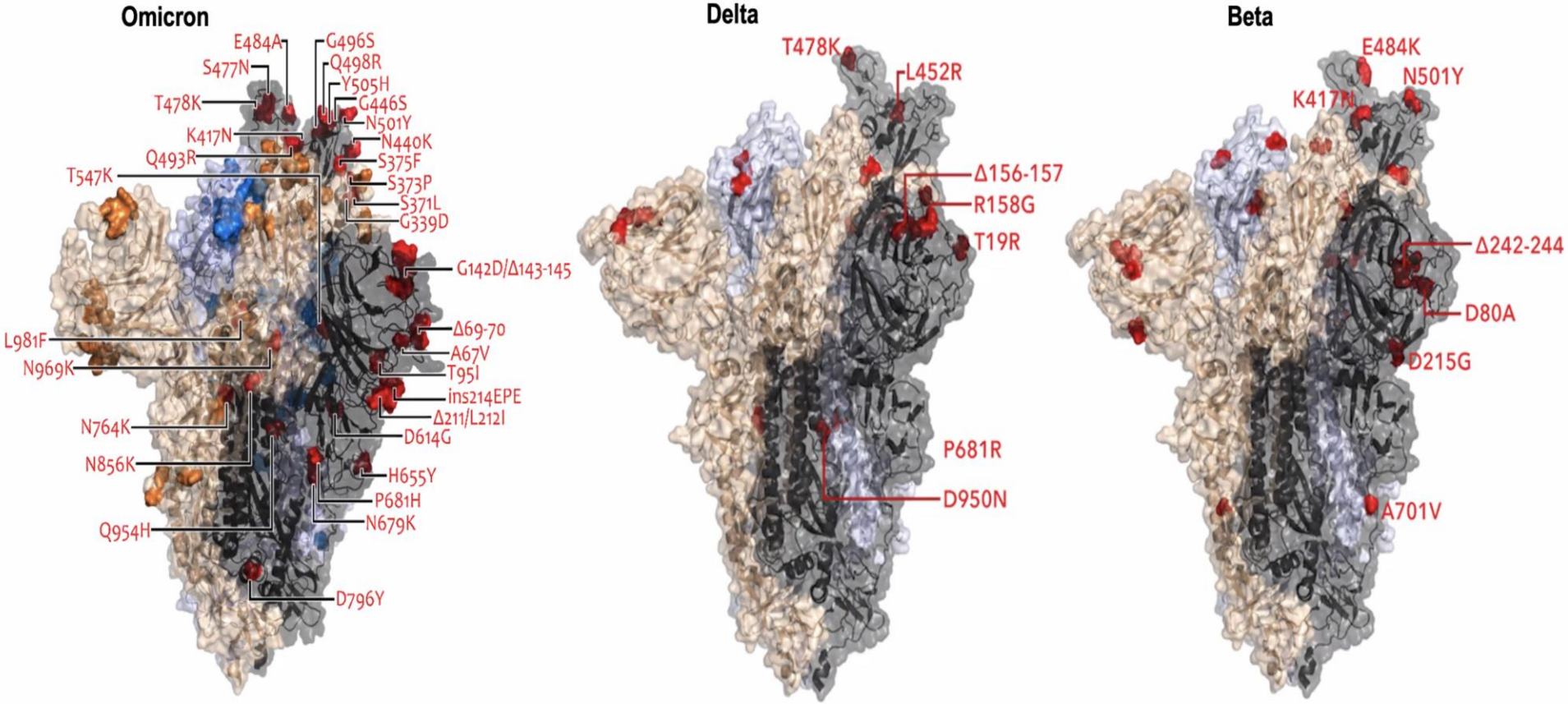

Pfizer
LOYALTY CARD
DOSE 1
DOSE 2
BOOSTER 1
BOOSTER 2
BOOSTER 3
BOOSTER 4
BOOSTER 5
BOOSTER 6
BOOSTER 7
Free
Pizza
BOOSTER 8

Omicron

Omicron is highly mutated

OMICRON IS A HIGHLY MUTATED AND DISTINCT LINEAGE

- >50 mutations, 26-32 concentrated in spike including **all four major neutralization sites** targeted by neutralizing antibodies
- Others with unclear consequences but implicated in increased ACE2 binding, immune escape and infectivity
- Not related to existing VOC lineages; still evolving: some sequences lack the del69-70 mutation traceable by PCR



https://nextstrain.org/ncov/gisaid/global?l=radial&m=div

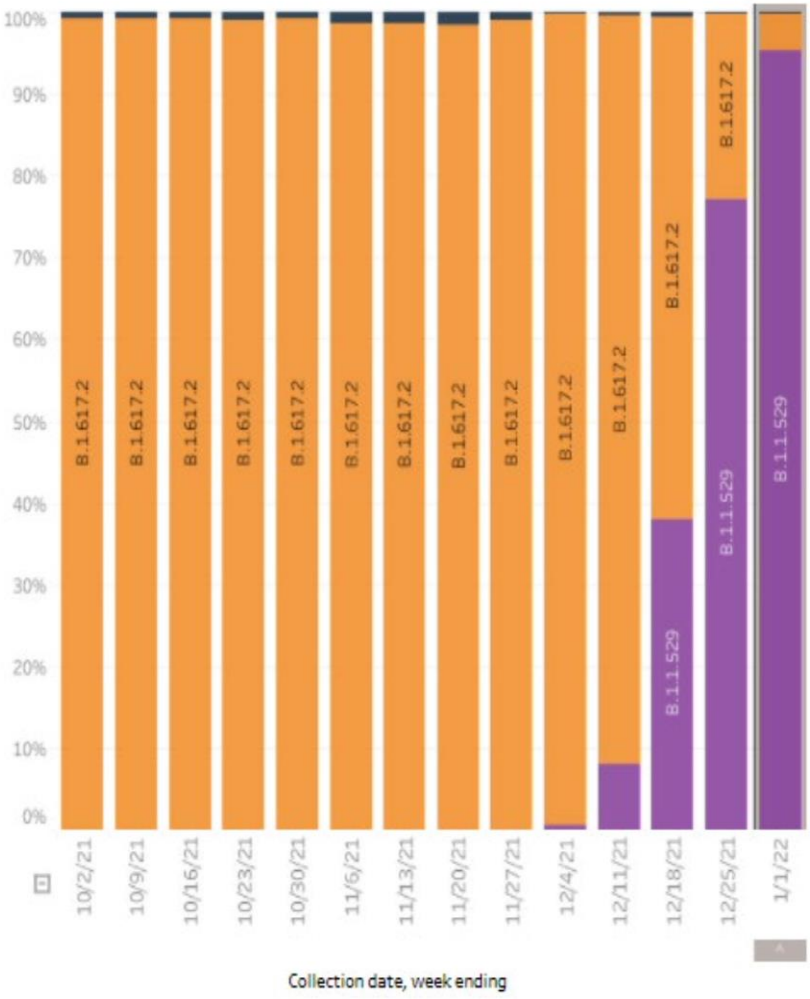
https://covdb.stanford.edu/page/mutation-viewer/

https://sars2.cvr.gla.ac.uk/cog-uk/

Why did omicron sweep through the US?

Estimated circulating SARS-CoV-2 variants in the United States

Variant Proportions, September 19 – Jan 1, 2021



USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	B.1.1.529	VOC	95.4%	92.9-97.0%
Delta	B.1.617.2	VOC	4.6%	2.9-7.0%
Other	Other*		0.0%	0.0-0.1%

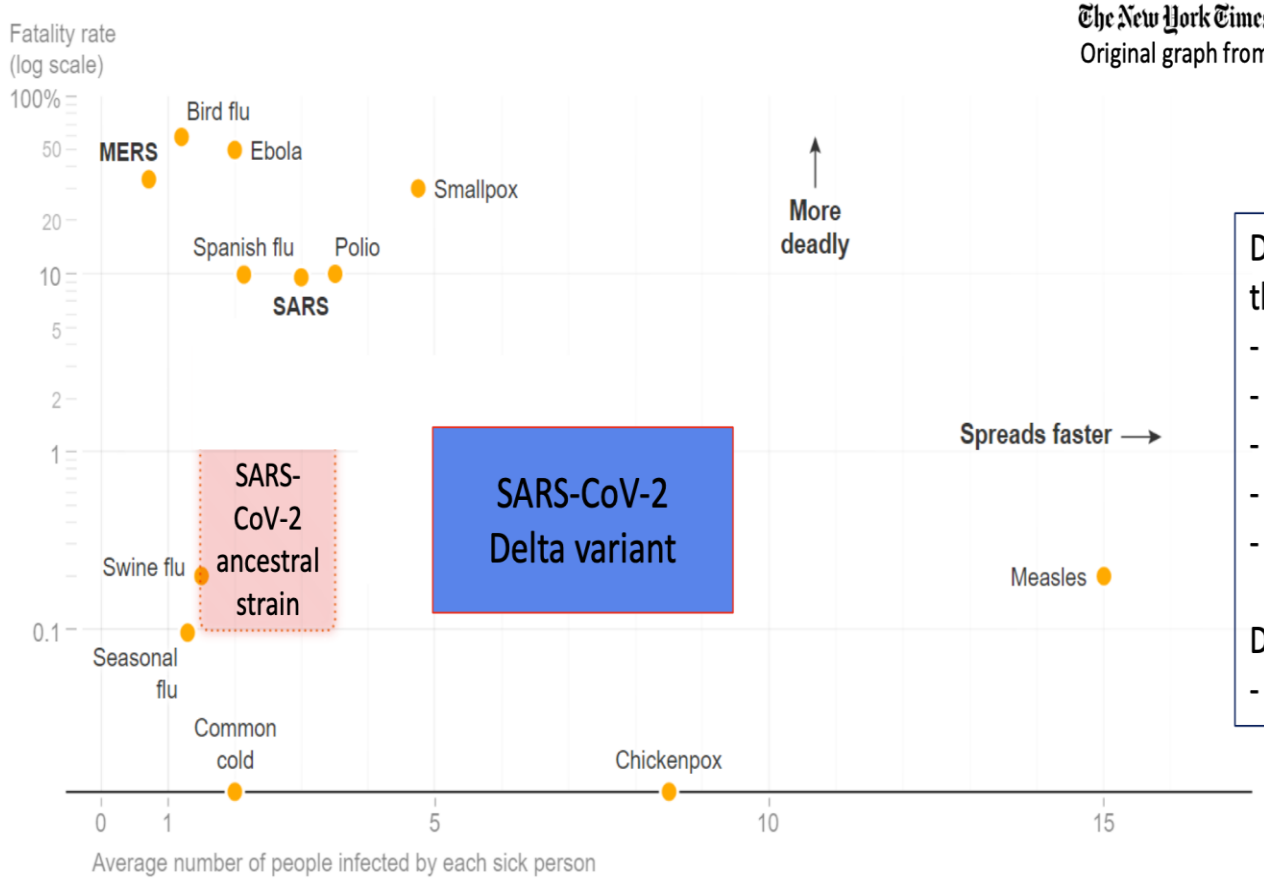
* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.

** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates

AY.1-AY.127 and their sublineages are aggregated with B.1.617.2. BA.1, BA.2 and BA.3 are aggregated with B.1.1.529.

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

Transmission of Delta variant vs. ancestral strain and other infectious diseases



The New York Times
Original graph from 2/28/2020.

Note: Average case-fatality rates and transmission numbers are shown. Estimates of case-fatality rates can vary, and numbers for the new coronavirus are preliminary estimates.

Delta variant is **more** transmissible than:
- MERS & SARS
- Ebola
- Common cold
- Seasonal flu & 1918 ("Spanish") flu
- Smallpox

Delta variant is **as** transmissible as:
- Chicken Pox

SARS-CoV-2 Omicron VOC Transmission in Danish Households

Frederik Plesner Lyngse[1,2,3,*], Laust Hvas Mortensen[4,5], Matthew J. Denwood[6], Lasse Engbo Christiansen[7], Camilla Holten Møller[3], Robert Leo Skov[3], Katja Spiess[3], Anders Fomsgaard[3], Maria Magdalena Lassaunière[3], Morten Rasmussen[3], Marc Stegger[8], Claus Nielsen[3], Raphael Niklaus Sieber[8], Arieh Sierra Cohen[3], Frederik Trier Møller[3], Maria Overvad[3], Kåre Mølbak[3], Tyra Grove Krause[3], Carsten Thure Kirkeby[6]

December 22, 2021

Table 3: Relative effect of the Omicron VOC

	Unvaccinated	Fully vaccinated	Booster-vaccinated
Omicron households	1.17	2.61	3.66
	(0.99-1.38)	(2.34-2.90)	(2.65-5.05)
Delta households	ref	ref	ref
	(.)	(.)	(.)
Number of observations	27,874	27,874	27,874
Number of households	11,937	11,937	11,937

Omicron less virulent

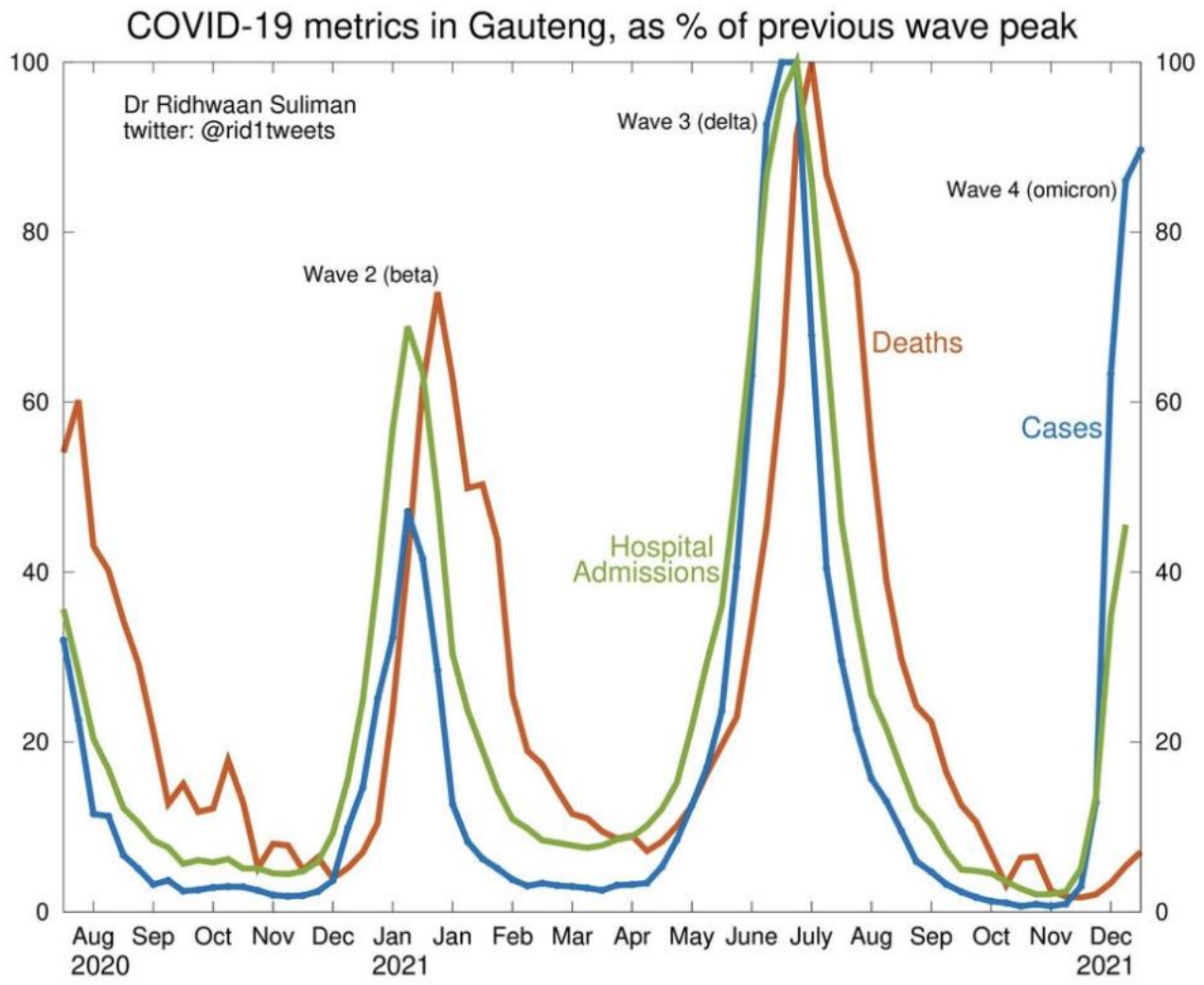
Comparison of outcomes from COVID infection in pediatric and adult patients before and after the emergence of Omicron

Lindsey Wang[1,2], Nathan A. Berger[2,3], David C. Kaelber[4], Pamela B. Davis[5], Nora D. Volkow[6], Rong Xu[1,3]*

[1]Center for Artificial Intelligence in Drug Discovery, Case Western Reserve University School of Medicine, Cleveland, OH, USA
[2]Center for Science, Health, and Society, Case Western Reserve University School of Medicine, Cleveland, OH, USA
[3]Case Comprehensive Cancer Center, School of Medicine, Case Western Reserve University, Cleveland, OH, USA
[4]The Center for Clinical Informatics Research and Education, The MetroHealth System, Cleveland, OH, USA
[5]Center for Community Health Integration, School of Medicine, Case Western Reserve University, Cleveland, OH, USA
[6]National Institute on Drug Abuse, National Institutes of Health, Bethesda, MD, USA

Omicron is less virulent than Delta

- ED visits: 15.2% for delta, 4.5% for omicron.
- Hospitalizations: 3.95% for delta, 1.75% for omicron.
- ICU admissions: 0.78% for delta, 0.26% for omicron.
- Mechanical ventilation: 0.43% for delta, 0.07% for omicron.
- Similar results for children 12-17, 5-11, and less than 5 years of age.


COVID-19 metrics in Gauteng, as % of previous wave peak
Dr Ridhwaan Suliman
twitter: @rid1tweets
Wave 2 (beta)
Wave 3 (delta)
Wave 4 (omicron)
Deaths
Cases
Hospital Admissions
100
80
60
40
20
0
Aug Sep Oct Nov Dec Jan Jan Feb Mar Apr May June July Aug Sep Oct Nov Dec
2020
2021
2021

Find us online:

vaccine.chop.edu

Children's Hospital of Philadelphia®

Vaccine Education Center

To ask a question:

- **Type your question into the chat box, not the Q&A box**

Pennsylvania Chapter

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®

Thank You!

- Instructions on how to claim credit for your participation in today's Let's Talk webinar ***"COVID-19 Update: Kids, Omicron and Boosters "*** will be emailed to all of today's participants, along with a recording of the session.

- If you have any additional questions or issues, please email info@paaap.org.

- Registration is open for our 2022 Pediatric Conference, which will take place on March 19th and 20th, 2022 at the Gettysburg Hotel in Gettysburg, Pennsylvania! Make sure to register ASAP to qualify for a discounted registration fee.

PENNSYLVANIA IMMUNIZATION COALITION
PAIC

Pennsylvania Chapter

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®