Experience Rochester

COVID-19 RESEARCH: NEW KNOWLEDGE, NEW APPROACHES

Thursday, November 4, 2021

UNIVERSITY of ROCHESTER

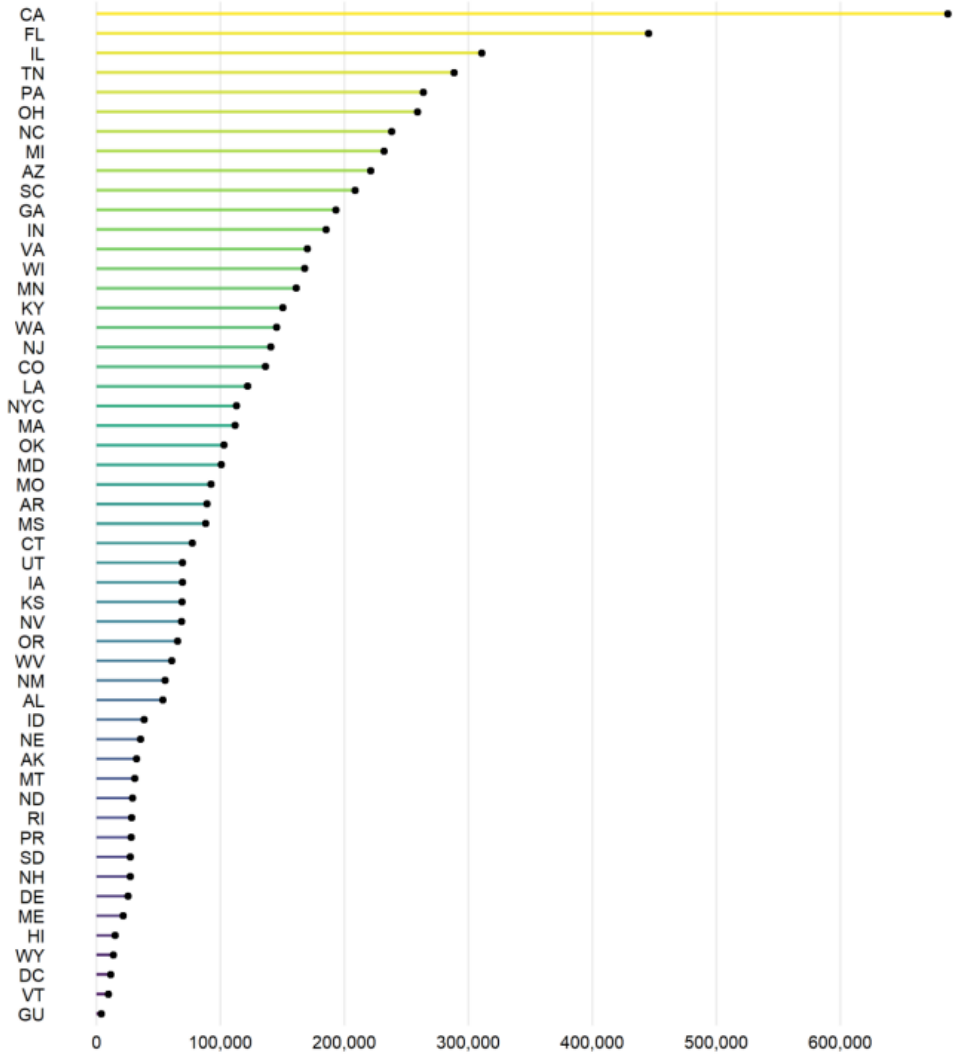
COVID-19 VACCINE TRIALS IN CHILDREN

Mary T. Caserta, MD

COVID-19 IN US CHILDREN

Fig 2. Cumulative Number of Child COVID-19 Cases: 10/28/21

- 6,396,278 total child COVID-19 cases (cumulative)
- Ten states reported 200,000+ child cases
- One state reported fewer than 10,000 child cases



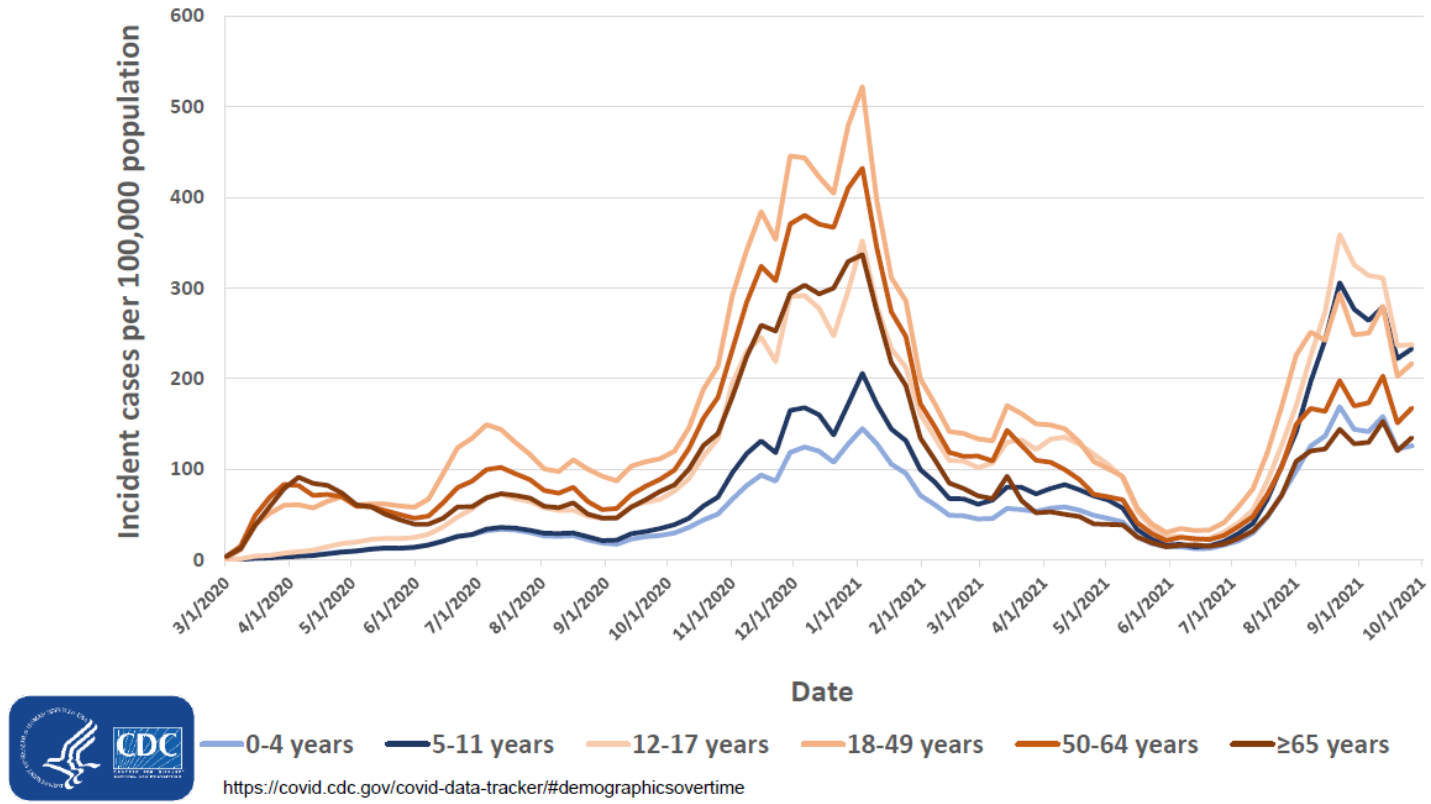
See detail in Appendix: Data from 48 states, NYC, DC, PR, and GU (TX excluded from figure)
All data reported by state/local health departments are preliminary and subject to change
Analysis by American Academy of Pediatrics and Children's Hospital Association
As of 6/30/21, NE COVID-19 dashboard is no longer available; NE cumulative cases through 6/24/21
Due to available data and changes made to dashboard, AL cumulative cases through 7/29/21

CHILDREN'S HOSPITAL ASSOCIATION
American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®

Amer Academ of Peds/Children's Hosp Assoc, 28 Oct 2021

COVID-19 IN US CHILDREN

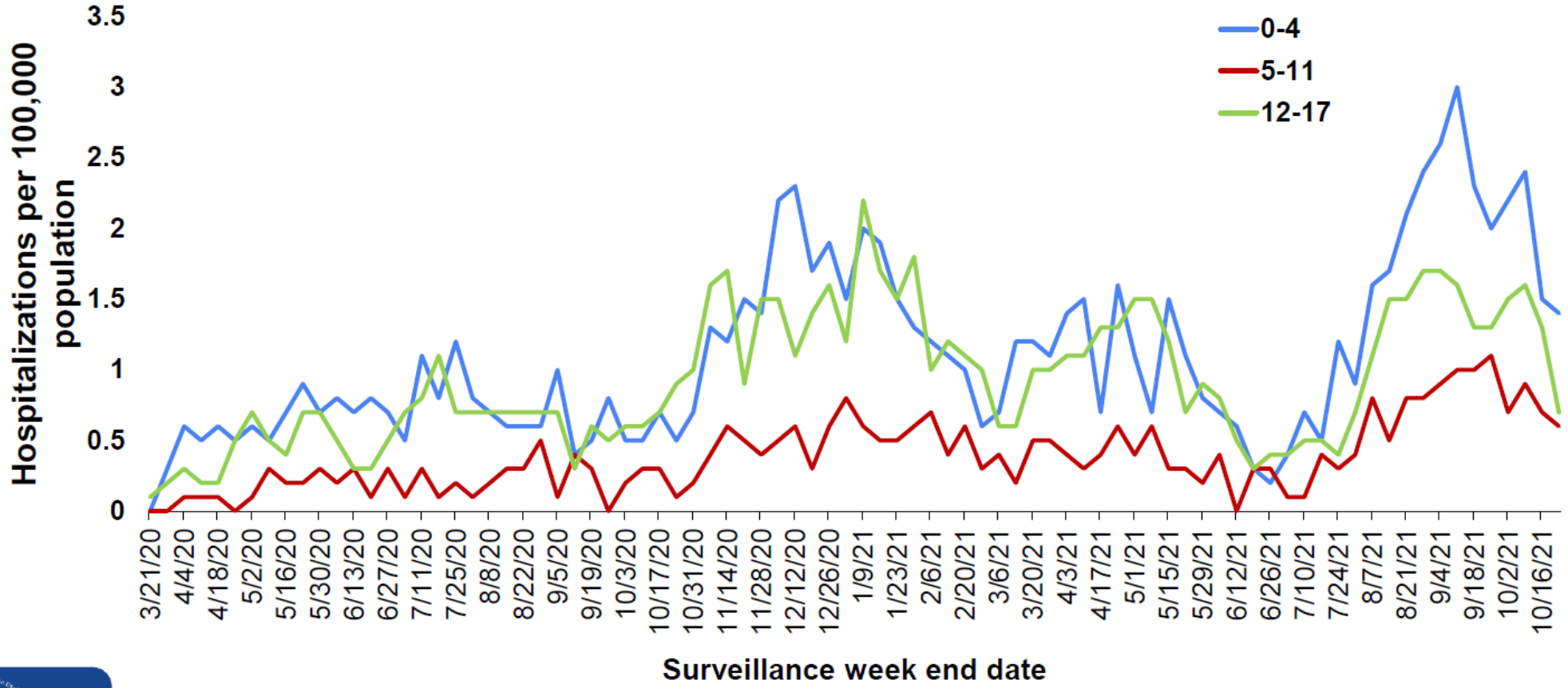
COVID-19 Weekly Cases per 100,000 Population by Age — United States, March 1, 2020–October 10, 2021



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

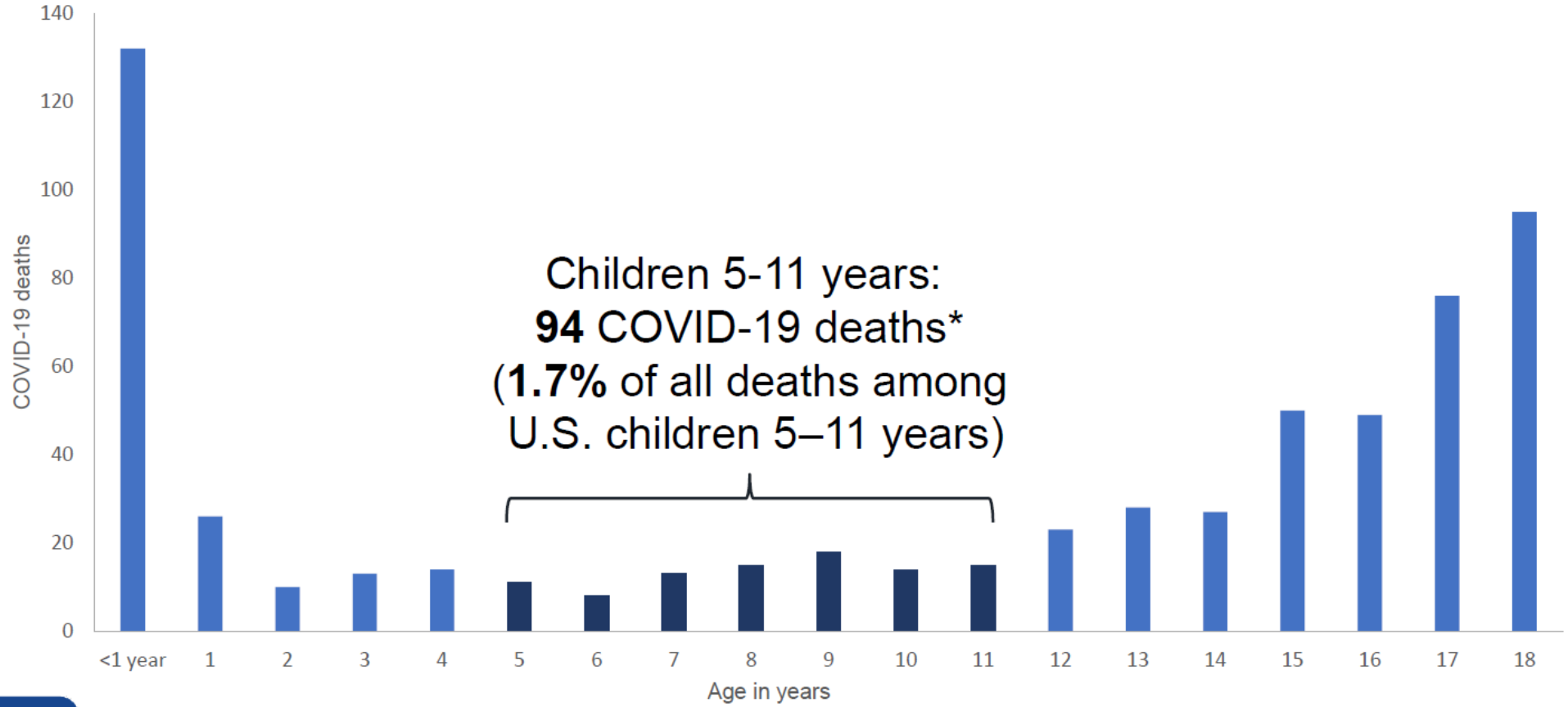
Jones, Epi Task Force, CDC COVID-19 Public Health Response, 2 Nov 2021

COVID-19-Associated Weekly Hospitalizations per 100,000 — COVID-NET by Age Group, March 21, 2020–October 23, 2021



https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covid-net/purpose-methods.html, Data are preliminary and subject to change

COVID-19 Deaths by Age Group, NCHS
— United States. January 1, 2020–October 16, 2021



*Lag in reporting of deaths might result in underestimate
https://data.cdc.gov/NCHS/Provisional-COVID-19-Deaths-Counts-by-Age-in-Years/3apk-4u4f/data

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

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

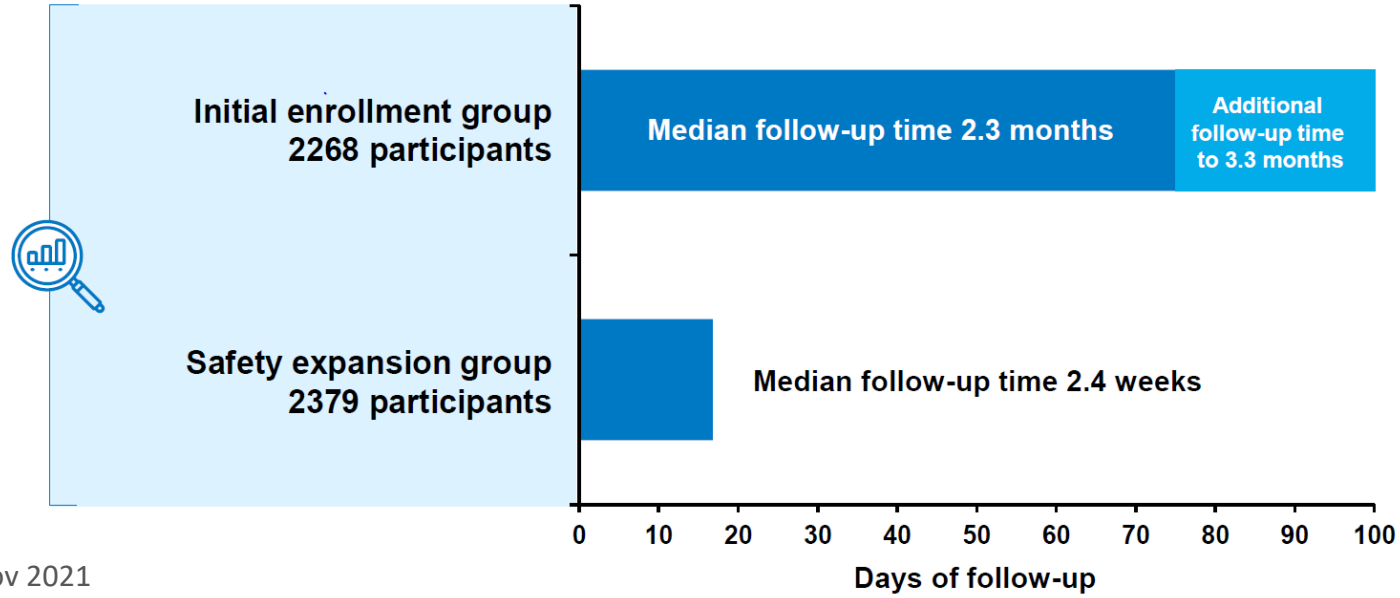
2:1
randomization

90 clinical trial sites

~1500 BNT162b2

750 placebo

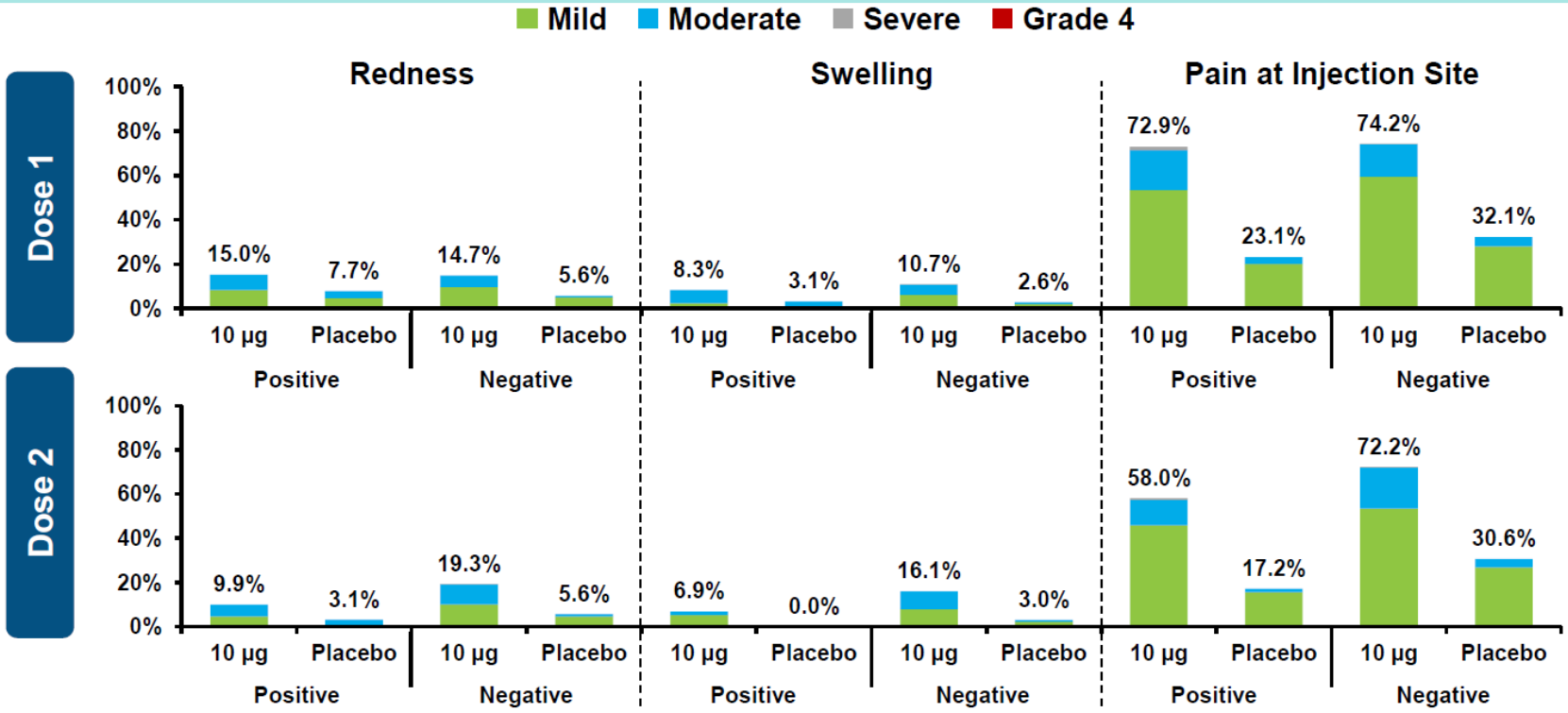
~Additional 1500 BNT162b2 and 750 placebo recipients most with ≥2 weeks post dose 2 safety data



Gurtman, Pfizer Clin Research and Dev. Presentation to FDA, 2Nov 2021

VACCINE REACTOGENICITY

Subjects Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose in 5 to <12 Year Olds by Baseline SARS-CoV-2 Status



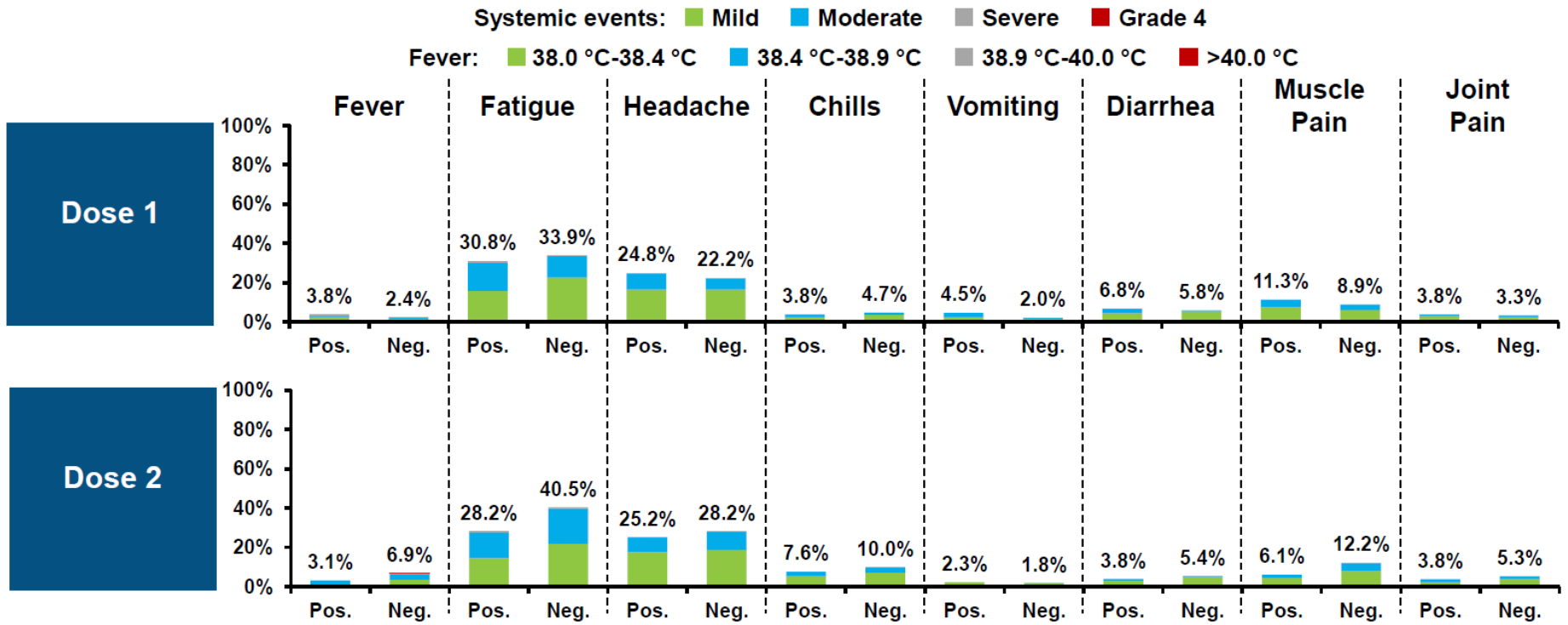
Redness and swelling severity definition: Mild= >2-5cm, Moderate= >5-10 cm; Severe= >10 cm; Grade 4= necrosis
Pain at injection site severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization
Dose 1: Positive N=198; Negative N=2062 Dose 2: Positive N=195; Negative N=2047

CC-12

Gurtman, Pfizer Clin Research and Dev. Presentation to FDA, 2Nov 2021

VACCINE REACTOGENICITY

Subjects Reporting Systemic Events, by Maximum Severity, Within 7 Days After Dose 1 and Dose 2 in 5 to <12 Year Olds by Baseline SARS-CoV-2 Status



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 1 Positive N=198; Negative N=2062 Dose 2: Positive N=195; Negative N=2047

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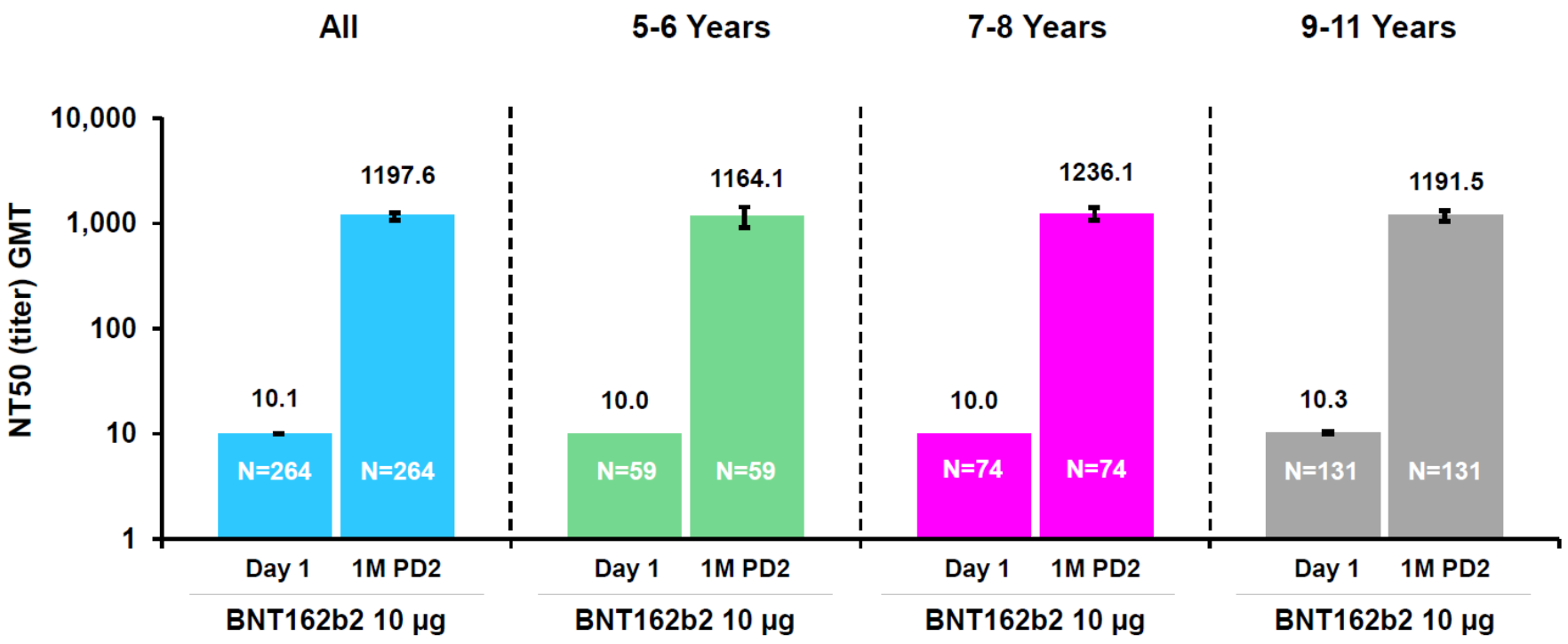
Gurtman, Pfizer Clin Research and Dev. Presentation to FDA, 2 Nov 2021

VACCINE IMMUNOGENICITY

Geometric Mean Titers (NT50), by Age Subgroup – Subjects 5 to <12 Years – Evaluable Immunogenicity Population

Immunogenicity Subset – Without Evidence of Prior Infection up to 1 Month Post Dose 2



NT50 = 50% neutralizing titers

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Gurtman, Pfizer Clin Research and Dev. Presentation to FDA, 2 Nov 2021

VACCINE EFFICACY

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

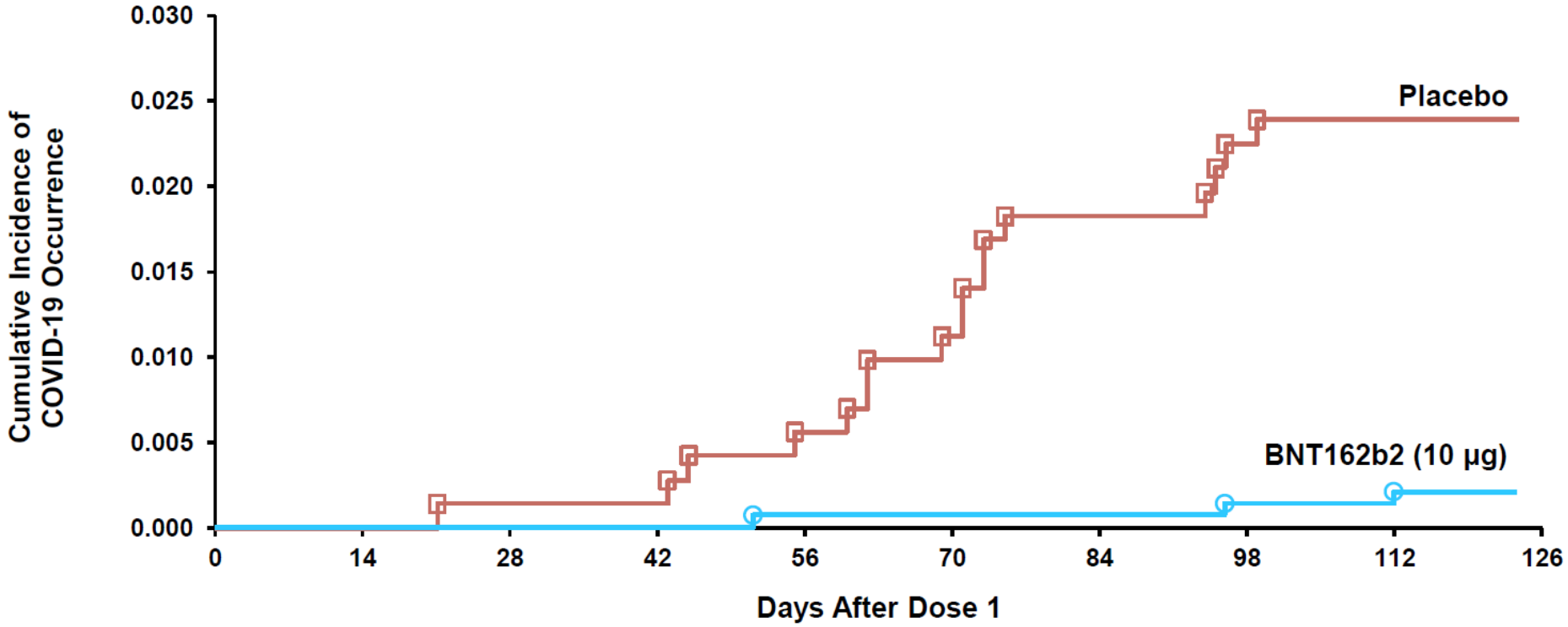
	BNT162b2 (10 µg) N=1305		Placebo N=663			
Efficacy Endpoint	n	Surveillance Time (n)	n	Surveillance Time (n)	VE (%)	(95% CI)
First COVID-19 occurrence ≥7 days after Dose 2	3	0.322 (1273)	16	0.159 (637)	90.7	(67.7, 98.3)

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

Gurtman, Pfizer Clin Research and Dev. Presentation to FDA, 2 Nov 2021

VACCINE EFFICACY

Cumulative Incidence of COVID-19 After Dose 1: 5 to <12 Years of Age



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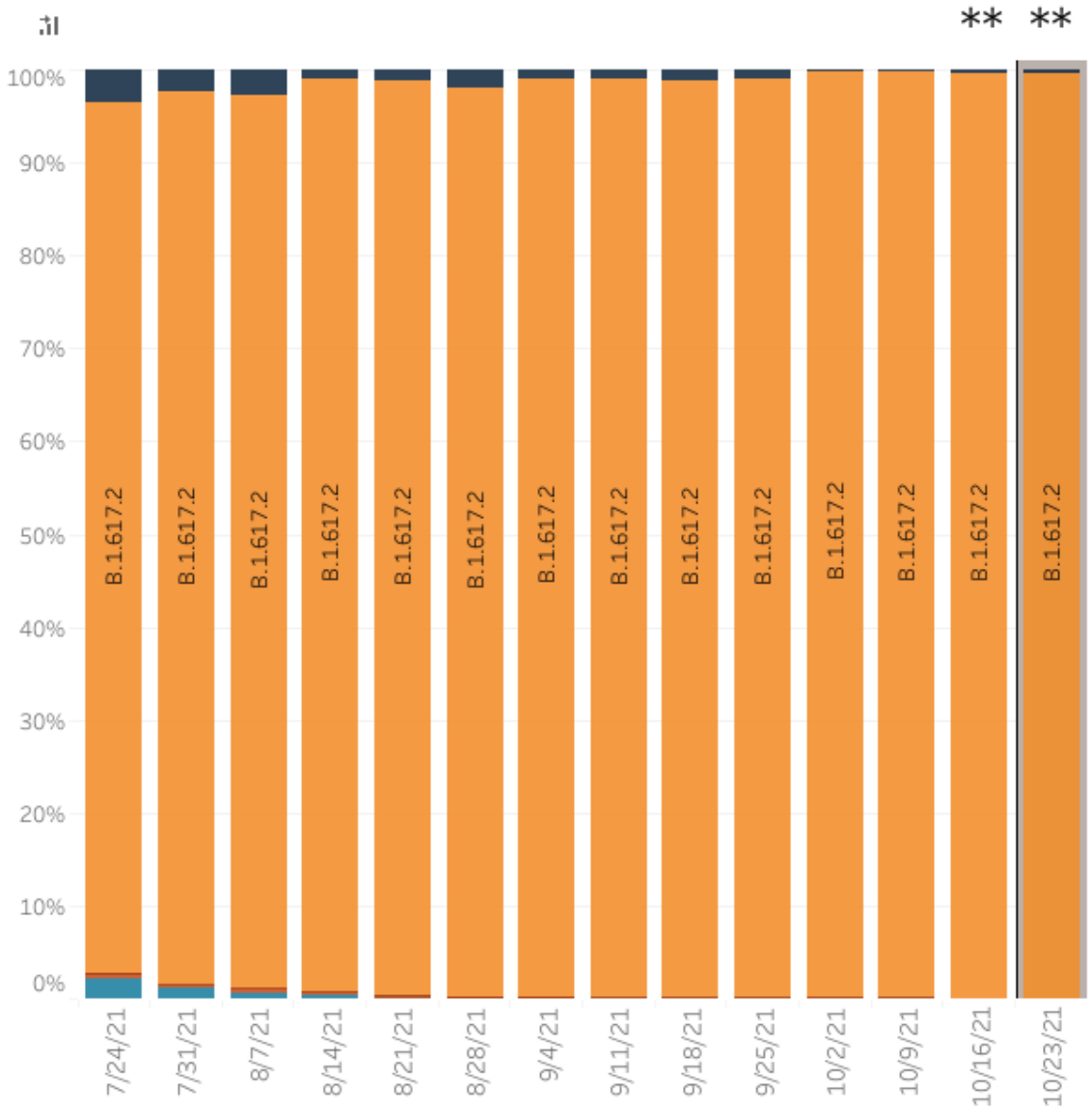
NEW COVID-19 VIRUS STRAINS, BREAKTHROUGH CASES, BOOSTERS

David J. Topham, PhD

UNIVERSITY of ROCHESTER
MEDICAL CENTER
Translational Immunology and Infectious Disease Institute

In the US, the Delta variant is responsible for nearly 100% of COVID-19 infections.



USA

WHO label	Lineage #	US Class	%Total	95%PI
Alpha	B.1.1.7	VBM	0.0%	0.0-0.0%
Delta	B.1.617.2	VOC	99.5%	99.2-99.7%
	AY.1	VOC	0.1%	0.0-0.1%
	AY.2	VOC	0.0%	0.0-0.0%
Other	Other*		0.4%	0.3-0.8%

* 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

Q.1-Q.8 are aggregated with B.1.1.7. AY.3-AY.38 and their sublineages are aggregated with B.1.617.2.

Breakthrough infections: A vaccine breakthrough infection is defined as the detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected from a person ≥14 days after they have completed all recommended doses of an FDA authorized COVID-19 vaccine. (CDC)

Hospitalized or fatal COVID-19 vaccine breakthrough cases reported to CDC as of October 18, 2021

As of October 18, 2021, more than 189 million people in the United States had been fully vaccinated against COVID-19.

During the same time, CDC received reports from 50 U.S. states and territories of 41,127 patients with COVID-19 vaccine breakthrough infection who were hospitalized or died.

	Deaths		Hospitalized, non-fatal*	
Total	N=10,857		N=30,270	
Females	4,619	(43%)	14,453	(48%)
People aged ≥65 years	9,172	(85%)	20,008	(66%)
Asymptomatic or not COVID-related**	2,299	(21%)	7,866	(26%)

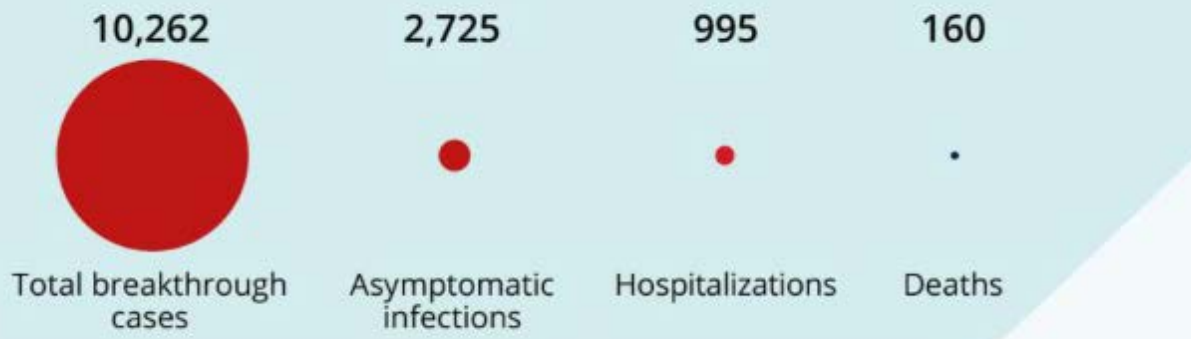
*This table separates all reported vaccine breakthrough infections that resulted in hospitalization and/or death into two columns. While most deaths were also among hospitalized individuals, a small number were not.

**Includes cases in which the patient did not have symptoms of COVID-19, or their hospitalization or death was not COVID-related. For example, people may be hospitalized for reasons other than COVID-19, such as an auto accident, and test positive when screened upon hospital admission.

0.02% of 189M vaccinated people in the US

Breakthrough Covid-19 Cases Remain Rare In The U.S.

Number of breakthrough Covid-19 cases reported in the U.S. as of April 30, 2021*



101 million
Total number fully vaccinated

* Vaccinated Americans who were infected with Covid-19.

Source: Centers for Disease Control and Prevention

Forbes statista

Colin Powell, first Black US secretary of state, dies of Covid-19 complications amid cancer battle

By Devan Cole, CNN

Updated 5:29 AM ET, Tue October 19, 2021

CURRENT RECOMMENDATIONS FOR RECEIVING A BOOSTER DOSE IF YOU INITIALLY RECEIVED AN mRNA VACCINE:

PFIZER-BIONTECH

- Received last dose > 6months ago
- Anyone 65 and older.
- All adults aged 18 to 64 who have cancer, dementia, diabetes, heart disease, HIV and other medical conditions that increase their likelihood of Covid complications.
- Anyone 18 or older who live or work in a long-term care facility, homeless shelter and prison or other congregate setting.
- Front-line personnel 18 or older who are at a higher risk of Covid exposure due to their job, including first responders, teachers, supermarket staff and mass transit employees.

MODERNA

- Received last dose > 6months ago
- Anyone 65 and older.
- All adults aged 18 to 64 who have cancer, dementia, diabetes, heart disease, HIV and other medical conditions that increase their likelihood of Covid complications.
- Anyone 18 or older who live or work in a long-term care facility, homeless shelter and prison or other congregate setting.
- Front-line personnel 18 or older who are at a higher risk of Covid exposure due to their job, including first responders, teachers, supermarket staff and mass transit employees.

Recommendations are the same for both Pfizer and Moderna.

CURRENT RECOMMENDATIONS FOR RECEIVING A BOOSTER DOSE IF YOU INITIALLY RECEIVED THE J&J VACCINE:

JOHNSON & JOHNSON

The CDC adopted a slightly different criteria for J&J's one-shot Covid vaccine, making almost 13 million recipients eligible.

That includes

- All adults who were vaccinated with J&J's Covid vaccine at least **two months ago,** instead of six months with Pfizer and Moderna.

- **All adult J&J recipients are eligible for a booster even if they don't have underlying medical conditions or work in a profession or live where there's a higher risk of Covid.**

BENEFITS OF BOOSTER (FOR ANY VACCINE TYPE)

- Rise in protective serum antibodies
- Antibodies more cross-reactive against variants
- Increased frequencies of Memory B cells and Memory T cells
    - Can prevent serious illness, hospitalization, and death

FDA/CDC also recommend getting <u>any</u> one of the three approved vaccines as a boost

THE CHANGING LANDSCAPE OF COVID-19 VACCINES

Angela Branche, MD

ADDING TO THE BOOSTER CONTROVERSY

Heterologous SARS-CoV-2 Booster Vaccinations—Preliminary Report

The NEW ENGLAND JOURNAL of MEDICINE

- Phase 1/2 open-label clinical trial conducted at ten U.S. sites, adults who received one of three EUA Covid-19 vaccines at least 12 weeks prior received a booster injection with one of three vaccines (Moderna mRNA-1273 100-µg, Janssen Ad26.COV2.S 5×1010 virus particles, or Pfizer-BioNTech BNT162b2 30-µg.

- The primary outcomes were safety, reactogenicity, and humoral immunogenicity on study days 15 and 29.

Table 1. Characteristics of the Participants at Enrollment

Group	1	2	3	4	5	6	7	8	9
Primary EUA Immunization Vaccine	Janssen Ad26.COV2-S $5x10^{10}$ vp	Moderna mRNA-1273 100-mcg	Pfizer/BioNTech BNT162b2 30-mcg	Janssen Ad26.COV2-S $5x10^{10}$ vp	Moderna mRNA-1273 100-mcg	Pfizer/BioNTech BNT162b2 30-mcg	Janssen Ad26.COV2-S $5x10^{10}$ vp	Moderna mRNA-1273 100-mcg	Pfizer/BioNTech BNT162b2 30-mcg
Booster	Moderna mRNA-1273 100-mcg			Janssen Ad26.COV2-S $5x10^{10}$ vp			Pfizer/BioNTech BNT162b2 30-mcg		
Total Number	53	51	50	50	49	51	53	51	50

HETEROLOGOUS SARS-COV-2 BOOSTER VACCINATIONS – PRELIMINARY REPORT (MIX AND MATCH)

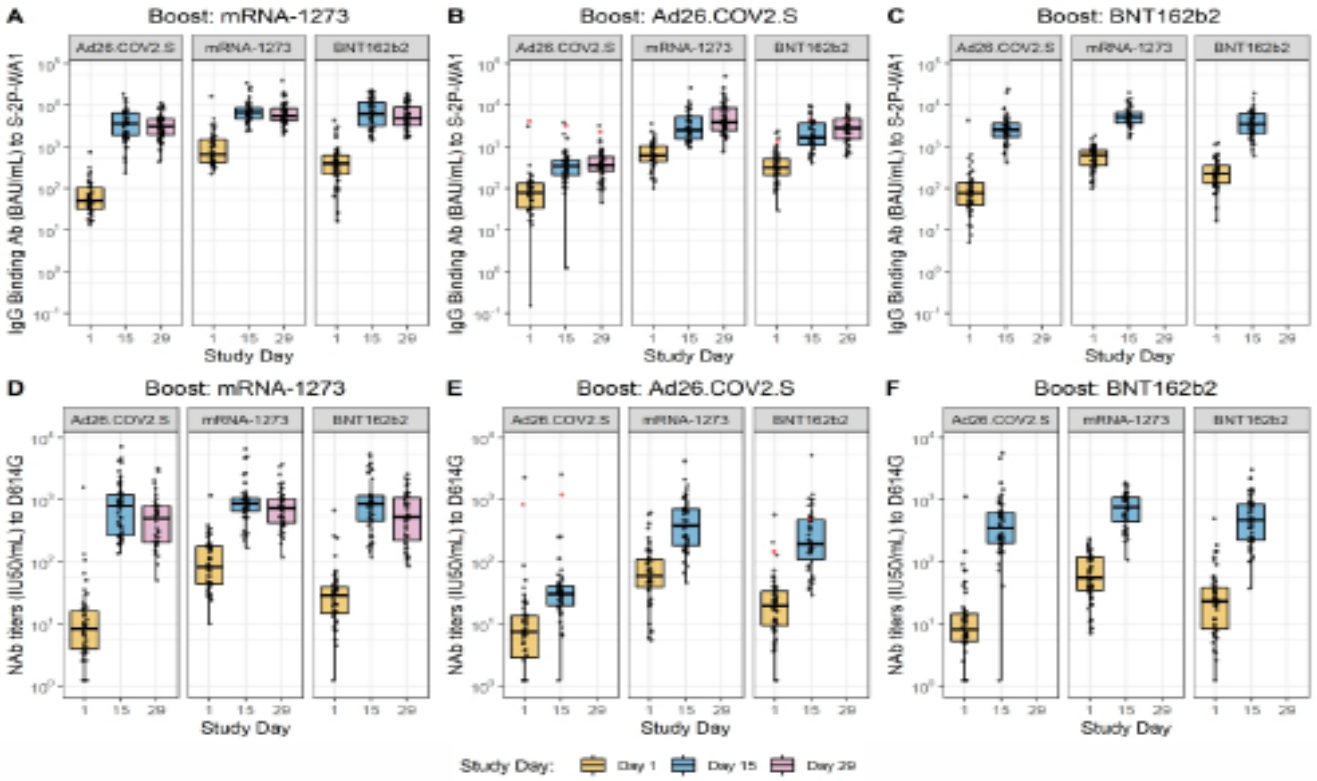


Figure 2 | Binding Antibody and Neutralizing Antibody Titers

VACCINATION AND PREGNANCY

Design: From December 14, 2020, to February 28, 2021, we used data from the "v-safe after vaccination, the v-safe pregnancy registry, and the Vaccine Adverse Event Reporting System (VAERS) to characterize the initial safety of mRNA Covid-19 vaccines in pregnant persons.

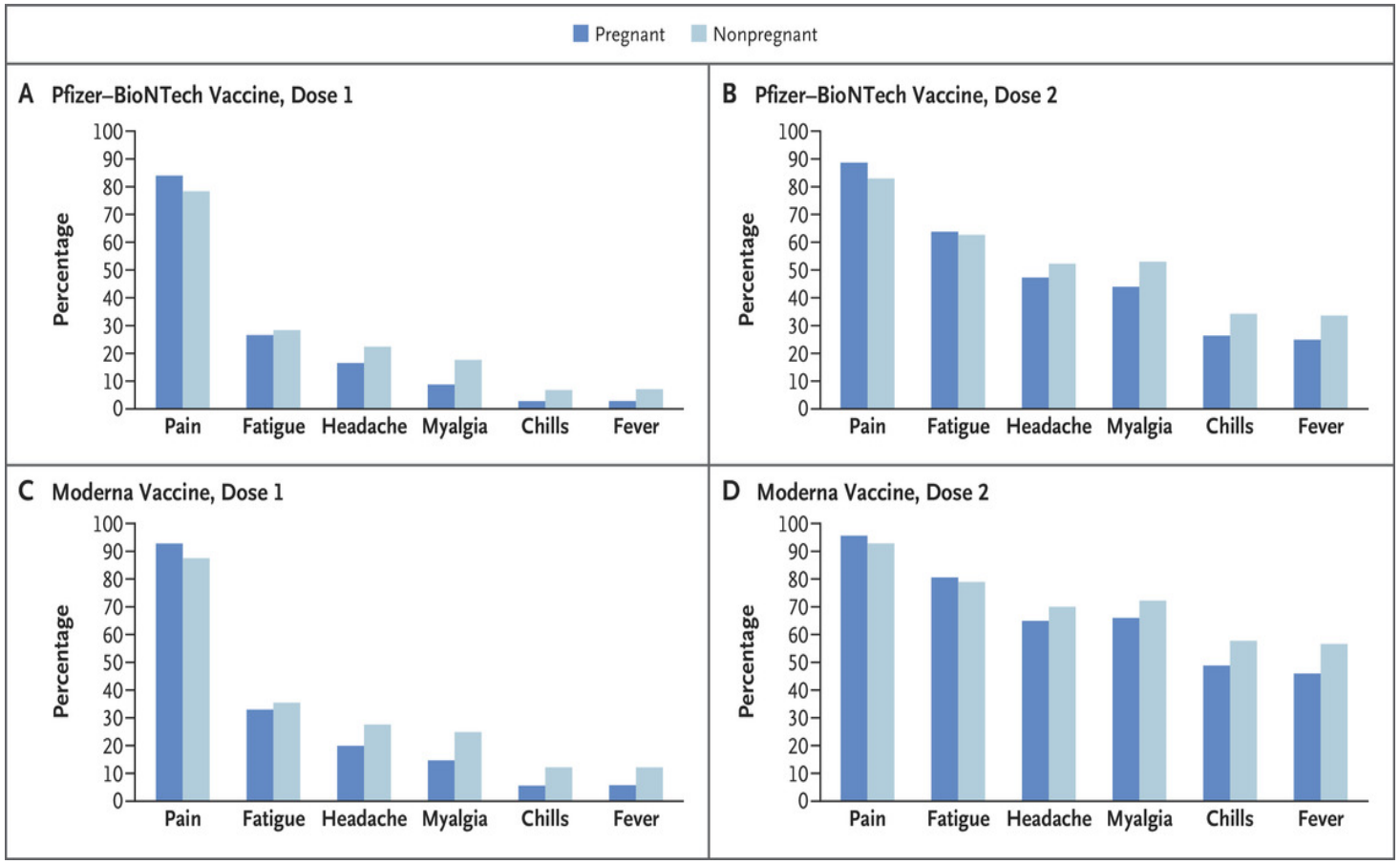
Results: 35,691 v-safe participants 16 to 54 years of age identified as pregnant.

Table 3. Characteristics of V-safe Pregnancy Registry Participants.*

Characteristic	Pfizer–BioNTech Vaccine	Moderna Vaccine	Total
	number (percent)		
Total	2136 (54.0)	1822 (46.0)	3958 (100)
Timing of first eligible dose			
Periconception: within 30 days before last menstrual period	55 (2.6)	37 (2.0)	92 (2.3)
First trimester: <14 wk	615 (28.8)	517 (28.4)	1132 (28.6)
Second trimester: ≥14 and <28 wk	932 (43.6)	782 (42.9)	1714 (43.3)
Third trimester: ≥28 wk	533 (25.0)	486 (26.7)	1019 (25.7)
Missing data	1 (<0.1)	0	1 (<0.1)

VACCINATION AND PREGNANCY

Most Frequent Local and Systemic Reactions Reported in the V-safe Surveillance System on the Day after mRNA Covid-19 Vaccination.



TT Shimabukuro et al. N Engl J Med 2021;384:2273-2282.

VACCINATION AND PREGNANCY

Pregnancy Loss and Neonatal Outcomes in Published Studies and V-safe Pregnancy Registry Participants.

Table 4. Pregnancy Loss and Neonatal Outcomes in Published Studies and V-safe Pregnancy Registry Participants.

Participant-Reported Outcome	Published Incidence*	V-safe Pregnancy Registry†
	%	*no./total no. (%)*
Pregnancy loss among participants with a completed pregnancy		
Spontaneous abortion: <20 wk[15-17]‡	Not applicable	104
Stillbirth: ≥ 20 wk[18-20]	<1	1/725 (0.1)§
Neonatal outcome among live-born infants		
Preterm birth: <37 wk[21,22]	8–15	60/636 (9.4)¶
Small size for gestational age[23,24]‖	3.5	23/724 (3.2)
Congenital anomalies[25]**	3	16/724 (2.2)
Neonatal death[26]††	<1	0/724

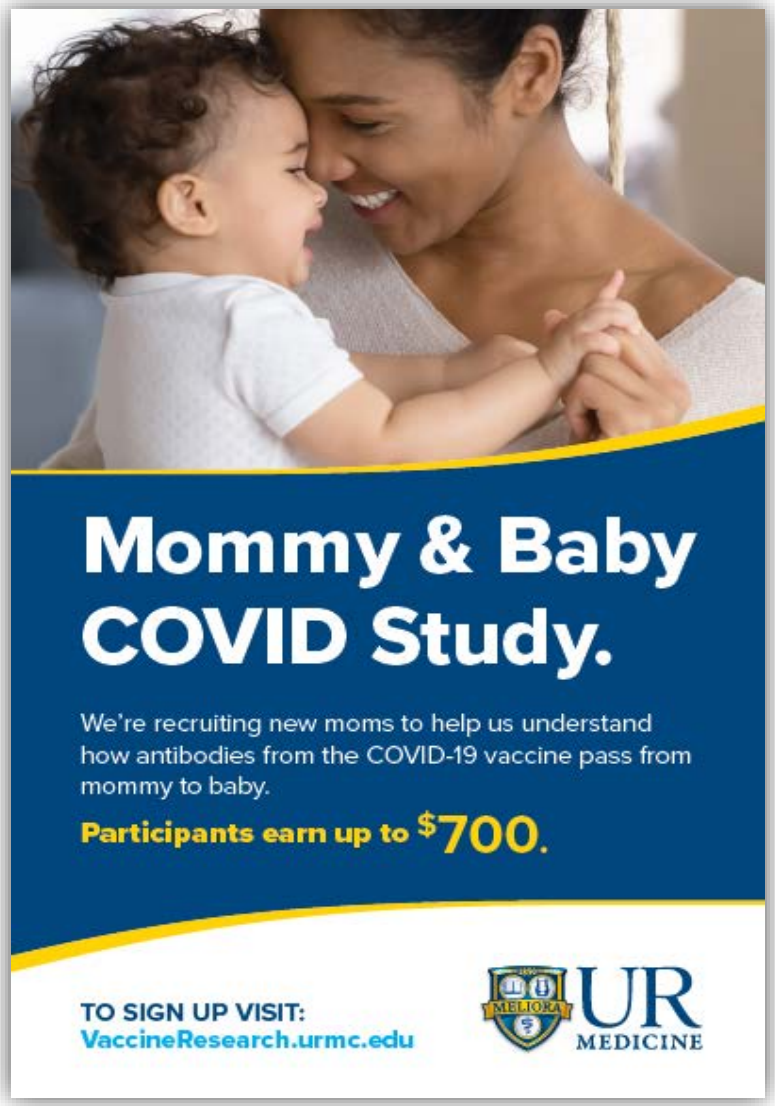
TT Shimabukuro et al. N Engl J Med 2021;384:2273-2282.

MomiVax

Observational, Prospective Cohort Study of the Immunogenicity and Safety of SARS-CoV-2 Vaccines Administered during Pregnancy or Postpartum and Evaluation of Antibody Transfer and Durability in Infants.

APPROXIMATELY 2,000 STUDY PARTICIPANTS IN 3 GROUPS:

- **GROUP 1**: Individuals who receive a COVID19 vaccine during pregnancy and their Infants.
- **GROUP 2:** Individuals who receive a COVID19 vaccine postpartum and their infants.
- **GROUP 3:** Individuals who receive a COVID19 booster during pregnancy and their infants.



NEW VACCINE PLATFORMS—CAN WE DO BETTER THAN MRNA?

- A Phase 1 open label dose ranging trail to evaluate safety, and immunogenicity of CVXGA1.

- A live recombinant parainfluenza virus 5 (PIV5) expressing SARS-CoV 2 spike (S) protein administered as:

- Single Dose
- Intranasally

CYANVAC

CVXGA1-001

NEW HORIZONS…

- Are there benefits to mixing vaccine types?
- Will new variants emerge against which current vaccines have little or no neutralizing activities?
- How many doses will be required before durable immunity is achieved?
- Can COVID vaccines be combined with other seasonal vaccines?