COVID-19 Vaccine Effectiveness in the United States

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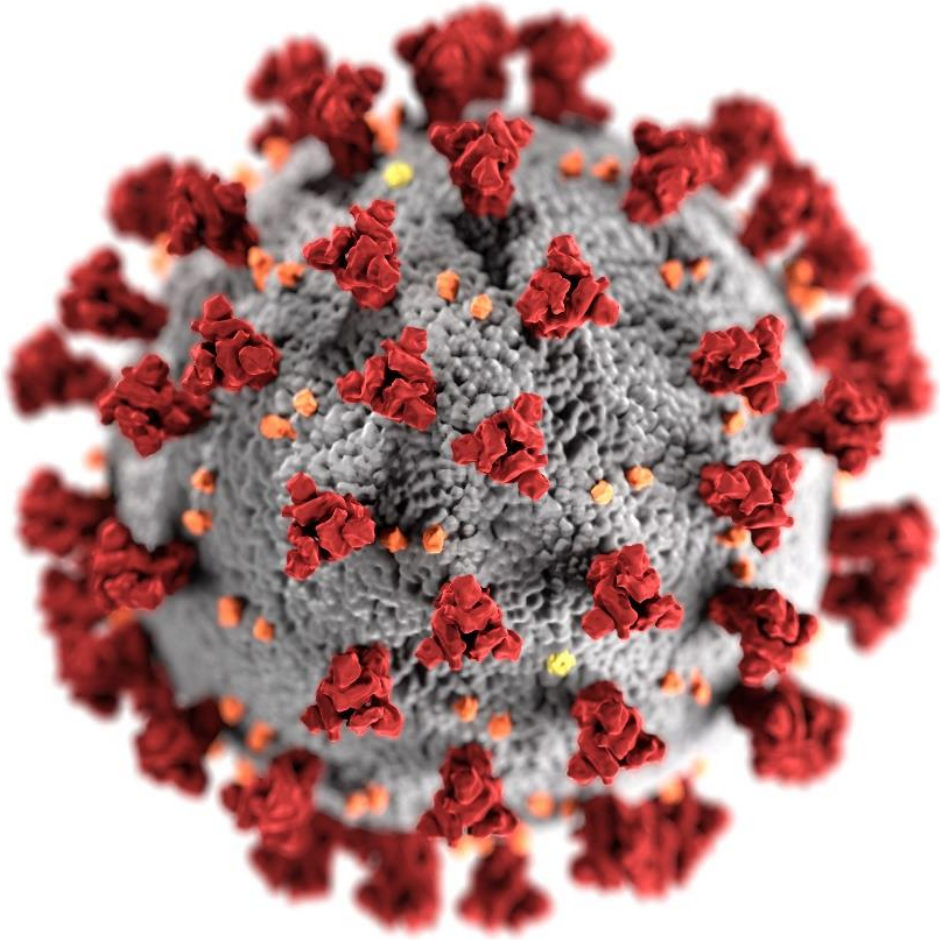
CDC COVID-19 Response
LCDR, US Public Health Service

COCA Call
September 28, 2021



cdc.gov/coronavirus

Monitoring vaccine effectiveness (VE) evidence by risk group, outcome, and product over time

By time since vaccination *and/or* pre-/post-Delta

Risk group X **Outcome** X **Product**

Desired, but often limited by sample size

Increasing Community Access to Testing (ICATT) Partnership

Waning of immunity by Delta predominance in the general population

Increasing Community Access to Testing (ICATT) Partnership: VE analysis for symptomatic infection, March 13–August 31, 2021

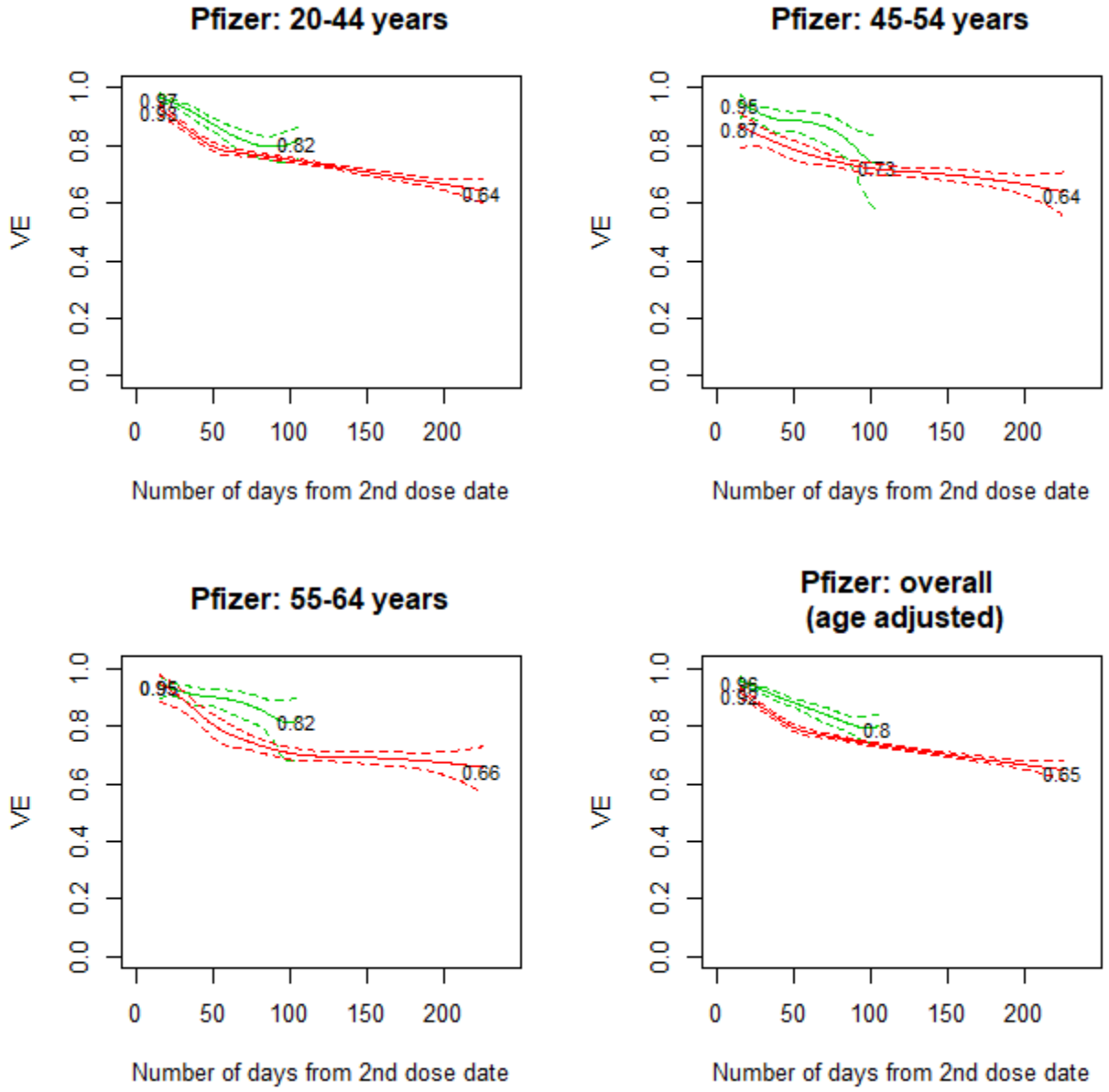
- Nationwide community-based COVID-19 testing via pharmacies and partners
- Self-reported vaccine history at time of registration for COVID-19 testing; excluded those who did not report vaccination status (18%)
- **Design**: Test-negative, case-control assessment
- **Period**: Pre-Delta: March 13–May 29 (N=255,519); Delta: July 18–August 31 (N=519,699)
- **Population**: Persons aged 20–64 years of age with COVID-like illness (CLI) and laboratory-based nucleic acid amplification testing (NAAT)
- **Adjusted for**:
  - Calendar day, race, ethnicity, gender, site's HHS region and state, site census tract's social vulnerability index (SVI)
  - **Not** adjusted for underlying conditions or prior infection

Pfizer-BioNTech VE against symptomatic infection by age group and time since vaccination in pre-Delta vs Delta periods

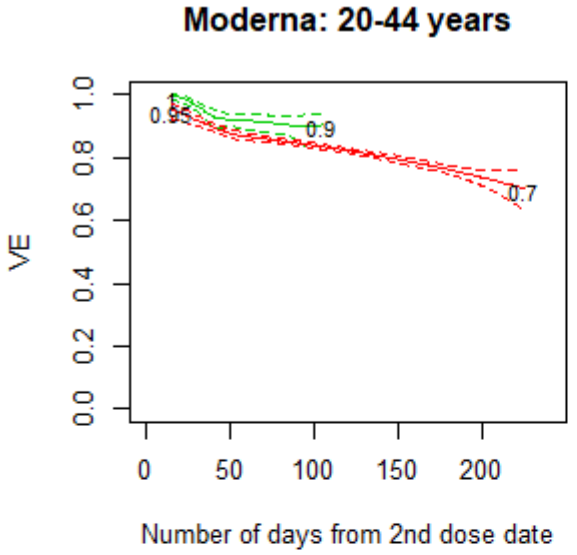
- Significant waning of VE in both time periods
- VE is lower during Delta period at all time points
- Curves look similar across age groups

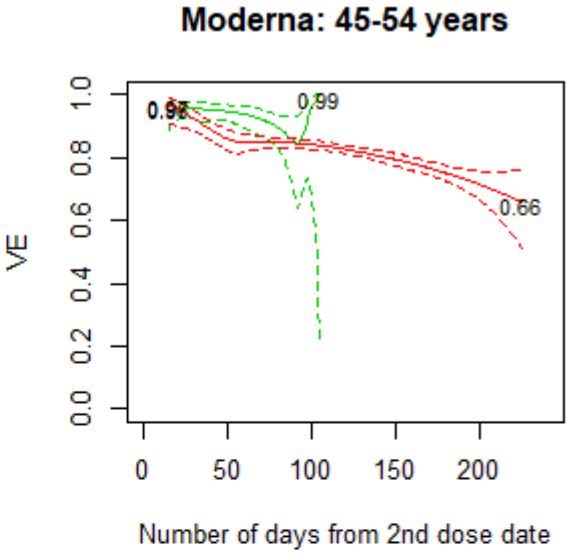
Pre-Delta (March 13–May 29) with 95% CIs in dotted lines

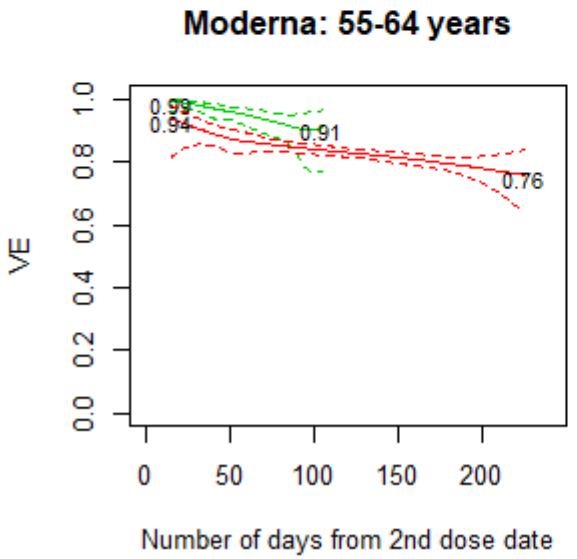
Delta (July 18–August 31) with 95% CIs in dotted lines

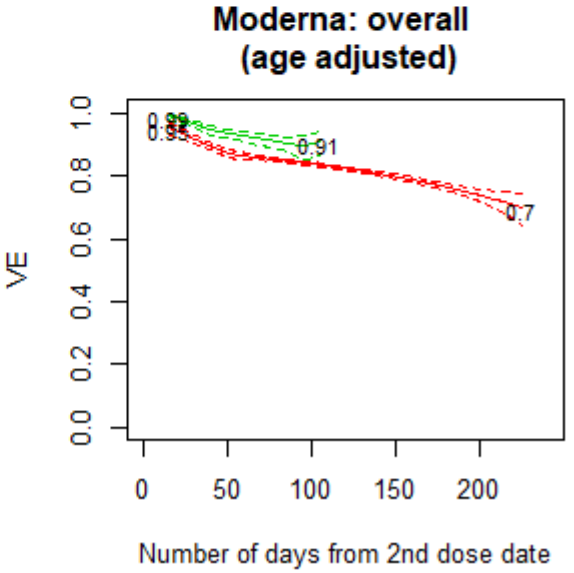


Moderna VE against symptomatic infection by age group and time since vaccination in pre-Delta and Delta periods









- Moderna VE is higher than Pfizer-BioNTech
- VE wanes during Delta
- Curves look similar across age groups

Pre-Delta (March 13–May 29) with 95% CIs in dotted lines

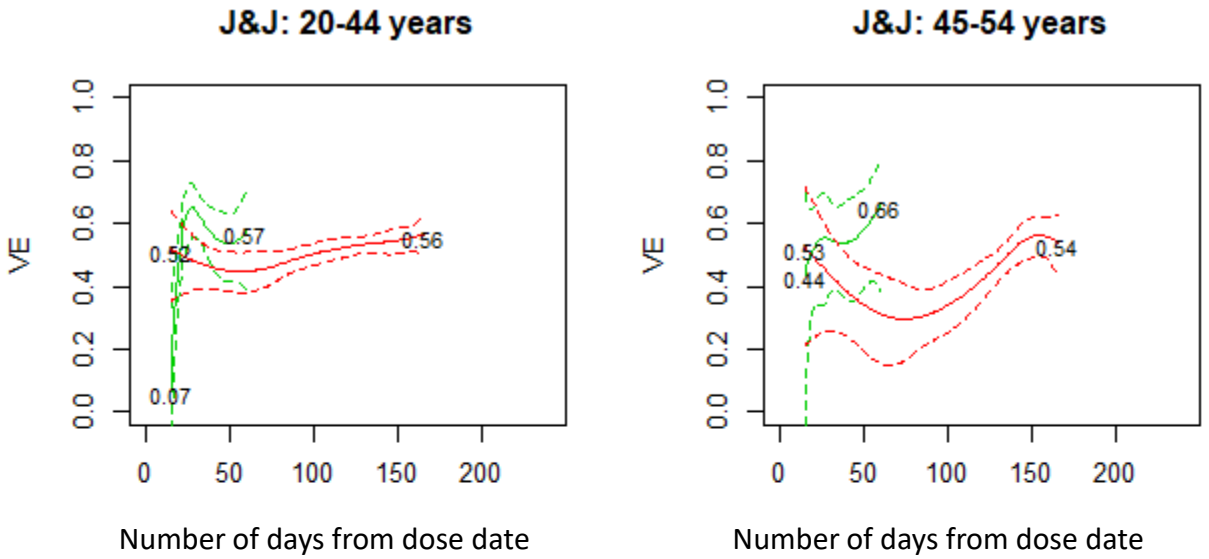
Delta (July 18–August 31) with 95% CIs in dotted lines

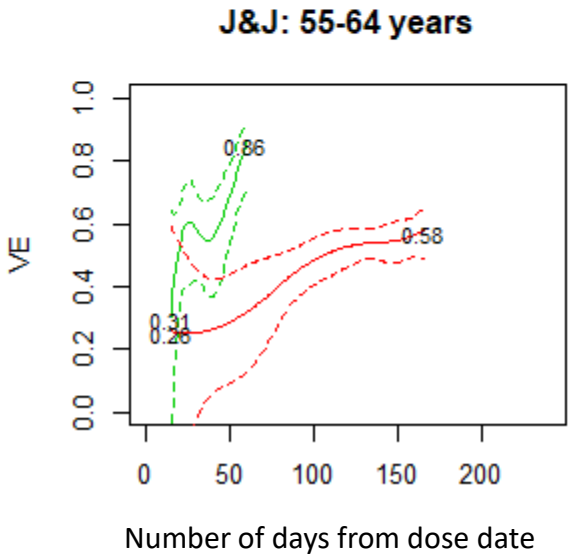
Johnson & Johnson (J&J, Janssen) VE against symptomatic infection by age group and time since vaccination in pre-Delta and Delta periods

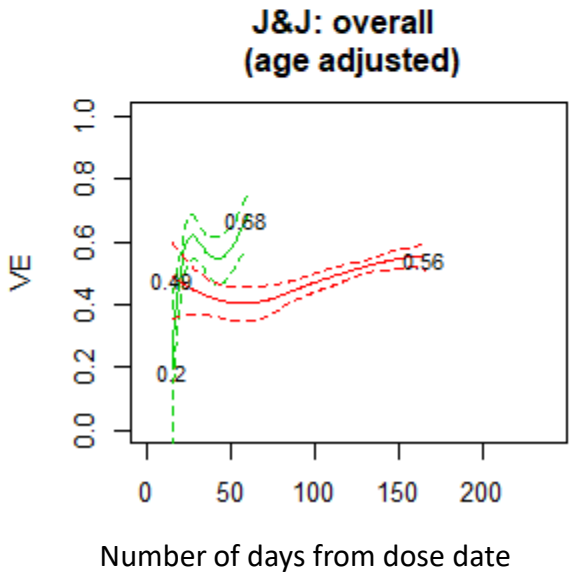
- VE increases with time in both periods
- No clear Delta effect on VE
- Curves look similar across age groups

Pre-Delta (March 13–May 29) with 95% CIs in dotted lines

Delta (July 18–August 31) with 95% CIs in dotted lines







ICATT limitations for VE against symptomatic infection

- Self-reported vaccination data, no clinical assessment
  - By limiting to persons with known vaccination status, a substantial proportion of records were lost, possibly introducing bias
- No information on co-morbidities, prior infection, risk behaviors
- Analysis based on tests, no unique identifiers to track individuals in data
- No genetic sequencing results
  - Pre-Delta: March 13–May 29
  - Delta: July 18–August 31

Vaccine effectiveness in individuals ≥65 years of age, including residents of long-term care facilities

COVID-19-Associated Hospitalization Surveillance Network (COVID-NET)

- **Population-based** surveillance **for laboratory-confirmed** COVID-19-associated **hospitalizations**
- Defined catchment area: >250 acute care hospitals in 99 counties in 14 states, representing 10% of U.S. population
- **Case definition**: Resident of the surveillance area and positive SARS-CoV-2 test within 14 days prior to or during hospitalization
- **VE estimates:** variation of **screening method**
  - Immunization information systems (ISS)
  - Representative sample of hospitalized cases (>37,000 to date)
  - Underlying population in catchment area by week

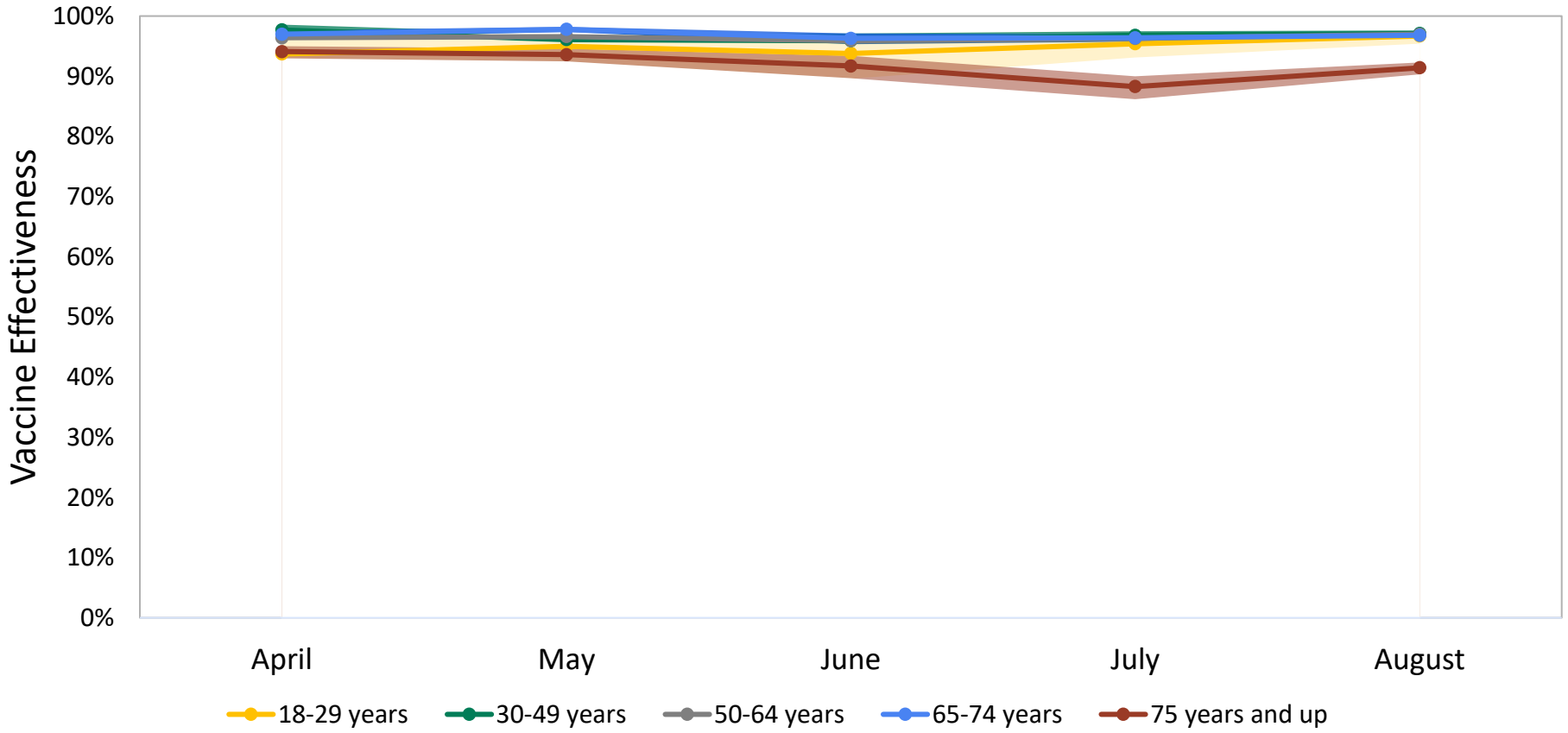
Represents ~10% of U.S. population (32 million people)

- VE estimates adjusted for time, but cannot adjust for other important potential confounders (e.g., comorbidities, prior infection)

*Vaccine effectiveness calculated using previously described methods: Moline et al. Effectiveness of COVID-19 Vaccines in Preventing Hospitalization Among Adults Aged ≥65 Years — COVID-NET, 13 States, February–April 2021. MMWR, August 13, 2021

‡California, Colorado, Connecticut, Georgia, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah are included in these analyses

COVID-NET vaccine effectiveness against hospitalization, by month and age group, mRNA vaccines



No significant differences in VE by age group or calendar month of hospitalization

Among **fully vaccinated** patients, defined as receipt of both doses of Moderna or Pfizer-BioNTech vaccine, with second dose received ≥14 days before hospitalization

Source: Unpublished COVID-NET data, 2021

COVID-19-associated hospitalizations among vaccinated adults ≥18 years with COVID-19 as primary reason for admission — COVID-NET, January 1–July 31, 2021

- Fully vaccinated cases more likely to be:
  - Older
  - Long-term care facility resident
  - DNR/DNI code
- More underlying medical conditions

Category	Unvaccinated weighted % N=5,513	Fully vaccinated weighted % N=465
Age group (median, IQR)	59 (47–71)	72 (62–80)
18–49 years	28	11
50–64 years	33	16
≥65 years	40	72
LTCF residence	5	13
DNR/DNI/CMO	6	16
Underlying medical conditions		
Cardiovascular disease	34	50
Neurologic disease	17	28
Renal disease	16	29
Immunosuppressive condition	12	29
Rheumatologic or autoimmune	3	7
Blood disorder	3	4
≥3 Underlying medical conditions	55	66

* All characteristics were significantly different on univariate analysis

VE against infection and hospitalization: Data from NY State, May–July 2021

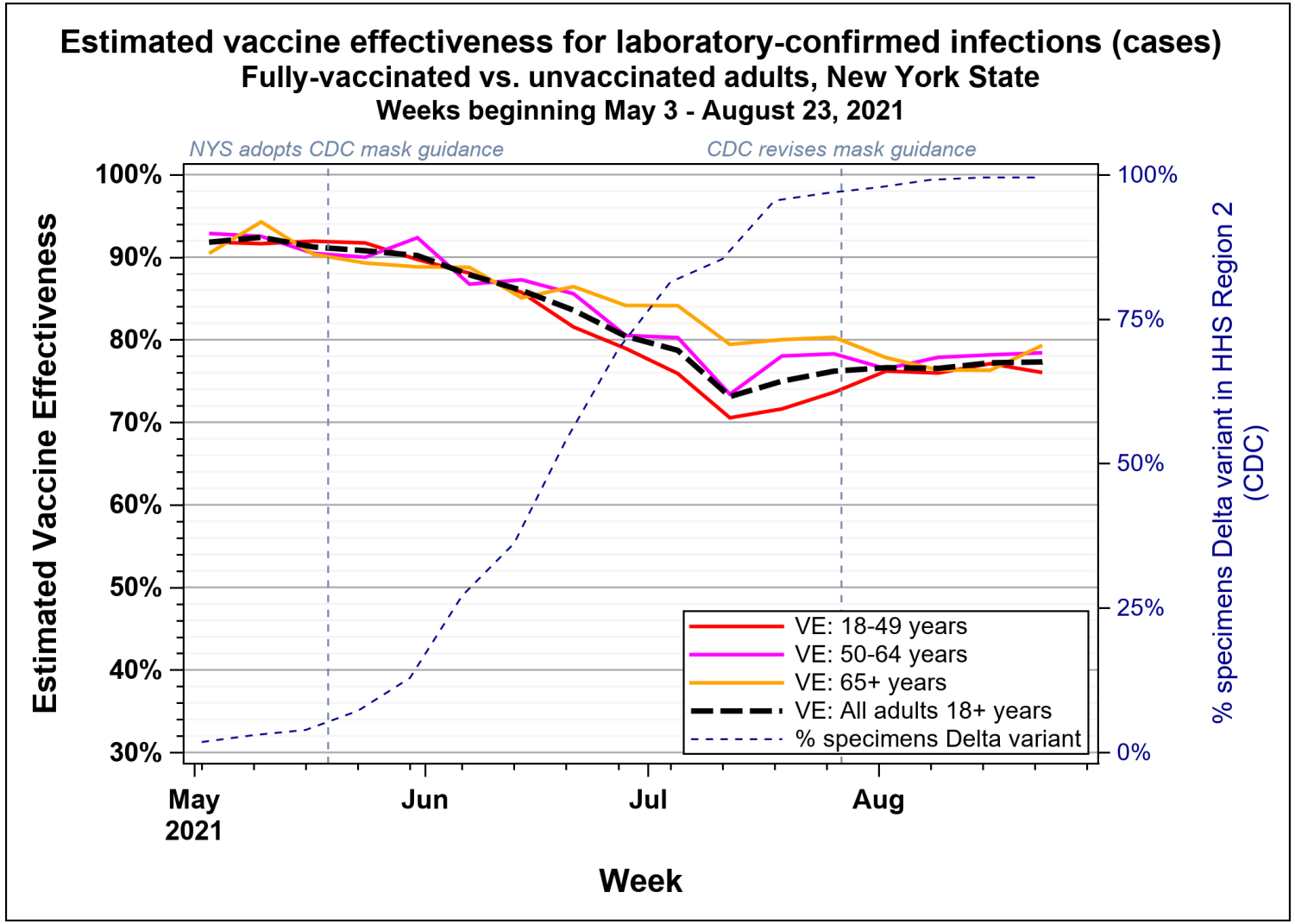
- NY State linked lab, immunization, and hospitalization data to estimate VE from May 3–August 29, 2021
  - 147,937 new diagnoses among fully vaccinated and unvaccinated persons
  - 16,261 new hospitalizations among fully vaccinated and unvaccinated persons

- Breakdown by vaccine:
  - Pfizer-BioNTech: 52%
  - Moderna: 39%
  - Johnson & Johnson/Janssen: 9%

- Delta proportion: <2% (May 2–8) to >99% (August 22–28) (CDC NS3, HHS Reg. 2)

Update of published study: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e1.htm

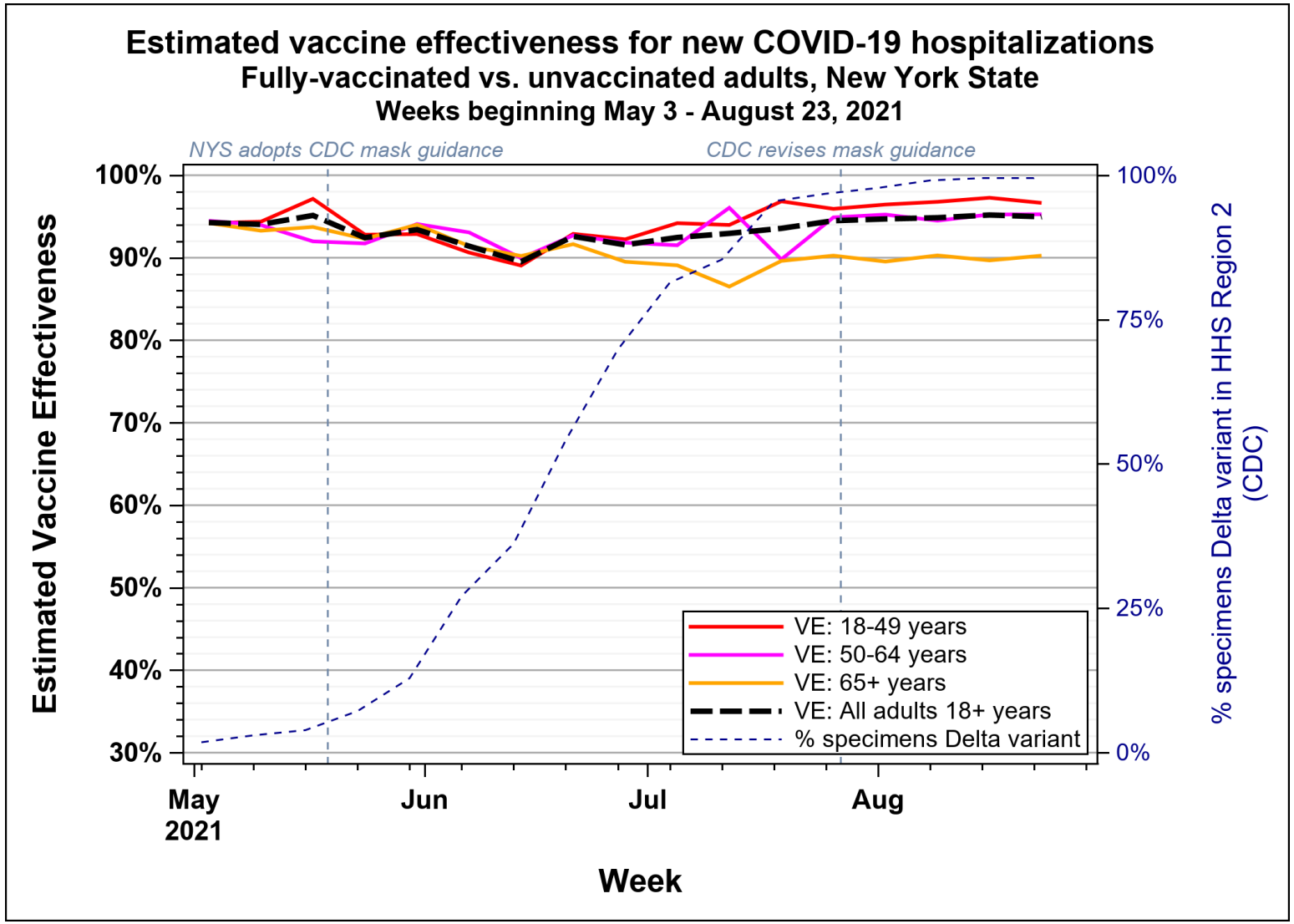
VE against infection: Data from NY State, May–August 2021



Age-adjusted VE against new COVID-19 infections declined from 92% (May 3–9) to 73% (July 12–18), when Delta reached 85%. Then, decline ceased, with plateau around 77%.

Update of published study: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e1.htm

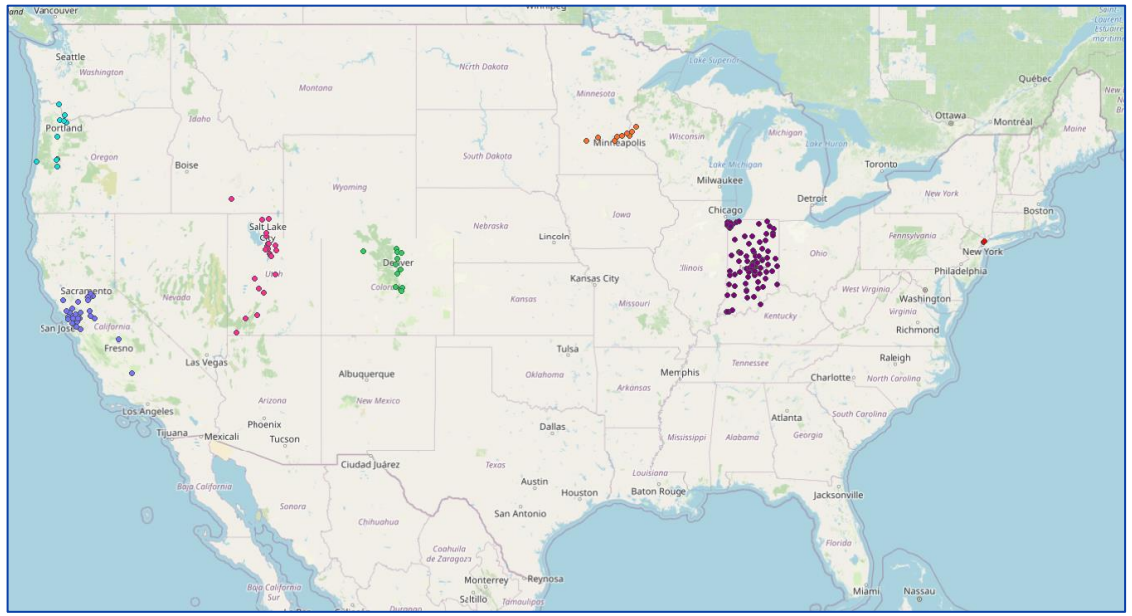
VE against hospitalization: Data from NY State, May-August 2021



Age-adjusted VE against new COVID-19 hospitalizations remained stable at 90%–95%.

Update of published study: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e1.htm

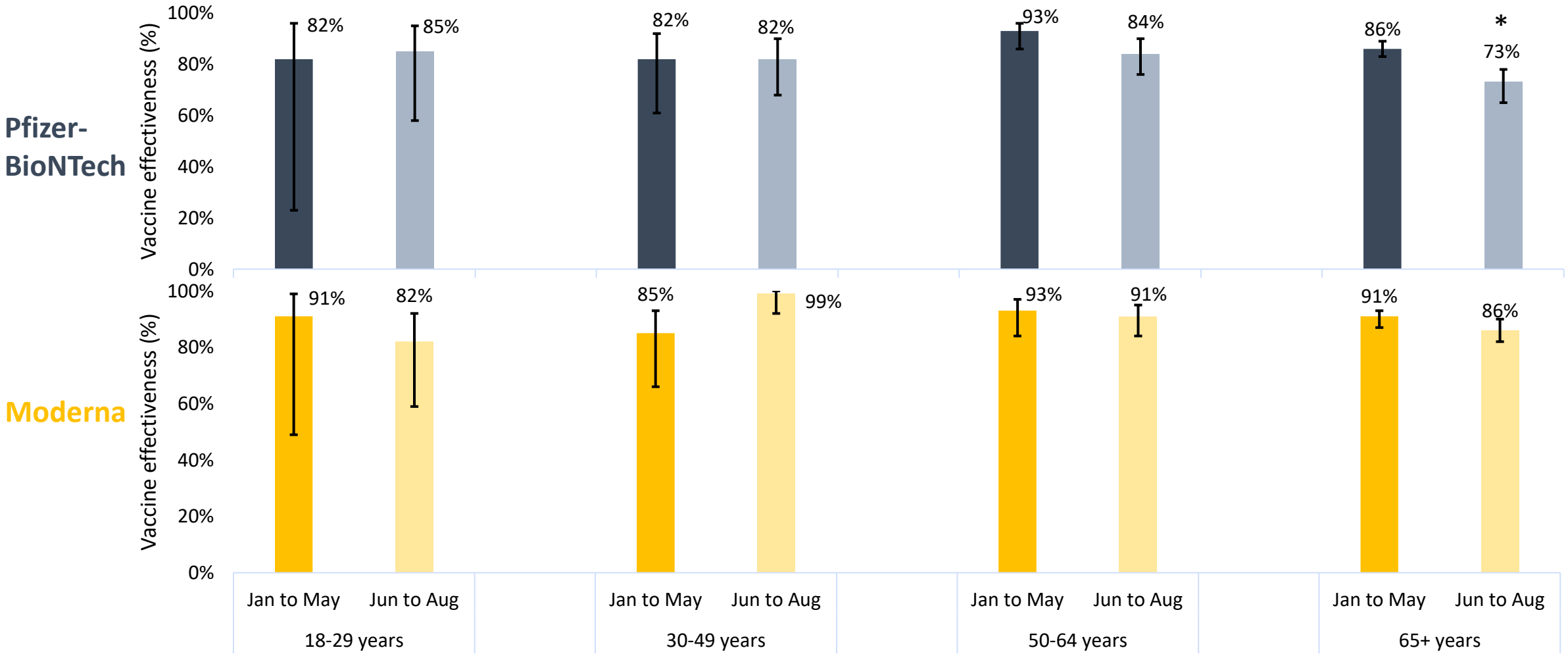
VISION Multi-State Network of Electronic Health Records for VE against hospitalization



Estimates are from over 74,000 hospitalizations across 187 hospitals

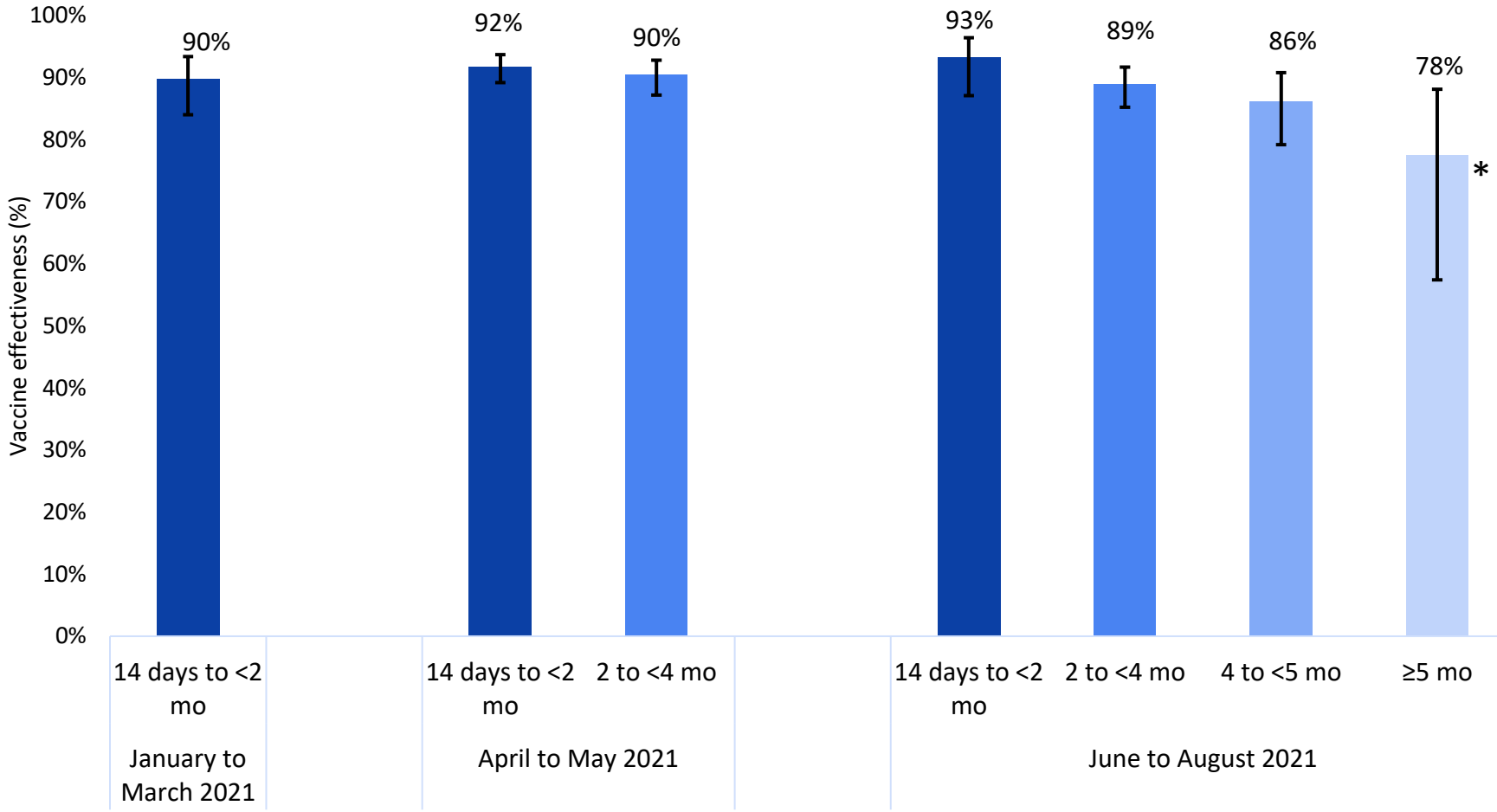
- VE for adults aged ≥18 years
- **Cases**: COVID-like illness (CLI) with positive PCR for SARS-CoV-2
- **Controls**: CLI with negative PCR for SARS-CoV-2
- VE adjusted for propensity to be vaccinated, calendar time, site-region, local virus circulation, and age
  - Waning VE models are matched on calendar week and site and restricted to six of seven VISION sites
- Vaccination documented by electronic health records and state and city registries
- Median age of cases: 65 years (IQR 48-77)

VISION Network: VE against hospitalization by time period and age group, Pfizer-BioNTech and Moderna



* p<0.05

VISION Network: Preliminary VE against hospitalization by time since vaccination in each calendar period, adults ≥18 years, mRNA products



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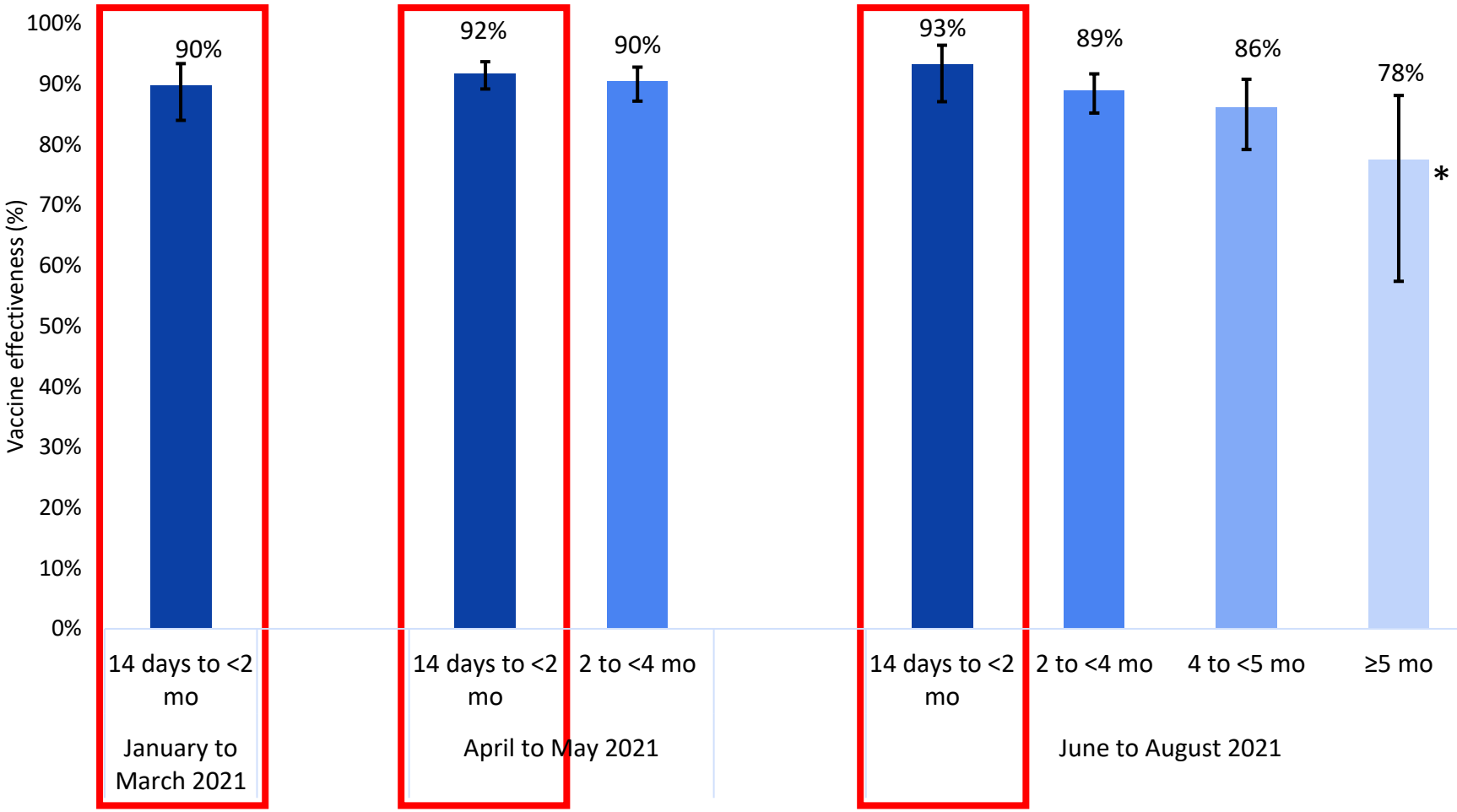
VISION Network: Preliminary VE against hospitalization by time since vaccination in each calendar period, adults ≥18 years, mRNA products



Among people recently vaccinated (<2 months), VE against hospitalization has remained high. VE has declined among those who have been vaccinated for longer periods of time.

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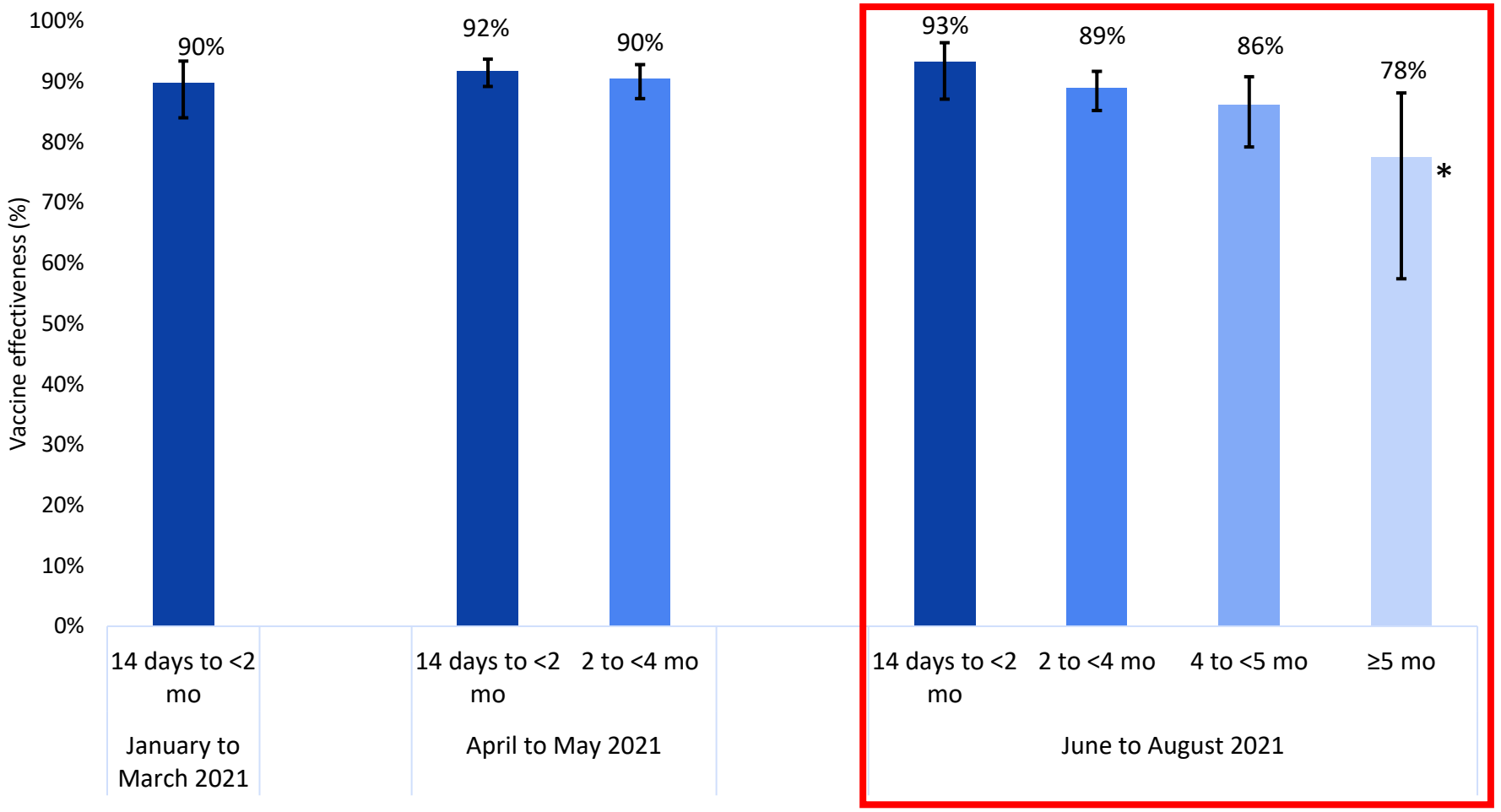
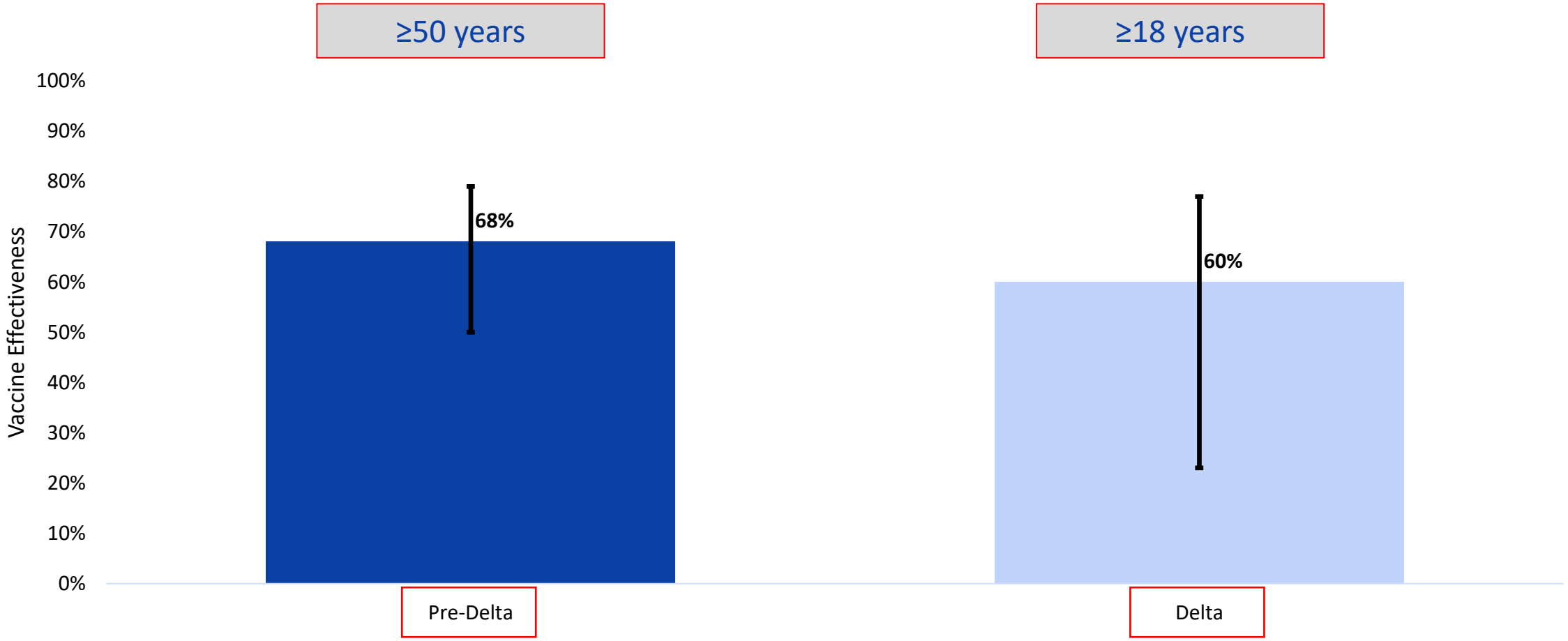
VISION Network: Preliminary VE against hospitalization by time since vaccination in each calendar period, adults ≥18 years, mRNA products



Among people recently vaccinated (<2 months), VE against hospitalization has remained high. VE has declined among those who have been vaccinated for longer periods of time.

* p<0.05 for trend

VISION Network: VE against hospitalization by time period and age group, *Johnson & Johnson/Janssen*



https://www.nejm.org/doi/full/10.1056/NEJMoa2110362
https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e2.htm

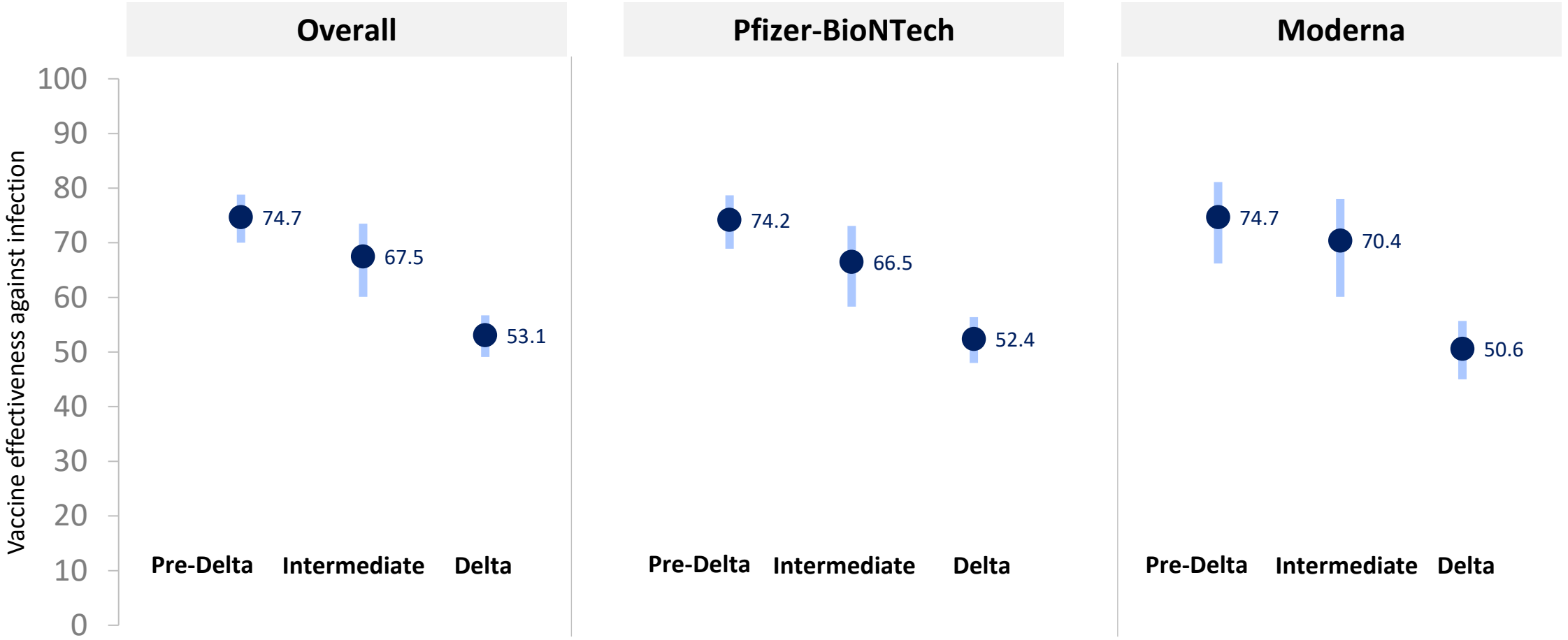
VE of mRNA vaccines against infection among nursing home residents before and during widespread Delta circulation

- Data from National Healthcare Safety Network (NHSN)
- Nursing homes report weekly aggregate number of residents and cases by vaccination status (product and number of doses received) to NHSN
- VE estimated for three periods:
  1) Pre-Delta (March 1–May 9)
  2) Intermediate (May 10–June 20)
  3) Delta (June 21–August 1)

	Pre-Delta (Mar 1–May 9)	Intermediate (May 10–Jun 20)	Delta (Jun 20–Aug 1)
No. of weekly reports	17,407	33,160	85,593
No. of facilities	3,862	11,581	14,917

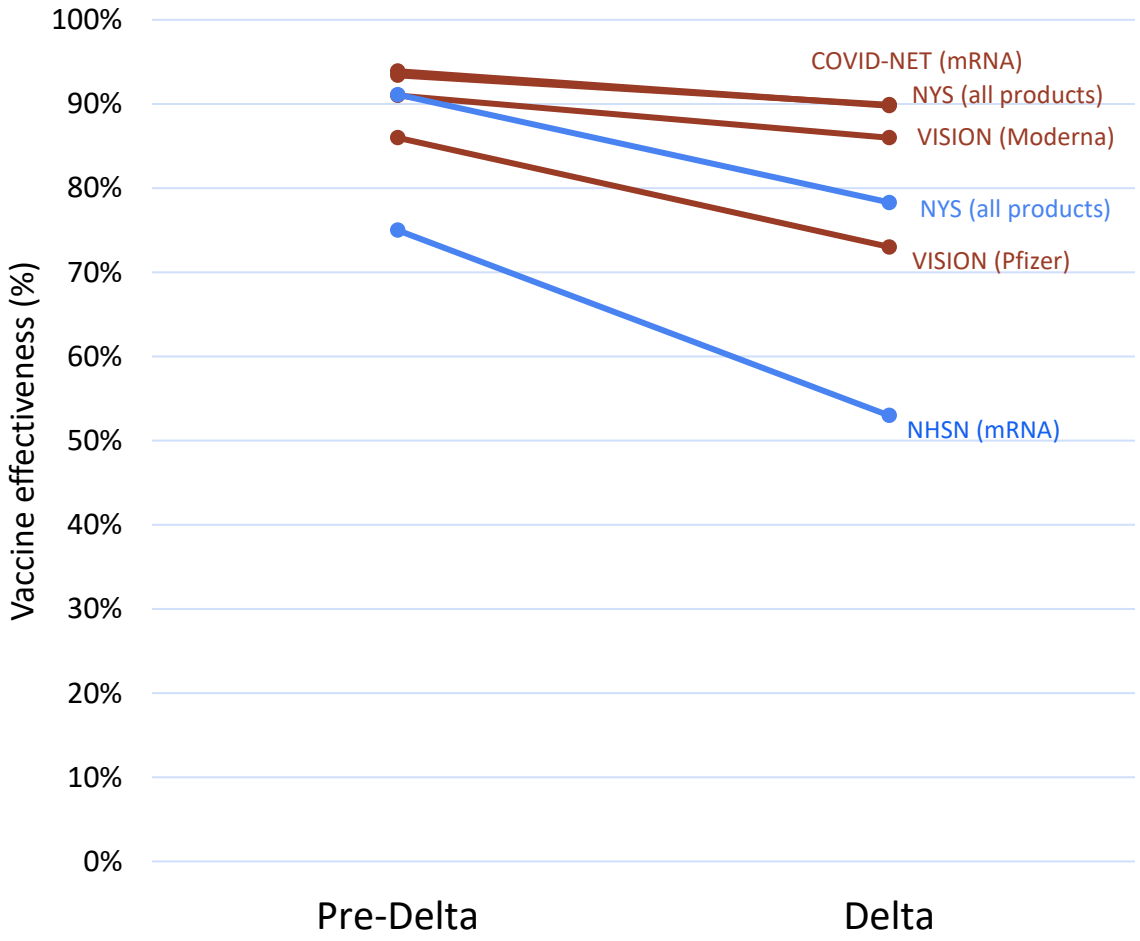
Nanduri et al. *MMWR*: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e2.htm

NHSN: VE against infection during Delta period differed significantly from pre-Delta period



Adapted from: Nanduri S. Effectiveness of Pfizer-BioNTech and Moderna Vaccines in Preventing SARS-CoV-2 Infection Among Nursing Home Residents Before and During Widespread Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant — National Healthcare Safety Network, March 1–August 1, 2021. MMWR Morbidity and Mortality Weekly Report. 2021 2021;70. Slide courtesy of Ian Plumb.

Magnitude of VE against infection or hospitalization by Delta predominance for adults ≥65 years of age, by study



- Decline of 15–25 percentage points for point estimates against infection
- Hospitalization data mixed
  - Larger decline for Pfizer-BioNTech (VISION)
  - Smaller declines for combined mRNA products and Moderna alone

NHSN: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e3.htm
COVID-NET: CDC unpublished VISION: CDC unpublished

Vaccine effectiveness for adults with underlying medical conditions

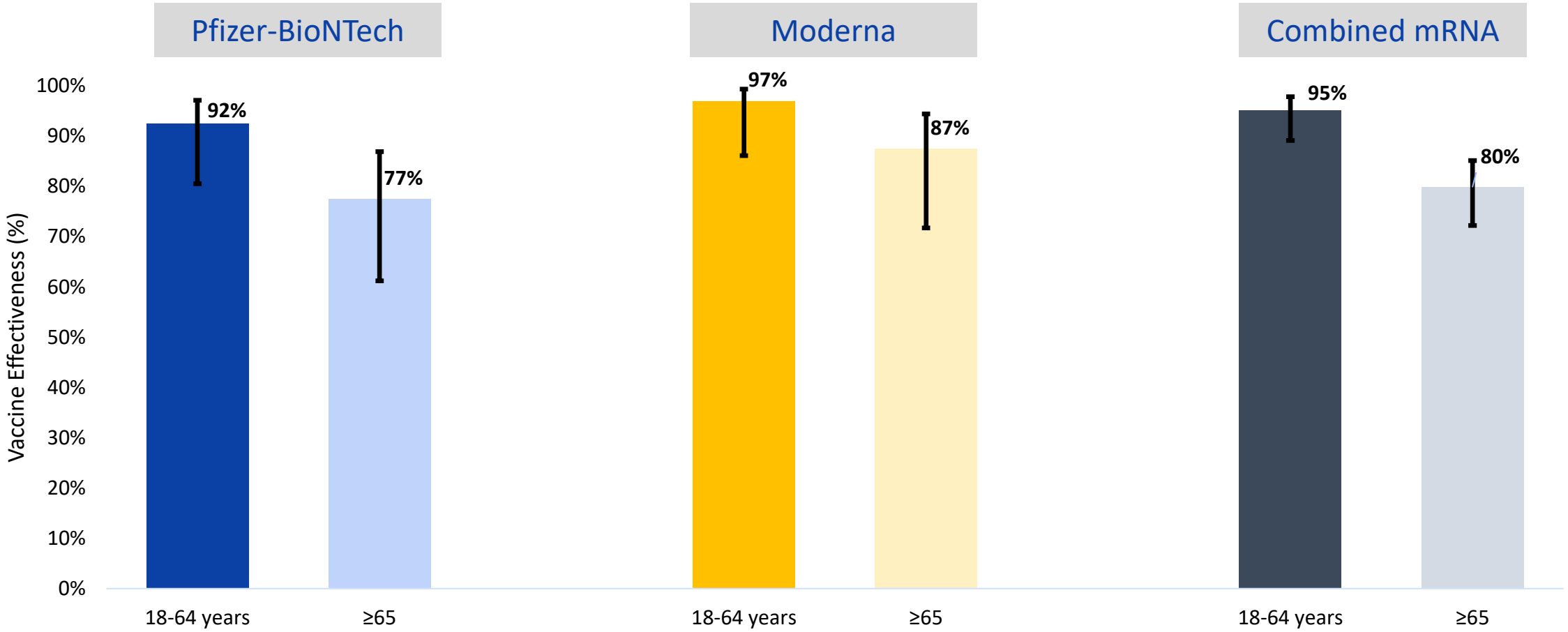
Vaccine effectiveness of mRNA vaccines against COVID-19-associated hospitalization: SUPERNOVA Network

- **Design**: Test-negative, case-control assessment
- **Period**: February 1–August 6, 2021
- **Population**: U.S. Veterans (aged ≥18 years) hospitalized at 5 Veterans Administration Medical Centers
- **Participants**
  - Cases: COVID-like illness (CLI) and SARS-CoV-2-positive test results by RT-PCR
  - Controls: CLI and SARS-CoV-2-negative test results by RT-PCR
- **Demographics:**
  - Median age: 68 years
  - 49% Black, non-Hispanic
  - 44% with Charlson Comorbidity Index score ≥3
    - 70% hypertension; 47% obesity; 43% diabetes

SUrveillance **P**latform for **E**nteric and **R**espiratory i**N**fectious **O**rganisms at the **VA**

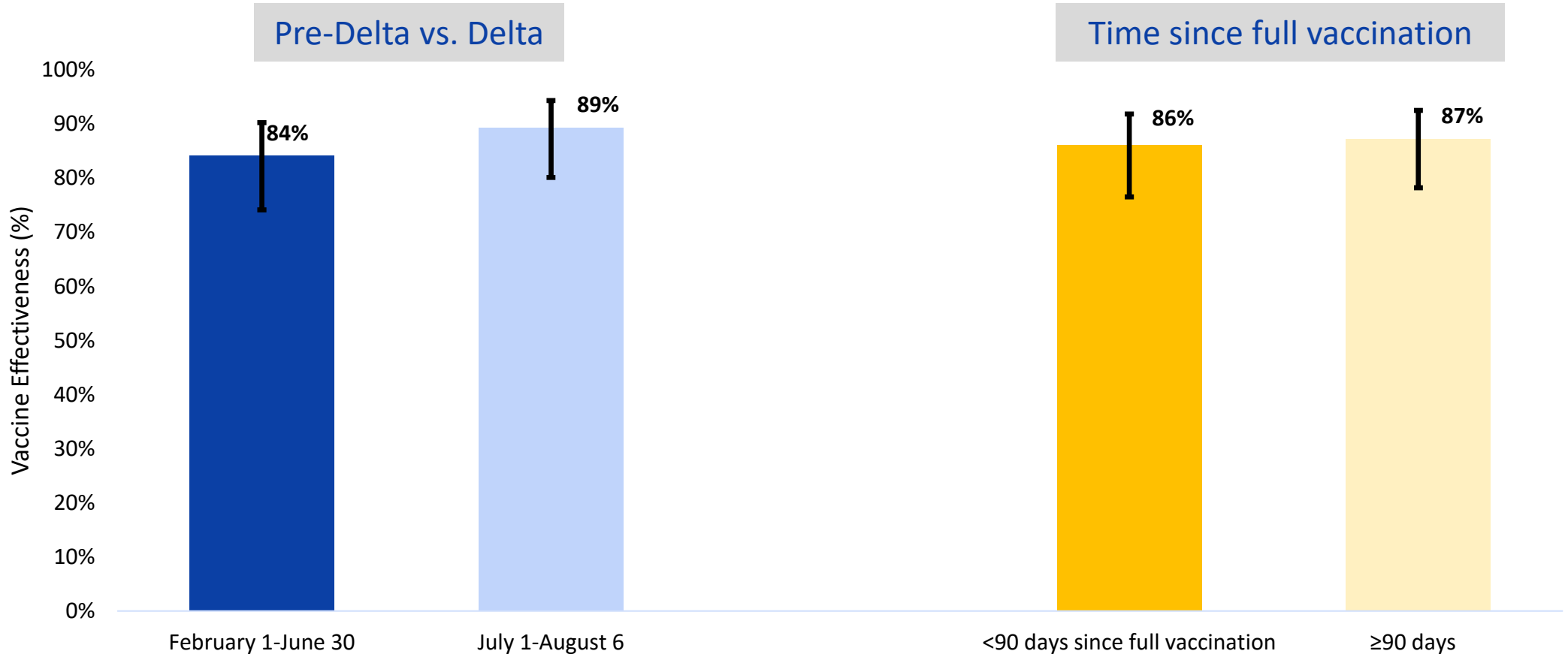
https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e3.htm

SUPERNOVA: VE against COVID-19-associated hospitalization, by mRNA vaccine



https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e3.htm

SUPERNOVA: mRNA VE against COVID-19-associated hospitalization, by Delta variant predominance and time since vaccination



https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e3.htm

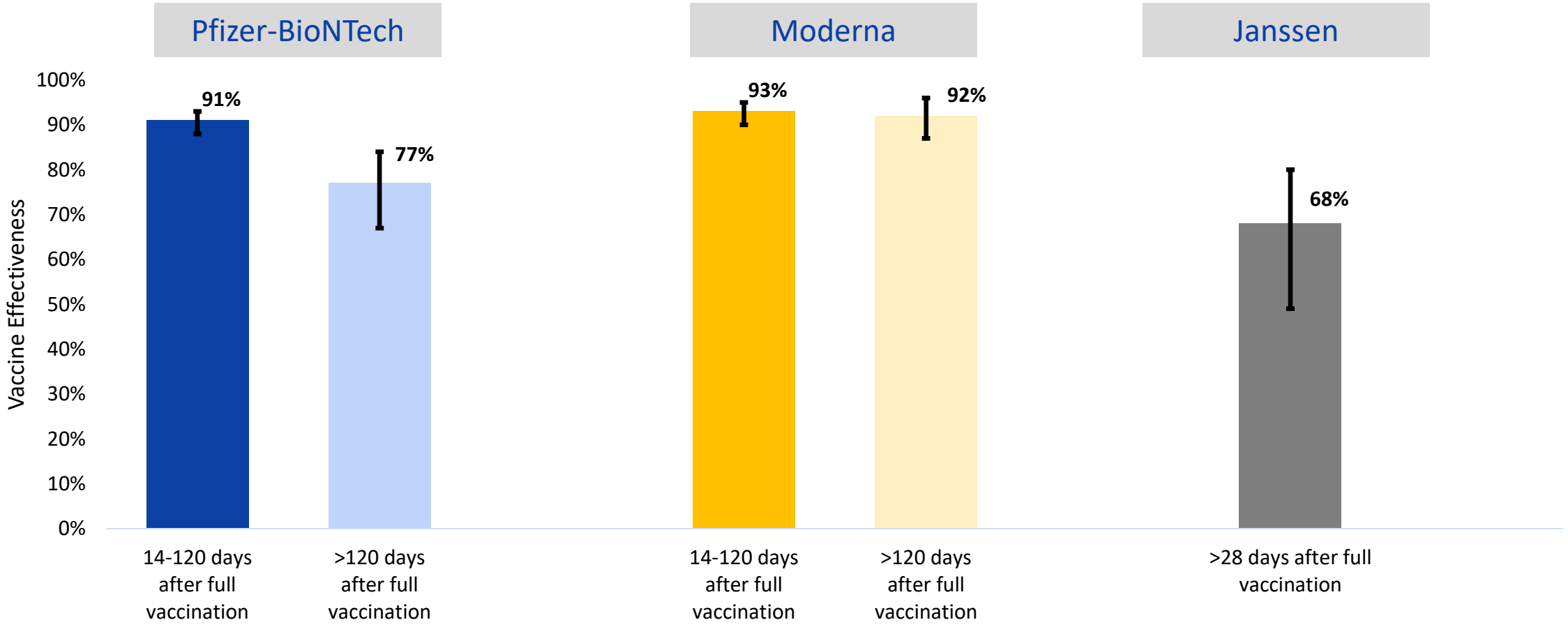
Effectiveness of mRNA vaccines for preventing COVID-19 hospitalization, IVY Network

IVY
INFLUENZA AND OTHER VIRUSES IN THE ACUTELY ILL

- **Population**: Adults (≥18 years) hospitalized at 21 medical centers in 18 states
- **Case status**:
  - Cases with COVID-19-like illness and SARS-CoV-2 antigen / RT-PCR (+)
  - Controls: SARS-CoV-2 RT-PCR (-)
- SARS-CoV-2 testing within 10 days of admission, and admission within 14 days of illness onset
- **Analytic period**: Admitted March 11–August 15, 2021

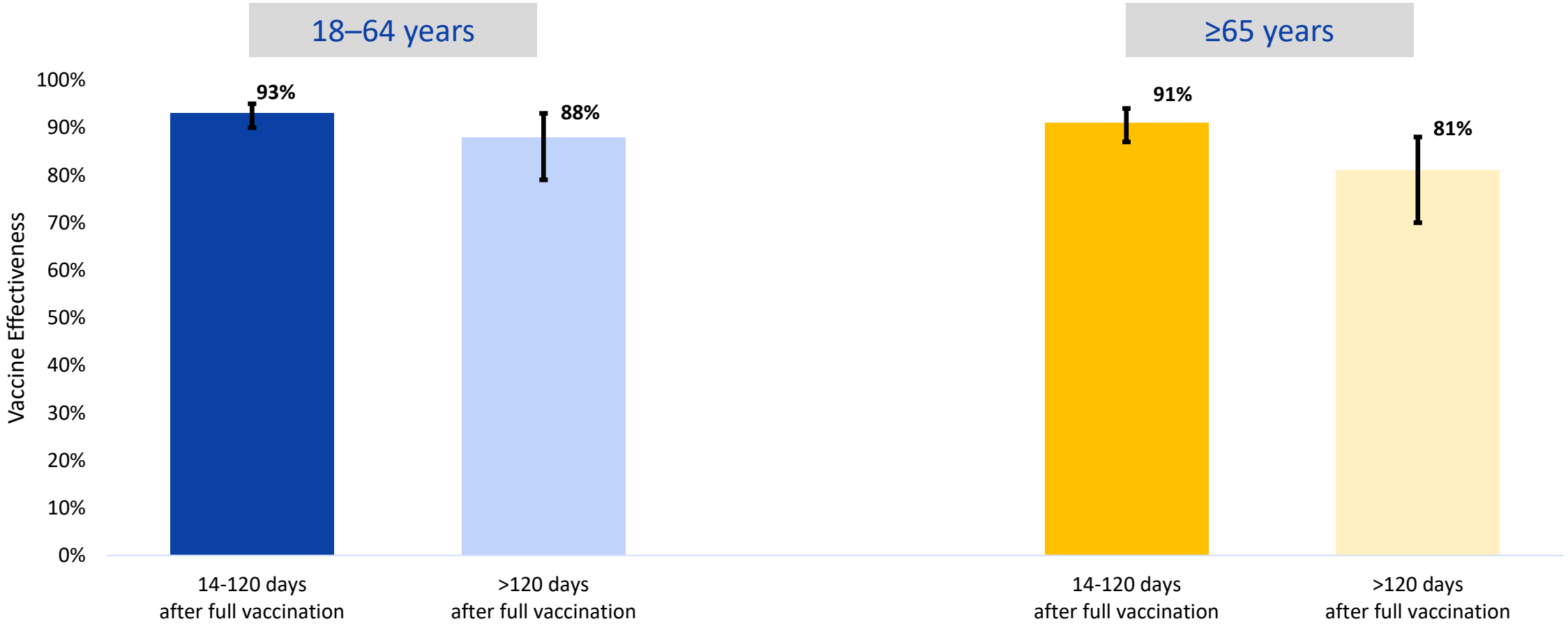
Tenforde et al. *MMWR* https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e2.htm

IVY Network: COVID-19 vaccine effectiveness against hospitalization by vaccine product and time since vaccination, adults ≥18 years without immunocompromising conditions

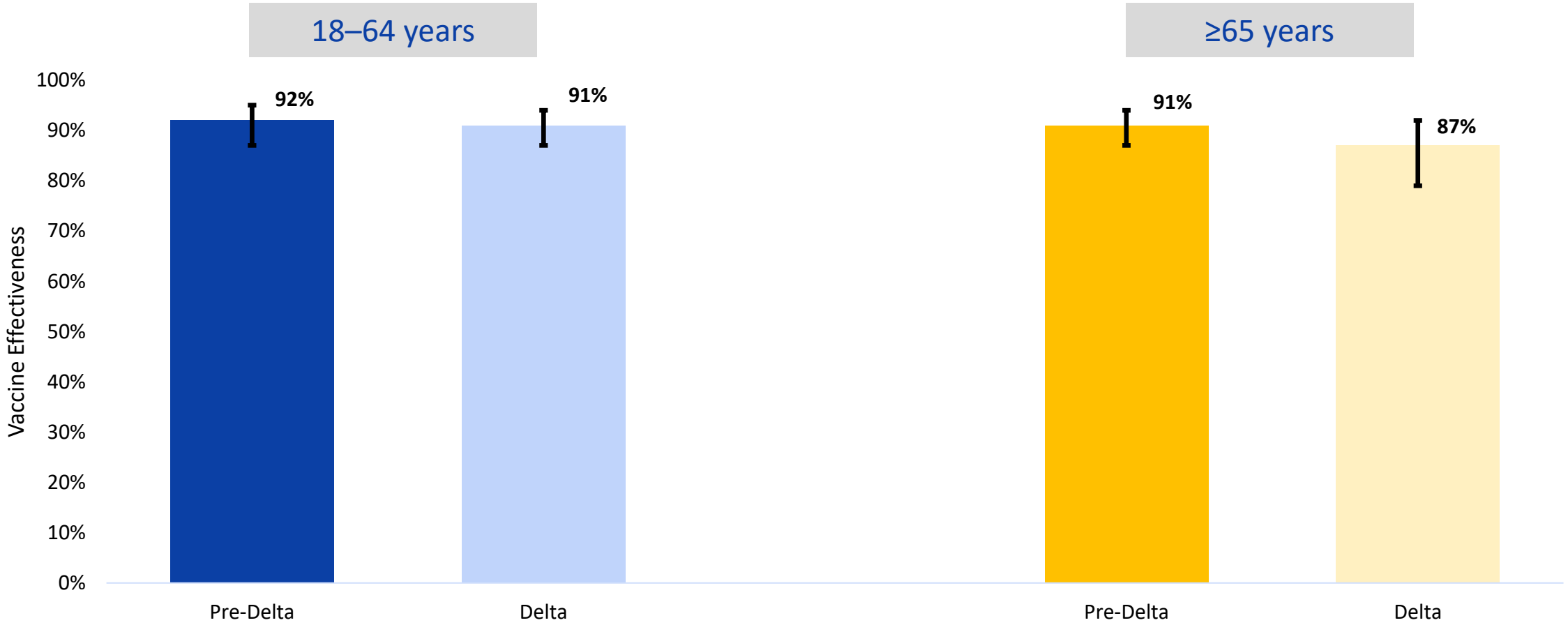


* Adjusted for admission date (biweekly), HHS region, age, sex, race/ethnicity. Not enough recipients of Janssen to assess by time since vaccination.

IVY Network: COVID-19 vaccine effectiveness against hospitalization by age group and time since vaccination, adults without immunocompromising conditions, mRNA vaccines

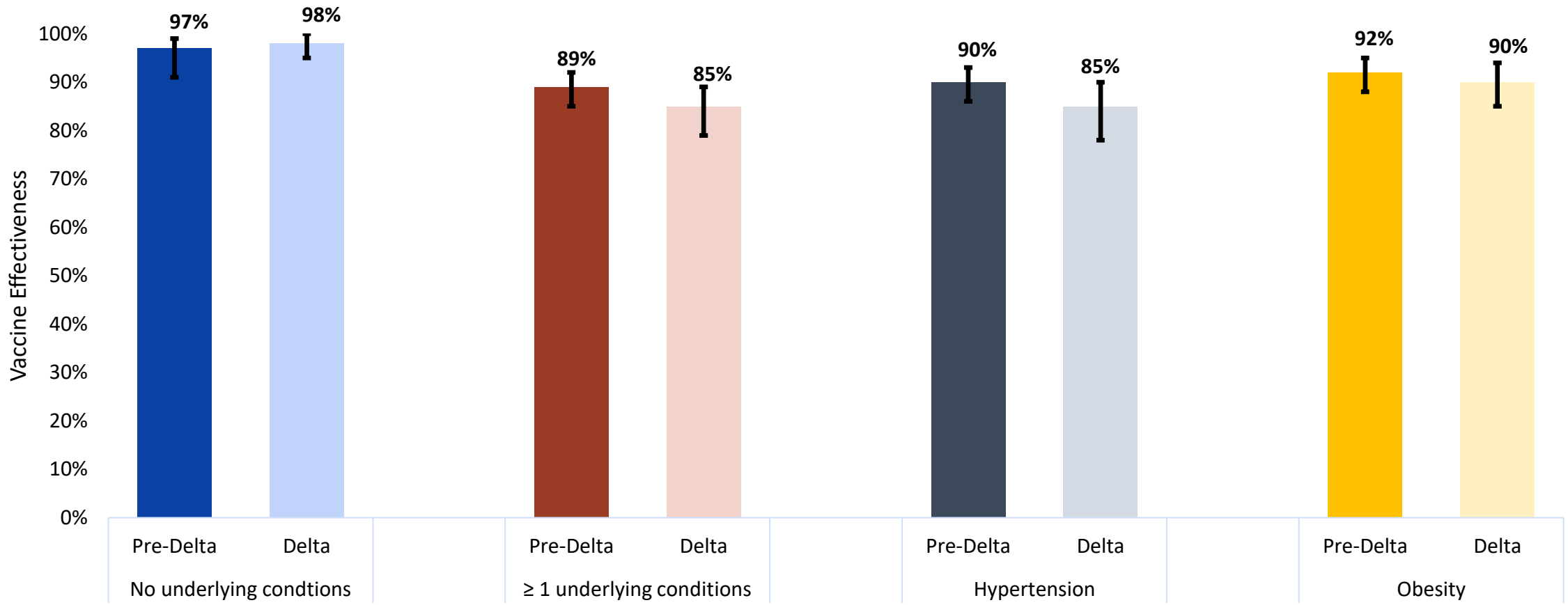


IVY Network: COVID-19 vaccine effectiveness against hospitalization by age group and Delta predominance, adults without immunocompromising conditions, mRNA vaccines



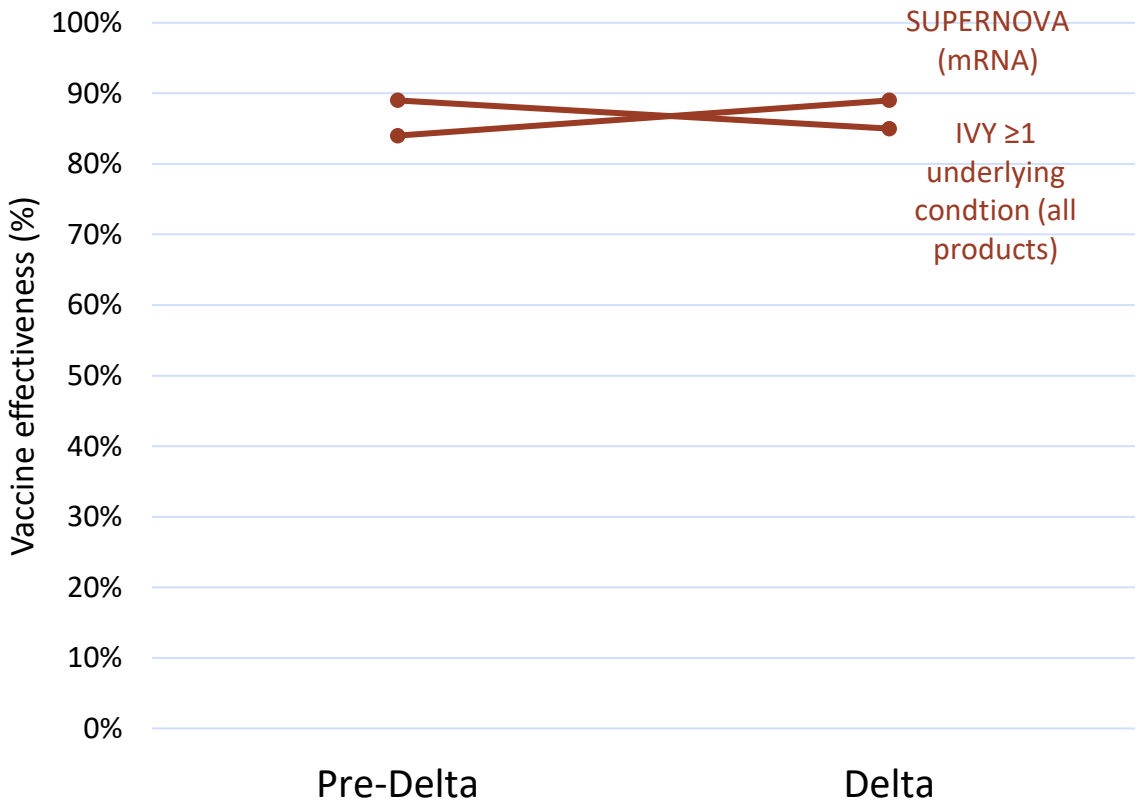
https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e2.htm

IVY Network: COVID-19 mRNA vaccine effectiveness against hospitalization among adults by risk group and Delta predominance, excluding patients with immunocompromising conditions



CDC unpublished; estimates are controlled for age.

Magnitude of VE against infection or hospitalization by Delta predominance for adults with underlying medical conditions, by study

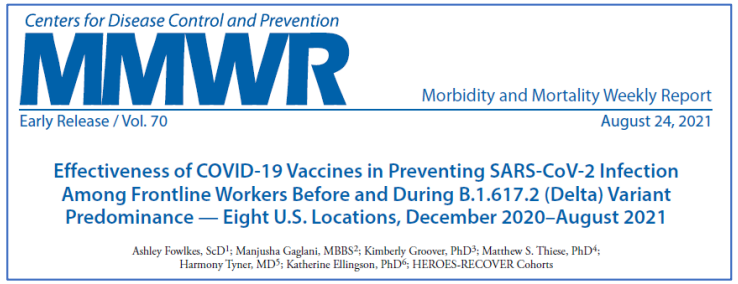


- No VE estimates available for infection
- VE estimates for hospitalization, remain high during Delta

SUPERNOVA: https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e3.htm
IVY: CDC unpublished data

Vaccine effectiveness for workers employed in occupations with high risk of exposure to SARS-CoV-2

HEROES-RECOVER Cohorts


Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 70
August 24, 2021

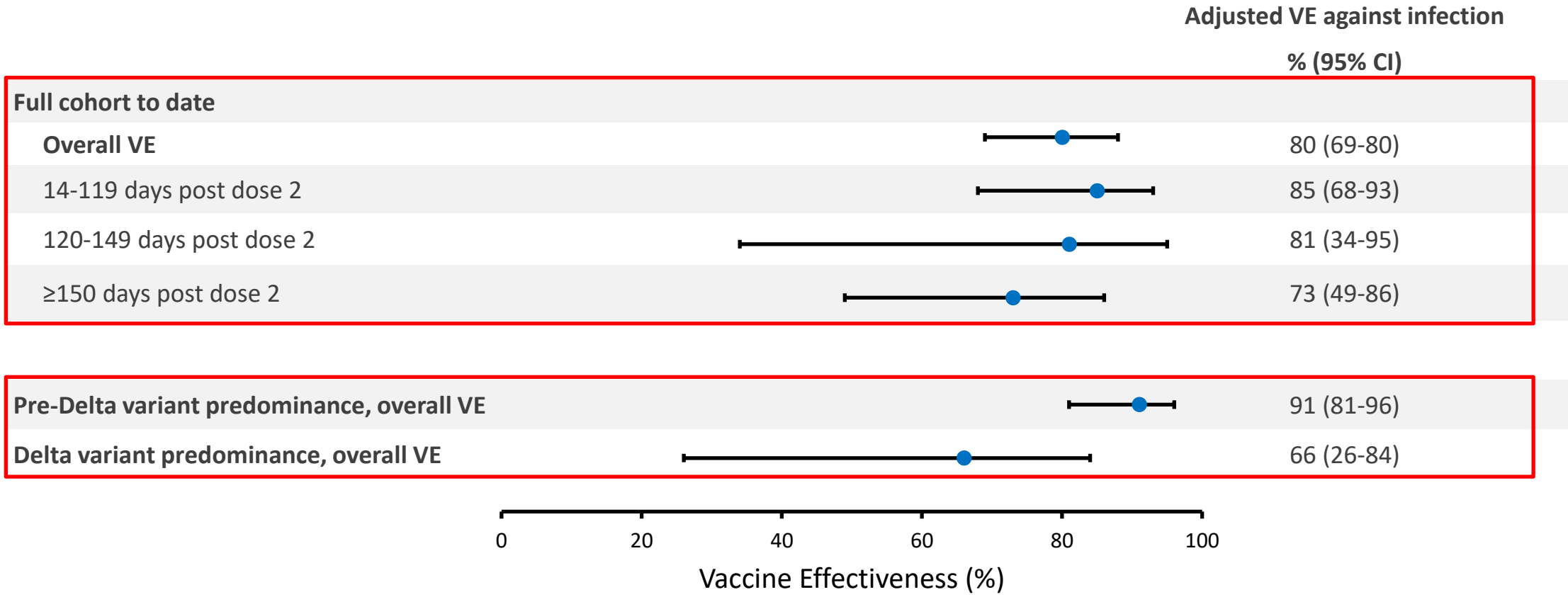
Effectiveness of COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Frontline Workers Before and During B.1.617.2 (Delta) Variant Predominance — Eight U.S. Locations, December 2020–August 2021

Ashley Fowlkes, ScD[1]; Manjusha Gaglani, MBBS[2]; Kimberly Groover, PhD[3]; Matthew S. Thiese, PhD[4]; Harmony Tyner, MD[5]; Katherine Ellingson, PhD[6]; HEROES-RECOVER Cohorts

- Prospective cohort of over 4,000 **healthcare personnel, first responders, and other frontline workers in 8 U.S. locations**
- VE of full vaccination in preventing symptomatic and asymptomatic SARS-CoV-2 infection
  - Routine weekly swabbing plus illness specimens
  - Multi-method vaccination documentation; 95% mRNA vaccines
  - Hazard person-time model adjusted for study site, occupation, and local virus circulation and weighted for propensity to be vaccinated (socio-demographics, health, frequency of close contact and mask use)
  - 62% female; 72% aged 18–49 years; 31% with ≥1 underlying medical condition

https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e4.htm

HEROES/RECOVER: VE against SARS-CoV-2 infection by Delta variant predominance and time since full vaccination

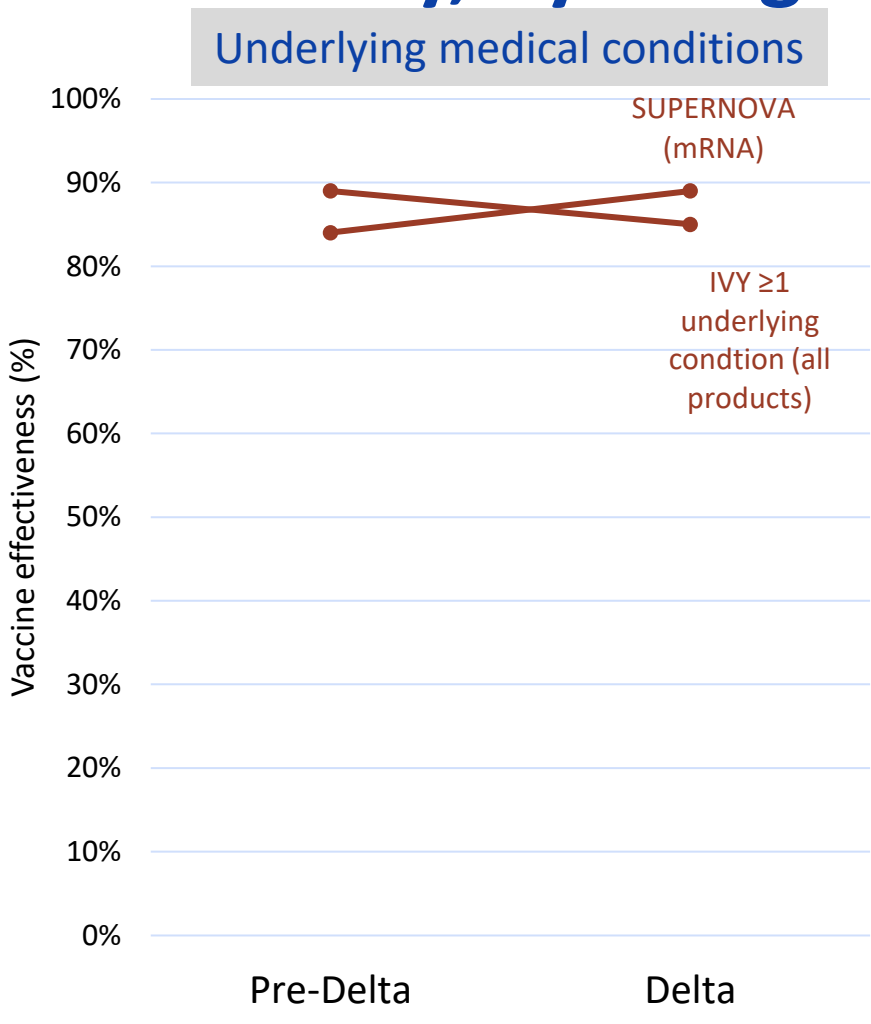


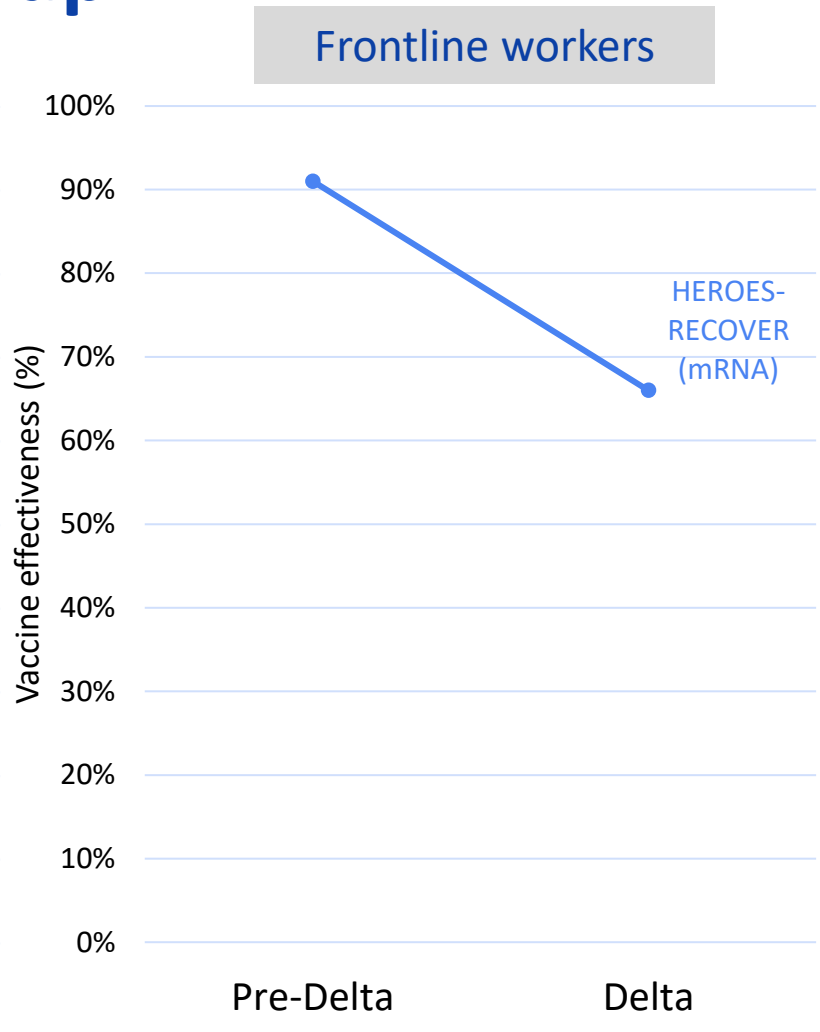
- VE against infection (80% symptomatic) declined from 91% pre-Delta to 66% during Delta
- Did not have enough power to look at time since vaccination pre-Delta and during Delta
- Do not see significant difference between mRNA products

https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e4.htm

Summary and conclusions

Magnitude of VE against infection or hospitalization by Delta predominance and study, by risk group





NHSN: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e3.htm
COVID-NET: CDC unpublished
IVY: CDC unpublished data
NYS: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e1.htm

VISION: https://www.nejm.org/doi/10.1056/NEJMoa2110362/ https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e2.htm
SUPERNOVA: https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e3.htm
HEROES-RECOVER: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e4.htm

Summary & conclusions

- Individuals ≥65 years of age
  - Significant declines in VE against infection for mRNA products in during Delta-variant predominant period
  - Declines for hospitalization (with Pfizer-BioNTech greater than Moderna) in Delta-variant predominant period
  - Evidence of waning in Delta-variant predominant period

- Individuals with underlying conditions
  - No data on VE against infection; likely similar to overall population
  - Similar patterns for VE for hospitalization as in general adult population

- Occupations with high risk of exposure to SARS-CoV-2
  - No data on VE against hospitalization; likely similar to overall population
  - Similar patterns for VE for infection as in general adult population

Acknowledgements

- New York State Health Department
  - Eli Rosenberg and co-authors
- Site PIs and teams for IVY, VISION, Signature, NHSN, HEROES/RECOVER, SUPERNOVA, COVID-NET

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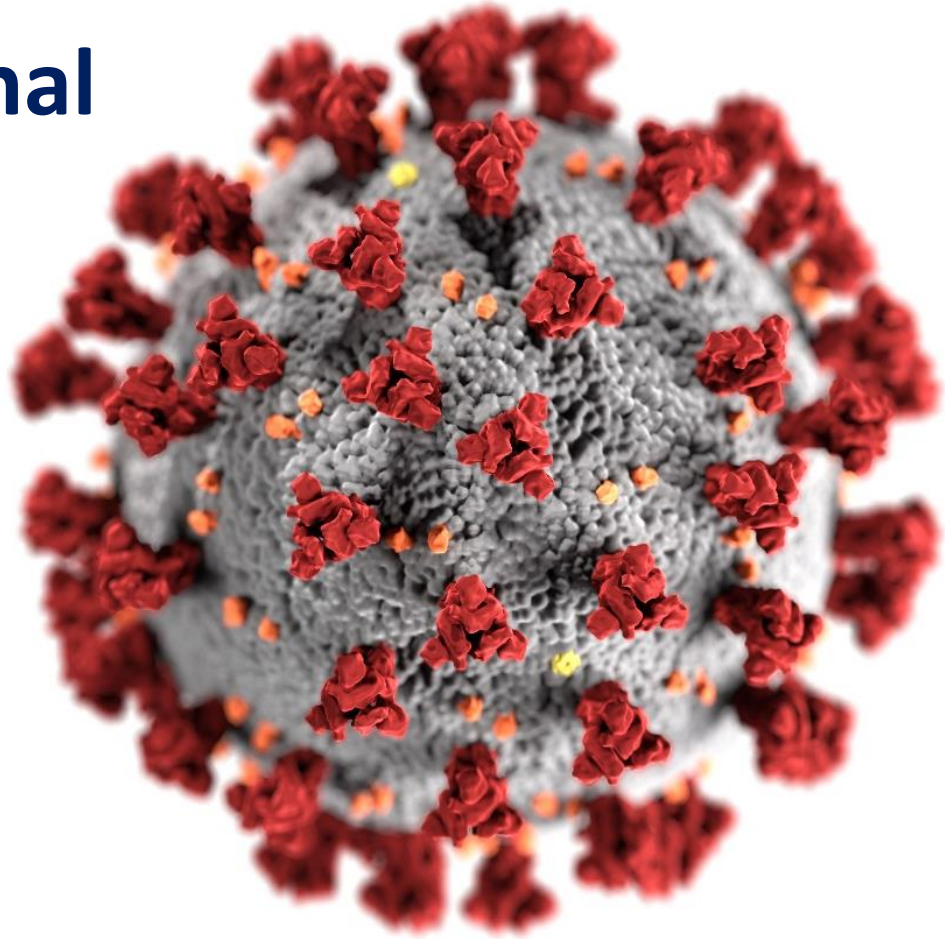
  - Jessica Smith
  - Manish Patel

Early safety monitoring for additional COVID-19 vaccine doses: Reports to VAERS and v-safe

Clinician Outreach and Communication Activity

September 28, 2021

Anne M. Hause, PhD MSPH
v-safe Team Co-Lead
COVID-19 Vaccine Task Force



cdc.gov/coronavirus

CDC vaccine safety monitoring

- COVID-19 vaccines are being administered under **the most intensive vaccine safety monitoring effort in U.S. history**
- Strong, complementary systems are in place—both new and established

v-safe

VAERS

VSD

CISA Project

Full list of U.S. COVID-19 vaccine safety monitoring systems

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html

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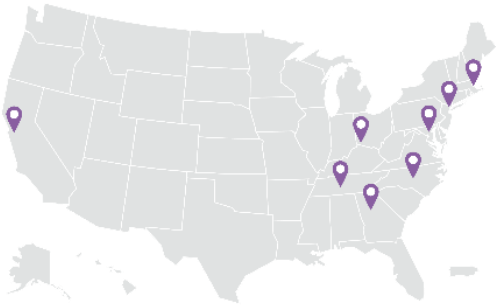


Full list of U.S. COVID-19 vaccine safety monitoring systems

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html

VAERS is the nation's early warning system for vaccine safety

CDC + FDA

VAERS

Vaccine Adverse Event Reporting System

http://vaers.hhs.gov

VAERS accepts reports from everyone

Regardless of the plausibility of the vaccine causing the event or the clinical seriousness of the event

Key strengths

- Rapidly detects potential safety problems
- Can detect rare adverse events

Key limitations

- Inconsistent quality and completeness of information
- Reporting biases
- Generally, cannot determine cause and effect

Reports to VAERS following dose 3 of mRNA COVID-19 vaccination, by age group and sex

Age group, years	n (%)
12–17	48 (2)
18–49	622 (24)
50–64	654 (26)
≥65	1,239 (48)
Total	**2,563**

Sex	n (%)
Male	979 (38)
Female	1,570 (61)
Unknown	14 (1)
Total	**2,563**

- Median age 64 years (range: 12–100)
- Most reports (61%) among women

Includes data collected during December 14, 2020–September 17, 2021

Reports to VAERS following dose 3 of mRNA COVID-19 vaccination, by race and ethnicity

- Most reports either
  - Unknown/not reported race or ethnicity (49%)
  - White, non-Hispanic race and ethnicity (39%)

Race or ethnicity	Reports (%)
Hispanic or Latino	143 (6)
Non-Hispanic	
AI/AN	11 (<1)
Asian	51 (2)
Black or African American	89 (3)
NHPI	1 (<1)
White	998 (39)
Multiracial	14 (1)
Other	8 (<1)
Unknown/not reported	1,248 (49)
Total	**2,563**

Includes data collected during December 14, 2020–September 17, 2021 for persons aged 12 years and older. Hispanic also includes persons identified of Hispanic ethnicity of unknown race. Abbreviations: AI/AN = American Indian/Alaska Native; NHPI = Native Hawaiian or other Pacific Islander.

Reports to VAERS following dose 3 of mRNA COVID-19 vaccination

Manufacturer	Non-serious	Serious	Total
Pfizer-BioNTech	1,175 (95%)	68 (5%)	1,243
Moderna	1,257 (95%)	63 (5%)	1,320
Total	**2,432 (95%)**	**131 (5%)**	**2,563**

- Regardless of manufacturer, 95% of reports non-serious

Includes data collected during December 14, 2020–September 17, 2021 for persons aged 12 years and older.
Per federal law, includes reports of hospitalization, prolongation of existing hospitalization, life threatening condition, permanent disability, congenital deformity or birth defect, or death

Most frequently reported adverse events to VAERS following dose 3 of mRNA COVID-19 vaccination, by seriousness

Serious (n = 131)

Rank	Adverse event*	n (%)
1	Extra dose administered	40 (31)
2	Fever	27 (21)
3	Dyspnea	23 (18)
4	Death	18 (14)
5	Fatigue	14 (11)

Non-serious (n= 2,432)

Rank	Adverse event*	n (%)
1	Extra dose administered	945 (39)
2	Fever	323 (13)
3	Headache	274 (11)
4	Fatigue	269 (11)
5	No adverse event	243 (10)

Includes data collected during December 14, 2020–September 17, 2021 for persons aged 12 years and older. Per federal law, includes reports of hospitalization, prolongation of existing hospitalization, life threatening condition, permanent disability, congenital deformity or birth defect, or death.

* Not mutually exclusive

Reports of death to VAERS following dose 3 of mRNA COVID-19 vaccination

- Median age = 76 years (range: 47–93)
- Median time from third dose to death = 1 day (range: 0 – 12)

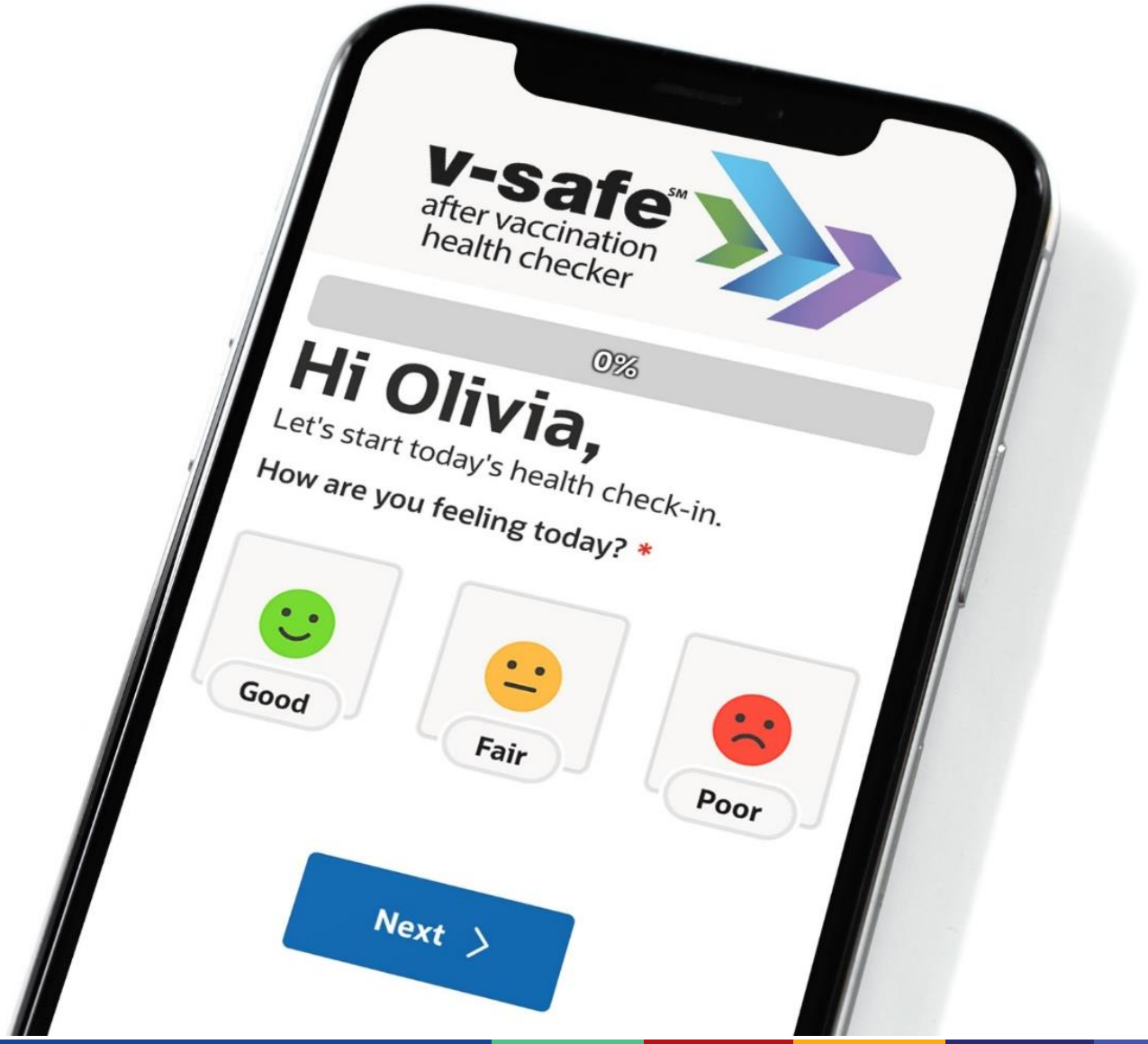
Preliminary impression of cause of death*	Reports
Respiratory and/or cardiac arrest	7
Unable to assess	4
Pulmonary embolism	2
Sepsis	1
Accident/trauma	1
Cancer	1
COVID-19 pneumonia	1
Total	**18**

Includes data collected during December 14, 2020–September 17, 2021

* Based upon physician review of initial report and available documentation, including death certificates

Smartphone-based active safety monitoring

v-safe[SM]
after vaccination
health checker



http://cdc.gov/vsafe

Active safety monitoring for COVID-19 vaccines

v-safe is a CDC smart phone based monitoring program for COVID-19 vaccine safety

- Uses text messaging and web surveys to check in with vaccine recipients after vaccination
- Can register at any time: after first, second, or third dose
- Solicits participants' reports on how they feel after COVID-19 vaccination
  - Local injection site reactions (i.e., pain, redness, swelling)
  - Systemic reactions (i.e., fatigue, headache, joint pain)
  - Health impacts (unable to perform normal daily activities, missed school or work, or received care)

v-safe after vaccination health checker

Demographic summary of 22,191 v-safe participants who reported an additional dose

Characteristic	% of participants
Sex	
Female	63.3
Male	35.7
Unknown	1.0
Age group (years)	
0-17	0.3
18-49	29.1
50-64	29.8
65-74	30.5
75-84	9.5
≥85	0.9

Characteristic	% of participants
Ethnicity	
Hispanic or Latino	8.2
Not Hispanic/ Latino	87.6
Unknown	4.2
Race	
AI/AN	0.5
Asian	5.6
Black or AA	5.9
NHPI	0.3
White	81.4
Multiracial	1.9
Other	2.1
Unknown	2.4

Includes participants who completed at least one survey in the first week after additional dose, data collected during August 12–September 19, 2021
Abbreviations: AI/AN = American Indian/Alaska Native; NHPI = Native Hawaiian or other Pacific Islander; AA=African American.

Patterns of vaccination for 22,191 v-safe participants who reported an additional dose

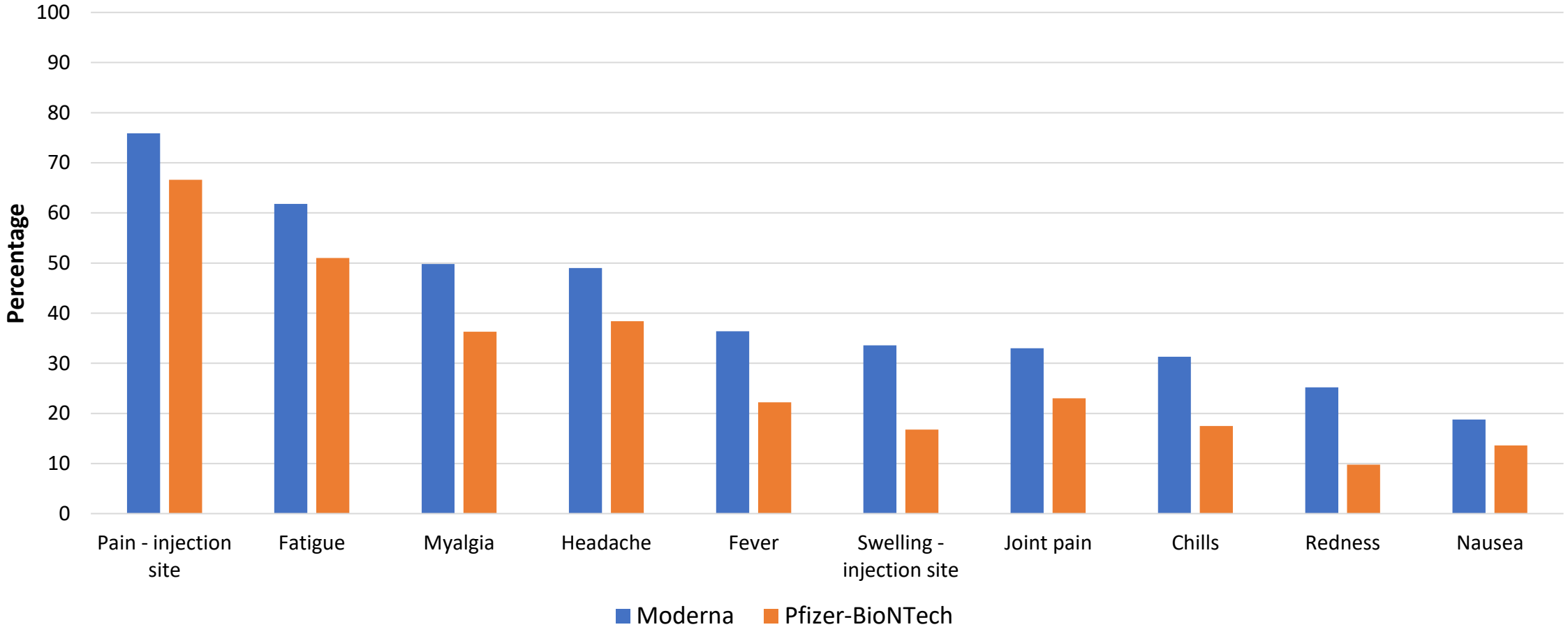
Primary series

Additional dose	Moderna (%)	Pfizer-BioNTech (%)	Janssen (%)*	Total
Moderna	**10,453 (98.6)**	197	64	10,714
Pfizer-BioNTech	144	**11,209 (98.2)**	66	11,419
Janssen	4	6	**48 (27.0)**	58
Total	10,601	11,412	178	**22,191**

Includes participants who completed at least one survey in the first week after additional dose, data collected during August 12–September 19, 2021

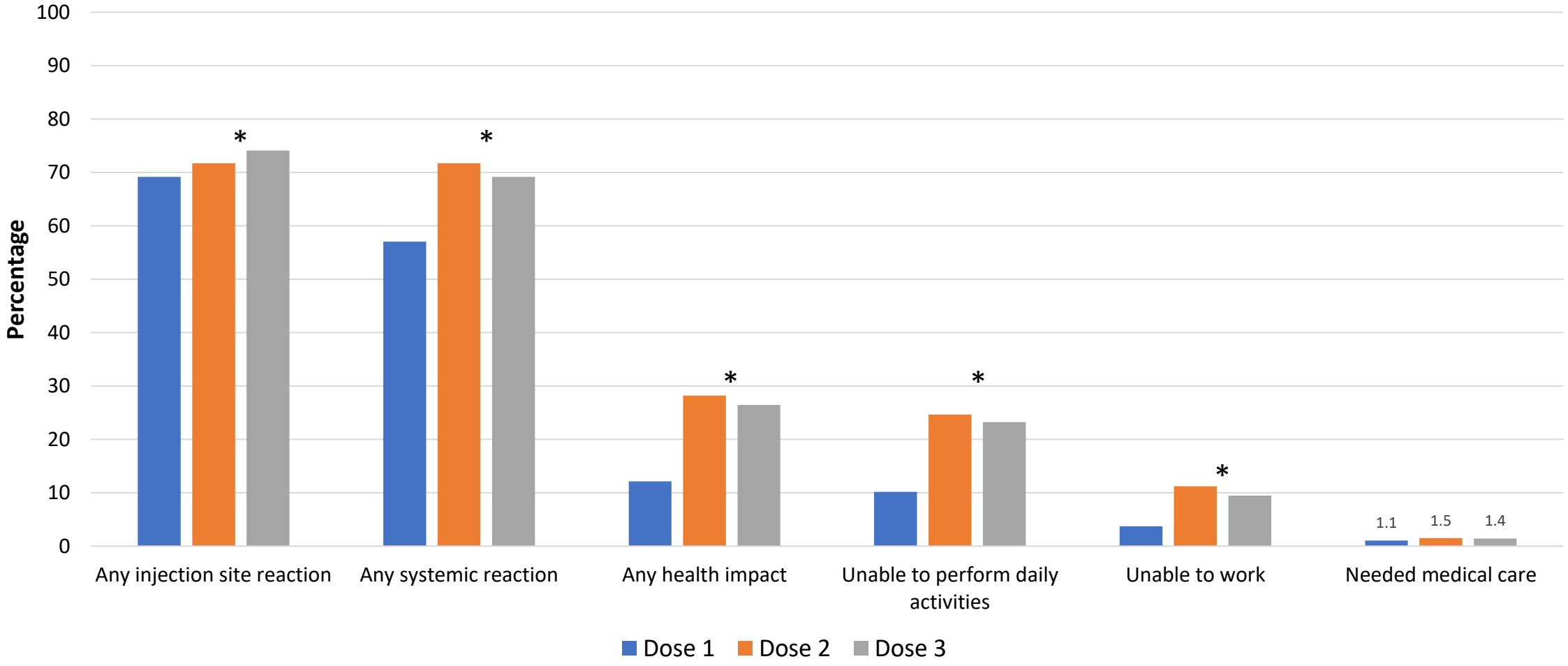
* Includes persons who received Janssen as their primary series and one additional dose of vaccine from the listed manufacturers

Top 10 solicited reactions reported at least once 0-7 days after dose 3 of Moderna or Pfizer-BioNTech vaccine



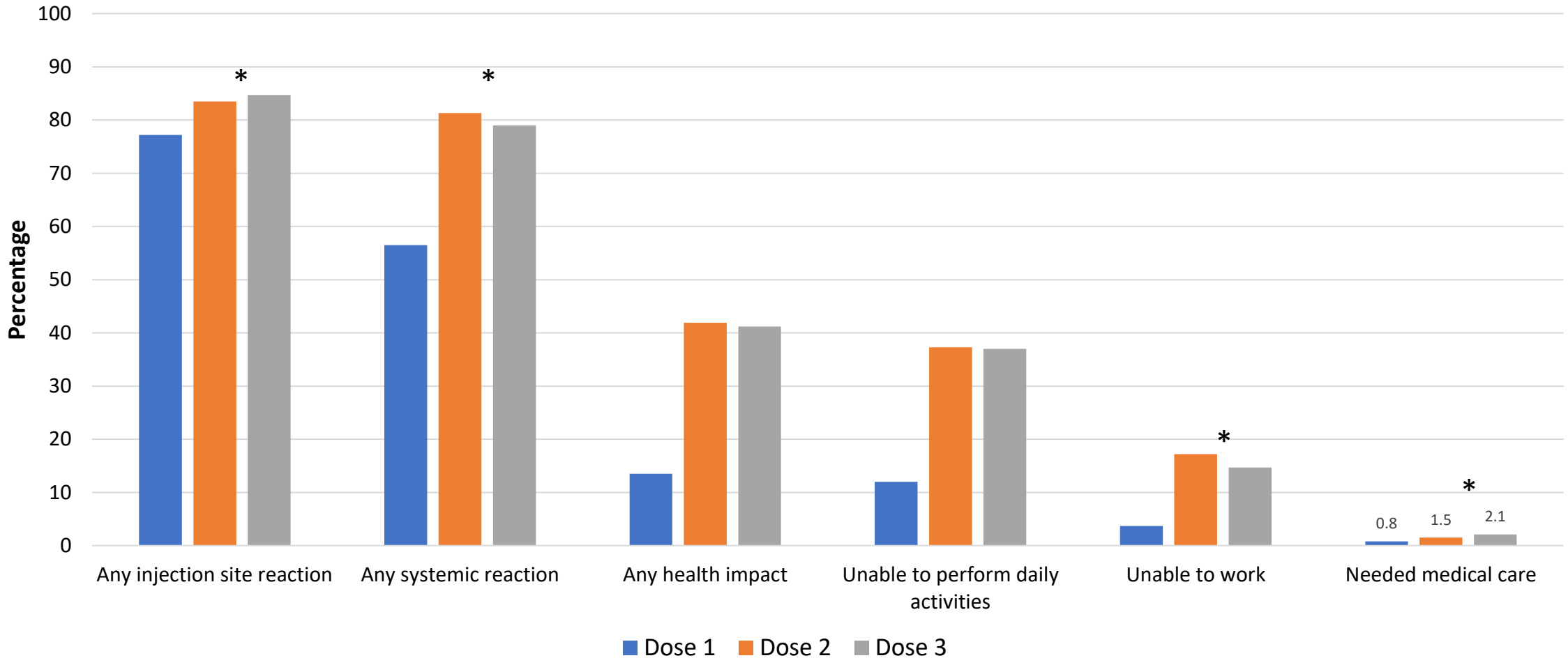
Includes 22,191 participants who completed at least one survey in the first week after additional dose, data collected during August 12–September 19, 2021

Reactions and health impact events reported at least once in days 0-7 after Pfizer-BioNTech vaccination, by dose



Includes 6,308 participants who completed at least one survey in the first week after each dose, data collected during August 12–September 19, 2021
* Statistically significant difference (p-value <0.05). Odds of reporting an event following dose 2 and 3 compared using multivariable generalized estimating equations model that accounted for the correlation between registrants and adjusted for demographic variables.

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



Includes 6,283 participants who completed at least one survey in the first week after each dose, data collected during August 12–September 19, 2021
* Statistically significant difference)p-value <0.05). Odds of reporting an event following dose 2 and 3 compared using multivariable generalized estimating equations model that accounted for the correlation between registrants and adjusted for demographic variables.

Limitations of early safety monitoring for an additional COVID-19 vaccine dose

- V-safe population likely not representative of the vaccinated U.S. population
- Additional dose recipients likely included immunocompromised and non-immunocompromised persons
  - V-safe does not include information about immune status
  - Immunocompromised persons might have different reactogenicity than immunocompetent persons
- Data available now are insufficient
  - To determine patterns of adverse events after receipt of an additional dose from a manufacturer different from the primary series
  - To identify rare adverse events
- Complete medical review of deaths following vaccination reported to VAERS is dependent on availability of medical records, death certificates, and autopsy reports, which may be delayed or not available

Summary

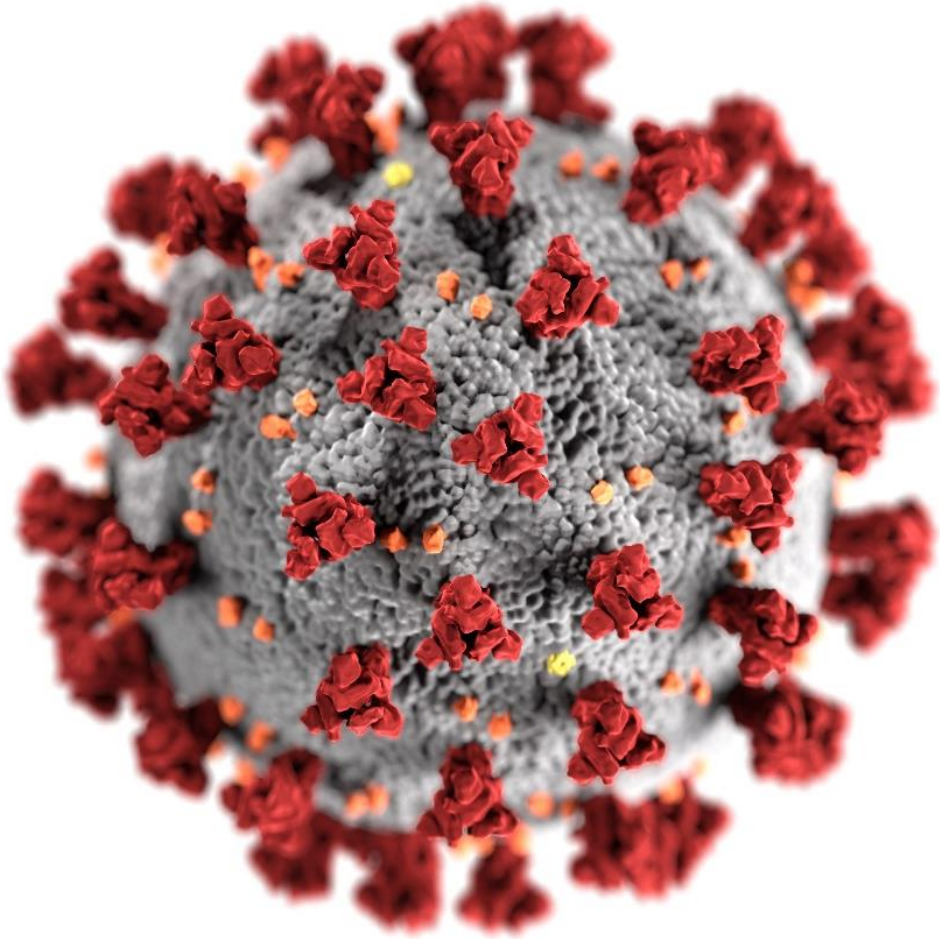
- No unexpected patterns of adverse events were identified
- 95% of VAERS reports following dose 3 of COVID-19 vaccination were non-serious
- Over 22,000 v-safe registrants reported an additional dose
  - Most reported a primary mRNA vaccine series followed by dose 3 from the same manufacturer
  - Local reactions were reported slightly more frequently and systemic reactions slightly less frequently following dose 3 than dose 2
    - Similar to Pfizer-BioNTech phase 3 clinical trial (included 306 persons)[1]

[1] https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-initiate-rolling-submission

Next steps

- VAERS and v-safe will continue to monitor safety of additional doses of COVID-19 vaccination
- The Vaccine Safety Datalink (VSD) will incorporate additional doses of COVID-19 vaccination into weekly near real-time sequential monitoring
- The Clinical Immunization Safety Assessment (CISA) Project will continue to be available to consult on clinically complex adverse events following additional dose of COVID-19 vaccination
- CDC will update the Advisory Committee on Immunization Practices as additional data become available

Interim Clinical Considerations for Pfizer-BioNTech COVID-19 Vaccine Booster Doses



Neela Goswami, MD, MPH

September 28, 2021

Context of updated CDC COVID-19 vaccine recommendations

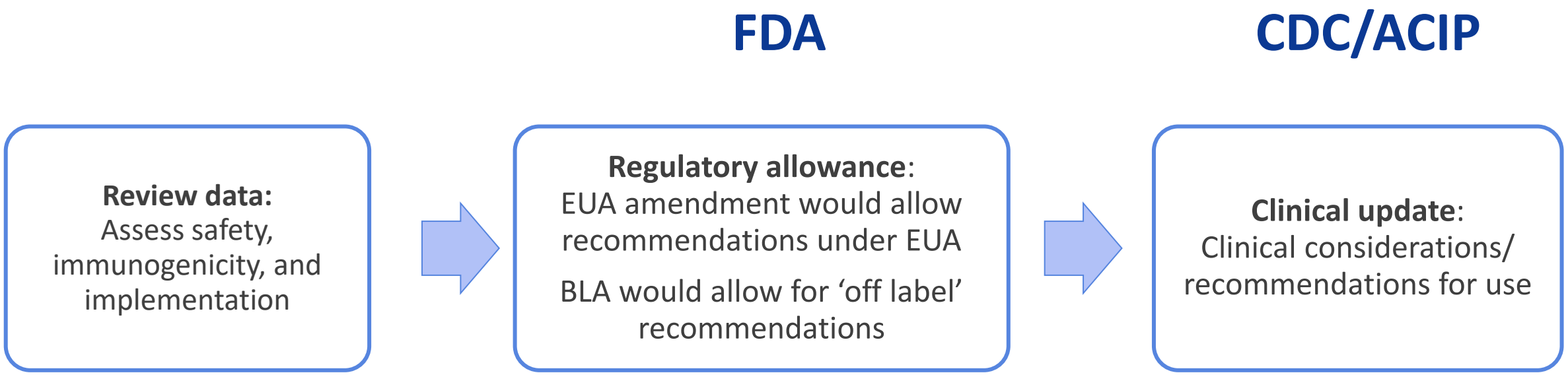
- Getting people vaccinated with a COVID-19 primary vaccine series remains the highest priority and is fundamental to reducing COVID-related morbidity and mortality
- **All COVID-19 vaccines currently approved or authorized in the United States remain effective against severe disease, hospitalization, and death**
- Persons of all ages who have received a primary vaccine series are much less likely than unvaccinated persons to become infected with SARS-CoV-2 and to require hospitalization or die because of COVID-19
- CDC's COVID-19 vaccine recommendations will be updated, as needed, to reflect changes in U.S. COVID-19 disease trends, new information on COVID-19 vaccine effectiveness and safety, and updated benefit-risk analyses

CDC's definition of 'fully vaccinated' is unchanged

For public health purposes, a person is considered fully vaccinated against COVID-19 ≥2 weeks after receipt of the second dose in a 2-dose series (Pfizer-BioNTech and Moderna) or ≥2 weeks after receipt of the single dose Janssen vaccine

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated.html

COVID-19 vaccine booster dose evaluation



FDA = Food and Drug Administration; ACIP = Advisory Committee on Immunization Practices
EUA= Emergency Use Authorization; BLA= Biologics License Application

Definitions

There are two distinct potential uses for an additional dose of COVID-19 vaccine:

- **Additional dose after a primary vaccine series**: administration of an additional vaccine dose when the initial immune response following a primary vaccine series is likely to be insufficient. An additional mRNA COVID-19 vaccine dose is recommended for moderately to severely immunocompromised people at least 28 days after an initial 2-dose mRNA primary vaccine series.

- **Booster dose:** an additional dose of vaccine administered when the initial sufficient immune response to a primary vaccine is likely to have waned over time. A single Pfizer-BioNTech vaccine booster dose at least 6 months after completion of a Pfizer-BioNTech COVID-19 primary vaccine series is recommended in some populations.

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Rationale for guidance

- SARS-CoV-2 infections with the Delta variant in fully vaccinated persons are associated with less severe clinical outcomes than infections in unvaccinated persons
- Starting around 6 months after primary series vaccination, gradual reduction in COVID-19 vaccine effectiveness is being observed against asymptomatic and mild symptomatic infections with the delta variant of SARS-CoV-2
- Waning of COVID-19 vaccine effectiveness against severe disease (hospitalization and death) is being observed in people aged ≥65yrs
- Data continue to emerge as more fully vaccinated people reach a 6-month interval after their primary vaccine series
- Early data suggest use of a Pfizer-BioNTech COVID-19 booster vaccine dose in people who received a primary Pfizer-BioNTech COVID-19 vaccine series may enhance immune response

Recommendation – Part 1

CDC recommends that the following groups **should** receive a booster dose of Pfizer-BioNTech's COVID-19 vaccine at least 6 months after completing their Pfizer-BioNTech primary vaccine series:

- People aged 65 years and older
- Residents aged 18 years and older in long-term care settings
- People aged 50–64 years with underlying medical conditions

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

Underlying medical conditions

- In unvaccinated persons, there are certain underlying medical conditions that are associated with severe illness from COVID-19
- Improved management of a person's underlying medical condition may decrease risk of severe illness from COVID-19
- Among fully vaccinated persons, having underlying medical conditions may be associated with increased risk of severe illness from COVID-19 over time as antibody titers wane
- Examples:

• Cancer • Chronic kidney disease • COPD (chronic obstructive pulmonary disease) • Diabetes mellitus, type 1 and type 2	• Heart conditions (such as heart failure, coronary artery disease, or cardiomyopathies) • Obesity (BMI ≥30 kg/m2) • Pregnancy and recent pregnancy

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

Recommendation – Part 2

CDC recommends that a booster dose of Pfizer-BioNTech's COVID-19 vaccine should be made available so that the following groups **may** receive a booster dose of Pfizer-BioNTech's COVID-19 vaccine at least 6 months after completing their Pfizer-BioNTech primary vaccine series, based on their individual benefits and risks:

- People aged 18–49 years with underlying medical conditions
- People aged 18–64 years at increased risk for SARS-CoV-2 exposure and transmission because of occupational or institutional setting

https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

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https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

Individual risk benefit assessment considerations

Given the rapidly changing clinical, public health, and scientific landscape amidst the COVID-19 pandemic, an individual level assessment considering potential benefits and risks of a COVID-19 booster dose is needed where the data are uncertain

Risk and benefit considerations for a COVID-19 booster dose

- **Potential risks**
  - Very rare risks of myocarditis and pericarditis
  - Likely even rarer risk of anaphylaxis
  - Reactogenicity, including transient local and systemic symptoms
    - The third dose of Pfizer-BioNTech COVID-19 vaccine appears to have similar reactogenicity as the second dose
- **Potential benefits**
  - Reduced risk of SARS-CoV-2 infection and reduced risk of severe disease
  - Strongest evidence for reductions in the risk of **severe disease** has been observed in older adults (aged ≥65 years); effectiveness of an mRNA COVID-19 primary vaccine series against severe disease remains high for younger age groups
  - Reduced risk of SARS-CoV-2 infection could reduce transmission of virus to other at-risk-persons, but the immediate and sustained impact of a booster dose on SARS-CoV-2 transmission is not yet known

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#Patient-counseling

Additional considerations

- People at highest risk for work-related exposure include those whose work-related duties are performed indoors outside their homes, involve close proximity (<6 feet) to other people, and involve unavoidable frequent interactions with unvaccinated people (e.g., healthcare workers, teachers)
- Congregate living settings, such as correctional and detention facilities, may be associated with an increased risk of SARS-CoV-2 exposure for both staff and residents depending on the ability to follow current prevention measures
- A person's risk of developing severe COVID-19, if infected, may vary by the type, number, and level of control of specific medical conditions, as well as other yet to be defined variables
- While a primary vaccination series decreases the risk of future infections in people with prior SARS-CoV-2 infection, the efficacy of a booster dose for fully vaccinated people who have already had COVID-19 is not yet known

Administration- booster dose

- Pfizer-BioNTech COVID-19 vaccine (BTN162b2), 0.3ml, intramuscular administration (same dose used in primary series)
- Timing: at least 6 months after completion of the primary series
  - Immunity wanes gradually over time, therefore a booster may be given at an interval greater than 6 months
- **Co-administration: a Pfizer-BioNTech COVID-Vaccine booster dose may be given with other vaccines (e.g., influenza), without regard to timing, including administration of COVID-19 and other vaccines on the same day**

Contraindications and precautions

- Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a component of the Pfizer BioNTech COVID-19 vaccine
- Immediate allergic reaction of any severity to a previous dose or known (diagnosed) allergy to a component of the vaccine
- Known polysorbate allergy is a precaution to mRNA COVID-19 vaccination

- Note: Myocarditis after a dose of mRNA COVID-19 vaccine is **not** an absolute contraindication:
  - Recommend deferral of a subsequent dose
  - People who choose to receive a subsequent dose should wait until myocarditis has completely resolved

https://www.cdc.gov/vaccines/covid-19/downloads/IntermConsid-Anaphylaxis-covid19-vaccine-sites.pdf

Looking ahead

- Currently there are insufficient data to support the use of the Pfizer-BioNTech COVID-19 vaccine as a booster dose in people who received the Moderna or Janssen COVID-19 vaccines as a primary vaccination series

- There is uncertainty around the risk of transmission following a vaccine booster dose

- Therefore, at this time, people who have received a booster dose should continue to mask indoors in public where SARS-CoV-2 transmission is substantial or high and follow other guidance for fully vaccinated persons to minimize spread of SARS-CoV-2 to others

Additional clinical resources

Pfizer-BioNTech COVID-19 Vaccine
Standing Orders for Administering Vaccine to Persons 12 Years of Age and Older

Purpose

- To reduce morbidity and mortality from coronavirus disease 2019 (COVID-19) by vaccinating persons who meet the criteria established by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP).

Policy

- Where authorized under state law, standing orders enable eligible nurses and other healthcare professionals (e.g., pharmacists) to assess and vaccinate persons wh… "Procedure" section below without examination or direct order from th… time of the interaction.

Procedure

- Assess persons 12 years of age and… Pfizer-BioNTech COVID-19 Vaccine…
  - History of myocarditis or pericar… dose of an mRNA COVID-19 vacc…
    - Defer the second dose of an m… Administration of the second … vaccine series can be consider… after the episode of myocardit… completely resolved. Consider… www.cdc.gov/vaccines/covid-… covid-19-vaccines-us.html#un…
  - History of myocarditis or pericar… vaccination
    - May receive any FDA-authorize… episode of myocarditis or perica…
  - Has not completed a COVID-19 v… brand. If 2 doses of an mRNA vac… or a single dose of Janssen vacci… additional doses are recommenc…
  - If the recipient has received 1 pre… COVID-19 Vaccine, administer th… least 21 days (but preferably befo…
  - If the vaccine product given as th… determined or is no longer availa… vaccine product may be adminis… first dose.
- Inform recipients, especially males… and their parents/legal representat… possibility of myocarditis or pericar… COVID-19 vaccines and the need to… myocarditis or pericarditis develop…
- For people who received a COVID-…
- Defer vaccination with Pfizer-BioNTech COVID-19 Vaccine for at least 90 days for persons who received passive antibody therapy (monoclonal antibodies or convalescent plasma) as part of COVID-19 treatment.
- Screen for contraindications and precautions.
  - Contraindications:
    - Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a component of an mRNA COVID-19 vaccine (Moderna or Pfizer-BioNTech)
    - Immediate allergic reaction[§] of any severity to a previous dose or

Moderna COVID-19 Vaccine
Standing Orders for Administering Vaccine to Persons 18 Years of Age and Older

Purpose

- To reduce morbidity and mortality from coronavirus disease 2019 (COVID-19) by vaccinating persons who meet the criteria established by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP).

Policy

- Where authorized under state law, standing orders enable eligible nurses and other healthcare professionals (e.g., pharmacists) to assess and vaccinate persons who meet the criteria in the "Procedure" section below without the need for clinician examination or direct order from the attending provider at the time of the interaction.

Procedure

- Assess persons 18 years of age and older for vaccination with Moderna COVID-19 Vaccine based on the following criteria:
  - History of myocarditis or pericarditis after receiving the first dose of an mRNA COVID-19 vaccine
    - Defer the second dose of an mRNA COVID-19 vaccine. Administration of the second dose of an mRNA COVID-19 vaccine series can be considered in certain circumstances after the episode of myocarditis or pericarditis has completely resolved. Considerations can be found at https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#underlying-conditions
  - History of myocarditis or pericarditis prior to COVID-19 vaccination
    - May receive any FDA-authorized COVID-19 vaccine after the episode of myocarditis or pericarditis has completely resolved
  - Has not completed a COVID-19 vaccination series, regardless of brand. If 2 doses of an mRNA vaccine have been administered or a single dose of Janssen vaccine has been administered, no additional doses are recommended.
  - If the recipient has received 1 previous dose of Moderna COVID-19 Vaccine, administer the second dose at an interval of least 28 days (but preferably before 42 days).*
  - If the vaccine product given as the first dose cannot be determined or is no longer available, any mRNA COVID-19 vaccine product may be administered at least 28 days after the first dose.
- Inform recipients, especially males 12 through 29 years of age and their parents/legal representative (when relevant) of the possibility of myocarditis or pericarditis following receipt of mRNA COVID-19 vaccines and the need to seek care if symptoms of myocarditis or pericarditis develop after vaccination.†
- For people who received a COVID-19 vaccine that is not currently authorized in the United States, guidance can be found at: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html#not-authorized-vaccines
- Moderna COVID-19 vaccine may be coadministered with other vaccines - on the same day, as well as within 14 days of each other.‡
- Defer vaccination with Moderna COVID-19 Vaccine for at least 90 days for persons who received passive antibody therapy (monoclonal antibodies or convalescent plasma) as part of COVID-19 treatment.
- Screen for contraindications and precautions.
  - Contraindications:
    - Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a component of an mRNA COVID-19 vaccine (Moderna or Pfizer-BioNTech)
    - Immediate allergic reaction[§] of any severity to a previous dose or known (diagnosed) allergy to a component of the vaccine (see Table 1 in this document for a list of vaccine components)

Note: Persons who have a contraindication to an mRNA COVID-19 vaccine (Moderna or Pfizer-BioNTech) may be able to receive the Janssen COVID-19 Vaccine (see footnote).[¶] Prior to administration of Janssen COVID-19 Vaccine, inform women 18-49 years of the increased risk of thrombosis with thrombocytopenia syndrome (TTS) in their age group.[#] Persons at risk for or with a history of other thrombosis not associated with thrombocytopenia can receive any FDA-authorized vaccine.

  - Precautions:
    - Most people determined to have a precaution to a COVID-19 vaccine at their appointment can and should be administered vaccine.
    - History of an immediate allergic reaction[§] of any severity to any other vaccine or injectable therapy (i.e., intramuscular, intravenous, or subcutaneous vaccines or therapies)
      - This includes persons with a reaction to a vaccine or injectable therapy that contains multiple components, one of which is polyethylene glycol (PEG) or another vaccine component, but for whom it is unknown which component elicited the immediate allergic reaction.
      - People with a contraindication to Janssen COVID-19 Vaccine have a precaution to both mRNA vaccines (see footnote).[¶]
    - Moderate to severe acute illness

*Administer the second dose as close as possible to the recommended interval (28 days). If the second dose is not administered within 42 days of the first dose, the series does not need to be restarted. Doses inadvertently administered less than 28 days apart do not need to be repeated.
†Educational materials are available at www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html
‡When deciding whether to coadminister COVID-19 vaccine and other vaccines, providers should consider whether the patient is behind or at risk of becoming behind on recommended vaccines. They should also consider the patient's risk of vaccine-preventable diseases (e.g., during an outbreak) and the reactogenicity profile of the vaccines.
§An immediate allergic reaction is defined as any hypersensitivity-related signs or symptoms such as urticaria, angioedema, respiratory distress (e.g., wheezing, stridor), or anaphylaxis that occur within 4 hours following exposure to a vaccine or medication.
¶Consider consultation with an allergist-immunologist to help determine if a patient with a contraindication to an mRNA vaccine can safely receive the Janssen COVID-19 vaccine. Healthcare providers and health departments may also request a consultation from the Clinical Immunization Safety Assessment COVIDvax project. Vaccination of these individuals should only be done in an appropriate setting under the supervision of a healthcare provider experienced in the management of severe allergic reactions.
- People with a contraindication to mRNA COVID-19 vaccines (including due to a known PEG allergy) have a precaution to Janssen COVID-19 vaccination. People who have previously received an mRNA COVID-19 vaccine dose should wait at least 28 days to receive Janssen COVID-19 Vaccine.
- People with a contraindication to Janssen COVID-19 Vaccine (including due to a known polysorbate allergy) have a precaution to mRNA COVID-19 vaccination.

#Educational materials are available at: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/JJUpdate.html

Prevaccination Checklist for COVID-19 Vaccines

vaccine recipients:
llowing questions will help us determine if there is any reason ould not get the COVID-19 vaccine today. **If you answer "yes" question, it does not necessarily mean you should not be ated.** It just means additional questions may be asked. If a on is not clear, please ask your healthcare provider to explain it.

Name _____

Age _____

	Yes	No	Don't know
e you feeling sick today?	☐	☐	☐
ve you ever received a dose of COVID-19 vaccine?	☐	☐	☐
f yes, which vaccine product did you receive? Pfizer ☐ Moderna ☐ Janssen (Johnson & Johnson) ☐ Another Product _____			
cination record card or other documentation? *(yes/no)*	☐	☐	
ergic reaction to: *gic reaction [e.g., anaphylaxis] that required treatment with epinephrine or EpiPen® or that caused you include an allergic reaction that caused hives, swelling, or respiratory distress, including wheezing.)*			
ID-19 vaccine, including either of the following:			
PEG), which is found in some medications, such as laxatives and noscopy procedures	☐	☐	☐
found in some vaccines, film coated tablets, and intravenous steroids	☐	☐	☐
/ID-19 vaccine	☐	☐	☐
ergic reaction to another vaccine *(other than COVID-19 vaccine)* on? *gic reaction [e.g., anaphylaxis] that required treatment with epinephrine or EpiPen® or that It would also include an allergic reaction that caused hives, swelling, or respiratory distress,*	☐	☐	☐
u:			
ages 18 and 49 years old			
ges 12 and 29 years old			
carditis or pericarditis			
eaction to something other than a vaccine or injectable therapy such as food, pet, venom, medication allergies			
s treated with monoclonal antibodies or convalescent serum			
system Inflammatory Syndrome (MIS-C or MIS-A) after a COVID-19 infection			
nune system (i.e., HIV infection, cancer)			
sive drugs or therapies			
der			
arin-induced thrombocytopenia (HIT)			
t or breastfeeding			
fillers			

Date _____

Adapted with appreciation from the Immunization Action Coalition (IAC) screening checklists

1

Updates will be posted at: https://www.cdc.gov/vaccines/covid-19/info-by-product/index.html

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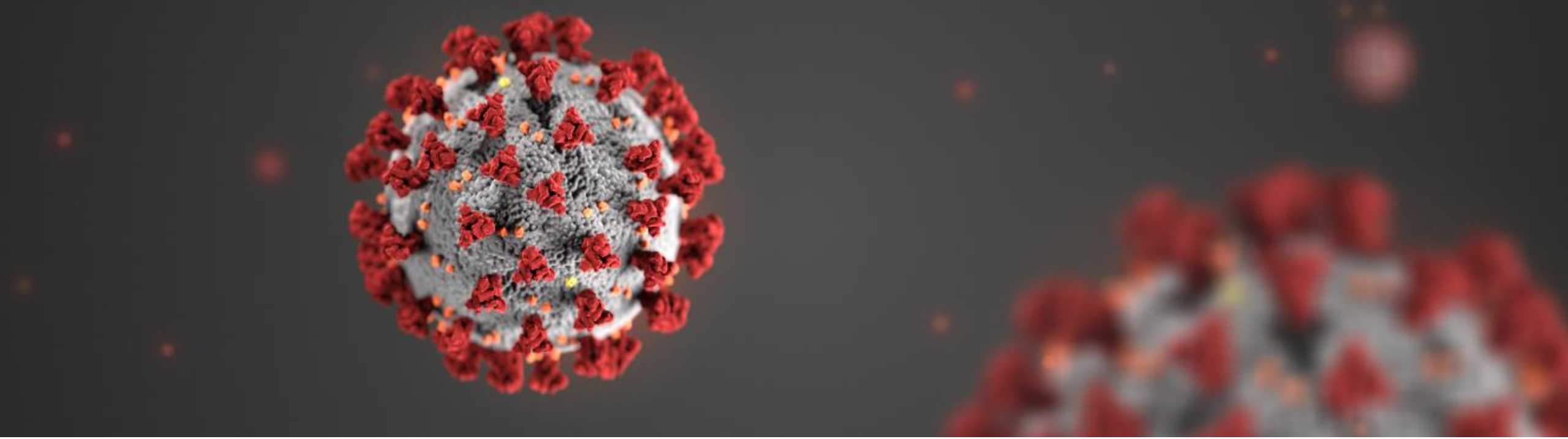

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

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