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

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

- **Risk group** × **Outcome** × **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

- 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

Among fully vaccinated patients, defined as receipt of both doses of Moderna or Pfizer-BioNTech vaccine, with second dose received ≥14 days before hospitalization. No significant differences in VE by age group or calendar month of 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

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

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

- 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)

Estimates are from over 74,000 hospitalizations across 187 hospitals
VISION Network: VE against hospitalization by time period and age group, Pfizer-BioNTech and Moderna

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Vaccine Effectiveness (VE) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan to May</td>
<td>82% 82% 93% 91%</td>
</tr>
<tr>
<td>Jan to May</td>
<td>85% 82% 93% 91%</td>
</tr>
<tr>
<td>Jan to May</td>
<td>99% 91% 91% 91%</td>
</tr>
<tr>
<td>Jan to May</td>
<td>99% 93% 91% 86%</td>
</tr>
<tr>
<td>Jun to Aug</td>
<td>82% 82% 84% 73%</td>
</tr>
<tr>
<td>Jun to Aug</td>
<td>85% 99% 91% 86%</td>
</tr>
<tr>
<td>Jun to Aug</td>
<td>82% 82% 85% 86%</td>
</tr>
<tr>
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<td>85% 99% 91% 86%</td>
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</tr>
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<td>Jun to Aug</td>
<td>82% 82% 85% 86%</td>
</tr>
<tr>
<td>18-29 years</td>
<td>91% 82% 85% 86%</td>
</tr>
<tr>
<td>30-49 years</td>
<td>85% 99% 91% 86%</td>
</tr>
<tr>
<td>50-64 years</td>
<td>93% 91% 91% 86%</td>
</tr>
<tr>
<td>65+ years</td>
<td>91% 86% 73% 86%</td>
</tr>
</tbody>
</table>

* p<0.05
VISION Network: Preliminary VE against hospitalization by time since vaccination in each calendar period, adults ≥18 years, mRNA products

* p<0.05 for trend
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: 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

-Vaccine Effectiveness

≥50 years

-68%

Pre-Delta

≥18 years

-60%

Delta

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)

<table>
<thead>
<tr>
<th></th>
<th>Pre-Delta (Mar 1–May 9)</th>
<th>Intermediate (May 10–Jun 20)</th>
<th>Delta (Jun 20–Aug 1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of weekly reports</td>
<td>17,407</td>
<td>33,160</td>
<td>85,593</td>
</tr>
<tr>
<td>No. of facilities</td>
<td>3,862</td>
<td>11,581</td>
<td>14,917</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th></th>
<th>Vaccine Effectiveness (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pfizer-BioNTech</strong></td>
<td></td>
</tr>
<tr>
<td>18-64 years</td>
<td>92%</td>
</tr>
<tr>
<td>≥65</td>
<td>77%</td>
</tr>
</tbody>
</table>

| **Moderna**      |                           |
| 18-64 years      | 97%                       |
| ≥65              | 87%                       |

| **Combined mRNA** |                           |
| 18-64 years      | 95%                       |
| ≥65              | 80%                       |

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

Vaccine Effectiveness (%)

Pre-Delta vs. Delta

<table>
<thead>
<tr>
<th>Time period</th>
<th>Vaccine Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>February 1-June 30</td>
<td>84%</td>
</tr>
<tr>
<td>July 1-August 6</td>
<td>89%</td>
</tr>
</tbody>
</table>

Time since full vaccination

<table>
<thead>
<tr>
<th>Time since vaccination</th>
<th>Vaccine Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;90 days</td>
<td>86%</td>
</tr>
<tr>
<td>≥90 days</td>
<td>87%</td>
</tr>
</tbody>
</table>
Effectiveness of mRNA vaccines for preventing COVID-19 hospitalization, IVY Network

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

<table>
<thead>
<tr>
<th>Vaccine Product</th>
<th>14-120 days after full vaccination</th>
<th>&gt;120 days after full vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer-BioNTech</td>
<td>91%</td>
<td>77%</td>
</tr>
<tr>
<td>Moderna</td>
<td>93%</td>
<td>92%</td>
</tr>
<tr>
<td>Janssen</td>
<td>68%</td>
<td></td>
</tr>
</tbody>
</table>

* 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

Vaccine Effectiveness

18–64 years

- Pre-Delta: 92%
- Delta: 91%

≥65 years

- Pre-Delta: 91%
- Delta: 87%

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

- 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

<table>
<thead>
<tr>
<th>Time since dose 2</th>
<th>Overall VE</th>
<th>Adjusted VE against infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>14-119 days</td>
<td>85 (68-93)</td>
<td>80 (69-80)</td>
</tr>
<tr>
<td>120-149 days</td>
<td>81 (34-95)</td>
<td></td>
</tr>
<tr>
<td>≥150 days</td>
<td>73 (49-86)</td>
<td></td>
</tr>
</tbody>
</table>

Pre-Delta variant predominance, overall VE: 91 (81-96)

Delta variant predominance, overall VE: 66 (26-84)

- 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](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

- **≥ 65 years of age**
  - **Underlying medical conditions**
  - **Frontline workers**

Vaccine effectiveness (%) against Delta predominance and study, by risk group.

**Pre-Delta**

- NHSN (mRNA)
- COVID-NET (mRNA)
- VISION (Modern)
- VISION (Pfizer)
- NYS (all products)

**Delta**

- NHSN (mRNA)
- COVID-NET (mRNA)
- VISION (Modern)
- VISION (Pfizer)
- NYS (all products)

NHSN: [https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e3.htm](https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e3.htm)
COVID-NET: CDC unpublished
VISION (Pfizer): [https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e2.htm](https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e2.htm)
VISION (Moderna): [https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e3.htm](https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e3.htm)
NYS: [https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e1.htm](https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e1.htm)
PROVIDER: [https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e4.htm](https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e4.htm)
HEROES-RECOVER: [https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e4.htm](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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  - John Jernigan
  - Nong Shang
  - Gordana Derado
  - Stephanie Bialek
  - Meredith McMorrow
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- CDC
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  - Mila Prill
  - Kristina Bajema
  - Mark Thompson
  - Jill Ferdinands
  - Ian Plumb
  - Fiona Havers
  - Heidi Moline
  - 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 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

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

CDC vaccine safety monitoring

• COVID-19 vaccines are being administered under the most intensive vaccine safety monitoring effort in U.S. history

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

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

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

<table>
<thead>
<tr>
<th>Age group, years</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12–17</td>
<td>48 (2)</td>
</tr>
<tr>
<td>18–49</td>
<td>622 (24)</td>
</tr>
<tr>
<td>50–64</td>
<td>654 (26)</td>
</tr>
<tr>
<td>≥65</td>
<td>1,239 (48)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>2,563</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>979 (38)</td>
</tr>
<tr>
<td>Female</td>
<td>1,570 (61)</td>
</tr>
<tr>
<td>Unknown</td>
<td>14 (1)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>2,563</td>
</tr>
</tbody>
</table>

- 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%)

<table>
<thead>
<tr>
<th>Race or ethnicity</th>
<th>Reports (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic or Latino</td>
<td>143 (6)</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td></td>
</tr>
<tr>
<td>AI/AN</td>
<td>11 (&lt;1)</td>
</tr>
<tr>
<td>Asian</td>
<td>51 (2)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>89 (3)</td>
</tr>
<tr>
<td>NHPI</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>White</td>
<td>998 (39)</td>
</tr>
<tr>
<td>Multiracial</td>
<td>14 (1)</td>
</tr>
<tr>
<td>Other</td>
<td>8 (&lt;1)</td>
</tr>
<tr>
<td>Unknown/not reported</td>
<td>1,248 (49)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2,563</strong></td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Non-serious</th>
<th>Serious</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer-BioNTech</td>
<td>1,175 (95%)</td>
<td>68 (5%)</td>
<td>1,243</td>
</tr>
<tr>
<td>Moderna</td>
<td>1,257 (95%)</td>
<td>63 (5%)</td>
<td>1,320</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2,432 (95%)</strong></td>
<td><strong>131 (5%)</strong></td>
<td><strong>2,563</strong></td>
</tr>
</tbody>
</table>

- 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

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

<table>
<thead>
<tr>
<th>Rank</th>
<th>Adverse event*</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Extra dose administered</td>
<td>40 (31)</td>
</tr>
<tr>
<td>2</td>
<td>Fever</td>
<td>27 (21)</td>
</tr>
<tr>
<td>3</td>
<td>Dyspnea</td>
<td>23 (18)</td>
</tr>
<tr>
<td>4</td>
<td>Death</td>
<td>18 (14)</td>
</tr>
<tr>
<td>5</td>
<td>Fatigue</td>
<td>14 (11)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rank</th>
<th>Adverse event*</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Extra dose administered</td>
<td>945 (39)</td>
</tr>
<tr>
<td>2</td>
<td>Fever</td>
<td>323 (13)</td>
</tr>
<tr>
<td>3</td>
<td>Headache</td>
<td>274 (11)</td>
</tr>
<tr>
<td>4</td>
<td>Fatigue</td>
<td>269 (11)</td>
</tr>
<tr>
<td>5</td>
<td>No adverse event</td>
<td>243 (10)</td>
</tr>
</tbody>
</table>
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)

<table>
<thead>
<tr>
<th>Preliminary impression of cause of death*</th>
<th>Reports</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory and/or cardiac arrest</td>
<td>7</td>
</tr>
<tr>
<td>Unable to assess</td>
<td>4</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>2</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1</td>
</tr>
<tr>
<td>Accident/trauma</td>
<td>1</td>
</tr>
<tr>
<td>Cancer</td>
<td>1</td>
</tr>
<tr>
<td>COVID-19 pneumonia</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>18</strong></td>
</tr>
</tbody>
</table>

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

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.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>% of participants</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>63.3</td>
</tr>
<tr>
<td>Male</td>
<td>35.7</td>
</tr>
<tr>
<td>Unknown</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Age group (years)</strong></td>
<td></td>
</tr>
<tr>
<td>0-17</td>
<td>0.3</td>
</tr>
<tr>
<td>18-49</td>
<td>29.1</td>
</tr>
<tr>
<td>50-64</td>
<td>29.8</td>
</tr>
<tr>
<td>65-74</td>
<td>30.5</td>
</tr>
<tr>
<td>75-84</td>
<td>9.5</td>
</tr>
<tr>
<td>≥85</td>
<td>0.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>% of participants</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>8.2</td>
</tr>
<tr>
<td>Not Hispanic/Latino</td>
<td>87.6</td>
</tr>
<tr>
<td>Unknown</td>
<td>4.2</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
</tr>
<tr>
<td>AI/AN</td>
<td>0.5</td>
</tr>
<tr>
<td>Asian</td>
<td>5.6</td>
</tr>
<tr>
<td>Black or AA</td>
<td>5.9</td>
</tr>
<tr>
<td>NHPI</td>
<td>0.3</td>
</tr>
<tr>
<td>White</td>
<td>81.4</td>
</tr>
<tr>
<td>Multiracial</td>
<td>1.9</td>
</tr>
<tr>
<td>Other</td>
<td>2.1</td>
</tr>
<tr>
<td>Unknown</td>
<td>2.4</td>
</tr>
</tbody>
</table>
Patterns of vaccination for 22,191 v-safe participants who reported an additional dose

<table>
<thead>
<tr>
<th>Additional dose</th>
<th>Primary series</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Moderna (%)</td>
</tr>
<tr>
<td>Moderna</td>
<td>10,453 (98.6)</td>
</tr>
<tr>
<td>Pfizer-BioNTech</td>
<td>144</td>
</tr>
<tr>
<td>Janssen</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>10,601</td>
</tr>
</tbody>
</table>

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)\(^1\)

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

COVID-19 vaccine booster dose evaluation

**Regulatory allowance:**
- EUA amendment would allow recommendations under EUA
- BLA would allow for ‘off label’ recommendations

**FDA**

**CDC/ACIP**

**Clinical update:**
- Clinical considerations/recommendations for use

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**Review data:**
- Assess safety, immunogenicity, and implementation

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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.
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.
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

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

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

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

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

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.
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- Jennifer Layden
- Alison Albert
- CDC COVID-19 Response Colleagues
For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.