Evidence to Recommendation Framework:
Moderna & Janssen
COVID-19 Vaccine Booster Dose

Kathleen Dooling, MD, MPH
ACIP Meeting, Oct 21, 2021
Evidence to Recommendations (EtR) Framework

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<td>Public Health Problem</td>
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</table>
Booster doses of COVID-19 vaccines

- Policy on booster doses will be coordinated with FDA for regulatory allowance and ACIP/CDC for recommendations for use.
CDC recommends the following groups for Pfizer-BioNTech COVID-19 vaccine boosters

- The following recipients of Pfizer-BioNTech COVID-19 vaccine primary series **should receive** a single booster dose ≥6 months after completion of the primary series:
  - ≥65 years
  - ≥18 years and reside in long-term care settings
  - Aged 50-64 years with certain underlying medical conditions

- The following recipients of Pfizer-BioNTech COVID-19 vaccine primary series **may receive** a single booster dose ≥6 months after completion of the primary series based on their individual risks and benefits:
  - Aged 18-49 years with certain underlying medical conditions
  - Aged 18-64 years at increased risk for SARS-CoV-2 exposure and transmission because of occupational or institutional setting
Evidence to Recommendations (EtR) Framework

Policy Questions

1) Among risk groups for whom CDC recommends a Pfizer-BioNTech booster dose, should those who received a Moderna COVID-19 vaccine primary series be recommended to receive a single Moderna COVID-19 booster dose (50µg) ≥6 months after completion of the primary series?

2) Among people aged ≥18 years who received Janssen COVID-19 vaccine for their primary COVID-19 vaccine, should a booster dose of Janssen COVID-19 be recommended ≥2 months after receipt of the initial dose?
Number of people fully vaccinated in the U.S. by COVID-19 vaccine series type

- **Pfizer-BioNTech 2-dose**: 104,672,981
- **Moderna 2-dose**: 69,603,147
- **J&J/Janssen single dose**: 15,096,805
- **Unknown 2-dose**: 114,860

Total: 189,487,793 Fully Vaccinated

Evidence to Recommendations Framework
Booster doses of COVID-19 vaccines

Public Health Problem
Daily trends in number of COVID-19 cases in the United States

44,857,861 total cases

Pfizer-BioNTech booster dose recommended

Daily trends in number of hospitalized COVID-19 cases in the United States

New Hospitalizations for COVID-19 with a 7-Day Moving Average, August 2020-October 2021

Age-adjusted weekly COVID-19-associated hospitalization rates among adults by week of admission and age group* — COVID-NET, January 24–August 28, 2021

*Data are preliminary and case counts and rates for recent hospital admissions are subject to lag. As data are received each week, prior case counts and rates are updated accordingly.

†Cumulative rate ratio from January 24 – August 28, 2021.

COVID Data Tracker: https://covid.cdc.gov/covid-data-tracker/#covidnet-hospitalizations-vaccination

18-49 years

50-64 years

≥65 years

Vaccinated vs. Unvaccinated †

14x higher

15x higher

9x higher

Unvaccinated rate

Fully vaccinated rate

Rate per 100,000 population

Rate per 100,000 population

Rate per 100,000 population

1/30/2021

2/13/2021

2/27/2021

3/13/2021

3/27/2021

4/10/2021

4/24/2021

5/8/2021

5/22/2021

6/5/2021

6/19/2021

7/3/2021

7/17/2021

7/31/2021

8/14/2021

8/28/2021

1/30/2021

2/13/2021

2/27/2021

3/13/2021

3/27/2021

4/10/2021

4/24/2021

5/8/2021

5/22/2021

6/5/2021

6/19/2021

7/3/2021

7/17/2021

7/31/2021

8/14/2021

8/28/2021

1/30/2021

2/13/2021

2/27/2021

3/13/2021

3/27/2021

4/10/2021

4/24/2021

5/8/2021

5/22/2021

6/5/2021

6/19/2021

7/3/2021

7/17/2021

7/31/2021

8/14/2021

8/28/2021
Long COVID-19 and risk in vaccinated people

- Prevalence of post-COVID-19 conditions, among vaccinated and unvaccinated, reported from 5%–80%\(^1\)
- Prevalence of long COVID-19 among fully vaccinated persons who develop COVID-19 ranges from 5% (U.K. adults)\(^2\) to 19% (Israeli healthcare workers)\(^3\)
- Among COVID-19 cases in a U.K. study, odds of long COVID-19 were reduced by half among fully vaccinated compared to unvaccinated\(^2\)

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Magnitude of vaccine effectiveness (VE) against infection or hospitalization by Delta predominance and study, by risk group

≥ 65 years of age

Underlying medical conditions

Frontline workers

Vaccine effectiveness (%)

Pre-Delta

Delta

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 (Pfizer): https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e2.htm
VISION (Moderna): https://www.cdc.gov/mmwr/volumes/70/wr/mm7037e3.htm
NYS (all products): https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e1.htm
HEROES-RECOVER: https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e4.htm

SuperNova (mRNA)

IVY ≥1 underlying condition (all products)
Vaccine effectiveness against **infection** over time
Adults ≥18 years of age

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Keehner J, Horton LE, Binkin NJ et al. Resurgence of SARS-CoV-2 Infection in a Highly Vaccinated Health System Workforce. NEJM, September 1, 2021. DOI: 10.1056/NEJMoa2112981
Vaccine effectiveness against **hospitalization** by month
Adults ≥18 years of age

![Diagram showing vaccine effectiveness against hospitalization by month]

- Tenforde, et al.*
- Rosenberg, et al.
- Puranik, et al. (Pfizer)
- Puranik, et al. (Moderna)
- Bajema et al.

* February estimates from platform’s May 2021 MMWR

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Vaccine effectiveness against **hospitalization** over time

Adults ≥16 years of age


Summary

- More than 189 million people in the U.S. are fully vaccinated (~57% total population)
- Hospitalization rates are ~9X-15X higher in unvaccinated as compared to vaccinated adults
- Moderna COVID-19 Vaccine (37% of fully vaccinated people)
  - Infection: Declines in VE against infection over time and during Delta period
  - Hospitalization: Minimal to no declines in VE against hospitalization in younger adults and mild declines observed in some for platforms among older adults
- Janssen COVID-19 Vaccine (8% of fully vaccinated people)
  - Lower VE compared to mRNA vaccines, but most study platforms show persistent VE over time against infection and hospitalization, even among older adults
Evidence to Recommendations Framework
Booster doses of COVID-19 vaccines

Benefits and Harms
## PICO Question

<table>
<thead>
<tr>
<th></th>
<th>Moderna</th>
<th>Janssen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>Persons aged ≥18 years who completed a COVID-19 vaccine primary series  ≥6 months ago</td>
<td>Persons aged ≥18 years who completed a COVID-19 vaccine primary series  ≥2 months ago</td>
</tr>
<tr>
<td><strong>Comparison</strong></td>
<td>No booster dose</td>
<td></td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Symptomatic laboratory-confirmed COVID-19*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hospitalization due to COVID-19*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Death due to COVID-19</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transmission of SARS-CoV-2 infection</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Serious adverse events*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reactogenicity</td>
<td></td>
</tr>
</tbody>
</table>

* Critical outcomes
**Evidence Retrieval**

### Janssen booster

- Records identified from WHO/IVAC literature review*: (n = 0)
- Additional records identified through other sources**: (n = 2)

#### Records screened
- (n = 2)

#### Records assessed for eligibility
- (n = 2)

#### Records included in evidence synthesis (n = 2)
- 2 clinical trial records
- 0 vaccine effectiveness studies

### Moderna booster

- Records identified from WHO/IVAC literature review*: (n = 0)
- Additional records identified through other sources**: (n = 2)

#### Records screened
- (n = 2)

#### Records assessed for eligibility
- (n = 2)

#### Records included in evidence synthesis (n = 2)
- 2 clinical trial records
- 0 vaccine effectiveness studies

*See https://view-hub.org/resources** clinicaltrials.gov and Sponsor
## Moderna booster ≥6 months after primary series

### Summary of GRADE

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Importance</th>
<th>Design (# of studies)</th>
<th>Findings</th>
<th>Evidence type</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benefits (prevention of outcome)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic laboratory-confirmed COVID-19</td>
<td>Critical</td>
<td>RCT (0) OBS (2)</td>
<td>Moderna COVID-19 booster dose (50 µg) induced immune response (GMR) noninferior to that following dose 2 of the 100 µg primary series</td>
<td>4</td>
</tr>
<tr>
<td>Hospitalization due to COVID-19</td>
<td>Critical</td>
<td>RCT (0) OBS (0)</td>
<td>No data available</td>
<td>ND</td>
</tr>
<tr>
<td>Death due to COVID-19</td>
<td>Important</td>
<td>RCT (0) OBS (0)</td>
<td>No data available</td>
<td>ND</td>
</tr>
<tr>
<td>Transmission of SARS-CoV-2 infection</td>
<td>Important</td>
<td>RCT (0) OBS (0)</td>
<td>No data available</td>
<td>ND</td>
</tr>
<tr>
<td><strong>Harms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>Critical</td>
<td>RCT (0) OBS (2)</td>
<td>No SAEs were attributed to Moderna COVID-19 booster dose (50 µg) during follow-up. No imbalance between booster and comparison group</td>
<td>4</td>
</tr>
<tr>
<td>Reactogenicity</td>
<td>Important</td>
<td>RCT (0) OBS (2)</td>
<td>Grade ≥3 reactogenicity occurred in 10.8% of Moderna COVID-19 booster dose (50 µg) recipients vs 19.7% primary series (100ug)</td>
<td>4</td>
</tr>
</tbody>
</table>

Evidence type: 1=high; 2=moderate; 3=low; 4=very low; ND= no data
## Janssen booster ≥2 months after primary dose

### Summary of GRADE

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Importance</th>
<th>Design (# of studies)</th>
<th>Findings</th>
<th>Evidence type</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benefits (prevention of outcome)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic laboratory-confirmed COVID-19</td>
<td>Critical</td>
<td>RCT (0) OBS (2)</td>
<td>Janssen COVID-19 booster dose is more effective at preventing symptomatic laboratory-confirmed COVID-19 than the primary dose</td>
<td>4</td>
</tr>
<tr>
<td>Hospitalization due to COVID-19</td>
<td>Critical</td>
<td>RCT (0) OBS (2)</td>
<td>Janssen COVID-19 booster dose may be more effective at preventing hospitalization due to COVID-19 (severe COVID-19) than the primary dose</td>
<td>4</td>
</tr>
<tr>
<td>Death due to COVID-19</td>
<td>Important</td>
<td>RCT (0) OBS (2)</td>
<td>Janssen COVID-19 booster dose may be more effective at preventing death due to COVID-19 than the primary dose</td>
<td>4</td>
</tr>
<tr>
<td>Transmission of SARS-CoV-2 infection</td>
<td>Important</td>
<td>RCT (0) OBS (0)</td>
<td>No data available</td>
<td>ND</td>
</tr>
<tr>
<td><strong>Harms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>Critical</td>
<td>RCT (1) OBS (0)</td>
<td>3 SAEs were attributed to Janssen COVID-19 booster dose (facial paresis, pulmonary embolism, and cerebrovascular accident). SAE were balanced between booster and placebo arms</td>
<td>4</td>
</tr>
<tr>
<td>Reactogenicity</td>
<td>Important</td>
<td>RCT (1) OBS (0)</td>
<td>Grade ≥3 systemic adverse events occurred in 2.1% of Janssen COVID-19 booster dose recipients- similar or less than after the primary dose</td>
<td>4</td>
</tr>
</tbody>
</table>

Evidence type: 1=high; 2=moderate; 3=low; 4=very low; ND=no data
Number of people needed to vaccinate with a booster dose to prevent one hospitalization over 6 months

** Not estimable due to pre-booster efficacy estimated at >95%
Methods for calculations included in backup slides
Myocarditis and Pericarditis

- Postmarketing data demonstrate increased risks of myocarditis and pericarditis, particularly within 7 days following the second dose. The observed risk is higher among males under 40 years of age than among females and older males. The observed risk is highest in males 18 through 24 years of age. Although some cases required intensive care support, available data from short-term follow-up suggest that most individuals have had resolution of symptoms with conservative management. Information is not yet available about potential long-term sequelae.¹

- Highest reporting rate in 18-24yo males (0-7 days post dose 2)= 39 cases/1M doses administered²

¹ Moderna COVID-19 Vaccine Fact Sheet for Health Care Providers (fda.gov)
² VAERS
Thrombosis with thrombocytopenia syndrome (TTS)
- Blood clots involving blood vessels in the brain, lungs, abdomen, and legs along with low levels of platelets (blood cells that help your body stop bleeding), have occurred in some people who have received the Janssen COVID-19 Vaccine. In people who developed these blood clots and low levels of platelets, symptoms began approximately one to two weeks after vaccination. Reporting of these blood clots and low levels of platelets has been highest in females ages 18 through 49 years. The chance of having this occur is remote.¹

- Highest reporting rate in 30-39 year old females (0-21 days post dose)= 10 cases/1M doses administered²

¹ Janssen COVID-19 Vaccine Fact Sheet for Recipients and Caregivers (fda.gov)
² VAERS
GBS following Janssen

- Guillain Barré syndrome (GBS)
  - has occurred in some people who have received the Janssen COVID-19 Vaccine. In most of these people, symptoms began within 42 days following receipt of the Janssen COVID-19 Vaccine. The chance of having this occur is very low.¹

  - Highest reporting rate in 50-64 year old males (1-42d post dose)= 16 cases/1M doses administered²

1. Janssen COVID-19 Vaccine Fact Sheet for Recipients and Caregivers (fda.gov)
Heterologous Boosting (Mix and Match)

- Use of Moderna, Janssen, and Pfizer-BioNTech COVID-19 vaccines as boosters led to strong serologic responses in groups primed by all three vaccines.
- For a given primary COVID-19 vaccine, heterologous boosts elicited similar or higher serologic responses as compared to their respective homologous booster responses.
- mRNA vaccines resulted in higher antibody titers in the first 28 days after the boost.
- The study arms were small (n=49-53), but no safety concerns were identified.

https://www.medrxiv.org/content/10.1101/2021.10.10.21264827v1.full.pdf
Evidence to Recommendations Framework
Booster dose of COVID-19 vaccines

Values and Acceptability
Values and Acceptability

- In published surveys completed in August (n=5), **76%-87%** of vaccinated adults reported they would get a booster dose, if available\(^1-5\)
  - In one survey, this increased to **93%** of surveyed adults if it was recommended by their primary care provider

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Cumulative Number of COVID-19 Vaccine Booster/Additional Doses

Total booster/additional doses administered: 10.9M

Potential underreporting due to reporting lag

Evidence to Recommendations Framework
Booster doses of COVID-19 vaccines
Completed primary vaccination regime, by week

CDC Immunization Data Lake. Data as of September 9, 2021
Completed primary vaccination regime, by week

Completed primary series 6 months prior

CDC Immunization Data Lake. Data as of September 9, 2021
Number of U.S. persons potentially eligible (in millions) for a booster dose on October 22, 2021

<table>
<thead>
<tr>
<th>Age group</th>
<th>Pfizer-BioNTech ≥6m</th>
<th>Moderna ≥6m</th>
<th>Janssen ≥2m</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-29 years old</td>
<td>4.7</td>
<td>3.0</td>
<td>2.4</td>
<td>10.1</td>
</tr>
<tr>
<td>30-49 years old</td>
<td>11.9</td>
<td>8.3</td>
<td>4.5</td>
<td>24.7</td>
</tr>
<tr>
<td>50-64 years old</td>
<td>13.2</td>
<td>10.1</td>
<td>4.0</td>
<td>27.3</td>
</tr>
<tr>
<td>65+ years old</td>
<td>17.3</td>
<td>17.7</td>
<td>1.9</td>
<td>36.9</td>
</tr>
<tr>
<td>Total</td>
<td>47.1</td>
<td>39.1</td>
<td>12.9</td>
<td>99.1</td>
</tr>
</tbody>
</table>
Implementation

Long-term care (LTC) facility residents

- CDC’s federal pharmacy program provides vaccination support to LTC settings, including on-site vaccination clinics where needed, to help residents access vaccine in local community

- 8.1 million doses administered during original LTC program (December 2020-March 2021): 6.2M (76%) were Pfizer-BioNTech, 1.9M (24%) were Moderna

- Thus far, the support for booster doses has been restricted to Pfizer-BioNTech recipients based on current FDA and CDC guidance
Evidence to Recommendations Framework
Booster doses of COVID-19 vaccines
Summary - Resource Use

- All COVID-19 vaccines, including booster doses, will be provided **free of charge** to the U.S. population
  - Health systems or health departments incur costs for vaccination program planning and implementation
  - Fees for administration of COVID-19 vaccines recommended by ACIP/CDC are reimbursable by insurance or other federal programs

- Cost effectiveness analyses will take on increased importance in the future, when public health emergency is over
Evidence to Recommendations Framework
Booster doses of COVID-19 vaccines
Percentage of Booster Dose Administrations by Race/Ethnicity

Data shown for 9.8M people with a booster/additional dose administration and known race/ethnicity, vaccinated since August 13, 2021

Source: Immunization Data Lake Aggregate Dataset (includes TX). Data reported as of 19OCT2021 0600.

Notes: Census populations used to calculate Group Percentage of U.S. Population are from the Census 2019 Vintage files. The Multiple/Other category includes vaccine recipients that were identified as Multiple Race or Other Race. The Census populations used to calculate the Group Percentage of U.S. Population for this group represent the non-Hispanic Two or More Race population only, since Other is not a Census-recognized group.
Summary - Equity

- COVID-19 disease and COVID-19 vaccination varies by socioeconomic and sociodemographic groups
  - However, vaccine effectiveness does not vary by race and ethnicity

- At present, only recipients of Pfizer-BioNTech COVID-19 vaccine have been recommended to receive a booster, thus creating inequity for recipients of Moderna or Janssen COVID-19 vaccine
  - Janssen COVID-19 vaccine may have been used more commonly for outreach to homeless or medically underserved communities because it is a single dose regime
Summary
Work Group interpretation

- **Top priority** should be **continued vaccination** of unvaccinated individuals

- Goals of booster program:
  - Prevention of **severe disease**, including hospitalization and death
  - Other considerations are important, such as maintaining workforce and healthcare capacity, prevention of transmission, individual benefit/risk balance

- Balance of benefits and risks **varies by age**
  - Adults ≥65 years have the clearest benefit>risk
  - Moderna: Benefits are incrementally smaller with decreasing age, given high effectiveness maintained from primary series. Myocarditis risk higher in young adults.
  - Janssen: Benefits may be smaller across age groups compared with mRNA vaccines. TTS risk higher in young females.
Work Group interpretation

- For people who received Moderna COVID-19 vaccine as a primary series, the Work Group supports using a single booster dose ≥ 6 months following the primary series in certain populations (consistent with CDC recommended populations for Pfizer-BioNTech COVID-19 booster).

- For people who received Janssen COVID-19 vaccine as primary vaccination, the Work Group supports using a single booster ≥ 2 months following the initial dose in all people aged ≥ 18 years and older.

- A single dose of Janssen COVID-19 vaccine results in lower VE and antibody levels compared to mRNA vaccine primary series - data demonstrate that a single dose of Janssen or mRNA COVID-19 vaccines boost immune response in these individuals.
Acknowledgments

- Monica Godfrey
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- Hannah Rosenblum
- Heather Scobie
- Ian Plumb
- Amy Blain
- Neela Goswami
- Mary Chamberland
- CDC/University of Iowa
- VTF ACIP WG Team
- ACIP COVID-19 Vaccines Work Group
- Vaccine Task Force
- Epi Task Force
- Respiratory Viruses Branch
Clinical Considerations
## Evidence to Recommendations Framework

### Summary: Work Group Interpretations

<table>
<thead>
<tr>
<th>Type of recommendation</th>
<th>We do not recommend the intervention</th>
<th>We recommend the intervention for individuals based on assessment of benefits and risks</th>
<th>We recommend the intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Used when the <strong>risks</strong> clearly outweigh the <strong>benefits</strong> in a population</td>
<td>Used when there is diversity of the <strong>benefits</strong> and <strong>risks</strong> in a population</td>
<td>Used when the <strong>benefits</strong> clearly outweigh the <strong>risks</strong> in a population</td>
<td>Can allow flexibility across a population</td>
</tr>
</tbody>
</table>
Policy question #1

Among risk groups for whom CDC recommends a Pfizer-BioNTech booster dose, should those who received a Moderna COVID-19 vaccine primary series be recommended to receive a single Moderna COVID-19 booster dose (50ug) ≥6 months after completion of the primary series?

Policy question #2

Among people aged ≥18 years who received Janssen COVID-19 vaccine for their primary COVID-19 vaccine, should a booster dose of Janssen COVID-19 be recommended ≥2 months after receipt of the initial dose?
ACIP Vote #1
Interim Recommendation

A single Moderna COVID-19 vaccine booster dose (50ug) is recommended at least 6 months after completion of the Moderna primary series, in the same risk groups for whom CDC recommended a booster dose of Pfizer-BioNTech, under the FDA’s Emergency Use Authorization.
ACIP Vote #2
Interim Recommendation

A single Janssen COVID-19 vaccine booster dose is recommended for persons aged ≥18 years, at least 2 months after receipt of the initial Janssen dose, under the FDA’s Emergency Use Authorization.
CDC recommends the following groups for Pfizer-BioNTech COVID-19 vaccine boosters

- The following recipients of Pfizer-BioNTech COVID-19 vaccine primary series should receive a single booster dose ≥6 months after completion of the primary series:
  - ≥65 years
  - ≥18 years and reside in long-term care settings
  - Aged 50-64 years with certain underlying medical conditions

- The following recipients of Pfizer-BioNTech COVID-19 vaccine primary series may receive a single booster dose ≥6 months after completion of the primary series based on their individual risks and benefits:
  - Aged 18-49 years with certain underlying medical conditions
  - Aged 18-64 years at increased risk for SARS-CoV-2 exposure and transmission because of occupational or institutional setting
Among groups recommended to receive booster vaccination after a Pfizer-BioNTech, Moderna, or Janssen COVID-19 vaccine primary series, a single booster dose of any of the authorized or approved COVID-19 vaccines may be administered as a heterologous booster dose, under FDA’s Emergency Use Authorization.
Thank you

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.
Incidence among vaccinated people, for hospitalization by month in United States and for severe disease by time since 2nd dose in Israel

*Israel estimates were derived from rate of severe COVID-19 (per 1,000 persons) from July 11, 2021 to July 31, 2021. Each data point represents all person stratified by when second dose of COVID-19 vaccine received.
## Summary of GRADE- Pfizer-BioNTech

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Importance</th>
<th>Design (# of studies)</th>
<th>Findings</th>
<th>Evidence type</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benefits</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic laboratory-confirmed COVID-19</td>
<td>Critical</td>
<td>RCT (2) OBS (1)</td>
<td>Pfizer-BioNTech COVID-19 booster dose induced immune responses (GMR, seroresponse) noninferior to those following dose 2. Observational data suggest increased protective effect against any SARS-CoV-2 infection.</td>
<td>4</td>
</tr>
<tr>
<td>Hospitalization due to COVID-19</td>
<td>Critical</td>
<td>RCT (0) OBS (1)</td>
<td>Observational data suggest increased protective effect against severe COVID-19.</td>
<td>4</td>
</tr>
<tr>
<td>Death due to COVID-19</td>
<td>Important</td>
<td>RCT (0) OBS (0)</td>
<td>No data available.</td>
<td>ND</td>
</tr>
<tr>
<td>Transmission of SARS-CoV-2 infection</td>
<td>Important</td>
<td>OBS (0)</td>
<td>No data available.</td>
<td>ND</td>
</tr>
<tr>
<td><strong>Harms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>Critical</td>
<td>RCT (1)</td>
<td>No SAEs were attributed to booster dose.</td>
<td>4</td>
</tr>
<tr>
<td>Reactogenicity</td>
<td>Important</td>
<td>RCT (1)</td>
<td>Grade ≥3 reactogenicity was reported by 6.6% of booster dose recipients.</td>
<td>4</td>
</tr>
</tbody>
</table>

Evidence type: 1=high; 2=moderate; 3=low; 4=very low; ND, no data
Methods for number needed to vaccinate

Calculated per 1 million booster doses using current COVID-19 vaccine and disease data to estimate number of cases and hospitalizations occurring among vaccinated

- Age groups: 18 – 29 years, 30 – 49 years, 50 – 64 years, ≥65 years
- Time Horizon: 180-day period, with stable incidence and VE

| Input                                      | Source                                                              |
|--------------------------------------------|                                                                    |
| Number fully vaccinated                    | CDC Data Tracker (Sept 10, 2021)<sup>1</sup>                      |
| Case Incidence                             | CDC Data Tracker (Sept 9, 2021)<sup>2</sup>                       |
| Hospitalization Incidence                  | COVID-NET (Aug 21, 2021)<sup>3</sup>                              |
| Vaccine Effectiveness (primary series)     | Averaged VE estimates from four platforms                          |
| Vaccine Effectiveness booster              | Assumption (VE post-booster is unknown) 95% VE for hospitalization |

VE: Vaccine Effectiveness

<sup>1</sup>https://covid.cdc.gov/covid-data-tracker/#vaccination-demographic
<sup>2</sup>https://covid.cdc.gov/covid-data-tracker/#trends_dailycases
Around 1/3 of unvaccinated respondents said that COVID-19 booster vaccines would make them less likely to get vaccinated at all.
Cumulative COVID-19 associated hospitalizations in the United States by race/ethnicity, March 7, 2020 – September 11, 2021
Among VE platforms able to provide specific estimates for vaccine effectiveness by race or ethnicity, no differences noted.

VE against hospitalization among adults ≥50 years of age:
- Overall: 89% (95% CI: 87-91%)
- Black individuals: 86% (95% CI: 75-92%)
- Hispanic individuals: 90% (95% CI: 85-93%)

VE against hospitalization among VA centers:
- Black individuals: 86% (95% CI: 77-93%)
- White individuals: 88% (95% CI: 77-94%)
Percentage of people who have received at least one dose of the COVID-19 vaccine by race/ethnicity over time

Implications for public health recommendations
Definition of ‘fully vaccinated’

- For public health purposes, people who have completed a primary vaccine series (i.e., 2-dose mRNA vaccine series or a single dose of the Janssen vaccine) are considered fully vaccinated ≥2 weeks after completion of the primary series.
- The above definition applies to all people including those recommended to receive an additional single dose due to moderate to severe immunocompromise and those recommended to receive a booster dose.
- People who have received a booster dose should continue to follow guidance for fully vaccinated persons to minimize spread of SARS-CoV-2.