Framework for booster doses of COVID-19 vaccines

Sara Oliver MD, MSPH
ACIP Meeting
August 30, 2021
Roles of an Additional Dose

There are two distinct potential uses for an additional dose:

- **Additional dose after an initial primary vaccine series**: administration of an additional vaccine dose when the initial immune response following a primary vaccine series is likely to be insufficient.

- **Booster dose**: a dose of vaccine administered when the initial sufficient immune response to a primary vaccine series is likely to have waned over time.
Booster doses of COVID-19 vaccines

- Are booster doses of COVID-19 vaccines needed for those previously vaccinated with a primary series?

- Policy on booster doses will be coordinated with FDA for regulatory allowance, and ACIP for recommendations for use.
COVID-19 vaccines administered
As of August 26, 2021

Total Vaccine Doses Administered: 365,767,674

% of Population Fully Vaccinated:

≥12 years of age: 60.7%
≥18 years of age: 62.8%
≥65 years of age: 81.4%

CDC. https://covid.cdc.gov/covid-data-tracker
COVID-19 vaccines
As of August 26, 2021

Daily Count of Newly Fully Vaccinated People

A person is considered fully vaccinated against COVID-19 ≥2 weeks after receipt of the second dose in a two-dose series (Pfizer-BioNTech and Moderna) or ≥2 weeks after receipt of the single dose of the Janssen vaccine; CDC. [https://covid.cdc.gov/covid-data-tracker](https://covid.cdc.gov/covid-data-tracker)
COVID-19 vaccines

As of August 11, 2021

Weekly Count of Newly Fully Vaccinated People in US, by age group

A person is considered fully vaccinated against COVID-19 ≥2 weeks after receipt of the second dose in a two-dose series (Pfizer-BioNTech and Moderna) or ≥2 weeks after receipt of the single dose of the Janssen vaccine; CDC, https://covid.cdc.gov/covid-data-tracker
Booster doses of COVID-19 vaccines

What are the key considerations for decision making?

What data are available for decision making?

Does ACIP recommend booster doses of COVID-19 vaccines in any populations?
Booster doses of COVID-19 vaccines

What are the **key considerations** for decision making?

**ACIP Meeting Aug 13**: Framework for COVID-19 booster doses presented

What **data** are available for decision making?

**ACIP Meeting Aug 30**: Begin to provide data to inform booster dose policy

Does ACIP **recommend** booster doses of COVID-19 vaccines in any populations?
Booster doses of COVID-19 vaccines

**Do we need them?**

- Is vaccine effectiveness (VE) \textit{wanning} over time?
- Is VE \textit{reduced} for the \textit{Delta} variant?
- Does the need vary by \textit{sub-population}?

**Do they work?**

- Are booster doses of COVID-19 vaccines \textit{safe} and \textit{immunogenic}?
- Will booster doses reduce COVID-19 \textit{incidence, hospitalization} and/or \textit{mortality}?
- Do booster doses \textit{improve} VE against the \textit{Delta} variant?
Booster doses of COVID-19 vaccines: Data to inform recommendations

Is vaccine effectiveness (VE) waning over time?

Is VE recently similar to what was noted at 2 months after vaccination?

How do these data vary by severity of disease?

How do these data vary by vaccine?
Booster doses of COVID-19 vaccines: Is vaccine effectiveness waning over time?

- Initial VE reviewed during EUA application

- Will work with manufacturers to review longer-term follow up from clinical trials
## Recent U.S. Publications

<table>
<thead>
<tr>
<th>Author</th>
<th>Publication (Date)</th>
<th>Population</th>
<th>Outcomes</th>
<th>Time Assessed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenforde et al.</td>
<td>MMWR (8/18/21)</td>
<td>Multi-state network of hospitalized adults</td>
<td>Hospitalization</td>
<td>March – July 2021</td>
</tr>
<tr>
<td>Rosenberg et al.</td>
<td>MMWR (8/18/21)</td>
<td>Adult residents of NY</td>
<td>Documented infection Hospitalization</td>
<td>May – July 2021</td>
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<tr>
<td>Nanduri et al.</td>
<td>MMWR (8/18/21)</td>
<td>Nursing home residents</td>
<td>Documented infection</td>
<td>March – July 2021</td>
</tr>
<tr>
<td>Puranik et al.</td>
<td>Preprint (8/9/21)</td>
<td>Adults within the Mayo Clinic health system</td>
<td>Documented infection Hospitalization</td>
<td>February – July 2021</td>
</tr>
</tbody>
</table>


Booster doses of COVID-19 vaccines: Vaccine effectiveness against hospitalization

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

* February estimates from platform’s May 2021 MMWR
Booster doses of COVID-19 vaccines: Vaccine effectiveness against infection

Booster doses of COVID-19 vaccines: Vaccine effectiveness against infection

Introduction of Delta variant
Late May
Delta: 7%
Mid-July
Delta: 94%

Booster doses of COVID-19 vaccines: Data to inform recommendations

- Is VE reduced for the Delta variant?
- How does this vary by severity of disease?
- How would this information impact VE for future variants?
Booster doses of COVID-19 vaccines: Is effectiveness reduced because of the Delta variant?

- Globally, among studies assessing infections with Alpha vs Delta: mild decrease in Delta VE
- Other factors may include study methods, **interval** between doses, and **timing** with vaccination and variant increases

References:
3. Tang et al. https://www.medrxiv.org/content/10.1101/2021.08.11.21261885v1
6. Bernal Lopez et al. https://www.medrxiv.org/content/10.1101/2021.05.22.21257658v1

*Included other variants
Vaccine effectiveness in the Pre-Delta and Delta Periods

In studies comparing the ‘Pre-Delta’ and ‘Delta’ periods:

- Pre-Delta vaccine effectiveness estimates high (87% or higher)
- Since the introduction of the Delta variant (varies by region)
  - VE against infection ranges from 39–84%
  - VE against hospitalization ranges from 75–95%

References:
1. Israel Ministry of Health (committee/he/files_publications_corona_two-dose-vaccination-data.pdf)
2. Haas et al. (Israel) https://doi.org/10.1016/S0140-6736(21)00947-8
3. Pouwels et al. (UK) survey/finalfinalcombinedve20210816.pdf
4. Puranik https://www.medrxiv.org/content/10.1101/2021.08.06.21261707v2
5. Rosenberg (US) https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e1.htm
6. Tenforde (US) https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e2.htm
Summary of vaccine effectiveness estimates since introduction of the Delta variant

- Vaccines remain effective in preventing hospitalization and severe disease but might be less effective in preventing infection or milder symptomatic illness.
- Reasons for lower effectiveness likely include both waning over time and Delta variant.

See reference list in later slides.
Booster doses of COVID-19 vaccines: Data to inform recommendations

Does the need vary by sub-population?

- Adults ≥65 years of age
- Residents of long-term care facilities
- Healthcare personnel
Booster doses of COVID-19 vaccines: Adults ≥60 years of age

VE for **symptomatic infection** ≥7 days after dose 2, Pfizer-BioNTech vaccine

- VE against **symptomatic infection** in adults ≥60 years of age is high, but some decreases noted against VoC
  - Differences were not significantly different: small numbers and wide confidence intervals

Nasreen et al. [https://www.medrxiv.org/content/10.1101/2021.06.28.21259420v2.supplementary-material](https://www.medrxiv.org/content/10.1101/2021.06.28.21259420v2.supplementary-material)  
VoC= Variants of Concern
 Booster doses of COVID-19 vaccines: Adults ≥65 years of age

- VE against hospitalization in adults ≥65 years of age decreases over time but remained high
  - Differences by interval since vaccination were not significantly different

Tenforde et al. [https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e2.htm](https://www.cdc.gov/mmwr/volumes/70/wr/mm7034e2.htm)
Booster doses of COVID-19 vaccines: Adults ≥65 years of age

Preliminary VE against COVID-19–associated hospitalization among fully vaccinated patients aged ≥18 years by age group and month — COVID-NET

- Preliminary VE against hospitalization in adults ≥75 years of age decreased in July, but remains >80%
Booster doses of COVID-19 vaccines: Healthcare personnel

- VE against infection among frontline workers (including healthcare personnel) declined somewhat over time and from the pre-Delta period to Delta period
  - VEs were not significantly different

Data from HEROES-RECOVER Cohort

Booster doses of COVID-19 vaccines: Long-term care facility residents

- Initially, VE against infection among long-term care facility residents was high.
Booster doses of COVID-19 vaccines:
Long-term care facility residents

- VE against infection among long-term care facility residents differed significantly from pre-Delta period to Delta period

Summary of vaccine effectiveness estimates since introduction of the Delta variant

- Lower vaccine effectiveness estimated against infection for long term care facility resident
- Vaccine effectiveness among older age groups and healthcare personnel comparable with other subgroups; follow up needed to monitor VE estimates over time

See reference list in later slides
Booster doses of COVID-19 vaccines: Data to inform recommendations

Are booster doses of COVID-19 vaccines safe and immunogenic?

Do COVID-19 vaccines provide a boost in neutralizing antibody response?

How do neutralizing antibodies correlate to clinical protection from COVID-19?
Booster doses of COVID-19 vaccines: Are booster doses safe and immunogenic?

- Pfizer-BioNTech, Moderna, and Janssen (Johnson & Johnson) conducting studies to evaluate safety and immunogenicity of COVID-19 vaccine booster doses

- Important to include sufficient safety data for booster doses
Booster doses of COVID-19 vaccines: Data to inform recommendations

Will booster doses of COVID-19 vaccines reduce COVID-19 incidence, hospitalization and/or mortality?
Booster doses of COVID-19 vaccines:
Will booster doses reduce COVID-19 morbidity and mortality?

- Evaluating data available to assess the potential **impact** of COVID-19 booster doses in a variety of populations and settings
Booster doses of COVID-19 vaccines: Data to inform recommendations

Do boosters improve VE against the Delta variant and other variants of concern (VoC)?

How can we use this data to inform VE for future variants?
Booster doses of COVID-19 vaccines: Do booster doses improve VE against Delta and other VoC?

- **Immunogenicity** data (including sera from study participants who received a booster dose) can evaluate neutralizing antibody data for variants of concern (including Delta)

- No correlate of protection available, but growing understanding around impact of **neutralizing antibodies**
  - Can infer impact of booster doses on neutralizing antibodies to clinical protection (VE) against Delta and other VoC
Booster doses of COVID-19 vaccines: Data to inform recommendations

Are booster doses of COVID-19 feasible to implement?
Booster doses of COVID-19 vaccines: Are booster doses feasible to implement?

- Some aspects of implementation will be more feasible than primary series roll-out:
  - Supply and number of vaccination sites not a serious limitation

- Some aspects of implementation will be more complex:
  - Different primary series
    - Individuals received a variety of primary series
    - Upcoming data will evaluate booster response for same (homologous) and different (heterologous) series
    - Booster dose policy will need to address individuals who received all primary series
  - Different doses
    - Some COVID-19 vaccine booster studies have evaluated various doses for booster vaccines for the same product
Summary and Work Group Considerations
Booster doses of COVID-19 vaccines: Summary

- Not uncommon for a vaccine series to require several doses
- Vaccines that require >1 dose do not necessarily mean annual boosters needed
  - For many vaccines, the final dose is given at least 6 months after the initial dose

<table>
<thead>
<tr>
<th>Sample of adult vaccines requiring &gt;1 dose</th>
<th>1st dose</th>
<th>2nd dose</th>
<th>3rd dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpes zoster (shingles)</td>
<td>Initial</td>
<td>2-6 months</td>
<td></td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Initial</td>
<td>6 months</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Initial</td>
<td>1-2 months</td>
<td>6-18 months</td>
</tr>
<tr>
<td>Human papillomavirus (HPV) (Age ≥15 at initial vaccination)</td>
<td>Initial</td>
<td>1-2 months</td>
<td>6 months</td>
</tr>
</tbody>
</table>
Booster doses of COVID-19 vaccines:

Summary

Initial dose(s) of vaccine: **Prime**

Subsequent doses of vaccine: ‘**Boost**’ Effect

*Time* between the doses can allow for a 'boosting' effect with the immune system

- B-cells
- Antibodies
- T-cells

- B-cells
- Antibodies
- T-cells
Booster doses of COVID-19 vaccines:

Summary

- COVID-19 vaccines continue to maintain **high protection** against severe disease, hospitalization, and death

- Protection against infection (including asymptomatic or mild infections) appears lower in recent months
  - Difficult to distinguish role of **time** since primary series and **Delta variant**

- Reported data through July; data through August shown at future ACIP meetings
  - Important to monitor **trends** of effectiveness by severity of disease over time

- Policy around booster doses requires **continued evaluation** of effectiveness, monitoring impact of both **time** and **variants**, and ability of booster doses to **improve** protection
Recommendations for Allocation of Initial Doses of COVID-19 Vaccines
December 2020–Early 2021

Phase 1a
- LTCF Residents
- Healthcare Personnel

Phase 1b
- Adults ≥75 years of age
- Frontline Essential Workers

Phase 1c
- Adults ≥65 years of age
- All Essential Workers
- Adults 16-64 years of age with high-risk medical conditions

- Early in vaccine roll-out, ACIP voted for a risk-based approach to allocation of COVID-19 vaccines
- Variation in implementation across states/jurisdictions
Booster doses of COVID-19 vaccines: Work Group considerations

- **Top priority** should be continued vaccination of unvaccinated individuals
  
  – Planning for delivery of booster doses to vaccinated individuals should not deter outreach for delivery of primary series to unvaccinated individuals

- Priority for booster dose policy:
  
  Prevention of severe disease in at-risk populations

- **Simplicity** and **flexibility** will be important to support equitable and efficient delivery of booster doses
Booster doses of COVID-19 vaccines: Work Group considerations

- Important to ensure **global vaccine availability**
  - Uncontrolled spread globally that could result in new variants threaten control of the pandemic everywhere

- Policy around booster doses should also consider **equity** in the U.S. population
  - Access to booster doses may vary by population and setting
  - **Lessons learned** around equitable access in early primary series roll-out
Booster doses of COVID-19 vaccines: Work Group considerations

- In addition to immunogenicity data, need to review available safety data for booster doses

- Balance of benefits and risks for booster doses may vary by age
  - Policy for booster doses needs to take this benefit/risk balance into account

- Critical to wait for additional safety data and regulatory allowance for booster doses
Booster doses of COVID-19 vaccines: Work Group considerations

- At this time, the Work Group discussed a risk-based approach for booster dose recommendations
  - Prevent severe disease in the most at-risk populations:
    - LTCF residents
    - Older adults (≥65 or ≥75 years of age)
  - Support strained healthcare infrastructure:
    - Healthcare personnel with mild disease cannot work, so prevention of mild disease takes on greater importance as a public health goal in this population

- Time since vaccination with primary series also important
  - For many vaccines, a minimum interval beneficial for full ‘boosting effect’
  - Ability to benefit from ‘boosting effect’ extends well beyond the minimum interval
Booster doses of COVID-19 vaccines

Recommendations for Allocation of Initial Doses of COVID-19 Vaccines

- **Phase 1a**: LTCF Residents, Healthcare Personnel
- **Phase 1b**: Adults ≥75 years of age, Frontline Essential Workers
- **Phase 1c**: Adults ≥65 years of age, All Essential Workers, Adults 16-64 years of age with high-risk medical conditions

**Highest Risk Individuals**

**Time since recommendation**
Booster doses of COVID-19 vaccines

Recommendations for Allocation of Initial Doses of COVID-19 Vaccines

**Phase 1a**
- LTCF Residents
- Healthcare Personnel

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- Adults ≥65 years of age
- All Essential Workers
- Adults 16-64 years of age with high-risk medical conditions

**Highest Risk Individuals**

Time since recommendation

**Possible Recommendations for Initial Booster Doses**

- LTCF Residents
- Healthcare Personnel
- Adults ≥65/75 years of age

Time interval since receipt of last dose
Booster doses of COVID-19 vaccines

- ACIP will continue to review additional data:
  - Manufacturer data on safety + immunogenicity of booster doses
  - Effectiveness, breakthrough infections and epi data through August

- Further discussions around feasibility, implementation, and balance of benefit and risks by age group and population
Booster doses of COVID-19 vaccines

What are the **key considerations** for decision making?

**ACIP Meeting Aug 13**: Framework for COVID-19 booster doses presented

What **data** are available for decision making?

**ACIP Meeting Aug 30**: Begin to provide data to inform booster dose policy

Does ACIP **recommend** booster doses of COVID-19 vaccines in any populations?
Booster doses of COVID-19 vaccines

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- **ACIP Meeting Aug 13**: Framework for COVID-19 booster doses presented

What **data** are available for decision making?

- **ACIP Meeting Aug 30**: Begin to provide data to inform booster dose policy
- **ACIP Meeting mid-September**: Additional data to inform policy

Does ACIP **recommend** booster doses of COVID-19 vaccines in any populations?

- **ACIP Meeting after FDA authorization**: Possible vote
Acknowledgements

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- Eddie Shanley
- Megan Wallace
- Neela Goswami
- Kristine Schmidt

- Vaccine Task Force
- Epi Task Force
- Respiratory Viruses Branch
Questions for ACIP

1. Does ACIP agree with the proposed risk-based approach for COVID-19 booster dose recommendations?

2. What other questions would be important for ACIP to address?
Reference list for recent estimates of vaccine effectiveness against the Delta variant

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.