Summary and Work Group Interpretation:
Extended intervals for mRNA COVID-19 vaccines

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cdc.gov/coronavirus
Policy question for previous ACIP vote

Should vaccination with the Moderna COVID-19 vaccine (Spikevax, 2-dose primary series) be recommended for persons 18 years of age and older?

Regulatory action, GRADE, Evidence to Recommendation Framework, Vote

| Moderna COVID-19 vaccine | Compared to | No COVID-19 vaccine |
Question for discussion

- Based on new and emerging data, should CDC consider guidance around the interval between dose 1 and 2 for mRNA COVID-19 vaccines?

  Implementation;
  Discussions around myocarditis and intervals

- Moderna COVID-19 vaccine
- Pfizer-BioNTech COVID-19 vaccine
VaST assessment – Myocarditis/pericarditis following Moderna and Pfizer-BioNTech COVID-19 vaccination

- VaST reviewed the most recent data from three U.S. safety monitoring systems*, and well as data from international partners.
- Reported rates of myocarditis/pericarditis following mRNA COVID-19 vaccination are higher than background; rates are highest after dose 2 in adolescent and young adult males.
- In most safety monitoring systems, myocarditis/pericarditis risk appears higher after dose 2 Moderna than dose 2 Pfizer-BioNTech COVID-19 vaccination.
- Data are limited on myocarditis/pericarditis risk following different dose 1-dose 2 intervals+.

VaST: Vaccine Safety Technical (VaST) Work Group  *VAERS, v-safe, VSD
Summary: International data
Myocarditis after mRNA COVID-19 vaccines

- Risk of myocarditis/pericarditis was higher for Moderna than Pfizer vaccine
  - The highest risk was seen after the second dose among younger males

- Rates of myocarditis/pericarditis were lower with extended interval (≥8 weeks) between first and second dose of mRNA vaccine primary series
Summary
Extended primary series interval and mRNA COVID-19 vaccine effectiveness

- An extended primary series interval may improve immunogenicity and vaccine effectiveness
  - Antibody responses were higher following an extended interval (6–14 weeks) between the first and second doses of mRNA vaccine, compared to a standard interval (3–4 weeks)
  - mRNA vaccine effectiveness against infection and hospitalization was higher with an extended interval (6–8 weeks), compared to a standard interval (3–4 weeks)
Benefits and risks balance for mRNA COVID-19 vaccines
Adults ages 18–39 years

**Benefits**
- mRNA COVID-19 vaccines
  - Moderna COVID-19 vaccine
  - Pfizer-BioNTech COVID-19 vaccine

**Risks**
- mRNA COVID-19 vaccines
  - Moderna COVID-19 vaccine
  - Pfizer-BioNTech COVID-19 vaccine
Methods for assessment of benefit-risk balance

Benefits — Calculated per 1 million fully vaccinated people

- Age group: 18 – 39 years
  - Selected because this age group has the highest rates of myocarditis and lowest hospitalization rates among adults, and would therefore have the closest benefit/risk margin
- Age/sex specific hospitalization rates: COVID-NET (average of rates from Dec 11-Jan 1, 2022)\(^1\)
- Pooled vaccine-specific VE estimates from two platforms\(^2\)
- Time Horizon: 150-day period

Harms — Calculated per 1 million fully vaccinated people

- Vaccine-specific myocarditis rates from Vaccine Safety Datalink (VSD)

VE: Vaccine Effectiveness

\(^1\)https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html
\(^2\)https://covid.cdc.gov/covid-data-tracker/#vaccine-effectiveness
### Vaccine-specific estimates of effectiveness against COVID-19 hospitalization

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>IVY Network(^2), Oct – Nov, 2021 % (95% CI)</th>
<th>VISION(^2), Aug – Dec, 2021, % (95% CI)</th>
<th>Pooled VE Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderna</td>
<td>91 (89-93)</td>
<td>92 (91-93)</td>
<td>92</td>
</tr>
<tr>
<td>Pfizer-BioNTech</td>
<td>86 (83-88)</td>
<td>87 (86-88)</td>
<td>87</td>
</tr>
</tbody>
</table>

VE= vaccine effectiveness; VE reported for 2 doses of mRNA COVID-19 vaccines

2. VE estimate for 17-179 days after 2\(^{nd}\) dose
Reporting rates of myocarditis following mRNA COVID-19 vaccination (per million 2nd doses administered) among persons ages 18–39 years

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Sex</th>
<th>Rate per 1M 2nd Doses in 7-day risk period among persons ages 18–39 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderna</td>
<td>Males</td>
<td>67.5</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>33.0</td>
</tr>
<tr>
<td>Pfizer-BioNTech</td>
<td>Males</td>
<td>46.8</td>
</tr>
<tr>
<td></td>
<td>All</td>
<td>24.1</td>
</tr>
</tbody>
</table>

2. Data through Jan 15, 2022
Benefits and risks after mRNA COVID-19 vaccines among persons ages 18–39 years

- COVID-19-associated hospitalizations prevented by mRNA COVID-19 vaccines compared with myocarditis cases expected
- Presented by vaccine product
Benefits and risks after mRNA COVID-19 vaccines among males ages 18–39 years

*per million 2nd doses*

- COVID-19-associated hospitalizations prevented by mRNA COVID-19 vaccines compared with myocarditis cases expected
- Presented by vaccine product

COVID-19-Associated Hospitalizations Prevented per Million 2nd Doses of Moderna and Pfizer-BioNTech Vaccine

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Moderna</th>
<th>Pfizer-BioNTech</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-39</td>
<td>1903</td>
<td>1799</td>
</tr>
</tbody>
</table>

Cases of Myocarditis Expected per Million 2nd Doses of Moderna and Pfizer-BioNTech Vaccine

<table>
<thead>
<tr>
<th>Cases of Myocarditis Expected</th>
<th>Moderna</th>
<th>Pfizer-BioNTech</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-39</td>
<td>68</td>
<td>47</td>
</tr>
</tbody>
</table>
Limitations

- Benefit-risk analysis focuses on individuals 18–39 years of age, considers direct benefits and risk over a 150-day period, and compares vaccine vs. no vaccine

- VE assumptions used in the model do not yet include Omicron-specific VE estimates

- The model assumes static hospitalization rate over 5 months
  - Benefit/risk profile might change as hospitalization rates change

- Model does not account for booster doses or prior infection
Benefits and risks balance for mRNA COVID-19 vaccines

**Benefits**

- COVID-19 hospitalizations averted by Moderna COVID-19 vaccine greater than Pfizer-BioNTech COVID-19 vaccine

**Risks**

- Myocarditis after Moderna COVID-19 vaccine likely greater than Pfizer-BioNTech COVID-19 vaccine
Summary:
Benefit/risk balance

- Benefits for both mRNA COVID-19 vaccines far outweigh risk of myocarditis, compared with no vaccine.

- When compared to the benefit-risk balance for Pfizer-BioNTech COVID-19 vaccine, the Moderna vaccine prevents more COVID-19 hospitalizations, however more myocarditis cases would also be expected.
Summary: Myocarditis and Intervals

- When comparing the two mRNA COVID-19 vaccines, the risk of myocarditis/pericarditis was higher for Moderna than Pfizer vaccine
  - The highest risk was seen after the second dose among younger males

- Rates of myocarditis/pericarditis were lower with extended interval between first and second dose of mRNA vaccine primary series

- Extended primary series interval may improve immunogenicity and vaccine effectiveness
Question for discussion

- Based on new and emerging data, should CDC consider guidance around the interval between dose 1 and 2 for mRNA COVID-19 vaccines?

Implementation; Discussions around myocarditis and intervals

- Moderna COVID-19 vaccine
- Pfizer-BioNTech COVID-19 vaccine
Who would this apply to?
Number and percent of people with 0 doses administered, by age group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number (M)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>12–17 yrs</td>
<td>8.3</td>
<td>35</td>
</tr>
<tr>
<td>18–24 yrs</td>
<td>7.9</td>
<td>25</td>
</tr>
<tr>
<td>25–39 yrs</td>
<td>16.5</td>
<td>25</td>
</tr>
<tr>
<td>40–49 yrs</td>
<td>6.1</td>
<td>15</td>
</tr>
<tr>
<td>50–64 yrs</td>
<td>4.7</td>
<td>8</td>
</tr>
<tr>
<td>65–74 yrs</td>
<td>0.5</td>
<td>5</td>
</tr>
<tr>
<td>75+ yrs</td>
<td>0.5</td>
<td>5</td>
</tr>
</tbody>
</table>

Source: https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-people-onedose-pop-5yr

~33 million unvaccinated individuals ages 12–39 years
Considerations regarding extended intervals between first and second doses of mRNA vaccine (primary series)

Possible Benefits

- **Safety:**
  - Extended interval appears to reduce the risk of myocarditis
  - Lowest rates of myocarditis with interval at 8 weeks

- **Effectiveness:**
  - Extended interval appears to increase VE for primary series
  - Benefit may ‘level out’ at ≥8 weeks

- **Implementation:**
  - Possibility that uptake for COVID-19 vaccine primary series could increase if individuals/parents desire action to lower risk for myocarditis
Considerations regarding extended intervals between first and second doses of mRNA vaccine (primary series)

Possible Risks

- **Effectiveness**: Longer duration of time where individual only have the benefit of a single dose of mRNA vaccine

- **Implementation**: For aspects that require being ‘fully vaccinated’ (shorter quarantine, travel or restaurants, etc), extending interval would extend the time before being ‘fully vaccinated’
An individual’s risk of getting COVID-19 likely increases the longer they are only partially vaccinated with a single dose.

The risk would need to be balanced with the benefits of lowering rates of myocarditis and optimizing the long-term vaccine effectiveness.

This balance is influenced by trajectory of pandemic and recent epidemiology of COVID-19, and can change over time.

Early in the pandemic, the priority was for individuals to have optimum protection from the primary series as quickly as possible.

– Guidance around COVID-19 vaccines can be updated as new data become available and the focus expands to the future of the COVID-19 vaccine program.
Clear communication for COVID-19 vaccines and preferred intervals is important.

May be populations where the benefits of earlier interval (3 or 4 weeks) would outweigh possible risks of myocarditis.

- Licensed intervals of 3 weeks (Pfizer-BioNTech) or 4 weeks (Moderna) continue to be recommended, especially in circumstances where early protection is desired.

The Work Group supported a preferred interval of 8 weeks between the first and second dose of an mRNA COVID-19 vaccine primary series.
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- ACIP COVID-19 Vaccines Work Group
- Vaccine Task Force
- Epi Task Force
- Data Analytics and Visualization Task Force
- Respiratory Viruses Branch
Questions for ACIP

- What does ACIP think about an **extended interval** between the first and second doses of the mRNA COVID-19 vaccine primary series?

- What **time frame** does ACIP think would be preferred for the interval between first and second doses of the mRNA COVID-19 vaccine primary series?
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.