Pfizer-BioNTech COVID-19 vaccine and myocarditis in individuals aged 16-29 years: Benefits-Risk Discussion

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ACIP Meeting
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Benefits and risks of Pfizer-BioNTech COVID-19 vaccine by age and sex in individuals aged 16-29 years

**Benefits** of Pfizer-BioNTech COVID-19 vaccination

**Risk** of myocarditis after Pfizer-BioNTech COVID-19 vaccination
Background
There have been more than 38 million cases of COVID-19 in the United States since January 2020

January 23, 2020—August 26, 2021
Total number of cases: 38,341,339
New COVID-19 hospital admissions are increasing among young individuals

United States: 0-17 years
Total number of admissions Aug 1, 2020-Aug 24, 2021: 51,008

United States: 18-29 years
Total number of admissions Aug 1, 2020-Aug 24, 2021: 134,410

Forecasts of U.S. COVID-19 cases and hospitalizations project ongoing increases

Severe outcomes among patients hospitalized for COVID-19 in COVID-NET*, by age

*Source: COVID-NET March 1, 2020—June 30, 2021; LOS = Length of stay
MIS-C and MIS-A are severe inflammatory disorders occurring after SARS-CoV-2 and affecting younger individuals.

- 4,573* cases of multisystem inflammatory syndrome in children (MIS-C) reported in the United States.

- MIS-C cases trends follow SARS-CoV-2 infections by 2-6 weeks.

- With rising cases, a rise in MIS-C and multisystem inflammatory syndrome in adults (MIS-A) cases is expected to be reported.

https://www.cdc.gov/mis-c/cases/index.html; Of 4573 cases of MIS-C, the 4,533 reports with onset data available are plotted on this graph.
Risk of myocarditis following SARS-CoV-2 infection is described in several recent studies

- Patients with SARS-CoV-2 infection had **16-18 times higher risk for myocarditis** compared with patients without SARS-CoV-2; risk varied by age and sex
  - Retrospective cohort using administrative data from >800 U.S. hospitals\(^1\)
  - In a large national study from Israel\(^2\)

- Risk of myocarditis in individuals post-SARS-CoV-2 infection was **6-34 times higher** compared to those who received mRNA vaccine
  - Administrative dataset analysis of 48 large healthcare organizations in the U.S.\(^3\)
  - Retrospective cohort using EHR data from 42 U.S. healthcare systems\(^4\)

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\(^1\) Boehmer & Kompaniyets, et al., Association between COVID-19 and myocarditis using hospital-based administrative data. Pre-publication; CDC authors.


\(^4\) Block et al., Occurrence of myocarditis, pericarditis, and anaphylaxis in children and young adults after COVID-19 vaccination compared to SARS-CoV-2 infection. Pre-publication; CDC and university-affiliated authors.
Rare reports of myocarditis after mRNA COVID-19 vaccines

- **Myocarditis** following mRNA COVID-19 vaccination is a rare event observed primarily in males aged < 30 years, particularly after the second dose

- Benefit-risk assessment presented for adolescents (Pfizer-BioNTech) and young adults (Pfizer-BioNTech and Moderna) to ACIP June 23, 2021; benefits outweigh risks

- Benefit-risk assessment presented for adults 18+ to ACIP on July 22, 2021; benefits outweigh risks
Clinical outcomes of patients hospitalized with myocarditis after mRNA vaccination in recent preprint/publications

- Case series (n=7) of hospitalized patients\(^1\)
  - All 7 resolved their symptoms rapidly; all discharged home

- Case series of children <19 years (n=15) hospitalized with myocarditis following Pfizer-BioNTech vaccination\(^2\)
  - No ICU admissions; authors conclude these individuals had benign short-term clinical course

- Retrospective multi-center study across 16 hospitals (n=63) comparing 12-20-year-old patients with post-vaccination myocarditis to a cohort with MIS-C\(^3\)
  - Post-vaccination myocarditis patients had a mild hospital course with quick clinical recovery. Of patients followed up, all had normal ventricular function on echocardiography

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Clinical outcomes of patients hospitalized with myocarditis after Pfizer-BioNTech vaccination in safety surveillance systems

- **Vaccine Adverse Event Reporting System (VAERS)**
  - 16-29-year-olds, N=368:
    - 93% (344/368) hospitalized
    - 4% (16/368) admitted to ICU
    - 95% discharged to home
    - 0 deaths
    - Additional follow up ongoing

- **Vaccine Safety Datalink (VSD)**
  - 16-29-year-olds, N=16:
    - 94% (15/16) hospitalized; mean LOS: 1.9 days
      - 25% (4/16) admitted to ICU
      - 100% discharged to home
    - 0 deaths
    - Additional follow up ongoing

Source: Vaccine Safety Team; CDC and VSD. ICU = Intensive Care Unit; LOS = Length of Stay;

*VAERS reports received 8/18/21, reviewed through 8/25/21, following dose 1 or 2 within 21 days of vaccination*
Background summary

- COVID-19 incidence and hospitalization rates are increasing rapidly.

- Rare myocarditis occurs after mRNA vaccination, at higher rates in young males <30 years.

- Myocarditis can occur in patients with SARS-CoV-2 infection and at higher rates than in those who received mRNA vaccination.

- Hospitalization, COVID-19 in young adults:
  - Mean length of stay: 5 days, ~5% required mechanical ventilation; deaths occur.

- Hospitalization, post-vaccination myocarditis in young adults:
  - Mean length of stay: 1-2 days; no deaths.
Benefits-Risk Analysis for Pfizer-BioNTech COVID-19 Vaccine
Methods for assessment of benefit-risk balance similar to prior presentations to ACIP

Benefits

- Expected protection provided per 1 million second doses of Pfizer-BioNTech COVID-19 vaccine using:
  - Case incidence data and COVID-NET hospitalization and severity data through July 31 and projected hospitalization rates from CDC forecasts
  - Phase 3 trial VE for hospitalization (95%) and for COVID-19 symptomatic cases (95%)
  - 120-day period assumed

VE = vaccine efficacy
Methods for assessment of benefit-risk balance similar to prior presentations to ACIP

**Benefits**
- Expected protection provided per 1 million second doses of Pfizer-BioNTech COVID-19 vaccine using:
  - Case incidence data and COVID-NET hospitalization and severity data through July 31 and projected hospitalization rates from CDC forecasts
  - Phase 3 trial VE for hospitalization (95%) and for COVID-19 symptomatic cases (95%)
  - 120-day period assumed

**Potential harms**
- Estimated cases of myocarditis per 1 million second doses of Pfizer-BioNTech COVID-19 vaccine dose, by age and sex using VAERS data received and reviewed through August 18

21-day risk window for myocarditis used

VE = vaccine efficacy
Methods were adjusted to account for rising COVID-19 cases

- Cases increasing at rates not seen with previous benefit-risk analyses
- Adjustments made to account for increases:
  - Multiplied by ratio of current case incidence compared to July 31: 1.5 times higher
  - Four-week average for hospitalizations allows for more robust estimates by age and sex
  - Multiplied by ratio of current hospitalizations (August 22) compared to July 31: 3 times higher
- Estimated benefits over longer periods of time to account for future benefits likely to accrue

**Current Policy Discussion:**
Use of Pfizer-BioNTech COVID-19 vaccine in individuals ≥16 years of age

- Will update with additional ages and/or vaccines for future policy questions
# Myocarditis cases and reporting rates after Pfizer-BioNTech COVID-19 vaccination

- Over 17 million 2\textsuperscript{nd} Pfizer-BioNTech vaccine doses administered and 327 confirmed myocarditis cases in VAERS as of August 18, 2021 in persons aged 16-29 years

<table>
<thead>
<tr>
<th>Age group</th>
<th>Females</th>
<th></th>
<th>Males</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Doses admin</td>
<td>Reporting rate(\dagger)</td>
<td>Cases</td>
</tr>
<tr>
<td>16-17 years old</td>
<td>15</td>
<td>1,834,838</td>
<td>8.2</td>
<td>124</td>
</tr>
<tr>
<td>18-24 years old</td>
<td>12</td>
<td>4,279,917</td>
<td>2.8</td>
<td>140</td>
</tr>
<tr>
<td>25-29 years old</td>
<td>4</td>
<td>3,056,893</td>
<td>1.3</td>
<td>32</td>
</tr>
</tbody>
</table>

\*Source of doses administered: [https://covid.cdc.gov/covid-data-tracker/#vaccinations](https://covid.cdc.gov/covid-data-tracker/#vaccinations); some age- and sex-specific doses administered data were imputed

\(\dagger\)Reporting rate = myocarditis cases per 1 million mRNA COVID-19 mRNA second vaccine doses administered
Estimated COVID-19 cases prevented vs. myocarditis cases for every million Pfizer-BioNTech COVID-19 vaccinations over 120 days

Females 16-17 Years

- 77,800 COVID-19 cases prevented
- 520 hospitalizations prevented
- 100 ICU admissions prevented
- 4 deaths prevented
- 8 myocarditis cases

Males 16-17 Years

- 56,700 COVID-19 cases prevented
- 500 hospitalizations prevented
- 170 ICU admissions prevented
- 4 deaths prevented
- 73 myocarditis cases

Case incidence based on week of July 31 x 1.5; Hospitalizations, ICU admissions and deaths based on data for weeks of July 10-July 31 x 3 based on CDC forecasts
Estimated COVID-19 cases prevented vs. myocarditis cases for every million Pfizer-BioNTech COVID-19 vaccinations over 120 days

Females 18-24 Years

- **107,000** COVID-19 cases prevented
- **3,000** hospitalizations prevented
- **240** ICU admissions prevented
- **21** deaths prevented
- **3** myocarditis cases

Males 18-24 Years

- **75,200** COVID-19 cases prevented
- **1,000** hospitalizations prevented
- **230** ICU admissions prevented
- **2** deaths prevented
- **39** myocarditis cases

Case incidence based on week of July 31 x 1.5; Hospitalizations, ICU admissions and deaths based on data for weeks of July 10-July 31 x 3 based on CDC forecasts.
Estimated COVID-19 cases prevented vs. myocarditis cases for every million Pfizer-BioNTech COVID-19 vaccinations over 120 days

<table>
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<tr>
<th>Females 25-29 Years</th>
<th>Males 25-29 Years</th>
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<tr>
<td>105,000 COVID-19 cases prevented</td>
<td>76,600 COVID-19 cases prevented</td>
</tr>
<tr>
<td>4,100 hospitalizations prevented</td>
<td>2,200 hospitalizations prevented</td>
</tr>
<tr>
<td>240 ICU admissions prevented</td>
<td>490 ICU admissions prevented</td>
</tr>
<tr>
<td>16 deaths prevented</td>
<td>44 deaths prevented</td>
</tr>
<tr>
<td>1 myocarditis cases</td>
<td>12 myocarditis cases</td>
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Case incidence based on week of July 31 x 1.5; Hospitalizations, ICU admissions and deaths based on data for weeks of July 10-July 31 x 3 based on CDC forecasts.
Benefits and risks after Pfizer-BioNTech COVID-19 vaccination

For every million doses of vaccine given with US exposure risk and hospitalization rates projected through August 2021

COVID-19-Associated Hospitalizations & ICU Admissions Prevented by Pfizer-BioNTech vaccine

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Females</th>
<th>Males</th>
<th>Cases of myocarditis</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-17</td>
<td>520</td>
<td>500</td>
<td>8</td>
</tr>
<tr>
<td>18-24</td>
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For every million doses of vaccine given with US exposure risk and hospitalization rates projected through August 2021

- **Females**: 520 cases of COVID-19-associated hospitalizations, 100 cases of ICU admissions prevented by Pfizer-BioNTech vaccine.
- **Males**: 500 cases of COVID-19-associated hospitalizations, 170 cases of ICU admissions prevented by Pfizer-BioNTech vaccine.

**Cases of myocarditis**
- **16-17**: 8 cases
- **18-24**: 3 cases
- **25-29**: 1 case

**Benefits and risks**
- **Males**: 1,000 cases prevented, 73 myocarditis cases.
- **Females**: 4,100 cases prevented, 39 myocarditis cases.
Benefits and risks after Pfizer-BioNTech COVID-19 vaccination, lower VE

For every million doses of vaccine given with US exposure risk and hospitalization rates projected through August 2021, assuming vaccine effectiveness (VE) for cases: 74.6%; VE for hospitalizations: 84%.

COVID-19-Associated Hospitalizations & ICU Admissions Prevented by Pfizer-BioNTech vaccine

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<td>16-17</td>
<td>460</td>
<td>450</td>
</tr>
<tr>
<td>18-24</td>
<td>260</td>
<td>920</td>
</tr>
<tr>
<td>25-29</td>
<td>3,600</td>
<td>1,950</td>
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Cases of myocarditis

- 16-17: 8 cases for females, 73 cases for males
- 18-24: 3 cases for females, 39 cases for males
- 25-29: 1 case for females, 12 cases for males

Benefits and risks after Pfizer-BioNTech COVID-19 vaccination among males, over longer periods of time: 120 days

For every million doses of vaccine given with US exposure risk and hospitalization rates projected through August 2021

- COVID-19 associated hospitalizations prevented
- Myocarditis cases estimated

- Males 16-17 Years
- Males 18-24 Years
Benefits and risks after Pfizer-BioNTech COVID-19 vaccination among males, over longer periods of time: 180 days

For every million doses of vaccine given with US exposure risk and hospitalization rates projected through August 2021

- COVID-19 associated hospitalizations prevented
- Myocarditis cases estimated

Males 16-17 Years

Males 18-24 Years

Days

Cases (per million doses)
Benefits and risks after Pfizer-BioNTech COVID-19 vaccination among males, over longer periods of time: 365 days

For every million doses of vaccine given with US exposure risk and hospitalization rates projected through August 2021

**Males 16-17 Years**
- COVID-19 associated hospitalizations prevented
- Myocarditis cases estimated

**Males 18-24 Years**
- COVID-19 associated hospitalizations prevented
- Myocarditis cases estimated
## Benefits and risks after Pfizer-BioNTech COVID-19 vaccination

*For every million doses of vaccine given with US exposure risk and hospitalization rates projected through August 2021*

<table>
<thead>
<tr>
<th>Age Group</th>
<th>COVID-19 cases prevented</th>
<th>COVID-19 hospitalizations Prevented</th>
<th>COVID-19 ICU admissions prevented</th>
<th>Myocarditis cases expected per million</th>
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Summary of benefit-risk balance for Pfizer-BioNTech COVID-19 vaccination and myocarditis in individuals aged 16-29 years

- Direct risk assessment for Pfizer-BioNTech COVID-19 vaccine & myocarditis
  - Considers individual benefits of vaccination vs. individual risks
  - Considers receipt of vaccine versus no vaccine
  - Indirect benefits of vaccine were not considered in this analysis

- The Work Group assessed that the **benefits** of vaccination **outweigh** the risks for each age/sex group evaluated
  - As with previous analyses, balance of benefits and risks varies by age/sex
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