Updated Guidance for Clinicians on COVID-19 Vaccines

Clinician Outreach and Communication Activity (COCA) Call
Friday, December 17, 2021
Continuing Education

- Continuing education is not offered for this webinar.
To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov
Today’s Presenters

- Isaac See, MD
  Vaccine Safety Team
  Vaccine Task Force
  COVID-19 Response
  Centers for Disease Control and Prevention

- Sara Oliver, MD, MSPH
  LCDR, U.S. Public Health Service
  Lead, Advisory Committee for Immunization Practices COVID-19 Vaccines Work Group
  Vaccine Task Force
  COVID-19 Response
  Centers for Disease Control and Prevention
Updates on Thrombosis with Thrombocytopenia Syndrome (TTS)

Clinician Outreach and Communication Activity (COCA)

Dec 17, 2021

Isaac See, MD
Vaccine Safety Team
CDC COVID-19 Vaccine Task Force

cdc.gov/coronavirus
Background
Thrombosis with thrombocytopenia syndrome (TTS): new syndrome recognized after adenoviral-vectored COVID-19 vaccines

AstraZeneca’s COVID-19 vaccine: EMA finds possible link to very rare cases of unusual blood clots

News 07/04/2021

EMA confirms overall benefit-risk remains positive

EMA’s safety committee (PRAC) has concluded today that unusual blood clots in very rare cases of AstraZeneca’s COVID-19 vaccine are no longer listed as very rare side effects of Vaxzevria (formally known as AstraZeneca COVID-19 Vaccine) and will be reassessed as rare side effects.

In reaching its conclusion, the committee took into account advice from an ad hoc expert group.

Thrombosis with thrombocytopenia syndrome (TTS): new syndrome recognized after adenoviral-vectored COVID-19 vaccines

Thrombosis with thrombocytopenia syndrome (TTS), also known as de novo antiphospholipid syndrome, is a rare but serious complication that can occur after the adenoviral-vectored COVID-19 vaccines. It is a new syndrome recognized by the European Medicines Agency (EMA) following reports of very rare cases of unusual blood clots.

References:

- https://jamanetwork.com/journals/jama/fullarticle/2779731
- https://www.cdc.gov/mmwr/volumes/70/rr/mm7018e2.htm?s_cid=mm7018e2_w
Cerebral Venous Sinus Thrombosis (CVST)

Features of severe CVST

- CVST is often under-diagnosed due to its nonspecific presentation
- Short-term death from CVST usually caused by brain herniation
  - Resulting from large or multiple hemorrhages (bleed) or from diffuse brain edema (swelling)
- Reported prognostic factors for poor short-term outcome include:
  - Anatomical: brain herniation, hemorrhage
  - Clinical presentation: seizures, depressed consciousness, altered mental status

Timeline for initial U.S. events for TTS following Janssen COVID-19 Vaccine, 2021

- **Feb 27**: FDA authorizes Janssen COVID-19 Vaccine
- **Mar 2**: First post-authorization U.S. doses of Janssen COVID-19 Vaccine
- **Apr 13**: CDC/FDA announce pause in use of Janssen COVID-19 Vaccine after identification of 6 cases of CVST with thrombocytopenia
- **Apr 23**: ACIP reviews data; Reaffirms recommendation for Janssen COVID-19 Vaccine; CDC/FDA lift pause; CDC interim clinical considerations and FDA EUA fact sheets updated with information about risk of TTS particularly in women <50 years of age
- **Jul 22**: ACIP reviews Janssen COVID-19 Vaccine benefit/risk data again in light of Guillain-Barré syndrome (TTS data included)

[Links]
- https://www.cdc.gov/media/releases/2021/s0413-jj-vaccine.html
- https://www.fda.gov/media/146304/download
- https://www.cdc.gov/mmwr/volumes/70/wr/mm7032e4.htm
VAERS is the nation’s early warning system for vaccine safety

Vaccine Adverse Event Reporting System

http://vaers.hhs.gov
CISA
Clinical Immunization Safety Assessment (CISA) Project

7 participating medical research centers with vaccine safety experts

- clinical consult services*
- clinical research

Case finding in VAERS for TTS following COVID-19 vaccines

- VAERS database search conducted daily for possible TTS reports
  - Healthcare providers directly contacted CDC with potential TTS
  - CDC initiates an investigation and facilitates submission of a VAERS report
- Medical records requested for all potential TTS case reports to confirm thrombosis with laboratory evidence of thrombocytopenia, using working case definition, reviewed by CDC and FDA medical officers
- CISA experts, including hematology/neurology, confirm clinical syndrome consistent with TTS and rule out other causes of thrombosis and thrombocytopenia
CDC working case definition for TTS following COVID-19 Vaccine

<table>
<thead>
<tr>
<th>TTS category</th>
<th>Thrombosis location</th>
<th>Platelet count</th>
<th>Positive PF4 ELISA* test required?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tier 1</td>
<td>Unusual location, e.g., CVST, abdominal venous or arterial thrombosis</td>
<td>&lt;150,000 cells/µL</td>
<td>No</td>
</tr>
<tr>
<td>Tier 2</td>
<td>Only in ‘typical’ location(s), e.g., pulmonary embolism, deep vein thrombosis of extremity</td>
<td>&lt;150,000 cells/µL</td>
<td>Yes</td>
</tr>
</tbody>
</table>

- Reports where only thrombosis is ischemic stroke or myocardial infarction are excluded
- Cases with concurrent COVID-19 infection excluded

*PF4 ELISA: platelet factor 4 enzyme-linked immunosorbent assay
Analytic periods

- Descriptive epidemiology and reporting rates for TTS cases receiving Janssen COVID-19 Vaccine March 2–August 31, 2021
- Summarize information about all deaths among TTS cases following Janssen COVID-19 Vaccine confirmed by December 9, 2021
- Reporting rates for TTS deaths receiving Janssen COVID-19 Vaccine March 2–August 31, 2021
Epidemiology of U.S. TTS cases following Janssen COVID-19 vaccination (March 2–August 31, 2021)
Characteristics of U.S. TTS cases after Janssen COVID-19 vaccination*, N=54 (Tier 1=46, Tier 2=8)

- Median age: 44.5 years (range 18–70 years)
- Female (n=37), male (n=17)
- 26 (48%) are women aged <50 years
- 83% in white non-Hispanic persons
- 29 of the TTS cases (54%) have a cerebral venous sinus thrombosis (CVST)
- Pregnant or postpartum (n=0)
- Known or newly diagnosed thrombophilia (n=0)
- Past SARS-CoV-2 infection (n=7); 5 by history, 2 by nucleocapsid serology testing only

*Vaccinated March 2–August 31, 2021
Characteristics of U.S. TTS cases after Janssen COVID-19 vaccination*, N=54 (continued)

- Median time from vaccination to symptom onset: 9 days (range 0–18 days)
- Median time from symptom onset to admission: 5 days (range: 0–30 days)
- 39 (72%) received the Janssen COVID-19 Vaccine before the pause on April 13, 2021
- All after dose 1 of Janssen COVID-19 Vaccine (i.e., none after booster doses)

*Vaccinated March 2–August 31, 2021
Number of TTS cases following Janssen COVID-19 vaccination, by month of vaccination* (N=54)

*Vaccinated March 2–August 31, 2021
U.S. TTS cases, by time from Janssen COVID-19 vaccination to symptom onset, (N=53*)

*Exact symptom onset could not be determined for one case but known to be ≤12 days after vaccination. Vaccinations March 2–August 31, 2021
Venous thrombosis risk factors in U.S. TTS cases following Janssen COVID-19 vaccination*, N=54

<table>
<thead>
<tr>
<th>Risk factor** (not mutually exclusive)</th>
<th>n (%)</th>
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</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>25 (46)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>16 (30)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7 (13)</td>
</tr>
<tr>
<td>Systemic estrogen therapy†</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Other venous thrombosis risk factor‡</td>
<td>3 (6)</td>
</tr>
<tr>
<td>None of the above risk factors</td>
<td>21 (39)</td>
</tr>
</tbody>
</table>

* Vaccinated March 2–August 31, 2021
† 2 receiving combined oral contraceptives and 1 on estradiol patch for hormone replacement therapy
‡ Other venous thrombosis risk factors include cirrhosis, malignancy, fertility treatment, venous catheter at thrombosis site; one case had both venous catheter at thrombosis site and malignancy
Outcomes among U.S. TTS cases following Janssen COVID-19 vaccination, N=54*

- All hospitalized
- ICU admission (n=36)
- Length of stay for patients surviving hospitalization
  - Median 9 days
  - Range: 1–132 days
  - Interquartile range: 6–17 days
- Outcome of hospitalization
  - Death (n=8)
  - Discharged to post-acute care facility (n=9)
  - Discharged home (n=37)

*Vaccinated March 2–August 31, 2021
Reporting rates of TTS after Janssen COVID-19 vaccine, vaccination through August 31, 2021 (N=54)

14.1 million total Janssen COVID-19 vaccine doses administered*

<table>
<thead>
<tr>
<th>Age group</th>
<th>Females</th>
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<th></th>
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<th></th>
<th>Males</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>TTS cases</td>
<td>Doses admin</td>
<td>Reporting rate† (per million)</td>
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<td></td>
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<tr>
<td>18-29 yrs old</td>
<td>5</td>
<td>1,089,649</td>
<td>4.59</td>
<td>3</td>
<td>1,565,212</td>
<td>1.92</td>
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<tr>
<td>30-39 yrs old</td>
<td>11</td>
<td>1,037,386</td>
<td>10.60</td>
<td>3</td>
<td>1,443,900</td>
<td>2.08</td>
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<tr>
<td>40-49 yrs old</td>
<td>10</td>
<td>1,108,495</td>
<td>9.02</td>
<td>6</td>
<td>1,392,990</td>
<td>4.30</td>
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</tr>
<tr>
<td>50-64 yrs old</td>
<td>9</td>
<td>2,002,984</td>
<td>4.49</td>
<td>5</td>
<td>2,338,263</td>
<td>2.14</td>
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<tr>
<td>65+ yrs old</td>
<td>2</td>
<td>1,096,923</td>
<td>1.82</td>
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<td>1,004,285</td>
<td>0</td>
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</tbody>
</table>

Overall reporting rate: 3.83 cases per million Janssen doses

*Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations
† Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered
### Reporting rates of TTS after Janssen COVID-19 vaccine, vaccination March 2–August 31, 2021 (N=54)

14.1 million total Janssen COVID-19 vaccine doses administered*

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Overall reporting rate: 3.83 cases per million Janssen doses
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Overall reporting rate: 3.83 cases per million Janssen doses

Similar rates
Reporting rates of TTS after Janssen COVID-19 vaccine, females: data presented to ACIP Jul 2021 vs Dec 2021

<table>
<thead>
<tr>
<th>Age group</th>
<th>Females (Jul ACIP*)</th>
<th></th>
<th>Females (Dec ACIP**)</th>
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<tbody>
<tr>
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<td>TTS cases</td>
<td>Doses admin</td>
<td>Reporting rate†</td>
<td>TTS cases</td>
</tr>
<tr>
<td>18-29 yrs old</td>
<td>4</td>
<td>946,358</td>
<td>4.22</td>
<td>5</td>
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<tr>
<td>30-49 yrs old</td>
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<td>1,934,574</td>
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<td>50-64 yrs old</td>
<td>7</td>
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<td>1,028,190</td>
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<tr>
<td>Total</td>
<td>28</td>
<td>5,774,494</td>
<td>4.85</td>
<td>37</td>
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† Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered
Reporting rates of TTS after Janssen COVID-19 vaccine, males: data presented to ACIP Jul 2021 vs Dec 2021

<table>
<thead>
<tr>
<th>Age group</th>
<th>Males (Jul ACIP*)</th>
<th>Males (Dec ACIP**)</th>
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<tbody>
<tr>
<td></td>
<td>TTS cases</td>
<td>Doses admin</td>
</tr>
<tr>
<td>18-29 yrs old</td>
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<td>1,281,479</td>
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<td>30-49 yrs old</td>
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<td>2,440,773</td>
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<tr>
<td><strong>Total</strong></td>
<td>10</td>
<td>6,795,823</td>
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</table>

† Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered
U.S. TTS Deaths Following Janssen COVID-19 Vaccination
Epidemiology of TTS deaths following Janssen COVID-19 vaccination through December 9, 2021 (N=9*)

- All after dose 1 of Janssen COVID-19 Vaccine
- Median age: 45 years (range: 28–62)
- Sex: female (n=7), male (n=2)
- Race/ethnicity: all non-Hispanic white
- Underlying medical conditions:
  - Obesity (n=7)
  - Hypertension (n=3)
  - Diabetes (n=2)
  - None of the above (n=2)
  - Iron deficiency anemia (n=2)
  - Hypothyroidism (n=2)
  - Other** (n=4)

* One TTS death confirmed in a person vaccinated with Janssen COVID-19 Vaccine after August 31, 2021
** Other includes (n=1 each) asthma, gastroesophageal reflux disease, obstructive sleep apnea, hyperlipidemia, seizure disorder; one patient with both hyperlipidemia and seizure disorder
Clinical description of TTS deaths following Janssen COVID-19 vaccination through December 9, 2021 (N=9)

- All have features of severe CVST: large or multiple cerebral hemorrhages; evidence of intracranial edema and/or mass effect; depressed consciousness and/or seizure
- 7 with confirmed CVST
- None received IV heparin for treatment
- Four received craniectomy/craniotomy for brain hemorrhage
- Median time from symptom onset to admission: 3 days (range: 0-5)
- Median time from admission to death: 1 day (range: 0-2)
Revisit TTS updates to ACIP 2021

<table>
<thead>
<tr>
<th>Date of meeting</th>
<th>Purpose of discussion</th>
<th>Cut-off for data</th>
<th>No. Janssen doses given</th>
<th>Total TTS cases</th>
<th>Total TTS deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apr 23</td>
<td>Discuss resolution of Janssen pause</td>
<td>Apr 21</td>
<td>7.98 million</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>May 12</td>
<td>General follow-up on TTS</td>
<td>May 7</td>
<td>8.73 million</td>
<td>28</td>
<td>3</td>
</tr>
<tr>
<td>Jul 22</td>
<td>Updated benefit-risk discussion (including Guillain-Barré)</td>
<td>Jul 8</td>
<td>12.5 million</td>
<td>38</td>
<td>4</td>
</tr>
</tbody>
</table>
Revisit TTS updates to ACIP 2021: comparing previously presented data with data as of Dec 9, 2021

<table>
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<tr>
<td></td>
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<td>50</td>
<td>6</td>
</tr>
<tr>
<td>Dec 16</td>
<td>TTS update</td>
<td>Aug 31</td>
<td>14.1 million</td>
<td>54</td>
<td>8</td>
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</tbody>
</table>
TTS death reporting rate with Janssen COVID-19 vaccination by August 31, 2021 (N=8 confirmed deaths)

Overall death reporting rate: 0.57 per million Janssen COVID-19 Vaccine doses

<table>
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<tr>
<th>Age group</th>
<th>Females</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TTS</td>
<td>Doses</td>
<td>Reporting rate↑</td>
<td>TTS</td>
<td>Doses</td>
</tr>
<tr>
<td></td>
<td>deaths</td>
<td>admin</td>
<td>(per million)</td>
<td>deaths</td>
<td>admin</td>
</tr>
<tr>
<td>18-29 yrs old</td>
<td>0</td>
<td>1,089,649</td>
<td>0</td>
<td>1</td>
<td>1,565,212</td>
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<td>1,037,386</td>
<td>1.93</td>
<td>0</td>
<td>1,443,900</td>
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<td>1</td>
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<td>2,002,984</td>
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<td>0</td>
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<td>1,004,285</td>
</tr>
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</table>

Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations;
↑ Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered
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**Highest rates**

Source of doses administered: [https://covid.cdc.gov/covid-data-tracker/#vaccinations]; † Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered
TTS death reporting rate with Janssen COVID-19 vaccination by August 31, 2021 (N=8 confirmed deaths)

Overall death reporting rate: 0.57 per million Janssen COVID-19 Vaccine doses

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<tbody>
<tr>
<td></td>
<td>TTS deaths</td>
<td>Doses admin</td>
<td>Reporting rate† (per million)</td>
<td>TTS deaths</td>
</tr>
<tr>
<td>18-29 yrs old</td>
<td>0</td>
<td>1,089,649</td>
<td>0</td>
<td>1</td>
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<tr>
<td>30-39 yrs old</td>
<td>2</td>
<td>1,037,386</td>
<td>1.93</td>
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<tr>
<td>40-49 yrs old</td>
<td>2</td>
<td>1,108,495</td>
<td>1.80</td>
<td>1</td>
</tr>
<tr>
<td>50-64 yrs old</td>
<td>2</td>
<td>2,002,984</td>
<td>1.00</td>
<td>0</td>
</tr>
<tr>
<td>65+ yrs old</td>
<td>0</td>
<td>1,096,923</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

% of TTS cases with death: Vaccinated before pause**: 5/39 (13%)
Vaccinated after pause**: 3/15 (20%)

Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations;

† Reporting rate = TTS cases per 1 million Janssen COVID-19 vaccine doses administered
In addition: two possible TTS deaths with Janssen COVID-19 vaccination*

- Features shared with confirmed TTS deaths after Janssen COVID-19 vaccine
  - Symptoms beginning within 7–14 days of vaccination
  - Large cerebral hemorrhage with mass effect and thrombocytopenia
  - Rapid progression from admission to death (1–2 days)
- Difference: no definitive imaging for CVST; no imaging for other thrombosis
- Reviewed with CISA investigators
  - Difficult to confirm as TTS cases because of lack of documented thrombosis
  - Clinically concerned that TTS with CVST is underlying cause of hemorrhage

*Of these two possible TTS deaths following Janssen COVID-19 vaccination, one is in a woman between 50–64 years of age and the other in a man 40–49 years. Both vaccinated before the pause in Janssen COVID-19 vaccination.
Limitations

- Possible underdiagnosis of CVST and TTS
- VAERS is passive surveillance system
- Therefore, case and death reporting rates might be underestimates
Summary

- U.S. TTS case reporting rate (3.8 per million doses) following Janssen COVID-19 vaccination higher than previously presented
  - Case reporting rates for men 40–49 years and women 50–64 years similar to women 18–29 years (~4–5 per million doses)
- U.S. TTS deaths following Janssen COVID-19 vaccination:
  - Have typical features of severe CVST: clinical course from symptoms to admission, and admission to death is rapid
  - Are more common than known during previous presentations to ACIP (TTS death reporting rate following Janssen: ~2 per million doses in women 30–49 years)
  - Proportion of TTS cases with death did not decrease after Janssen pause on April 13
Acknowledgements

- VAERS (CDC and FDA teams)
- CISA Project and Investigators
- COVID-19 Vaccine Task Force
- COVID-19 Vaccine Task Force, Vaccine Safety Team
- Immunization Safety Office
- People reporting to VAERS
Thank you!

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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.

Mention of a product or company name is for identification purposes only and does not constitute endorsement by CDC or FDA.
Updates to the benefit/risk assessment for Janssen COVID-19 vaccines: Applying the Evidence to Recommendation Framework

Sara Oliver, MD MSPH
COCA Call
December 17, 2021
Evidence to Recommendations (EtR) Framework
Policy Question

- Should vaccination with the Janssen COVID-19 vaccine (1 dose) be recommended for persons 18 years of age and older under an Emergency Use Authorization?
Public Health Problem
Trends in COVID-19 cases in the United States

January 23, 2020 – December 13, 2021

50,052,008 total cases

7-day average: 117,890 cases

SARS-CoV-2 Variants Circulating in the United States

Variant Proportions, August 29 - December 11, 2021

https://covid.cdc.gov/covid-data-tracker/#variant-proportions
Thrombosis with Thrombocytopenia Syndrome (TTS) after Janssen COVID-19 vaccine in the United States

- Through August 31, 2021: 54 cases of TTS identified after Janssen COVID-19 vaccine, for an overall reporting rate of 3.83 per million Janssen doses
  - TTS rates highest among females 30–39 years of age (10.6 per million doses) and 40–49 years of age (9.0 per million doses)

- Through December 2, 2021: 9 TTS deaths following Janssen COVID-19 vaccine, for an overall reporting rate of 0.57 per million Janssen doses
  - TTS death rates highest among females 30–39 years of age (1.93 per million doses) and 40–49 years of age (1.8 per million doses)
Thrombosis with Thrombocytopenia Syndrome (TTS) after AstraZeneca COVID-19 vaccine in Europe

- April 2021: EU reporting ~10 cases per million vaccinated adults
  - Most cases in women aged <60 years within 2 weeks of receiving 1st vaccine dose

- September 2021: EMA’s PRAC updated the product information by removing the previous statement reporting TTS cases occurred mostly in women <60 years of age
  - 43% of cases in males and 37% in vaccinated person >60 years
  - 1503 cases of TTS reported, 592 million doses administered worldwide as of 25 July 2021

- December 2021: UK reported 428 cases of blood clotting with low platelets
  Rate: 15.3 per million doses (49 million doses given)
  - 50% of cases in women. Age range: 18–93 years. 74 deaths (17%); 6 deaths after second dose
  - Most cases occurred after first vaccine dose; 47 cases occurred after second dose

EU: European Union  EMA: European Medicines Agency  PRAC: Pharmacovigilance Risk Assessment Committee

Vaccine policy for adenovirus vector vaccines

- Vaccine policy evaluated from 16 countries*
  - Primarily higher income countries with broad access to mRNA and adenovirus vector vaccines, not globally representative of all adenovirus vector vaccine policy

- All 16 had recommendations for use of the AstraZeneca COVID-19 vaccine:
  - 5 (31%) halted use of the vaccine
  - 7 (44%) use the vaccine, but have a preferential recommendation for other COVID-19 vaccines
  - 2 (12%) don’t have a preferential recommendation, but recommend use only in older ages
  - 2 (12%) recommend use of the vaccine in all ages/populations

- 12 had recommendations for use of the Janssen COVID-19 vaccine:
  - 3 (25%) halted use of the vaccine
  - 4 (33%) use the vaccine, but have a preferential recommendation for other COVID-19 vaccines
  - 1 (8%) doesn’t have a preferential recommendation, but recommend use only in older ages
  - 4 (33%) recommend use of the vaccine in all ages/populations

*Australia, Canada, Denmark, Finland, France, Germany, Israel, Japan, Mexico, Netherlands, Norway, Philippines, South Africa, Spain, Sweden, United Kingdom
Benefit-Risk Analysis for Janssen COVID-19 vaccine
Timeline of Janssen COVID-19 benefit-risk review

Benefit-risk to inform decision making during the Janssen COVID-19 vaccine pause

April 2021

Benefit-risk review of all vaccine-associated events (TTS, GBS, myocarditis)

July 2021

Benefit-risk of Janssen COVID-19 vaccine in the context of additional data, sufficient vaccine supply

December 2021

TTS= Thrombosis with thrombocytopenia syndrome; GBS= Guillain-Barré syndrome
1. MacNeil et al. http://dx.doi.org/10.15585/mmwr.mm7017e4
2. Rosenblum et al. http://dx.doi.org/10.15585/mmwr.mm7032e4
Methods for assessment of benefit-risk balance

**Benefits** — Calculated per 1 million fully vaccinated people

- Age groups: 18 – 49 years, 50 – 64 years, ≥65 years
- Age/sex specific hospitalization rates: COVID-NET (week ending Nov 13, 2021)\(^2\)
- Age/vaccine specific VE estimates from IVY Network\(^3\)
- Time Horizon: 180-day period

**Harms** — Calculated per 1 million fully vaccinated people

- TTS rates from cases reported to VAERS and reviewed with clinicians from CDC’s Clinical Immunization Safety Assessment (CISA) Project
- Previously presented GBS\(^4\) and myocarditis\(^5\) rates from VAERS

VE: Vaccine Effectiveness

3. Self et al. MMWR 2021
### Vaccine-specific estimates of effectiveness against COVID-19 hospitalization

<table>
<thead>
<tr>
<th>Age group</th>
<th>Janssen, % (95% CI)</th>
<th>mRNA, % (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-49 years</td>
<td>73 (37-88)</td>
<td>92 (88-95)</td>
</tr>
<tr>
<td>50-64 years</td>
<td>69 (38-84)</td>
<td>92 (88-94)</td>
</tr>
<tr>
<td>65+ years</td>
<td>76 (48-89)</td>
<td>88 (84-91)</td>
</tr>
</tbody>
</table>

VE= vaccine effectiveness; VE reported for 1 dose of Janssen COVID-19 vaccine, and 2 doses of mRNA COVID-19 vaccines

1. [https://www.cdc.gov/mmwr/volumes/70/wr/mm7038e1.htm](https://www.cdc.gov/mmwr/volumes/70/wr/mm7038e1.htm)
2. For age strata specific estimates, adjusted for continuous age in years, calendar date (biweekly), HHS region, sex, and race/ethnicity
# Reporting rates of TTS following Janssen COVID-19 vaccination (per million doses administered)

<table>
<thead>
<tr>
<th>Age group</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TTS case rate</td>
<td>TTS death rate</td>
</tr>
<tr>
<td>18-49 years old</td>
<td>8.7</td>
<td>1.2</td>
</tr>
<tr>
<td>50-64 years old</td>
<td>4.5</td>
<td>1.0</td>
</tr>
<tr>
<td>≥65 years old</td>
<td>1.8</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Data as of August 31, 2021.
Framework for benefit-risk analysis

Benefits vs risks of Janssen COVID-19 vaccine compared with no vaccine, by age and sex

Differential benefits and risks of Janssen COVID-19 vaccine compared with mRNA COVID-19 vaccines, including risks of GBS and myocarditis
Benefits and risks after Janssen COVID-19 vaccine

*per million fully vaccinated people*

- COVID-19-associated hospitalizations prevented by Janssen COVID-19 vaccine compared with TTS cases expected
- Presented by age groups and sex

**COVID-19-Associated Hospitalizations Prevented Among Males and Females**

- Age groups (years)
  - 18-49
  - 50-64
  - ≥65

**Cases of TTS Expected Among Males and Females**

- Age groups (years)
  - 18-49
  - 50-64
  - ≥65

- Numbers represent cases per million fully vaccinated people.
Benefits and risks after Janssen COVID-19 vaccine, Females
per million fully vaccinated people

- COVID-19 associated hospitalizations prevented by Janssen COVID-19 vaccine compared with TTS and GBS cases expected
- Presented by age groups for females

**COVID-19-Associated Hospitalizations Prevented per Million Doses of Janssen COVID-19 vaccines**

- Age groups (years)
  - 18-49: 3729
  - 50-64: 11181
  - ≥65: 24149

**TTS and GBS Cases Expected per Million Janssen Doses**

- Age groups
  - 18-49: 9
  - 50-64: 5
  - ≥65: 7
Benefits and risks after Janssen and mRNA COVID-19 vaccine, Females

*per million fully vaccinated people*

- COVID-19 associated hospitalizations prevented by Janssen COVID-19 vaccine (1 dose) compared with TTS and GBS cases expected
- COVID-19 associated hospitalizations prevented by mRNA COVID-19 vaccines (2 dose) compared with myocarditis cases expected
- Presented by age groups for females

**COVID-19-Associated Hospitalizations Prevented per Million Doses of Janssen and per Million 2nd doses of mRNA COVID-19 vaccines**

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>COVID-19-Associated Hospitalizations Prevented</th>
<th>TTS and GBS Cases Expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-49</td>
<td>3729</td>
<td>9</td>
</tr>
<tr>
<td>50-64</td>
<td>11181</td>
<td>5</td>
</tr>
<tr>
<td>≥65</td>
<td>24149</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>27962</td>
<td>2</td>
</tr>
</tbody>
</table>

**Myocarditis Cases Expected per Million mRNA 2nd doses**

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>Myocarditis Cases Expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-49</td>
<td>9</td>
</tr>
<tr>
<td>50-64</td>
<td>7</td>
</tr>
<tr>
<td>≥65</td>
<td>2</td>
</tr>
</tbody>
</table>
Benefits and risks after Janssen and mRNA COVID-19 vaccine, Males

For every million doses of vaccine given

- COVID-19 associated hospitalizations prevented by Janssen COVID-19 vaccine (1 dose) compared with TTS and GBS cases expected
- COVID-19 associated hospitalizations prevented by mRNA COVID-19 vaccines (2 dose) compared with myocarditis cases expected
- Presented by age groups for males

COVID-19-Associated Hospitalizations Prevented per Million Doses of Janssen and per Million 2nd doses of mRNA COVID-19 vaccines

TTS and GBS Cases Expected per Million Janssen Doses and Myocarditis Cases Expected per Million mRNA 2nd doses
Severity of vaccine associated events

Myocarditis after mRNA COVID-19 vaccines
- At 3 month follow-up, over 90% are ‘fully recovered’ by cardiologist or healthcare provider
- No confirmed deaths

TTS after Janssen COVID-19 vaccines
- ~15% mortality rate
- 17% required discharge to post-acute care/rehabilitation facility

GBS after Janssen COVID-19 vaccines
- ~1% mortality rate
- 10% required mechanical ventilation

---

2Presentation, Dr. See:
Limitations

- Benefit-risk analysis considers direct benefits and risk over a 180-day period comparing vaccine vs. no vaccine
- Model compares single dose Janssen series with 2-dose mRNA series
- Model assumes static hospitalization rate and VE over a 6-month period
- Model does not account for booster doses or prior infection
Summary of benefit-risk balance for Janssen COVID-19 vaccine

- Direct benefit-risk assessment for Janssen COVID-19 vaccine & TTS
  - Considers individual benefits of vaccination vs. individual risks

- Using current VE estimates, benefit/risk balance of Janssen COVID-19 vaccine is still favorable for all age and sex groups \textit{compared with no vaccine}

- When compared to benefit-risk balance for mRNA COVID-19 vaccines, the Janssen vaccine prevents \textit{fewer} COVID-19 hospitalizations, ICU admissions, and deaths

- \textbf{More severe} health impacts from TTS and GBS after Janssen COVID-19 vaccine, compared to impacts from myocarditis after mRNA COVID-19 vaccines

- In a setting where mRNA and Janssen COVID-19 vaccines are both available, \textbf{benefit/risk balance} for mRNA COVID-19 vaccines likely \textit{more favorable} across all age and sex groups
Values
Acceptability
Feasibility
U.S. COVID-19 vaccine administration by vaccine type
As of December 15, 2021

- **Pfizer-BioNTech**: 284,069,934 doses
- **Moderna**: 186,454,785 doses
- **J&J/Janssen**: 17,272,247 doses
- **Other**: 499,123 doses

Total doses administered: 488,296,089
Number of people with a booster dose in the U.S. by COVID-19 vaccine type
As of December 15, 2021

- Pfizer-BionTech: 30,289,141
- Moderna: 24,905,140
- J&J/Janssen: 873,139
- Other: 12,745

56.1 million booster doses

COVID-19 booster dose type by primary series type
United States, as of December 15, 2021

Data on booster dose type by primary series type for Texas are unavailable. As such, these metrics do not include people who received doses of vaccine in Texas.

Administration of Janssen COVID-19 vaccines in the U.S. since authorization by age and sex, primary series and booster doses

Pause in administration of Janssen COVID-19 vaccines

Authorization of booster doses
Administration of Janssen COVID-19 vaccines in the U.S. among males since pause, primary series and booster doses

Primary dose (since early September)
~65,000 doses administered per week

Booster dose (since authorization)
~50,000 doses administered per week
Administration of Janssen COVID-19 vaccines in the U.S. among females since pause, primary series and booster doses

Primary dose (since early September)
~45,000 doses
administered per week

Booster dose (since authorization)
~50,000 doses
administered per week
Administration of Janssen COVID-19 vaccines in the U.S. since pause, by race and ethnicity

![Graph showing the doses administered by race and ethnicity from January to December 2021.](image-url)
Most populations can receive the Janssen vaccine
Jurisdictional survey, December 2021

Jurisdictions reported that the Janssen vaccine was available to nearly all populations.

Q: Which populations are offered the Janssen vaccine?

- Experiencing homelessness: 70%
- Homebound populations: 70%
- Incarcerated individuals: 63%
- Migrant or seasonal populations: 59%
- Rural populations: 57%
- College students: 50%
- Those at higher risk of COVID-19: 48%
- Educators: 48%
- LCTFS: 39%

Jurisdictions also conveyed easier, more widespread access to all populations:

- "Any individual may receive Janssen if they go to a provider that offers it."
- "All providers are given the option to order and administer J+J."
- "Pretty much anyone who wants the Janssen vaccine can have it as long as they go to a provider who carries it."
- "It is offered specifically if requested by the person setting up the clinic, but it is also offered as a choice at all community clinics and mass vaccination sites."

Jurisdictional survey on Janssen vaccine, December 12-15, 2021 (n=46)
ACIP reaffirmed its interim recommendation for use of the Janssen COVID-19 vaccine in all persons aged ≥18 years under FDA’s EUA, including a warning that rare clotting events might occur after vaccination, primarily among women aged 18-49 years.

- Education around the risk for TTS with Janssen COVID-19 vaccine, as well as the availability of alternative COVID-19 vaccines, is required to guide vaccine decision-making.
GBS after Janssen vaccine identified and benefit/risk balance reassessed

ACIP determined that overall, the benefits of COVID-19 vaccination in preventing COVID-19 morbidity and mortality outweigh the risks for these rare serious adverse events

- Balance of benefits and risks varies by sex
• Additional case review and ongoing safety surveillance identified cases (previous and newly occurring) of TTS, including deaths

• No longer in the setting of limited mRNA COVID-19 vaccine supply in the US
Proposed policy options for Janssen COVID-19 recommendations discussed with the Work Group

• Reaffirm recommendations for all age and sex
  – In setting of FDA warning on EUA, guidance in clinical considerations

• Recommend vaccination only for older adults (≥50 or ≥65 years of age)

• Recommend against use for all persons

• Preferential recommendations for mRNA COVID-19 vaccines over the Janssen COVID-19 vaccines
Work Group Summary

• In the setting where there are no alternative COVID-19 vaccines, the benefits of Janssen COVID-19 vaccines outweigh the risks
  – Important for global situations where there may not be other COVID-19 vaccines available

• Due to both higher vaccine effectiveness of mRNA vaccines and severity of safety issues with the Janssen vaccine, in the setting of widely available mRNA COVID-19 vaccines in the US, the benefit/risk balance of mRNA COVID-19 vaccines is more favorable than for Janssen COVID-19 vaccines
Work Group Summary

• Based on reviewing the totality of the data, the Work Group supported a **preferential recommendation** for mRNA COVID-19 vaccines
  – Similar to other countries with mRNA and adenovirus-vector vaccines available

• Will continue to review available data on vaccine effectiveness and safety; updates to recommendations can be made as needed

• **Education** around the risks associated with adenovirus-vector vaccines will be critical for those who may choose to receive Janssen vaccine

• Ensuring **access** to mRNA COVID-19 vaccines in all individuals is critical
  – If Janssen COVID-19 vaccine is only vaccine offered to some harder-to-reach populations, could result in inequitable distribution of risk for TTS and GBS
ACIP Vote

mRNA COVID-19 vaccines are preferred over the Janssen COVID-19 vaccine for the prevention of COVID-19 for those ≥18 years of age
Guidance for a preferential recommendation

- In most situations, mRNA COVID-19 vaccines are **preferred** over the Janssen COVID-19 vaccine for primary and booster vaccination, including those who received Janssen COVID-19 vaccine for their single dose primary series.

- Janssen COVID-19 vaccines **may be offered** to the following populations:
  - Persons with a contraindication to mRNA COVID-19 vaccines (e.g. severe allergic reaction after a previous dose or to a component of an mRNA COVID-19 vaccine)
  - Persons who would otherwise remain unvaccinated for COVID-19 due to limited access to mRNA COVID-19 vaccines
  - Persons who would prefer the Janssen COVID-19 vaccine despite safety concerns identified
Guidance for a preferential recommendation

- Persons who elect to receive a Janssen COVID-19 vaccine should be informed, as part of the pre-vaccination discussion with the vaccine provider, about the risk and symptoms of TTS that could occur in the 2 weeks after vaccination, the need to seek immediate medical care should symptoms develop, and the availability of mRNA COVID-19 vaccines.

- Vaccine providers should start the two-dose mRNA COVID-19 vaccine series, even if there is uncertainty about how the patient will receive their second dose; two-dose mRNA vaccines can be used in any population or setting.

- It is contraindicated to administer Janssen COVID-19 vaccine to persons with a history of TTS following receipt of Janssen or other adenovirus vector-based COVID-19 vaccines (e.g. AstraZeneca’s COVID-19 vaccine).
Acknowledgements

- Megan Wallace
- Stephen Hadler
- Sarah Mbaeyi
- Jack Gersten
- Monica Godfrey
- Jefferson Jones
- Eddie Shanley
- Agam Rao
- Valerie Morelli
- JoEllen Wolicki
- Anthony Fiore
- Susan Goldstein

- Erin Ricketts
- Faisal Minhaj
- Roodly Archer
- Amanda Cohn
- Tom Shimabukuro
- John Su
- Fiona Havers
- Christopher Taylor
- Ruth Link-Gelles
- Mark Tenforde

- COVID-NET Team
- DAV Vaccine Team
- Vaccine Safety Team
- Epidemiology and Surveillance Task Force
- Vaccine Task Force
For more information, contact CDC
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Thank you

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  - Submit your question

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- **What:** Video recording

- **Where:** On the COCA Call webpage
  
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