



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.

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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)

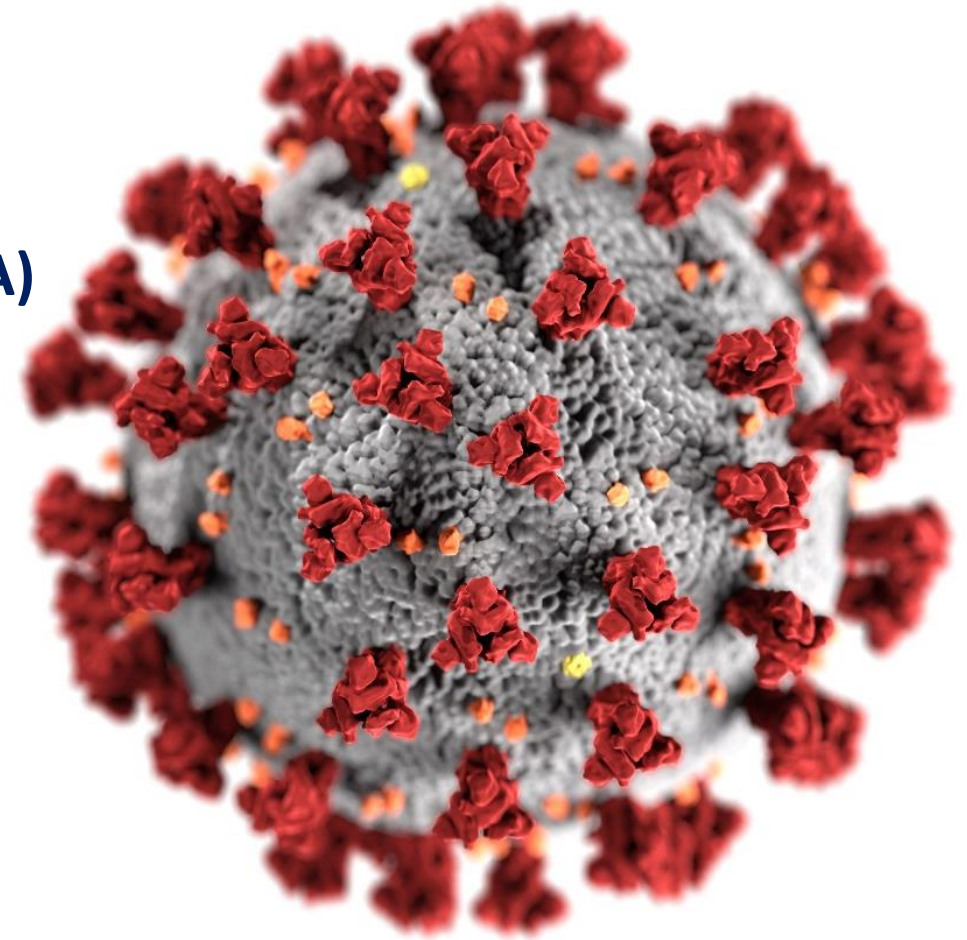
Clinician Outreach and Communication Activity (COCA)

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



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

Share

News 07/04/2021

EMA confirms overall benefit-risk remains positive

EMA's safety committee (PRAC) has concluded today that the very rare cases of unusual blood clots should be listed as very rare side effects of Vaxzevria (from

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

Research

JAMA | Original Investigation

US Case Reports of Cerebral Venous Sinus Thrombosis With Thrombocytopenia After Ad26.COVS.2S Vaccination: March 2 to April 21, 2021

Isaac See, MD; John R. Su, MD, PhD, MPH; Allison Lale, MD, MPH; Emily Jane Woo, MD, MPH; Alice Y. Guh, MD, MPH; Tom T. Shimabukuro, MD, MPH, MBA; Michael B. Streiff, MD; Agam K. Rao, MD; Allison P. Wheeler, MD, MSCI; Suzanne F. Beavers, MD; Anna P. Durbin, MD; Kathryn Edwards, MD; Elaine Miller, RN, MPH; Theresa A. Harrington, MD, MPH&TM; Adamma Mba-Jonas, MD, MPH; Narayan N. Duong T. Nguyen, DO; Kawsar R. Talaat, MD; Victor C. Urrutia, MD; Shannon C. Walker, MD; C. Buddy Creech, MD; Thomas A. Clark, MD, MPH; Frank DeStefano, MD, MPH; Karen R. Broder, MD

Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Early Release / Vol. 70

April 30, 2021

Safety Monitoring of the Janssen (Johnson & Johnson) COVID-19 Vaccine — United States, March–April 2021

David K. Shay, MD¹; Julianne Gee, MPH¹; John R. Su, MD, PhD¹; Tanya R. Myers, PhD¹; Paige Marquez, MSPH¹; Ruiling Liu, PhD¹; Bicheng Zhang, MS¹; Charles Licata, PhD¹; Thomas A. Clark, MD¹; Tom T. Shimabukuro, MD¹

On February 27, 2021, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for Janssen (Ad.26.COVS.2S) COVID-19 vaccine (Janssen Biotech, Inc., a Janssen Pharmaceutical company, Johnson

VAERS reports reviewed, 97% were classified as nonserious and 3% as serious,[†] including three reports among women of cases of thrombosis in large arteries or veins accompanied by thrombocytopenia during the second week after vaccination.

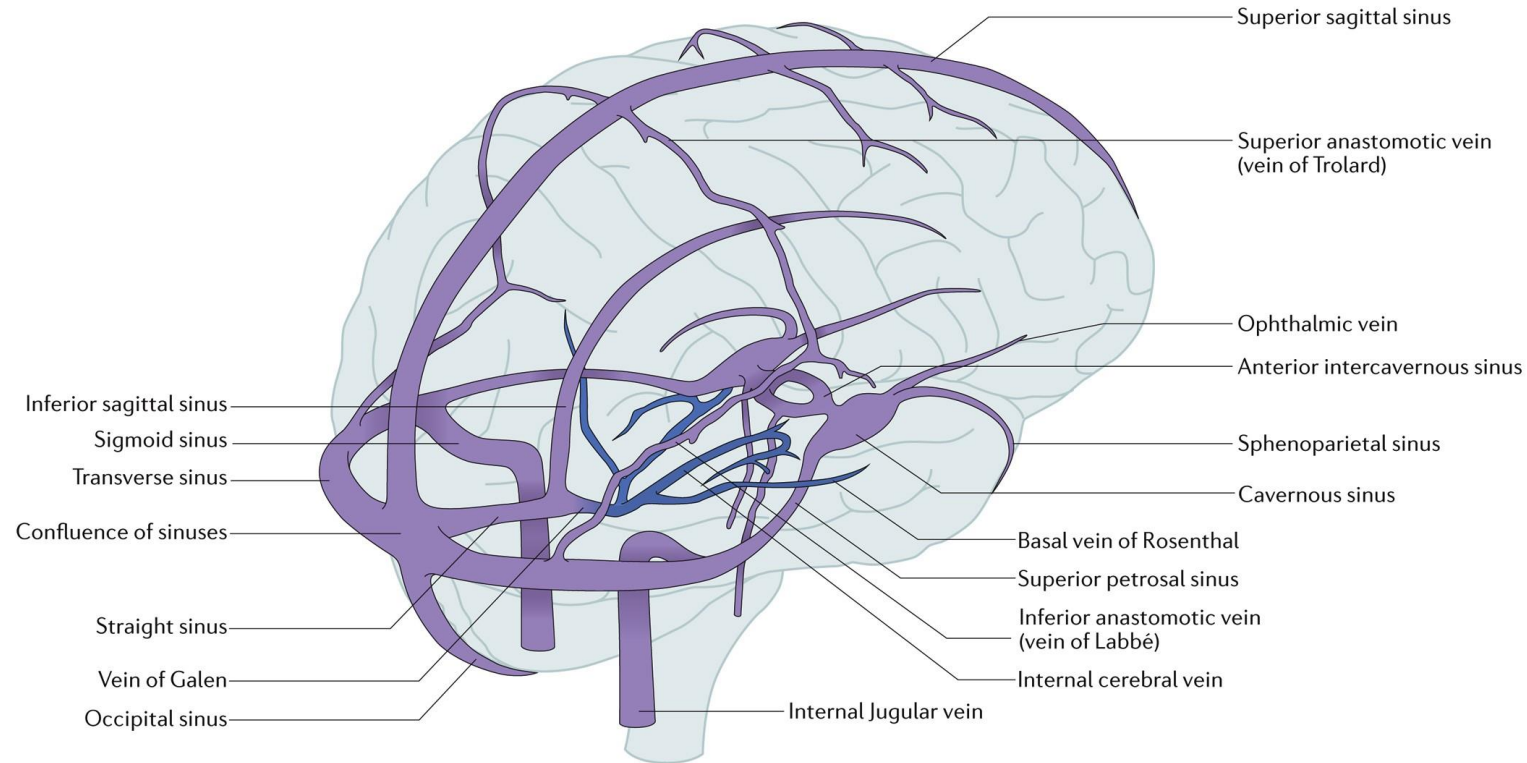
<https://www.ema.europa.eu/en/news/astrazenecas-covid-19-vaccine-ema-finds-possible-link-very-rare-cases-unusual-blood-clots-low-blood>

<https://jamanetwork.com/journals/jama/fullarticle/2779731>

https://www.cdc.gov/mmwr/volumes/70/wr/mm7018e2.htm?s_cid=mm7018e2_w



Cerebral Venous Sinus Thrombosis (CVST)



Nature Reviews | Neurology



Source: Silvis SM et al, Nature Reviews Neurology **13**, 555-565 (2017).

Features of severe CVST

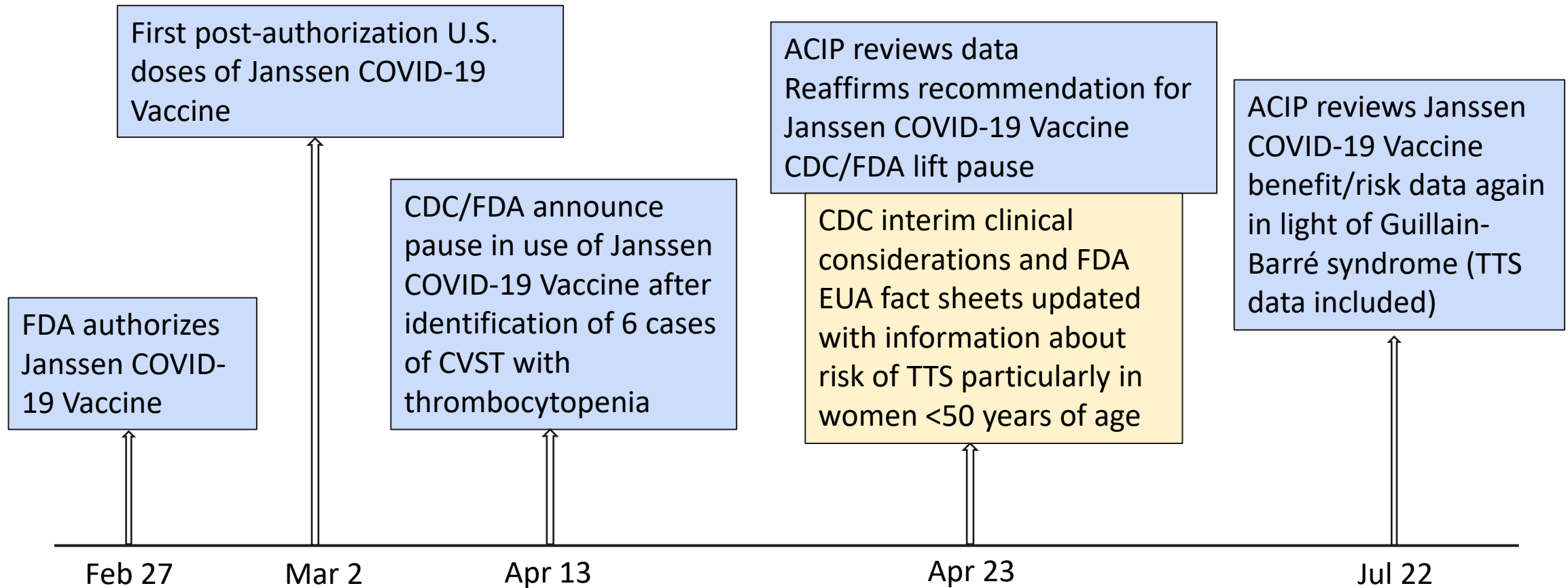
- CVST is often under-diagnosed due to its nonspecific presentation
- Short-term death from CVST usually caused by brain herniation
 - Resulting from large or multiple hemorrhages (bleed) or from diffuse brain edema (swelling)
- Reported prognostic factors for poor short-term outcome include:
 - Anatomical: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



Idiculla PS et al. Cerebral Venous Thrombosis: a comprehensive review. *Eur Neuro* 2020;83:369-379.

Saposnik G, et al. AHA/ASA scientific statement. Diagnosis and management of cerebral venous thrombosis. *Stroke* 2011;42:1158-1192.

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



<https://www.cdc.gov/media/releases/2021/s0413-JJ-vaccine.html>; <https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.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



VAERS

Vaccine Adverse Event Reporting System

<http://vaers.hhs.gov>

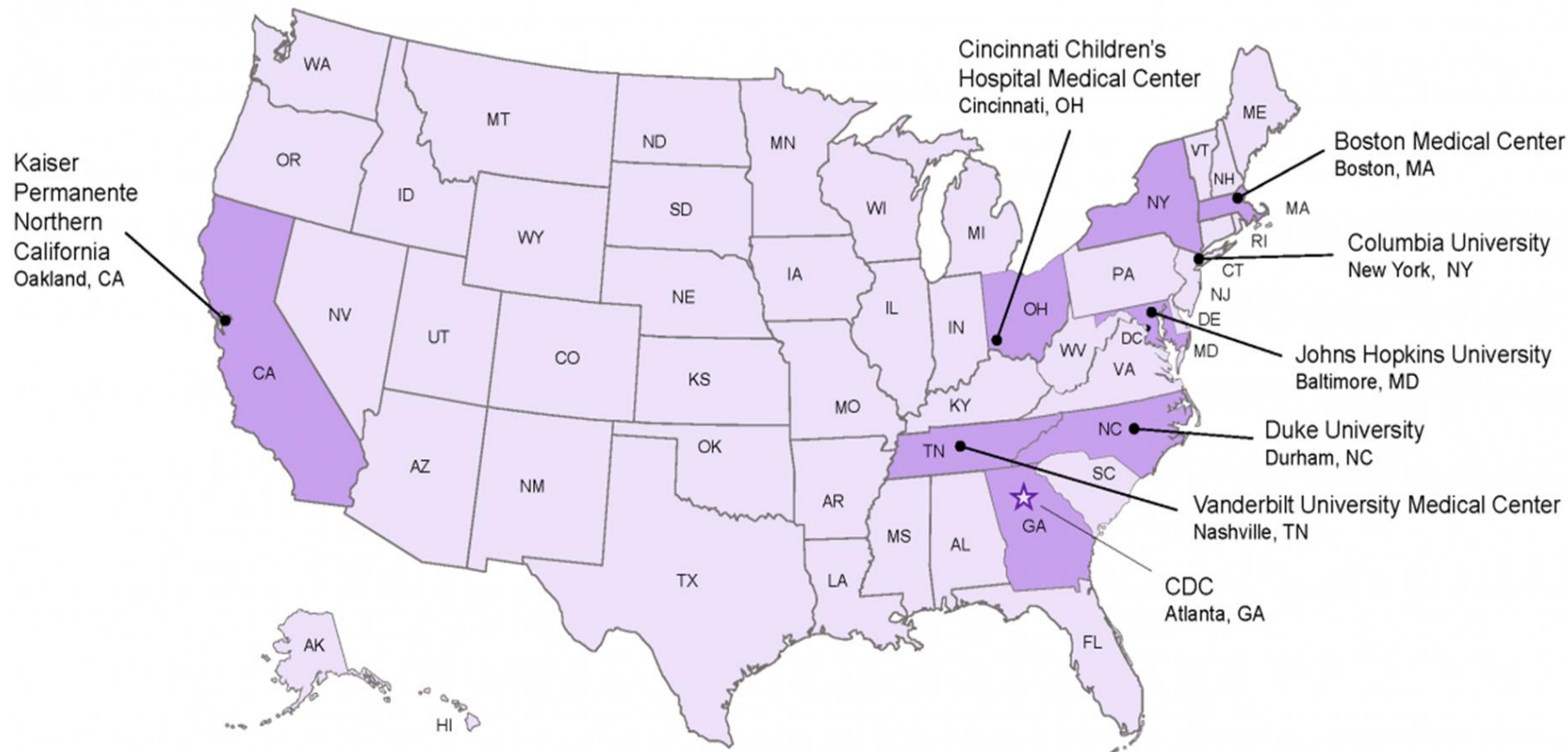




CISA

Clinical Immunization Safety Assessment (CISA) Project

7 participating medical research centers with vaccine safety experts



- clinical consult services*
- clinical research

*More information about clinical consults available at <http://www.cdc.gov/vaccinesafety/Activities/CISA.html>



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

TTS category	Thrombosis location	Platelet count	Positive PF4 ELISA* test required?
Tier 1	Unusual location, e.g., CVST, abdominal venous or arterial thrombosis	<150,000 cells/ μ L	No
Tier 2	Only in 'typical' location(s), e.g., pulmonary embolism, deep vein thrombosis of extremity	<150,000 cells/ μ L	Yes

- 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

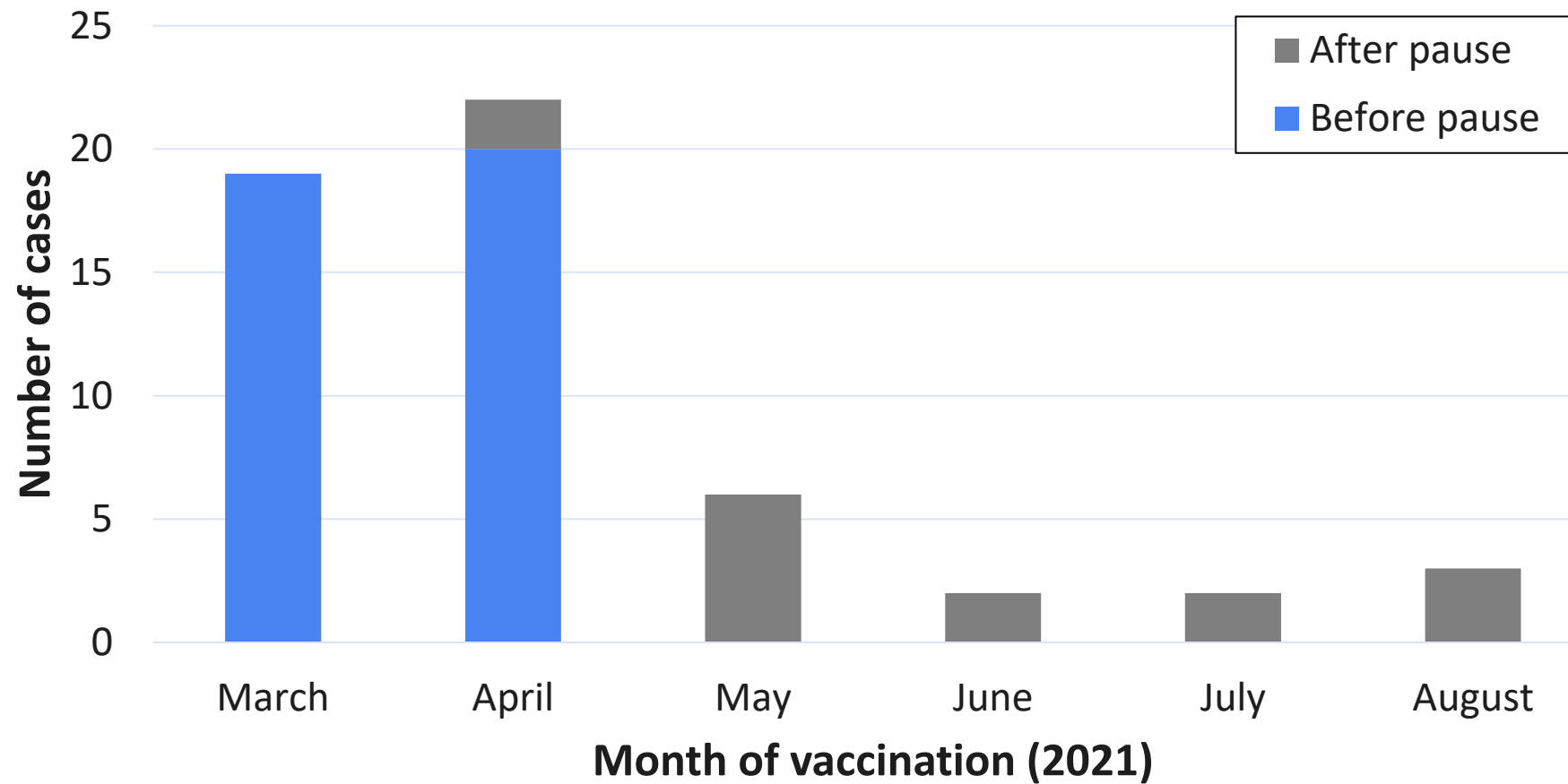
Characteristics of U.S. TTS cases after Janssen COVID-19 vaccination*, N=54 (continued)

- 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)



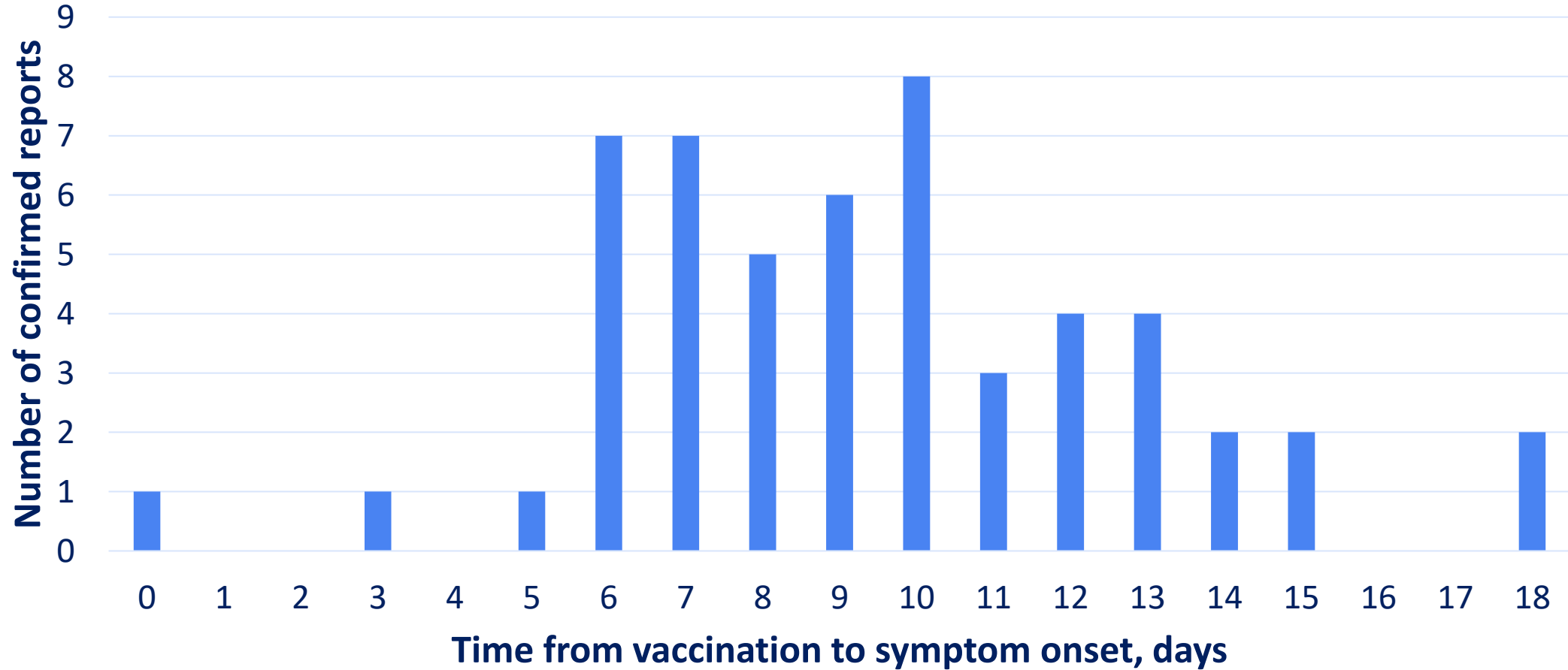
*Vaccinated March 2–August 31, 2021

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

Risk factor** (not mutually exclusive)	n (%)
Obesity	25 (46)
Hypertension	16 (30)
Diabetes	7 (13)
Systemic estrogen therapy [†]	3 (6)
Other venous thrombosis risk factor [‡]	3 (6)
None of the above risk factors	21 (39)

* Vaccinated March 2–August 31, 2021

** Venous thrombosis risk factors as described in Lijfering WM et al, Br J Haematol 2020; and Crous-Bou M et al, Semin Thromb Hemost 2016.

[†] 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*

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

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

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40-49 yrs old	10	1,108,495	9.02	6	1,392,990	4.30
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Highest rates

Overall reporting rate: 3.83 cases per million Janssen doses



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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, vaccination March 2–August 31, 2021 (N=54)

14.1 million total Janssen COVID-19 vaccine doses administered*

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

Similar rates

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, females: data presented to ACIP Jul 2021 vs Dec 2021

Age group	Females (Jul ACIP*)			Females (Dec ACIP**)		
	TTS cases	Doses admin	Reporting rate [†] (per million)	TTS cases	Doses admin	Reporting rate [†] (per million)
18-29 yrs old	4	946,358	4.22	5	1,089,649	4.59
30-49 yrs old	17	1,934,574	8.79	21	2,145,881	9.79
50-64 yrs old	7	1,865,372	3.75	9	2,002,984	4.49
65+ yrs old	0	1,028,190	0	2	1,096,923	1.82
Total	28	5,774,494	4.85	37	6,335,437	5.84



* Jul ACIP: vaccination through Jul 8, 2021 <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/05-COVID-Rosenblum-508.pdf>

** Current data: vaccination through August 31, 2021. 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, males: data presented to ACIP Jul 2021 vs Dec 2021

Age group	Males (Jul ACIP*)			Males (Dec ACIP**)		
	TTS cases	Doses admin	Reporting rate [†] (per million)	TTS cases	Doses admin	Reporting rate [†] (per million)
18-29 yrs old	3	1,281,479	2.34	3	1,565,212	1.92
30-49 yrs old	4	2,440,773	1.64	9	2,836,890	3.17
50-64 yrs old	3	2,130,473	1.41	5	2,338,263	2.14
65+ yrs old	0	943,098	0	0	1,004,285	0
Total	10	6,795,823	1.47	17	7,744,650	2.20



* Jul ACIP: vaccination through Jul 8, 2021 <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/05-COVID-Rosenblum-508.pdf>

** Current data: vaccination through August 31, 2021. 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

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

Date of meeting	Purpose of discussion	Cut-off for data	No. Janssen doses given	Total TTS cases	Total TTS deaths
Apr 23	Discuss resolution of Janssen pause	Apr 21	7.98 million	15	3
May 12	General follow-up on TTS	May 7	8.73 million	28	3
Jul 22	Updated benefit-risk discussion (including Guillain-Barré)	Jul 8	12.5 million	38	4



Revisit TTS updates to ACIP 2021: comparing previously presented data with data as of Dec 9, 2021

Date of meeting	Purpose of discussion	Cut-off for data	No. Janssen doses given	Total TTS cases	Total TTS deaths
Apr 23	Discuss resolution of Janssen pause	Apr 21	7.98 million	15 39	3 5
May 12	General follow-up on TTS	May 7	8.73 million	28 43	3 6
Jul 22	Updated benefit-risk discussion (including Guillain-Barré)	Jul 8	12.5 million	38 50	4 6
Dec 16	TTS update	Aug 31	14.1 million	54	8



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

Age group	Females			Males		
	TTS deaths	Doses admin	Reporting rate [†] (per million)	TTS deaths	Doses admin	Reporting rate [†] (per million)
18-29 yrs old	0	1,089,649	0	1	1,565,212	0.64
30-39 yrs old	2	1,037,386	1.93	0	1,443,900	0
40-49 yrs old	2	1,108,495	1.80	1	1,392,990	0.72
50-64 yrs old	2	2,002,984	1.00	0	2,338,263	0
65+ yrs old	0	1,096,923	0	0	1,004,285	0



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)

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40-49 yrs old	2	1,108,495	1.80	1	1,392,990	0.72
50-64 yrs old	2	2,002,984	1.00	0	2,338,263	0
65+ yrs old	0	1,096,923	0	0	1,004,285	0

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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18-29 yrs old	0	1,089,649	0	1	1,565,212	0.64
30-39 yrs old	2	1,037,386	1.93	0	1,443,900	0
40-49 yrs old	2	1,108,495	1.80	1	1,392,990	0.72
50-64 yrs old	2	2,002,984	1.00	0	2,338,263	0
65+ yrs old	0	1,096,923	0	0	1,004,285	0

% 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

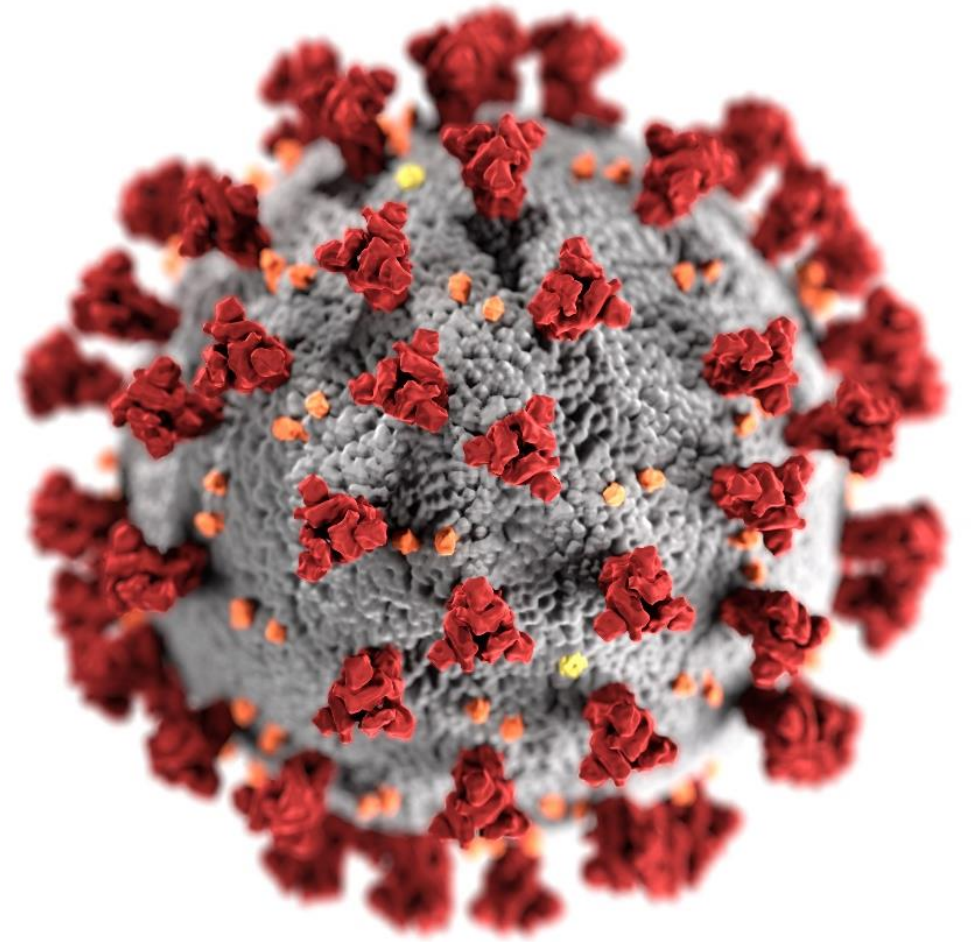


Acknowledgements

- 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!



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

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

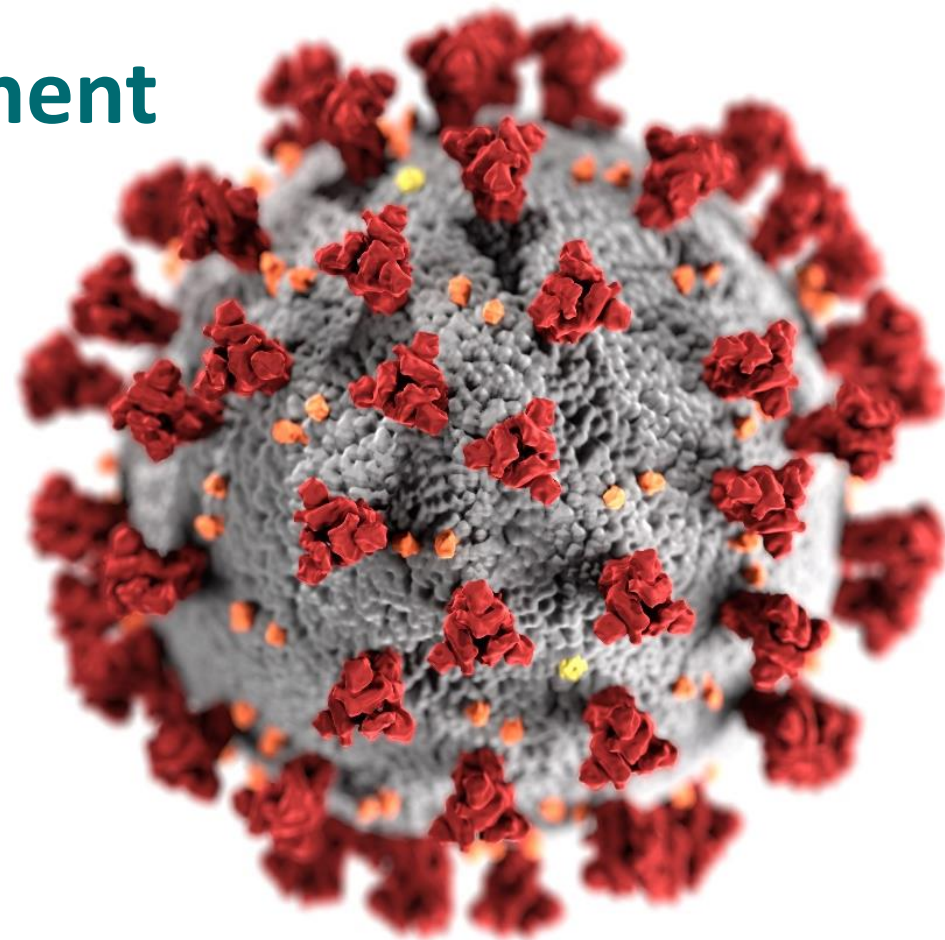
FDA.

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



cdc.gov/coronavirus

Evidence to Recommendations (EtR) Framework

Policy Question

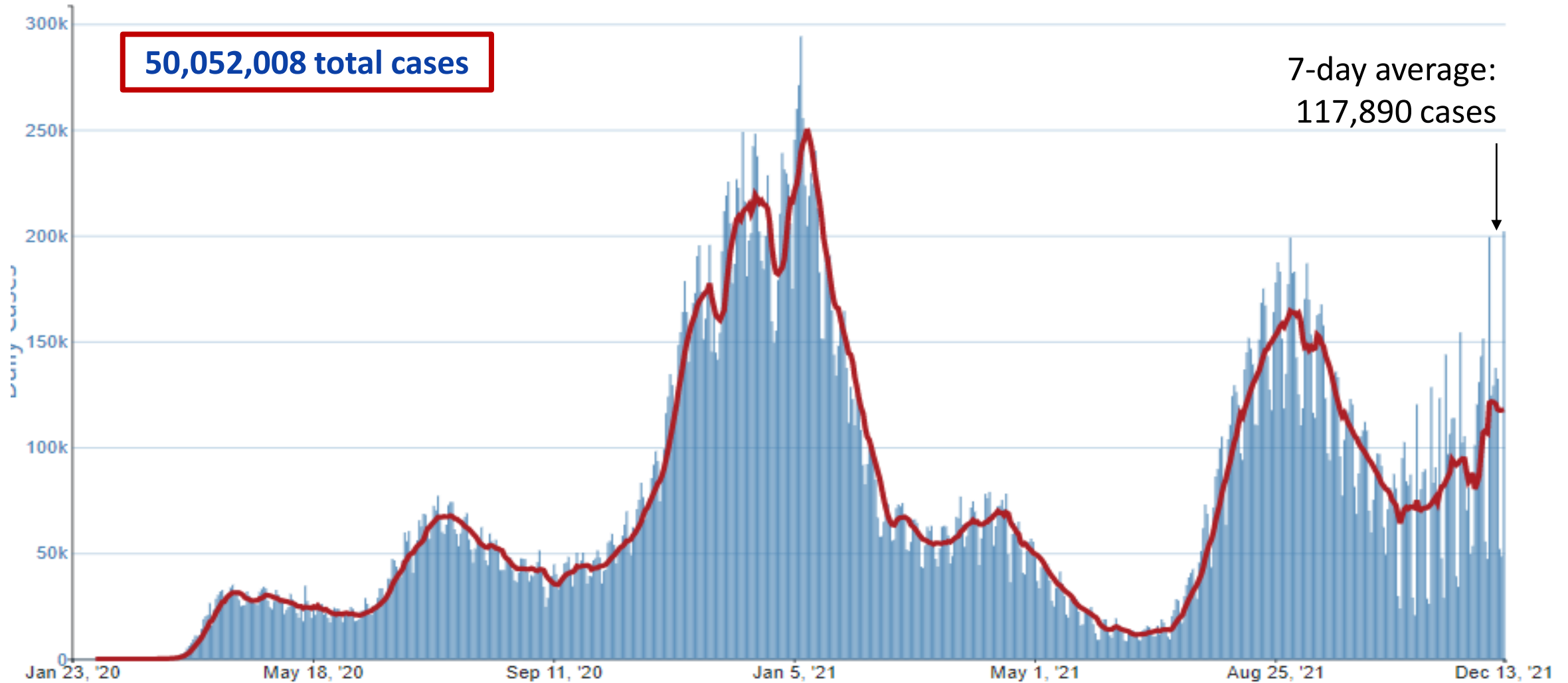
- Should vaccination with the Janssen COVID-19 vaccine (1 dose) be recommended for persons 18 years of age and older under an Emergency Use Authorization?

Public Health Problem



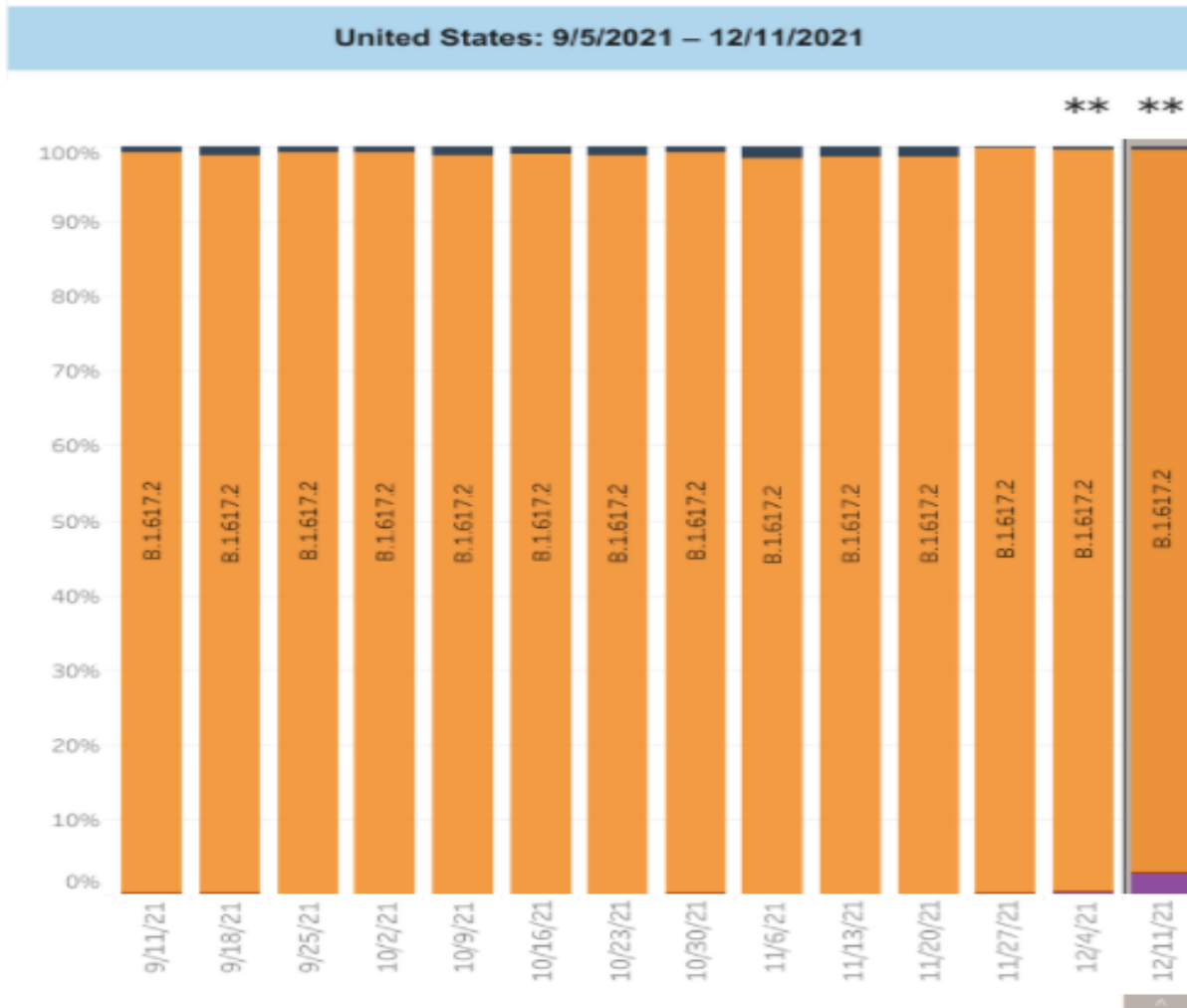
Trends in COVID-19 cases in the United States

January 23, 2020 – December 13, 2021



SARS-CoV-2 Variants Circulating in the United States

Variant Proportions, August 29 - December 11, 2021



WHO label	Lineage #	US Class	%Total	95%PI
Delta	B.1.617.2	VOC	96.7%	85.9-99.6%
	AY.1	VOC	0.1%	0.0-0.1%
	AY.2	VOC	0.0%	0.0-0.0%
Omicron	B.1.1.529	VOC	2.9%	0.2-14.7%
Other	Other*		0.3%	0.2-0.6%

* Enumerated lineages are US VOC and lineages circulating above 1% nationally in at least one week period. "Other" represents the aggregation of lineages which are circulating <1% nationally during all weeks displayed.

** These data include Nowcast estimates, which are modeled projections that may differ from weighted estimates generated at later dates

AY.3-AY.125 and their sublineages are aggregated with B.1.617.2. BA.1 and BA.2 are aggregated with B.1.1.529.

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

[https://www.who.int/news/item/16-04-2021-global-advisory-committee-on-vaccine-safety-\(gacvs\)-review-of-latest-evidence-of-rare-adverse-blood-coagulation-events-with-astrazeneca-covid-19-vaccine-\(vaxzevria-and-covishield\)](https://www.who.int/news/item/16-04-2021-global-advisory-committee-on-vaccine-safety-(gacvs)-review-of-latest-evidence-of-rare-adverse-blood-coagulation-events-with-astrazeneca-covid-19-vaccine-(vaxzevria-and-covishield))
https://www.ema.europa.eu/en/documents/prac-recommendation/signal-assessment-report-embolic-thrombotic-events-smq-covid-19-vaccine-chadox1-s-recombinant_en.pdf
https://www.ema.europa.eu/en/documents/covid-19-vaccine-safety-update/covid-19-vaccine-safety-update-vaxzevria-previously-covid-19-vaccine-astrazeneca-8-september-2021_en.pdf
<https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting#yellow-card-reports>

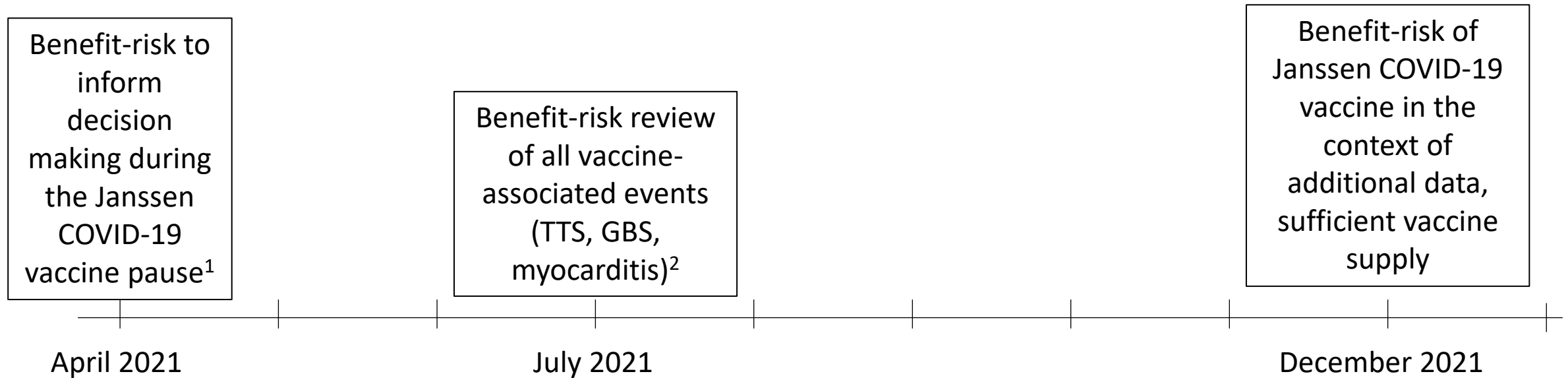
Vaccine policy for adenovirus vector vaccines

- 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

Benefit-Risk Analysis for Janssen COVID-19 vaccine



Timeline of Janssen COVID-19 benefit-risk review



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 Network³
- 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 GBS⁴ and myocarditis⁵ rates from VAERS

VE: Vaccine Effectiveness

¹https://covid.cdc.gov/covid-data-tracker/#trends_dailycases

²https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html

³Self et al. MMWR 2021

⁴<https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/02-COVID-Alimchandani-508.pdf>

⁵<https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-11-2-3/04-COVID-Oster-508.pdf>

Vaccine-specific estimates of effectiveness against COVID-19 hospitalization

VE against COVID-19 hospitalization		
Age group	IVY Network, March–August 2021 ^{1,2}	
	Janssen, % (95% CI)	mRNA, % (95%)
18-49 years	73 (37-88)	92 (88-95)
50-64 years	69 (38-84)	92 (88-94)
65+ years	76 (48-89)	88 (84-91)

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>

2. For age strata specific estimates, adjusted for continuous age in years, calendar date (biweekly), HHS region, sex, and race/ethnicity

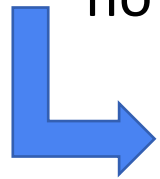
Reporting rates of TTS following Janssen COVID-19 vaccination (per million doses administered)

	Females		Males	
Age group	TTS case rate	TTS death rate	TTS case rate	TTS death rate
18-49 years old	8.7	1.2	2.8	0.5
50-64 years old	4.5	1.0	2.1	0
≥65 years old	1.8	0.0	0.0	0

Framework for benefit-risk analysis



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

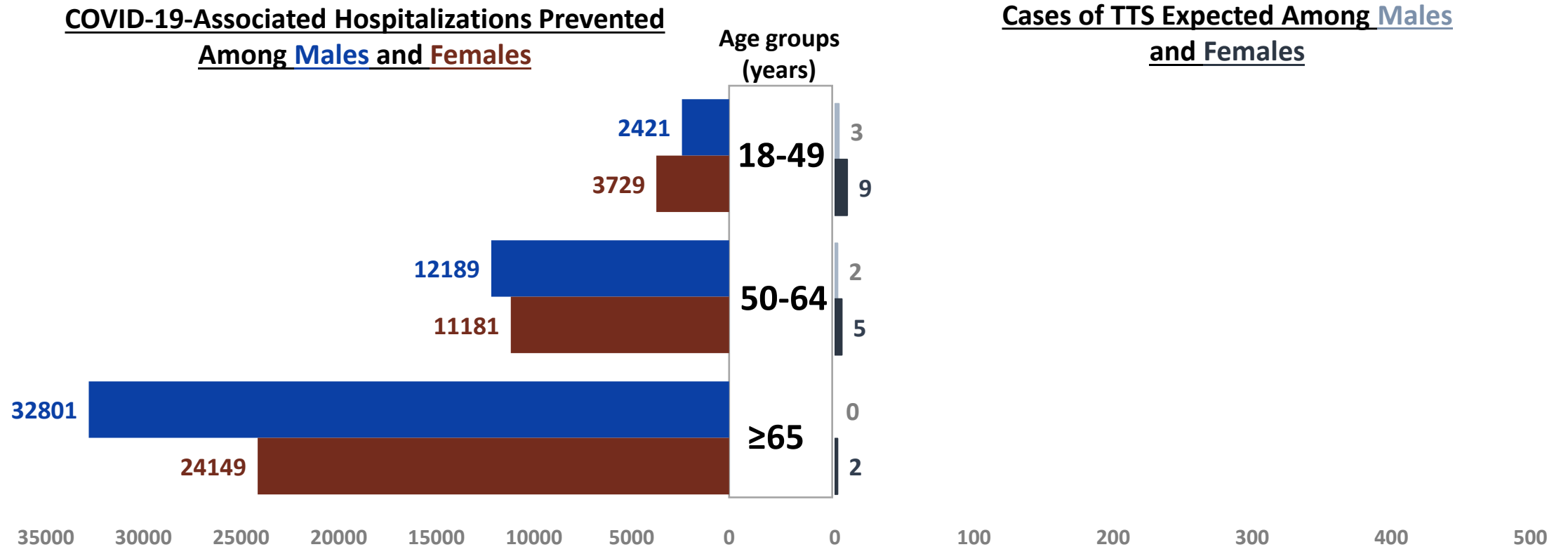


Differential benefits and risks of Janssen COVID-19 vaccine compared with mRNA COVID-19 vaccines, including risks of GBS and myocarditis

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



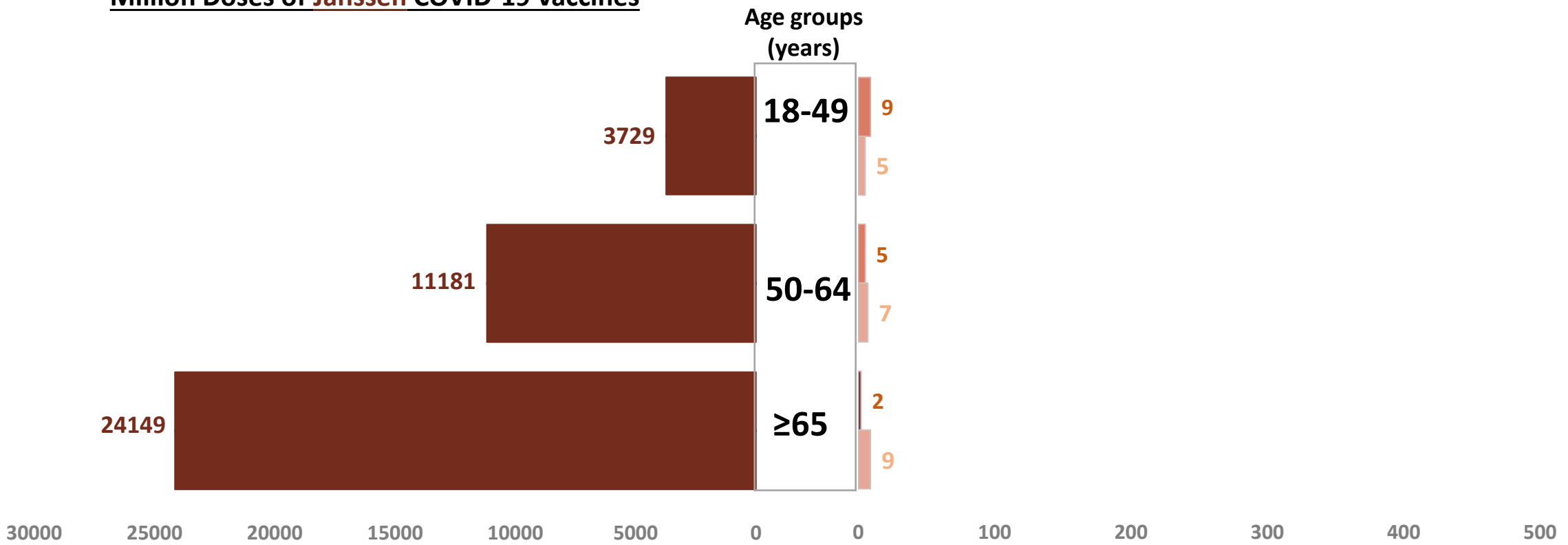
Benefits and risks after Janssen COVID-19 vaccine, Females

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

TTS and GBS Cases Expected per Million Janssen Doses



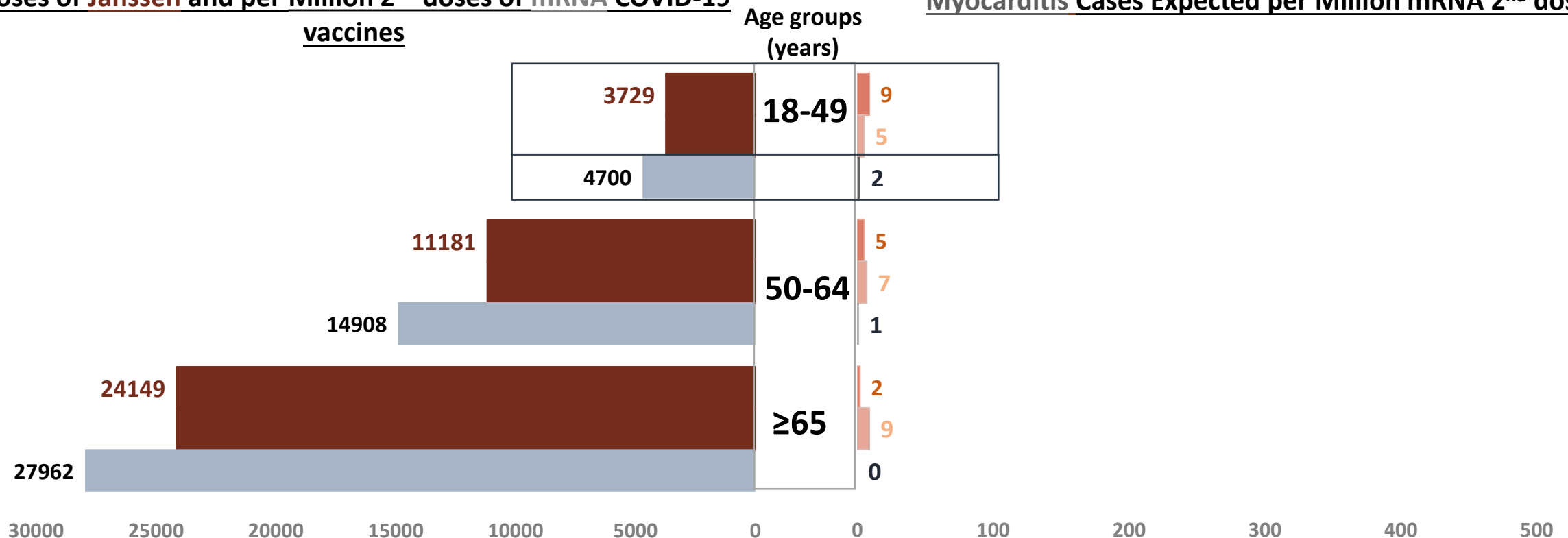
Benefits and risks after Janssen and mRNA COVID-19 vaccine, Females

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

TTS and GBS Cases Expected per Million Janssen Doses and Myocarditis Cases Expected per Million mRNA 2nd doses



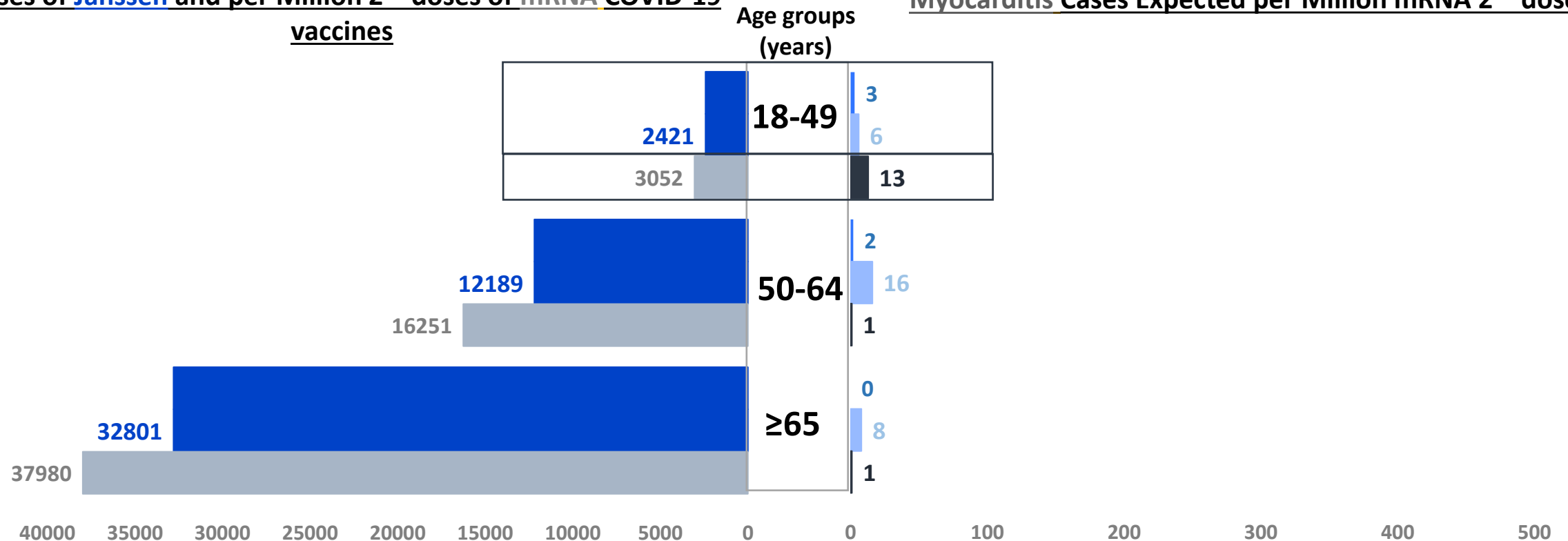
Benefits and risks after Janssen and mRNA COVID-19 vaccine, Males

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 vaccines¹

- At 3 month follow-up, over 90% are 'fully recovered' by cardiologist or healthcare provider
- No confirmed deaths

TTS after Janssen COVID-19 vaccines²

- ~15% mortality rate
- 17% required discharge to post-acute care/rehabilitation facility

GBS after Janssen COVID-19 vaccines³

- ~1% mortality rate
- 10% required mechanical ventilation

¹ACIP Presentation, Dr. Oster: November 2, 2021 <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-11-2-3/04-COVID-Oster-508.pdf>

²Presentation, Dr. See:

³ACIP Presentation, Dr. Alimchandani: July 22, 2021 <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/02-COVID-Alimchandani-508.pdf>

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

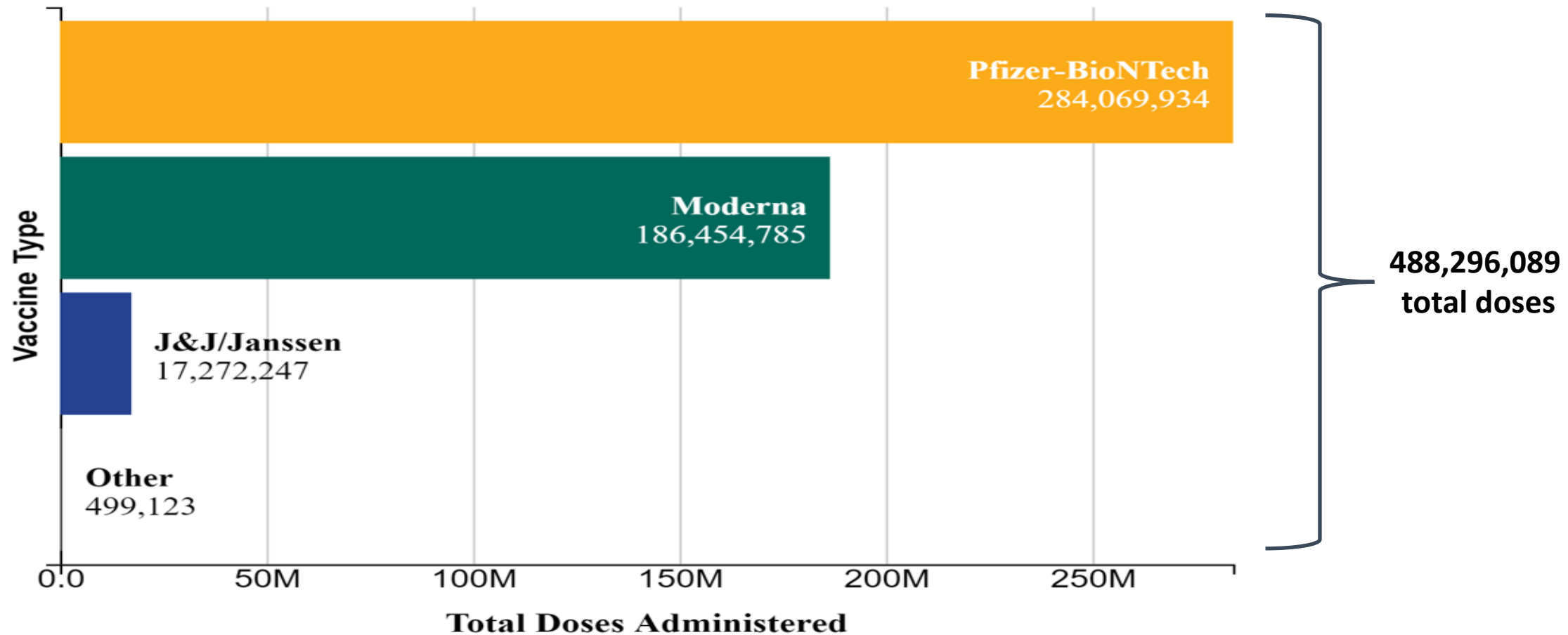
- Direct benefit-risk assessment for Janssen COVID-19 vaccine & TTS
 - Considers individual benefits of vaccination vs. individual risks
- Using current VE estimates, benefit/risk balance of Janssen COVID-19 vaccine is still favorable for all age and sex groups **compared with no vaccine**
- When compared to benefit-risk balance for mRNA COVID-19 vaccines, the Janssen vaccine prevents **fewer** COVID-19 hospitalizations, ICU admissions, and deaths
- **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, **benefit/risk balance** for mRNA COVID-19 vaccines likely **more favorable** across all age and sex groups

Values
Acceptability
Feasibility



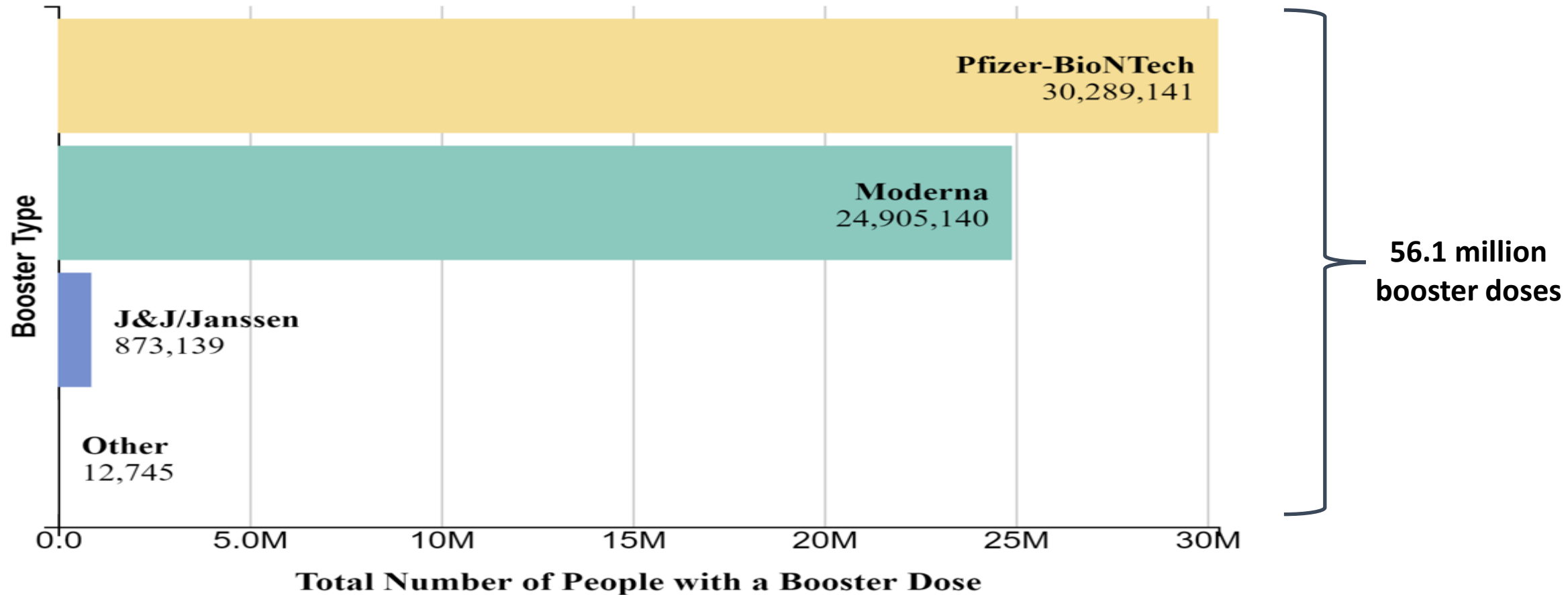
U.S. COVID-19 vaccine administration by vaccine type

As of December 15, 2021



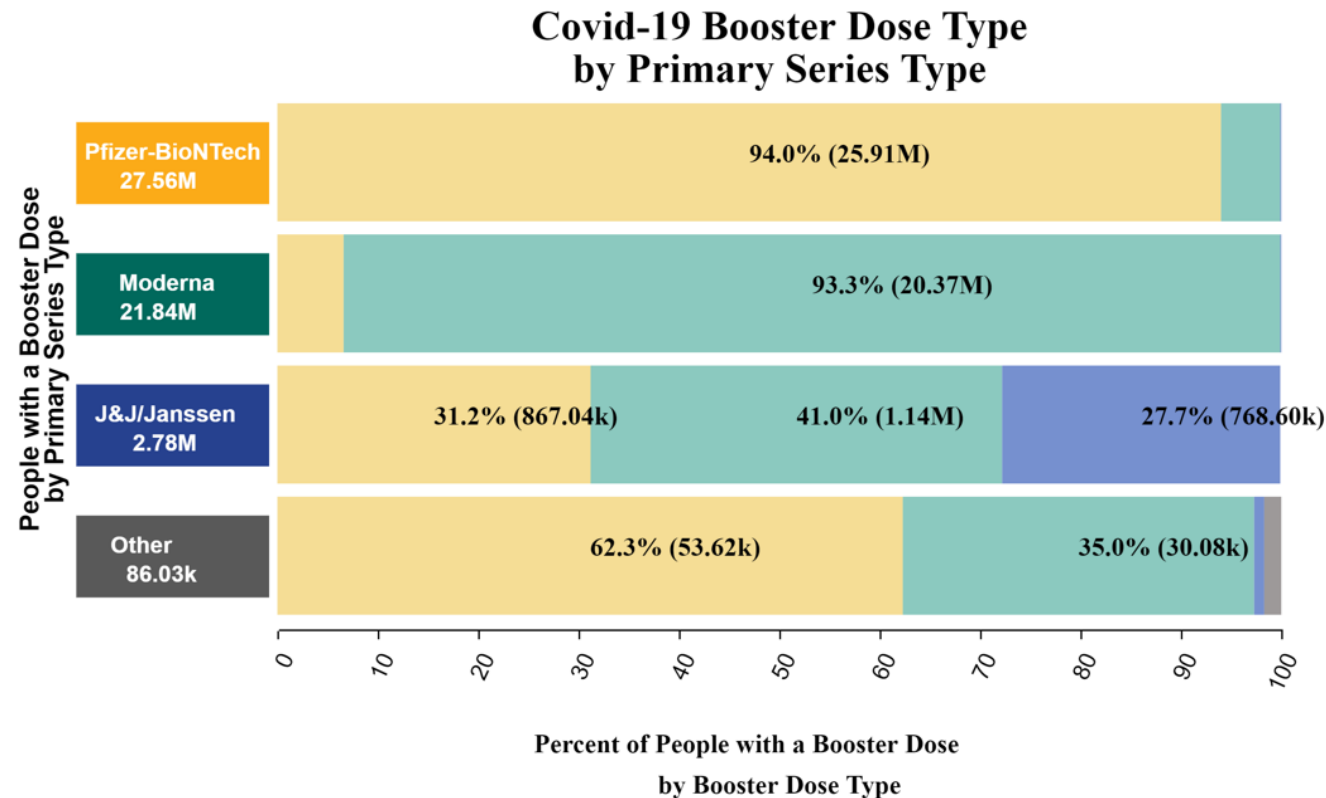
Number of people with a booster dose in the U.S. by COVID-19 vaccine type

As of December 15, 2021



COVID-19 booster dose type by primary series type

United States, as of December 15, 2021

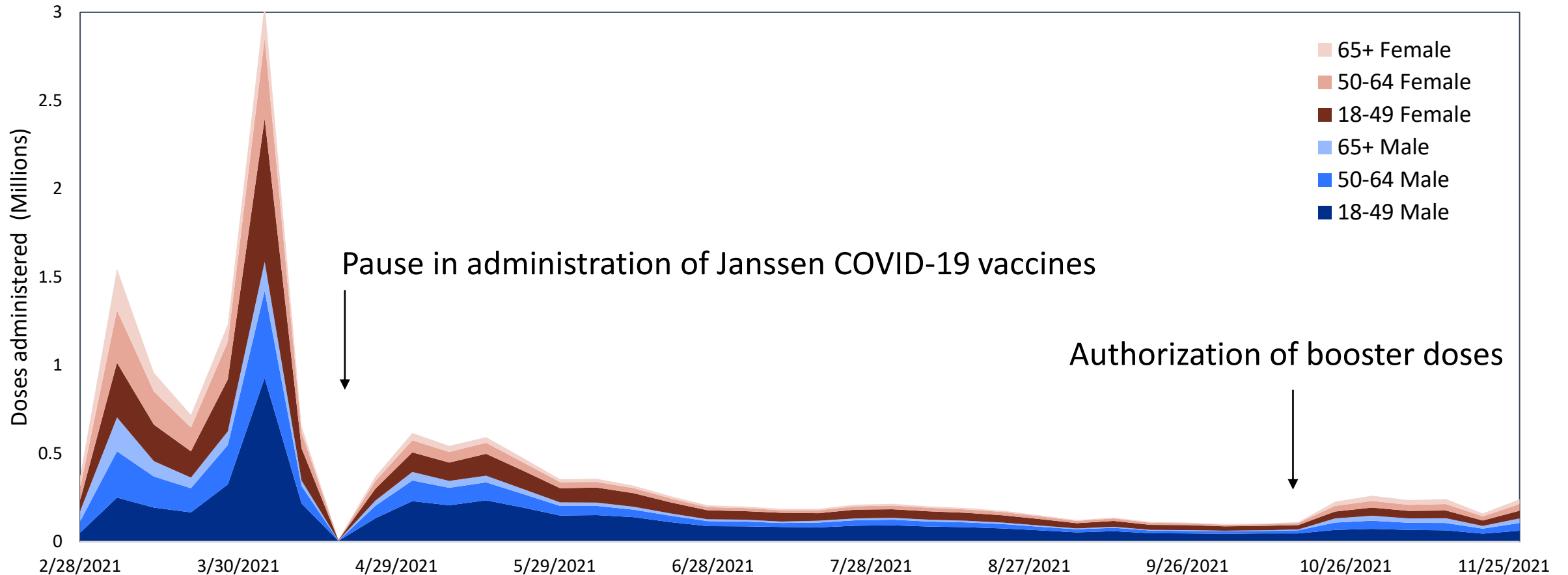


Total Number of People with Booster Doses

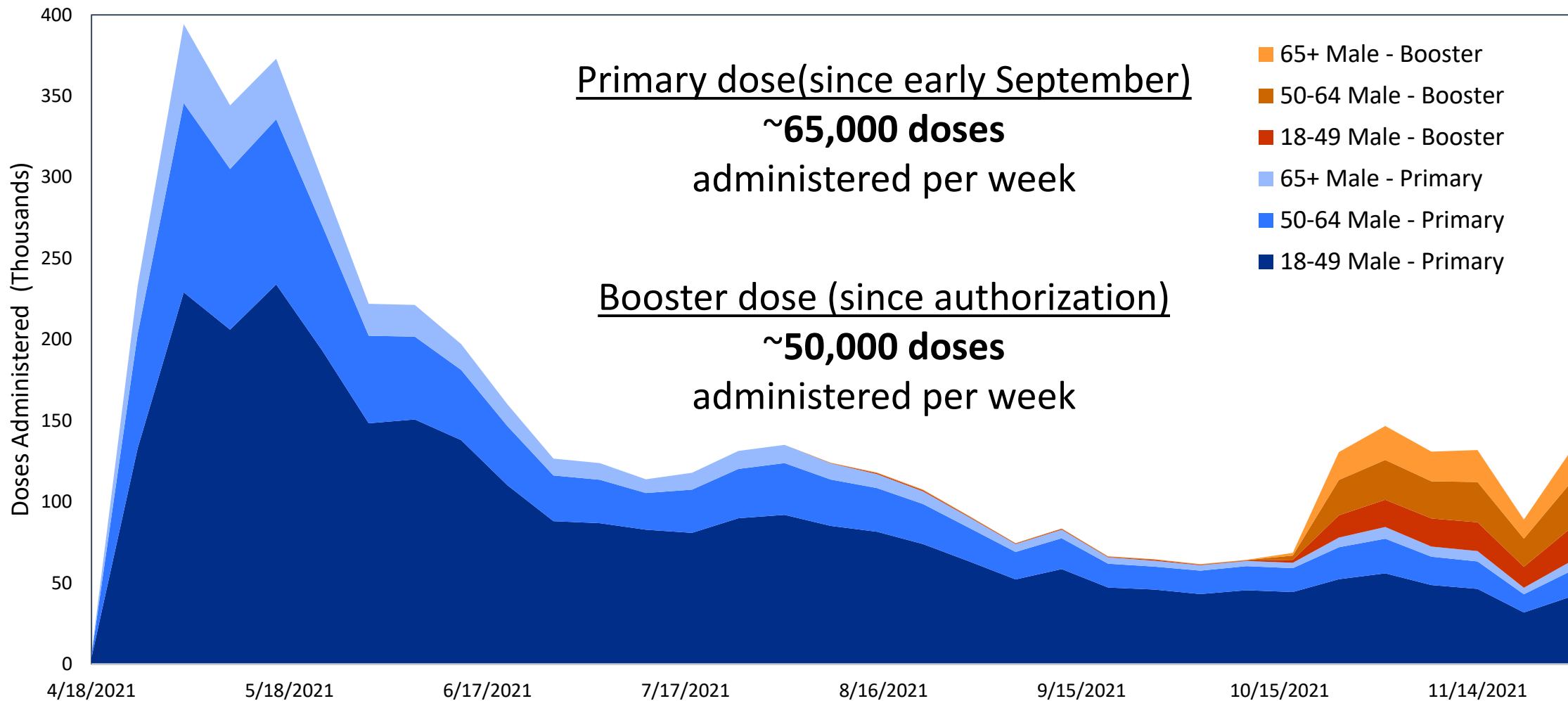
	by Primary Series Type:	by Booster Dose Type:
Pfizer-BioNTech	27.56M	28.27M
Moderna	21.84M	23.16M
J&J/Janssen	2.78M	810.88k
Other	86.03k	12.64k

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.

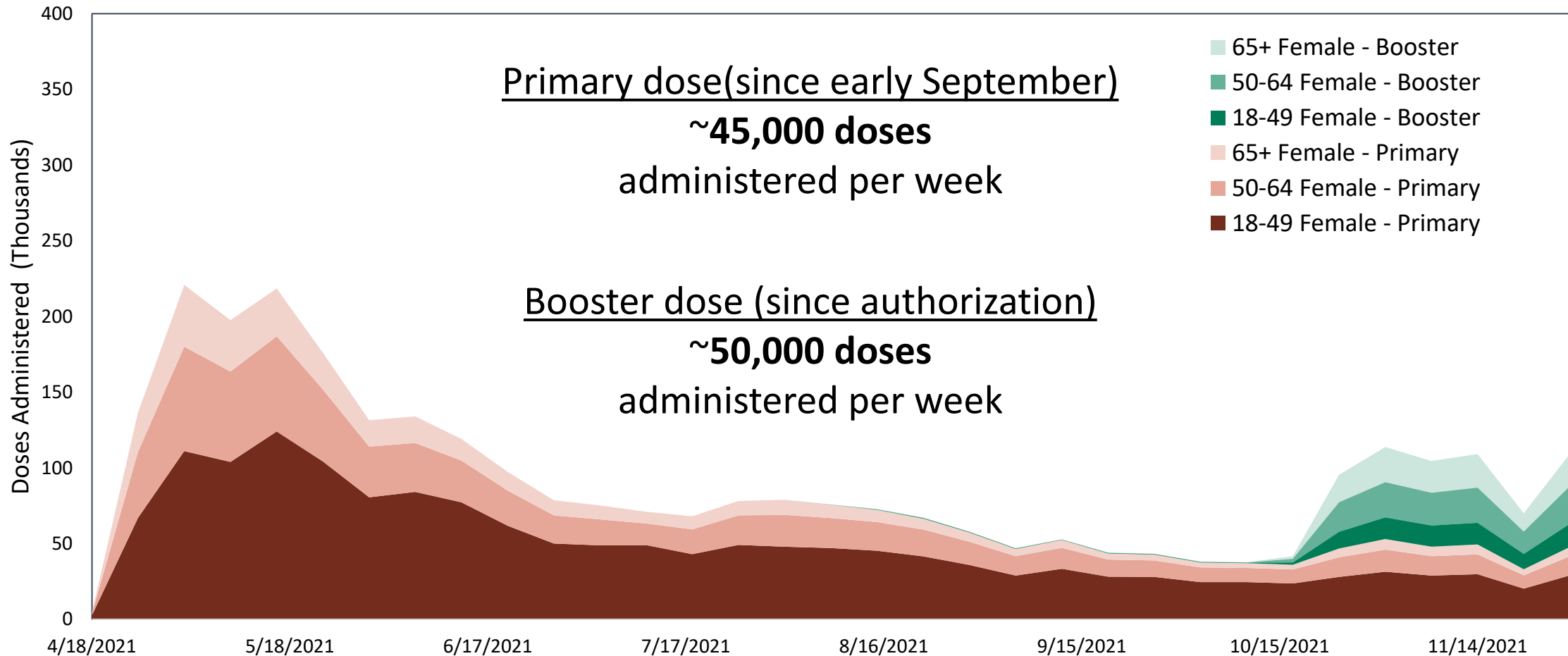
Administration of Janssen COVID-19 vaccines in the U.S. since authorization by age and sex, primary series and booster doses



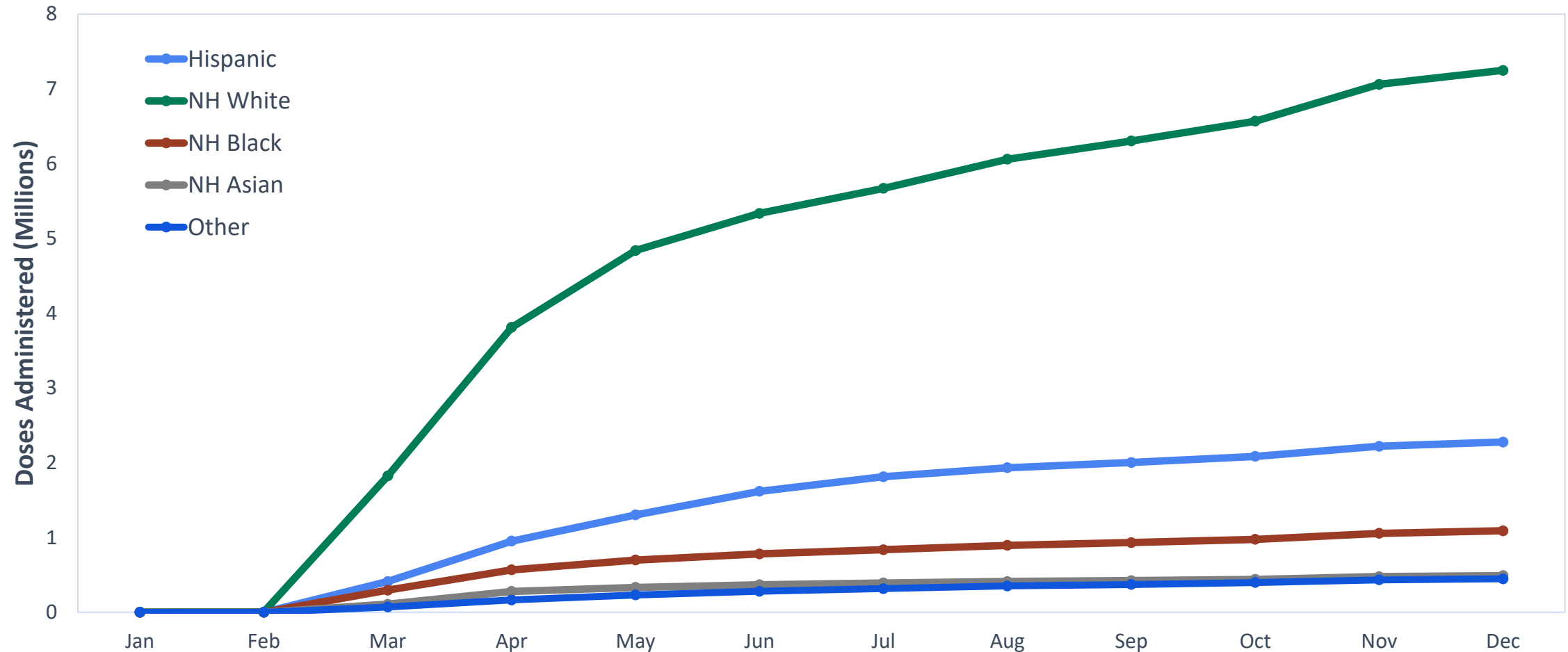
Administration of Janssen COVID-19 vaccines in the U.S. among males since pause, primary series and booster doses



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



Administration of Janssen COVID-19 vaccines in the U.S. since pause, by race and ethnicity

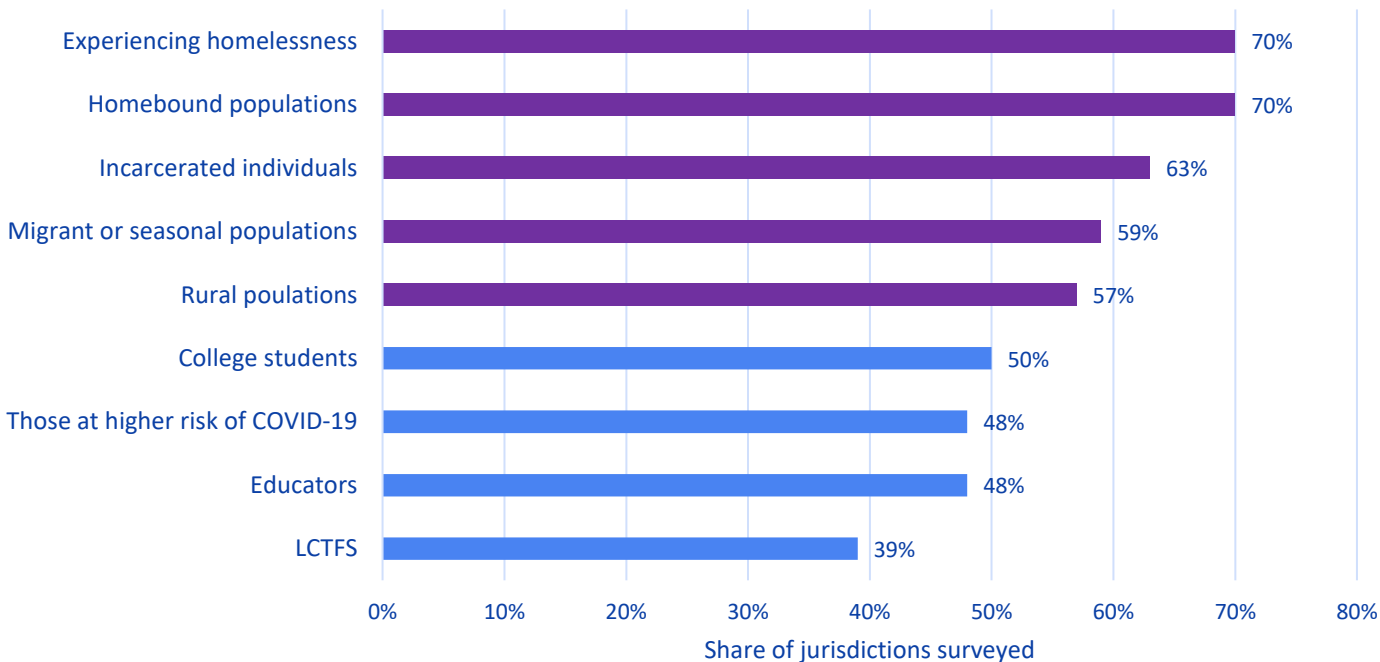


Most populations can receive the Janssen vaccine

Jurisdictional survey, December 2021

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

Q: Which populations are offered the Janssen vaccine?



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."

Summary



Timeline of Janssen COVID-19 vaccine benefit-risk review

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

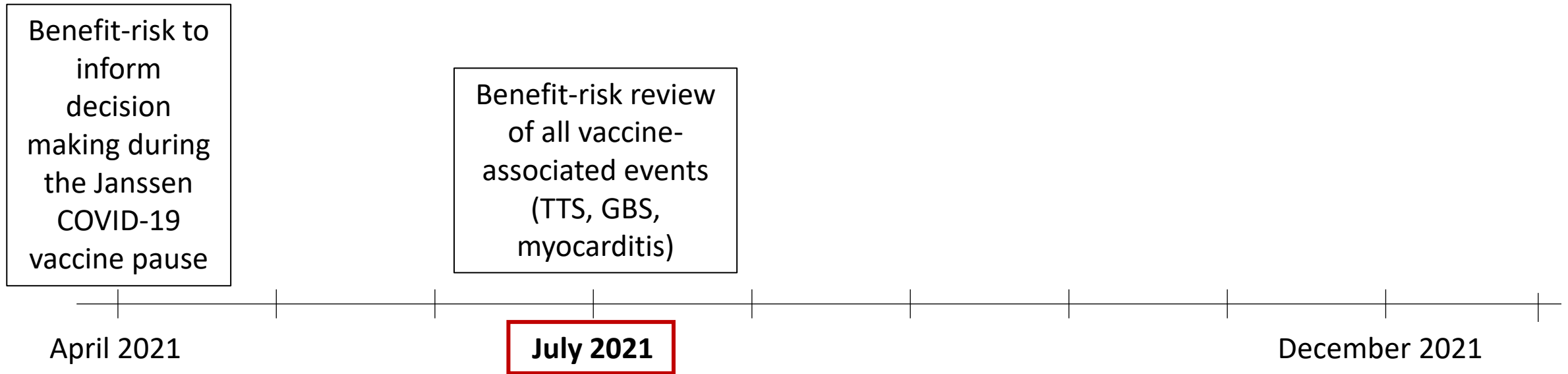
Limited supply of mRNA COVID-19 vaccines

- Estimated that if Janssen COVID-19 vaccine not resumed, could take nearly **3 months** for all vaccine-intending adults to complete a COVID-19 vaccine series, based on supply at that time



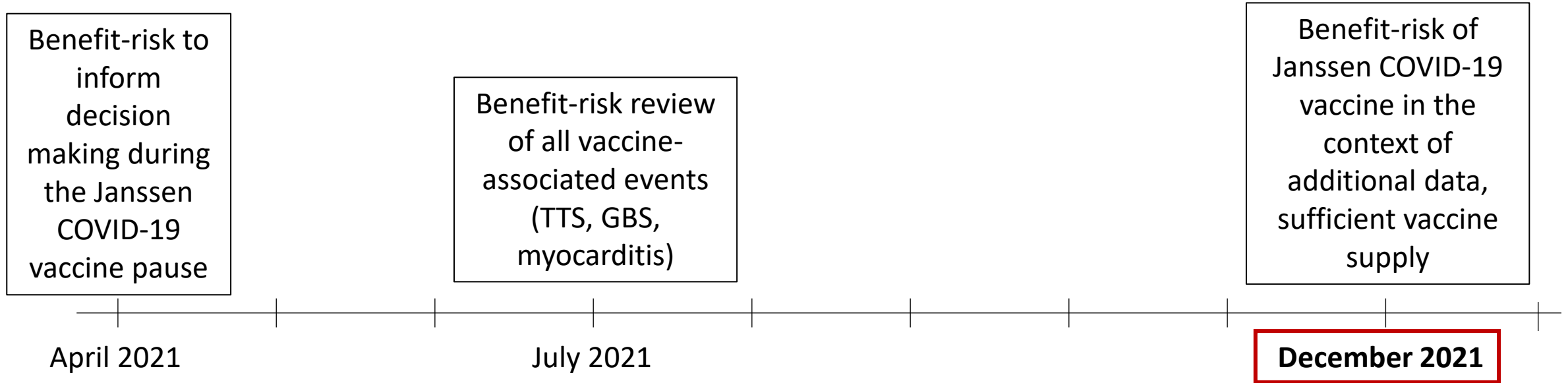
- ACIP reaffirmed its interim recommendation for use of the Janssen COVID-19 vaccine in all persons aged ≥ 18 years under FDA's EUA, including a warning that rare clotting events might occur after vaccination, primarily among women aged 18-49 years
 - Education around the **risk for TTS** with Janssen COVID-19 vaccine, as well as the **availability of alternative COVID-19 vaccines**, is required to guide vaccine decision-making

Timeline of Janssen COVID-19 vaccine benefit-risk review



- 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

Timeline of Janssen COVID-19 vaccine benefit-risk review



- 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

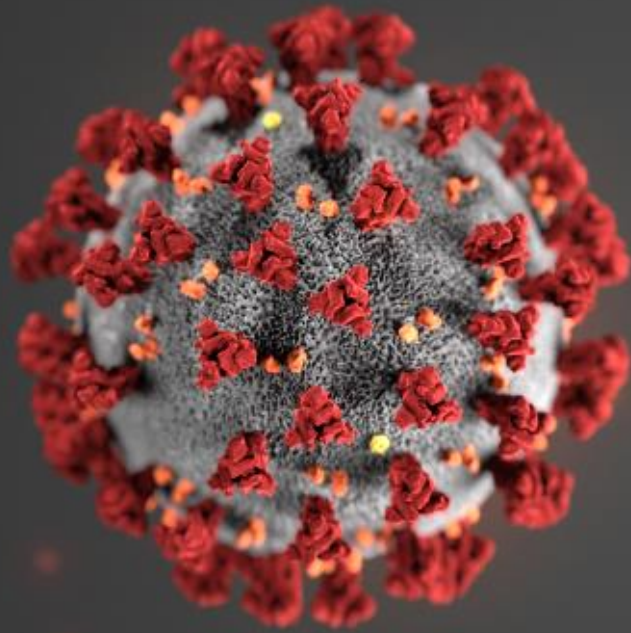
- In most situations, mRNA COVID-19 vaccines are **preferred** over the Janssen COVID-19 vaccine for primary and booster vaccination, including those who received Janssen COVID-19 vaccine for their single dose primary series
- Janssen COVID-19 vaccines may be offered to the following populations:
 - 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)

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- Roodly Archer
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- 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
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

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.



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 COCA Call Will Be Available to View On-Demand

- **When:** A few hours after the live call ends*
- **What:** Video recording
- **Where:** On the COCA Call webpage
https://emergency.cdc.gov/coca/calls/2021/callinfo_121721.asp

**A transcript and closed-captioned video will be available shortly after the original video recording posts at the above link.*

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- Continue to visit emergency.cdc.gov/coca to get more details about upcoming COCA Calls, as COCA intends to host more COCA Calls to keep you informed of the latest guidance and updates on COVID-19.
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- Share call announcements with colleagues.
- Sign up to receive weekly **COVID-19 Science Updates** by visiting cdc.gov/library/covid19/scienceupdates.html?Sort=Date%3A%3Adesc.

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The screenshot shows the Facebook profile for COCA (CDC Clinician Outreach and Communication Activity). The profile picture features a group of diverse healthcare professionals. The cover photo shows a group of six people, including a woman in a black blazer with a stethoscope, a man in a white lab coat, and others in medical attire. The page includes a navigation menu on the left with options like Home, About, Posts, Photos, Events, and Community, along with a 'Create a Page' button. The main content area shows a 'Status' section with a text input field and a 'Posts' section featuring a recent event announcement: 'CDC Clinician Outreach and Communication Activity - COCA shared their event. October 31 at 1:18pm - Clinicians, you can earn FREE CE with this COCA Call! Join us for this COCA Call November 7, 2017 at 2:00PM.' The right sidebar displays the location 'Government Organization in Atlanta, Georgia', community statistics (21,420 likes, 21,217 followers), and a map of the location.

Thank you for joining us today!



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