COVID-19 Vaccine Safety Technical (VaST) Work Group

Assessment

Grace M. Lee, MD MPH (ACIP Chair)

Robert H. Hopkins, Jr., MD (NVAC Chair)

Advisory Committee on Immunization Practices

August 30, 2021

COVID-19 Vaccine Safety Technical (VaST) Work Group

Objectives

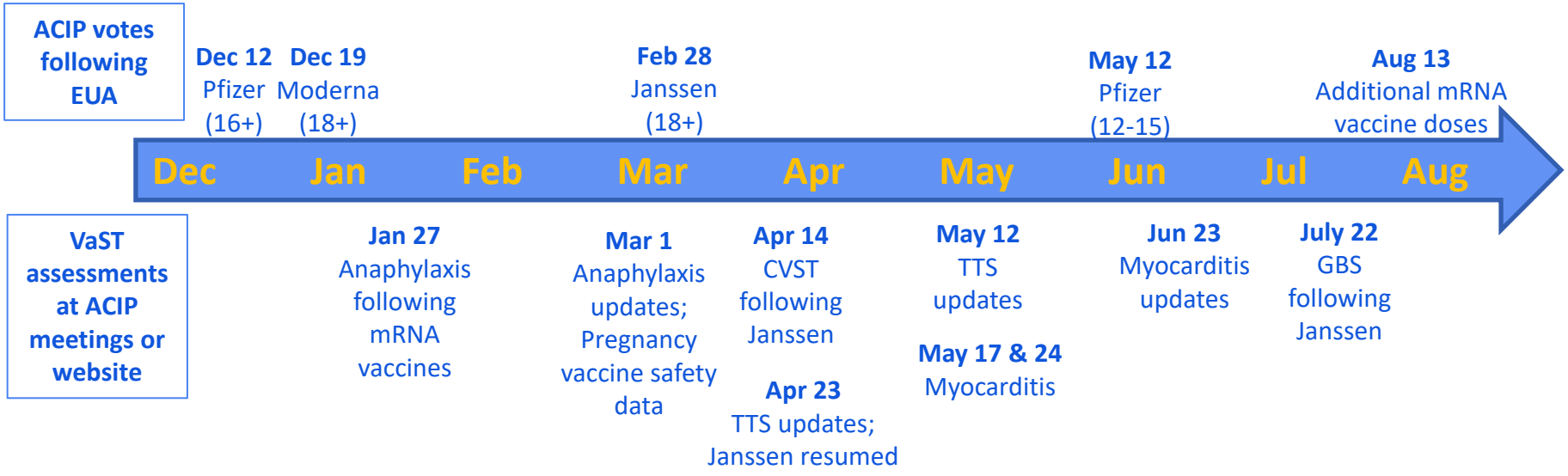
- Review, evaluate, and interpret post-authorization/approval COVID-19 vaccine safety data
- Serve as the central hub for technical subject matter expertise from federal agencies conducting post-authorization/approval safety monitoring
- Advise on analyses, interpretation, and data presentation
- Provide updates to the ACIP COVID-19 Vaccines Work Group and the ACIP on COVID-19 vaccine safety

VaST Activities

Dec 21, 2020 – present

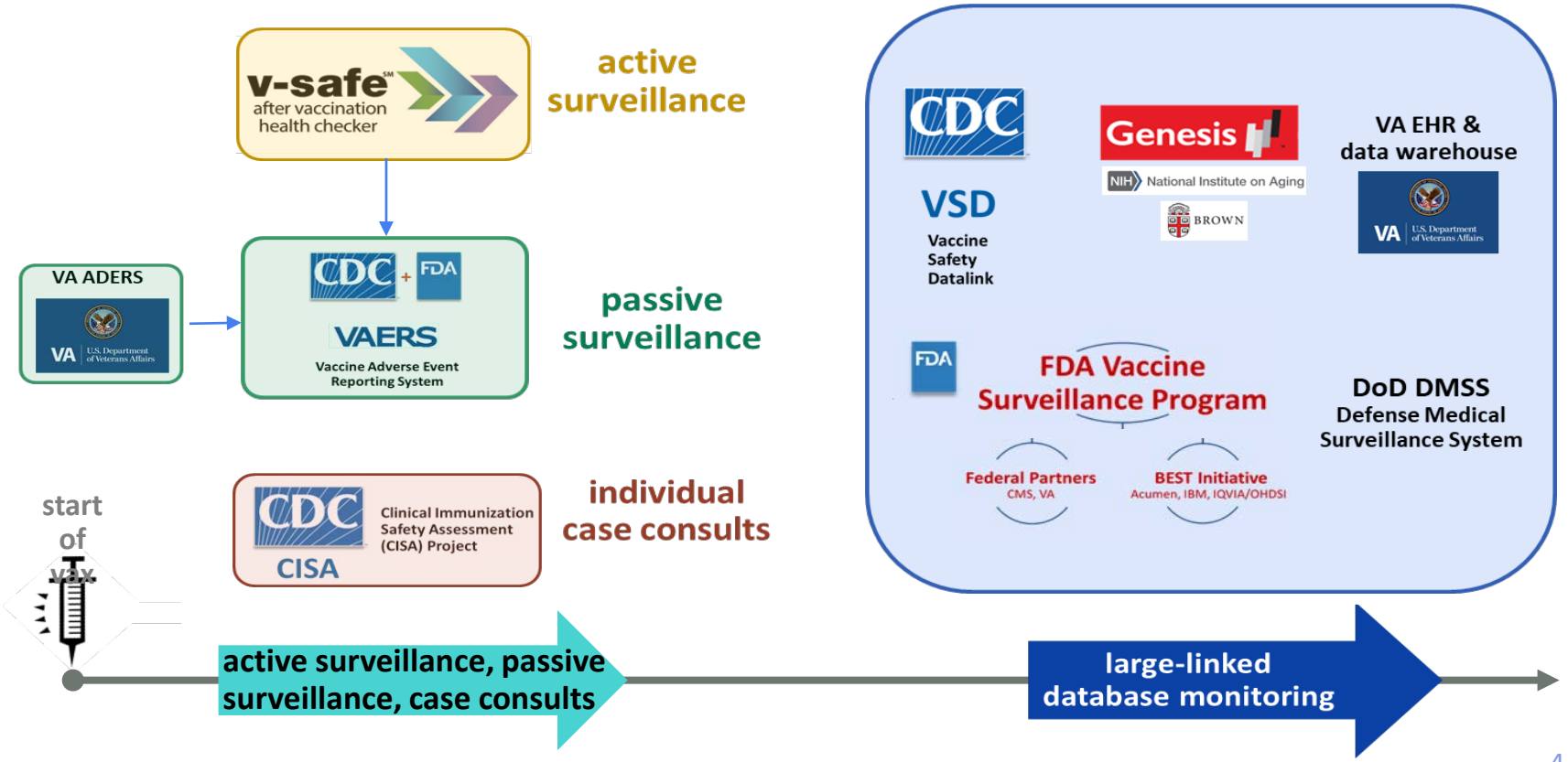
32 independent meetings to review vaccine safety data

8 joint meetings with COVID-19 Vaccines Work Group focused on safety



CVST, cerebral venous sinus thrombosis; TTS, thrombosis with thrombocytopenia syndrome; GBS, Guillain-Barré syndrome

U.S. Vaccine Safety Monitoring Systems and Timelines



Monitoring and Responding to Safety Data

Safety monitoring

- mRNA COVID-19 vaccines
  - Anaphylaxis
  - Myocarditis
- Janssen COVID-19 vaccine
  - TTS
  - GBS
- Pre-specified AESI
- Maternal immunization

Incorporating safety data into decision-making

- Dynamic benefit-risk balance
- Risk mitigation strategies
  - Support informed discussions about benefits and risks of available vaccines
  - Clinical guidance to support early detection and appropriate management
- Guidance for use of post-approval safety data in GRADE

TTS, thrombosis with thrombocytopenia syndrome; GBS, Guillain-Barré syndrome

VaST continues to review data on myocarditis, GBS and TTS from passive and active surveillance systems

- Data from
  - U.S. systems including VAERS, VSD
    - Most updated data on myocarditis presented today
  - U.S. data from VA, DoD, FDA, and IHS
  - Israel, Canada, Global Advisory Committee on Vaccine Safety

Anaphylaxis following mRNA COVID-19 vaccination

- Anaphylaxis following mRNA COVID-19 vaccination identified Dec 2020
- Safety data and VaST assessment presented at January and March 2021 ACIP meetings*
- CDC and FDA recommended risk mitigation strategies, including:
  - Screening for risk prior to vaccination
  - Monitoring for symptoms post-vaccination
  - Early recognition and management of anaphylaxis on-site
  - Provider and patient education by CDC and partners

*https://www.cdc.gov/vaccines/acip/meetings/slides-2021-1-27-21.html; https://www.cdc.gov/vaccines/acip/meetings/slides-2021-02-28-03-01.html

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 70
January 6, 2021

Allergic Reactions In
Pfizer-BioNTech COVI

As of January 3, 2021, a total o
coronavirus disease 2019 (COVID-1
ated deaths have been reported in th
term sequalae of COVID-19 over t

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 70
January 22, 2021

Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Moderna COVID-19 Vaccine — United States, December 21, 2020–January 10, 2021

As of January 20, 2021
coronavirus disease 2019 (C
deaths had been reported in
cdc.gov/covid-data-tracker

JAMA Insights | CLINICAL UPDATE

Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine

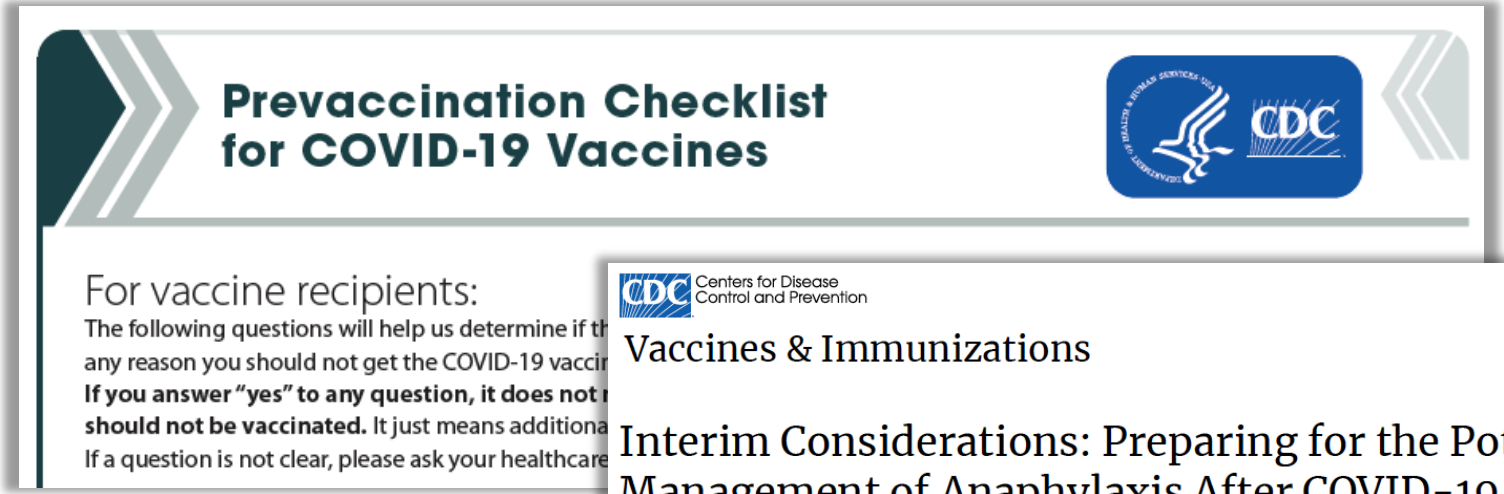
Tom Shimabukuro, MD, MPH, MBA; Narayan Nair, MD

On December 11, 2020, the US Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the Pfizer-BioNTech coronavirus disease 2019 (COVID-19) vaccine, administered as 2 doses separated by 21 days.[1] Shortly after, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for its use.[2]

Multimedia

Following implementation of vaccination, reports of anaphylaxis after the first dose of the Pfizer-BioNTech COVID-19 vaccine emerged.[3] Anaphylaxis is a life-threatening allergic reaction that occurs rarely after vaccination, with onset typically within minutes to hours.[4]

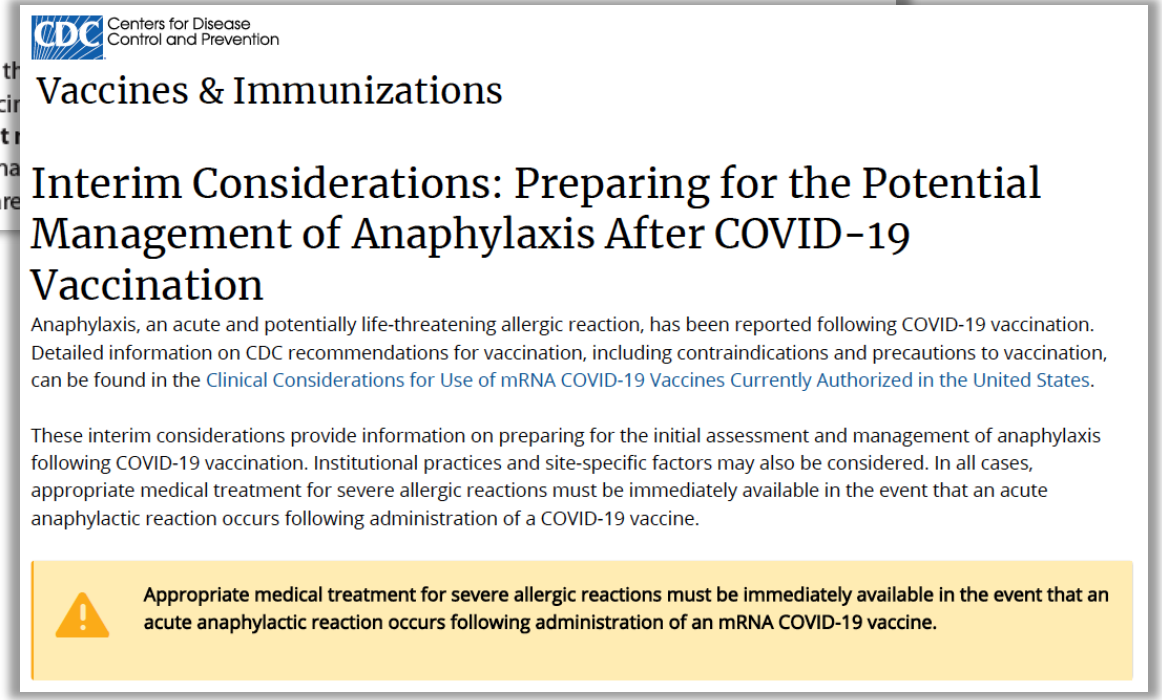
Notifications and reports of suspected severe allergic reactions and anaphylaxis following vaccination were captured in the Vaccine Adverse Event Reporting System (VAERS), the national



Prevaccination Checklist for COVID-19 Vaccines

For vaccine recipients:

The following questions will help us determine if th
any reason you should not get the COVID-19 vacci
If you answer "yes" to any question, it does not
should not be vaccinated. It just means additiona
If a question is not clear, please ask your healthcare



CDC Centers for Disease Control and Prevention

Vaccines & Immunizations

Interim Considerations: Preparing for the Potential Management of Anaphylaxis After COVID-19 Vaccination

Anaphylaxis, an acute and potentially life-threatening allergic reaction, has been reported following COVID-19 vaccination. Detailed information on CDC recommendations for vaccination, including contraindications and precautions to vaccination, can be found in the Clinical Considerations for Use of mRNA COVID-19 Vaccines Currently Authorized in the United States.

These interim considerations provide information on preparing for the initial assessment and management of anaphylaxis following COVID-19 vaccination. Institutional practices and site-specific factors may also be considered. In all cases, appropriate medical treatment for severe allergic reactions must be immediately available in the event that an acute anaphylactic reaction occurs following administration of a COVID-19 vaccine.

Appropriate medical treatment for severe allergic reactions must be immediately available in the event that an acute anaphylactic reaction occurs following administration of an mRNA COVID-19 vaccine.

Anaphylaxis: VaST Discussion and Interpretation

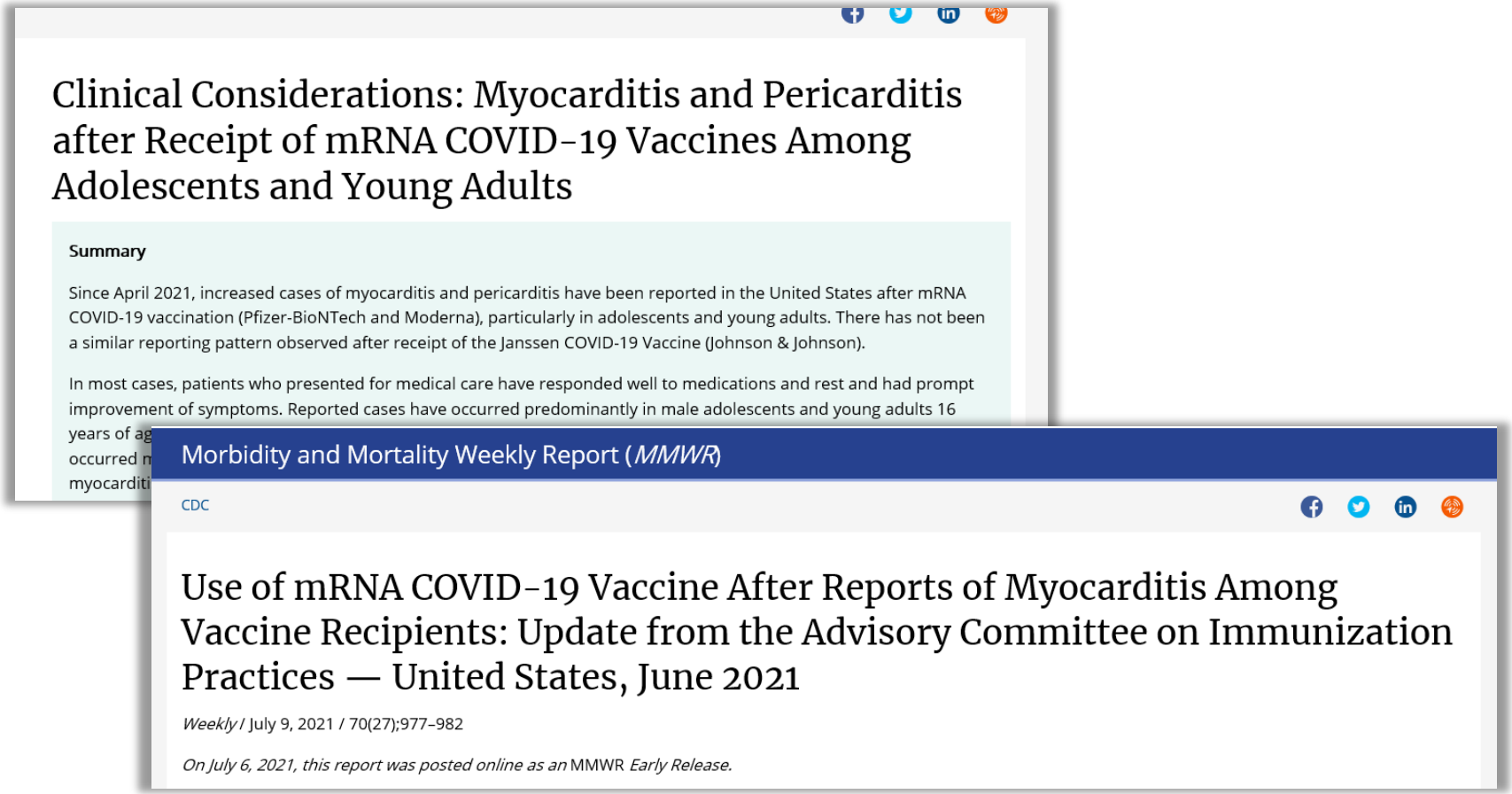
- Initial data from VAERS
  - Rate for Pfizer-BioNTech: 11.1 per million doses admin (Dec 14-Dec 23) https://www.cdc.gov/mmwr/volumes/70/wr/mm7002e1.htm
  - Rate for Moderna vaccine: 2.5 per million doses admin (Dec 21-Jan 10) https://www.cdc.gov/mmwr/volumes/70/wr/mm7004e1.htm
- Most recent data from VSD among persons aged 12 and older*
  - 5.0 (95% CI 3.5, 6.9) (Pfizer-BioNTech) and 4.9 (95% CI 3.2, 7.2) (Moderna) per million doses administered
  - Most in females after first dose
- No substantial change in benefit-risk balance with risk mitigation strategies in place

*1-day risk interval

Myocarditis following mRNA COVID-19 vaccination

- Myocarditis following mRNA COVID-19 vaccination identified in May 2021[1]
- CDC issued clinical guidance for myocarditis/pericarditis following mRNA vaccines, May 2021
- Data presented at the Vaccines and Related Biologics Products Advisory Committee (VRBPAC), June 10
- Data and VaST assessment presented at ACIP meeting on June 23[2] and MMWR published
- EUA fact sheets revised with warning added, June 25
- FDA approval of Pfizer BioNTech COVID-19 vaccine on August 23
  - Information on myocarditis/pericarditis in package insert[3]

[1]https://www.cdc.gov/vaccines/acip/work-groups-vast/index.html; [2]https://www.cdc.gov/vaccines/acip/meetings/slides-2021-06.htm; [3]https://www.fda.gov/media/151707/download



Clinical Considerations: Myocarditis and Pericarditis after Receipt of mRNA COVID-19 Vaccines Among Adolescents and Young Adults

Summary

Since April 2021, increased cases of myocarditis and pericarditis have been reported in the United States after mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna), particularly in adolescents and young adults. There has not been a similar reporting pattern observed after receipt of the Janssen COVID-19 Vaccine (Johnson & Johnson).

In most cases, patients who presented for medical care have responded well to medications and rest and had prompt improvement of symptoms. Reported cases have occurred predominantly in male adolescents and young adults 16 years of ag
occurred m
myocarditi

Morbidity and Mortality Weekly Report (*MMWR*)

CDC

Use of mRNA COVID-19 Vaccine After Reports of Myocarditis Among Vaccine Recipients: Update from the Advisory Committee on Immunization Practices — United States, June 2021

Weekly / July 9, 2021 / 70(27);977–982

On July 6, 2021, this report was posted online as an MMWR *Early Release.*

Myocarditis/Pericarditis – 0-7 day risk interval

	VAERS reporting rates per million doses administered				VSD excess cases per million doses based on chart confirmed data			
Ages (yrs)	Pfizer Dose 1	Pfizer Dose 2	Moderna Dose 1	Moderna Dose 2	Pfizer Dose 1	Pfizer Dose 2	Moderna Dose 1	Moderna Dose 2
12–15	2.6	20.9			0.7	14.4	4.9	19.7
16–17	2.5	34.0						
18–24	1.1	18.5	2.7	20.2				
25–29	1.0	7.2	1.7	10.3				
30–39	0.8	3.4	1.0	4.2				

Data presented at Aug 30, 2021 ACIP Meeting

Myocarditis following vaccination – Clinical course

- VAERS reports for individuals <30 years of age (N=845 cases reviewed)
  - 88% of reviewed cases met CDC case definition
  - 77% were known to have recovered from symptoms at time of VAERS report
- VSD cases among individuals 12-39 years of age (N=98 cases reviewed)
  - 56% of cases met chart confirmation criteria for myocarditis within 0-21 days of vaccination
  - 100% with chest pain/pressure/discomfort
  - Elevated troponin, abnormal EKG findings, abnormal MRI common
  - 76% discharged within 0-2 days; 100% discharged to home

Myocarditis: VaST Discussion and Interpretation

- Data available to date suggest association of myocarditis with mRNA vaccination in adolescents and young adults
- Further data are being compiled to understand potential risk factors, optimal management strategies, and long-term outcomes
  - Patient survey on functional status, clinical symptoms, quality of life and ongoing need for medication or treatment
  - Provider survey on cardiac health and functional status

Comirnaty and Pfizer-BioNTech COVID-19 Vaccine

Share | Tweet | Linkedin | Email | Print

August 23, 2021: **FDA approves Comirnaty (COVID-19 Vaccine, mRNA), which was previously known as Pfizer-BioNTech COVID-19 Vaccine, for the prevention of COVID-19 disease in individuals 16 years of age and older.** View Comirnaty information, press release and frequently asked questions.

On August 23, 2021, the FDA approved the first COVID-19 vaccine. The vaccine has been known as the Pfizer-BioNTech COVID-19 Vaccine, and will now be marketed as Comirnaty, for the prevention of COVID-19 disease in individuals 16 years of age and older. The vaccine also continues to be available under emergency use authorization (EUA), including for individuals 12 through 15 years of age and for the administration of a third dose in certain immunocompromised individuals.

Comirnaty Prescribing Information

Pfizer-BioNTech Fact Sheets

Pfizer-BioNTech Fact Sheet Translations

Myocarditis: FDA Post-Marketing Requirements for Pfizer-BioNTech COVID-19 mRNA vaccine

- Non-Interventional Post-Approval Safety Study to evaluate occurrence of myocarditis and pericarditis *in the U.S.*
- Post Conditional Approval Active Surveillance Study to evaluate occurrence of myocarditis and pericarditis *in Europe*
  - Sub-study to describe the *natural history* of myocarditis and pericarditis
- Prospective cohort study ≥5 years for potential *long-term sequelae of myocarditis* after vaccination (in collaboration with Pediatric Heart Network)
- Sub-studies of clinical trials to prospectively assess the *incidence of subclinical myocarditis* following 2nd dose in subset of participants aged 5-15 years and 16-30 years

https://www.fda.gov/media/151710/download

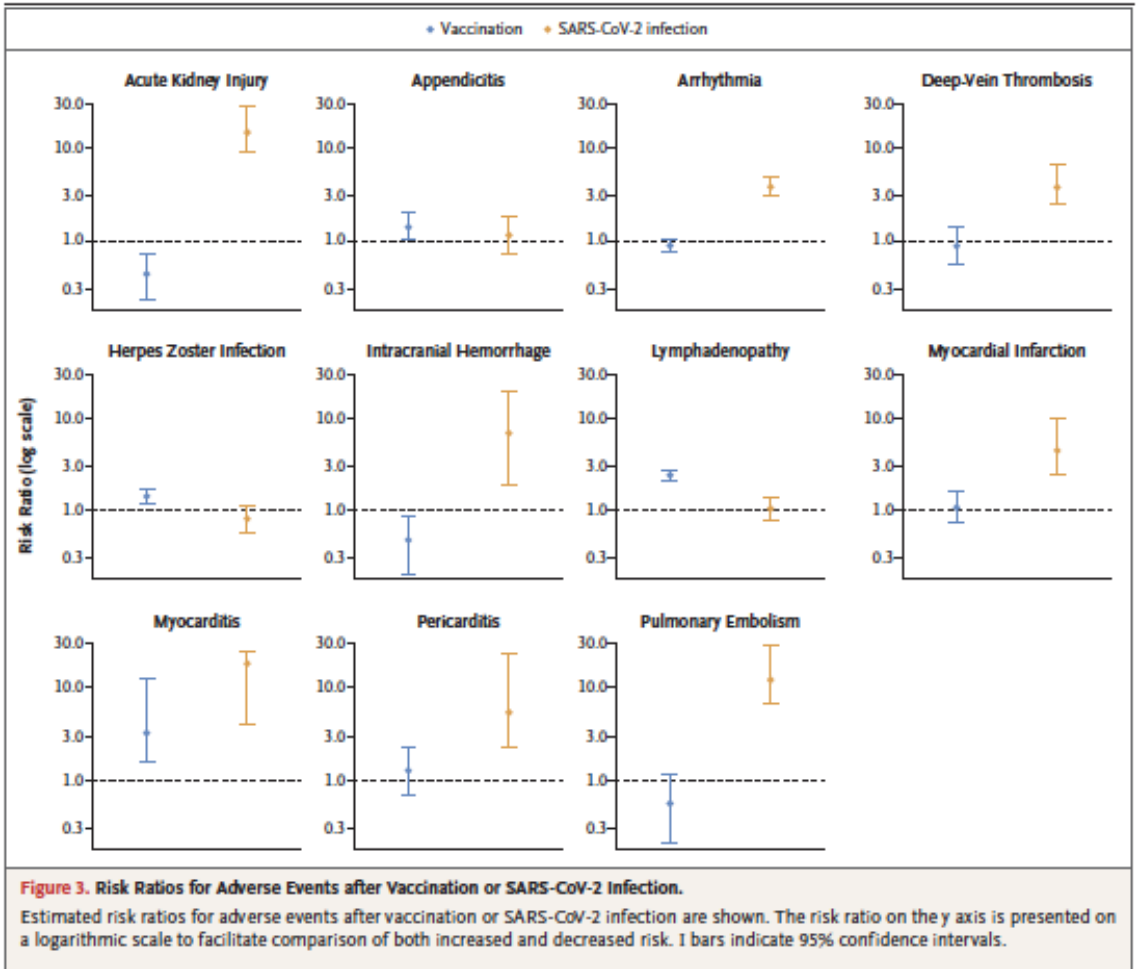


Figure 3. Risk Ratios for Adverse Events after Vaccination or SARS-CoV-2 Infection.

Estimated risk ratios for adverse events after vaccination or SARS-CoV-2 infection are shown. The risk ratio on the y axis is presented on a logarithmic scale to facilitate comparison of both increased and decreased risk. I bars indicate 95% confidence intervals.

- In a 42-day risk window for myocarditis:
  - **Risk ratio 3.2** after vaccination **vs. 18.3** after SARS-CoV-2 infection
  - **Risk difference of 2.7** per 100,000 persons after vaccination **vs. 11.0** events per 100,000 persons after SARS-CoV-2 infection
- Adverse events substantially increased after infection
- Protective effects of vaccination observed

Barda et al., NEJM 2021

Safety Monitoring and VaST Next Steps

- Continue near real-time monitoring of vaccine safety in the U.S.
  - Collaboration across U.S. federal agencies
- Continue collaboration with global vaccine safety colleagues on key issues that impact benefit-risk balance
  - Myocarditis
  - Booster doses
- Continue to provide updates to the ACIP COVID-19 Vaccines Workgroup and the ACIP at future meetings

VaST Members

VaST Members
Grace Lee (ACIP)
Robert Hopkins (NVAC)
Matt Daley
Veronica McNally
Keipp Talbot
Kathy Edwards
Lisa Jackson
Jennifer Nelson
Laura Riley
Robert Schechter
Patricia Whitley-Williams

CDC Co-Leads
Lauri Markowitz
Melinda Wharton

Ex Officio and Liaison Representatives
Tatiana Beresnev (NIH)
Karen Farizo; Hui Lee Wong (FDA)
Judith Steinberg (OIDP)
Jeffrey Kelman (CMS)
Matthew Clark (IHS)
Mary Rubin (HRSA)
Fran Cunningham (VA)
Limone Collins (DoD)

Administrative Support
Jared Woo

Reporting rates of myopericarditis (per million doses administered), by manufacturer, sex, and dose number, 7-day risk period* (as of Aug 18, 2021)

	Pfizer		Moderna		Janssen	Pfizer		Moderna		Janssen	Pfizer		Moderna		Janssen
	(All)		(All)		(All)	(Males)		(Males)		(Males)	(Females)		(Females)		(Females)
Ages† (yrs)	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1	Dose 1	Dose 2	Dose 1	Dose 2	Dose 1
12–15	2.6	20.9	0.0	not calc.	0.0	4.8	42.6	0.0	not calc.	0.0	0.5	4.3	0.0	0.0	0.0
16–17	2.5	34.0	0.0	14.6	0.0	5.2	71.5	0.0	31.2	0.0	0.0	8.1	0.0	0.0	0.0
18–24	1.1	18.5	2.7	20.2	2.7	2.4	37.1	5.1	37.7	3.0	0.0	2.6	0.7	5.3	1.6
25–29	1.0	7.2	1.7	10.3	1.9	1.8	11.1	3.2	14.9	2.0	0.3	1.3	0.4	6.3	0.0
30–39	0.8	3.4	1.0	4.2	0.4	1.1	6.8	1.6	8.0	0.0	0.6	1.0	0.4	0.7	1.0

* Reports with time to symptom onset within 7 days of vaccination

† Reports among persons 12–29 years of age were verified by provider interview of medical record review