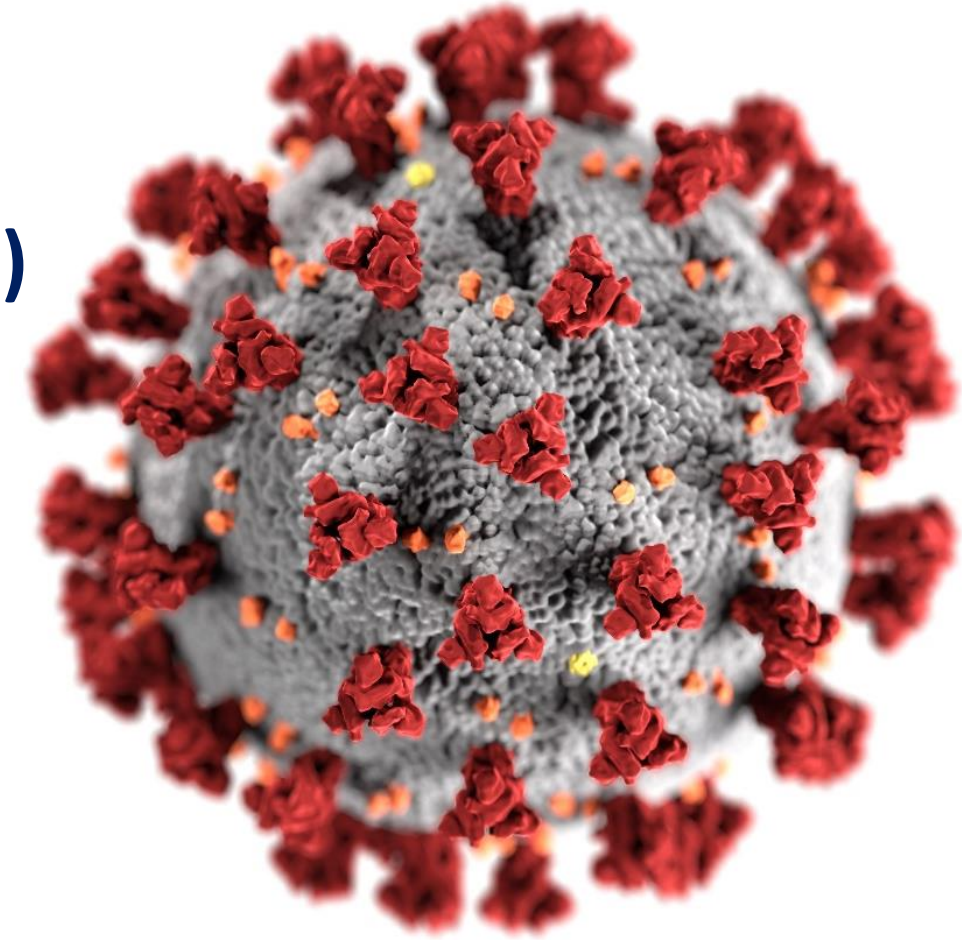
Myopericarditis following COVID-19 vaccination: Updates from the Vaccine Adverse Event Reporting System (VAERS)

Oct 21, 2021



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Disclaimer

- 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 (CDC) or the U.S. Food and Drug Administration (FDA)
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Myopericarditis reports to VAERS

Reports of myocarditis and myocarditis with pericarditis (myopericarditis) following COVID-19 vaccination

- As of Oct 6, 2021, a total of **402,469,096** doses of COVID-19 vaccines were administered (Pfizer-BioNTech, Moderna, and Janssen)
  - **3,336** reports of myocarditis and pericarditis
    - Myopericarditis: 2,459 reports
    - Pericarditis alone: 877 reports

Preliminary myopericarditis reports to VAERS following COVID-19 vaccination, by dose number (data thru Oct 6, 2021)

Manufacturer	Reports after dose 1	Reports after dose 2	Reports after unknown dose
Pfizer-BioNTech (n=1,651)	250	1,160	241
Moderna (n=723)	198	419	106
Janssen (n=71)	50	1	20
Not reported (n=14)	1	8	5
Total (N=2,459)	**499**	**1,588**	**372**

- Includes total preliminary reports identified through VAERS database searches for reports with myopericarditis MedDRA* codes and pre-screened VAERS reports with signs and symptoms consistent with myopericarditis; **excludes reports of solely pericarditis**
  - Follow-up, medical record review, application of CDC working case definition, and adjudication is ongoing or pending

* Medical Dictionary for Regulatory Activities https://www.meddra.org/

Characteristics of preliminary* myopericarditis reports to VAERS following known mRNA COVID-19 vaccination† (data thru Oct 6, 2021)

Characteristics	Dose 1 (mRNA only) (n=448)†	Dose 2 (n=1,579)†
Median age, years (IQR**)	28 (19–42)	20 (16–31)
Median time to symptom onset, days (IQR)	3 (1–10)	2 (1–4)
Sex (%)		
Male	299 (67%)	1,273 (81%)
Female	142 (32%)	295 (19%)
Not reported/not available	7 (2%)	11 (1%)

* Includes reports identified through VAERS database searches for reports with myopericarditis MedDRA codes, with signs and symptoms consistent with myopericarditis, and with dose number documented; and pre-process VAERS reports with follow-up, medical record review, and application of CDC case definition for myopericarditis

† Excludes 50 reports after Janssen, and 1 report that did not specify manufacturer after Dose 1; excludes 1 report after Janssen and 8 reports that did not specify manufacturer after Dose 2

** IQR = interquartile range

Reporting rates of myocarditis (per 1 million doses administered) after mRNA COVID-19 vaccines, 7-day risk period (N=935)*

- **366,062,239** doses of mRNA vaccine administered (dose 1 and dose 2)*
- Reporting rates exceed background incidence**
  - After dose 1 of Pfizer (12–17 years) and Moderna (18–24 years)
  - After dose 2 of Pfizer (12–39 years) and Moderna (18–49 years)

	Pfizer		Moderna	
	(All)		(All)	
Ages	**Dose 1**	**Dose 2**	**Dose 1**	**Dose 2**
12-15	**2.3**	**21.5**	0.0	not calculated
16-17	**2.8**	**37.4**	0.0	not calculated
18-24	1.2	**18.1**	**3.1**	**20.7**
25-29	0.7	**5.7**	1.8	**11.2**
30-39	0.6	**2.8**	1.4	**3.6**
40-49	0.2	1.5	0.2	**2.1**
50-64	0.3	0.4	0.5	0.5
65+	0.1	0.2	0.0	0.3

* As of Oct 6, 2021; 935 of 1,181 reports of myocarditis after doses 1 and 2 of mRNA vaccines occurred during days 0–6 after vaccination; reports verified to meet case definition by provider interview or medical record review

** An estimated 1–10 cases of myocarditis per 100,000 person years occurs among people in the United States, regardless of vaccination status; adjusted for the 7-day risk period, this estimated background is **0.2 to 1.9 per 1 million person 7-day risk period**

Reporting rates (per 1 million doses administered) of myocarditis among males after mRNA COVID-19 vaccines, 7-day risk period (N=797)*

- **169,740,953** doses of mRNA vaccine administered to males (dose 1 and dose 2) *
- Reporting rates exceed background incidence**
  - After dose 1 of Pfizer (12–24 years) and Moderna (18–39 years)
  - After dose 2 of Pfizer (12–39 years) and Moderna (18–49 years)

	Pfizer		Moderna	
	(Males)		(Males)	
Ages	**Dose 1**	**Dose 2**	**Dose 1**	**Dose 2**
12-15	**4.2**	**39.9**	0.0	not calculated
16-17	**5.7**	**69.1**	0.0	not calculated
18-24	**2.3**	**36.8**	**6.1**	**38.5**
25-29	1.3	**10.8**	**3.4**	**17.2**
30-39	0.5	**5.2**	**2.3**	**6.7**
40-49	0.3	2.0	0.2	**2.9**
50-64	0.2	0.3	0.5	0.6
65+	0.2	0.1	0.1	0.3

* As of Oct 6, 2021; 797 of 935 reports after doses 1 and 2 of mRNA vaccines occurred during Days 0–6 after vaccination among males; reports verified to meet case definition by provider interview or medical record review

** An estimated 1–10 cases of myocarditis per 100,000 person years occurs among people in the United States, regardless of vaccination status; adjusted for the 7-day risk period, this estimated background is **0.2 to 1.9 per 1 million person 7-day risk period**

Reporting rates (per 1 million doses administered) of myocarditis among females after mRNA COVID-19 vaccines, 7-day risk period (N=138)*

- **193,215,313** doses of mRNA vaccine administered to females (dose 1 and dose 2)*
- Reporting rates exceed background incidence**
  - After dose 2 of Pfizer (12–24 years) and dose 2 Moderna (18–29 years)

	Pfizer		Moderna	
	(Females)		(Females)	
Ages	**Dose 1**	**Dose 2**	**Dose 1**	**Dose 2**
12-15	0.4	**3.9**	0.0	0.0
16-17	0.0	**7.9**	0.0	0.0
18-24	0.2	**2.5**	0.6	**5.3**
25-29	0.2	1.2	0.4	**5.7**
30-39	0.6	0.7	0.5	0.4
40-49	0.1	1.1	0.2	1.4
50-64	0.3	0.5	0.5	0.4
65+	0.1	0.3	0.0	0.3

* As of Oct 6, 2021; 138 of 935 reports after doses 1 and 2 of mRNA vaccines occurred during Days 0–6 after vaccination among females; reports verified to meet case definition by provider interview or medical record review

** An estimated 1–10 cases of myocarditis per 100,000 person years occurs among people in the United States, regardless of vaccination status; adjusted for the 7-day risk period, this estimated background is **0.2 to 1.9 per 1 million person 7-day risk period**

Care and outcomes

Care and outcomes of preliminary myopericarditis cases reported to VAERS after COVID-19 vaccination in persons ≤29 years old (N=1,640)

(data thru Oct 6, 2021)

1,640 total preliminary reports

- **877** met CDC case definition* of myocarditis or myopericarditis
- 637 under review

Of 877 meeting case definition:

- 829 were hospitalized
  - 789 discharged
    - **607 (77%) known to have recovered from symptoms at time of report**
  - 19 still hospitalized (5 in ICU)
  - 21 with unknown disposition
- 34 were not hospitalized (seen in emergency dept., urgent care, outpatient clinic, not specified)

* Gargano JW, Wallace M, Hadler SC, et al. 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. MMWR Morb Mortal Wkly Rep 2021;70:977–982.

https://www.cdc.gov/mmwr/volumes/70/wr/pdfs/mm7027e2-H.pdf

Summary

Summary

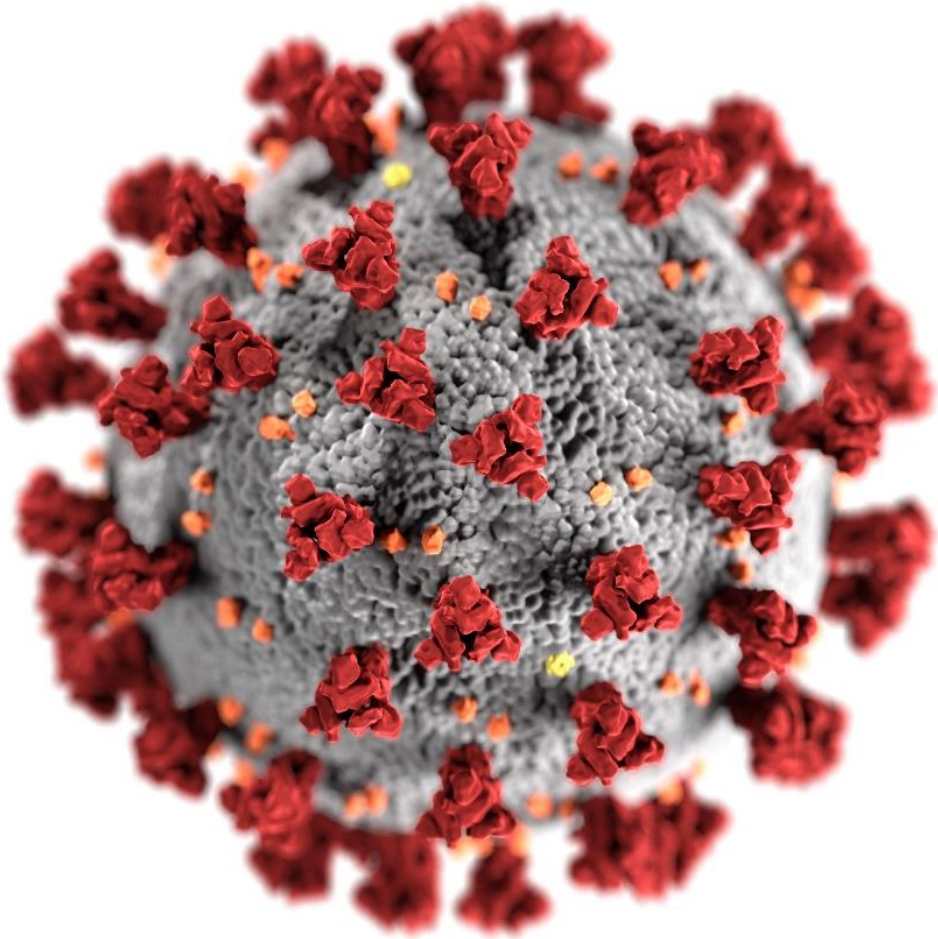
- 3,336 reports of myopericarditis or pericarditis to VAERS (as of October 6, 2021)
  - 2,459 myopericarditis, 877 pericarditis
- Epidemiology of myopericarditis following COVID-19 vaccination similar to previously reported updates
  - Primarily in younger males, after dose 2 mRNA vaccination, symptom onset clustering within several days of vaccination
- Limited follow-up information in VAERS case reports suggests most patients (77%) symptomatically recover
- Reporting rates of myocarditis > background rates for males (12–49 years, depending upon dose and manufacturer) and females (after dose 2, 12–29 years, depending upon manufacturer)
- Data subject to limitations of VAERS

Acknowledgments

Thanks to the many people who made analysis of these data possible:

- **VAERS Team**
  - VAERS TTS abstraction team
  - VAERS Myopericarditis abstraction team
  - VAERS Data team
- **Clinical Immunization Safety Assessment Project**
- **COVID-19 Vaccine Task Force Data Monitoring and Reporting Group**
- **FDA/Center for Biologics Evaluation and Research**

Thank you!



For more information, contact CDC
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TTY: 1-888-232-6348 www.cdc.gov

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Extra slides

MedDRA terms to search for myocarditis and pericarditis

Atypical mycobacterium pericarditis
Autoimmune myocarditis
Autoimmune pericarditis
Bacterial pericarditis
Coxsackie myocarditis
Coxsackie pericarditis
Cytomegalovirus myocarditis
Cytomegalovirus pericarditis
Enterovirus myocarditis
Eosinophilic myocarditis
Hypersensitivity myocarditis
Immune-mediated myocarditis
Myocarditis
Myocarditis bacterial
Myocarditis helminthic
Myocarditis infectious
Myocarditis meningococcal
Myocarditis mycotic
Myocarditis post infection
Myocarditis septic
Pericarditis
Pericarditis adhesive
Pericarditis constrictive
Pericarditis helminthic
Pericarditis infective
Pericarditis mycoplasmal
Pleuropericarditis
Purulent pericarditis
Viral myocarditis
Viral pericarditis

CDC case definitions of probable and confirmed myocarditis, pericarditis, and myopericarditis

Gargano JW, Wallace M, Hadler SC, et al. 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. MMWR Morb Mortal Wkly Rep 2021;70:977–982.

https://www.cdc.gov/mmwr/volumes/70/wr/pdfs/mm7027e2-H.pdf

a mainstay of treatment, with targeted cardiac medications or interventions as needed. Current guidelines from the American Heart Association and American College of Cardiology recommend exercise restriction until the heart recovers.[††]

As of June 11, 2021, approximately 296 million doses of mRNA COVID-19 vaccines had been administered in the United States, with 52 million administered to persons aged 12–29 years; of these, 30 million were first and 22 million were second doses. Within the Vaccine Adverse Event Reporting System (VAERS) (*4*), the national vaccine safety passive monitoring system, 1,226 reports of myocarditis after mRNA vaccination were received during December 29, 2020–June 11, 2021. Among persons with reported myocarditis after mRNA vaccination, the median age was 26 years (range = 12–94 years), with median symptom onset interval of 3 days after vaccination (range = 0–179). Among 1,194 reports for which patient age was known, 687 were among persons aged <30 years and 507 were among persons aged ≥30 years; of 1,212 with sex reported, 923 were male, and 289 were female.[§§] Among 1,094 patients with number of vaccine doses received reported, 76% occurred after receipt of dose 2 of mRNA vaccine; cases were reported after both Pfizer-BioNTech and Moderna vaccines. Informed by early reports, CDC prioritized rapid review of myocarditis in persons aged <30 years reported during May 1–June 11, 2021; the 484 patient records in this subset were evaluated by physicians at CDC, and several reports were also reviewed with Clinical Immunization Safety Assessment Project investigators,[¶¶] including cardiologists. At the time of this report, 323 of these 484 cases were determined to meet criteria in CDC's case definitions for myocarditis, pericarditis, or myopericarditis by provider interview or medical record review (Table 1). The median age of the 323 patients meeting CDC's case definitions was 19 years (range = 12–29 years); 291 were male, and 32 were female. The median interval from vaccination to symptom onset was 2 days (range = 0–40 days); 92% of patients experienced onset of symptoms within 7 days of vaccination. Of the 323 persons meeting CDC's case definitions, 309 (96%) were hospitalized. Acute clinical courses were generally mild; among 304 hospitalized patients with known clinical outcomes, 95% had been discharged at time of review, and none had died. Treatment data in VAERS are preliminary and incomplete; however, many patients have experienced resolution of symptoms with conservative treatment, such as receipt of nonsteroidal antiinflammatory drugs. Follow-up is

[††] https://www.ahajournals.org/doi/10.1161/CIR.0000000000000239?url_

TABLE 1. Case definitions of probable and confirmed myocarditis, pericarditis, and myopericarditis

Condition	Definition	
	Probable case	**Confirmed case**
Acute myocarditis	Presence of ≥1 new or worsening of the following clinical symptoms:* • chest pain, pressure, or discomfort • dyspnea, shortness of breath, or pain with breathing • palpitations • syncope OR, infants and children aged <12 years might instead have ≥2 of the following symptoms: • irritability • vomiting • poor feeding • tachypnea • lethargy AND ≥1 new finding of • troponin level above upper limit of normal (any type of troponin) • abnormal electrocardiogram (ECG or EKG) or rhythm monitoring findings consistent with myocarditis[§] • abnormal cardiac function or wall motion abnormalities on echocardiogram • cMRI findings consistent with myocarditis[¶] AND • No other identifiable cause of the symptoms and findings	Presence of ≥1 new or worsening of the following clinical symptoms:* • chest pain, pressure, or discomfort • dyspnea, shortness of breath, or pain with breathing • palpitations • syncope OR, infants and children aged <12 years might instead have ≥2 of the following symptoms: • irritability • vomiting • poor feeding • tachypnea • lethargy AND ≥1 new finding of • Histopathologic confirmation of myocarditis[†] • cMRI findings consistent with myocarditis[¶] in the presence of troponin level above upper limit of normal (any type of troponin) AND • No other identifiable cause of the symptoms and findings
Acute pericarditis**	Presence of ≥2 new or worsening of the following clinical features: • acute chest pain[††] • pericardial rub on exam • new ST-elevation or PR-depression on EKG • new or worsening pericardial effusion on echocardiogram or MRI	
Myopericarditis	This term may be used for patients who meet criteria for both myocarditis and pericarditis.	

Abbreviations: AV = atrioventricular; cMRI = cardiac magnetic resonance imaging; ECG or EKG = electrocardiogram.

* Persons who lack the listed symptoms but who meet other criteria may be classified as subclinical myocarditis (probable or confirmed).

† Using the Dallas criteria (Aretz HT, Billingham ME, Edwards WD, et al. Myocarditis. A histopathologic definition and classification. Am J Cardiovasc Pathol 1987; 1:3–14). Autopsy cases may be classified as confirmed clinical myocarditis on the basis of meeting histopathologic criteria if no other identifiable cause.

§ To meet the ECG or rhythm monitoring criterion, a probable case must include at least one of 1) ST-segment or T-wave abnormalities; 2) Paroxysmal or sustained atrial, supraventricular, or ventricular arrhythmias; or 3) AV nodal conduction delays or intraventricular conduction defects.

¶ Using either the original or the revised Lake Louise criteria. https://www.

Expected vs. Observed cases of myocarditis reported to VAERS after Pfizer-BioNTech dose 2, 7-day risk period (N=518)*

Age group, years	Females		Males	
	Cases of myopericarditis, expected	Cases of myopericarditis, observed	Cases of myopericarditis, expected	Cases of myopericarditis, observed
12–15	0–4	14	1–7	143
16–17	0–2	17	0–4	139
18–24	1–5	12	1–8	152
25–29	0–4	4	1–6	33
30–39	1–14	5	1–13	34
40–49	1–14	8	1–12	13
50–64	2–24	6	2–21	3
65+	2–23	3	2–18	1

* As of Oct 6, 2021; assumes a 7-day observation window, with 518 of 682 reports after Pfizer-BioNTech dose 2 occurring during Days 0–6 after vaccination; counts from reports meeting case definition for myopericarditis; expected estimates for females 12–29 years adjusted to reflect reduced incidence in this age group

Expected vs. Observed cases of myocarditis reported to VAERS after Moderna dose 2, 7-day risk period (N=216)*

Age group, years	Females		Males	
	Cases of myopericarditis, expected	Cases of myopericarditis, observed	Cases of myopericarditis, expected	Cases of myopericarditis, observed
12–15	0	0	0	1
16–17	0	0	0	1
18–24	0–3	14	0–4	89
25–29	0–2	12	0–4	33
30–39	1–9	2	1–8	29
40–49	1–10	7	1–9	13
50–64	2–18	4	2–17	5
65+	2–23	3	2–19	3

Moderna vaccine not authorized in 12-17 y/o

* As of Oct 6, 2021; assumes a 7-day observation window, with 216 of 254 reports after Moderna dose 2 occurring during Days 0–6 after vaccination; counts from reports meeting case definition for myopericarditis; expected estimates for females 12–29 years adjusted to reflect reduced incidence in this age group

Observed/Expected vs Reporting Rates

- Previous observed/expected analyses assumed same background incidence*, regardless of age group
  - As presented, implied different incidence by age group
- Reporting rates (per 100,000 doses administered) more neutral indicator
  - Adjusting for time (COVID-19 vaccines in use for 81.10% of a year), reporting rates among females < background incidence
    - Also adjusting for lower incidence among females**, rates slightly > background incidence after dose 2 Moderna among females 18–29 years of age

* An estimated 1–10 cases of myocarditis per 100,000 person years occurs among people in the United States
**Adjusted by factor of 1.7, estimated background incidence among females ~ 0.5–4.8 per 100,000 person years; (Fairweather, D. et al, *Curr Probl Cardiol.* 2013;38(1):7-46).

VAERS

VAERS accepts all reports from everyone regardless of the plausibility of the vaccine causing the event or the clinical seriousness of the event

key strengths

- Rapidly detects potential safety problems
- Can detect rare adverse events

key limitations

- Inconsistent quality and completeness of information
- Reporting biases
- Generally, cannot determine cause and effect

Adjusting for background rate of myocarditis

- 1–10 per 100,000 person years = 10–100 per 1 million person years
- 10–100 per 1 million person years x (7 days/365 days per year) = 0.2–1.9 per 1 million person 7-day period