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Incidence of Myocarditis/Pericarditis Following mRNA COVID-19 Vaccination Among Children and Younger Adults in the United States

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Background:

Vaccine safety monitoring systems worldwide have reported cases of myocarditis/pericarditis after mRNA-based COVID-19 vaccines (Pfizer-BioNTech and Moderna), especially among younger male persons 0 to 7 days after they received dose 2 (1, 2). Less is known about the incidence of myocarditis/pericarditis after booster doses.

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Reproducible Research Statement: *Study protocol:* <https://www.cdc.gov/vaccinesafety/pdf/COVID19-RCA-Protocol-1342-508.pdf>.

Statistical Code: Available to interested readers by contacting Kristin Goddard at kristin.x.goddard@kp.org. *Data set:* VSD data may be requested through the VSD data sharing program: <https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vsd/accessing-data.html#datasharing>.

Disclaimer: The findings and conclusions in this paper are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC). Mention of a product or company name is for identification purposes only and does not constitute endorsement by CDC.

Objective

To estimate the incidence of myocarditis/pericarditis during days 0 to 7 after mRNA vaccination by age, sex, dose number, and product.

Methods

The Vaccine Safety Datalink (VSD) is a collaborative of 8 integrated health care delivery systems with comprehensive medical records that has conducted active, population-based surveillance of prespecified outcomes after COVID-19 vaccination since December 2020 (1, 3). We identified all potential cases of myocarditis/pericarditis in emergency department and inpatient settings 1 to 98 days after vaccination, using myocarditis/pericarditis-specific ICD-10 codes, among 5- to 39-year-old persons (Table). We validated cases through review of medical records with physician adjudication and classified according to the Centers for Disease Control and Prevention case definition (1).

Findings

From 14 December 2020 through 31 May 2022 (persons 18–39 years) and 20 August 2022 (persons 5–17 years), 320 potential cases of myocarditis/pericarditis were identified 1 to 98 days after 6 992 340 vaccine doses as part of primary series COVID-19 vaccination, with 224 (70%) verified. Of these, 137 (61%) occurred 0 to 7 days after vaccination; 18 were after the first dose (of 3 562 311 doses administered) and 119 were after the second dose (of 3 430 029 doses administered).

In all age groups, incidence per million doses 0 to 7 days after vaccination was numerically higher in male than in female persons and after dose 2, although confidence intervals were wide and overlapped across sex for some age groups. Incidence was highest for male adolescents ages 12 to 15 years and 16 to 17 years following dose 2 (Table).

From 24 September 2021 through 20 August 2022, 101 potential cases of myocarditis/pericarditis were identified 1 to 98 days after 1 848 723 first booster doses, with 77 (76%) verified with a median onset of 4.5 days after vaccination; 39 cases (51%) were verified in the first week versus 38 during the subsequent 13 weeks.

In all age groups, incidence 0 to 7 days after first booster was higher for male compared to female persons, with adolescent males having the highest incidence in 16- to 17-year-olds and in 12- to 15-year-olds. In adults for whom both vaccine products were available, post-booster incidence was higher in male than in female adults and higher in males aged 18 to 29 compared to males aged 30 to 39.

Discussion

In this population-based surveillance, we found that myocarditis/pericarditis 0 to 7 days after mRNA vaccination in persons aged 5 to 39 years occurred in approximately 1 in 200 000 doses after the first dose and 1 in 30 000 doses after second dose of the primary series, and 1 in 50 000 doses after the first booster. The incidence varied markedly by age and sex,

however, with a disproportionate number of cases occurring in male persons, notably among adolescents after dose 2 and first boosters.

Our observed incidence after first boosters was generally higher than after dose 1, consistent with reporting from Israel (4). However, in contrast to this earlier report, we did not consistently observe a lower incidence after the first booster than after the second dose in the primary vaccination series. Incidence rates of myocarditis/pericarditis observed in the VSD population were higher, particularly after first boosters, than those reported to the U.S. Vaccine Adverse Event Reporting System (VAERS), but patterns noted by sex and age subgroups were similar (2, 5). Rates from VAERS may be lower because of the passive nature of VAERS reporting versus VSD's identification of cases using active surveillance. Both VSD and VAERS found incidence rates during days 0 to 7 after vaccination that were higher than the pre-pandemic background rates noted by Oster and colleagues (2); however, pre-pandemic rates may not be directly comparable with post vaccination rates because underdiagnosis of myocarditis/pericarditis in this age range was more likely pre-pandemic than post vaccination when surveillance was greater.

This study was strengthened by active surveillance of a large diverse population and by verification of cases through medical record review and physician adjudication. Important limitations include the lack of a control group, precluding causal inference. Cases were also identified only in emergency or inpatient settings using myocarditis/pericarditis-specific ICD-10 codes. Thus, cases were not identified if they were seen only in outpatient settings or if they received less-specific diagnosis codes such as chest pain (R07.9). Further limitations included potential reporting and ascertainment bias, potential differences between individuals who received Moderna versus Pfizer vaccines, and underreporting of SARS-CoV-2 infection.

Our findings can inform risk-benefit analyses, which thus far have consistently found the benefits of mRNA vaccination greatly outweigh the risks. Continued communication with patients and providers about risk for myocarditis/pericarditis after mRNA COVID-19 vaccination, as well as ongoing population-based safety surveillance, is warranted.

Acknowledgment

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The study sponsor, CDC, participated as a coinvestigator and contributed to protocol development; conduct of the study; interpretation of the data; review and revision of the manuscript; approval of the manuscript through official CDC scientific clearance processes; and the decision to submit the manuscript for publication. CDC authors must receive approval through the CDC scientific clearance process to submit an article for publication. Final decision to

submit rests with the first author. The study sponsor does not have the right to direct the submission to a particular journal.

References

1. Klein NP, Lewis N, Goddard K, et al. Surveillance for adverse events after COVID-19 mRNA vaccination. *JAMA*. 2021;326:1390–1399. doi:10.1001/jama.2021.15072 [PubMed: 34477808]
2. Oster ME, Shay DK, Su JR, et al. Myocarditis cases reported after mRNA-based COVID-19 vaccination in the US from December 2020 to August 2021. *JAMA*. 2022;327:331–340. [doi:10.1001/jama.2021.24110 [PubMed: 35076665]]
3. Goddard K, Lewis N, Fireman B, et al. Risk of myocarditis and pericarditis following BNT162b2 and mRNA-1273 COVID-19 vaccination. *Vaccine*. 2022;40:5153–5159. doi:10.1016/j.vaccine.2022.07.007 [PubMed: 35902278]
4. Oliver S Updates to the Evidence to Recommendation Framework: Pfizer-BioNTech Vaccine Booster Doses in 12-15 Year Olds. Advisory Committee on Immunization Practices. Accessed at www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-01-05/06_COVID_Oliver_2022-01-05.pdf on 5 January 2022.
5. Oliver S Updates to the Evidence to Recommendation Framework: Bivalent COVID-19 Vaccine Booster Doses. Accessed at: www.cdc.gov/vaccines/acip/meetings/live-mtg-2022-9-1.html on 18 September 2022.

Incidence Rate of Verified Myocarditis/Pericarditis in the 0 to 7 Days After mRNA COVID-19 Vaccination Among Persons Aged 5 to 39 Years by Product, Age Group, Sex, and Dose Number*

Table.

Product and Patient Group	Dose 1			Dose 2			First Booster		
	Cases/Doses Administered [†]	Incidence Rate/ Million Doses (95% CI)	Cases/Doses Administered	Incidence Rate/ Million Doses (95% CI)	Cases/Doses Administered	Incidence Rate/ Million Doses (95% CI)	Cases/Doses Administered [†]	Incidence Rate/ Million Doses (95% CI)	
Pfizer[‡]									
Male, age									
5–11 y	0/221 975	0.0 (0.0–13.5)	3/207 958	1.4 (3.0–42.2)	0/50 415	0.0 (0.0–59.4)			
12–15 y [§]	2/212 977	9.39 (1.1–33.9)	31/205 955	150.5 (102.3–213.6)	5/81 613	61.3 (19.9–143.0)			
16–17 y	1/105 147	9.51 (0.2–53.0)	14/102 091	137.1 (75.0–230.1)	9/47 874	188.0 (86.0–356.9)			
18–29 y	4/348 080	11.5 (3.1–29.4)	27/331 889	81.4 (53.6–118.4)	7/166 973	41.9 (16.9–86.4)			
30–39 y	1/352 403	2.8 (0.1–15.8)	5/341 527	14.6 (4.8–34.2)	3/197 554	15.2 (3.1–44.4)			
Female, age									
5–11 y	0/215 986	0.0 (0.0–13.9)	0/202 596	0.0 (0.0–14.8)	0/49 261	0.0 (0.0–60.8)			
12–15 y	0/210 741	0.0 (0.0–14.2)	5/204 074	24.5 (8.0–57.2)	0/84 114	0.0 (0.0–35.6)			
16–17 y	1/110 066	9.1 (0.2–50.6)	1/107 173	9.3 (0.2–52.0)	2/55 004	36.4 (4.4–131.3)			
18–29 y	1/414 730	2.4 (0.1–13.4)	2/400 321	5.0 (0.6–18.0)	1/240 226	4.2 (0.1–23.2)			
30–39 y	0/420 934	0.0 (0.0–7.1)	3/410 713	7.3 (1.5–21.3)	1/268 412	3.7 (0.1–20.8)			
Moderna[¶]									
Male, age									
18–29 y	5/207 073	24.2 (7.8–56.3)	19/195 809	97.0 (58.4–151.5)	7/109 337	64.0 (25.7–131.9)			
30–39 y	1/223 064	4.5 (0.1–25.0)	8/216 583	36.9 (15.9–72.8)	1/149 468	6.7 (0.2–37.3)			
Female, age									
18–29 y	1/253 773	3.9 (0.1–22.0)	0/243 560	0.0 (0.0–12.3)	1/156 707	6.4 (0.2–35.6)			
30–39 y	1/265 362	3.8 (0.1–21.0)	1/259 780	3.9 (0.1–21.4)	2/191 765	10.4 (1.3–37.7)			

* From the Vaccine Safety Datalink (VSD), 14 December 2020 Through 20 August 2022. The VSD population covered by the 8 data-contributing health plans is made up of approximately 12.5 million people, representing 3.6% of the U.S. population, and includes all ages, with approximately 20% younger than 18 years. Participating sites (Kaiser Permanente; Colorado, Northern California, Northwest Southern California, and Washington; Marshfield Clinic; HealthPartners; and Denver Health) have comprehensive medical records for their members. Potential cases were identified using myocarditis- and pericarditis-specific ICD Codes (B33.22 viral myocarditis; B33.23 viral pericarditis; I30.* acute pericarditis; I31.9 disease of pericardium, unspecified; I40.* acute myocarditis; and I51.4 myocarditis, unspecified) in emergency and inpatient settings (first in 60 days) in the 1 to 98 days post-vaccination. All identified cases underwent medical record review and then adjudication by a specialist (infectious disease physician, cardiologist, or both). Onset dates occasionally shifted to day 0 based on medical record review. All verified cases that met the Centers for Disease Control and Prevention case definition

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of confirmed or probable myocarditis, pericarditis, or myopericarditis without a clear alternative etiology were included. Case patients with a COVID-19 diagnosis code or positive COVID-19 laboratory test result in the 30 days prior to vaccination were excluded. Approximately 15% of case patients after a primary series dose and 21% of case patients after a first booster dose had a more distant COVID-19 infection identified and were included.

[‡] Vaccination date, manufacturer, and dose number for each COVID-19 vaccine were recorded at the participating sites for the doses administered. All sites capture COVID-19 vaccines administered internal to their health care system as well as outside of their health care system, including those administered in nursing homes, retail pharmacies, and government-run vaccination clinics; self-reported vaccinations; and those recorded in state immunization registries. Only 2 primary series doses and first booster doses were monitored in VSD. Primary series third doses were not included or monitored in these data.

[‡] Pfizer-BioNTech dose totals among all age groups and both sexes: dose 1: 2 613 039; dose 2: 2 514 297; first booster: 1 241 446.

[§] One person had separate occurrences of confirmed myocarditis in the 0 to 7 days following dose 2 of the primary series and their first booster dose. Because these were clinically distinct events, both were included in the appropriate rate estimates.

^{||} Moderna dose totals among all age groups and both sexes: dose 1: 949 272; dose 2: 915,732, first booster: 607 277.

[¶] Moderna COVID-19 vaccine was not authorized for use in children or adolescents aged <18 years during the study period.