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Monkeypox in a Traveler Returning from Nigeria — Dallas, Texas, July 2021

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Monkeypox is a rare, sometimes life-threatening zoonotic infection that occurs in west and central Africa. It is caused by *Monkeypox virus*, an orthopoxvirus similar to *Variola virus* (the causative agent of smallpox) and *Vaccinia virus* (the live virus component of orthopoxvirus vaccines) and can spread to humans. After 39 years without detection of human disease in Nigeria, an outbreak involving 118 confirmed cases was identified during 2017–2018 (*1*); sporadic cases continue to occur. During September 2018–May 2021, six unrelated persons traveling from Nigeria received diagnoses of monkeypox in non-African countries: four in the United Kingdom and one each in Israel and Singapore. In July 2021, a man who traveled from Lagos, Nigeria, to Dallas, Texas, became the seventh traveler to a non-African country with diagnosed monkeypox. Among 194 monitored contacts, 144 (74%) were flight contacts. The patient received tecovirimat, an antiviral for treatment of orthopoxvirus infections, and his home required large-scale decontamination. Whole genome sequencing showed that the virus was consistent with a strain of *Monkeypox virus* known to circulate in Nigeria, but the specific source of the patient's infection was not identified. No epidemiologically linked cases were reported in Nigeria; no contact received postexposure prophylaxis (PEP) with the orthopoxvirus vaccine ACAM2000.

Findings

On July 13, 2021, an emergency department (ED) physician in Dallas evaluated an early middle-aged man* with a 2-week history of fever, cough, and fatigue, followed by onset of a diffuse rash. Less than 1 week earlier, the patient had been in Nigeria for a large social gathering. Because of the extensive pustular rash on his face, hospital staff members immediately placed the patient in an airborne isolation room, where he was managed with airborne and contact precautions plus eye protection. After reviewing CDC's Travelers' Health destination webpage for Nigeria,† the ED physician suspected monkeypox, and public health authorities were immediately notified. The following day, the Dallas County Health and

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* Past medical history and identifying information withheld to protect patient confidentiality.

† https://wwwnc.cdc.gov/travel/destinations/traveler/none/nigeria?s_cid%20=%20ncezid-dgmq-travel-single-001

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Human Services Laboratory Response Network laboratory confirmed, by real-time polymerase chain reaction (PCR), the presence of nonvariola orthopoxvirus DNA from lesion swabs. Subsequent testing by species-specific real-time PCR at CDC confirmed West African clade *Monkeypox virus*.

Interviews revealed that the patient had arrived in Nigeria on June 25 and stayed in three urban centers during his trip (Figure). By June 30, he began experiencing diarrhea, vomiting, cough, subjective fever, and fatigue, all characteristic signs and symptoms of the monkeypox prodrome, which also mark the onset of transmissibility of the virus to others (e.g., through infected body fluids or respiratory droplets). On July 8, 1 day before boarding the first of two return flights, the patient developed a purulent rash confined to a covered part of his body. After a brief layover in the Atlanta airport, he took a domestic flight to Dallas, and then a ride-share vehicle to his residence, where he lives alone. The next day, the rash had worsened and was visible on his face, prompting a friend to drive him to the hospital on July 13. Like many persons his age, the patient had never received the smallpox vaccine, which would have provided cross-protection against monkeypox (*2*) but has not been routinely administered following the eradication of smallpox in 1980 (*3*).

Public Health Response

CDC, state and local public health authorities, and the treating clinicians launched an intensive investigation during July 13–September 4. Investigators reviewed what is known about orthopoxviruses and, through iterative discussions, categorized exposures as high, intermediate, low/uncertain, or no risk (Table). Exposures were ascertained through information collected from airport video surveillance, the patient's report of his activities and interactions with others, and flight seating assignments. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[§]

Notifications were immediately issued to the public via press releases; clinicians through the Health Alert Network; country national focal points, including those in Nigeria, under guidelines of the *International Health Regulations (2005)*; public health officials via an Epi-X[¶]; and a call with state health departments. Airline and federal partners provided information for flight contacts. Simultaneously, investigators discussed disinfection of potentially contaminated surfaces. Transmission to passengers on subsequent flights was considered unlikely because the disinfectants used between flights included a label claim for inactivation of *Vaccinia virus*, suggesting effective inactivation of *Monkeypox virus*. Airport bathrooms used by the patient were confirmed to have been regularly cleaned with similarly effective products. The owners of the two cars used by the patient were instructed to disinfect high-touch surfaces in the car with such products.

[§] 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

[¶] https://emergency.cdc.gov/epix/index.asp

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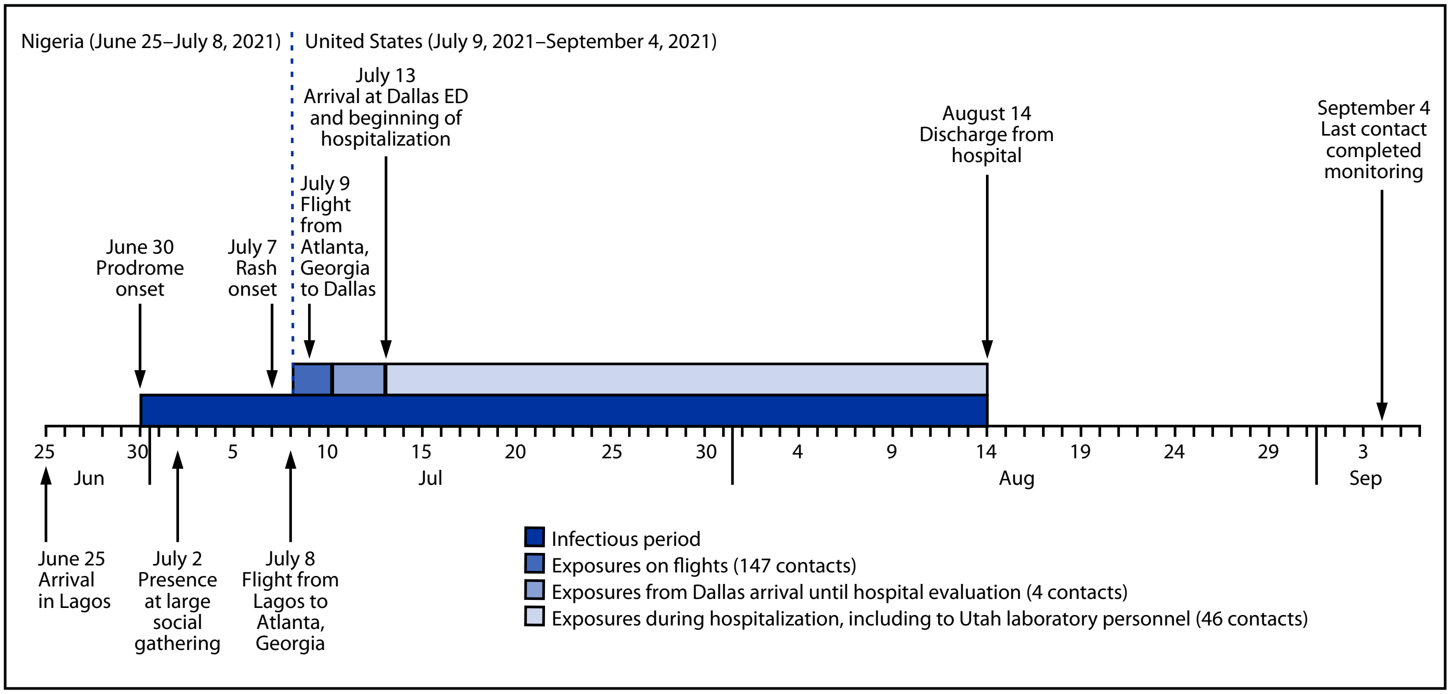
FIGURE. Time line of patient activities and potential exposures to *Monkeypox virus* from patient's arrival in Lagos, Nigeria to completion of monitoring for the last exposed known contact — Dallas, Texas, June–September 2021



Abbreviation: ED = emergency department.

A total of 223 contacts were identified. A 24/7 CDC monkeypox call center was established to coordinate daily monitoring from 21 U.S. jurisdictions where contacts resided and to provide clinical consultations to physicians who suspected additional cases. Recommendations about monitoring and PEP were strongest for persons with high (no persons) or intermediate (34 persons) risk. Some exposures were categorized or recategorized to a higher or lower risk level because of circumstances unique to this event. For example, typically, persons who used the same lavatory as the patient would be categorized as no risk; however, because the patient used the mid-cabin aircraft lavatory while he had a purulent rash on his body, investigators included passengers who used that same lavatory in the "low/uncertain" risk group. Similarly, persons seated adjacent to the patient on the domestic flight (<3 hours) had increased opportunities for contact with the patient's skin or contaminated materials (e.g., shared arm rest); however, because it was uncertain whether this exposure had occurred, investigators categorized these as "low/uncertain" risk. Reaching identified travel contacts was challenging; some travelers were non-U.S. residents, had already departed the United States, or had provided inaccurate telephone numbers to airlines, all of which hindered timely contact tracing.

Approximately 1 week after the investigation began, investigators learned that early in the patient's hospitalization, clinical specimens from the patient had been sent from the hospital to a laboratory in Utah for additional diagnostics. Conversations with the laboratory's biosafety manager revealed that instrumentation used to process these specimens during July 13–19 might have resulted in aerosol generation outside of a biosafety cabinet where personnel were not wearing respirators; six laboratory personnel were accordingly added to contact monitoring.

Most (189; 85%) contacts were categorized as having "low/uncertain" risk. All monitoring of known contacts concluded on September 4, 2021, and no secondary cases in the United States were identified, including among persons with suspected cases reported by clinicians to the CDC call center. ACAM2000, the orthopoxvirus vaccine recommended after exposure to smallpox (*4*), might be helpful after exposure to *Monkeypox virus* and was available for this potential indication through a CDC Investigational New Drug Protocol. Local public health officials were recommended to consider ACAM2000 for the 34 contacts with intermediate risk; no contact for whom ACAM2000 was offered received the vaccine. The patient completed a 32-day hospitalization that included treatment with tecovirimat because of severe disease. Hospital discharge had been delayed until a remaining lesion tested negative for *Monkeypox virus* DNA by PCR; this ensured no infectious risk upon discharge but extended the hospitalization.

TABLE. Recommendations for monitoring and postexposure prophylaxis with the orthopoxvirus vaccine ACAM2000,[*] by risk level of exposure to a monkeypox patient during the period of interest[†] (N = 223 contacts)[§] — Dallas, Texas, July 2021

Exposure risk level	Recommendations		Exposure characteristic	Specific population for this event	No. of persons monitored/ Total no. (%)
	Monitoring[§]	PEP[¶]			
High	Monitoring	Recommended	Contact between a person's broken skin or mucous membranes and the materials,[**] skin, lesions, or body fluids from patient (e.g., saliva from patient inadvertently splashes eye or oral cavity of a person)	NA	0 (—)
			Presence near patient during aerosol-generating procedure (e.g., intubation) while not wearing a surgical face mask or respirator		
			Exposure that, at the discretion of public health authorities, was recategorized to this risk level (i.e., exposure that ordinarily would be considered a lower risk exposure, raised to this risk level because of unique circumstances)		
Intermediate	Monitoring	Might be recommended after consultation with public health authorities and consideration of the risks and benefits	Contact between a person's intact skin and the materials,[**] skin, lesions, or body fluids from patient	Friend who visited patient and touched patient's used or potentially soiled clothing	1/1 (100)
				Flight crew who provided service to patient and had opportunities for direct contact with patient materials[**] (e.g., handling of used drinking cups or improper doffing of gloves)	6/7 (86)
			Presence ≤6 ft of patient for >3 hrs	Passengers seated ≤6 ft of patient during the Lagos to Atlanta flight	21/23 (91)
			Care provided to patient by health care provider not wearing gown, gloves, eye protection, and N95 or other respirator on one or more occasions	NA	0 (—)
			Exposure that, at the discretion of public health authorities, was recategorized to this risk level because of unique circumstances (e.g., if the potential for an aerosol exposure is uncertain, public health authorities may choose to decrease risk level from high to intermediate)	Laboratory personnel ≤6 ft from a laboratory instrument that had the potential for aerosol generation during analysis of patient specimens	3/3 (100)
Low/Uncertain	Monitoring	None	Care provided to patient by a health care provider who, during all interactions, wore gown, gloves, eye protection, and N95 or other respirator	Health care provider who cared for patient	43/43 (100)
			Exposure that, at the discretion of public health authorities, was recategorized to this risk level based on unique circumstances (e.g., uncertainty about whether *Monkeypox virus* was present on a surface and uncertainty about whether a person touched that surface)	Passengers on the international flight who might have used the mid-cabin lavatory used by patient	112/138 (81)
				Passengers on the domestic flight, seated adjacent to patient with potential for contact with patient or contaminated materials[**] because of narrow space (e.g., sharing armrest)	5/5 (100)
				Ride-share driver of an enclosed vehicle who drove patient while both wore cloth masks	1/1 (100)
				Friend who visited patient's home, but denied contact with any surfaces or with patient	1/1 (100)
				Unspecified community contact	1/1 (100)

See table footnotes on the next page.

TABLE. (*Continued*) **Recommendations for monitoring and postexposure prophylaxis with the orthopoxvirus vaccine ACAM2000,[*] by risk level of exposure to a monkeypox patient during the period of interest[†] (N = 223 contacts)[§] — Dallas, Texas, July 2021**

Exposure risk level	Recommendations		Exposure characteristic	Specific population for this event	No. of persons monitored/ Total no. (%)
	Monitoring[§]	PEP[¶]			
No risk	None	None	Exposure that public health authorities deemed did not meet criteria for other risk categories	Example: Customs and Border Protection officers who briefly handled patient materials (e.g., passport)[**] while wearing gloves Example: persons at gate of an airport at the same time as patient Example: cleaners of mid-cabin lavatory of international flight and janitorial staff in airport bathrooms who were confirmed to have worn eye protection, gloves, gowns, and surgical masks	0 (—)

Abbreviations: NA = not applicable; PEP = postexposure prophylaxis.

[*] https://www.fda.gov/vaccines-blood-biologics/vaccines/acam2000-smallpox-vaccine-questions-and-answers

[†] Period of interest was from onset of prodromal symptoms through resolution of the rash (i.e., shedding of crusts and observation of healthy pink tissue at all former lesion sites).

[§] Monitoring includes ascertainment of selected signs and symptoms of monkeypox: fever (≥100.4°F [≥38°C]), chills, new lymphadenopathy (periauricular, axillary, cervical, inguinal), and new skin rash through 21 days after the exposure to the patient or the patient's materials. Monitoring could involve in-person visits, regular communications (e.g., phone call or another system) between public health representatives and the person under monitoring, self-monitoring by persons and reporting of symptoms to health departments only if symptoms appear, or another reliable system determined by the health department. Health departments should take into consideration the person's exposure risk level, the number of persons needing monitoring, time since exposure, and available resources, when determining the type of monitoring to be conducted. Persons should be advised to self-isolate if any symptoms develop. Persons who report only chills or lymphadenopathy should remain at their residence, self-isolate for 24 hours, and monitor their temperature for fever; if fever or rash do not develop and chills or lymphadenopathy persist, the person should be evaluated by a clinician for the potential cause. Clinicians can consult with the state health department if monkeypox is suspected. If a fever or rash develops, CDC should immediately be consulted.

[¶] During this investigation, no contacts received PEP with ACAM2000.

[**] Linens, health care equipment used for patient care, surfaces potentially soiled by patient, and personal items belonging to patient.

Procedures for disinfection of his home were extrapolated from guidance previously developed by CDC for smallpox[**] and by Public Health England for monkeypox.[††] Whole genome sequencing confirmed that the *Monkeypox virus* strain was closely related to strains known to circulate in Nigeria. No specific source of his infection was identified in Nigeria; local staff members dispatched to the urban centers visited by the patient found no reported cases linked to him.

Discussion

This was the first travel-associated monkeypox case in the United States, and the seventh such case worldwide, since a large 2017 outbreak in Nigeria (*5*,*6*). Case recognition launched a large public health response involving extrapolation of limited data about monkeypox to develop a framework for managing potentially exposed persons and preventing additional cases.

The reservoir for *Monkeypox virus* has not been identified but is suspected to be a rodent or other small mammal or mammals (*2*). Before the 2017 Nigeria outbreak, most human monkeypox cases occurred in rural, forested areas of Africa; however, in Nigeria, monkeypox cases have occurred in urban areas, suggesting novel risk factors (*1*). Two distinct clades of *Monkeypox virus* circulate in Africa: the West African clade, which is endemic in west Africa, and the Congo Basin clade, which occurs in central Africa (*2*). Complicating the public health response, cases in Nigeria, although confirmed to be caused by the West African clade, have clinically been distinct: the West African Clade is historically believed to cause milder human disease, few deaths, and limited human-to-human transmission. However, some cases in Nigeria have been severe, even resulting in death, most commonly in persons with HIV infection (*1*,*7*). In addition, epidemiologic and genomic analyses have shown multiple human-to-human transmission events in Nigeria, including within households and a prison; secondary cases occurred in a health care provider and in family members of one patient whose illness was diagnosed in the United Kingdom (*1*,*7*,*8*).

Fortuitously, mask use during the ongoing COVID-19 pandemic ensured that contacts, including fellow airline passengers and crew members, community contacts, and health care providers, were at reduced risk for being infected with *Monkeypox virus* from this patient. Sparse data on *Monkeypox*

[**] https://biotech.law.lsu.edu/blaw/bt/smallpox/CDC-28feb2010/index.htm

[††] https://www.gov.uk/guidance/monkeypox#guidance-for-environmental-cleaning-and-decontamination

virus epidemiology, increasing numbers of immunocompromised persons in the United States (*9*) (e.g., from chemotherapy and other therapeutics), and waning of immunity to orthopoxviruses since the eradication of smallpox and cessation of routine smallpox vaccination (*2*) led investigators in this situation to take a cautious approach. Clinical laboratory personnel are typically not at risk for exposure to *Monkeypox virus*; however, use of specific laboratory instruments near persons not wearing adequate personal protective equipment caused investigators to be concerned about exposure to aerosols. The possible presence of *Monkeypox virus* on the patient's covered body during lavatory use similarly prompted a guarded approach; passengers who used that lavatory were monitored in the "low/uncertain" risk group. Most exposures occurred during airline flights that, relative to the time the patient was in the community and admitted to the hospital, were brief.

Four months after this case, an eighth travel-associated monkeypox case in a traveler from Nigeria occurred, also in the United States, prompting CDC to issue a Level 1 (Watch) Travel Health Notice for travel to Nigeria.[§§] Multiple reasons have been proposed for continued human cases in Nigeria, including population growth, increased human interaction with *Monkeypox virus* reservoirs because of deforestation and climate change, accumulation of unvaccinated cohorts, and declining smallpox vaccine immunity (*1*,*10*). The Nigerian Federal Ministry of Health continues to work to prevent, detect, and investigate monkeypox cases in Nigeria, but as cases continue to occur, U.S. public health and hospital authorities might consider developing local strategies for responding to future imported cases. Early clinical suspicion facilitated by elicitation of a complete travel history, use of appropriate infection control precautions, and timely identification of activities performed during the period of infectivity were among the most critical actions taken. Understanding the types of exposures that are most concerning for *Monkeypox virus* transmission, knowing contaminated surfaces need to be quickly identified and decontaminated, and anticipating potentially long hospitalizations and contact monitoring periods might also aid in planning for future cases (Box).

Summary

What is already known about this topic?

Monkeypox is a rare, potentially serious zoonotic infection. During September 2018–June 2021, six cases among travelers from Nigeria to non-African countries were identified; two instances resulted in secondary cases.

What is added by this report?

In July 2021, *Monkeypox virus* was confirmed in a U.S. resident who had returned from Nigeria. The public health investigation included identifying and monitoring exposed persons and disinfecting potentially contaminated surfaces. No secondary cases occurred.

What are the implications for public health practice?

Continued *Monkeypox virus* transmission in Nigeria might lead to additional sporadic U.S. importations. Early clinical suspicion, prompt reporting to public health authorities, and awareness of the types of exposures that might be high risk are among the lessons learned.

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[§§] https://wwwnc.cdc.gov/travel/notices/watch/monkeypox-nigeria

BOX. Critical actions taken during response to an imported case of monkeypox in the United States and lessons learned — Dallas, Texas, July 2021

- Elicitation of past-month travel history as part of every initial patient encounter in the treating hospital's ED; facilitated expedited clinical diagnosis and isolation of the patient.
- Assurance of airborne and contact precautions, plus eye protection*; minimal numbers of staff members entering patient's room; and log of all persons entering rooms ensured limited exposures and a record of persons to be monitored.
- Immediate notification of clinical suspicion to the local health department† as part of the treating hospital's ED protocol for situations such as this; enabled swift public health investigation.
- Consultation with CDC about antivirals and clinical management needs§; can be helpful early in the clinical course, particularly for severe infections.
- Collaboration with local LRN laboratory facilitated earliest testing to confirm that specimens from the patient had a DNA signature consistent with nonvariola orthopoxvirus; in the United States, this testing only possible at LRN laboratories and CDC.
- Identification of patient's period of infectivity; enabled identification of potential contacts during period of interest,¶ but required iterative interviews at multiple time points with patient.
- Establishment of local capacity to monitor contacts for 21 days from last exposure; was challenging, particularly with public health authorities strained by ongoing COVID-19 pandemic. Successful monitoring often involved providing case-by-case guidance (e.g., about delaying international travel plans) and negotiating with exposed persons regarding strategy that was least disruptive.
- Consideration of patient as infectious until all lesions are fully healed was safest approach; resulted in protracted hospitalization that local health authorities and treating hospitals should plan for.**
- Patient unwillingness, because of privacy concerns, to share details that would have aided the public health investigation in Nigeria hindered identification of infection source; patient trust, including in international authorities, is essential to determining infection source.
- Multiple communal settings identified for rapid decontamination despite the relatively short period between the patient's flight and his hospitalization; common over-the-counter cleaning products with label claim for *Vaccinia virus* used for most surfaces, but additional steps needed in hospital and residence because of extensive contamination.
- Assurance by laboratories that specimens are handled according to the BMBL to prevent unintentional exposures.††

Abbreviations: BMBL = Biosafety in Microbiological and Biomedical Laboratories; ED = emergency department; LRN = Laboratory Response Network.

[*] CDC recommends at least droplet precautions for monkeypox, but whenever possible, airborne precautions should be used out of an abundance of caution.

[†] Early notification, even while other diagnoses are being considered, is critical to the investigation. Public health authorities can facilitate CDC consultation and laboratory confirmation; timely communication of suspicions is essential to timely decontamination of contaminated surfaces (e.g., airplanes) and to begin contact tracing.

[§] Therapeutics stockpiled by the U.S. Government for prevention and treatment of smallpox can be considered for patients with monkeypox; these are available through Investigational New Drug protocols at CDC. https://www.cdc.gov/smallpox/prevention-treatment/index.html

[¶] Patients with monkeypox are infectious from the onset of prodromal symptoms until crusts separate and a fresh layer of skin forms underneath.

[**] Health care facilities and public health authorities should be familiar with the tiered U.S. Regional Treatment Network for special pathogens, including how to contact the Regional Ebola and other Special Pathogen Treatment Center for their jurisdiction for further consultation about persons with suspected or confirmed infection with a special pathogen. https://www.phe.gov/Preparedness/planning/hpp/reports/Documents/RETN-Ebola-Report-508.pdf

[††] https://www.cdc.gov/labs/BMBL.html

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Morbidity and Mortality Weekly Report

Cardiac Complications After SARS-CoV-2 Infection and mRNA COVID-19 Vaccination — PCORnet, United States, January 2021–January 2022

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Cardiac complications, particularly myocarditis and pericarditis, have been associated with SARS-CoV-2 (the virus that causes COVID-19) infection (*1*–*3*) and mRNA COVID-19 vaccination (*2*–*5*). Multisystem inflammatory syndrome (MIS) is a rare but serious complication of SARS-CoV-2 infection with frequent cardiac involvement (*6*). Using electronic health record (EHR) data from 40 U.S. health care systems during January 1, 2021–January 31, 2022, investigators calculated incidences of cardiac outcomes (myocarditis; myocarditis or pericarditis; and myocarditis, pericarditis, or MIS) among persons aged ≥5 years who had SARS-CoV-2 infection, stratified by sex (male or female) and age group (5–11, 12–17, 18–29, and ≥30 years). Incidences of myocarditis and myocarditis or pericarditis were calculated after first, second, unspecified, or any (first, second, or unspecified) dose of mRNA COVID-19 (BNT162b2 [Pfizer-BioNTech] or mRNA-1273 [Moderna]) vaccines, stratified by sex and age group. Risk ratios (RR) were calculated to compare risk for cardiac outcomes after SARS-CoV-2 infection to that after mRNA COVID-19 vaccination. The incidence of cardiac outcomes after mRNA COVID-19 vaccination was highest for males aged 12–17 years after the second vaccine dose; however, within this demographic group, the risk for cardiac outcomes was 1.8–5.6 times as high after SARS-CoV-2 infection than after the second vaccine dose. The risk for cardiac outcomes was likewise significantly higher after SARS-CoV-2 infection than after first, second, or unspecified dose of mRNA COVID-19 vaccination for all other groups by sex and age (RR 2.2–115.2). These findings support continued use of mRNA COVID-19 vaccines among all eligible persons aged ≥5 years.

This study used EHR data from 40 health care systems* participating in PCORnet, the National Patient-Centered Clinical Research Network (7), during January 1, 2021–January 31, 2022. PCORnet is a national network of networks that facilitates access to health care data and interoperability through use of a common data model across participating health care systems (https://pcornet.org/data). The PCORnet Common Data Model contains information captured from EHRs and other health care data sources (e.g., health insurance claims), including demographic characteristics, diagnoses, prescriptions, procedures, and laboratory test results, among other elements. The study population included persons with documented SARS-CoV-2 testing, viral illness diagnostic codes, or COVID-19 vaccination during the study period. Data were obtained through a single query that was executed by participating health care systems to generate aggregated results.

Five cohorts were created using coded EHR data among persons aged ≥5 years: 1) an infection cohort (persons who received ≥1 positive SARS-CoV-2 molecular or antigen test result); 2) a first dose cohort (persons who received a first dose of an mRNA COVID-19 vaccine); 3) a second dose cohort (persons who received a second dose of an mRNA COVID-19 vaccine); 4) an unspecified dose cohort (persons who received an mRNA COVID-19 vaccine dose not specified as a first or second dose); and 5) an any dose cohort (persons who received any mRNA COVID-19 vaccine dose). The any dose cohort is a combination of the other three vaccination cohorts; persons who received 2 doses were included twice in this cohort, once for each dose.[†] Vaccine doses specifically coded as booster or extra doses were excluded. Persons with a positive SARS-CoV-2 test result ≤30 days before receipt of an mRNA COVID-19 vaccine were excluded from the vaccine cohorts; persons who had received an mRNA COVID-19 vaccine dose ≤30 days before a positive SARS-CoV-2 test result were excluded from the infection cohort. In the infection cohort, there were no other exclusions based on vaccination status. The following index dates were used for cohort entrance: first positive SARS-CoV-2 test result for the infection cohort; first vaccination for the first dose cohort; second vaccination for the second dose cohort; the single vaccination for the unspecific dose cohort; and the first, second, and unspecified vaccination for the any dose cohort. Persons could be represented twice in the any dose cohort if they received a first and second dose; they would have a different index date for each of the doses.

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* The 40 PCORnet sites were AdventHealth, Allina Health, Children's Hospital Colorado, Cincinnati Children's Hospital, Columbia Health, Duke University, Fenway Health, Health Choice Network, Johns Hopkins University, Lurie Children's Hospital, Medical College of Wisconsin, Medical University of South Carolina, Montefiore Medical Center, Mount Sinai Health System, Nationwide Children's Hospital, Nemours Children's Hospital, New York University Langone Medical Center, Northwestern University, OCHIN, Inc., Ochsner Health System, Ohio State University, Orlando Health System, Penn State College of Medicine and Penn State Health Milton S. Hershey Medical Center, Seattle Children's Hospital, Temple University, University of Florida Health, University of Iowa Healthcare, University of Kansas, University Medical Center New Orleans, University of Miami, University of Michigan, University of Missouri Health Care, University of Nebraska, University of North Carolina, University of Pittsburgh Medical Center, University of Texas Southwest Medical Center, University of Utah, Vanderbilt University Medical Center, Wake Forest Baptist Health, and Weill Cornell Medicine. These sites represent academic and community hospitals that serve patients who are self-pay or have public or private insurance.

Incidence of three cardiac outcomes (myocarditis; myocarditis or pericarditis; and myocarditis, pericarditis, or MIS) were defined using *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) diagnostic codes[§] within 7-day or 21-day risk windows after the index date; persons who had received any of these diagnoses during the year preceding the index date were excluded. The outcome including MIS was only assessed for the infection cohort because the rare reports of MIS after mRNA COVID-19 vaccination typically had evidence of previous SARS-CoV-2 infection (*8*); a 42-day risk window also was used for this outcome to allow for a possible long latency between infection and diagnosis of MIS (*6*).[¶] Because persons with MIS who have cardiac involvement might only receive an ICD-10-CM code for MIS, rather than myocarditis or pericarditis, this combined outcome allowed for a comprehensive capture of potential cardiac complications after infection. Nearly 80% of cases of MIS have cardiac involvement (*9*). Cohorts were stratified by sex and age group.

The sex- and age-stratified incidences of the cardiac outcomes (cases per 100,000 persons) were calculated within 7-, 21-, or 42-day risk windows. Unadjusted RRs and 95% CIs were calculated as the incidences of the outcomes within the infection cohort divided by the incidences in the first, second, unspecified, and any dose cohorts separately for each sex and age stratum. RRs whose CIs did not include 1.0 were considered statistically significant; RRs were not compared across outcomes, risk windows, vaccine dose, or sex and age stratum. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[**]

The study population consisted of 15,215,178 persons aged ≥5 years, including 814,524 in the infection cohort; 2,548,334 in the first dose cohort; 2,483,597 in the second dose cohort; 1,681,169 in the unspecified dose cohort; and 6,713,100 in the any dose cohort (Table 1).[††] Among the four COVID-19 vaccination cohorts, 77%–79% of persons were aged ≥30 years; within the SARS-CoV-2 infection cohort, 63% were aged ≥30 years.

Among males aged 5–11 years, the incidences of myocarditis and myocarditis or pericarditis were 12.6–17.6 cases per 100,000 after infection, 0–4 after the first vaccine dose, and 0 after the second dose; incidences of myocarditis, pericarditis, or MIS were 93.0–133.2 after infection (Table 2). Because there were no or few cases of myocarditis or pericarditis after vaccination, the RRs for several comparisons could not be calculated or were not statistically significant. The RRs were significant when comparing myocarditis, pericarditis, or MIS in the 42 days after infection (133.2 cases per 100,000) with myocarditis or pericarditis after the first (4.0 cases per 100,000; RR 33.3) or second (4.7 cases per 100,000; RR 28.2) vaccine dose.

Among males aged 12–17 years, the incidences of myocarditis and myocarditis or pericarditis were 50.1–64.9 cases per 100,000 after infection, 2.2–3.3 after the first vaccine dose, and 22.0–35.9 after the second dose; incidences of myocarditis, pericarditis, or MIS were 150.5–180.0 after infection. RRs for cardiac outcomes comparing infected persons with first dose recipients were 4.9–69.0, and with second dose recipients, were 1.8–5.6; all RRs were statistically significant.

Among males aged 18–29 years, the incidences of myocarditis and myocarditis or pericarditis were 55.3–100.6 cases per 100,000 after infection, 0.9–8.1 after the first vaccine dose, and 6.5–15.0 after the second dose; incidences of myocarditis, pericarditis, or MIS were 97.2–140.8 after infection. RRs for

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[†] The first dose cohort included persons who had either the first of 2 doses ≥20 days before a second dose or a specific code for a first dose; the second dose cohort included persons who had either the second of 2 doses ≥20 days after a first dose or a specific code for a second dose. The unspecified dose cohort included persons who had only one code for an mRNA COVID-19 vaccination that was not specified as a first or second dose. The any dose cohort was the combination of the first, second, and unspecified dose cohorts; this cohort included all doses captured, with duplication of persons who received 2 doses. Vaccination and infection exclusions were provided before but not after exposures; thus, persons who had an infection soon after a vaccination would still be included in the vaccination cohort or vice versa. The cohorts were not mutually exclusive; persons vaccinated and infected could be in both vaccination and infection cohorts. However, because the outcomes were assessed in short time periods after index dates, overlap in outcomes was unlikely, unless an outcome was experienced more than once.

[§] Myocarditis was defined as presence of ICD-10-CM codes B33.22, I40, I40.0, I40.1, I40.8, I40.9, or I51.4. Pericarditis was defined as presence of ICD-10-CM codes B33.23, I30, I30.0, I30.1, I30.8, I30.9, or I31.9. MIS was defined as presence of ICD-10-CM code M35.81.

[¶] MIS often occurs in the absence of prior positive SARS-CoV-2 test results; these cases were not captured in the infection cohorts.

[**] 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. Sect. 3501 et seq.

[††] In the first and second dose vaccine cohorts, 27% of persons received Moderna and 73% received Pfizer-BioNTech. In the unspecified dose cohort, 36% received Moderna and 64% Pfizer-BioNTech, and in the any dose cohort, 29% received Moderna and 71% Pfizer-BioNTech.

TABLE 1. Demographic characteristics of persons who were infected with SARS-CoV-2 or received a first, second, unspecified, or any dose of an mRNA COVID-19 vaccine* — National Patient-Centered Clinical Research Network, United States, January 1, 2021–January 31, 2022

Characteristic	No. (%)				
	SARS-CoV-2 infection cohort†	mRNA COVID-19 vaccination cohort			
		First dose*,§	Second dose*,§	Unspecified dose*,¶	Any dose*,**
Cohort total	**814,524 (100)**	**2,548,334 (100)**	**2,483,597 (100)**	**1,681,169 (100)**	**6,713,100 (100)**
Age group, yrs					
5–11	76,960 (9)	48,986 (2)	41,742 (2)	30,199 (2)	120,927 (2)
12–17	70,336 (9)	190,810 (7)	179,612 (7)	113,775 (7)	484,197 (7)
18–29	151,950 (19)	308,892 (12)	297,560 (12)	241,787 (14)	848,239 (13)
30–50	255,103 (31)	665,876 (26)	652,947 (26)	490,808 (29)	1,809,631 (27)
51–65	152,243 (19)	601,615 (24)	588,873 (24)	404,445 (24)	1,594,933 (24)
≥66	107,932 (13)	732,155 (29)	722,863 (29)	400,155 (24)	1,855,173 (28)
Sex					
Female	457,506 (56)	1,497,984 (59)	1,463,746 (59)	997,741 (59)	3,959,471 (59)
Male	357,018 (44)	1,050,350 (41)	1,019,851 (41)	683,428 (41)	2,753,629 (41)
Race/Ethnicity††					
Hispanic	133,784 (16)	309,468 (12)	298,270 (12)	169,688 (10)	777,426 (12)
Asian	23,684 (3)	133,445 (5)	131,205 (5)	83,937 (5)	348,587 (5)
Black or African American	162,434 (20)	408,657 (16)	395,283 (16)	283,534 (17)	1,087,474 (16)
Other	34,473 (4)	93,100 (4)	90,122 (4)	54,305 (3)	237,527 (4)
White	408,152 (50)	1,441,573 (57)	1,407,974 (57)	1,001,686 (60)	3,851,233 (57)
Missing§§	58,980 (7)	205,834 (8)	204,224 (8)	98,299 (6)	508,357 (8)

* In the first and second dose cohorts, 27% of persons received mRNA-1273 (Moderna) vaccine and 73% received BNT162b2 (Pfizer-BioNTech) vaccine. In the unspecified dose cohort, 36% received Moderna and 64% Pfizer-BioNTech. In the any dose cohort, 29% received Moderna and 71% Pfizer-BioNTech.

† Persons in the infection cohort included those who received ≥1 positive SARS-CoV-2 molecular or antigen test result.

§ The first dose cohort included persons who had either the first of 2 doses ≥20 days before a second dose or a specific code for a first dose; the second dose cohort included persons who had either the second of 2 doses ≥20 days after a first dose or a specific code for a second dose.

¶ The unspecified dose cohort included persons who had a single dose that was not specified as a first or second dose; doses specified as booster doses were excluded.

** The any dose cohort is the first, second, and unspecified dose cohorts combined; persons who had 2 doses are represented twice in the cohort but had different index dates for their first and second doses.

†† Persons of Hispanic origin could be of any race; Asian, Black or African American, White, or other (which includes American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, multiple race, and other race) persons are not Hispanic.

§§ Missing race category includes no information, refused to answer, unknown, or missing.

cardiac outcomes comparing infected persons with first dose recipients were 7.2–61.8, and with second dose recipients, were 6.7–8.5; all RRs were statistically significant.

Among males aged ≥30 years, the incidences of myocarditis and myocarditis or pericarditis were 57.2–114.0 cases per 100,000 after infection, 0.9–7.3 after the first vaccine dose, and 0.5–7.3 after the second dose; incidences of myocarditis, pericarditis, or MIS were 109.1–136.8 after infection. RRs for cardiac outcomes among infected persons compared with first dose recipients were 10.7–67.2, and compared with second dose recipients, were 10.8–115.2; all RRs were statistically significant.

Among females aged 5–11 years, incidences of myocarditis and myocarditis or pericarditis were 5.4–10.8 cases per 100,000 after infection, and incidences of myocarditis, pericarditis, or MIS were 67.3–94.2 after infection (Table 3). No cases of myocarditis or pericarditis after vaccination were identified. The incidences of cardiac outcomes did not vary by age among females aged ≥12 years. In this group, the incidences of myocarditis and myocarditis or pericarditis were 11.9–61.7 cases per 100,000 after infection, 0.5–6.2 after the first vaccine dose, and 0.5–5.4 after the second dose; incidences of myocarditis, pericarditis, or MIS were 27.1–93.3 after infection. Among females aged ≥12 years, RRs for cardiac outcomes comparing infected persons with first dose recipients were 7.4–42.6, and with second dose recipients, were 6.4–62.9; all RRs were statistically significant.

Discussion

Analysis of EHR data from 40 U.S. health care systems found that the incidences of cardiac complications after SARS-CoV-2 infection or mRNA COVID-19 vaccination were low overall but were higher after infection than after vaccination for both males and females in all age groups. Two studies from Israel (*2*) and the United Kingdom (*3*) have found similar higher risk for myocarditis after SARS-CoV-2 infection compared with that after mRNA COVID-19 vaccination.

Myocarditis or pericarditis incidence after mRNA COVID-19 vaccination in the current study (0–35.9 per 100,000 for males and 0–10.9 for females across age groups and vaccine cohorts) was similar to estimates found in a study from eight U.S. health systems in the Vaccine Safety Datalink (*10*). Previous CDC estimates found the highest risk for post-vaccination myocarditis among males aged 16–17 years (10.6 per 100,000)

TABLE 2. Incidence of cardiac outcomes among males aged ≥5 years after SARS-CoV-2 infection or mRNA COVID-19 vaccination and risk ratios, by age group and risk window — National Patient-Centered Clinical Research Network, United States, January 1, 2021–January 31, 2022

Age group, yrs/ Outcome/ Risk window	Incidence[*] among males					Risk ratio (95% CI) SARS-CoV-2 infection versus mRNA COVID-19 vaccination			
	SARS-CoV-2 infection cohort[†]	mRNA COVID-19 vaccination cohort				mRNA COVID-19 vaccination cohort			
		First dose[§]	Second dose[§]	Unspecified dose[¶]	Any dose[**]	First dose[§]	Second dose[§]	Unspecified dose[¶]	Any dose[**]
5–11[††]									
Myocarditis									
7-day	12.6	0	0	0	0	NC	NC	NC	NC
21-day	17.6	4.0	0	6.5	3.2	4.4 (0.5–35.7)	NC	2.7 (0.3–22.1)	5.4 (1.1–26.1)
Myocarditis or pericarditis									
7-day	12.6	0	0	0	0	NC	NC	NC	NC
21-day	17.6	4.0	0	6.5	3.2	4.4 (0.5–35.7)	NC	2.7 (0.3–22.1)	5.4 (1.1–26.1)
Myocarditis, pericarditis, or MIS[§§]									
7-day	93.0	—[¶¶]	—	—	—	NC	NC	NC	NC
21-day	103.0	—	—	—	—	25.7 (3.5–187.0)	NC	16.0 (2.2–116.0)	31.7 (7.7–131.2)
42-day	133.2	—	—	—	—	33.3 (4.6–240.5)	28.2 (3.9–203.9)	10.3 (2.5–42.3)	20.5 (7.4–56.7)
12–17[††]									
Myocarditis									
7-day	50.1	2.2	22.0	16.7	12.9	23.0 (5.3–99.5)	2.3 (1.2–4.4)	3.0 (1.3–6.7)	3.9 (2.1–7.0)
21-day	59.0	3.3	26.7	20.4	16.0	18.0 (5.4–60.6)	2.2 (1.2–4.0)	2.9 (1.4–6.0)	3.7 (2.1–6.4)
Myocarditis or pericarditis									
7-day	56.0	2.2	26.7	22.3	16.0	25.7 (6.0–110.3)	2.1 (1.1–3.9)	2.5 (1.2–5.2)	3.5 (2.0–6.1)
21-day	64.9	3.3	35.9	29.7	21.6	19.8 (5.9–66.2)	1.8 (1.0–3.1)	2.2 (1.1–4.2)	3.0 (1.8–5.0)
Myocarditis, pericarditis, or MIS[§§]									
7-day	150.5	—	—	—	—	69.0 (16.8–283.2)	5.6 (3.5–9.2)	6.8 (3.6–12.7)	9.4 (6.2–14.4)
21-day	159.3	—	—	—	—	48.7 (15.2–155.7)	4.4 (2.9–6.9)	5.4 (3.1–9.4)	7.4 (5.0–10.8)
42-day	180.0	—	—	—	—	4.9 (3.2–7.4)	4.6 (3.0–6.9)	5.4 (3.2–9.1)	4.9 (3.5–6.7)
18–29									
Myocarditis									
7-day	55.3	0.9	6.5	7.0	4.6	61.8 (8.5–451.8)	8.5 (3.7–19.1)	7.9 (3.3–19.0)	12.0 (6.4–22.5)
21-day	63.7	3.6	8.4	11.6	7.5	17.8 (6.4–49.8)	7.6 (3.7–15.7)	5.5 (2.7–11.0)	8.4 (5.0–14.2)
Myocarditis or pericarditis									
7-day	85.5	2.7	12.1	22.0	11.5	31.8 (9.9–102.0)	7.0 (3.8–12.9)	3.9 (2.3–6.6)	7.4 (4.8–11.5)
21-day	100.6	8.1	15.0	27.8	16.1	12.5 (6.2–25.2)	6.7 (3.9–11.7)	3.6 (2.3–5.8)	6.3 (4.3–9.1)
Myocarditis, pericarditis, or MIS[§§]									
7-day	97.2	—	—	—	—	36.2 (11.3–115.5)	8.0 (4.4–14.6)	4.4 (2.6–7.4)	8.5 (5.6–12.9)
21-day	112.3	—	—	—	—	13.9 (7.0–28.0)	7.5 (4.4–13.0)	4.0 (2.5–6.4)	7.0 (4.8–10.1)
42-day	140.8	—	—	—	—	7.2 (4.5–11.4)	8.4 (5.0–13.9)	4.5 (2.9–6.9)	6.4 (4.6–8.8)
≥30									
Myocarditis									
7-day	57.2	0.9	0.5	3.0	1.3	67.2 (31.4–143.8)	115.2 (42.6–311.7)	18.9 (11.2–31.7)	45.7 (30.2–69.2)
21-day	63.0	1.9	1.2	4.2	2.2	32.4 (19.3–54.3)	50.8 (26.7–96.4)	15.1 (9.7–23.7)	28.3 (20.4–39.3)
Myocarditis or pericarditis									
7-day	100.2	3.8	3.1	15.0	6.3	26.6 (18.2–38.7)	32.3 (21.3–48.8)	6.7 (5.2–8.6)	16.0 (12.9–19.8)
21-day	114.0	7.3	7.3	20.1	10.4	15.6 (11.8–20.7)	15.6 (11.7–20.7)	5.7 (4.5–7.1)	10.9 (9.1–13.1)
Myocarditis, pericarditis, or MIS[§§]									
7-day	109.1	—	—	—	—	28.9 (19.9–42.0)	35.1 (23.3–53.0)	7.3 (5.7–9.4)	17.4 (14.1–21.5)
21-day	123.0	—	—	—	—	16.8 (12.7–22.3)	16.8 (12.7–22.2)	6.1 (4.9–7.7)	11.8 (9.9–14.0)
42-day	136.8	—	—	—	—	10.7 (8.6–13.4)	10.8 (8.6–13.5)	5.4 (4.4–6.7)	8.7 (7.4–10.1)

Abbreviations: MIS = multisystem inflammatory syndrome; NC = not calculated.

[*] Cases per 100,000 persons.

[†] Persons in the infection cohort included those who received ≥1 positive SARS-CoV-2 molecular or antigen test result.

[§] The first dose cohort included persons who had either the first of 2 doses ≥20 days before a second dose or a specific code for a first dose; the second dose cohort included persons who had either the second of 2 doses ≥20 days after a first dose or a specific code for a second dose.

[¶] The unspecified dose cohort included persons who had a single dose that was not specified as a first or second dose; doses specified as booster doses were excluded.

[**] The any dose cohort is the first, second, and unspecified dose cohorts combined; persons who had 2 doses are represented twice in the cohort but had different index dates for their first and second doses.

[††] BNT162b2 (Pfizer-BioNTech) is the only mRNA COVID-19 vaccine approved for persons aged 5–17 years.

[§§] Diagnoses of myocarditis, pericarditis, or MIS after a positive SARS-CoV-2 test result compared with diagnoses of myocarditis or pericarditis after vaccination. The 42-day risk ratios were only calculated for this outcome and comparison. The incidence of myocarditis or pericarditis in this risk window was 4.0, 37.1, 19.7, and 12.8 cases per 100,000 for males aged 5–11, 12–17, 18–29, and ≥30 years after a first dose of an mRNA COVID-19 vaccine; 4.7, 39.4, 16.8, and 12.7 cases per 100,000 after a second dose; 12.9, 33.4, 31.3, and 25.3 cases per 100,000 after an unspecified dose; and 6.5, 37.1, 22.0, and 15.8 cases per 100,000 after any dose.

[¶¶] Dashes indicate the incidence for vaccination cohorts was not applicable because the comparison for incidence of myocarditis, pericarditis, or MIS after infection was to myocarditis or pericarditis after vaccination.

TABLE 3. Incidence of cardiac outcomes among females aged ≥5 years after SARS-CoV-2 infection or mRNA COVID-19 vaccination and risk ratios, by age group and risk window — National Patient-Centered Clinical Research Network, United States, January 1, 2021–January 31, 2022

	Incidence* among females					Risk ratio (95% CI) SARS-CoV-2 infection versus mRNA COVID-19 vaccination			
		mRNA COVID-19 vaccination cohort				mRNA COVID-19 vaccination cohort			
Age group, yrs/ Outcome/ Risk window	SARS-CoV-2 infection cohort[†]	First dose[§]	Second dose[§]	Unspecified dose[¶]	Any dose**	First dose[§]	Second dose[§]	Unspecified dose[¶]	Any dose**
5–11[††]									
Myocarditis									
7-day	5.4	0	0	0	0	NC	NC	NC	NC
21-day	8.1	0	0	0	0	NC	NC	NC	NC
Myocarditis or pericarditis									
7-day	8.1	0	0	0	0	NC	NC	NC	NC
21-day	10.8	0	0	0	0	NC	NC	NC	NC
Myocarditis, pericarditis, or MIS[§§]									
7-day	67.3	—[¶¶]	—	—	—	NC	NC	NC	NC
21-day	80.7	—	—	—	—	NC	NC	NC	NC
42-day	94.2	—	—	—	—	NC	NC	NC	NC
12–17[††]									
Myocarditis									
7-day	24.7	1.0	1.1	0	0.8	24.5 (3.1–193.3)	23.1 (2.9–182.0)	NC	31.2 (6.7–144.3)
21-day	35.7	1.0	3.2	1.7	2.0	35.4 (4.6–270.5)	11.1 (3.2–39.0)	21.4 (2.8–163.4)	18.0 (6.4–50.5)
Myocarditis or pericarditis									
7-day	24.7	2.0	2.1	0	1.6	12.2 (2.6–56.7)	11.5 (2.5–53.4)	NC	15.6 (4.8–50.6)
21-day	35.7	2.0	5.4	3.3	3.6	17.7 (4.0–78.4)	6.7 (2.4–18.7)	10.7 (2.4–47.4)	10.0 (4.3–23.4)
Myocarditis, pericarditis, or MIS[§§]									
7-day	63.1	—	—	—	—	31.3 (7.4–132.7)	29.5 (6.9–125.0)	NC	39.8 (13.8–115.2)
21-day	79.6	—	—	—	—	39.5 (9.4–165.4)	14.9 (5.7–38.3)	23.8 (5.7–99.9)	22.3 (10.6–47.2)
42-day	93.3	—	—	—	—	11.6 (5.4–25.0)	12.4 (5.5–28.1)	14.0 (5.0–39.4)	12.4 (7.1–21.7)
18–29									
Myocarditis									
7-day	11.9	0.5	1.6	3.9	1.8	23.5 (3.0–182.0)	7.6 (2.1–27.1)	3.1 (1.1–8.4)	6.5 (2.8–15.2)
21-day	19.5	1.0	2.1	5.8	2.8	19.2 (4.5–82.9)	9.3 (3.1–27.5)	3.4 (1.5–7.5)	7.1 (3.6–14.0)
Myocarditis or pericarditis									
7-day	23.8	2.5	3.1	7.1	4.0	9.4 (3.6–24.8)	7.6 (3.1–18.7)	3.4 (1.6–7.0)	5.9 (3.3–10.6)
21-day	33.6	4.6	5.2	10.9	6.6	7.4 (3.5–15.5)	6.4 (3.1–13.1)	3.1 (1.7–5.6)	5.1 (3.1–8.2)
Myocarditis, pericarditis, or MIS[§§]									
7-day	27.1	—	—	—	—	10.7 (4.1–27.9)	8.6 (3.5–21.0)	3.8 (1.9–7.8)	6.7 (3.8–11.9)
21-day	40.1	—	—	—	—	8.8 (4.2–18.2)	7.6 (3.8–15.4)	3.7 (2.1–6.5)	6.1 (3.8–9.6)
42-day	67.2	—	—	—	—	8.3 (4.8–14.3)	11.6 (6.1–22.1)	5.2 (3.2–8.7)	7.8 (5.3–11.3)
≥30									
Myocarditis									
7-day	32.6	0.8	0.5	1.0	0.7	42.6 (21.5–84.4)	62.9 (27.6–143.6)	31.3 (15.2–64.3)	44.0 (27.9–69.3)
21-day	36.3	1.4	0.9	1.6	1.3	25.2 (15.1–42.0)	38.3 (20.6–71.3)	23.2 (12.8–42.2)	28.2 (19.6–40.6)
Myocarditis or pericarditis									
7-day	53.8	3.1	1.7	8.2	3.9	17.1 (12.0–24.5)	31.2 (19.6–49.7)	6.6 (4.9–8.8)	13.9 (11.0–17.7)
21-day	61.7	6.2	4.1	10.7	6.5	10.0 (7.6–13.1)	14.9 (10.8–20.5)	5.8 (4.5–7.5)	9.4 (7.7–11.5)
Myocarditis, pericarditis, or MIS[§§]									
7-day	58.6	—	—	—	—	18.7 (13.1–26.6)	34.0 (21.4–54.0)	7.1 (5.4–9.5)	15.2 (12.0–19.2)
21-day	68.2	—	—	—	—	11.0 (8.4–14.4)	16.5 (12.0–22.6)	6.4 (4.9–8.3)	10.4 (8.6–12.7)
42-day	79.6	—	—	—	—	8.4 (6.7–10.5)	10.0 (7.9–12.8)	5.6 (4.5–7.0)	7.9 (6.7–9.4)

Abbreviations: MIS = multisystem inflammatory syndrome; NC = not calculated.

* Cases per 100,000 persons.

[†] Persons in the infection cohort included those who received ≥1 positive SARS-CoV-2 molecular or antigen test result.

[§] The first dose cohort included persons who had either the first of 2 doses ≥20 days before a second dose or a specific code for a first dose; the second dose cohort included persons who had either the second of 2 doses ≥20 days after a first dose or a specific code for a second dose.

[¶] The unspecified dose cohort included persons who had a single dose that was not specified as a first or second dose; doses specified as booster doses were excluded.

** The any dose cohort is the first, second, and unspecified dose cohorts combined; persons who had 2 doses are represented twice in the cohort but had different index dates for their first and second doses.

[††] BNT162b2 (Pfizer-BioNTech) is the only mRNA COVID-19 vaccine approved for persons aged 5–17 years.

[§§] Diagnoses of myocarditis, pericarditis, or MIS after a positive SARS-CoV-2 test result compared with diagnoses of myocarditis or pericarditis after vaccination. The 42-day risk ratios were only calculated for this outcome and comparison. The incidence of myocarditis or pericarditis in this risk window was 0, 8.1, 8.1, 9.5 cases per 100,000 for females 5-11, 12-17, 18-29, and ≥30 years after a first dose of an mRNA COVID-19 vaccine; 0, 7.5, 5.8, and 8.0 cases per 100,000 after a second dose; 0, 6.7, 12.9, and 14.2 cases per 100,000 after an unspecified dose; and 0, 7.5, 8.7, and 10.1 cases per 100,000 after any dose.

[¶¶] Dashes indicate the incidence for vaccination cohorts was not applicable because the comparison for incidence of myocarditis, pericarditis, or MIS after infection was to myocarditis or pericarditis after vaccination.

during a 7-day risk window after receipt of a second mRNA COVID-19 vaccine dose (*5*). Estimates from the current study (22.0 per 100,000 males aged 12–17 years) are higher, likely because outcomes were captured using ICD-10-CM codes alone rather than through passive reporting with subsequent verification through medical record review. Even among males aged 12–17 years, the group with the highest incidence of cardiac complications after receipt of a second mRNA COVID-19 vaccine dose, the risk was 1.8–5.6 times as high after SARS-CoV-2 infection than after vaccination.

The findings in this report are subject to at least six limitations. First, data were obtained using a query that returned aggregate data from sites, precluding adjustment for potential confounders. Stratification by age and sex was performed because of their clear prior association with cardiac outcomes. Second, outcomes were rare in some cohorts, leading to wide CIs around RR estimates. Third, only SARS-CoV-2 test results and mRNA COVID-19 vaccinations documented in EHRs were available for assessment. SARS-CoV-2 infections were not captured if testing occurred in homes, schools, community sites, or pharmacies. Similarly, EHR data in this study captured ≥1 dose of mRNA COVID-19 vaccine for 28% of persons aged ≥5 years. Nationally, 82% of persons aged ≥5 years were reported to have received any COVID-19 vaccination; 97% of all vaccinations administered were mRNA COVID-19 vaccines.[§§] Underascertainment of SARS-CoV-2 infections and mRNA COVID-19 vaccinations reduced sample size and might have introduced bias if capture of infection or vaccination within the EHR occurred differentially for those with cardiac outcomes.[¶¶] Fourth, case definitions for myocarditis, pericarditis, or MIS were ICD-10-CM code–based; diagnoses were not confirmed with chart review and are subject to misclassification. Fifth, cases of MIS among persons without documented SARS-CoV-2 infection were not included (*9*). Finally, some overlap might have occurred in risk windows for persons who had a SARS-CoV-2 infection soon after vaccination or a vaccination soon after infection. Exclusions were made for persons who received COVID-19 vaccine doses ≤30 days before infection or who had infections ≤30 days before vaccination.

Cardiac complications were rare after SARS-CoV-2 infection or mRNA COVID-19 vaccination. However, the risks for these complications were higher after infection than after vaccination among males and females in all age groups. These findings provide important context for balancing risks and benefits of mRNA COVID-19 vaccination among eligible persons ≥5 years.

Summary

What is already known about this topic?

Studies have found an increased risk for cardiac complications after SARS-CoV-2 infection and mRNA COVID-19 vaccination, but few have compared these risks.

What is added by this report?

Data from 40 health care systems participating in a large network found that the risk for cardiac complications was significantly higher after SARS-CoV-2 infection than after mRNA COVID-19 vaccination for both males and females in all age groups.

What are the implications for public health practice?

These findings support continued use of recommended mRNA COVID-19 vaccines among all eligible persons aged ≥5 years.

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[§§] https://covid.cdc.gov/covid-data-tracker/#vaccinations (Accessed March 29, 2022).

[¶¶] If patients who received a SARS-CoV-2–positive test result at a health care system were more likely to return to the same health care system for myocarditis, pericarditis, or MIS treatment than were patients who had their mRNA COVID-19 vaccination documented at the health care system, then the underascertainment of outcomes might be higher in the vaccination cohorts, introducing bias away from the null. This scenario might occur if a person was more likely to visit a tertiary care referral center participating in this study if they were more severely ill with a cardiac complication after SARS-CoV-2 infection than a perhaps mild cardiac complication after COVID-19 vaccination. However, if the cardiac complications were more commonly linked to vaccination than infection in the EHR, bias would be toward the null. This scenario might occur if clinicians were more likely to document an mRNA COVID-19 vaccination in the EHR if a cardiac complication was noted after vaccination than if the cardiac complication occurred after SARS-CoV-2 infection.

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Notes from the Field

SARS-CoV-2 Omicron Variant Infection in 10 Persons Within 90 Days of Previous SARS-CoV-2 Delta Variant Infection — Four States, October 2021–January 2022

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Vaccination protects against infection with SARS-CoV-2 (the virus that causes COVID-19) and related hospitalizations (*1*,*2*), and surviving a previous infection protects against B.1.1.7 (Alpha) and B.1.617.2 (Delta) variant reinfections[†] (*2*). Since the SARS-CoV-2 B.1.1.529 (Omicron) variant became predominant in the United States in late December 2021, reported reinfections have increased[§] (*3*). Early reinfections (those occurring within 90 days of previous infection) are not well understood (*4*). Because some persons have prolonged detection of viral RNA after infection,[¶] repeat positive nucleic acid amplification test (NAAT) results within 90 days could reflect prolonged shedding from earlier infection, presenting technical challenges to documenting and characterizing early reinfections. This report describes 10 patients from four states, with whole genome sequencing (WGS)–confirmed Omicron variant infections within 90 days of a previous Delta infection. This activity was reviewed by CDC, approved by respective institutional review boards, and was conducted consistent with applicable federal law and CDC policy.[**]

An early reinfection was defined as a SARS-CoV-2 WGS test result (performed at a state, university, or contracted commercial laboratory[††]) from a new NAAT-positive specimen, collected during October 2021–January 2022 and <90 days after a first positive specimen from a previous WGS-confirmed SARS-CoV-2 infection, that demonstrated a different lineage from the first infection. Vermont Department of Health case investigators noted an increase in suspected early reinfections; five of these cases were confirmed through Vermont's passive WGS surveillance system, which sequences the highest percentage (15.8%) of total state cases nationwide.[§§] Wisconsin Department of Health Services was notified by university researchers of suspected early reinfections in members of a household enrolled in a longitudinal respiratory disease surveillance study.[¶¶] Public Health – Seattle & King County was notified after Washington testing guidance for K–12 schools led to identification of a suspected early reinfection in a student at a school sporting event. Rhode Island screening protocols for hospitals and long-term care facilities led to collection of two NAAT-positive specimens within 90 days from a long-term care facility resident.

Ten patients with early reinfections were identified (Table). WGS identified Delta variant in all specimens from first infections and Omicron in all reinfection specimens.[***] Median age at first infection was 11 years. Eight patients were aged <18 years, one was a long-term care facility resident, and one was a health care worker[†††]; five were male. Intervals between initial and subsequent specimen collections ranged from 23 to 87 days (median = 54.5 days). Patient E had completed a 2-dose mRNA COVID-19 vaccination series 6–10 weeks before the first infection; patients A and B each had received a single dose of mRNA COVID-19 vaccine between infections. The seven

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[*] These authors contributed equally to this report.

[†] https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/vaccine-induced-immunity.html

[§] https://coronavirus.health.ny.gov/covid-19-reinfection-data

[¶] https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html

[**] Inclusion of Wisconsin case data was approved by University of Wisconsin-Madison, Minimal Risk Research Institutional Review Board; 45 C.F.R. part 46; 21 C.F.R. part 56. Remaining activity was determined not to be research; 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

[††] Despite potential differences in established WGS protocols among laboratories, all lineage and sublineage determinations, which are based upon universally accepted genetic sequence markers, are comparable among laboratories.

[§§] In the 90 days preceding April 4, 2022, the percentage of state cases sequenced and shared with GISAID ranged from 0.45% (Oklahoma) to 15.83% (Vermont). https://www.gisaid.org/submission-tracker-usa

[¶¶] https://www.fammed.wisc.edu/orchards

[***] Multiple Delta variant sublineages (AY.3, AY.4, AY.25, AY.33, AY.44, AY.47, and AY.100) and two Omicron variant sublineages (BA.1 and BA1.1) were identified.

[†††] Patient E was a non-Vermont resident who was living and working as a health care worker (caring for COVID-19 patients) in Vermont during both infections.

remaining patients were unvaccinated. In Wisconsin, household transmission during patient G's reinfection likely resulted in reinfections of patients F and H.[§§§,¶¶¶] Nine patients were symptomatic during first infection (median duration = 9 days; range = 0–20 days).[****] Among eight patients with available clinical data during reinfection, six were symptomatic during reinfection (median duration = 5 days; range = 0–10 days).

Expansion of SARS-CoV-2 WGS, through public health surveillance and longitudinal research,[††††] might enable rapid identification of reinfections with distinct lineages and detection of novel variants. Current CDC guidance for identifying early reinfections requires demonstration of different lineages by genetic sequencing.[§§§§] Limited capacity for strain testing, including WGS, diminishes opportunities for first and reinfection NAAT specimens from the same person to undergo additional testing.[¶¶¶¶] Moreover, antigen tests are increasingly performed at home, resulting in specimens being unavailable for strain testing. Thus, most early reinfections are likely not identified.

The findings from this case series might not be generalizable to the U.S. population and are specific to the transition period between Delta and Omicron variant predominance. Nonetheless, this study highlights potential limits of infection-induced immunity against novel variants.

One patient in this case series had received a full primary COVID-19 vaccine series but was not yet eligible for a booster. No other eligible patient was up to date on recommended COVID-19 vaccinations,[*****] which provides additional protection, even among those with previous infection (*2*,*5*). These patients might have had increased risk for SARS-CoV-2 infection because of low vaccination rates[†††††] and high rates of close contact[§§§§§] in school-aged cohorts, and higher frequency and intensity of exposures in health care and congregate settings. Although the epidemiology of COVID-19 might change as new variants emerge, vaccination remains the safest strategy for preventing future SARS-CoV-2 infections (*2*,*5*).

[§§§] The index member in this household cluster of persons with early reinfections with SARS-CoV-2 was patient G, who began to experience respiratory illness symptoms on January 3, 2022, and was the only person to receive a positive SARS-CoV-2 test result the next day when specimens were collected from all household members. On January 8, patient F began to experience respiratory illness symptoms and was the only person to receive a positive SARS-CoV-2 test result when specimens from remaining household members (including patient G) were tested on January 11. On January 15, patient H began to experience symptoms of respiratory illness and was the only person to receive a positive SARS-CoV-2 test result when specimens from remaining household members (including patients F and G) were tested on January 18.

[¶¶¶] Household secondary transmission during patient B's early reinfection likely also resulted in an early reinfection in a parent, but WGS data from this parent's reinfection were not available for confirmation. This parent is not included in this case series.

[****] Calculation of median duration of symptoms during first infection does not include patient D because information on the full duration of this patient's symptoms was unavailable.

[††††] The Seattle Flu Study, like the Oregon Child Absentee due to Respiratory Disease Study (ORCHARDS), is a community-based, longitudinal surveillance study of influenza and viral respiratory diseases. Seattle Flu Study researchers were instrumental in the first identification of COVID-19 in the Seattle area. http://www.seattleflu.org

[§§§§] https://ndc.services.cdc.gov/case-definitions/coronavirus-disease-2019-2021/

[¶¶¶¶] Although S-gene target failure, which detects a deletion in the gene that encodes for the SARS-CoV-2 spike protein, is a commonly used screening method for the Omicron variant, this deletion is not unique to this variant and is not present in all Omicron variant sublineages. Other strain testing methods only target a portion of a strain's genome. In contrast, WGS analyzes a strain's entire genome and is therefore the preferred method for lineage confirmation.

[*****] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html

[†††††] https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends

[§§§§§] https://www.nature.com/articles/s41598-021-81673-y

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TABLE. Characteristics of SARS-CoV-2 Omicron variant infection in 10 persons within 90 days of a previous SARS-CoV-2 B.1.617.2 (Delta) variant infection — four states, October 2021–January 2022

Patient	State	Age group, yrs[*]	Race and ethnicity	High-risk preexisting condition[†]	Infection no.[§]	Test date	COVID-19 vaccination status	Suspected exposure	Symptoms	No. of days between infections
A	Vermont	5–11	White, NH	No	1	Oct 19, 2021	None	School	Yes	87
					2	Jan 14, 2022	1 mRNA dose (Dec 17, 2021)	Household	Yes	
B	Vermont	5–11	White, NH	No	1	Oct 30, 2021	None	School	Yes	77
					2	Jan 15, 2022	1 mRNA dose (Jan 8, 2022)	Family gathering	Yes	
C	Vermont	5–11	White, NH	Yes	1	Nov 21, 2021	None	Household	Yes	69
					2	Jan 29, 2022	None	Household	Yes	
D	Vermont	0–4	White, NH	No	1	Nov 11, 2021	None	School	Yes	76
					2	Jan 26, 2022	None	Unknown	Unknown	
E	Vermont	25–39	Black, NH	Yes	1	Dec 16, 2021	2 mRNA doses (Sep/Oct 2021)	Health care	Yes (hospitalized)	40
					2	Jan 25, 2022	(As above)	Health care	No	
F[¶]	Wisconsin	5–11	White, NH	No	1	Nov 27, 2021	None	School	Yes	45
					2	Jan 11, 2022	None	Household (patient G)	Yes	
G[¶]	Wisconsin	5–11	White, NH	No	1	Dec 4, 2021	None	Household (patient F)	Yes	31
					2	Jan 4, 2022	None	Unknown	Yes	
H[¶]	Wisconsin	5–11	White, NH	No	1	Nov 27, 2021	None	Household (patient F)	Yes	52
					2	Jan 18, 2022	None	Household (patient G)	Yes	
I	Washington	12–17	White, NH	No	1	Nov 23, 2021	None	Household	Yes	23
					2	Dec 16, 2021	None	School sport	No	
J	Rhode Island	65–74	Unknown	Unknown	1	Nov 15, 2021	None	LTCF	No	57
					2	Jan 11, 2022	None	LTCF	Unknown	

Abbreviations: LTCF = long-term care facility; NH = non-Hispanic.

[*] At time of first infection.

[†] Obesity, diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease and bronchiectasis, neurocognitive disorders, coronary arteriosclerosis, and other heart disease.

[§] In all cases, the first infection was with Delta variant and the second was with Omicron variant.

[¶] Patients were in one household.

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Notes from the Field

Enteropathogenic *Escherichia coli* Outbreak at a Child Care Center — Oregon, August 2021

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On August 16, 2021, the Oregon Health Authority Public Health Division (OPHD) was notified of two pediatric cases of Shiga toxigenic *Escherichia coli* among members of the same household. Each of the patients received a positive polymerase chain reaction test result for Shiga toxin in a stool specimen. *E. coli* O157:H7 was subsequently isolated from stool culture from both patients. During routine case investigation, the local health department determined that one patient, aged 2 years, had attended an in-home child care center. OPHD visited the child care center on August 18 to conduct case ascertainment among staff members and children, share recommendations for rapid isolation and exclusion of those ill, observe infection prevention practices during diaper changing, and educate staff members on infection prevention measures for toys and high-touch surfaces. The investigation team requested parental consent and attempted to collect clinical information on gastrointestinal symptoms during July 30–August 18 and stool specimens from all staff members and children on the day of the visit. A child care center staff member followed up with other staff members and children who were not present on the day of the visit to obtain clinical information and provide them with specimen collection kits and instructions. Stool specimens were placed in Cary-Blair transport medium, transported to OPHD, and tested for 22 enteric pathogens using the BioFire FilmArray Gastrointestinal Panel (BioFire Diagnostics, LLC).

Clinical information was provided for each of the 17 children and four staff members enrolled or employed at the child care center. Among these, six of 17 (35%) children and one of four staff members reported diarrhea, vomiting, or other gastrointestinal symptoms. Stool specimens were collected from 18 (86%) children and staff members. Initially, culture for *E. coli* O157 was performed on 10 specimens; all were negative for *E. coli* O157:H7. Twelve specimens were acceptable for testing using BioFire; nine specimens contained evidence of an enteric pathogen, including seven with enteropathogenic *E. coli* (EPEC), four with norovirus, and one each with rotavirus, sapovirus, astrovirus, and *Campylobacter*. Four specimens yielded more than one pathogen. Among seven persons with EPEC, three were symptomatic, as were three of four with norovirus infection. Two persons infected with EPEC were coinfected with norovirus, one of whom was symptomatic. After reviewing laboratory results, the local health officer recommended temporarily closing the child care center for 7 days; the child care center complied, household members of children and staff members were informed of the outbreak and asked to monitor for symptoms, and no additional cases were reported.

This outbreak during August 2021 is the first EPEC outbreak detected in Oregon. Several patients experienced coinfection with other enteric pathogens. EPEC causes diarrhea by adhering to the small intestine endothelium, damaging microvilli, and affecting absorption (*1*). The public health implications of asymptomatic EPEC infection remain unclear (*2*). With the advent of multiplex gastrointestinal assays, in use in Oregon since 2015, more EPEC outbreaks are likely to be detected (*3*). During 1971–2018, 58 EPEC outbreaks were reported to the National Outbreak Reporting System; 43 (74%) of these outbreaks were detected during 2016–2018. Among the 13 EPEC outbreaks at child care centers, 12 were detected during 2016–2018.* As detection of EPEC increases through broader use of multiplex assays, a need exists to develop guidance for case and outbreak management of EPEC outbreaks in congregate settings and child care centers.

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* The National Outbreak Reporting System (NORS) provides a publicly available download of all NORS Dashboard data, including etiology, exposure location, and year of report. https://wwwn.cdc.gov/norsdashboard/

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All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

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Erratum

Vol. 71, No. 6

The report "Genomic Surveillance for SARS-CoV-2 Variants: Predominance of the Delta (B.1.617.2) and Omicron (B.1.1.529) Variants — United States, June 2021–January 2022" contained several errors.

On page 206, the list of authors should have read, "Anastasia S. Lambrou, PhD[1,2,*]; Philip Shirk, PhD[1,*]; Molly K. Steele, PhD[1]; Prabasaj Paul, PhD[1]; Clinton R. Paden, PhD[1]; Betsy Cadwell, MSPH[1]; Heather E. Reese, PhD[1]; Yutaka Aoki, PhD[1]; Norman Hassell, MS[1]; **Jason Caravas, PhD[1,3]; Nicholas A. Kovacs, PhD[1,4]; Jonathan G. Gerhart, MS[5]; Han Jia Ng, PhD[1,6];** Xiao-yu Zheng, PhD[1,7]; **Andrew Beck, PhD[1]; Reina Chau, MS[1]; Roxana Cintron, MS[1]; Peter W. Cook, PhD[1]; Christopher A. Gulvik, PhD[1]; Dakota Howard[1]; Yunho Jang, PhD[1]; Kristen Knipe, MS[1]; Kristine A. Lacek, MS[1]; Kara A. Moser, PhD[8]; Adrian C. Paskey, PhD[1]; Benjamin L. Rambo-Martin, PhD[1]; Roopa R. Nagilla, MS[7]; Adam C. Retchless, PhD[1]; Matthew W. Schmerer, PhD[1]; Sandra Seby, MS[1]; Samuel S. Shepard, PhD[1]; Richard A. Stanton, PhD[1]; Thomas J. Stark, PhD[1]; Anna Uehara, PhD[1]; Yvette Unoarumhi, MS[1,4]; Meghan L. Bentz[1]; Alex Burgin[1]; Mark Burroughs[1]; Morgan L. Davis, MS[1,5]; Matthew W. Keller, PhD[1]; Lisa M. Keong[7]; Shoshona S. Le[1]; Justin S. Lee, DVM, PhD[1]; Joseph C. Madden Jr, PhD[1]; Sarah Nobles, MS[1]; D. Collins Owuor, PhD[1]; Jasmine Padilla[1,5]; Mili Sheth, PhD[1]; Malania M. Wilson, MS, MBA[1];** Sarah Talarico, PhD[1]; Jessica C. Chen, PhD[1]; M. Steven Oberste, PhD[1]; Dhwani Batra, MS, MBA[1]; Laura K. McMullan, PhD[1]; Alison Laufer Halpin, PhD[1]; Summer E. Galloway, PhD[1]; Duncan R. MacCannell, PhD**[3]**; Rebecca Kondor, PhD[1]; John Barnes, PhD[1]; Adam MacNeil, PhD[1]; Benjamin J. Silk, PhD[1]; Vivien G. Dugan, PhD[1]; Heather M. Scobie, PhD[1]; David E. Wentworth, PhD[1]."

On pages 210–11 the acknowledgments should have read, "**Eric Chirtel, Victoria Caban Figueroa, Tymeckia Kendall, Garrett Longmire, Brian Mann, Nicole Patterson, Catherine Smith, Erica Sula, Subblakshmi Voleti, Jonathan Zhong.**"

On page 211, the author affiliations should have read, "[1]CDC COVID-19 Emergency Response Team; [2]Epidemic Intelligence Service, CDC; **[3]**Office of Advanced Molecular Detection, National Center for Emerging and Zoonotic Infectious Diseases, CDC; **[4]Oak Ridge Institute for Science and Education, Oak Ridge, Tennessee; [5]ASRT Inc., Smyrna, Georgia; [6]Eagle Global Scientific, LLC, San Antonio, Texas;** [7]General Dynamics Information Technology, Inc., Falls Church, Virginia; **[8]Goldbelt C6, LLC, Chesapeake, Virginia.**"

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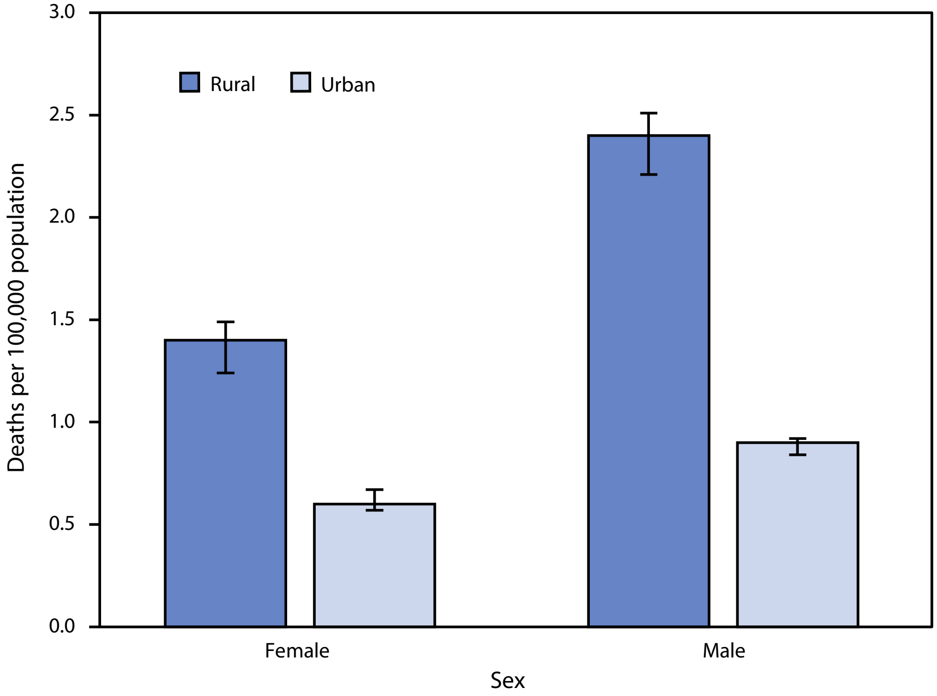
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Rate* of Deaths Attributed to Unintentional Injury from Fire or Flames,† by Sex and Urban-Rural Status§ — National Vital Statistics System, United States, 2020



* Crude rate of deaths per 100,000 population; 95% CIs indicated by error bars.

† Deaths attributed to unintentional injury from fire or flames were identified using the *International Classification of Diseases, Tenth Revision* underlying cause-of-death codes X00–X09.

§ Urban-rural status is determined by the Office of Management and Budget's February 2013 delineation of metropolitan statistical areas (MSAs), in which each MSA must have at least one urban area of ≥50,000 inhabitants. Areas with <50,000 inhabitants are grouped into the rural category.

In 2020, the death rate attributed to unintentional injury from fire or flames was higher in rural areas than in urban areas for females and males. The rate for females was 1.4 per 100,000 in rural areas and 0.6 in urban areas. The rate for males was 2.4 per 100,000 in rural areas and 0.9 in urban areas. Males had higher death rates than females in both rural and urban areas.

Source: National Center for Health Statistics, National Vital Statistics System, Mortality Data, 2020. https://www.cdc.gov/nchs/deaths.htm

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