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Epidemiologic and Clinical Features of Mpox in Transgender and Gender-Diverse Adults — United States, May–November 2022

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As of November 9, 2022, a total of 28,730 cases of monkeypox (mpox) had been reported in the United States,* primarily among adult cisgender men reporting recent male-to-male sexual contact (*1*). Transgender and gender-diverse persons, who constitute an estimated 0.5% of the U.S. adult population,† face unique health disparities and barriers to care (*2–4*). However, data on the epidemiologic and clinical features of *Monkeypox virus* infections in this population are limited (*5*). CDC analyzed U.S. case surveillance data on mpox cases in transgender and gender-diverse adults reported during May 17–November 4, 2022. During this period, 466 mpox cases in transgender and gender-diverse adults were reported, accounting for 1.7% of reported cases among adults. Most were in transgender women (43.1%) or gender-diverse persons (42.1%); 14.8% were in transgender men. Among 374 (80.3%) mpox cases in transgender and gender-diverse adults with information available on sexual or close intimate contact, 276 (73.8%) reported sexual or close intimate contact with a cisgender male partner during the 3 weeks preceding symptom onset. During the ongoing outbreak, transgender and gender-diverse persons have been disproportionately affected by mpox. Members of this population frequently reported recent sexual or close intimate contact with cisgender men, who might be in sexual networks experiencing the highest incidence of mpox. These findings highlight the importance of tailoring public health prevention and outreach efforts to transgender and gender-diverse communities and could guide strategies to reduce mpox transmission.

Data on confirmed and probable cases of mpox are electronically reported by jurisdictional health departments to CDC using a standardized case report form§ or the National Notifiable Diseases Surveillance System.¶ CDC analyzed case report form

* https://www.cdc.gov/poxvirus/monkeypox/response/2022/index.html (Accessed November 9, 2022).

† Transgender and gender-diverse persons are those whose gender identity might differ from their assigned sex at birth. This description includes transgender women, transgender men, and gender-diverse persons identifying as another gender (i.e., not transgender or cisgender), such as nonbinary, genderqueer, and gender nonconforming. Using data from CDC's 2017–2020 Behavior Risk Factor Surveillance System and 2017 and 2019 Youth Risk Behavior Survey, which rely on self-reporting of gender identity, the Williams Institute estimates that 1.3 million transgender and gender-diverse adults live in the United States; however, this percentage might be an underestimate because some persons might have been reluctant to disclose their gender identity because of fear of stigma or other reasons.

§ https://www.cdc.gov/poxvirus/monkeypox/pdf/sCRF-Short-Form.pdf

¶ https://www.cdc.gov/nndss/index.html

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data for persons aged ≥18 years with probable or confirmed mpox reported through November 4, 2022. CDC identified persons as transgender or gender-diverse if their self-reported gender** was transgender or "another gender identity" (i.e., not cisgender or transgender); in addition, persons whose self-reported gender identity differed from their assigned sex at birth were considered transgender.†† This descriptive analysis included demographic and epidemiologic characteristics, exposure characteristics, symptoms, HIV status, and hospitalization status. Data were stratified by gender identity. Because of the high level of missingness of some variables, statistical testing was not performed. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.§§

As of November 4, 2022, a total of 28,072 cases of mpox had been reported in U.S. adults, primarily among cisgender men (94.8%); 2.6% of cases occurred in cisgender women (Table 1). A total of 466 (1.7%) adults with mpox were transgender or gender-diverse; among these persons, most were transgender women (43.1%) or gender-diverse persons (42.1%); 14.8% were transgender men. A total of 223 persons with missing age were excluded. Among 157 (80.1%) cases in gender-diverse adults with available data on assigned sex at birth, 151 (96.2%) were assigned male sex at birth.

Overall, approximately 52.1% of cases in transgender and gender-diverse adults were reported from New York City (26.0%) or California (26.2%). The median age of transgender and

TABLE 1. Gender identity* of adults who received a diagnosis of mpox (N = 28,072) — United States, May–November 2022

Gender identity	No. (%)
Cisgender, total	**27,352 (97.4)**
Cisgender men	26,616 (94.8)
Cisgender women	736 (2.6)
Transgender and gender-diverse, total	**466 (1.7)**
Gender-diverse persons†	196 (0.7)
Transgender women	201 (0.7)
Transgender men	69 (0.2)
Missing	254 (0.9)
All persons	**28,072 (100)**

* Because of differences in collection of sex and gender information among jurisdictions, both sex and gender were used to represent gender identity. Persons whose reported sex differed from their reported gender were classified as transgender (59). Self-reported gender or sex assigned at birth were missing for 10,370 (36.9%) adults and their gender identity was presumed to be cisgender consistent with the available response unless their gender identity was reported as transgender or "another gender identity."

† Persons whose self-reported gender was "another gender identity" (i.e., not transgender or cisgender), such as nonbinary, genderqueer, and gender nonconforming, were classified as gender-diverse.

** Case report form responses to "Do you currently describe yourself as male, female, or transgender?" include "male," "female," "transgender female," "transgender male," and "another gender identity."

†† Thirty-six adults assigned male sex at birth identified as women and were classified as transgender women; 23 adults assigned female sex at birth identified as men and were classified as transgender men. Information on assigned sex at birth or gender identity was available for 98.4% of all adults with mpox. Among 10,370 (36.9%) persons for whom self-reported gender or assigned sex at birth was missing, gender identity was presumed to be cisgender consistent with the available response, unless their gender (if reported) was transgender or "another gender identity."

§§ 45 C.F.R. part 46.102(l)(2), 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.

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TABLE 2. Demographic, epidemiologic, and clinical features of transgender, gender-diverse, and cisgender adults who received a diagnosis of mpox — United States, May–November 2022

Characteristic	No. (%)* Transgender and gender-diverse persons (n = 466)	Cisgender persons (n = 27,352)
Median age, yrs (range)	32 (18–71)	34 (18–89)
Race and ethnicity†		
American Indian or Alaska Native	2 (0.5)	104 (0.5)
Asian	11 (2.6)	691 (3.0)
Black or African American	115 (27.6)	7,417 (32.2)
Hispanic or Latino	154 (37.0)	7,132 (30.9)
Native Hawaiian or other Pacific Islander	1 (0.2)	65 (0.3)
White	117 (28.1)	6,939 (30.1)
Multiracial or other race or ethnicity	16 (3.8)	716 (3.1)
Missing	50 (—)	4,288 (—)
Sex or close intimate contact in the 3 wks before symptom onset		
Any recently reported sexual or close intimate contact	316 (84.5)	13,556 (82.1)
Recent partners exclusively cisgender men	261 (69.8)	11,610 (70.3)
Recent partners include cisgender men and other genders	15 (4.0)	418 (2.5)
Recent partners exclude cisgender men	10 (2.7)	752 (4.6)
Genders of all partners unknown or not specified	30 (8.0)	776 (4.7)
No recently reported sexual or close intimate contact	58 (15.5)	2,962 (17.9)
Missing	92 (—)	10,834 (—)
HIV infection status		
HIV positive	79 (47.6)	3,469 (55.1)
HIV negative	87 (52.4)	2,825 (44.9)
Missing	300 (—)	21,058 (—)
Hospitalized		
Yes§	21 (6.9)	800 (6.5)
No	284 (92.8)	11,574 (93.5)
Missing	160 (—)	14,978 (—)

* Percentages were calculated using nonmissing data.
† Persons of Hispanic or Latino (Hispanic) origin might be of any race but are categorized as Hispanic; all racial groups are non-Hispanic.
§ Among the 21 transgender and gender-diverse persons who were hospitalized, reason for hospitalization was available for 11 (52%): five were hospitalized for pain control, two for treatment of secondary infections, two for exacerbation of an underlying condition, and two for breathing problems, one of whom required mechanical ventilation; five were hospitalized for other reasons (patients could be hospitalized for more than one reason). HIV status was available for 18 (86%) of the hospitalized transgender and gender-diverse persons, among whom 13 had HIV infection.

gender-diverse adults with mpox was 32 years (range = 18–71 years) (Table 2). Among the 416 (89.3%) transgender and gender-diverse adults with mpox for whom race and ethnicity were reported, 37.0% of cases occurred in Hispanic or Latino (Hispanic)¶¶ persons, 28.1% in non-Hispanic White persons, 27.6% in non-Hispanic Black or African American (Black) persons, and the remainder in persons of another race or ethnicity. The racial and ethnic distribution among transgender and gender-diverse persons with mpox was generally similar to that among cisgender persons.

¶¶ Persons of Hispanic origin might be of any race but are categorized as Hispanic; all racial groups are non-Hispanic.

Summary

What is already known about this topic?

Epidemiologic data on and clinical characteristics of monkeypox (mpox) in transgender and gender-diverse persons are limited.

What is added by this report?

The ongoing mpox outbreak has disproportionately affected transgender and gender-diverse (i.e., not cisgender or transgender) adults. The most commonly reported potential exposure among transgender and gender-diverse adults with mpox was recent sexual contact with cisgender men; these men might be in sexual networks experiencing the highest mpox incidence.

What are the implications for public health practice?

Addressing the unique health needs faced by many transgender and gender-diverse adults is an important public health priority. Tailoring prevention and outreach efforts to transgender and gender-diverse communities might reduce the disproportionate incidence of mpox in this population.

Among 374 (80.3%) transgender and gender-diverse adults with sexual and close intimate contact information available, 316 (84.5%) reported engaging in any sexual or close intimate contact during the 3 weeks preceding symptom onset, including 276 (73.8%) who reported sexual or close intimate contact with a cisgender man (261 had exclusively cisgender men as partners, and 15 had partners who included cisgender men and persons of other genders). Ten (2.7%) transgender and gender-diverse adults with mpox reported exclusive sexual or close intimate contact with partners who were not cisgender men. Similarly, among 16,518 (60.4%) cisgender adults with this information available, 13,556 (82.1%) reported engaging in sex or close intimate contact during the 3 weeks before symptom onset, most often with a cisgender man.

The most frequently reported signs and symptoms reported by transgender and gender-diverse adults with mpox included rash (91.8%), malaise (67.3%), fever (64.9%), pruritis (63.9%), headache (63.7%), chills (62.2%) myalgia (61.9%), and enlarged lymph nodes (58.9%). Among 166 (35.6%) transgender and gender-diverse adult mpox patients with data available on HIV status, 79 (47.6%) had HIV infection, including 34 of 57 (59.6%) transgender women, six of 21 (28.6%) transgender men, and 39 of 88 (44.3%) gender-diverse persons. HIV prevalence among cisgender adults with mpox with available data was 55.1%. Among 306 transgender and gender-diverse adults with hospitalization data, 21 (6.9%) were hospitalized, similar to 6.5% of cisgender adults with available data. Among the 21 transgender and gender-diverse persons who were hospitalized, nine (43%) were transgender women, seven (33%) were gender-diverse persons, and five (24%) were transgender men. To date, no mpox-associated deaths have been reported among the transgender or gender-diverse adults identified in this analysis.

Discussion

Mpox cases among transgender and gender-diverse adults have accounted for 1.7% of total U.S. cases. Based on the estimated percentage of U.S. adults who identify as transgender or gender-diverse (0.5%), this population has been overrepresented among mpox cases during the ongoing outbreak (*2*). Among transgender and gender-diverse persons with available sexual and close intimate contact information, a commonly reported potential exposure was recent sexual or close intimate contact with a cisgender man (73.8%); these cisgender men might be in sexual networks experiencing the highest prevalence of mpox (*1*). These findings are similar to those from an analysis of mpox cases occurring in 62 transgender women in Europe and the Americas during May–October 2022 (*6*); in that study, the likeliest route of transmission for most transgender women (89%) was sexual contact, with a majority reporting having had a male sexual partner during the preceding month.

Similar to cisgender adults with mpox, Hispanic (37.0%) and Black (27.6%) transgender and gender-diverse persons were disproportionately represented among mpox cases compared with the racial and ethnic percentage distribution of the overall U.S. population.*** Unique health disparities and barriers to prevention and care faced by transgender and gender-diverse persons might be exacerbated by racial and ethnic health disparities (*3*,*4*). Ensuring the prioritization of eligible transgender and gender-diverse persons for mpox vaccination, expanding community engagement and outreach to improve prevention messages, and ensuring equity in approaches to mpox testing, treatment, and prevention strategies are critical public health priorities.

The findings in this report are subject to at least three limitations. First, data on certain variables such as symptoms reported, HIV status, hospitalization status, and exposure information were frequently missing in national case surveillance data. Recent sexual and close intimate contact information was missing for approximately one in five cases in transgender and gender-diverse persons, and among those with available information, approximately one in four did not report recent sexual or close intimate contact with a cisgender man. These missing data limit the ability to fully characterize the epidemiologic and clinical features of transgender and gender-diverse persons with mpox. In-depth collection of accurate exposure information is vital to understanding how persons without recent sexual or close intimate contact with cisgender men are likely being exposed to mpox virus, which could guide expanded prevention messaging. Second, methods for collecting sex and gender information are not standardized across all U.S. states and territories. Self-reported gender or sex assigned at birth were missing for 10,370 (36.9%) adults, and for these persons, gender identity was presumed to be cisgender unless gender identity was reported as transgender or another gender identity. This limitation could have resulted in undercounting persons who identify as transgender or gender-diverse, particularly in jurisdictions that do not routinely collect information about transgender and gender-diverse identities. Finally, in the absence of available data on sex assigned at birth, current sex might have been reported, potentially leading to misclassification of gender identity. Improving collection of data on transgender and gender-diverse persons, such as standardizing approaches to collection of sex and gender information and routinely capturing the diversity of gender identities, is important to better understanding and addressing health inequities.

This analysis found that transgender and gender-diverse adults have been experiencing a disproportionate prevalence of *Monkeypox virus* infections, particularly among those who are Hispanic and Black. Meeting the unique health needs and addressing barriers to prevention and care faced by many transgender and gender-diverse persons is a critical public health priority, particularly during the current mpox outbreak. Adequately addressing the needs of this population will require standardized collection of data on sex and gender identity. Tailoring public health prevention and outreach efforts to transgender and gender-diverse communities, including the prioritization of eligible transgender and gender-diverse persons for mpox vaccination and expanding community engagement efforts, might reduce the disproportionate prevalence of mpox among this population.

*** According to 2021 U.S. Census Bureau estimates, Black and Hispanic persons constitute 13.6% and 18.9% of the U.S. population, respectively. https://www.census.gov/quickfacts/fact/table/US/PST045221 (Accessed November 15, 2022).

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Morbidity and Mortality Weekly Report

Demographic and Clinical Characteristics of Mpox in Persons Who Had Previously Received 1 Dose of JYNNEOS Vaccine and in Unvaccinated Persons — 29 U.S. Jurisdictions, May 22–September 3, 2022

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As of November 14, 2022, monkeypox (mpox) cases had been reported from more than 110 countries, including 29,133 cases in the United States.* Among U.S. cases to date, 95% have occurred among males (*1*). After the first confirmed U.S. mpox case on May 17, 2022, limited supplies of JYNNEOS vaccine (Modified Vaccinia Ankara vaccine, Bavarian Nordic) were made available to jurisdictions for persons exposed to mpox. JYNNEOS vaccine was approved by the Food and Drug Administration (FDA) in 2019 as a 2-dose series (0.5 mL per dose, administered subcutaneously) to prevent smallpox and mpox disease.† On August 9, 2022, FDA issued an emergency use authorization to allow administration of JYNNEOS vaccine by intradermal injection (0.1 mL per dose) (*2*). A previous report on U.S. mpox cases during July 31–September 3, 2022, suggested that 1 dose of vaccine offers some protection against mpox (*3*). This report describes demographic and clinical characteristics of cases occurring ≥14 days after receipt of 1 dose of JYNNEOS vaccine and compares them with characteristics of cases among unvaccinated persons with mpox and with the vaccine-eligible vaccinated population in participating jurisdictions. During May 22–September 3, 2022, among 14,504 mpox cases reported from 29 participating U.S. jurisdictions,§ 6,605 (45.5%) had available vaccination information and were included in the analysis. Among included cases, 276 (4.2%) were among persons who had received 1 dose of vaccine ≥14 days before illness onset. Mpox cases that occurred in these vaccinated persons were associated with lower percentage of hospitalization (2.1% versus 7.5%), fever, headache, malaise, myalgia, and chills, compared with cases in unvaccinated persons. Although 1 dose of JYNNEOS vaccine offers some protection from disease, mpox infection can occur after receipt of 1 dose, and the duration of protection conferred by 1 dose is unknown. Providers and public health officials should therefore encourage persons at risk for acquiring mpox to complete the 2-dose vaccination series and provide guidance and education regarding nonvaccine-related prevention strategies (*4*).

Probable and confirmed mpox cases¶ among persons with illness onset during May 22–September 3, 2022, in the 29 jurisdictions were eligible for inclusion. Persons who had received 1 dose of JYNNEOS vaccine ≥14 days before illness onset were considered vaccinated for the purposes of this study**; those who had not received 1 vaccine dose during the current outbreak or who reported illness onset before receipt of their first vaccine dose were considered unvaccinated. Cases were excluded if 1) no vaccination date or vaccination status was available, 2) receipt of vaccine occurred before May 2022, or 3) illness onset occurred ≤13 days after receipt of 1 vaccine dose.

Participating jurisdictions collected data using a standardized data collection form†† including self-reported demographic characteristics, vaccination history, medical history, and possible exposures. Participating jurisdictions linked vaccination data from immunization registries when available or by self-report during case investigation and transmitted the linked data to CDC.

Demographic characteristics of persons with mpox who had received 1 vaccine dose (i.e., were vaccinated) were compared with those of unvaccinated persons with mpox. In addition, characteristics of persons with mpox who were vaccinated were compared with those of all vaccine-eligible persons who were vaccinated, irrespective of case status; these data were obtained through jurisdictional immunization registries reporting first doses administered. Comparisons were made using Pearson's chi-square test, Fisher's exact test, or the Wilcoxon rank-sum test as appropriate. P-values <0.05 were considered statistically significant.

* https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html
† https://www.fda.gov/media/131078/download
§ California; Chicago, Illinois; Colorado; Connecticut; Delaware; District of Columbia; Florida; Georgia; Illinois; Massachusetts; Maryland; Michigan; Minnesota; Missouri; Montana; Nebraska; New Mexico; New York (not including New York City); Oregon; Pennsylvania; Philadelphia, Pennsylvania; Puerto Rico; Rhode Island; South Carolina; Tennessee; Utah; Virginia; Washington; and Wisconsin.
¶ https://www.cdc.gov/poxvirus/monkeypox/clinicians/case-definition.html
** For this analysis, persons were considered vaccinated ≥14 days after receipt of 1 dose of JYNNEOS vaccine, based on previous immunogenicity studies showing an immunologic response 14 days after vaccination.
†† https://www.cdc.gov/poxvirus/monkeypox/pdf/scrf-short-form.pdf

To assess differences in illness among vaccinated and unvaccinated persons with mpox, clinical characteristics were compared between these two groups among persons with data reported for one or more clinical symptoms. Missing individual symptom data were imputed as "no" when there was evidence that the reporting jurisdiction collected symptom data in a "check-all-that-apply" format.[§§] Odds ratios and 95% CIs were calculated to compare clinical characteristics of vaccinated and unvaccinated mpox patients. Persons with missing data for relevant variables of interest were excluded from individual analyses.

Because JYNNEOS vaccine was administered for postexposure prophylaxis at the beginning of the outbreak, and because the mpox incubation period can be as long as 21 days, a sensitivity analysis including only persons with mpox who received 1 vaccine dose ≥22 days before illness onset as the vaccinated group was conducted. SAS (version 9.4; SAS Institute) and R (version 4.0.3; R Foundation) were used to conduct all analyses. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[¶¶]

During May 22, 2022–September 3, 2022, a total of 14,504 mpox cases were reported in the 29 included jurisdictions. Among the 6,605 (45.5%) persons with mpox who had available information and who were included in the analysis,[***] 6,329 (95.8%) were unvaccinated, and 276 (4.2%) had illness onset ≥14 days after receiving 1 vaccine dose (Table 1). Among vaccinated patients, the median interval from vaccination to illness onset was 23 days (IQR = 17.5–30 days). The age distribution differed for vaccinated mpox patients compared with the vaccine-eligible population identified through immunization registries (p<0.001), but not compared with unvaccinated mpox patients (p = 0.07); 91.2% of vaccinated mpox patients were aged 18–49 years. Overall, 68.2% of vaccinated mpox patients and 49.9% of unvaccinated mpox patients reported White race, whereas 12.4% and 30.9% of vaccinated and unvaccinated patients, respectively, reported Black or African American race (p<0.001). Among 345,220 vaccine-eligible persons in the population who had received 1 dose of JYNNEOS vaccine, a significantly smaller percentage identified as White (46.7%) compared with vaccinated mpox patients (62.8%; p = 0.02). Overall, 259 (98.1%) vaccinated and 5,710 (96.1%) unvaccinated mpox cases occurred in persons identifying as male.

Information on at least one clinical finding was available for 202 (73.2%) of 276 vaccinated persons with mpox and 5,326 (84.2%) of 6,329 unvaccinated mpox patients. Among those who were vaccinated, the most commonly reported signs and symptoms were rash (96.5%), pruritis (33.5%), and enlarged lymph nodes (31.6%) (Table 2). Among unvaccinated persons, the most common signs and symptoms were rash (97.3%), fever (46.5%), and malaise (43.0%). The odds of fever, headache, malaise, abdominal pain, vomiting or nausea, myalgia, and chills were significantly lower among vaccinated than among unvaccinated patients (Figure). Odds of rectal signs and symptoms (e.g., proctitis, rectal bleeding, tenesmus, and rectal pain) were similar among vaccinated and unvaccinated mpox patients.

Among both vaccinated and unvaccinated patients, the genital area was the rash location most commonly reported (55.0% of vaccinated patients and 46.7% of unvaccinated patients) (Table 2). The odds of reporting rash in all other locations except the perianal area were significantly lower among vaccinated than among unvaccinated patients. The median number of rash locations reported by vaccinated patients (two) was significantly lower than that reported by unvaccinated patients (three) (p<0.001). Among 129 persons with mpox who received 1 vaccine dose ≥22 days before illness onset, demographic and clinical findings were not different from those in persons who had received vaccine ≥14 days earlier.

Among 3,142 unvaccinated persons with mpox, 237 (7.5%) were hospitalized compared with two (2.1%) of 95 vaccinated mpox patients (odds ratio = 0.27; 95% CI = 0.06–1.09). No deaths were reported in either group.

Discussion

In this analysis of 276 mpox cases in persons who received 1 dose of JYNNEOS vaccine ≥14 days before illness onset and 6,329 cases in unvaccinated persons during the 2022 U.S. outbreak, vaccinated patients reported signs and symptoms similar to those described earlier in the outbreak (*1*); however, some symptoms were reported less frequently among vaccinated than among unvaccinated mpox patients. In addition, the percentage of vaccinated patients who were hospitalized (2%) was lower than that among unvaccinated patients (8%), and the odds of systemic signs and symptoms, such as fever and chills, were lower among vaccinated patients. These findings indicate that 1 dose of the JYNNEOS vaccine might attenuate the severity of mpox illness in persons who are infected after vaccination.

The frequent presentation of rash in the genital and perianal areas among both vaccinated and unvaccinated mpox patients suggests that sexual transmission in this population was a common mechanism of transmission. The fewer number of reported rash locations among vaccinated patients suggests possible prevention of spread of rash from site of inoculation among even partially vaccinated persons.

The predominance of White persons among vaccinated mpox patients compared with unvaccinated patients reflects

[§§] Jurisdictions were considered to have collected symptom variables in a "check-all-that-apply" manner if a case patient had a "yes" response for one or more clinical symptoms, but all other symptoms were reported as missing.

[¶¶] 5 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.

[***] A total of 6,856 (47.3%) cases were excluded because information on vaccination status or date of vaccination was missing, 106 (0.7%) had a vaccine date before May 2022 and were excluded, and 927 (6.4%) were excluded because they had been vaccinated <14 days from illness onset.

TABLE 1. Characteristics of mpox patients, by vaccination status (N = 6,605) and of recipients of 1 dose of JYNNEOS vaccine (N = 345,220) — 29 U.S. jurisdictions,* May 22–September 3, 2022

Characteristic	Mpox patient vaccination status, n/N (%)†				
	Vaccinated§ (n = 276)	Unvaccinated¶ (n = 6,329)	p-value**	Recipients of 1 vaccine dose, n/N (column %) (N = 345,220)**	p-value**,§§
Age group, yrs					
Mean (median)	36.9 (36.0)	35.3 (34.0)	<0.01	NA	NA
18–29	57/275 (20.7)	1,755/6,282 (27.9)	0.07	72,998/345,215 (21.1)	<0.001
30–39	134/275 (48.7)	2,714/6,282 (43.2)		113,503/345,215 (32.9)	
40–49	60/275 (21.8)	1,266/6,282 (20.2)		64,481/345,215 (18.7)	
≥50	24/275 (8.7)	547/6,282 (8.7)		93,768/345,215 (27.2)	
Missing	1	47		5	
Race					
American Indian or Alaska Native	2/266 (0.8)	43/6,140 (0.7)	<0.001	975/345,220 (0.2)	0.02
Asian	17/266 (6.4)	196/6,140 (3.2)		23,598/345,220 (6.8)	
Black or African American	33/266 (12.4)	1,901/6,140 (30.9)		37,325/345,220 (10.8)	
Native Hawaiian or other Pacific Islander	1/266 (0.4)	19/6,140 (0.3)		783/345,220 (0.2)	
White	167/266 (62.8)	3,054/6,140 (49.9)		161,203/345,220 (46.7)	
Multiracial or other	8/266 (3.0)	275/6,140 (4.5)		15,247/345,220 (4.4)	
Unknown	38/266 (14.3)	652/6,140 (10.6)		34,948/345,220 (10.1)	
Missing	10	189		0	
Ethnicity					
Hispanic or Latino	64/269 (23.8)	1,880/6,159 (30.5)	0.06	71,141/345,220 (20.6)	0.02
Non-Hispanic	177/269 (65.8)	3,929/6,159 (63.8)		274,079/345,220 (79.4)	
Unknown	28/269 (10.4)	350/6,159 (5.7)		0	
Missing	7	170		0	
Sex at birth					
Female	0	137/5,956 (2.3)	0.02	24,306/345,220 (7.0)	<0.001
Male	216/257 (84.1)	5,408/5,956 (90.8)		315,940/345,220 (91.5)	
Unknown	41/257 (15.4)	411/5,956 (6.9)		4,974/345,220 (1.4)	
Missing	19	373		0	
Gender					
Female	1/264 (0.3)	127/5,939 (2.2)	0.20	NA	NA
Male	259/264 (98.1)	5,710/5,939 (96.1)		NA	
Transgender female	0	37/5,939 (0.6)		NA	
Transgender male	1/264 (0.3)	18/5,939 (0.3)		NA	
Another gender identity	3/264 (1.1)	47/5,939 (0.8)		NA	
Missing	12	390		NA	

Abbreviations: mpox = monkeypox; NA = not applicable.

* California; Chicago, Illinois; Colorado; Connecticut; Delaware; District of Columbia; Florida; Georgia; Illinois; Massachusetts; Maryland; Michigan; Minnesota; Missouri; Montana; Nebraska; New Mexico; New York (not including New York City); Oregon; Pennsylvania; Philadelphia, Pennsylvania; Puerto Rico; Rhode Island; South Carolina; Tennessee; Utah; Virginia; Washington; and Wisconsin.

† Percentages were calculated using cases with available data as the denominator.

§ Cases of probable and confirmed mpox in persons with illness onset ≥14 days after receipt of 1 vaccine dose.

¶ Cases of probable and confirmed mpox in persons with illness onset before the date of vaccination or who did not report receipt of vaccine.

** Medians were compared using a Wilcoxon rank sum test. Proportions were compared using Pearson's chi-square test or Fisher's exact test.

†† Includes all persons within the vaccine-eligible population who received 1 vaccine dose, including vaccinated mpox patients.

§§ Comparison between recipients of 1 vaccine dose in the vaccine-eligible population and vaccinated mpox patients.

the ongoing racial and ethnic disparities in receipt of the JYNNEOS vaccine nationwide (*5*,*6*) and could indicate differential access to or acceptance of the vaccine. Disparities in access to health care and additional treatment options could also have played a role in decreasing the severity of illness in vaccinated White persons.

The findings in this report are subject to at least four limitations. First, 47% of cases were excluded because of missing vaccination information; therefore, results might not be generalizable to all persons with mpox in the United States. Second, persons with mpox who received vaccine outside of their respective jurisdictions of residence might not have had documentation of vaccine receipt, which could lead to potential undercounting of cases among vaccinated persons (*7*), although many jurisdictions did report sharing vaccination data with one another (Sarah Gillani, District of Columbia Department of Health, personal communication, September 2022). Third, self-reported doses were included to optimize ascertainment of vaccination status, but self-report is less accurate than documented vaccine receipt and could result in misclassification of vaccination status. Finally, clinical data were not available for all cases. In particular, HIV status was unknown or missing for two thirds of vaccinated and more than one half

TABLE 2. Clinical characteristics of mpox patients, by vaccination status* — 29 U.S. jurisdictions,† May 22–September 3, 2022

Characteristic	Mpox patient vaccination status, n/N (%)		
	Vaccinated§ (n = 202)	Unvaccinated¶ (n = 5,326)	Odds ratio (95% CI)
HIV status			
Positive	19/78 (24.4)	1,074/2,585 (41.6)	Not calculated
Negative	46/78 (58.9)	1,153/2,585 (44.5)	
Unknown or missing	137	3,099	
Signs and symptoms			
Abdominal pain	5/190 (2.6)	420/5,069 (8.3)**	0.29 (0.12–0.72)
Chills	23/193 (11.9)	2,015/5,207 (38.7)**	0.21 (0.14–0.33)
Conjunctivitis	2/65 (3.1)	148/2,703 (5.5)	0.57 (0.14–2.36)
Enlarged lymph nodes	62/196 (31.6)	1,841/5,237 (35.2)	0.84 (0.62–1.14)
Fever	55/198 (27.8)	2,451/5,266 (46.5)**	0.44 (0.32–0.60)
Headache	39/195(20.0)	1,908/5,217 (36.6)**	0.43 (0.30–0.61)
Malaise	47/192 (24.5)	2,240/5,204 (43.0)**	0.43 (0.31–0.60)
Myalgia	39/194 (20.1)	1,696/5,212 (32.5)**	0.52 (0.36–0.74)
Proctitis	11/187 (5.9)	360/4,983 (7.2)	0.81 (0.44–1.50)
Pruritis	65/194 (33.5)	1,840/5,193 (35.4)	0.93 (0.68–1.26)
Pus in stool	12/191 (6.3)	558/5,169 (10.8)**	0.55 (0.30–0.99)
Rectal bleeding	17/193 (8.8)	684/5,182 (13.2)	0.63 (0.38–1.04)
Rectal pain	38/194 (19.6)	1,255/5,211 (24.1)	0.77 (0.53–1.10)
Tenesmus	16/190 (8.4)	573/5,164 (11.1)	0.74 (0.44–1.24)
Vomiting or nausea	6/199 (3.0)	494/5,263 (9.4)**	0.31 (0.13–0.69)
Rash			
Presence of rash	195/202 (96.5)	5,173/5,318 (97.3)	0.73 (0.34–1.58)
Rash location			
Arms	20/160 (12.5)	1,860/4,140 (44.9)**	0.18 (0.11–0.28)
Face	26/160 (16.3)	1,386/4,140 (33.5)**	0.39 (0.25–0.59)
Genitals	88/160 (55.0)	1,933/4,140 (46.7)**	1.40 (1.02–1.92)
Head	27/160 (16.9)	1,376/4,140 (33.2)**	0.41 (0.27–0.62)
Legs	19/160 (11.9)	1,628/4,140 (39.3)**	0.21 (0.13–0.34)
Mouth, lips, or oral mucosa	7/160 (4.4)	400/4,140 (9.7)**	0.43 (0.20–0.92)
Neck	5/160 (3.13)	545/4,140 (13.2)**	0.21 (0.09–0.52)
Palms of hands	6/160 (3.8)	806/4,140 (19.5)**	0.16 (0.07–0.37)
Perianal	42/160 (26.3)	1,212/4,140 (29.3)	0.86 (0.60–1.23)
Soles of feet	1/160 (0.6)	445/4,140 (10.8)**	0.05 (0.01–0.37)
Trunk	18/160 (11.3)	1,521/4140 (36.7)**	0.22 (0.13–0.36)
Other locations	68/160 (42.5)	1,574/4,140 (38.0)	1.21 (0.88–1.66)
Number of rash locations reported			
Median (IQR)**	2.0 (1.0–3.0)	3.0 (2.0–5.0)**	<0.001††
Severity			
Hospitalization related to mpox	2/95 (2.1)	237/3,142 (7.5)	0.27 (0.06–1.09)

Abbreviation: mpox = monkeypox.

* Persons with complete data for one or more clinical symptom were included in analysis; for vaccinated persons 73.2% were included (202/276), and for unvaccinated persons 84.2% were included (5,326/6,329).

† California; Chicago, Illinois; Colorado; Connecticut; Delaware; District of Columbia; Florida; Georgia; Illinois; Massachusetts; Maryland; Michigan; Minnesota; Missouri; Montana; Nebraska; New Mexico; New York (not including New York City); Oregon; Pennsylvania; Philadelphia, Pennsylvania; Puerto Rico; Rhode Island; South Carolina; Tennessee; Utah; Virginia; Washington; and Wisconsin.

§ Cases of probable and confirmed mpox in persons with illness onset ≥14 days after receipt of 1 vaccine dose (202/276).

¶ Cases of probable and confirmed mpox in persons with illness onset before the date of vaccination or who did not report receipt of vaccine (5,326/6,329).

** Statistically significant difference using odds ratios.

†† Median rash locations reported from 160 vaccinated and 4,140 unvaccinated mpox patients.

Summary

What is already known about this topic?

Evidence suggests that 1 dose of JYNNEOS vaccine offers some protection against monkeypox (mpox).

What is added by this report?

Analysis of mpox infections among unvaccinated persons and those who had received 1 JYNNEOS vaccine dose ≥14 days before illness onset found that the odds of fever, headache, malaise, myalgia, and chills were significantly lower among vaccinated patients than among unvaccinated patients. Overall, 2% of vaccinated persons with mpox and 8% of unvaccinated patients were hospitalized.

What are the implications for public health practice?

One dose of JYNNEOS vaccine might attenuate the severity of illness and reduce hospitalization in persons who become infected after vaccination; however, to optimize protection, all eligible persons are recommended to complete the 2-dose vaccination series.

of unvaccinated patients. Because HIV infection might affect the trajectory and illness severity, future studies with additional data for real-world use of JYNNEOS vaccine against clinical outcomes, including data on HIV history, are needed.

The more limited distribution of rash and reduced severity of illness among persons who had mpox after receiving 1 JYNNEOS vaccine dose supports the potential benefit of vaccination on attenuation of disease. Although infection ≥14 days after receipt of 1 JYNNEOS vaccine dose is infrequent, the occurrence of such cases and the unknown duration of protection conferred by 1 vaccine dose highlights the need for providers and public health officials to encourage completion of the 2-dose vaccination series among persons at risk and continue to provide guidance and education regarding nonvaccine-related prevention strategies (*4*) until optimal immune protection from the second dose is achieved.

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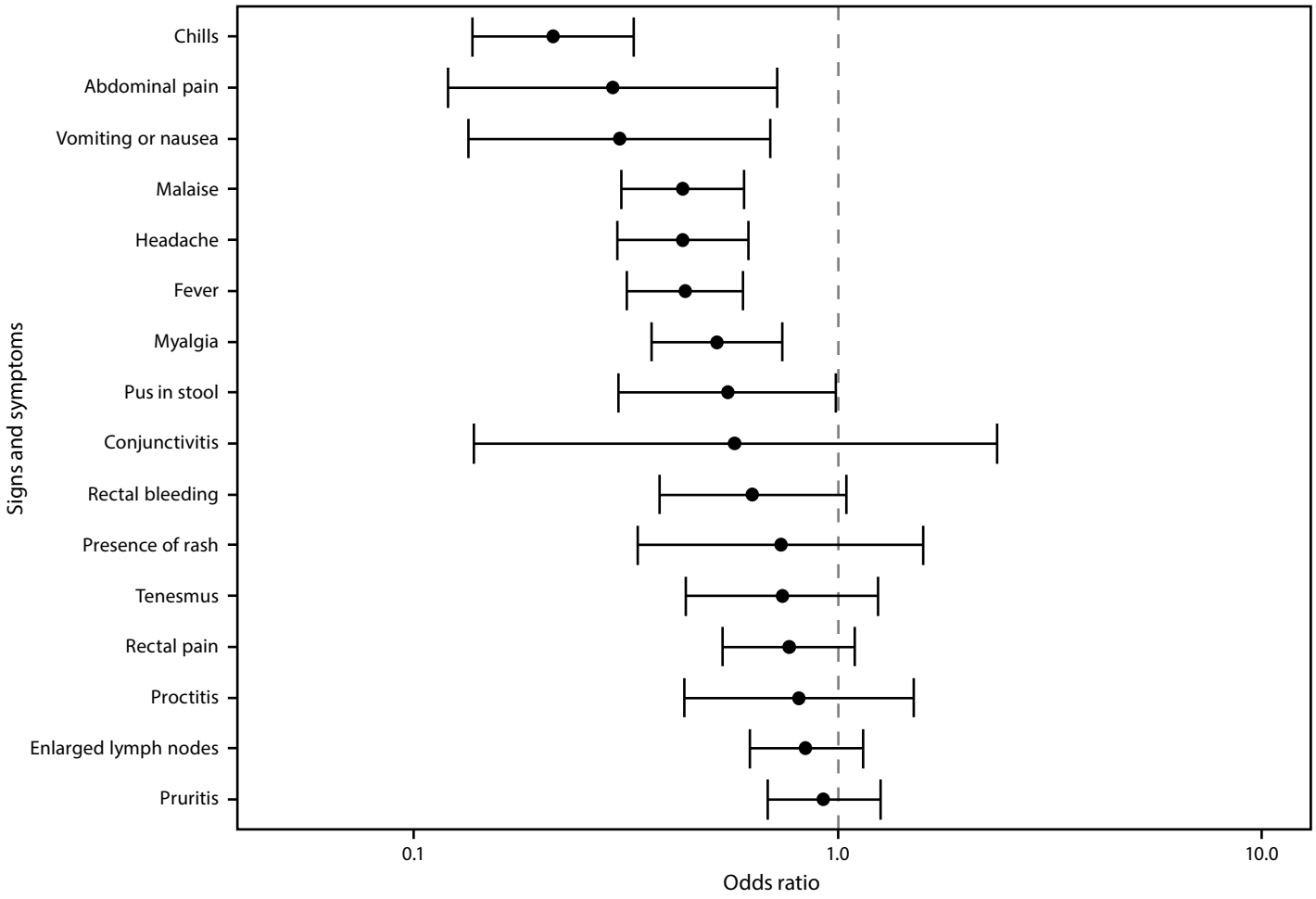
FIGURE. Odds* of signs and symptoms present among persons with mpox who received 1 dose of JYNNEOS vaccine compared with those in unvaccinated persons with mpox — 29 U.S. jurisdictions,† May 22–September 3, 2022



* With 95% CIs indicated by error bars.

† California; Chicago, Illinois; Colorado; Connecticut; Delaware; District of Columbia; Florida; Georgia; Illinois; Massachusetts; Maryland; Michigan; Minnesota; Missouri; Montana; Nebraska; New Mexico; New York (not including New York City); Oregon; Pennsylvania; Philadelphia, Pennsylvania; Puerto Rico; Rhode Island; South Carolina; Tennessee; Utah; Virginia; Washington; and Wisconsin.

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Morbidity and Mortality Weekly Report

Early Estimates of Bivalent mRNA Vaccine Effectiveness in Preventing COVID-19–Associated Emergency Department or Urgent Care Encounters and Hospitalizations Among Immunocompetent Adults — VISION Network, Nine States, September–November 2022

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During June–October 2022, the SARS-CoV-2 Omicron BA.5 sublineage accounted for most of the sequenced viral genomes in the United States, with further Omicron sublineage diversification through November 2022.* Bivalent mRNA vaccines contain an ancestral SARS-CoV-2 strain component plus an updated component of the Omicron BA.4/BA.5 sublineages. On September 1, 2022, a single bivalent booster dose was recommended for adults who had completed a primary vaccination series (with or without subsequent booster doses), with the last dose administered ≥2 months earlier (*1*). During September 13–November 18, the VISION Network evaluated vaccine effectiveness (VE) of a bivalent mRNA booster dose (after 2, 3, or 4 monovalent doses) compared with 1) no previous vaccination and 2) previous receipt of 2, 3, or 4 monovalent-only mRNA vaccine doses, among immunocompetent adults aged ≥18 years with an emergency department/urgent care (ED/UC) encounter or hospitalization for a COVID-19–like illness.† VE of a bivalent booster dose (after 2, 3, or 4 monovalent doses) against COVID-19–associated ED/UC encounters was 56% compared with no vaccination, 31% compared with monovalent vaccination only with last dose 2–4 months earlier, and 50% compared with monovalent vaccination only with last dose ≥11 months earlier. VE of a bivalent booster dose (after 2, 3, or 4 monovalent doses) against COVID-19–associated hospitalizations was 57% compared with no vaccination, 38% compared with monovalent vaccination only with last dose 5–7 months earlier, and 45% compared with monovalent vaccination only with last dose ≥11 months earlier. Bivalent vaccines administered after 2, 3, or 4 monovalent doses were effective in preventing medically attended COVID-19 compared with no vaccination and provided additional protection compared with past monovalent vaccination only, with relative protection increasing with time since receipt of the last monovalent dose. All eligible persons should stay up to date with recommended COVID-19 vaccinations, including receiving a bivalent booster dose. Persons should also consider taking additional precautions to avoid respiratory illness this winter season, such as masking in public indoor spaces, especially in areas where COVID-19 community levels are high.

Monovalent COVID-19 mRNA vaccines were developed against the spike protein of the ancestral SARS-CoV-2 virus and were found to provide cross-reactive immune protection against Alpha and Delta SARS-CoV-2 variants (*2*). The SARS-CoV-2 Omicron variant emerged in November 2021 and diversified into sublineages. These Omicron sublineages were associated with decreased protection from vaccination with monovalent vaccine (*3*). A single booster dose of bivalent mRNA vaccine (Pfizer-BioNTech or Moderna) containing an updated BA.4/BA.5 component was recommended by CDC on September 1, 2022, (*1*) for adults who had completed a primary series with any Food and Drug Administration–approved or –authorized monovalent vaccine or who had previously received a monovalent booster dose ≥2 months earlier.§

* SARS-CoV-2 variant proportions are monitored by CDC, and available online. https://covid.cdc.gov/covid-data-tracker/#variant-proportions

† Medical events with a discharge code consistent with COVID-19–like illness were included. COVID-19–like illness diagnoses were obtained from *International Classification of Diseases, Tenth Revision* (ICD-10) discharge codes. The specific codes used were: COVID-19 pneumonia: J12.81 and J12.82; influenza pneumonia: J09.X1, J10.0, J10.00, J10.01, J10.08, J11.0, J11.00, and J11.08; other viral pneumonia: J12*; bacterial and other pneumonia: J13, J14, J15*, J16*, J17, and J18*; influenza disease: J09*, J10.1, J10.2, J10.8*, J11.1, J11.2, and J11.8*; acute respiratory distress syndrome: J80; chronic obstructive pulmonary disease with acute exacerbation: J44.1; asthma acute exacerbation: J45.21, J45.22, J45.31, J45.32, J45.41, J45.42, J45.51, J45.52, J45.901, and J45.902; respiratory failure: J96.0*, J96.2*, and R09.2; other acute lower respiratory tract infections: J20*, J21*, J22, J40, J44.0, J41*, J42, J43*, J47*, J85, J85.0, J85.2, J85.3, J85.1, and J86*; acute and chronic sinusitis: J01* and J32*; acute upper respiratory tract infections: J00*, J02*, J03*, J04*, J05*, and J06*; acute respiratory illness signs and symptoms: R04.2, R05, R05.1, R05.2, R05.4, R05.8, R05.9, R06.00, R06.02, R06.03, R06.1, R06.2, R06.8, R06.81, R06.82, R06.89, R07.1, R09.0*, R09.01, R09.02, R09.1, R09.2, R09.3, and R09.8*; acute febrile illness signs and symptoms: R50*, R50.81, R50.9, and R68.83; acute nonrespiratory illness signs and symptoms: R19.7, R43*, R43.9, R51*, R51.9, M79.1*, M79.10, M79.18, R65*, R53.81, R53.83, R57.9, R41.82, R40*, R40.0, R40.1, R53.1, R11*, R11.0, R11.1, R11.10, R11.11, R11.15, R11.2, R21*, R10*, R10.0, R10.1*, R10.2, R10.3*, R10.8, R10.81, R10.81*, R10.84, and R10.9. All ICD-10 codes with * include all child codes under the specific parent code.

§ https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html

The VISION Network[¶] evaluated the effectiveness of a bivalent booster dose among immunocompetent adults during September 13–November 18, 2022, a period during which the Omicron BA.5 sublineage predominated and additional Omicron sublineages emerged. Seven health systems in nine states contributed data for this analysis. VISION methods have been described (*3*). Briefly, ED/UC encounters and hospitalizations associated with a COVID-19–like illness among adults who received a SARS-CoV-2 molecular test result during the 14 days before through 72 hours after the encounter were included.[**] Patients were classified as unvaccinated (zero doses received), vaccinated with 2, 3, or 4 doses of a monovalent-only mRNA vaccine, or vaccinated with 2, 3, or 4 monovalent doses plus a bivalent booster dose ≥60 days after receipt of their last monovalent dose. Encounters were excluded if 1) the patient likely had an immunocompromising condition (*4*); 2) only one mRNA monovalent vaccine dose was received, a second monovalent vaccine dose was received <14 days before the encounter date, or a third or fourth monovalent vaccine dose or a bivalent booster dose was received <7 days before the encounter date; 3) any dose of a non-mRNA vaccine (e.g., Janssen [Johnson & Johnson]) was received; or 4) a vaccine dose was received before being recommended by CDC.[††] VE was estimated using a test-negative case-control design, comparing the odds of having received versus having not received a bivalent booster dose among case-patients (those who received a positive SARS-CoV-2 test result) and control patients (those who received a negative SARS-CoV-2 test result).

Odds ratios and 95% CIs were calculated using multivariable logistic regression, adjusting for age, race and ethnicity, sex, calendar day (days since January 1, 2021), geographic region, and local SARS-CoV-2 circulation (percentage of SARS-CoV-2–positive results from testing within the counties surrounding the facility on the date of the encounter). Age, calendar day, and local circulation were modeled as natural cubic splines. A single, combined model was fit for each outcome (ED/UC encounters and hospitalizations) with those who had received a bivalent booster dose (after 2, 3, or 4 monovalent doses) as the referent group with the following vaccination groups: those who had received no vaccine doses (unvaccinated) (i.e., absolute VE) and those who had received 2, 3, or 4 monovalent doses but not a bivalent booster dose (i.e., relative VE). Varying time intervals between the last dose and the index date (2–4, 5–7, 8–10, or ≥11 months)[§§] were used to calculate relative VE. Analyses were conducted using R (version 4.2.2; R Foundation). This study was conducted consistent with applicable federal law and CDC policy and was reviewed and approved by Institutional Review Boards at participating sites or under reliance agreement with the Institutional Review Board of Westat, Inc.[¶¶]

Among 78,303 ED/UC encounters with COVID-19–like illness that met inclusion criteria, 9,009 (12%) case-patients and 69,294 (89%) control patients were identified (Table 1). Overall, 24,142 (31%) were unvaccinated. Among persons who had not received a bivalent dose, 18,812 (24%), 23,042 (29%), and 8,402 (11%) had received 2, 3, and 4 doses of monovalent mRNA vaccine, respectively. Among the 3,905 (5%) adults who had received a bivalent booster dose (median interval since receipt of bivalent booster dose = 25 days), 216 (6%) had received 2 monovalent doses, 1,679 (43%) had received 3 monovalent doses, and 2,010 (51%) had received 4 monovalent vaccine doses. Bivalent booster dose recipients were older (median age = 68 years) than were those who had not received a bivalent booster dose (median age = 55 years). VE of a bivalent booster dose (after 2, 3, or 4 monovalent doses) against ED/UC encounters for COVID-19–associated illness was 56% (95% CI = 49%–62%) compared with no vaccination, 31% (95% CI = 19%–41%) compared with receipt of last monovalent dose 2–4 months earlier, and 50% (95% CI = 43%–57%) compared with receipt of last monovalent dose ≥11 months earlier (Table 2).

Among 15,527 hospitalizations with COVID-19–like illness that met inclusion criteria, 1,453 (9%) case-patients and 14,074 (91%) control patients were identified (Table 3). Overall, 4,092 (26%) were unvaccinated. Among those who had not received a bivalent dose, 3,355 (22%), 4,766 (31%), and 2,531 (16%) had received 2, 3, and 4 doses of monovalent mRNA vaccine, respectively. Among the 783 (5%) adults

[¶] Sites from the CDC-funded VISION Network that contributed data for this analysis were Baylor Scott & White Health (Texas), Columbia University Irving Medical Center (New York), HealthPartners (Minnesota and Wisconsin), Intermountain Healthcare (Utah), Kaiser Permanente Northern California (California), Kaiser Permanente Center for Health Research (Oregon and Washington), and University of Colorado (Colorado).

[**] The encounter date was either the date of collection of a respiratory specimen associated with the most recent positive or negative SARS-CoV-2 test result before the admission or visit date, or the date of the medical visit if testing occurred only after the admission or visit.

[††] Encounters were excluded if a first mRNA booster dose (third dose) was received before it was recommended by CDC on September 23, 2021; the interval between the second and third doses was <5 months, a second mRNA booster dose (fourth dose) was received before it was authorized for adults aged ≥50 years on March 29, 2022; the interval between the third and fourth doses was <4 months; a bivalent booster dose was received before recommended and generally available to the public (September 6, 2022); or the interval between the last monovalent vaccine dose (second, third, or fourth dose) and the bivalent booster dose was <2 months. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html

[§§] Sixty–149 days was classified as 2–4 months, 150–239 days as 5–7 months, 240–329 days as 8–10 months, and ≥330 days as ≥11 months.

[¶¶] 45 C.F.R. part 46.102(l)(2), 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.

TABLE 1. Characteristics of emergency department and urgent care encounters among immunocompetent adults aged ≥18 years with COVID-19–like illness,* by mRNA COVID-19 vaccination status and SARS-CoV-2 test result — nine states,† September–November 2022

Characteristic	Overall, no. (column %)	SARS-CoV-2 test result status, no. (row %)		SMD¶	mRNA COVID-19 vaccination status,§ no. (row %)						
		Case-patients (positive)	Control patients (negative)		Unvaccinated	Received 2, 3, or 4 MV doses only, interval since last dose (mos) 2–4	5–7	8–10	≥11	Received BV booster dose ≥7 days earlier	SMD¶
All ED/UC encounters	**78,303**	**9,009 (11.5)**	**69,294 (88.5)**	—	**24,142 (30.8)**	**5,668 (7.2)**	**6,891 (8.8)**	**14,220 (18.2)**	**23,477 (30.0)**	**3,905 (5.0)**	—
Site											
Baylor Scott & White Health	**13,516 (17.3)**	1,390 (10.3)	12,126 (89.7)	0.37	7,014 (51.9)	288 (2.1)	374 (2.8)	1,244 (9.2)	4,513 (33.4)	83 (0.6)	3.8
Columbia University	**3,243 (4.1)**	253 (7.8)	2,990 (92.2)		1,421 (43.8)	110 (3.4)	209 (6.4)	508 (15.7)	941 (29.0)	54 (1.7)	
HealthPartners	**14,214 (18.2)**	1,637 (11.5)	12,577 (88.5)		3,523 (24.8)	1,236 (8.7)	1,296 (9.1)	3,006 (21.1)	3,683 (25.9)	1,470 (10.3)	
Intermountain Healthcare	**16,110 (20.6)**	2,746 (17.0)	13,364 (83.0)		5,290 (32.8)	924 (5.7)	1,189 (7.4)	2,933 (18.2)	5,538 (34.4)	236 (1.5)	
KPNC	**19,484 (24.9)**	1,326 (6.8)	18,158 (93.2)		2,431 (12.5)	2,350 (12.1)	3,052 (15.7)	4,787 (24.6)	5,339 (27.4)	1,525 (7.8)	
KPCHR	**5,840 (7.5)**	736 (12.6)	5,104 (87.4)		1,405 (24.1)	617 (10.6)	602 (10.3)	1,190 (20.4)	1,611 (27.6)	415 (7.1)	
University of Colorado	**5,896 (7.5)**	921 (15.6)	4,975 (84.4)		3,058 (51.9)	143 (2.4)	169 (2.9)	552 (9.4)	1,852 (31.4)	122 (2.1)	
Age group, yrs											
18–49	**39,190 (50.0)**	4,035 (10.3)	35,155 (89.7)	0.14	16,470 (42.0)	870 (2.2)	1,661 (4.2)	7,211 (18.4)	12,048 (30.7)	930 (2.4)	3.41
50–64	**14,692 (18.8)**	1,710 (11.6)	12,982 (88.4)		3,903 (26.6)	1,362 (9.3)	1,328 (9.0)	3,085 (21.0)	4,308 (29.3)	706 (4.8)	
65–74	**10,533 (13.5)**	1,311 (12.4)	9,222 (87.6)		1,898 (18.0)	1,362 (12.9)	1,478 (14.0)	1,714 (16.3)	3,100 (29.4)	981 (9.3)	
75–84	**8,844 (11.3)**	1,275 (14.4)	7,569 (85.6)		1,202 (13.6)	1,277 (14.4)	1,536 (17.4)	1,424 (16.1)	2,532 (28.6)	873 (9.9)	
≥85	**5,044 (6.4)**	678 (13.4)	4,366 (86.6)		669 (13.3)	797 (15.8)	888 (17.6)	786 (15.6)	1,489 (29.5)	415 (8.2)	
Sex											
Female	**48,342 (61.7)**	5,343 (11.1)	42,999 (88.9)	0.06	14,554 (30.1)	3,431 (7.1)	4,182 (8.7)	9,033 (18.7)	14,819 (30.7)	2,323 (4.8)	0.15
Male	**29,961 (38.3)**	3,666 (12.2)	26,295 (87.8)		9,588 (32.0)	2,237 (7.5)	2,709 (9.0)	5,187 (17.3)	8,658 (28.9)	1,582 (5.3)	
Race and ethnicity											
Black or African American, NH	**9,261 (11.8)**	823 (8.9)	8,438 (91.1)	0.17	3,837 (41.4)	516 (5.6)	694 (7.5)	1,421 (15.3)	2,553 (27.6)	240 (2.6)	1.17
Hispanic or Latino	**14,703 (18.8)**	1,345 (9.1)	13,358 (90.9)		5,119 (34.8)	850 (5.8)	1,096 (7.5)	2,767 (18.8)	4,492 (30.6)	379 (2.6)	
Other, NH**	**7,417 (9.5)**	841 (11.3)	6,576 (88.7)		1,746 (23.5)	659 (8.9)	785 (10.6)	1,743 (23.5)	2,031 (27.4)	453 (6.1)	
Unknown	**1,255 (1.6)**	154 (12.3)	1,101 (87.7)		547 (43.6)	46 (3.7)	73 (5.8)	240 (19.1)	321 (25.6)	28 (2.2)	
White, NH	**45,667 (58.3)**	5,846 (12.8)	39,821 (87.2)		12,893 (28.2)	3,597 (7.9)	4,243 (9.3)	8,049 (17.6)	14,080 (30.8)	2,805 (6.1)	
Documented previous SARS-CoV-2 infection††											
Yes	**15,750 (20.1)**	1,247 (7.9)	14,503 (92.1)	0.19	4,682 (29.7)	1,036 (6.6)	1,351 (8.6)	2,916 (18.5)	5,136 (32.6)	629 (4.0)	0.15
No	**62,553 (79.9)**	7,762 (12.4)	54,791 (87.6)		19,460 (31.1)	4,632 (7.4)	5,540 (8.9)	11,304 (18.1)	18,341 (29.3)	3,276 (5.2)	
SARS-CoV-2 status											
Positive test result (case-patient)	**9,009 (11.5)**	9,009 (100.0)	0 (—)	—	3,040 (33.7)	537 (6.0)	725 (8.0)	1,677 (18.6)	2,783 (30.9)	247 (2.7)	0.24
Negative test result (control patient)	**69,294 (88.5)**	0 (—)	69,294 (100.0)		21,102 (30.5)	5,131 (7.4)	6,166 (8.9)	12,543 (18.1)	20,694 (29.9)	3,658 (5.3)	

See table footnotes on the next page.

TABLE 1. (*Continued*) Characteristics of emergency department and urgent care encounters among immunocompetent adults aged ≥18 years with COVID-19–like illness,* by mRNA COVID-19 vaccination status and SARS-CoV-2 test result — nine states,† September–November 2022

Characteristic	Overall, no. (column %)	SARS-CoV-2 test result status, no. (row %)			mRNA COVID-19 vaccination status,§ no. (row %)						
		Case-patients (positive)	Control patients (negative)	SMD¶	Unvaccinated	Received 2, 3, or 4 MV doses only, interval since last dose (mos) 2–4	5–7	8–10	≥11	Received BV booster dose ≥7 days earlier	SMD¶
No. of MV mRNA vaccine doses received											
None	**24,142**	3,040	21,102	0.08	24,142	0	0	0	0	0	—
	(30.8)	(12.6)	(87.4)		(100.0)	(—)	(—)	(—)	(—)	(—)	
2	**19,028**	2,158	16,870		0	277	606	1,391	16,538	216	
	(24.3)	(11.3)	(88.7)		(—)	(1.5)	(3.2)	(7.3)	(86.9)	(1.1)	
3	**24,721**	2,752	21,969		0	1,006	2,268	12,829	6,939	1,679	
	(31.6)	(11.1)	(88.9)		(—)	(4.1)	(9.2)	(51.9)	(28.1)	(6.8)	
4	**10,412**	1,059	9,353		0	4,385	4,017	0	0	2,010	
	(13.3)	(10.2)	(89.8)		(—)	(42.1)	(38.6)	(—)	(—)	(19.3)	
Most recent dose product manufacturer											
Pfizer-BioNTech	**34,596**	3,821	30,775	0.07	0	3,610	4,451	8,441	15,290	2,804	—
	(44.2)	(11.0)	(89.0)		(—)	(10.4)	(12.9)	(24.4)	(44.2)	(8.1)	
Moderna	**19,565**	2,148	17,417		0	2,058	2,440	5,779	8,187	1,101	
	(25.0)	(11.0)	(89.0)		(—)	(10.5)	(12.5)	(29.5)	(41.8)	(5.6)	
None	**24,142**	3,040	21,102		24,142	0	0	0	0	0	
	(30.8)	(12.6)	(87.4)		(100.0)	(—)	(—)	(—)	(—)	(—)	
Any chronic condition											
Yes	**23,892**	2,311	21,581	0.12	6,782	2,114	2,466	4,056	7,313	1,161	0.46
	(30.5)	(9.7)	(90.3)		(28.4)	(8.8)	(10.3)	(17.0)	(30.6)	(4.9)	
No	**54,411**	6,698	47,713		17,360	3,554	4,425	10,164	16,164	2,744	
	(69.5)	(12.3)	(87.7)		(31.9)	(6.5)	(8.1)	(18.7)	(29.7)	(5.0)	
≥1 chronic respiratory condition											
Yes	**12,316**	1,060	11,256	0.13	3,606	1,014	1,203	2,067	3,863	563	0.2
	(15.7)	(8.6)	(91.4)		(29.3)	(8.2)	(9.8)	(16.8)	(31.4)	(4.6)	
No	**65,987**	7,949	58,038		20,536	4,654	5,688	12,153	19,614	3,342	
	(84.3)	(12.0)	(88.0)		(31.1)	(7.1)	(8.6)	(18.4)	(29.7)	(5.1)	
≥1 chronic non-respiratory condition											
Yes	**17,268**	1,836	15,432	0.05	4,869	1,600	1,794	2,853	5,389	763	0.4
	(22.1)	(10.6)	(89.4)		(28.2)	(9.3)	(10.4)	(16.5)	(31.2)	(4.4)	
No	**61,035**	7,173	53,862		19,273	4,068	5,097	11,367	18,088	3,142	
	(77.9)	(11.8)	(88.2)		(31.6)	(6.7)	(8.4)	(18.6)	(29.6)	(5.1)	

Abbreviations: BV = bivalent; ED/UC = emergency department/urgent care; KPCHR = Kaiser Permanente Center for Health Research; KPNC = Kaiser Permanente Northern California; MV = monovalent; NH = non-Hispanic; SMD = standardized mean or proportion difference.

* ED/UC encounters with a discharge code consistent with COVID-19–like illness were included. COVID-19–like illness diagnoses included acute respiratory illness, respiratory signs or symptoms, or febrile signs or symptoms using diagnosis codes from the *International Classification of Diseases, Tenth Revision*. Clinician-ordered molecular assays (e.g., real-time reverse transcription–polymerase chain reaction) for SARS-CoV-2 occurring ≤14 days before to <72 hours after the encounter date were included.

† California (Sep 13–Nov 18, 2022), Colorado (Sep 13–Nov 7, 2022), Minnesota and Wisconsin (Sep 13–Nov 18, 2022), New York (Sep 13–Nov 18, 2022), Oregon and Washington (Sep 13–Nov 14, 2022), Texas (Sep 13–Nov 13, 2022), and Utah (Sep 13–Nov 18, 2022).

§ Vaccination was defined as having received the last monovalent or bivalent dose within the specified range of months or days before the ED/UC encounter date, which was the date of respiratory specimen collection associated with the most recent positive or negative SARS-CoV-2 test result before the encounter start date or the encounter start date if testing only occurred after the admission.

¶ An absolute SMD >0.20 indicates a nonnegligible difference in variable distributions between ED/UC encounters for vaccinated versus unvaccinated patients or for patients with positive SARS-CoV-2 test results versus patients with negative SARS-CoV-2 test results. For mRNA COVID-19 vaccination status, a single SMD was calculated by averaging the absolute SMDs obtained from pairwise comparisons of each vaccinated category versus unvaccinated. Specifically, it was calculated as the average of the absolute value of the SMDs for 1) vaccinated with only monovalent doses, ≥11 months earlier versus unvaccinated, 2) vaccinated with only monovalent doses, 8–10 months earlier versus unvaccinated, 3) vaccinated with only monovalent doses 5–7 months earlier versus unvaccinated, 4) vaccinated with only monovalent doses 2–4 months earlier versus unvaccinated, and 5) vaccinated with bivalent booster ≥7 days earlier versus unvaccinated.

** Other race includes Asian, Hawaiian or other Pacific Islander, American Indian or Alaska Native, other not listed, and multiple races. Because of small numbers, these categories were combined.

†† Previous SARS-CoV-2 infection was defined as having a positive SARS-CoV-2 test result (molecular or antigen) documented in the electronic health record ≥15 days before the hospital admission date. This does not capture previous infections in which testing was not performed or testing was performed but not available in the electronic health record (e.g., at-home testing).

TABLE 2. Bivalent booster COVID-19 vaccine effectiveness* against laboratory confirmed COVID-19–associated emergency department and urgent care encounters and hospitalizations among immunocompetent adults aged 18 years — nine states,† September–November 2022

mRNA dosage pattern	Total	Negative SARS-CoV-2 test result, no. (%)	Positive SARS-CoV-2 test result, no. (%)	Median interval since last dose, days (IQR)	VE % (95% CI)
ED/UC encounters					
Relative VE					
Only MV doses, last dose 2–4 mos earlier	**5,668**	5,131 (91)	537 (9)	115 (91–134)	Ref
BV booster dose, ≥7 days earlier	**3,905**	3,658 (94)	247 (6)	25 (16–37)	31 (19–41)
Only MV doses, last dose 5–7 mos earlier	**6,891**	6,166 (89)	725 (11)	184 (166–209)	Ref
BV booster dose, ≥7 days earlier	**3,905**	3,658 (94)	247 (6)	25 (16–37)	42 (32–50)
Only MV doses, last dose 8–10 mos earlier	**14,220**	12,543 (88)	1,677 (12)	294 (273–312)	Ref
BV booster dose, ≥7 days earlier	**3,905**	3,658 (94)	247 (6)	25 (16–37)	53 (46–60)
Only MV doses, last dose ≥11 mos earlier	**23,477**	20,694 (88)	2,783 (12)	459 (365–542)	Ref
BV booster dose, ≥7 days earlier	**3,905**	3,658 (94)	247 (6)	25 (16–37)	50 (43–57)
Absolute VE					
Unvaccinated	**24,142**	21,102 (87)	3,040 (13)	NA	Ref
BV booster dose, ≥7 days earlier	**3,905**	3,658 (94)	247 (6)	25 (16–37)	56 (49–62)
Hospitalizations					
Relative VE					
Only MV doses, last dose 2–4 mos earlier	—§	—	—	—	—
BV booster dose, ≥7 days earlier	—	—	—	—	—
Only MV doses, last dose 5–7 mos earlier	**1,819**	1,652 (91)	167 (9)	178 (164–201)	Ref
BV booster dose, ≥7 days earlier	**783**	734 (94)	49 (6)	23 (14–34)	38 (13–56)
Only MV doses, last dose 8–10 mos earlier	**2,655**	2,422 (91)	233 (9)	294 (273–313)	Ref
BV booster dose, ≥7 days earlier	**783**	734 (94)	49 (6)	23 (14–34)	42 (19–58)
Only MV doses, last dose ≥11 mos earlier	**4,595**	4,147 (90)	448 (10)	472 (362–556)	Ref
BV booster dose, ≥7 days earlier	**783**	734 (94)	49 (6)	23 (14–34)	45 (25–60)
Absolute VE					
Unvaccinated	**4,092**	3,658 (89)	434 (11)	NA	Ref
BV booster dose, ≥7 days earlier	**783**	734 (94)	49 (6)	23 (14–34)	57 (41–69)

Abbreviations: BV = bivalent; ED/UC = emergency department/urgent care; MV = monovalent; NA = not applicable; Ref = referent group; VE = vaccine effectiveness.
* VE was calculated as ([1 − odds ratio] x 100%), estimated using a test-negative case-control design, adjusted for age, sex, race and ethnicity, geographic region, calendar time (days since January 1, 2021), and local virus circulation (percentage of positive SARS-CoV-2 test results from testing within the counties surrounding the facility on the date of the encounter).
† California (Sep 13, 2022–Nov 18, 2022), Colorado (Sep 13, 2022–Nov 7, 2022), Minnesota and Wisconsin (Sep 13, 2022–Nov 18, 2022), New York (Sep 13, 2022–Nov 18, 2022), Oregon and Washington (Sep 13, 2022–Nov 14, 2022), Texas (Sep 13, 2022–Nov 13, 2022), and Utah (Sep 13, 2022–Nov 18, 2022).
§ Dashes indicate that estimated VE had a CI width ≥50%. Estimates with CI widths ≥50% are not shown here because of imprecision. The associated data are also omitted.

who had received a bivalent booster dose (median interval since receipt of bivalent booster dose = 23 days), 49 (6%) had received 2 monovalent doses, 252 (32%) had received 3 monovalent doses, and 482 (62%) had received 4 monovalent doses. Bivalent booster dose recipients were similar in age to vaccinated adults who had not received a bivalent booster dose (median age = 76 and 73 years, respectively). VE of a bivalent booster dose (after 2, 3, or 4 monovalent doses) against hospitalization for COVID-19–associated illness was 57% (95% CI = 41%–69%) compared with no vaccination and 45% (95% CI = 25%–60%) compared with receipt of last monovalent doses, with last dose ≥11 months earlier (Table 2).

Discussion

Analysis of data from the multistate VISION Network found that during September–November 2022, when the BA.5 and other Omicron sublineages were the predominant circulating SARS-CoV-2 variants in the United States, bivalent booster doses (after receipt of 2, 3, or 4 monovalent doses) were effective in preventing medically attended COVID-19 compared with no previous vaccination among immunocompetent adults and provided additional protection when compared with previous monovalent mRNA vaccine doses only. VE was similar against COVID-19–associated ED/UC encounters and hospitalizations, which might reflect changing severity of hospitalized cases over time (*5*). Additional studies are needed to evaluate VE against outcomes such as COVID-19–associated severe respiratory illness or death. The IVY Network, an adult inpatient VE network, recently found higher estimated VE in adults aged ≥65 years compared with estimates for those aged ≥18 years included in this analysis (*6*). This might reflect differences in population subgroups evaluated. Long-term durability of bivalent booster vaccination protection also could not be assessed because of the short period of observation since bivalent dose receipt. In a recent analysis from VISION, during BA.4/BA.5–predominant circulation, 3-dose monovalent VE against COVID-19–associated hospitalization was observed to wane from 68% at 7–119 days after vaccination to 36% at ≥120 days (*5*). This might explain why, among patients who had received 2, 3, or 4 monovalent vaccine doses only, a longer

TABLE 3. Characteristics of hospitalizations among immunocompetent adults aged ≥18 years with COVID-19–like illness,* by mRNA COVID-19 vaccination status and SARS-CoV-2 test result — nine states,† September–November 2022

Characteristic	Overall, no. (col %)	SARS-CoV-2 test result status no. (row %)			mRNA COVID-19 vaccination status.§ no. (row %)						
		Case-patients (positive)	Control patients (negative)	SMD¶	Unvaccinated	Received 2, 3, or 4 MV doses only, interval since last dose (mos) 2–4	5–7	8–10	≥11	Received BV booster dose ≥7 days earlier	SMD¶
All hospitalizations	**15,527 (100.0)**	**1,453 (9.4)**	**14,074 (90.6)**	—	**4,092 (26.4)**	**1,583 (10.2)**	**1,819 (11.7)**	**2,655 (17.1)**	**4,595 (29.6)**	**783 (5.0)**	—
Site											
Baylor Scott & White Health	**3,782 (24.4)**	331 (8.8)	3,451 (91.2)	0.19	1,545 (40.9)	117 (3.1)	136 (3.6)	433 (11.4)	1,516 (40.1)	35 (0.9)	3.91
Columbia University	**1,125 (7.2)**	128 (11.4)	997 (88.6)		432 (38.4)	69 (6.1)	109 (9.7)	200 (17.8)	292 (26.0)	23 (2.0)	
HealthPartners	**1,504 (9.7)**	165 (11.0)	1,339 (89.0)		311 (20.7)	206 (13.7)	183 (12.2)	267 (17.8)	349 (23.2)	188 (12.5)	
Intermountain Healthcare	**1,693 (10.9)**	219 (12.9)	1,474 (87.1)		506 (29.9)	167 (9.9)	167 (9.9)	285 (16.8)	536 (31.7)	32 (1.9)	
KPNC	**5,489 (35.4)**	438 (8.0)	5,051 (92.0)		582 (10.6)	838 (15.3)	1,076 (19.6)	1,193 (21.7)	1,384 (25.2)	416 (7.6)	
KPNW	**1,028 (6.6)**	82 (8.0)	946 (92.0)		305 (29.7)	135 (13.1)	104 (10.1)	181 (17.6)	238 (23.2)	65 (6.3)	
University of Colorado	**906 (5.8)**	90 (9.9)	816 (90.1)		411 (45.4)	51 (5.6)	44 (4.9)	96 (10.6)	280 (30.9)	24 (2.6)	
Age group, yrs											
18–49	**2,928 (18.9)**	160 (5.5)	2,768 (94.5)	0.34	1,315 (44.9)	72 (2.5)	138 (4.7)	506 (17.3)	822 (28.1)	75 (2.6)	2.74
50–64	**2,988 (19.2)**	212 (7.1)	2,776 (92.9)		1,006 (33.7)	229 (7.7)	284 (9.5)	574 (19.2)	812 (27.2)	83 (2.8)	
65–74	**3,244 (20.9)**	300 (9.2)	2,944 (90.8)		717 (22.1)	390 (12.0)	404 (12.5)	528 (16.3)	1,016 (31.3)	189 (5.8)	
75–84	**3,626 (23.4)**	410 (11.3)	3,216 (88.7)		599 (16.5)	482 (13.3)	565 (15.6)	639 (17.6)	1,085 (29.9)	256 (7.1)	
≥85	**2,741 (17.7)**	371 (13.5)	2,370 (86.5)		455 (16.6)	410 (15.0)	428 (15.6)	408 (14.9)	860 (31.4)	180 (6.6)	
Sex											
Female	**8,405 (54.1)**	748 (8.9)	7,657 (91.1)	0.06	2,147 (25.5)	873 (10.4)	990 (11.8)	1,447 (17.2)	2,525 (30.0)	423 (5.0)	0.19
Male	**7,122 (45.9)**	705 (9.9)	6,417 (90.1)		1,945 (27.3)	710 (10.0)	829 (11.6)	1,208 (17.0)	2,070 (29.1)	360 (5.1)	
Race and ethnicity											
Black or African American, NH	**1,788 (11.5)**	116 (6.5)	1,672 (93.5)	0.2	634 (35.5)	138 (7.7)	171 (9.6)	248 (13.9)	546 (30.5)	51 (2.9)	1.18
Hispanic or Latino	**2,395 (15.4)**	178 (7.4)	2,217 (92.6)		696 (29.1)	212 (8.9)	248 (10.4)	490 (20.5)	683 (28.5)	66 (2.8)	
Other,** NH	**1,502 (9.7)**	117 (7.8)	1,385 (92.2)		279 (18.6)	197 (13.1)	240 (16.0)	303 (20.2)	381 (25.4)	102 (6.8)	
Unknown	**239 (1.5)**	21 (8.8)	218 (91.2)		111 (46.4)	13 (5.4)	24 (10.0)	29 (12.1)	58 (24.3)	4 (1.7)	
White, NH	**9,603 (61.8)**	1,021 (10.6)	8,582 (89.4)		2,372 (24.7)	1,023 (10.7)	1,136 (11.8)	1,585 (16.5)	2,927 (30.5)	560 (5.8)	
Documented prior SARS-CoV-2 infection††											
Yes	**2,450 (15.8)**	141 (5.8)	2,309 (94.2)	0.2	641 (26.2)	217 (8.9)	253 (10.3)	415 (16.9)	828 (33.8)	96 (3.9)	0.19
No	**13,077 (84.2)**	1,312 (10.0)	11,765 (90.0)		3,451 (26.4)	1,366 (10.4)	1,566 (12.0)	2,240 (17.1)	3,767 (28.8)	687 (5.3)	
SARS-CoV-2 status											
Positive test result (case-patient)	**1,453 (9.4)**	1,453 (100.0)	0 (—)	—	434 (29.9)	122 (8.4)	167 (11.5)	233 (16.0)	448 (30.8)	49 (3.4)	0.27
Negative test result (control patient)	**14,074 (90.6)**	0 (—)	14,074 (100.0)		3,658 (26.0)	1,461 (10.4)	1,652 (11.7)	2,422 (17.2)	4,147 (29.5)	734 (5.2)	

See table footnotes on the next page.

TABLE 3. (*Continued*) Characteristics of hospitalizations among immunocompetent adults aged ≥18 years with COVID-19–like illness,* by mRNA COVID-19 vaccination status and SARS-CoV-2 test result — nine states,† September–November 2022

Characteristic	Overall, no. (col %)	SARS-CoV-2 test result status no. (row %)			mRNA COVID-19 vaccination status.§ no. (row %)						
		Case-patients (positive)	Control patients (negative)	SMD¶	Unvaccinated	Received 2, 3, or 4 MV doses only, interval since last dose (mos) 2–4	5–7	8–10	≥11	Received BV booster dose ≥7 days earlier	SMD¶
No. of monovalent mRNA vaccine doses received											
None	**4,092**	434	3,658	0.1	4,092	0	0	0	0	0	—
	(26.4)	(10.6)	(89.4)		(100.0)	(—)	(—)	(—)	(—)	(—)	
2	**3,404**	322	3,082		0	48	82	196	3,029	49	
	(21.9)	(9.5)	(90.5)		(—)	(1.4)	(2.4)	(5.8)	(89.0)	(1.4)	
3	**5,018**	443	4,575		0	216	525	2,459	1,566	252	
	(32.3)	(8.8)	(91.2)		(—)	(4.3)	(10.5)	(49.0)	(31.2)	(5.0)	
4	**3,013**	254	2,759		0	1,319	1,212	0	0	482	
	(19.4)	(8.4)	(91.6)		(—)	(43.8)	(40.2)	(—)	(—)	(16.0)	
Most recent dose product manufacturer											
Pfizer-BioNTech	**7,085**	620	6,465	0.09	0	1,006	1,132	1,450	2,914	583	—
	(45.6)	(8.8)	(91.2)		(—)	(14.2)	(16.0)	(20.5)	(41.1)	(8.2)	
Moderna	**4,350**	399	3,951		0	577	687	1,205	1,681	200	
	(28.0)	(9.2)	(90.8)		(—)	(13.3)	(15.8)	(27.7)	(38.6)	(4.6)	
None	**4,092**	434	3,658		4,092	0	0	0	0	0	
	(26.4)	(10.6)	(89.4)		(100.0)	(—)	(—)	(—)	(—)	(—)	
Any chronic condition											
Yes	**14,671**	1,411	13,260	0.14	3,748	1,558	1,782	2,472	4,363	748	0.83
	(94.5)	(9.6)	(90.4)		(25.5)	(10.6)	(12.1)	(16.8)	(29.7)	(5.1)	
No	**856**	42	814		344	25	37	183	232	35	
	(5.5)	(4.9)	(95.1)		(40.2)	(2.9)	(4.3)	(21.4)	(27.1)	(4.1)	
≥1 chronic respiratory condition											
Yes	**9,261**	921	8,340	0.08	2,324	1,049	1,174	1,540	2,700	474	0.44
	(59.6)	(9.9)	(90.1)		(25.1)	(11.3)	(12.7)	(16.6)	(29.2)	(5.1)	
No	**6,266**	532	5,734		1,768	534	645	1,115	1,895	309	
	(40.4)	(8.5)	(91.5)		(28.2)	(8.5)	(10.3)	(17.8)	(30.2)	(4.9)	
≥1 chronic non-respiratory condition											
Yes	**14,141**	1,370	12,771	0.14	3,530	1,535	1,745	2,402	4,197	732	1.07
	(91.1)	(9.7)	(90.3)		(25.0)	(10.9)	(12.3)	(17.0)	(29.7)	(5.2)	
No	**1,386**	83	1,303		562	48	74	253	398	51	
	(8.9)	(6.0)	(94.0)		(40.5)	(3.5)	(5.3)	(18.3)	(28.7)	(3.7)	
ICU admission											
Yes	**2,568**	182	2,386	0.13	751	232	300	449	729	107	0.29
	(16.5)	(7.1)	(92.9)		(29.2)	(9.0)	(11.7)	(17.5)	(28.4)	(4.2)	
No	**12,959**	1,271	11,688		3,341	1,351	1,519	2,206	3,866	676	
	(83.5)	(9.8)	(90.2)		(25.8)	(10.4)	(11.7)	(17.0)	(29.8)	(5.2)	
Receipt of invasive mechanical ventilation											
Yes	**1,580**	97	1,483	0.14	567	112	128	227	497	49	0.75
	(10.2)	(6.1)	(93.9)		(35.9)	(7.1)	(8.1)	(14.4)	(31.5)	(3.1)	
No	**13,947**	1,356	12,591		3,525	1,471	1,691	2,428	4,098	734	
	(89.8)	(9.7)	(90.3)		(25.3)	(10.5)	(12.1)	(17.4)	(29.4)	(5.3)	

See table footnotes on the next page.

interval since the most recent dose was associated with more relative protection after receipt of the bivalent booster dose.

Bivalent COVID-19 booster vaccines were developed to improve protection against circulating Omicron sublineages because of immune escape potentially associated with these subvariants and waning of monovalent vaccine-conferred protection over time (*7*). Real-world data suggest that bivalent boosters provide a modest degree of protection against symptomatic infection among adults compared with receipt of 2, 3, or 4 doses of monovalent vaccines only (*8*). Results from this study also demonstrate protection against ED/UC encounters and hospitalization during a period when BA.5 and other Omicron sublineage viruses predominated in the United States. With co-circulation of multiple respiratory viruses, including SARS-CoV-2, influenza, and respiratory syncytial virus, vaccination against respiratory diseases for which vaccines are available is especially important to prevent illnesses resulting in health care encounters and to reduce strain on the health care system (*9*). Additional studies will be critical to evaluating the durability of added protection, especially with circulation of sublineages of the BA.4/BA.5 Omicron variants such as BQ.1 and BQ.1.1.

TABLE 3. (*Continued*) Characteristics of hospitalizations among immunocompetent adults aged ≥18 years with COVID-19–like illness,* by mRNA COVID-19 vaccination status and SARS-CoV-2 test result — nine states,† September–November 2022

Characteristic	Overall, no. (col %)	SARS-CoV-2 test result status no. (row %)			mRNA COVID-19 vaccination status.§ no. (row %)						
		Case-patients (positive)	Control patients (negative)	SMD¶	Unvaccinated	Received 2, 3, or 4 MV doses only, interval since last dose (mos) 2–4	5–7	8–10	≥11	Received BV booster dose ≥7 days earlier	SMD¶
In-hospital death§§											
Yes	**466**	51	415	0.03	129	61	57	58	139	22	0.11
	(3.0)	(10.9)	(89.1)		(27.7)	(13.1)	(12.2)	(12.4)	(29.8)	(4.7)	
No	**15,061**	1,402	13,659		3,963	1,522	1,762	2,597	4,456	761	
	(97.0)	(9.3)	(90.7)		(26.3)	(10.1)	(11.7)	(17.2)	(29.6)	(5.1)	

Abbreviations: BV = bivalent; ICU = intensive care unit; KPCHR = Kaiser Permanente Center for Health Research; KPNC = Kaiser Permanente Northern California; MV = monovalent; NH = non-Hispanic; SMD = standardized mean or proportion difference.

* Hospitalizations with a discharge code consistent with COVID-19–like illness were included. COVID-19–like illness diagnoses included acute respiratory illness, respiratory signs or symptoms or febrile signs or symptoms using diagnosis codes from the *International Classification of Diseases, Tenth Revision*. Clinician-ordered molecular assays (e.g., real-time reverse transcription–polymerase chain reaction) for SARS-CoV-2 occurring ≤14 days before to <72 hours after the encounter date were included.

† California (Sep 13–Nov 18, 2022), Colorado (Sep 13–Nov 7, 2022), Minnesota and Wisconsin (Sep 13–Nov 18, 2022), New York (Sep 13–Nov 18, 2022), Oregon and Washington (Sep 13–Nov 14, 2022), Texas (Sep 13–Nov 13, 2022), and Utah (Sep 13–Nov 18, 2022).

§ Vaccination was defined as having received the last monovalent or bivalent dose within the specified range of months/days before the hospitalization encounter date, which was the date of respiratory specimen collection associated with the most recent positive or negative SARS-CoV-2 test result before the admission date or the admission date if testing only occurred after the admission.

¶ An absolute SMD >0.20 indicates a nonnegligible difference in variable distributions between hospitalizations for vaccinated versus unvaccinated patients or for patients with a positive SARS-Cov-2 test result versus patients with a negative SARS-CoV-2 test result. For mRNA COVID-19 vaccination status, a single SMD was calculated by averaging the absolute SMDs obtained from pairwise comparisons of each vaccinated category versus unvaccinated. Specifically, it was calculated as the average of the absolute value of the SMDs for 1) vaccinated with only monovalent doses, ≥11 months earlier versus unvaccinated, 2) vaccinated with only monovalent doses, 8–10 months earlier versus unvaccinated, 3) vaccinated with only monovalent doses 5–7 months earlier versus unvaccinated, 4) vaccinated with only monovalent doses 2–4 months earlier versus unvaccinated, and 5) vaccinated with bivalent booster ≥7 days earlier versus unvaccinated.

** Other race includes Asian, Hawaiian or other Pacific Islander, American Indian or Alaska Native, other not listed, and multiple races. Because of small numbers, these categories were combined.

†† Previous SARS-CoV-2 infection was defined as having a positive SARS-CoV-2 test result (molecular or antigen) documented in the electronic health record ≥15 days before the hospital admission date. This does not capture infections in which testing was not performed or testing was performed but not available in the electronic health record, e.g., at-home testing.

§§ In-hospital death was identified at each individual site and was defined as a death while hospitalized and ≤28 days after admission.

Summary

What is already known about this topic?

Bivalent mRNA COVID-19 booster doses containing an Omicron BA.4/BA.5 sublineage component were recommended on September 1, 2022. The effectiveness of these updated vaccines against COVID-19–associated medical encounters has not been established.

What is added by this report?

Bivalent booster doses provided additional protection against COVID-19–associated emergency department/urgent care encounters and hospitalizations in persons who previously received 2, 3, or 4 monovalent vaccine doses. Because of waning of monovalent vaccine-conferred immunity, relative effectiveness of bivalent vaccines was higher with increased time since the previous monovalent dose.

What are the implications for public health practice?

All persons should stay up to date with recommended COVID-19 vaccinations, including receiving a bivalent booster dose if eligible.

The findings in this study are subject to at least six limitations. First, previous SARS-CoV-2 infection was not accounted for in this analysis. A large proportion of the population has now experienced SARS-CoV-2 infection which decreases the risk of future medically attended COVID-19 illness and might affect observed VE due to background immunity (*10*). Second, although models adjusted for relevant confounders, residual confounding is possible, including by behavioral differences and use of COVID-19 treatments such as nirmatrelvir/ritonavir (Paxlovid). Third, sublineage-specific VE could not be estimated. Fourth, this analysis did not compare product-specific bivalent booster VE estimates. Fifth, relative VE was estimated using the interval since receipt of last monovalent dose; this study was not statistically powered to estimate whether relative VE differed by number of previous monovalent vaccine doses received. Finally, because these data are from nine states, the patients in this analysis might not be representative of the entire population of the United States. Further, this analysis included adults who received bivalent booster doses shortly after authorization who might not be fully representative of the vaccine-eligible population. For example, over one half of bivalent booster recipients had previously received 4 monovalent vaccine doses. Additional VE studies are needed as coverage of bivalent boosters increases.

In this early study of immunocompetent adults, significant protection from a booster dose of bivalent mRNA COVID-19 vaccine (after receipt of 2, 3, or 4 monovalent doses) compared

with no vaccination was found, as well as significant relative benefits of a bivalent booster dose when compared with previous receipt of monovalent doses only. These findings support efforts to improve coverage with bivalent vaccines, although optimal timing for receipt of bivalent vaccine booster doses needs to be established. All eligible persons should stay up to date with recommended COVID-19 vaccination, including receiving a bivalent booster dose. In addition, persons should consider taking other precautions to avoid respiratory illness this winter season, including masking in public indoor spaces, especially in areas where COVID-19 community levels are high, to protect themselves and others and reduce strain on the health care system during an ongoing surge in multiple respiratory viruses.

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Early Estimates of Bivalent mRNA Vaccine Effectiveness in Preventing COVID-19–Associated Hospitalization Among Immunocompetent Adults Aged ≥65 Years — IVY Network, 18 States, September 8–November 30, 2022

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Monovalent COVID-19 mRNA vaccines, designed against the ancestral strain of SARS-CoV-2, successfully reduced COVID-19–related morbidity and mortality in the United States and globally (*1*,*2*). However, vaccine effectiveness (VE) against COVID-19–associated hospitalization has declined over time, likely related to a combination of factors, including waning immunity and, with the emergence of the Omicron variant and its sublineages, immune evasion (*3*). To address these factors, on September 1, 2022, the Advisory Committee on Immunization Practices recommended a bivalent COVID-19 mRNA booster (bivalent booster) dose, developed against the spike protein from ancestral SARS-CoV-2 and Omicron BA.4/BA.5 sublineages, for persons who had completed at least a primary COVID-19 vaccination series (with or without monovalent booster doses) ≥2 months earlier (*4*). Data on the effectiveness of a bivalent booster dose against COVID-19 hospitalization in the United States are lacking, including among older adults, who are at highest risk for severe COVID-19–associated illness. During September 8–November 30, 2022, the Investigating Respiratory Viruses in the Acutely Ill (IVY) Network[§] assessed effectiveness of a bivalent booster dose received after ≥2 doses of monovalent mRNA vaccine against COVID-19–associated hospitalization among immunocompetent adults aged ≥65 years. When compared with unvaccinated persons, VE of a bivalent booster dose received ≥7 days before illness onset (median = 29 days) against COVID-19–associated hospitalization was 84%. Compared with persons who received ≥2 monovalent-only mRNA vaccine doses, relative VE of a bivalent booster dose was 73%. These early findings show that a bivalent booster dose provided strong protection against COVID-19–associated hospitalization in older adults and additional protection among persons with previous monovalent-only mRNA vaccination. All eligible persons, especially adults aged ≥65 years, should receive a bivalent booster dose to maximize protection against COVID-19 hospitalization this winter season. Additional strategies to prevent respiratory illness, such as masking in indoor public spaces, should also be considered, especially in areas where COVID-19 community levels are high (*4*,*5*).

During September 8–November 30, 2022, adults aged ≥65 years admitted for COVID-19–like illness[¶] to any of 22 hospitals in 18 states participating in the IVY Network were eligible for inclusion in this test-negative design, case-control analysis. Among patients hospitalized with COVID-19–like illness who received testing for SARS-CoV-2 by nucleic acid amplification test or antigen test, those who received a positive test result ≤10 days after illness onset and ≤3 days after hospital admission were classified as case-patients, and those who received a negative test result during the same interval were classified as control patients. Upper respiratory specimens were collected from enrolled patients and retested by reverse transcription–polymerase chain reaction for SARS-CoV-2 and influenza at a central laboratory (Vanderbilt University Medical

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[§] The IVY Network includes the following hospitals: Baystate Medical Center (Springfield, Massachusetts), Beth Israel Deaconess Medical Center (Boston, Massachusetts), Montefiore Medical Center (New York, New York), Vanderbilt University Medical Center (Nashville, Tennessee), University of Miami Medical Center (Miami, Florida), Emory University Medical Center (Atlanta, Georgia), Johns Hopkins Hospital (Baltimore, Maryland), Wake Forest University Baptist Medical Center (Winston-Salem, North Carolina), Baylor Scott & White Health – Baylor Scott & White Medical Center (Temple, Texas), University of Iowa Hospitals (Iowa City, Iowa), University of Michigan Hospital (Ann Arbor, Michigan), Hennepin County Medical Center (Minneapolis, Minnesota), Barnes-Jewish Hospital (St. Louis, Missouri), Cleveland Clinic (Cleveland, Ohio), The Ohio State University Wexner Medical Center (Columbus, Ohio), Stanford University Medical Center (Stanford, California), UCLA Medical Center (Los Angeles, California), UCHealth University of Colorado Hospital (Aurora, Colorado), Oregon Health & Sciences University Hospital (Portland, Oregon), Intermountain Medical Center (Murray, Utah), University of Washington (Seattle, Washington), and Baylor Scott & White Health – Baylor University Medical Center (Dallas, Texas).

[¶] COVID-19–like illness was defined as including any one of the following: fever, cough, shortness of breath, new or worsening findings on chest imaging consistent with pneumonia, or hypoxemia defined as oxygen saturation (SpO2) <92% on room air or supplemental oxygen to maintain SpO2 ≥92%. For patients on chronic oxygen therapy, hypoxemia was defined as SpO2 below baseline or an escalation of supplemental oxygen to maintain a baseline SpO2.

Center). Patients who were initially enrolled as controls on the basis of negative SARS-CoV-2 test results at their local hospital, but whose test results by central laboratory testing were positive, were reclassified as case-patients in the analysis. Control patients whose influenza test results were positive were excluded from the analysis because of potential correlation between COVID-19 and influenza vaccination behaviors (*6*).

Demographic and clinical data were obtained through electronic medical record (EMR) review and patient (or proxy) interview. COVID-19 mRNA vaccination status was verified from EMR, state-based registries, vaccination cards, or self-report. Three COVID-19 vaccination groups were defined as: 1) unvaccinated (no COVID-19 vaccine doses received); 2) vaccinated with ≥2 monovalent-only mRNA vaccine doses with last dose ≥2 months before illness onset; and 3) vaccinated with ≥2 monovalent-only mRNA vaccine doses plus a bivalent booster dose ≥2 months after receipt of the last monovalent mRNA vaccine dose. Analyses excluded patients with immunocompromising conditions,** those who received a bivalent booster dose <7 days before illness onset or ≤2 months after their last monovalent vaccine dose, those who received a non-mRNA COVID-19 vaccine, and those with other exclusions.††

Absolute VE against COVID-19–associated hospitalization was estimated by comparing the odds of bivalent booster dose receipt with no COVID-19 vaccination between case-patients and control patients. Relative VE, which is a measure of the additional protection against COVID-19 hospitalization from a bivalent booster dose compared with residual protection from previous monovalent vaccination, was estimated by comparing the odds of bivalent booster vaccination with receipt of ≥2 monovalent-only mRNA vaccine doses between case-patients and control patients. Relative VE was stratified by number of months (i.e., 2–5, 6–11, or ≥12) between the last monovalent vaccine dose and illness onset. Using multivariable logistic regression models, VE was estimated as (1 – adjusted odds ratio [aOR]) x 100). Models were adjusted for U.S. Department of Health and Human Services region, admission date in 2-week intervals, continuous age, sex, race, and Hispanic or Latino (Hispanic) ethnicity. Estimates with nonoverlapping 95% CIs were considered statistically significant. Analyses were conducted using SAS (version 9.4; SAS Institute). This activity was determined to be public health surveillance by each participating site and CDC, and was conducted consistent with all applicable federal laws and CDC policy.§§

During September 8–November 30, 2022, a total of 1,168 immunocompetent adults aged ≥65 years were enrolled in the IVY Network. After exclusion of 370 patients,¶¶ 798 (68%) were included in this analysis (381 case-patients and 417 control patients) (Table 1). The median age of included patients was 76 years (IQR = 70–83 years), 118 (15%) were non-Hispanic Black or African American, 78 (10%) were Hispanic, 588 (74%) had at least two underlying conditions, and 66 (8%) had self-reported or documented SARS-CoV-2 infection before the current illness episode during the Omicron period (December 26, 2021–November 30, 2022). Among the 381 case-patients, 81 (21%) were unvaccinated, 280 (73%) had received ≥2 monovalent-only mRNA vaccine doses, and 20 (5%) had received a bivalent booster dose. Among 417 control patients, 62 (15%) were unvaccinated, 296 (71%) had received ≥2 monovalent-only mRNA vaccine doses, and 59 (14%) had received a bivalent booster dose.

The median interval between receipt of a bivalent booster dose and illness onset was 29 days (IQR = 15–45 days) (Table 2). When compared with unvaccinated patients, VE of a bivalent booster dose in preventing COVID-19–associated hospitalization was 84%. When compared with patients who had received ≥2 monovalent-only mRNA vaccine doses ≥2 months before illness onset, relative VE of a bivalent booster dose was 73%. When compared with patients whose last monovalent dose was 6–11 months and ≥12 months before illness onset, relative VE of a bivalent booster dose was 78% and 83%, respectively. Small sample size precluded estimation of the relative VE of a bivalent booster dose compared with receipt of ≥2 monovalent-only mRNA vaccine doses with last dose 2–5 months before illness onset.***

** Immunocompromising conditions were defined as active solid tumor or hematologic cancer (i.e., newly diagnosed cancer or cancer treatment within the previous 6 months); solid organ transplant; bone marrow or stem cell transplant; HIV infection; congenital immunodeficiency syndrome; use of an immunosuppressive medication within the previous 30 days; splenectomy; or another condition that causes moderate or severe immunosuppression.

†† Exclusions: 1) immunocompromising conditions; 2) illness onset after hospital admission; 3) enrollment >7 days after hospital admission; 4) SARS-CoV-2-positive test result >3 days after hospital admission; 5) co-infection with influenza or respiratory syncytial virus (RSV); 6) positive influenza test result in control patients; 7) receipt of non-mRNA vaccine; 8) partial vaccination (receipt of only 1 mRNA vaccine dose); 9) receipt of last monovalent vaccine dose <2 months before illness onset; 10) receipt of bivalent vaccine dose <2 months after last monovalent dose; or 11) withdrawal from study.

§§ 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.

¶¶ A total of 370 patients were excluded from the analysis for the following reasons (not mutually exclusive): patient did not meet COVID-19–like illness definition (two); illness onset occurred after hospital admission (12); patient enrolled >7 days after hospital admission (21); inability to obtain an upper respiratory sample for central laboratory testing among controls (19); SARS-CoV-2 test >3 days after hospital admission (three); SARS-CoV-2 testing indeterminate (seven); case-patient received a positive influenza test result (three); control patient received a positive influenza test result (100); influenza testing indeterminate or not done (42); case-patient received a positive RSV test result (five); inability to verify vaccination status (71); received non-mRNA vaccine (66); partial vaccination (30); received last monovalent dose <2 months before illness onset (10); received bivalent COVID-19 mRNA booster dose <2 months after last monovalent dose (three); received COVID-19 vaccines outside of CDC guidelines (13); other sex (two); or withdrew (two).

*** VE estimates with 95% CIs >50 percentage points were not reported because of lack of precision.

TABLE 1. Characteristics of immunocompetent adults aged ≥65 years, hospitalized with COVID-like illness,* by COVID-19 case status — IVY Network, 22 hospitals,† 18 U.S. states, September 8, 2022–November 30, 2022

Characteristic	No. (%) Total (N = 798)	COVID-19 case-patients (n = 381)	Test-negative control patients (n = 417)
Vaccination status			
Unvaccinated	**143 (18)**	81 (21)	62 (15)
≥2 Monovalent-only mRNA doses	**576 (72)**	280 (73)	296 (71)
Bivalent booster dose§	**79 (10)**	20 (5)	59 (14)
Female sex	**442 (55)**	210 (55)	232 (56)
Median age, yrs (IQR)	**76 (70–83)**	78 (71–85)	75 (69–81)
Age group, yrs			
65–74	**345 (43)**	140 (37)	205 (49)
≥75	**453 (57)**	241 (63)	212 (51)
Race and ethnicity			
Black or African American, non-Hispanic	**118 (15)**	52 (14)	66 (16)
Hispanic or Latino, any race	**78 (10)**	40 (11)	38 (9)
White, non-Hispanic	**551 (69)**	264 (69)	287 (69)
Other race, non-Hispanic¶	**18 (2)**	8 (2)	10 (2)
Other**	**33 (4)**	17 (4)	16 (4)
HHS region†			
1	**155 (19)**	91 (24)	64 (15)
2	**50 (6)**	29 (8)	21 (5)
3	**9 (1)**	4 (1)	5 (1)
4	**94 (12)**	40 (11)	54 (13)
5	**125 (16)**	66 (17)	59 (14)
6	**99 (12)**	42 (11)	57 (14)
7	**68 (9)**	27 (7)	41 (10)
8	**145 (18)**	58 (15)	87 (21)
9	**29 (4)**	14 (4)	15 (4)
10	**24 (3)**	10 (3)	14 (3)
No. of underlying medical conditions			
0	**38 (5)**	15 (4)	23 (6)
1	**172 (22)**	91 (24)	81 (19)
2	**243 (30)**	115 (30)	128 (31)
≥3	**345 (43)**	160 (42)	185 (44)
Previous Omicron infection††	**66 (8)**	24 (6)	42 (10)

TABLE 1. (*Continued*) Characteristics of immunocompetent adults aged ≥65 years, hospitalized with COVID-like illness,* by COVID-19 case status — IVY Network, 22 hospitals,† 18 U.S. states, September 8, 2022–November 30, 2022

Abbreviation: HHS = U.S. Department of Health and Human Services.

* COVID-19–like illness was defined as including any one of the following: fever, cough, shortness of breath, new or worsening findings on chest imaging consistent with pneumonia, or hypoxemia defined as oxygen saturation (SpO2) <92% on room air or supplemental oxygen to maintain SpO2 ≥92%. For patients on chronic oxygen therapy, hypoxemia was defined as SpO2 below baseline or an escalation of supplemental oxygen to maintain a baseline SpO2.

† Hospitals by HHS region included *Region 1:* Baystate Medical Center (Springfield, Massachusetts) and Beth Israel Deaconess Medical Center (Boston, Massachusetts); *Region 2:* Montefiore Medical Center (New York, New York); *Region 3:* Johns Hopkins Hospital (Baltimore, Maryland); *Region 4:* Emory University Medical Center (Atlanta, Georgia), University of Miami Medical Center (Miami, Florida), Vanderbilt University Medical Center (Nashville, Tennessee), and Wake Forest University Baptist Medical Center (Winston-Salem, North Carolina); *Region 5:* Cleveland Clinic (Cleveland, Ohio), Hennepin County Medical Center (Minneapolis, Minnesota), The Ohio State University Wexner Medical Center (Columbus, Ohio), and University of Michigan Hospital (Ann Arbor, Michigan); *Region 6:* Baylor Scott & White Health – Baylor Scott & White Medical Center (Temple, Texas) and Baylor Scott & White Health – Baylor University Medical Center (Dallas, Texas); *Region 7:* Barnes-Jewish Hospital (St. Louis, Missouri) and University of Iowa Hospitals (Iowa City, Iowa); *Region 8:* Intermountain Medical Center (Murray, Utah) and UCHealth University of Colorado Hospital (Aurora, Colorado); *Region 9:* Stanford University Medical Center (Stanford, California) and UCLA Medical Center (Los Angeles, California); and *Region 10:* Oregon Health & Science University Hospital (Portland, Oregon) and University of Washington (Seattle, Washington).

§ Bivalent COVID-19 mRNA booster dose recipients received ≥2 monovalent COVID-19 mRNA doses ≥2 months before their bivalent booster dose.

¶ Other race, non-Hispanic includes Asian, Native American or Alaska Native, and Native Hawaiian or other Pacific Islander; these groups were combined because of small counts.

** Self-reported race and ethnicity as other, or patients for whom information on race and ethnicity was unavailable.

†† Previous Omicron infection was defined by date of self-reported or documented previous SARS-CoV-2 infection that occurred during December 26, 2021–November 30, 2022.

Discussion

Among immunocompetent adults aged ≥65 years hospitalized within the IVY Network in 18 states, a bivalent booster dose received after ≥2 monovalent mRNA doses provided strong protection against COVID-19–associated hospitalization during a period of Omicron BA.5 or BQ.1/BQ.1.1 predominance (*7*). Substantial additional protection from a bivalent booster dose was observed when compared with remote monovalent-only mRNA vaccination, which suggests important incremental benefit for persons eligible to receive a bivalent vaccine booster. These early findings from a cohort of adults aged ≥65 years, 74% of whom had multiple underlying conditions, are among the first to document real-world evidence that receipt of a bivalent booster dose after completion of at least a primary COVID-19 mRNA vaccination series is protective against COVID-19 hospitalization. Continued monitoring will be important to understand ongoing protection in the context of expanding Omicron sublineages and new emerging variants, as well as whether waning of bivalent vaccine-induced immunity over time is observed, similar to that seen after monovalent COVID-19 mRNA vaccine booster doses.

Recent findings from the United Kingdom and the United States have also demonstrated protection of a bivalent mRNA booster dose against COVID-19 hospitalization (*8*,*9*). The bivalent mRNA booster vaccine used in the United Kingdom contains spike protein mRNA from ancestral SARS-CoV-2 plus Omicron BA.1, in contrast to the bivalent booster vaccines used in the United States, which contain mRNA from ancestral SARS-CoV-2 and Omicron BA.4/BA.5. In the United Kingdom, among adults aged ≥50 years or those in clinical risk groups, a BA.1 bivalent booster dose was found to have a relative VE of 57% (95% CI = 48%–65%) compared with ≥2 COVID-19 vaccine doses received ≥6 months earlier (*8*). Similarly, a report among adults aged ≥18 years from the VISION Network in the United States using BA.4/BA.5 bivalent booster doses showed a relative VE of

TABLE 2. Effectiveness of a bivalent COVID-19 mRNA booster dose against COVID-19–associated hospitalization among immunocompetent adults aged ≥65 years — IVY Network, 22 hospitals,* 18 states, September 8, 2022–November 30, 2022

Characteristic	Received BV vaccine dose, by case status, n/N (%)		Median interval† from last vaccine dose to illness onset (IQR), days	Adjusted VE, % (95% CI)§
	Case-patients	Control patients		
Absolute VE (BV booster dose versus no vaccine)				
Unvaccinated (Ref)	—	—	NA	—
BV booster dose¶ ≥7 days before illness onset	20/101 (20)	59/121 (49)	29 (15–45)	84 (64–93)
Relative VE (BV booster dose versus MV-only, by interval since last dose)				
≥2 MV-only mRNA doses, last dose ≥2 mos before illness onset (Ref)	—	—	305 (168–377)	—
BV booster dose ≥7 days before illness onset	20/300 (7)	59/355 (17)	29 (15–45)	73 (52–85)
≥2 MV-only mRNA doses, last dose 2–5 mos before illness onset (Ref)	—	—	137 (111–155)	—
BV booster dose ≥7 days before illness onset	20/82 (24)	59/155 (38)	29 (15–45)	—**
≥2 MV-only mRNA doses, last dose 6–11 mos before illness onset (Ref)	—	—	304 (258–333)	—
BV booster dose ≥7 days before illness onset	20/155 (13)	59/176 (34)	29 (15–45)	78 (57–89)
≥2 MV-only mRNA doses, last dose ≥12 mos before illness onset (Ref)	—	—	528 (386–575)	—
BV booster dose ≥7 days before illness onset	20/103 (19)	59/142 (42)	29 (15–45)	83 (63–92)

Abbreviations: BV = bivalent; MV = monovalent; NA = not applicable; Ref = referent group; VE = vaccine effectiveness.

* The IVY Network includes the following hospitals: Baystate Medical Center (Springfield, Massachusetts), Beth Israel Deaconess Medical Center (Boston, Massachusetts), Montefiore Medical Center (New York, New York), Vanderbilt University Medical Center (Nashville, Tennessee), University of Miami Medical Center (Miami, Florida), Emory University Medical Center (Atlanta, Georgia), Johns Hopkins Hospital (Baltimore, Maryland), Wake Forest University Baptist Medical Center (Winston-Salem, North Carolina), Baylor Scott & White Health – Baylor Scott & White Medical Center (Temple, Texas), University of Iowa Hospitals (Iowa City, Iowa), University of Michigan Hospital (Ann Arbor, Michigan), Hennepin County Medical Center (Minneapolis, Minnesota), Barnes-Jewish Hospital (St. Louis, Missouri), Cleveland Clinic (Cleveland, Ohio), The Ohio State University Wexner Medical Center (Columbus, Ohio), Stanford University Medical Center (Stanford, California), UCLA Medical Center (Los Angeles, California), UCHealth University of Colorado Hospital (Aurora, Colorado), Oregon Health & Sciences University Hospital (Portland, Oregon), Intermountain Medical Center (Murray, Utah), University of Washington (Seattle, Washington), and Baylor Scott & White Health – Baylor University Medical Center (Dallas, Texas).

† For patients who received a BV booster dose, median time since last dose refers to the number of days between receipt of the BV booster dose and illness onset. For patients who received ≥2 MV doses without a BV booster dose, median time since last dose refers to the number of days between receipt of the last MV dose and illness onset.

§ VE was estimated by comparing the odds of being BV-vaccinated among case-patients to the odds of being BV-vaccinated among control patients, calculated as VE = 100 × (1 − odds ratio). Logistic regression models were adjusted for date of hospital admission (biweekly intervals), U.S. Department of Health and Human Services (10 regions), continuous age, sex, and race and ethnicity (non-Hispanic Black or African American, Hispanic of any race, non-Hispanic White, non-Hispanic other race, or other or unknown).

¶ BV COVID-19 mRNA booster dose recipients received ≥2 MV COVID-19 mRNA doses ≥2 months before their BV booster dose.

** VE estimate was not reported because of insufficient sample size. 95% CI width >50 percentage points.

42% (95% CI = 19%–58%) against COVID-19–associated hospitalization compared with ≥2 monovalent COVID-19 vaccine doses received 8–10 months earlier (*9*). Overall, these results were similar to the relative VE findings in the current study, suggesting that bivalent booster doses provide important benefits.

The findings in this report are subject to at least five limitations. First, the sample size was not sufficient to estimate VE by the number of COVID-19 monovalent vaccine doses received before the bivalent booster dose or compared with patients whose most recent monovalent vaccine dose was received 2–5 months before illness onset. Second, because use of monovalent COVID-19 mRNA vaccines as a booster dose is no longer authorized in the United States,††† this analysis could not compare the effectiveness of a bivalent booster dose with a monovalent booster dose administered during the same period. Third, the analysis period includes both BA.5- and BQ.1/BQ.1.1–predominant periods; therefore, variant-specific VE could not be evaluated. Fourth, previous SARS-CoV-2 infection during the Omicron period was rarely reported or documented among patients in this analysis, which prevented evaluation of the impact of previous infection on VE. Finally, selection bias and residual confounding bias cannot be excluded, including from risk behaviors or preventive treatments.

These early findings from a multistate network show that among adults aged ≥65 years, many of whom have multiple comorbid conditions and who are at highest risk of severe COVID-19, recent bivalent booster vaccination offers substantial added protection against COVID-19 hospitalization. Although prevention of COVID-19 hospitalizations is a core goal of the U.S. vaccination program, bivalent booster dose coverage in the United States remains low among adults aged ≥18 years (16%) and adults aged ≥65 years (36%) (*10*). Increasing bivalent booster coverage among eligible U.S. adults has the potential to prevent COVID-19 hospitalizations as COVID-19 incidence and transmission increase. All eligible persons, especially adults aged ≥65 years, should receive a bivalent booster dose to maximize protection against COVID-19 hospitalization this winter season. Additional strategies to

††† https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-moderna-pfizer-biontech-bivalent-covid-19-vaccines-use (Accessed December 9, 2022).

Summary

What is already known about this topic?

Immunity from monovalent COVID-19 mRNA vaccination wanes over time. A bivalent COVID-19 mRNA booster dose is recommended for all eligible persons; however, little is known about its effectiveness against COVID-19 hospitalization.

What is added by this report?

Among immunocompetent adults aged ≥65 years hospitalized in the multistate IVY Network, a bivalent booster dose provided 73% additional protection against COVID-19 hospitalization compared with past monovalent mRNA vaccination only.

What are the implications for public health practice?

To maximize protection against severe COVID-19 this winter season, all eligible persons, especially adults aged ≥65 years, should receive a bivalent booster dose and consider additional prevention strategies, including masking in indoor public spaces.

prevent respiratory illness, such as masking in indoor public spaces, should also be considered, especially in areas where COVID-19 community levels are high (*4*,*5*).

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Notes from the Field

Clinical and Epidemiologic Characteristics of Mpox Cases from the Initial Phase of the Outbreak — New York City, May 19–July 15, 2022

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Monkeypox virus (MPXV), an *Orthopoxvirus* that can cause monkeypox (mpox) disease in humans, was rarely seen outside Africa before 2022. Since May 2022, mpox has been reported in multiple countries and regions without endemic transmission, including the United States (*1*). New York City (NYC) quickly became one of the major foci of the 2022 outbreak after the first case in a NYC resident was diagnosed on May 19.* Epidemiologic profiles and clinical characteristics of mpox cases in the United States during this outbreak have been described (*2*,*3*), but previous summaries were limited by incomplete data or inclusion of only a subset of cases (*2*,*3*). Most case investigation data from mpox cases reported to the NYC Department of Health and Mental Hygiene (DOHMH) surveillance system have a high degree of completeness for gender, race or ethnicity, sexual orientation, and clinical signs and symptoms. To describe the characteristics of mpox in NYC, case investigation data for NYC residents with mpox diagnosed during May 19–July 15, 2022, were analyzed. Using a standardized form, DOHMH staff members attempted to interview all NYC residents with probable (a positive non-variola Orthopoxvirus polymerase chain reaction [PCR] test result)† or confirmed (a positive MPXV–specific PCR test result) mpox reported to DOHMH through mandated laboratory reporting. For patients who declined an interview or were unreachable, information obtained from medical care providers during DOHMH consultation calls was used. This activity was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.§

Among 719 NYC patients with probable or confirmed mpox, 704 (97.9%) were men; 566 (78.7%) were gay, lesbian, or queer; and 40 (5.6%) were bisexual (Table). Among 651 patients with available data on intimate or sexual exposure, 505 (77.6%) reported intimate or sexual contact with men, and among 611 patients with known contact data, 103 (16.9%) reported contact with persons with suspected mpox during the 3 weeks preceding their symptom onset. Prodromal symptoms were reported by 234 (38.1%) of 614 patients with symptom data; 277 patients (45.1%) reported proctitis or rectal symptoms (e.g., constipation, tenesmus, rectal pain, rectal bleeding, or blood in stool), 192 (69.3%) of whom did not observe perianal skin lesions, and eight (3.0%) of whom did not have any skin lesions when rectal symptoms began. Among 584 patients reporting skin lesions, 216 (37.0%) and 117 (20.0%) had genital and perianal involvement, respectively. Ophthalmic manifestations¶ were reported by 38 (6.2%) patients. The median interval from symptom onset to diagnosis was 5 days (range = 3–7 days); 101 (14.0%) patients received tecovirimat, and 35 (4.9%) were hospitalized.

Data on gender, race or ethnicity, and sexual orientation from the DOHMH surveillance system were >80% complete for patients with mpox diagnosed during the study period; these data informed public health outreach and intervention efforts.** Whereas ophthalmic involvement has been rarely reported in the current global mpox outbreak, 38 (6.2%) of 614 patients in this analysis reported ophthalmic manifestations, which can require urgent clinical management and result in longer-term sequelae (*4*). More than two thirds of patients with proctitis or rectal symptoms did not report perianal skin lesions. Moreover, a small number of these patients reported no skin lesions at onset of rectal symptoms. Although the current recommended method of swabbing skin lesions to diagnose mpox does not include collection of anorectal swabs, MPXV can be detected from anorectal swabs in patients with rectal symptoms†† (*5*). Additional studies evaluating anorectal swabs for use in mpox diagnosis might expand the range of potential specimens and enhance the possibility for early diagnosis among symptomatic persons at risk for mpox but without cutaneous lesions.

The findings in this report are subject to at least two limitations. First, data were missing for approximately 15% of

* https://www.nyc.gov/site/doh/data/health-tools/monkeypox.page

† Swabs from skin lesions were tested for *Orthopoxvirus* or non-variola *Orthopoxvirus* at DOHMH Public Health Laboratory, commercial, or academic laboratories. CDC tested swabs submitted from DOHMH for *Orthopoxvirus* or non-variola *Orthopoxvirus* in addition to an MPXV-specific test.

§ 45 C.F.R. part 46.102(l)(2), 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.

¶ Includes eye lesion, conjunctivitis, red eyes, or eye discharge.

** https://www.nyc.gov/site/doh/about/press/pr2022/health-department-releases-monkeypox-vaccination-demographic-data.page

†† https://www.cdc.gov/poxvirus/monkeypox/about/science-behind-transmission.html

TABLE. Characteristics of patients with probable and confirmed mpox (N = 719) — New York City, May 19–July 15, 2022

Characteristic (no. with available information)*	No. (%)
Age, yrs, median (IQR)	35 (31–41)
Gender†	
Female	2 (0.3)
Male	704 (97.9)
Transgender, nonbinary, or genderqueer	12 (1.7)
Unknown	1 (0.1)
Sexual orientation	
Bisexual	40 (5.6)
Gay, lesbian, or queer	566 (78.7)
Straight or heterosexual	18 (2.5)
Unknown	95 (13.2)
Race and ethnicity	
Asian or Pacific Islander	37 (5.2)
Black or African American	148 (20.6)
Hispanic or Latino	212 (29.5)
White	247 (34.4)
Unknown	75 (10.4)
Possible exposure ≤3 weeks before symptom onset	
Had intimate or sexual contact (n = 651)§	**521 (80.0)**
No. of partners, median (IQR)	3 (1–5)
Contact with men	505 (77.6)
No. of partners, median (IQR)	3 (1–5)
Contact with women	17 (2.6)
No. of partners, median (IQR)	1 (1–2)
Contact with persons who identify as transgender, nonbinary, genderqueer, or other gender identity	7 (1.1)
No. of partners, median (IQR)	1.5 (1–5)
Contact with persons with unknown gender identities	6 (0.9)
No. of partners, median (IQR)	1 (1–3)
Self-reported contact with a person with suspected mpox (n = 611)¶,**	**103 (16.9)**
Intimate or sexual contact	66 (64.1)
Household contact	5 (4.8)
Other	13 (12.6)
Unknown	20 (19.4)
Symptomatic	
Yes	614 (85.4)
Unknown	105 (14.6)
Presence of prodrome (n = 614)††	**234 (38.1)**
Sign or symptom (n = 614)§§	
Fever	360 (58.6)
Body or muscle ache, myalgia, or back pain	327 (53.3)
Fatigue	319 (51.9)
Chills	299 (48.7)
Lymphadenopathy	298 (48.5)
Itching or pruritus	291 (47.4)
Proctitis or rectal sign or symptom¶¶	277 (45.1)
Proctitis	111 (40.0)
Constipation	100 (36.1)
Tenesmus	102 (36.8)
Rectal pain	211 (76.2)
Rectal bleeding	108 (39.0)
Blood in stool	97 (35.0)
Headache	253 (41.2)
Night sweats	253 (41.2)
Malaise	236 (38.4)
Sore throat	173 (28.2)
Runny nose or cough	118 (19.2)
Gastrointestinal***	96 (15.6)
Ophthalmic manifestations†††	38 (6.2)

TABLE. (*Continued*) Characteristics of patients with probable and confirmed mpox (N = 719) — New York City, May 19–July 15, 2022

Characteristic (no. with available information)*	No. (%)
Presence of skin lesion (n = 614)	
Yes	584 (95.1)
Unknown	30 (4.9)
No. of skin lesions (n = 584)	
1–9	227 (38.9)
10–49	192 (32.8)
50–99	20 (3.4)
≥100	4 (0.7)
Unknown	141 (24.1)
Location of skin lesion (n = 584)§§§	
Upper or lower extremities	234 (40.1)
Genitals	216 (37.0)
Face, mouth, or lip	194 (33.2)
Torso (i.e., chest, abdomen, back, or trunk)	184 (31.5)
Perianal	117 (20.0)
Hand or foot	116 (19.9)
Buttocks	108 (18.5)
Scalp, head, or neck	108 (18.4)
Palms or soles	81 (13.9)
Eye	3 (0.5)
Other	85 (14.5)
Location where skin lesion began (n = 584)	
Genitals	178 (30.5)
Upper or lower extremities	134 (22.9)
Face, mouth, or lip	98 (16.8)
Torso or back	76 (13.0)
Perianal	72 (12.3)
Palms or soles	42 (7.2)
Neck	28 (4.8)
Other	87 (14.9)
Unknown	143 (24.5)
HIV infection, self- or provider-reported	181 (25.2)
Interval from symptom onset to diagnosis, days, median (IQR)	5 (3–7)
Receipt of PEP with JYNNEOS vaccine 0–14 days after last exposure	10 (1.4)
Initiated treatment with tecovirimat	101 (14.0)
Hospitalized	35 (4.9)

Abbreviations: mpox = monkeypox; PEP = postexposure prophylaxis.

* Unknown category included patients with missing data or patients who responded "do not know" or "declined to answer" to the survey question.
† Transgender women or men are included with transgender, nonbinary, or genderqueer. Groups are mutually exclusive.
§ Patients could report intimate or sexual contact with more than one gender.
¶ Suspected mpox case defined as a person with a diagnosis of mpox or with compatible signs or symptoms. Patient could report more than one type of contact.
** Percentage of persons who reported contact with a person with suspected mpox.
†† Presence of nondermatologic signs or symptoms before onset of skin lesion.
§§ Patients could have more than one sign or symptom.
¶¶ Percentage of patients with proctitis or rectal signs or symptoms.
*** Includes nausea, vomiting, abdominal pain, or discomfort.
††† Includes eye lesion, conjunctivitis, red eyes, or eye discharge.
§§§ Patient could have skin lesions in more than one location.

patients, more than one half of whom were unreachable for interview; these persons might differ systematically from those who were interviewed. Second, mpox testing and treatment resources were limited during the study period, and the epidemiology has since evolved; thus, these findings might not be generalizable throughout the outbreak.

These findings can guide development of public health messaging to communities with increased likelihood of exposure to mpox; in addition to avoiding close personal contact with someone with mpox and recommendations for eligible persons to receive mpox vaccine, the clinical manifestations described in this report can guide providers managing patients with mpox. Further studies are needed to assess the potential utility of anorectal swabs in early diagnosis of mpox.

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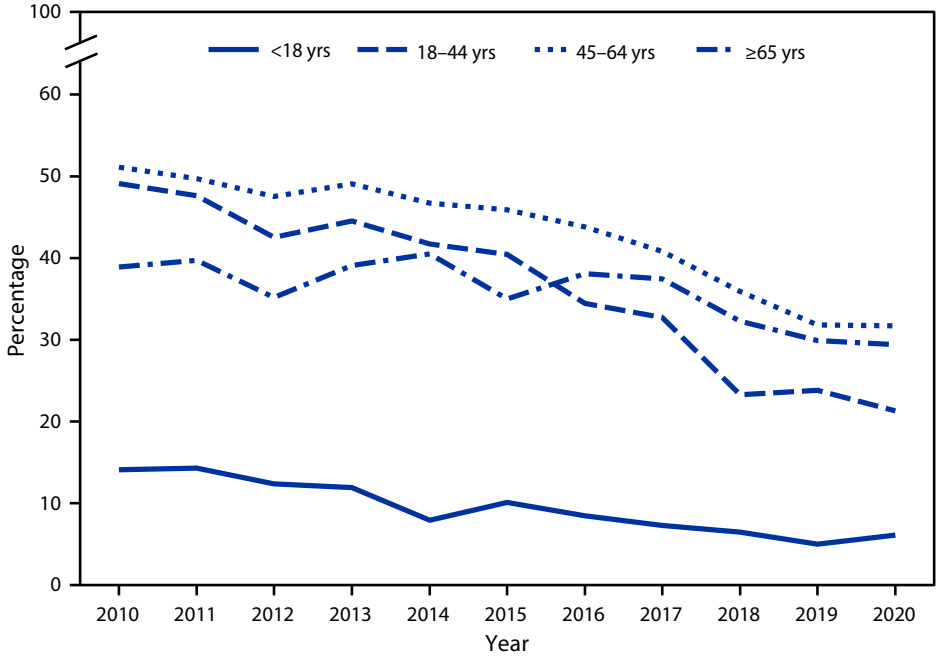
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage of Emergency Department Visits for Pain* at Which Opioids† Were Given or Prescribed, by Patient Age and Year — National Hospital Ambulatory Medical Care Survey, United States, 2010–2020



Abbreviation: ED = emergency department.

* Based on a sample of visits to EDs in noninstitutional general and short-stay hospitals, exclusive of federal, military, and Veterans Administration hospitals, located in the 50 states and the District of Columbia. Pain-related visits were defined using up to three reasons for visit coded according to the National Center for Health Statistics Reason for Visit Classification (https://www.cdc.gov/nchs/data/series/sr_02/sr02_078.pdf) and grouped using an algorithm (https://jamanetwork.com/journals/jama/fullarticle/1149438).

† Visits with at least one opioid given in the ED or prescribed at discharge. Opioids were defined using the Cerner Multum (https://www.cerner.com/solutions/drug-database) third-level therapeutic category codes for narcotic analgesics (code 60) and narcotic-analgesic combinations (code 191). Visits with only buprenorphine or buprenorphine-naloxone given or prescribed were not included.

During 2010–2020, the percentages of ED visits for pain in which an opioid was given or prescribed decreased for all age groups. During this period, visits were lowest for persons aged <18 years, decreasing from 14.1% in 2010 to 6.1% in 2020. Among the adult age groups, adults aged 18–44 years experienced the greatest decrease during the period, declining from 49.1% to 21.3%. At the beginning of the period, percentages were lower for adults aged ≥65 years compared with those aged 18–44 years, but in 2016 that pattern reversed.

Source: National Center for Health Statistics. National Hospital Ambulatory Medical Care Survey, 2010–2020. https://www.cdc.gov/nchs/ahcd/index.htm

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For more information on this topic, CDC recommends the following link: https://www.cdc.gov/drugoverdose/index.html

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