Potential for Recurrent Mpox Outbreaks Among Gay, Bisexual, and Other Men Who Have Sex with Men — United States, 2023

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More than 30,000 monkeypox (mpox) cases have been diagnosed in the United States since May 2022, primarily among gay, bisexual, and other men who have sex with men (MSM) (*1,2*). In recent months, diagnoses have declined to one case per day on average. However, mpox vaccination coverage varies regionally, suggesting variable potential risk for mpox outbreak recurrence (*3*). CDC simulated dynamic network models representing sexual behavior among MSM to estimate the risk for and potential size of recurrent mpox outbreaks at the jurisdiction level for 2023 and to evaluate the benefits of vaccination for preparedness against mpox reintroduction. The risk for outbreak recurrence after mpox reintroduction is linearly (inversely) related to the proportion of MSM who have some form of protective immunity: the higher the population prevalence of immunity (from vaccination or natural infection), the lower the likelihood of recurrence in that jurisdiction across all immunity levels modeled. In contrast, the size of a potential recurrent outbreak might have thresholds: very small recurrences are predicted for jurisdictions with mpox immunity of 50%–100%; exponentially increasing sizes of recurrences are predicted for jurisdictions with 25%–50% immunity; and linearly increasing sizes of recurrences are predicted for jurisdictions with <25% immunity. Among the 50 jurisdictions examined, 15 are predicted to be at minimal risk for recurrence because of their high levels of population immunity. This analysis underscores the ongoing need for accessible and sustained mpox vaccination to decrease the risk for and potential size of future mpox recurrences.

CDC adapted models of mpox transmission to estimate the risk for and size of potential mpox recurrences at varying levels of population-level mpox immunity (*4,5*). Immunity varied from 0%–99% in increments of approximately 4%. Immunity levels included persons who had received 1 or 2 vaccine doses or had a history of infection, which conveyed 37%, 67%, and 100% reduction in susceptibility to infection, respectively (*6*). At each immunity level modeled, 29%, 67%, and 4% of those with some immunity were assumed to have 1-dose, 2-dose, or infection-acquired immunity, respectively, with immunity concentrated among MSM with higher levels of sexual activity (*3,4*). Sensitivity analyses considered 65% and 83% reductions in susceptibility associated with receipt of 1 or 2 doses, respectively (*6*).

To model mpox reintroduction, five MSM with infectious mpox and high levels of sexual activity were introduced to the sexual network. Depending on the level of immunity and chance, introduced cases either initiated an outbreak (of variable size) or failed to sustain transmission. An outbreak

Continuing Education examination available at https://www.cdc.gov/mmwr/mmwr_continuingEducation.html

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was defined as a simulation with sustained mpox incidence 3 months after reintroduction. For each immunity level, model simulations were conducted until 50 simulated recurrent outbreaks occurred. This analysis assumed no additional vaccination after April 28, 2023, no behavioral adaptation (such as decreasing partner acquisition rates) among MSM in response to new mpox cases, and no loss of immunity due to demographic turnover during the 2-year period modeled.

Risk was assessed at the jurisdiction level for the 50 non-state, Ending the HIV Epidemic (EHE) Initiative jurisdictions based on these results and each jurisdiction's case and vaccine administration data, through April 2023 (4,5). These jurisdictions, many of which contain urban centers with large MSM populations, account for more than one half of all new HIV diagnoses.* The numerator for jurisdiction immunity level was the sum of persons who had received 1 and 2 doses of JYNNEOS vaccine and those who had already been infected, accounting for potential incomplete reporting (2,3,5). The denominator was based on the population at increased risk for *Monkeypox virus* exposure, estimated as the number of MSM aged ≥16 years who were recommended to receive HIV preexposure prophylaxis and the number of MSM aged ≥13 years living with HIV in each jurisdiction, using publicly available data (7,8). The estimated population was then increased by 25% for each jurisdiction to account for additional persons

eligible for vaccination (e.g., MSM with lower levels of sexual activity than their already-eligible partners). Statistical models were fit to the simulated outbreak results to summarize the relationship between immunity level and both risk for and size of outbreak recurrence; each jurisdiction's risk for and size of outbreak recurrence was then then inferred based on jurisdiction-specific immunity using these fitted curves. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[†]

Conditional on mpox reintroduction into a jurisdiction, the risk for a recurrent mpox outbreak is linearly related to immunity: each percentage point increase in population immunity reduces outbreak risk by 0.62 percentage points across all immunity levels modeled (Figure 1). For example, Suffolk County, Massachusetts, with an estimated at-risk population immunity of 64%, has a 21% risk for a recurrent outbreak, whereas Harris County, Texas, with 17% immunity has a 50% risk, conditional on reintroduction (Table). No critical threshold to avert a recurrent mpox outbreak was identified; higher vaccination coverage among MSM at risk provides continued decreased recurrence risk across all immunity levels modeled. Sensitivity analyses using higher efficacy estimates of 65% and 83%, respectively, decreased the recurrence risk by 6 percentage points when population immunity was >20% (Supplementary Figure, https://stacks.cdc.gov/view/cdc/128422).

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* https://www.cdc.gov/endhiv/about.html

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

FIGURE 1. Risk* for recurrent mpox outbreak lasting >3 months, by immunity level[†] — United States, 2023
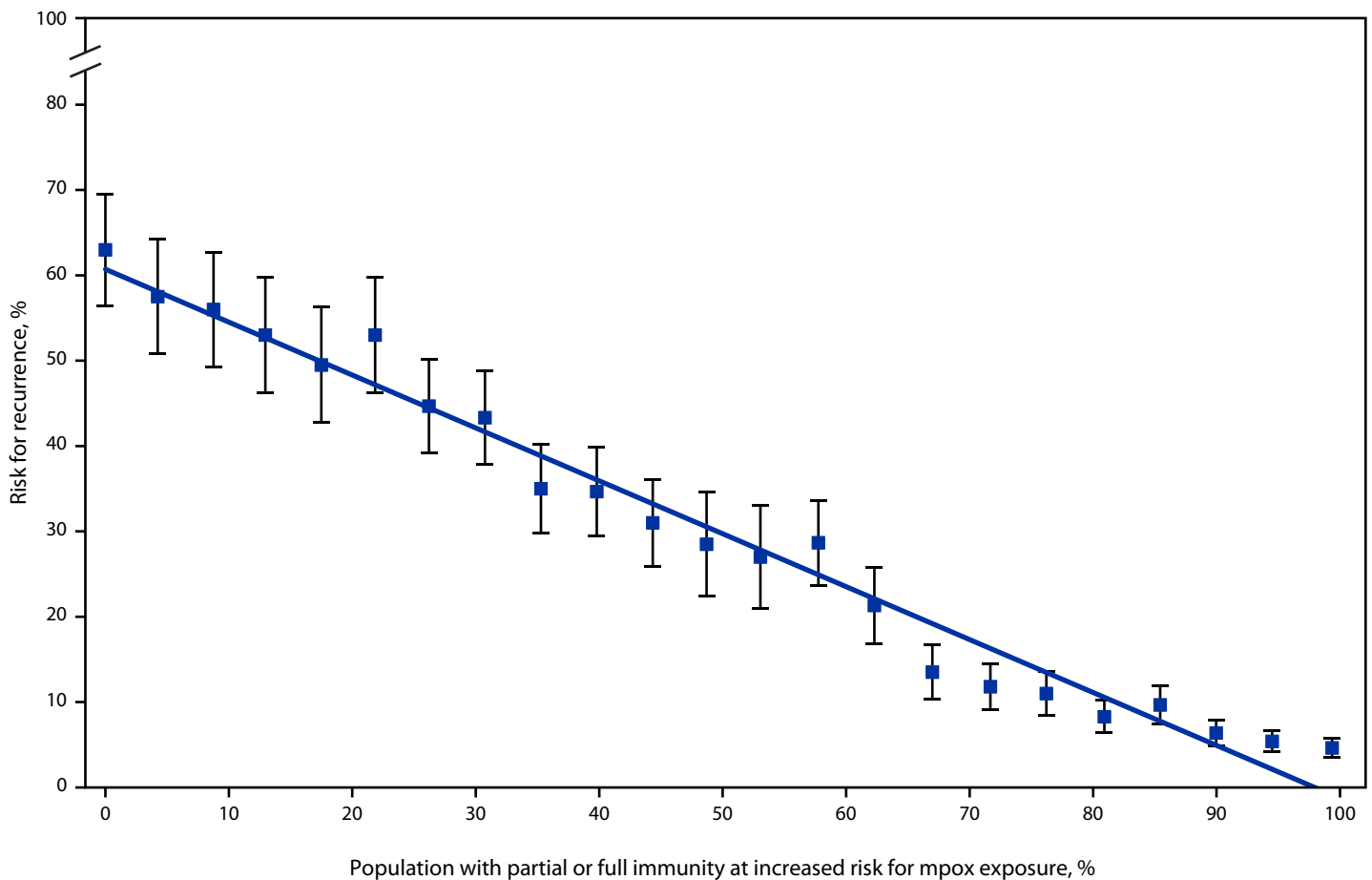
Abbreviations: mpox = monkeypox; MSM = gay, bisexual, and other men who have sex with men.
* Data points reflect simulated risk for a specific immunity level; line reflects predictions from linear model using immunity level as the independent variable and risk for recurrence as the dependent variable; error bars indicate 95% CIs assuming a binomial distribution based on the number of simulations required to produce 50 outbreaks.
[†] Immunity was varied from 0% to 99% in increments of approximately 4%; at each level of immunity, 29%, 67%, and 4% of MSM with some immunity are assumed to have 1-dose, 2-dose, or infection-acquired immunity, conveying 37%, 67%, and 100% protection, respectively.

In contrast to the linear relationship between increasing levels of immunity in the population at risk and the risk for a recurrent outbreak, immunity does have a threshold effect on the size of a recurrent outbreak (Figure 2). Three distinct jurisdictional groupings were identified: those with high, medium, and low immunity, defined as 50%–100%, 25%–49%, and <25% vaccine- or infection-induced immunity, respectively. High-immunity jurisdictions were predicted to experience small recurrences that resolved within 1 year. Medium-immunity jurisdictions were transitional, with more uncertainty: recurrence size increased exponentially and lasted 12–17 months. Finally, low-immunity jurisdictions were predicted to experience recurrences lasting 18–20 months that increased linearly in size with decreasing levels of immunity.

Overall, 44% of MSM at increased risk for *Monkeypox virus* exposure who live in EHE jurisdictions live in high-immunity jurisdictions that are likely to have minimal risk for recurrence, including Los Angeles, New York City, San Francisco, and Washington, DC (Table). However, 56% of MSM at increased risk for exposure who live in EHE jurisdictions live in low- or medium-immunity jurisdictions that are potentially at risk for mpox recurrences capable of sustained transmission should reintroduction occur (Table).

Discussion

This analysis, which highlights the association between population mpox immunity and the risk for outbreak recurrence, underscores the need for accessible and sustained mpox vaccination services, particularly in communities with

TABLE. Jurisdiction-specific estimates of immunity and inferred* risk and size of mpox recurrence — United States, 2023

Jurisdiction	Estimated immunity level, %[†]	Inferred* risk for recurrence, %	Inferred* cumulative *Monkeypox virus* infections vs. 2022[§]	Jurisdictional immunity grouping[¶]	MSM at increased risk for *Monkeypox virus* exposure**
Duval County, Florida	6	57	4.08	Low	12,425
Shelby County, Tennessee	10	55	3.77	Low	10,626
Hamilton County, Ohio	10	55	3.79	Low	9,970
Bexar County, Texas	11	54	3.67	Low	17,916
Dallas County, Texas	12	53	3.62	Low	45,264
Tarrant County, Texas	15	51	3.32	Low	15,909
Palm Beach County, Florida	15	52	3.36	Low	12,824
Hillsborough County, Florida	15	52	3.39	Low	17,802
Wayne County, Michigan	16	51	3.29	Low	14,705
Harris County, Texas	17	50	3.16	Low	60,769
San Bernardino County, California	18	49	3.07	Low	15,829
East Baton Rouge Parish, Louisiana	18	50	3.14	Low	3,735
Baltimore City, Maryland	19	49	3.04	Low	10,800
Pinellas County, Florida	20	48	2.96	Low	13,430
Gwinnett County, Georgia	21	48	2.89	Low	5,672
Marion County, Indiana	24	46	2.60	Low	12,681
Fulton County, Georgia	25	45	2.58	Low	27,831
Prince George's County, Maryland	26	44	2.03	Medium	9,007
Orange County, Florida	26	45	2.09	Medium	21,838
Dekalb County, Georgia	26	45	2.12	Medium	14,053
Cuyahoga County, Ohio	27	44	1.90	Medium	11,470
Cobb County, Georgia	27	44	1.96	Medium	5,980
Essex County, New Jersey	29	43	1.66	Medium	7,806
Franklin County, Ohio	31	42	1.41	Medium	15,752
Travis County, Texas	32	41	1.30	Medium	16,218
San Juan Municipio, Puerto Rico	32	41	1.30	Medium	3,773
Maricopa County, Arizona	32	41	1.33	Medium	33,513
Mecklenburg County, North Carolina	33	40	1.18	Medium	12,947
Montgomery County, Maryland	34	40	1.10	Medium	7,515
Clark County, Nevada	36	39	0.97	Medium	20,231
Bronx County, New York	36	39	0.98	Medium	19,723
Hudson County, New Jersey	37	38	0.86	Medium	8,009
Miami-Dade County, Florida	40	36	0.72	Medium	40,489
Orange County, California	45	33	0.48	Medium	17,090
Philadelphia County, Pennsylvania	47	32	0.42	Medium	18,771
Sacramento County, California	52	28	0.20	High	9,723
San Diego County, California	54	27	0.19	High	27,536
Riverside County, California	58	25	0.18	High	21,314
Broward County, Florida	59	24	0.18	High	33,886
Orleans Parish, Louisiana	61	23	0.18	High	8,057
Cook County, Illinois	63	22	0.17	High	60,444
Los Angeles County, California	63	22	0.17	High	117,361
Suffolk County, Massachusetts	64	21	0.17	High	10,356
King County, Washington	65	20	0.16	High	24,308
Alameda County, California	75	14	0.14	High	14,167
Queens County, New York	78	12	0.13	High	20,057
District of Columbia	98	<1	0.08	High	22,348
Kings County, New York	99	<1	0.07	High	30,540
New York County, New York	100	<1	0.07	High	37,900
San Francisco County, California	100	<1	0.07	High	23,577

Abbreviations: mpox = monkeypox; MSM = gay, bisexual, and other men who have sex with men.
  * Risk and size of potential recurrence inferred from each jurisdiction's estimated immunity level based on primary simulated results.
  [†] At each level of immunity, 29%, 67%, and 4% of MSM with some immunity are assumed to have 1-dose, 2-dose, or infection-acquired immunity, conveying 37%, 67%, and 100% protection, respectively.
  [§] Median cumulative infections from simulations, relative to the size of the CDC-modeled 2022 mpox outbreak in the absence of additional vaccination or behavioral adaptation.
  [¶] Grouping based on thresholds identified in primary analysis. Threshold values are as follows: high >50%, medium = 25%–50%, and low <25%.
** Estimated as the number of MSM aged ≥16 years who were recommended to receive HIV preexposure prophylaxis and the number of MSM aged ≥13 years living with HIV in each jurisdiction, using publicly available data. The estimated population was then increased by 25% for each jurisdiction to account for additional persons eligible for vaccination (e.g., MSM with lower levels of sexual activity than their already-eligible partners).

FIGURE 2. Cumulative *Monkeypox virus* infections* relative to 2022, by immunity level[†] — United States, 2023
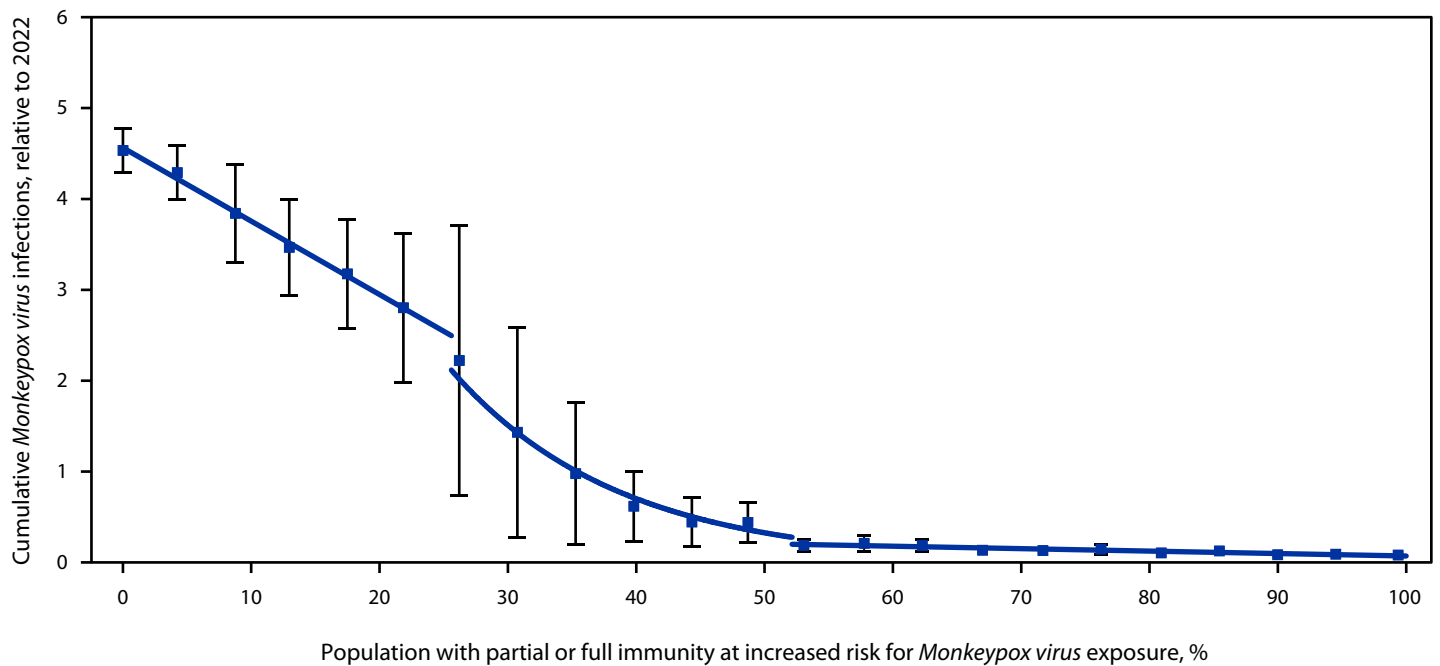
Abbreviations: mpox = monkeypox; MSM = gay, bisexual, and other men who have sex with men.
* Median cumulative infections from simulations, measured among simulations in which an outbreak occurred, relative to the size of the CDC-modeled 2022 mpox outbreak; data points reflect simulated cumulative infection magnitude for a specific immunity level; lines reflect three separate linear model fits using immunity level as the independent variable and median cumulative incidence as the dependent variable among each threshold; first and last threshold were fit using estimates directly, and middle threshold was fit using log-transformed incidence estimates to reflect the rapid change in outbreak magnitude during this period; error bars indicate 25th–75th quartile observed across outbreaks.
[†] Immunity was varied from 0% to 99% in increments of approximately 4%; at each level of immunity, 29%, 67%, and 4% of MSM with some immunity are assumed to have 1-dose, 2-dose, or infection-acquired immunity, conveying 37%, 67%, and 100% protection, respectively.

low vaccination coverage and among MSM at highest risk. Jurisdictions that achieved high vaccination coverage among populations at risk are not expected to experience large recurrences in the immediate future. Success in achieving high coverage in these jurisdictions was partially driven by early prioritization for vaccine distribution because of high early case counts when there was high vaccination demand. In other jurisdictions, vaccines became available after the outbreak had peaked and when demand had declined because of reduced perception of risk (*5*).

The findings in this report are subject to at least four limitations. First, to consider the downstream effects of mpox reintroduction and guide preparedness, mpox reintroduction was assumed to be certain. However, actual reintroduction risk will be influenced by global and local mpox infection dynamics. Although the intensity of the 2022 multinational outbreak has diminished substantially, areas with ongoing transmission remain. Attendance at large social engagements that attract domestic and international MSM travelers could result in reintroduction of mpox into local sexual networks. Assuming reintroduction is independent of subsequent outbreak recurrence risk, reintroduction has a proportional effect on recurrence:

for example, if there were a 50% probability of reintroduction, the risk for recurrence would be 50% lower than that presented in the current analysis. In the absence of additional vaccination or mpox cases, immunity will decline in future years because of demographic turnover, thereby increasing recurrence risk. In addition, small outbreaks might occur even when the estimated risk for a large outbreak is relatively low. As an example, based on this model, Cook County, Illinois, has an estimated 22% risk for a sustained mpox recurrence; however, the city of Chicago, which is part of Cook County, has reported a new cluster of mpox cases that emerged in April 2023 (*9*). Second, inferred estimates of vaccine efficacy from Israel and the United States show a range of effectiveness (*6*). Conservative estimates for 1- and 2-dose efficacy of 37% and 67%, respectively, were used in the primary analysis, although sensitivity analysis examining higher efficacy did not appreciably change the results. Third, many of the sexual behavior data were derived from surveys conducted in 2012, and it is possible that patterns have changed over time and in response to recent disruptive public health events, including this mpox outbreak (*10*). The actual risk for and size of recurrent outbreaks might differ among the actual social and sexual engagements of

Summary

What is already known about this topic?

Monkeypox (mpox) has disproportionately affected gay, bisexual, and other men who have sex with men (MSM); the percentage of MSM with immunity due to vaccination or infection varies among jurisdictions.

What is added by this report?

Mathematical modeling suggests that the risk for future outbreaks depends linearly on the level of immunity in the population at risk; cumulative incidence, on the other hand, has multiple thresholds. More than 592,000 MSM live in jurisdictions with risk for mpox recurrences capable of sustained transmission if a cluster of infectious cases were reintroduced.

What are the implications for public health practice?

Increasing vaccination coverage among MSM at risk and in jurisdictions with low immunity has the potential to reduce the risk for and potential size of future mpox outbreaks.

MSM, which might also vary between communities. Finally, this analysis assumed no interventions took place in response to mpox reintroduction. However, this assumption highlights the benefits of vaccination for preparedness against mpox reintroduction. Delays between detection of reintroduction, mobilization of additional vaccination sites, vaccine administration, and immunologic protection are difficult to shorten, potentially leaving vulnerable communities at risk.

This analysis highlights the importance of public health programs identifying opportunities to promote vaccination before Pride-related and other events when vaccination interest might be higher, rather than vaccinating after reintroduction is identified. Focusing these vaccination efforts in low-coverage areas, and even in high-coverage areas, among MSM who are younger and newly sexually active and among groups with disproportionally low vaccination coverage, can help protect both individual persons and the entire community against a resurgence of mpox. CDC continues to recommend a full 2-dose course of the JYNNEOS vaccine for MSM and others at risk for *Monkeypox virus* exposure.

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Urban and Rural Mpox Incidence Among Persons Aged 15–64 Years — United States, May 10–December 31, 2022

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During May 10–December 31, 2022, a total of 29,980 confirmed and probable[†] U.S. monkeypox (mpox) cases were reported to CDC, predominantly in cisgender adult men reporting recent same-gender sexual partners (1). Urban-rural differences in health (2) and diagnosis of HIV (3,4) and other sexually transmitted infections (5) are well documented nationally. This report describes urban-rural differences in mpox incidence (cases per 100,000 population) among persons aged 15–64 years, by gender and race and ethnicity. Urbanicity was assessed using the 2013 National Center for Health Statistics (NCHS) Urban-Rural Classification Scheme for Counties (2). Substantial differences in incidence by urbanicity, gender, and race and ethnicity were observed; most (71.0%) cases occurred in persons residing in large central urban areas. Among the cases in large central urban areas, most (95.7%) were in cisgender men. The overall incidence of mpox in the United States was 13.5 per 100,000 persons aged 15–64 years and peaked in August in both urban and rural areas. Among cisgender men, incidence in rural areas was approximately 4% that in large central urban areas (risk ratio [RR] = 0.04). Among cisgender women, incidence in rural areas was approximately 11% that in large central urban areas (RR = 0.11). In both urban and rural areas, incidence among non-Hispanic Black or African American (Black) and Hispanic or Latino (Hispanic) persons was consistently higher than that among non-Hispanic White (White) persons; RRs between Black and White persons were highest in rural areas. Support and maintenance of mpox surveillance and prevention efforts including vaccinations should focus on urban areas with the highest incidence of mpox during the 2022 outbreak; however, surveillance and prevention efforts should include all genders, persons of color, and persons residing in both urban and rural areas who are at increased risk for mpox.

Jurisdictional health departments electronically reported data on confirmed and probable mpox cases as part of the national case surveillance through a standardized case report form or via the National Notifiable Diseases Surveillance System.[§] Urbanicity of county of residence was defined using the NCHS six-level classification scheme: four levels for metropolitan (urban) counties (large central, large fringe, medium, and small) and two levels for nonmetropolitan (rural) counties (micropolitan and noncore)[¶] (2). Two U.S. counties were not represented in the analyses because they were not assigned an NCHS urban-rural classification; however, neither of these counties reported cases in 2022. Because of small case numbers, micropolitan and noncore groups were combined into one rural group. Incidence by each of the five levels of urbanicity was calculated by 1) summing cases from counties of the same level of urbanicity (numerator) and 2) summing county-level 2021 CDC WONDER population for persons aged 15–64 years[**] from counties with the same level of urbanicity (denominator). This analysis was limited to incidence estimates among persons aged 15–64 years because the majority of mpox cases were in this age range and to reduce bias that might be introduced by differential age distribution by urbanicity. Incidence estimates were stratified by month, gender, or race and ethnicity. RRs with 95% CIs were calculated between groups (e.g., urban compared with rural areas). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[††]

The 29,980 confirmed and probable mpox cases reported to CDC in 2022 included 29,311 (97.8%) cases among persons aged 15–64 years in the 50 states and the District of Columbia. Most cases among persons aged 15–64 years occurred in large central urban areas (71.0%); however, cases were reported at each level of urbanicity, including 440 (1.5%) in rural areas (Table 1). The median age (34 years) and distribution of mpox patients by age group were similar for all urban-rural categories. In large central urban areas, 95.7% and 2.3% of cases were in cisgender men and cisgender women, respectively, and in rural areas, 94.7% and 4.6% of cases were in these groups, respectively.

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[†] https://www.cdc.gov/poxvirus/mpox/health-departments/case-reporting.html (Accessed January 21, 2023).

[§] https://www.cdc.gov/nndss/index.html (Accessed January 21, 2023).

[¶] https://www.cdc.gov/nchs/data/data_acces_files/2014-rural-urban-chartbook-update.pdf

[**] Single-Race Population Estimates, United States, 2020–2021. July 1 resident population by state, county, age, sex, single-race, and Hispanic origin, on CDC WONDER. CDC county-level data are available in 5-year data increments. Vintage 2021 estimates were released by the U.S. Census Bureau on June 30, 2022. https://wonder.cdc.gov/single-race-v2021.html (Accessed December 27, 2022).

[††] 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. Demographic characteristics of persons aged 15–64 years with mpox,* by urban-rural classification[†] of county of residence — United States,[§] May 10–December 31, 2022

Characteristic (no. with available information)	Urban-rural classification, no. (%)						
	Overall[¶] (N = 29,176)	Large central (n = 20,710)	Large fringe (n = 5,321)	Medium (n = 2,177)	Small (n = 528)	Nonmetro or rural (n = 440)	Missing county of residence (n = 135)
Age, median, yrs (IQR)	**34 (29–42)**	35 (29–42)	34 (28–41)	33 (27–40)	32 (26–40)	34 (27–41)	33 (28–40)
Age group, yrs (29,176)							
15–29	**7,939 (27.2)**	5,276 (25.5)	1,599 (30.1)	729 (33.5)	190 (36.0)	145 (33.0)	43 (31.9)
30–39	**12,156 (41.7)**	8,860 (42.8)	2,107 (39.6)	841 (38.6)	193 (36.6)	155 (35.2)	58 (43.0)
40–49	**6,010 (20.6)**	4,385 (21.2)	1,041 (19.6)	396 (18.2)	92 (17.4)	96 (21.8)	28 (20.7)
50–64	**3,071 (10.5)**	2,189 (10.6)	574 (10.8)	211 (9.7)	53 (10.0)	44 (10.0)	6 (4.4)
Gender** (28,941)							
Cisgender men	**27,597 (95.4)**	19,725 (95.7)	4,943 (94.9)	2,036 (93.7)	484 (92.9)	409 (94.7)	129 (97.7)
Cisgender women	**820 (2.8)**	475 (2.3)	195 (3.7)	101 (4.7)	29 (5.6)	20 (4.6)	2 (1.5)
Transgender men	**70 (0.2)**	42 (0.2)	14 (0.3)	9 (0.4)	4 (0.8)	1 (0.2)	1 (0.8)
Transgender women	**249 (0.9)**	191 (0.9)	38 (0.7)	16 (0.7)	2 (0.4)	2 (0.5)	0 (—)
Another sex or gender	**205 (0.7)**	173 (0.8)	20 (0.4)	10 (0.5)	2 (0.4)	0 (—)	0 (—)
Race and ethnicity[††] (27,503)							
AI/AN	**112 (0.4)**	79 (0.4)	6 (0.1)	15 (0.7)	4 (0.8)	8 (1.9)	0 (—)
Asian	**779 (2.8)**	623 (3.2)	112 (2.2)	33 (1.6)	2 (0.4)	9 (2.1)	5 (6.2)
Black or African American	**9,151 (33.3)**	6,000 (30.8)	2,019 (40.1)	784 (37.8)	197 (39.2)	151 (35.1)	20 (24.7)
NH/OPI	**70 (0.3)**	48 (0.2)	8 (0.2)	12 (0.6)	0 (—)	2 (0.5)	0 (—)
White	**8,050 (29.3)**	5,487 (28.2)	1,421 (28.2)	741 (35.8)	215 (42.8)	186 (43.3)	29 (35.8)
Hispanic or Latino	**8,500 (30.9)**	6,584 (33.8)	1,334 (26.5)	445 (21.5)	72 (14.3)	65 (15.1)	26 (32.1)
Multiple or other races	**841 (3.1)**	642 (3.3)	136 (2.7)	42 (2.0)	12 (2.4)	9 (2.1)	1 (1.2)

Abbreviations: AI/AN = American Indian or Alaska Native; NH/OPI = Native Hawaiian or other Pacific Islander.

* Includes confirmed and probable cases among persons aged 15–64 years; data were updated as of January 31, 2023. Cases missing information on age (207) were not included.

[†] Urban-rural classification of county of residence is based on the 2013 National Center for Health Statistics Urban-Rural Classification Scheme for Counties. The two nonmetro categories were combined into one rural (i.e., nonmetropolitan) category.

[§] Counties from the 50 states and the District of Columbia reporting at least one resident aged 15–64 years with mpox are included. A total of 983 of 3,141 (31%) counties are represented in this table, and the percentages of counties represented by urbanicity were as follows: 100% in large central urban areas, 70% in large fringe urban areas, 59% in medium urban areas, 47% in small urban areas, and 14% in nonmetro or rural areas.

[¶] Cases with missing information on county of residence (135) are not included in the overall category.

** Methods for collecting gender information are not standardized across all jurisdictions. When self-reported gender was missing, current sex or sex assigned at birth was used, and gender identity was presumed to be cisgender. Among the 29,311 cases reported in 2022, a total of 238 cases were missing data on gender (i.e., gender, sex, and sex assigned at birth).

[††] All persons who reported Hispanic or Latino (Hispanic) ethnicity, regardless of race, were categorized as Hispanic. Persons who did not report ethnicity as Hispanic (including missing ethnicity) were categorized as non-Hispanic and reported race in the following categories: AI/AN, Asian, Black or African American, NH/OPI, White, and multiple races (more than one race category selected) or other race. Persons with missing data on race and ethnicity were categorized as missing or unknown.

Racial and ethnic distributions of cases differed by urbanicity. Hispanic persons accounted for 33.8% and 26.5% of cases in large central urban and large fringe urban areas, respectively, but only 14.3% and 15.1% in small urban and rural areas, respectively. The proportion of cases in small urban and rural areas among White persons (42.8% and 43.3% respectively), was higher than that in other urban areas (28.2% in large central, 28.2% in large fringe, and 35.8% in medium). The proportion of cases among Black persons differed across each category of urbanicity, ranging from 30.8% in large central urban areas to 40.1% in large fringe urban areas. The number of mpox cases in other racial and ethnic groups was small, and the relationship with urbanicity could not be assessed.

Overall mpox incidence was 13.5 per 100,000 (Table 2) but varied by urbanicity. Rates in large fringe urban areas (9.7), medium urban areas (4.9), small urban areas (2.8), and rural areas (1.5) were 32%, 16%, 9%, and 5% the rate in large central

urban areas (30.6), respectively (Table 2) (Supplementary Table 1, https://stacks.cdc.gov/view/cdc/128431). In all areas, incidence peaked in August and then declined during October–December.

Overall, incidence was 27.2 in cisgender men and 0.7 in cisgender women (Supplementary Table 2, https://stacks.cdc.gov/view/cdc/128432). Among both groups, rates were highest in large central urban areas and were lower in small urban areas (Figure), (Supplementary Table 1, https://stacks.cdc.gov/view/cdc/128431) (Supplementary Table 2, https://stacks.cdc.gov/view/cdc/128432). Among cisgender men, incidence in rural areas (2.8 per 100,000) was approximately 4% that in large central urban areas (65.0; RR = 0.04). Among cisgender women, rates in rural areas (0.1) were approximately 11% that in large central urban areas (1.3; RR = 0.11).

In urban and rural areas, incidence was higher among cisgender men than among cisgender women, with the highest

TABLE 2. Mpox incidence* among persons aged 15–64 years, by month[†] and urban-rural classification[§] of county of residence — United States, May 10–December 31, 2022

Urban-rural classification	Incidence, by month						Overall risk ratio (95% CI)**
	May–Jun	Jul[¶]	Aug[¶]	Sep[¶]	Oct–Dec[¶]	Overall	
All areas	**0.5**	**4.2**	**5.3**	**2.3**	**1.3**	**13.5**	—
Urban							
Large central urban	1.3	10.0	11.7	4.9	2.6	**30.6**	Ref
Large fringe urban	0.3	2.9	3.9	1.6	1.0	**9.7**	0.32 (0.31–0.33)
Medium urban	0.1	1.0	1.9	1.1	0.7	**4.9**	0.16 (0.15–0.17)
Small urban	0.1	0.6	1.0	0.7	0.5	**2.8**	0.09 (0.08–0.10)
Rural							
Nonmetropolitan	0	0.3	0.6	0.4	0.2	**1.5**	0.05 (0.05–0.06)

Abbreviation: Ref = reference group.
* Cases per 100,000 population, calculated using summed case counts and population size (persons aged 15–64 years) for all areas and for each level of urbanicity, multiplied by 100,000.
[†] Incidence during May–June and during October–December was combined because case counts were low during those periods.
[§] Urban-rural classification of county of residence is based on the 2013 National Center for Health Statistics Urban-Rural Classification Scheme for Counties. The two nonmetro categories were combined into one rural (i.e., nonmetropolitan) category. Among the 29,311 cases reported in 2022, 135 were missing data on county of residence; therefore, incidences were calculated based on a total of 29,176 mpox cases.
[¶] The number of cases in each period (numerator) was subtracted from the denominator for the following period when calculating incidence.
** Risk ratio was calculated by comparing large fringe urban, medium urban, small urban, and rural (nonmetropolitan) areas with large central urban areas.

RR (51.2) in large central urban areas where the incidence in cisgender men was highest (Supplementary Table 1, https://stacks.cdc.gov/view/cdc/128431). In rural areas, the relative difference in incidence between cisgender men and cisgender women was lower (RR = 19.8).

In both urban and rural areas, incidence was higher among Black persons compared with White persons (Figure) (Supplementary Table 3, https://stacks.cdc.gov/view/cdc/128433). The relative difference in incidence between Black and White persons was highest in rural areas (RR = 7.2) (Supplementary Table 1, https://stacks.cdc.gov/view/cdc/128431); however, the absolute difference was highest in large central urban areas where incidence per 100,000 persons aged 15–64 years in Black persons was 52.3 and in White persons was 19.7 (Supplementary Table 3, https://stacks.cdc.gov/view/cdc/128433). In addition, in urban and rural areas, rates were higher among Hispanic persons than among White persons (Figure). Lastly, in urban and rural areas, incidence was higher among Black persons than among Hispanic persons.

Discussion

In the United States, 85% of the population lives in areas classified as urban (2), and the majority of mpox cases occurred in urban areas (1), with the highest incidence in large central urban areas. Across all urban-rural levels, incidence peaked in August 2022. Although the number of mpox cases decreased sharply after this date, the risk for outbreak and recurrence is dependent on the estimated immunity level, which is calculated by the number of cases during the 2022 outbreak and vaccination rates (6).

During the 2022 mpox outbreak, approximately 95% of mpox cases were among cisgender men. Among both cisgender men and cisgender women, incidence was lower with decreasing urbanicity. Incidence was consistently higher among cisgender men than among cisgender women in all urban-rural areas; however, the relative difference in incidence was less in rural areas.

In large central urban areas, proportions of cases among Black, Hispanic, and White persons were similar; however, the incidence was much higher among Black and Hispanic persons than among White persons. In rural areas, most cases were among both Black (35%) and White (43%) persons; however, rates among Black (6.2) and Hispanic (2.4) persons were approximately six and two times higher, respectively, than incidence among White persons (0.9).

During the multinational outbreak in 2022, 1- and 2- dose mpox vaccination coverage, among persons at risk in the United States, reached an estimated 37% and 23%, respectively, with wide variation across the country (7). Preventive efforts, including vaccination campaigns, were concentrated in urban areas because of the large number of cases in these areas during the mpox response (7). The estimated higher incidence in urban areas underscores the need for services, especially in large central urban areas; however, mpox prevention, recognition, diagnosis, and treatment services are still needed in less urban and rural areas. In addition, in light of the lower incidence observed in less urban areas and potentially lower levels of immunity acquired through natural infection, larger proportions of the population in smaller urban and rural areas might be susceptible to infection.

FIGURE. Mpox incidence* among persons aged 15–64 years, by gender[†] (A), race and ethnicity[§] (B), and urban-rural classification[¶] of county of residence — United States, May 10–December 31, 2022

A. Gender

B. Race and ethnicity
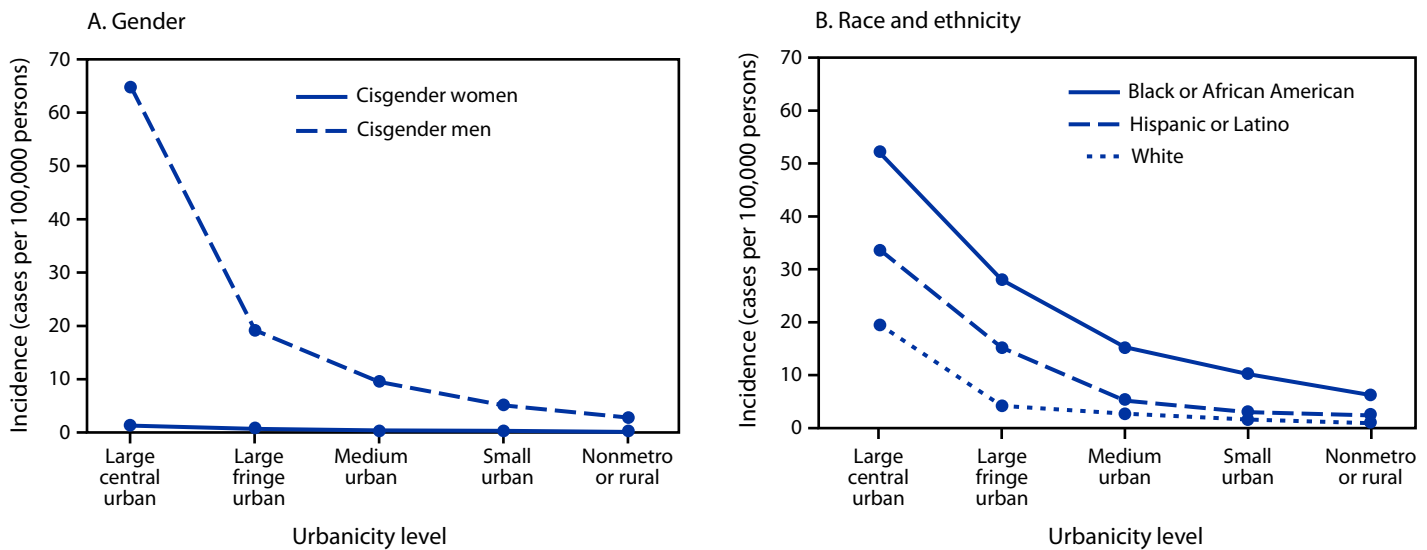
* Cases per 100,000 population. Risk was calculated by using summed case counts and population size (persons aged 15–64 years) by gender and race and ethnicity and each level of urban-rural classification, multiplied by 100,000.

[†] Methods for collecting gender information are not standardized across all jurisdictions. When self-reported gender was missing, current sex or sex assigned at birth was used, and gender identity was presumed to be cisgender. Among the 29,311 cases reported in 2022, 238 cases were missing data on gender (i.e., gender, sex, and sex assigned at birth). Among cases reported in cisgender men (27,726), 129 were missing information on county of residence, and risk for cisgender men was calculated from a total of 27,597 mpox cases among cisgender men. Among cases reported in cisgender women (822), two were missing information on county of residence, and incidence among cisgender women was calculated from a total of 820 mpox cases.

[§] All persons who reported Hispanic or Latino (Hispanic) ethnicity, regardless of race, were categorized as Hispanic. Persons who did not report ethnicity as Hispanic (including missing ethnicity) were categorized as non-Hispanic and reported race in the following categories: American Indian or Alaska Native, Asian, Black or African American (Black), Native Hawaiian or other Pacific Islander, White, and multiple races (more than one race category selected) or other race. This figure includes Black, Hispanic, and White racial and ethnic groups; incidence in all other groups was unreliable because of small sample sizes and were not included (https://stacks. cdc.gov/view/cdc/128433). Persons with missing data on ethnicity and race were categorized as missing or unknown. Among the 29,311 cases reported in 2022, 1,727 cases were missing data on race and ethnicity. Incidences among Black, Hispanic, and White persons were calculated using 9,151, 8,500, and 8,500 cases, respectively, because of the number of cases missing information on county of residence (20 of 9,171 [Black], 26 of 8,526 [Hispanic], and 29 of 8,079 [White]).

[¶] Urban-rural classification of county of residence is based on the 2013 National Center for Health Statistics Urban-Rural Classification Scheme for Counties. The two nonmetro categories were combined into one rural (i.e., nonmetropolitan) category.

Previously published information indicated that barriers to accessing prevention services in rural areas might result from fewer service locations, shortages in providers, cultural barriers, stigma, and fewer provider referrals for testing and vaccination (5,8). Further, these barriers exist in the context of persistent racial and ethnic health disparities, particularly among men, in rural areas (9). In rural areas, the higher incidence observed among Black and Hispanic persons compared with White persons might be attributed to known barriers to accessing care combined with existing health inequalities. Further research into mpox risk factors, incidence, transmission potential, vaccination coverage, and access to prevention and care services by urbanicity, gender, and race and ethnicity is needed for public health decision-making and improving equitable prevention and care among those at risk.

The findings in this report are subject to at least three limitations. First, sample sizes did not permit reliable estimation of incidence by urbanicity among transgender or gender diverse persons, or among some racial and ethnic groups. Second, methods for collecting gender information are not standardized across the United States. When self-reported gender data were missing, current sex or sex assigned at birth was used, and gender identity was presumed to be cisgender. This limitation could have resulted in undercounting transgender or gender-diverse persons, particularly in jurisdictions that do not routinely collect this information. Finally, persons with mpox might have been less likely to receive an mpox diagnosis in rural areas, potentially because of inadequate access or limited testing availability. If mpox was less likely to be detected and consequently diagnosed in less urban and rural areas, than in large central urban areas, incidence might have been underestimated in rural and less urban areas.

The 2022 U.S. mpox outbreak was largely driven by transmission among cisgender men reporting recent same-gender sexual partners in large central urban areas (1). However, although incidence was lower in less urban areas, this analysis

Summary

What is already known about this topic?

Monkeypox (mpox) has disproportionately affected gay, bisexual, and other men who have sex with men (MSM). Information on urbanicity of mpox cases during the 2022 outbreak is limited.

What is added by this report?

During May–December 2022, U.S. mpox incidence was 13.5 per 100,000 persons peaking in August. Among cisgender men and cisgender women, incidence in rural areas was 4% and 11% of incidence in large central urban areas, respectively. Incidence among Black or African American and Hispanic or Latino persons was higher than among White persons.

What are the implications for public health practice?

National mpox surveillance should be continued to ensure persons at risk for mpox get tested and treated. Prevention efforts should be focused on MSM in urban areas.

found that cases also occurred among cisgender men in less urban areas, and among cisgender women in both urban and rural areas. Efforts to support and maintain mpox surveillance should be continued nationally in all areas of urbanicity to ensure all persons at risk for mpox get tested and treated. The current analysis demonstrated that racial and ethnic disparities in mpox incidence that were previously documented (*10*) were higher in absolute magnitude in urban areas and higher in relative magnitude in smaller urban and rural areas. This underscores the need for continued implementation of equity-based vaccination strategies focused on gay, bisexual, and other men who have sex with men (MSM) in urban areas where most mpox cases have been reported. In addition, comprehensive prevention strategies should include all persons at risk for mpox. CDC continues to recommend a full 2-dose course of the JYNNEOS vaccines for MSM and others at risk for *Monkeypox virus* exposure.

Acknowledgments

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[1]CDC Mpox Emergency Response Team.

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Estimates of Bivalent mRNA Vaccine Durability in Preventing COVID-19–Associated Hospitalization and Critical Illness Among Adults with and Without Immunocompromising Conditions — VISION Network, September 2022–April 2023

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On September 1, 2022, CDC's Advisory Committee on Immunization Practices (ACIP) recommended a single bivalent mRNA COVID-19 booster dose for persons aged ≥12 years who had completed at least a monovalent primary series. Early vaccine effectiveness (VE) estimates among adults aged ≥18 years showed receipt of a bivalent booster dose provided additional protection against COVID-19–associated emergency department and urgent care visits and hospitalizations compared with that in persons who had received only monovalent vaccine doses (*1*); however, insufficient time had elapsed since bivalent vaccine authorization to assess the durability of this protection. The VISION Network* assessed VE against COVID-19–associated hospitalizations by time since bivalent vaccine receipt during September 13, 2022–April 21, 2023, among adults aged ≥18 years with and without immunocompromising conditions. During the first 7–59 days after vaccination, compared with no vaccination, VE for receipt of a bivalent vaccine dose among adults aged ≥18 years was 62% (95% CI = 57%–67%) among adults without immunocompromising conditions and 28% (95% CI = 10%–42%) among adults with immunocompromising conditions. Among adults without immunocompromising conditions, VE declined to 24% (95% CI = 12%–33%) among those aged ≥18 years by 120–179 days after vaccination. VE was generally lower for adults with immunocompromising conditions. A bivalent booster dose provided the highest protection, and protection was sustained through at least 179 days against critical outcomes, including intensive care unit (ICU) admission or

in-hospital death. These data support updated recommendations allowing additional optional bivalent COVID-19 vaccine doses for certain high-risk populations. All eligible persons should stay up to date with recommended COVID-19 vaccines.

The VISION Network evaluated VE of bivalent vaccines against COVID-19–associated hospitalization by length of time since receipt of the most recent dose during September 13, 2022–April 21, 2023, across five sites in seven states. VE methods used by the VISION Network have been previously described (*2*). For this analysis, adults aged ≥18 years with and without immunocompromising conditions who were hospitalized with COVID-19–like illness† were included if the patient received molecular testing (e.g., real-time reverse transcription–polymerase chain reaction) for SARS-CoV-2 during the 14 days preceding or up to 72 hours after hospital

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* Sites from the CDC-funded VISION Network that contributed data for this analysis were HealthPartners (Minnesota and Wisconsin), Intermountain Healthcare (Utah), Kaiser Permanente Northern California (California), Kaiser Permanente Center for Health Research (Oregon and Washington), and Regenstrief Institute (Indiana).

† Medical events with a discharge code consistent with COVID-19–like illness were included. COVID-19–like illness diagnoses were obtained from 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, J85.1, J85.2, J85.3, 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*, R09.1, R09.2, R09.3, and R09.8*; acute febrile illness signs and symptoms: R50*, R50.81, and R68.83; acute nonrespiratory illness signs and symptoms: R19.7, R43*, R51*, R51.9, M79.1*, M79.10, M79.18, R65*, R53.81, R53.83, R57.9, R41.82, R40*, R53.1, R11.0, R11.10, R11.11, R11.15, R11.2, R21*, R10.0, R10.1*, R10.2, R10.3*, R10.8, R10.81*, R10.84, and R10.9. All ICD-10 codes with * include all child codes under the specific parent code.

admission. Patients were categorized as immunocompromised or not based on *International Classification of Diseases, Tenth Revision* (ICD-10) discharge codes.[§] Patients were classified on the index date[¶] as unvaccinated (no COVID-19 vaccine doses received), vaccinated with monovalent doses only, or vaccinated with one mRNA bivalent booster dose (regardless of number of previous monovalent doses received). Patients who received only monovalent doses were included if they received any combination of 1–4 doses (or 1–5 doses if immunocompromised) monovalent mRNA (Moderna or Pfizer-BioNTech), Janssen (Johnson & Johnson), or Novavax vaccine doses; recipients of a single monovalent mRNA dose or a single Novavax dose were excluded. In addition, patients were excluded if any vaccine dose was received <7 days before the index date, if a bivalent dose was received ≥180 days before the index date, or if >1 bivalent dose was received.[**] Patients aged <50 years without documented immunocompromising conditions were excluded if they had received >3 monovalent doses. Patients were considered to have critical illness if they were admitted to an ICU, died, or both.[††]

Absolute VE was estimated using a test-negative case-control design comparing the odds of vaccination (either bivalent booster or monovalent doses only versus being unvaccinated)

among case- and control patients. Relative VE was calculated by comparing those who received a bivalent booster with those who received monovalent doses only. A combined model was generated and included patients who had only received monovalent vaccination ≥7 days before their index date, or a bivalent mRNA booster dose at 7–59, 60–119, or 120–179 days before their index date, compared with an unvaccinated reference group. Odds ratios and 95% CIs were estimated using multivariable logistic regression controlling for age, race and ethnicity, sex, calendar day (days since January 1, 2021), and geographic region. Age and calendar day were modeled as natural cubic splines. VE was modeled separately for persons with and without immunocompromising conditions, by age group (18–64 and ≥65 years), and for each outcome (hospitalization and critical illness).[§§] Analyses were conducted using R (version 4.2.2; The 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 a reliance agreement with the Institutional Review Board of Westat, Inc.[¶¶]

Among 66,141 hospitalized patients without immunocompromising conditions who met inclusion criteria, 6,907 (10.4%) were case-patients and 59,234 (89.6%) were control patients (Table 1). Median age of case- and control patients was 76 years and 71 years, respectively. Among case- and control patients, 25.9% and 23.2% were unvaccinated, respectively; a bivalent vaccine dose had been received by 16.3% of case-patients and 20.6% of control patients. VE against COVID-19–associated hospitalization was similar across age groups, but waned over time, from 62% during the first 7–59 days after the bivalent dose to 24% by 120–179 days among adults aged ≥18 years (Table 2). Among those who received monovalent doses only, VE was 21% a median 376 days after the last dose. VE against critical illness was 69% during the 7–59 days after receipt of a bivalent dose and was more sustained (50% at 120–179 days after bivalent vaccination) than VE against hospitalization.

Among 18,934 hospitalized patients with immunocompromising conditions who met inclusion criteria, 1,834 (9.7%) were case-patients and 17,100 (90.3%) were control patients (Table 3); these persons represented 22.3% of the overall hospitalized population who met inclusion criteria. Median age of case- and control patients was 73 years and 70 years, respectively. Within this group, 17.1% of case-patients and 16.3% of control patients were unvaccinated; 21.0% of case-patients

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[§] Immunocompromising conditions were obtained from ICD-10 discharge codes. The specific codes used were Hematological Malignancy: C81.*, C82.*, C83.*, C84.*, C85.*, C86.*, C88.*, C90.*, C91.*, C92.*, C93.*, C94.*, C95.*, C96.*, D46.*, D61.0*, D61.2, D61.9, D70.0, and D71.*; Solid Malignancy: C00.*, C01.*, C02.*, C03.*, C04.*, C05.*, C06.*, C07.*, C08.*, C09.*, C10.*, C11.*, C12.*, C13.*, C14.*, C15.*, C16.*, C17.*, C18.*, C19.*, C20.*, C21.*, C22.*, C23.*, C24.*, C25.*, C26.*, C27.*, C28.*, C29.*, C30.*, C31.*, C32.*, C33.*, C34.*, C35.*, C36.*, C37.*, C38.*, C39.*, C40.*, C41.*, C42.*, C43.*, C44.*, C45.*, C46.*, C47.*, C48.*, C49.*, C50.*, C51.*, C52.*, C53.*, C54.*, C55.*, C56.*, C57.*, C58.*, C59.*, C60.*, C61.*, C62.*, C63.*, C64.*, C65.*, C66.*, C67.*, C68.*, C69.*, C70.*, C71.*, C72.*, C73.*, C74.*, C75.*, C76.*, C77.*, C78.*, C79.*, C7A.*, C7B.*, C80.*, D3A.*, Z51.0, Z51.1*, and C4A.*; Transplant: T86.0, T86.1, T86.2, T86.3, T86.4, T86.5, T86.81, T86.85, D47.Z1, Z48.2.*, Z94.*, and Z98.85; rheumatologic/inflammatory disorders: D86.*, E85, E85.1, E85.2, E85.3, E85.4, E85.8*, E85.9, G35.*, J67.9.*, L40.54, L40.59, L93.0.*, L93.2.*, L94.*, M05.*, M06.*, M07.*, M08.*, M30.*, M31.3*, M31.5*, M32.*, M33.*, M34.*, M35.3*, M35.8*, M35.9*, M46.*, and T78.40*; Other intrinsic immune condition of immunodeficiency: D27.9, D72.89, D80.*, D81, D81.0, D81.1, D81.2, D81.4, D81.5, D81.6, D81.7, D81.8*, D81.9, D82.*, D83.*, D84.*, D87.89, D89, D89.0, D89.1, D89.3, D89.4*, D89.8*, D89.9, K70.3*, K70.4*, K72.*, K74.3, K74.4, K74.5, K74.6, N04.*, R18.0; HIV: B20.*, B21.*, B22.*, B23.*, B24.*, B97.35, O98.7*, and Z21*. All ICD-10 codes with * include all child codes under the specific parent code.

[¶] The index date for each hospitalization was defined as either the date of collection of a respiratory specimen associated with the most recent positive or negative SARS-CoV-2 test result before the hospital admission or the admission date (if testing occurred only after the admission).

[**] On April 19, 2023, CDC authorized an additional bivalent vaccine dose for adults aged ≥65 years and additional doses for persons who are immunocompromised. https://www.cdc.gov/media/releases/2023/s0419-covid-vaccines.html

[††] Death was identified at each individual site and was defined as a death while hospitalized or ≤28 days after hospital admission.

[§§] For VE against critical illness, case-patients were persons admitted to an ICU or who experienced in-hospital death associated with COVID-19, and control patients were persons hospitalized without COVID-19.

[¶¶] 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 hospitalizations among immunocompetent adults aged ≥18 years with COVID-19–like illness,* by COVID-19 vaccination status and SARS-CoV-2 test result — seven states,[†] September 2022–April 2023

Characteristic	Overall, no. (column %)	SARS-CoV-2 test result status, no. (row %)		SMD[§]	Vaccination status,[¶] no. (row %)					SMD[§]
		Case-patients (positive)	Control patients (negative)		Unvaccinated	Primary series with or without MV booster, ≥7 days earlier**	BV mRNA dose, 7–59 days earlier	BV mRNA dose, 60–119 days earlier	BV mRNA dose, 120–179 days earlier	
All hospitalizations (row %)	66,141 (100.0)	6,907 (10.4)	59,234 (89.6)	NA	15,514 (23.5)	37,269 (56.3)	4,857 (7.3)	5,191 (7.8)	3,310 (5.0)	NA
Variant-predominant period[††]										
BA.4/BA.5–related	47,065 (71.2)	5,219 (11.1)	41,846 (88.9)	0.11	11,240 (23.9)	27,594 (58.6)	4,439 (9.4)	3,525 (7.5)	267 (0.6)	1.09
XBB-related	19,076 (28.8)	1,688 (8.8)	17,388 (91.2)		4,274 (22.4)	9,675 (50.7)	418 (2.2)	1,666 (8.7)	3,043 (16.0)	
Site										
HealthPartners	5,354 (8.1)	646 (12.1)	4,708 (87.9)	0.11	969 (18.1)	2,716 (50.7)	678 (12.7)	643 (12.0)	348 (6.5)	2.72
Intermountain Healthcare	7,572 (11.4)	933 (12.3)	6,639 (87.7)		2,041 (27.0)	3,994 (52.7)	538 (7.1)	595 (7.9)	404 (5.3)	
KPCHR	4,974 (7.5)	414 (8.3)	4,560 (91.7)		1,232 (24.8)	2,565 (51.6)	458 (9.2)	465 (9.3)	254 (5.1)	
KPNC	23,294 (35.2)	2,271 (9.7)	21,023 (90.3)		2,147 (9.2)	15,152 (65.0)	2,017 (8.7)	2,338 (10.0)	1,640 (7.0)	
Regenstrief Institute	24,947 (37.7)	2,643 (10.6)	22,304 (89.4)		9,125 (36.6)	12,842 (51.5)	1,166 (4.7)	1,150 (4.6)	664 (2.7)	
Age group, yrs										
18–49	9,656 (14.6)	552 (5.7)	9,104 (94.3)	0.35	4,047 (41.9)	4,880 (50.5)	288 (3.0)	283 (2.9)	158 (1.6)	2.25
50–64	13,200 (20.0)	995 (7.5)	12,205 (92.5)		3,986 (30.2)	7,488 (56.7)	671 (5.1)	652 (4.9)	403 (3.1)	
65–74	15,002 (22.7)	1,496 (10.0)	13,506 (90.0)		3,206 (21.4)	8,531 (56.9)	1,240 (8.3)	1,242 (8.3)	783 (5.2)	
75–84	16,791 (25.4)	2,155 (12.8)	14,636 (87.2)		2,702 (16.1)	9,671 (57.6)	1,582 (9.4)	1,726 (10.3)	1,110 (6.6)	
≥85	11,492 (17.4)	1,709 (14.9)	9,783 (85.1)		1,573 (13.7)	6,699 (58.3)	1,076 (9.4)	1,288 (11.2)	856 (7.4)	
Sex										
Men	30,327 (45.9)	3,412 (11.3)	26,915 (88.7)	0.08	7,503 (24.7)	16,802 (55.4)	2,163 (7.1)	2,333 (7.7)	1,526 (5.0)	0.23
Women	35,814 (54.1)	3,495 (9.8)	32,319 (90.2)		8,011 (22.4)	20,467 (57.1)	2,694 (7.5)	2,858 (8.0)	1,784 (5.0)	
Race and ethnicity										
Black or African American, non-Hispanic	5,953 (9.0)	481 (8.1)	5,473 (91.9)	0.11	1,923 (32.3)	3,317 (55.7)	263 (4.4)	275 (4.6)	175 (2.9)	1.17
White, non-Hispanic	45,101 (68.2)	4,976 (11.0)	40,125 (89.0)		10,399 (23.1)	24,751 (54.9)	3,593 (8.0)	3,892 (8.6)	2,466 (5.5)	
Hispanic or Latino	5,622 (8.5)	517 (9.2)	5,105 (90.8)		944 (16.8)	3,736 (66.5)	364 (6.5)	350 (6.2)	228 (4.1)	
Other,[§§] non-Hispanic	6,054 (9.2)	566 (9.3)	5,488 (90.7)		926 (15.3)	3,716 (61.4)	496 (8.2)	553 (9.1)	363 (6.0)	
Unknown	3,411 (5.2)	367 (10.8)	3,044 (89.2)		1,322 (38.8)	1,749 (51.3)	141 (4.1)	121 (3.5)	78 (2.3)	

See table footnotes on page 583.

and 25.1% of control patients had received a bivalent dose. Among patients aged ≥18 years with immunocompromising conditions, VE against COVID-19–associated hospitalization was 28% during the first 7–59 days after receipt of the bivalent dose and declined to 13% by 120–179 days. VE for those who received monovalent doses only was 3% (median 355 days after the last dose). Estimates of relative and absolute VE were similar (Supplementary Table, https://stacks.cdc.gov/view/cdc/128421).

Discussion

In this multistate analysis of 85,075 hospitalizations of persons with COVID-19–like illness, bivalent doses were 62% effective among adults without immunocompromising conditions, and 28% effective in those with immunocompromising conditions in preventing COVID-19–associated hospitalization during the first 7–59 days after vaccination. Waning was evident in adults without immunocompromising conditions from 60–179 days (2–6 months) after vaccination. VE was more sustained against critical illness (50% at

TABLE 1. (*Continued*) Characteristics of hospitalizations among immunocompetent adults aged ≥18 years with COVID-19–like illness,* by COVID-19 vaccination status and SARS-CoV-2 test result — seven states,† September 2022–April 2023

| Characteristic | Overall, no. (column %) | SARS-CoV-2 test result status, no. (row %) | | SMD§ | Vaccination status,¶ no. (row %) | | | | | SMD§ |
		Case-patients (positive)	Control patients (negative)		Unvaccinated	Primary series with or without MV booster, ≥7 days earlier**	BV mRNA dose, 7–59 days earlier	BV mRNA dose, 60–119 days earlier	BV mRNA dose, 120–179 days earlier	
SARS-CoV-2 test result status										
Case-patients (positive)	**6,907 (10.4)**	6,907 (100.0)	0 (—)	NA	1,791 (25.9)	3,988 (57.7)	327 (4.7)	486 (7.0)	315 (4.6)	NA
Control patients (negative)	**59,234 (89.6)**	0 (—)	59,234 (100.0)		13,723 (23.2)	33,281 (56.2)	4,530 (7.6)	4,705 (7.9)	2,995 (5.1)	
No. of MV doses received										
0	**15,599 (23.6)**	1,798 (11.5)	13,801 (88.5)	NA	15,514 (99.5)	0 (—)	36 (0.2)	30 (0.2)	19 (0.1)	NA
1	**1,402 (2.1)**	116 (8.3)	1,286 (91.7)		0 (—)	1,259 (89.8)	53 (3.8)	54 (3.9)	36 (2.6)	
2	**12,948 (19.6)**	1,340 (10.3)	11,608 (89.7)		0 (—)	11,936 (92.2)	404 (3.1)	407 (3.1)	201 (1.6)	
3	**21,860 (33.1)**	2,199 (10.1)	19,661 (89.9)		0 (—)	16,684 (76.3)	1,959 (9.0)	1,972 (9.0)	1,245 (5.7)	
4	**14,332 (21.7)**	1,454 (10.1)	12,878 (89.9)		0 (—)	7,390 (51.6)	2,405 (16.8)	2,728 (19.0)	1,809 (12.6)	
MV product received, by manufacturer¶¶										
Pfizer-BioNTech	**29,721 (58.7)**	2,950 (9.9)	26,771 (90.1)	NA	NA	21,435 (72.1)	3,018 (10.1)	3,203 (10.8)	2,065 (6.9)	NA
Moderna	**23,048 (45.5)**	2,384 (10.3)	20,664 (89.7)		NA	16,887 (73.3)	2,242 (9.7)	2,409 (10.4)	1,510 (6.6)	
Janssen (Johnson & Johnson)	**3,230 (6.4)**	286 (8.9)	2,944 (91.1)		NA	2,770 (85.8)	176 (5.4)	177 (5.5)	107 (3.3)	
Novavax	**1 (0)**	0 (—)	1 (100.0)		NA	1 (100.0)	0 (—)	0 (—)	0 (—)	
COVID-19 vaccination status										
Unvaccinated	**15,514 (23.5)**	1,791 (11.5)	13,723 (88.5)	0.14	15,514 (100.0)	0 (—)	0 (—)	0 (—)	0 (—)	NA
Primary series with or without MV booster	**37,269 (56.3)**	3,988 (10.7)	33,281 (89.3)		0 (—)	37,269 (100.0)	0 (—)	0 (—)	0 (—)	
mRNA BV dose, 7–59 days earlier	**4,857 (7.3)**	327 (6.7)	4,530 (93.3)		0 (—)	0 (—)	4,857 (100.0)	0 (—)	0 (—)	
mRNA BV dose, 60–119 days earlier	**5,191 (7.8)**	486 (9.4)	4,705 (90.6)		0 (—)	0 (—)	0 (—)	5,191 (100.0)	0 (—)	
mRNA BV dose, 120–179 days earlier	**3,310 (5.0)**	315 (9.5)	2,995 (90.5)		0 (—)	0 (—)	0 (—)	0 (—)	3,310 (100.0)	
Most recent dose product manufacturer										
Pfizer-BioNTech	**29,892 (59.0)**	2,968 (9.9)	26,924 (90.1)	0.04	0 (—)	20,271 (67.8)	3,441 (11.5)	3,732 (12.5)	2,448 (8.2)	NA
Moderna	**19,084 (37.7)**	2,004 (10.5)	17,080 (89.5)		0 (—)	15,347 (80.4)	1,416 (7.4)	1,459 (7.6)	862 (4.5)	
Janssen (Johnson & Johnson)	**1,650 (3.3)**	144 (8.7)	1,506 (91.3)		0 (—)	1,650 (100.0)	0 (—)	0 (—)	0 (—)	
Novavax	**1 (0)**	0 (—)	1 (100.0)		0 (—)	1 (100.0)	0 (—)	0 (—)	0 (—)	

See table footnotes on page 583.

120–179 days after vaccination) in adults without immunocompromising conditions, which suggests that bivalent vaccines provide durable protection against the most severe outcomes from COVID-19.

In this analysis, receipt of a bivalent dose boosted protection against COVID-19–associated hospitalization that had waned since receipt of previous monovalent doses; however, protection afforded by a bivalent dose against COVID-19–associated hospitalization in adults without immunocompromising conditions waned in a similar pattern to that seen after receipt of a monovalent dose during Omicron predominance, with high initial VE and a decrease over time since the last dose. Among adults without immunocompromising conditions, bivalent VE was similar against COVID-19–associated hospitalization and critical illness within the first 2 months after vaccination but appeared to be more durable against critical illness, consistent with previous CDC research showing durable protection by monovalent mRNA vaccines against critical illness, defined as invasive mechanical ventilation or death (*3*). Although VE point estimates were lower among persons with immunocompromising conditions compared with those without such conditions, waning was not evident in this group, possibly because of heterogeneity in immune response among those with immunocompromising conditions or because of limited

TABLE 1. (*Continued*) Characteristics of hospitalizations among immunocompetent adults aged ≥18 years with COVID-19–like illness,* by COVID-19 vaccination status and SARS-CoV-2 test result — seven states,[†] September 2022–April 2023

Characteristic	Overall, no. (column %)	SARS-CoV-2 test result status, no. (row %)		SMD[§]	Vaccination status,[¶] no. (row %)					SMD[§]
		Case-patients (positive)	Control patients (negative)		Unvaccinated	Primary series with or without MV booster, ≥7 days earlier**	BV mRNA dose, 7–59 days earlier	BV mRNA dose, 60–119 days earlier	BV mRNA dose, 120–179 days earlier	
One or more chronic respiratory condition										
Yes	**39,469** (59.7)	4,286 (10.9)	35,183 (89.1)	0.05	8,602 (21.8)	22,383 (56.7)	3,067 (7.8)	3,314 (8.4)	2,103 (5.3)	0.46
No	**26,672** (40.3)	2,621 (9.8)	24,051 (90.2)		6,912 (25.9)	14,886 (55.8)	1,790 (6.7)	1,877 (7.0)	1,207 (4.5)	
One or more chronic nonrespiratory condition										
Yes	**54,754** (82.8)	5,843 (10.7)	48,911 (89.3)	0.05	11,322 (20.7)	31,413 (57.4)	4,344 (7.9)	4,679 (8.5)	2,996 (5.5)	1.28
No	**11,387** (17.2)	1,064 (9.3)	10,323 (90.7)		4,192 (36.8)	5,856 (51.4)	513 (4.5)	512 (4.5)	314 (2.7)	
ICU admission										
Yes	**12,197** (18.4)	1,023 (8.4)	11,174 (91.6)	0.11	3,146 (25.8)	6,763 (55.4)	848 (7.0)	886 (7.3)	554 (4.5)	0.22
No	**53,944** (81.6)	5,884 (10.9)	48,060 (89.1)		12,368 (22.9)	30,506 (56.6)	4,009 (7.4)	4,305 (8.0)	2,756 (5.1)	
Receipt of invasive mechanical ventilation										
Yes	**3,293** (5.0)	250 (7.6)	3,043 (92.4)	0.08	804 (24.4)	1,857 (56.4)	229 (7.0)	254 (7.7)	149 (4.5)	1.89
No	**44,995** (68.0)	4,814 (10.7)	40,181 (89.3)		7,984 (17.7)	26,340 (58.5)	3,850 (8.6)	4,151 (9.2)	2,670 (5.9)	
Unknown	**17,853** (27.0)	1,843 (10.3)	16,010 (89.7)		6,726 (37.7)	9,072 (50.8)	778 (4.4)	786 (4.4)	491 (2.8)	
In-hospital death***										
Yes	**2,735** (4.1)	331 (12.1)	2,404 (87.9)	0.04	727 (26.6)	1,433 (52.4)	183 (6.7)	246 (9.0)	146 (5.3)	0.09
No	**63,406** (95.9)	6,576 (10.4)	56,830 (89.6)		14,787 (23.3)	35,836 (56.5)	4,674 (7.4)	4,945 (7.8)	3,164 (5.0)	

Abbreviations: BV = bivalent; ICU = intensive care unit; KPCHR = Kaiser Permanente Center for Health Research; KPNC = Kaiser Permanente Northern California; MV = monovalent; NA = not applicable; 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 date of admission were included.

[†] California (September 13, 2022–April 21, 2023), Indiana (September 13, 2022–April 12, 2023), Minnesota and Wisconsin (September 13, 2022–April 21, 2023), Oregon and Washington (September 13, 2022–April 14, 2023), and Utah (September 13, 2022–April 21, 2023).

[§] 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 MV doses, ≥7 days earlier versus unvaccinated, 2) vaccinated with an mRNA BV dose, 7–59 days earlier versus unvaccinated, 3) vaccinated with an mRNA BV dose, 60–119 days earlier versus unvaccinated, and 4) vaccinated with an mRNA BV dose, 120–179 days earlier versus unvaccinated.

[¶] Vaccination was defined as having received the last MV or BV dose within the specified range of days before the index 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.

** Includes persons who received a single dose of Janssen (Johnson & Johnson) vaccine. Persons who received a single dose of Pfizer-BioNTech, Moderna, or Novavax vaccine were excluded from the analysis.

[††] Variant predominance was defined as the period when a variant accounted for ≥50% of all sequenced specimens in the U.S. Department of Health and Human Services region where the site is located. XBB-related sublineages predominated at Intermountain Healthcare beginning January 28, 2023; at HealthPartners, KPNC, and Regenstrief Institute beginning February 4, 2023; and at KPCHR beginning February 11, 2023.

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

[¶¶] Because persons might have received vaccine from more than one manufacturer, columns might sum to >100%.

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

statistical power to detect differences by time. Previous analyses have shown differences in VE by type of immunocompromising condition (*4*); however, this analysis did not have sufficient statistical power to differentiate VE by condition type.

As of May 10, 2023, only one in five (20.5%) U.S. adults had received a bivalent booster dose.*** Among U.S. adults who previously received a monovalent vaccine but had yet to receive a bivalent mRNA booster, most received their last vaccine dose >1 year ago.[†††] Results of this analysis indicate that these adults might have relatively little remaining protection against COVID-19–associated hospitalization compared with unvaccinated persons, although might have more remaining protection against critical illness.

*** https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-people-booster-percent-pop5

[†††] https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-09-01/08-COVID-Oliver-508.pdf

TABLE 2. COVID-19 vaccine effectiveness* against laboratory-confirmed COVID-19–associated hospitalizations and critical illness† among adults aged ≥18 years, by age group and immunocompromise status — seven states,§ September 2022–April 2023

Clinical status/Age group, yrs/Vaccine type and doses received, interval since receipt of BV dose	Without documented immunocompromising conditions				With documented immunocompromising conditions			
	Total	Positive SARS-CoV-2 test result, no. (%)	Median interval since last dose, days (IQR)	VE, % (95% CI)	Total	Positive SARS-CoV-2 test result, no. (%)	Median interval since last dose, days (IQR)	VE, % (95% CI)
Hospitalization								
≥18								
Unvaccinated (Ref)	15,514	1,791 (11.5)	NA	Ref	3,109	314 (10.1)	NA	Ref
MV only	37,269	3,988 (10.7)	376 (270 to 505)	21 (16 to 26)	11,140	1,134 (10.2)	355 (237 to 474)	3 (−12 to 16)
BV, 7–59 days earlier	4,857	327 (6.7)	34 (21 to 47)	62 (57 to 67)	1,612	143 (8.9)	33 (19 to 46)	28 (10 to 42)
BV, 60–119 days earlier	5,191	486 (9.4)	87 (73 to 103)	47 (41 to 53)	1,829	140 (7.6)	88 (74 to 104)	41 (26 to 53)
BV, 120–179 days earlier	3,310	315 (9.5)	144 (132 to 159)	24 (12 to 33)	1,244	103 (8.3)	144 (131 to 159)	13 (−13 to 33)
18–64								
Unvaccinated (Ref)	8,033	591 (7.4)	NA	Ref	NA	NA	NA	NA
MV only	12,368	821 (6.6)	403 (306 to 534)	17 (7 to 26)	NA	NA	NA	NA
BV, 7–59 days earlier	959	38 (4.0)	33 (21 to 45)	61 (44 to 72)	NA	NA	NA	NA
BV, 60–119 days earlier	935	66 (7.1)	86 (72 to 101)	25 (1 to 43)	NA	NA	NA	NA
BV, 120–179 days earlier	561	31 (5.5)	143 (131 to 158)	16 (−24 to 43)¶	NA	NA	NA	NA
≥65								
Unvaccinated (Ref)	7,481	1,200 (16.0)	NA	Ref	NA	NA	NA	NA
MV only	24,901	3,167 (12.7)	362 (245 to 484)	24 (18 to 29)	NA	NA	NA	NA
BV, 7–59 days earlier	3,898	289 (7.4)	35 (21 to 48)	64 (58 to 68)	NA	NA	NA	NA
BV, 60–119 days earlier	4,256	420 (9.9)	87 (73 to 103)	51 (45 to 57)	NA	NA	NA	NA
BV, 120–179 days earlier	2,749	284 (10.3)	145 (132 to 159)	27 (15 to 37)	NA	NA	NA	NA
Critical illness**								
≥18								
Unvaccinated (Ref)	14,090	367 (2.6)	NA	Ref	2,881	86 (3.0)	NA	Ref
MV only	33,925	644 (1.9)	375 (269 to 505)	31 (21 to 40)	10,263	257 (2.5)	354 (235 to 474)	16 (−10 to 36)
BV, 7–59 days earlier	4,579	49 (1.1)	34 (21 to 47)	69 (57 to 77)	1,501	32 (2.1)	33 (19 to 46)	40 (7 to 61)¶
BV, 60–119 days earlier	4,790	85 (1.8)	86 (73 to 103)	46 (30 to 58)	1,725	36 (2.1)	88 (74 to 104)	43 (14 to 63)
BV, 120–179 days earlier	3,028	33 (1.1)	144 (132 to 159)	50 (26 to 66)	1,155	14 (1.2)	144 (131 to 159)	53 (13 to 75)¶

Abbreviations: BV = bivalent; 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, and calendar time (days since January 1, 2021).

† Patients were considered to have critical illness if they were admitted to an intensive care unit or died. Death was identified at each individual site and was defined as a death while hospitalized or ≤28 days after admission.

§ California (September 13, 2022–April 21, 2023), Indiana (September 13, 2022–April 12, 2023), Minnesota and Wisconsin (September 13, 2022–April 21, 2023), Oregon and Washington (September 13, 2022–April 14, 2023), and Utah (September 13, 2022–April 21, 2023).

¶ These estimates are imprecise, which might be because of a relatively small number of persons in each level of vaccination or case status. This imprecision indicates the actual VE could be substantially different from the point estimate shown, and estimates should therefore be interpreted with caution. Additional data accrual could increase precision and allow appropriate interpretation.

** For VE against critical illness, case-patients were persons admitted to an intensive care unit or who experienced death associated with COVID-19, and control patients were persons hospitalized without COVID-19.

On April 19, 2023, CDC amended recommendations to permit adults aged ≥65 years and those with immunocompromising conditions to receive ≥1 additional bivalent dose. In this analysis, waning VE patterns were the same in younger and older adults; however, rates of COVID-19–associated hospitalization and death remain substantially higher among older adults, which suggests that an additional dose might confer additional benefit. In addition, although this analysis did not demonstrate clear evidence of waning VE in immunocompromised adults, overall VE among immunocompromised adults was lower than among those without immunocompromising conditions. Like older adults, persons with immunocompromising conditions remain at higher risk for COVID-19 hospitalization and death and might benefit from additional bivalent doses, although this will require future evaluation.

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. According to a national seroprevalence survey, a large proportion of the population has now experienced SARS-CoV-2 infection; infection-induced immunity decreases the risk for future medically attended COVID-19 illness and might affect observed VE.§§§ The findings of this analysis should therefore be interpreted in the context of this underlying immunity as the incremental benefit provided by COVID-19 vaccination. Second, although all case-patients included in the analysis had COVID-19–like illness and a positive SARS-CoV-2 test result at the time of the included hospitalization, some might have had relatively mild COVID-19 disease and been hospitalized because of reasons unrelated to COVID-19, which could lower measured VE. Third, although models adjusted for relevant confounders, such as age and

§§§ https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-04-19/06-COVID-Oliver-508.pdf

TABLE 3. Characteristics of hospitalizations among immunocompromised adults aged ≥18 years with COVID-19–like illness,* by COVID-19 vaccination status and SARS-CoV-2 test result — seven states,[†] September 2022–April 2023

| Characteristic | Overall, no. (column %) | SARS-CoV-2 test result status, no. (row %) | | SMD[§] | Vaccination status,[¶] no. (row %) | | | | | SMD[§] |
		Case-patients (positive)	Control patients (negative)		Unvaccinated	Primary series with or without MV booster, ≥7 days earlier**	BV mRNA dose, 7–59 days earlier	BV mRNA dose, 60–119 days earlier	BV mRNA dose, 120–179 days earlier	
All hospitalizations (row %)	**18,934 (100.0)**	1,834 (9.7)	17,100 (90.3)	NA	3,109 (16.4)	11,140 (58.8)	1,612 (8.5)	1,829 (9.7)	1,244 (6.6)	NA
Variant-predominant period[††]										
BA.4/BA.5–related	**13,310 (70.3)**	1,347 (10.1)	11,963 (89.9)	0.08	2,261 (17.0)	8,282 (62.2)	1,480 (11.1)	1,196 (9.0)	91 (0.7)	1.17
XBB-related	**5,624 (29.7)**	487 (8.7)	5,137 (91.3)		848 (15.1)	2,858 (50.8)	132 (2.3)	633 (11.3)	1,153 (20.5)	
Site										
HealthPartners	**1,896 (10.0)**	217 (11.4)	1,679 (88.6)	0.13	288 (15.2)	1,014 (53.5)	244 (12.9)	218 (11.5)	132 (7.0)	2.7
Intermountain Healthcare	**2,092 (11.0)**	244 (11.7)	1,848 (88.3)		446 (21.3)	1,171 (56.0)	154 (7.4)	188 (9.0)	133 (6.4)	
KPCHR	**1,633 (8.6)**	132 (8.1)	1,501 (91.9)		346 (21.2)	853 (52.2)	167 (10.2)	161 (9.9)	106 (6.5)	
KPNC	**8,957 (47.3)**	795 (8.9)	8,162 (91.1)		652 (7.3)	5,726 (63.9)	823 (9.2)	1,016 (11.3)	740 (8.3)	
Regenstrief Institute	**4,356 (23.0)**	446 (10.2)	3,910 (89.8)		1,377 (31.6)	2,376 (54.5)	224 (5.1)	246 (5.6)	133 (3.1)	
Age group, yrs										
18–49	**2,080 (11.0)**	140 (6.7)	1,940 (93.3)	0.21	677 (32.5)	1,174 (56.4)	95 (4.6)	77 (3.7)	57 (2.7)	2.03
50–64	**4,220 (22.3)**	351 (8.3)	3,869 (91.7)		892 (21.1)	2,610 (61.8)	259 (6.1)	290 (6.9)	169 (4.0)	
65–74	**5,567 (29.4)**	508 (9.1)	5,059 (90.9)		808 (14.5)	3,255 (58.5)	492 (8.8)	585 (10.5)	427 (7.7)	
75–84	**4,807 (25.4)**	550 (11.4)	4,257 (88.6)		526 (10.9)	2,795 (58.1)	501 (10.4)	582 (12.1)	403 (8.4)	
≥85	**2,260 (11.9)**	285 (12.6)	1,975 (87.4)		206 (9.1)	1,306 (57.8)	265 (11.7)	295 (13.1)	188 (8.3)	
Sex										
Men	**9,187 (48.5)**	930 (10.1)	8,257 (89.9)	0.05	1,512 (16.5)	5,334 (58.1)	773 (8.4)	921 (10.0)	647 (7.0)	0.08
Women	**9,747 (51.5)**	904 (9.3)	8,843 (90.7)		1,597 (16.4)	5,806 (59.6)	839 (8.6)	908 (9.3)	597 (6.1)	
Race and ethnicity										
Black or African American, non-Hispanic	**1,609 (8.5)**	155 (9.6)	1,454 (90.4)	0.06	292 (18.1)	1,008 (62.6)	132 (8.2)	108 (6.7)	69 (4.3)	1.09
White, non-Hispanic	**12,656 (66.8)**	1,250 (9.9)	11,406 (90.1)		2,156 (17.0)	7,142 (56.4)	1,148 (9.1)	1,324 (10.5)	886 (7.0)	
Hispanic or Latino	**2,027 (10.7)**	192 (9.5)	1,835 (90.5)		255 (12.6)	1,366 (67.4)	138 (6.8)	168 (8.3)	100 (4.9)	
Other,[§§] non-Hispanic	**2,064 (10.9)**	172 (8.3)	1,892 (91.7)		191 (9.3)	1,325 (64.2)	173 (8.4)	199 (9.6)	176 (8.5)	
Unknown	**578 (3.1)**	65 (11.2)	513 (88.8)		215 (37.2)	299 (51.7)	21 (3.6)	30 (5.2)	13 (2.2)	
SARS-CoV-2 test result status										
Case-patients (positive)	**1,834 (9.7)**	1,834 (100.0)	0 (—)	NA	314 (17.1)	1,134 (61.8)	143 (7.8)	140 (7.6)	103 (5.6)	NA
Control patients (negative)	**17,100 (90.3)**	0 (—)	17,100 (100.0)		2,795 (16.3)	10,006 (58.5)	1,469 (8.6)	1,689 (9.9)	1,141 (6.7)	
No. of MV doses received										
0	**3,133 (16.5)**	315 (10.1)	2,818 (89.9)	NA	3,109 (99.2)	0 (—)	6 (0.2)	15 (0.5)	3 (0.1)	NA
1	**332 (1.8)**	34 (10.2)	298 (89.8)		0 (—)	296 (89.2)	15 (4.5)	15 (4.5)	6 (1.8)	
2	**3,207 (16.9)**	289 (9.0)	2,918 (91.0)		0 (—)	2,951 (92.0)	87 (2.7)	107 (3.3)	62 (1.9)	
3	**6,376 (33.7)**	649 (10.2)	5,727 (89.8)		0 (—)	4,854 (76.1)	579 (9.1)	580 (9.1)	363 (5.7)	
4	**5,689 (30.0)**	523 (9.2)	5,166 (90.8)		0 (—)	2,903 (51.0)	902 (15.9)	1,093 (19.2)	791 (13.9)	
5	**197 (1.0)**	24 (12.2)	173 (87.8)		0 (—)	136 (69.0)	23 (11.7)	19 (9.6)	19 (9.6)	

See table footnotes on page 587.

TABLE 3. (*Continued*) Characteristics of hospitalizations among immunocompromised adults aged ≥18 years with COVID-19–like illness,* by COVID-19 vaccination status and SARS-CoV-2 test result — seven states,[†] September 2022–April 2023

Characteristic	Overall, no. (column %)	SARS-CoV-2 test result status, no. (row %)		SMD§	Vaccination status,[¶] no. (row %)					SMD§
		Case-patients (positive)	Control patients (negative)		Unvaccinated	Primary series with or without MV booster, ≥7 days earlier**	BV mRNA dose, 7–59 days earlier	BV mRNA dose, 60–119 days earlier	BV mRNA dose, 120–179 days earlier	
MV product received, by manufacturer[¶¶]										
Pfizer-BioNTech	9,634 (60.9)	937 (9.7)	8,697 (90.3)	NA	NA	6,644 (69.0)	1,021 (10.6)	1,167 (12.1)	802 (8.3)	NA
Moderna	6,923 (43.7)	659 (9.5)	6,264 (90.5)		NA	4,879 (70.5)	715 (10.3)	788 (11.4)	541 (7.8)	
Janssen (Johnson & Johnson)	982 (6.2)	89 (9.1)	893 (90.9)		NA	821 (83.6)	55 (5.6)	59 (6.0)	47 (4.8)	
Novavax	3 (0)	1 (33.3)	2 (66.7)		NA	3 (100.0)	0 (—)	0 (—)	0 (—)	
COVID-19 vaccination status										
Unvaccinated	3,109 (16.4)	314 (10.1)	2,795 (89.9)	NA	3,109 (100.0)	0 (—)	0 (—)	0 (—)	0 (—)	NA
Primary series with or without MV booster dose(s)	11,140 (58.8)	1,134 (10.2)	10,006 (89.8)		0 (—)	11,140 (100.0)	0 (—)	0 (—)	0 (—)	
mRNA BV dose, 7–59 days earlier	1,612 (8.5)	143 (8.9)	1,469 (91.1)		0 (—)	0 (—)	1,612 (100.0)	0 (—)	0 (—)	
mRNA BV dose, 60–119 days earlier	1,829 (9.7)	140 (7.7)	1,689 (92.3)		0 (—)	0 (—)	0 (—)	1,829 (100.0)	0 (—)	
mRNA BV dose, 120–179 days earlier	1,244 (6.6)	103 (8.3)	1,141 (91.7)		0 (—)	0 (—)	0 (—)	0 (—)	1,244 (100.0)	
Most recent dose product manufacturer										
Pfizer-BioNTech	9,757 (61.7)	936 (9.6)	8,821 (90.4)	0.03	0 (—)	6,317 (64.7)	1,179 (12.1)	1,335 (13.7)	926 (9.5)	NA
Moderna	5,646 (35.7)	546 (9.7)	5,100 (90.3)		0 (—)	4,401 (77.9)	433 (7.7)	494 (8.7)	318 (5.6)	
Janssen (Johnson & Johnson)	419 (2.6)	37 (8.8)	382 (91.2)		0 (—)	419 (100.0)	0 (—)	0 (—)	0 (—)	
Novavax	3 (0)	1 (33.3)	2 (66.7)		0 (—)	3 (100.0)	0 (—)	0 (—)	0 (—)	
One or more chronic respiratory condition										
Yes	12,146 (64.1)	1,259 (10.4)	10,887 (89.6)	0.11	1,966 (16.2)	7,102 (58.5)	1,056 (8.7)	1,209 (10.0)	813 (6.7)	0.13
No	6,788 (35.9)	575 (8.5)	6,213 (91.5)		1,143 (16.8)	4,038 (59.5)	556 (8.2)	620 (9.1)	431 (6.3)	
One or more chronic nonrespiratory condition										
Yes	17,973 (94.9)	1,753 (9.8)	16,220 (90.2)	0.11	2,855 (15.9)	10,600 (59.0)	1,554 (8.6)	1,771 (9.9)	1,193 (6.6)	0.13
No	961 (5.1)	81 (8.4)	880 (91.6)		254 (26.4)	540 (56.2)	58 (6.0)	58 (6.0)	51 (5.3)	
Solid malignancy										
Yes	8,202 (43.3)	639 (7.8)	7,563 (92.2)	0.19	1,240 (15.1)	4,871 (59.4)	712 (8.7)	822 (10.0)	557 (6.8)	0.3
No	10,732 (56.7)	1,195 (11.1)	9,537 (88.9)		1,869 (17.4)	6,269 (58.4)	900 (8.4)	1,007 (9.4)	687 (6.4)	
Hematologic malignancy										
Yes	2,775 (14.7)	324 (11.7)	2,451 (88.3)	0.09	409 (14.7)	1,639 (59.1)	250 (9.0)	294 (10.6)	183 (6.6)	0.2
No	16,159 (85.3)	1,510 (9.3)	14,649 (90.7)		2,700 (16.7)	9,501 (58.8)	1,362 (8.4)	1,535 (9.5)	1,061 (6.6)	
Rheumatologic or inflammatory disorder										
Yes	4,752 (25.1)	550 (11.6)	4,202 (88.4)	0.12	746 (15.7)	2,752 (57.9)	458 (9.6)	488 (10.3)	308 (6.5)	0.19
No	14,182 (74.9)	1,284 (9.1)	12,898 (90.9)		2,363 (16.7)	8,388 (59.1)	1,154 (8.1)	1,341 (9.5)	936 (6.6)	
Other intrinsic immune condition or immunodeficiency										
Yes	6,056 (32.0)	647 (10.7)	5,409 (89.3)	0.08	1,105 (18.2)	3,593 (59.3)	456 (7.5)	534 (8.8)	368 (6.1)	0.4
No	12,878 (68.0)	1,187 (9.2)	11,691 (90.8)		2,004 (15.6)	7,547 (58.6)	1,156 (9.0)	1,295 (10.1)	876 (6.8)	

See table footnotes on page 587.

TABLE 3. (*Continued***) Characteristics of hospitalizations among immunocompromised adults aged ≥18 years with COVID-19–like illness,* by COVID-19 vaccination status and SARS-CoV-2 test result — seven states,[†] September 2022–April 2023**

Characteristic	Overall, no. (column %)	SARS-CoV-2 test result status, no. (row %)		SMD[§]	Vaccination status,[¶] no. (row %)					SMD[§]
		Case-patients (positive)	Control patients (negative)		Unvaccinated	Primary series with or without MV booster, ≥7 days earlier**	BV mRNA dose, 7–59 days earlier	BV mRNA dose, 60–119 days earlier	BV mRNA dose, 120–179 days earlier	
Organ or stem cell transplant										
Yes	**1,298** (6.9)	172 (13.3)	1,126 (86.7)	0.1	162 (12.5)	783 (60.3)	122 (9.4)	133 (10.2)	98 (7.6)	0.3
No	**17,636** (93.1)	1,662 (9.4)	15,974 (90.6)		2,947 (16.7)	10,357 (58.7)	1,490 (8.4)	1,696 (9.6)	1,146 (6.5)	
HIV/AIDS										
Yes	**350** (1.8)	30 (8.6)	320 (91.4)	0.02	79 (22.6)	191 (54.6)	32 (9.1)	26 (7.4)	22 (6.3)	0.19
No	**18,584** (98.2)	1,804 (9.7)	16,780 (90.3)		3,030 (16.3)	10,949 (58.9)	1,580 (8.5)	1,803 (9.7)	1,222 (6.6)	
ICU admission										
Yes	**4,094** (21.6)	335 (8.2)	3,759 (91.8)	0.09	747 (18.2)	2,411 (58.9)	323 (7.9)	367 (9.0)	246 (6.0)	0.29
No	**14,840** (78.4)	1,499 (10.1)	13,341 (89.9)		2,362 (15.9)	8,729 (58.8)	1,289 (8.7)	1,462 (9.9)	998 (6.7)	
Receipt of invasive mechanical ventilation										
Yes	**1,403** (7.4)	131 (9.3)	1,272 (90.7)	0.02	274 (19.5)	839 (59.8)	99 (7.1)	114 (8.1)	77 (5.5)	1.47
No	**15,220** (80.4)	1,467 (9.6)	13,753 (90.4)		2,104 (13.8)	9,038 (59.4)	1,402 (9.2)	1,589 (10.4)	1,087 (7.1)	
Unknown	**2,311** (12.2)	236 (10.2)	2,075 (89.8)		731 (31.6)	1,263 (54.7)	111 (4.8)	126 (5.5)	80 (3.5)	
In-hospital death***										
Yes	**1,638** (8.7)	169 (10.3)	1,469 (89.7)	0.02	336 (20.5)	946 (57.8)	102 (6.2)	155 (9.5)	99 (6.0)	0.35
No	**17,296** (91.3)	1,665 (9.6)	15,631 (90.4)		2,773 (16.0)	10,194 (58.9)	1,510 (8.7)	1,674 (9.7)	1,145 (6.6)	

Abbreviations: BV = bivalent; ICU = intensive care unit; KPCHR = Kaiser Permanente Center for Health Research; KPNC = Kaiser Permanente Northern California; MV = monovalent; NA = not applicable; 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 date of admission were included.

[†] California (September 13, 2022–April 21, 2023), Indiana (September 13, 2022–April 12, 2023), Minnesota and Wisconsin (September 13, 2022–April 21, 2023), Oregon and Washington (September 13, 2022–April 14, 2023), and Utah (September 13, 2022–April 21, 2023).

[§] 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 MV doses, ≥7 days earlier versus unvaccinated, 2) vaccinated with an mRNA BV dose, 7–59 days earlier versus unvaccinated, 3) vaccinated with an mRNA BV dose, 60–119 days earlier versus unvaccinated, and 4) vaccinated with an mRNA BV dose, 120–179 days earlier versus unvaccinated.

[¶] Vaccination was defined as having received the last MV or BV dose within the specified range of days before the index 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.

** Includes persons who received a single dose of Janssen (Johnson & Johnson) vaccine. Persons who received a single dose of Pfizer-BioNTech, Moderna, or Novavax vaccine were excluded from the analysis.

[††] Variant predominance was defined as the period when a variant accounted for ≥50% of all sequenced specimens in the U.S. Department of Health and Human Services region where the site is located. XBB-related sublineages predominated at Intermountain Healthcare beginning January 28, 2023; at HealthPartners, KPNC, and Regenstrief Institute beginning February 4, 2023; and at KPCHR beginning February 11, 2023.

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

[¶¶] Because persons might have received vaccine from more than one manufacturer, columns might sum to >100%.

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

calendar time, residual confounding is possible, including by behavioral differences, history of previous SARS-CoV-2 infection, and use of COVID-19 treatments such as nirmatrelvir-ritonavir (Paxlovid). Fourth, differences in sublineage-specific VE could not be compared because of limited statistical power. Fifth, this analysis did not compare product-specific bivalent booster VE estimates. Finally, because these data are from seven states, the patients in this analysis might not be representative of the entire U.S. population.

In this study of durability of bivalent VE, bivalent doses helped provide protection against COVID-19–associated hospitalization and critical disease. Although waning of protection was evident in some groups, VE was more sustained for critical illness, indicating the vaccines are continuing to help protect adults from the most severe COVID-19 outcomes. All adults should stay up to date with recommended COVID-19 vaccines.

Summary

What is already known about this topic?

Bivalent mRNA COVID-19 vaccines help provide protection against medically attended COVID-19–associated illness. However, the durability of this protection is uncertain.

What is added by this report?

Among adults aged ≥18 years without immunocompromising conditions, bivalent booster vaccine effectiveness (VE) against COVID-19–associated hospitalization declined from 62% at 7–59 days postvaccination to 24% at 120–179 days compared with VE among unvaccinated adults. Among immunocompromised adults, lower bivalent booster VE was observed. However, bivalent booster VE was sustained against critical COVID-19–associated outcomes, including intensive care unit admission or death.

What are the implications for public health practice?

Adults should stay up to date with recommended COVID-19 vaccines. Optional additional bivalent vaccine doses are available for older adults and persons with immunocompromising conditions.

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Notes from the Field

Multistate, Multiserotype Outbreak of *Salmonella* Infections Linked to Cashew Brie — United States, 2021

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On March 30, 2021, during weekly analysis of sequenced isolates, the Tennessee Department of Health identified two *Salmonella* Duisburg isolates that had been determined to be closely related by whole genome sequencing (WGS). The specimens containing the isolates were from two patients who reported eating the same brand of cashew brie (a vegan brie cheese alternative) at the same restaurant. A search of the National Center for Biotechnology Information (NCBI) Pathogen Detection Isolates Browser identified three additional *Salmonella* isolates, two from patients in California and one in Florida, that were closely related genetically to the Tennessee isolates. The California Department of Public Health confirmed that one patient consumed the same brand of cashew brie before becoming ill. The Florida Department of Health reported the patient followed a vegan diet, which excluded some potential food exposures. A multistate investigation to characterize illnesses and identify the outbreak source was initiated. Open-source access to WGS data through NCBI facilitated rapid investigation of this outbreak before it was large enough to be identified through standard multistate outbreak detection methods (*1*). Rapid detection, investigation, and product recall prevented additional illnesses.

A case was defined as a *Salmonella* infection with one of four outbreak strains (identified using WGS) with illness onset during December 1, 2020–May 9, 2021 (Figure). State and local officials interviewed patients about the foods they consumed before illness onset, including cashew brie, and where the foods were purchased. Product and environmental sampling were conducted at retail locations or at the sole cashew brie production facility identified during of the Food and Drug Administration (FDA) traceback investigation. Outbreak strains of *S.* Chester, *S.* Typhimurium, and *S.* Urbana were included in the investigation because patients reported consuming cashew brie and cashew brie and component ingredients tested positive for these strains of *Salmonella*. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.*

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* 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.
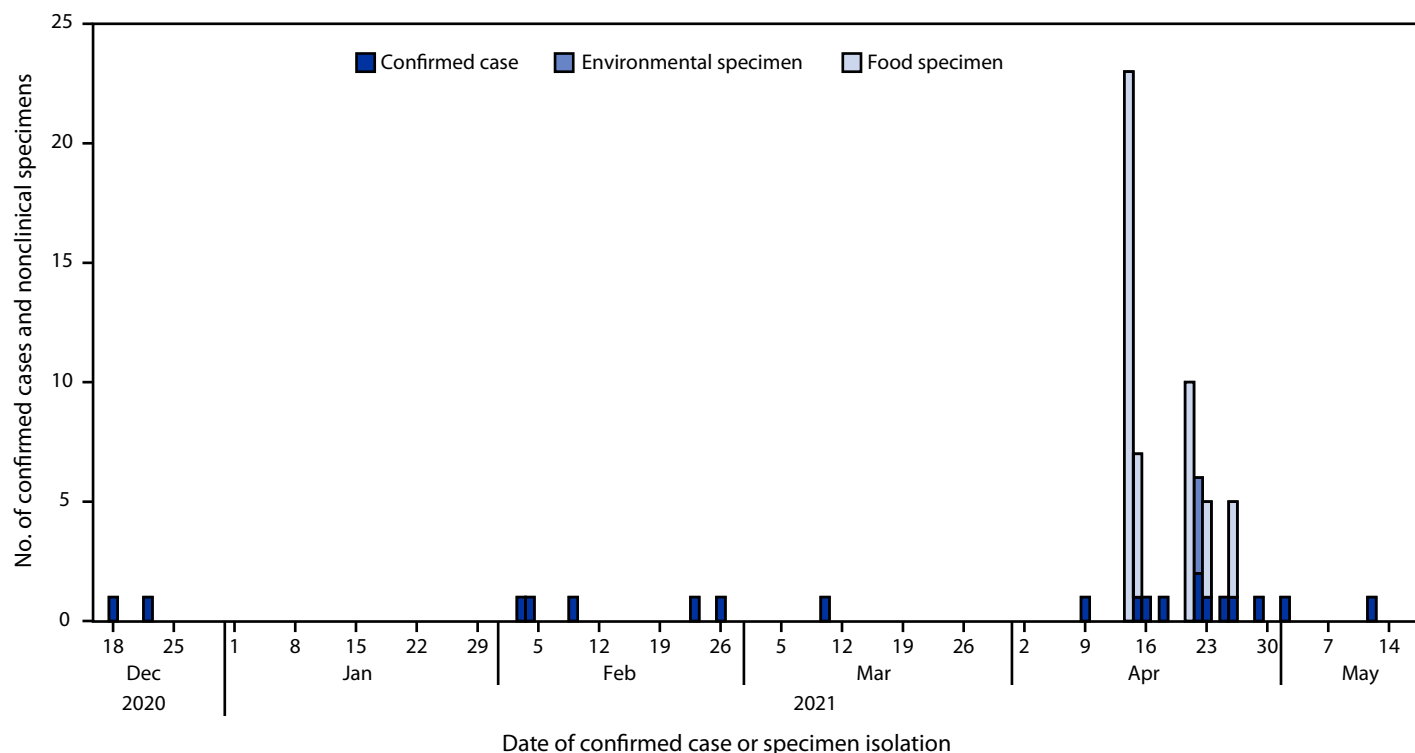
Overall, 20 cases were identified in four states: California (seven *S.* Typhimurium, three *S.* Chester, three *S.* Urbana, two *S.* Duisburg), Florida (one *S.* Chester, one *S.* Duisburg), Maryland (one *S.* Urbana), and Tennessee (two *S.* Duisburg). The median patient age was 26 years (range = 1–72 years); 65% were female. Five patients were hospitalized, and none died.

Among 19 patients who were interviewed, 15 reported eating the same brand of cashew brie during the week before illness onset. Thirty-six samples were collected by state and federal officials from component ingredients, in-process and finished products, and environmental swabs from the cashew brie production facility. Twenty-three (64%) samples yielded 51 *Salmonella* isolates, including 19 (95%) of 20 retail samples and four (25%) of 16 samples collected from the production facility. On the basis of these findings, the cashew brie producer voluntarily recalled all products. Four *Salmonella* strains were isolated from 51 food and environmental samples; the results of WGS analysis indicated that only *S.* Chester and *S.* Urbana detected in non-clinical samples were associated with human illness. In addition, *S.* Duisburg and *S.* Typhimurium were only isolated from clinical samples and not found in food or environmental samples.

On the basis of the food sample results and FDA traceback, the cashew ingredients used to make the brie products were the likely source of contamination. Review of cashew brie production revealed no lethality treatment (e.g., pasteurizing or irradiation) (*2*) before cashew processing. FDA worked with the cashew supplier to ensure potentially contaminated cashews were no longer on the market and the supplier implemented corrective actions.

Outbreaks associated with raw nut and seed products are well documented (*3*), and *Salmonella* outbreaks associated with cashew cheese have been reported (*4*). The lack of a lethality treatment for component ingredients can increase the risk of contamination in products that are served ready-to-eat and perceived as safe by the public. The identification of two persons who became ill after eating the same uncommon food at the same restaurant, paired with detection of a rare *S.* Duisburg serotype, led to an early hypothesis about the source of this outbreak. Open-source access to WGS data through NCBI enabled rapid investigation of this outbreak before it was large enough to be identified using the standard multistate outbreak detection methods (*1*). Rapid detection, investigation, and product recall prevented additional illnesses, given the detection of *Salmonella* in 95% of cashew brie products collected at retail locations during this investigation.

FIGURE. Number of confirmed cases (n = 20) and nonclinical (environmental and food) specimens of *Salmonella* (n = 51) linked to cashew brie by date of isolation — United States, December 2020–May 2021

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QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Age-Adjusted Percentage* of Adults Aged ≥18 Years Who Take Prescription Medication for Depression,[†] by Sex and Race and Hispanic Origin — National Health Interview Survey,[§] United States, 2021
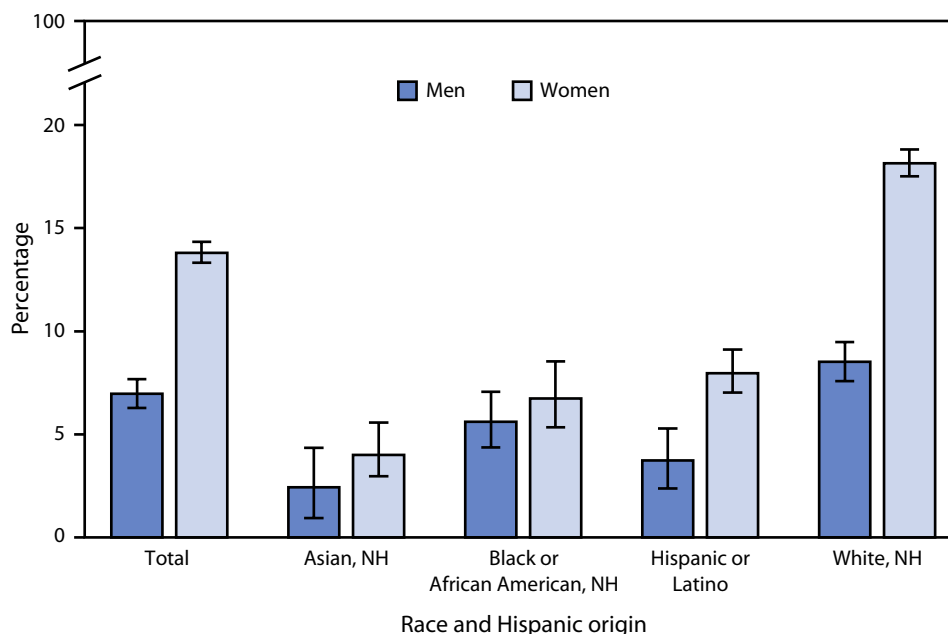
Abbreviation: NH = non-Hispanic.
* Age-adjusted percentages are based on the 2000 U.S. Census Bureau standard population; using age groups 18–44, 45–64, 65–74, and ≥75 years; with 95% CIs indicated by error bars.
[†] Based on a positive response to the question, "Do you take prescription medication for depression?"
[§] Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population.

In 2021, among adults aged ≥18 years, women were more likely to take prescription medication for depression than were men (13.8% versus 7.0%). This pattern was found among non-Hispanic White (White) (18.1% versus 8.5%) and Hispanic or Latino (8.0% versus 3.7%) adults, but differences by sex were not statistically significant among non-Hispanic Black or African American (Black) (6.7% versus 5.6%) and non-Hispanic Asian (Asian) (4.0% versus 2.4%) adults. Among men, Asian adults were less likely than White and Black adults to take prescription medication for depression, but the difference compared with Hispanic adults was not statistically significant. Among women, Asian adults were the least likely to take prescription medication for depression.

Source: National Center for Health Statistics, National Health Interview Survey, 2021. https://www.cdc.gov/nchs/nhis/index.htm
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