Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 71 / No. 42
October 21, 2022

Progress Toward Poliomyelitis Eradication — Pakistan, January 2021–July 2022

Chukwuma Mbaeyi, DDS[1]; Shahzad Baig, MD[2]; Muhammad Rana Safdar, MD[2]; Zainul Khan, MD[3]; Hamish Young[4]; Jaume Jorba, PhD[5]; Zubair M. Wadood, MD[6]; Hamid Jafari, MD[7]; Muhammad Masroor Alam, PhD[7]; Richard Franka, PhD[1]

After reporting a single wild poliovirus (WPV) type 1 (WPV1) case in 2021, Pakistan reported 14 cases during April 1–July 31, 2022. Pakistan and Afghanistan are the only countries where endemic WPV transmission has never been interrupted (*1*). In its current 5-year strategic plan, the Global Polio Eradication Initiative (GPEI) has set a goal of interrupting all WPV1 transmission by the end of 2023 (*1*–*3*). The reemergence of WPV cases in Pakistan after 14 months with no case detection has uncovered transmission in southern Khyber Pakhtunkhwa province, the most historically challenging area. This report describes Pakistan's progress toward polio eradication during January 2021–July 2022 and updates previous reports (*4*,*5*). As of August 20, 2022, all but one of the 14 WPV1 cases in Pakistan during 2022 have been reported from North Waziristan district in Khyber Pakhtunkhwa. In underimmunized populations, excretion of vaccine virus can, during a period of 12–18 months, lead to reversion to neurovirulence, resulting in circulating vaccine-derived polioviruses (cVDPVs), which can cause paralysis and outbreaks. An outbreak of cVDPV type 2 (cVDPV2), which began in Pakistan in 2019, has been successfully contained; the last case occurred in April 2021 (*1*,*6*). Despite program improvements, 400,000–500,000 children continue to be missed during nationwide polio supplementary immunization activities (SIAs),* and recent isolation of poliovirus from sewage samples collected in other provinces suggests wider WPV1 circulation during the ongoing high transmission season. Although vaccination efforts have been recently complicated by months of flooding during the summer of 2022, to successfully interrupt WPV1 transmission in the core reservoirs in southern Khyber Pakhtunkhwa and reach the GPEI goal, emphasis should be placed on further improving microplanning and supervision of SIAs and on systematic tracking and vaccination of persistently missed children in these reservoir areas of Pakistan.

Immunization Activities

Essential (routine) immunization. The World Health Organization (WHO) and UNICEF estimated Pakistan's 2021 national polio vaccination coverage (3 doses of oral poliovirus vaccine [OPV] and 1 dose of inactivated poliovirus vaccine by age 12 months) at 83% (*7*). A 2021 survey sponsored by

* SIAs are mass house-to-house vaccination campaigns targeting children aged <5 years with OPV, irrespective of the child's vaccination history.

INSIDE

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

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

WHO and Gavi, the Vaccine Alliance,[†] indicated that the proportion of children aged 12–23 months who had received 3 OPV doses, by province, ranged from 45.1% in Balochistan to 94.9% in Punjab. None of the districts in the provinces of Balochistan, Khyber Pakhtunkhwa, and Sindh achieved ≥80% coverage. By comparison, 31 of 36 (86%) districts in Punjab province achieved ≥80% 3-dose OPV coverage.

Supplementary immunization activities. After the declaration of eradication of WPV type 2 in 2015,[§] Pakistan joined other countries in GPEI in implementing a synchronized withdrawal of trivalent OPV (tOPV; containing Sabin-strain types 1, 2, and 3) in 2016 as part of containment efforts for all type 2 polioviruses (*8*). However, with the emergence of cVDPV2 in Pakistan in 2019, GPEI authorized the use of tOPV along with the recommended monovalent Sabin-strain OPV type 2 (mOPV2) for outbreak response vaccination activities. During 2021, 4 national immunization days (NIDs) and 2 subnational immunization days (SNIDs) directed at children aged <5 years were conducted using bivalent OPV (bOPV; containing Sabin-strain types 1 and 3) and, in areas with cVDPV2 transmission, either mOPV2 or tOPV. The November 2021 NIDs were combined with a measles-rubella vaccination campaign that reached 90 million persons aged 9 months–15 years with measles-rubella vaccine in addition to doses of bOPV administered to 41 million children aged <5 years.

Two NIDs (in March and May) and 2 SNIDs (in January and June) targeting children aged <5 years have been conducted to date in 2022 using bOPV. SNIDs took place in designated, high-risk districts for poliovirus transmission and other priority areas for the polio program mostly in the provinces of Khyber Pakhtunkhwa, Balochistan, Sindh, and Punjab. Limited SIAs were conducted in response to identification of WPV1 cases and environmental isolates in March, April, and June. An NID was conducted in August; another is planned for November, and an SNID is planned for October 2022.

During SIAs conducted in 25 very high-risk districts,[¶] including approximately 10–12 million children aged <5 years, the number of children missed because the child was absent from the household declined 9%, from 184,597 in September 2021 to 167,934 in May 2022, and the number of refusals among eligible children decreased 23%, from 66,875 to 51,577. Collectively, among 43 million children targeted during each NID, 400,000–500,000 (0.9%–1.2%) children were repeatedly being missed. Lot quality assurance sampling (LQAS)[**]

[†] https://www.gavi.org

[§] https://polioeradication.org/news-post/global-eradication-of-wild-poliovirus-type-2-declared

[¶] Based on priority history, current transmission patterns, and community polio vaccination status.

[**] LQAS surveys use a small sample size to assess the quality of vaccination activities within a few days after SIAs in union councils (i.e., subdistricts referred to as "lots"). LQAS surveys seek evidence of vaccination (i.e., finger marking) by random selection of 60 children within each lot. If the number of unvaccinated persons in the sample exceeds three, then the union council SIA is classified as having failed at a threshold of ≥90%, and additional vaccination activities in those areas are recommended. If the threshold of ≥90% (three or fewer unvaccinated children) is met, then the union council SIA is classified as having passed.

The *MMWR* series of publications is published by the Center for Surveillance, Epidemiology, and Laboratory Services, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30329-4027.

Suggested citation: [Author names; first three, then et al., if more than six.] [Report title]. MMWR Morb Mortal Wkly Rep 2022;71:[inclusive page numbers].

survey results have also indicated performance gaps in districts identified to be at highest risk for poliovirus transmission. Only 67%–80% of these districts reached the 90% LQAS threshold for SIAs conducted during September 2021–May 2022.

Poliovirus Surveillance

Acute flaccid paralysis surveillance. Detection of two or more cases of nonpolio acute flaccid paralysis (AFP) per 100,000 children and adolescents aged <15 years per year is an indicator of adequately sensitive polio surveillance.[††] Pakistan reported a national nonpolio AFP rate of 13 per 100,000 children and adolescents in 2021; provincial rates ranged from 9.5 to 18.8. As of July 27, 2022, the annualized 2022 nonpolio AFP rate was 14.2; stool adequacy[§§] rates, a measure of completeness of case investigation, was ≥80% nationally and in each province during 2021 and 2022.

Environmental surveillance. Laboratory testing of sewage samples routinely collected at designated sites supplements AFP surveillance in facilitating timely detection of circulating polioviruses. Pakistan has 77 environmental surveillance sampling sites. During 2021, 65 (8%) of 833 sewage samples tested positive for WPV1 compared with 407 (52%) of 786 samples tested in 2020. In 2022, to date, 13 (2%) of 748 samples have tested positive for WPV1, including eight from Khyber Pakhtunkhwa province, four from Punjab province, and one from Islamabad. The earliest isolates detected in samples collected from environmental surveillance sites in Bannu district (Khyber Pakhtunkwa) in April 2022 were orphan viruses (i.e., ≥1.5% divergent from their closest genetic match), indicating gaps in AFP surveillance sensitivity; subsequent isolates were genetically linked to WPV1 cases detected in North Waziristan.

Epidemiology of poliomyelitis cases. During 2021, a single Pakistan WPV1 case was reported in Killa Abdullah, Balochistan, compared with 84 cases reported from several provinces in 2020 and 147 cases reported during 2019 (Figure 1). As of August 20, 2022, 14 WPV1 cases had been reported from two districts in Khyber Pakhtunkhwa in 2022, including North Waziristan (13) and Lakki Marwat (one) (Figure 2).

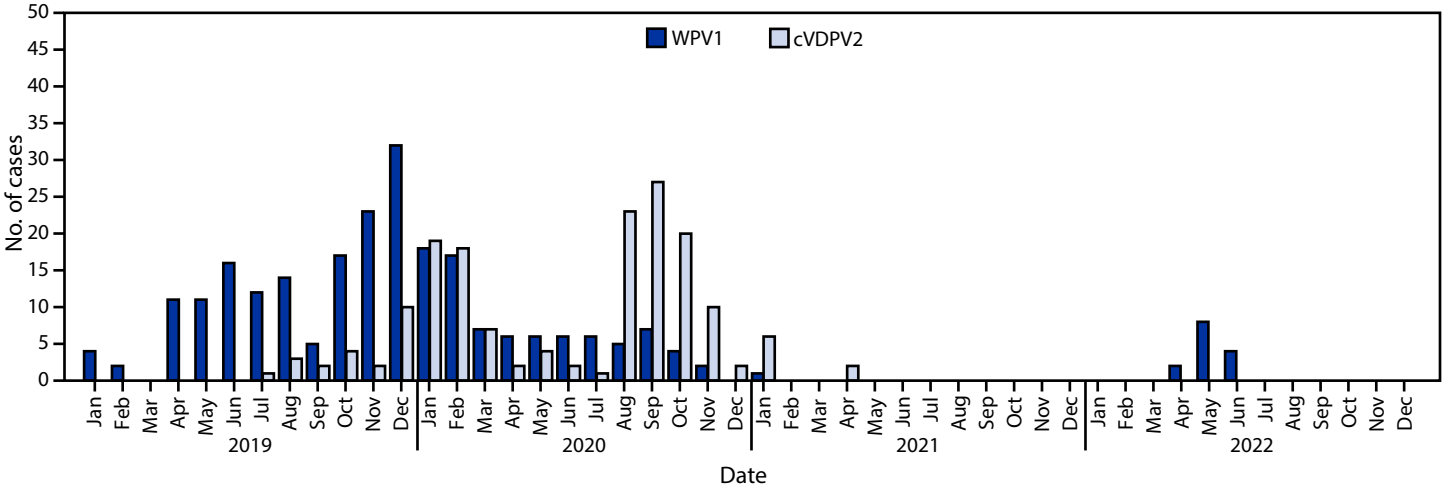
Of the 15 WPV1 cases reported during January 2021–July 2022, patients' ages ranged from 7 to 28 months (median = 15 months); 87% had never received OPV through essential immunization (zero-dose children), and 13% had received 1–3 OPV doses through essential immunization. Genetic analysis of the viruses identified in the WPV1 cases indicated that all belong to a single genetic cluster (groups of polioviruses sharing ≥95% sequence identity in the region coding the VP1 capsid protein). However, three additional genetic clusters were identified from environmental surveillance isolates during January 2021–July 2022, again an indication of AFP surveillance gaps, although only one genetic cluster has been detected since June 2021.

Transmission of cVDPV2 from several emergences in Pakistan resulted in 165 cVDPV2 cases during July 2019–April 2021 (22 cases in 2019, 135 in 2020, and eight in 2021). In the most recent case, the patient had paralysis onset on April 23, 2021 (Table) (Figure 1) (Figure 2).

[††] Nonpolio AFP cases are those that are discarded as not having laboratory or other proof of poliovirus as the cause. The expected background rate of nonpolio AFP illnesses is ≥2 per 100,000 children and adolescents aged <15 years per year, the standard WHO performance indicator target for sufficiently sensitive detection. The standard WHO stool specimen indicator target is adequate stool specimen collection from ≥80% of AFP cases.

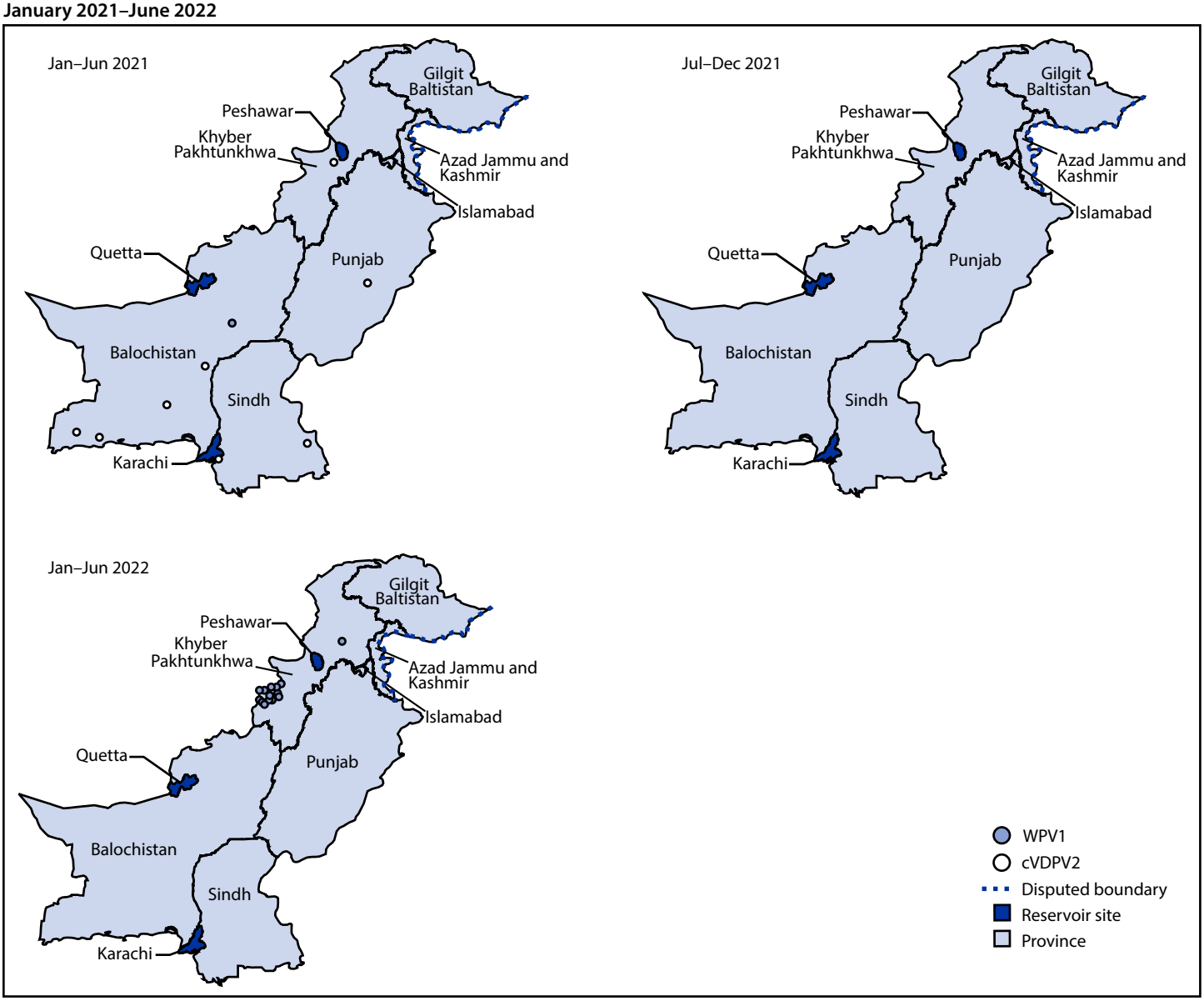
[§§] Stool specimens are considered adequate if two specimens are collected ≥24 hours apart within 14 days of paralysis onset and arrive at a WHO-accredited laboratory with reverse cold chain maintained and without leakage or desiccation.

FIGURE 1. Wild poliovirus type 1 and circulating vaccine-derived poliovirus type 2 cases, by month — Pakistan, January 2019–July 2022



Abbreviations: cVDPV2 = circulating vaccine-derived poliovirus type 2; WPV1 = wild poliovirus type 1.

FIGURE 2. Location of cases of wild poliovirus type 1 and circulating vaccine-derived poliovirus type 2, by province and period — Pakistan, January 2021–June 2022



Abbreviations: cVDPV2 = circulating vaccine-derived poliovirus type 2; WPV1 = wild poliovirus type 1.

Discussion

The number of WPV1 cases and areas of poliovirus transmission identified in Pakistan declined markedly during January 2021–July 2022 compared with the preceding 2 years. The limited genetic divergence among WPV1 isolations since 2020 suggests that the reduction in cases and apparent geographic scope of virus spread are likely reflective of a decrease in WPV1 circulation during the reporting period. Disruptions to implementation of polio eradication activities because of the COVID-19 pandemic have been ameliorated since late 2020 (*1*,*6*), and a cVDPV2 outbreak that began in 2019 was interrupted by 2021 after a robust vaccination response.

The resurgence of WPV1 cases in 2022 and the isolation of WPV1 from environmental surveillance samples have demonstrated that Pakistan's recent progress toward interrupting endemic WPV1 transmission has been jeopardized by persistent circulation in a historically challenging geographic area as well as by AFP surveillance limitations. Of note, an outbreak of WPV1 genetically linked to viral strains in Pakistan was identified during this period in Malawi and Mozambique, countries located in the WHO African Region, which was certified free of indigenous WPV1 transmission in September 2020 (*1*,*9*).

The clustering of WPV1 cases in North Waziristan demonstrates the progress of the Pakistan program in limiting the geographic scope of transmission. However, recent environmental

TABLE. Acute flaccid paralysis surveillance indicators, number of wild poliovirus cases reported, and number of circulating vaccine-derived poliovirus type 2 cases reported, by region and period — Pakistan, January 2021–July 2022

	AFP surveillance indicators				Poliomyelitis cases							
	No. of AFP cases (nonpolio AFP rate*)		% With adequate stool specimens†		Reported WPV1 cases				Reported cVDPV2 cases			
Region	2021	2022§	2021	2022	Jan–Jun 2021	Jul–Dec 2021	Jan–Jun 2022	Total	Jan–Jun 2021	Jul–Dec 2021	Jan–Jun 2022	Total
Azad Jammu Kashmir	273 (14.5)	212 (20.7)	89.7	93.4	0	0	0	**0**	0	0	0	0
Balochistan	564 (9.5)	245 (7.6)	87.4	89.4	1	0	0	**1**	4	0	0	4
Gilgit-Baltistan	129 (18.8)	88 (23.6)	83.0	84.1	0	0	0	**0**	0	0	0	0
Islamabad	172 (17.2)	104 (19.0)	84.3	81.7	0	0	0	**0**	0	0	0	0
Khyber Pakhtunkhwa	3,311 (15.8)	1,934 (17.5)	83.1	86.2	0	0	14	**14**	1	0	0	1
Punjab	6,300 (12.2)	3,705 (13.2)	84.2	87.9	0	0	0	**0**	1	0	0	1
Sindh	2,369 (10.5)	1,460 (11.9)	89.4	86.9	0	0	0	**0**	2	0	0	2
Total	**13,118 (13.0)**	**7,748 (14.2)**	**85.2**	**87.2**	**1**	**0**	**14**	**15**	**8**	**0**	**0**	**8**

Abbreviations: AFP = acute flaccid paralysis; cVDPV2 = circulating vaccine-derived poliovirus type 2; WPV1 = wild poliovirus type 1.
* Nonpolio AFP cases per 100,000 children and adolescents aged <15 years. Recommended benchmark: two cases per 100,000 persons aged <15 years.
† Defined as two stool specimens collected ≥24 hours apart within 14 days of paralysis onset and arriving at a World Health Organization–accredited laboratory with reverse cold chain maintained and without leakage or desiccation.
§ Annualized.

Summary

What is already known about this topic?

Pakistan is one of two countries (including Afghanistan) where wild poliovirus type 1 (WPV1) transmission has never been interrupted.

What is added by this report?

WPV1 cases in Pakistan decreased from 147 in 2019 and 84 in 2020 to a single case in 2021 but increased to 14 cases in 2022 as of July 31. These 14 WPV1 cases are clustered among children in southern Khyber Pakhtunkhwa province, many of whom have never received poliovirus vaccine (zero-dose children).

What are the implications for public health practice?

Ensuring the highest quality vaccination activities in priority areas of Pakistan will enable the polio program to improve the chances of interrupting ongoing transmission of WPV1.

surveillance isolations of WPV1 from sites in Islamabad and Punjab, genetically linked to WPV1 in circulation in southern Khyber Pakhtunkhwa, indicate the potential for further spread to other parts of the country. Months of flooding in the summer of 2022 in several areas of the country and associated displacement of persons, in addition to limiting the reach of SIAs, could increase the likelihood of further spread of the virus.

Although performance benchmarks for AFP surveillance are met nationally and at the provincial levels, priority should be given to enhancing the quality of AFP surveillance through continued training of health care workers and enlisting of more community informants. The planned expansion of environmental surveillance should be prioritized to include traditional poliovirus reservoirs without current environmental surveillance sites.

Despite high levels of poliovirus vaccination coverage during the reporting of SIAs nationally, the considerable challenges to quality of vaccination activities in the highest priority districts, as evidenced by repeatedly missed children and performance gaps indicated by LQAS survey results, could be addressed by improving microplanning of and supervision during SIAs in these areas. Postcampaign monitoring findings after the completion of vaccination activities should guide specific interventions focusing on areas with challenges to reaching and vaccinating children who are continually missed during SIAs. Vaccination activities should continue to be synchronized with neighboring Afghanistan, when and where feasible; tracking and vaccinating children in highly mobile populations and displaced families must also remain a priority for the Pakistan polio eradication program. With the return of targeted attacks on polio workers in Pakistan and Afghanistan by militants (*10*), efforts must be enhanced to ensure the safety of everyone serving at the frontlines of polio eradication.

There is an urgent need to take advantage of the window of opportunity presented by the current relative attenuation of poliovirus spread in Pakistan to end national and global transmission of WPV1. This will require expanding initiatives that foster more community engagement, providing incentives for participation in vaccination and empowering frontline polio workers, as well as mitigating the challenges posed by the flooding. To stop the spread of wild poliovirus in Pakistan and globally by the end of 2023, the country's polio eradication program must ensure that no child is missed in the quest to administer life-saving vaccines.

Acknowledgments

Beth Henderson, Casey Smith, National Center for Immunization and Respiratory Diseases, CDC; Geospatial Research, Analysis, and Services Program, Agency for Toxic Substances and Disease Registry; M. Salman, National Institute of Health Pakistan Polio Laboratory; Global Polio Laboratory Network, World Health Organization Eastern Mediterranean Region Office, Cairo, Egypt.

Corresponding author: Chukwuma Mbaeyi, cmbaeyi@cdc.gov, 404-823-7764.

[1]Global Immunization Division, Center for Global Health, CDC; [2]National Emergency Operation Center, Islamabad, Pakistan; [3]World Health Organization, Islamabad, Pakistan; [4]UNICEF, Islamabad, Pakistan; [5]Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, CDC; [6]Polio Eradication Department, World Health Organization, Geneva, Switzerland; [7]World Health Organization, Amman, Jordan.

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

References

1. Rachlin A, Patel JC, Burns CC, et al. Progress toward polio eradication—worldwide, January 2020–April 2022. MMWR Morb Mortal Wkly Rep 2022;71:650–5. PMID:35552352 https://doi.org/10.15585/mmwr.mm7119a2
2. Sadigh KS, Akbar IE, Wadood MZ, et al. Progress toward poliomyelitis eradication—Afghanistan, January 2020–November 2021. MMWR Morb Mortal Wkly Rep 2022;71:85–9. PMID:35051135 https://doi.org/10.15585/mmwr.mm7103a3
3. Global Polio Eradication Initiative. Delivering on a promise: GPEI strategy 2022–2026. Geneva, Switzerland: World Health Organization; 2021. https://polioeradication.org/gpei-strategy-2022-2026
4. Mbaeyi C, Baig S, Khan Z, et al. Progress toward poliomyelitis eradication—Pakistan, January 2020–July 2021. MMWR Morb Mortal Wkly Rep 2021;70:1359–64. PMID:34591827 https://doi.org/10.15585/mmwr.mm7039a1
5. Hsu CH, Rehman MS, Bullard K, et al. Progress toward poliomyelitis eradication—Pakistan, January 2019–September 2020. MMWR Morb Mortal Wkly Rep 2020;69:1748–52. PMID:33211676 https://doi.org/10.15585/mmwr.mm6946a5
6. Zomahoun DJ, Burman AL, Snider CJ, et al. Impact of COVID-19 pandemic on global poliovirus surveillance. MMWR Morb Mortal Wkly Rep 2021;69:1648–52. PMID:33382673 https://doi.org/10.15585/mmwr.mm695152a4
7. World Health Organization. Immunization analysis and insights. Geneva, Switzerland: World Health Organization; 2022. https://www.who.int/teams/immunization-vaccines-and-biologicals/immunization-analysis-and-insights/global-monitoring/immunization-coverage/who-unicef-estimates-of-national-immunization-coverage
8. Hampton LM, Farrell M, Ramirez-Gonzalez A, et al.; Immunization Systems Management Group of the Global Polio Eradication Initiative. Cessation of trivalent oral poliovirus vaccine and introduction of inactivated poliovirus vaccine—worldwide, 2016. MMWR Morb Mortal Wkly Rep 2016;65:934–8. PMID:27606675 https://doi.org/10.15585/mmwr.mm6535a3
9. Davlantes E; Malawi Ministry of Health; Global Polio Eradication Initiative. Notes from the field: initial outbreak response activity following wild poliovirus type 1 detection—Malawi, February 2022. MMWR Morb Mortal Wkly Rep 2022;71:776–7. PMID:35679180 https://doi.org/10.15585/mmwr.mm7123a3
10. Ahmad J, Mehsud S. Militants in Pakistan attack polio vaccination team, killing three. Reuters. June 28, 2022. https://www.reuters.com/business/healthcare-pharmaceuticals/militants-pakistan-attack-polio-vaccination-team-killing-three-2022-06-28

Influenza and COVID-19 Vaccination Coverage Among Health Care Personnel — United States, 2021–22

Hilda Razzaghi, PhD[1]; Anup Srivastav, PhD[2]; Marie A. de Perio, MD[3]; A. Scott Laney, PhD[4]; Carla L. Black, PhD[1]

The Advisory Committee on Immunization Practices (ACIP) and CDC recommend that all health care personnel (HCP) receive annual influenza vaccination to reduce influenza-related morbidity and mortality among these personnel and their patients (*1*). ACIP also recommends that all persons aged ≥6 months, including HCP, be vaccinated with COVID-19 vaccines and remain up to date (*2*,*3*). During March 29–April 19, 2022, CDC conducted an opt-in Internet panel survey of 3,618 U.S. HCP to estimate influenza vaccination coverage during the 2021–22 influenza season as well as receipt of the primary COVID-19 vaccination series and a booster dose. Influenza vaccination coverage was 79.9% during the 2021–22 season, and 87.3% of HCP reported having completed the primary COVID-19 vaccination series; among these HCP, 67.1% reported receiving a COVID-19 booster dose. Among HCP, influenza, COVID-19 primary series, and COVID-19 booster dose vaccination coverage were lowest among assistants and aides, those working in long-term care (LTC) or home health care settings, and those whose employer neither required nor recommended the vaccines. Overall, employer requirements for influenza and COVID-19 primary series vaccines were reported by 43.9% and 59.9% of HCP, respectively; among HCP who completed the primary series of COVID-19 vaccines, 23.5% reported employer requirements for COVID-19 booster vaccines. Vaccination coverage for all three vaccine measures was higher among HCP who reported employer vaccination requirements and ranged from 95.8% to 97.3% for influenza, 90.2% to 95.1% for COVID-19 primary series, and 76.4% to 87.8% for COVID-19 booster vaccinations among HCP who completed the primary series of COVID-19 vaccines, by work setting. Implementing workplace strategies demonstrated to improve vaccination coverage among HCP, including vaccination requirements or active promotion of vaccination, can increase influenza and COVID-19 vaccination coverage among HCP and reduce influenza and COVID-19–related morbidity and mortality among HCP and their patients (*4*).

An Internet panel survey of HCP was conducted during March 29–April 19, 2022, to provide estimates of influenza and COVID-19 vaccination coverage among HCP during the 2021–22 influenza season. Similar surveys have been conducted annually since the 2010–11 influenza season, and previously published results from the 2020–21 season are available (*5*). Respondents were recruited from two preexisting national opt-in Internet sources: Medscape,* a medical website managed by WebMD Health Professional Network, and general population Internet panels operated by Dynata.† Responses were weighted to the distribution of the U.S. population of HCP§ by occupation,¶ age, sex, race and ethnicity, work setting, and U.S. Census Bureau region. A poststratification weight for each survey respondent was calculated by fitting a generalized exponential model and estimating the model parameters using calibration equations (*6*). Among 3,830 eligible participants, a total of 3,679 completed the survey (completion rate = 96.1%**). Sixty-one participants were excluded because they did not report their occupational setting or indicated a setting other than those listed, and the verbatim description did not qualify as a health care setting, leaving 3,618 respondents in the analytic sample. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.††

Estimated (weighted) proportions and corresponding 95% CIs for three vaccination measures (influenza vaccination coverage for the 2021–22 season, COVID-19 vaccination coverage [i.e., receipt of ≥1 dose and completion of primary series§§], and

* Physicians, nurse practitioners, physician assistants, nurses, dentists, pharmacists, allied health professionals, technicians, and technologists were recruited from the current membership roster of Medscape. https://www.medscape.com

† Assistants, aides, and nonclinical personnel (e.g., administrators, clerical support workers, janitors, food service workers, and housekeepers) were recruited from general population Internet panels operated by Dynata. https://www.dynata.com

§ Population control totals of U.S. HCP by occupation and work setting were obtained from the U.S. Department of Commerce Bureau of Labor Statistics' occupational employment and wage statistics (https://www.bls.gov/oes/current/oessrci.htm). Population control totals by other demographic characteristics were obtained from the Bureau of Labor Statistics' labor force statistics from the current population survey. https://www.bls.gov/cps/data.htm

¶ Major occupational categories included physicians and dentists, nurse practitioners and physician assistants, nurses, pharmacists, other clinical personnel (including allied health professionals, technicians and technologists, and emergency medical technicians and paramedics), assistants and aides, and nonclinical personnel (including administrative support staff members and managers, and nonclinical support staff members).

** A survey response rate requires specification of the denominator at each stage of sampling. During recruitment of an online opt-in survey sample, such as the Internet panels described in this report, these numbers are not available; therefore, a response rate cannot be calculated. Instead, the survey completion rate is provided.

†† 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.

§§ Completion of primary series of COVID-19 vaccines was defined as the receipt of a 2-dose primary mRNA COVID-19 vaccine series for respondents who did not report being immunocompromised, or an additional dose after completion of a 2-dose mRNA COVID-19 vaccine series for respondents who reported being immunocompromised. For respondents whose initial vaccine was Janssen (Johnson & Johnson), completion of primary COVID-19 vaccination series was defined as the receipt of 1 dose for those who were not immunocompromised, or a second COVID-19 vaccine (either Janssen or mRNA) for those who were immunocompromised (because of solid organ transplant, blood or bone marrow transplant, immune deficiencies, HIV, use of corticosteroids, or use of other immune-weakening medicines).

COVID-19 booster vaccination[¶¶]) were estimated for each work setting, occupation, and demographic characteristic. LTC settings include nursing homes, assisted living facilities, other long-term care facilities, home health agencies, and home health care. Employer requirements for all three vaccination measures were assessed through three separate questions.[***] The Korn-Graubard method was used to calculate CIs for proportions, assuming that the weighted estimates were approximately unbiased.[†††] CDC's National Center for Health Statistics reliability criteria for proportions were applied to the estimates in the descriptive analyses of HCP characteristics (*7*). T-tests were used to assess differences among subgroups; $p<0.05$ was considered statistically significant. SAS (version 9.4; SAS Institute) and SAS-callable SUDAAN (version 11.0.1; RTI International) were used to conduct all analyses.

Overall, 79.9% of HCP reported having received an influenza vaccination during the 2021–22 season, not significantly different from the 75.9% reported during the 2020–21 season (Table 1). During the 2021–22 season, higher influenza vaccination coverage was reported among HCP with either a master's, professional, or doctoral degree (92.3%) and an associate or bachelor's degree (80.2%) than among those with some college education or less (66.7%). Influenza vaccination coverage was lower among nurse practitioners and physician assistants (92.4%), nurses (87.8%), other clinical personnel (87.8%), nonclinical HCP (75.7%), and assistants and aides (68.8%) compared with coverage among physicians (96.8%). Influenza vaccination coverage during 2021–22 was highest among HCP working in hospitals (92.0%) and lowest among HCP working in LTC settings (66.4%). Coverage was higher among HCP who reported an employer requirement for influenza vaccination (96.8%) than among those who reported an employer recommendation (76.5%) or no recommendation or requirement for vaccination (48.1%). Compared with the 2020–21 influenza season, increases in influenza vaccination coverage were observed among HCP aged 30–45 years (7.5 percentage points), those with more than a college degree (10.9 percentage points), physicians (5.5 percentage points), and pharmacists (4.3 percentage points).

Overall, 89.9% of HCP reported having received ≥1 dose of a COVID-19 vaccine, and 87.3% reported having completed the primary COVID-19 vaccination series (Table 2). Among those who completed the primary series, 67.1% reported having received a COVID-19 booster vaccine dose. Completion of primary COVID-19 vaccination was higher among HCP with more than a college degree (97.0%), those with an associate or bachelor's degree (87.3%), physicians (98.7%), those who received an influenza vaccination during the 2020–21 influenza season (94.1%), and those working in hospitals (91.6%), nonrural areas (88.6%), and facilities where their employer required COVID-19 vaccination (93.1%) compared with the respective reference groups. Similar patterns were observed for receipt of a COVID-19 booster vaccine dose, with the addition of higher coverage among HCP aged 45–59 years (71.7%) and ≥60 years (87.0%), and lower coverage among female HCP (64.7%) and those working in the U.S. Census Bureau South Region (59.8%).

Employer requirements for receipt of influenza and COVID-19 primary series vaccination were reported by 43.9% and 59.9% of HCP, respectively (Figure). Overall, among HCP who completed the primary series of COVID-19 vaccines, 23.5% reported employer requirement for COVID-19 booster vaccination. HCP working in LTC settings were less likely to report requirements for receipt of any vaccine compared with HCP working in hospitals and ambulatory care settings. Coverage with influenza vaccine, the primary COVID-19 series, and a COVID-19 booster dose was higher among HCP who reported an employer requirement for vaccination than among those who reported an employer recommendation or neither a recommendation nor requirement for vaccination. Among HCP who reported employer vaccination requirements, influenza vaccination coverage ranged from 95.8% to 97.3%, COVID-19 primary series vaccination coverage ranged from 90.2% to 95.1%, and COVID-19 booster vaccination coverage among HCP who completed the primary series of COVID-19 vaccines ranged from 76.4% to 87.8%, by work setting. Among HCP who reported that their employer neither recommended nor required vaccinations, influenza vaccination coverage ranged from 40.1% to 64.2%, COVID-19 primary series vaccination coverage ranged from 54.4% to 62.8%, and among HCP who completed the primary series of COVID-19 vaccines, COVID-19 booster vaccination coverage ranged from 46.1% to 59.7%, by work setting.

[¶¶] COVID-19 booster vaccination was defined as the receipt of a third dose of COVID-19 vaccine after completion of a 2-dose primary mRNA COVID-19 vaccine series for respondents who did not report being immunocompromised, or a fourth dose of COVID-19 vaccine after completion of a 3-dose mRNA COVID-19 vaccine series for respondents who reported being immunocompromised. For respondents whose initial vaccine was Janssen, booster vaccination was defined as the receipt of a second COVID-19 vaccine (either Janssen or mRNA) for respondents who were not immunocompromised or 3 total doses for respondents who were immunocompromised.

[***] Questions included, "Since July 1, 2021, has your employer recommended or required that you be vaccinated for flu?," "Since December 2020, has your employer recommended or required that you be vaccinated for COVID-19?," and "Has your employer recommended or required that you be vaccinated with a COVID-19 booster vaccine?" Analyses of employer requirements for COVID-19 vaccine booster doses were restricted to 2,256 HCP who completed the primary series and excluded 1,044 HCP who encountered an erroneous skip pattern, which was corrected on the second day of the survey.

[†††] https://www.aapor.org/AAPOR_Main/media/MainSiteFiles/NPS_TF_Report_Final_7_revised_FNL_6_22_13.pdf; https://www.aapor.org/getattachment/Education-Resources/For-Researchers/AAPOR_Guidance_Nonprob_Precision_042216.pdf

TABLE 1. Receipt of influenza vaccination during 2020–21 and 2021–22 influenza seasons among health care personnel, by selected characteristics — Internet panel surveys,* United States, April 2021 and April 2022

Characteristic	2020–21 Influenza season		2021–22 Influenza season		Percentage point change in weighted % vaccinated, 2020–21 to 2021–22 (95% CI)†
	No. (weighted %)	Weighted % vaccinated (95% CI)†	No. (weighted %)	Weighted % vaccinated (95% CI)†	
Total	**2,391**	**75.9 (71.3 to 80.1)**	**3,618**	**79.9 (76.6 to 82.9)**	**4.0 (−1.4 to 9.4)**
Age group, yrs					
18–30 (Ref)	263 (17.5)	65.0 (48.1 to 79.5)§	343 (17.3)	71.4 (55.7 to 84.0)	6.4 (−14.7 to 27.5)
30–45	1,007 (38.9)	76.3 (69.8 to 82.0)	1,616 (39.7)	83.8 (80.8 to 86.5)	7.5 (0.8 to 14.2)¶
45–60	774 (29.0)	79.2 (72.0 to 85.3)	1,112 (29.1)	77.7 (73.6 to 81.5)	−1.5 (−9.2 to 6.2)
≥60	346 (14.6)	81.3 (71.2 to 89.0)	547 (13.9)	83.7 (77.5 to 88.8)	2.4 (−8.1 to 12.9)
Race and ethnicity**					
White, non-Hispanic (Ref)	1,419 (61.4)	79.9 (75.1 to 84.1)	2,329 (60.7)	80.9 (76.6 to 84.7)	1.0 (−5.1 to 7.1)
Black, non-Hispanic	316 (17.0)	67.4 (52.9 to 79.9)	319 (16.5)	77.3 (70.3 to 83.3)	9.9 (−5.1 to 24.9)
Hispanic or Latino	399 (14.1)	68.0 (48.5 to 83.8)§	485 (14.3)	78.5 (65.5 to 88.3)	10.5 (−10.5 to 31.5)
Other, non-Hispanic	253 (7.5)	77.1 (62.7 to 87.9)	471 (8.5)	80.4 (71.9 to 87.2)	3.3 (−11.4 to 18.0)
Education					
Some college education or less (Ref)	541 (29.1)	66.7 (58.2 to 74.6)	526 (27.3)	66.7 (59.9 to 73.1)	0.0 (−10.5 to 10.5)
Associate or bachelor's degree	767 (45.2)	78.7 (70.7 to 85.3)††	1,038 (45.0)	80.2 (74.3 to 85.2)††	1.5 (−7.6 to 10.6)
Master's, professional, or doctoral degree	1,082 (25.7)	81.4 (74.4 to 87.1)††	2,053 (27.7)	92.3 (89.7 to 94.5)††	10.9 (4.1 to 17.7)¶
Occupation§§					
Physician (Ref)	283 (3.4)	91.3 (85.2 to 95.5)	591 (3.6)	96.8 (94.9 to 98.1)	5.5 (0.1 to 10.9)¶
Nurse practitioner/Physician assistant	147 (1.4)	88.9 (56.0 to 99.5)§	333 (1.7)	92.4 (88.7 to 95.1)††	3.5 (−18.5 to 25.5)
Nurse	179 (18.4)	90.3 (82.2 to 95.5)	362 (18.7)	87.8 (82.7 to 91.8)††	−2.5 (−10.6 to 5.6)
Pharmacist	309 (1.3)	90.3 (86.4 to 93.4)	509 (1.5)	94.6 (92.2 to 96.4)	4.3 (0.2 to 8.4)¶
Other clinical personnel¶¶	561 (18.8)	83.0 (75.5 to 89.0)††	916 (18.8)	87.8 (85.2 to 90.1)††	4.8 (−2.4 to 12.0)
Assistant/Aide	577 (24.2)	64.8 (60.4 to 68.9)††	540 (24.8)	68.8 (64.4 to 73.0)††	4.0 (−2.0 to 10.0)
Nonclinical personnel***	306 (32.5)	69.0 (55.8 to 80.2)††	333 (30.9)	75.7 (65.9 to 83.9)††	6.7 (−8.5 to 21.9)
**Work setting††† **					
Hospital	914 (38.8)	91.6 (87.8 to 94.5)††	1,488 (40.3)	92.0 (89.6 to 94.1)††	0.4 (−3.6 to 4.4)
Ambulatory care	734 (22.8)	77.3 (63.9 to 87.6)	1,335 (31.2)	81.2 (77.2 to 84.7)	3.9 (−8.5 to 16.3)
Long-term care facility/Home health care§§§	576 (41.6)	66.0 (57.6 to 73.6)††	646 (29.3)	66.4 (57.5 to 74.4)††	0.4 (−11.0 to 12.0)
Other clinical setting¶¶¶	629 (10.9)	66.8 (54.6 to 77.5)	754 (9.5)	79.4 (72.4 to 85.3)	12.6 (−0.5 to 25.7)
Location of primary workplace**					
Rural (Ref)	308 (12.2)	71.6 (60.1 to 81.4)	496 (14.8)	76.5 (70.7 to 81.6)	4.9 (−7.1 to 16.9)
Nonrural	2,080 (87.8)	76.5 (71.3 to 81.2)	3,117 (85.2)	80.5 (76.7 to 83.9)	4.0 (−2.1 to 10.1)
**U.S. Census Bureau region†††† **					
Northeast (Ref)	456 (19.8)	83.6 (76.5 to 89.2)	791 (19.9)	84.0 (79.0 to 88.1)	0.4 (−7.4 to 8.2)
Midwest	399 (23.3)	73.9 (63.3 to 82.9)	816 (23.1)	82.8 (78.5 to 86.4)	8.9 (−1.7 to 19.5)
South	1,024 (36.1)	75.5 (67.5 to 82.3)	1,251 (35.8)	77.7 (70.8 to 83.7)	2.2 (−7.6 to 12.0)
West	507 (20.8)	71.5 (57.5 to 83.1)	760 (21.1)	76.5 (67.7 to 84.0)	5.0 (−10.2 to 20.2)
Employer influenza vaccination requirement					
Required (Ref)	843 (34.2)	95.9 (92.6 to 98.0)	1,714 (43.9)	96.8 (95.3 to 98.0)	0.9 (−2.1 to 3.9)
Recommended	1,024 (42.4)	76.2 (69.9 to 81.8)††	1,293 (36.5)	76.5 (69.6 to 82.5)††	0.3 (−8.5 to 9.1)
Not required or recommended	524 (23.4)	46.0 (33.7 to 58.7)††	611 (19.5)	48.1 (40.3 to 55.9)††	2.1 (−12.6 to 16.8)
Receipt of ≥1 dose of a COVID-19 vaccine					
Yes	1,780 (68.2)	87.6 (83.4 to 91.1)††	3,361 (89.9)	85.5 (81.8 to 88.7)††	−2.1 (−7.3 to 3.1)
No (Ref)	609 (31.8)	51.0 (41.7 to 60.2)	257 (10.1)	29.4 (21.2 to 38.8)	−21.6 (−34.4 to −8.8)¶

See table footnotes on the next page.

Discussion

Overall influenza vaccination coverage among HCP during the 2021–22 season was similar to that during the previous season. As observed during previous influenza seasons, nonclinical personnel, assistants and aides, HCP working in LTC settings, HCP with less than a college degree, and HCP who reported their employer neither required nor recommended the influenza vaccine had the lowest vaccination coverage (*5*). Similar patterns were observed for COVID-19 vaccination coverage, although coverage with the primary COVID-19 vaccination series was ≥80% in all work settings, including LTC settings, possibly, in part, because of the prioritization of HCP when the U.S. vaccination program commenced in December 2020 and a relatively high prevalence of employers

TABLE 1. (*Continued*) Receipt of influenza vaccination during 2020–21 and 2021–22 influenza seasons among health care personnel, by selected characteristics — Internet panel surveys,* United States, April 2021 and April 2022

Abbreviation: Ref = referent group.

* Respondents were recruited from two preexisting national opt-in Internet sources: Medscape, a medical website managed by WebMD Health Professional Network, and general population Internet panels operated by Dynata.

† Korn-Graubard 95% CI.

§ Estimate does not meet CDC's National Center for Health Statistics standards of reliability (https://www.cdc.gov/nchs/data/series/sr_02/sr02_175.pdf). These estimates are presented in this report for comparison purposes and should be interpreted with caution.

¶ Statistically significant (p<0.05) when compared across seasons. The difference between percentages is based on unrounded percentages in each season.

** Race and ethnicity were self-reported. Respondents who identified as Hispanic or Latino might be of any race. The "Other" race category included persons who identified as Asian, American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, and persons who selected "Other" or "multiple races."

†† Statistically significant (p<0.05) when compared with Ref in the same season. The difference between percentages is based on unrounded percentages in each season.

§§ Excludes students (34).

¶¶ Includes dentists, allied health professionals, technicians and technologists, emergency technicians, emergency medical technicians, and paramedics.

*** Includes administrative support staff members and managers, and nonclinical support staff members.

††† Respondents could select more than one work setting. Each work setting is represented by a separate variable with two values (yes and no, where reference value is no).

§§§ Nursing home, assisted living facility, other long-term care facility, home health agency, or home health care.

¶¶¶ Includes dentist office or dental clinic, pharmacy, emergency medical services, and other settings where clinical care or related services were provided to patients.

**** Rurality was defined using zip codes in which >50% of the population resides in a nonmetropolitan county, a rural U.S. Census Bureau tract, or both, according to the Health Resources and Services Administration's definition of rural population. https://www.hrsa.gov/rural-health/about-us/what-is-rural

†††† https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf

TABLE 2. Receipt of ≥1 COVID-19 vaccine dose, completion of primary series,* and receipt of 1 COVID-19 booster dose† among health care personnel, by selected characteristics — Internet panel surveys,§ United States, April 2022

Characteristic	Total no. (weighted %) (N = 3,618)	Weighted % (95% CI)¶		
		Received ≥1 dose of COVID-19 vaccine (N = 3,618)	Completed primary COVID-19 vaccination series (N = 3,618)	Receipt of first COVID-19 booster dose among HCP who completed primary COVID-19 vaccination series (N = 3,300)
Overall	**3,618**	**89.9 (88.2–91.5)**	**87.3 (85.4–89.1)**	**67.1 (63.6–70.4)**
Age group, yrs				
18–29 (Ref)	343 (17.3)	91.1 (86.4–94.6)	86.4 (80.2–91.3)	50.9 (37.2–64.5)
30–44	1,616 (39.7)	88.5 (85.2–91.2)	84.8 (81.3–87.9)	63.1 (58.8–67.3)
45–59	1,112 (29.1)	89.7 (86.6–92.2)	88.9 (85.9–91.5)	71.7 (66.8–76.2)**
≥60	547 (13.9)	93.2 (88.6–96.4)	92.0 (87.2–95.4)	87.0 (81.8–91.1)**
Race and ethnicity††				
White, non-Hispanic (Ref)	2,329 (60.7)	89.2 (86.8–91.2)	87.1 (84.6–89.3)	66.4 (61.7–71.0)
Black, non-Hispanic	319 (16.5)	88.9 (83.6–93.0)	84.9 (78.6–89.9)	60.1 (51.8–68.1)
Hispanic or Latino	485 (14.3)	92.1 (87.2–95.6)	88.4 (82.8–92.7)	68.8 (60.2–76.6)
Other, non-Hispanic	471 (8.5)	94.4 (89.8–97.4)**	92.1 (85.8–96.2)	81.3 (73.5–87.6)**
Sex				
Male (Ref)	1,081 (21.9)	92.2 (87.3–95.7)	90.0 (85.0–93.8)	75.2 (69.1–80.7)
Female	2,537 (78.1)	89.3 (87.4–91.0)	86.5 (84.4–88.5)	64.7 (60.5–68.6)**
Education				
Some college education or less (Ref)	526 (27.3)	81.0 (76.3–85.1)	77.5 (72.6–81.9)	50.8 (43.2–58.4)
Associate or bachelor's degree	1,038 (45.0)	90.6 (87.9–92.8)**	87.3 (84.1–90.0)**	65.9 (59.7–71.7)**
Master's, professional, or doctoral degree	2,053 (27.7)	97.7 (96.5–98.6)**	97.0 (95.6–98.0)**	81.5 (77.7–84.9)**
Occupation§§				
Physician (Ref)	591 (3.6)	98.7 (97.3–99.5)	98.7 (97.3–99.5)	89.6 (86.6–92.2)
Nurse practitioner/ Physician assistant	333 (1.7)	95.1 (92.2–97.2)**	93.8 (90.5–96.1)**	72.8 (67.0–78.1)**
Nurse	362 (18.7)	95.4 (92.7–97.3)**	92.8 (88.8–95.7)**	75.5 (69.2–81.1)**
Pharmacist	509 (1.5)	96.6 (94.3–98.2)**	96.2 (93.8–97.8)**	83.0 (79.3–86.4)**
Other clinical personnel¶¶	916 (18.8)	95.2 (92.2–97.3)**	93.9 (90.9–96.2)**	73.4 (69.1–77.5)**
Assistant/Aide	540 (24.8)	79.9 (75.9–83.5)**	76.5 (72.4–80.3)**	51.1 (45.3–56.8)**
Nonclinical personnel***	333 (30.9)	89.8 (85.2–93.3)**	86.4 (81.4–90.5)**	64.5 (54.6–73.5)**
Work setting†††				
Hospital	1,488 (40.3)	94.1 (91.2–96.3)**	91.6 (88.4–94.2)**	72.7 (68.3–76.7)**
Ambulatory care	1,335 (31.2)	92.0 (89.0–94.5)	89.5 (86.1–92.3)	66.4 (61.3–71.2)
Long-term care facility/Home health care§§§	646 (29.3)	83.6 (79.6–87.0)**	80.0 (75.6–84.0)**	61.0 (51.5–69.9)
Other clinical setting¶¶¶	754 (9.5)	87.9 (81.4–92.7)	84.8 (77.6–90.3)	63.9 (54.9–72.3)

See table footnotes on the next page.

TABLE 2. (*Continued*) Receipt of ≥1 COVID-19 vaccine dose, completion of primary series,* and receipt of 1 COVID-19 booster dose† among health care personnel, by selected characteristics — Internet panel surveys,§ United States, April 2022

Characteristic	Total no. (weighted %) (N = 3,618)	Weighted % (95% CI)¶ Received ≥1 dose of COVID-19 vaccine (N = 3,618)	Completed primary COVID-19 vaccination series (N = 3,618)	Receipt of first COVID-19 booster dose among HCP who completed primary COVID-19 vaccination series (N = 3,300)
Location of primary workplace**				
Rural (Ref)	496 (14.8)	82.5 (77.1–87.2)	80.6 (75.0–85.4)	62.5 (55.2–69.4)
Nonrural	3,117 (85.2)	91.3 (89.5–93.0)**	88.6 (86.5–90.4)**	67.8 (63.8–71.5)
U.S. Census Bureau region†††				
Northeast (Ref)	791 (19.9)	90.4 (86.5–93.4)	89.4 (85.4–92.6)	71.7 (65.3–77.6)
Midwest	816 (23.1)	90.7 (86.1–94.2)	87.8 (83.0–91.7)	66.3 (60.3–72.0)
South	1,251 (35.8)	88.7 (85.5–91.3)	84.7 (81.0–87.9)	59.8 (52.7–66.6)**
West	760 (21.1)	90.8 (86.9–93.9)	89.1 (85.0–92.5)	75.1 (67.7–81.6)
Employer COVID-19 vaccination recommendation				
Required (Ref)	2,155 (59.9)	95.4 (93.3–97.0)	93.1 (90.8–95.0)	70.4 (67.0–73.8)
Recommended	1,179 (32.1)	86.3 (82.6–89.4)**	83.3 (79.2–86.8)**	63.4 (57.1–69.4)**
Not recommended or required	245 (8.0)	64.9 (56.2–72.9)**	60.9 (51.9–69.3)**	61.6 (49.6–72.6)
Receipt of influenza vaccine during 2020–2021				
Yes	3,115 (79.9)	96.3 (94.7–97.5)**	94.1 (92.3–95.6)**	71.0 (68.0–73.9)**
No (Ref)	503 (20.1)	64.7 (57.0–71.9)	60.3 (52.1–68.1)	42.4 (29.1–56.6)
Place of first dose of COVID-19 vaccination				
At work	1,900 (50.5)	NA	NA	NA
Place other than work§§§§	1,461 (49.5)	NA	NA	NA

Abbreviations: HCP = health care personnel; NA = not applicable; Ref = referent group.

* Completion of primary series of COVID-19 vaccines was defined as the receipt of a 2-dose primary mRNA COVID-19 vaccine series for respondents who did not report being immunocompromised, or an additional dose after completion of a 2-dose mRNA COVID-19 vaccine series for respondents who reported being immunocompromised. For respondents whose initial vaccine was Janssen (Johnson & Johnson), completion of primary COVID-19 vaccination series was defined as the receipt of 1 dose for those who were not immunocompromised, or a second COVID-19 vaccine (either Janssen or mRNA) for those who were immunocompromised.

† COVID-19 booster vaccination was defined as the receipt of a third dose of COVID-19 vaccine after completion of a 2-dose primary mRNA COVID-19 vaccine series for respondents who did not report being immunocompromised, or a fourth dose of COVID-19 vaccine after completion of a 3-dose mRNA COVID-19 vaccine series for respondents who reported being immunocompromised. For respondents whose initial vaccine was Janssen, booster vaccination was defined as the receipt of a second COVID-19 vaccine dose (either Janssen or mRNA) for respondents who were not immunocompromised or 3 total doses for respondents who were immunocompromised.

§ Respondents were recruited from two preexisting national opt-in Internet sources: Medscape, a medical website managed by WebMD Health Professional Network, and general population Internet panels operated by Dynata.

¶ Korn-Graubard 95% CI.

** Statistically significant (p<0.05) when compared with Ref.

†† Race and ethnicity were self-reported. Respondents who identified as Hispanic or Latino might be of any race. The "Other" race category included persons who identified as Asian, American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, and persons who selected "Other" or "multiple races."

§§ Excludes students (34).

¶¶ Includes dentists, allied health professionals, technicians and technologists, emergency technicians, emergency medical technicians, and paramedics.

*** Includes administrative support staff members and managers, and nonclinical support staff members.

††† Respondents could select more than one work setting. Each work setting is represented by a separate variable with two values (yes and no, where reference value is no).

§§§ Nursing home, assisted living facility, other long-term care facility, home health agency, or home health care.

¶¶¶ Includes dentist office or dental clinic, pharmacy, emergency medical services, and other settings where clinical care or related services were provided to patients.

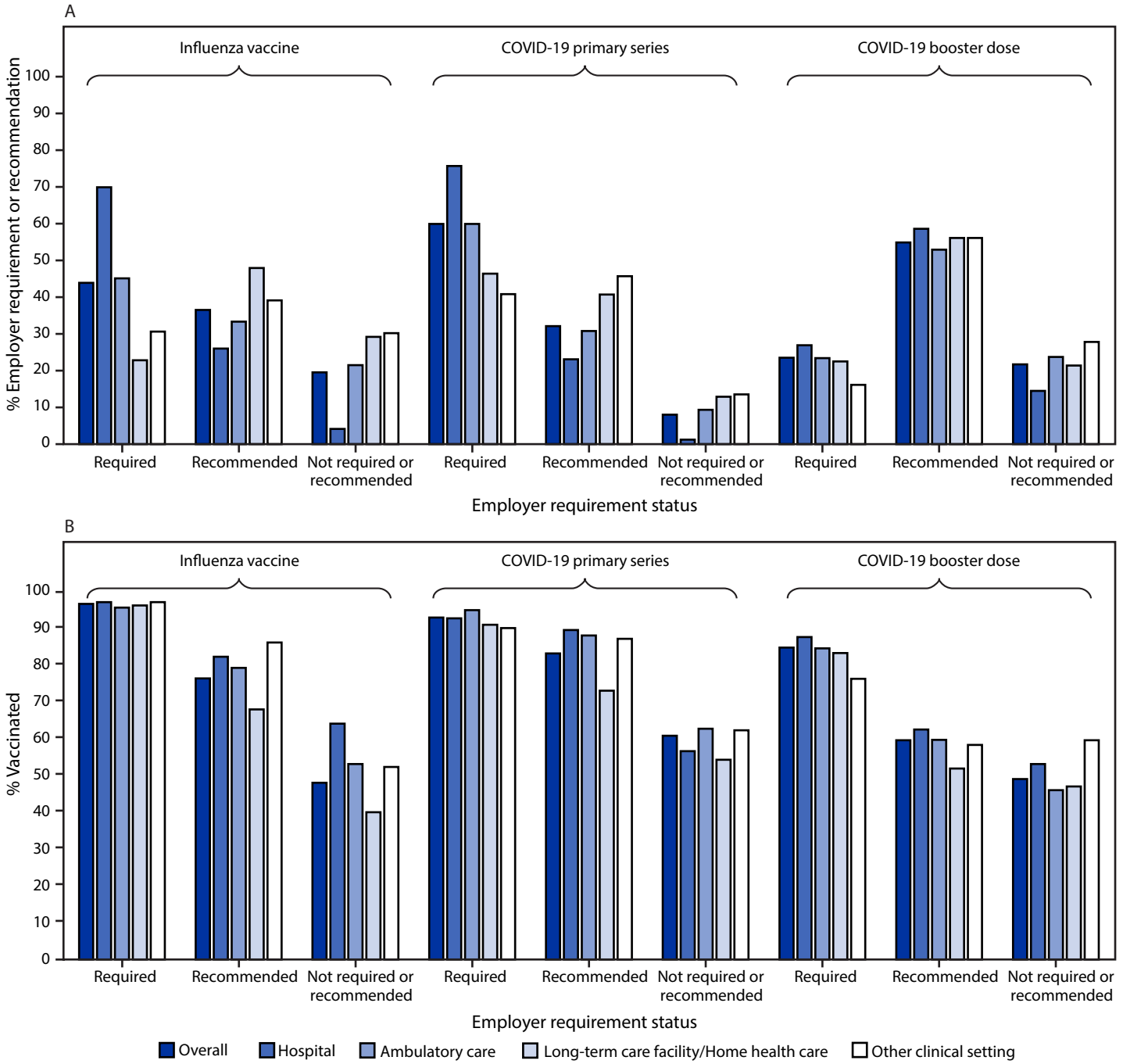
**** Rurality was defined using zip codes in which >50% of the population resides in a nonmetropolitan county, a rural U.S. Census Bureau tract, or both, according to the Health Resources and Services Administration's definition of rural population. https://www.hrsa.gov/rural-health/about-us/what-is-rural

†††† https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf

§§§§ "Other" place of first or only COVID-19 vaccination includes other medically or nonmedically related place, such as a drugstore, supermarket, and pharmacy.

required COVID-19 vaccination among HCP. Although the prevalence of reported requirements for influenza vaccination during the 2021–22 season increased by approximately 10 percentage points compared with those during the 2020–21 season, requirements for influenza vaccination were lower than were those for COVID-19 vaccination in most work settings, especially LTC settings. Requirements for COVID-19 booster vaccination were infrequently reported in all work settings by HCP who had completed the primary COVID-19 vaccination series, even among hospitals, a large percentage of which had requirements for influenza and COVID-19 primary vaccination. Thus, compared with primary COVID-19 vaccination coverage, influenza vaccination coverage was lower in nonhospital settings, and COVID-19 booster vaccination coverage was lower in all settings. Given that vaccine-induced immunity wanes over time after vaccination, remaining up to date with all COVID-19 recommended vaccination is important for all eligible persons to prevent COVID-19–related hospitalization and severe outcomes, and for HCP to protect their patients (*3*,*8*). In September 2022, CDC recommended an updated

FIGURE. Prevalence of employer requirement or recommendation for influenza and COVID-19* vaccination (A) and vaccination coverage,† by employer requirement status (B) among health care personnel, by work setting§ — Internet panel surveys,¶ United States, April 2022



* COVID-19 booster vaccination coverage was restricted to health care personnel who completed the primary series of COVID-19 vaccines. Analysis specific to employer requirements for COVID-19 booster vaccines was restricted to 2,256 health care personnel who completed the primary series of COVID-19 vaccines and excluded 1,044 health care providers who encountered an erroneous skip pattern which was corrected on the second day of the survey.

† Completion of primary series of COVID-19 vaccines was defined as the receipt of a 2-dose primary mRNA COVID-19 vaccine series for respondents who did not report being immunocompromised, or an additional dose after completion of a 2-dose mRNA COVID-19 vaccine series for respondents who reported being immunocompromised. For respondents whose initial vaccine was Janssen (Johnson & Johnson), completion of primary COVID-19 vaccination series was defined as the receipt of 1 dose for those who were not immunocompromised, or a second COVID-19 vaccine (either Janssen or mRNA) for those who were immunocompromised.

§ Includes dentist office or dental clinic, pharmacy, emergency medical services, and other settings where clinical care or related services were provided to patients.

¶ Respondents were recruited from two preexisting national opt-in Internet sources: Medscape, a medical website managed by WebMD Health Professional Network, and general population Internet panels operated by Dynata.

Summary

What is already known about this topic?

Influenza and COVID-19 vaccines are recommended for all persons aged ≥6 months, including health care personnel (HCP).

What is added by this report?

HCP influenza vaccination coverage was 79.9% during the 2021–22 season; 87.3% completed primary COVID-19 vaccination, 67.1% of whom received a COVID-19 booster dose. Influenza, primary COVID-19, and COVID-19 booster coverage was higher among HCP who reported employer vaccination requirements for those vaccines; coverage was lowest among HCP working in long-term care settings.

What are the implications for public health practice?

Enhanced efforts are needed to improve HCP vaccination coverage, especially with COVID-19 booster doses and annually for influenza vaccines. Staying up to date with COVID-19 and influenza vaccines can protect HCP and their patients.

bivalent COVID-19 booster vaccination to provide enhanced protection against circulating strains of COVID-19 (*9*).

The findings in this report are subject to at least four limitations. First, the study used a nonprobability sample of volunteer members of Medscape and Dynata Internet panels. Responses were weighted to be representative of the U.S. population of HCP; however, some bias might remain in the coverage estimates. Second, the self-selection of respondents to the panels and to the survey might introduce selection bias if participation in the panel or survey is related to likelihood of being vaccinated. Third, vaccination status was self-reported and might be subject to recall or social desirability bias. Finally, insufficient sample size resulted in the coverage estimates in some subgroups not meeting the National Center for Health Statistics reliability criteria for reporting proportions.

HCP coverage with influenza vaccine, the primary COVID-19 vaccination series, and a booster COVID-19 dose was highest among those who reported employer vaccination requirements for the respective vaccines. Work settings that successfully implemented requirements for primary COVID-19 vaccination could consider the same requirements for COVID-19 booster doses to restore protection among HCP that has declined since their previous vaccination. In addition, many LTC settings now have experience implementing COVID-19 vaccine requirements and could consider these requirements for influenza vaccination to improve influenza vaccination coverage. The Centers for Medicare & Medicaid Services requires that many health care settings report both influenza[§§§] and COVID-19[¶¶¶] HCP vaccination data to CDC's National Healthcare Safety Network; the interim final rule published by the Centers for Medicare & Medicaid Services also requires LTC settings to offer the COVID-19 vaccine to staff members and residents and to educate them about benefits and potential side effects, which might increase vaccination coverage in these settings.[****] In addition, useful resources that can help to increase vaccination coverage among HCP include CDC's long term care web-based toolkit,[††††] which provides access to resources, strategies, and educational materials, and interventions recommended by the Community Preventive Services Task Force and CDC (*4*,*10*). Annual influenza vaccination and staying up to date with recommended COVID-19 vaccines are critical in prevention of severe disease as well as reduction of influenza and COVID-19–related morbidity and mortality among HCP and their patients.

Corresponding author: Hilda Razzaghi, hrazzaghi@cdc.gov.

[1]Immunization Services Division, National Center for Immunization and Respiratory Diseases, CDC; [2]Leidos, Inc., Atlanta, Georgia; [3]Office of the Director, National Institute for Occupational Safety and Health, CDC; [4]Division of Respiratory Health, National Institute for Occupational Safety and Health, CDC.

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

§§§ https://www.cdc.gov/nhsn/pdfs/cms/cms-reporting-requirements.pdf

¶¶¶ https://www.cdc.gov/nhsn/pdfs/covid19/ltcf/cms-covid19-req-508.pdf

**** https://www.cms.gov/medicareprovider-enrollment-and-certificationsurveycertificationgeninfopolicy-and-memos-states-and/interim-final-rule-covid-19-vaccine-immunization-requirements-residents-and-staff

†††† https://www.cdc.gov/flu/toolkit/long-term-care/index.htm

References

1. Advisory Committee on Immunization Practices; CDC. Immunization of health-care personnel: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2011;60(No. RR-7):1–45. PMID:22108587
2. CDC. Vaccines & immunizations: interim clinical considerations for use of COVID-19 vaccines currently approved or authorized in the United States. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. Accessed June 29, 2022. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html
3. CDC. COVID-19: stay up to date with COVID-19 vaccines including boosters. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. Accessed July 19, 2022. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html
4. Community Preventive Services Task Force. Worksite: seasonal influenza vaccinations using interventions with on-site, free, actively promoted vaccinations—healthcare workers. Atlanta, GA: US Department of Health and Human Services, CDC, Community Preventive Services Task Force; 2021. https://www.thecommunityguide.org/findings/worksite-seasonal-influenza-vaccinations-healthcare-on-site
5. Masalovich S, Razzaghi H, Duque J, et al. Influenza (flu): influenza vaccination coverage among health care personnel—United States, 2020–21 influenza season. Atlanta, GA: US Department of Health and Human Services, CDC; 2021. https://www.cdc.gov/flu/fluvaxview/hcp-coverage_1920-21-estimates.htm

6. Folsom, Jr. RE, Singh AC. The generalized exponential model for sampling weight calibration for extreme values, nonresponse, and poststratification. Alexandria, VA: American Statistical Association; 2000. http://www.asasrms.org/Proceedings/papers/2000_099.pdf
7. Parker JD, Talih M, Malec DJ, et al. National Center for Health Statistics data presentation standards for proportions. Vital Health Stat 2 2017; 175:1–22. PMID:30248016
8. Ferdinands JM, Rao S, Dixon BE, et al. Waning 2-dose and 3-dose effectiveness of mRNA vaccines against COVID-19–associated emergency department and urgent care encounters and hospitalizations among adults during periods of Delta and Omicron variant predominance—VISION network, 10 states, August 2021–January 2022. MMWR Morb Mortal Wkly Rep 2022;71:255–63. PMID:35176007 https://doi.org/10.15585/mmwr.mm7107e2
9. CDC. CDC newsroom: CDC recommends the first updated COVID-19 booster. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. https://www.cdc.gov/media/releases/2022/s0901-covid-19-booster.html
10. CDC. Vaccines & immunizations: promoting COVID-19 vaccine in long-term care settings. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. Accessed September 6, 2022. https://www.cdc.gov/vaccines/covid-19/long-term-care/pharmacy-partnerships.html

Effectiveness of Monovalent mRNA Vaccines Against COVID-19–Associated Hospitalization Among Immunocompetent Adults During BA.1/BA.2 and BA.4/BA.5 Predominant Periods of SARS-CoV-2 Omicron Variant in the United States — IVY Network, 18 States, December 26, 2021–August 31, 2022

Diya Surie, MD[1,*]; Levi Bonnell, PhD[1,*]; Katherine Adams, MPH[1]; Manjusha Gaglani, MBBS[2,3]; Adit A. Ginde, MD[4]; David J. Douin, MD[4]; H. Keipp Talbot, MD[5]; Jonathan D. Casey, MD[5]; Nicholas M. Mohr, MD[6]; Anne Zepeski, PharmD[6]; Tresa McNeal, MD[3,4]; Shekhar Ghamande, MD[3,4]; Kevin W. Gibbs, MD[7]; D. Clark Files, MD[7]; David N. Hager, MD, PhD[8]; Arber Shehu, MD[8]; Anne P. Frosch, MD[9]; Heidi L. Erickson, MD[9]; Michelle N. Gong, MD[10]; Amira Mohamed, MD[10]; Nicholas J. Johnson, MD[11]; Vasisht Srinivasan, MD[11]; Jay S. Steingrub, MD[12]; Ithan D. Peltan, MD[13]; Samuel M. Brown, MD[13]; Emily T. Martin, PhD[14]; Akram Khan, MD[15]; William S. Bender, MD[16]; Abhijit Duggal, MD[17]; Jennifer G. Wilson, MD[18]; Nida Qadir, MD[19]; Steven Y. Chang, MD, PhD[19]; Christopher Mallow, MD[20]; Carolina Rivas[20]; Jennie H. Kwon, DO[21]; Matthew C. Exline, MD[22]; Adam S. Lauring, MD, PhD[23]; Nathan I. Shapiro, MD[24]; Natasha Halasa, MD[5]; James D. Chappell, MD, PhD[5]; Carlos G. Grijalva, MD[5]; Todd W. Rice, MD[5]; William B. Stubblefield, MD[5]; Adrienne Baughman[5]; Kelsey N. Womack, PhD[5]; Kimberly W. Hart, MA[5]; Sydney A. Swan, MPH[5]; Yuwei Zhu, MD[5]; Jennifer DeCuir, MD, PhD[1]; Mark W. Tenforde, MD, PhD[1]; Manish M. Patel, MD[1]; Meredith L. McMorrow, MD[1,*]; Wesley H. Self, MD[5,*]; IVY Network

The SARS-CoV-2 Omicron variant (B.1.1.529 or BA.1) became predominant in the United States by late December 2021 (*1*). BA.1 has since been replaced by emerging lineages BA.2 (including BA.2.12.1) in March 2022, followed by BA.4 and BA.5, which have accounted for a majority of SARS-CoV-2 infections since late June 2022 (*1*). Data on the effectiveness of monovalent mRNA COVID-19 vaccines against BA.4/BA.5-associated hospitalizations are limited, and their interpretation is complicated by waning of vaccine-induced immunity (*2*–*5*). Further, infections with earlier Omicron lineages, including BA.1 and BA.2, reduce vaccine effectiveness (VE) estimates because certain persons in the referent unvaccinated group have protection from infection-induced immunity. The IVY Network[†] assessed effectiveness of 2, 3, and 4 doses of monovalent mRNA vaccines compared with no vaccination against COVID-19–associated hospitalization among immunocompetent adults aged ≥18 years during December 26, 2021–August 31, 2022. During the BA.1/BA.2 period, VE 14–150 days after a second dose was 63% and decreased to 34% after 150 days. Similarly, VE 7–120 days after a third dose was 79% and decreased to 41% after 120 days. VE 7–120 days after a fourth dose was 61%. During the BA.4/BA.5 period, similar trends were observed, although CIs for VE estimates between categories of time since the last dose overlapped. VE 14–150 days and >150 days after a second dose was 83% and 37%, respectively. VE 7–120 days and >120 days after a third dose was 60%and 29%, respectively. VE 7–120 days after the fourth dose was 61%. Protection against COVID-19–associated hospitalization waned even after a third dose. The newly authorized bivalent COVID-19 vaccines include mRNA from the ancestral SARS-CoV-2 strain and from shared mRNA components between BA.4 and BA.5 lineages and are expected to be more immunogenic against BA.4/BA.5 than monovalent mRNA COVID-19 vaccines (*6*–*8*). All eligible adults aged ≥18 years[§] should receive a booster dose, which currently consists of a bivalent mRNA vaccine, to maximize protection against BA.4/BA.5 and prevent COVID-19–associated hospitalization.

During December 26, 2021–August 31, 2022, adults aged ≥18 years admitted for COVID-19–like illness[¶] within the IVY Network of 21 hospitals in 18 states were eligible for inclusion in this test-negative, case-control analysis. Among patients hospitalized with COVID-19–like illness, case-patients

[*] These authors contributed equally to this report.

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

[§] On October 12, 2022, the Food and Drug Administration amended the emergency use authorizations of the Moderna COVID-19 vaccine and the Pfizer-BioNTech COVID-19 vaccine to authorize bivalent formulations of the vaccines for use as a single booster dose. The Moderna COVID-19 Vaccine, Bivalent, is authorized for use as a single booster dose in persons aged ≥6 years. The Pfizer-BioNTech COVID-19 Vaccine, Bivalent, is authorized for use as a single booster dose in persons aged ≥5 years. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-moderna-and-pfizer-biontech-bivalent-covid-19-vaccines

[¶] COVID-19–like illness was defined as having any one of the following: fever, cough, shortness of breath, loss of taste, loss of smell, new or worsening findings on chest imaging consistent with pneumonia, or use of respiratory support (e.g., high flow nasal cannula, noninvasive ventilation, or invasive mechanical ventilation).

received a positive SARS-CoV-2 nucleic acid amplification test (NAAT) or antigen test result within 14 days of illness onset and control-patients received a negative SARS-CoV-2 NAAT result. Upper respiratory specimens were collected from all enrolled patients and tested by reverse transcription–polymerase chain reaction (RT-PCR) at a central laboratory (Vanderbilt University Medical Center, Nashville, Tennessee). Specimens testing positive for SARS-CoV-2 were sent to the University of Michigan (Ann Arbor, Michigan) for whole genome sequencing to determine SARS-CoV-2 lineages.** Periods of lineage predominance were defined based on when >50% of sequenced specimens within the IVY Network represented a particular lineage.

Demographic and clinical data were obtained through electronic medical record (EMR) review and patient (or proxy) interview. COVID-19 mRNA vaccination status was verified from EMRs, state-based registries, vaccination cards, or self-report and adjudicated based on vaccination dates. Four vaccination groups were defined: 1) patients who received no vaccine doses before illness onset, 2) patients who received 2 doses of a monovalent mRNA vaccine ≥14 days before illness onset, 3) patients who received 3 doses of a monovalent mRNA vaccine ≥7 days before illness onset, and 4) patients who received 4 doses of a monovalent mRNA vaccine ≥7 days before illness onset. Patients were excluded if they had an immunocompromising condition,†† had an incomplete vaccination series, or had received a non-mRNA vaccine.§§

VE to prevent COVID-19–associated hospitalization was estimated by comparing the odds of antecedent monovalent mRNA vaccination (2, 3, or 4 doses) versus no previous vaccination between case-patients and control-patients. Using multivariable logistic regression models, VE was calculated as (1 – adjusted odds ratio [aOR]) × 100. Models were adjusted for U.S. Department of Health and Human Services region, calendar time in biweekly intervals, age group (18–49, 50–64, and ≥65 years), sex, race, and Hispanic or Latino (Hispanic) ethnicity. Results were stratified by periods of Omicron variant predominance (i.e., December 26, 2021–June 19, 2022 [BA.1/BA.2 period] and June 20–August 31, 2022 [BA.4/BA.5 period]), and by days since the last monovalent vaccine dose (14–150 days versus >150 days for 2 doses and 7–120 versus >120 days for 3 or 4 doses to align with previous guidance for next dose eligibility).¶¶ Differences with nonoverlapping 95% CIs were considered to be statistically significant. Analyses were conducted using Stata (version 17; StataCorp). This activity was determined to be public health surveillance by each participating site and CDC and was conducted consistent with applicable federal law and CDC policy.***

During December 26, 2021–August 31, 2022, a total of 6,599 immunocompetent patients were enrolled in the IVY Network, and 4,730 (72%) adult patients were included in the analysis (Table 1) (Figure). (A total of 1,869 patients were excluded from this analysis for the following reasons: non-mRNA vaccine receipt [390]; partially vaccinated [158]; implausible or unverified vaccination dates [632]; received vaccination before CDC recommendations [169]; illness onset >10 days before test date [125]; illness onset >14 days before hospitalization [12]; missing data [274]; withdrew [nine]; other [100].) Among the 4,730 patients included, 3,352 (71%) were enrolled during the BA.1/BA.2 period (1,699 case-patients and 1,653 control-patients) and 1,378 (29%) during the BA.4/BA.5 period (707 case-patients and 671 control-patients).

Case-patients' median ages during the BA.1/BA.2 period and the BA.4/BA.5 period were 65 and 69 years, respectively. Among patients enrolled during the BA.1/BA.2 period, 1,144 (34%) were unvaccinated, 1,016 (30%) had received 2 doses, 1,126 (34%) had received 3 doses, and 66 (2%) had received 4 doses. Among 1,378 patients included during the BA.4/BA.5 period, 369 (27%) were unvaccinated, 329 (24%) had received 2 doses, 510 (37%) had received 3 doses, and 170 (12%) had received 4 doses.

During the BA.1/BA.2 period, the overall VE of 3 COVID-19 mRNA vaccine doses against COVID-19–associated hospitalization (median interval between the last dose and illness onset = 145 days) was 69% (Table 2), and during the BA.4/BA.5 period (median interval between the last dose and illness onset = 233 days) was 31%; whereas overall VE of 2 or 4 doses between lineage periods was similar (39% versus 41% for 2 doses and 61% versus 60% for 4 doses). During the BA.1/BA.2 period, VE of 2 doses waned from 63% at 14–150 days since the second dose to 34% at >150 days,

** During the early BA.1 period (December 26, 2021–January 14, 2022), all specimens testing positive for SARS-CoV-2 by RT-PCR were submitted for whole genome sequencing; from January 15, 2022, onward, only specimens testing positive for SARS-CoV-2 by RT-PCR with a cycle threshold <32 for at least one of two nucleocapsid gene targets tested underwent whole genome sequencing. SARS-CoV-2 lineages were assigned by using PANGO on genomes with >80% coverage.

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

§§ Other exclusions included 1) receipt of a non-mRNA vaccine; 2) partial vaccination, including receipt of only 1 mRNA vaccine dose; 3) inability to verify vaccination status; 4) vaccination before CDC recommendations; 5) illness onset >10 days before test date; 6) illness onset >14 days before hospitalization; 7) missing data; and 8) withdrawal from participation.

¶¶ https://www.cdc.gov/vaccines/covid-19/clinical-considerations/archived-covid-19-vacc-schedule.html (Accessed September 27, 2022).

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

TABLE 1. Characteristics of immunocompetent adults hospitalized during BA.1/BA.2 and BA.4/BA.5 predominant periods of SARS-CoV-2 Omicron variant circulation* — IVY Network, 21 hospitals† in 18 U.S. states, December 26, 2021–August 31, 2022

Characteristic	No. (%)				
		BA.1/BA.2 period		BA.4/BA.5 period	
	Total (N = 4,730)	COVID-19 case-patients (n = 1,699)	Test-negative control-patients (n = 1,653)	COVID-19 case-patients (n = 707)	Test-negative control-patients (n = 671)
Vaccination status, no. of COVID-19 vaccine doses received					
Unvaccinated	1,513 (32)	709 (42)	435 (26)	214 (30)	155 (23)
2	1,345 (28)	533 (31)	483 (29)	148 (21)	181 (27)
3	1,636 (35)	432 (25)	694 (42)	277 (39)	233 (35)
4	236 (5)	25 (1)	41 (2)	68 (10)	102 (15)
Female sex	2,319 (49)	807 (47)	823 (50)	360 (51)	329 (49)
Median age, yrs (IQR)	**65 (52–76)**	**65 (52–77)**	**63 (50–74)**	**69 (54–79)**	**64 (54–74)**
Age group, yrs					
18–49	1,012 (21)	363 (21)	392 (24)	141 (20)	116 (17)
50–64	1,345 (28)	460 (27)	496 (30)	151 (21)	238 (35)
65–74	1,071 (23)	380 (22)	386 (23)	150 (21)	155 (23)
75–84	862 (18)	323 (19)	260 (16)	170 (24)	109 (16)
≥85	440 (9)	173 (10)	119 (7)	95 (13)	53 (8)
Race or ethnicity					
Black, non-Hispanic	910 (19)	314 (18)	352 (21)	114 (16)	130 (19)
White, non-Hispanic	2,846 (60)	999 (59)	985 (60)	457 (65)	405 (60)
Hispanic, any race	631 (13)	245 (14)	199 (12)	91 (13)	96 (14)
Other race, non-Hispanic§	251 (5)	108 (6)	79 (5)	36 (5)	28 (4)
Other¶	92 (2)	33 (2)	38 (2)	9 (1)	12 (2)
HHS Region					
1	941 (20)	403 (24)	303 (18)	113 (16)	122 (18)
2	266 (6)	62 (4)	90 (5)	51 (7)	63 (9)
3	153 (3)	59 (3)	62 (4)	17 (2)	15 (2)
4	879 (19)	356 (21)	366 (22)	85 (12)	75 (11)
5	564 (12)	208 (12)	216 (13)	74 (10)	66 (10)
6	486 (10)	116 (7)	136 (8)	121 (17)	113 (17)
7	346 (7)	118 (7)	101 (6)	61 (9)	66 (10)
8	643 (14)	207 (12)	219 (13)	119 (17)	98 (15)
9	174 (4)	67 (4)	63 (4)	24 (3)	20 (3)
10	278 (6)	103 (6)	100 (6)	42 (6)	33 (5)
No. of underlying conditions					
0	563 (12)	258 (15)	161 (10)	75 (11)	69 (10)
1	1,223 (26)	445 (26)	413 (25)	200 (28)	165 (25)
2	1,387 (29)	473 (28)	482 (29)	201 (28)	231 (34)
≥3	1,557 (33)	523 (31)	597 (36)	231 (33)	206 (31)

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

* BA.1/BA.2 period was during December 26, 2021–June 19, 2022; BA.4/BA.5 period was during June 20–August 31, 2022.

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

§ Other race includes Asian, Native American or Alaska Native, and Native Hawaiian or other Pacific Islander, which were combined because of small counts.

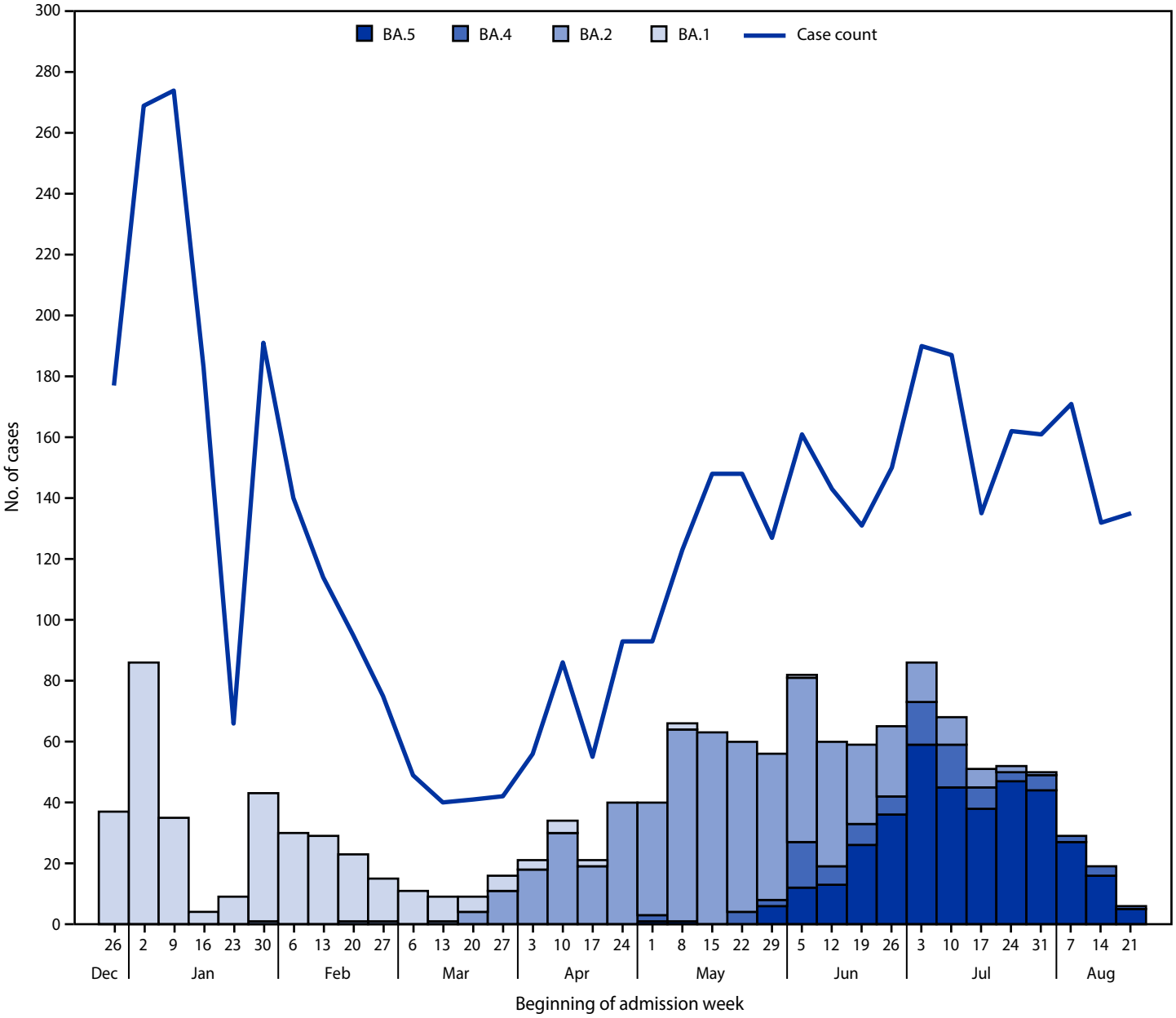
¶ Self-reported race and ethnicity as other or non-Hispanic, or patients for whom information on race and ethnicity was unavailable.

VE of 3 doses waned from 79% at 7–120 days since the last dose to 41% at >120 days, and VE of 4 doses 7–120 days after vaccination was 61%. During the BA.4/BA.5 period, VE estimates of 2 doses 14–150 days and >150 days after the second dose were 83% and 37%, respectively; VE estimates of 3 doses 7–120 days and >120 days from the last dose were 60% and 29%, respectively. VE of 4 doses 7–120 days after vaccination was 61%.

Discussion

Among immunocompetent adults hospitalized within the IVY Network in 18 states, a monovalent booster dose of mRNA COVID-19 vaccine had limited overall effectiveness against hospitalization caused by currently circulating SARS-CoV-2 Omicron variants, likely because of waning immunity. Waning protection against COVID-19–associated hospitalizations was

FIGURE. Numbers of COVID-19 cases* and SARS-CoV-2 whole genome–sequenced lineages[†,§,¶] among immunocompetent adults hospitalized with COVID-19 — IVY Network, 21 hospitals in 18 U.S. states, December 26, 2021–August 24, 2022[††]**



* N = 4,543.

† Number of SARS-CoV-2 whole genome–sequenced lineages: BA.1 = 349; BA.2 = 568; BA.4 = 91; BA.5 = 376.

§ Upper respiratory specimens collected from COVID-19 patients for detection of SARS-CoV-2 by reverse transcription–polymerase chain reaction (RT-PCR) were eligible for whole genome sequencing. During the early BA.1 period (December 26, 2021–January 14, 2022), all specimens testing positive for SARS-CoV-2 by RT-PCR were submitted for whole genome sequencing; from January 15, 2022 onward, only specimens testing positive for SARS-CoV-2 by RT-PCR with a cycle threshold <32 for at least one of two nucleocapsid gene targets tested underwent whole genome sequencing. SARS-CoV-2 lineages were assigned using PANGO on genomes with >80% coverage.

¶ BA.1, BA.2, BA.4, and BA.5 lineages. Among specimens from 568 patients who received test results indicating BA.2 lineage, 343 (60%) indicated BA.2.12.1 lineage.

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

†† Sequencing results complete through August 24, 2022. Low numbers of COVID-19 cases and SARS-CoV-2 whole genome–sequenced lineages in late January reflect an administrative pause in IVY Network enrollment during January 25–31, 2022.

TABLE 2. Effectiveness of monovalent mRNA vaccines against COVID-19–associated hospitalization during the BA.1/BA.2 and BA.4/BA.5 predominant periods of SARS-CoV-2 Omicron variant circulation* among immunocompetent adults — IVY Network, 21 hospitals in 18 U.S. states,† December 26, 2021–August 31, 2022

Group/No. of doses	Interval from last vaccine dose to illness onset, days§	Median interval (IQR) from last vaccine dose to illness, days	Vaccinated case-patients, no./total no. (%)	Vaccinated control-patients, no./total no. (%)	Adjusted VE, % (95% CI)¶
BA.1/BA.2 period					
2	≥14	277 (216–341)	533/1,242 (43)	483/918 (53)	39 (26–49)
	14–150	111 (87–130)	62/771 (8)	79/514 (15)	63 (46–75)
	>150	290 (241–351)	471/1,180 (40)	404/839 (48)	34 (20–46)
3	≥7	145 (92–190)	432/1,141 (38)	694/1,129 (61)	69 (62–74)
	7–120	80 (55–100)	167/876 (19)	393/828 (47)	79 (74–84)
	>120	180 (154–208)	265/974 (27)	301/736 (41)	41 (23–55)
4	≥7	26 (16–39)	25/734 (3)	41/476 (9)	61 (29–78)
	7–120	26 (16–39)	25/734 (3)	41/476 (9)	61 (29–78)
	>120	—	—	—	—
BA.4/BA.5 period					
2	≥14	428 (324–468)	131/317 (41)	181/336 (54)	41 (17–57)
	14–150	102 (77–123)	3/189 (2)	13/168 (8)	83 (35–96)
	>150	430 (329–471)	128/314 (41)	168/323 (52)	37 (12–55)
3	≥7	233 (196–267)	232/418 (56)	232/387 (60)	31 (7–49)
	7–120	74 (33–110)	13/199 (7)	24/179 (13)	60 (12–81)
	>120	237 (204–269)	219/405 (54)	208/363 (57)	29 (3–48)
4	≥7	69 (54–103)	63/249 (25)	102/257 (40)	60 (36–75)
	7–120	66 (51–85)	56/242 (23)	95/250 (38)	61 (37–76)
	>120	131 (126–137)	7/193 (4)	7/162 (4)	—

Abbreviation: VE = vaccine effectiveness.

* BA.1/BA.2 period was during December 26, 2021–June 19, 2022; BA.4/BA.5 period was during June 20–August 31, 2022.

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

§ An interval of 14 days was used to estimate the time needed to acquire immunity after receipt of a primary COVID-19 vaccination series; after the initial priming of the immune system, a shorter interval of 7 days was used to estimate the time required for response to booster doses. A threshold of 150 days was used to assess waning of 2-dose VE because eligibility for a third dose occurs >150 days after receipt of the second dose. Similarly, a threshold of 120 days was used to assess waning VE of a third dose because eligibility for the fourth dose occurs after 120 days. Follow-up time after 120 days from the fourth dose was insufficient to determine VE for this subgroup.

¶ VE was estimated by comparing the odds of being vaccinated with 2 and either 3 or 4 doses of a COVID-19 mRNA vaccine in cases and controls during the BA.1/BA.2 and BA.4/BA.5 periods, calculated as VE = 100 × (1 − odds ratio). Logistic regression models were adjusted for date of hospital admission (biweekly intervals), U.S. Department of Health and Human Services region, age group (18–49, 50–64, and ≥65 years), sex, and race or ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic of any race, non-Hispanic Other, or unknown). Age-specific models were adjusted for age as a continuous variable.

observed with either 2 or 3 doses of mRNA vaccine during the BA.1/BA.2 period with similar emerging trends during the BA.4/BA.5 periods. These findings demonstrate the importance of staying up to date with COVID-19 vaccinations through receipt of booster doses, which currently consist of bivalent mRNA vaccines for all eligible adults.

Three phenomena likely contributed to the lower overall VE estimated for 3 monovalent mRNA doses during the BA.4/BA.5 period compared with VE during the BA.1/BA.2 period. First, waning protection of mRNA vaccines against COVID-19–associated hospitalizations has been shown previously, and the current findings add to this evidence (*2*,*9*). Although the analysis was stratified by time since last vaccination during each lineage predominance period, the median interval between receipt of the third dose and illness onset during the BA.4/BA.5 period in this analysis was 233 days compared with 145 days during the BA.1/BA.2 period; thus, the BA.4/BA.5 period disproportionately included patients further removed from vaccination, which likely contributed to the lower VE during this period. Waning immunity between lineage periods was less discernible for 2 doses, likely because the median interval between receipt of the second dose and illness onset during the earliest period in this analysis (i.e., BA.1/BA.2) was 277 days, which might already be past the period during which waning can be demonstrated and instead reflects residual protection of 2 doses against COVID-19 hospitalization. In contrast, waning immunity from 4 doses between lineage periods could not be assessed because the median interval from the fourth dose and illness onset during the BA.1/BA.2 and BA.4/BA.5 periods was 26–69 days, which is too recent to show a decrease in protection

Summary

What is already known about this topic?

Monovalent mRNA vaccine effectiveness (VE) against COVID-19–associated hospitalization wanes over time; less is known about durability of protection during the SARS-CoV-2 Omicron BA.4/BA.5–predominant period.

What is added by this report?

Three-dose monovalent mRNA VE estimates against COVID-19–associated hospitalization decreased with time since vaccination. Three-dose VE during the BA.1/BA.2 and BA.4/BA.5 periods was 79% and 60%, respectively, during the initial 120 days after the third dose and decreased to 41% and 29%, respectively, after 120 days from vaccination.

What are the implications for public health practice?

Eligible adults aged ≥18 years should receive an updated bivalent COVID-19 mRNA vaccine to maximize protection against BA.4/BA.5 lineages and to prevent COVID-19–associated hospitalization.

against COVID-19 hospitalization. Second, increased immune evasion of BA.4/BA.5 lineages has been shown in neutralization assessments and may contribute to lower VE (*10*). However, the extent to which reduced neutralization in vitro correlates with reduced protection against severe disease is unknown; available studies have shown mixed results (*2*–*5*). A study from South Africa showed no difference in VE of 3 monovalent mRNA vaccine doses against hospitalization during the BA.4/BA.5 period compared with the BA.1/BA.2 period at the same intervals from vaccination, which was corroborated by findings from the United Kingdom showing similar VE against BA.2– or BA.4/BA.5–related hospitalizations (*2*,*3*). In contrast, a cohort study in Portugal found reduced protection against severe outcomes during BA.5 predominance (*4*). This was similar to U.S. findings, which indicated that 3-dose VE against hospitalization was lower during the BA.4/BA.5 period compared with the BA.1 period, although these VE estimates did not account for time after the last vaccine dose (*5*). Third, infection-induced immunity in the population substantially increased during and after the BA.1 period. National seroprevalence estimates indicate a 1.8-fold increase in SARS-CoV-2 infections during December 2021–February 2022, with 58% of the U.S. population infected by the end of February 2022.††† Cumulative previous infection during the BA.4/BA.5 period compared with that during the BA.1/BA.2 period likely resulted in a larger proportion of unvaccinated persons having infection-induced immunity during the BA.4/BA.5 period than during the BA.1/BA.2 period; thus, lower VE was observed.

††† https://covid.cdc.gov/covid-data-tracker/#national-lab (Accessed September 9, 2022).

The findings in this report are subject to at least four limitations. First, sample size was insufficient to assess VE varying over time for the BA.2 period separately, resulting in use of a combined BA.1/BA.2 group instead, or to demonstrate substantial waning during the BA.4/BA.5 period. Second, because lineage periods were pooled, the unique contributions of immune evasion associated with each lineage to VE could not be ascertained. Third, because previous infection could not be measured, its effect on VE estimates could only be inferred, not quantified. Finally, follow-up time after the fourth dose to assess waning immunity associated with this dose was insufficient.

Overall, these findings indicate that by the time BA.4/BA.5 lineages became predominant in the United States, effectiveness of 2 or 3 doses of monovalent mRNA vaccines against COVID-19–associated hospitalization had waned. Augmenting population immunity before the winter season through receipt of an updated bivalent COVID-19 booster is important to maximize protection against the predominant BA.5 lineages and prevent COVID-19–associated hospitalizations.

IVY Network

Nicole Calhoun, Baylor Scott & White Health; Judy Herrick, Baylor Scott & White Health; Eric Hoffman, Baylor Scott & White Health; Amanda McKillop, Baylor Scott & White Health; Kempapura Murthy, Baylor Scott & White Health; Michael Smith, Baylor Scott & White Health; Martha Zayed, Baylor Scott & White Health; Lesley De Souza, Baystate Medical Center; Lori-Ann Kozikowski, Baystate Medical Center; Scott Ouellette, Baystate Medical Center; Kiran Ashok, Cleveland Clinic; Susan Gole, Cleveland Clinic; Alexander King, Cleveland Clinic; Omar Mehkri, Cleveland Clinic; Bryan Poynter, Cleveland Clinic; Caitlin ten Lohuis, Emory University; Nicholas Stanley, Emory University; Sean Caspers, Hennepin County Medical Center; Audrey Hendrickson, Hennepin County Medical Center; Olivia Kaus, Hennepin County Medical Center; Leyla Taghizadeh, Hennepin County Medical Center; Walker Tordsen, Hennepin County Medical Center; Valerie Aston, Intermountain Medical Center; Robert Bowers, Intermountain Medical Center; Jeffrey Jorgensen, Intermountain Medical Center; Jennifer King, Intermountain Medical Center; Harith Ali, Johns Hopkins University; Richard E. Rothman, Johns Hopkins University; Jen-Ting Chen, Montefiore Medical Center; Rahul Nair, Montefiore Medical Center; Gopal Allada, Oregon Health & Science University; Genesis Briceno, Oregon Health & Science University; Shewit Giovanni, Oregon & Health Science University; Kinsley A. Hubel, Oregon Health & Science University; Jesus Martinez, Oregon Health & Science University; Minn Oh, Oregon Health & Science University; Jonathan Pak, Oregon Health & Science University; Jose Pena, Oregon Health & Science University; Alexandra Jun Gordon, Stanford University; Joe Levitt, Stanford University; Cynthia Perez, Stanford University; Jonasel Roque, Stanford University; Anita Visweswaran, Stanford University; Sarah Karow, The Ohio State University; Maryiam Khan, The Ohio State University, Austin Klingler, The Ohio State University; Sarah Pannu, The Ohio State University; David Smith, The Ohio State University, Elizabeth Schwartz,

The Ohio State University, Connor Snyder, The Ohio State University, Madison So, The Ohio State University; Preston So, The Ohio State University; Gabrielle Swoope, The Ohio State University; Michael Weigand, The Ohio State University; Michael Carricato, UCHealth University of Colorado Hospital; Ian Chambers, UCHealth University of Colorado Hospital; Conner Driver, UCHealth University of Colorado Hospital; Jennifer Goff, UCHealth University of Colorado Hospital; David Huynh, UCHealth University of Colorado Hospital; Kelly Jensen, UCHealth University of Colorado Hospital; Sukantha Chandrasekaran, University of California, Los Angeles; Trevor Frankel, University of California, Los Angeles; Omai Garner, University of California, Los Angeles; Catherine Fairfield, University of Iowa; Shannon Landers, University of Iowa; Paul Nassar, University of Iowa; Cameron Williams, University of Iowa; Hayley Gershengorn, University of Miami; Ramsay Bielak, University of Michigan; Christopher Blair, University of Michigan; William J. Fitzsimmons, University of Michigan; Rebecca Fong, University of Michigan; Julie Gilbert, University of Michigan; EJ McSpadden, University of Michigan; Lara Thomas, University of Michigan; Rachel Truscon, University of Michigan; Weronika Damek Valvano, University of Michigan; Layla A. Anderson, University of Washington; Christine D. Crider, University of Washington; Thomas C. Paulson, University of Washington; Kyle A. Steinbock, University of Washington; Marica Blair, Vanderbilt University Medical Center; Lauren J. Ezzell, Vanderbilt University Medical Center; Samarian J. Hargrave, Vanderbilt University Medical Center; Christy Kampe, Vanderbilt University Medical Center; Jakea Johnson, Vanderbilt University Medical Center; Jennifer L. Luther, Vanderbilt University Medical Center; Rendie E. McHenry, Vanderbilt University Medical Center; Bryan P. M. Peterson, Vanderbilt University Medical Center; Claudia Guevara Pulido, Vanderbilt University Medical Center; Laura L. Short, Vanderbilt University Medical Center; Margaret E. Whitsett, Vanderbilt University Medical Center; Madeline Hicks, Wake Forest University; Leigha Landreth, Wake Forest University; Mary LaRose, Wake Forest University; Lisa Parks, Wake Forest University; Hilary Babcock, Washington University; Tiffany Hink, Washington University; Kevin Jolani, Washington University; David McDonald, Washington University; Caroline O'Neal, Washington University; Bijal Parikh, Washington University; Katie Parrish, Washington University; Carleigh Samuels, Washington University.

Corresponding author: Diya Surie, dsurie@cdc.gov.

[1]CDC COVID-19 Emergency Response Team; [2]Baylor Scott & White Health, Temple, Texas; [3]Texas A&M University College of Medicine, Temple, Texas; [4]University of Colorado School of Medicine, Aurora, Colorado; [5]Vanderbilt University Medical Center, Nashville, Tennessee; [6]University of Iowa, Iowa City, Iowa; [7]Wake Forest University Baptist Medical Center, Winston-Salem, North Carolina; [8]Johns Hopkins Hospital, Baltimore, Maryland; [9]Hennepin County Medical Center, Minneapolis, Minnesota; [10]Montefiore Healthcare Center, Albert Einstein College of Medicine, New York, New York; [11]University of Washington School of Medicine, Seattle, Washington; [12]Baystate Medical Center, Springfield, Massachusetts; [13]Intermountain Medical Center and University of Utah, Salt Lake City, Utah; [14]University of Michigan School of Public Health, Ann Arbor, Michigan; [15]Oregon Health & Science University Hospital, Portland, Oregon; [16]Emory University School of Medicine, Atlanta, Georgia; [17]Cleveland Clinic, Cleveland, Ohio; [18]Stanford University School of Medicine, Stanford, California; [19]Ronald Reagan UCLA Medical Center, Los Angeles, California; [20]University of Miami, Miami, Florida; [21]Washington University, St. Louis, Missouri; [22]The Ohio State University Wexner Medical Center, Columbus, Ohio; [23]University of Michigan School of Medicine, Ann Arbor, Michigan; [24]Beth Israel Deaconess Medical Center, Boston, Massachusetts.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Samuel M. Brown reports personal fees from Hamilton Ventilators outside the submitted work. Jonathan D. Casey reports grants from the National Institutes of Health (NIH) and U.S. Department of Defense (DoD), outside the submitted work. Steven Y. Chang reports consulting for PureTech Health in 2020 and Kiniksa Pharmaceuticals and membership on the safety monitoring board (DSMB) for an investigator-initiated study at UCLA. James D. Chappell reports grants from NIH and DoD during the conduct of the study. David J. Douin reports grants received from NIH and National Institute of General Medical Sciences, outside the submitted work. Abhijit Duggal reports grants from NIH and participation on a steering committee for ALung technologies, outside the submitted work. Matthew C. Exline reports grants from the NIH and Regeneron, as well as support from Abbott Labs for sponsored talks, outside the submitted work. D. Clark Files reports personal consultant fees from Cytovale and membership on DSMB from Medpace, outside the submitted work. Anne P. Frosch reports grants from NIH, outside the submitted work. Manjusha Gaglani reports grants from Abt Associates, Westat, Janssen, and participation as co-chair on the Infection Diseases and Immunizations Committee for the Texas Pediatric Society, outside the submitted work. Kevin W. Gibbs reports grants from NIH and DoD, and DoD funds for Military Health System Research Symposium travel in 2022, outside the submitted work. Adit A. Ginde reports grants from NIH, DoD, AbbVie, and Faron Pharmaceuticals, outside the submitted work. Michelle N. Gong reports grants from NIH, speaking at medicine grand rounds at New York Medical College, travel support for the American Thoracic Society executive meeting, DSMB membership fees from Regeneron, and participation on the scientific advisory panel for Endpoint, outside the submitted work. Carlos G. Grijalva reports consultancy fees from Pfizer, Merck, and Sanofi-Pasteur; grants from Campbell Alliance/Syneos Health, NIH, the Food and Drug Administration, Agency for Healthcare Research and Quality, and Sanofi, outside the submitted work. David N. Hager grants from NIH, outside the submitted work. Natasha Halasa reports grants and nonfinancial support from Sanofi, and grants from Quidel outside the submitted work. Nicholas J. Johnson reports grants from the NIH, DoD, University of Washington, and Medic One Foundation, outside the submitted work. Akram Khan reports grants from United Therapeutics, Johnson & Johnson, Ely Lilly, 4D Medical, Dompe Pharmaceuticals, and GlaxoSmithKline, outside the submitted work. Jennie H. Kwon reports grants from National Institute of Allergy and Infectious Diseases (NIAID), outside the submitted work. Adam S. Lauring reports personal fees from Sanofi and Roche and grants from NIAID, Burroughs Wellcome Fund, Flu Lab, outside the submitted work. Emily T. Martin reports grants from Merck, outside the submitted work. Tresa McNeal reports participation as a webinar invited panelist and a Practice Management Committee member for Society of Hospital Medicine, outside the submitted work. Ithan D. Peltan reports grants from NIH, Janssen Pharmaceuticals and institutional support from Asahi Kasei Pharma and Regeneron,

outside the submitted work. Todd W. Rice reports grants from Abbvie Inc, and personal fees from Cumberland Pharmaceuticals, Inc, Cytovale, Inc., and Sanofi, Inc., outside the submitted work. William B. Stubblefield reports grants from NIH, outside the submitted work. Jennifer G. Wilson reports grants from NIH, and personal funds from the American College of Emergency Physicians and American Board of Internal Medicine, outside the submitted work. No other potential conflicts of interest were disclosed.

References

1. CDC. COVID data tracker. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. Accessed September 4, 2022. https://covid.cdc.gov/covid-data-tracker/#variant-proportions
2. Collie S, Nayager J, Bamford L, Bekker L-G, Zylstra M, Gray G. Effectiveness and durability of the BNT162b2 vaccine against Omicron sublineages in South Africa. N Engl J Med 2022;387:1332–3. PMID:36103455 https://doi.org/10.1056/NEJMc2210093
3. Kirsebom FCM, Andrews N, Stowe J, Ramsay M, Bernal JL. Effectiveness of the COVID-19 vaccines against severe disease with Omicron sublineages BA.4 and BA.5 in England. medRxiv [Preprint posted online September 1, 2022]. https://www.medrxiv.org/content/10.1101/2022.08.31.22279444v1.full.pdf
4. Kislaya I, Casaca P, Borges V, et al. SARS-CoV-2 BA.5 vaccine breakthrough risk and severity compared with BA.2: a case-case and cohort study using electronic health records in Portugal. medRxiv [Preprint posted online July 25, 2022]. https://www.medrxiv.org/content/10.1101/2022.07.25.22277996v1.full.pdf
5. Tseng HF, Ackerson BK, Bruxvoort KJ, et al. Effectiveness of mRNA-1273 against infection and COVID-19 hospitalization with SARS-CoV-2 Omicron subvariants: BA.1, BA.2, BA.2.12.1, BA.4, and BA.5. medRxiv [Preprint posted online October 1, 2022]. https://www.medrxiv.org/content/medrxiv/early/2022/10/01/2022.09.30.22280573.full.pdf?%253fcollection=
6. Chalkias S, Harper C, Vrbicky K, et al. A bivalent Omicron-containing booster vaccine against COVID-19. N Engl J Med 2022;387:1279–91. PMID:36112399 https://doi.org/10.1056/NEJMoa2208343
7. Food and Drug Administration. Coronavirus (COVID-19) update: FDA authorizes Moderna, Pfizer-BioNTech bivalent COVID-19 vaccines for use as a booster dose. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2022. https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-moderna-pfizer-biontech-bivalent-covid-19-vaccines-use
8. CDC. Vaccines & immunizations: use of COVID-19 vaccines in the United States. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. Accessed September 6, 2022. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html
9. Ferdinands JM, Rao S, Dixon BE, et al. Waning 2-dose and 3-dose effectiveness of mRNA vaccines against COVID-19–associated emergency department and urgent care encounters and hospitalizations among adults during periods of Delta and Omicron variant predominance—VISION Network, 10 states, August 2021–January 2022. MMWR Morb Mortal Wkly Rep 2022;71:255–63. PMID:35176007 https://doi.org/10.15585/mmwr.mm7107e2
10. Qu P, Faraone J, Evans JP, et al. Neutralization of the SARS-CoV-2 Omicron BA.4/5 and BA.2.12.1 Subvariants. N Engl J Med 2022;386:2526–8. PMID:35704428 https://doi.org/10.1056/NEJMc2206725

Effectiveness of COVID-19 mRNA Vaccines Against COVID-19–Associated Hospitalizations Among Immunocompromised Adults During SARS-CoV-2 Omicron Predominance — VISION Network, 10 States, December 2021–August 2022

Amadea Britton, MD[1,*]; Peter J. Embi, MD[2,3,4,*]; Matthew E. Levy, PhD[5]; Manjusha Gaglani, MBBS[6,7]; Malini B. DeSilva, MD[8]; Brian E. Dixon, PhD[2,9]; Kristin Dascomb, MD, PhD[10]; Palak Patel, MBBS[1]; Kristin E. Schrader, MA[5]; Nicola P. Klein, MD, PhD[11]; Toan C. Ong, PhD[12]; Karthik Natarajan, PhD[13,14]; Emily Hartmann, MPP[15]; Anupam B. Kharbanda, MD[16]; Stephanie A. Irving, MHS[17]; Monica Dickerson[1]; Margaret M. Dunne, MSc[5]; Chandni Raiyani, MPH[6]; Shaun J. Grannis, MD[2,9]; Edward Stenehjem, MD[10]; Ousseny Zerbo, PhD[11]; Suchitra Rao, MBBS[12]; Jungmi Han[13]; Chantel Sloan-Aagard, PhD[15,18]; Eric P. Griggs, MPH[1]; Zachary A. Weber, PhD[5]; Kempapura Murthy, MBBS[6]; William F. Fadel, PhD[2,9]; Nancy Grisel, MPP[10]; Charlene McEvoy, MD[8]; Ned Lewis, MPH[11]; Michelle A. Barron, MD[12]; Juan Nanez[15]; Sarah E. Reese, PhD[5]; Mufaddal Mamawala, MBBS[6]; Nimish R. Valvi, DrPH[2]; Julie Arndorfer, MPH[10]; Kristin Goddard, MPH[11]; Duck-Hye Yang, PhD[5]; Bruce Fireman, MA[11]; Sarah W. Ball, ScD[5]; Ruth Link-Gelles, PhD[1]; Allison L. Naleway, PhD[17,†]; Mark W. Tenforde, MD, PhD[1,†]

Persons with moderate-to-severe immunocompromising conditions might have reduced protection after COVID-19 vaccination, compared with persons without immunocompromising conditions (*1*–*3*). On August 13, 2021, the Advisory Committee on Immunization Practices (ACIP) recommended that adults with immunocompromising conditions receive an expanded primary series of 3 doses of an mRNA COVID-19 vaccine. ACIP followed with recommendations on September 23, 2021, for a fourth (booster) dose and on September 1, 2022, for a new bivalent mRNA COVID-19 vaccine booster dose, containing components of the BA.4 and BA.5 sublineages of the Omicron (B.1.1.529) variant (*4*). Data on vaccine effectiveness (VE) of monovalent COVID-19 vaccines among persons with immunocompromising conditions since the emergence of the Omicron variant in December 2021 are limited. In the multistate VISION Network,[§] monovalent 2-, 3-, and 4-dose mRNA VE against COVID-19–related hospitalization were estimated among adults with immunocompromising conditions[¶] hospitalized with COVID-19–like illness,[**] using a test-negative design comparing odds of previous vaccination among persons with a positive or negative molecular test result (case-patients and control-patients) for SARS-CoV-2 (the virus that causes COVID-19). During December 16, 2021–August 20, 2022, among SARS-CoV-2 test-positive case-patients, 1,815 (36.3%), 1,387 (27.7%), 1,552 (31.0%), and 251 (5.0%) received 0, 2, 3, and 4 mRNA COVID-19 vaccine doses, respectively. Among test-negative control-patients during this period, 6,928 (23.7%), 7,411 (25.4%), 12,734 (43.6%), and 2,142 (7.3%) received these respective doses. Overall, VE against COVID-19–related hospitalization among adults with immunocompromising conditions hospitalized for COVID-like illness during Omicron predominance was 36% ≥14 days after dose 2, 69% 7–89 days after dose 3, and 44% ≥90 days after dose 3. Restricting the analysis to later periods when Omicron sublineages BA.2/BA.2.12.1 and BA.4/BA.5 were predominant and 3-dose recipients were eligible to receive a fourth dose, VE was 32% ≥90 days after dose 3 and 43% ≥7 days after dose 4. Protection offered by vaccination among persons with immunocompromising conditions during Omicron predominance was moderate even after a 3-dose monovalent primary series or booster dose. Given the incomplete protection against hospitalization afforded by monovalent COVID-19 vaccines, persons with immunocompromising conditions might benefit from updated bivalent vaccine booster doses that target recently circulating Omicron sublineages, in line with ACIP recommendations. Further, additional protective recommendations for persons with immunocompromising conditions, including the use of prophylactic antibody therapy, early access to and use of

* These authors contributed equally to this report.
† These senior authors contributed equally to this report.
§ VISION Network includes partner sites in California (Kaiser Permanente Northern California), Colorado (University of Colorado), Indiana (Regenstrief Institute), Minnesota (HealthPartners), New York (Columbia University Irving Medical Center), Oregon (Kaiser Permanente Northwest), Texas (Baylor Scott & White Health and Paso Del Norte Health Information Exchange), Utah (Intermountain Healthcare), Washington (Kaiser Permanente Northwest), and Wisconsin (HealthPartners).
¶ Immunocompromised status was defined as the presence of at least one discharge diagnosis, using *International Classification of Diseases, Ninth Revision* (ICD-9) and *International Classification of Diseases, Tenth Revision* (ICD-10) diagnosis codes for solid malignancy (C00–C80, C7A, C7B, D3A, Z51.0, and Z51.1), hematologic malignancy (C81–C86, C88, C90–C96, D46, D61.0, D70.0, D61.2, D61.9, and D71), rheumatologic or inflammatory disorder (D86, E85 [except E85.0], G35, J67.9, L40.54, L40.59, L93.0, L93.2, L94, M05–M08, M30, M31.3, M31.5, M32–M34, M35.3, M35.8, M35.9, M46, and T78.40), other intrinsic immune condition or immunodeficiency (D27.9, D61.09, D72.89, D80, D81 [except D81.3], D82–D84, D89 [except D89.2], K70.3, K70.4, K72, K74.3–K74.6 [except K74.60 and K74.69], N04, and R18), or organ or stem cell transplant (T86 [except T86.82–T86.84, T86.89, and T86.9], D47.Z1, Z48.2, Z94, and Z98.85).
** Hospitalizations with a discharge diagnosis code consistent with COVID-19–like illness were included. COVID-19–like illness diagnoses included acute respiratory illness (e.g., respiratory failure or pneumonia) or related signs or symptoms (e.g., cough, fever, dyspnea, vomiting, or diarrhea) using ICD-9 and ICD-10 diagnosis codes.

antivirals, and enhanced nonpharmaceutical interventions such as well-fitting masks or respirators, should also be considered.

VISION Network methods to assess VE have been previously described (*3*,*5*). For this analysis, among adults aged ≥18 years, eligible medical encounters were defined as hospitalizations of patients with one or more immunocompromising conditions and a COVID-19–like illness diagnosis who underwent SARS-CoV-2 molecular testing ≤14 days before to <72 hours after the encounter date. Immunocompromising conditions were identified from electronic medical records based on *International Classification of Diseases, Ninth Revision* (ICD-9) and *International Classification of Diseases, Tenth Revision* (ICD-10) discharge diagnosis codes associated with being immunocompromised (*3*). Vaccination status was obtained from electronic health records or immunization registries. Two-dose vaccination was defined as receipt of a second dose of mRNA-1273 (Moderna) or BNT162b2 (Pfizer-BioNTech) vaccine ≥14 days before the index date;[††] 3- and 4-dose vaccinations were defined as receipt of the most recent dose ≥7 days before the index date. Persons with no documented COVID-19 vaccine doses were considered unvaccinated. Encounters for persons who received a non-mRNA COVID-19 vaccine, only 1 dose, >4 doses, dose 2 <14 days before the index date, dose 3 or 4 <7 days before the index date, or who received doses before vaccine was recommended by ACIP were excluded.[§§] The study period began on the date when ≥50% of sequenced specimens for each study site yielded an Omicron variant based on local surveillance data (site-specific start dates ranged from December 16 to 29, 2021) and ended August 20, 2022; start and end dates for Omicron sublineage predominance periods for BA.1 (including the original BA.1.1.529 variant and BA.1.1 and BA.1 sublineages), BA.2/BA.2.12.1, and BA.4/BA.5 were defined as the site-specific dates of ≥50% sublineage predominance[¶¶,***,†††].

VE was estimated using a test-negative design, comparing the odds of being vaccinated versus unvaccinated between persons with a positive or negative SARS-CoV-2 molecular test result (case-patients and control-patients, respectively). Multivariable logistic regression models were adjusted for age, geographic region,[§§§] calendar time, and local percentage of positive SARS-CoV-2 test results[¶¶¶] and weighted for the inverse propensity to be vaccinated or unvaccinated[****] (*5*). VE of 2- and 3-doses was estimated for the full Omicron period (all sublineages combined) and for each sublineage predominance period. VE estimates for 4 doses were restricted to a combined period including BA.2/BA.2.12.1 and BA.4/BA.5 periods because of limited 4-dose coverage among eligible persons before mid-March 2022.[††††] VE was estimated among all persons with one or more immunocompromising condition and then separately among persons who had a single condition in one

[††] The index date for each encounter 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).

[§§] Encounters among persons who received dose 3 before recommended by ACIP (August 13, 2021) or doses outside recommended dosing intervals (<28 days between doses 2 and 3 or <90 days between doses 3 and 4) were excluded. A fifth dose (second booster) was recommended for persons with immunocompromising conditions on March 29, 2022, ≥4 months after their fourth dose. However, only eight of 223 (3.6%) potentially eligible persons during the study period had received a fifth dose ≥7 days before the index date; because of the limited sample size these persons were excluded from analyses.

[¶¶] Partners contributing data on hospitalizations during dates of estimated ≥50% Omicron BA.1 predominance were in California (December 21, 2021–March 20, 2022), Colorado (December 19, 2021–March 20, 2022), Indiana (December 26, 2021–March 20, 2022), Minnesota and Wisconsin (December 25, 2021–March 21, 2022), New York (December 18, 2021–March 16, 2022), Oregon and Washington (December 24, 2021–March 23, 2022), Texas (Baylor Scott & White Health: December 16, 2021–March 18, 2022; Paso Del Norte Health Information Exchange: December 29, 2021–March 29, 2022), and Utah (December 24, 2021–March 18, 2022).

[***] Partners contributing data on hospitalizations during dates of estimated ≥50% Omicron BA.2/BA.2.12.1 predominance were in California (March 21–June 24, 2022), Colorado (March 21–June 18, 2022), Indiana (March 21–June 18, 2022), Minnesota and Wisconsin (March 22–June 21, 2022), New York (March 17–June 28, 2022), Oregon and Washington (March 24–June 28, 2022), Texas (Baylor Scott & White Health: March 19–June 21, 2022; Paso Del Norte Health Information Exchange: March 30–June 21, 2022), and Utah (March 19–June 22, 2022).

[†††] Partners contributing data on hospitalizations during dates of estimated ≥50% Omicron BA.4/BA.5 predominance were in California (June 25–August 20, 2022), Colorado (June 19–August 20, 2022), Indiana (June 19–August 20, 2022), Minnesota and Wisconsin (June 22–August 20, 2022), New York (June 29–August 20, 2022), Oregon and Washington (June 29–August 20, 2022), Texas (Baylor Scott & White Health: June 22–August 20, 2022; Paso Del Norte Health Information Exchange: June 22–August 20, 2022), and Utah (June 23–August 20, 2022).

[§§§] VISION Network site partners categorized their medical facilities into a total of 43 geographic subregions based on locations of included facilities.

[¶¶¶] Local SARS-CoV-2 circulation on the day of each medical visit was defined as percentage of positive local test results reported in the U.S. Department of Health and Human Services (HHS) Protect database; data present in HHS Protect are representative of diagnostic specimens being tested and reflects the majority of, but not all, laboratory-based COVID-19 testing being conducted in the United States.

[****] Covariates considered for inclusion in propensity score models and evaluated for imbalances after inverse propensity-to-be-vaccinated weighting have been previously published. An absolute standardized mean or proportion difference (SMD) >0.20 indicated a nonnegligible difference in variable distributions among events for vaccinated versus unvaccinated patients. All covariates with SMD >0.20 after weighting were also included in the multivariable logistic regression model for the respective VE estimate to minimize residual confounding.

[††††] The initial recommendation for a third vaccine dose in immunocompromised persons was made on August 13, 2021; a fourth dose was recommended on September 23, 2021. The initial recommended interval between doses 3 and 4 was ≥6 months, but this was shortened to ≥5 months on January 4, 2022, and then to 3 months on February 11, 2022. Persons who received their additional primary series dose after the August 2021 recommendation and were in the initial 6-month interval would have first been eligible for a fourth dose in late February 2022. As a result, very few persons received a fourth vaccine dose before March 2022. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us-appendix.html

of five mutually exclusive immunocompromising condition categories: 1) solid malignancies, 2) hematologic malignancies, 3) rheumatologic or inflammatory disorders, 4) other intrinsic immune conditions or immunodeficiencies, or 5) organ or stem cell transplants. VE was also estimated among recipients of an organ or stem cell transplant without excluding those with other immunocompromising conditions and among persons with any immunocompromising condition except an organ or stem cell transplant. Estimates with nonoverlapping 95% CIs were considered significantly different. Analyses were conducted using R software (version 4.1.1; R Foundation). The study was reviewed and approved by institutional review boards at participating sites or under a reliance agreement with the institutional review board of Westat, Inc. This activity was conducted consistent with applicable federal law and CDC policy.[§§§§]

During December 16, 2021–August 20, 2022, among 34,220 eligible hospitalizations for COVID-19–like illness in adults with immunocompromising conditions (median age = 69 years; IQR = 58–78 years), 8,798 (25.7%), 14,286 (41.7%), and 2,393 (7.0%) patients had received 2, 3, and 4 COVID-19 vaccine doses, respectively, including 11,088 (32.4% of all patients included) who received dose 3 ≥90 days before the index date and were therefore eligible for a fourth dose (Table 1). VE during the full Omicron period was 36% (95% CI = 30–41) ≥14 days after dose 2, 69% (95% CI = 63–74) 7–89 days after dose 3, and 44% (95% CI = 37–49) ≥90 days after dose 3 (Table 2). When stratified by sublineage period, VE was higher ≥7 days after receipt of dose 3 during the BA.1 period (67%; median interval since vaccination = 99 days) than during the BA.2/BA.2.12.1 (32%; median interval = 172 days) and BA.4/BA.5 periods (35%; median interval = 239 days). During the combined BA2/BA.2.12.1 and BA.4/BA.5 periods, when persons with immunocompromising conditions were eligible to receive a fourth dose, VE ≥90 days after dose 3 was 32% (median interval = 196 days), and ≥7 days after dose 4 was 43% (median interval = 61 days).

VE ≥7 days after receipt of dose 3 varied by immunocompromising condition, ranging from 43% among persons with an organ or stem cell transplant (with or without another condition) to 70% among those with a solid malignancy only (Table 3).

Discussion

In this multistate analysis of over 34,000 hospitalizations for COVID-19–like illness among adults with immunocompromising conditions, 2 doses of monovalent mRNA COVID-19 vaccine were 36% effective against COVID-19–associated hospitalization during a period of Omicron variant predominance. VE increased to 67% with the addition of a third dose of monovalent vaccine during BA.1 predominance but declined during the combined BA.2/BA.2.12.1 and BA.4/BA.5 periods to 32% ≥90 days after dose 3 and 43% ≥7 days after a monovalent fourth dose. These results suggest that monovalent COVID-19 vaccination among persons with immunocompromising conditions conferred moderate protection against COVID-19–associated hospitalization during Omicron circulation, with lower protection during BA.2/BA.2.12.1 and BA.4/BA.5 sublineage predominance periods.

Although protection increased after receipt of a third monovalent vaccine dose (compared with 2 doses), estimated 3-dose VE was lower in this study than in other similar studies among immunocompetent persons during Omicron predominance, including recent VISION Network analyses (*6*,*7*). Consistent with previous studies restricted to persons with immunocompromising conditions, VE in this study was lower among persons with certain immunocompromising conditions that might be associated with being more severely immunocompromised, particularly solid organ or stem cell transplant recipients.

Estimated VE among persons with immunocompromising conditions during Omicron predominance was lower than VE in comparable studies during Delta variant predominance (*2*). Protection was also lower during Omicron BA.2/BA.2.12.1 and BA.4/BA.5 than during BA.1 predominance, although the median interval since receipt of last vaccine dose was lower during BA.1, and waning effectiveness over time might have also contributed to the lower VE observed during these later sublineage periods. In either case, these findings suggest that the newly authorized bivalent booster vaccines, which target BA.4/BA.5 might offer additional benefit to persons with immunocompromising conditions (*8*).

Given the moderate protection observed even after monovalent booster doses, persons with immunocompromising conditions might also benefit from other recommended protective measures including preexposure prophylaxis with the antibody treatment tixagevimab/cilgavimab (Evusheld),[¶¶¶¶] which was authorized in December 2021 for persons with moderate-to-severe immunocompromising conditions and was associated with a reduction in risk for both symptomatic and severe COVID-19 in clinical trials (*9*). However, recent in vitro data suggest protection against emerging Omicron sublineages might be reduced and additional clinical data are needed (*10*).

The findings in this report are subject to at least four limitations. First, immunocompromising conditions were based on discharge diagnosis codes and a range of immune suppression is associated with each code. Second, residual confounding in VE models is possible. For example, history of previous infection could not be accurately ascertained, but might have differed between vaccinated and unvaccinated persons, which could affect VE estimates. Third, data on the use of outpatient

[§§§§] 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.

[¶¶¶¶] https://www.fda.gov/drugs/drug-safety-and-availability/fda-releases-important-information-about-risk-covid-19-due-certain-variants-not-neutralized-evusheld

TABLE 1. Characteristics of hospitalizations among immunocompromised* adults aged ≥18 years with COVID-19–like illness,† by mRNA COVID-19 vaccination status and SARS-CoV-2 test result — VISION Network, 10 states, December 2021–August 2022

Characteristic	Total No. (column %)	mRNA COVID-19 vaccination status§ No. (row %)						Positive SARS-CoV-2 test result	
			2 doses	3 doses	3 doses	4 doses			
		Unvaccinated	≥14 days earlier	7–89 days earlier	≥90 days earlier	≥7 days earlier	SMD¶	No. (row %)	SMD¶
All hospitalizations	**34,220 (100.0)**	**8,743 (25.5)**	**8,798 (25.7)**	**3,198 (9.3)**	**11,088 (32.4)**	**2,393 (7.0)**	**NA**	**5,005 (14.6)**	**NA**
Omicron sublineage predominance period									
BA.1**	**15,049 (44.0)**	4,422 (29.4)	4,486 (29.8)	2,638 (17.5)	3,503 (23.3)	0 (—)	0.67	3,190 (21.2)	0.55
BA.2/BA.2.12.1††	**12,470 (36.4)**	2,807 (22.5)	2,892 (23.2)	476 (3.8)	5,172 (41.5)	1,123 (9.0)		862 (6.9)	
BA.4/BA.5§§	**6,701 (19.6)**	1,514 (22.6)	1,420 (21.2)	84 (1.3)	2,413 (36.0)	1,270 (19.0)		953 (14.2)	
Site									
Baylor Scott & White Health	**7,513 (22.0)**	2,722 (36.2)	2,640 (35.1)	397 (5.3)	1,639 (21.8)	115 (1.5)	0.83	1,194 (15.9)	0.17
Columbia University	**2,375 (6.9)**	650 (27.4)	646 (27.2)	248 (10.4)	737 (31.0)	94 (4.0)		355 (14.9)	
HealthPartners	**2,043 (6.0)**	337 (16.5)	353 (17.3)	259 (12.7)	834 (40.8)	260 (12.7)		251 (12.3)	
Intermountain Healthcare	**2,323 (6.8)**	607 (26.1)	539 (23.2)	268 (11.5)	776 (33.4)	133 (5.7)		483 (20.8)	
KPNC	**9,355 (27.3)**	958 (10.2)	1,810 (19.3)	1,157 (12.4)	4,079 (43.6)	1,351 (14.4)		1,253 (13.4)	
KPNW	**1,966 (5.7)**	493 (25.1)	355 (18.1)	203 (10.3)	675 (34.3)	240 (12.2)		211 (10.7)	
PHIX	**189 (0.6)**	72 (38.1)	49 (25.9)	15 (7.9)	45 (23.8)	8 (4.2)		37 (19.6)	
Regenstrief Institute	**5,132 (15.0)**	1,829 (35.6)	1,390 (27.1)	402 (7.8)	1,424 (27.7)	87 (1.7)		758 (14.8)	
University of Colorado	**3,324 (9.7)**	1,075 (32.3)	1,016 (30.6)	249 (7.5)	879 (26.4)	105 (3.2)		463 (13.9)	
Age group, yrs									
18–49	**4,605 (13.5)**	2,044 (44.4)	1,358 (29.5)	302 (6.6)	820 (17.8)	81 (1.8)	0.54	666 (14.5)	0.03
50–64	**8,617 (25.2)**	2,658 (30.8)	2,552 (29.6)	788 (9.1)	2,256 (26.2)	363 (4.2)		1,304 (15.1)	
65–74	**9,684 (28.3)**	2,084 (21.5)	2,372 (24.5)	956 (9.9)	3,515 (36.3)	757 (7.8)		1,373 (14.2)	
75–84	**7,885 (23.0)**	1,390 (17.6)	1,759 (22.3)	747 (9.5)	3,174 (40.3)	815 (10.3)		1,142 (14.5)	
≥85	**3,429 (10.0)**	567 (16.5)	757 (22.1)	405 (11.8)	1,323 (38.6)	377 (11.0)		520 (15.2)	
Sex									
Male	**16,533 (48.3)**	4,296 (26.0)	4,100 (24.8)	1,544 (9.3)	5,383 (32.6)	1,210 (7.3)	0.03	2,449 (14.8)	0.01
Female	**17,687 (51.7)**	4,447 (25.1)	4,698 (26.6)	1,654 (9.4)	5,705 (32.3)	1,183 (6.7)		2,556 (14.5)	
Race and ethnicity									
White, non-Hispanic	**22,318 (65.2)**	5,498 (24.6)	5,458 (24.5)	2,050 (9.2)	7,632 (34.2)	1,680 (7.5)	0.27	3,149 (14.1)	0.08
Black, non-Hispanic	**3,805 (11.1)**	1,226 (32.2)	1,118 (29.4)	364 (9.6)	966 (25.4)	131 (3.4)		642 (16.9)	
Hispanic	**4,530 (13.2)**	1,211 (26.7)	1,357 (30.0)	430 (9.5)	1,264 (27.9)	268 (5.9)		728 (16.1)	
Other,¶¶ non-Hispanic	**2,805 (8.2)**	489 (17.4)	671 (23.9)	318 (11.3)	1,021 (36.4)	306 (10.9)		380 (13.5)	
Unknown	**762 (2.2)**	319 (41.9)	194 (25.5)	36 (4.7)	205 (26.9)	8 (1.0)		106 (13.9)	
Documented previous SARS-CoV-2 infection* **									
Yes	**4,672 (13.7)**	1,313 (28.1)	1,423 (30.5)	357 (7.6)	1,330 (28.5)	249 (5.3)	0.09	543 (11.6)	0.10
No	**29,548 (86.3)**	7,430 (25.1)	7,375 (25.0)	2,841 (9.6)	9,758 (33.0)	2,144 (7.3)		4,462 (15.1)	
Chronic respiratory condition†††									
Yes	**21,648 (63.3)**	5,419 (25.0)	5,555 (25.7)	2,073 (9.6)	7,067 (32.6)	1,534 (7.1)	0.04	3,519 (16.3)	0.18
No	**12,572 (36.7)**	3,324 (26.4)	3,243 (25.8)	1,125 (8.9)	4,021 (32.0)	859 (6.8)		1,486 (11.8)	
Solid malignancy									
Yes	**13,875 (40.5)**	3,234 (23.3)	3,458 (24.9)	1,290 (9.3)	4,858 (35.0)	1,035 (7.5)	0.10	1,433 (10.3)	0.29
No	**20,345 (59.5)**	5,509 (27.1)	5,340 (26.2)	1,908 (9.4)	6,230 (30.6)	1,358 (6.7)		3,572 (17.6)	
Hematologic malignancy									
Yes	**4,992 (14.6)**	1,086 (21.8)	1,231 (24.7)	494 (9.9)	1,765 (35.4)	416 (8.3)	0.10	789 (15.8)	0.04
No	**29,228 (85.4)**	7,657 (26.2)	7,567 (25.9)	2,704 (9.3)	9,323 (31.9)	1,977 (6.8)		4,216 (14.4)	
Rheumatologic or inflammatory disorder									
Yes	**8,341 (24.4)**	2,062 (24.7)	2,184 (26.2)	804 (9.6)	2,689 (32.2)	602 (7.2)	0.03	1,443 (17.3)	0.12
No	**25,879 (75.6)**	6,681 (25.8)	6,614 (25.6)	2,394 (9.3)	8,399 (32.5)	1,791 (6.9)		3,562 (13.8)	
Other intrinsic immune condition or immunodeficiency									
Yes	**13,183 (38.5)**	3,754 (28.5)	3,554 (27.0)	1,114 (8.5)	3,951 (30.0)	810 (6.1)	0.14	2,242 (17.0)	0.15
No	**21,037 (61.5)**	4,989 (23.7)	5,244 (24.9)	2,084 (9.9)	7,137 (33.9)	1,583 (7.5)		2,763 (13.1)	
Organ or stem cell transplant									
Yes	**2,951 (8.6)**	509 (17.2)	747 (25.3)	263 (8.9)	1,150 (39.0)	282 (9.6)	0.14	699 (23.7)	0.20
No	**31,269 (91.4)**	8,234 (26.3)	8,051 (25.7)	2,935 (9.4)	9,938 (31.8)	2,111 (6.8)		4,306 (13.8)	

See table footnotes on the next page.

TABLE 1. (*Continued*) Characteristics of hospitalizations among immunocompromised* adults aged ≥18 years with COVID-19–like illness,† by mRNA COVID-19 vaccination status and SARS-CoV-2 test result — VISION Network, 10 states, December 2021–August 2022

Characteristic	Total No. (column %)	mRNA COVID-19 vaccination status§ No. (row %) Unvaccinated	2 doses ≥14 days earlier	3 doses 7–89 days earlier	3 doses ≥90 days earlier	4 doses ≥7 days earlier	SMD¶	Positive SARS-CoV-2 test result No. (row %)	SMD¶
mRNA COVID-19 vaccination product received									
Moderna (mRNA-1273)	**9,555 (37.5)**	NA	3,461 (36.2)	1,284 (13.4)	3,913 (41.0)	897 (9.4)	NA	1,098 (11.5)	0.11
Pfizer-BioNTech (BNT162b2)	**14,769 (58.0)**	NA	5,293 (35.8)	1,620 (11.0)	6,584 (44.6)	1,272 (8.6)		1,983 (13.4)	
Heterologous	**1,153 (4.5)**	NA	44 (3.8)	294 (25.5)	591 (51.3)	224 (19.4)		109 (9.5)	
ICU admission									
Yes	**7,840 (22.9)**	2,276 (29.0)	2,119 (27.0)	685 (8.7)	2,307 (29.4)	453 (5.8)	0.11	1,100 (14.0)	0.03
No	**26,380 (77.1)**	6,467 (24.5)	6,679 (25.3)	2,513 (9.5)	8,781 (33.3)	1,940 (7.4)		3,905 (14.8)	
In-hospital death§§§									
Yes	**2,741 (8.0)**	915 (33.4)	702 (25.6)	213 (7.8)	746 (27.2)	165 (6.0)	0.12	609 (22.2)	0.16
No	**31,479 (92.0)**	7,828 (24.9)	8,096 (25.7)	2,985 (9.5)	10,342 (32.9)	2,228 (7.1)		4,396 (14.0)	

Abbreviations: ICD-9 = *International Classification of Diseases, Ninth Revision*; ICD-10 = *International Classification of Diseases, Tenth Revision;* ICU = intensive care unit; KPNC = Kaiser Permanente Northern California; KPNW = Kaiser Permanente Northwest; NA = not applicable; PHIX = Paso del Norte Health Information Exchange; SMD = standardized mean or proportion difference.

* Immunocompromised status was defined as the presence of at least one discharge diagnosis using ICD-9 and ICD-10 diagnosis codes for solid malignancy (ICD-10 codes: C00–C80, C7A, C7B, D3A, Z51.0, and Z51.1), hematologic malignancy (ICD-10 codes: C81–C86, C88, C90–C96, D46, D61.0, D70.0, D61.2, D61.9, and D71), rheumatologic or inflammatory disorder (ICD-10 codes: D86, E85 [except E85.0], G35, J67.9, L40.54, L40.59, L93.0, L93.2, L94, M05–M08, M30, M31.3, M31.5, M32–M34, M35.3, M35.8, M35.9, M46, and T78.40), other intrinsic immune condition or immunodeficiency (ICD-10 codes: D27.9, D61.09, D72.89, D80, D81 [except D81.3], D82–D84, D89 [except D89.2], K70.3, K70.4, K72, K74.3–K74.6 [except K74.60 and K74.69], N04, and R18), or organ or stem cell transplant (ICD-10 codes: T86 [except T86.82–T86.84, T86.89, and T86.9], D47.Z1, Z48.2, Z94, and Z98.85).

† Hospitalizations with a discharge code consistent with COVID-19–like illness and molecular testing for SARS-CoV-2 ≤14 days before to <72 hours after the encounter date were included. COVID-19–like illness diagnoses included acute respiratory illness (e.g., respiratory failure or pneumonia) or related signs or symptoms (cough, fever, dyspnea, vomiting, or diarrhea) using ICD-9 and ICD-10 diagnosis codes.

§ mRNA COVID-19 vaccination status was defined as having received the listed number of doses of an mRNA COVID-19 vaccine within the specified range of number of days before the encounter 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 hospital admission or the admission date if testing only occurred after the admission.

¶ An absolute SMD >0.20 indicates a nonnegligible difference in variable distributions between hospitalizations for vaccinated versus unvaccinated patients or for patients with positive SARS-CoV-2 test results versus patients with negative SARS-CoV-2 test results. For mRNA COVID-19 vaccination status, a single SMD was calculated by averaging the absolute SMDs obtained from pairwise comparisons of each vaccinated category versus unvaccinated. Specifically, it was calculated as the average of the absolute value of the SMDs for 1) vaccinated with 2 doses ≥14 days earlier versus unvaccinated, 2) vaccinated with 3 doses 7–89 days earlier versus unvaccinated, 3) vaccinated with 3 doses ≥90 days earlier versus unvaccinated, and 4) vaccinated with 4 doses ≥7 days earlier versus unvaccinated.

** Partners contributing data on hospitalizations during dates of estimated ≥50% Omicron BA.1 predominance were in California (December 21, 2021–March 20, 2022), Colorado (December 19, 2021–March 20, 2022), Indiana (December 26, 2021–March 20, 2022), Minnesota and Wisconsin (December 25, 2021–March 21, 2022), New York (December 18, 2021–March 16, 2022), Oregon and Washington (December 24, 2021–March 23, 2022), Texas (Baylor Scott & White Health: December 16, 2021–March 18, 2022; PHIX: December 29, 2021–March 29, 2022), and Utah (December 24, 2021–March 18, 2022).

†† Partners contributing data on hospitalizations during dates of estimated ≥50% Omicron BA.2/BA.2.12.1 predominance were in California (March 21–June 24, 2022), Colorado (March 21–June 18, 2022), Indiana (March 21–June 18, 2022), Minnesota and Wisconsin (March 22–June 21, 2022), New York (March 17–June 28, 2022), Oregon and Washington (March 24–June 28, 2022), Texas (Baylor Scott & White Health: March 19–June 21, 2022; PHIX: March 30–June 21, 2022), and Utah (March 19–June 22, 2022).

§§ Partners contributing data on hospitalizations during dates of estimated ≥50% Omicron BA.4/BA.5 predominance were in California (June 25–August 20, 2022), Colorado (June 19–August 20, 2022), Indiana (June 19–August 20, 2022), Minnesota and Wisconsin (June 22–August 20, 2022), New York (June 29–August 20, 2022), Oregon and Washington (June 29–August 20, 2022), Texas (Baylor Scott & White Health: June 22–August 20, 2022; PHIX: June 22–August 20, 2022), and Utah (June 23–August 20, 2022).

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

*** Previous SARS-CoV-2 infection was defined as having a positive SARS-CoV-2 test result (molecular or antigen) documented in the electronic health record ≥15 days before the hospital admission date.

††† Chronic respiratory condition was defined by corresponding discharge codes for asthma, chronic obstructive pulmonary disease, or other lung disease using ICD-9 and ICD-10 diagnosis codes.

§§§ In-hospital death was defined as death while hospitalized within 28 days after admission.

treatments such as nirmatelvir/ritonavir (Paxlovid) or prophylaxis with Evusheld were not available. Finally, SARS-CoV-2 genomic sequencing data were unavailable for individual encounters, and date of testing was used to assign likely sublineage ecologically.

Persons with immunocompromising conditions have been disproportionately affected by the COVID-19 pandemic. Whereas monovalent vaccination remains moderately protective in persons with immunocompromising conditions, VE has decreased compared with that during pre-Omicron periods, most notably during recent Omicron sublineage predominance periods, despite expanded dosing recommendations. Given the incomplete protection against hospitalization afforded by monovalent COVID-19 vaccines, persons with immunocompromising conditions might benefit from updated bivalent boosters that target BA.4/BA.5 sublineages. In addition, other

TABLE 2. Vaccine effectiveness* of 2-, 3-, and 4-dose mRNA COVID-19 vaccination against COVID-19–associated† hospitalizations among immunocompromised§ adults aged ≥18 years, by Omicron (and Omicron sublineage) predominance period¶ and mRNA COVID-19 vaccination status — VISION Network, 10 states, December 2021–August 2022**

Omicron predominance period/Vaccination status	Total	SARS-CoV-2 positive test result, no. (%)	Median interval since last dose, days (IQR)	VE % (95% CI)
Omicron predominance period				
Unvaccinated (Ref)	**8,743**	1,815 (20.8)	NA	NA
2 doses (≥14 days earlier)	**8,798**	1,387 (15.8)	316 (250–387)	36 (30–41)
3 doses (≥7 days earlier)	**14,286**	1,552 (10.9)	147 (96–202)	57 (53–61)
3 doses (7–89 days earlier)	**3,198**	335 (10.5)	59 (38–76)	69 (63–74)
3 doses (≥90 days earlier)	**11,088**	1,217 (11.0)	169 (131–218)	44 (37–49)
BA.1 sublineage predominance††				
Unvaccinated (Ref)	**4,422**	1,373 (31.1)	NA	NA
2 doses (≥14 days earlier)	**4,486**	1,008 (22.5)	283 (222–321)	40 (34–46)
3 doses (≥7 days earlier)	**6,141**	809 (13.2)	99 (65–133)	67 (63–71)
3 doses (7–89 days earlier)	**2,638**	302 (11.4)	59 (38–75)	75 (71–79)
3 doses (≥90 days earlier)	**3,503**	507 (14.5)	128 (109–152)	49 (41–57)
BA.2/BA.2.12.1 sublineage predominance§§				
Unvaccinated (Ref)	**2,807**	190 (6.8)	NA	NA
2 doses (≥14 days earlier)	**2,892**	204 (7.1)	371 (286–414)	7 (−16–25)
3 doses (≥7 days earlier)	**5,648**	372 (6.6)	172 (134–210)	32 (16–46)
3 doses (7–89 days earlier)	—¶¶	—	—	—
3 doses (≥90 days earlier)	**5,172**	351 (6.8)	179 (145–214)	32 (15–45)
BA.4/BA.5 sublineage predominance* **				
Unvaccinated (Ref)	**1,514**	252 (16.6)	NA	NA
2 doses (≥14 days earlier)	**1,420**	175 (12.3)	445 (336–488)	38 (23–50)
3 doses (≥7 days earlier)	**2,497**	371 (14.9)	239 (199–276)	35 (21–47)
3 doses (7–89 days earlier)	—	—	—	—
3 doses (≥90 days earlier)	**2,413**	359 (14.9)	241 (204–278)	36 (22–47)
BA.2/BA.2.12.1/BA.4/BA.5 sublineage predominance†††				
Unvaccinated (Ref)	**4,321**	442 (10.2)	NA	NA
2 doses (≥14 days earlier)	**4,312**	379 (8.8)	386 (305–441)	22 (10–33)
3 doses (≥7 days earlier)	**8,145**	743 (9.1)	190 (147–234)	33 (22–42)
3 doses (7–89 days earlier)	—	—	—	—
3 doses (≥90 days earlier)	**7,585**	710 (9.4)	196 (156–238)	32 (21–42)
4 doses (≥7 days earlier)	**2,393**	251 (10.5)	61 (34–91)	43 (27–56)

Abbreviations: ICD-9 = *International Classification of Diseases, Ninth Revision*; ICD-10 = *International Classification of Diseases, Tenth Revision*; NA = not applicable; PHIX = Paso del Norte Health Information Exchange; Ref = referent group; VE = vaccine effectiveness.

* VE was calculated as ([1 − odds ratio] x 100%), estimated using a test-negative design, adjusted for age, geographic region, calendar time (days since January 1, 2021), and local virus circulation (percentage of SARS-CoV-2–positive results from testing within the counties surrounding the facility on the date of the encounter) and weighted for inverse propensity to be vaccinated or unvaccinated (calculated separately for each VE estimate). Generalized boosted regression trees were used to estimate the propensity to be vaccinated based on sociodemographic characteristics, underlying medical conditions, and facility characteristics.

† Hospitalizations with a discharge code consistent with COVID-19–like illness and molecular testing for SARS-CoV-2 ≤14 days before to <72 hours after the encounter date were included. COVID-19–like illness diagnoses included acute respiratory illness (e.g., respiratory failure or pneumonia) or related signs or symptoms (cough, fever, dyspnea, vomiting, or diarrhea) using ICD-9 and ICD-10 diagnosis codes.

§ Immunocompromised status was defined as the presence of at least one discharge diagnosis using ICD-9 and ICD-10 diagnosis for solid malignancy (ICD-10 codes: C00–C80, C7A, C7B, D3A, Z51.0, and Z51.1), hematologic malignancy (ICD-10 codes: C81–C86, C88, C90–C96, D46, D61.0, D70.0, D61.2, D61.9, and D71), rheumatologic or inflammatory disorder (ICD-10 codes: D86, E85 [except E85.0], G35, J67.9, L40.54, L40.59, L93.0, L93.2, L94, M05–M08, M30, M31.3, M31.5, M32–M34, M35.3, M35.8, M35.9, M46, and T78.40), other intrinsic immune condition or immunodeficiency (ICD-10 codes: D27.9, D61.09, D72.89, D80, D81 [except D81.3], D82–D84, D89 [except D89.2], K70.3, K70.4, K72, K74.3–K74.6 [except K74.60 and K74.69], N04, and R18), or organ or stem cell transplant (ICD-10 codes: T86 [except T86.82–T86.84, T86.89, and T86.9], D47.Z1, Z48.2, Z94, and Z98.85).

¶ Based on ≥50% of sequenced specimens yielding a specific Omicron sublineage.

** mRNA COVID-19 vaccination status was defined as having received the listed number of doses of an mRNA COVID-19 vaccine within the specified range of number of days before the encounter 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 hospital admission or the admission date if testing only occurred after the admission.

†† Partners contributing data on hospitalizations during dates of estimated ≥50% Omicron BA.1 predominance were in California (December 21, 2021–March 20, 2022), Colorado (December 19, 2021–March 20, 2022), Indiana (December 26, 2021–March 20, 2022), Minnesota and Wisconsin (December 25, 2021–March 21, 2022), New York (December 18, 2021–March 16, 2022), Oregon and Washington (December 24, 2021–March 23, 2022), Texas (Baylor Scott & White Health: December 16, 2021–March 18, 2022; PHIX: December 29, 2021–March 29, 2022), and Utah (December 24, 2021–March 18, 2022).

§§ Partners contributing data on hospitalizations during dates of estimated ≥50% Omicron BA.2/BA.2.12.1 predominance were in California (March 21–June 24, 2022), Colorado (March 21–June 18, 2022), Indiana (March 21–June 18, 2022), Minnesota and Wisconsin (March 22–June 21, 2022), New York (March 17–June 28, 2022), Oregon and Washington (March 24–June 28, 2022), Texas (Baylor Scott & White Health: March 19–June 21, 2022; PHIX: March 30–June 21, 2022), and Utah (March 19–June 22, 2022).

¶¶ Dashes indicate that estimated VE had a CI width ≥50%. Estimates with CI widths ≥50% are not shown here due to imprecision. The associated data (total number of tests, number of SARS-CoV-2 positive tests, and median interval since last dose) are also omitted.

*** Partners contributing data on hospitalizations during dates of estimated ≥50% Omicron BA.4/BA.5 predominance were in California (June 25–August 20, 2022), Colorado (June 19–August 20, 2022), Indiana (June 19–August 20, 2022), Minnesota and Wisconsin (June 22–August 20, 2022), New York (June 29–August 20, 2022), Oregon and Washington (June 29–August 20, 2022), Texas (Baylor Scott & White Health: June 22–August 20, 2022; PHIX: June 22–August 20, 2022), and Utah (June 23–August 20, 2022).

††† Partners contributing data on hospitalizations during dates of estimated ≥50% Omicron BA.2/BA.2.12.1/BA.4/BA.5 predominance were in California (March 21–August 20, 2022), Colorado (March 21–August 20, 2022), Indiana (March 21–August 20, 2022), Minnesota and Wisconsin (March 22–August 20, 2022), New York (March 17–August 20, 2022), Oregon and Washington (March 24–August 20, 2022), Texas (Baylor Scott & White Health: March 19–August 20, 2022; PHIX: March 30–August 20, 2022), and Utah (March 19–August 20, 2022).

TABLE 3. Vaccine effectiveness* of 2- and 3-dose mRNA COVID-19 vaccination against COVID-19–associated† hospitalization among immunocompromised§ adults aged ≥18 years, by immunocompromising condition category and mRNA COVID-19 vaccination status,¶ during period of Omicron predominance — VISION Network, 10 states, December 2021–August 2022**

Immunocompromising condition	Total	SARS-CoV-2 positive test result, no. (%)	Median interval since last dose, days (IQR)	VE % (95% CI)
Solid malignancy only				
Unvaccinated (Ref)	**2,467**	411 (16.7)	NA	NA
2 doses (≥14 days earlier)	**2,574**	282 (11.0)	322 (257–390)	47 (36–55)
3 doses (≥7 days earlier)	**4,523**	296 (6.5)	148 (96–203)	70 (64–76)
3 doses (7–89 days earlier)	**991**	55 (5.5)	57 (37–75)	81 (72–87)
3 doses (≥90 days earlier)	**3,532**	241 (6.8)	171 (131–219)	61 (52–69)
Hematologic malignancy only				
Unvaccinated (Ref)	**562**	117 (20.8)	NA	NA
2 doses (≥14 days earlier)	— ††	—	—	—
3 doses (≥7 days earlier)	**1,209**	162 (13.4)	147 (94–204)	58 (40–70)
3 doses (7–89 days earlier)	—	—	—	—
3 doses (≥90 days earlier)	**924**	104 (11.3)	171 (131–219)	63 (45–75)
Rheumatologic or inflammatory disorder only				
Unvaccinated (Ref)	**1,549**	378 (24.4)	NA	NA
2 doses (≥14 days earlier)	**1,528**	281 (18.4)	321 (249–394)	38 (24–49)
3 doses (≥7 days earlier)	**2,395**	253 (10.6)	141 (90–195)	61 (51–69)
3 doses (7–89 days earlier)	**599**	57 (9.5)	61 (38–76)	76 (63–84)
3 doses (≥90 days earlier)	**1,796**	196 (10.9)	166 (129–212)	48 (34–60)
Other intrinsic immune condition or immunodeficiency only				
Unvaccinated (Ref)	**2,334**	465 (19.9)	NA	NA
2 doses (≥14 days earlier)	**1,852**	279 (15.1)	304 (239–375)	40 (28–51)
3 doses (≥7 days earlier)	**2,222**	210 (9.4)	140 (87–196)	64 (54–72)
3 doses (7–89 days earlier)	**576**	46 (8.0)	59 (37–76)	76 (62–85)
3 doses (≥90 days earlier)	**1,646**	164 (10.0)	168 (129–215)	45 (27–58)
Organ or stem cell transplant only				
Unvaccinated (Ref)	**151**	47 (31.1)	NA	NA
2 doses (≥14 days earlier)	—	—	—	—
3 doses (≥7 days earlier)	—	—	—	—
3 doses (7–89 days earlier)	—	—	—	—
3 doses (≥90 days earlier)	—	—	—	—
Organ or stem cell transplant (not mutually exclusive of other conditions)§§				
Unvaccinated (Ref)	**509**	151 (29.7)	NA	NA
2 doses (≥14 days earlier)	**747**	178 (23.8)	310 (248–378)	40 (17–56)
3 doses (≥7 days earlier)	**1,413**	326 (23.1)	153 (107–210)	43 (22–58)
3 doses (7–89 days earlier)	—	—	—	—
3 doses (≥90 days earlier)	**1,150**	265 (23.0)	170 (134–223)	30 (4–49)
Any immunocompromising condition, except organ or stem cell transplant¶¶				
Unvaccinated (Ref)	**8,234**	1,664 (20.2)	NA	NA
2 doses (≥14 days earlier)	**8,051**	1,209 (15.0)	317 (250–387)	37 (31–42)
3 doses (≥7 days earlier)	**12,873**	1,226 (9.5)	146 (95–201)	60 (56–64)
3 doses (7–89 days earlier)	**2,935**	274 (9.3)	60 (39–76)	70 (64–75)
3 doses (≥90 days earlier)	**9,938**	952 (9.6)	169 (130–217)	47 (41–53)

Abbreviations: ICD-9 = *International Classification of Diseases, Ninth Revision*; ICD-10 = *International Classification of Diseases, Tenth Revision*; NA = not applicable; Ref = referent group; VE = vaccine effectiveness.

* VE was calculated as ([1 − odds ratio] x 100%), estimated using a test-negative design, adjusted for age, geographic region, calendar time (days since January 1, 2021), and local virus circulation (percentage of SARS-CoV-2–positive results from testing within the counties surrounding the facility on the date of the encounter) and weighted for inverse propensity to be vaccinated or unvaccinated (calculated separately for each VE estimate). Generalized boosted regression trees were used to estimate the propensity to be vaccinated based on sociodemographic characteristics, underlying medical conditions, and facility characteristics.

† Hospitalizations with a discharge code consistent with COVID-19–like illness and molecular testing for SARS-CoV-2 ≤14 days before to <72 hours after the encounter date were included. COVID-19–like illness diagnoses included acute respiratory illness (e.g., respiratory failure or pneumonia) or related signs or symptoms (cough, fever, dyspnea, vomiting, or diarrhea) using ICD-9 and ICD-10 diagnosis codes.

§ Immunocompromised status was defined as the presence of at least one discharge diagnosis using ICD-9 and ICD-10 diagnosis codes (ICD-10 codes: C00–C80, C7A, C7B, D3A, Z51.0, and Z51.1), hematologic malignancy (ICD-10 codes: C81–C86, C88, C90–C96, D46, D61.0, D70.0, D61.2, D61.9, and D71), rheumatologic or inflammatory disorder (ICD-10 codes: D86, E85 [except E85.0], G35, J67.9, L40.54, L40.59, L93.0, L93.2, L94, M05–M08, M30, M31.3, M31.5, M32–M34, M35.3, M35.8, M35.9, M46, and T78.40), other intrinsic immune condition or immunodeficiency (ICD-10 codes: D27.9, D61.09, D72.89, D80, D81 [except D81.3], D82–D84, D89 [except D89.2], K70.3, K70.4, K72, K74.3–K74.6 [except K74.60 and K74.69], N04, and R18), or organ or stem cell transplant (ICD-10 codes: T86 [except T86.82–T86.84, T86.89, and T86.9], D47.Z1, Z48.2, Z94, and Z98.85).

¶ mRNA COVID-19 vaccination status was defined as having received the listed number of doses of an mRNA COVID-19 vaccine within the specified range of number of days before the encounter 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 hospital admission or the admission date if testing only occurred after the admission.

†† Dashes indicate that estimated VE had a CI width ≥50%. Estimates with CI widths ≥50% are not shown here due to imprecision. The associated data (total number of tests, number of SARS-CoV-2 positive tests, and median interval since last dose) are also omitted.

§§ Category includes persons with at least organ or stem cell transplant, but these categories are not mutually exclusive (i.e., persons might have one or more additional immunocompromising conditions).

See table footnotes on the next page.

TABLE 3. (*Continued*) Vaccine effectiveness* of 2- and 3-dose mRNA COVID-19 vaccination against COVID-19–associated† hospitalization among immunocompromised§ adults aged ≥18 years, by immunocompromising condition category and mRNA COVID-19 vaccination status,¶ during period of Omicron predominance — VISION Network, 10 states, December 2021–August 2022**

¶¶ Category includes persons with one or more immunocompromising conditions: solid malignancy, hematologic malignancy, rheumatologic or inflammatory disorder, and other intrinsic immune condition or immunodeficiency; all persons with organ or stem cell transplant were excluded.

Summary

What is already known about this topic?

COVID-19 vaccine effectiveness (VE) data among immunocompromised persons during SARS-CoV-2 Omicron variant predominance are limited.

What is added by this report?

Among immunocompromised adults hospitalized with a COVID-like illness, 2-dose monovalent mRNA COVID-19 vaccine VE against COVID-19–associated hospitalization during Omicron predominance was 36%. VE was 67% ≥7 days after a third dose during BA.1 predominance but declined during BA.2/BA.2.12.1 and BA.4/BA.5 predominance to 32% ≥90 days after dose 3 and 43% ≥7 days after dose 4.

What are the implications for public health practice?

Monovalent COVID-19 vaccine protection among persons with immunocompromising conditions during Omicron predominance was moderate after a 3-dose primary series or booster dose. Persons with immunocompromising conditions might benefit from updated bivalent boosters that target circulating BA.4/BA.5 sublineages.

protective measures recommended for persons with immunocompromising conditions, including prophylactic antibody treatments, early access to and use of antivirals, and nonpharmaceutical interventions, such as the use of well-fitting masks or respirators, should also be considered. Further study of VE of updated vaccines in persons with immunocompromising conditions is warranted.

Corresponding author: Amadea Britton, lto7@cdc.gov.

[1]CDC COVID-19 Emergency Response Team; [2]Center for Biomedical Informatics, Regenstrief Institute, Indianapolis, Indiana; [3]School of Medicine, Indiana University, Indianapolis, Indiana; [4]Vanderbilt University Medical Center, Nashville, Tennessee; [5]Westat, Rockville, Maryland; [6]Baylor Scott & White Health, Temple, Texas; [7]School of Medicine, Texas A&M University, Bryan, Texas; [8]HealthPartners Institute, Minneapolis, Minnesota; [9]Richard M. Fairbanks School of Public Health, Indiana University, Indianapolis, Indiana; [10]Division of Infectious Diseases and Clinical Epidemiology, Department of Medicine, Intermountain Healthcare, Salt Lake City, Utah; [11]Vaccine Study Center, Division of Research, Kaiser Permanente Northern California, Oakland, California; [12]School of Medicine, University of Colorado Anschutz Medical Campus, Aurora, Colorado; [13]Department of Biomedical Informatics, Columbia University Irving Medical Center, New York, New York; [14]New York-Presbyterian Hospital, New York, New York; [15]Paso del Norte Health Information Exchange, El Paso, Texas; [16]Children's Minnesota, Minneapolis, Minnesota; [17]Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon; [18]Department of Public Health, College of Life Sciences, Brigham Young University, Provo, Utah.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Brian E. Dixon reported grant support from the National Institutes of Health, Agency for Healthcare Research and Quality, and the U.S. Department of Veterans Affairs; personal fees from Elsevier and Springer Nature; and consulting fees from Merck. Nicola P. Klein reported institutional grant support from Pfizer, Inc., Merck, GSK, and Sanofi Pasteur. Allison L. Naleway reported institutional support from Pfizer, Inc. and Vir Biotechnology. Suchitra Rao reported grant support from GSK. Charlene McEvoy reported institutional support from AstraZeneca. No other potential conflicts of interest were disclosed.

References

1. Singson JRC, Kirley PD, Pham H, et al.; COVID-NET Surveillance Team. Factors associated with severe outcomes among immunocompromised adults hospitalized for COVID-19—COVID-NET, 10 states, March 2020–February 2022. MMWR Morb Mortal Wkly Rep 2022;71:878–84. https://doi.org/10.15585/mmwr.mm7127a3
2. Tenforde MW, Patel MM, Gaglani M, et al.; IVY Network. Effectiveness of a third dose of Pfizer-BioNTech and Moderna vaccines in preventing COVID-19 hospitalization among immunocompetent and immunocompromised adults—United States, August–December 2021. MMWR Morb Mortal Wkly Rep 2022;71:118–24. PMID:35085218 https://doi.org/10.15585/mmwr.mm7104a2
3. Embi PJ, Levy ME, Naleway AL, et al. Effectiveness of 2-dose vaccination with mRNA COVID-19 vaccines against COVID-19–associated hospitalizations among immunocompromised adults—nine states, January–September 2021. MMWR Morb Mortal Wkly Rep 2021;70:1553–9. PMID:34735426 https://doi.org/10.15585/mmwr.mm7044e3
4. CDC. Use of COVID-19 vaccines in the United States. Interim clinical considerations for use of COVID-19 vaccines currently authorized or approved in the United States. Atlanta, GA: US Department of Health and Human Services; 2022.Accessed September 2, 2022. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html
5. Thompson MG, Stenehjem E, Grannis S, et al. Effectiveness of Covid-19 vaccines in ambulatory and inpatient care settings. N Engl J Med 2021;385:1355–71. PMID:34496194 https://doi.org/10.1056/NEJMoa2110362
6. Link-Gelles R, Levy ME, Gaglani M, et al. Effectiveness of 2, 3, and 4 COVID-19 mRNA vaccine doses among immunocompetent adults during periods when SARS-CoV-2 Omicron BA.1 and BA.2/BA.2.12.1 sublineages predominated—VISION Network, 10 states, December 2021–June 2022. MMWR Morb Mortal Wkly Rep 2022;71:931–9. PMID:35862287 https://doi.org/10.15585/mmwr.mm7129e1
7. Tartof SY, Slezak JM, Puzniak L, et al. Immunocompromise and durability of BNT162b2 vaccine against severe outcomes due to omicron and delta variants. Lancet Respir Med 2022;10:e61–2. PMID:35533699 https://doi.org/10.1016/S2213-2600(22)00170-9
8. Oliver S. Evidence to recommendations framework: bivalent COVID-19 vaccine booster. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-09-01/08-covid-oliver-508.pdf
9. Levin MJ, Ustianowski A, De Wit S, et al.; PROVENT Study Group. Intramuscular AZD7442 (tixagevimab-cilgavimab) for prevention of Covid-19. N Engl J Med 2022;386:2188–200. PMID:35443106 https://doi.org/10.1056/NEJMoa2116620
10. Takashita E, Yamayoshi S, Simon V, et al. Efficacy of antibodies and antiviral drugs against Omicron BA.2.12.1, BA.4, and BA.5 subvariants. N Engl J Med 2022;387:468–70. PMID:35857646 https://doi.org/10.1056/NEJMc2207519

Ocular Monkeypox — United States, July–September 2022

Shama Cash-Goldwasser, MD[1,2,3]; Sarah M. Labuda, MD[1]; David W. McCormick, MD[1]; Agam K. Rao, MD[1]; Andrea M. McCollum, PhD[1]; Brett W. Petersen, MD[1]; James Chodosh, MD[4]; Catherine M. Brown, DVM[5]; Suk Yin Chan-Colenbrander, MD[6]; Caitlin M. Dugdale, MD[7]; Michael Fischer, MD[8]; Amy Forrester[9]; Jayne Griffith, MPH[3]; Rachel Harold, MD[10]; Bruce W. Furness, MD[1,10]; Vivian Huang, MD[11]; Aaron R. Kaufman, MD[12]; Ellen Kitchell, MD[13]; Rachel Lee, DO[14]; Nicholas Lehnertz, MD[3]; Ruth Lynfield, MD[3]; Ketzela Jacobowitz Marsh, MD[6]; Lawrence C. Madoff, MD[5]; Nelson Nicolasora, MD[15]; Dharmendra Patel, MD[16]; Roberto Pineda II, MD[12]; Trey Powrzanas, FNP[17]; Afsoon Roberts, MD[14]; Maria Teresa Seville, MD[16]; Ami Shah, MD[16]; Joshua M. Wong, MD[1]; Jana M. Ritter, DVM[1]; Caroline A. Schrodt, MD[1]; Elliot Raizes, MD[1]; Sapna Bamrah Morris, MD[1]; Jeremy A. W. Gold, MD[1]; CDC Monkeypox Clinical Escalations Team

On October 17, 2022, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

As of October 11, 2022, a total of 26,577 monkeypox cases had been reported in the United States.* Although most cases of monkeypox are self-limited, lesions that involve anatomically vulnerable sites can cause complications. Ocular monkeypox can occur when *Monkeypox virus* (MPXV) is introduced into the eye (e.g., from autoinoculation), potentially causing conjunctivitis, blepharitis, keratitis, and loss of vision (*1*,*2*). This report describes five patients who acquired ocular monkeypox during July–September 2022. All patients received treatment with tecovirimat (Tpoxx)†; four also received topical trifluridine (Viroptic).§ Two patients had HIV-associated immunocompromise and experienced delays between clinical presentation with monkeypox and initiation of monkeypox-directed treatment. Four patients were hospitalized, and one experienced marked vision impairment. To decrease the risk for autoinoculation, persons with monkeypox should be advised to practice hand hygiene and to avoid touching their eyes, which includes refraining from using contact lenses (*3*). Health care providers and public health practitioners should be aware that ocular monkeypox, although rare, is a sight-threatening condition. Patients with signs and symptoms compatible with ocular monkeypox should be considered for urgent ophthalmologic evaluation and initiation of monkeypox-directed treatment. Public health officials should be promptly notified of cases of ocular monkeypox. Increased clinician awareness of ocular monkeypox and of approaches to prevention, diagnosis, and treatment might reduce associated morbidity.

During the 2022 multinational outbreak, CDC has provided consultation to clinicians treating patients with monkeypox.¶ This report describes demographic characteristics, clinical features, and outcomes as of October 11 for five patients who received a diagnosis of ocular monkeypox during July–September 2022. Ocular monkeypox was defined as the presence of new ocular disease compatible with *Orthopoxvirus* (OPXV) infection in a patient with probable or confirmed monkeypox** and no alternative explanation for the ocular disease. CDC obtained data during clinical consultation and worked with treating clinicians and jurisdictional health departments to follow patient progress. Patient permission for the use of the clinical image was obtained. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.††

Patient A

In August 2022, a man aged 20–29 years with HIV disease (Table) (Figure 1) (CD4 = 25 cells/mm^3, not receiving antiretroviral therapy [ART]) was evaluated in an outpatient clinic for a rash on his buttocks, chest, arms, and hands that was compatible with monkeypox.§§ Swabs collected from lesions on his chest were sent for polymerase chain reaction (PCR) testing for OPXV, and results were negative. Ten days later, the patient presented for care again, this time with progressive rash as well as left eye symptoms, including pain, itching, swelling, discharge, foreign body sensation, photosensitivity, and vision changes. The rash was swabbed again to test for OPXV, and he was provided a referral to ophthalmology. Seven days later, PCR testing returned positive results for OPXV, and he

* Case counts included confirmed and probable monkeypox cases. https://www.cdc.gov/poxvirus/monkeypox/response/2022/us-map.html (Accessed October 11, 2022).

† Tecovirimat, an FDA-approved treatment for smallpox, is an antiviral drug that has demonstrated effectiveness in animal MPXV models. Interim CDC guidance currently recommends that tecovirimat be considered in patients with severe monkeypox, those at high risk for severe disease, or those whose infection involves accidental implantation in the eyes or other sensitive anatomic areas where monkeypox might constitute a special hazard. https://www.cdc.gov/poxvirus/monkeypox/clinicians/Tecovirimat.html

§ Trifluridine, an antiviral drug used to treat herpes simplex keratitis, can be considered to treat conjunctivitis and keratitis caused by MPXV, in consultation with an ophthalmologist. Trifluridine is a preferred treatment for ocular infection with vaccinia virus, which can occur as a complication of autoinoculation after vaccination with ACAM 2000. https://www.cdc.gov/poxvirus/monkeypox/clinicians/ocular-infection.html

¶ CDC is offering a monkeypox clinical consultation service during the ongoing monkeypox outbreak. Health care providers seeking additional clinical guidance can contact CDC Emergency Operations by phone (770-488-7100) or by email (eocevent482@cdc.gov).

** Case definitions for use in the 2022 monkeypox response. https://www.cdc.gov/poxvirus/monkeypox/clinicians/case-definition.html

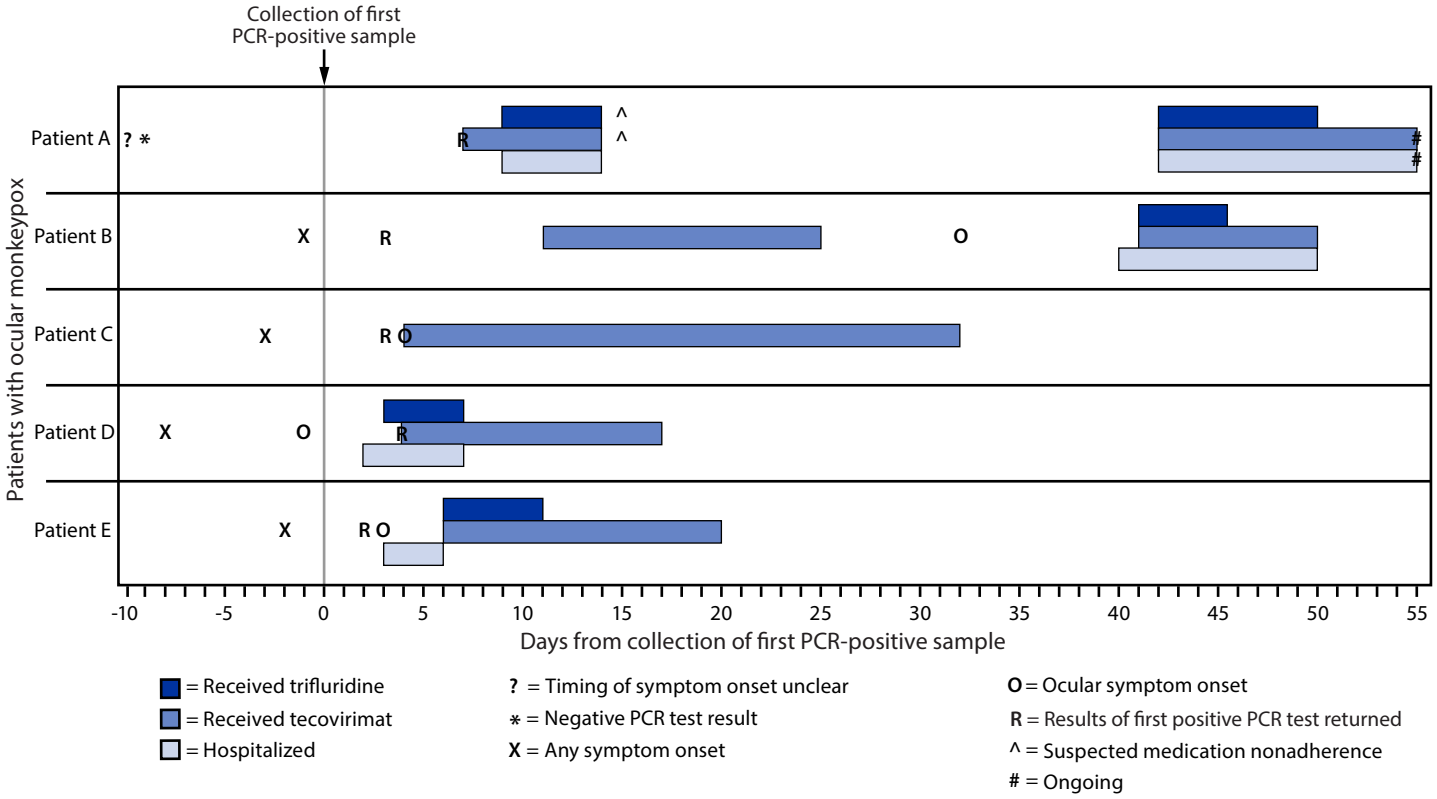
†† 45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

§§ Clinical recognition, monkeypox. https://www.cdc.gov/poxvirus/monkeypox/clinicians/clinical-recognition.html

TABLE. Demographic characteristics, clinical characteristics, and outcomes among patients with ocular monkeypox — United States, July–September 2022

Patient	Age group, yrs, sex	HIV status (CD4 count, cells/mm^3)	Signs and symptoms	Ocular exam findings	Outcomes
A	20–29, male	Positive (25)	Nonocular: rash on arms, hands, chest, and buttocks Ocular: redness, pain, itching, swelling, discharge, foreign body sensation, photosensitivity, and vision changes	Unilateral conjunctivitis, conjunctival lesion, and keratitis	Hospitalization: 22 days and ongoing Vision impairment ongoing and treatment for active ocular monkeypox ongoing
B	30–39, male	Positive (78)	Nonocular: rash on face, chest, legs, and perianal area Ocular: redness, pain, itching, and photosensitivity	Unilateral medial canthus lesion, conjunctivitis, conjunctival lesion, and corneal lesion	Hospitalization: 10 days No vision changes
C	30–39, male	Negative	Nonocular: rectal pain and perianal rash Ocular: redness, pain, and discharge	Bilateral conjunctivitis	Hospitalization: none No vision changes
D	30–39, male	Negative	Nonocular: rash on penis, abdomen, and wrist Ocular: redness, pain, and periorbital swelling	Unilateral eyelid lesion, conjunctivitis, conjunctival lesion, and preseptal cellulitis	Hospitalization: 5 days No vision changes
E	30–39, female	Negative	Nonocular: rash on vaginal labia, buttocks, back, chin, and forehead Ocular: redness and pain	Unilateral eyelid lesion, conjunctivitis, conjunctival lesion, and subconjunctival nodule	Hospitalization: 3 days No vision changes

FIGURE 1. Timeline of testing, symptom onset, and initiation of medical countermeasures for patients with ocular monkeypox — United States, July–September 2022



Abbreviation: PCR = polymerase chain reaction.

commenced treatment with oral tecovirimat. Two days later, he was admitted to a hospital because of worsening ocular symptoms. Ophthalmologic exam was notable for left eye conjunctivitis. Visual acuity in the left eye was 20/40. The patient started intravenous tecovirimat and topical trifluridine drops to his left eye on admission, and he was initiated on ART. His ocular symptoms improved, and he was discharged after 5 days with prescriptions for oral tecovirimat, topical

trifluridine, and ART. During the next 4 weeks he developed new facial lesions and decreasing left eye vision, for which he was readmitted to the hospital; health care providers suspected nonadherence with prescribed medications. Ophthalmologic examination revealed left eye conjunctivitis, keratitis, and a conjunctival ulcer (Figure 2). Left eye visual acuity was measured at 20/300. A swab of the conjunctival lesion yielded a positive PCR test result for OPXV, and biopsy showed necroulcerative conjunctivitis with extensive intralesional orthopoxviral antigen detected by immunohistochemistry. The patient was restarted on intravenous tecovirimat, and his left eye was treated with topical trifluridine for 1 week as well as topical povidone-iodine. Currently, the patient is on day 14 of intravenous tecovirimat and remains hospitalized for treatment of ocular monkeypox. He has experienced waxing and waning of left eye pain, irritation, and photosensitivity. Left eye visual acuity was most recently measured at 20/800 (profound visual impairment), although bedside visual acuity assessments have been challenging. His prognosis for vision recovery is currently unknown.

Patient B

In July 2022, a man aged 30–39 years with HIV disease (CD4 = 78 cells/mm^3, not on ART) was evaluated at an emergency department with a rash on his chest, legs, perianal area, and face, including on the bridge of his nose near his right eye (Table) (Figure 1). Swabs of lesions from his face and scalp were taken to test for OPXV, but because tecovirimat was not available in the emergency department, he was referred to an outpatient clinic to receive tecovirimat. The swabs tested PCR-positive for OPXV. The patient was evaluated at an outpatient clinic 9 days after testing and was prescribed ART and 14 days of oral tecovirimat. His rash began to resolve during treatment. Two weeks after completion of tecovirimat, he developed new and worsening facial lesions. The lesion on his nose expanded onto the right medial canthus and over the conjunctiva, and he experienced right eye redness, pain, itching, and photosensitivity, for which he was hospitalized. He did not experience vision changes. Ophthalmologic exam results were notable for right eye conjunctivitis, several small conjunctival nodular lesions, and corneal ulcers. He was treated again with intravenous tecovirimat for 10 days and with topical trifluridine drops for 5 days and antibacterial eye drops to the right eye. He was discharged upon regression of the eye lesion and improvement in conjunctivitis 10 days after admission, without further treatment for monkeypox.

Patient C

In August 2022, a previously healthy man aged 30–39 years developed rectal pain and perianal lesions. He went to an emergency department 3 days later and swabs of those lesions were taken for OPXV testing (Table) (Figure 1). Three days later, when the swabs yielded positive PCR test results for OPXV, the patient was prescribed oral tecovirimat for rectal pain. Two days later, he was evaluated again in the emergency department with right eye pain, redness and discharge. He did not experience vision changes. Ophthalmologic exam was notable for right eye conjunctivitis. He subsequently developed bilateral

FIGURE 2. Left eye in a patient* with HIV-associated immunocompromise and ocular monkeypox, with conjunctivitis and conjunctival lesion earlier in the course of monkeypox illness (A), and with conjunctival ulcer and peripheral keratitis later in the course of monkeypox illness (B) — United States, August–September 2022

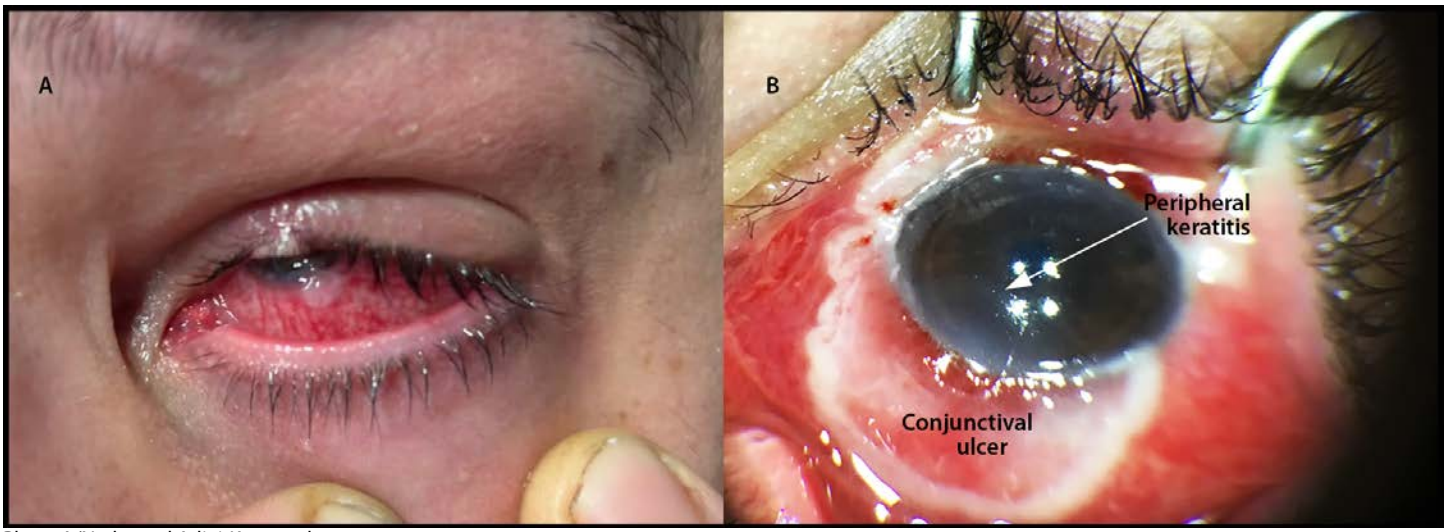


Photo A/Nathanael Adjei-Kyeremeh
Photo B/Dharmendra R. Patel
* Patient has consented to the publication of these photographs.

Summary

What is already known about this topic?

Patients with monkeypox can experience serious ocular complications, which are not well described during the current outbreak.

What is added by this report?

This report describes five cases of ocular monkeypox identified in the United States during July–September 2022. Patients with ocular monkeypox, including those with HIV-associated immunocompromise, have experienced delays in treatment initiation, prolonged illness, hospitalization, and vision impairment.

What are the implications for public health practice?

Health care providers and public health practitioners should be aware that ocular monkeypox, although rare, is a sight-threatening condition. Patients with signs and symptoms compatible with ocular monkeypox should be considered for urgent ophthalmologic evaluation and treatment. Prompt notification of public health officials can help support these efforts.

conjunctivitis; the treating physicians suspected the patient had autoinoculated both eyes with MPXV by rubbing them. The patient's bilateral conjunctivitis persisted for 3 weeks after resolution of his perianal lesions. The course of tecovirimat was extended until all ocular symptoms resolved, which occurred after 1 month of treatment.

Patient D

In August 2022, a previously healthy man aged 30–39 years developed a groin rash (Table) (Figure 1). One week later, he was examined at an emergency department for right eye redness, pain, and eyelid swelling. He reported rubbing his right eye. Lesions were noted on his penis, abdomen, and one wrist. Samples were collected from the body lesions for OPXV testing; the patient received empiric treatment for gonorrhea and chlamydia. Providers attributed the eye symptoms to bacterial preseptal cellulitis and he was discharged on oral antibiotics. Two days later, the patient returned with multiple right eyelid lesions, periorbital swelling, and eye pain, for which he was admitted to a hospital. He did not experience vision changes. Ophthalmologic exam was notable for right eye conjunctivitis as well as four ulcers on the eyelid margin and three lesions on the palpebral conjunctiva, which were swabbed for OPXV testing. He was started on oral tecovirimat empirically, after which all test results from swabs of skin and eye lesions returned PCR-positive for OPXV. The patient also received topical trifluridine for 5 days and antibacterial drops to the right eye, as well as intravenous antibiotics for preseptal cellulitis. He was discharged upon clinical improvement 5 days after admission, to complete a 14-day course of oral tecovirimat.

Patient E

In July 2022, a previously healthy woman aged 30–39 years was evaluated for pustular lesions on her vaginal labia (Table) (Figure 1). A swab of those lesions tested PCR-positive for OPXV. During the week after symptom onset, lesions spread to her back, buttocks, chin, forehead, and left lower eyelid. She began experiencing left eye pain and redness. She sought medical care after noticing a lesion on the globe of her left eye, for which she was admitted to a hospital. Ophthalmologic exam was notable for left eye conjunctivitis, a bulbar conjunctival lesion, and a subconjunctival nodule. She did not experience vision changes. Neither tecovirimat nor trifluridine was immediately available; the patient was treated with naproxen. Her ocular symptoms improved, and she was discharged after 3 days with a 14-day course of oral tecovirimat and a 5-day course of topical trifluridine (*2*).

Discussion

This report highlights the varying clinical manifestations of ocular monkeypox and the importance of prompt evaluation and treatment to prevent sight-threatening complications. All five patients with ocular monkeypox described in this report suffered prolonged illness, four were hospitalized, and one experienced significant vision impairment. Two patients had HIV-associated immunocompromise and experienced delays in initiation of treatment for monkeypox. One of these patients experienced vision loss; he remains in treatment and his prognosis for vision recovery is currently unknown. Urgent referral for ophthalmologic evaluation and prompt antiviral therapy should be considered for patients with monkeypox and ocular signs or symptoms (e.g., vision changes or eye pain, itching, redness, swelling, or foreign body sensation) or lesions near the eye. Clinicians should consider initiation of prompt systemic antiviral therapy as well as topical trifluridine for patients with ocular monkeypox.[¶¶]

Several strategies might help prevent ocular monkeypox and associated complications. To decrease the risk for autoinoculation, persons with monkeypox should be advised to practice hand hygiene and to avoid touching their eyes, which includes refraining from using contact lenses (*3*). Short turnaround times for OPXV/MPXV PCR test results might help prevent delays in treatment initiation. For persons with suspected ocular monkeypox, or for persons with suspected monkeypox who are at risk for severe manifestations of the disease (e.g., those with HIV-associated immunocompromise), clinicians might consider initiating empiric treatment for monkeypox while test results are pending. Health care providers can

[¶¶] Interim clinical considerations for management of ocular monkeypox virus infection. https://www.cdc.gov/poxvirus/monkeypox/clinicians/ocular-infection.html

contact their public health jurisdictions and CDC for support on the use of medical countermeasures to treat patients with monkeypox*** (*4*).

The findings in this report are subject to at least two limitations. First, the cases described might not be representative of patients with ocular monkeypox in the United States, and conclusions cannot be drawn about the frequency of reported events. Although the frequency of ocular monkeypox during the current outbreak is unknown, national surveillance data from the United States suggest that 5% of patients with monkeypox report ocular symptoms††† (*5*). Second, not every patient underwent testing of ocular lesions for OPXV/MPXV or exhaustive testing for other ocular infections. However, the clinical findings in these patients were compatible with descriptions of ocular monkeypox from other studies (*6,7*).

Ocular monkeypox is a potentially sight-threatening infection. Urgent ophthalmologic evaluation and the provision of timely medical countermeasures for patients with suspected or confirmed ocular monkeypox might help prevent poor outcomes.

*** Interim clinical guidance for the treatment of monkeypox. https://www.cdc.gov/poxvirus/monkeypox/clinicians/treatment.html#anchor_1655488233196

††† This frequency is lower than that reported from the Democratic Republic of the Congo, where 23% of patients with monkeypox had conjunctivitis, a difference that might be related to the virulence of the MPXV clade causing infection during the ongoing outbreak, or to epidemiologic or clinical factors. https://www.cdc.gov/poxvirus/monkeypox/clinicians/ocular-infection.html

Acknowledgments

Isaac Bleicher, Harvard Medical School; Shade Brady, Arizona Department of Health Sciences; Steven Yeh, University of Nebraska Medical Center; Melissa Yuan, Massachusetts Eye and Ear Infirmary.

CDC Monkeypox Clinical Escalations Team

Amimah Asif, CDC; Amy Beeson, CDC; Ramon Bhatia, CDC; Brian F. Borah, CDC; Kevin Chatham-Stevens, CDC; Rewa Choudhary, CDC; Eleanor Click, CDC; Thomas D. Filardo, CDC; Romeo R. Galang, CDC; Julia Haston, CDC; Sophia Hsu, CDC; Gurpreet Kaur, CDC; Anne Kimball, CDC; James T. Lee, CDC; Grace Marx, CDC; Janet McNicholl, CDC; Maureen J. Miller, CDC; Rebecca Noe, CDC; Siobhan O'Connor, CDC; Kevin O'Laughlin, CDC; Kia Padgett, CDC; Gail Thompson, CDC; Farrell Tobolowsky, CDC; Isaac Zulu, CDC.

Corresponding author: Shama Cash-Goldwasser, tqx7@cdc.gov.

[1]CDC Monkeypox Emergency Response Team; [2]Epidemic Intelligence Service, CDC; [3]Minnesota Department of Health; [4]University of New Mexico School of Medicine, Albuquerque, New Mexico; [5]Massachusetts Department of Public Health; [6]University of Minnesota Medical Center, Minneapolis, Minnesota; [7]Massachusetts General Hospital, Boston, Massachusetts; [8]Texas Department of State Health Services; [9]Dallas County Health and Human Services, Dallas, Texas; [10]District of Columbia Department of Health, Washington, D.C.; [11]Maricopa County Department of Health, Phoenix, Arizona; [12]Massachusetts Eye and Ear Infirmary, Boston, Massachusetts; [13]University of Texas Southwestern Medical Center, Dallas, Texas; [14]The George Washington University School of Medicine and Health Sciences, Washington, D.C.; [15]Banner University Medical Center, University of Arizona, Phoenix, Arizona; [16]Mayo Clinic Hospital, Phoenix, Arizona; [17]Pueblo Family Physicians, Phoenix, Arizona.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. James Chodosh is a consultant to the Food and Drug Administration, where he chairs an advisory committee for new ophthalmic medications. He also receives grant support from the National Institutes of Health (NIH) to study adenovirus keratitis. Caitlin M. Dugdale reports institutional support from the National Institute for Child Health and Human Development, NIH; Harvard University Center for AIDS Research; the Massachusetts General Hospital Executive Committee on Research; the International AIDS Vaccine Initiative; and the International Maternal, Pediatric, Adolescent AIDS Clinical Trials (IMPAACT) Network, NIH. Aaron R. Kaufman reports support by a Heed Fellowship awarded by the Heed Ophthalmic Foundation. Roberto Pineda II reports royalties from Elsevier and consulting fees from Sanofi-Genzyme. No other potential conflicts of interest were disclosed.

References

1. Abdelaal A, Serhan HA, Mahmoud MA, Rodriguez-Morales AJ, Sah R. Ophthalmic manifestations of monkeypox virus. Eye (Lond) 2022. PMID:35896700 https://doi.org/10.1038/s41433-022-02195-z
2. Foos W, Wroblewski K, Ittoop S. Subconjunctival nodule in a patient with acute monkeypox. JAMA Ophthalmol. 2022;140:e223742. PMID: 36069930 https://doi.org/10.1001/jamaophthalmol.2022.3742
3. CDC. Monkeypox. Isolation and infection control at home. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. Accessed October 12, 2022. https://www.cdc.gov/poxvirus/monkeypox/clinicians/infection-control-home.html
4. CDC. Emergency preparedness and response. Severe manifestations of monkeypox among people who are immunocompromised due to HIV or other conditions. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. Accessed October 6, 2022. https://emergency.cdc.gov/han/2022/han00475.asp
5. CDC. Monkeypox. Technical report 3: multi-national monkeypox outbreak, United States, 2022. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. Accessed October 12, 2022. https://www.cdc.gov/poxvirus/monkeypox/cases-data/technical-report/report-3.html
6. Hughes C, McCollum A, Pukuta E, et al. Ocular complications associated with acute monkeypox virus infection, DRC. Int J Infect Dis 2014;21:276–7 https://doi.org/10.1016/j.ijid.2014.03.994
7. Mazzotta V, Mondi A, Carletti F, et al. Ocular involvement in monkeypox: description of an unusual presentation during the current outbreak. J Infect 2022. Epub August 18, 2022. https://doi.org/10.1016/j.jinf.2022.08.011

Monkeypox Virus Infection Resulting from an Occupational Needlestick — Florida, 2022

Rafael Mendoza, MPH[1,*]; Julia K. Petras, MSPH[2,3,*]; Patrick Jenkins, MPH[1]; Margaret J. Gorensek, MD[4]; Susan Mableson[4]; Philip A. Lee, MSc[5]; Ann Carpenter, DVM[2,3]; Heather Jones, DNP[2]; Marie A. de Perio, MD[2]; Zeshan Chisty, MPH[2]; Scott Brueck, MS[2]; Agam K. Rao, MD[2]; Johanna S. Salzer, DVM, PhD[2]; Danielle Stanek, DVM[5]; Carina Blackmore, DVM, PhD[5]

On October 17, 2022, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

In August 2022, the Florida Department of Health notified CDC of a nurse who acquired monkeypox through an occupational exposure while providing care to a patient with monkeypox. To date, occupationally acquired *Monkeypox virus* (MPXV) infections in health care personnel (HCP) have been rarely reported during the 2022 multinational outbreak (*1*,*2*). This report describes the first reported U.S. case and recommends approaches for preventing occupationally acquired MPXV infections in HCP.

On July 12, 2022, a Florida county health department (HD) received notification of an emergency department nurse who was exposed to MPXV through a needlestick that occurred earlier that day. While obtaining swabs from a patient with suspected monkeypox, the nurse used a needle to create an opening in the vesicular lesion to facilitate direct contact of the swab with fluid in the lesion. The needlestick occurred when recapping the used needle by hand before disposal; it caused a break in the skin on the index finger through the nurse's gloved hand, accompanied by a small amount of bleeding. The wound was immediately washed with soap and water and drenched with Betadine antiseptic solution (10% povidone-iodine). The incident was promptly reported to the hospital's infection control practitioner and occupational health department, and to the county HD. Later that day, the lesion swab collected from the patient by the nurse tested positive for nonvariola *Orthopoxvirus* using a real-time polymerase chain reaction (PCR) assay at the Florida Department of Health Bureau of Public Health Laboratories reference laboratory; a duplicate swab subsequently tested positive for Clade II (previously known as West African clade) MPXV at CDC using a real-time PCR assay specific for the detection of West African Clade II MPXV.

Within approximately 15 hours of the incident, the nurse, who had no relevant past medical history or previous orthopoxvirus vaccination, received the first dose of a 2-dose JYNNEOS vaccination series as postexposure prophylaxis. In accordance with CDC guidance (*3*), the nurse continued to work while asymptomatic and was actively monitored by the hospital infectious disease specialist and the county HD. The nurse wore a surgical mask, consistent with CDC COVID-19 guidance, and chose to wear medical gloves when interacting with patients.[†]

Ten days after the exposure, a single skin lesion formed at the site of the needlestick. The nurse immediately began isolating at home and kept the lesion covered until it had crusted over, the scab had fallen off, and a new layer of skin had formed beneath the lesion 19 days later.

The day after the single small vesicular lesion appeared, it was swabbed and subsequently tested positive by PCR for *Orthopoxvirus* and MPXV at a commercial laboratory; a duplicate swab tested at the Florida Department of Health Bureau of Public Health Laboratories reference laboratory using PCR was positive for nonvariola *Orthopoxvirus*. During the next 19 days, the lesion at the needlestick site increased in size (remaining <1 cm in diameter) and became pruritic, deep-seated, and umbilicated, then scabbed over and a new layer of skin formed under the scab. Apart from this single lesion at the puncture site, no additional lesions or other clinical signs or symptoms were reported, and tecovirimat was not indicated.[§] No secondary cases were identified.

This report describes the first occupationally acquired MPVX infection in a U.S. health care worker during the 2022 monkeypox outbreak. CDC advises against unroofing, opening, or aspirating[¶] (*4*) monkeypox lesions with sharp instruments (e.g., needles) and recapping used needles[**] because of the risk for sharps injuries. During the current outbreak, MPXV PCR testing cycle threshold values from swabbed skin and mucosal lesion specimens have been very low, indicating that surface swabbing collects sufficient amounts of viral material without a need to unroof lesions. Because of the reliability and sensitivity of real-time PCR assays used (*4*,*5*), vigorous swabbing of the outer surface of a lesion is adequate to collect enough viral material for testing and will minimize the potential for needlesticks. Employers should ensure that

[*] These authors contributed equally to this report.

[†] A mask was worn consistent with CDC's health care guidance for the COVID-19 pandemic. https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html (Accessed October 14, 2022.) CDC does not recommend work restriction or use of additional personal protective equipment for asymptomatic HCP while being monitored for symptoms compatible with monkeypox.

[§] https://www.cdc.gov/poxvirus/monkeypox/clinicians/Tecovirimat.html

[¶] https://www.cdc.gov/poxvirus/monkeypox/clinicians/prep-collection-specimens.html

[**] https://www.cdc.gov/niosh/newsroom/feature/needlestick_disposal.html

HCP are trained in proper specimen collection methods, follow recommended infection prevention and control precautions for the care of patients with monkeypox, and implement safety practices for managing sharps[††] if they are used during other aspects of patient care. HCP with exposures should be evaluated promptly to ensure postexposure recommendations are implemented (*3*). As of October 6, 2022, among 326[§§] HCP in Florida who have been occupationally exposed to patients with monkeypox during the 2022 outbreak, only this HCP with a reported needlestick exposure developed a clinical MPXV infection. Overall, with routine adherence to standard infection control practices, among U.S. HCP with nonpercutaneous exposure to monkeypox patients, the risk for acquiring monkeypox appears to be low (*6*).

[††] https://www.cdc.gov/sharpssafety/index.html

[§§] Thirty-one of these 326 exposures were determined to be high risk, 47 intermediate risk, and 248 low or uncertain risk using the exposure criteria in effect at the time of risk assessment. http://web.archive.org/web/20220706182701/https:/www.cdc.gov/poxvirus/monkeypox/clinicians/monitoring.html

Acknowledgments

Kevin Chatham-Stephens, Christina Hutson, Alexander Kallen, David Lowe, Andrea McCollum, Faisal Minhaj, Siobhán O'Connor, Melissa K. Schaefer, Caroline Schrodt, Dawn Smith, Elliot Raizes, CDC Monkeypox Emergency Response Team.

Corresponding author: Julia Petras, jpetras@cdc.gov.

[1]Florida Department of Health in Broward County, Fort Lauderdale, Florida; [2]CDC Monkeypox Emergency Response Team; [3]Epidemic Intelligence Service, CDC; [4]Holy Cross Health, Fort Lauderdale, Florida; [5]Florida Department of Health.

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

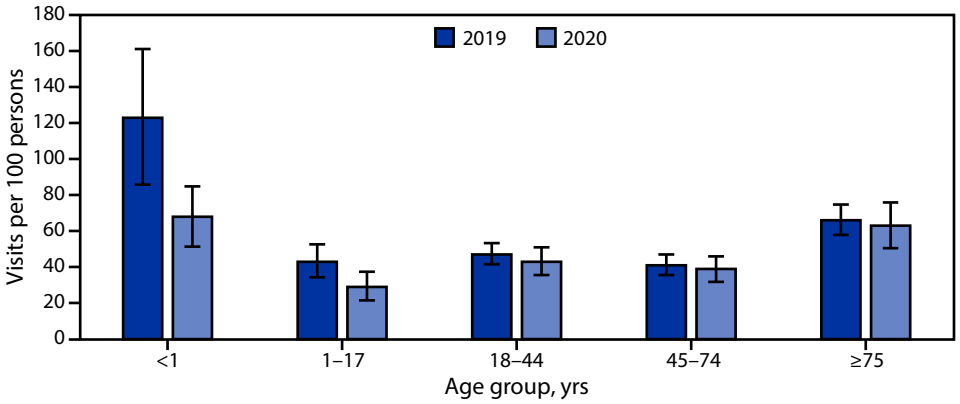
References

1. Toohey G. Nation's first MPX case in healthcare worker exposed on the job is reported in L.A. County. Los Angeles Times. September 13, 2022. https://www.latimes.com/california/story/2022-09-13/los-angeles-county-nations-first-mpx-case-in-healthcare-worker
2. Carvalho LB, Casadio LVB, Polly M, et al. Monkeypox virus transmission to healthcare worker through needlestick injury, Brazil. Emerg Infect Dis 2022. Epub September 22, 2022. PMID:36121391 https://doi.org/10.3201/eid2811.221323
3. CDC. Monkeypox: infection prevention and control of monkeypox in healthcare settings. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. https://www.cdc.gov/poxvirus/monkeypox/clinicians/infection-control-healthcare.html
4. CDC. Monkeypox: tips for adequate collection of a lesion specimen from a suspect monkeypox virus case. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. https://www.cdc.gov/poxvirus/monkeypox/pdf/mpox-adequatespecimencollection_508.pdf
5. Li Y, Zhao H, Wilkins K, Hughes C, Damon IK. Real-time PCR assays for the specific detection of monkeypox virus West African and Congo Basin strain DNA. J Virol Methods 2010;169:223–7. PMID:20643162 https://doi.org/10.1016/j.jviromet.2010.07.012
6. Marshall KE, Barton M, Nichols J, et al.; Colorado Healthcare Personnel Monitoring Team. Health care personnel exposures to subsequently laboratory-confirmed monkeypox patients—Colorado, 2022. MMWR Morb Mortal Wkly Rep 2022;71:1216–9. PMID:36136939 https://doi.org/10.15585/mmwr.mm7138e2

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Emergency Department Visit Rates,*,† by Age Group — United States, 2019–2020



* Based on a sample of visits to emergency departments in noninstitutional general and short-stay hospitals, excluding federal, military, and Veterans Administration hospitals, located in 50 states and the District of Columbia. Visit rates are based on sets of estimates of the U.S. civilian, noninstitutionalized population developed by the Population Division of the U.S. Census Bureau and reflect the population as of July 1 of each year.
† With 95% CIs indicated by error bars.

The emergency department (ED) visit rate for infants aged <1 year declined by nearly one half from 123 visits per 100 infants during 2019 to 68 during 2020. The ED visit rate for children and adolescents aged 1–17 years also decreased from 43 to 29 visits per 100 persons during the same period. Decreases among adults aged 18–44 (47 to 43 per 100 adults), 45–74 (41 to 39), and ≥75 years (66 to 63) from 2019 to 2020 were not statistically significant. ED visit rates were highest for infants aged <1 year followed by adults aged ≥75 years.

Source: National Center for Health Statistics, National Hospital Ambulatory Medical Care Survey, 2019–2020.

Reported by: Christopher Cairns, MPH, ovw7@cdc.gov, 301-458-4186; Jill J. Ashman, PhD.

The *Morbidity and Mortality Weekly Report (MMWR)* Series is prepared by the Centers for Disease Control and Prevention (CDC) and is available free of charge in electronic format. To receive an electronic copy each week, visit *MMWR* at *https://www.cdc.gov/mmwr/index.html*.

Readers who have difficulty accessing this PDF file may access the HTML file at https://www.cdc.gov/mmwr/index2022.html. Address all inquiries about the *MMWR* Series to Editor-in-Chief, *MMWR* Series, Mailstop V25-5, CDC, 1600 Clifton Rd., N.E., Atlanta, GA 30329-4027 or to mmwrq@cdc.gov.

ISSN: 0149-2195 (Print)