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Geospatial Transmission Hotspots of Recent HIV Infection — Malawi, October 2019–March 2020

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Persons infected with HIV are more likely to transmit the virus during the early stages (acute and recent) of infection, when viral load is elevated and opportunities to implement risk reduction are limited because persons are typically unaware of their status (*1*,*2*). Identifying recent HIV infections (acquired within the preceding 12 months)* is critical to understanding the factors and geographic areas associated with transmission to strengthen program intervention, including treatment and prevention (*2*). During June 2019, a novel recent infection surveillance initiative was integrated into routine HIV testing services in Malawi, a landlocked country in southeastern Africa with one of the world's highest prevalences of HIV infection.† The objectives of this initiative were to collect data on new HIV diagnoses, characterize the epidemic, and guide public health response (*2*). New HIV diagnoses were classified as recent infections based on a testing algorithm that included results from the rapid test for recent infection (RTRI)§ and HIV viral load testing (*3*,*4*). Among 9,168 persons aged ≥15 years with a new HIV diagnosis who received testing across 103 facilities during October 2019–March 2020, a total of 304 (3.3%) were classified as having a recent infection. Higher proportions of recent infections were detected among females, persons aged <30 years, and clients at maternal and child health and youth clinics. Using a software application that analyzes clustering in spatially referenced data, transmission hotspots were identified

* As defined by the HIV-1 recent infection surveillance using point-of-care test for recent infection in Malawi protocol.
† https://www.unaids.org/en/regionscountries/countries/malawi
§ https://trace-recency.org/ufaqs/what-is-a-rapid-test-for-hiv-1-recent-infection-rtri/

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with rates of recent infection that were significantly higher than expected. These near real-time HIV surveillance data highlighted locations across Malawi, allowing HIV program stakeholders to assess program gaps and improve access to HIV testing, prevention, and treatment services. Hotspot investigation information could be used to tailor HIV testing, prevention, and treatment to ultimately interrupt transmission.

During June 2019, a phased approach was used to integrate recent infection surveillance into HIV testing services in 11 of Malawi's 28 districts. For persons aged ≥13 years who received a new HIV diagnosis and consented to recent infection surveillance, providers performed a finger prick to conduct an RTRI using the Asante HIV-1 Rapid Recency Assay (Sedia Biosciences). If RTRI results indicated recent infection, additional specimens were collected for viral load testing. Using the testing algorithm for recent infections, new diagnoses were classified as recent if RTRI results indicated a recent infection and viral load was ≥1,000 copies/mL.

This analysis included 103 facilities in five districts that carried out surveillance activities during October 2019-March 2020. These districts were selected based on availability of HIV-testing data disaggregated by age and sex at the facility level. Among 9,295 persons with a new diagnosis of HIV during this period meeting eligibility criteria, 127 (1.4%) declined participation. Two persons aged <15 years were excluded to prevent inclusion of persons who might have been infected through mother-to-child transmission; another four persons who self-reported a previous HIV diagnosis or antiretroviral therapy (ART), were also excluded. In addition, 252 persons whose RTRI results indicated recent infection with a viral load <1,000 copies/mL were excluded because viral suppression likely indicated previous ART use and HIV diagnosis.

Transmission hotspots were defined as one or more facilities in which the observed rate of recent infections was significantly higher ($p<0.05$) than the expected rate. Transmission hotspot analysis was conducted using SaTScan software (version 9.6; Harvard Medical School) via spatial scan statistic in a Poisson probability model to identify clustering of facilities, using facility geographic coordinates, with significantly higher diagnosis rates of recent HIV infection compared with what was expected based on the overall rate of recent infection (*5*,*6*). Rates of recent infection were calculated as the number of recent HIV infections per 100,000 persons at risk for HIV (total number of recent infections plus the total number of negative HIV tests). Relative risks were calculated as the risk for recent infection among facilities inside a given hotspot compared with the risk outside of the hotspot. Facilities reported the total number of HIV negative test results quarterly. Because not all facilities were collecting recent infection surveillance data by October 1, 2019, the number of total HIV-negative tests was adjusted proportionally, assuming testing uniformity across quarters. Hotspots were ranked by probability of occurrence based on log-likelihood and reported using the letter "P." The analysis was adjusted for sex and age (<30 years or ≥30 years),

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and did not allow cluster overlap.[¶] A maximum cluster radius (20 kilometers [12.4 miles]) was selected to identify smaller hotspots and to allow response efforts to focus on facilities that contributed most to high rates of recent infection. Given its population density, a secondary analysis was conducted in Blantyre district in the southern region of the country, with a maximum radius of 5 kilometers (3.1 miles), to identify potential micro-hotspots within this district. Hotspots from this secondary analysis were also ranked according to the log-likelihood and reported using the letter "S." Statistical analyses were conducted using R (version 3.5.0; R Foundation) to analyze the percentage of recent HIV infections among total tests performed, by district, age group, sex, HIV testing service entry point, and facility urban-rural classification. This activity was reviewed and approved by the Malawi National Health Science Research Institutional Review Board and was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.[**]

Among 9,168 new HIV diagnoses, 3.3% (304) were recent infections (Table 1). The number of recent infections was highest in Blantyre district (116). The percentages of new diagnoses that were recent infections was highest in Machinga district (6.9%) and lowest in Blantyre (2.4%) and Mangochi (2.4%) districts. The percentage of new diagnoses that were recent infections was highest among persons aged <30 years (4.6%), females (4.0%), clients at youth clinics (12.8%) and maternal/child health clinics (6.3%) and those who received a diagnosis in rural facilities (3.8%).

Spatial analyses identified six transmission hotspots: three in the primary analysis (P) and three in the secondary analysis (S) (Table 2) (Figure). In the primary analysis, the median age (range = 26–30 years) of persons with recent infection was similar across hotspots. Hotspot P1 was in Blantyre district, a mostly urban area[††] that includes four facilities within a radius of 10.2 kilometers (6.3 miles). The recent infection rate in Blantyre district was 575 per 100,000 persons at risk for HIV (relative risk [RR] = 3.1; p <0.001); the highest percentage of recent infections occurred among females (81.5%). Hotspot P2 included four facilities located across the border of Machinga and Zomba districts within a radius of 16.1 kilometers (9.9 miles), but were primarily in Machinga district, a mostly rural area. The recent infection rate in hotspot P2 was 376 per 100,000 persons at risk (RR = 2.0; p = 0.018). Hotspot P3 was a single facility in Blantyre with a recent infection rate of 818 per 100,000 persons at risk (RR = 4.2; p = 0.025). In the secondary analysis limited to Blantyre district, hotspot S1 included two facilities that were also part of hotspot P1 of the primary analysis, suggesting these facilities contributed most to the high rate of recent infection in their respective localities. Hotspots S2 and S3 included facilities with significantly elevated rates that were not identified in the primary analysis. Median age (range = 25–30 years) and percentage of females (range = 60%–78%) among hotspots in the secondary analysis were similar to hotspots in the primary analysis.

TABLE 1. Demographic characteristics of persons with new HIV diagnoses at health facilities implementing recent HIV infection surveillance — Malawi, October 2019–March 2020

Characteristic	No. of new HIV diagnoses	No. of recent infections (%)
Overall	9,168	304 (3.3)
District		
Blantyre	4,770	116 (2.4)
Lilongwe	945	48 (5.1)
Machinga	1,057	73 (6.9)
Mangochi	801	19 (2.4)
Zomba	1,595	48 (3.0)
Age group, yrs		
<30	3,871	177 (4.6)
≥30	5,297	127 (2.4)
Sex		
Male	3,655	85 (2.3)
Female	5,513	219 (4.0)
Entry point		
HTC or VCT	5,724	179 (3.1)
Antenatal care	820	27 (3.3)
Inpatient department	560	15 (2.7)
Maternal and child health	80	5 (6.3)
Outpatient department	1,604	51 (3.2)
Youth clinic	86	11 (12.8)
Other	294	16 (5.4)
Residence		
Urban	4,979	147 (3.0)
Rural	4,165	157 (3.8)
Unknown	24	0 (—)

Abbreviations: HTC = HIV testing and counseling; VCT = voluntary counseling and testing.

Discussion

This report describes demographic characteristics of persons with recent HIV infection and identifies geospatial hotspots of health facilities with significantly higher rates of recent HIV infection across five districts in Malawi. These findings were consistent with the last national HIV household survey that estimated high HIV incidence in persons aged 15–24 years and females (all ages) (*7*). Location of the most likely hotspots in Blantyre district, a primarily urban district, was consistent with previous evidence from household surveys conducted in 2016 identifying Blantyre as an area with high HIV prevalence and lower rates of viral suppression (*7*). Previous evidence indicated

[¶] Specified as no geographic overlap criteria for reporting hierarchical clusters.
[**] 45 C.F.R. part 46; 21 C.F.R. part 56.
[††] Rural and urban classification based on European Commission's Global Human Settlement categorization.

TABLE 2. Characteristics of persons with recent HIV infection in geospatial transmission hotspots among health facilities that implemented surveillance for recent HIV infection — Malawi, October 2019–March 2020

District*	Transmission hotspot rank†	No. of facilities (radius)	No. of persons at risk for HIV	Recent infection rate (per 100,000 population)§	No. of observed recent infections¶	No. of expected recent infections**	RR†† (p-value)	Median age, yrs (range)¶	% Aged <30 yrs¶	% of females¶
Primary analysis										
Blantyre	1	4 (10.2 km)	4,699	575	27	9	3.1 (<0.001)	26 (15–38)	55.6	81.5
Machinga and Zomba	2	4 (16.1 km)	10,365	376	39	21	2.0 (0.018)	26 (18–45)	61.5	79 5
Blantyre	3	1 (—)	1,223	818	10	2	4.2 (0.025)	30 (19–44)	50.0	60.0
Secondary analysis										
Blantyre	1	2 (2.1 km)	2,959	608	18	6	3.1 (<0.001)	29 (18–36)	50.0	77.8
	2	1 (—)	1,223	818	10	3	3.9 (0.005)	30 (19–44)	50.0	60.0
	3	1 (—)	3,406	470	16	7	2.3 (0.048)	25 (19–60)	62.5	68.8

Abbreviation: RR = relative risk.
* Spatial analyses identified six transmission hotspots: three in the primary analysis and three in the secondary analysis.
† Ranked by probability of occurrence based on log-likelihood.
§ Cases per 100,000 population. Denominator for rate calculation was total persons at risk for HIV, calculated as the sum of recent infections observed and total negative HIV test results.
¶ Among recent infections included in a cluster.
** Expected number of recent infections in facilities included in a cluster based on the rate of infection across all facilities.
†† RR for recent infection among persons tested within a cluster.

that primarily rural Machinga and Zomba districts were also areas with high prevalence but higher viral load suppression; hotspots of recent infections suggested there might still be significant transmission (*8*). Investigations of these hotspots should seek to understand variation in transmission dynamics between urban and rural areas that may warrant implementation of a tailored response and program strengthening efforts. High proportions of females and similar median ages also warrant further investigation into factors contributing to recent transmission in these subpopulations and potential delayed diagnoses or gaps in HIV services for males (*7*).

Findings from this analysis underscore important considerations when examining recent HIV infection surveillance data. Although Blantyre district had a lower percentage of recent infections among new HIV diagnoses (2.4%) than did the overall analysis population percentage (3.3%), geospatial analysis identified hotspots with significantly higher rates of recent infection that might have otherwise gone unrecognized. This supports the importance of using the number of recent infections in the numerator and total recent infections plus total negative HIV tests (total at risk) in the denominator to identify hotspots of increased transmission (*9*). In addition, triangulation of various surveillance data sources and indicators of recent infection is important to understand the true prevalence and transmission of HIV across time and space. Moreover, geographic analyses can be conducted at various levels rather than just administrative borders (e.g., district).

The findings in this report are subject to at least five limitations. First, analysis was limited to five districts in Malawi, thus results might not be generalizable to other settings. Second, although only persons reporting a new HIV diagnosis were eligible for recent infection surveillance, in the absence of unique identifiers and case surveillance, it might not have been possible to determine whether a person had previously received an HIV diagnosis. Third, focusing only on HIV diagnoses overlooks persons with HIV who do not know their status or have not enrolled in treatment. Fourth, HIV testing frequency and behavior might vary across populations. For this analysis, mapping was done using health facility location, which might not reflect client residence, where transmission occurred, or population mobility. Future analyses could map residential-level hotpots, while protecting client privacy. Finally, performance of the test used to identify recent infections was assumed to be similar across all facilities.

Summary

What is already known about this topic?

A novel HIV infection surveillance initiative was implemented in Malawi to collect data on recent HIV infections among new diagnoses to characterize the epidemic and guide the public health response.

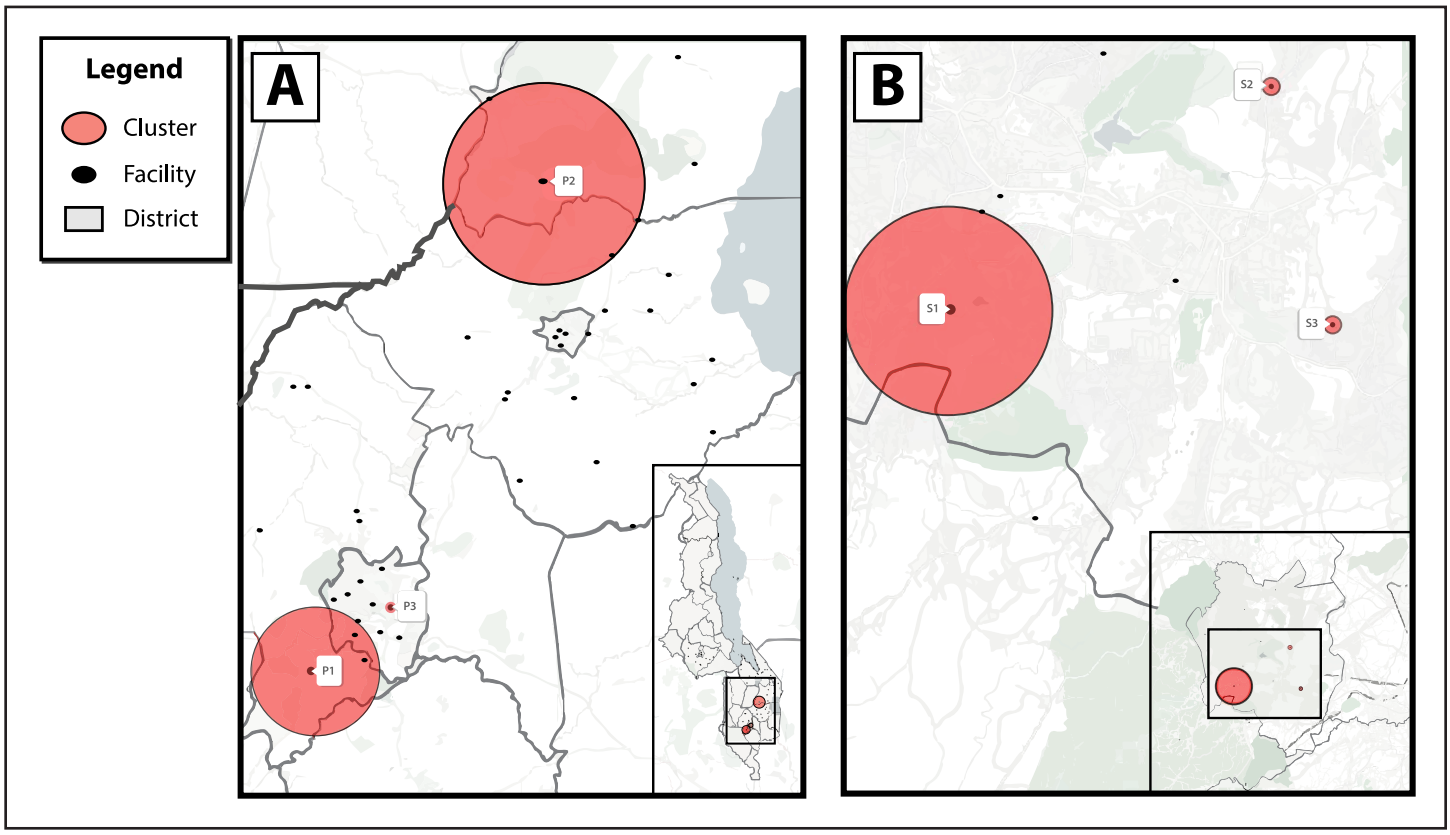
What is added by this report?

Higher proportions of recent infections were identified among females, persons aged <30 years, and clients at maternal and child health and youth clinics. Spatial analysis identified three hotspots of health facilities with significantly higher rates of recent infection than expected across five districts.

What are the implications for public health practice?

Geospatial analysis of recent HIV infection surveillance data can identify potential transmission hotspots. This information could be used to tailor program activities to strengthen HIV testing, prevention, and treatment services and ultimately interrupt transmission.

FIGURE. Geospatial transmission hotspots of recent HIV infection among health facilities implementing recent HIV infection surveillance in (A) five districts in Malawi and (B) Blantyre district, Malawi* — October 2019–March 2020



* The primary analysis (A) in five districts (Blantyre, Lilongwe, Machinga, Mangochi, and Zomba) in Malawi with a 20-km (12.4-mi) maximum cluster radius identified three HIV transmission hotspots (P1 = Blantyre, P2 = Machinga and Zomba, P3 = Blantyre [one facility]); a secondary analysis (B) focused on Blantyre district alone with a 5-km (3.1-mi) maximum cluster radius identified three additional HIV transmission hotspots (S1, S2, S3 = all Blantyre district).

Surveillance for recent HIV infection can help identify trends across sub-populations, map geographic areas where transmission has occurred in the past year, detect hotspots including facilities with higher-than-expected rates of recent infection, and guide prevention activities (*10*). After identifying a potential hotspot, investigations can include triangulation of surveillance and HIV program data to examine data quality, collection and reporting issues, programmatic gaps, and factors that elevate risk for infection. Hotspot investigation information could be used to tailor HIV testing, prevention and treatment to ultimately interrupt transmission.

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References

1. Vasylyeva TI, Friedman SR, Smyrnov P, Bondarenko K. A new approach to prevent HIV transmission: Project Protect intervention for recently infected individuals. AIDS Care 2015;27:223–8. PMID:25244688 https://doi.org/10.1080/09540121.2014.947913
2. Kim AA, Behel S, Northbrook S, Parekh BS. Tracking with recency assays to control the epidemic: real-time HIV surveillance and public health response. AIDS 2019;33:1527–9. PMID:31021850 https://doi.org/10.1097/QAD.0000000000002239
3. Parekh, B. Performance evaluation of Asante™ Rapid Recency Assay for HIV diagnosis and detection of recent infection: potential for surveillance and prevention. IAS 2017 [Abstract A-854–0164–05286]. International AIDS Society Conference on HIV Science; July 23–26, 2017; Paris, France; 2017. https://trace-recency.org/wp-content/uploads/2021/06/Parekh_IAS-2017-Asante-Poster11.pdf
4. Kassanjee R, Pilcher CD, Busch MP, et al.; Consortium for the Evaluation and Performance of HIV Incidence Assays (CEPHIA). Viral load criteria and threshold optimization to improve HIV incidence assay characteristics. AIDS 2016;30:2361–71. PMID:27454561 https://doi.org/10.1097/QAD.0000000000001209

5. Kulldorff M. A spatial scan statistic. Commun Stat Theory Methods 1997;26:1481–96. https://doi.org/10.1080/03610929708831995
6. Latash J, Greene SK, Stavinsky F, et al. Salmonellosis outbreak detected by automated spatiotemporal analysis—New York City, May–June 2019. MMWR Morb Mortal Wkly Rep 2020;69:815–9. PMID:32614808 https://doi.org/10.15585/mmwr.mm6926a2
7. Malawi Ministry of Health. Malawi population-based HIV impact assessment (MPHIA) 2015–16. Lilongwe, Malawi: Malawi Ministry of Health; 2018. https://phia.icap.columbia.edu/wp-content/uploads/2019/08/MPHIA-Final-Report_web.pdf
8. Nutor JJ, Duah HO, Agbadi P, Duodu PA, Gondwe KW. Spatial analysis of factors associated with HIV infection in Malawi: indicators for effective prevention. BMC Public Health 2020;20:1167. PMID:32711500 https://doi.org/10.1186/s12889-020-09278-0
9. Godin A, Eaton J, Giguere K, et al. Inferring population HIV incidence trends from surveillance data of recent HIV infection among HIV testing clients. AIDS 2021;35:2383–88. PMID:34261098 https://doi.org/10.1097/QAD.0000000000003021
10. Wand H, Ramjee G. Targeting the hotspots: investigating spatial and demographic variations in HIV infection in small communities in South Africa. J Int AIDS Soc 2010;13:41. PMID:20979651 https://doi.org/10.1186/1758-2652-13-41

Disparities in COVID-19 Vaccination Coverage Between Urban and Rural Counties — United States, December 14, 2020–January 31, 2022

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Higher COVID-19 incidence and mortality rates in rural than in urban areas are well documented (*1*). These disparities persisted during the B.1.617.2 (Delta) and B.1.1.529 (Omicron) variant surges during late 2021 and early 2022 (*1*,*2*). Rural populations tend to be older (aged ≥65 years) and uninsured and are more likely to have underlying medical conditions and live farther from facilities that provide tertiary medical care, placing them at higher risk for adverse COVID-19 outcomes (*2*). To better understand COVID-19 vaccination disparities between urban and rural populations, CDC analyzed county-level vaccine administration data among persons aged ≥5 years who received their first dose of either the BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna) COVID-19 vaccine or a single dose of the Ad.26.COV2.S (Janssen [Johnson & Johnson]) COVID-19 vaccine during December 14, 2020–January 31, 2022, in 50 states and the District of Columbia (DC). COVID-19 vaccination coverage with ≥1 doses in rural areas (58.5%) was lower than that in urban counties (75.4%) overall, with similar patterns across age groups and sex. Coverage with ≥1 doses varied among states: 46 states had higher coverage in urban than in rural counties, one had higher coverage in rural than in urban counties. Three states and DC had no rural counties; thus, urban-rural differences could not be assessed. COVID-19 vaccine primary series completion was higher in urban than in rural counties. However, receipt of booster or additional doses among primary series recipients was similarly low between urban and rural counties. Compared with estimates from a previous study of vaccine coverage among adults aged ≥18 years during December 14, 2020–April 10, 2021, these urban-rural disparities among those now eligible for vaccination (aged ≥5 years) have increased more than twofold through January 2022, despite increased availability and access to COVID-19 vaccines. Addressing barriers to vaccination in rural areas is critical to achieving vaccine equity, reducing disparities, and decreasing COVID-19–related illness and death in the United States (*2*).

Data on COVID-19 vaccine doses administered in the United States are reported to CDC by jurisdictions, pharmacies, and federal entities through immunization information systems (IISs),* the Vaccine Administration Management System (VAMS),† or through direct data submission.§ Persons aged ≥5 years with a valid county of residence in one of the 50 states or DC who received their first dose of a COVID-19 vaccine¶ during December 14, 2020–January 31, 2022, and whose deidentified data were reported to CDC were included in the analysis.** Urban-rural comparisons could not be made for three states (Delaware, New Jersey, and Rhode Island) and DC because they only had urban counties. In addition, eight counties in California with population size <20,000 were excluded because they have data-sharing restrictions on county-level information reported to CDC. Vaccine doses administered to persons residing in U.S. territories and freely associated states were also excluded because jurisdictional divisions could not be mapped to urban-rural classifications at the county level.

Receipt of the first dose of COVID-19 vaccine was matched by county of residence to one of six urban-rural categories according to the 2013 National Center for Health Statistics Urban-Rural Classification Scheme (*3*). To further classify counties into two categories (urban versus rural), four of these six categories (large central metropolitan, large fringe metropolitan, medium metropolitan, and small metropolitan) were combined into an urban category, and two (micropolitan and noncore) were combined into a rural category (*3*).

Vaccination coverage for persons aged ≥5 years who received ≥1 doses of a 2-dose COVID-19 primary vaccination series or a single dose of the Janssen COVID-19 vaccine was calculated overall and by age group (5–11, 12–17, 18–64, and ≥65 years), sex, jurisdiction, and urban-rural classification (two- and six-level). Population size was obtained by county, age group, and sex from the U.S. Census Bureau's 2020 Population Estimates

* IISs are confidential, computerized, population-based systems that collect and consolidate vaccination data from providers in 64 public health jurisdictions nationwide and can be used to track administered vaccines and measure vaccination coverage. The 64 IIS jurisdictions comprise the 50 U.S. states, five U.S. territories (American Samoa, Guam, Northern Mariana Islands, Puerto Rico, and U.S. Virgin Islands), three freely associated states (Federated States of Micronesia, Marshall Islands, and Palau), and six local jurisdictions (Chicago, Illinois; Houston, Texas; New York, New York; Philadelphia, Pennsylvania; San Antonio, Texas; and Washington, DC).

† https://www.cdc.gov/vaccines/covid-19/reporting/vams/program-information.html

§ https://www.cdc.gov/vaccines/covid-19/reporting/overview/IT-systems.html

¶ Includes the first dose of a 2-dose vaccination series (Pfizer-BioNTech or Moderna) as well as a single dose of the Janssen vaccine.

** Providers are required to document vaccination in their medical records within 24 hours of administration and in their jurisdiction's IISs within 72 hours of administration. A total of 5 days of observation were included to account for any delays in reporting and transmission of records to CDC.

Program (*4*). Because only the first dose of a 2-dose primary vaccination series or the single dose for Janssen vaccine was analyzed, the total number of doses per county was capped at the county's population size.†† Primary series completion§§ was also calculated and stratified by urban-rural classification. Among those aged ≥12 years who had completed their primary COVID-19 vaccination series, the proportions eligible for a booster dose and with sufficient time to receive it,¶¶ as well as the proportions of eligible persons who did and did not receive a booster dose, were calculated and stratified by urban-rural classification. Tests for statistical significance were not conducted because the data represent the U.S. population (excluding eight counties in California) and were not based on population samples. All analyses were conducted using SAS software (version 9.4; SAS Institute). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.***

Overall, during December 14, 2020–January 31, 2022, rural counties had lower first-dose vaccination coverage (58.5%) than did urban counties (75.4%) (Table 1). Females and males had lower first-dose coverage in rural counties (61.4% and 55.7%, respectively) than in urban counties (77.6% and 73.2%, respectively). Among all age groups, vaccination coverage with ≥1 doses was lower in rural counties, with the largest absolute difference (26.2 percentage points) among those aged 12–17 years (38.7% rural, 64.9% urban) and the largest relative difference among those aged 5–11 years (14.7% rural, 30.5% urban). Across jurisdictions, vaccination coverage with ≥1 doses varied by urban-rural classification. Among jurisdictions for which the urban-rural classification could be calculated, 46 jurisdictions had higher coverage in urban than rural counties, and one jurisdiction (Arizona) had higher coverage in rural than urban counties (Table 2). Primary series completion was lower in rural counties (52.1%) than in urban counties (66.2%) (Table 3).

†† For statistical analysis, the number of doses per county was capped at the county's population size minus one for a maximum vaccination coverage of 100%.

§§ Primary series completion is defined as receiving either both doses of a 2-dose mRNA COVID-19 vaccination series (Pfizer-BioNTech or Moderna) or a single dose of the Janssen vaccine. Series completion includes receipt of the same vaccine type for both mRNA doses or mismatched products for the first and second dose (e.g., Pfizer-BioNTech for the first dose and Moderna for the second dose, or vice versa).

¶¶ Eligible population is defined as persons aged ≥12 years who completed a primary COVID-19 vaccination series and were eligible to receive a booster or additional primary dose by the end of the analysis period, January 31, 2022. Those aged 12–17 years were eligible to receive their booster dose beginning January 5, 2022, and persons aged ≥18 years were eligible beginning November 19, 2021. These differences in eligibility dates were accounted for in analyses by restricting data to these eligibility dates by age. For Pfizer-BioNTech and Moderna vaccines, the primary series must have been completed by August 31, 2021 (i.e., ≥5 months earlier); for Janssen recipients, 1 dose must have been received by December 1, 2021 (i.e., ≥2 months earlier).

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

TABLE 1. COVID-19 vaccination coverage for persons aged ≥5 years who have received their first dose of the Moderna or Pfizer-BioNTech vaccine or a single dose of the Janssen (Johnson & Johnson) vaccine,* by sex, age group, and urban-rural classification† — United States, December 14, 2020–January 31, 2022

	No. (%)								
		Six-level urban-rural classification						Two-level urban-rural classification	
Characteristic	Overall	Large central metropolitan	Large fringe metropolitan	Medium metropolitan	Small metropolitan	Micropolitan	Noncore	Urban	Rural
Total	**226,621,879 (73.1)**	**76,387,928 (80.4)**	**59,624,160 (76.1)**	**47,054,083 (72.2)**	**18,185,028 (64.4)**	**15,549,920 (60.4)**	**9,820,760 (55.8)**	**201,251,199 (75.4)**	**25,370,680 (58.5)**
Sex									
Male	**107,681,923 (70.7)**	36,514,502 (78.7)	28,228,944 (73.6)	22,236,671 (69.6)	8,633,027 (61.9)	7,393,069 (57.6)	4,675,710 (52.8)	95,613,144 (73.2)	12,068,779 (55.7)
Female	**118,939,956 (75.4)**	39,873,426 (82.0)	31,395,216 (78.6)	24,817,412 (74.7)	9,552,001 (66.8)	8,156,851 (63.2)	5,145,050 (58.8)	105,638,055 (77.6)	13,301,901 (61.4)
Age group, yrs									
5–11	**8,046,457 (28.4)**	3,007,534 (34.7)	2,363,850 (32.5)	1,591,017 (26.3)	517,209 (20.4)	373,368 (16.1)	193,479 (12.5)	7,479,610 (30.5)	566,847 (14.7)
12–17	**15,398,653 (61.3)**	5,419,083 (73.0)	4,346,283 (65.4)	3,203,152 (59.9)	1,080,652 (48.5)	866,250 (41.7)	483,233 (34.2)	14,049,170 (64.9)	1,349,483 (38.7)
18–64	**152,499,838 (75.9)**	54,096,094 (84.4)	40,059,543 (79.1)	30,972,242 (74.4)	11,706,128 (65.3)	9,782,658 (61.0)	5,883,173 (55.7)	136,834,007 (78.5)	15,665,831 (58.9)
≥65	**50,676,931 (91.1)**	13,865,217 (93.5)	12,854,484 (93.7)	11,287,672 (93.0)	4,881,039 (87.6)	4,527,644 (85.4)	3,260,875 (80.2)	42,888,412 (92.7)	7,788,519 (83.2)

* Excludes doses with state of residence reported as a territory, freely associated state, or county of residence in California with population <20,000. Completeness of county data varied by jurisdiction.

† First doses of COVID-19 vaccine were matched by county of residence to one of six urban-rural categories according to the 2013 National Center for Health Statistics Urban-Rural Classification Scheme (https://www.cdc.gov/nchs/data/series/sr_02/sr02_166.pdf). To further classify counties into two categories (urban versus rural), four of these six categories were combined into urban areas (large central metropolitan, large fringe metropolitan, medium metropolitan, and small metropolitan), and two were combined into rural areas (micropolitan and noncore).

TABLE 2. COVID-19 vaccination coverage for persons aged ≥5 years who have received their first dose of the Moderna or Pfizer-BioNTech vaccine, or a single dose of the Janssen (Johnson & Johnson) vaccine, by jurisdiction* and urban-rural classification† — December 14, 2020–January 31, 2022

Jurisdiction	Vaccination coverage, no. (%)								
	Overall no. (%) with available county-level data	Six-level urban-rural classification						Two-level urban-rural classification	
		Large central metropolitan	Large fringe metropolitan	Medium metropolitan	Small metropolitan	Micropolitan	Noncore	Urban	Rural
All	**226,621,879 (73.1)**	**76,387,928 (80.4)**	**59,624,160 (76.1)**	**47,054,083 (72.2)**	**18,185,028 (64.4)**	**15,549,920 (60.4)**	**9,820,760 (55.8)**	**201,251,199 (75.4)**	**25,370,680 (58.5)**
Alabama	2,757,503 (59.6)	455,302 (74.2)	221,709 (47.0)	823,384 (66.2)	696,028 (56.4)	267,428 (53.9)	293,652 (51.5)	2,196,423 (61.6)	561,080 (52.6)
Alaska	457,999 (68.1)	—§	—§	254,919 (68.8)	63,589 (71.6)	35,442 (82.1)	104,049 (61.1)	318,508 (69.4)	139,491 (65.4)
Arizona	4,902,381 (70.1)	2,893,327 (67.2)	278,396 (61.2)	815,028 (81.1)	628,677 (70.1)	203,258 (85.9)	83,695 (86.7)	4,615,428 (69.3)	286,953 (86.1)
Arkansas	1,648,929 (58.0)	—§	24,271 (55.1)	887,427 (63.8)	175,592 (49.6)	282,910 (53.4)	278,729 (53.1)	1,087,290 (60.7)	561,639 (53.3)
California	30,179,535 (81.6)	19,997,305 (85.1)	3,877,313 (78.7)	5,036,170 (75.1)	790,163 (70.7)	363,889 (68.2)	114,695 (67.3)	29,700,951 (81.9)	478,584 (68.0)
Colorado	4,185,782 (76.3)	586,633 (84.6)	1,679,502 (78.9)	1,274,961 (76.2)	183,689 (59.7)	276,592 (72.7)	184,405 (61.6)	3,724,785 (77.5)	460,997 (67.8)
Connecticut	3,088,922 (91.5)	748,852 (88.9)	259,254 (86.5)	1,927,679 (93.4)	—§	153,137 (88.9)	—§	2,935,785 (91.6)	153,137 (88.9)
Delaware	742,926 (79.7)	—§	448,379 (84.6)	180,672 (78.6)	113,875 (66.0)	—§	—§	742,926 (79.7)	—§
District of Columbia	640,686 (95.8)	640,686 (95.8)	—§	—§	—§	—§	—§	640,686 (95.8)	—§
Florida	15,798,256 (76.7)	5,897,602 (82.8)	4,508,848 (78.2)	4,160,855 (71.2)	854,221 (72.5)	215,083 (61.3)	161,647 (48.4)	15,421,526 (77.4)	376,730 (55.0)
Georgia	5,818,300 (57.8)	676,861 (66.5)	2,805,562 (59.7)	685,239 (60.1)	818,217 (54.8)	470,916 (49.5)	361,505 (47.6)	4,985,879 (59.7)	832,421 (48.7)
Hawaii	1,166,364 (88.2)	—§	—§	833,497 (92.1)	127,790 (80.7)	205,077 (78.9)	—§	961,287 (90.4)	205,077 (78.9)
Idaho	989,974 (57.8)	—§	—§	459,601 (63.4)	237,160 (54.1)	227,660 (55.3)	65,553 (47.8)	696,761 (59.9)	293,213 (53.4)
Illinois	9,268,865 (78.2)	4,100,438 (85.3)	3,117,807 (80.6)	582,524 (68.8)	666,813 (67.6)	491,120 (61.4)	310,163 (56.3)	8,467,582 (80.6)	801,283 (59.3)
Indiana	3,927,951 (62.0)	591,225 (65.9)	1,405,574 (68.3)	582,136 (63.0)	647,621 (59.3)	490,631 (52.2)	210,764 (49.1)	3,226,556 (64.9)	701,395 (51.3)
Iowa	1,995,392 (67.2)	—§	—§	847,442 (73.0)	438,094 (69.6)	286,111 (62.4)	423,745 (58.6)	1,285,536 (71.8)	709,856 (60.1)
Kansas	1,889,944 (69.2)	—§	708,348 (84.2)	399,033 (65.6)	285,569 (65.9)	300,857 (60.9)	196,137 (55.5)	1,392,950 (74.0)	496,994 (58.6)
Kentucky	2,679,957 (63.7)	558,304 (77.5)	429,089 (65.4)	474,368 (69.0)	247,934 (58.1)	455,933 (56.4)	514,329 (56.6)	1,709,695 (68.7)	970,262 (56.5)
Louisiana	2,641,765 (60.7)	303,080 (82.5)	590,214 (71.3)	958,914 (58.3)	437,889 (53.3)	191,525 (52.8)	160,143 (49.1)	2,290,097 (62.6)	351,668 (51.0)
Maine	1,108,287 (86.1)	—§	—§	489,231 (94.5)	198,983 (80.5)	94,230 (80.6)	325,843 (80.5)	688,214 (90.0)	420,073 (80.5)
Maryland	4,826,509 (84.7)	418,821 (76.1)	3,967,335 (87.9)	215,045 (68.3)	124,839 (71.5)	49,943 (76.4)	50,526 (65.3)	4,726,040 (85.1)	100,469 (70.4)
Massachusetts	5,706,211 (87.2)	697,974 (91.7)	3,659,320 (91.9)	1,174,555 (85.1)	113,507 (34.9)	60,355 (71.7)	500 (4.7)	5,645,356 (87.6)	60,855 (64.2)
Michigan	5,826,988 (61.9)	1,381,910 (61.6)	1,823,505 (64.6)	990,899 (63.7)	640,707 (59.3)	626,474 (58.3)	363,493 (57.6)	4,837,021 (62.8)	989,967 (58.1)
Minnesota	3,830,405 (72.1)	1,387,321 (81.5)	1,114,942 (69.0)	164,688 (73.9)	425,982 (70.7)	416,618 (66.3)	320,854 (59.2)	3,092,933 (74.7)	737,472 (63.0)
Mississippi	1,679,842 (60.3)	—§	162,000 (63.8)	583,623 (63.8)	82,810 (58.6)	510,014 (58.7)	341,395 (56.3)	828,433 (63.2)	851,409 (57.7)
Missouri	3,582,610 (61.9)	688,006 (73.1)	1,557,395 (69.1)	256,709 (54.9)	386,917 (57.1)	333,686 (49.7)	359,897 (46.6)	2,889,027 (66.6)	693,583 (48.1)
Montana	632,670 (62.0)	—§	—§	—§	228,239 (64.0)	202,588 (62.9)	201,843 (59.1)	228,239 (64.0)	404,431 (60.9)
Nebraska	1,117,283 (61.8)	—§	—§	797,578 (73.1)	53,722 (52.7)	129,210 (42.5)	136,773 (43.9)	851,300 (71.3)	265,983 (43.2)
Nevada	2,098,894 (71.1)	1,566,670 (72.0)	—§	345,349 (76.1)	40,393 (76.4)	130,281 (54.4)	16,201 (53.3)	1,952,412 (72.7)	146,482 (54.3)
New Hampshire	1,193,635 (91.6)	—§	393,877 (93.2)	361,471 (91.0)	—§	394,069 (90.4)	44,218 (93.2)	755,348 (92.1)	438,287 (90.7)
New Jersey	7,314,550 (87.4)	1,750,970 (92.5)	4,786,993 (86.2)	603,833 (86.7)	172,754 (76.7)	—§	—§	7,314,550 (87.4)	—§
New Mexico	1,604,088 (80.7)	—§	—§	723,609 (82.7)	413,490 (88.1)	406,316 (72.9)	60,673 (70.6)	1,137,099 (84.6)	466,989 (72.6)
New York	15,684,228 (86.0)	8,401,387 (90.2)	—§	1,353,652 (78.8)	627,694 (79.5)	634,961 (69.1)	237,481 (65.1)	14,811,786 (87.4)	872,442 (68.0)
North Carolina	7,803,797 (78.1)	1,935,906 (91.3)	956,059 (70.6)	2,815,151 (79.9)	657,630 (73.8)	1,036,172 (68.7)	402,879 (67.6)	6,364,746 (80.7)	1,439,051 (68.4)
North Dakota	429,616 (60.3)	—§	—§	—§	236,356 (65.4)	88,397 (52.1)	104,863 (57.9)	236,356 (65.4)	193,260 (55.1)
Ohio	6,925,142 (62.9)	2,244,625 (71.1)	1,540,587 (65.1)	1,790,442 (63.5)	241,601 (52.5)	920,736 (51.6)	187,151 (44.7)	5,817,255 (66.1)	1,107,887 (50.3)
Oklahoma	2,502,179 (67.1)	618,215 (82.7)	381,909 (65.1)	695,416 (67.7)	89,297 (75.5)	440,229 (59.1)	277,113 (55.1)	1,784,837 (72.0)	717,342 (57.5)
Oregon	3,093,299 (76.9)	708,636 (91.4)	903,139 (80.5)	570,920 (73.6)	482,396 (69.0)	361,879 (65.8)	66,329 (67.6)	2,665,091 (79.0)	428,208 (66.1)
Pennsylvania	9,420,480 (77.9)	2,315,543 (88.2)	3,001,055 (85.3)	2,588,460 (74.7)	724,186 (64.7)	583,977 (59.2)	207,259 (54.6)	8,629,244 (80.4)	791,236 (58.0)
Rhode Island	850,640 (84.8)	494,329 (82.3)	356,311 (88.5)	—§	—§	—§	—§	850,640 (84.8)	—§
South Carolina	3,115,559 (63.2)	—§	246,655 (61.9)	2,108,729 (63.5)	352,130 (69.4)	240,259 (56.9)	167,786 (60.3)	2,707,514 (64.1)	408,045 (58.3)
South Dakota	602,302 (72.4)	—§	—§	—§	315,121 (76.2)	152,801 (69.7)	134,380 (67.2)	315,121 (76.2)	287,181 (68.6)
Tennessee	3,996,653 (61.7)	1,100,667 (72.4)	804,507 (61.3)	1,057,733 (64.2)	307,777 (56.0)	422,790 (50.9)	303,179 (49.1)	3,270,684 (65.0)	725,969 (50.1)
Texas	17,422,544 (63.6)	8,869,150 (68.5)	3,451,074 (62.3)	2,947,901 (68.8)	827,824 (47.8)	765,416 (49.9)	561,179 (41.4)	16,095,949 (65.7)	1,326,595 (45.9)
Utah	2,175,366 (72.3)	876,508 (80.8)	45,977 (66.7)	870,732 (70.0)	184,278 (62.8)	116,968 (65.5)	80,903 (58.2)	1,977,495 (73.5)	197,871 (62.3)
Vermont	510,091 (85.7)	—§	—§	—§	185,762 (88.2)	194,964 (84.5)	129,365 (84.2)	185,762 (88.2)	324,329 (84.4)
Virginia	5,802,571 (71.8)	890,652 (71.6)	3,414,756 (76.5)	393,085 (61.8)	513,580 (67.8)	142,629 (58.1)	447,869 (60.8)	5,212,073 (73.4)	590,498 (60.1)
Washington	5,661,229 (78.2)	1,936,717 (90.1)	1,596,654 (75.5)	971,606 (70.8)	652,690 (74.4)	391,498 (68.1)	112,064 (71.4)	5,157,667 (79.2)	503,562 (68.8)
West Virginia	1,098,194 (64.8)	—§	41,649 (76.3)	206,145 (66.3)	462,288 (67.5)	173,245 (62.5)	214,867 (58.7)	710,082 (67.6)	388,112 (60.4)
Wisconsin	3,909,379 (71.0)	654,306 (74.2)	635,142 (71.5)	793,672 (80.9)	927,701 (69.6)	469,365 (63.6)	429,193 (62.6)	3,010,821 (73.8)	898,558 (63.1)
Wyoming	315,207 (57.5)	—§	—§	—§	101,453 (59.6)	142,281 (62.4)	71,473 (47.6)	101,453 (59.6)	213,754 (56.5)

* Excludes doses with state of residence reported as a territory, freely associated state, or county of residence in California with population <20,000. Completeness of county data varied by jurisdiction.

† First doses of COVID-19 vaccine were matched by county of residence to one of six urban-rural categories according to the 2013 National Center for Health Statistics Urban-Rural Classification Scheme (https://www.cdc.gov/nchs/data/series/sr_02/sr02_166.pdf). To further classify counties into two categories (urban versus rural), four of these six categories were combined into urban areas (large central metropolitan, large fringe metropolitan, medium metropolitan, and small metropolitan), and two were combined into rural areas (micropolitan and noncore).

§ State has no counties at this level of urban-rural classification.

TABLE 3. COVID-19 vaccine series completion* and receipt of booster or additional dose among eligible population,† by urban-rural classification§ — United States, December 14, 2020–January 31, 2022

Characteristic	No. (%)								
		Six-level urban-rural classification						Two-level urban-rural classification	
	Overall	Large central metropolitan	Large fringe metropolitan	Medium metropolitan	Small metropolitan	Micropolitan	Noncore	Urban	Rural
Completed series*	**199,221,855 (64.2)**	66,993,451 (70.5)	52,606,393 (67.2)	40,925,558 (62.8)	16,107,552 (57.0)	13,783,465 (53.6)	8,805,436 (50.0)	176,632,954 (66.2)	22,588,901 (52.1)
Eligible for booster dose†	**151,089,493**	49,090,381	39,909,203	32,033,567	12,472,784	10,892,636	6,690,922	133,505,935	17,583,558
Received booster or additional dose									
Yes	**75,983,349 (50.3)**	24,689,986 (50.3)	20,439,141 (51.2)	15,878,242 (49.6)	6,244,751 (50.1)	5,343,170 (49.1)	3,388,059 (50.6)	67,252,120 (50.4)	8,731,229 (49.7)
No	**75,106,144 (49.7)**	24,400,395 (49.7)	19,470,062 (48.8)	16,155,325 (50.4)	6,228,033 (49.9)	5,549,466 (50.9)	3,302,863 (49.4)	66,253,815 (49.6)	8,852,329 (50.3)

* Persons aged ≥5 years who received a single dose of Janssen (Johnson & Johnson) vaccine or 2 doses of an mRNA vaccine (Pfizer-BioNTech or Moderna). This includes those who received the same vaccine type for both mRNA vaccine doses, as well as those who received heterologous products for the first and second dose (e.g., Pfizer-BioNTech for first dose and Moderna for the second dose, or vice versa). Excludes doses with state of residence reported as a territory, freely associated state, or county of residence in California with population <20,000. Completeness of county data varied by jurisdiction.

† Eligible population is defined as persons aged ≥12 years who completed a primary COVID-19 vaccination series and were eligible to receive a booster or additional primary dose by the end of the analysis period, January 31, 2022. For Pfizer-BioNTech and Moderna, the primary series must have been completed by August 31, 2021 (i.e., ≥5 months earlier); for Janssen recipients, 1 dose must have been received by December 1, 2021 (i.e., ≥2 months earlier). Excludes residents in Texas and persons aged <18 years from Idaho.

§ Doses of COVID-19 vaccine were matched by county of residence to one of six urban-rural categories according to the 2013 National Center for Health Statistics Urban-Rural Classification Scheme (https://www.cdc.gov/nchs/data/series/sr_02/sr02_166.pdf). To further classify counties into two categories (urban versus rural), four of these six categories were combined into urban areas (large central metropolitan, large fringe metropolitan, medium metropolitan, and small metropolitan), and two were combined into rural areas (micropolitan and noncore).

Receipt of booster or additional doses among those eligible was similar between urban (50.4%) and rural counties (49.7%).

Discussion

Across the United States, COVID-19 vaccination coverage was lower in rural counties than in urban counties, and this disparity persisted across sex and age groups. Compared with estimates from a previous study of vaccine coverage among adults aged ≥18 years during December 14, 2020–April 10, 2021, these urban-rural disparities among those now eligible (persons aged ≥5 years) for vaccination have increased overall and across sex and age groups, despite increased availability and access to COVID-19 vaccines (*5*). During December 14, 2020–April 10, 2021, urban-rural differences in first-dose COVID-19 vaccination coverage among adults aged ≥18 years were 6.8 percentage points (*5*); this gap has increased more than twofold to 16.9 percentage points in the current analysis among persons aged ≥5 years.

Various factors might have contributed to these increasing disparities. First, access to health care remains challenging in rural counties. Before the pandemic, persons in rural areas were more likely to report not having enough health care providers or hospitals to serve the community compared with persons living in urban areas, which might pose access issues for rural Americans seeking COVID-19 vaccination (*6*). Second, variations in views regarding the seriousness of COVID-19 infection and intention to implement COVID-19 prevention strategies exist and are often shaped by sociocultural identities and political ideologies that vary across the urban-rural continuum (*7*). Third, vaccine hesitancy has been historically higher in rural††† than urban areas for routinely recommended vaccines and continues to drive lower COVID-19 vaccination coverage in rural areas. Adults in rural areas were nearly three times as likely to report that they "definitely won't" get a COVID-19 vaccine than were those in urban areas (*8*). Targeted efforts are critical to increase vaccine confidence to address gaps in vaccination coverage between urban and rural communities.

Similar factors have also affected pediatric COVID-19 vaccination coverage. Parents in rural communities were approximately twice as likely to state that their child will "definitely not" get a COVID-19 vaccine compared with those in urban communities (*8*). Notably, 76% of parents in rural areas indicated that their trusted source of vaccination information for their children is their health care provider. However, nearly 40% of rural parents reported that their child's pediatrician did not recommend a COVID-19 vaccine, compared with only 8% of parents in urban communities (*8*). Health care providers remain a trusted source of information for parents, and vaccine recommendations from a health care provider are strong predictors of COVID-19 vaccination (*9*). This reported

††† https://www.ruralhealthinfo.org/rural-monitor/increasing-vaccination-rates/

Summary

What is already known about this topic?

COVID-19 incidence and mortality are higher in rural than in urban communities. Disparities in COVID-19 vaccination coverage between urban and rural communities have been recognized.

What is added by this report?

COVID-19 vaccination coverage with the first dose of the primary vaccination series was lower in rural (58.5%) than in urban counties (75.4%); disparities have increased more than twofold since April 2021. Receipt of booster or additional doses was similarly low in both rural and urban counties.

What are the implications for public health practice?

Addressing barriers to vaccination in rural areas is critical to achieving vaccine equity, reducing disparities, and decreasing COVID-19–related illness and death in the United States.

disparity between urban and rural pediatricians highlights the importance of partnering with health care providers and provider organizations to reduce vaccine hesitancy and increase vaccination coverage. Ongoing joint efforts by the CDC, local and state health departments, and other local partners through the Vaccinate with Confidence[§§§] initiative are designed to enhance trust and vaccine confidence in rural areas.

Some exceptions to the general trends were observed in this study. Although vaccination coverage was nearly universally higher in urban than rural counties, Arizona was the only state where coverage in rural counties was higher than that in urban counties; the reasons for this finding are not well understood. Rapid research will be important to identify and implement innovative approaches to bridge the gap in coverage between urban and rural counties. Despite pronounced urban-rural differences being noted in first dose COVID-19 vaccination coverage, receipt of booster or additional doses among those eligible was similarly low in urban and rural counties. Although booster doses for adolescents aged 12–17 years were authorized for only approximately 3 weeks during this study period (which might account for low booster dose coverage in this age group), all other age groups had more time to receive booster vaccination. The low booster dose coverage in urban and rural counties highlights the importance of developing and implementing innovative strategies to promote COVID-19 vaccines among all persons who are eligible for booster or additional doses and to receive these doses at the recommended intervals.

[§§§] https://www.cdc.gov/vaccines/covid-19/vaccinate-with-confidence/strategy.html

The findings in this report are subject to at least four limitations. First, eight counties with population size <20,000 in California were excluded, which might minimally bias coverage estimates. Second, race and ethnicity were unknown for approximately 35% of persons; therefore, vaccination coverage could not be estimated based on race and ethnicity. Third, booster doses could not be distinguished from additional primary doses because of absence of information on the immunocompromise status of vaccine recipients, which can thereby affect the interpretation of these findings. Finally, the National Center for Health Statistics Urban-Rural Classification was developed in 2013, and counties once classified as rural in 2013 might no longer be rural in 2022.

Addressing barriers to vaccination in rural areas is critical to achieving vaccine equity, reducing disparities, and decreasing COVID-19–related illness and death in the United States. Public health practitioners could focus on collaborating with health care providers, pharmacies, schools, community-based organizations, faith leaders, and local employers[¶¶¶] to improve vaccine confidence, ensure equitable vaccine access, and encourage staying up to date with recommended COVID-19 vaccinations in rural communities (*10*).

[¶¶¶] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/essentialworker/workplace-vaccination-program.html

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References

1. Dobis EA, McGranahan D. Rural residents appear to be more vulnerable to serious infection or death from coronavirus COVID-19. Washington, DC: U.S. Department of Agriculture; 2021. Accessed February 6, 2022. https://www.ers.usda.gov/amber-waves/2021/february/rural-residents-appear-to-be-more-vulnerable-to-serious-infection-or-death-from-coronavirus-covid-19
2. Ullrich F, Mueller K. COVID-19 Cases and deaths, metropolitan and nonmetropolitan counties over time (update). Iowa City, IA: Rural Policy research Institute, Center for Rural Health Policy Analysis; 2022. Accessed February 6, 2022. https://rupri.public-health.uiowa.edu/publications/policybriefs/2020/COVID%20Longitudinal%20Data.pdf
3. Ingram DD, Franco SJ. 2013 NCHS urban–rural classification scheme for counties. Hyattsville, MD: US Department of Health and Human Services, CDC, National Center for Health Statistics; 2014. https://www.cdc.gov/nchs/data/series/sr_02/sr02_166.pdf
4. US Census Bureau. Population and housing unit estimates. Washington, DC: US Department of Commerce, US Census Bureau; 2021. https://www.census.gov/programs-surveys/popest.html
5. Murthy BP, Sterrett N, Weller D, et al. Disparities in COVID-19 vaccination coverage between urban and rural counties—United States, December 14, 2020–April 10, 2021. MMWR Morb Mortal Wkly Rep 2021;70:759–64. PMID:34014911 https://doi.org/10.15585/mmwr.mm7020e3
6. Hamel L, Wu B, Brodie M. The health care views and experiences of rural Americans: findings from the Kaiser Family Foundation/Washington Post Survey of Rural America. Oakland, CA: Kaiser Family Foundation; 2017. Accesssed February 9, 2022. https://www.kff.org/report-section/the-health-care-views-and-experiences-of-rural-americans-findings
7. Porteny T, Corlin L, Allen JD, et al. Associations among political voting preference, high-risk health status, and preventative behaviors for COVID-19. BMC Public Health 2022;22:225. PMID:35114966 https://doi.org/10.1186/s12889-022-12633-y
8. Sparks G, Hamel L, Kirzinger A, Stokes M, Brodie M. KFF COVID-19 vaccine monitor: differences in vaccine attitudes between rural, suburban, and urban areas. Oakland, CA: Kaiser Family Foundation; 2021. Accessed February 7, 2022. https://www.kff.org/coronavirus-covid-19/poll-finding/kff-covid-19-vaccine-monitor-vaccine-attitudes-rural-suburban-urban/
9. Nguyen KH, Yankey D, Lu PJ, et al. Report of health care provider recommendation for COVID-19 vaccination among adults, by recipient COVID-19 vaccination status and attitudes—United States, April–September 2021. MMWR Morb Mortal Wkly Rep 2021;70:1723–30. PMID:34914669 https://doi.org/10.15585/mmwr.mm7050a1
10. Piltch-Loeb R, DiClemente R. The vaccine uptake continuum: applying social science theory to shift vaccine hesitancy. Vaccines (Basel) 2020;8:76. PMID:32046228 https://doi.org/10.3390/vaccines8010076

SARS-CoV-2 B.1.1.529 (Omicron) Variant Transmission Within Households — Four U.S. Jurisdictions, November 2021–February 2022

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The B.1.1.529 (Omicron) variant, first detected in November 2021, was responsible for a surge in U.S. infections with SARS-CoV-2, the virus that causes COVID-19, during December 2021–January 2022 (*1*). To investigate the effectiveness of prevention strategies in household settings, CDC partnered with four U.S. jurisdictions to describe Omicron household transmission during November 2021–February 2022. Persons with sequence-confirmed Omicron infection and their household contacts were interviewed. Omicron transmission occurred in 124 (67.8%) of 183 households. Among 431 household contacts, 227 were classified as having a case of COVID-19 (attack rate [AR] = 52.7%).† The ARs among household contacts of index patients who had received a COVID-19 booster dose, of fully vaccinated index patients who completed their COVID-19 primary series within the previous 5 months, and of unvaccinated index patients were 42.7% (47 of 110), 43.6% (17 of 39), and 63.9% (69 of 108), respectively. The AR was lower among household contacts of index patients who isolated (41.2%, 99 of 240) compared with those of index patients who did not isolate (67.5%, 112 of 166) (p-value <0.01). Similarly, the AR was lower among household contacts of index patients who ever wore a mask at home during their potentially infectious period (39.5%, 88 of 223) compared with those of index patients who never wore a mask at home (68.9%, 124 of 180) (p-value <0.01). Multicomponent COVID-19 prevention strategies, including up-to-date vaccination, isolation of infected persons, and mask use at home, are critical to reducing Omicron transmission in household settings.

Persons with sequence-confirmed Omicron variant infections during November 2021–February 2022 were identified from four U.S. jurisdictions (Chicago, Illinois; Connecticut; Milwaukee, Wisconsin; and Utah) and contacted by telephone to assess eligibility of the household to participate in the investigation.§ A household was eligible if the index patient did not live in a congregate setting and did live with at least one other person for most of their potentially infectious period, defined as 2 days before through 10 days after the index date (the date of the index patient's positive SARS-CoV-2 nucleic acid amplification test result or antigen test result or symptom onset, whichever occurred first). Index patients were defined as the first person within each household to recently experience COVID-19–compatible symptoms¶ or have a positive SARS-CoV-2 test result. Household contacts were defined as any persons who spent one or more overnights in the residence with the index patient during their potentially infectious period. If it was unclear who within the household was the index patient (e.g., if multiple persons developed COVID-19–compatible symptoms in the household on the same day or had the same SARS-CoV-2 exposure) or if household contacts had confirmed or probable cases and were known to have a SARS-CoV-2 exposure to someone other than the index patient, the household was excluded from analyses.

Index patients and household contacts participated in voluntary telephone interviews to retrospectively collect information on demographic characteristics, SARS-CoV-2 testing, symptoms, COVID-19 vaccination history, previous SARS-CoV-2 infection, index patient isolation practices (defined as always or sometimes isolating in a room by oneself at any point during

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† In this investigation, a confirmed case in a household contact was defined as having received a positive SARS-CoV-2 nucleic acid amplification test result or antigen test result ≤14 days after the index date (date of the index patient's symptom onset or positive SARS-CoV-2 nucleic acid amplification test result or antigen test result), and a probable case in a household contact was defined as the presence of COVID-19–compatible symptoms during the same 14-day period but without a positive SARS-CoV-2 test confirmation. Persons without symptoms and who did not have a positive SARS-CoV-2 test result were not considered to have a case of COVID-19. Analysis of AR among household contacts excluded eight persons with unknown case status (persons for whom it was not known whether COVID-19–compatible symptoms were present and whether SARS-CoV-2 testing had occurred [or if testing occurred, the results were unknown]).

§ Jurisdictions identified persons who were considered potentially eligible for participation through obtaining laboratory line lists of persons who had sequence-confirmed Omicron (B.1.1.529 lineage and its sublineages) or whose sequencing results were pending. Two jurisdictions attempted to contact all households on their line lists, and two jurisdictions attempted to contact households on their line lists based on specimen collection date.

¶ Persons were provided with the following list of signs and symptoms compatible with COVID-19: fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, and diarrhea or abdominal pain during the course of their recent illness. Persons who reported any signs or symptoms during the course of their recent illness were considered to have COVID-19–compatible symptoms. Persons who only had signs or symptoms (and no positive SARS-CoV-2 test result) were considered to have a probable case.

their potentially infectious period), and index patient mask use practices (defined as ever wearing a mask at home during their potentially infectious period). For this investigation, a confirmed case in a household contact was defined as a positive SARS-CoV-2 nucleic acid amplification test result or antigen test result (through local or home testing)** ≤14 days after the index date. A probable case in a household contact was defined as the presence of COVID-19–compatible symptoms in a household contact during the same 14-day period, but without confirmation by a SARS-CoV-2 test.†† Vaccination status was based primarily on self-report§§; participants were categorized as having received a booster dose, fully vaccinated (<5 or ≥5 months before the index date), partially vaccinated, or unvaccinated.¶¶

The interval between the index date and onset of symptoms or positive test result in a household contact was calculated. ARs among household contacts were estimated overall, by household contact characteristics, and by index patient characteristics, by dividing the number of household contacts with confirmed and probable cases by the total number of household contacts within a given stratum. P-values comparing differences in stratum-specific ARs were calculated using a generalized estimating equation approach to account for clustering by household (*2*). Statistical significance was defined as $p<0.05$. Subanalyses were conducted to examine potential secondary transmission (as opposed to all household transmission); the interval was calculated for households of two persons (index patient and another household contact), and ARs were calculated after restricting the case definition to cases identified ≤7 days*** after the index date. Data were collected and managed using REDCap (version 11.1.8; Vanderbilt University) and analyzed using R (version 4.0.3; R Foundation). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.†††

A total of 3,558 persons were considered potentially eligible for participation in the investigation, among whom jurisdictions attempted to contact 1,461 (41.1%). Of the 562 households successfully contacted, 175 (31.1%) declined to participate, and 204 (36.3%) were excluded; 183 (32.6%) were enrolled. §§§ Enrolled households included 183 index patients and 439 household contacts (Table). The median index patient age was 37 years (IQR = 23–54 years). A majority of index patients were White (59.0%, 108 of 183), and 21.3% (39 of 183) were Hispanic/Latino.

Index dates occurred during November 21, 2021–February 3, 2022.¶¶¶ Among index patients, 172 (94.0%) had a positive SARS-CoV-2 test result (confirmed COVID-19) and 11 (6.0%) had COVID-19–compatible symptoms but without SARS-CoV-2 test confirmation (probable COVID-19). Among 439 household contacts, cases were identified in 227 (51.7%), including 178 (40.5%) confirmed and 49 (11.2%) probable cases; among the remaining household contacts, 204 (46.5%) were classified as non–COVID-19 patients and eight (1.8%) as having unknown status.**** A negative SARS-CoV-2 test result was reported on the day of or after symptom onset by 38.8% (19 of 49) of household contacts classified as having probable COVID-19 and 68.6% (140 of 204) of those classified as not having COVID-19. The median interval between index patient onset date and household contact onset date was 4 days (IQR = 2–7 days) (Figure 1).

Most index patients (88.4%, 152 of 172) and household contacts (78.7%, 140 of 178) with confirmed cases reported COVID-19–compatible symptoms. Of those with known SARS-CoV-2 infection history, eleven (6.1%) of 181 index patients and nine (4.7%) of 192 household contacts with confirmed or probable COVID-19 reported a previous SARS-CoV-2 infection.

** Persons provided retrospective information about any SARS-CoV-2 testing that they chose and were able to perform. Thus, whether someone was tested and how many times they were tested depended on individual and social factors. Interviewers encouraged household contacts who had not received testing to receive testing if the telephone interview occurred ≤14 days after the index date and instructed them to call back with test results. When possible, SARS-CoV-2 testing data were supplemented with or verified using state or jurisdiction registry data.

†† Persons with probable cases included symptomatic persons who did not have SARS-CoV-2 testing and symptomatic persons who received negative SARS-CoV-2 test results.

§§ When possible, vaccination data were supplemented with or verified using state or jurisdiction registry data.

¶¶ Received a booster dose was defined as having received an additional dose after completion of the primary COVID-19 vaccination series before the index date. Fully vaccinated was defined as completion of the primary vaccination series ≥2 weeks before the index date and stratified into completion <5 months or ≥5 months before the index date. Some persons who were fully vaccinated had unknown dates for completion of their primary vaccination series. Partially vaccinated was defined as having only 1 dose of a 2-dose series or completing the primary vaccination series <2 weeks before the index date.

*** Seven days was chosen for this analysis, because 75% of cases occurred ≤7 days after the index date.

††† 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.

§§§ Among the 204 excluded households, 143 did not meet eligibility criteria, 47 were excluded because the index patient could not be identified, 11 were excluded because household contacts had confirmed or probable cases and were known to have a SARS-CoV-2 exposure other than exposure to the index patient, and three were excluded when sequencing results (pending at the time of interview) indicated a variant that was not Omicron. All but one of the 183 included households had sequence-confirmed Omicron; this one household had probable Omicron through variant specific qPCR in which the specimen had mutations consistent with the Omicron variant (K417N+ and L452R–).

¶¶¶ The median interval between index date and date of interview was 24 days (IQR = 17–29 days).

**** Case status of household contacts was unknown if the occurrence of COVID-19–compatible symptoms was not known and if the contact's testing results were unknown.

Transmission occurred within 67.8% (124 of 183) of households, and the overall AR among household contacts with known status was 52.7% (227 of 431) (Figure 2). Similar ARs were observed across age groups for household contacts, including those aged 0–4 years (51.2%, 21 of 41). ARs were high across all household contact vaccination categories but lowest among those who received a booster dose (47.8%, 54 of 113) or were fully vaccinated <5 months before the index date (50.0%, 14 of 28). The AR among household contacts with previous SARS-CoV-2 infection was 40.9% (9 of 22) compared with 59.8% (183 of 306) among those without previous infection (p-value = 0.08).

Household contact ARs ranged from a low of 47.5% (19 of 40) when the index patient was aged 5–11 years to a high of 72.0% (18 of 25) when the index patient was aged 0–4 years. The ARs among household contacts by index patient vaccination status were lowest among those who received a booster dose (42.7%, 47 of 110) and those who were fully vaccinated <5 months before the index date (43.6%, 17 of 39). The AR was lower among household contacts of index patients who isolated (41.2%, 99 of 240) compared with those of index patients who did not isolate (67.5%, 112 of 166, p-value<0.01). The AR was lower among household contacts of index patients who reported ever wearing a mask at home during their potentially infectious period (39.5%, 88 of 223) compared with household contacts of index patients who reported never wearing a mask at home during this period (68.9%, 124 of 180, p-value<0.01). Subanalyses focusing on secondary household

TABLE. Characteristics* and vaccination status of index COVID-19 patients (n = 183) and their household contacts (n = 439) — four U.S. jurisdictions, November 2021–February 2022

Characteristic	No. (column %)		
	Index patients, n = 183	Household contacts, n = 439	Total, N = 622
Jurisdiction			
Chicago, Illinois	26 (14.2)	51 (11.6)	**77 (12.4)**
Connecticut	93 (50.8)	218 (49.7)	**311 (50.0)**
Milwaukee, Wisconsin	36 (19.7)	101 (23.0)	**137 (22.0)**
Utah	28 (15.3)	69 (15.7)	**97 (15.6)**
Age group, yrs†			
0–4	8 (4.4)	41 (9.3)	**49 (7.9)**
5–11	11 (6.0)	51 (11.6)	**62 (10.0)**
12–17	14 (7.7)	42 (9.6)	**56 (9.0)**
18–64	134 (73.2)	262 (59.7)	**396 (63.7)**
≥65	14 (7.7)	27 (6.2)	**41 (6.6)**
Unknown	2 (1.1)	16 (3.6)	**18 (2.9)**
Gender			
Female	95 (51.9)	229 (52.2)	**324 (52.1)**
Male	88 (48.1)	199 (45.3)	**287 (46.1)**
Unknown	0 (—)	11 (2.5)	**11 (1.8)**
Race			
White	108 (59.0)	209 (47.6)	**317 (51.0)**
Black	27 (14.8)	35 (8.0)	**62 (10.0)**
Asian	15 (8.2)	25 (5.7)	**40 (6.4)**
Other/Multiple§	16 (8.7)	33 (7.5)	**49 (7.9)**
Unknown	17 (9.3)	137 (31.2)	**154 (24.8)**
Ethnicity			
Non-Hispanic/Latino	130 (71.0)	219 (49.9)	**349 (56.1)**
Hispanic/Latino	39 (21.3)	98 (22.3)	**137 (22.0)**
Other/Unknown	14 (7.7)	122 (27.8)	**136 (21.9)**
COVID-19 vaccination status¶			
Received a booster	57 (31.1)	114 (26.0)	**171 (27.5)**
Fully vaccinated	85 (46.4)	154 (35.1)	**239 (38.4)**
<5 months before index date	12 (6.6)	28 (6.4)	**40 (6.4)**
≥5 months before index date	70 (38.3)	88 (20.0)	**158 (25.4)**
Timing of vaccination unknown	3 (1.6)	38 (8.7)	**41 (6.6)**
Partially vaccinated	2 (1.1)	15 (3.4)	**17 (2.7)**
Not vaccinated	36 (19.7)	129 (29.4)	**165 (26.5)**
Unknown	3 (1.6)	27 (6.2)	**30 (4.8)**
Previous COVID-19 infection status			
Previous infection	11 (6.0)	22 (5.0)	**33 (5.3)**
No previous infection	170 (92.9)	306 (69.7)	**476 (76.5)**
Unknown	2 (1.1)	111 (25.3)	**113 (18.2)**
COVID-19 case status**			
Confirmed	172 (94.0)	178 (40.5)	**350 (56.3)**
Probable	11 (6.0)	49 (11.2)	**60 (9.6)**
Not a case	0 (—)	204 (46.5)	**204 (32.8)**
Unknown	0 (—)	8 (1.8)	**8 (1.3)**

* Persons self-reported their race (White, Black, Asian, American Indian or Alaska Native, or Native Hawaiian or other Pacific Islander), ethnicity (Hispanic/Latino or non-Hispanic/Latino), and gender (male or female) from lists of options and had the opportunity to state another option if their race, ethnicity, or gender was not listed.

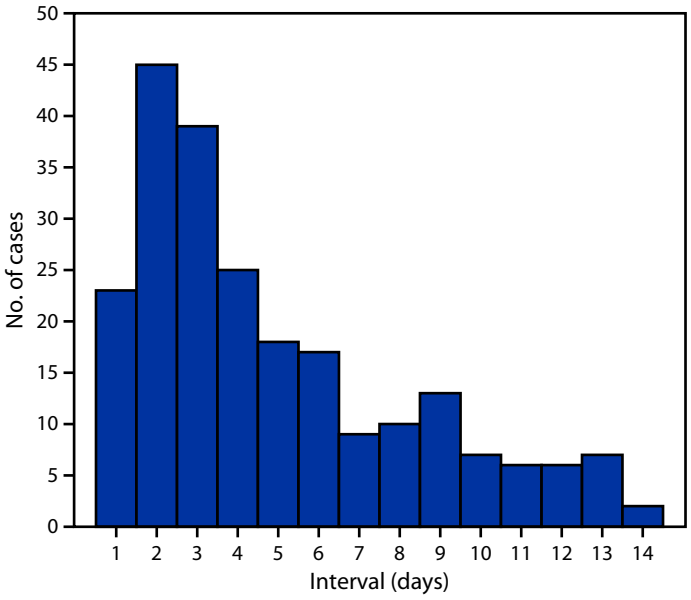
† Age at index date was determined from date of birth or self-reported age.

§ The "other/multiple" race category included American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, another race specified by the person not in the provided list, or multiple races.

¶ Received a booster dose was defined as having received an additional dose after completion of the primary COVID-19 vaccination series before the index date. Fully vaccinated was defined as completion of the primary vaccination series ≥2 weeks before the index date and stratified into completion <5 months or ≥5 months before the index date. Some persons who were fully vaccinated had unknown dates for completion of their primary vaccination series. Partially vaccinated was defined as having only 1 dose of a 2-dose series or completing the primary vaccination series <2 weeks before the index date.

** An index patient with a confirmed COVID-19 case was the first person with a positive SARS-CoV-2 nucleic acid amplification test result or antigen test result (through local or home testing) reported in a household. An index patient with a probable COVID-19 case was the first person with onset of any symptom consistent with COVID-19, but without a positive SARS-CoV-2 test confirmation, reported in a household. A confirmed case in a household contact was receipt of a positive SARS-CoV-2 nucleic acid amplification test result or antigen test result (through local or home testing) reported ≤14 days after the index date. A probable case in a household contact was the presence of any symptom consistent with COVID-19 during the same 14-day period but without a positive SARS-CoV-2 test confirmation.

FIGURE 1. Interval*,† between index patient onset date and household contact onset date — four U.S. jurisdictions, November 2021–February 2022



* The interval was estimated by calculating the number of days between the symptom onset or positive test result date for the index patient and that of the household contact. For both index patients and household contacts, the onset date was either the date of SARS-CoV-2 positive test result or date of symptom onset, whichever occurred first.

† Transmission can occur within a household setting on the first day an index patient is infected or on any subsequent day during which they are still shedding viable virus.

transmission demonstrated a similar interval (median = 3 days, IQR = 2–5) (Supplementary Figure 1, https://stacks.cdc.gov/view/cdc/114723) and similar patterns in ARs (Supplementary Figure 2, https://stacks.cdc.gov/view/cdc/114722).

Discussion

Omicron infection resulted in high ARs among household contacts in this investigation, particularly among those who lived with index patients who were not vaccinated or who did not practice prevention measures (isolating or ever wearing a mask at home). The estimated overall AR in this investigation is consistent with the range of ARs observed in other Omicron transmission studies†††† (*3*), and higher than those associated with some other SARS-CoV-2 variants.§§§§ These findings underscore the importance of implementation of multicomponent prevention measures for reducing SARS-CoV-2 transmission in household settings, including from the Omicron variant (*4*).

ARs were consistently high across household contact and index patient age groups, including those aged 0–4 years. This age group is currently not eligible for vaccination and is a population in which some prevention strategies, such as isolation and mask use, might be difficult or impractical to implement. These findings further highlight young children's potential contribution to household transmission of SARS-CoV-2, as well as their ongoing susceptibility to infection when SARS-CoV-2 is introduced in the home¶¶¶¶ (*5*).

These findings are subject to at least six limitations. First, this investigation used a convenience sample of persons with sequence-confirmed Omicron infections, and participation in this investigation was voluntary. The small sample size, especially for certain stratum-specific ARs, may limit overall generalizability of the results. Households with high transmission or with more attention to public health measures may have been more likely to participate. Second, the investigation relied primarily on self-reported data. Vaccination status was not always verified, and the analysis did not account for potential variations in prevention practices (e.g., frequency of mask use). Third, COVID-19 prevention measures (vaccination, isolation, and mask use) are likely highly correlated within households, and the identified risk factors might not be independent predictors of transmission. Fourth, the interval analysis reflected time between dates of a positive test result or symptom onset, not date of infection, and did not account for duration of symptoms and prevention strategies, such as frequency of mask use. Fifth, this investigation did not definitively distinguish between secondary and potential tertiary cases within a household. Finally, this investigation occurred during a period when testing and sequencing capacity was strained and when many persons traveled and attended gatherings, increasing the possibility that household contacts had unknown SARS-CoV-2 exposures outside the home (*6*).

Summary

What is already known about this topic?

The SARS-CoV-2 B.1.1.529 (Omicron) variant contributed to a surge of SARS-CoV-2 infections in the United States during December 2021–January 2022.

What is added by this report?

In a study of household transmission in four U.S. jurisdictions, Omicron infection resulted in high transmission among household contacts, particularly among those who lived with index patients who were not vaccinated or who did not take measures to reduce the risk of transmission to household contacts.

What are the implications for public health practice?

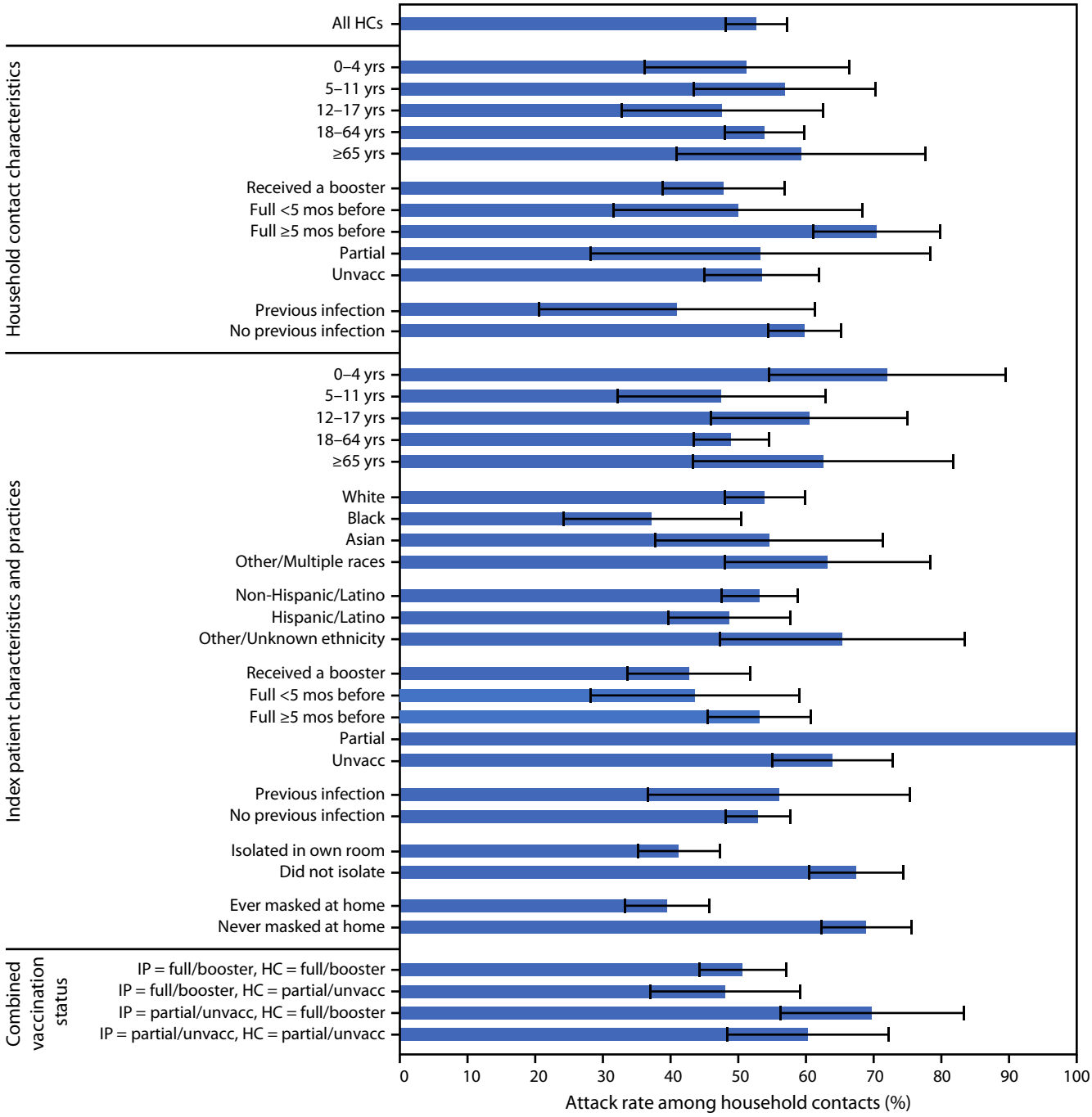
Multicomponent COVID-19 prevention strategies, including up-to-date vaccination, isolation of infected persons, and mask use at home, are important to reduce Omicron transmission in household settings.

†††† https://www.medrxiv.org/content/10.1101/2021.12.27.21268278v1

§§§§ https://www.medrxiv.org/content/10.1101/2022.01.09.22268984v1

¶¶¶¶ https://www.medrxiv.org/content/10.1101/2021.08.16.21262121v2

FIGURE 2. SARS-CoV-2 infection attack rates* among household contacts (N = 431) with known case status, by household contact characteristics,†,§ index patient characteristics and practices,†,§,¶ and combined vaccination status — four U.S. jurisdictions, November 2021–February 2022**



Abbreviations: Full = fully vaccinated; HC = household contact; IP = index patient; Partial = partially vaccinated; Unvacc = unvaccinated.

* Analysis of attack rates among HCs excluded persons with unknown case status or "unknown" categorization within a given stratum. 95% CIs for attack rates are represented by error bars.

† Age at index date was determined from date of birth or self-reported age.

§ Received a booster dose was defined as having received an additional dose after completion of the primary COVID-19 vaccination series before the index date. Fully vaccinated was defined as completion of the primary vaccination series ≥2 weeks before the index date and stratified into completion <5 months or ≥5 months before the index date. Some persons who were fully vaccinated had unknown dates for completion of their primary vaccination series. Partially vaccinated was defined as having only 1 dose of a 2-dose series or completing the primary vaccination series <2 weeks before the index date.

¶ Persons reported their race (White, Black, Asian, American Indian or Alaska Native, or Native Hawaiian or other Pacific Islander) and ethnicity (Hispanic/Latino or non-Hispanic/Latino) from lists of options and had the opportunity to state another option if their race or ethnicity was not listed. The "other/multiple races" category included American Indian or Alaskan Native, Native Hawaiian or other Pacific Islander, another race specified by the person not in the provided list, or multiple races.

** Analysis for attack rates by combined vaccination status combined persons who were fully vaccinated or had received a booster dose into one category (full/booster) and persons who were partially vaccinated or unvaccinated into another category (partial/unvacc).

Because SARS-CoV-2 testing was not available for all household contacts, ability to detect asymptomatic infections was limited. Without sequencing results for all household contact cases, it was not possible to confirm that transmission occurred from index patients to household contacts or that household contacts were infected with the same variant.

The findings from this investigation reinforce the importance of multi-component prevention strategies, including up-to-date vaccination, isolation of infected persons, and mask use at home, to reduce Omicron transmission in household settings.

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References

1. Iuliano AD, Brunkard JM, Boehmer TK, et al. Trends in disease severity and health care utilization during the early Omicron variant period compared with previous SARS-CoV-2 high transmission periods—United States, December 2020–January 2022. MMWR Morb Mortal Wkly Rep 2022;71:146–52. PMID:35085225 https://doi.org/10.15585/mmwr.mm7104e4
2. Zeger SL, Liang KY, Albert PS. Models for longitudinal data: a generalized estimating equation approach. Biometrics 1988;44:1049–60. PMID:3233245 https://doi.org/10.2307/2531734
3. Song JS, Lee J, Kim M, et al. Serial intervals and household transmission of SARS-CoV-2 Omicron variant, South Korea, 2021. Emerg Infect Dis 2022;28:756–9. PMID:35107418 https://doi.org/10.3201/eid2803.212607
4. CDC COVID-19 Response Team. SARS-CoV-2 B.1.1.529 (Omicron) variant—United States, December 1-8, 2021. MMWR Morb Mortal Wkly Rep 2021;70:1731–4. PMID:34914670 https://doi.org/10.15585/mmwr.mm7050e1
5. Lopez AS, Hill M, Antezano J, et al. Transmission dynamics of COVID-19 outbreaks associated with child care facilities—Salt Lake City, Utah, April–July 2020. MMWR Morb Mortal Wkly Rep 2020;69:1319–23. PMID:32941418 https://doi.org/10.15585/mmwr.mm6937e3
6. US Travel Association. Monthly travel data report. Washington, DC: US Travel Association; 2021. Accessed February 23, 2022. https://www.ustravel.org/research/monthly-travel-data-report

Safety Monitoring of COVID-19 Vaccine Booster Doses Among Persons Aged 12–17 Years — United States, December 9, 2021–February 20, 2022

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As of February 20, 2022, only BNT162b2 (Pfizer-BioNTech) COVID-19 vaccine has been authorized for use in persons aged 12–17 years in the United States (*1*). The Food and Drug Administration (FDA) amended the Emergency Use Authorization (EUA) for Pfizer-BioNTech vaccine on December 9, 2021, to authorize a homologous* booster dose for persons aged 16–17 years ≥6 months after receipt of dose 2 (*1*). On January 3, 2022, authorization was expanded to include persons aged 12–15 years, and for all persons aged ≥12 years, the interval between dose 2 and booster dose was shortened to ≥5 months (*1*). To characterize the safety of Pfizer-BioNTech booster doses among persons aged 12–17 years (adolescents), CDC reviewed adverse events and health impact assessments during the week after receipt of a homologous Pfizer-BioNTech booster dose reported to v-safe, a voluntary smartphone–based safety surveillance system for adverse events after COVID-19 vaccination, and adverse events reported to the Vaccine Adverse Event Reporting System (VAERS), a passive vaccine safety surveillance system managed by CDC and FDA. During December 9, 2021–February 20, 2022, approximately 2.8 million U.S. adolescents received a Pfizer-BioNTech booster dose.† During this period, receipt of 3,418 Pfizer-BioNTech booster doses were reported to v-safe for adolescents. Reactions were reported to v-safe with equal or slightly higher frequency after receipt of a booster dose than after dose 2, were primarily mild to moderate in severity, and were most frequently reported the day after vaccination. VAERS received 914 reports of adverse events after Pfizer-BioNTech booster dose vaccination of adolescents; 837 (91.6%) were nonserious and 77 (8.4%) were serious. Health care providers, parents, and adolescents should be advised that local and systemic reactions are expected among adolescents after homologous Pfizer-BioNTech booster vaccination, and that serious adverse events are rare.

V-safe is a voluntary, smartphone–based U.S. active safety surveillance system established to monitor adverse events after COVID-19 vaccination (https://vsafe.cdc.gov/en/). The v-safe platform allows current registrants to report receipt of a booster dose of COVID-19 vaccine and new registrants to enter information about all doses received. Registrants aged ≤15 years must be enrolled by a parent or guardian. Health surveys are sent daily during the first week after administration of each dose and include questions about local injection site and systemic reactions and health impacts.§ CDC's v-safe call center contacts registrants who indicate that medical care was sought after vaccination and encourages completion of a VAERS report, if indicated.

VAERS is a U.S. national passive vaccine safety surveillance system managed by CDC and FDA that monitors adverse events after vaccination (*2*). VAERS accepts reports from health care providers, vaccine manufacturers, and members of the public.¶ VAERS reports are classified as serious if there are any reports of hospitalization, prolongation of hospitalization, life-threatening illness, permanent disability, congenital anomaly or birth defect, or death.** VAERS staff members assign Medical Dictionary for Regulatory Activities (MedDRA) preferred terms to the signs, symptoms, and diagnostic findings in VAERS reports.†† Serious reports to VAERS were reviewed by CDC physicians to form a clinical impression based on available data. Reports of myocarditis and pericarditis, rare adverse events that have been associated with mRNA-based COVID-19 vaccines (*3*), after receipt of a booster vaccine were identified by a search for selected MedDRA preferred terms; CDC staff members attempted to collect information about clinical course and determined whether the CDC myocarditis case definition was met.§§

* Homologous refers to a booster dose of the same product administered for the primary series.

† https://covid.cdc.gov/covid-data-tracker/#vaccination-demographic

§ Health surveys are sent for the most recent dose entered via text messages that link to web-based surveys on days 0–7 after vaccination; then weekly through 6 weeks after vaccination; and then 3, 6, and 12 months after vaccination.

¶ Health care providers are required by COVID-19 vaccine EUAs to report certain adverse events after vaccination to VAERS, including death. https://vaers.hhs.gov/faq.html

** VAERS reports are classified as serious based on the Code of Federal Regulations Title 21 (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm?fr). Reports of serious adverse events receive follow-up by VAERS staff to obtain additional information, including medical records and, for reports of death, death certificates and autopsy reports, if available.

†† Each VAERS report might be assigned more than one MedDRA preferred term. A MedDRA-coded event does not indicate a medically confirmed diagnosis. https://www.meddra.org/how-to-use/basics/hierarchy

§§ Acute myocarditis was defined as presence of signs and symptoms (one or more new or worsening of the following: chest pain/pressure/discomfort, dyspnea/shortness of breath/pain with breathing, palpitations, or syncope; or two or more of the following in children aged ≤11 years: irritability, vomiting, poor feeding, tachypnea, or lethargy); and one or more new finding of elevated troponin, electrocardiogram findings consistent with myocarditis, abnormal cardiac function or wall motion on echocardiogram, cardiac magnetic resonance imaging findings consistent with myocarditis, or histopathologic findings consistent with myocarditis; and no other identifiable cause for these findings.

This report assessed local and systemic reactions and health impacts reported during the week after vaccination among adolescent v-safe registrants who received a homologous Pfizer-BioNTech booster dose ≥5 months after completion of their primary series during December 9, 2021–February 20, 2022. The odds of reporting an adverse reaction or health impact after dose 2 and booster dose were compared using a multivariable generalized estimating equations model; p<0.05 was defined as statistically significant.[¶¶] VAERS reports for adolescents who received a Pfizer-BioNTech booster dose during December 9, 2021–February 20, 2022, were described by serious and nonserious classification, demographic characteristics (i.e., sex and age), and MedDRA preferred terms.[***] Reporting rates for myocarditis were stratified by sex and age group. SAS software (version 9.4; SAS Institute) was used to conduct all analyses. These surveillance activities were reviewed by CDC and conducted consistent with applicable federal law and CDC policy.[†††]

Review of v-safe Data

During December 9, 2021–February 20, 2022, v-safe recorded a total of 3,418 Pfizer-BioNTech booster doses administered to adolescents, including 1,952 administered to persons aged 12–15 years and 1,466 to those aged 16–17 years. Local injection site reactions (2,802; 82.0%) and systemic reactions (2,659; 77.8%) were frequently reported during the week after booster dose vaccination for all adolescents (Table 1); the most frequently reported adverse reactions were injection site pain (2,736; 80.0%), fatigue (1,998; 58.5%), headache (1,911; 55.9%), and myalgia (1,578; 46.2%). Reactions were mostly mild to moderate in severity and most frequently reported the day immediately after vaccination. Local injection site reactions were more commonly reported after booster dose (82.0%) than dose 2 (77.8%) (p<0.001), and systemic reactions were similarly reported after booster dose (77.8%) and dose 2 (77.2%) (p = 0.48) (Figure).

In the week after booster dose vaccination, 20.0% (682) of adolescents were reported as being unable to attend school or work. Approximately 0.9% (32) of adolescents reportedly received medical care during the week after booster dose vaccination; most (15; 0.4%) care was received via a clinic appointment. One (0.03%) adolescent received care at a hospital during the week after booster dose vaccination for treatment of a new onset migraine; whether hospitalization was the result of vaccination could not be determined. Inability to perform daily activities was less frequently reported after receipt of the booster dose (25.8%) than after dose 2 (28.8%) (p<0.001) (Figure), whereas inability to work or attend school was more frequently reported (20.0% and 9.4%, respectively) (p<0.001). Receipt of medical care was more frequently reported after receipt of the booster dose than dose 2 (0.9% and 0.6%, respectively); however, the difference was not statistically significant (p = 0.12).

Review of VAERS Data

During December 9, 2021–February 20, 2022, VAERS received and processed 914 reports of adverse events after receipt of a Pfizer-BioNTech booster dose for adolescents; the median age was 16 years, and 459 (50.2%) reports were for adolescent girls. Most VAERS reports were for nonserious events (837; 91.6%); the most commonly reported nonserious events included product storage error (123; 14.7%), dizziness (100; 12.0%), and syncope (87; 10.4%) (Table 2). Sixty-four preliminary reports of myocarditis were received,

TABLE 1. Adverse reactions and health impacts reported to v-safe for persons aged 12–17 years[*] (N = 3,418) who received a homologous Pfizer-BioNTech COVID-19 vaccine booster dose — United States, December 9, 2021–February 20, 2022

	No. (%) reporting reaction or health impact after receipt of a homologous Pfizer-BioNTech vaccine[†]	
Reported event	**Dose 2**	**Booster dose**
Any local injection site reaction	**2,660 (77.8)**	**2,802 (82.0)**
Itching	250 (7.3)	252 (7.4)
Pain	2,596 (76.0)	2,736 (80.0)
Redness	287 (8.4)	350 (10.2)
Swelling	483 (14.1)	644 (18.8)
Any systemic reaction	**2,638 (77.2)**	**2,659 (77.8)**
Abdominal pain	318 (9.3)	291 (8.5)
Myalgia	1,399 (40.9)	1,578 (46.2)
Chills	949 (27.8)	1,115 (32.6)
Diarrhea	153 (4.5)	118 (3.5)
Fatigue	2,006 (58.7)	1,998 (58.5)
Fever	1,310 (38.3)	1,213 (35.5)
Headache	1,914 (56.0)	1,911 (55.9)
Joint pain	578 (16.9)	672 (19.7)
Nausea	643 (18.8)	647 (18.9)
Rash	52 (1.5)	41 (1.2)
Vomiting	93 (2.7)	78 (2.3)
Any health impact	**1,094 (32.0)**	**1,224 (35.8)**
Unable to perform normal daily activities	986 (28.8)	881 (25.8)
Unable to attend school or work	320 (9.4)	682 (20.0)
Needed medical care	21 (0.6)	32 (0.9)
Telehealth	4 (0.1)	6 (0.2)
Clinic	4 (0.1)	15 (0.4)
Emergency visit	8 (0.2)	5 (0.1)
Hospitalization	2 (0.1)	1 (0.03)

[*] Registrants aged ≤15 years must be enrolled by a parent or guardian.
[†] Percentage of registrants who reported a reaction or health impact at least once during days 0–7 after vaccination.

[¶¶] This model adjusted for demographic variables (i.e., age, sex, race, and ethnicity) and accounted for repeated measures among doses reported by each registrant.
[***] This analysis excluded reports to v-safe or VAERS of persons aged 12–15 and 16–17 years who were vaccinated before authorization for a booster dose for their age group (January 3, 2022, and December 9, 2021, respectively).
[†††] 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.

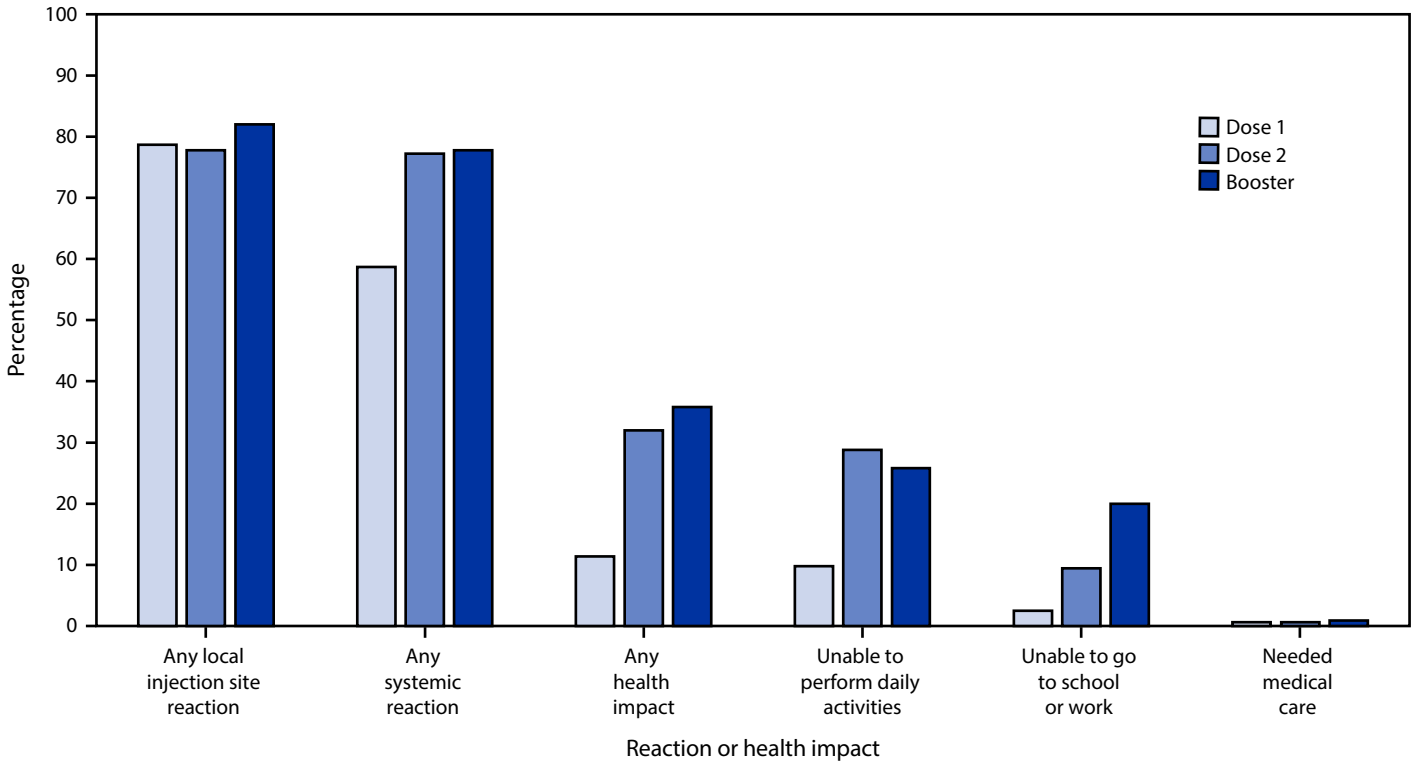
among which 47 were considered serious; 32 (68.1%) of these reports were confirmed by provider interview or medical record review to meet the CDC working definition of myocarditis. All 32 reports were among adolescent boys and 27 (84.4%) patients were hospitalized; as of February 20, 2022, all had been discharged, 18 had recovered, and nine were recovering. Among adolescent boys, the reporting rate for confirmed cases of myocarditis after Pfizer-BioNTech booster vaccination was 11.4 per 1 million booster doses administered. No deaths were reported to VAERS.

Discussion

This report provides findings from v-safe and VAERS data collected during the first 7–11 weeks of administration of homologous Pfizer-BioNTech booster doses to persons aged 12–17 years, during which time approximately 2.8 million booster doses were administered. Among adolescents, reports to v-safe and VAERS after receipt of a booster dose were generally similar to those previously described after a primary series dose, reinforcing that vaccination among this population is safe (*4*,*5*). Health care providers, parents, and adolescents should be advised that local and systemic reactions are expected among adolescents after Pfizer-BioNTech booster vaccination and that serious adverse events are rare.

Reports to v-safe after receipt of a booster dose in an adolescent were generally similar to those previously described for persons aged ≥18 years who received a homologous booster dose of Pfizer-BioNTech vaccine (*6*,*7*); however, reactions among adolescents were reported to v-safe with equal or slightly higher frequency after receipt of a booster dose than after dose 2. Reactions reported after both dose 2 and booster dose vaccination were mostly mild to moderate in severity. Most were reported the day after vaccination. Inability to attend school was more frequently reported after a booster dose than after dose 2; however, for many in this age group, receipt of dose 2 occurred during a period of remote learning or summer vacation, which might have affected reporting. Hospitalization in the week after booster dose vaccination was reported for one adolescent with new onset migraine; whether hospitalization was the result of COVID-19 vaccination could not be determined.

FIGURE. Adverse reactions and health impacts reported* among persons aged 12–17 years (N = 3,274) who received a homologous Pfizer-BioNTech COVID-19 vaccine booster, by vaccine dose — United States, December 9, 2021–February 20, 2022



* Registrants aged ≤15 years must be enrolled by a parent or guardian. The odds of reporting an event after dose 2 and booster dose were compared for registrants who completed at least one v-safe health check-in survey on days 0–7 after each vaccination using a multivariable generalized estimating equations model. This model adjusted for demographic variables and accounted for repeated measures among doses reported by each registrant (needed medical care was not adjusted due to small numbers); $p<0.05$ was considered statistically significant. All dose 2 and booster dose comparisons were statistically significant, except any systemic reaction and needed medical care.

TABLE 2. Reports of nonserious and serious events to Vaccine Adverse Event Reporting System for persons aged 12–17 years (N = 914) who received a Pfizer-BioNTech COVID-19 vaccine booster — United States, December 9, 2021–February 20, 2022

Reported event	No. (%) reporting
Nonserious VAERS reports	
Symptom, sign, diagnostic result, or condition (MedDRA PT*)	**837 (100.0)**
Product storage error	123 (14.7)
Dizziness	100 (11.9)
Syncope	87 (12.0)
Fever	75 (9.0)
No adverse event†	70 (8.4)
Headache	69 (8.2)
Inappropriate schedule of product administration	56 (6.7)
Fatigue	55 (6.6)
Nausea	52 (6.2)
Pain	52 (6.2)
Expired product administered	40 (4.8)
Pain in extremity	40 (4.8)
Chest pain	39 (4.7)
Underdose	39 (4.7)
Vomiting	39 (4.7)
Serious VAERS reports§,¶	
Clinical impression	**77 (100.0)**
Myocarditis	47 (61.0)
Insufficient data to make a clinical impression	10 (13.0)
Appendicitis	3 (3.9)
Acute embolic stroke	2 (2.6)
Anaphylaxis or allergic reaction	2 (2.6)
Tachycardia	2 (2.6)
Acute pancreatitis	1 (1.3)
Exacerbation of existing genetic disorder	1 (1.3)
Guillain-Barré syndrome	1 (1.3)
Immune thrombocytopenia	1 (1.3)
Injection site pain	1 (1.3)
Pericardial effusion	1 (1.3)
Rhabdomyolysis	1 (1.3)
Severe headache	1 (1.3)
Side effect of prescription medication	1 (1.3)
Spontaneous tension pneumothorax	1 (1.3)
Transverse myelitis	1 (1.3)

Abbreviations: MedDRA = Medical Dictionary for Regulatory Activities; PT = preferred term; VAERS = Vaccine Adverse Event Reporting System.

* Signs and symptoms in VAERS reports are assigned MedDRA PTs by VAERS staff members. Each VAERS report might be assigned more than one MedDRA PT, which can include normal diagnostic findings; thus, the events listed in the table might sum to more than the total number of reports. A MedDRA PT does not indicate a medically confirmed diagnosis.

† Reports of no adverse event were often accompanied by product storage error, inappropriate schedule of product administration, expired product administered, or underdose.

§ VAERS reports are classified as serious if there are any reports of hospitalization, prolongation of hospitalization, life-threatening illness, permanent disability, congenital anomaly or birth defect, or death.

¶ Serious reports to VAERS were reviewed by CDC physicians to form a clinical impression. Reports of myocarditis were identified using a combination of MedDRA PTs; in some cases, reports of myocarditis (identified by fulfilling criteria of the CDC working case definition of myocarditis) did not have the MedDRA PT "myocarditis" assigned to them. https://www.meddra.org/how-to-use/basics/hierarchy

Most (91.6%) reports to VAERS for adolescents after a Pfizer-BioNTech booster dose were nonserious and generally similar to those reported for this age group after primary series vaccination (*4*). The most common adverse events reported to VAERS in this age group were administration errors and events, including dizziness, related to syncope, a vasovagal response to vaccination that is common among adolescents after any vaccination (*8*). Most reports of administration errors mentioned that no adverse event was associated with receipt of an incorrect dose.

Among the 64 VAERS reports of myocarditis, a rare adverse event that has been associated with mRNA-based COVID-19 vaccines (*3*), after Pfizer-BioNTech booster dose vaccination among adolescents, 32 cases were confirmed at the time of this report. The reporting rate of confirmed cases of myocarditis among adolescent boys after Pfizer-BioNTech booster dose vaccination (11.4 per 1 million doses administered) was lower than for dose 2 Pfizer-BioNTech vaccination for boys aged 12–15 years (70.7 per 1 million doses administered) or 16–17 years (105.9 per 1 million doses administered) (*3*). CDC will follow up on myocarditis reports at 3–6 months after onset to assess health and functional status.

The findings in this report are subject to at least four limitations. First, v-safe is a voluntary program; therefore, data might not be representative of the vaccinated population. Second, it is possible that vaccinees who experience an adverse event could be more likely to respond to v-safe surveys. Third, as a passive surveillance system, VAERS is subject to reporting biases and underreporting, especially of nonserious events (*2*). Finally, assessment of myocarditis reports to VAERS is ongoing, and counts are subject to change.

The Advisory Committee on Immunization Practices recommends that all persons aged ≥12 years receive a booster dose of COVID-19 vaccine ≥5 months after the second dose of the mRNA vaccine primary series (*9*). Preliminary safety findings for booster doses among adolescents are generally similar to those reported after a primary series in this age group. Health care providers, parents, and adolescents should be advised that local and systemic reactions are expected among adolescents after homologous Pfizer-BioNTech booster vaccination, and that serious adverse events are rare. CDC and FDA will continue to monitor vaccine safety and will provide updates as needed to guide COVID-19 vaccination recommendations.

Summary

What is already known about this topic?

Adults aged ≥18 years reported adverse reactions less frequently after receipt of a homologous Pfizer-BioNTech COVID-19 booster dose than after the second primary dose.

What is added by this report?

Among persons aged 12–17 years, reactions after Pfizer-BioNTech booster vaccination were generally mild to moderate and transient; the frequency of local and systemic reactions reported to v-safe after a booster dose were equal to or slightly higher than after the second primary dose. Myocarditis was less frequently reported after a booster dose than a second primary dose.

What are the implications for public health practice?

Health care providers, parents, and adolescents should be advised that local and systemic reactions are expected among adolescents after a homologous Pfizer-BioNTech booster vaccination and that serious adverse events are rare.

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References

1. Food and Drug Administration. Pfizer-BioNTech COVID-19 vaccine letter of authorization. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2021. https://www.fda.gov/media/150386/download
2. Shimabukuro TT, Nguyen M, Martin D, DeStefano F. Safety monitoring in the Vaccine Adverse Event Reporting System (VAERS). Vaccine 2015;33:4398–405. PMID:26209838 https://doi.org/10.1016/j.vaccine.2015.07.035
3. Oster ME, Shay DK, Su JR, et al. Myocarditis cases reported after mRNA-based COVID-19 vaccination, United States, December 2020–August 2021. JAMA 2022;327:331–40. PMID:35076665 https://doi.org/10.1001/jama.2021.24110
4. Hause AM, Gee J, Baggs J, et al. COVID-19 vaccine safety in adolescents aged 12–17 years—United States, December 14, 2020–July 16, 2021. MMWR Morb Mortal Wkly Rep 2021;70:1053–8. PMID:34351881 https://doi.org/10.15585/mmwr.mm7031e1
5. Frenck RW Jr, Klein NP, Kitchin N, et al.; C4591001 Clinical Trial Group. Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. N Engl J Med 2021;385:239–50. PMID:34043894 https://doi.org/10.1056/NEJMoa2107456
6. Hause AM, Baggs J, Marquez P, et al. Safety monitoring of COVID-19 vaccine booster doses among adults—United States, September 22, 2021–February 6, 2022. MMWR Morb Mortal Wkly Rep 2022;71:249–54. PMID:35176008 https://doi.org/10.15585/mmwr.mm7107e1
7. Gruber WC. BNT162b2 [COMIRNATY (COVID-19 vaccine, mRNA)] booster (third) dose. Advisory Committee on Immunization Practices meeting; September 22, 2021; Atlanta, Georgia. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-09-22/02-COVID-Gruber-508.pdf
8. CDC. Syncope after vaccination—United States, January 2005–July 2007. MMWR Morb Mortal Wkly Rep 2008;57:457–60. PMID:18451756
9. CDC. 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, CDC; 2021. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

Effectiveness of COVID-19 Pfizer-BioNTech BNT162b2 mRNA Vaccination in Preventing COVID-19–Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Nonimmunocompromised Children and Adolescents Aged 5–17 Years — VISION Network, 10 States, April 2021–January 2022

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The efficacy of the BNT162b2 (Pfizer-BioNTech) vaccine against laboratory-confirmed COVID-19 exceeded 90% in clinical trials that included children and adolescents aged 5–11, 12–15, and 16–17 years (*1*–*3*). Limited real-world data on 2-dose mRNA vaccine effectiveness (VE) in persons aged 12–17 years (referred to as adolescents in this report) have also indicated high levels of protection against SARS-CoV-2 (the virus that causes COVID-19) infection and COVID-19–associated hospitalization (*4*–*6*); however, data on VE against the SARS-CoV-2 B.1.1.529 (Omicron) variant and duration of protection are limited. Pfizer-BioNTech VE data are not available for children aged 5–11 years. In partnership with CDC, the VISION Network* examined 39,217 emergency department (ED) and urgent care (UC) encounters and 1,699 hospitalizations† among persons aged 5–17 years with COVID-19–like illness across 10 states during April 9, 2021–January 29, 2022,§ to estimate VE using a case-control test-negative design. Among children aged 5–11 years, VE against laboratory-confirmed COVID-19–associated ED and UC encounters 14–67 days after dose 2 (the longest interval after dose 2 in this age group) was 46%. Among adolescents aged 12–15 and 16–17 years, VE 14–149 days after dose 2 was 83% and 76%, respectively; VE ≥150 days after dose 2 was 38% and 46%, respectively. Among adolescents aged 16–17 years, VE increased to 86% ≥7 days after dose 3 (booster dose). VE against COVID-19–associated ED and UC encounters was substantially lower during the Omicron predominant period than the B.1.617.2 (Delta) predominant period among adolescents aged 12–17 years, with no significant protection ≥150 days after dose 2 during Omicron predominance. However, in adolescents aged 16–17 years, VE during the Omicron predominant period increased to 81% ≥7 days after a third booster dose. During the full study period, including pre-Delta, Delta, and Omicron predominant periods, VE against laboratory-confirmed COVID-19–associated hospitalization among children aged 5–11 years was 74% 14–67 days after dose 2, with wide CIs that included zero. Among adolescents aged 12–15 and 16–17 years, VE 14–149 days after dose 2 was 92% and 94%, respectively; VE ≥150 days after dose 2 was 73% and 88%, respectively. All eligible children and adolescents should remain up to date with recommended COVID-19 vaccinations, including a booster dose for those aged 12–17 years.

VISION Network VE methods have been previously published (*7*). In brief, eligible medical encounters were defined as ED and UC encounters and hospitalizations among persons aged ≥5 years with a COVID-19–like illness diagnosis¶ who had received SARS-CoV-2 molecular testing (primarily by reverse transcription–polymerase

* Funded by CDC, the VISION Network includes Baylor Scott & White Health (Texas), Columbia University Irving Medical Center (New York), HealthPartners (Minnesota and Wisconsin), Intermountain Healthcare (Utah), Kaiser Permanente Northern California (California), Kaiser Permanente Northwest (Oregon and Washington), Regenstrief Institute (Indiana), and University of Colorado (Colorado).

† The data in these analyses come from 306 ED and UC clinics and 164 hospitals.

§ The study period at Baylor Scott and White Health began on September 11, 2021.

¶ Medical events with an encounter or discharge code consistent with COVID-19–like illness were included, using *International Classification of Disease, Ninth Revision* and *International Classification of Diseases, Tenth Revision* (ICD-10). Four categories of codes were considered: 1) acute respiratory illness, including COVID-19, respiratory failure, viral or bacterial pneumonia, asthma exacerbation, influenza, and viral illness not otherwise specified; 2) nonrespiratory COVID-19–like illness diagnoses including cause-unspecified gastroenteritis, thrombosis, and acute myocarditis; 3) respiratory signs and symptoms consistent with COVID-19–like illness, including hemoptysis, cough, dyspnea, painful respiration, or hypoxemia; 4) signs and symptoms of acute febrile illness. One code in any of the four categories was sufficient for inclusion. Clinician-ordered molecular assays (e.g., real-time reverse transcription–polymerase chain reaction) for SARS-CoV-2 occurring ≤14 days before to <72 hours after the encounter date were included.

chain reaction assay) during the 14 days before through 72 hours after the encounter. For adolescents aged 16–17 years, the study period began when COVID-19 vaccines were recommended and became available to persons aged ≥16 years at each study site (April–May 2021).** For children aged 5–11 years and adolescents aged 12–15 years, the study period began 5 weeks after the Pfizer-BioNTech vaccine was recommended for their age group.†† The dates when the Delta and Omicron variants became predominant (accounted for >50% of sequenced viruses) were determined for each study site based on state and national surveillance data.§§ Patients were excluded if they 1) were vaccinated before the CDC recommendation date for their age group, 2) received a third dose before booster doses were recommended for their age group, 3) received a booster dose <5 months after dose 2, 4) received 1 or >3 doses of the vaccine, or 5) if <14 days had elapsed since receipt of dose 2 or <7 days since dose 3. Patients who were likely immunocompromised based on diagnosis codes were also excluded.¶¶ VE was estimated using a case-control test-negative design comparing the odds of a positive SARS-CoV-2 test result between vaccinated (received at least 2 doses ≥14 days earlier or 3 doses ≥7 days earlier) and unvaccinated (received no doses) patients using multivariable logistic regression models*** (*7*). VE was not calculated for exposure categories with fewer than 20 encounters or with no SARS-CoV-2 test–positive cases. A statistically significant difference in VE or distributions of vaccination or infection status was indicated by nonoverlapping 95% CIs or standardized mean or proportion differences ≥0.2. All statistical analyses were conducted using R software (version 4.1.2; R Foundation). This study was reviewed and approved by the institutional review boards at participating sites or under a reliance agreement with the Westat, Inc. institutional review board.†††

Emergency Department and Urgent Care Encounters

Among 39,217 eligible encounters at 306 ED and UC facilities, 23.4%, 46.2%, and 30.3% were among persons aged 5–11, 12–15, and 16–17 years, respectively (Table 1). Most encounters among adolescents aged 12–15 years and 16–17 years occurred during the Delta predominant period (14,491 [79.9%] and 8,800 [74.0%], respectively); among children aged 5–11 years, most (6,424 [70.0%]) occurred during the Omicron predominant period, reflecting differences in the dates when vaccines became available for the respective age groups.

Among children aged 5–11 years, VE of 2 doses received 14–67 days earlier against COVID-19–associated ED and UC encounters was 46% (Table 2). Among adolescents aged 12–15 and 16–17 years, VE of 2 doses 14–149 days earlier against COVID-19–associated ED and UC encounters was 83% and 76%, respectively; VE was significantly lower for 2 doses received ≥150 days earlier (38% and 46%, respectively). Among adolescents aged 16–17 years, VE after receipt of a third dose ≥7 days earlier increased to 86%, significantly higher than the VE of 2 doses received ≥150 days earlier. The number of observations was insufficient to estimate 3-dose VE for adolescents aged 12–15 years. Compared with the Delta predominant period, estimated 2-dose VE for adolescents aged 12–15 and 16–17 years declined significantly once Omicron became the predominant variant: among adolescents aged 16–17 years, VE of 2 doses received ≥150 days earlier against COVID-19–associated ED and UC encounters declined from 77% during Delta predominance to a null VE (–3%) during Omicron predominance; however, effectiveness of a third dose received ≥7 days earlier against COVID-19–associated ED and UC encounters during Omicron predominance was 81%. Among children aged 5–11 years, VE of 2 doses received 14–67 days earlier against COVID-19–associated ED and UC encounters during Omicron predominance was 51%.

** The Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the Pfizer-BioNTech vaccine for persons aged ≥16 years on December 11, 2020 (https://www.fda.gov/news-events/press-announcements/fda-takes-key-action-fight-against-covid-19-issuing-emergency-use-authorization-first-covid-19), and CDC recommended the Pfizer-BioNTech vaccine on December 12, 2020 (https://www.cdc.gov/media/releases/2020/s1213-covid-vaccine.html). CDC recommended a booster dose for adolescents aged 16–17 years on December 9, 2021 (https://www.cdc.gov/media/releases/2021/s1208-16-17-booster.html).

†† FDA amended the EUA for the Pfizer-BioNTech vaccine to include adolescents aged 12–15 years on May 10, 2021 (https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-pfizer-biontech-covid-19-vaccine-emergency-use), and CDC recommended the Pfizer-BioNTech vaccine in this age group on May 12, 2021 (https://www.cdc.gov/media/releases/2021/s0512-advisory-committee-signing.html). FDA authorized the EUA for the Pfizer-BioNTech vaccine for children aged 5–11 years on October 29, 2021 (https://www.fda.gov/news-events/press-announcements/fda-authorizes-pfizer-biontech-covid-19-vaccine-emergency-use-children-5-through-11-years-age), and CDC recommended the Pfizer-BioNTech vaccine for this age group on November 2, 2021 (https://www.cdc.gov/media/releases/2021/s1102-PediatricCOVID-19Vaccine.html). On January 5, 2022, CDC expanded its recommendation for a booster 5 months after receipt of the second dose of the Pfizer-BioNTech vaccine to include adolescents aged 12–15 years (https://www.cdc.gov/media/releases/2022/s0105-Booster-Shot.html).

§§ Estimated date of Delta and Omicron predominance at contributing sites: California (Delta: June 23, 2021; Omicron: December 21, 2021); Colorado (Delta: June 3, 2021; Omicron: December 19, 2021); Indiana (Delta: June 23, 2021; Omicron: December 26, 2021); Minnesota and Wisconsin (Delta: June 28, 2021; Omicron: December 25, 2021); New York (Delta: June 30, 2021; Omicron: December 18, 2021); Oregon and Washington (Delta: June 30, 2021; Omicron: December 24, 2021); Texas (Delta: July 3, 2021; Omicron: December 16, 2021); Utah (Delta: June 1, 2021; Omicron December 24, 2021). Pre-Delta refers to the period before Delta predominance.

¶¶ Immunocompromised status was defined using ICD-9 and ICD-10 as the presence of discharge codes for solid malignancy, hematologic malignancy, rheumatologic or inflammatory disorder, other intrinsic immune condition or immunodeficiency, or organ or stem cell transplant.

*** With a test-negative design, vaccine performance is assessed by comparing the odds of antecedent vaccination among case-patients with acute laboratory-confirmed COVID-19 and control-patients without acute COVID-19. This odds ratio was adjusted for age, geographic region, calendar time (days from January 1), and local virus circulation in the community and weighted for inverse propensity to be vaccinated or unvaccinated.

††† 45 C.F.R. part 46; 21 C.F.R. part 56.

TABLE 1. Characteristics of emergency department and urgent care encounters among children aged 5–17 years with COVID-19–like illness,* by COVID-19 Pfizer-BioNTech vaccination status† and SARS-CoV-2 test result — 10 states,§ April 2021–January 2022

Characteristic	Total no. (column %)	No. (row %) Pfizer-BioNTech vaccination status				SMD¶	No. (row %)	SMD¶
		Unvaccinated	2 doses (14–149 days earlier)	2 doses (≥150 days earlier)	3 doses (≥7 days earlier)		Positive SARS-CoV-2 test result	
All ED and UC encounters	**39,217**	**28,084 (71.6)**	**7,821 (19.9)**	**3,238 (8.3)**	**74 (0.2)**	—	**9,252 (23.6)**	—
Variant predominance period**								
Pre-Delta	955 (2.4)	851 (89.1)	104 (10.9)	0 (—)	0 (—)	0.84	113 (11.8)	0.81
B.1.617.2 (Delta)	26,048 (66.4)	17,596 (67.6)	6,496 (24.9)	1,954 (7.5)	2 (0.0)		3,655 (14.0)	
B.1.1.529 (Omicron)	12,214 (31.1)	9,637 (78.9)	1,221 (10.0)	1,284 (10.5)	72 (0.6)		5,484 (44.9)	
Site								
Baylor Scott & White Health	4,408 (11.2)	3,932 (89.2)	313 (7.1)	163 (3.7)	0 (—)	0.83	1,653 (37.5)	0.48
Columbia University	1,564 (3.9)	1,260 (80.6)	226 (14.5)	77 (4.9)	1 (0.1)		510 (32.6)	
HealthPartners	2,089 (5.3)	988 (47.3)	844 (40.4)	257 (12.3)	0 (—)		231 (11.1)	
Intermountain Healthcare	12,993 (33.1)	8,314 (64.0)	3,274 (25.2)	1,372 (10.6)	33 (0.3)		2,002 (15.4)	
Kaiser Permanente Northern California	2,287 (5.8)	1,134 (49.6)	795 (34.8)	339 (14.8)	19 (0.8)		578 (25.3)	
Kaiser Permanente Northwest	1,508 (3.8)	841 (55.8)	447 (29.6)	212 (14.1)	8 (0.5)		354 (23.5)	
Regenstrief Institute	7,374 (18.8)	6,008 (81.5)	972 (13.2)	384 (5.2)	10 (0.1)		2,391 (32.4)	
University of Colorado	6,994 (17.8)	5,607 (80.2)	950 (13.6)	434 (6.2)	3 (0.0)		1,533 (21.9)	
Age group, yrs								
5–11	9,181 (23.4)	8,599 (93.7)	582 (6.3)	0 (—)	0 (—)	1.07	2,776 (30.2)	0.20
12–15	18,138 (46.2)	12,064 (66.5)	4,547 (25.1)	1,517 (8.4)	10 (0.1)		3,873 (21.4)	
16–17	11,898 (30.3)	7,421 (62.4)	2,692 (22.6)	1,721 (14.5)	64 (0.5)		2,603 (21.9)	
Sex								
Male††	18,907 (48.2)	13,658 (72.2)	3,713 (19.6)	1,505 (8.0)	31 (0.2)	0.07	4,369 (23.1)	0.03
Female	20,310 (51.7)	14,426 (71.0)	4,108 (20.2)	1,733 (8.5)	43 (0.2)		4,883 (24.0)	
Race/Ethnicity								
Hispanic	9,316 (23.7)	7,069 (75.9)	1,662 (17.8)	571 (6.1)	14 (0.2)	0.36	2,458 (26.4)	0.29
White, non-Hispanic	20,177 (51.4)	13,934 (69.1)	4,295 (21.3)	1,913 (9.5)	35 (0.2)		3,888 (19.3)	
Black, non-Hispanic	4,106 (10.4)	3,405 (82.9)	503 (12.3)	195 (4.7)	3 (0.1)		1,504 (36.6)	
Other, non-Hispanic§§	2,987 (7.6)	1,876 (62.8)	779 (26.1)	318 (10.6)	14 (0.5)		718 (24.0)	
Unknown	2,631 (6.7)	1,800 (68.4)	582 (22.1)	241 (9.2)	8 (0.3)		684 (26.0)	
Chronic respiratory condition¶¶								
Yes††	3,183 (8.1)	2,160 (67.9)	728 (22.9)	284 (8.9)	11 (0.3)	0.11	456 (14.3)	0.17
No	36,034 (91.8)	25,924 (71.9)	7,093 (19.7)	2,954 (8.2)	63 (0.2)		8,796 (24.4)	
Chronic nonrespiratory condition***								
Yes††	1,815 (4.6)	1,260 (69.4)	372 (20.5)	178 (9.8)	5 (0.3)	0.05	379 (20.9)	0.03
No	37,402 (95.3)	26,824 (71.7)	7,449 (19.9)	3,060 (8.2)	69 (0.2)		8,873 (23.7)	

Abbreviations: ED = emergency department; ICD-9 = *International Classification of Diseases, Ninth Revision;* ICD-10 = *International Classification of Diseases, Tenth Revision;* SMD = standardized mean or proportion difference; UC = urgent care.

* Medical events with an encounter or discharge code consistent with COVID-19–like illness were included, using ICD-9 and ICD-10. Four categories of codes were considered: 1) acute respiratory illness, including COVID-19, respiratory failure, viral or bacterial pneumonia, asthma exacerbation, influenza, and viral illness not otherwise specified; 2) nonrespiratory COVID-19–like illness diagnoses including cause-unspecified gastroenteritis, thrombosis, and acute myocarditis; 3) respiratory signs and symptoms consistent with COVID-19–like illness, including hemoptysis, cough, dyspnea, painful respiration, or hypoxemia; and 4) signs and symptoms of acute febrile illness. One code in any of the four categories was sufficient for inclusion. Clinician-ordered molecular assays (e.g., real-time reverse transcription–polymerase chain reaction) for SARS-CoV-2 occurring ≤14 days before to <72 hours after the encounter date were included.

† Vaccination was defined as having received the listed number of doses of COVID-19 Pfizer-BioNTech BNT162b2 vaccine ≥14 days (for 2 doses) or ≥7 days (for 3 doses) before the medical event index date, which was the date of respiratory specimen collection associated with the most recent positive or negative SARS-CoV-2 test result before medical event or the admission date if testing only occurred after the admission.

§ Partners contributing data on medical events were in California (vaccine availability: April 30, 2021), Colorado (May 22, 2021), Indiana (April 27, 2021), Minnesota and Wisconsin (April 21, 2021), New York (April 27, 2021), Oregon and Washington (April 28, 2021), Texas (March 29, 2021), Utah (April 9, 2021). The study period began in September 2021 for partners located in Texas. For adolescents aged 16–17 years, the study period began when COVID-19 vaccines became available to all persons aged ≥16 years at each study site. For children aged 5–11 and persons aged 12–15 years, the study period began 5 weeks after the Pfizer-BioNTech vaccine was authorized for each age group (November 2, 2021, and May 12, 2021, respectively).

¶ An absolute SMD ≥0.20 indicates a nonnegligible difference in variable distributions between medical events for vaccinated versus unvaccinated patients; single SMD calculated by averaging pairwise comparisons of each vaccinated category versus unvaccinated and separately for patients with SARS-CoV-2–positive versus SARS-CoV-2–negative test results. For example, the age SMD calculation comparing unvaccinated versus different vaccinated categories was generated by averaging the pairwise SMD calculations for unvaccinated and 2 doses (14–149 days earlier), unvaccinated and 2 doses (≥150 days earlier), and unvaccinated and 3 doses (≥7 days earlier). In addition, the age SMD calculation comparing negative SARS-CoV-2 test result and positive SARS-CoV-2 test result was generated by directly calculating the SMD for negative SARS-CoV-2 test result and positive SARS-CoV-2 test result.

** Estimated date of Delta and Omicron predominance at contributing sites: California (Delta: June 23, 2021; Omicron: December 21, 2021); Colorado (Delta: June 3, 2021; Omicron: December 19, 2021); Indiana (Delta: June 23, 2021; Omicron: December 26, 2021); Minnesota and Wisconsin (Delta: June 28, 2021; Omicron: December 25, 2021); New York (Delta: June 30, 2021; Omicron: December 18, 2021); Oregon and Washington (Delta: June 30, 2021; Omicron: December 24, 2021); Texas (Delta: July 3, 2021; Omicron: December 16, 2021); Utah (Delta: June 1, 2021; Omicron December 24, 2021). Pre-Delta refers to the period before Delta predominance.

†† Indicates the reference group used for standardized mean or proportion difference calculations for dichotomous variables.

§§ Other race includes Asian, Native Hawaiian or other Pacific islander, American Indian or Alaska Native, Other not listed, and multiple races.

¶¶ Chronic respiratory condition was defined as the presence of discharge code for asthma, sleep apnea, or other lung disease using ICD-9 and ICD-10 diagnosis codes.

*** Chronic nonrespiratory condition was defined as the presence of discharge code for heart failure, ischemic heart disease, hypertension, other heart disease, stroke, other cerebrovascular disease, diabetes type I or II, other diabetes, metabolic disease, clinical obesity, clinically underweight, renal disease, liver disease, blood disorder, immunosuppression, organ transplant, cancer, neurologic disorder, musculoskeletal disorder, Down Syndrome, congenital heart disease, neurologic conditions, muscular dystrophy, sickle cell disease, prematurity (<24 weeks), developmental delay, technology dependence, or chronic gastrointestinal disease/irritable bowel syndrome.

TABLE 2. COVID-19 Pfizer-BioNTech vaccine effectiveness* against laboratory-confirmed COVID-19–associated† emergency department and urgent care clinic encounters and hospitalizations among children aged 5–17 years, by number and timing of vaccine doses§ and predominant circulating SARS-CoV-2 variant — VISION Network, 10 states,¶ April 2021 to January 2022

Encounter type/Vaccination status	Total	SARS-CoV-2 test-positive, no. (%)	VE %* (95% CI)
ED or UC encounters during Delta or Omicron predominance, by age group			
5–11 yrs			
Unvaccinated (Ref)	8,599	2,652 (30.8)	—
2 doses (14–67 days earlier)	582	124 (21.3)	46 (24–61)
12–15 yrs			
Unvaccinated (Ref)	12,064	3,238 (26.8)	—
2 doses (14–149 days earlier)	4,547	254 (5.6)	83 (80–85)
2 doses (≥150 days earlier)	1,517	378 (24.9)	38 (28–48)
3 doses (≥7 days earlier)	10	3 (30)	NC
16–17 yrs			
Unvaccinated (Ref)	7,421	2,068 (27.9)	—
2 doses (14–149 days earlier)	2,692	193 (7.2)	76 (71–80)
2 doses (≥150 days earlier)	1,721	329 (19.1)	46 (36–54)
3 doses (≥7 days earlier)	64	13 (20.3)	86 (73–93)
ED or UC encounters, by age group and predominant variant			
5–11 yrs**			
Omicron predominant††			
Unvaccinated (Ref)	5,938	2,409 (40.6)	—
2 doses (14–67 days earlier)	486	118 (24.3)	51 (30–65)
12–15 yrs			
Delta predominant††			
Unvaccinated (Ref)	9,633	1,978 (20.5)	—
2 doses (14–149 days earlier)	4,060	80 (2.0)	92 (89–94)
2 doses (≥150 days earlier)	798	32 (4.0)	79 (68–86)
Omicron predominant††			
Unvaccinated (Ref)	2,336	1,254 (53.7)	—
2 doses (14–149 days earlier)	472	174 (36.9)	45 (30–57)
2 doses (≥150 days earlier)	719	346 (48.1)	−2 (−25–17)
3 doses (≥7 days earlier)	10	3 (30.0)	NC
16–17 yrs			
Delta predominant††			
Unvaccinated (Ref)	5,302	1,191 (22.5)	—
2 doses (14–149 days earlier)	2,340	78 (3.3)	85 (81–89)
2 doses (≥150 days earlier)	1,156	47 (4.1)	77 (67–84)
3 doses (≥7 days earlier)	2	0 (—)	NC
Omicron predominant††			
Unvaccinated (Ref)	1,363	771 (56.6)	—
2 doses (14–149 days earlier)	263	114 (43.4)	34 (8–53)
2 doses (≥150 days earlier)	565	282 (49.9)	−3 (−30–18)
3 doses (≥7 days earlier)	62	13 (21.0)	81 (59–91)
Hospitalizations during Delta or Omicron predominance, by age group			
5–11 yrs			
Unvaccinated (Ref)	262	59 (22.5)	—
2 doses (14–67 days earlier)	23	2 (8.7)	74 (−35–95)
12–15 yrs			
Unvaccinated (Ref)	496	149 (30)	—
2 doses (14–149 days earlier)	182	7 (3.8)	92 (79–97)
2 doses (≥150 days earlier)	63	13 (20.6)	73 (43–88)
16–17 yrs			
Unvaccinated (Ref)	437	136 (31.1)	—
2 doses (14–149 days earlier)	150	7 (4.7)	94 (87–97)
2 doses (≥150 days earlier)	82	14 (17.1)	88 (72–95)
3 doses (≥7 days earlier)	4	1 (25.0)	NC

TABLE 2. (*Continued*) COVID-19 Pfizer-BioNTech vaccine effectiveness* against laboratory-confirmed COVID-19–associated† emergency department and urgent care clinic encounters and hospitalizations among children aged 5–17 years, by number and timing of vaccine doses§ and predominant circulating SARS-CoV-2 variant — VISION Network, 10 states,¶ April 2021 to January 2022

Abbreviations: ED = emergency department; NC = not calculated; Ref = referent group; UC = urgent care; 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. Generalized boosted regression trees were used to estimate the propensity to be vaccinated based on sociodemographic characteristics, underlying medical conditions, and facility characteristics.

† Medical events with an encounter or discharge code consistent with COVID-19–like illness were included, using *International Classification of Disease, Ninth Revision* and *International Classification of Diseases, Tenth Revision*. Four categories of codes were considered: 1) acute respiratory illness, including COVID-19, respiratory failure, viral or bacterial pneumonia, asthma exacerbation, influenza, and viral illness not otherwise specified; 2) nonrespiratory COVID-19–like illness diagnoses including cause-unspecified gastroenteritis, thrombosis, and acute myocarditis; 3) respiratory signs and symptoms consistent with COVID-19–like illness, including hemoptysis, cough, dyspnea, painful respiration, or hypoxemia; and 4) signs and symptoms of acute febrile illness. One code in any of the four categories was sufficient for inclusion. Clinician-ordered molecular assays (e.g., real-time reverse transcription–polymerase chain reaction) for SARS-CoV-2 occurring ≤14 days before to <72 hours after the encounter date were included.

§ Vaccination was defined as having received the listed number of doses of an mRNA-based COVID-19 Pfizer-BioNTech vaccine ≥14 days (for 2 doses) or ≥7 days (for 3 doses) before the medical event index date, which was the date of respiratory specimen collection associated with the most recent positive or negative SARS-CoV-2 test result before medical event or the admission date if testing only occurred after the admission.

¶ Partners contributing data on medical events were in California (vaccine availability: April 30, 2021), Colorado (May 22, 2021), Indiana (April 27, 2021), Minnesota and Wisconsin (April 21, 2021), New York (April 27, 2021), Oregon and Washington (April 28, 2021), Texas (March 29, 2021), Utah (April 9, 2021). The study period began in September 2021 for partners located in Texas. For adolescents aged 16–17 years, the study period began when COVID-19 vaccines became available to all those aged ≥16 years at each study site. For children aged 5–11 and persons aged 12–15 years, the study period began 5 weeks after the Pfizer-BioNTech vaccine was authorized for each age group (November 2, 2021, and May 12, 2021, respectively).

** VE during the period of Delta predominance was not calculated for children aged 5–11 years because of the short eligibility interval in this age group during that time.

†† Estimated date of Delta and Omicron predominance at contributing sites: California (Delta: June 23, 2021; Omicron: December 21, 2021); Colorado (Delta: June 3, 2021; Omicron: December 19, 2021); Indiana (Delta: June 23, 2021; Omicron: December 26, 2021); Minnesota and Wisconsin (Delta: June 28, 2021; Omicron: December 25, 2021); New York (Delta: June 30, 2021; Omicron: December 18, 2021); Oregon and Washington (Delta: June 30, 2021; Omicron: December 24, 2021); Texas (Delta: July 3, 2021; Omicron: December 16, 2021); Utah (Delta: June 1, 2021; Omicron December 24, 2021).

Hospitalizations

Among 1,699 eligible hospitalizations at 164 hospitals, 16.8%, 43.6%, and 39.6% were among children and adolescents aged 5–11, 12–15 and 16–17 years, respectively (Table 3). Most hospitalizations of adolescents aged 12–15 years (613 [82.7%]) and 16–17 years (476 [70.7%]) occurred during Delta predominance, whereas two thirds of hospitalizations

TABLE 3. Characteristics of hospitalizations among children aged 5–17 years with COVID-19–like illness* by COVID-19 Pfizer-BioNTech vaccination status† and SARS-CoV-2 test result — 10 states,§ April 2021 to January 2022

Characteristic	Total, no. (column %)	No. (row %) Pfizer-BioNTech vaccination status: Unvaccinated	2 doses (14–149 days earlier)	2 doses (≥150 days earlier)	3 doses (≥7 days earlier)	SMD¶	No. (row %) Positive SARS-CoV-2 test result	SMD¶
All hospitalizations	**1,699**	**1,195 (70.3)**	**355 (20.9)**	**145 (8.5)**	**4 (0.2)**	–	**388 (22.8)**	–
Variant predominance period**								
Pre-Delta	110 (6.4)	91 (82.7)	19 (17.3)	0 (—)	0 (—)	1.11	13 (11.8)	0.46
B.1.617.2 (Delta)	1,184 (69.6)	812 (68.6)	288 (24.3)	84 (7.1)	0 (—)		224 (18.9)	
B.1.1.529 (Omicron)	405 (23.8)	292 (72.1)	48 (11.9)	61 (15.1)	4 (1.0)		151 (37.3)	
Site								
Baylor Scott & White Health	189 (11.1)	167 (88.4)	14 (7.4)	7 (3.7)	1 (0.5)	1.4	42 (22.2)	0.49
Columbia University	162 (9.5)	118 (72.8)	35 (21.6)	9 (5.6)	0 (—)		19 (11.7)	
HealthPartners	40 (2.3)	22 (55.0)	13 (32.5)	5 (12.5)	0 (—)		3 (7.5)	
Intermountain Healthcare	403 (23.7)	261 (64.8)	97 (24.1)	45 (11.2)	0 (—)		113 (28.0)	
Kaiser Permanente Northern California	265 (15.5)	115 (43.4)	105 (39.6)	42 (15.8)	3 (1.1)		31 (11.7)	
Kaiser Permanente Northwest	57 (3.3)	32 (56.1)	21 (36.8)	4 (7.0)	0 (—)		9 (15.8)	
Regenstrief Institute	371 (21.8)	315 (84.9)	37 (10.0)	19 (5.1)	0 (—)		121 (32.6)	
University of Colorado	212 (12.4)	165 (77.8)	33 (15.6)	14 (6.6)	0 (—)		50 (23.6)	
Age group, yrs								
5–11	285 (16.8)	262 (91.9)	23 (8.1)	0 (—)	0 (—)	1.03	61 (21.4)	0.04
12–15	741 (43.6)	496 (66.9)	182 (24.6)	63 (8.5)	0 (—)		169 (22.8)	
16–17	673 (39.6)	437 (64.9)	150 (22.3)	82 (12.2)	4 (0.6)		158 (23.5)	
Sex								
Male††	805 (47.3)	570 (70.8)	171 (21.2)	61 (7.6)	3 (0.4)	0.24	161 (20.0)	0.15
Female	894 (52.6)	625 (69.9)	184 (20.6)	84 (9.4)	1 (0.1)		227 (25.4)	
Race/Ethnicity								
Hispanic	454 (26.7)	326 (71.8)	100 (22.0)	28 (6.2)	0 (—)	0.53	93 (20.5)	0.13
White, non-Hispanic	733 (43.1)	493 (67.3)	159 (21.7)	79 (10.8)	2 (0.3)		186 (25.4)	
Black, non-Hispanic	242 (14.2)	193 (79.8)	31 (12.8)	17 (7.0)	1 (0.4)		50 (20.7)	
Other, non-Hispanic§§	207 (12.1)	131 (63.3)	58 (28.0)	17 (8.2)	1 (0.5)		45 (21.7)	
Unknown	63 (3.7)	52 (82.5)	7 (11.1)	4 (6.3)	0 (—)		14 (22.2)	
Chronic respiratory condition¶¶								
Yes††	1,090 (64.1)	756 (69.4)	249 (22.8)	82 (7.5)	3 (0.3)	0.18	150 (13.8)	0.70
No	609 (35.8)	439 (72.1)	106 (17.4)	63 (10.3)	1 (0.2)		238 (39.1)	
Chronic nonrespiratory condition***								
Yes††	930 (54.7)	647 (69.6)	202 (21.7)	78 (8.4)	3 (0.3)	0.17	207 (22.3)	0.04
No	769 (45.2)	548 (71.3)	153 (19.9)	67 (8.7)	1 (0.1)		181 (23.5)	

Abbreviations: ICD-9 = *International Classification of Diseases, Ninth Revision;* ICD-10 = *International Classification of Diseases, Tenth Revision;* SMD = standardized mean or proportion difference.

* Medical events with an encounter or discharge code consistent with COVID-19–like illness were included, using ICD-9 and ICD-10. Four categories of codes were considered: 1) acute respiratory illness, including COVID-19, respiratory failure, viral or bacterial pneumonia, asthma exacerbation, influenza, and viral illness not otherwise specified; 2) nonrespiratory COVID-19–like illness diagnoses including cause-unspecified gastroenteritis, thrombosis, and acute myocarditis; 3) respiratory signs and symptoms consistent with COVID-19–like illness, including hemoptysis, cough, dyspnea, painful respiration, or hypoxemia; and 4) signs and symptoms of acute febrile illness. One code in any of the four categories was sufficient for inclusion. Clinician-ordered molecular assays (e.g., real-time reverse transcription–polymerase chain reaction) for SARS-CoV-2 occurring ≤14 days before to <72 hours after the encounter date were included.

† Vaccination was defined as having received the listed number of doses of COVID-19 Pfizer-BioNTech vaccine ≥14 days (for 2 doses) or ≥7 days (for 3 doses) before the medical event index date, which was the date of respiratory specimen collection associated with the most recent positive or negative SARS-CoV-2 test result before medical event or the admission date if testing only occurred after the admission.

§ Partners contributing data on medical events were in California (vaccine availability: April 30, 2021), Colorado (May 22, 2021), Indiana (April 27, 2021), Minnesota and Wisconsin (April 21, 2021), New York (April 27, 2021), Oregon and Washington (April 28, 2021), Texas (March 29, 2021), Utah (April 9, 2021). The study period began in September 2021 for partners located in Texas. For adolescents aged 16–17 years, the study period began when COVID-19 vaccines became available to all those aged ≥16 years at each study site. For children aged 5–11 and persons aged 12–15 years, the study period began 5 weeks after the Pfizer-BioNTech vaccine was authorized for each age group (November 2, 2021, and May 12, 2021, respectively).

¶ An absolute SMD ≥0.20 indicates a nonnegligible difference in variable distributions between medical events for vaccinated versus unvaccinated patients; single SMD calculated by averaging pair-wise comparisons of each vaccinated category versus unvaccinated and separately for patients with SARS-CoV-2–positive versus SARS-CoV-2–negative test results. For example, the age SMD calculation comparing unvaccinated versus different vaccinated categories was generated by averaging the pairwise SMD calculations for unvaccinated and 2 doses (14–149 days earlier), unvaccinated and 2 doses (≥150 days earlier), and unvaccinated and 3 doses (≥7 days). In addition, the age SMD calculation comparing negative SARS-CoV-2 test result and positive SARS-CoV-2 test result was generated by directly calculating the SMD for negative SARS-CoV-2 test result and positive SARS-CoV-2 test result.

** Estimated date of Delta and Omicron predominance at contributing sites: California (Delta: June 23, 2021; Omicron: December 21, 2021); Colorado (Delta: June 3, 2021; Omicron: December 19, 2021); Indiana (Delta: June 23, 2021; Omicron: December 26, 2021); Minnesota and Wisconsin (Delta: June 28, 2021; Omicron: December 25, 2021); New York (Delta: June 30, 2021; Omicron: December 18, 2021); Oregon and Washington (Delta: June 30, 2021; Omicron: December 24, 2021); Texas (Delta: July 3, 2021; Omicron: December 16, 2021); Utah (Delta: June 1, 2021; Omicron December 24, 2021). Pre-Delta refers to the period before Delta predominance.

†† Indicates the reference group used for SMD calculations for dichotomous variables.

§§ Other race includes Asian, Native Hawaiian or other Pacific islander, American Indian or Alaska Native, Other not listed, and multiple races.

¶¶ Chronic respiratory condition was defined as the presence of discharge code for asthma, sleep apnea, or other lung disease using ICD-9 and ICD-10 diagnosis codes.

*** Chronic nonrespiratory condition was defined as the presence of discharge code for heart failure, ischemic heart disease, hypertension, other heart disease, stroke, other cerebrovascular disease, diabetes type I or II, other diabetes, metabolic disease, clinical obesity, clinically underweight, renal disease, liver disease, blood disorder, immunosuppression, organ transplant, cancer, neurologic disorder, musculoskeletal disorder, Down Syndrome, congenital heart disease, neurologic conditions, muscular dystrophy, sickle cell disease, prematurity (<24 weeks), developmental delay, technology dependence, or chronic gastrointestinal disease/irritable bowel syndrome.

Summary

What is already known about this topic?

Two doses of Pfizer-BioNTech vaccine provided protection against COVID-19 in persons aged 12–17 years during Delta predominance, but data during Omicron predominance and among children aged 5–11 years are lacking.

What is added by this report?

Two doses protect against COVID-19–associated emergency department and urgent care encounters among children and adolescents. However, vaccine effectiveness (VE) was lower during Omicron predominance and decreased with time since vaccination; a booster dose restored VE to 81% among adolescents aged 16–17 years. Overall, 2-dose VE against COVID-19–associated hospitalization was 73%–94%.

What are the implications for public health practice?

All eligible children and adolescents should remain up to date with recommended COVID-19 vaccinations, including a booster dose for those aged 12–17 years.

among children aged 5–11 years (190 [66.7%]) occurred during Omicron predominance.

Among children aged 5–11 years, estimated VE of 2 vaccine doses received 14–67 days earlier against COVID-19–associated hospitalization was 74%, with wide confidence intervals that included zero (95% CI = –35% to 95%) (Table 2). Among adolescents aged 12–15 and 16–17 years, VE of 2 doses received 14–149 days earlier was 92% and 94%, respectively, and VE of 2 doses received ≥150 days earlier was 73% and 88%, respectively. Differences by time since vaccination were not statistically significant.

Discussion

In a multistate analysis of 39,217 ED and UC encounters with COVID-19–like illness among nonimmunocompromised patients aged 5–17 years through January 29, 2022, estimates of Pfizer-BioNTech VE against COVID-19–associated ED and UC encounters varied by time since vaccination and by predominant circulating SARS-CoV-2 variant. Among adolescents aged 12–17 years during the full study period including pre-Delta, Delta, and Omicron predominant periods, 2-dose VE estimates were higher (76%–83%) 14–149 days after receipt of a second dose, and significantly lower (38%–46%) at ≥150 days postvaccination. However, a third vaccine dose restored VE against COVID-19–associated ED or UC encounters to 86% among adolescents aged 16–17 years. Among children aged 5–11 years during the full study period, VE of 2 doses (14–67 days earlier) against COVID-19–associated ED or UC encounters was 46%, which was significantly lower than overall estimates for adolescents aged 12–17 years. However, most encounters among children aged 5–11 years occurred during Omicron predominance, when VE significantly declined for adolescents aged 12–17 years. During Omicron predominance, VE of a second dose received 14–149 days earlier was 45% and 34% for adolescents aged 12–15 and 16–17 years, respectively, suggesting that the lower VE observed among children aged 5–11 years was likely driven by the predominant variant rather than differences in VE across age groups. During Omicron predominance, there was no evidence of protection for adolescents aged 12–17 years from 2 doses received ≥150 days earlier; however, a third vaccine restored VE to 81% among adolescents aged 16–17 years.

Receipt of 2 Pfizer-BioNTech vaccine doses in persons aged 12–17 years provided a high level of protection (>90%) against COVID-19–associated hospitalizations within 149 days of receipt of the second dose. VE point estimates for second dose received ≥150 days earlier were 73% to 88%; however, differences by time since vaccination were not statistically significant. Additional data are needed to better understand duration of protection against COVID-19–associated hospitalization in adolescents aged 12–17 years, the protection from 3 doses, and the level of protection among children aged 5–11 years.

These findings are consistent with previously published data showing high effectiveness of the Pfizer-BioNTech vaccine among adolescents before Omicron became the predominant variant (*4*–*6*), and with data from adults demonstrating relatively higher protection against more severe outcomes (*7*). These findings are also consistent with data showing a decline in mRNA VE over time since receipt of the second dose among adolescents and adults (*8*–*10*). The findings in this report also align with studies among adults that report lower VEs during Omicron variant predominance (*9*,*10*) and an increase in VE after receipt of a third vaccine dose (*9*,*10*).

The findings in this report are subject to at least six limitations. First, comparison of VE estimates between age groups should be made with caution because of differences in the timing of vaccine availability and predominant variants when the vaccine became available to different age groups. Second, statistical power for estimating VE against COVID-19–associated hospitalizations was limited, resulting in wide CIs for some groups, particularly children aged 5–11 years. Third, among adolescents aged 16–17, the estimated 3-dose VE was based on a relatively short period after vaccination. Fourth, despite adjustments to balance the differences between unvaccinated and vaccinated persons, unmeasured and residual confounding (e.g., mask use and physical distancing) might have biased the estimates. Fifth, genetic characterization of patients' viruses was not available, and Delta and Omicron predominance periods were based on surveillance data. Finally, although the facilities in this study serve heterogeneous populations in 10 states, the findings might not be generalizable to the U.S. population.

This report provides real-world evidence of protection by the Pfizer-BioNTech vaccine against COVID-19–associated ED and UC encounters and hospitalizations among children and adolescents aged 5–17 years and supports the role of third (booster) doses in maintaining high levels of VE in the setting of Omicron predominance. All eligible children and adolescents should remain up to date with recommended COVID-19 vaccinations, including a booster dose for those aged 12–17 years.[§§§]

[§§§] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/children-teens.html (Accessed January 11, 2022).

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References

1. Walter EB, Talaat KR, Sabharwal C, et al.; C4591007 Clinical Trial Group. Evaluation of the BNT162b2 Covid-19 vaccine in children 5 to 11 years of age. N Engl J Med 2022;386:35–46. PMID:34752019 https://doi.org/10.1056/NEJMoa2116298
2. Frenck RW Jr, Klein NP, Kitchin N, et al.; C4591001 Clinical Trial Group. Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. N Engl J Med 2021;385:239–50. PMID:34043894 https://doi.org/10.1056/NEJMoa2107456
3. Polack FP, Thomas SJ, Kitchin N, et al.; C4591001 Clinical Trial Group. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020;383:2603–15. PMID:33301246 https://doi.org/10.1056/NEJMoa2034577
4. Reis BY, Barda N, Leshchinsky M, et al. Effectiveness of BNT162b2 vaccine against Delta variant in adolescents. N Engl J Med 2021;385:2101–3. PMID:34670036 https://doi.org/10.1056/NEJMc2114290
5. Olson SM, Newhams MM, Halasa NB, et al.; Overcoming Covid-19 Investigators. Effectiveness of BNT162b2 vaccine against critical Covid-19 in adolescents. N Engl J Med 2022;386:713–23. PMID:35021004 https://doi.org/10.1056/NEJMoa2117995
6. Lutrick K, Rivers P, Yoo YM, et al. Interim estimate of vaccine effectiveness of BNT162b2 (Pfizer-BioNTech) vaccine in preventing SARS-CoV-2 infection among adolescents aged 12–17 years—Arizona, July–December 2021. MMWR Morb Mortal Wkly Rep 2021;70:1761–5. PMID:34968373 https://doi.org/10.15585/mmwr.mm705152a2
7. 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
8. Britton A, Fleming-Dutra KE, Shang N, et al. Association of COVID-19 vaccination with symptomatic SARS-CoV-2 infection by time since vaccination and Delta variant predominance. JAMA 2022. Epub February 14, 2022. PMID:35157002 https://doi.org/10.1001/jama.2022.2068
9. Thompson MG, Natarajan K, Irving SA, et al. Effectiveness of a third dose 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;71:139–45. PMID:35085224 https://doi.org/10.15585/mmwr.mm7104e3
10. Accorsi EK, Britton A, Fleming-Dutra KE, et al. Association between 3 doses of mRNA COVID-19 vaccine and symptomatic infection caused by the SARS-CoV-2 Omicron and Delta variants. JAMA 2022;327:639–51. PMID:35060999 https://doi.org/10.1001/jama.2022.0470

Notes from the Field

First Reports of Locally Transmitted Seoul Hantavirus Infection — District of Columbia, May 2018–December 2018

Nivedita Ravi-Caldwell, DVM[1]; Preetha Iyengar, MD[1]; John Davies-Cole, PhD[1]

In May 2018, patient A, a previously healthy man aged 30 years, was evaluated at a District of Columbia (DC) health care facility for a 4-day history of chills, diarrhea, fever (103°F [39.5°C]), headache, sore throat, and vomiting. Despite symptomatic treatment with antipyretics, he subsequently experienced hemoconcentration (hematocrit = 60.4% [normal = 38.8%–50%]), thrombocytopenia (<10,000 platelets/μL [normal = 150,000–450,000]), and acute kidney injury (blood urea nitrogen [BUN] = 95 mg/dL [normal = 9–20] and creatinine = 4.95 mg/dL [normal = 0.66–1.50]) over several days (*1*). Approximately 1 week later, he experienced signs consistent with hemophagocytic lymphohistiocytosis, a potentially fatal systemic inflammatory syndrome, including elevated ferritin, triglycerides, and interleukin-2 levels, and hemophagocytosis cells on bone marrow biopsy (*2*). Patient A was a maintenance worker with frequent rodent sightings at his workplace. Serology results were positive for hantavirus immunoglobulin (Ig) M and IgG. Additional tests sent to CDC returned with hantavirus IgG and IgM titers >1:6,400, confirming recent infection with Seoul hantavirus (SEOV). Virus isolation was unsuccessful (*1*). Comprehensive testing for other infectious etiologies returned negative results. The patient responded to supportive treatment and was eventually discharged.

Five months later, in November 2018, patient B, a man aged 37 years with history of chronic kidney disease, was evaluated in a DC emergency department with a 3-day history of chills, fever (104°F [40.1°C]), headache, myalgia, and productive cough, followed later by diarrhea, nausea, and vomiting. On further evaluation, he had elevated hepatic transaminases (aspartate aminotransferase = 164 units/L [normal = 3–34], alanine aminotransferase = 78 units/L [normal = 15–41]), thrombocytopenia (43,000/μL), and acute kidney injury (BUN = 36 mg/dL and creatinine = 7.6 mg/dL) during his admission. The patient worked as a dishwasher and plumber's assistant, had no recent history of travel outside the United States, and did not own any pets. He was unaware of exposure to rodents at work, at home, or during his commute. Serology sent to rule out hemorrhagic fever-renal syndrome returned with IgG and IgM titers of >1:6,400, confirming recent infection with SEOV. Comprehensive testing for other infectious etiologies returned negative results. The patient responded to supportive treatment and was eventually discharged.

SEOV is a type of hantavirus previously associated with hemorrhagic fever-renal syndrome.* Patient A is believed to have had the first case of hemophagocytic lymphohistiocytosis related to hantavirus infection reported in the United States and the second worldwide (*1*,*3*). Past studies have documented that Norway rats serve as the reservoir species for SEOV in the United States (*1*,*4*), and previous cases of hantavirus infection have been linked to wild or pet rodents (*4*,*5*). Humans can become infected with SEOV through aerosol exposure to virus shed in rodent feces, saliva, or urine. Rodent overpopulation in DC is well documented by increased complaints via the Citywide Call Center to the Rodent Control Program, and the DC Department of Health has amplified efforts to address this public health threat.† Although extremely rare, the two SEOV cases presented in this report highlight the importance of physicians including hantavirus infection in their differential diagnoses in patients with compatible symptoms and history of animal exposure or travel and underscore the importance of reporting notifiable infectious disease cases to health departments for investigation and response. These cases also serve as a reminder to the public to minimize risk for infection by following recommended hygiene practices.§

* https://www.cdc.gov/hantavirus/hfrs/index.html (Accessed June 21, 2019).
† https://www.washingtonpost.com/graphics/2018/local/rat-calls/
§ https://www.cdc.gov/hantavirus/outbreaks/seoul-virus/cleaning-up-pet-rodents.html

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References

1. Shastri B, Kofman A, Hennenfent A, et al. Domestically acquired Seoul virus causing hemophagocytic lymphohistiocytosis—Washington, DC, 2018. Open Forum Infect Dis 2019;6:ofz404. PMID:31660366 https://doi.org/10.1093/ofid/ofz404
2. Rouphael NG, Talati NJ, Vaughan C, Cunningham K, Moreira R, Gould C. Infections associated with haemophagocytic syndrome. Lancet Infect Dis 2007;7:814–22. PMID:18045564 https://doi.org/10.1016/S1473-3099(07)70290-6
3. Lee J-J, Chung I-J, Shin D-H, et al. Hemorrhagic fever with renal syndrome presenting with hemophagocytic lymphohistiocytosis. Emerg Infect Dis 2002;8:209–10. PMID:11897077 https://doi.org/10.3201/eid0802.010299
4. Easterbrook JD, Kaplan JB, Vanasco NB, et al. A survey of zoonotic pathogens carried by Norway rats in Baltimore, Maryland, USA. Epidemiol Infect 2007;135:1192–9. PMID:17224086 https://doi.org/10.1017/S0950268806007746
5. Knust B, Brown S, de St Maurice A, et al. Multistate Seoul Virus Outbreak Investigation Team. Seoul virus infection and spread in United States home-based ratteries: rat and human testing results from a multistate outbreak investigation. J Infect Dis 2020;222:1311–9. PMID:32484879 https://doi.org/10.1093/infdis/jiaa307

Notes from the Field

Readiness for Use of Type 2 Novel Oral Poliovirus Vaccine in Response to a Type 2 Circulating Vaccine-Derived Poliovirus Outbreak — Tajikistan, 2020–2021

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On January 13, 2021, a vaccine-derived poliovirus type 2 (VDPV2) was identified by the Regional Reference Laboratory for Polio in Moscow, Russia* in a specimen from a patient with acute flaccid paralysis (AFP) in Jaloliddin Balkhi district, Khatlon Region, in Tajikistan. Paralysis onset occurred on November 22, 2020. On February 6, 2021, a second, genetically linked VDPV2 paralytic case, with onset of paralysis on January 17, 2021, was confirmed from Khatlon Region in the neighboring Vakhsh district, indicating local transmission. Genetic sequencing of the isolate by the Regional Reference Laboratory for Polio in Moscow found a 20-nucleotide divergence from Sabin vaccine virus strain, and a 14-nucleotide divergence from a circulating VDPV2 (cVDPV2) reported from Khikorgangi, Pakistan on December 7, 2020, which suggests undetected circulation for approximately 12 months (*1*). On the basis of high-quality AFP surveillance in Tajikistan, the researchers concluded these cases likely represent recent importation (*2*). During 2014, the Director-General of the World Health Organization (WHO) declared polio a Public Health Emergency of International Concern under the International Health Regulations; the isolation of any poliovirus requires immediate reporting and prompt response (*3*).

Children born after the global cessation of use of type 2–containing oral poliovirus vaccine (OPV) from routine immunization schedules in April 2016 have no mucosal immunity against type 2 polioviruses. Therefore, cVDPV2 outbreak immunization responses require the use of type 2–containing OPVs; however, in low-coverage settings, use of type 2 oral poliovirus vaccine increases the risk for seeding† of new cVDPV2 emergences (*1*,*4*). Current type 2–containing poliovirus vaccines are Sabin strain monovalent type 2 oral poliovirus vaccine (mOPV2) and trivalent oral poliovirus vaccine (tOPV); tOPV is preferred where cocirculation of wild poliovirus 1 and cVDPV2 occurs. To mitigate new seeding events, WHO granted Emergency Use Listing status for a recently developed, genetically stabilized, novel OPV type 2 (nOPV2) during November 2020. The Tajik Ministry of Health and Social Protection of the Population (MoHSPP), in consultation with partners, conducted a rigorous risk assessment and determined that nOPV2 was the best vaccine outbreak response option that also served to protect the polio-free status of the WHO European Region. MoHSPP completed and documented the 25 Emergency Use Listing readiness criteria for the initial use phase§ for vaccine release in 8 weeks, which was then authorized by the WHO Director-General, making Tajikistan the first country outside the WHO African Region to use nOPV2 (*5*). MoHSPP incorporated nOPV2 into three rounds of outbreak response, including supplementary immunization activities (SIAs) (Figure). The targeted age group for rounds 1 and 2 was children aged 0–65 months and for round 3 was children aged 0–55 months.

A total of 31 cVDPV2 cases were confirmed during November 22, 2020–June 26, 2021, with none occurring after the second SIA; virus was also isolated from close contacts of AFP cases, community-based stool collection surveys, and environmental samples.¶ The geographic spread of cVDPV2 included 10 districts within Khatlon Region, and in a broad central belt including Dushanbe, the capital. The first Outbreak Response Assessment was conducted during August 16–20, 2021, and an additional nOPV2 SIA was recommended at the end of August 2021 to ensure that transmission had been interrupted. Despite the challenges related to responding to a cVDPV2 outbreak during the COVID-19 pandemic, MoHSPP imported and distributed nOPV2, trained staff members, and conducted high-quality outbreak response activities (assessed via lot quality assurance

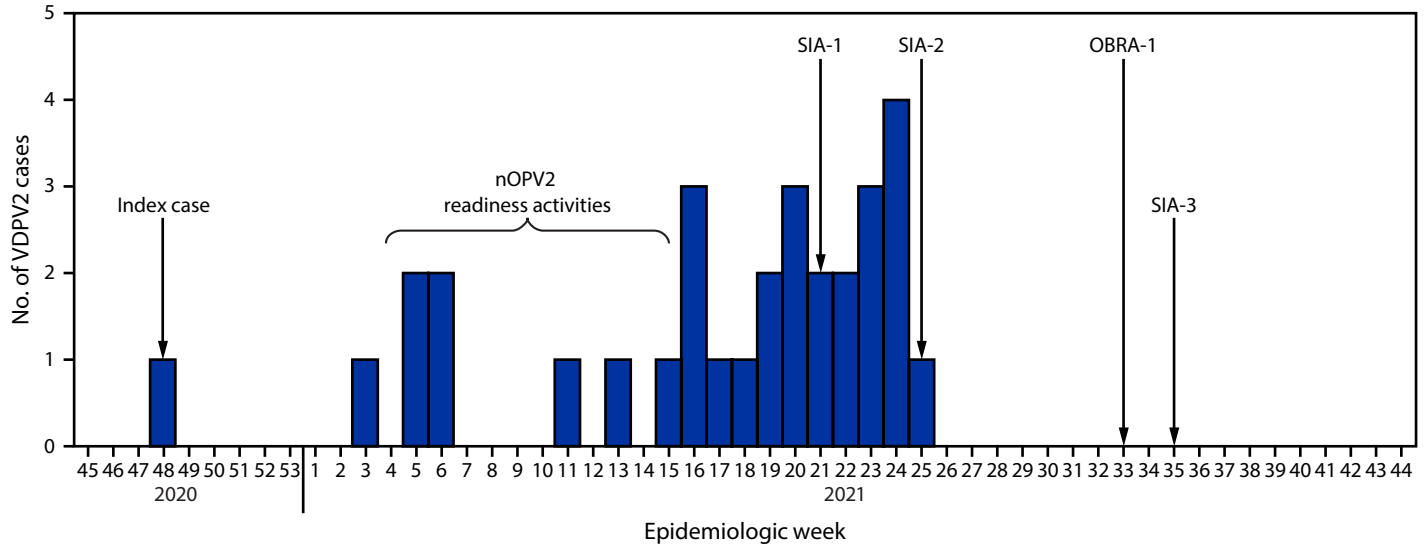
* Tajikistan does not have a national polio laboratory; therefore, specimens are transported to the Regional Reference Laboratory for Polio in Moscow, Russia for testing on a regular basis. During the COVID-19 pandemic, regularly scheduled flights to and from Tajikistan were interrupted, and this affected the transportation of specimens.

† Oral poliovirus vaccines are live attenuated virus vaccines and provide intestinal immunity; poliovirus replicates in the intestinal tract. The vaccine virus is excreted in stool and can spread from person to person. However, in communities with low immunization coverage, vaccine virus can circulate during an extended period leading to reversion to neurovirulence, which can result in paralysis identical to that caused by wild polioviruses. https://www.cdc.gov/vaccines/vpd/polio/hcp/vaccine-derived-poliovirus-faq.html

§ The 25 nOPV2 readiness criteria are in nine categories: 1) coordination; 2) nOPV2 approvals; 3) cold chain logistics and vaccine management; 4) AFP surveillance; 5) environmental surveillance; 6) safety monitoring; 7) advocacy, communication, and social mobilization; 8) laboratory; and 9) campaign operations. https://polioeradication.org/wp-content/uploads/2020/12/nOPV2-Readiness-Verification-and-Dose-Release-Process-20201208.pdf

¶ As part of the nOPV2 readiness criteria, an environmental (sewage) collection point was identified in Dushanbe. The first specimen was collected the week of February 7, 2021 (epidemiologic week 6). Testing of specimens was supported by the Regional Reference Laboratories for Polio in Islamabad, Pakistan and Bilthoven, Netherlands. Data are current as of August 13, 2021.

FIGURE. Circulating vaccine-derived poliovirus type 2 cases, novel oral poliovirus vaccine type 2 readiness activities, and outbreak supplementary immunization activities — Tajikistan, 2020–2021*,†



Abbreviations: nOPV2 = novel oral poliovirus vaccine type 2; OBRA-1 = first outbreak response assessment; SIA = supplementary immunization activity; SIA-1 = first SIA; SIA-2 = second SIA; SIA-3 = third SIA; VDPV2 = vaccine-derived poliovirus type 2.
* Date of onset of paralysis for the index case: November 22, 2020; nOPV2 readiness activities: February 10–April 11, 2021; first nOPV2 SIA: May 31–June 6, 2021; second nOPV2 SIA: June 29–July 3, 2021; third nOPV2 SIA: August 30–September 4, 2021; OBRA-1: August 16–20, 2021.
† National Expanded Program on Immunization data from weekly acute flaccid paralysis surveillance, Tajikistan, 2020–2021.

sampling**). These efforts by MoHSPP resulted in administrative coverage of >99%, following mop-ups, in all three rounds, in this first use of nOPV2 outside the WHO Africa Region.

** Assessing vaccination coverage levels using clustered lot quality assurance sampling. https://polioeradication.org/wp-content/uploads/2016/09/Assessing-Vaccination-Coverage-Levels-Using-Clustered-LQAS_Apr2012_EN.pdf

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

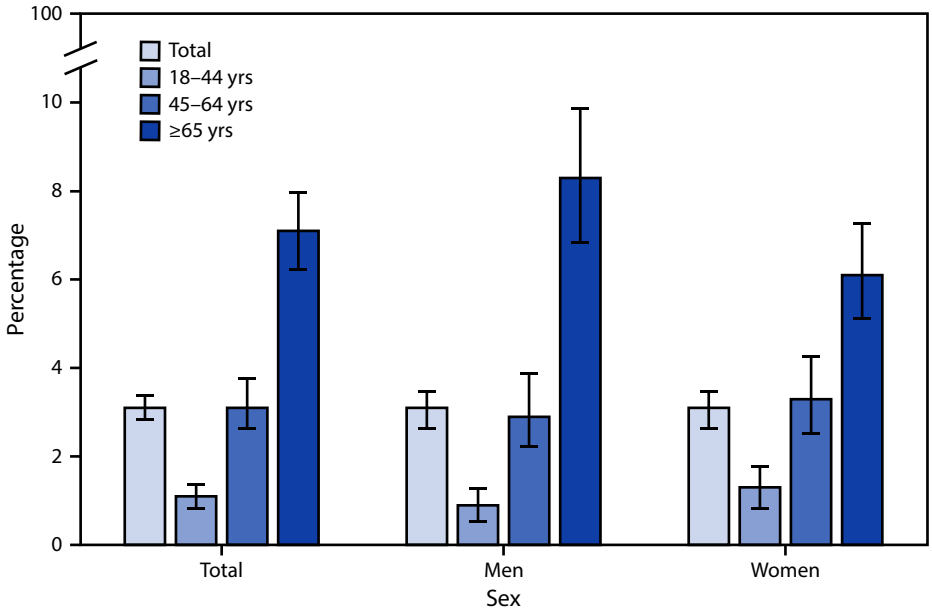
References

1. Alleman MM, Jorba J, Greene SA, et al. Update on vaccine-derived poliovirus outbreaks—worldwide, July 2019–February 2020. MMWR Morb Mortal Wkly Rep 2020;69:489–95. PMID:32324719 https://doi.org/10.15585/mmwr.mm6916a1
2. Global Polio Eradication Initiative. Reporting and classification of vaccine-derived polioviruses: GPEI guidelines. Geneva, Switzerland: Global Polio Eradication Initiative; 2015. https://polioeradication.org/wp-content/uploads/2016/07/VDPV_ReportingClassification.pdf
3. World Health Organization. Statement of the twenty-seventh polio IHR emergency committee. Geneva, Switzerland: World Health Organization; 2021. https://www.who.int/news/item/19-02-2021-statement-of-the-twenty-seventh-polio-ihr-emergency-committee
4. 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
5. Global Polio Eradication Initiative. GPEI strategy for the response to cVDPV2 2020–2021. Geneva, Switzerland: Global Polio Eradication Initiative; 2020. https://polioeradication.org/wp-content/uploads/2022/01/GPEI_cVDPV2-nOPV2_Factsheet_13-Jan-2022-EN.pdf

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage* of Adults Aged ≥18 Years with Kidney Disease,† by Age Group and Sex — National Health Interview Survey,§ United States, July–December 2020



* With 95% CIs indicated by error bars.
† Based on an affirmative response to the survey question, "Have you ever been told by a doctor or other health professional that you had weak or failing kidneys?" Because data are self-reported and not based on clinical diagnosis, prevalence estimates might differ from other published sources of kidney disease data.
§ Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population.

During July–December 2020, 3.1% of adults aged ≥18 years had kidney disease. The prevalence of kidney disease increased with age, from 1.1% among adults aged 18–44 years to 3.1% among those aged 45–64 years and to 7.1% among those aged ≥65 years. Among adults aged ≥65 years, a higher percentage of men had kidney disease (8.3%) compared with women (6.1%). No significant differences were observed by sex for adults aged 18–44 years (0.9% for men versus 1.3% for women) and those aged 45–64 years (2.9% for men versus 3.3% for women).

Source: National Center for Health Statistics, National Health Interview Survey, 2020. https://www.cdc.gov/nchs/nhis.htm

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

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