Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 71 / No. 48
December 2, 2022

HIV Services and Outcomes During the COVID-19 Pandemic — United States, 2019–2021

Karen W. Hoover, MD[1]; Weiming Zhu, MD, PhD[1]; Zanetta C. Gant, PhD[1]; Kevin P. Delaney, PhD[1]; Jeffrey Wiener, PhD[1]; Neal Carnes, PhD[1]; Dominique Thomas, MPA[1]; John Weiser, MD[1]; Ya-Lin A. Huang, PhD[1]; Laura W. Cheever, MD[2]; Athena P. Kourtis, MD, PhD[1]

Increasing HIV testing, preexposure prophylaxis (PrEP), and antiretroviral therapy (ART) are pillars of the federal Ending the HIV Epidemic in the U.S. (EHE) initiative, with a goal of decreasing new HIV infections by 90% by 2030.* In response to the COVID-19 pandemic, a national emergency was declared in the United States on March 13, 2020, resulting in the closure of nonessential businesses and most nonemergency health care venues; stay-at-home orders also limited movement within communities (*1*). As unemployment increased during the pandemic (*2*), many persons lost employer-sponsored health insurance (*3*). HIV testing and PrEP prescriptions declined early in the COVID-19 pandemic (*4*–*6*); however, the full impact of the pandemic on use of HIV prevention and care services and HIV outcomes is not known. To assess changes in these measures during 2019–2021, quarterly data from two large U.S. commercial laboratories, the IQVIA Real World Data — Longitudinal Prescription Database (IQVIA),† and the National HIV Surveillance System (NHSS)§ were analyzed. During quarter 1 (Q1)¶ 2020, a total of 2,471,614 HIV tests were performed, 190,955 persons were prescribed PrEP, and 8,438 persons received a diagnosis of HIV infection. Decreases were observed during quarter 2 (Q2), with 1,682,578 HIV tests performed (32% decrease), 179,280 persons prescribed PrEP (6% decrease), and 6,228 persons receiving an HIV diagnosis (26% decrease). Partial rebounds were observed during quarter 3 (Q3), with 2,325,554 HIV tests performed, 184,320 persons prescribed PrEP, and 7,905 persons receiving an HIV diagnosis. The proportion of persons linked to HIV care, the number who were prescribed ART, and proportion with a suppressed viral load test (<200 copies of HIV RNA per mL) among those tested were stable during the study period. During public health emergencies, delivery of HIV services outside of traditional clinical settings or that use nonclinical delivery models are needed to facilitate access to HIV testing, ART, and PrEP, as well as to support adherence to ART and PrEP medications.

* https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview
† https://www.iqvia.com/locations/belgium/library/fact-sheets/real-world-longitudinal-prescription-data
§ The study period for analyses using NHSS data was January 2019–December 2020.
¶ Quarters were defined as Q1 (January 1–March 31), Q2 (April 1–June 30), Q3 (July 1–September 30), and Q4 (October 1–December 31).

INSIDE

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

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

Data from four data sources were used to estimate HIV service use and outcomes by quarter: 1) LabCorp, 2) Quest Diagnostics, 3) IQVIA, and 4) NHSS. Combined LabCorp and Quest Diagnostics laboratory data were analyzed to estimate the number of HIV tests performed during 2019–2021; Current Procedural Terminology codes were used to identify HIV antigen and antibody test results and HIV RNA test results. Laboratory data were also used to estimate the number of HIV viral load tests performed and the proportion of those tests indicating viral load suppression. IQVIA data on antiretroviral drugs dispensed by U.S. retail pharmacies and mail-order pharmacies during 2019–2021 were analyzed using a validated algorithm to estimate the number of persons prescribed PrEP or ART (*7*). Laboratory and IQVIA data were analyzed to assess the change from each quarter to the following quarter in the number of HIV tests and persons prescribed PrEP during 2019–2021, stratified by age group (15–24, 25–34, and ≥35 years). NHSS data from 2019–2020 were analyzed to identify the number of persons who received a diagnosis of HIV infection and the proportion of those persons linked to care within 1 month of diagnosis** as well as to assess the quarterly change in the number of persons who received an HIV diagnosis during 2019–2020, by age group, race and ethnicity, and transmission category. Incomplete race and ethnicity data and no transmission data were available in either the laboratory or IQVIA data; in addition, the number of persons who received an HIV diagnosis and the percentage linked to care were not available for 2021. Poisson regression models were used to assess trends in service use and outcomes by calculating the estimated quarterly percent change (EQPC) during 2019–2021 and 95% CIs; these models were also used to assess whether changes in the number of HIV tests and number of persons prescribed PrEP from Q1 to Q2 during 2020 differed significantly among age groups. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.††

The number of HIV tests and number of persons prescribed PrEP decreased early in the COVID-19 pandemic but started to rebound by mid-2020. During 2020, the number of HIV tests decreased 32% from Q1 (2,471,614) to Q2 (1,682,578) but increased in Q3 to 2,325,554 (2019–2021 EQPC = 0.33%) (Table 1). Similarly, during 2020, the number of persons prescribed PrEP decreased 6% from Q1 (190,955) to Q2 (179,280) but increased to 184,320 in Q3 (2019–2021 EQPC = 3.45%). Following a similar pattern, during 2020, HIV diagnoses decreased 6% from Q1 (8,438) to Q2 (6,228) but increased to 7,905 in Q3 (2019–2020 EQPC = –3.99%).

** Data included in this study are from 46 jurisdictions (45 states and the District of Columbia) that had complete laboratory reporting for all data years. Linkage to care was defined as having one or more CD4 or viral load tests within 1 month of HIV diagnosis.

†† 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.

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

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

TABLE 1. HIV testing, preexposure prophylaxis, HIV diagnoses, linkage to HIV care, antiretroviral therapy, and viral suppression, by quarter* — United States, 2019–2021

HIV service or outcome	No. or % (% change from previous quarter)												2019–2021 EQPC, % (95% CI)
	2019				2020				2021				
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	
No. of HIV tests†,§	2,101,633 (—)	2,523,317 (20.1)	2,572,963 (2.0)	2,451,303 (−4.7)	2,471,614 (0.8)	1,682,578 (−31.9)	2,325,554 (38.2)	2,274,593 (−2.2)	2,346,191 (3.1)	2,646,562 (12.8)	2,643,539 (−0.1)	2,453,114 (−7.2)	0.33 (0.31 to 0.34)
No. of persons prescribed PrEP¶	159,434 (—)	168,543 (5.7)	176,180 (4.5)	181,016 (2.7)	190,955 (5.5)	179,280 (−6.1)	184,320 (2.8)	187,478 (1.7)	193,587 (3.3)	215,715 (11.4)	236,323 (9.6)	243,515 (3.0)	3.45 (3.41 to 3.49)
No. of persons with diagnosed HIV infection**,††	9,488 (—)	9,431 (−0.6)	9,164 (−2.8)	8,392 (−8.4)	8,438 (0.5)	6,228 (−26.2)	7,905 (26.9)	7,758 (−1.9)	NA	NA	NA	NA	−3.99 (−4.31 to −3.67)§§
% of persons linked to care**,††,¶¶	88.0 (—)	87.9 (−0.1)	88.4 (0.6)	88.5 (0.1)	87.8 (−0.8)	89.2 (1.6)	89.4 (0.2)	89.3 (−0.1)	NA	NA	NA	NA	0.24 (−0.12 to 0.60)§§
No. of viral load tests†	225,149 (—)	270,189 (20.0)	269,265 (−0.3)	261,143 (−3.0)	259,026 (−0.8)	206,586 (−20.2)	252,643 (22.3)	250,823 (−0.7)	259,659 (3.5)	273,282 (5.2)	265,562 (−2.8)	254,675 (−4.1)	0.45 (0.42 to 0.48)
% with suppressed viral load†,***	86.7 (—)	87.2 (0.6)	87.3 (0.1)	87.8 (0.6)	87.3 (−0.6)	88.9 (1.8)	88.9 (0)	88.9 (0)	89.0 (0.1)	88.9 (−0.1)	88.8 (−0.1)	89.4 (0.7)	0.26 (0.23 to 0.30)
No. of persons prescribed ART¶	586,169 (—)	591,874 (1.0)	600,396 (1.4)	603,634 (0.5)	615,339 (1.9)	613,100 (−0.4)	600,336 (−2.1)	596,251 (−0.7)	604,627 (1.4)	605,727 (0.2)	609,394 (0.6)	611,884 (0.4)	0.24 (0.22 to 0.26)

Abbreviations: ART = antiretroviral therapy; EQPC = estimated quarter percentage change; PrEP = preexposure prophylaxis; Q1 = quarter 1; Q2 = quarter 2; Q3 = quarter 3; Q4 = quarter 4.

* Quarters were defined as Q1 (January 1–March 31), Q2 (April 1–June 30), Q3 (July 1–September 30), and Q4 (October 1–December 31).

† Commercial laboratory testing data from LabCorp and Quest Diagnostics, 2019–2021.

§ HIV antigen/antibody testing data were missing for January 2019 from LabCorp; therefore, the total number of HIV tests in Q1 2019 is underreported. The EQPC for HIV testing was calculated for Q2 2019 through Q4 2019.

¶ IQVIA Real-World Data — Longitudinal Prescription Database, 2019–2021.

** National HIV Surveillance System, 2019–2020.

†† Data included in this study are from 46 jurisdictions (45 states and the District of Columbia) that had complete laboratory reporting for all data years. Linkage to care was defined as having one or more CD4 or viral load tests within 1 month of the HIV diagnosis. Data include 53 and 17 cases with missing month of HIV diagnosis for 2019 and 2020, respectively.

§§ EQPC calculated for 2019–2020. The number of persons who received an HIV diagnosis and the percentage linked to care were not available for 2021.

¶¶ Data include 48 and 17 cases with missing month of HIV diagnosis for 2019 and 2020, respectively.

*** Suppressed viral load calculation is for persons who had a viral load test result.

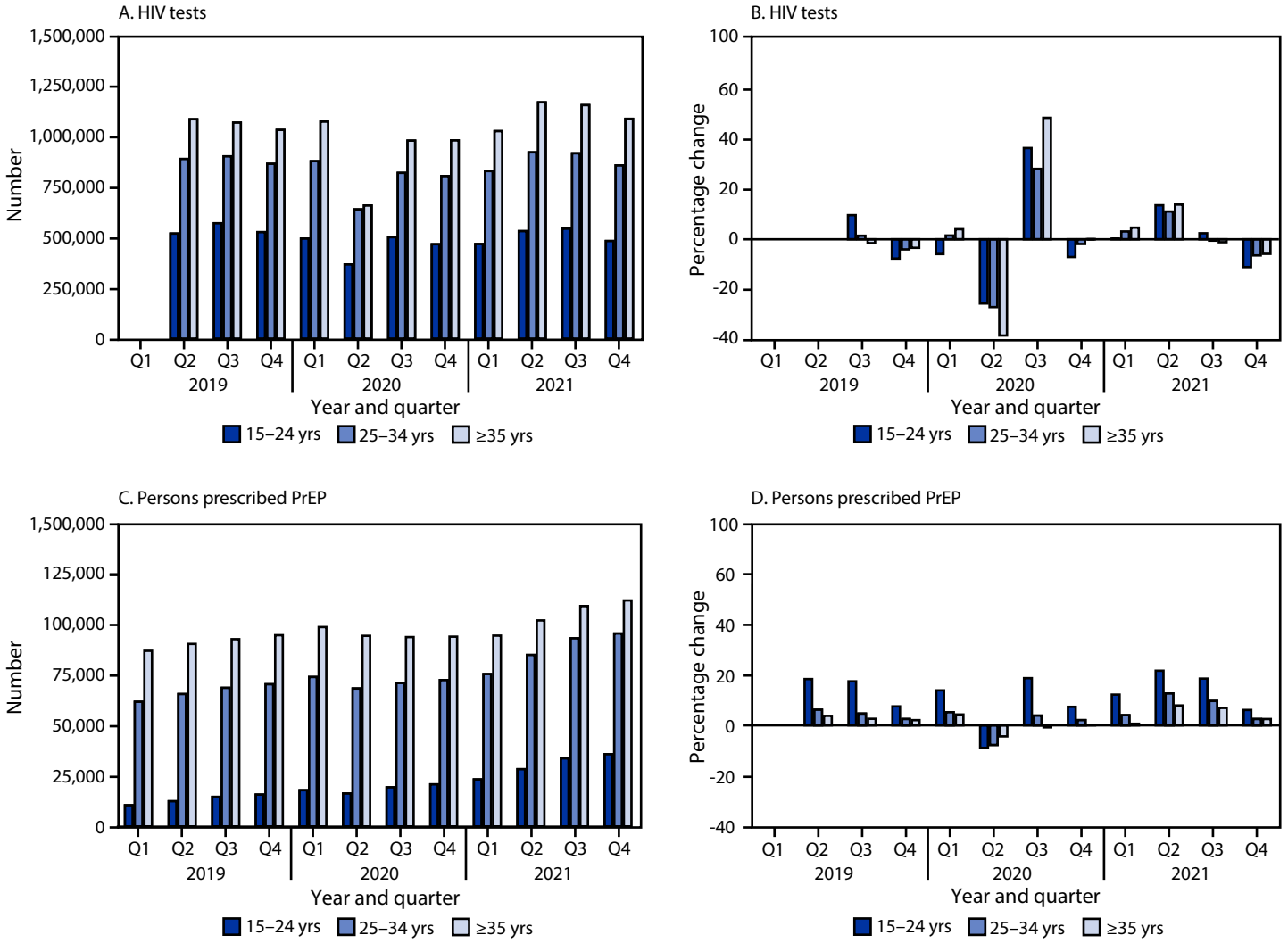
The proportion of persons linked to HIV care, the number who were prescribed ART, and the proportion with a suppressed viral load test result among those tested was stable during the study period. Among persons who received a diagnosis of HIV infection, the percentage who were linked to care did not vary during 2019–2020, ranging from 88.0% to 89.4% (2019–2020 EQPC = 0.24%). During 2020, viral load tests performed decreased 20% from Q1 (259,026) to Q2 (206,586) but increased to 252,643 in Q3 (2019–2021 EQPC = 0.45%). The number of persons prescribed ART did not vary (2019–2021 EQPC = 0.24%). Similarly, the proportion of tests indicating viral load suppression did not vary and ranged from 86.7% to 89.0% (2019–2021 EQPC = 0.26%).

During 2020, among all age groups, persons aged ≥35 years experienced the largest quarter-to-quarter decrease in number of HIV tests from Q1 (1,076,548) to Q2 (660,593), representing a 39% decline (Figure). During the same period, persons aged 15–24 years experienced the largest quarter-to-quarter decrease in receipt of PrEP prescriptions (from 17,909 to 16,316, a 9% decrease). Among all racial and ethnic groups and HIV transmission categories, the number of persons who received a diagnosis of HIV infection in 2020 decreased from Q1 to Q2 (range = −21.1 [White] to −29.4 [Other] and −25.7 [male-to-male sexual contact and heterosexual contact, females] to −29.0 [heterosexual contact, males]) and then partially rebounded in Q3 (Table 2).

Discussion

Compared with the performance of the U.S. HIV prevention and care service system before the COVID-19 pandemic, the system performed as well as it did during the first 2 years of the pandemic when access to services decreased as a result of shutdowns and loss of employer-sponsored health insurance (*1–3*). HIV testing and PrEP prescriptions were disrupted during Q2 2020 but rebounded during Q3 after which PrEP prescriptions followed prepandemic trends, increasing each

FIGURE. Change in the number of HIV tests (A),* percentage change in number of HIV tests from quarter to quarter (B),† change in the number of persons prescribed preexposure prophylaxis (C),§ and percentage change in the number of persons prescribed preexposure prophylaxis from quarter to quarter (D),¶ by age group — United States 2019–2021



Abbreviations: PrEP = preexposure prophylaxis; Q1 = quarter 1; Q2 = quarter 2; Q3 = quarter 3; Q4 = quarter 4.

* Commercial laboratory HIV antigen/antibody testing data from LabCorp and Quest Diagnostics, 2019–2021. Because data were incomplete for January 2019, the Q1–Q2 change was not calculated.

† The percentage change in the number of HIV tests from Q1 2020 to Q2 2020 was larger among persons aged ≥35 years (−38.6%; 95% CI = −38.8 to −38.4) compared with persons aged 15–24 years (−25.7%; 95% CI = −26.0 to −25.4) and 25–34 years (−27.2%; 95% CI = −27.4 to −27.0).

§ IQVIA Real-World Data — Longitudinal Prescription Database, 2019–2021.

¶ The percentage change in the number of persons prescribed PrEP from Q1 2020 to Q2 2020 was larger among persons aged 15–24 years (−8.9%; 95% CI = −10.8 to −6.9) compared with persons aged 25–34 years (−7.8%; 95% CI = −8.7 to −6.8) and ≥35 years (−4.4%; 95% CI = −5.2 to −3.5).

quarter through 2021. The decrease in HIV diagnoses might be attributable to decreases in HIV testing as well as decreases in transmission during the pandemic. Despite the decline in HIV diagnoses, similar proportions of persons receiving a diagnosis were linked to care compared with prepandemic proportions. Although viral load tests decreased in Q2 2020, ART prescriptions remained stable, suggesting that prescriptions were provided without recommended viral load testing.[§§] This is consistent with guidelines recommending providers and their patients to weigh the risks and benefits of in-person care, including visits for laboratory testing, during periods of high COVID-19 community transmission.[¶¶]

Interventions to increase HIV testing and PrEP use outside of clinical settings were being implemented in the United States before and during the COVID-19 pandemic and can be expanded during future public health emergencies or other

[§§] https://clinicalinfo.hiv.gov/en/guidelines

[¶¶] https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/guidelines-covid-19-hiv.pdf

TABLE 2. Number of persons diagnosed with HIV infection, by age, race and ethnicity, and transmission category by quarter* — National HIV Surveillance System, United States, 2019–2020

Characteristic	No. of HIV diagnoses (% change from previous quarter)								2019–2020 EQPC (95% CI)
	2019				2020				
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	
Age group, yrs									
13–24	2,062	1,964	1,916	1,682	1,702	1,279	1,570	1,526	−5.17
	(—)	(−4.8)	(−2.4)	(−12.2)	(1.2)	(−24.9)	(22.8)	(−2.8)	(−5.86 to −4.47)
25–34	3,322	3,398	3,320	3,018	3,076	2,314	2,969	2,894	−3.13
	(—)	(2.3)	(−2.3)	(−9.1)	(1.9)	(−24.8)	(28.3)	(−2.5)	(−3.66 to −2.59)
≥35	4,104	4,069	3,928	3,692	3,660	2,635	3,366	3,338	−4.15
	(—)	(−0.9)	(−3.5)	(−6.0)	(−0.9)	(−28.0)	(27.7)	(−0.8)	(−4.63 to −3.66)
Race and ethnicity									
Black or African American	4,036	3,956	3,875	3,584	3,577	2,588	3,353	3,300	−3.98
	(—)	(−2.0)	(−2.0)	(−7.5)	(−0.2)	(−27.6)	(29.6)	(−1.6)	(−4.47 to −3.49)
Hispanic or Latino†	2,539	2,524	2,516	2,292	2,276	1,640	2,043	2,035	−4.48
	(—)	(−0.6)	(−0.3)	(−8.9)	(−0.7)	(−27.9)	(24.6)	(−0.4)	(−5.09 to −3.86)
White	2,385	2,399	2,246	2,025	2,108	1,663	2,042	2,012	−3.37
	(—)	(0.6)	(−6.4)	(−9.8)	(4.1)	(−21.1)	(22.8)	(−1.5)	(−4.00 to −2.73)
Other§	528	552	527	491	477	337	467	411	−4.50
	(—)	(4.5)	(−4.5)	(−6.8)	(−2.9)	(−29.4)	(38.6)	(−12.0)	(−5.82 to −3.16)
Transmission category¶									
Heterosexual contact, female	1,424	1,526	1,425	1,347	1,300	966	1,182	1,087	−5.00
	(—)	(7.2)	(−6.6)	(−5.5)	(−3.5)	(−25.7)	(22.4)	(−8.0)	(−5.80 to −4.19)
Heterosexual contact, male	720	682	653	614	600	426	511	475	−6.46
	(—)	(−5.3)	(−4.3)	(−6.0)	(−2.3)	(−29.0)	(20.0)	(−7.0)	(−7.63 to −5.27)
Male-to-male sexual contact	6,261	6,146	6,043	5,487	5,614	4,174	5,399	5,372	−3.25
	(—)	(−1.8)	(−1.7)	(−9.2)	(2.3)	(−25.7)	(29.3)	(−0.5)	(−3.65 to −2.86)
Persons who inject drugs**	1,059	1,057	1,020	920	896	645	789	804	−5.52
	(—)	(−0.2)	(−3.5)	(−9.8)	(−2.6)	(−28.0)	(22.3)	(1.9)	(−6.48 to −4.56)

Abbreviations: EQPC = estimated quarter percentage change; Q1 = quarter 1; Q2 = quarter 2; Q3 = quarter 3; Q4 = quarter 4.
* Quarters were defined as Q1 (January 1–March 31), Q2 (April 1–June 30), Q3 (July 1–September 30), and Q4 (October 1–December 31).
† Hispanic or Latino persons can be of any race.
§ Other includes American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, and multiracial.
¶ Classified based on a hierarchy of the risk factors most likely responsible for HIV transmission; classification is determined based on the person's sex assigned at birth. Data have been statistically adjusted to account for missing transmission category.
** Includes persons who inject drugs and engage in male-to-male sexual contact.

periods of decreased health care access. HIV and PrEP self-test kits are in various stages of development, evaluation, and distribution (*8*–*10*). The use of such testing kits, along with health service models that include telehealth clinical services and an expanded role for pharmacies, can provide opportunities for PrEP initiation and continued use over time during periods of decreased access to health care venues.

In 2020, the Coronavirus Aid, Relief, and Economic Security Act appropriated $90 million to Ryan White HIV/AIDS Program (RWHAP) recipients to facilitate response to clients' COVID-19–related health service needs.*** The Health Resources and Services Administration (HRSA) HIV/AIDS Bureau (HAB) waived certain administrative requirements for RWHAP recipients and subrecipients. These include eligible clients be persons with HIV infection, so that COVID-19 prevention measures could be provided to close contacts who did not have HIV; penalty provisions, including requirements for obligation of funds and core medical services budgets; and the requirement for a nominal charge for clients with incomes above the federal poverty level. Recipients were encouraged to be flexible in client eligibility determinations and recertification processes, including adoption of self-attestation and electronic signatures for jurisdictions that did not already use them.

Summary

What is already known about this topic?

HIV service use decreased after the COVID-19 public health emergency declaration in March 2020.

What is added by this report?

In 2020, the number of HIV tests and the number of persons prescribed preexposure prophylaxis (PrEP) decreased between the first and second calendar quarters but rebounded by the third quarter. The proportion of persons linked to HIV care, the number prescribed antiretroviral therapy, and the proportion with a suppressed viral load among those tested remained stable during the study period.

What are the implications for public health practice?

Innovative service delivery models for HIV testing and PrEP care are needed to ensure that these services are accessible during public health emergencies.

*** https://ryanwhite.hrsa.gov/grants/coronavirus

HRSA HAB encouraged adoption of telehealth services and mobile technology to increase access to services.

The findings in this report are subject to at least four limitations. First, although HIV antigen and antibody and viral load tests were not nationally representative, they included more than one half of laboratory tests performed in the United States. Second, IQVIA data were not nationally representative but included prescriptions from 93% of retail pharmacies and 77% of mail-order pharmacies. Third, HIV and viral load testing data were not deduplicated across LabCorp and Quest Diagnostics. A person might have had more than one test result, resulting in an overestimation of persons with an HIV or viral load test result. Finally, viral suppression estimates did not include persons out of care; these persons might have been less likely to be virally suppressed. The viral suppression method in this study differs from the viral suppression measure used to monitor the EHE initiative, which is calculated using NHSS data on all persons with diagnosed HIV infection in the United States. However, viral suppression rates in this study are similar to EHE initiative measures for persons who received care or a viral load test.

The HIV prevention and care service system was resilient during the COVID-19 pandemic. Although HIV testing and PrEP services were disrupted in the spring of 2020, these services started to rebound by summer 2020; ART services for treatment remained unchanged because of interventions such as telehealth and ART home delivery. HIV testing and PrEP provision using self-test kits and nonclinical delivery models are needed to ensure robust prevention services during public health emergencies. Data on the impact of disrupted services and outcomes during the pandemic, along with risk behavior change data, can be used in models to predict the impact on HIV transmission and delays in achieving goals of the EHE initiative. Communities can use this information to assess resources and activities needed to offset decreased prevention services during the pandemic.

Acknowledgment

Xiaohong Hu, Division of HIV Prevention, National Center for HIV, Viral Hepatitis, STD, and TB Prevention, CDC.

Corresponding author: Karen W. Hoover, ffw6@cdc.gov.

[1]Division of HIV Prevention, National Center for HIV, Viral Hepatitis, STD, and TB Prevention, CDC; [2]HIV/AIDS Bureau, Health Resources and Services Administration, Rockville, Maryland.

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. Moreland A, Herlihy C, Tynan MA, et al.; CDC Public Health Law Program; CDC COVID-19 Response Team, Mitigation Policy Analysis Unit. Timing of state and territorial COVID-19 stay-at-home orders and changes in population movement—United States, March 1–May 31, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1198–203. PMID:32881851 https://doi.org/10.15585/mmwr.mm6935a2
2. Bundorf MK, Gupta S, Kim C. Trends in US health insurance coverage during the COVID-19 pandemic. Chicago, IL: JAMA Health Forum; 2021. https://jamanetwork.com/journals/jama-health-forum/fullarticle/2783874
3. Smith SM, Edwards R, Duong HC. Unemployment rises in 2020, as the country battles the COVID-19 pandemic. Washington, DC: US Department of Labor, Bureau of Labor Statistics; 2021. https://www.bls.gov/opub/mlr/2021/article/pdf/unemployment-rises-in-2020-as-the-country-battles-the-covid-19-pandemic.pdf
4. DiNenno EA, Delaney KP, Pitasi MA, et al. HIV testing before and during the COVID-19 pandemic—United States, 2019–2020. MMWR Morb Mortal Wkly Rep 2022;71:820–4. PMID:35737573 https://doi.org/10.15585/mmwr.mm7125a2
5. Huang YLA, Zhu W, Wiener J, Kourtis AP, Hall HI, Hoover KW. Impact of coronavirus disease 2019 (COVID-19) on human immunodeficiency virus (HIV) pre-exposure prophylaxis prescriptions in the United States—a time-series analysis. Clin Infect Dis 2022;75:e1020–7. PMID:35040928 https://doi.org/10.1093/cid/ciac038
6. Zhu W, Huang YA, Wiener J, et al. Impact of the coronavirus disease 2019 pandemic on prescriptions for antiretroviral drugs for HIV treatment in the United States, 2019–2021. AIDS 2022;36:1697–705. PMID:35848572 https://doi.org/10.1097/QAD.0000000000003315
7. Huang YA, Zhu W, Smith DK, Harris N, Hoover KW. HIV preexposure prophylaxis, by race and ethnicity—United States, 2014–2016. MMWR Morb Mortal Wkly Rep 2018;67:1147–50. PMID:30335734 https://doi.org/10.15585/mmwr.mm6741a3
8. MacGowan RJ, Chavez PR, Borkowf CB, et al.; eSTAMP Study Group. Effect of Internet-distributed HIV self-tests on HIV diagnosis and behavioral outcomes in men who have sex with men: a randomized clinical trial. JAMA Intern Med 2020;180:117–25. PMID:31738378 https://doi.org/10.1001/jamainternmed.2019.5222
9. Touger R, Wood BR. A review of telehealth innovations for HIV pre-exposure prophylaxis (PrEP). Curr HIV/AIDS Rep 2019;16:113–9. PMID:30701404 https://doi.org/10.1007/s11904-019-00430-z
10. Sullivan PS, Mena L, Elopre L, Siegler AJ. Implementation strategies to increase PrEP uptake in the South. Curr HIV/AIDS Rep 2019;16:259–69. PMID:31177363 https://doi.org/10.1007/s11904-019-00447-4

Appliances Used by Consumers to Prepare Frozen Stuffed Chicken Products — United States, May–July 2022

Katherine E. Marshall, MPH[1,*]; Michelle Canning, MPH[1,2,*]; Michael Ablan, MPH[1]; Tamara N. Crawford, DBH[1]; Misha Robyn, DVM[1]

Frozen stuffed breaded raw chicken products have repeatedly been implicated in *Salmonella* outbreaks (*1*). These products are partially cooked to set the breading, often making them appear cooked (*2*). Despite their appearance, these products need to be cooked to an internal temperature of 165°F (74°C) to ensure that they are safe to eat. Producers began implementing labeling changes in 2006 to more clearly identify these products as raw; many warn against using microwave ovens (microwaves) to prepare them and provide validated cooking instructions solely for conventional ovens (ovens) (*3*,*4*). However, outbreaks continued to occur after implementation of these labeling changes (*4*). To describe the demographic characteristics of persons who prepare frozen stuffed chicken products and which appliances they use to prepare them, data from a May–July 2022 representative panel survey were analyzed. Although most (82.7%) respondents used an oven as one of their cooking methods, more than one half (54.0%) of respondents also used another appliance, including 29.0% who used a microwave. Oven use was lower among respondents with household income <$25,000 (68.9%), and who lived in mobile homes or other portable types of homes (66.5%). Among respondents who reported using microwaves to cook these products, 8% reported using a microwave with ≤750 W of power, which might be insufficient to thoroughly cook such products (*1*,*5*,*6*). Economic and other factors might influence some groups' access to recommended cooking appliances. Companies could consider implementing additional interventions that rely less on labeling and consumer preparation practices and focus on controlling or reducing levels of *Salmonella* in these products, such as selling them fully cooked, or monitoring and testing *Salmonella* levels, to ensure safety. These findings highlight challenges consumers might face in preparing frozen stuffed chicken products safely and can guide strategies for regulatory authorities and industry to prevent outbreaks and illnesses associated with them.

During May 31–July 6, 2022, Porter Novelli Public Services conducted the SummerStyles survey using the Ipsos KnowledgePanel. Panel members are recruited nationwide by mail using probability-based sampling by address and are provided with a laptop or tablet and access to the Internet if needed. Among 5,990 members invited to participate, 4,156 (69.3%) completed the survey. Fourteen respondents did not provide responses to the questions of interest, resulting in a final sample of 4,142.

To assess use of cooking appliances to prepare frozen stuffed chicken products, respondents were asked, "What appliances do you use to prepare frozen stuffed chicken products, such as chicken stuffed with broccoli and cheese, chicken cordon bleu, or chicken Kiev?" followed by a list of appliances, or an option to select "I don't eat these products." Respondents could select more than one appliance. To assess respondents' knowledge of their microwaves' wattage, respondents were asked, "What is the wattage of your household microwave?" To align with the U.S. population distribution, the sample was weighted by sex, age group, household income, race and ethnicity, household size, whether the respondent was the parent of a child or adolescent aged 11–17 years, educational attainment, U.S. Census Bureau region,[†] and metropolitan status.

Point estimates and 95% CIs were calculated overall and by demographic characteristic (age group, sex, race and ethnicity, U.S. Census Bureau region, household income, highest educational attainment, home type, home ownership, and health insurance status) and compared among respondents who did and did not report preparing frozen stuffed chicken products, and among those who did, the appliances they used and their knowledge of microwave wattage, using Wald chi-square tests. P-values <0.05 were considered statistically significant. All weighted analyses were conducted using SAS (version 9.4; SAS Institute). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[§]

Among 4,142 adults who participated in this survey, 2,546 (61.5%) reported preparing frozen stuffed chicken products (Table 1). A higher percentage of men than women (50.8% versus 44.3%) reported preparing these products as did a higher percentage of younger participants (35.1%) compared with respondents aged ≥60 years (29.1%). A lower percentage of respondents who lived in U.S. Census Bureau West Region (21.8%) reported preparing the products compared with those who lived in other regions (27.4%).

Overall, 2,107 (82.7%) of the 2,546 respondents reported using an oven as one of the cooking appliances used for

[*] These authors contributed equally to this report.

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

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

TABLE 1. Demographic and socioeconomic characteristics of survey respondents who do and do not prepare frozen stuffed chicken products (N = 4,142) — Porter Novelli Public Services, United States, May–July 2022

Characteristic	Prepares frozen stuffed chicken products, weighted % (95% CI)		
	Yes (n = 2,546)	No (n = 1,596)	p-value*
Overall	**61.5 (59.7–63.3)**	**38.5 (36.7–40.3)**	—
Age group, yrs			
18–29	19.6 (17.3–21.9)	18.0 (15.1–20.9)	0.001
30–44	27.2 (25.1–29.3)	26.0 (23.3–28.8)	0.001
45–59	24.1 (22.2–26.0)	20.9 (18.6–23.2)	0.001
≥60	29.1 (27.2–30.9)	35.1 (32.5–37.6)	0.001
Sex			
Female	48.9 (46.6–51.3)	55.3 (52.4–58.2)	0.003
Male	50.8 (48.5–53.2)	44.3 (41.4–47.3)	0.003
Prefer to self-describe	0.2 (0.0–0.4)	0.4 (0.0–0.7)	0.003
Race and ethnicity			
AI/AN, NH	0.8 (0.3–1.20)	1.0 (0.3–1.8)	0.082
Asian or NH/OPI, NH	5.7 (4.4–6.9)	7.4 (5.6–9.2)	0.082
Black or African American, NH	11.8 (10.1–13.4)	12.2 (10.0–14.3)	0.082
Hispanic or Latino	18.5 (16.4–20.7)	14.1 (11.7–16.4)	0.082
White, NH	61.7 (59.3–64.1)	64.0 (61.0–67.0)	0.082
Multiple races, NH	1.5 (1.1–2.0)	1.3 (0.8–1.8)	0.082
Annual household income, US$			
<25,000	13.5 (11.8–15.3)	11.4 (9.4–13.4)	0.465
25,000–49,999	16.9 (15.1–18.7)	17.2 (14.8–19.5)	0.465
50,000–74,999	16.4 (14.6–18.2)	16.3 (14.1–18.6)	0.465
≥75,000	53.2 (50.9–55.6)	55.1 (52.1–13.4)	0.465
Highest educational attainment			
High school diploma or less	38.0 (35.7–40.4)	37.1 (34.1–40.1)	0.374
Some college	27.6 (25.6–29.7)	26.2 (23.6–28.7)	0.374
College graduate or higher	34.3 (32.2–36.5)	36.7 (34.0–39.5)	0.374
U.S. Census Bureau region†			
Northeast	18.0 (16.2–19.7)	16.1 (14.1–18.2)	0.009
Midwest	21.4 (19.5–23.3)	19.3 (17.0–21.6)	0.009
South	38.8 (36.5–41.1)	37.2 (34.2–40.1)	0.009
West	21.8 (19.8–23.8)	27.4 (24.7–30.1)	0.009
Housing type			
One-family house, townhouse, or condominium	79.6 (77.6–81.6)	79.5 (77.0–82.0)	0.933
Building with two or more apartments	16.1 (14.3–17.9)	16.5 (14.2–18.8)	0.933
Other (e.g., mobile home, RV, boat, or van)	4.2 (3.2–5.3)	4.0 (2.8–5.2)	0.933
Housing ownership			
Owned	69.6 (67.3–71.9)	71.4 (68.5–74.2)	0.536
Rented	28.4 (26.1–30.6)	27.0 (24.2–29.8)	0.536
Occupied without payment of rent§	2.1 (1.4–2.7)	1.6 (0.7–2.5)	0.536
Health insurance			
Yes	91.7 (89.7–93.7)	92.1 (89.7–94.5)	0.775
No	8.3 (6.3–10.3)	7.9 (5.5–10.3)	0.775
Visited primary health care provider during last 12 mos			
Yes	78.4 (76.4–80.5)	75.2 (72.4–77.9)	0.064
No	21.6 (19.5–23.6)	24.8 (22.1–27.6)	0.064

Abbreviations: AI/AN = American Indian or Alaska Native; NH = non-Hispanic; NH/OPI = Native Hawaiian or other Pacific Islander; RV = recreational vehicle.

* The p-value for weighted Wald chi-square test; p-values <0.05 were considered statistically significant.

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

§ Housing that is occupied without payment of rent could include housing owned by friends or relatives who live elsewhere and who allow occupancy without charge or could include housing provided as compensation for persons such as caretakers, ministers, tenant farmers, or others.

preparing frozen stuffed chicken products (Table 2). Oven usage was lower among respondents with an annual household income of <$25,000 (68.9%) than among those with household incomes ≥$25,000 (84.9%; p<0.001), those who completed some college or less (80.4%) than among those who completed college (87.2%; p = 0.0002), respondents living in mobile homes, recreational vehicles, boats, vans, or other types of home (66.5%) compared with those living in a one-family house, townhouse, condominium, or apartment (83.5%; p = 0.014), and among those who occupied their home without payment of rent¶ (63.1%) compared with those who owned or rented their home (83.1%; p = 0.037).

More than one half (54.0%) of respondents reported preparing frozen stuffed chicken products using appliances other than or in addition to ovens, including air fryers (29.7%), microwaves (29.0%), toaster ovens (13.7%), or another appliance (3.8%). Microwave usage was higher among men (33.7%), respondents with household incomes <$25,000 (37.2%), and those who occupied their home without payment of rent (49.9%), compared with women (24.2%; p≤0.001), respondents with incomes ≥$25,000 (27.7%; p = 0.011), and those who rented or owned their home (28.5%; p = 0.031).

Among 730 respondents who reported using a microwave to prepare frozen stuffed chicken products, approximately one third (34%) did not know the wattage of their microwave (Figure). A higher percentage of respondents aged 18–29 years did not know their microwave's wattage (46%) compared with respondents aged ≥30 years (31%; p = 0.03). Overall, 8% of respondents who reported preparing frozen stuffed chicken products using a microwave had microwaves with a power level ≤750 W.

Discussion

Although ovens were the most commonly reported appliance used to cook frozen stuffed chicken products, more than one half of respondents (54.0%) reported using other appliances instead of or in addition to ovens, including microwaves (29.0%), a circumstance that historically has been reported frequently by ill persons in outbreaks associated with frozen stuffed chicken products (*1*). Respondents with lower incomes and who live in mobile types of homes reported lower oven use and higher microwave use. Persons within these groups might be at increased risk for illness related to both challenges in preparing these foods and access to appliances.

¶ Housing that is occupied without payment of rent could include housing owned by friends or relatives who live elsewhere and who allow occupancy without charge or could include housing provided as compensation for persons such as caretakers, ministers, tenant farmers, or others.

TABLE 2. Appliances used to prepare frozen stuffed chicken products,* by appliance type and user characteristics (N = 2,546) — Porter Novelli Public Services, United States, May–July 2022

Characteristic	Appliance type: Microwave oven No. (weighted %)	Microwave oven 95% CI	Toaster oven No. (weighted %)	Toaster oven 95% CI	Air fryer No. (weighted %)	Air fryer 95% CI	Appliance not listed No. (weighted %)	Appliance not listed 95% CI	Conventional oven No. (weighted %)	Conventional oven 95% CI	Total
Total	**738 (29.0)**	**26.8–31.1**	**349 (13.7)**	**12.1–15.3**	**755 (29.7)**	**27.5–31.9**	**97 (3.8)**	**2.8–4.8**	**2,107 (82.7)**	**80.8–84.6**	**2,546**
Age group, yrs											
18–29	146 (29.3)	23.0–35.5	71 (14.3)	9.5–19.0	186 (37.4)	30.7–44.1	24 (4.9)	1.9–7.9	432 (86.6)	81.7–91.5	**499**
30–44	196 (28.3)	24.1–32.6	98 (14.2)	11.0–17.4	227 (32.8)	28.5–37.1	30 (4.3)	2.4–6.2	563 (81.2)	77.4–85.1	**693**
45–59	160 (26.1)	22.1–30.1	93 (15.2)	11.9–18.5	179 (29.2)	25.1–33.2	28 (4.6)	2.6–6.5	499 (81.1)	77.4–84.9	**614**
≥60	235 (31.7)	28.5–34.9	86 (11.6)	9.5–13.8	162 (21.9)	19.0–24.9	15 (2.0)	1.0–3.0	613 (82.9)	80.1–85.6	**740**
Sex											
Female	301 (24.2)	21.2–27.2	142 (11.4)	9.1–13.6	361 (29.0)	25.8–32.2	42 (3.4)	2.1–4.6	1,052 (84.4)	81.8–87.0	**1,246**
Male	437 (33.7)	30.7–36.8	207 (16.0)	13.6–18.4	392 (30.3)	27.3–33.4	55 (4.2)	2.8–5.7	1,051 (81.2)	78.5–83.9	**1,294**
Prefer to self-describe	0 (—)	—	0 (—)	—	2 (36.3)	0.0–78.1	0 (—)	—	4 (74.1)	32.8–100.0	**6**
Race and ethnicity											
AI/AN, NH	2 (11.2)	0.0–25.6	3 (13.9)	0.0–38.6	4 (21.5)	0.0–48.7	4 (22.4)	0.0–45.7	15 (77.0)	49.3–100.0	**19**
Asian or NH/OPI, NH	61 (42.4)	31.2–53.7	36 (25.2)	15.6–34.8	62 (43.2)	31.9–54.6	12 (8.6)	2.6–14.6	96 (66.3)	55.5–77.1	**144**
Black or African American, NH	86 (28.6)	21.9–35.3	32 (10.7)	6.1–15.2	101 (33.7)	26.5–40.9	2 (0.7)	0.0–1.5	239 (79.9)	73.6–86.1	**300**
Hispanic or Latino	126 (26.8)	20.9–32.6	63 (13.4)	9.2–17.6	149 (31.6)	25.5–37.7	25 (5.2)	2.0–8.3	371 (78.5)	73.0–84.0	**472**
White, NH	454 (28.9)	26.4–31.4	213 (13.6)	11.6–15.5	430 (27.3)	24.9–29.8	49 (3.1)	2.1–4.1	1,353 (86.1)	84.2–88.0	**1,572**
Multiple races, NH	8 (20.1)	10.5–29.8	2 (4.5)	0.0–9.5	9 (22.4)	12.3–32.6	4 (10.5)	0.0–21.6	33 (84.3)	75.4–93.3	**39**
Annual household income, US$											
<25,000	128 (37.2)	30.3–44.0	44 (12.8)	7.9–17.7	115 (33.2)	26.6–39.9	21 (6.0)	2.5–9.5	237 (68.9)	(62.3–75.6)	**344**
25,000–49,999	115 (26.7)	21.5–31.9	59 (13.8)	9.9–17.7	144 (33.4)	27.6–39.2	15 (3.5)	1.1–6.0	350 (81.5)	77.1–86.0	**430**
50,000–74,999	107 (25.8)	20.6–31.0	53 (12.7)	8.7–16.8	99 (23.7)	18.6–28.8	16 (4.0)	1.7–6.2	348 (83.4)	78.5–88.3	**417**
≥75,000	387 (28.6)	25.8–31.4	193 (14.2)	12.0–16.4	399 (29.4)	26.5–32.3	44 (3.3)	2.1–4.4	1,171 (86.4)	84.2–88.6	**1,355**
Education											
High school diploma or less	299 (30.8)	26.9–34.7	126 (13.0)	10.2–15.9	298 (30.8)	26.8–34.8	28 (2.8)	1.5–4.2	763 (78.8)	75.3–82.3	**969**
Some college	177 (25.1)	21.3–28.9	92 (13.1)	10.0–16.2	216 (30.7)	26.6–34.8	41 (5.8)	3.3–8.2	582 (82.7)	79.2–86.2	**703**
Completed college or higher	262 (30.0)	26.7–33.4	131 (15.0)	12.4–17.5	241 (27.6)	24.3–30.9	29 (3.3)	2.1–4.5	762 (87.2)	84.7–89.7	**874**
U.S. Census Bureau region†											
Northeast	113 (24.8)	20.2–29.4	67 (14.6)	10.9–18.3	124 (27.2)	22.1–32.3	13 (2.9)	1.0–4.8	389 (85.0)	81.1–88.8	**458**
Midwest	164 (30.0)	25.5–34.6	65 (11.9)	8.5–15.2	156 (28.6)	24.2–33.1	26 (4.8)	2.7–6.9	455 (83.5)	79.6–87.4	**545**
South	276 (27.9)	24.5–31.4	125 (12.6)	10.0–15.2	297 (30.1)	26.5–33.7	28 (2.9)	1.5–4.2	825 (83.4)	80.5–86.4	**989**
West	184 (33.2)	28.3–38.1	93 (16.7)	12.9–20.6	177 (32.0)	27.0–37.0	29 (5.2)	2.6–7.8	437 (78.9)	74.5–83.3	**555**
Housing type											
One-family house, townhouse, or condominium	582 (28.7)	26.4–31.1	266 (13.1)	11.4–14.9	585 (28.9)	26.5–31.3	69 (96.6)	95.6–97.6	1,706 (84.1)	82.2–86.1	**2,027**
Building with two or more apartments	113 (27.4)	22.0–32.8	58 (14.2)	9.9–18.5	132 (32.2)	26.3–38.1	19 (4.5)	1.8–7.2	329 (80.0)	75.1–85.0	**411**
Other (e.g., mobile home, RV, boat, or van)	43 (39.6)	27.0–52.2	25 (22.9)	11.1–34.8	38 (35.0)	22.6–47.4	9 (8.8)	0.4–17.1	72 (66.5)	54.2–78.8	**108**
Housing ownership											
Owned	495 (27.9)	25.5–30.4	245 (13.8)	11.9–15.7	506 (28.6)	26.1–31.1	60 (3.4)	2.4–4.4	1,502 (84.8)	82.8–86.8	**1,772**
Rented	216 (29.9)	25.5–34.4	97 (13.4)	10.0–16.7	231 (32.1)	27.5–36.6	35 (4.9)	2.6–7.2	571 (79.1)	75.1–83.2	**722**
Occupied without payment of rent§	26 (49.9)	33.1–66.7	8 (15.0)	1.9–28.2	18 (33.3)	17.2–49.4	2 (2.9)	0.0–8.6	33 (63.1)	46.3–79.9	**53**
Health insurance											
Yes	432 (28.9)	26.1–31.7	199 (13.3)	11.2–15.5	435 (29.1)	26.3–31.9	61 (4.1)	2.8–5.4	1,255 (83.9)	81.5–86.2	**1,496**
No	41 (30.1)	18.5–41.7	16 (11.8)	4.4–19.2	53 (38.8)	26.3–51.3	4 (3.0)	0.0–6.5	103 (76.2)	65.4–87.0	**136**
Accessed primary health care provider in last 12 mos											
Yes	571 (29.3)	26.8–31.7	251 (12.8)	11.1–14.6	576 (29.5)	27.1–32.0	70 (3.6)	2.6–4.6	1,617 (82.9)	80.8–85.0	**1,951**
No	144 (26.8)	21.9–31.7	88 (16.5)	12.4–20.5	163 (30.3)	25.1–35.5	25 (4.7)	2.1–7.2	450 (83.9)	79.6–88.1	**536**

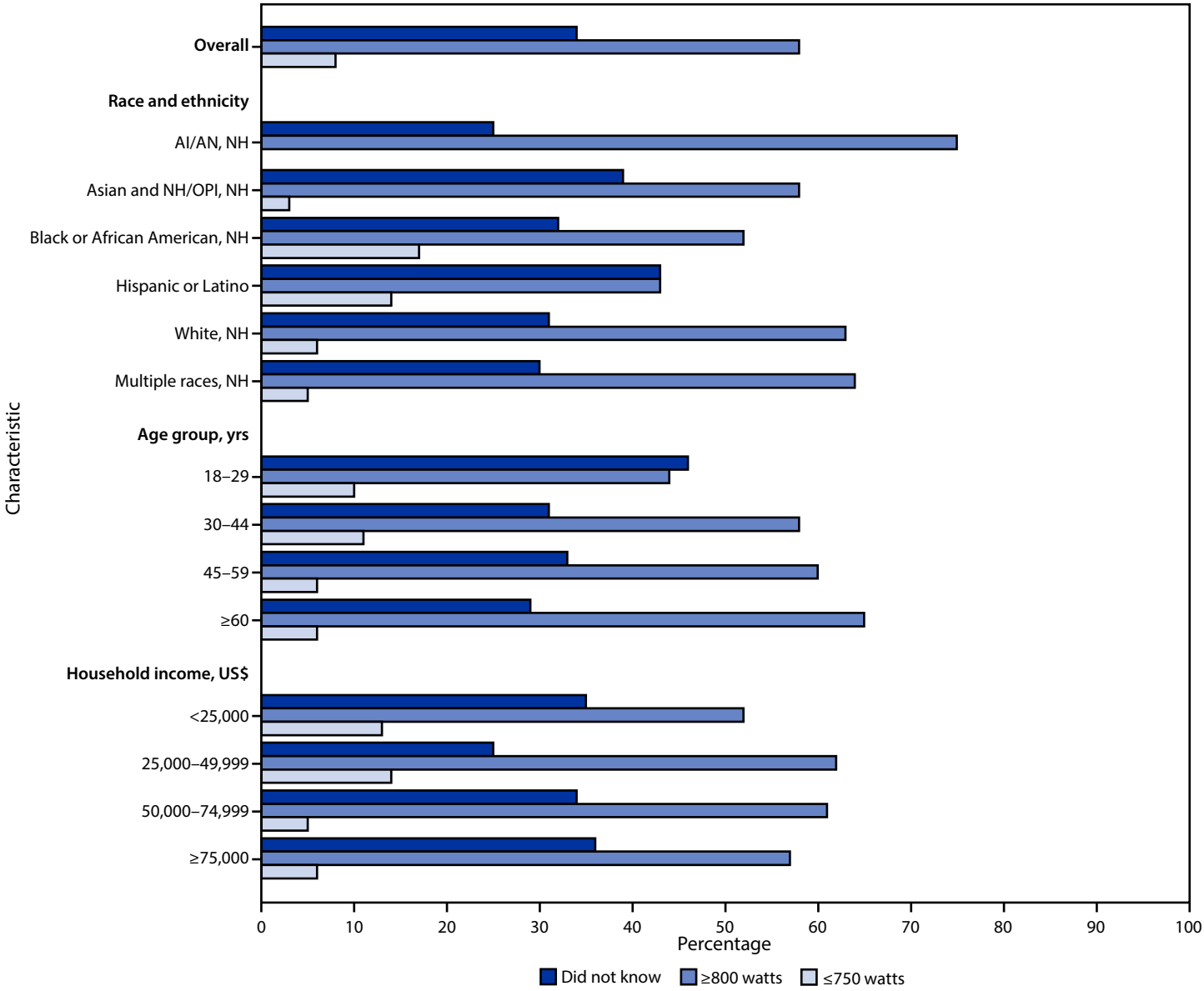
Abbreviations: AI/AN = American Indian or Alaska Native; NH = non-Hispanic; NH/OPI = Native Hawaiian or other Pacific Islander; RV = recreational vehicle.

* Such as chicken stuffed with broccoli and cheese, chicken cordon bleu, or chicken Kiev.

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

§ Housing that is occupied without payment of rent could include housing owned by friends or relatives who live elsewhere and who allow occupancy without charge or could include housing provided as compensation for persons such as caretakers, ministers, tenant farmers, or others.

FIGURE. Characteristics of respondents who prepared frozen stuffed chicken products using a microwave oven, by reported microwave wattage (N = 730)* — United States, May–July 2022



Abbreviations: AI/AN = American Indian or Alaska Native; NH = non-Hispanic; NH/OPI = Native Hawaiian or other Pacific Islander.
* Seven respondents who reported, "I don't have a microwave" when asked about the wattage of their household microwave but reported preparing the product in a microwave were excluded.

Efforts to prevent *Salmonella* infections linked to frozen stuffed chicken products have relied on manufacturers to develop validated cooking instructions and labeling to alert the consumer to which appliances are recommended to cook them (i.e., ovens). Studies indicate that microwaves, air fryers, and toaster ovens inconsistently heat frozen stuffed chicken or frozen raw breaded chicken (*4*,*6*,*7*). Therefore, cooking instructions often do not include information about cooking the product in air fryers or toaster ovens and might warn against using microwaves. However, previous studies have found that some consumers infrequently read package instructions (*8*,*9*), including one report that found some consumers discarded packaging when the products were brought home and never saw cooking instructions (*9*). In this survey, 30% of respondents reported using an air fryer, 29% a microwave, and 14% a toaster oven. These findings suggest that relying on labeling and cooking instructions might not be sufficient to prevent illness. Further, even when cooking these products in an oven, verifying the temperature of the finished product is important (*7*). However, food thermometer usage can be

Summary

What is already known about this topic?

Frozen stuffed chicken products remain a source of *Salmonella* outbreaks despite changes to packaging instructing consumers to cook these products in ovens and to avoid using microwaves.

What is added by this report?

More than one half of respondents to an Internet panel survey reported using an appliance other than an oven to cook frozen stuffed chicken products; 29% used a microwave. Respondents with lower incomes and who live in mobile types of homes reported lower oven use and higher microwave use.

What are the implications for public health practice?

Economic and other factors might influence access to recommended cooking appliances. Companies could consider implementing interventions that rely less on labeling and consumer preparation practices to ensure safety.

low; one study found that even among persons who owned a food thermometer, only 38% typically used them to check doneness of frozen chicken products (*2*).

Preparing frozen stuffed chicken products in an oven requires access to a working oven. In this survey, persons with lower income, who live in mobile types of homes, and who live in their home without payment of rent reported lower oven use. Persons who live in mobile types of homes might have less or insufficient space for a conventional oven. Appliances like microwaves are small, often portable, and cost less to own and operate than an oven. These findings suggest that economic and other factors might influence some groups' access to recommended cooking appliances.

Barriers to using ovens, combined with the convenience of microwaves' shorter cooking times, might encourage consumers to use microwaves. Microwaves require adjusting cooking times based on the microwave's wattage. Consumers who do not know their microwave's wattage, as was the case among approximately one third of respondents in this survey, might not be able to adjust cooking times and might therefore be less likely to prepare these products safely. In addition, 8% of all respondents who reported using a microwave to prepare these products and knew the wattage had microwaves with a power level ≤750 W. Studies suggest that lower wattage microwaves might be insufficient to cook these products (*1*,*5*,*6*).

Current measures to prevent *Salmonella* infections linked to contaminated frozen raw stuffed chicken products rely on consumers' ability to identify them as raw, to read and recall cooking instructions, to adequately cook the products according to validated cooking instructions, typically in conventional ovens, and to verify the product's internal temperature using a food thermometer. Results from this survey highlight possible challenges consumers face preparing these products safely and the need for additional action. Given the substantial percentage of respondents who reported using an appliance other than an oven, and socioeconomic characteristics of respondents with lower oven usage, companies could consider implementing additional interventions that rely less on labeling and consumer preparation practices and instead control or reduce levels of *Salmonella* in these products, such as selling them fully cooked, or monitoring and testing *Salmonella* levels, to ensure safety.

The findings in this report are subject to at least four limitations. First, responses were self-reported and therefore subject to recall and social desirability biases. Second, although weighted to represent the U.S. population, the survey sample might not be representative. Third, the survey did not specify raw frozen stuffed chicken products; therefore, consumers possibly reported appliances that they use to prepare fully cooked stuffed chicken products. However, previous studies indicate that some consumers might be unaware that these products are usually raw (*2*). Finally, the survey did not include questions about whether cooking instructions were noticed or followed, or which appliances respondents owned; therefore, reasons that specific appliances were used could not be assessed.

Although *Salmonella* has not historically been considered an adulterant in not-ready-to-eat products, including raw frozen stuffed chicken products, the U.S. Department of Agriculture Food Safety and Inspection Service recently announced its intention to declare it an adulterant in these products (*10*). These findings can guide regulatory policy and prevention strategies for the industry.

Corresponding author: Katherine E. Marshall, uwj0@cdc.gov, 404-639-4405.

[1]Division of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC; [2]Oak Ridge Institute for Science and Education, Oak Ridge, Tennessee.

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. Smith KE, Medus C, Meyer SD, et al. Outbreaks of salmonellosis in Minnesota (1998 through 2006) associated with frozen, microwaveable, breaded, stuffed chicken products. J Food Prot 2008;71:2153–60. PMID:18939771 https://doi.org/10.4315/0362-028X-71.10.2153
2. Sheryl C, Cates ES, Brophy J, et al. Food safety consumer research project: meal preparation experiment on raw stuffed chicken breasts. Washington, DC: U.S. Department of Agriculture, Food Safety and Inspection Service; 2020. https://www.fsis.usda.gov/sites/default/files/media_file/2021-04/fscrp-yr3-nrte-final-report.pdf
3. Kremer S. Stuffed, not ready-to-eat poultry products. Washington, DC: U.S. Department of Agriculture; 2021. https://www.fsis.usda.gov/sites/default/files/media_file/2021-09/NACMPI-092021-pesentation-Stuffed-Not-Ready-to-Eat-Poultry-Products.pdf

4. Food Safety and Inspection Service. *Salmonella* enteritidis outbreak linked to frozen, raw, breaded, stuffed chicken products outbreak investigation after action review, report 2021–07. Washington, DC: U.S. Department of Agriculture, Food Safety and Inspection Service; 2022. https://www.fsis.usda.gov/sites/default/files/media_file/2022-04/FSIS-After-Action-Review-2021-07.pdf
5. Phebus R, Powell D, Thippareddi H. Beyond intent: assessment and validation of on-package handling and cooking instructions for uncooked, breaded meat and poultry products to promote consumer practices that reduce foodborne illness risks. Washington, DC: Foundation for Meat and Poultry Research and Education; 2009. http://meatpoultryfoundation.org/namif/wp-content/uploads/06-411.pdf
6. Food Safety and Inspection Service. Information on validation of labeled cooking instructions for products containing raw or partially cooked poultry. Washington, DC: U.S. Department of Agriculture, Food Safety and Inspection Service; 2017. https://www.fsis.usda.gov/guidelines/2017-0017
7. Rao M, Klappholz A, Tamber S. Effectiveness of preparation practices on the inactivation of *Salmonella enterica* serovar Enteritidis in frozen breaded chicken strips. J Food Prot 2020;83:1289–95. PMID:32221539 https://doi.org/10.4315/JFP-19-601
8. Cates S, Blitstein J, Shumaker E, et al. Modernizing safe handling and ready-to-eat/not-ready-to-eat labeling instructions: behavior change study. Research Triangle Park, NC: RTI International; 2020. https://www.fsis.usda.gov/sites/default/files/media_file/2022-02/SHI_Behavior_Change_Study%20Final%20Report_9_23_20.pdf
9. Carvalho JP, Benusic M, Codat R, Gruescu R, Haydu L, Loh LC. Health risks of frozen raw breaded chicken products: a local health unit perspective. Can Commun Dis Rep 2020;46:403–8. PMID:33447162 https://doi.org/10.14745/ccdr.v46i1112a07
10. Food Safety and Inspection Service. USDA announces action to declare *Salmonella* an adulterant in breaded stuffed raw chicken products [Press release]. Washington, DC: U.S. Department of Agriculture; 2022. https://www.usda.gov/media/press-releases/2022/08/01/usda-announces-action-declare-salmonella-adulterant-breaded-stuffed

Outbreak of *Burkholderia stabilis* Infections Associated with Contaminated Nonsterile, Multiuse Ultrasound Gel — 10 States, May–September 2021

Matthew J. Hudson, MD[1,*]; Stacy C. Park, MD[2,*]; Amy Mathers, MD[2]; Hardik Parikh, PhD[2]; Janet Glowicz, PhD[3]; David Dar, MPH[4]; Marjan Nabili, PhD[4]; John J. LiPuma, MD[5]; Amy Bumford[5]; Matthew A. Pettengill, PhD[6]; Mark R. Sterner, Jr.[6]; Julie Paoline, MA[7]; Stacy Tressler, PhD[7]; Tiina Peritz, MS[8]; Jane Gould, MD[8]; Stuart R. Hutter, MS, MPH[9]; Heather Moulton-Meissner, PhD[3]; Kiran M. Perkins, MD[3]

In July 2021, the Virginia Department of Health notified CDC of a cluster of eight invasive infections with *Burkholderia stabilis*, a bacterium in the *Burkholderia cepacia* complex (BCC), among hospitalized patients at hospital A. Most patients had undergone ultrasound-guided procedures during their admission. Culture of MediChoice M500812 nonsterile ultrasound gel used in hospital A revealed contamination of unopened product with *B. stabilis* that matched the whole genome sequencing (WGS) of *B. stabilis* strains found among patients. CDC and hospital A, in collaboration with partner health care facilities, state and local health departments, and the Food and Drug Administration (FDA), identified 119 *B. stabilis* infections in 10 U.S. states, leading to the national recall of all ultrasound gel products produced by Eco-Med Pharmaceutical (Eco-Med), the manufacturer of MediChoice M500812. Additional investigation of health care facility practices revealed frequent use of nonsterile ultrasound gel to assist with visualization in preparation for or during invasive, percutaneous procedures (e.g., intravenous catheter insertion). This practice could have allowed introduction of contaminated ultrasound gel into sterile body sites when gel and associated viable bacteria were not completely removed from skin, leading to invasive infections. This outbreak highlights the importance of appropriate use of ultrasound gel within health care settings to help prevent patient infections, including the use of only sterile, single-use ultrasound gel for ultrasonography when subsequent percutaneous procedures might be performed.

Investigation and Results

On July 21, 2021, the Virginia Department of Health notified CDC that eight patients with invasive *B. stabilis* infection (mostly bloodstream infections) had been identified by hospital A during May 18–July 20, 2021. At least seven of the eight patients had undergone ultrasound-guided procedures at hospital A. Unopened bottles of nonsterile ultrasound gel, MediChoice M500812, present at the facility were sampled and cultured. Initial cultures identified BCC organisms in eight of 13 unopened bottles; subsequent WGS identified BCC as *B. stabilis* among bottles representing three lots of MediChoice M500812 ultrasound gel. Quantitative testing yielded high bacterial bioburden (7.0×10^6–5.8×10^7 colony-forming units/mL) in bottles from two of these lots. The genetic sequences of *B. stabilis* for all eight clinical (seven from blood and one from ascites fluid) and three product isolates collected at hospital A were closely related (0–11 single nucleotide variants with coverage of >99% of the full reference genome). Hospital A reported these results to CDC on July 23, 2021.

During the week of July 18, 2021, hospital A posted a query regarding unusual BCC blood cultures on an American Society of Microbiology Listserv. On July 22, the Philadelphia Department of Public Health notified CDC about seven patients in an acute care hospital (hospital B) with BCC bloodstream infections identified during July 7–July 20, 2021, four of whom had undergone ultrasound-guided percutaneous procedures. Hospital B cultured bottles from 21 lots of ultrasound gel and identified BCC in two of these lots, including one of the three lots in which BCC had previously been identified by hospital A and an additional fourth lot of unopened MediChoice M500812 ultrasound gel. Hospital B shared these clinical and product isolates with hospital A for WGS, which confirmed isolates to be *B. stabilis* and demonstrated that patient and product isolates from the two facilities were closely related (1–7 single nucleotide variants, >99% genome coverage), raising concern about contamination of the ultrasound gel during manufacturing or distribution. Although nonsterile, multiuse ultrasound gel is intended only for external, noninvasive ultrasonography (e.g., transthoracic echocardiogram and diagnostic abdominal ultrasound), both hospitals noted that health care personnel often use this ultrasound gel to visualize anatomic structures during percutaneous procedures (e.g., locating veins to guide peripheral intravenous catheter insertion). This practice could have left gel containing viable bacteria on the skin that is difficult to remove before the procedure, preventing adequate skin antisepsis and allowing introduction of BCC into sterile body sites.

CDC subsequently collected information on demographic and clinical characteristics for any patients with *B. stabilis* infections reported to CDC during July 21–October 15, 2021, with the assistance of state and local health departments, which collected this information from health care facilities. CDC also facilitated sharing of isolates and WGS information

*These authors contributed equally to this report.

among facilities with patient infections and hospital A, which conducted WGS comparisons for isolates among facilities reporting cases. The University of Michigan *Burkholderia cepacia* Research Laboratory and Repository performed repetitive extragenic palindromic polymerase chain reaction (rep-PCR) for selected isolates. For this investigation, a case was defined as a positive culture for *B. stabilis* in a patient specimen collected from any body site on or after January 1, 2021, in which the isolate was genetically related to the outbreak strain by WGS (match within 12 single nucleotide variants, >99% coverage across the entire *B. stabilis* reference genome) or rep-PCR (match defined as similarity coefficient >85%).

CDC was notified of 119 *B. stabilis* patient infections among 10 states meeting the case definition (Table). Reported isolates were collected during May 15–September 14, 2021. The median patient age was 61 years (range = 4 days–92 years). Median interval from hospital admission to detection of *B. stabilis* infection was 1 day (range = 0–118 days). Most infections were bloodstream infections (106, 89%). Among 87 patients with available clinical data, 59 (68%) had signs and symptoms of infection (e.g., fever and tachycardia). Among 102 patients with vital status information, 14 (14%) deaths were reported during the hospitalization in which *B. stabilis* infection was identified. Cause of death was available for 10 patients and was attributed to *B. stabilis* infection in two of these. Cause of death for the remaining eight patients included septic shock unrelated to BCC (three), cardiac arrest (two), hypoxemic respiratory failure (one), respiratory failure secondary to COVID-19 (one), and sickle cell crisis (one). Among 117 patients with available information, 104 (89%) are known to have undergone ultrasonography during their admission, and 103 (94%) underwent an ultrasound-associated percutaneous procedure (e.g., peripheral intravenous catheter insertion or paracentesis). An Eco-Gel 200 product was documented to have been used among 31 (26%) of all infections and was known to have been present in all facilities reporting cases.

TABLE. Demographics, clinical characteristics, and exposures of patients with *Burkholderia stabilis* infections associated with contaminated ultrasound gel (N = 119) — United States, May–September 2021

Characteristic (no. with available information)	No. (%)
Age, yrs, median (range) (n = 68)	**61 (4 days–92 yrs)**
Sex (n = 89)	
Female	44 (49)
Male	45 (51)
Jurisdiction (n = 119)	
California	12 (10)
Illinois	6 (5)
Minnesota	23 (19)
New Jersey	4 (3)
New Mexico	1 (1)
New York	6 (5)
Ohio	4 (3)
Pennsylvania (not including Philadelphia)	19 (16)
Philadelphia	35 (29)
Virginia	8 (7)
Washington	1 (1)
Signs and symptoms of infection* (n = 87)	**59 (68)**
Site of infection (n = 119)	
Blood	106 (89)
Ascites or abdominal fluid	5 (4)
Sputum	3 (3)
Wound	3 (3)
Amniotic fluid	1 (1)
Bile	1 (1)
Days from admission to detection of infection, median (range) (n = 113)	**1 (0–118)**
Treated for *Burkholderia cepacia* complex infection (n = 63)	**51 (81)**
Deaths (n = 102)†	14 (14)
Underwent ultrasonography during admission (n = 117)	**104 (89)**
Number of ultrasounds during admission, mean (range)	1.8 (0–11)
Underwent ultrasound-guided percutaneous procedure (n = 109)	103 (94)
Peripheral intravenous catheter placement	59 (57)
Central venous catheter (includes peripherally inserted central catheter and hemodialysis catheter)	14 (14)
Arterial line	10 (10)
Paracentesis	7 (7)
Aspiration of fluid collection	4 (4)
Thoracentesis or chest tube	3 (3)
Nerve block	2 (2)
Percutaneous biopsy of lesion	2 (2)
Amniocentesis	1 (1)
Gallbladder aspiration	1 (1)
Underwent intracavitary ultrasound§ (n = 100)	3 (3)

See table footnotes on the next page.

Public Health Response

Because of the concern for product contamination, CDC notified FDA on July 23, 2021, of the epidemiologic and laboratory findings. FDA and CDC informed Eco-Med on July 29, 2021, of the patient infections, resulting in a voluntary recall of eight product lots on August 4, 2021, including the four lots initially identified by hospitals A and B (*1*). The recall also advised facilities to quarantine all associated products from Eco-Med, including all MediChoice M500812 gel and its other ultrasound gel product line, Eco-Gel 200, while investigation was ongoing (*1*). On August 4, 2021, CDC issued an Epidemic Information Exchange communication to relevant professional organizations to alert public health and clinical communities of the infections and product recall (*2*).

Additional FDA investigation of manufacturing protocols revealed concern for potential bacterial product contamination beyond the eight recalled lots, in light of the company's inappropriate testing of finished product, inadequate testing of raw materials, and a lack of environmental controls, although the root cause and extent of the bacterial contamination was not identified (*3*). On August 18, 2021, FDA advised immediate discontinuation of use and discarding of all ultrasound gels and lotions manufactured by Eco-Med (*3*). The manufacturer ceased operation and FDA engaged the multiple distributors of the product to ensure execution of an expanded recall of all

Summary

What is already known about this topic?

Burkholderia cepacia complex (BCC) is a group of opportunistic pathogens that can cause infection in healthy persons who become exposed to contaminated medical products.

What is added by this report?

In 2021, a total of 119 BCC infections were associated with multiple lots of nonsterile ultrasound gel contaminated with BCC organisms. Use of this contaminated gel before percutaneous procedures likely contributed to patient infections.

What are the implications for public health practice?

Ensuring quality system practices during manufacturing and appropriate use of products in clinical practice are crucial to preventing infections. Health care personnel who perform ultrasounds and ultrasound-associated procedures should be trained for the appropriate use of ultrasound gel associated with these procedures.

ultrasound gels and lotions manufactured by Eco-Med. After the recall, FDA also collected samples of product from distributor sites and a point of importation for laboratory analysis and confirmation of contamination. Subsequent FDA testing identified bacterial contamination in eight of the 13 tested lots of ultrasound gel manufactured by Eco-Med, seven of which were contaminated with BCC (and an additional lot contaminated with *Bacillus circulans*). One of these contaminated lots had been identified by hospital A; the other seven were additional lots not included in the original product recall, validating FDA's recommendation for expansion of the initial recall.

Health departments in cities and states with facilities reporting cases reported that all affected facilities removed all ultrasound gels and lotions manufactured by Eco-Med from clinical areas and destroyed the products or returned them to their distributors. No additional cases were reported to CDC after October 12, 2021.

Discussion

BCC is a group of opportunistic pathogens with intrinsic resistance to certain preservatives and antimicrobial agents often used in aqueous products and can cause clinical infection in healthy persons who are exposed to contaminated medical products or devices (*4*,*5*). Infection with BCC has been associated with ultrasound gel in previous outbreaks (*4*–*6*). In this outbreak, BCC-contaminated ultrasound gel was likely introduced into sterile body sites during invasive procedures when needles were advanced through skin on which the contaminated gel had been applied before or during the procedure. Such practices, including the routine use of ultrasonography and multiuse ultrasound gel to guide peripheral intravenous catheter placement, were reported as occurring in affected facilities across multiple jurisdictions. Only single-use, sterile ultrasound gel packets should be used for ultrasonography in anticipation of, preparation for, or during percutaneous procedures (*7*). Ultrasound probes and other related devices (e.g., consoles and handles) should also be completely cleaned and disinfected according to manufacturers' instructions to avoid the transmission of pathogens to patients (*7*). A high bioburden of bacteria noted on quantitative testing and BCC's intrinsic resistance to antiseptics commonly used in clinical practice might have further contributed to this outbreak by rendering skin antiseptics less effective when used as part of aseptic preparation for such procedures (*8*,*9*). After all external ultrasonographic examinations, ultrasound gel should be thoroughly removed from the skin, and care must be taken to ensure that any residual gel is completely cleaned off. Once all residual ultrasound gel is removed, skin antisepsis as indicated for the procedure should be performed at the site before proceeding with any associated invasive procedure. Additional considerations for the appropriate use of ultrasound gel might also prevent infections (Box).

This investigation highlights that BCC can pose a risk for invasive infections because of contamination of nonsterile aqueous medical products even when intended use is limited to skin. Other, nonsterile aqueous medical products implicated in health care–associated outbreaks due to BCC contamination include nasal sprays, mouthwashes, preoperative skin solutions, and hand sanitizers, among others. Manufacturers of water-based medical products and medical devices (e.g., ultrasound gels) should ensure that quality system processes

TABLE. (*Continued*) Demographics, clinical characteristics, and exposures of patients with *Burkholderia stabilis* infections associated with contaminated ultrasound gel (N = 119) — United States, May–September 2021

Characteristic (no. with available information)	No. (%)
Hospital location where ultrasound was performed (n = 72)¶	
Emergency department or trauma bay	34 (47)
Inpatient room	24 (33)
Radiology suite	9 (13)
Operating room	6 (8)
Outpatient clinic	5 (7)
Known exposure to Eco-Med 200 product (n = 39)	**31 (79)**

* Signs and symptoms of infection included fever, tachycardia, and leukocytosis. It is hypothesized that a proportion of blood cultures were positive for *Burkholderia cepacia* complex without sign of infection because of specimen contamination, whereby the specimen was drawn directly at the site where the ultrasound gel had been applied and not completely removed.

† Cause of death was only available for 10 patients and was attributed to *Burkholderia stabilis* infection in two of these. Cause of death for the remaining eight patients included septic shock unrelated to *Burkholderia cepacia* complex (three), cardiac arrest (two), hypoxemic respiratory failure (one), respiratory failure secondary to COVID-19 (one), and sickle cell crisis (one).

§ All intracavitary ultrasound procedures were transesophageal echocardiograms.

¶ Categories are not mutually exclusive.

Box. Considerations for the use of ultrasound gel*

Sterile ultrasound gel

- Use single-use, sterile ultrasound gel for ultrasonography performed in preparation for or during percutaneous procedures (e.g., placement of central and peripheral intravenous lines, amniocentesis, paracentesis, tissue biopsy, and surgical procedures).†
  - Do not use nonsterile ultrasound gel for visualization before such procedures.
  - If nonsterile ultrasound gel is inadvertently used before such procedures (e.g., unanticipated procedure), care must be taken to ensure that all residual gel is removed from the skin and the appropriate skin antisepsis is performed before the procedure.
- Use single-use, sterile ultrasound gel for all ultrasound procedures performed on nonintact skin or near fresh surgical sites.†
- Whenever feasible, use single-use, sterile ultrasound gel inside single-use or sterile ultrasound probe covers.†

Nonsterile ultrasound gel

- If multiuse containers are used†:
  - Do not refill; discard and replace multidose containers when empty.
  - Seal container when not in use.
  - Avoid direct contact between gel container dispensing tip and any persons or instrumentation, including the ultrasound transducer.
- If a patient under contact precautions undergoes an ultrasound using gel dispensed from a multiuse container, discard the container after use.†
- After ultrasonography, clean the skin, ensuring that all residual ultrasound gel is removed.§

Reprocessing of ultrasound equipment

- Follow manufacturer's instructions for ultrasound probe reprocessing to ensure recommended cleaning and disinfection protocols are being followed.†,¶
- Clean and thoroughly disinfect ultrasound consoles and other parts of the ultrasound device that do not come into direct contact with the patient (e.g., handles, cables, connectors, and holders) and any warming devices or other noncritical surfaces associated with ultrasound procedures before use on another patient.† Containers for ultrasound gel and consoles should be considered high-touch surfaces.
- All transducers used on either mucous membranes or nonintact skin (e.g., use in transvaginal, transrectal, and transesophageal procedures) require high-level disinfection or sterilization before use on another patient.†,§,¶,**

* For all ultrasonography, standard precautions including adherence to hand hygiene and the use of personal protective equipment are recommended. Surgical hand scrub and use of sterile barriers is recommended for sterile procedures.
† https://www.aium.org/officialstatements/57
§ https://www.cdc.gov/infectioncontrol/guidelines/disinfection/
¶ https://doi.org/10.1002/jum.15653
** https://www.fda.gov/media/71100/download

include pathogen prevention and identification as part of their contamination and environmental control requirements.† Health care personnel should be trained for the appropriate use of ultrasound gel associated with ultrasounds and ultrasound-associated procedures, including that only sterile, single-use ultrasound gel should be used before and during invasive percutaneous procedures to prevent additional outbreaks of serious patient infections (*7*).

Acknowledgments

April Attai, Joan Buckner, Sarah Schumacher, School of Medicine, University of Virginia; Courtney Mitchell, Kelly Zabriskie, Sidney Kimmel College of Medicine, Thomas Jefferson University; Raquel DeLeon-Gonsalves, Temple University Hospital; Shane Zelencik, Chicago Department of Public Health; Ira Heimler, Illinois Department of Public Health; Moon Kim, County of Los Angeles Department of Public Health; Amanda Beaudoin, Jennifer Dale, Paula Snippes Vagnone, Laura Tourdot, Minnesota Department of Health; Michel Masters, Montgomery County Office of Public Health, Pennsylvania; Jason Mehr, New Jersey Department of Public Health; Marla Sievers, New Mexico Department of Health; Kara Mitchell, New York State Department of Health; Marika Mohr, Ohio Department of Health; Cara Bicking Kinsey, Jenna Sinkevitch, Pennsylvania Department of Health; Beth Morris, Philadelphia Department of Public Health; Rehab Abdelfattah, Sarah Lineberger, Dawn Saady, Virginia Department of Health; Marisa D'Angeli, Washington State Department of Health; Joseph Perz, CDC; Center for Devices and Radiological Health, FDA Office of Regulatory Affairs; Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, CDC.

Corresponding author: Kiran M. Perkins, guu9@cdc.gov.

[1]Epidemic Intelligence Service, CDC; [2]School of Medicine, University of Virginia, Charlottesville, Virginia; [3]Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, CDC; [4]Food and Drug Administration, Silver Spring, Maryland; [5]University of Michigan Medical School, Ann Arbor, Michigan; [6]Sidney Kimmel College of Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania; [7]Pennsylvania Department of Health; [8]Philadelphia Department of Public Health, Philadelphia, Pennsylvania; [9]Virginia Department of Health.

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

† Quality System Regulation, 21 C.F.R. 820.70 (2022). Items c and e. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=820.70

References

1. Food and Drug Administration. Eco-Med Pharmaceutical issues voluntary recall of Eco-Gel 200. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2021. https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/eco-med-pharmaceutical-issues-voluntary-recall-eco-gel-200
2. CDC. Healthcare-associated infections (HAIs). Multistate outbreak of *Burkholderia cepacia* infections associated with contaminated ultrasound gel. Atlanta, GA: US Department of Health and Human Services, CDC; 2021. Accessed March 1, 2022. https://www.cdc.gov/hai/outbreaks/b-cepacia-ultrasound-gel/index.html
3. Food and Drug Administration. Stop using all Eco-Med ultrasound gels and lotions due to risk of bacterial contamination – letter to health care providers. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2021. Accessed March 1, 2022. https://www.fda.gov/medical-devices/letters-health-care-providers/stop-using-all-eco-med-ultrasound-gels-and-lotions-due-risk-bacterial-contamination-letter-health
4. Hutchinson J, Runge W, Mulvey M, et al. *Burkholderia cepacia* infections associated with intrinsically contaminated ultrasound gel: the role of microbial degradation of parabens. Infect Control Hosp Epidemiol 2004;25:291–6. PMID:15108725 https://doi.org/10.1086/502394
5. Food and Drug Administration. FDA advises drug manufacturers that *Burkholderia cepacia* complex poses a contamination risk in non-sterile, water-based drug products. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2021. Accessed March 1, 2022. https://www.fda.gov/drugs/drug-safety-and-availability/fda-advises-drug-manufacturers-burkholderia-cepacia-complex-poses-contamination-risk-non-sterile
6. Torbeck L, Raccasi D, Guilfoyle DE, Friedman RL, Hussong D. *Burkholderia cepacia*: this decision is overdue. PDA J Pharm Sci Technol 2011;65:535–43. PMID:22293841 https://doi.org/10.5731/pdajpst.2011.00793
7. American Institute for Ultrasound in Medicine. Official statements: guidelines for cleaning and preparing external- and internal-use ultrasound transducers and equipment between patients as well as safe handling and use of ultrasound coupling gel. Laurel, MD: American Institute for Ultrasound in Medicine; 2021. Accessed March 1, 2022. https://www.aium.org/officialstatements/57
8. Kim JM, Ahn Y, LiPuma JJ, Hussong D, Cerniglia CE. Survival and susceptibility of *Burkholderia cepacia* complex in chlorohexidine gluconate and benzalkonium chloride. J Ind Microbiol Biotechnol 2015;42:905–13. PMID:25794566 https://doi.org/10.1007/s10295-015-1605-x
9. Ahn Y, Kim JM, Lee Y-J, et al. Effects of extended storage of chlorhexidine gluconate and benzalkonium chloride solutions on the viability of *Burkholderia cenocepacia*. J Microbiol Biotechnol 2017;27:2211–20. PMID:29032643 https://doi.org/10.4014/jmb.1706.06034

SARS-CoV-2 Serology and Self-Reported Infection Among Adults — National Health and Nutrition Examination Survey, United States, August 2021–May 2022

Lara J. Akinbami, MD[1]; Deanna Kruszon-Moran, MS[1]; Chia-Yih Wang, PhD[1]; Renee J. Storandt, MT, MSPH[1]; Jason Clark, MS[2]; Minsun K. Riddles, PhD[2]; Leyla K. Mohadjer, PhD[2]

CDC COVID-19 surveillance systems monitor SARS-CoV-2 antibody prevalence to collect information about asymptomatic, undiagnosed, and unreported disease using national convenience samples of blood donor data from commercial laboratories (*1*,*2*). However, nonrandom sampling of data from these systems could affect prevalence estimates (*1*–*3*). The National Health and Nutrition Examination Survey (NHANES) collects SARS-CoV-2 serology data among a sample of the general U.S. civilian population (*4*). In addition, NHANES collects self-reported COVID-19 vaccination and disease history, and its statistical sampling design is not based on health care access or blood donation. Therefore, NHANES data can be used to better quantify asymptomatic SARS-CoV-2 infection prevalence and seropositivity attained through infection without vaccination. Preliminary NHANES 2021–2022 results indicated that 41.6% of adults aged ≥18 years had serology indicative of past infection and that 43.7% of these adults, including 57.1% of non-Hispanic Black or African American (Black) adults, reported never having had COVID-19, possibly representing asymptomatic infection. In addition, 25.5% of adults whose serology indicated past infection reported never having received COVID-19 vaccination. Prevalences of seropositivity in the absence of vaccination were higher among younger adults and Black adults, reflecting the lower observed vaccination rates among these groups (*5*). These findings raise health equity concerns given the disparities observed in SARS-CoV-2 infection and COVID-19 vaccination. Results from NHANES 2021–2022 can guide ongoing efforts to achieve vaccine equity in COVID-19 primary vaccination series and booster dose coverage.*

The 2-year sample design of NHANES 2021–2022, includes 30 primary sampling units (usually a county) that are visited sequentially. In each 12-month data collection period, a nationally representative sample of 15 primary sampling units are visited. Preliminary data for adults aged ≥18 years from the first 10 primary sampling units (visited during periods of SARS-CoV-2 Delta [August–November 2021] and Omicron [December 2021–May 2022] variant predominance) (*6*) were analyzed as a convenience sample because data for all 15 primary sampling units were not yet available.† Analysis of preliminary unweighted NHANES data was conducted to examine SARS-CoV-2 antibody status in association with demographic characteristics and self-report of ever having had COVID-19 illness and having received ≥1 dose of COVID-19 vaccine. Sera were tested for anti-spike (anti-S) antibodies (which are produced in response to COVID-19 vaccination, SARS-CoV-2 infection, or both) using the Ortho VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack.§ Anti-nucleocapsid (anti-N) antibodies, which are produced only in response to SARS-CoV-2 infection, were assessed with the Total N Antibody Reagent Pack.¶ Seroprevalence was calculated by age, sex, race and Hispanic origin, and education in persons with combined anti-S–positive and anti-N–positive test results (infected, possibly vaccinated) and those with combined anti-S–positive and anti-N–negative test results (vaccinated, not infected). Among 1,581 participants with serology results, seven were excluded (including three with "don't know" or "refused" responses for self-reported COVID-19 history and four with a combined serology result of anti-S–negative and anti-N–positive**) leaving an analytic sample of 1,574. Analyses were performed using SAS software (version 9.4; SAS Institute). Final survey weights were unavailable at the time of this report because they are not calculated until the conclusion of the 2-year data collection cycle. Because NHANES uses a complex sampling design, simple random sampling assumptions for statistical testing are not appropriate. Therefore, statistical comparisons were not performed and references to differences among groups are based on observation only. The NHANES protocol was approved by the National Center for Health Statistics Ethics

* https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html (Accessed September 12, 2022).

† Public release of the full data set for 30 primary sampling units for the 2021–2022 NHANES cycle on the NHANES website occurs upon completion of data collection and processing. The 10 primary sampling unit data set used for this analysis is available in the National Center for Health Statistics Research Data Center. The locations of the primary sampling units included in NHANES are never publicly released to protect respondent confidentiality. https://www.cdc.gov/nchs/nhanes/participant/participant-confidentiality.htm

§ https://www.fda.gov/media/136967/download (Accessed September 5, 2022).

¶ https://www.fda.gov/media/151027/download (Accessed September 5, 2022).

** This pattern might reflect more recent infection given that anti-S antibody levels might rise more slowly than anti-N antibody levels after infection. However, these participants were still excluded for clarity of presentation. https://www.frontiersin.org/articles/10.3389/fmicb.2020.584251/full

Review Board and was conducted consistent with applicable federal law and CDC policy.[††]

During August 2021–May 2022, a total of 91.5% of adults included in NHANES had SARS-CoV-2 anti-S antibodies and 41.6% had anti-N antibodies. The percentage of adults with anti-S–positive, anti-N–positive serology (infected, possibly vaccinated) (Figure 1) was 41.6% overall and declined with age (59.7% among adults aged 18–29 years versus 30.2% among those aged ≥70 years); anti-S–positive, anti-N–positive prevalences were equivalent to anti-N–positive prevalences. The percentage of adults with this serologic profile also varied by race and Hispanic origin; 59.2% Hispanic, 45.9% Black, and 30.6% non-Hispanic White (White) adults were infected and possibly vaccinated. Percentages also declined with increasing education level, with 49.0% adults with less than high school education versus 37.5% of those with at least some college being infected and possibly vaccinated. In contrast, the percentage of adults with anti-S–positive, anti-N–negative results (vaccinated, not infected) (Figure 1) was 49.9% overall, increased with age (28.1% among adults aged 18–29 years versus 64.7% among those aged ≥70 years), was lower among Hispanic (35.3%) and Black adults (46.7%) and higher in White adults (58.9%), and lower in adults with less than high school education (42.5%) and higher in those with at least some college (55.4%).

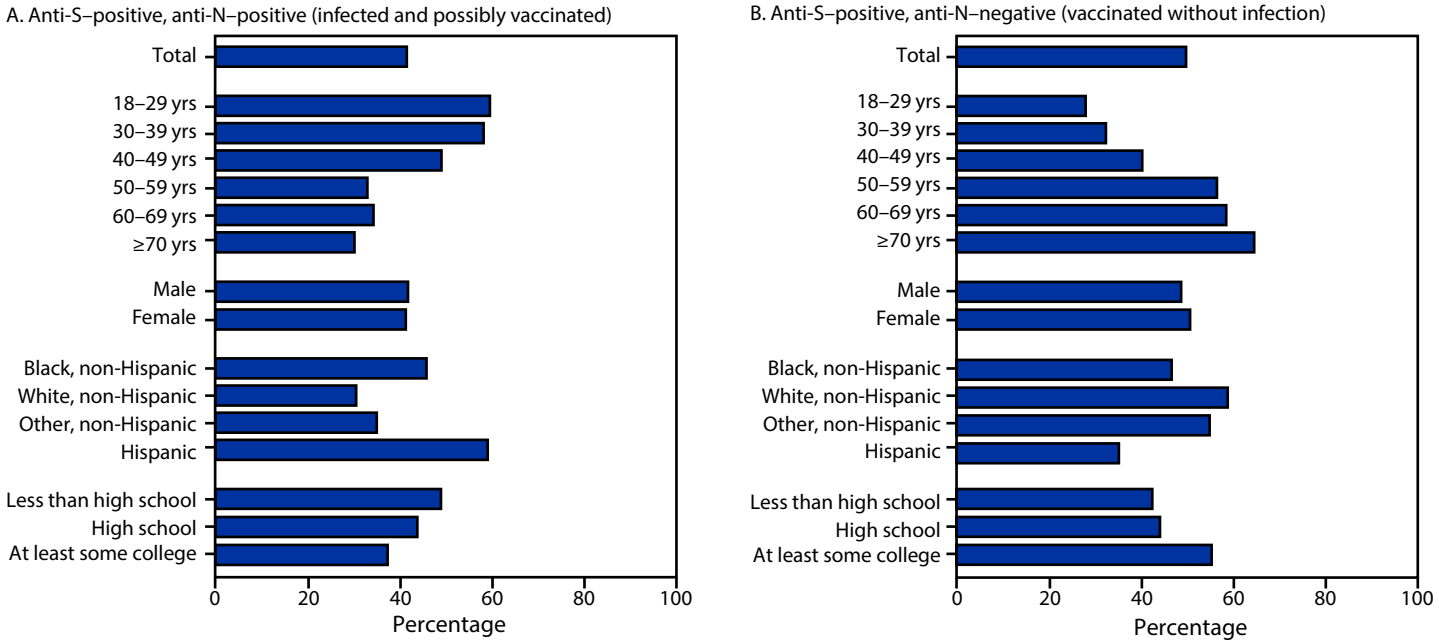
Among 655 adult participants with anti-S–positive, anti-N–positive serology results (indicating infection), 43.7% reported that they had never had COVID-19 (Figure 2). This percentage was higher among Black adults (57.1%) and adults with less than high school education (57.8%) than among adults of other racial and ethnic groups and among those with higher educational attainment. Among anti-S-positive, anti-N-positive adults, 25.5% reported never having received any COVID-19 vaccination (Figure 2). Percentages of respondents who reported not having been vaccinated decreased with age (31.6% among adults aged 18–29 years versus 18.8% among adults aged ≥70 years). A higher percentage of Black adults (31.3%) and a lower percentage of Hispanic adults (21.4%) with serologic evidence of infection reported never having received COVID-19 vaccination.

Discussion

Preliminary analyses of unweighted NHANES data during August 2021–May 2022, found that 41.6% of adults had SARS-CoV-2 anti-N antibodies, consistent with previous infection. CDC's nationwide commercial laboratory surveillance system estimated a higher anti-N seroprevalence (57.7%)

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

FIGURE 1. Combined SARS-CoV-2 anti-spike* and anti-nucleocapsid† antibody testing results among adults aged ≥18 years who were infected and possibly vaccinated (A) and those vaccinated without infection (B), by age group, sex, race and Hispanic origin,§ and education — National Health and Nutrition Examination Survey, United States, August 2021–May 2022¶



Abbreviations: anti-N = anti-nucleocapsid; anti-S = anti-spike.

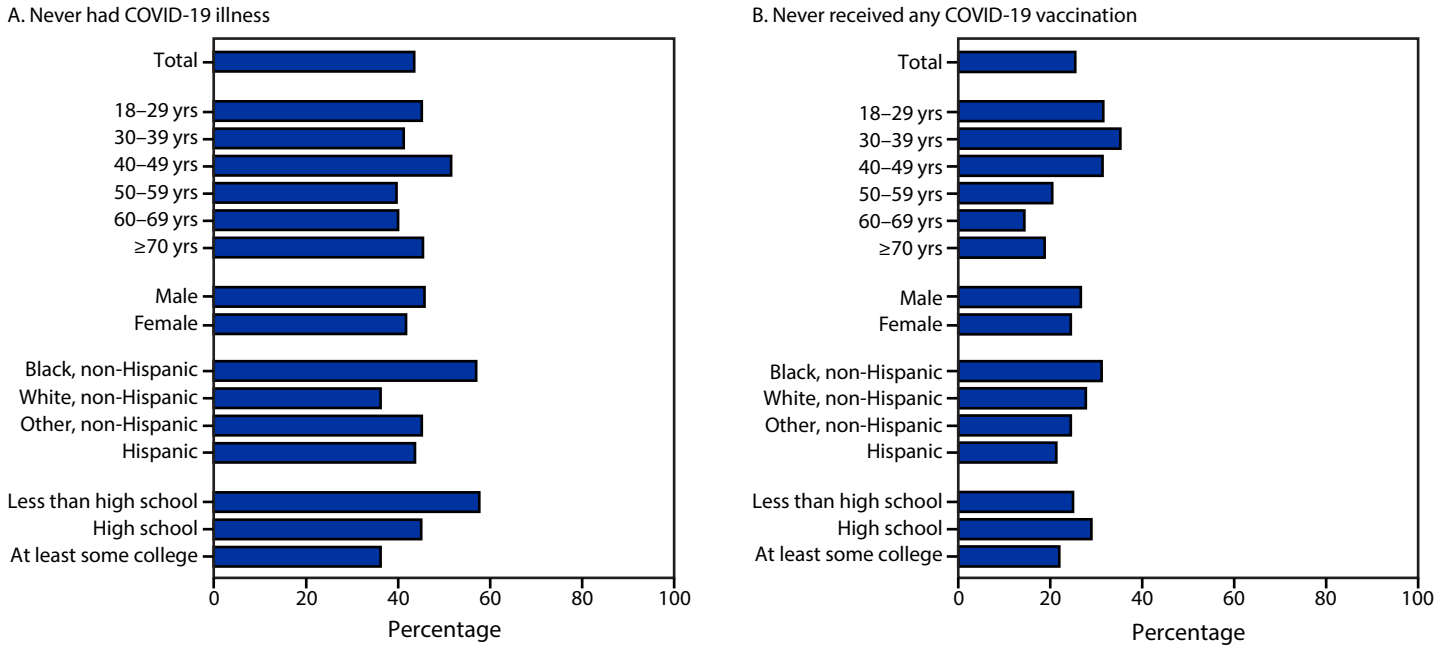
* Positivity for SARS-CoV-2 anti-S antibodies (previous infection, vaccination, or both).

† Positivity for SARS-CoV-2 anti-N antibodies (previous infection).

§ The category "other, non-Hispanic" includes non-Hispanic participants who reported being either American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, or multiple race.

¶ Preliminary sample = 1,574, unweighted data; information on education was missing for 63 adults.

FIGURE 2. Percentage of adults aged ≥18 years with both SARS-CoV-2 anti-spike* and anti-nucleocapsid† antibodies who reported never having had COVID-19 (A)§ or never having received any COVID-19 vaccine (B),¶ by age group, sex, race and Hispanic origin, and education — National Health and Nutrition Examination Survey, United States, August 2021–May 2022††**



* Positivity for SARS-CoV-2 anti-spike antibodies (previous infection, vaccination, or both).
† Positivity for SARS-CoV-2 anti-nucleocapsid antibodies (previous infection).
§ Negative response to the question, "Have you ever had COVID-19, or the illness caused by the Coronavirus Disease 2019?"
¶ Responded "zero doses" to the question, "How many doses of COVID-19 vaccine have you received? Please include booster shots and any additional doses."
** The category "other, non-Hispanic" includes non-Hispanic participants who reported being either American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, or multiple race.
†† Preliminary sample = 655, unweighted data; information on education was missing for 36 adults.

Summary

What is already known about this topic?

A high percentage of U.S. adults have antibodies to SARS-CoV-2, attained through vaccination, infection, or both.

What is added by this report?

During August 2021–May 2022, 41.6% of a convenience sample of adults had both anti-spike antibodies (indicating previous infection or vaccination) and anti-nucleocapsid antibodies (indicating previous infection only); 43.7% of these persons were possibly asymptomatically infected. Prevalence of serologic patterns consistent with vaccination without infection was lower among adults who were younger, Hispanic and non-Hispanic Black or African American adults, and persons with less education.

What are the implications for public health practice?

CDC recommends that everyone stay up to date with COVID-19 vaccination. These results can guide ongoing efforts that are needed to achieve equity in primary series vaccination and booster dose coverage.

among persons of all ages for the period January–February 2022 (*2*). This difference was not unexpected, given that the commercial laboratory estimate included sampling only after the more infectious SARS-CoV-2 Omicron wave (*6*) and included children, whose seroprevalence is higher than that of adults (*2*). However, patterns by age group and sex were similar between NHANES and commercial laboratory data sources, with declining anti-N antibody prevalence associated with increasing age and similar prevalences among males and females. Similar to the patterns in anti-N antibody seroprevalence by race and Hispanic origin observed in NHANES, CDC national blood donor surveillance data for persons aged ≥16 years through December 2021 also found higher anti-N seroprevalence in persons belonging to racial and ethnic minority groups (*1*,*2*). Antibody patterns in seropositive racial and ethnic minority adults were less likely to be consistent with vaccination and more likely to suggest past infection than those observed in seropositive White adults. These patterns are consistent with survey data indicating lower vaccination coverage and higher infection rates among Hispanic and Black adults than among White adults (*5*,*7*,*8*).

These findings confirm many patterns observed in other seroprevalence studies based on convenience samples that reflect increased vaccination rates among older persons and higher infection rates among younger persons (*2*). Currently, few U.S. data sources can provide data on antibody status and

self-reported COVID-19 illness and vaccination. Preliminary NHANES data indicated that 43.7% of adults with serologic evidence of SARS-CoV-2 infection reported never having had COVID-19 and approximately one half of Black adults and those with lower educational attainment were possibly asymptomatically infected. Younger adults and Black adults with unidentified infections might have been more likely to lack access to testing and to have unknowingly exposed others, resulting in disparities in community transmission. In this way, undiagnosed infections could have amplified disparities in infection rates and outcomes (*2*,*3*). Furthermore, estimates of infection based on antigen testing results are likely underestimated. In addition, among anti-S–positive, anti-N–positive (infected and possibly vaccinated) adults, a higher percentage of younger and Black adults did not report any COVID-19 vaccination, suggesting that higher percentages of these groups acquired antibodies through infection rather than vaccination. Conversely, the antibody pattern consistent with vaccination without infection (anti-S–positive, anti-N–negative) was lower among Hispanic and Black adults and those with less than high school education.

The findings in this report are subject to at least five limitations. First, self-reported COVID-19 vaccination and infection history could be subject to social desirability bias. Second, to provide preliminary results, data from the first 10 primary sampling units were analyzed before completion of the 2-year NHANES data collection cycle. Because final survey weights were unavailable, no adjustment was made for nonresponse and unequal probability of selection by age. In addition, the unweighted sample is subject to bias and does not represent a particular population. For example, the population aged ≥60 years is overrepresented in this sample. Third, among the 10 primary sampling units included, those visited earlier in the survey cycle, during the predominance of the Delta variant, are combined with those visited later during the Omicron-predominant period. Thus, the seroprevalence estimates during these two variant periods are averaged over the period represented by NHANES data. Fourth, the observed seroprevalence in these 10 primary sampling units might differ from that in the primary sampling units that were not yet visited. Finally, seroprevalence might further underestimate the cumulative number of vaccinations and infections: some persons with infection or vaccination might remain seronegative (*9*), and infection after vaccination might result in lower anti-N titers (*10*).

CDC recommends that everyone remain up-to-date with COVID-19 vaccination. Consistent with findings from other seroprevalence studies, preliminary NHANES 2021–2022 results raise health equity concerns given the disparities observed in SARS-CoV-2 infection and COVID-19 vaccination. These results can guide ongoing efforts to achieve vaccine equity in COVID-19 primary vaccination series and booster dose coverage.

Acknowledgments

Marisol Iniquez, Suruchi Mishra, Tony D. Nguyen, Cynthia Ogden, Ryne Paulose, and David Woodwell, Division of Health and Nutrition Examination Surveys, National Center for Health Statistics, CDC; Laurie Barker, Jan Drobeniuc, Claire Hartloge, Kathleen N. Ly, Lili Punkova, Alexandra Tejada, Division of Viral Hepatitis, National Center for HIV, Viral Hepatitis, STD, and TB Prevention, CDC; Melissa Briggs Hagen, Jefferson Jones, National Center for Immunization and Respiratory Diseases, CDC.

Corresponding author: Lara J. Akinbami, lea8@cdc.gov.

[1]Division of Health and Nutrition Examination Surveys, National Center for Health Statistics, CDC; [2]Westat Corporation, Rockville, Maryland.

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. Jones JM, Stone M, Sulaeman H, et al. Estimated US infection- and vaccine-induced SARS-CoV-2 seroprevalence based on blood donations, July 2020–May 2021. JAMA 2021;326:1400–9. PMID:34473201 https://doi.org/10.1001/jama.2021.15161
2. CDC. COVID data tracker. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. Accessed August 25, 2022. https://covid.cdc.gov/covid-data-tracker/#datatracker-home
3. Bajema KL, Wiegand RE, Cuffe K, et al. Estimated SARS-CoV-2 seroprevalence in the US as of September 2020. JAMA Intern Med 2021;181:450–60. PMID:33231628 https://doi.org/10.1001/jamainternmed.2020.7976
4. National Center for Health Statistics. National Health and Nutrition Examination Survey: NHANES 2021–2022. Atlanta, GA: US Department of Health and Human Services, CDC; 2022. Accessed August 25, 2022. https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/default.aspx?BeginYear=2021
5. Siegel M, Critchfield-Jain I, Boykin M, et al. Racial/ethnic disparities in state-level COVID-19 vaccination rates and their association with structural racism. J Racial Ethn Health Disparities 2022;9:2361–74. PMID:34713336 https://doi.org/10.1007/s40615-021-01173-7
6. Lambrou AS, Shirk P, Steele MK, et al.; Strain Surveillance and Emerging Variants Bioinformatic Working Group; Strain Surveillance and Emerging Variants NS3 Working Group. Genomic surveillance for SARS-CoV-2 variants: predominance of the Delta (B.1.617.2) and Omicron (B.1.1.529) variants—United States, June 2021–January 2022. MMWR Morb Mortal Wkly Rep 2022;71:206–11. PMID:35143464 https://doi.org/10.15585/mmwr.mm7106a4
7. Kriss JL, Hung MC, Srivastav A, et al. COVID-19 vaccination coverage, by race and ethnicity – National Immunization Survey Adult COVID Module, United States, December 2020–November 2021. MMWR Morb Mortal Wkly Rep 2022;71:757–63. PMID:35679179 https://doi.org/10.15585/mmwr.mm7123a2
8. Zhang W, Wu YY, Wu B. Racial/ethnic disparities in getting COVID-19 vaccine: do age, gender, and education matter? Health Equity 2022;6:500–7. PMID:36186620 https://doi.org/10.1089/heq.2022.0025
9. Petersen LR, Sami S, Vuong N, et al. Lack of antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a large cohort of previously infected persons. Clin Infect Dis 2021;73:e3066–73. PMID:33147319 https://doi.org/10.1093/cid/ciaa1685
10. Follmann D, Janes HE, Buhule OD, et al. Antinucleocapsid antibodies after SARS-CoV-2 infection in the blinded phase of the randomized, placebo-controlled mRNA-1273 COVID-19 vaccine efficacy clinical trial. Ann Intern Med 2022;175:1258–65. PMID:35785530 https://doi.org/10.7326/M22-1300

Effectiveness of Bivalent mRNA Vaccines in Preventing Symptomatic SARS-CoV-2 Infection — Increasing Community Access to Testing Program, United States, September–November 2022

Ruth Link-Gelles, PhD[1]; Allison Avrich Ciesla, PhD[1,2]; Katherine E. Fleming-Dutra, MD[1]; Zachary R. Smith, MA[3]; Amadea Britton, MD[1]; Ryan E. Wiegand, PhD[1]; Joseph D. Miller, PhD[3]; Emma K. Accorsi, PhD[1,4]; Stephanie J. Schrag, DPhil[1]; Jennifer R. Verani, MD[1]; Nong Shang, PhD[1]; Gordana Derado, PhD[1]; Tamara Pilishvili, PhD[1]

On November 22, 2022, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

On September 1, 2022, bivalent COVID-19 mRNA vaccines, composed of components from the SARS-CoV-2 ancestral and Omicron BA.4/BA.5 strains, were recommended by the Advisory Committee on Immunization Practices (ACIP) to address reduced effectiveness of COVID-19 monovalent vaccines during SARS-CoV-2 Omicron variant predominance (*1*). Initial recommendations included persons aged ≥12 years (Pfizer-BioNTech) and ≥18 years (Moderna) who had completed at least a primary series of any Food and Drug Administration–authorized or –approved monovalent vaccine ≥2 months earlier (*1*). On October 12, 2022, the recommendation was expanded to include children aged 5–11 years. At the time of recommendation, immunogenicity data were available from clinical trials of bivalent vaccines composed of ancestral and Omicron BA.1 strains; however, no clinical efficacy data were available. In this study, effectiveness of the bivalent (Omicron BA.4/BA.5–containing) booster formulation against symptomatic SARS-CoV-2 infection was examined using data from the Increasing Community Access to Testing (ICATT) national SARS-CoV-2 testing program.* During September 14–November 11, 2022, a total of 360,626 nucleic acid amplification tests (NAATs) performed at 9,995 retail pharmacies for adults aged ≥18 years, who reported symptoms consistent with COVID-19 at the time of testing and no immunocompromising conditions, were included in the analysis. Relative vaccine effectiveness (rVE) of a bivalent booster dose compared with that of ≥2 monovalent vaccine doses among persons for whom 2–3 months and ≥8 months had elapsed since last monovalent dose was 30% and 56% among persons aged 18–49 years, 31% and 48% among persons aged 50–64 years, and 28% and 43% among persons aged ≥65 years, respectively. Bivalent mRNA booster doses provide additional protection against symptomatic SARS-CoV-2 in immunocompetent persons who previously received monovalent vaccine only, with relative benefits increasing with time since receipt of the most recent monovalent vaccine dose. Staying up to date with COVID-19 vaccination, including getting a bivalent booster dose when eligible, is critical to maximizing protection against COVID-19 (*1*).

The ICATT program was designed to increase access to COVID-19 testing in areas with high social vulnerability† through contracts with retail pharmacy chains to provide SARS-CoV-2 testing at no cost to the recipient at selected sites nationwide (*2*). ICATT vaccine effectiveness (VE) methods have been described previously (*3*). Briefly, at test registration, adults report their vaccination history§ and information on current COVID-19 symptoms, previous SARS-CoV-2 infection, and underlying medical conditions. Adults receiving testing at participating sites during September 14–November 11, 2022, (when Omicron variant BA.4/BA.5 lineages and their sublineages predominated¶) who reported one or more COVID-19–compatible symptoms were included; case-patients were persons who received a positive rapid or laboratory-based NAAT result; control-patients were those who received a negative NAAT result. Tests from persons who reported an immunocompromising condition (*4*), who received non-mRNA COVID-19 vaccines, who had received only a single monovalent mRNA vaccine dose or >4 monovalent mRNA doses, or who had received their last monovalent dose <2 months before the SARS-CoV-2 test were excluded from analyses.** In addition, tests from persons who reported a positive result during the preceding 90 days†† were excluded

* https://www.cdc.gov/icatt/index.html

† Social vulnerability index (SVI) is a tool that uses U.S. Census Bureau data on 16 social factors to rank social vulnerability by U.S. Census Bureau tract. The scale is from 0 to 1; higher SVIs represent more vulnerable communities. Tests with missing SVI data (<1% of total) were excluded from all analyses. https://www.atsdr.cdc.gov/placeandhealth/svi/data_documentation_download.html

§ Only month and year of receipt were reported for each vaccine dose from some participating pharmacies; therefore, the number of months between a vaccine dose and testing is a whole number calculated as the difference between the month and year of testing and the month and year of the vaccine dose. Persons reporting an mRNA booster dose on or after September 1, 2022, were assumed to have received a bivalent dose because no monovalent mRNA doses were authorized for use as booster doses at that time. For doses received in the same month or the month before SARS-CoV-2 testing, an additional question was asked to specify whether the dose was received ≥2 weeks before testing, and only doses received ≥2 weeks before testing were included.

¶ https://covid.cdc.gov/covid-data-tracker/#variant-proportions

** Test registration forms asked persons to report if they had an immunocompromising condition and provided the following examples: immunocompromising medications, solid organ or blood stem cell transplant, HIV, or other immunocompromising conditions.

†† https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/testing.html

to avoid analyzing repeated tests for the same illness episode or reinfections within a relatively short time frame. Absolute VE (aVE) was calculated by comparing the odds of receipt of a bivalent booster dose (after 2, 3, or 4 monovalent vaccine doses) to being unvaccinated (zero doses of any COVID-19 vaccine) among case- and control-patients. rVE was calculated by comparing the odds of receiving a bivalent booster dose (after 2, 3, or 4 monovalent doses) versus not receiving a bivalent booster dose (but receiving 2, 3, or 4 monovalent doses). To explore how waning of protection after receipt of the most recent monovalent vaccine dose influenced the measured relative effectiveness of a subsequent bivalent booster dose, rVE of a bivalent booster dose was calculated by interval since receipt of the most recent monovalent vaccine dose among those who had not received a bivalent booster (2–3 months, 4–5 months, 6–7 months, and ≥8 months). Odds ratios (ORs) were calculated using multivariable logistic regression[§§]; VE was calculated as (1 − OR) x 100. Analyses were conducted using R software (version 4.1.2; R Foundation). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[¶¶]

Among persons aged ≥18 years reporting COVID-19–compatible symptoms, 360,626 tests were included; of these, 121,687 (34%) persons received positive test results (Table 1). Among these case-patients, 28,874 (24%) reported being unvaccinated, 87,013 (72%) had received 2, 3, or 4 monovalent vaccine doses but no bivalent booster dose, and 5,800 (5%) had received a bivalent booster dose. Among 238,939 control-patients who received negative test results, 72,010 (30%) reported being unvaccinated, 150,455 (63%) had received 2, 3, or 4 monovalent vaccine doses but no bivalent booster dose, and 16,474 (7%) had received a bivalent booster dose. Median interval between receipt of the bivalent booster dose and SARS-CoV-2 testing was 1 month (range = 0–2 months) and did not vary by case status. Self-reported infection >90 days before the current test was more common among persons who received a negative test result (43%) than among those who received a positive test result (22%).

aVE of a bivalent booster dose received after ≥2 monovalent doses (compared with being unvaccinated) was similar among persons aged 50–64 years (28%) and ≥65 years (22%) but varied somewhat by number of previous monovalent vaccine doses (Table 2). Among adults aged 18–49 years, aVE after ≥2 monovalent doses (43%) was higher than that for older age groups and did not vary among those who received 2 or 3 previous monovalent vaccine doses.

Among persons who received ≥2 monovalent vaccine doses, rVE increased with time since the most recent monovalent vaccine dose in all age groups (Table 3). At 2–3 months and ≥8 months after receipt of the most recent monovalent dose, rVE of a bivalent mRNA COVID-19 vaccine dose was 30% and 56% among persons aged 18–49 years, 31% and 48% among persons aged 50–64 years, and 28% and 43% among persons aged ≥65 years, respectively.

Discussion

Among symptomatic adults who received testing for SARS-CoV-2 infection at pharmacies nationwide during September 14–November 11, 2022, bivalent mRNA vaccines provided additional protection against infection compared with previous vaccination with 2, 3, or 4 monovalent vaccines alone. These are the first published estimates of VE for newly authorized bivalent mRNA booster vaccines. In this study, relative benefits of a bivalent booster compared with monovalent vaccine doses alone increased with time since receipt of last monovalent dose.

Postauthorization immunogenicity studies have shown similar neutralizing antibody titers to BA.4/BA.5 after receipt of either a monovalent or BA.4/BA.5–containing bivalent vaccine as a fourth dose (*5*,*6*); however, immunogenicity studies are not generally designed to measure clinical impact. Findings from this real-world VE study indicate that the bivalent formulations authorized in the United States provide additional protection when administered to persons who previously received 2, 3, or 4 doses of monovalent mRNA vaccines.

Waning VE with time since monovalent vaccine receipt has been observed during the Omicron-predominant period, with more rapid waning during the period when Omicron BA.4/BA.5 lineages predominated.[***] Results from this study show that bivalent boosters provide protection against symptomatic SARS-CoV-2 infection during circulation of BA.4/BA.5 and their sublineages and restore protection observed to wane after monovalent vaccine receipt, as demonstrated by increased rVE with longer time since the most recent monovalent dose. Most tests (81%) in this study were conducted during a period of BA.4/BA.5 predominance. Results limited to the period of BA.4/BA.5 predominance were not meaningfully different

[§§] Multivariable logistic regression models were controlled for age, gender, race, ethnicity, SVI of the testing location, underlying conditions (presence versus absence), state of residence of person tested, pharmacy chain conducting the test, local incidence (cases per 100,000 by site zip code during the 7 days preceding test date), and date of testing. The following underlying conditions were included on the survey: heart conditions, high blood pressure, overweight or obesity, diabetes, current or former smoker, kidney failure or end stage renal disease, cirrhosis of the liver, chronic lung disease (such as chronic obstructive pulmonary disease, moderate to severe asthma, cystic fibrosis, or pulmonary embolism).

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

[***] https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-09-01/04-COVID-Link-Gelles-508.pdf

TABLE 1. Characteristics of patients with SARS-CoV-2 tests conducted at national pharmacy testing program locations (N = 360,626) — Increasing Community Access to Testing program, United States, September–November 2022

Characteristic	SARS-CoV-2 test result (col. %)		Number and type of mRNA COVID-19 vaccine doses received* before test date, no. (row %)					
	Positive (case-patients)	Negative (control-patients)	Unvaccinated	2 monovalent doses	3 monovalent doses	4 monovalent doses†	≥2 monovalent doses	≥2 monovalent plus bivalent booster
SARS-CoV-2 status§								
Positive (case-patients)	121,687 (100)	0 (—)	28,874 (24)	36,429 (30)	41,409 (34)	9,175 (8)	87,013 (72)	5,800 (5)
Negative (control-patients)	0 (—)	238,939 (100)	72,010 (30)	72,352 (30)	65,122 (27)	12,981 (5)	150,455 (63)	16,474 (7)
Time frame of test								
Sep 14–Oct 29, 2022	98,729 (81)	194,150 (81)	81,876 (28)	88,392 (30)	88,768 (30)	19,425 (7)	196,585 (67)	14,418 (5)
Oct 30–Nov 11, 2022	22,958 (19)	44,789 (19)	19,008 (28)	20,389 (30)	17,763 (26)	2,731 (4)	40,883 (60)	7,856 (12)
Age group, yrs								
18–49	75,012 (62)	171,125 (72)	81,296 (33)	82,488 (34)	71,881 (29)	0 (—)	154,369 (63)	10,472 (4)
50–64	29,896 (25)	43,179 (18)	14,366 (20)	19,688 (27)	22,580 (31)	11,055 (15)	53,323 (73)	5,386 (7)
≥65	16,779 (14)	24,635 (10)	5,222 (13)	6,605 (16)	12,070 (29)	11,101 (27)	29,776 (72)	6,416 (15)
Sex								
Female	68,487 (56)	150,790 (63)	57,988 (26)	66,662 (30)	66,983 (31)	13,661 (6)	147,306 (67)	13,983 (6)
Male	53,029 (44)	87,644 (37)	42,818 (30)	41,915 (30)	39,245 (28)	8,486 (6)	89,646 (64)	8,209 (6)
Other	171 (0.1)	505 (0.2)	78 (12)	204 (30)	303 (45)	9 (1)	516 (76)	82 (12)
Race and ethnicity								
Black or African American, non-Hispanic	15,881 (13)	39,592 (17)	20,759 (37)	19,729 (36)	11,190 (20)	2,321 (4)	33,240 (60)	1,474 (3)
Hispanic or Latino	22,694 (19)	48,109 (20)	22,074 (31)	25,281 (36)	19,408 (27)	2,141 (3)	46,830 (66)	1,899 (3)
Other, non-Hispanic	14,583 (12)	25,453 (11)	7,796 (19)	10,552 (26)	16,811 (42)	2,240 (6)	29,603 (74)	2,637 (7)
White, non-Hispanic	60,315 (50)	110,191 (46)	40,756 (24)	46,158 (27)	53,483 (31)	14,654 (9)	114,295 (67)	15,455 (9)
Unknown	8,214 (7)	15,594 (7)	9,499 (40)	7,061 (30)	5,639 (24)	800 (3)	13,500 (57)	809 (3)
HHS testing site region¶								
Region 1	8,705 (7)	15,181 (6)	5,088 (21)	5,653 (24)	9,005 (38)	1,943 (8)	16,601 (70)	2,197 (9)
Region 2	13,533 (11)	19,672 (8)	7,698 (23)	8,918 (27)	12,151 (37)	2,199 (7)	23,268 (70)	2,239 (7)
Region 3	9,802 (8)	17,519 (7)	7,090 (26)	7,618 (28)	8,564 (31)	1,957 (7)	18,139 (66)	2,092 (8)
Region 4	24,059 (20)	57,781 (24)	28,092 (34)	26,615 (33)	18,942 (23)	4,525 (6)	50,082 (61)	3,666 (4)
Region 5	25,382 (21)	44,689 (19)	19,072 (27)	20,873 (30)	20,740 (30)	4,403 (6)	46,016 (66)	4,983 (7)
Region 6	12,601 (10)	31,708 (13)	14,127 (32)	15,290 (35)	10,892 (25)	2,140 (5)	28,322 (64)	1,860 (4)
Region 7	3,451 (3)	6,715 (3)	3,004 (30)	3,318 (33)	2,735 (27)	537 (5)	6,590 (65)	572 (6)
Region 8	3,060 (3)	5,423 (2)	1,485 (18)	2,861 (34)	2,973 (35)	527 (6)	6,361 (75)	637 (8)
Region 9	18,771 (15)	35,126 (15)	14,080 (26)	15,321 (28)	17,755 (33)	3,433 (6)	36,509 (68)	3,308 (6)
Region 10	2,323 (2)	5,125 (2)	1,148 (15)	2,314 (31)	2,774 (37)	492 (7)	5,580 (75)	720 (10)
SVI, ** **mean (SD)**	0.5 (0.3)	0.5 (0.3)	0.6 (0.3)	0.5 (0.3)	0.5 (0.3)	0.5 (0.3)	0.5 (0.3)	0.5 (0.3)
History of self-reported SARS-CoV-2 positive test result								
None	95,378 (78)	136,420 (57)	59,380 (26)	63,497 (27)	73,538 (32)	18,420 (8)	155,455 (67)	16,963 (7)
Positive >90 days before current test	26,309 (22)	102,519 (43)	41,504 (32)	45,284 (35)	32,993 (26)	3,736 (3)	82,013 (64)	5,311 (4)

See table footnotes on the next page.

from the results shown, which include data from the period when BA.4/BA.5 sublineages (including BA.4.6, BA.5.2.6, BF.7, BQ.1, and BQ.1.1) predominated.

This study evaluated aVE and rVE by number of previous monovalent doses received and generally found similar additional benefit of the bivalent vaccine regardless of the number of previous monovalent vaccine doses received, when controlling for time since receipt of the last monovalent dose. These findings support the current COVID-19 vaccination policy recommending a bivalent booster dose for adults who have completed at least a primary mRNA vaccination series, irrespective of the number of monovalent doses previously received.

In the United States, >90% of adults have received ≥1 COVID-19 vaccine dose.††† Therefore, aVE should be interpreted with caution because unvaccinated persons might have different behaviors or a fundamentally different risk for acquiring COVID-19 compared with vaccinated persons. aVE in this study appeared lower in persons aged ≥50 years who received 3 or 4 monovalent doses before a bivalent booster dose compared with those who received only 2 monovalent doses before a bivalent booster dose; this might be because of differential rates of previous infection or differences in behaviors in those who had not previously received a booster dose

††† https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-people-onedose-pop-pop18

TABLE 1. (*Continued*) Characteristics of patients with SARS-CoV-2 tests conducted at national pharmacy testing program locations (N = 360,626) — Increasing Community Access to Testing program, United States, September–November 2022

Characteristic	SARS-CoV-2 test result (col. %)		Number and type of mRNA COVID-19 vaccine doses received* before test date, no. (row %)					
	Positive (case-patients)	Negative (control-patients)	Unvaccinated	2 monovalent doses	3 monovalent doses	4 monovalent doses†	≥2 monovalent doses	≥2 monovalent plus bivalent booster
SARS-CoV-2 test type								
Rapid NAAT††	39,729 (33)	84,511 (35)	33,055 (27)	44,280 (36)	34,218 (28)	6,281 (5)	84,779 (68)	6,406 (5)
Laboratory-based NAAT§§	81,958 (67)	154,428 (65)	67,829 (29)	64,501 (27)	72,313 (31)	15,875 (7)	152,689 (65)	15,868 (7)
Self-reported one or more chronic underlying condition¶¶								
No	94,236 (77)	187,842 (79)	85,207 (30)	86,234 (31)	81,463 (29)	13,581 (5)	181,278 (64)	15,593 (6)
Yes	27,451 (23)	51,097 (21)	15,677 (20)	22,547 (29)	25,068 (32)	8,575 (11)	56,190 (72)	6,681 (9)
For persons who received only monovalent mRNA doses, no. of mos since most recent dose								
2–3	3,718 (3)	7,540 (3)	0 (—)	1,966 (17)	3,446 (31)	5,846 (52)	11,258 (100)	0 (—)
4–5	7,188 (6)	12,284 (6)	0 (—)	2,907 (15)	5,517 (28)	11,048 (57)	19,472 (100)	0 (—)
6–7	6,110 (5)	11,396 (5)	0 (—)	4,002 (23)	9,061 (52)	4,443 (25)	17,506 (100)	0 (—)
≥8	69,592 (60)	118,304 (53)	0 (—)	99,906 (53)	87,943 (47)	47 (0.03)	187,896 (100)	0 (—)

Abbreviations: HHS = U.S. Department of Health and Human Services; ICATT = Increasing Community Access to Testing program; NAAT = nucleic acid amplification test; SVI = social vulnerability index.

* Only month and year of receipt were reported for each vaccination dose from some participating pharmacies; therefore, the number of months between a vaccine dose and testing is a whole number calculated as the difference between the month and year of testing and the month and year of the vaccine dose. Persons reporting an mRNA booster dose on or after September 1, 2022, were assumed to have received a bivalent dose because no monovalent mRNA doses were authorized for use as booster doses at that time. For doses received in the same month or the month before SARS-CoV-2 testing, an additional question was asked to specify whether the dose was received ≥2 weeks before testing, and only doses received ≥2 weeks before testing were included.

† Persons aged <50 years without moderate or severe immunocompromise were not eligible for a fourth monovalent (second booster) dose. Because of timing of authorization, not enough persons ≥8 months from the fourth dose (second monovalent booster) were available to include in analyses.

§ SARS-CoV-2 status after the most recent vaccine dose received.

¶ Regions defined by HHS and include only states and territories with ICATT sites. U.S. Virgin Islands (Region 2) and Federated States of Micronesia, Guam, Marshall Islands, Northern Mariana Islands, Palau, and American Samoa (Region 9) were not included because they did not have pharmacies participating in ICATT. https://www.hhs.gov/about/agencies/iea/regional-offices/index.html

** SVI is a tool that uses U.S. Census Bureau data on 16 social factors to rank social vulnerability by U.S. Census Bureau tract. The scale is from 0 to 1; higher SVIs represent more vulnerable communities. Tests with missing SVI data (<1% of total) were excluded from all analyses. https://www.atsdr.cdc.gov/placeandhealth/svi/data_documentation_download.html

†† Rapid NAAT was performed on-site on self-collected nasal swabs using ID Now (Abbott Diagnostics Scarborough Inc.) and Accula (Thermo Fisher Scientific).

§§ Laboratory-based NAAT was performed on self-collected nasal swabs at contracted laboratories using a variety of testing platforms.

¶¶ Underlying conditions included on the survey were heart conditions, high blood pressure, overweight or obesity, diabetes, current or former smoker, kidney failure or end stage renal disease, cirrhosis of the liver, chronic lung disease (such as chronic obstructive pulmonary disease, moderate to severe asthma, cystic fibrosis, or pulmonary embolism).

TABLE 2. Absolute vaccine effectiveness against symptomatic SARS-CoV-2 infection for a single bivalent mRNA COVID-19 booster dose received after 2, 3, or 4 doses of monovalent vaccine compared with no doses, by age group and number of monovalent COVID-19 vaccine doses — Increasing Community Access to Testing program, United States, September–November 2022

Age group, yrs	Absolute VE (95% CI), by no. of monovalent doses received before the bivalent vaccine dose			
	2 doses	3 doses	4 doses*	≥2 doses
18–49	41 (31–49)	43 (39–46)	NA	43 (39–46)
50–64	50 (35–61)	25 (17–33)	28 (20–34)	28 (22–33)
≥65	32 (9–49)	19 (8–29)	23 (15–30)	22 (15–29)

Abbreviations: NA = not applicable; VE = vaccine effectiveness.

* Persons aged <50 years without moderate or severe immunocompromise were not eligible for a fourth monovalent (second booster) dose.

compared with those who remained up to date with previous booster dose recommendations.

The findings in this study are subject to at least six limitations. First, vaccination status, previous infection history, and underlying medical conditions were self-reported and might be subject to recall bias. In particular, if previous infection provides protection against repeat infection, then VE estimates in this study would likely be biased toward the null, because self-reported previous infection differed by vaccination status, and statistical power was not sufficient to stratify VE estimates by presence of previous infection. In addition, previous infection might have been underreported (*7*). Second, acceptance of bivalent booster doses to date has been low (approximately 10% of persons aged ≥5 years as of November 15, 2022),§§§ which could bias the results if persons getting vaccinated early are systematically different from those vaccinated later. Third, important data including SARS-CoV-2 exposure risk and mask use were not collected, which might result in residual confounding. Fourth, the circulating variants in the United States continue to change, and results of this study might not be generalizable to future variants. Fifth, tests used in this study were collected predominantly (although not exclusively) in areas with higher social vulnerability; therefore, data might

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

Summary

What is already known about this topic?

Monovalent mRNA COVID-19 vaccines were less effective against symptomatic infection during the period of SARS-CoV-2 Omicron variant predominance.

What is added by this report?

In this study of vaccine effectiveness of the U.S.-authorized bivalent mRNA booster formulations, bivalent boosters provided significant additional protection against symptomatic SARS-CoV-2 infection in persons who had previously received 2, 3, or 4 monovalent vaccine doses. Due to waning immunity of monovalent doses, the benefit of the bivalent booster increased with time since receipt of the most recent monovalent vaccine dose.

What are the implications for public health practice?

All persons should stay up to date with recommended COVID-19 vaccinations, including bivalent booster doses for eligible persons.

TABLE 3. Relative vaccine effectiveness of a single bivalent mRNA COVID-19 booster dose against symptomatic SARS-CoV-2 infection* received after 2, 3, or 4 monovalent vaccine doses, by age group, number of monovalent COVID-19 vaccine doses received, and interval since last monovalent dose — Increasing Community Access to Testing program, United States, September–November 2022

Age group, yrs/mos since receipt of most recent monovalent dose	Relative VE (95% CI), by no. of monovalent doses received†			
	2 doses	3 doses	4 doses§	≥2 doses
18–49				
2–3	45 (31–56)	24 (14–33)	NA	30 (22–37)
4–5	47 (35–57)	41 (35–47)	NA	43 (38–48)
6–7	42 (30–52)	47 (42–52)	NA	46 (41–50)
≥8	53 (45–60)	58 (56–61)	NA	56 (53–58)
50–64				
2–3	—	15 (–4–31)	33 (24–41)	31 (24–38)
4–5	44 (18–62)	31 (18–42)	36 (29–43)	36 (30–41)
6–7	46 (22–62)	36 (25–45)	40 (32–47)	38 (32–43)
≥8	61 (49–70)	51 (45–55)	NA	48 (45–51)
≥65				
2–3	—	—	32 (23–40)	28 (19–35)
4–5	—	21 (1–36)	36 (29–42)	33 (27–39)
6–7	—	14 (–6–30)	40 (33–46)	36 (29–41)
≥8	45 (27–58)	42 (35–48)	NA	43 (39–46)

Abbreviations: NA = not applicable; VE = vaccine effectiveness.

* VE estimates with 95% CIs >50 percentage points are not shown because of imprecision.

† Total number of monovalent doses received for persons who did and did not receive a bivalent booster dose.

§ Persons aged <50 years without moderate or severe immunocompromise were not eligible for a fourth monovalent (second booster) dose. Because of timing of authorization, not enough persons ≥8 months from the fourth dose (second booster) were available to include in analyses.

not be fully representative of the broader U.S. population. Finally, these results might be susceptible to bias because of differences in testing behaviors between vaccinated and unvaccinated persons.

In this study of immunocompetent persons tested at ICATT locations, bivalent booster doses provided significant additional protection against symptomatic SARS-CoV-2 infection during a period when Omicron variant BA.4/BA.5 lineages and their sublineages predominated. All persons should stay up to date with recommended COVID-19 vaccines, including bivalent booster doses, if it has been ≥2 months since their last monovalent vaccine dose (*1*).

Corresponding author: Ruth Link-Gelles, media@cdc.gov.

[1]National Center for Immunization and Respiratory Diseases, CDC; [2]Eagle Health Analytics, San Antonio, Texas; [3]Center for Preparedness and Response, CDC; [4]Epidemic Intelligence Service, CDC.

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

References

1. Rosenblum HG, Wallace M, Godfrey M, et al. Interim recommendations from the Advisory Committee on Immunization Practices for the use of bivalent booster doses of COVID-19 vaccines—United States, October 2022. MMWR Morb Mortal Wkly Rep 2022;71:1436–41. PMID:36355612 https://doi.org/10.15585/mmwr.mm7145a2
2. Miller MF, Shi M, Motsinger-Reif A, Weinberg CR, Miller JD, Nichols E. Community-based testing sites for SARS-CoV-2—United States, March 2020–November 2021. MMWR Morb Mortal Wkly Rep 2021;70:1706–11. PMID:34882655 https://doi.org/10.15585/mmwr.mm7049a3
3. Fleming-Dutra KE, Britton A, Shang N, et al. Association of prior BNT162b2 COVID-19 vaccination with symptomatic SARS-CoV-2 infection in children and adolescents during Omicron predominance. JAMA 2022;327:2210–9. PMID:35560036 https://doi.org/10.1001/jama.2022.7493
4. Britton A, Embi PJ, Levy ME, et al. Effectiveness of COVID-19 mRNA vaccines against COVID-19–associated hospitalizations among immunocompromised adults during SARS-CoV-2 Omicron predominance—VISION Network, 10 states, December 2021–August 2022. MMWR Morb Mortal Wkly Rep 2022;71:1335–42. PMID:36264840 https://doi.org/10.15585/mmwr.mm7142a4
5. Wang Q, Bowen A, Valdez R, Gherasim C. Antibody responses to Omicron BA.4/BA.5 bivalent mRNA vaccine booster shot. bioRxiv [Preprint posted online October 24, 2022]. https://www.biorxiv.org/content/10.1101/2022.10.22.513349v1
6. Collier A, Miller J, Hachmann N. Immunogenicity of the BA.5 bivalent mRNA vaccine boosters. bioRxiv [Preprint posted online October 25, 2022]. https://www.biorxiv.org/content/10.1101/2022.10.24.513619v1
7. Clarke KE, Jones JM, Deng Y, et al. Seroprevalence of infection-induced SARS-CoV-2 antibodies—United States, September 2021–February 2022. MMWR Morb Mortal Wkly Rep 2022;71:606-8. PMID:35482574 http://dx.doi.org/10.15585/mmwr.mm7117e3

Paxlovid Associated with Decreased Hospitalization Rate Among Adults with COVID-19 — United States, April–September 2022

Melisa M. Shah, MD[1]; Brendan Joyce[2]; Ian D. Plumb, MBBS[1]; Sam Sahakian, MS[2]; Leora R. Feldstein, PhD[1]; Eric Barkley[2]; Mason Paccione, MSP[2]; Joseph Deckert, PhD[2]; Danessa Sandmann, MPH[2]; Jacqueline L. Gerhart, MD[2,*]; Melissa Briggs Hagen, MD[1,*]

On November 22, 2022, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

Nirmatrelvir-ritonavir (Paxlovid), an oral antiviral treatment, is authorized for adults with mild-to-moderate COVID-19 who are at increased risk for progression to severe illness. However, real-world evidence on the benefit of Paxlovid, according to vaccination status, age group, and underlying health conditions, is limited. To examine the benefit of Paxlovid in adults aged ≥18 years in the United States, a large electronic health record (EHR) data set (Cosmos[†]) was analyzed to assess the association between receiving a prescription for Paxlovid and hospitalization with a COVID-19 diagnosis in the ensuing 30 days. A Cox proportional hazards model was used to estimate this association, adjusted for demographic characteristics, geographic location, vaccination, previous infection, and number of underlying health conditions. Among 699,848 adults aged ≥18 years eligible for Paxlovid during April–August 2022, 28.4% received a Paxlovid prescription within 5 days of COVID-19 diagnosis. Being prescribed Paxlovid was associated with a lower hospitalization rate among the overall study population (adjusted hazard ratio [aHR] = 0.49), among those who had received ≥3 mRNA COVID-19 vaccines (aHR = 0.50), and across age groups (18–49 years: aHR = 0.59; 50–64 years: aHR = 0.40; and ≥65 years: aHR = 0.53). Paxlovid should be prescribed to eligible adults to reduce the risk of COVID-19–associated hospitalization.

Paxlovid is an oral antiviral medication that received Emergency Use Authorization by the Food and Drug Administration on December 22, 2021 (*1*), for use in patients with mild-to-moderate COVID-19 at high risk for progression to severe illness. Eligibility for Paxlovid includes 1) receipt of a positive SARS-CoV-2 test result (including home antigen test), 2) symptoms consistent with mild-to-moderate COVID-19, 3) symptom onset within the past 5 days, 4) age ≥18 years (or age ≥12 years and weight ≥40 kg), 5) one or more risk factors for progression to severe COVID-19, 6) no known or suspected severe renal or hepatic impairment, 7) no history of clinically significant reactions (e.g., toxic epidermal necrolysis or Stevens-Johnson syndrome) to the active ingredients (nirmatrelvir or ritonavir) or other components of the product, and 8) no contraindicated medications.[§]

A retrospective analysis was performed on patient records included in Cosmos, a data set that includes EHR information from >160 million persons in U.S. health systems covered by Epic, a health care software company (https://cosmos.epic.com). Inclusion criteria comprised 1) diagnosis of COVID-19 or a positive SARS-CoV-2 test result during April 1–August 31, 2022[¶]; 2) an outpatient encounter (telemedicine, in-person, urgent care, emergency department, or other)[**] associated with the COVID-19 diagnosis; 3) at least one previous face-to-face encounter in Cosmos during the 3 years preceding the COVID-19 diagnosis[††]; 4) age ≥50 years, or ≥18 years with a documented underlying health condition based on *International Classification of Diseases*, *Tenth Revision* (ICD-10) codes or medical record fields[§§]; 5) not known to be pregnant; and 6) not known to have pharmacologic or medical contraindications to Paxlovid use.[¶¶] For patients with multiple SARS-CoV-2 infections during the study period, only data from the first infection were used in the analysis; date of diagnosis (earliest COVID-19 diagnosis code or positive SARS-CoV-2 test result) was used as a proxy for symptom onset, and Paxlovid receipt was defined as receiving a prescription for Paxlovid during the 5 days after COVID-19 diagnosis.[***] The primary outcome was overnight

[*] These authors contributed equally to this report.
[†] https://cosmos.epic.com/
[§] https://www.fda.gov/media/158165/download

[¶] ICD-10 codes U07.1, J12.81, J12.82 and Systematized Nomenclature of Medicine–Clinical Terms (SNOMED-CT) code 840539006. Positive SARS-CoV-2 test results could be from a nucleic acid amplification test (NAAT) or an antigen test.
[**] Telemedicine included virtual, electronic, and telephone encounters. In-person included in-person outpatient encounters not in the urgent care or emergency department setting. Other included all other outpatient encounters which could not be categorized clearly.
[††] A previous documented face-to-face encounter suggests a person's familiarity with and ability to access care in this health system, which was used to increase the likelihood that subsequent hospitalizations were captured.
[§§] Underlying health conditions were identified using ICD-10 codes, with two exceptions, obesity and smoking, which were identified using dedicated EHR fields. Persons aged <50 years were required to have at least one underlying health condition to be considered eligible for Paxlovid in this study. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html (Accessed October 24, 2022).
[¶¶] Persons with ICD-10 codes consistent with Child-Pugh Class C (indicating advanced hepatic dysfunction) or estimated glomerular filtration rate <30 mL/minute within the past 6 months were considered ineligible to receive Paxlovid. Medications contraindicated with Paxlovid were taken from Food and Drug Administration's Fact Sheet for Healthcare Providers: Emergency Use Authorization for Paxlovid. https://www.fda.gov/media/155050/download
[***] Persons were excluded from the analysis if Paxlovid was prescribed within the 90 days preceding the diagnosis date for the present episode (because of concerns about not capturing the actual COVID-19 diagnosis date), if Paxlovid was prescribed 6–30 days after diagnosis date, or if the patient received other COVID-19–directed therapeutic agents prior to hospitalization.

COVID-19 hospitalization during the 30 days after the date of diagnosis; secondary outcomes were all-cause hospitalization and acute respiratory illness (ARI)–associated hospitalization.[†††]

Association between Paxlovid receipt and subsequent hospitalization was assessed using a Cox proportional hazards model, including age group, sex, race and ethnicity, social vulnerability index,[§§§] number of underlying health conditions, U.S. Census Bureau region of residence, previous COVID-19 infection, and COVID-19 vaccination status.[¶¶¶] In-hospital COVID-19 mortality during an admission commencing during the 30-day follow-up period was described but not used as an analytic outcome because of concern about underascertainment. Persons receiving Paxlovid contributed unexposed time until the prescription date and exposed time after the prescription date; those not receiving Paxlovid contributed unexposed time. Follow-up time ended when a hospitalization occurred or at 30 days after diagnosis, whichever came first. To assess possible bias related to symptom severity at diagnosis, primary analyses were repeated either excluding telemedicine visits, or excluding patients hospitalized during the 2 days after diagnosis. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[****]

Among 1,713,120 persons aged ≥18 years with a COVID-19 diagnosis during April 1–August 31, 2022, 699,848 (40.9%) met the inclusion criteria, including 198,927 who received Paxlovid within 5 days after diagnosis and 500,921 who did not (Figure). Among all persons with COVID-19 who were eligible for Paxlovid, 15.0% had documentation of previous infection and 68.8% were confirmed to have received ≥2 COVID-19 mRNA vaccine doses. Overall, 28.4% of eligible persons received Paxlovid. Paxlovid recipients were more likely to have a telehealth encounter (49.1%) than nonrecipients (18.4%, standardized mean difference = 0.69). Prevalences of underlying health conditions were similar among Paxlovid recipients and nonrecipients (Table 1), and 92.4% had at least one underlying condition. Persons who were immunocompromised[††††] accounted for 9.4% (64,911) of the study population, 30.2% of whom received Paxlovid. During the 30 days after a COVID-19 diagnosis, 5,229 (0.75%) persons were hospitalized; 3,311 (63.3%) of these hospitalizations occurred among persons aged ≥65 years. Among the 198,927 Paxlovid recipients, 930 (0.47%) were hospitalized,[§§§§] compared with 4,299 (0.86%) of nonrecipients. Among the 5,229 persons with a COVID-19 hospitalization, 930 (17.8%) received Paxlovid during the 5 days after diagnosis. Overall, 211 deaths were reported during a COVID-19 hospitalization. Among those who received Paxlovid, 0.01% (29 of 198,927) died compared with 0.04% (182 of 500,921) of persons who did not receive Paxlovid.

Paxlovid receipt was associated with protection against hospitalization overall (aHR = 0.49, 95% CI = 0.46–0.53) (Table 2), including among persons who had received ≥3 mRNA vaccine doses (0.50, 95% CI = 0.45–0.55) and 2 previous mRNA vaccine doses (0.50, 95% CI = 0.42–0.58). Paxlovid receipt was associated with lower hospitalization rates among persons aged 18–49 years (aHR = 0.59, 95% CI = 0.48–0.71), 50–64 years (0.40, 95% CI = 0.34–0.48), and ≥65 years (0.53, 95% CI = 0.48–0.58). Among persons aged 18–49 years, Paxlovid receipt was associated with lower hospitalization rates among persons who had received ≥3 mRNA vaccine doses (aHR = 0.75, 95% CI = 0.53–1.06) and those with only one underlying health condition (aHR = 0.91, 95% CI = 0.58–1.44), but these estimates did not reach statistical significance. Estimated protection by Paxlovid was similar by month of diagnosis. Findings from sensitivity analyses, excluding telemedicine encounters and patients hospitalized during the first 2 days after diagnosis, also indicated significant reduction in hospitalization among Paxlovid recipients.[¶¶¶¶] In the analysis of secondary outcomes, among the overall study population, Paxlovid receipt was associated with a lower rate of all-cause hospitalization (aHR = 0.45, 95% CI = 0.43–0.48) and ARI-associated hospitalization (aHR = 0.48, 95% CI = 0.45–0.51).

Discussion

In a sample of U.S. COVID-19 patients, many of whom had previous SARS-CoV-2 infection or were vaccinated against

[†††] COVID-19 hospitalization was defined as having a COVID-19–specific diagnosis code (ICD-10 U07.1 or SNOMED-CT 840539006) associated with the admission. ARI-associated hospitalizations were defined using ICD-10 codes (adapted from https://doi.org/10.1056/NEJMoa2110362).

[§§§] https://www.atsdr.cdc.gov/placeandhealth/svi/index.html

[¶¶¶] Previous infection was defined as a COVID-19 diagnosis code or positive SARS-CoV-2 test result (NAAT or antigen) >90 days earlier. Vaccination categories included 1) unvaccinated if no COVID-19 vaccine had been received; 2) 2 mRNA-dose recipients if ≥14 days had elapsed since receipt of the second dose and no subsequent doses had been received or <7 days since receipt of third dose; 3) ≥3 mRNA-dose recipients if ≥7 days had elapsed since receipt of the third dose; and 4) other recipient if any Janssen (Johnson & Johnson) vaccine, other vaccine, or only 1 mRNA vaccine dose had been received any time before COVID-19 diagnosis. The proportional hazards assumption was evaluated by plotting hazard functions for each variable in the model.

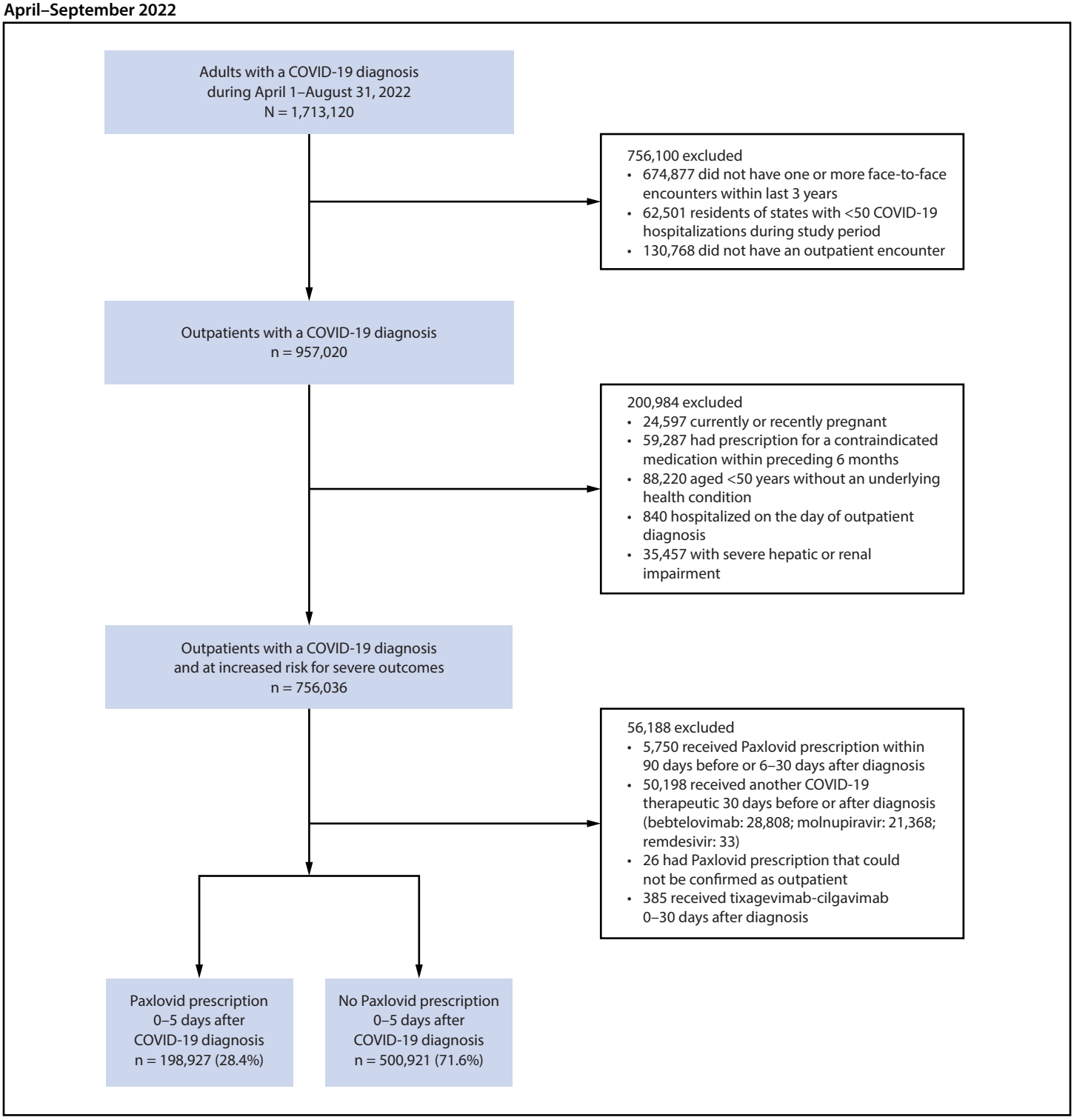
[****] 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

[††††] Immunocompromise was defined using ICD-10 codes (adapted from https://academic.oup.com/cid/article/73/11/e4353/6060064) or immunocompromising medication (adapted from https://www.atsjournals.org/doi/10.1513/AnnalsATS.201507-415BC) prescribed during the past 6 months.

[§§§§] COVID-19 hospitalizations occurred a median of 3 days (range = 1–30 days) after diagnosis. For those prescribed Paxlovid who were subsequently hospitalized, hospitalization occurred a median of 5 days after the Paxlovid prescription (range = 1–30 days).

[¶¶¶¶] In a sensitivity analysis limited to in-person encounters at the time of diagnosis, aHR was 0.53 (95% CI = 0.48–0.58). In a second sensitivity analysis excluding persons hospitalized during the first 2 days after diagnosis, aHR was 0.63 (95% CI = 0.58–0.69).

FIGURE. Identification of patients with COVID-19* who were eligible for treatment with Paxlovid (nirmatrelvir-ritonavir) — Cosmos,† United States, April–September 2022



Abbreviation: NAAT = nucleic acid amplification test.

* Patients were classified as having COVID-19 based on a diagnosis code for COVID-19 or based on a positive SARS-CoV-2 antigen or nucleic acid amplification test. Among 1,713,120 adults aged ≥18 years who met this definition during April 1–August 1, 2022, 930,847 had a diagnosis code only, 159,878 had a positive NAAT result only, 12,874 had a positive antigen test result only, and 609,521 had both a diagnosis code and positive test result (NAAT or antigen test). Exclusions summarized at each level of the flow chart are not mutually exclusive.

† Cosmos is an electronic health record dataset that includes information from >160 million persons in U.S. health systems covered by Epic. https://cosmos.epic.com

TABLE 1. Characteristics of persons eligible for Paxlovid (nirmatrelvir-ritonavir) by prescription receipt within 5 days after COVID-19 diagnosis — Cosmos,* United States, April–September 2022

Characteristic	No. (column %) Paxlovid prescribed (n = 198,927)	Paxlovid not prescribed (n = 500,921)	Standardized mean difference
Age group, yrs			
18–35	20,543 (10.3)	113,716 (22.7)	−0.34
36–49	36,077 (18.1)	107,373 (21.4)	−0.08
50–64	66,929 (33.7)	147,274 (29.4)	0.09
≥65	75,378 (37.9)	132,558 (26.5)	0.25
Sex			
Female	122,921 (61.8)	316,677 (63.2)	−0.03
Male	75,984 (38.2)	184,184 (36.8)	0.03
Race and ethnicity			
Black or African American, non-Hispanic	17,141 (8.6)	66,574 (13.3)	−0.15
Hispanic or Latino	12,088 (6.1)	38,487 (7.7)	−0.06
White, non-Hispanic	158,696 (79.8)	368,109 (73.5)	0.15
Other, non-Hispanic†	11,002 (5.5)	27,751 (5.5)	0.00
Social vulnerability index§			
0–0.25 (least vulnerable)	58,144 (29.5)	117,590 (23.7)	0.13
0.25–0.50	52,659 (26.7)	124,118 (25.0)	0.04
0.50–0.75	47,755 (24.2)	127,366 (25.7)	−0.03
0.75–1.00 (most vulnerable)	38,902 (19.7)	126,632 (25.6)	−0.14
U.S. Census Bureau region¶			
Northeast	47,737 (24.0)	134,818 (26.9)	−0.07
Midwest	78,925 (39.7)	189,000 (37.7)	0.04
South	51,784 (26.0)	140,818 (28.1)	−0.05
West	20,481 (10.3)	36,285 (7.2)	0.11
Outpatient encounter type**			
Telemedicine	97,644 (49.1)	91,916 (18.4)	0.69
In-person	56,793 (28.6)	245,004 (48.9)	−0.43
Urgent care	1,814 (0.9)	9,094 (1.8)	−0.08
Emergency department	19,872 (10.0)	98,359 (19.6)	−0.27
Other	22,804 (11.5)	56,548 (11.3)	0.01
Underlying health conditions††			
0	16,159 (8.1)	37,072 (7.4)	0.03
1	49,848 (25.1)	152,179 (30.4)	−0.12
≥2	132,920 (66.8)	311,670 (62.2)	0.10
Immunocompromised§§			
No	179,321 (90.1)	455,616 (91.0)	−0.03
Yes	19,606 (9.9)	45,305 (9.0)	0.03
Previous infection¶¶			
No	180,373 (90.7)	414,440 (82.7)	0.24
Yes	18,554 (9.3)	86,481 (17.3)	−0.24
Obesity			
No	100,035 (50.3)	257,590 (51.4)	−0.02
Yes	98,892 (49.7)	243,331 (48.6)	0.02
Smoker (current or former)			
No	119,770 (60.2)	287,747 (57.4)	0.06
Yes	79,157 (39.8)	213,174 (42.6)	−0.06
Diabetes			
No	161,177 (81.0)	424,246 (84.7)	−0.10
Yes	37,750 (19.0)	76,675 (15.3)	0.10
COVID-19 vaccination status***			
≥3 mRNA doses	119,324 (60.0)	209,614 (41.9)	0.37
2 mRNA doses	36,924 (18.6)	115,444 (23.1)	−0.11
Unvaccinated	30,619 (15.4)	141,931 (28.3)	−0.32
Other	12,060 (6.1)	33,932 (6.8)	−0.03
Month of COVID-19 diagnosis			
Apr 2022	10,581 (5.3)	50,116 (10.0)	−0.18
May 2022	36,326 (18.3)	104,105 (20.8)	−0.06
Jun 2022	40,747 (20.5)	104,418 (20.9)	−0.01
Jul 2022	58,961 (29.6)	126,991 (25.4)	0.10
Aug 2022	52,312 (26.3)	115,291 (23.0)	0.08

* Cosmos is an electronic health record dataset that includes information from >160 million persons in U.S. health systems covered by Epic. https://cosmos.epic.com

† Includes American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, or Asian, or other race.

§ https://www.atsdr.cdc.gov/placeandhealth/svi/index.html

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

** Telemedicine included virtual, electronic, and telephone encounters. In-person included in-person outpatient encounters not in the urgent care or emergency department setting. Other included all other outpatient encounters which could not be categorized clearly.

†† https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html (Accessed October 24, 2022).

§§ Immunocompromised status was defined using *International Classification of Diseases, Tenth Revision* codes (adapted from https://academic.oup.com/cid/article/73/11/e4353/6060064 or immunocompromising medication prescribed in the past 6 months (adapted from https://www.atsjournals.org/doi/10.1513/AnnalsATS.201507-415BC).

¶¶ Previous infection was defined as a COVID-19 diagnosis code or positive COVID-19 nucleic acid amplification test result or antigen test result >90 days before the current diagnosis.

*** Vaccination categories included 1) unvaccinated if no COVID-19 vaccine had been received; 2) 2 mRNA dose-recipients if ≥14 days had elapsed after the second dose and no subsequent doses had been received or <7 days since receipt of third dose; 3) ≥3 mRNA dose-recipients if ≥7 days had elapsed since receipt of the third dose; and 4) other recipient if any Janssen (Johnson & Johnson) vaccine, other vaccine, or 1 mRNA vaccine dose had been received any time before COVID-19 diagnosis.

Summary

What is already known about this topic?

Nirmatrelvir-ritonavir (Paxlovid) is an outpatient antiviral medication recommended for adults with mild-to-moderate COVID-19 who have elevated risk of severe illness.

What is added by this report?

Among U.S. adults diagnosed with COVID-19, including those with previous infection or vaccination, persons who were prescribed Paxlovid within 5 days of diagnosis had a 51% lower hospitalization rate within 30 days after diagnosis than those who were not prescribed Paxlovid.

What are the implications for public health practice?

Paxlovid should be offered to eligible adults irrespective of vaccination status, especially in groups with the highest risk for severe COVID-19 outcomes, such as older adults and those with multiple underlying health conditions.

TABLE 2. Adjusted hazard ratios for COVID-19–associated hospitalization based on Paxlovid prescription receipt (exposure) — Cosmos,* United States, April–September 2022

Characteristic	Adjusted HR (95% CI)†	No. of participants	No. hospitalized	Events per 100,000 person-days		
				Overall	Exposed§	Unexposed§
Total	**0.49 (0.46–0.53)**	**693,084**	**5,229**	**25.31**	**15.88**	**29.05**
COVID-19 vaccination status¶						
Vaccinated (≥3 mRNA doses)	**0.50 (0.45–0.55)**	310,196	2,126	**22.98**	14.30	27.87
Vaccinated (2 mRNA doses)	**0.50 (0.42–0.58)**	149,498	1,086	**24.37**	16.37	26.92
Unvaccinated	**0.50 (0.43–0.59)**	170,789	1,477	**29.05**	19.60	31.08
UHC**						
0	**0.89 (0.58–1.36)**	52,592	106	**6.73**	6.51	6.83
1	**0.57 (0.45–0.71)**	200,116	503	**8.40**	6.46	9.03
≥2	**0.47 (0.44–0.51)**	440,376	4,620	**35.29**	20.56	41.57
Previous infection††						
No	**0.48 (0.44–0.51)**	589,147	4,715	**26.86**	16.12	31.53
Yes	**0.76 (0.60–0.98)**	103,937	514	**16.56**	13.54	17.20
Immunocompromised§§						
No	**0.49 (0.45–0.53)**	628,706	3,770	**20.09**	12.61	23.03
Yes	**0.50 (0.44–0.58)**	64,378	1,459	**77.01**	45.99	90.49
Month of COVID-19 diagnosis						
Apr 2022	**0.54 (0.40–0.71)**	60,001	450	**25.16**	17.77	26.71
May 2022	**0.57 (0.48–0.67)**	139,062	979	**23.61**	17.06	25.88
Jun 2022	**0.51 (0.43–0.60)**	143,706	1,006	**23.48**	15.02	26.76
Jul 2022	**0.46 (0.40–0.53)**	184,153	1,432	**26.09**	15.65	30.94
Aug 2022	**0.44 (0.38–0.51)**	166,162	1,362	**27.52**	15.60	32.93
Age group, yrs						
18–49	**0.59 (0.48–0.71)**	275,930	886	**10.73**	6.99	11.68
50–64	**0.40 (0.34–0.48)**	211,940	1,032	**16.30**	7.90	20.10
≥65	**0.53 (0.48–0.58)**	205,214	3,311	**54.56**	29.72	68.80
By age group, yrs						
18–49						
Vaccinated (≥3 mRNA doses)	**0.75 (0.53–1.06)**	84,054	178	**7.07**	6.10	7.46
Vaccinated (2 mRNA doses)	**0.53 (0.35–0.82)**	70,159	198	**9.43**	6.20	10.16
Unvaccinated	**0.54 (0.39–0.76)**	97,637	417	**14.29**	9.09	15.13
1 UHC	**0.91 (0.58–1.44)**	109,620	157	**4.78**	4.11	4.91
≥2 UHC	**0.54 (0.43–0.67)**	166,310	729	**14.67**	8.35	16.54
50–64						
Vaccinated (≥3 mRNA doses)	**0.41 (0.30–0.55)**	98,699	284	**9.61**	5.28	12.11
Vaccinated (2 mRNA doses)	**0.46 (0.33–0.63)**	47,111	265	**18.84**	10.96	21.89
Unvaccinated	**0.38 (0.27–0.53)**	45,154	355	**26.39**	12.43	30.35
No UHC	**1.11 (0.46–2.68)**	32,519	25	**2.56**	2.87	2.46
1 UHC	**0.30 (0.17–0.55)**	53,493	109	**6.80**	2.45	8.72
≥2 UHC	**0.40 (0.33–0.48)**	125,928	898	**23.91**	11.04	30.26
≥65						
Vaccinated (≥3 mRNA doses)	**0.51 (0.46–0.57)**	127,443	1,664	**44.02**	24.51	57.35
Vaccinated (2 mRNA doses)	**0.53 (0.43–0.65)**	32,228	623	**65.58**	36.83	78.59
Unvaccinated	**0.58 (0.47–0.72)**	27,998	705	**85.92**	52.75	96.15
No UHC	**0.84 (0.51–1.36)**	20,073	81	**13.50**	10.34	15.49
1 UHC	**0.63 (0.47–0.85)**	37,003	237	**21.47**	13.66	26.77
≥2 UHC	**0.51 (0.47–0.56)**	148,138	2,993	**68.58**	37.33	85.48

Abbreviations: HR = hazard ratio; UHC = underlying health condition.

* Cosmos is an electronic health record dataset that includes information from >160 million persons in U.S. health systems covered by Epic. https://cosmos.epic.com

† 95% CIs that exclude 1 were considered to be statistically significant. Multivariable models were adjusted for age, sex, race and ethnicity, social vulnerability index, number of underlying health conditions, U.S. Census Bureau region of residence, previous infection, and COVID-19 vaccination status, excluding the stratum of interest.

§ Persons receiving Paxlovid contributed unexposed time until the prescription date and exposed time after the prescription date; those not receiving Paxlovid contributed unexposed time. Follow-up time ended when a hospitalization occurred or at 30-days after diagnosis, whichever came first.

¶ Vaccination categories included 1) unvaccinated if no COVID-19 vaccine had been received; 2) 2 mRNA-dose recipients if ≥14 days had elapsed after the second dose and no subsequent doses had been received or <7 days since receipt of third dose; 3) ≥3 mRNA-dose recipients if ≥7 days had elapsed since receipt of the third dose; and 4) other recipient if any Janssen (Johnson & Johnson) vaccine, other vaccine, or 1 mRNA vaccine dose had been received any time before COVID-19 diagnosis.

** https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html (Accessed October 24, 2022).

†† Previous infection was defined as a COVID-19 diagnosis code or positive COVID-19 nucleic acid amplification test result or antigen test result >90 days before the current diagnosis.

§§ Immunocompromised status was defined using *International Classification of Diseases, Tenth Revision* codes (adapted from https://academic.oup.com/cid/article/73/11/e4353/6060064 or immunocompromising medication prescribed during the past 6 months (adapted from https://www.atsjournals.org/doi/10.1513/AnnalsATS.201507-415BC).

COVID-19, the overall COVID-19 hospitalization rate was 51% lower among those who had received a prescription for Paxlovid for presumed mild-to-moderate COVID-19, compared with those who did not. Similar benefit was seen among persons who had received ≥2 COVID-19 mRNA vaccine doses. The initial randomized clinical trial of Paxlovid, which showed an 89% reduction in severe COVID-19 outcomes, was conducted in unvaccinated persons with no previous infection during the period preceding Omicron variant predominance (*2*). This real-word analysis demonstrated that being prescribed Paxlovid is associated with a substantially reduced hospitalization risk among persons with previous immunity from infection or vaccination in the setting of the current circulating Omicron subvariants. These findings parallel those of other studies indicating added protection from Paxlovid even among persons with previous infection or vaccination (*3*–*8*). Paxlovid conferred stable protection during a period in which multiple Omicron subvariants predominated in the United States. Protection against different predominant SARS-CoV-2 subvariants is consistent with Paxlovid's mechanism of action, which inhibits a highly conserved viral protease (*9*).

Current guidelines for Paxlovid indicate that persons who are at high risk for progression to severe COVID-19–associated outcomes should be considered for Paxlovid, with older age being a predominant risk factor (*10*). A study from Israel among persons with mild-to-moderate COVID-19 found comparable benefit from Paxlovid against severe outcomes among persons aged ≥65 years but did not find statistical evidence of protection among younger age groups (*3*). The current analysis adds to overall evidence of protection from Paxlovid by finding a statistically significant benefit among adults aged 18–64 years, specifically among adults aged 50–64 years with one or more underlying health condition and those aged 18–49 years with two or more underlying health conditions. Although ascertainment of deaths was limited to those with a documented death during the COVID-19 hospital admission, the proportion of persons with in-hospital death was also lower among persons who received Paxlovid (0.01%) than among those who did not (0.04%).

The findings in this report are subject to at least seven limitations. First, receipt of a Paxlovid prescription is a proxy for use of Paxlovid. Paxlovid course completion could not be confirmed, which might bias the results toward the null. Second, dates of diagnosis or test positivity were used to estimate illness onset but might not reflect date of symptom onset, or the presence of mild-to-moderate COVID-19 symptoms. Third, possible inclusion of asymptomatic COVID-19 infection in the nonrecipient comparison group could bias estimates toward the null. Fourth, participants with mild illness might be overrepresented among Paxlovid prescription recipients compared with nonrecipients, given the higher proportion of telemedicine visits, potentially leading to overestimation of protection from Paxlovid; however, a sensitivity analysis restricted to in-person encounters showed similar overall results. Fifth, underlying health conditions and immunocompromise were approximated using ICD-10 codes or medical record fields and might not capture the exact prevalences of these conditions. Sixth, although available vaccination information is automatically collected at each encounter, incomplete information could have limited differences in estimates by vaccination status. Finally, hospitalizations might be incompletely ascertained in Cosmos; this limitation was mitigated by including only persons with previous face-to-face encounters, indicating higher likelihood of hospitalization within a participating health system.

This study demonstrates that Paxlovid provides protection against severe COVID-19–associated outcomes among persons for whom it is recommended, including those with vaccine-conferred immunity, and that it is underutilized among eligible persons with COVID-19. In this analysis, only 28% of eligible persons were prescribed Paxlovid. The ease of oral administration, short duration of therapy, and lower likelihood for resistance make Paxlovid a useful antiviral. Reduction in nonsevere outcomes, such as duration, number, and intensity of COVID-19 symptoms, requires further study. Paxlovid should be offered to eligible persons to protect against COVID-19 hospitalizations, irrespective of vaccination status, and especially among groups with the highest risk for severe outcomes, such as older adults and those with multiple underlying health conditions.

Acknowledgments

Caleb Cox, Epic Research; Michael Feldstein; Stacey Adjei, Tegan Boehmer, Lara Bull, Preetika Rao, Olga Varechtchouk, Kristin Yeoman, CDC.

Corresponding author: Melisa M. Shah, bgn3@cdc.gov.

[1]Coronavirus and Other Respiratory Viruses Division (proposed), National Center for Immunization and Respiratory Diseases, CDC; [2]Epic Research, Epic Systems Corporation, Verona, Wisconsin.

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. Food and Drug Administration. Paxlovid emergency use authorization. Silver Spring, MD: Food and Drug Administration; 2022. https://www.fda.gov/media/155049/download
2. Hammond J, Leister-Tebbe H, Gardner A, et al.; EPIC-HR Investigators. Oral nirmatrelvir for high-risk, nonhospitalized adults with Covid-19. N Engl J Med 2022;386:1397–408. PMID:35172054 https://doi.org/10.1056/NEJMoa2118542
3. Arbel R, Wolff Sagy Y, Hoshen M, et al. Nirmatrelvir use and severe Covid-19 outcomes during the Omicron surge. N Engl J Med 2022;387:790–8. PMID:36001529 https://doi.org/10.1056/NEJMoa2204919

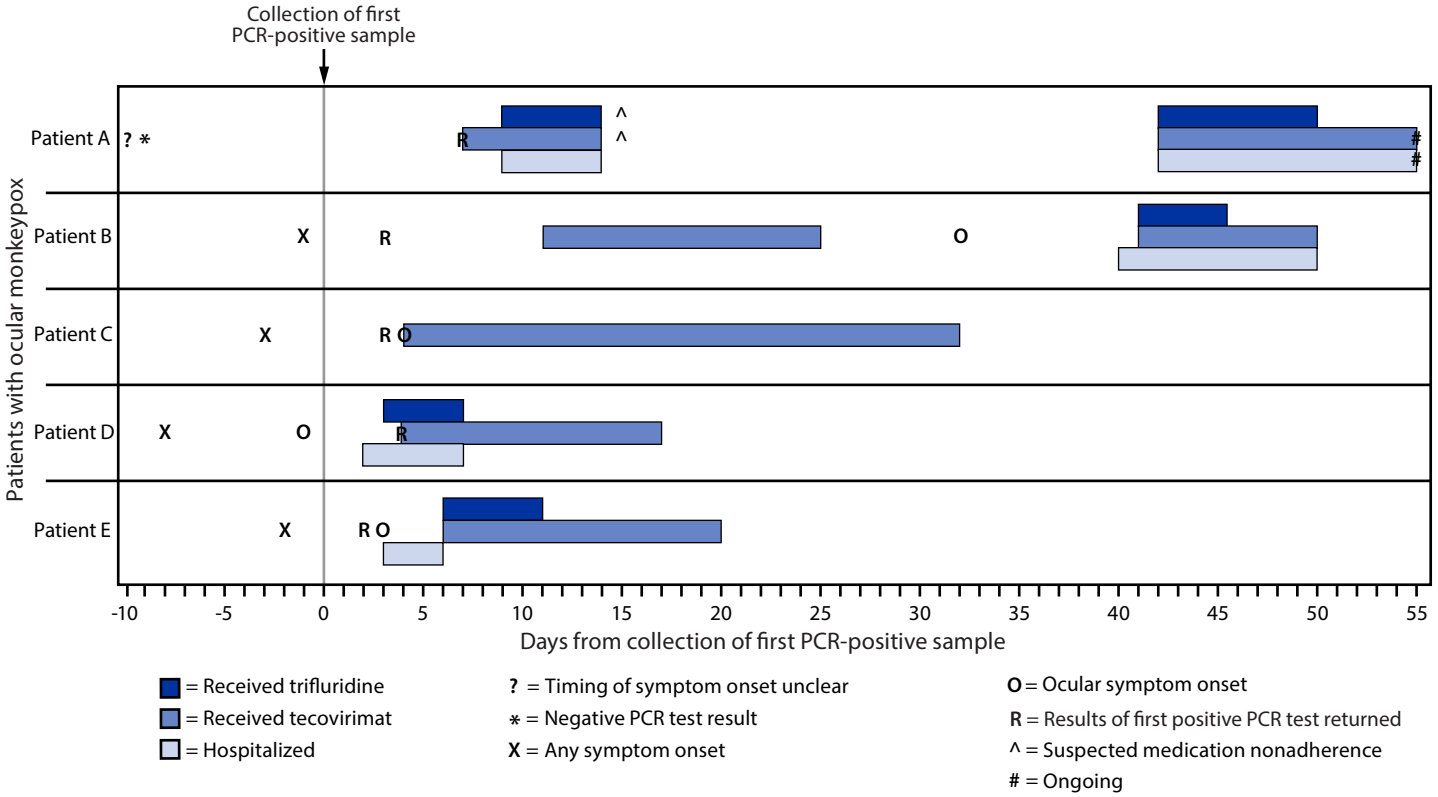
4. Dryden-Peterson S, Kim A, Kim AY, et al. Nirmatrelvir plus ritonavir for early COVID-19 and hospitalization in a large US health system. medRxiv [Preprint posted June 17, 2022]. https://doi.org/10.1101/2022.06.14.22276393
5. Lewnard JA, Malden D, Hong V, et al. Effectiveness of nirmatrelvir-ritonavir against hospital admission: a matched cohort study in a large US healthcare system. medRxiv [Preprint posted October 4, 2022]. https://doi.org/10.1101/2022.10.02.22280623
6. Wong CKH, Au ICH, Lau KTK, Lau EHY, Cowling BJ, Leung GM. Real-world effectiveness of molnupiravir and nirmatrelvir/ritonavir among COVID-19 inpatients during Hong Kong's Omicron BA.2 wave: an observational study. Lancet Infect Dis 2022;S14373–3099(22)00507–2. https://doi.org/10.1016/S1473-3099(22)00507-2
7. Ganatra S, Dani SS, Ahmad J, et al. Oral nirmatrelvir and ritonavir in nonhospitalized vaccinated patients with coronavirus disease 2019 (COVID-19). Clin Infect Dis 2022;ciac673. PMID:35986628 https://doi.org/10.1093/cid/ciac673
8. Najjar-Debbiny R, Gronich N, Weber G, et al. Effectiveness of Paxlovid in reducing severe coronavirus disease 2019 and mortality in high-risk patients. Clin Infect Dis 2022;ciac443. PMID:35653428 https://doi.org/10.1093/cid/ciac443
9. Vangeel L, Chiu W, De Jonghe S, et al. Remdesivir, molnupiravir and nirmatrelvir remain active against SARS-CoV-2 Omicron and other variants of concern. Antiviral Res 2022;198:105252. PMID:35085683 https://doi.org/10.1016/j.antiviral.2022.105252
10. Yek C, Warner S, Wiltz JL, et al. Risk factors for severe COVID-19 outcomes among persons aged ≥18 years who completed a primary COVID-19 vaccination series—465 health care facilities, United States, December 2020–October 2021. MMWR Morb Mortal Wkly Rep 2022;71:19–25. PMID:34990440 https://doi.org/10.15585/mmwr.mm7101a4

Erratum

Vol. 71, No. 42

In the report, "Ocular Monkeypox — United States, July–September 2022," the case report of patient E should have included a citation to a previously published case report that described the first 2 days of patient E's clinical course. On p. 1346, the last two sentences under the heading "Patient E" should have read "**Neither tecovirimat nor trifluridine was immediately available; the patient was treated with naproxen**. Her ocular symptoms improved, and she was discharged after 3 days with a 14-day course of oral tecovirimat and **a 5-day course of topical trifluridine (*2*)**. In the figure on p. 1344 (Figure 1), the timeline of treatment administration for patient E should have indicated 5 days of treatment with trifluridine. In addition, on p. 1347, the list of references should have included the following: "**2. Foos W, Wroblewski K, Ittoop S. Subconjunctival nodule in a patient with acute monkeypox. JAMA Ophthalmol 2022;140:e223742**."

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

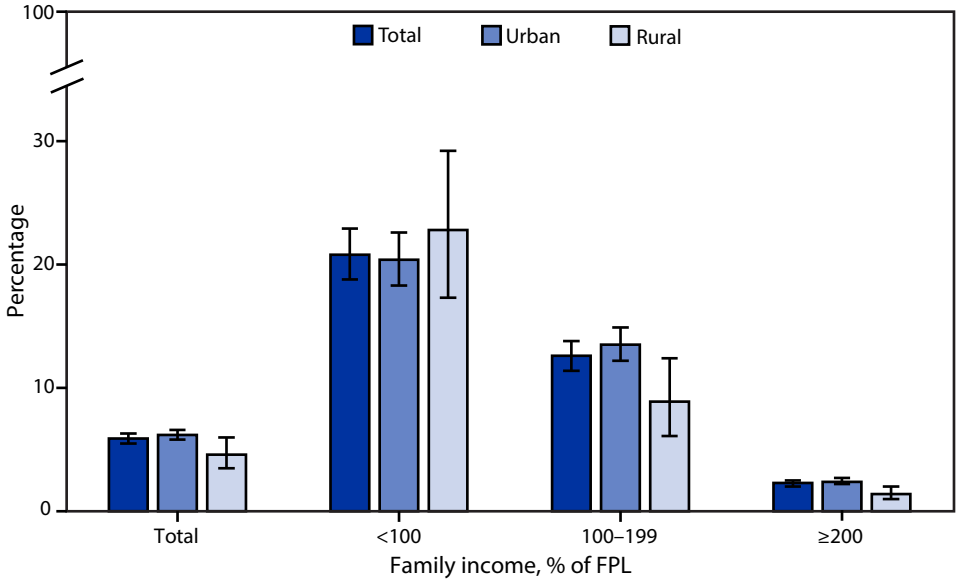


Abbreviation: PCR = polymerase chain reaction.

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage* of Adults Aged ≥18 Years Living in Families That Were Food-Insecure in the Past 30 Days,† by Family Income§ and Urbanicity¶ — National Health Interview Survey, United States, 2021**



Abbreviations: FPL = federal poverty level; MSA = metropolitan statistical area.

* With 95% CIs indicated by error bars.

† Based on a composite recode of responses to 10 questions developed by the U.S. Department of Agriculture to measure whether adults had problems with eating patterns or access, quality, variety, and quantity of food in the past 30 days. In the National Health Interview Survey, food insecurity was calculated at the family level, and families that reported six or more problems were considered to be food-insecure.

§ Income was calculated as a percentage of FPL, which is based on family income and family size, using the U.S. Census Bureau's poverty thresholds.

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

** Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population.

In 2021, 5.9% of adults aged ≥18 years lived in families that were food-insecure in the past 30 days. The percentage was higher in urban areas (6.2%) compared with rural areas (4.6%) overall and within households earning 100%–199% of FPL (13.5% versus 8.9%) and ≥200% of FPL (2.4% versus 1.4%). For adults living in families with incomes <100% of FPL, the percentage was similar in rural (22.8%) and urban (20.4%) areas. The percentage decreased with family income from 20.8% for those living in families earning <100% of FPL to 2.3% for those living in families earning ≥200% of FPL. The same pattern was found for adults living in urban and rural areas.

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

Reported by: Amanda E. Ng, MPH, qkd2@cdc.gov, 301-458-4587; John C. Lin.

For more information on this topic, CDC recommends the following link: https://www.cdc.gov/chronicdisease/programs-impact/sdoh.htm

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

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

ISSN: 0149-2195 (Print)