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Interim Effectiveness Estimates of 2024 Southern Hemisphere Influenza Vaccines in Preventing Influenza-Associated Hospitalization — REVELAC-i Network, Five South American Countries, March–July 2024

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Abstract

To reduce influenza-associated morbidity and mortality, countries in South America recommend annual influenza vaccination for persons at high risk for severe influenza illness, including young children, persons with preexisting health conditions, and older adults. Interim estimates of influenza vaccine effectiveness (VE) from Southern Hemisphere countries can provide early information about the protective effects of vaccination and help guide Northern Hemisphere countries in advance of their season. Using data from a multicountry network, investigators estimated interim VE against influenza-associated severe acute respiratory illness (SARI) hospitalization using a test-negative case-control design. During March 13–July 19, 2024, Argentina, Brazil, Chile, Paraguay, and Uruguay identified 11,751 influenza-associated SARI cases; on average, 21.3% of patients were vaccinated against influenza, and the adjusted VE against hospitalization was 34.5%. The adjusted VE against the predominating subtype A(H3N2) was 36.5% and against A(H1N1)pdm09 was 37.1%. These interim VE estimates suggest that although the proportion of hospitalized patients who were vaccinated was modest, vaccination with the Southern Hemisphere influenza vaccine significantly lowered the risk for hospitalization. Northern Hemisphere countries should, therefore, anticipate the need for robust influenza vaccination campaigns and early antiviral treatment to achieve optimal protection against influenza-associated complications.

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Introduction

Influenza epidemics typically occur during the cool weather months of April–September in the Southern Hemisphere and October–May in the Northern Hemisphere. Every year, it is estimated that influenza results in 716,000–829,000 hospitalizations and 41,007–71,710 deaths throughout the Americas (*1*,*2*). To prevent influenza-associated morbidity and mortality, most countries in the Americas have implemented influenza vaccination programs (*3*). The Pan American Health

INSIDE

869 COVID-19–Associated Hospitalizations Among U.S. Adults Aged ≥18 Years — COVID-NET, 12 States, October 2023–April 2024
876 Differences in COVID-19 Outpatient Antiviral Treatment Among Adults Aged ≥65 Years by Age Group — National Patient-Centered Clinical Research Network, United States, April 2022–September 2023
883 *Burkholderia multivorans* Infections Associated with Use of Ice and Water from Ice Machines for Patient Care Activities — Four Hospitals, California and Colorado, 2020–2024
888 QuickStats

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

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CENTERS FOR DISEASE CONTROL AND PREVENTION

Organization (PAHO) Network for the Evaluation of Vaccine Effectiveness in Latin America and the Caribbean - influenza (Red para la Evaluación de Vacunas en Latino América y el Caribe - influenza [REVELAC-i])[†] provides timely information about the vaccination status of hospitalized influenza patients and vaccine effectiveness (VE), which guides public health messaging and influenza vaccine composition decisions for each Southern Hemisphere season. Southern Hemisphere VE estimates also herald what Northern Hemisphere jurisdictions might anticipate about VE if the same influenza viruses circulate during their upcoming influenza season.

Methods

Data Sources

Patients with severe acute respiratory illness (SARI), defined as an acute respiratory illness with either a history of fever or measured body temperature ≥100.4°F (≥38°C), cough, and onset ≤10 days before hospitalization, were identified through the SARInet Plus network.[§,¶] Respiratory specimens were tested for influenza virus by reverse transcription–polymerase chain reaction (RT-PCR) and typed and subtyped in national reference laboratories.

The study population comprised SARI patients in three mutually exclusive PAHO target groups for vaccination: young children, persons with comorbidities, and older adults; definitions of young children and older adults varied among the countries.[**] March–July 2024 data were pooled from 2,535 hospitals, including 30 in Argentina, 2,477 in Brazil, 13 in Chile, five in Paraguay, and 10 in Uruguay. VE evaluation began 2 weeks after commencement of each country's influenza vaccination campaign.[††] All countries used World Health Organization (WHO)–recommended egg-based Southern Hemisphere formulations. Argentina, Brazil, Chile, and Uruguay used trivalent vaccines containing antigens from A/Victoria/4897/2022 (H1N1)pdm09–like virus, A/Thailand/8/2022 (H3N2)–like virus, and B/Austria/1359417/2021 (B/Victoria lineage)–like virus. Paraguay used quadrivalent vaccines that also contained the B/Yamagata lineage–like virus.[§§]

[†] https://www.paho.org/en/network-evaluation-vaccine-effectiveness-latinamerica-and-caribbean-influenza-revelac-i

[§] https://sarinet.org

[¶] https://www3.paho.org/revelac-i/wp-content/uploads/2015/10/2015-cha-operational-guidelines-sentinel-sari.pdf

[**] Young children were defined as those aged 6 months–2 years (Argentina), 6 months–3 years (Paraguay), 6 months–5 years (Chile and Uruguay), and 6 months–6 years (Brazil). Older adults were defined as those aged ≥60 years (Brazil and Paraguay) and those aged ≥65 years (Argentina, Chile, and Uruguay). The preexisting conditions tracked by REVELAC-i are asthma, cancer, hypertension, diabetes, cardiovascular disease, respiratory disease (excluding asthma), obesity, and immunocompromise.

[††] Influenza vaccination campaign start dates were Argentina: March 21; Brazil (except for the Northern Region): March 25, Chile: March 13, Paraguay: April 3, and Uruguay: April 24.

[§§] https://www.who.int/publications/m/item/recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2024-southern-hemisphere-influenza-season

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Study Design

VE against influenza-associated hospitalization was estimated using a test-negative case-control study design. Case-patients were SARI patients who received a positive influenza RT-PCR test result. Control patients were SARI patients who received negative RT-PCR test results for both influenza virus and SARS-CoV-2 (*4*). Vaccination status was ascertained using unique patient identifiers to link to national electronic immunization records. SARI patients who received the 2024 influenza vaccine ≥14 days before symptom onset were considered vaccinated. Those not vaccinated before symptom onset were considered unvaccinated, and those vaccinated 0–13 days before symptom onset were excluded from the evaluation.

Data Analysis

VE was calculated by comparing the odds of influenza vaccination between influenza test-positive SARI case-patients and influenza test-negative control patients using multivariable logistic regression, overall and by target group.¶¶ To reduce potential confounding, models were adjusted for country, sex, age in years (cubic spline), week of symptom onset (cubic spline), and presence of at least one comorbidity. Analyses were stratified by influenza type and subtype when at least five patients contributed to each stratum or when the width of the 95% CI was <140 percentage points from lower to upper bounds. Because Brazil accounted for the majority of SARI cases, a sensitivity analysis excluding Brazil was conducted. This activity was reviewed by CDC, deemed not research, and conducted consistent with applicable federal law and CDC policy.***

Results

Characteristics of the Study Population

During March 13–July 19, 2024, among a total of 111,856 SARI patients identified, 100,260 were excluded because of missing influenza RT-PCR results (70,055); ineligibility or not being in a vaccine target group (14,245); symptom onset before vaccine availability, outside the influenza season, or after hospital admission (7,581); unknown vaccination status or vaccination date (5,157); specimen collection >10 days after symptom onset (1,220); vaccination <14 days before symptom onset (911); receipt of a positive SARS-CoV-2 test result (503); not meeting the SARI case definition (251); or missing demographic information (201). A total of 11,751 patients met inclusion criteria, including 630 (5.4%) from Argentina, 9,095 (77.4%) from Brazil, 1,584 (13.5%) from Chile, 162 (1.4%) from Paraguay, and 280 (2.4%) from Uruguay (Table 1). Overall, 6,851 (58.3%) patients were young children, 1,702 (14.5%) were older children and adults with comorbidities, and 3,198 (27.2%) were older adults. The majority of SARI patients in Brazil were in the young children target group.

Characteristics of Influenza Case-Patients

Approximately one third (32.7%; 3,848) of SARI patients received a positive influenza test result; most (98.6%) viruses identified were influenza A viruses. Only 26 (0.7%) patients were infected with influenza B viruses, all of which were B/Victoria lineage; influenza virus type was missing for 28 (0.7%) case-patients. Among 2,382 (61.9%) influenza A viruses that were subtyped, 1,628 (68.3%) were A(H3N2) and 754 (31.7%) A(H1N1)pdm09 (Figure). The majority of influenza case-patients were older adults (59.2%), followed by persons with comorbidities (50.4%); the lowest percentage of cases (16.0%) occurred among young children (p<0.001).

Vaccination Status of Case- and Control Patients

Overall, 21.3% of SARI patients were vaccinated; vaccination coverage varied by target group: 29.3% of older adults, 19.4% of young children, and 14.5% of persons with comorbidities were vaccinated (p<0.001) (Table 1). Among 3,848 influenza case-patients, 704 (18.3%) had received a 2024 seasonal influenza vaccine compared with 1,804 of 7,903 (22.8%) control patients (p<0.001).

Vaccine Effectiveness

The adjusted VE against any influenza-associated hospitalization was 34.5% overall, including 58.7% among persons with comorbidities, 39.0% among young children, and 31.2% among older adults (Table 2). Among influenza A subtypes, VE was 36.5% against the predominating A(H3N2) and 37.1% against A(H1N1)pdm09. As of July 19, too few influenza B detections were available to estimate VE. Adjusted VE against SARI from any influenza virus was 42.2% in Argentina, 30.3% in Brazil, 56.9% in Chile, and 61.0% in Uruguay; VE was not calculated for Paraguay because data were insufficient. In the sensitivity analysis excluding Brazil, the adjusted VE for all other countries was 56.5%.

Genetic Characterization of Viruses Reported by REVELAC-i Countries

As of August 12, most A(H1N1)pdm09 viruses reported by REVELAC-i countries to the Global Initiative on Sharing All Influenza Data††† were clade 5a.2a.1 (64.2%) or 5a.2a (35.8%). Most reported A(H3N2) viruses were clade 2a.3a.1 subclade J.2 (92.3%), subclade J.1 (7.5%), or subclade J (0.1%).§§§

¶¶ VE was estimated using multivariable logistic regression as (1 – adjusted odds ratio) × 100%.

*** 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://gisaid.org

§§§ https://joss.theoj.org/papers/10.21105/joss.03773

TABLE 1. Seasonal vaccination status and influenza test results among hospitalized patients with severe acute respiratory illness, by select characteristics — REVELAC-i Network, five South American countries,* March–July 2024

	SARI patients					
				Influenza test result, no. (row %)		
Characteristic	No. (column %)	Vaccinated† no. (row %)	p-value§	Positive	Negative	p-value§
Overall	**11,751**	**2,508 (21.3)**	—	**3,848 (32.7)**	**7,903 (67.3)**	—
Target group¶						
Young children	6,851 (58.3)	1,326 (19.4)	<0.001	1,091 (16.0)	5,741 (84.0)	<0.001
Persons with comorbidities	1,702 (14.5)	246 (14.5)		858 (50.4)	844 (49.6)	
Older adults	3,198 (27.2)	936 (29.3)		1,894 (59.2)	1,304 (40.8)	
Sex						
Female	5,780 (49.3)	1,246 (21.6)	0.577	2,068 (35.8)	3,709 (64.2)	<0.001
Male	5,971 (50.8)	1,262 (21.1)		1,780 (29.8)	4,180 (70.2)	
Influenza test result						
Negative for influenza	7,903 (67.3)	1,804 (22.8)	<0.001	—	7,903 (100.0)	—
Positive for any influenza type A or B	3,848 (32.7)	704 (18.3)	—	3,848 (100.0)	—	
Positive for influenza A	3,794 (98.6)	697 (18.4)	<0.001	3,794 (100.0)	—	
Positive for influenza A(H3N2) subtype	1,628 (42.9)	292 (17.9)	<0.001	1,628 (100.0)	—	
Positive for influenza A(H1N1)pdm09 subtype	754 (19.9)	136 (18.0)	<0.001	754 (100.0)	—	
Positive for unknown A subtype	1,412 (37.2)	269 (19.1)	—	1,412 (100.0)	—	
Positive for influenza type B	26 (0.7)	5 (19.2)	<0.001	26 (100.0)	—	
Positive for unknown influenza virus type	28 (0.7)	2 (7.1)	—	28 (100.0)	—	
Country						
Argentina	630 (5.4)	125 (19.8)	—	203 (32.2)	427 (67.8)	—
Young children	228 (36.2)					
Persons with comorbidities	254 (40.3)					
Older adults	148 (23.5)					
Brazil	9,095 (77.4)	1,840 (20.2)		2,945 (32.4)	6,150 (67.6)	
Young children	6,080 (66.9)					
Persons with comorbidities	896 (9.9)					
Older adults	2,119 (23.3)					
Chile	1,584 (13.5)	507 (32.0)		537 (34.3)	1,028 (65.7)	
Young children	350 (22.1)					
Persons with comorbidities	493 (31.5)					
Older adults	741 (47.3)					
Paraguay	162 (1.4)	14 (8.6)		46 (28.4)	116 (71.6)	
Young children	76 (46.9)					
Persons with comorbidities	0 (—)					
Older adults	86 (53.1)					
Uruguay	280 (2.4)	22 (7.9)		112 (40.0)	168 (60.0)	
Young children	117 (41.8)					
Persons with comorbidities	59 (21.1)					
Older adults	104 (37.1)					

Abbreviations: REVELAC-i = La Red para la Evaluación de Vacunas en Latino América y el Caribe - influenza; SARI = severe acute respiratory infection.

* Argentina, Brazil, Chile, Paraguay, and Uruguay.

† Patients who received ≥1 dose of the 2024 season influenza vaccine ≥14 days before symptom onset were considered vaccinated; patients who did not receive any influenza vaccine during the 2024 season by the time of symptom onset were considered unvaccinated. Patients vaccinated 0–13 days before symptom onset or who received positive SARS-CoV-2 reverse transcription–polymerase chain reaction test results were excluded from the evaluation to avoid the risk of confounding.

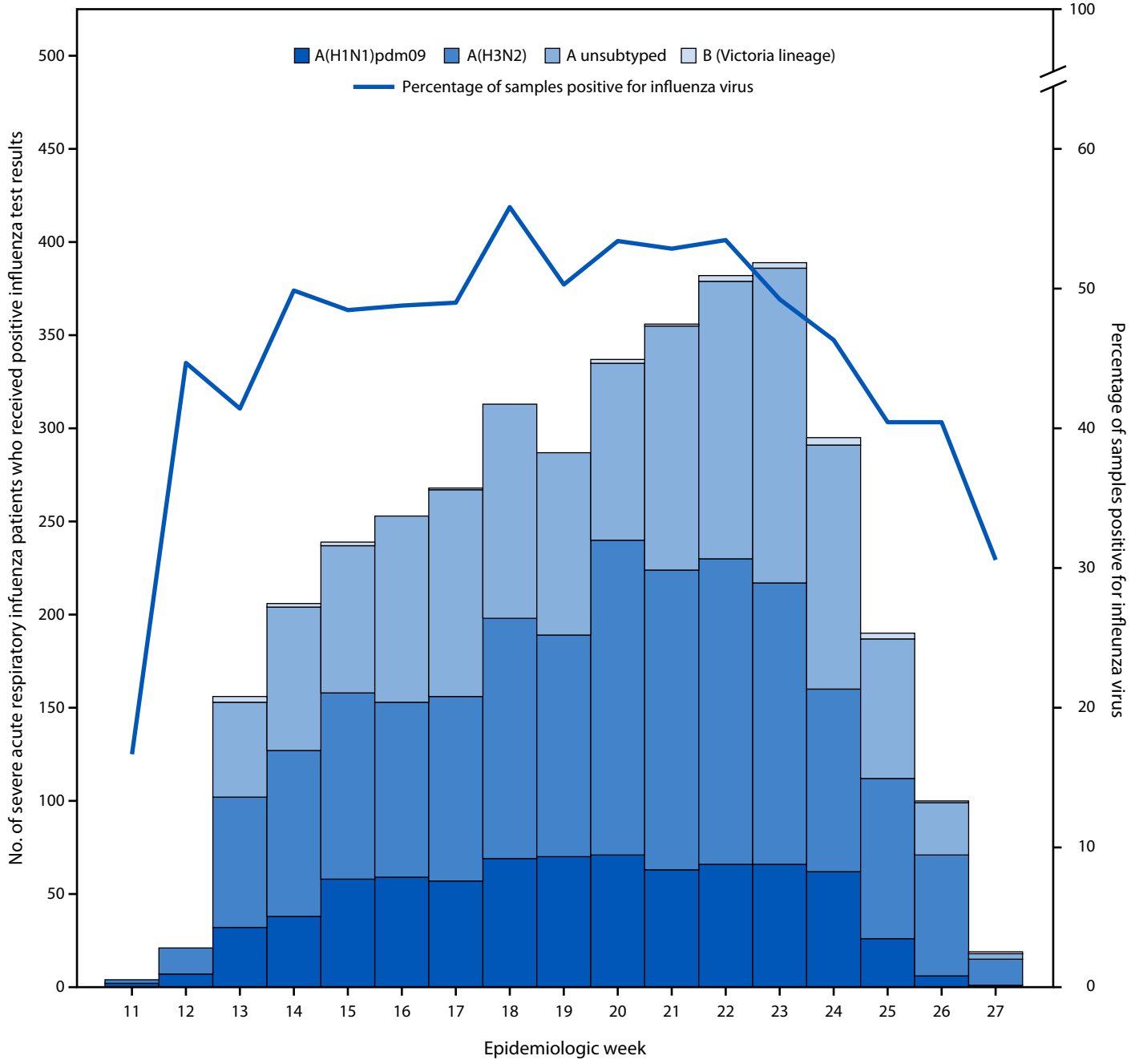
§ A Pearson's chi-square test was used to ascertain whether there were differences in the numbers of persons who were vaccinated and unvaccinated or who received positive and negative influenza test results.

¶ Target groups are included as mutually exclusive groups of patients considered to be at high risk for severe outcomes associated with influenza infection. Young children were defined as those aged 6 months–2 years (Argentina), 6 months–3 years (Paraguay), 6 months–5 years (Chile and Uruguay), and 6 months–6 years (Brazil). Older adults were defined as those aged ≥60 years (Brazil and Paraguay) and aged ≥65 years (Argentina, Chile, and Uruguay). The preexisting conditions tracked by REVELAC-i are asthma, cancer, hypertension, diabetes, cardiovascular disease, respiratory disease (excluding asthma), obesity, and immunocompromise.

Discussion

This evaluation suggests that while only one in five SARI patients had received the 2024 influenza vaccine, those who were vaccinated were at significantly lower risk for hospitalization from any influenza virus infection, including the predominant influenza A(H3N2) and influenza A(H1N1)pdm09 subtypes. Although South American countries prioritized young children, persons with comorbidities, and older adults for vaccination to prevent influenza illness complications, the documented influenza vaccination coverage levels (21.3%) were below pre–COVID-19 norms. This finding is consistent with postpandemic declines in vaccination coverage across the Americas associated with vaccine misinformation, hesitancy, and disruptions in routine immunization services, prevalent

FIGURE. Patients hospitalized with severe acute respiratory infection who received positive influenza virus test results,* by epidemiologic week,† (N = 11,751) — REVELAC-i Network, five South American countries,§ March–July 2024



* By reverse transcription–polymerase chain reaction testing at national reference laboratories.
† Epidemiologic week 11 began on March 10, 2024; epidemiologic week 27 ended on July 6, 2024.
§ Argentina, Brazil, Chile, Paraguay, and Uruguay.

during the COVID-19 pandemic (*3*). Vaccination remains one of the most effective measures to prevent influenza-associated complications, including death.¶¶¶ Annual influenza vaccination should be encouraged for young children, persons with comorbidities, and older adults (*5*). Influenza vaccine postintroduction evaluations and knowledge, attitudes, and practices surveys might identify additional reasons for low coverage and strategies for improved coverage for the next Southern Hemisphere season.

¶¶¶https://www.cdc.gov/flu/prevent/prevention.htm

TABLE 2. Interim 2024 Southern Hemisphere seasonal influenza vaccine effectiveness against influenza — REVELAC-i Network, five South American countries,* March–July 2024

Influenza type/Target group¶ and country	Influenza test-positive case-patients†		Influenza test-negative control patients		Vaccine effectiveness§	
	Total no.	Vaccinated, no. (%)	Total no.	Vaccinated, no. (%)	Unadjusted % (95% CI)	Adjusted§ % (95% CI)
Any influenza type A or B						
Overall	**3,848**	**704 (18.3)**	**7,889**	**1,804 (22.9)**	**24.3 (16.5 to 31.4)**	**34.5 (26.4 to 41.6)**
Young children	**1,096**	141 (12.9)	**5,741**	1,185 (20.6)	43.1 (31.0 to 53.0)	39.0 (25.6 to 50.0)
Persons with comorbidities	**858**	72 (8.4)	**844**	174 (20.6)	64.7 (52.3 to 74.1)	58.7 (43.4 to 69.8)
Older adults	**1,894**	491 (25.9)	**1,304**	445 (34.1)	32.4 (21.0 to 42.3)	31.2 (18.3 to 42.0)
Influenza type A						
Overall	**3,794**	**697 (18.4)**	**7,903**	**1,804 (22.8)**	**23.9 (16.0 to 31.1)**	**34.2 (26.0 to 41.4)**
Young children	**1,081**	140 (13.0)	**5,755**	1,185 (20.6)	42.6 (30.4 to 52.7)	38.1 (24.4 to 49.2)
Persons with comorbidities	**830**	70 (8.4)	**844**	174 (20.6)	64.5 (51.9 to 74.0)	58.3 (42.6 to 69.7)
Older adults	**1,883**	487 (25.9)	**1,304**	445 (34.1)	32.7 (21.2 to 42.5)	31.4 (18.5 to 42.2)
Influenza A(H1N1)pdm09 subtype						
Overall	**754**	**136 (18.0)**	**7,903**	**1,804 (22.8)**	**25.6 (9.4 to 39.1)**	**37.1 (21.9 to 49.4)**
Young children	**204**	16 (7.8)	**5,755**	1,185 (20.6)	67.4 (45.3 to 81.8)	60.0 (31.7 to 76.6)
Persons with comorbidities	**149**	12 (8.1)	**844**	174 (20.6)	66.3 (37.3 to 83.4)	57.6 (19.1 to 77.8)
Older adults	**400**	108 (27.0)	**1,304**	445 (34.1)	28.6 (7.9 to 44.9)	27.8 (5.1 to 45.0)
Influenza A(H3N2) subtype						
Overall	**1,628**	**292 (18.0)**	**7,903**	**1,804 (22.8)**	**26.1 (15.1 to 35.7)**	**36.5 (25.8 to 45.7)**
Young children	**453**	62 (13.8)	**5,755**	1,185 (20.6)	38.8 (19.2 to 54.3)	38.4 (17.3 to 54.1)
Persons with comorbidities	**384**	28 (7.3)	**844**	174 (20.6)	69.7 (53.6 to 80.8)	67.4 (49.3 to 79.0)
Older adults	**791**	202 (25.5)	**1,304**	445 (34.1)	33.8 (19.0 to 45.9)	30.8 (14.4 to 44.0)
Influenza type B						
Overall	**26**	**5 (19.2)**	**7,903**	**1,804 (22.8)**	**NC****	**NC****
Young children	**8**	0 (—)	**5,755**	1,185 (20.6)	NC**	NC**
Persons with comorbidities	**8**	1 (12.5)	**844**	174 (20.6)	NC**	NC**
Older adults	**10**	4 (40.0)	**1,304**	445 (34.1)	NC**	NC**
Any influenza type A or B						
Argentina	**203**	27 (13.3)	427	98 (23.0)	48.5 (16.8 to 68.9)	42.2 (6.9 to 64.1)
Brazil	**2,945**	561 (19.1)	**6,150**	1,279 (20.8)	10.4 (–0.3 to 19.9)	30.3 (19.9 to 39.4)
Chile	**542**	109 (20.3)	**1,042**	398 (38.2)	59.3 (47.7 to 68.4)	56.9 (42.5 to 67.7)
Paraguay	**46**	1 (2.2)	**116**	13 (11.2)	NC**	NC**
Uruguay	**112**	6 (5.4)	**168**	16 (9.5)	46.2 (–50.9 to 83.3)	61.0 (–11.5 to 86.4)

Abbreviation: NC = not calculated.

* Argentina, Brazil, Chile, Paraguay, and Uruguay.

† Reverse transcription polymerase–chain reaction testing for influenza was conducted at national reference laboratories.

§ Vaccine effectiveness estimated from logistic regression model adjusting for participating country, sex, age in years (fit as cubic spline), week of onset of symptoms (fit as cubic spline), and presence of at least one comorbidity.

¶ Young children were defined as those aged 6 months–2 years (Argentina), 6 months–3 years (Paraguay), 6 months–5 years (Chile and Uruguay), and 6 months–6 years (Brazil). Older adults were defined as those aged ≥60 years (Brazil and Paraguay) and aged ≥65 years (Argentina, Chile, and Uruguay).

** Percentage was NC when fewer than five patients were in each of the categories.

Despite the low influenza vaccination coverage, those vaccinated were protected against hospitalization. The 34.5% REVELAC-i VE against all influenza-associated hospitalization was within historical ranges of 34%–53% against A(H3N2) and 18%–56% against A(H1N1)pdm09 (*6*). Vaccination likely prevented 36.5% of influenza A(H3N2)–associated and 37.1% of influenza A(H1N1)pdm09–associated hospitalizations. VE was lowest in Brazil, likely because a higher proportion of cases in Brazil occurred among young children, a population with a VE estimate in the lower range among the three target groups. If these clades predominate during the Northern Hemisphere influenza season and the updated A/Thailand/8/2022 (H3N2)–like virus antigen provides similar protection against clade 2a.3a.1, health authorities might anticipate similar levels of protection from the 2024–25 vaccine (*7*). To enhance this year's modest influenza vaccine protection against hospitalization, providers should treat patients with suspected or confirmed influenza as soon as possible with antivirals.

Limitations

The findings in this report are subject to at least five limitations. First, small interim-estimate sample sizes precluded the estimation of VE against influenza B. Second, although the analyses were robust, 63% of patients were excluded because they did not receive RT-PCR results in time for the interim

Summary

What is already known about this topic?

Influenza vaccine effectiveness (VE) varies by season.

What is added by this report?

In five South American countries (Argentina, Brazil, Chile, Paraguay, and Uruguay) the 2024 Southern Hemisphere seasonal influenza vaccine reduced the risk for influenza-associated hospitalization among high-risk groups by 35%. VE might be similar in the Northern Hemisphere if similar A(H3N2) viruses predominate during the 2024–25 influenza season.

What are the implications for public health practice?

CDC recommends that all eligible persons aged ≥6 months receive seasonal influenza vaccine. Early antiviral treatment can complement vaccination to protect against severe influenza-related morbidity.

analysis. Third, Brazil, which is approximately three times as populous as the other countries combined,**** accounted for approximately 80% of the study population and included a higher percentage of SARI patients in the young children target group compared with that in other countries. Overall analyses were adjusted for country and target group but might still be more representative of Brazil's VE estimate. Fourth, this analysis does not distinguish between young children who received 1 or 2 vaccine doses; VE might be higher among young children who received 2 influenza vaccine doses. Finally, these results might not be generalizable to other target groups or to countries with different viral circulation and vaccination strategies.

Implications for Public Health Practice

Interim VE estimates from the REVELAC-i Network suggest that influenza vaccines are effective in preventing approximately one third of influenza-related hospitalizations among groups prioritized for vaccination. Although Southern Hemisphere influenza VE is not necessarily predictive of Northern Hemisphere VE, it can help the Northern Hemisphere plan contingencies for vaccination demand and use. These data suggest that influenza vaccine demand was still low post–COVID-19 but that vaccination prevented approximately one third of influenza-associated hospitalizations among groups at high risk for influenza-associated complications. These findings support CDC and WHO's recommendation that all eligible persons aged ≥6 months should receive influenza vaccination (*5*,*8*). If similar influenza viruses continue to predominate during Northern Hemisphere influenza season and the updated A/Thailand/8/2022 (H3N2)–like antigen provides similar protection against circulating influenza A(H3N2) viruses, health authorities might anticipate similar levels of protection. Nonpharmaceutical measures, such as hand washing and mask use, and early antiviral treatment can complement vaccination for stronger protection against influenza illness and its complications.

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REVELAC-i Network

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COVID-19–Associated Hospitalizations Among U.S. Adults Aged ≥18 Years — COVID-NET, 12 States, October 2023–April 2024

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Abstract

Among adults, COVID-19 hospitalization rates increase with age. Data from the COVID-19–Associated Hospitalization Surveillance Network were analyzed to estimate population-based COVID-19–associated hospitalization rates during October 2023–April 2024 and identify demographic and clinical characteristics of adults aged ≥18 years hospitalized with COVID-19. Adults aged ≥65 years accounted for 70% of all adult COVID-19–associated hospitalizations, and their COVID-19–associated hospitalization rates were higher than those among younger adult age groups. Cumulative rates of COVID-19–associated hospitalization during October 2023–April 2024 were the lowest for all adult age groups during an October–April surveillance period since 2020–2021. However, hospitalization rates among all adults aged ≥75 years approached one COVID-19–associated hospitalization for every 100 persons. Among adults hospitalized with COVID-19, 88.1% had not received the 2023–2024 formula COVID-19 vaccine before hospitalization, 80.0% had multiple underlying medical conditions, and 16.6% were residents of long-term care facilities (LTCFs). Guidance for adults at high risk for severe COVID-19 illness, including adults aged ≥65 years and residents of LTCFs, should continue to focus on adopting measures to reduce risk for contracting COVID-19, advocating for receipt of recommended COVID-19 vaccinations, and seeking prompt outpatient antiviral treatment after receipt of a positive SARS-CoV-2 test result.

Introduction

Hospitalization due to COVID-19 has remained a public health concern since the start of the COVID-19 pandemic. Persons of all ages remain at risk for COVID-19–associated hospitalization; among adults, the risk for hospitalization increases with age (*1*). Understanding the characteristics of adults hospitalized with COVID-19 can help guide appropriate recommendations as circulating SARS-CoV-2 variants change and vaccine recommendations are updated. Data from the COVID-19–Associated Hospitalization Surveillance Network (COVID-NET) were analyzed to estimate COVID-19–associated hospitalization rates during October 2023–April 2024 and identify demographic and clinical characteristics of adults aged ≥18 years hospitalized with COVID-19.

Methods

Data Source

COVID-NET conducts population-based surveillance for laboratory-confirmed COVID-19–associated hospitalization* among residents of predefined surveillance catchment areas. Demographic data were collected on all COVID-19–associated hospitalizations in 90 counties across 12 states† and were used to calculate overall, age-stratified, and age-adjusted hospitalization rates from October 1, 2023, through April 27, 2024,§ and compare these rates with those from previous surveillance periods.¶

Selection of Cases for Analysis

Using previously described methods (*2*), trained surveillance officers abstracted demographic and clinical data from the medical records of an age- and site-stratified monthly random sample of patients hospitalized during October 2023–April 2024. Analyses of sampled cases were limited to hospitalizations for which COVID-19–related illness was the likely primary complaint at the time of admission, based on information in the medical record (*3*). Data on receipt of the most recent patient COVID-19 vaccination** was obtained from state immunization information systems. Underlying conditions were defined as chronic or preexisting medical conditions present before or at the time of hospital admission. Long-term care facility (LTCF) residency was ascertained based on status upon admission.

* COVID-19–associated hospitalizations are defined as those among persons who have received a positive SARS-CoV-2 reverse transcription–polymerase chain reaction or rapid antigen detection test result during hospitalization or ≤14 days before admission.

† Selected counties and county equivalents in California, Colorado, Connecticut, Georgia, Maryland, Michigan, Minnesota, New Mexico, New York, Oregon, Tennessee, and Utah for the 2023–2024 surveillance season.

§ Age-adjusted rates were calculated using the direct method using the U.S. Census Bureau Vintage 2022 population estimates.

¶ The COVID-NET surveillance season extends year-round from epidemiologic week 40 through epidemiologic week 39, which roughly aligns with October–September of the following year. To compare with the analytic period in this study, the season was divided into surveillance weeks 40–17 (approximately October–April) and epidemiologic weeks 18–39 (approximately May–September). The 2019–2020 surveillance season began on March 1, 2020; data for that surveillance season are presented as epidemiologic weeks 10–17 and weeks 18–39.

** Vaccination status includes receipt of the 2022–2023 (bivalent) or 2023–2024 formula vaccine. The 2022–2023 formula (bivalent) vaccine was recommended by the Advisory Committee on Immunization Practices on September 1, 2022. The 2023–2024 formula vaccine was recommended on September 1, 2023. Vaccination status was assessed between September 1, 2022, and the date of hospital admission.

Data Analysis

For sampled data, unweighted case counts and weighted percentages that better represent the hospitalized population of the catchment area are presented (*2*). Data were analyzed using SAS (version 9.4; SAS Institute); variances were estimated using the Taylor series linearization method. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.[††]

Results

Age Distribution of Hospitalized Adults with COVID-19

During October 2023–April 2024, COVID-NET identified 40,761 COVID-19–associated hospitalizations, 38,900 (95.4%) of which were among adults aged ≥18 years.[§§] Among hospitalized adults, those aged 18–49, 50–64, 65–74, and ≥75 years accounted for 13.5%, 16.7%, 21.3%, and 48.6% (unweighted) of cases, respectively. Weekly proportions of adults with COVID-19–associated hospitalizations by age group have changed over time but were stable for this analytic period (Supplementary Figure 1, https://stacks.cdc.gov/view/cdc/162446).

Cumulative Age- and Season-Specific COVID-19 Hospitalization Rates

During October 2023–April 2024, cumulative COVID-19–associated hospitalization rates (hospitalizations per 100,000 population) among each adult age group were the lowest experienced during the months of October–April since the 2020–2021 surveillance season (Figure 1). Since 2020–2021, approximately 25% of COVID-19–associated hospitalizations among adults have occurred during May–September. During October 2023–April 2024, cumulative rates were highest among adults aged ≥75 years (936.4), approaching one COVID-19–associated hospitalization for every 100 persons. The rate in this group was also higher than that of any other age group during any previous October–April period. Relative to adults aged 18–49 years, cumulative rates among adults aged 50–64, 65–74, and ≥75 years during October 2023–April 2024 were 2.9, 7.3, and 24.1 times as high, respectively.

During October 2023–April 2024, weekly COVID-19–associated hospitalization rates increased during November–December, peaking in late December or early January, depending on the age group (Supplementary Figure 2, https://stacks.cdc.gov/view/cdc/162446). The peak weekly rate among adults aged ≥75 years (58.9) was 24.5 times as high as that among adults aged 18–49 years (2.4).

COVID-19 Hospitalization Rates Among Racial and Ethnic Groups

During the same period, cumulative, age-adjusted COVID-19–associated hospitalization rates were highest among non-Hispanic American Indian or Alaska Native (AI/AN) (205.9) and non-Hispanic Black or African American (Black) (198.2) adults (Figure 2); rates among both groups were 1.4 times as high as rates among Hispanic or Latino (Hispanic) adults (149.5) and 1.3 times as high as rates among non-Hispanic White (White) adults (151.4). Whereas AI/AN adults experienced the highest hospitalization rates throughout the season, rates among Black adults increased more sharply during December 2023–February 2024 relative to other groups, leading to cumulative rates that were similar to those among AI/AN adults.

Vaccination Status, Underlying Conditions, and Clinical Course Among Adults Hospitalized with COVID-19

Among a sample of 1,320 hospitalized adults,[¶¶] 88.1% had not received the 2023–2024 formula COVID-19 vaccine dose (Table). In addition, 57.7% had not received the 2022–2023 formula (bivalent) dose, including 66.7% of those aged 65–74 years, and 46.5% of those aged ≥75 years, representing 52.5% (95% CI = 46.7%–58.2%) of adults aged ≥65 years.

Among this sample of adults hospitalized with COVID-19, 80.0% had at least two underlying medical conditions, and 16.6% were residents of LTCFs. In addition, 18.4% were admitted to an intensive care unit, 8.4% received invasive mechanical ventilation, and 6.9% died during hospitalization. Among all in-hospital deaths, 45.0% (95% CI = 26.0%–65.0%) were among persons aged ≥75 years.

Discussion

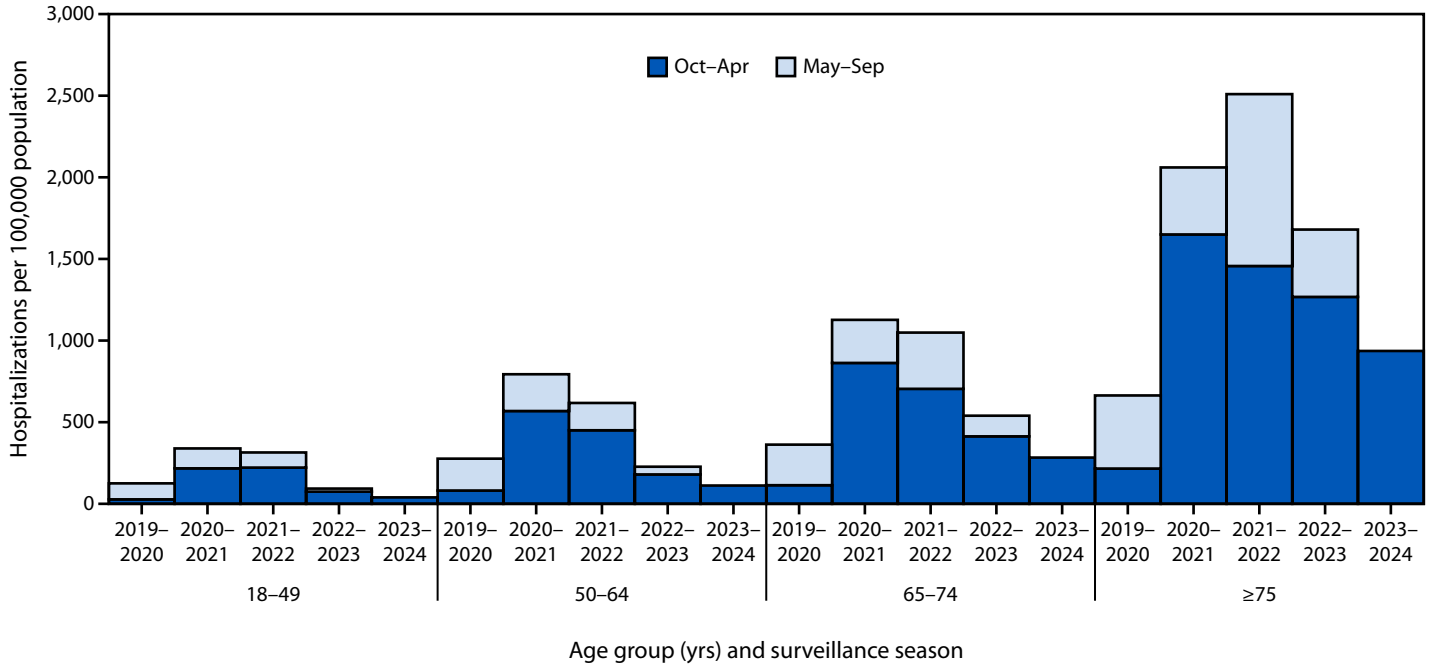
During October 2023–April 2024, cumulative COVID-19–associated hospitalization rates were lower than those during previous years. Similar to previous surveillance seasons, adults aged ≥65 years experienced COVID-19–associated hospitalization rates many times higher than did adults in other age groups (*3*). Adults aged ≥65 years accounted for approximately two thirds of all COVID-19–associated hospitalizations during October 2023–April 2024, with adults aged ≥75 years accounting for approximately one half of hospitalizations and in-hospital deaths. During the 7-month period, cumulative population-based hospitalization rates among all adults aged ≥75 years approached one in 100. These findings suggest that

[††] 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 1,861 COVID-19–associated hospitalizations among children and adolescents aged ≤17 years represented 4.6% of total COVID-19–associated hospitalizations and are not further described in this analysis.

[¶¶] Among the 38,900 COVID-19–associated hospitalizations among adults, data were abstracted from a sample of 1,754. Among these, 84 (4.8% [unweighted]) persons were pregnant, and 350 (19.9% [unweighted]) reported primary complaints upon admission that were not likely related to COVID-19–related illness and were excluded.

FIGURE 1. Cumulative* COVID-19–associated hospitalization† rates among adults aged ≥18 years, by age group and surveillance season§ — COVID-19–Associated Hospitalization Surveillance Network, 12 states,¶ March 2020–April 2024



* Cumulative rates are the sequential sum of weekly hospitalizations divided by the catchment area population.
† COVID-19–associated hospitalizations among patients who received a positive SARS-CoV-2 test result during hospitalization or ≤14 days before admission.
§ The COVID-19–Associated Hospitalization Surveillance Network surveillance season extends year-round from epidemiologic week 40 through epidemiologic week 39, which roughly aligns with October–September of the following year. To compare with the analytic period in this study, the season was divided into surveillance weeks 40–17 (approximately October–April) and epidemiologic weeks 18–39 (approximately May–September). The 2019–2020 surveillance season began on March 1, 2020; data for that surveillance season are presented as epidemiologic weeks 10–17 and weeks 18–39.
¶ Selected counties and county equivalents in California, Colorado, Connecticut, Georgia, Maryland, Michigan, Minnesota, New Mexico, New York, Oregon, Tennessee, and Utah.

COVID-19–associated hospitalization among adults aged ≥65 years remains a public health concern.

The Advisory Committee on Immunization Practices has updated COVID-19 vaccine recommendations as SARS-CoV-2 has continued to evolve (*4*,*5*). In this analysis, approximately 90% of adults hospitalized during October 2023–April 2024 had not received the recommended 2023–2024 formula dose; approximately one half had not received any COVID-19 vaccine since September 1, 2022, including adults aged ≥65 years. Receipt of COVID-19 vaccine has been demonstrated to reduce the risk for COVID-19–associated hospitalization (*6*).

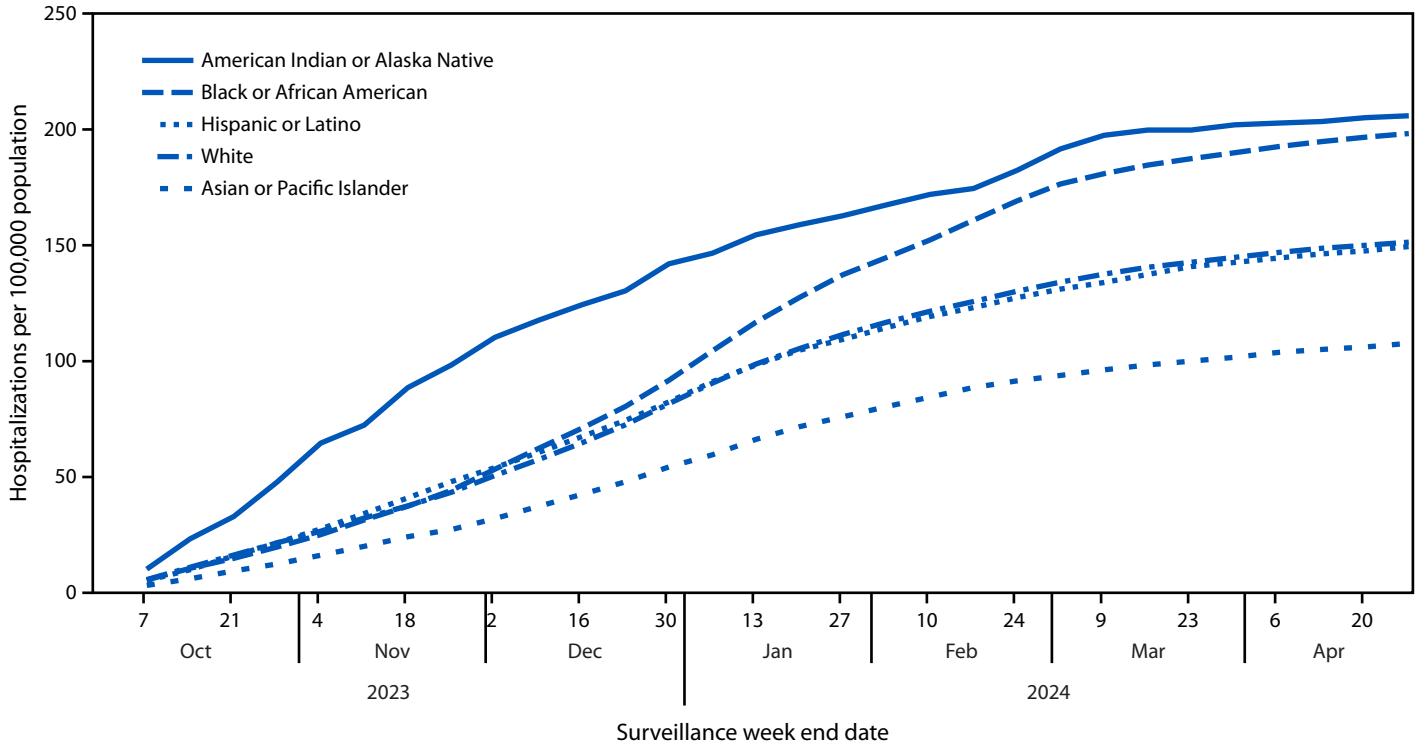
Disparities in COVID-19–associated hospitalization among adults by race and ethnicity persisted during the study period. Cumulative hospitalization rates among AI/AN and Black adults were 30%–40% higher than were those among Hispanic and White adults. Published data for July 2021–August 2022 showed that cumulative age-adjusted hospitalization rates among adults were approximately twice as high among AI/AN and Black adults as among White adults, and 40% as high compared with Hispanic adults (*7*). These data suggest that racial and ethnic disparities in rates of COVID-19–associated hospitalization among adults continue but might have decreased since July 2021–August 2022. In addition to disparities in rates of COVID-19–associated hospitalization, data from the National Immunization Survey indicate that racial and ethnic disparities among adults exist in COVID-19 vaccination coverage. The percentage of adults who received the 2023–2024 formula dose was highest among White adults relative to all other racial and ethnic groups.*** This disparity in vaccination coverage might contribute to continued racial and ethnic disparities in rates of COVID-19–associated hospitalizations among adults.

Approximately one in six adults hospitalized with COVID-19 was a resident of an LTCF. These findings are consistent with published literature demonstrating high rates of COVID-19–associated hospitalization and low prevalence of COVID-19 vaccination (40.5%) among nursing home residents during October 2023–February 2024 (*8*).

Most adults hospitalized with COVID-19 had two or more underlying medical conditions. A published analysis of

*** https://www.cdc.gov/covidvaxview/weekly-dashboard/adult-vaccination-coverage.html (Accessed September 27, 2024).

FIGURE 2. Cumulative* age-adjusted COVID-19–associated hospitalization† rates among adults aged ≥18 years, by race and ethnicity§ — COVID-19–Associated Hospitalization Surveillance Network, 12 states,¶ October 1, 2023–April 27, 2024



* Cumulative rates are the sequential sum of weekly hospitalizations divided by the catchment area population.
† COVID-19–associated hospitalizations among patients who received a positive SARS-CoV-2 test result during hospitalization or ≤14 days before admission.
§ Persons of Hispanic or Latino (Hispanic) origin might be of any race but are categorized as Hispanic; all racial groups are non-Hispanic.
¶ Selected counties and county equivalents in California, Colorado, Connecticut, Georgia, Maryland, Michigan, Minnesota, New Mexico, New York, Oregon, Tennessee, and Utah.

COVID-NET data from early in the pandemic found a fourfold increased risk for COVID-19–associated hospitalization among adults with two or more underlying medical conditions, even after adjusting for age, sex, and race and ethnicity (*9*). These data suggest that continued efforts are needed to prevent hospitalizations among adults with multiple underlying conditions.

Vaccination and nonpharmaceutical interventions such as hand hygiene and avoiding exposure to persons with respiratory symptoms can reduce the risk for contracting SARS-CoV-2. In addition, for persons with SARS-CoV-2 infection who are at high risk for progression to severe disease, receipt of early outpatient treatment with ritonavir-boosted nirmatrelvir (Paxlovid, Pfizer), remdesivir (Veklury, Gilead), or molnupiravir (Lagevrio, Merck & Co., Inc.) can reduce the risk for severe outcomes (*10*). Vaccination, other measures to reduce the risk for contracting SARS-CoV-2, and early antiviral treatment are important tools for preventing hospitalization among adults at increased risk for hospitalization, including those aged ≥65 years, residents of LTCFs, and persons with underlying medical conditions.

Limitations

The findings in this report are subject to at least five limitations. First, COVID-19–associated hospitalizations might have been missed because of hospital testing practices; therefore, hospitalization rates might be underestimated. Second, a patient's primary complaint at the time of admission is subject to misclassification, potentially resulting in cases being unintentionally included or excluded from this analysis. COVID-19–related illness can still affect the course of hospitalizations even if COVID-19–related illness was not the primary complaint upon admission. Third, vaccination status might be misclassified if immunization information systems data are incomplete; therefore, proportions of vaccinated patients might be underestimated. Fourth, these data only describe in-hospital deaths; deaths among patients discharged to hospice or who died elsewhere after hospitalization are not included. Finally, COVID-NET catchment areas include approximately 10% of the U.S. population; thus, these findings might not be nationally generalizable.

TABLE. Demographic characteristics of and clinical outcomes among a sample of adults aged ≥18 years hospitalized with laboratory-confirmed SARS-CoV-2 infection,* by age group — COVID-19–Associated Hospitalization Surveillance Network, 12 states,† October 2023–April 2024

Characteristic	Total		Age group, yrs: 18–49		50–64		65–74		≥75	
	No.	Weighted % (95% CI)	No.	Weighted % (95% CI)	No.	Weighted % (95% CI)	No.	Weighted % (95% CI)	No.	Weighted % (95% CI)
Total	**1,320**	**100 (100.0–100.0)**	**338**	**100 (100.0–100.0)**	**485**	**100 (100.0–100.0)**	**159**	**100 (100.0–100.0)**	**338**	**100 (100.0–100.0)**
Sex										
Female	**716**	**51.2 (46.7–55.6)**	192	54.8 (46.9–62.6)	250	46.9 (39.9–54.0)	83	45.3 (35.2–55.7)	191	54.5 (47.4–61.4)
Male	**604**	**48.8 (44.4–53.3)**	146	45.2 (37.4–53.1)	235	53.1 (46.0–60.1)	76	54.7 (44.3–64.8)	147	45.5 (38.6–52.6)
Race and ethnicity§										
A/PI	**54**	**5.3 (3.3–7.9)**	12	4.1 (1.7–8.1)	22	5.9 (3.1–10.0)	—¶	—¶	13	5.0 (2.3–9.4)
AI/AN	**17**	**1.1 (0.5–2.3)**	—¶	—¶	—¶	—¶	—¶	—¶	—¶	—¶
Black or African American	**270**	**19.8 (16.4–23.5)**	94	33.4 (26.1–41.4)	117	31.7 (25.1–39.0)	27	20.1 (12.9–29.1)	32	13.0 (8.2–19.3)
White	**818**	**64.5 (60.1–68.6)**	162	39.0 (31.7–46.7)	276	47.8 (40.8–54.9)	110	64.4 (53.9–74.0)	270	74.9 (68.0–81.0)
Hispanic or Latino	**133**	**7.3 (5.5–9.6)**	54	18.2 (12.4–25.2)	54	11.7 (7.9–16.7)	10	6.8 (2.6–14.0)	15	4.1 (2.0–7.4)
Unknown race	**19**	**1.1 (0.4–2.5)**	—¶	—¶	—¶	—¶	—¶	—¶	—¶	—¶
Resident of long-term care facility										
Yes	**171**	**16.6 (13.4–20.2)**	24	7.8 (4.0–13.4)	48	11.8 (7.3–17.6)	14	7.7 (3.4–14.4)	85	23.7 (18.1–30.0)
No	**1,148**	**83.4 (79.8–86.6)**	314	92.2 (86.6–96.0)	436	88.2 (82.4–92.7)	145	92.3 (85.6–96.6)	253	76.3 (70.0–81.9)
Underlying medical conditions										
0	**95**	**3.5 (2.5–4.9)**	47	12.1 (7.9–17.5)	36	5.1 (3.1–7.8)	—¶	—¶	—¶	—¶
1	**254**	**16.5 (13.5–19.9)**	99	29.2 (22.7–36.4)	74	16.0 (11.2–21.8)	30	21.7 (13.2–32.5)	51	12.1 (8.4–16.8)
≥1	**1,225**	**96.5 (95.1–97.5)**	291	87.9 (82.5–92.1)	449	94.9 (92.2–96.9)	155	98.1 (94.6–99.6)	330	97.8 (95.2–99.2)
≥2	**971**	**80.0 (76.4–83.2)**	192	58.7 (50.9–66.1)	375	78.9 (72.9–84.1)	125	76.4 (65.7–85.1)	279	85.7 (80.8–89.8)
Hospitalization, intervention or outcome										
Length of stay, days, median (IQR)	**3.4 (1.9–7.1)**		2.9 (1.4–5.5)		3.4 (1.9–7.9)		3.2 (1.8–6.8)		3.6 (2.0–7.2)	
ICU admission	**247**	**18.4 (15.0–22.1)**	64	17.9 (12.6–24.3)	99	21.5 (16.0–28.0)	36	21.4 (13.7–31.0)	48	16.0 (11.1–22.1)
Invasive mechanical ventilation	**95**	**8.4 (5.9–11.6)**	21	5.9 (3.1–10.2)	40	11.3 (7.0–17.0)	21	12.8 (6.9–21.0)	13	6.1 (2.6–11.8)
In-hospital death	**60**	**6.9 (4.6–9.9)**	—¶	—¶	20	6.4 (3.0–11.7)	16	11.3 (5.6–19.8)	17	6.1 (3.0–11.0)
Any respiratory viral codetection**										
Yes	**47**	**4.4 (2.7–6.8)**	13	4.0 (1.6–8.2)	16	5.2 (2.0–10.7)	—¶	—¶	10	4.1 (1.7–8.1)
Vaccination status††										
No record of 2022–2023 (bivalent) or 2023–2024 formula dose	**766**	**57.7 (53.3–62.1)**	236	75.0 (68.1–81.0)	295	70.3 (64.0–76.1)	92	66.7 (57.0–75.5)	143	46.5 (39.5–53.6)
Received 2022–2023 (bivalent) dose, but no 2023–2024 formula dose	**401**	**30.3 (26.4–34.5)**	81	20.8 (15.2–27.3)	150	24.2 (19.0–30.0)	44	23.8 (16.5–32.6)	126	36.9 (30.4–43.7)
Received 2023–2024 formula dose	**146**	**11.9 (9.2–15.2)**	20	4.3 (2.1–7.7)	35	5.5 (2.7–9.7)	22	9.5 (4.6–16.8)	69	16.6 (11.9–22.2)
Did not receive 2023–2024 formula dose	**1,167**	**88.1 (84.8–90.8)**	317	95.7 (92.3–97.9)	445	94.5 (90.3–97.3)	136	90.5 (83.2–95.4)	269	83.4 (77.8–88.1)

See table footnotes on the next page.

TABLE. (*Continued*) Demographic characteristics of and clinical outcomes among a sample of adults aged ≥18 years hospitalized with laboratory-confirmed SARS-CoV-2 infection,* by age group — COVID-19–Associated Hospitalization Surveillance Network, 12 states,† October 2023–April 2024

Abbreviations: A/PI = Asian or Pacific Islander; AI/AN = American Indian or Alaska Native; ICU = intensive care unit.

* The likely primary complaint upon admission is identified by trained COVID-19–Associated Hospitalization Surveillance Network surveillance officers using information in the medical record. The likely primary complaint is identified and categorized as COVID-19–related illness; inpatient surgery or procedures; psychiatric admission requiring acute medical care; trauma; "other" (with an accompanying free-text field); or unknown. CDC clinicians independently review the free-text field of complaints classified as "other" to determine if the complaint might be recategorized or remain in the "other" category (e.g., skin and soft tissue infections). Hospitalizations for which the likely primary complaint was not COVID-19–related illness were excluded from the analysis of clinical data.

† Selected counties and county equivalents in California, Colorado, Connecticut, Georgia, Maryland, Michigan, Minnesota, New Mexico, New York, Oregon, Tennessee, and Utah.

§ Persons of Hispanic or Latino (Hispanic) origin might be of any race but are categorized as Hispanic; all racial groups are non-Hispanic. Non-Hispanic persons of other races not listed are not presented due to small sample size.

¶ Data are not presented for cells with sample size <10.

** Denominators are the number of adults tested for respiratory viral codetections (1,134), accounting for 86.0% (95% CI = 82.5%–89.0%) of adults aged ≥18 years.

†† Vaccination status for the 2023–2024 surveillance season was only collected for vaccines administered on or after September 1, 2022.

Summary

What is already known about this topic?

Hospitalization due to COVID-19 remains a public health concern. The risk for hospitalization among adults increases with age.

What is added by this report?

During October 2023–April 2024, adults aged ≥65 years accounted for 70% of all COVID-19–associated hospitalizations among adults. Most hospitalized adults had multiple underlying medical conditions. Only 12% had received the recommended COVID-19 2023–2024 formula vaccine.

What are the implications for public health practice?

Adults at increased risk for COVID-19–associated hospitalization should reduce their risk for severe COVID-19 by adopting measures to reduce risk for contracting COVID-19, receiving recommended COVID-19 vaccinations, and seeking prompt outpatient antiviral treatment after a positive SARS-CoV-2 test result.

Implications for Public Health Practice

COVID-19–associated hospitalizations continue to largely affect adults aged ≥65 years. All adults, especially those aged ≥65 years and others at increased risk for progression to severe COVID-19 illness, including residents of LTCFs, should reduce their risk for COVID-19–related hospitalization and severe outcomes by receiving recommended COVID-19 vaccines, adopting measures to reduce risk for contracting SARS-CoV-2, and seeking early outpatient antiviral treatment after receipt of a positive SARS-CoV-2 test result.

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Differences in COVID-19 Outpatient Antiviral Treatment Among Adults Aged ≥65 Years by Age Group — National Patient-Centered Clinical Research Network, United States, April 2022–September 2023

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Abstract

Adults aged ≥65 years experience the highest risk for COVID-19–related hospitalization and death, with risk increasing with increasing age; outpatient antiviral treatment reduces the risk for these severe outcomes. Despite the proven benefit of COVID-19 antiviral treatment, information on differences in use among older adults with COVID-19 by age group is limited. Nonhospitalized patients aged ≥65 years with COVID-19 during April 2022–September 2023 were identified from the National Patient-Centered Clinical Research Network. Differences in use of antiviral treatment among patients aged 65–74, 75–89, and ≥90 years were assessed. Multivariable logistic regression was used to estimate the association between age and nonreceipt of antiviral treatment. Among 393,390 persons aged ≥65 years, 45.9% received outpatient COVID-19 antivirals, including 48.4%, 43.5%, and 35.2% among those aged 65–75, 76–89, and ≥90 years, respectively. Patients aged 75–89 and ≥90 years had 1.17 (95% CI = 1.15–1.19) and 1.54 (95% CI = 1.49–1.61) times the adjusted odds of being untreated, respectively, compared with those aged 65–74 years. Among 12,543 patients with severe outcomes, 2,648 (21.1%) had received an outpatient COVID-19 antiviral medication, compared with 177,874 (46.7%) of 380,847 patients without severe outcomes. Antiviral use is underutilized among adults ≥65 years; the oldest adults are least likely to receive treatment. To prevent COVID-19–associated morbidity and mortality, increased use of COVID-19 antiviral medications among older adults is needed.

Introduction

One of the most important factors associated with increased risk for hospitalization and death among patients with COVID-19 is age ≥50 years, with risk increasing with increasing age (*1*–*4*). Adults aged ≥65 years accounted for approximately two thirds of all COVID-19–associated hospitalizations during October 2023–April 2024, with adults aged ≥75 years accounting for nearly one half of hospitalizations and in-hospital deaths (*1*). In 2022, the COVID-19–related mortality rate among persons aged 65–74 and ≥85 years was approximately 100 and 800 times as high, respectively, as that among persons aged 15–24 years (*4*). Despite the continued effectiveness of COVID-19 oral antiviral medications to prevent hospitalization and death (*3*), studies suggest low use among persons aged ≥65 years; however, less is known about the differences in use among older patients (*5*,*6*). To examine differences in treatment by age and other factors associated with treatment, such as underlying medical conditions, race, and ethnicity, electronic health record data from the National Patient-Centered Clinical Research Network (PCORnet)* were analyzed.

Methods

Study Population and Criteria for Inclusion or Exclusion

This cross-sectional study used electronic health record data from 28,053,928 adults aged ≥20 years at 28 U.S. health care systems participating in PCORnet, during April 2022–September 2023. Patients with SARS-CoV-2 infection (1,298,966) were identified using at least one of the following inclusion criteria: 1) laboratory-confirmed SARS-CoV-2 test result identified with Logical Observation Identifiers Names and Codes (LOINC)†; 2) an *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM)§ diagnostic code for COVID-19 (U07.1 or U07.2); or 3) prescription or administration of an outpatient COVID-19 treatment (nirmatrelvir-ritonavir, molnupiravir, monoclonal antibody, or remdesivir).¶ The earliest COVID-19 diagnosis date by one of these three criteria was defined as the

* PCORnet is a national network that facilitates access to health care data and interoperability through the use of a common data model across participating health care systems. The PCORnet Common Data Model includes demographic characteristics, diagnoses, prescriptions, procedures, and laboratory test results, among other inpatient and outpatient elements, from approximately 30 million patients. https://pcornet.org/data

† LOINC is a code system that includes identifiers, names, and codes for clinical and laboratory observations, health care screening instruments, and document types. https://loinc.org

§ https://www.cdc.gov/nchs/icd/icd-10-cm/files.html

¶ Nirmatrelvir-ritonavir and molnupiravir are taken orally; remdesivir and monoclonal antibodies are administered intravenously. The only monoclonal antibody available for outpatient treatment during the study period was bebtelovimab. However, on November 30, 2022, the Food and Drug Administration announced that bebtelovimab was not authorized because it was not expected to neutralize the variants in circulation at that time.

index date. Persons hospitalized on or before their index date (1,297,899) were excluded to limit the analysis to outpatient COVID-19 diagnoses; thus, 393,390 patients aged ≥65 years were selected for inclusion in the analysis.

Population Characteristics and Outcome Definitions

Characteristics of patients aged 65–74, 75–89, and ≥90 years with COVID-19 were described by sex, race and ethnicity, area deprivation index (ADI),** underlying medical conditions, combined comorbidity index (CCI),†† use of immunosuppressive medication,§§ use of outpatient COVID-19 antivirals (overall and by medication) within 30 days of the index date, and outcome (*7*). Hospitalizations were inpatient encounters within 16 days of the index date. Severe outcome was defined as 1) hospitalization or 2) death or hospice (in-hospital death, out-of-hospital death, or discharge to hospice within 30 days of index date).¶¶

Statistical Analysis

To compare differences by age, Pearson's chi-square p-values were calculated. Because nearly all p-values were statistically significant at $p<0.05$, standardized mean differences (SMDs) were calculated among age groups to identify larger effect sizes; an SMD>0.2 was considered to represent large differences among groups.*** Logistic regression was used to estimate measures of association of age group with nontreatment, adjusting for sex, race, ethnicity, comorbidity index, and ADI score. To address a potential selection bias, a sensitivity analysis was conducted, excluding patients whose only index date was based on an antiviral prescription. All analyses were conducted using R software (version 4.2.3; R Foundation). This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.†††

Results

Population Characteristics, Outcomes, and Univariate Results by Age

Among 393,390 patients aged ≥65 years who received a COVID-19 diagnosis§§§ in an outpatient setting during April 2022–September 2023, a total of 221,798 (56.4%) were aged 65–74 years, 154,918 (39.4%) were aged 75–89 years, and 16,674 (4.2%) were aged ≥90 years (Table 1). Overall, 225,497 (57.3%) patients were women, 306,347 (80.7%) were non-Hispanic White, and 33,721 (8.9%) were non-Hispanic Black or African American. Among all 393,390 COVID-19 patients aged ≥65 years, 180,522 (45.9%) received outpatient antiviral treatment for COVID-19, 10,748 (2.7%) were hospitalized, and 2,422 (0.6%) died or were discharged to hospice. Statistically significant differences by age group were observed in the combined comorbidity score and several underlying medical conditions and treatment (Table 1). Prevalence of hospitalizations was 1.8% among patients aged 65–74 years, 3.5% among those aged 75–89 years, and 7.1% among those aged ≥90 years (SMD = 0.174) (Table 1) (Figure).

Differences in Receipt of Antiviral Treatment by Age

Receipt of outpatient antiviral treatment¶¶¶ varied across age groups: 48.4% among patients aged 65–74 years, 43.5% among those aged 75–89 years, and 35.2% among those aged ≥90 years received a COVID-19 antiviral (SMD = 0.180) (Figure). Among patients aged 65–74 years, 45.0% received an oral antiviral medication compared with 38.4% among those aged 75–89 years and 28.0% among those aged ≥90 years**** (SMD = 0.239). The percentage of patients aged ≥90 years who were treated with molnupiravir (4.5%) or intravenous remdesivir (4.1%) was higher than the percentage of those aged 65–74 years who received these medications (3.2% and 0.8%, respectively). Compared with COVID-19 patients aged 65–74 years, the adjusted odds ratio (aOR) for not being treated with outpatient antiviral medications for COVID-19 was 1.17 among patients aged 75–89 years and 1.54 among those aged ≥90 years. Compared with those with a CCI score <1 (lower mortality risk), those with a CCI score of 1–2 and

** ADI is a mapping tool that displays relative socioeconomic conditions of a neighborhood. Patients' 5-digit zip codes are mapped to socioeconomic status by normalized ADI value (0–100). Lower values are associated with lower deprivation and higher values with higher deprivation. Values are grouped into quartiles using the count of zip codes. Quartile 1 represents the lowest range and quartile 4 the highest range of ADI values (quartile 1 = 0–38; quartile 2 = 39–43; quartile 3 = 44–49; and quartile 4 = 50–100). https://www.neighborhoodatlas.medicine.wisc.edu

†† CCI score is a validated numerical value for the Medicare population used to predict 1-year mortality and ranges from −2 to 265. Higher values are associated with increased mortality risk.

§§ The use of immunosuppressive medications was defined as having a prescription for an immunosuppressing medication or corticosteroids (parenteral or oral) at least once during the 365 days before the index COVID-19 diagnosis.

¶¶ This outcome is determined only from data recorded in an electronic health record. PCORnet data identifies in-facility deaths but not out-of-facility deaths unless linked to a death or vital records registry.

*** SMDs were calculated by averaging all the pairwise absolute differences among the three groups scaled by their SDs.

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

§§§ Among 393,390 patients aged ≥65 years with COVID-19, 67% had a COVID-19 diagnostic code, 32.1% had received a laboratory-confirmed positive SARS-CoV-2 test result, 40.1% were prescribed an outpatient COVID-19 treatment, and 1.1% were administered an outpatient COVID-19 treatment. Patients could have met more than one of these criteria.

¶¶¶ A total of 1,818 (0.05%) patients aged ≥65 years with COVID-19 received more than one outpatient antiviral or monoclonal antibody, including 16 persons who received three different medications.

**** In this data asset, 80% of persons hospitalized received a COVID-19 diagnosis on or after their day of admission and were excluded from this analysis. Decreased oral antiviral use in older age groups when hospitalized patients were included was observed (42.1% among those aged 65–74 years, 33.6% among those aged 75–89 years, and 21.7% among those aged ≥90 years).

TABLE 1. Characteristics of persons aged 65–74, 75–89, and ≥90 years with an outpatient COVID-19 diagnosis — National Patient-Centered Clinical Research Network, United States, April 2022–September 2023

Characteristic	Age group, yrs no. (%)				SMD*
	All	65–74	75–89	≥90	
Total	**393,390 (100.0)**	**221,798 (56.4)**	**154,918 (39.4)**	**16,674 (4.2)**	—
COVID-19 outpatient medication received within 30 days of the index date†					
Any (nirmatrelvir-ritonavir, molnupiravir, monoclonal antibodies, or remdesivir)	**180,522 (45.9)**	107,320 (48.4)	67,338 (43.5)	5,864 (35.2)	0.180
Any oral (nirmatrelvir-ritonavir or molnupiravir)	**163,947 (41.7)**	99,863 (45.0)	59,420 (38.4)	4,664 (28.0)	0.239
Nirmatrelvir-ritonavir	**150,562 (38.3)**	93,149 (42.0)	53,441 (34.5)	3,972 (23.8)	0.262
Molnupiravir	**14,228 (3.6)**	7,190 (3.2)	6,295 (4.1)	743 (4.5)	0.042
Monoclonal antibodies	**12,316 (3.1)**	6,158 (2.8)	5,560 (3.6)	598 (3.6)	0.031
Remdesivir	**5,250 (1.3)**	1,725 (0.8)	2,839 (1.8)	686 (4.1)	0.148
Defining index event§					
COVID-19 diagnosis	**264,927 (67.3)**	149,333 (67.3)	104,252 (67.3)	11,342 (68.0)	0.010
COVID-19 laboratory test result (positive, detected, or presumptive)	**126,287 (32.1)**	65,975 (29.7)	53,598 (34.6)	6,714 (40.3)	0.148
COVID-19 medication prescription	**157,808 (40.1)**	94,912 (42.8)	57,996 (37.4)	4,900 (29.4)	0.188
COVID-19 medication administration	**4,133 (1.1)**	1,951 (0.9)	1,941 (1.3)	241 (1.4)	0.035
Comorbidities¶					
Cancer	**61,658 (15.7)**	31,352 (14.1)	27,914 (18.0)	2,392 (14.3)	0.071
Cardiac	**264,646 (67.3)**	137,878 (62.2)	113,473 (73.2)	13,295 (79.7)	0.262
HIV	**1,264 (0.3)**	1,028 (0.5)	228 (0.1)	8 (0.0)	0.057
Immunodeficiency	**84,969 (21.6)**	49,794 (22.5)	32,608 (21.0)	2,567 (15.4)	0.121
Kidney disease	**71,081 (18.1)**	29,689 (13.4)	35,782 (23.1)	5,610 (33.6)	0.327
Liver	**7,623 (1.9)**	5,298 (2.4)	2,192 (1.4)	133 (0.8)	0.086
Metabolic	**151,598 (38.5)**	89,273 (40.2)	57,745 (37.3)	4,580 (27.5)	0.181
Neurologic	**24,973 (6.3)**	7,255 (3.3)	14,204 (9.2)	3,514 (21.1)	0.383
Psychiatric and substance abuse	**79,769 (20.3)**	46,959 (21.2)	29,871 (19.3)	2,939 (17.6)	0.060
Pulmonary	**77,037 (19.6)**	43,331 (19.5)	30,850 (19.9)	2,856 (17.1)	0.048
Other	**4,203 (1.1)**	2,374 (1.1)	1,659 (1.1)	170 (1.0)	0.003
None of above comorbidities	**69,758 (17.7)**	43,687 (19.7)	23,802 (15.4)	2,269 (13.6)	0.109
Combined comorbidity index score**					
<0	**57,462 (15.0)**	36,530 (16.8)	19,528 (13.0)	1,404 (8.7)	0.484
0	**126,700 (33.0)**	80,988 (37.3)	42,637 (28.3)	3,075 (19.1)	
1	**71,240 (18.6)**	42,146 (19.4)	26,906 (17.9)	2,188 (13.6)	
2	**41,990 (10.9)**	21,425 (9.9)	18,420 (12.2)	2,145 (13.3)	
3	**26,342 (6.9)**	11,835 (5.5)	12,763 (8.5)	1,744 (10.8)	
4	**17,124 (4.5)**	7,078 (3.3)	8,602 (5.7)	1,444 (9.0)	
5	**12,457 (3.2)**	4,934 (2.3)	6,392 (4.2)	1,131 (7.0)	
>5	**30,515 (8.0)**	12,111 (5.6)	15,461 (10.3)	2,943 (18.3)	
Missing	**9,560 (—)**	4,751 (—)	4,209 (—)	600 (—)	
Immunosuppressive medication within year of index event					
Corticosteroid (one or more event)	**58,931 (15.0)**	34,667 (15.6)	22,493 (14.5)	1,771 (10.6)	0.099
Immunosuppressive medication (one or more event)	**13,250 (3.4)**	8,767 (4.0)	4,285 (2.8)	198 (1.2)	0.118
Sex					
Women	**225,497 (57.3)**	127,722 (57.6)	87,074 (56.2)	10,701 (64.2)	0.109
Men	**167,869 (42.7)**	94,060 (42.4)	67,836 (43.8)	5,973 (35.8)	
Race and ethnicity††					
AI/AN	**1,436 (0.4)**	949 (0.4)	464 (0.3)	23 (0.1)	0.110
Asian	**9,800 (2.6)**	5,514 (2.6)	3,775 (2.5)	511 (3.2)	
Black or African American	**33,721 (8.9)**	21,764 (10.2)	10,883 (7.3)	1,074 (6.7)	
NH/PI	**309 (0.1)**	195 (0.1)	104 (0.1)	10 (0.1)	
White	**306,347 (80.7)**	168,794 (78.9)	124,306 (83.1)	13,247 (83.1)	
Multiple races or other races	**8,050 (2.1)**	4,702 (2.2)	3,005 (2.0)	343 (2.2)	
Hispanic or Latino	**19,924 (5.2)**	12,128 (5.7)	7,055 (4.7)	741 (4.6)	
Missing	**13,803 (—)**	7,752 (—)	5,326 (—)	725 (—)	
COVID-19 vaccination history, no. of recorded doses§§					
1	**23,620 (6.0)**	13,948 (6.3)	8,783 (5.7)	889 (5.3)	0.114
2	**55,441 (14.1)**	30,314 (13.7)	22,766 (14.7)	2,361 (14.2)	
3	**71,279 (18.1)**	41,103 (18.5)	27,595 (17.8)	2,581 (15.5)	
≥4	**73,512 (18.7)**	40,706 (18.4)	30,188 (19.5)	2,618 (15.7)	
0 or missing	**169,538 (43.1)**	95,727 (43.2)	65,586 (42.3)	8,225 (49.3)	
Received ≥1 COVID-19 vaccine dose in the previous 6 months	**73,595 (18.7)**	41,768 (18.8)	29,152 (18.8)	2,595 (15.6)	0.058

See table footnotes on the next page.

TABLE 1. (*Continued*) Characteristics of persons aged 65–74, 75–89, and ≥90 years with an outpatient COVID-19 diagnosis — National Patient-Centered Clinical Research Network, United States, April 2022–September 2023

Characteristic	Age group, yrs no. (%)				
	All	65–74	75–89	≥90	SMD*
Area deprivation index¶¶					
Q1	**116,910 (35.4)**	64,827 (34.7)	47,074 (36.2)	5,009 (36.8)	0.050
Q2	**85,519 (25.9)**	47,702 (25.5)	34,248 (26.3)	3,569 (26.2)	
Q3	**73,275 (22.2)**	41,562 (22.3)	28,850 (22.2)	2,863 (21.0)	
Q4	**54,892 (16.6)**	32,695 (17.5)	20,016 (15.4)	2,181 (16.0)	
Missing	**62,794 (—)**	35,012 (—)	24,730 (—)	3,052 (—)	
Hospitalization					
Inpatient encounter 1–16 days after index event	**10,748 (2.7)**	4,087 (1.8)	5,471 (3.5)	1,190 (7.1)	0.174
No. of days after index event to hospitalization, mean (SD)	**4.50 (4.49)**	4.98 (4.70)	4.34 (4.41)	3.62 (3.89)	0.209
Death or discharge to hospice					
0–30 days after index event	**2,422 (0.6)**	623 (0.3)	1,309 (0.8)	490 (2.9)	0.147
No. of days after index, mean (SD)	**11.82 (8.88)**	12.00 (9.27)	11.90 (8.77)	11.38 (8.68)	0.047
No. of patients with hospitalization or death or discharge to hospice* **	**12,543**	**4,530**	**6,449**	**1,564**	—
With evidence of any outpatient treatment	**2,648 (21.1)**	933 (20.6)	1,372 (21.3)	343 (21.9)	0.022
With evidence of oral antiviral treatment	**1,808 (14.4)**	621 (13.7)	821 (12.7)	193 (12.3)	0.027
Without evidence of outpatient treatment	**9,895 (78.9)**	3,597 (79.4)	5,077 (78.7)	1,221 (78.1)	0.022
No. of patients with no hospitalization and no death or discharge to hospice	**380,847**	**217,268**	**148,469**	**15,110**	—
With evidence of any outpatient treatment	**177,874 (46.7)**	106,387 (49.0)	65,966 (44.4)	5,521 (36.5)	0.168
With evidence of oral antiviral treatment	**157,726 (41.4)**	99,242 (45.7)	58,599 (39.5)	4,471 (29.6)	0.224
Without evidence of outpatient treatment	**202,973 (53.3)**	110,881 (51.0)	82,503 (55.6)	9,589 (63.5)	0.168

Abbreviations: ADI = area deprivation index; AI/AN = American Indian or Alaska Native; BMI = body mass index; NH/PI = Native Hawaiian or Pacific Islander; Q = quartile; SMD = standardized mean difference.

* SMD values are reported because all p-values were significant at p<0.05, except for mean number of days from hospitalization to death or discharge to hospice (p = 0.453), COVID-19 diagnosis as index (p = 0.159), "Other" comorbidities (p = 0.821), and all values in hospitalized/died/discharge to hospice treatment status. SMDs were calculated for each characteristic or condition compared with not having that characteristic or condition. For characteristics with categories that are mutually exclusive (combined comorbidity index score, sex, race and ethnicity, COVID-19 vaccination history, number of recorded doses, and ADI) the SMD measured the effect size of each age group and category.

† A total of 1,818 (0.05%) patients aged ≥65 years with COVID-19 received more than one outpatient antiviral or monoclonal antibody, including 16 persons who received three different treatments.

§ Participants could have more than one qualifying index event; therefore, these categories are not mutually exclusive.

¶ At least one record in the 3 years preceding index date: Cardiac = cerebrovascular disease, congestive heart failure, arrythmia, coronary artery disease, hypertension, or peripheral vascular disease; Metabolic = type 1 diabetes, type 2 diabetes, overweight (BMI 25–30 kg/m^2), obesity (BMI ≥30 kg/m^2), or severe obesity (BMI ≥40 kg/m^2); Pulmonary = alpha-1 antitrypsin deficiency, bronchopulmonary dysplasia, chronic pulmonary disorder, asthma, chronic obstructive pulmonary disease, cystic fibrosis, or pulmonary circulation disorder; Kidney disease = chronic kidney disease, or end stage renal disease with dialysis; Immunodeficiency = primary immunodeficiency, inflammatory bowel disease, systemic lupus erythematosus, solid organ or stem cell transplant, rheumatoid arthritis, cancer, or multiple sclerosis;. Liver = cirrhosis, hepatitis B, or hepatitis C; Neurologic = dementia, seizure or epilepsy disorder, Parkinson disease, or hemiplegia; Psychiatric and substance abuse = alcohol abuse, smoking, substance use disorder, or mental health disorder; and Other = anemia, autism, coagulopathy, Down syndrome, or inactivity.

** Categories were generated from the combined comorbidity index score.

†† Persons of Hispanic or Latino (Hispanic) origin might be of any race but are categorized as Hispanic; all racial groups are non-Hispanic. The "Other" category includes persons of multiple racial and ethnicity groups.

§§ Vaccination data includes any COVID-19 vaccination before the index date.

¶¶ Patient 5-digit zip codes were mapped to socioeconomic status by normalized (ADI) value (0–100). Lower values are associated with lower deprivation, and higher values are associated with higher deprivation. For this mapping, values were grouped into quartiles using the count of zip codes. Q1 represents the lowest range of ADI values, and Q4 represents the highest range of ADI values (Q1 = 0–38; Q2 = 39–43; Q3 = 44–49; and Q4 = 50–100). Additional ADI index information is available at https://www.neighborhoodatlas.medicine.wisc.edu/.

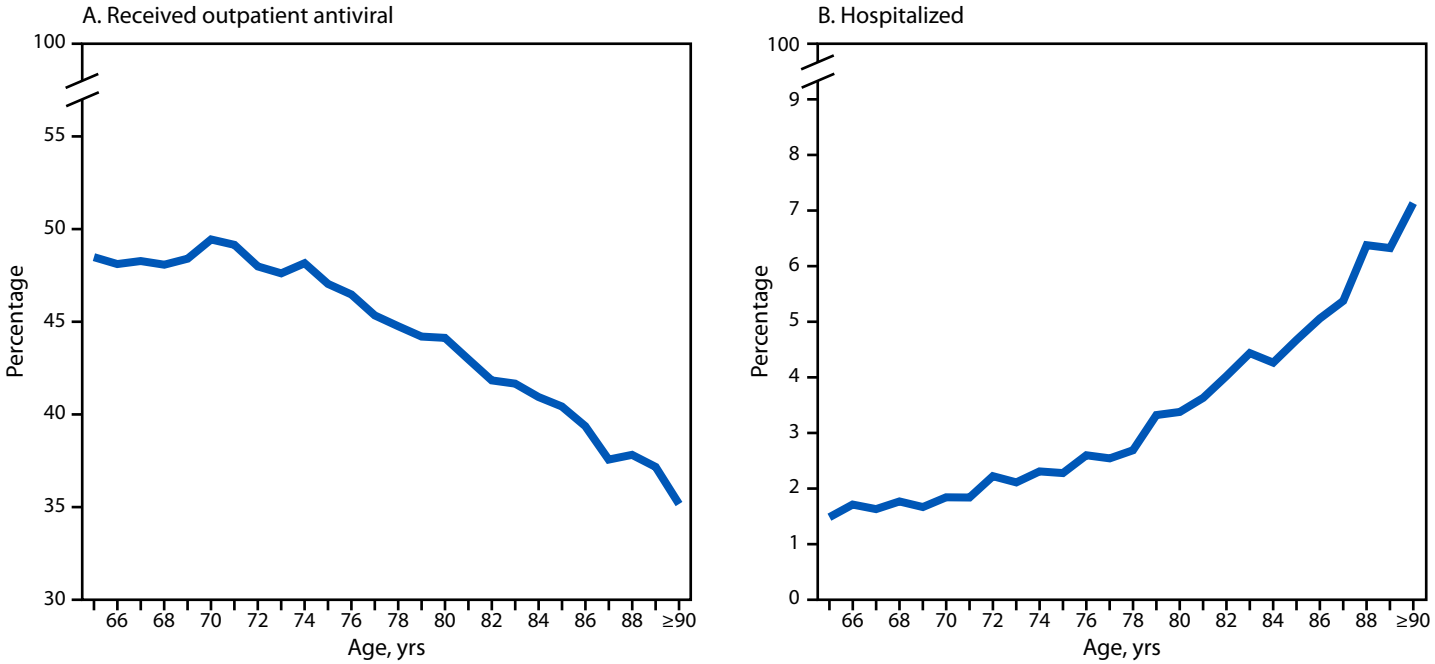
*** Hospitalization within 16 days of index diagnosis, or death or discharge to hospice within 30 days of index diagnosis.

≥3 had increased odds of not receiving antiviral treatment (aOR = 1.09 and 1.47, respectively) (Table 2). Similar results were found when 62,910 patients whose index date was based on a prescription only were excluded. Among 12,543 patients with severe outcomes, 2,648 (21.1%) had received an outpatient COVID-19 antiviral, compared with 177,874 (46.7%) of 380,847 patients without severe outcomes (Table 1).

Discussion

This analysis of nearly 400,000 COVID-19 patients aged ≥65 years found that fewer than one half received outpatient COVID-19 antiviral treatment. This finding is consistent with other studies: among patients aged 65–79 years and ≥80 years, one reported 37% and 9% antiviral use (*3*) and another reported 39.9% and 30.7% use, respectively (*6*). This study

FIGURE. Percentage of adults aged ≥65 years with COVID-19 who received an outpatient antiviral medication* (A) and who were hospitalized† (B), by age — National Patient-Centered Clinical Research Network, United States, April 2022–September 2023



* Patients with SARS-CoV-2 infection were identified using at least one of the following inclusion criteria: 1) laboratory-confirmed positive SARS-CoV-2 test result identified with Logical Observation Identifiers Names and Codes (LOINC); 2) an *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) diagnostic code for COVID-19 (U07.1 or U07.2); or 3) prescription or administration of an outpatient COVID-19 treatment (nirmatrelvir-ritonavir, molnupiravir, monoclonal antibody, or remdesivir). The earliest COVID-19 infection diagnosis date by one of these three criteria was defined as the index date.
† Hospitalizations were inpatient encounters within 16 days of the index date.

TABLE 2. Association of age and combined comorbidity index with odds of not receiving outpatient COVID-19 antiviral medication*,†,§ — National Patient-Centered Clinical Research Network, United States, April 2022–September 2023

Characteristic	Odds ratio (95% CI)	
	Unadjusted	Adjusted
Age group, yrs		
65–74	Ref	Ref
75–89	1.22 (1.20–1.24)	1.17 (1.15–1.19)
≥90	1.73 (1.67–1.79)	1.54 (1.49–1.61)
Combined comorbidity index¶		
≤0	Ref	Ref
1–2	1.09 (1.08–1.11)	1.09 (1.07–1.10)
≥3	1.58 (1.55–1.61)	1.47 (1.44–1.50)

Abbreviation: Ref = referent group.
* Nirmatrelvir-ritonavir, molnupiravir, monoclonal antibody, or remdesivir.
† Adjusted for sex, race and ethnicity, and area deprivation index.
§ Model sample size = 312,003 (cohort size = 393,390). Missing values: race = 3.5%; sex <0.01%; combined comorbidity index = 2.4%; area deprivation index = 16.0%.
¶ Combined comorbidity index is a validated score for the Medicare population used to predict 1-year mortality and ranges from −2 to 265. Higher values are associated with increased mortality risk.

found that prevalence of receipt of antivirals decreased progressively and substantially with increasing age in persons aged 65 to ≥90 years, after controlling for the number of underlying medical conditions and other demographic factors.

Several real-world studies, including those conducted since the emergence of SARS-CoV-2 Omicron variant in January 2022, have demonstrated that COVID-19 antivirals are effective in preventing hospitalization and death (*3*). Because older age is a strong risk factor for severe COVID-19–associated outcomes, and COVID-19 hospitalizations continue to disproportionately affect older patients (*1–4*), treatment of COVID-19, including cases in older adults, is critical to the prevention of severe outcomes.

Among older patients, frequent self-reported reasons for nonuse of antivirals include the presence of mild signs and symptoms, lack of awareness of eligibility, and absence of a provider recommendation (*8*). Other potential barriers to treatment among older patients include delays in seeking treatment after symptom onset and missing the treatment window (5–7 days after symptom onset) (*8*). Challenges to COVID-19 antiviral use include obtaining testing (*9*), acquiring an antiviral prescription after receiving a positive SARS-CoV-2 test result, and accessing treatment, with each step potentially requiring a separate visit to a health care facility.

Older age is associated with increasing numbers of comorbidities and potentially related medications, which might lead to patient and provider hesitation to commence treatment, based on concerns about drug interactions with nirmatrelvir-ritonavir

Summary

What is already known about this topic?

Older adults are at highest risk for hospitalization and death from COVID-19, with risk increasing with age. Outpatient antiviral treatment is effective at reducing these risks.

What is added by this report?

Fewer than one half of adults aged ≥65 years with an outpatient COVID-19 diagnosis received a recommended COVID-19 antiviral medication, including 48% among adults aged 65–74 years, 44% among those aged 75–89 years, and 35% among those aged ≥90 years. Among patients with severe outcomes, 21% had received an outpatient COVID-19 antiviral, compared with 47% of patients without severe outcomes.

What are the implications for public health practice?

Lower prevalence of outpatient antiviral treatment in the oldest age groups highlights the continued need to improve COVID-19 antiviral use by increasing awareness and testing, and facilitating early treatment in these groups.

or contraindications among patients with severe hepatic and renal disease. Lower antiviral use prevalence among persons who have more underlying medical conditions might be consistent with concern about drug interactions or difficulty in temporarily discontinuing or adjusting other concomitantly prescribed medications in older persons. However, absolute contraindications are unlikely to be the only reason for this finding because the decrease in antiviral use prevalence by age persisted even after controlling for CCI score. In addition, the use of the well-tolerated oral molnupiravir and intravenous remdesivir, which have few medication contraindications, increased only slightly with increasing age, and this analysis suggests that these medications have not closed the age-related treatment gap. Older adults and their providers might also have concerns about possible rebound after treatment, including the need to isolate should symptoms recur, although a review found similar frequencies of viral rebound among persons who received or did not receive treatment for COVID-19 (*10*).

Limitations

The findings in this report are subject to at least four limitations. First, this study excluded patients who received a COVID-19 diagnosis upon hospital admission, although the trend of decreasing oral antiviral use with age was similar when those diagnosed with COVID-19 during hospitalization were included. Second, selection bias might have resulted from exclusion of persons who did not have electronic health record documentation of receipt of a positive test result or treatment for COVID-19; this exclusion might also vary by age, possibly underestimating the prevalence of COVID-19 or treatment. Third, this data asset represents predominantly urban-based health care systems that identified a small portion of laboratory- or provider-confirmed cases during April 2022–September 2023; as such, the results might have overestimated overall receipt of treatment, but the effect by age is unclear. Finally, although few contraindications to receiving antivirals exist, this study could not exclude persons with contraindications to nirmatrelvir-ritonavir, possibly underestimating the prevalence of treatment. However, the effect of contraindications by age is unclear.

Implications for Public Health Practice

In this study of older adult patients with laboratory-confirmed COVID-19, antiviral treatment was underutilized, particularly among the oldest adults, who are at highest risk for severe outcomes. These findings highlight the importance of prioritizing public health efforts to improve antiviral use among older adults with COVID-19, particularly those aged ≥75 years. In addition to vaccination and access to early sensitive diagnostics such as polymerase chain reaction testing, COVID-19 treatment should be routinely discussed with older adults with mild or moderate COVID-19. Among eligible persons, antiviral treatment should be started within 5–7 days of symptom onset. Public health efforts to address provider hesitancy and patient knowledge of COVID-19 antivirals and to eliminate barriers to COVID-19 diagnostics and treatment are needed, especially among older adults.

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Burkholderia multivorans Infections Associated with Use of Ice and Water from Ice Machines for Patient Care Activities — Four Hospitals, California and Colorado, 2020–2024

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Abstract

Ice machines can harbor water-related organisms, and the use of ice or tap water for clinical care activities has been associated with infections in health care settings. During 2021–2022, a total of 23 cases of infection by *Burkholderia multivorans* (sequence type ST659) were reported at two southern California hospitals and linked to contaminated ice and water from ice machines. In addition to these 23 cases, this report also includes 23 previously unreported cases of *B. multivorans* ST659 infections that occurred during 2020–2024: 13 at a northern California hospital, eight at a hospital in Colorado, and two additional cases at one of the southern California hospitals. The same brand of ice machine and brands of filters, descaling, and sanitizing products were used by all four hospitals; *B. multivorans* was isolated from samples collected from ice machines in two of the hospitals. Whole genome sequencing indicated that all clinical and ice machine isolates were highly genetically similar (0–14 single nucleotide variant differences across 81% of the selected reference genome). Recommendations from public health officials to halt the outbreak included avoiding ice and tap water during clinical care activities. An investigation is ongoing to determine possible sources of ice machine contamination. During outbreaks of water-related organisms in health care facilities, health care personnel should consider avoiding the use of tap water, including ice and water from ice machines, for patient care.

Introduction

Ice machines contain several mechanical components that can favor microbial amplification and biofilm formation (*1*,*2*). Use of ice and tap water for clinical care activities has been recognized as a potential route of transmission of water-related opportunistic pathogens causing health care–associated infections, such as *Burkholderia* spp (*3*,*4*). *Burkholderia multivorans* is a member of the *Burkholderia cepacia* complex, a group of water-related, Gram-negative opportunistic bacteria commonly found in soil and water (*5*). Outbreaks of these organisms have been associated with contaminated medications, aqueous medical products, and medical devices and are of clinical importance because these organisms can be antibiotic-resistant and can lead to severe infections, especially among immunocompromised and critically ill patients (*4*,*6*,*7*). *B. multivorans* is often found in the sputum of patients with cystic fibrosis but is rarely isolated otherwise (*5*,*8*).

During August 2021–July 2022, two hospitals in a health care system in southern California (hospitals B and C) reported *B. multivorans* infections in 23 patients without cystic fibrosis (*9*). The outbreak investigation revealed that ice and water dispensed from ice machines were commonly used for clinical care activities (e.g., bed baths, swallow evaluations, and topical application of ice packs for analgesia). The same sequence type (ST659) of *B. multivorans* identified among the patients was isolated from ice and water samples collected from hospital B ice machines (*9*). This sequence type of *B. multivorans* had not been previously identified in the United States (*10*). Reports of patients without cystic fibrosis with *B. multivorans* infections from other hospitals in California and Colorado prompted CDC and state and local jurisdictions to conduct additional investigations. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.*

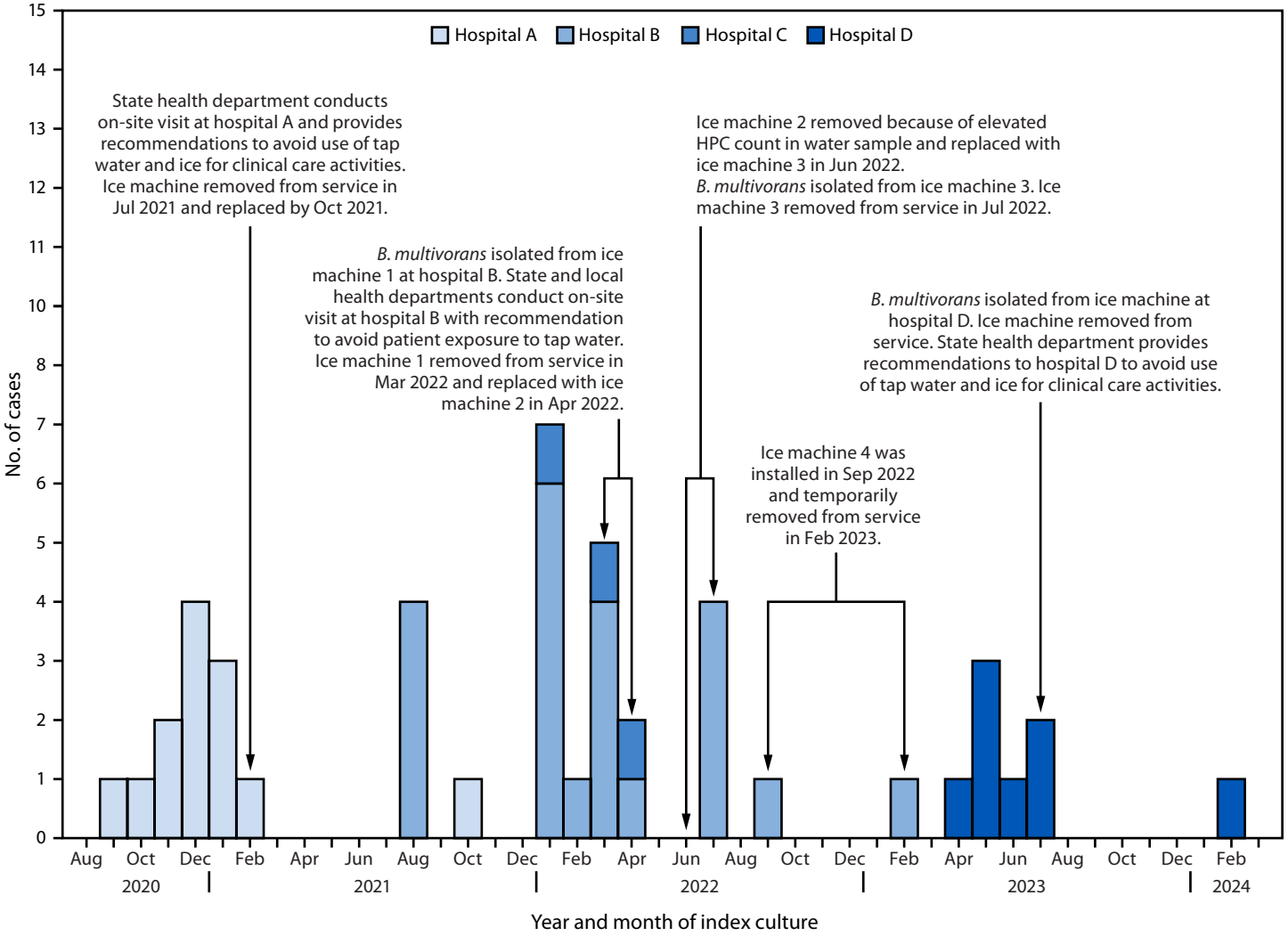
Investigation and Results

Case Identification

A case was defined as an infection with the outbreak strain (ST659) of *B. multivorans*, documented by isolation from a clinical specimen, in a patient without cystic fibrosis at one of the affected acute care hospitals during January 2020 or afterward. During September 2020–February 2024, a total of 46 cases were identified (Figure). During September 2020–October 2021, 13 cases were identified at a northern California hospital (hospital A). In addition to the 23 cases previously reported at the two southern California hospitals (hospital B = 20 and hospital C = three) during August 2021–July 2022, two additional cases were identified at hospital B during September 2022–February 2023. Eight cases were identified at a hospital in Colorado (hospital D) during

*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.

FIGURE. Timeline of the *Burkholderia multivorans* outbreak investigation associated with use of ice and water from ice — four hospitals,* California and Colorado, 2020–2024



Abbreviation: HPC = heterotrophic plate count.
* Hospital A is located in northern California, hospitals B and C in southern California, and hospital D in Colorado.

April 2023–February 2024. Medical records of all 46 cases were reviewed to identify common exposures.

Cases in three of the 46 patients were not temporally clustered with other cases: one patient was identified in October 2021 at hospital A, 8 months after the previous case at this hospital; this patient's previous admission to this hospital was during March–April 2021. The second patient was identified at hospital B in February 2023, 5 months after the previous case at this hospital. The third of these patients was identified at hospital D in February 2024, 7 months after the previous case at this hospital; this patient had multiple admissions to this hospital after undergoing solid organ transplantation in May 2023. These patients might have acquired *B. multivorans* months earlier, during a previous hospital admission.

A respiratory specimen was the source of the *B. multivorans* isolate for most patients identified at the three California hospitals (hospital A = 11 [85%] of 13; hospital B = 17 [77%] of 22; and hospital C = two [67%] of three). At hospital D, however, an intra-abdominal specimen was the isolate source for four of the eight identified patients (Table). Most of the 46 patients were admitted to a medical intensive care unit (ICU) at the time of index specimen collection: hospital A = 13 (100%) of 13; hospital B = 15 (68%) of 22; hospital C = two (67%) of three; and hospital D = five (62%) of eight. Review of medical records did not identify any common exposures.

Infection Prevention and Control Assessments

Public health officials conducted site visits at the affected hospitals at various times after report of the clusters to assess

TABLE. Characteristics of patients with *Burkholderia multivorans* — four hospitals, California and Colorado, 2020–2024

Characteristic	No. (%)				
	California			Colorado	
	Hospital A* n = 13	Hospital B† n = 22	Hospital C§ n = 3	Hospital D¶ n = 8	Total N = 46
Age, yrs, median (range)	60 (42–84)	61 (21–93)	61 (55–97)	56 (34–68)	**60 (21–97)**
Sex					
Female	4 (31)	10 (45)	0 (—)	4 (50)	**18 (39)**
Male	9 (69)	12 (55)	3 (100)	4 (50)	**28 (61)**
Source of index culture**					
Respiratory	11 (85)	17 (77)	2 (67)	2 (25)	**32 (70)**
Blood	2 (15)	3 (14)	1 (33)	2 (25)	**8 (17)**
Intra-abdominal††	0 (—)	0 (—)	0 (—)	4 (50)	**4 (9)**
Urine	0 (—)	2 (9)	0 (—)	0 (—)	**2 (4)**
Admission characteristics of index hospitalization§§					
Days from admission to index culture, median (range)	15 (8–22)	14 (0–117)	30 (0–57)	8 (2–17)	**14 (0–117)**
Patient location at time of specimen collection					
Medical intensive care unit	13 (100)	15 (68)	2 (67)	5 (62)	**35 (76)**
Medical-surgical ward	0 (—)	7 (32)	1 (33)	0 (—)	**8 (17)**
Other¶¶	0 (—)	0 (—)	0 (—)	3 (38)	**3 (7)**
Deceased***	8 (62)	9 (41)	0 (—)	4 (50)	**21 (46)**

* Hospital A was in northern California, and cases were identified during September 2020–October 2021.
† Hospital B was in southern California, and cases were identified during August 2021–February 2023.
§ Hospital C was in southern California, and cases were identified during January–April 2022.
¶ Hospital D cases were identified during April 2023–February 2024.
** Index culture is the first culture in which *Burkholderia multivorans* was isolated. If *B. multivorans* was isolated from blood and nonblood clinical specimens on the same day, the blood isolate was considered as the index culture.
†† Includes biliary fluid (two), peritoneal fluid (one), and perihepatic abscess fluid (one).
§§ Index hospitalization is the hospitalization that occurs when the index culture is identified and includes the period from admission to discharge. Transmission of *B. multivorans* before the index hospitalization cannot be ruled out for patients with frequent hospital admissions.
¶¶ Includes solid organ transplant unit (two) and medical telemetry unit (one).
*** Based on information from medical records; timing and cause of death was not ascertained.

general infection prevention and control practices and identify potential transmission routes for water-related organisms. Health care personnel were interviewed to identify clinical care activities that could have exposed patients to *B. multivorans.* These activities included use of ice and tap water for consumption or clinical care (e.g., placing ice or bags containing ice directly onto surgical incisions or wounds, before percutaneous procedures for analgesia, and when bathing patients with indwelling medical devices without covering and protecting insertion sites). These infection control assessments and health care personnel interviews revealed that 1) patients at all four hospitals might have consumed or been exposed to ice and water dispensed from ice machines during clinical care activities (e.g., swallow evaluations, topical application for analgesia and external cooling, and patient bathing) and 2) the same brand of ice machine and brands of filters, descaling, and sanitizing products were used by all four hospitals.

Environmental Sampling

Public health officials collected samples from ice machines in patient care areas at all four hospitals. Samples were also collected from sinks located in units where patients had been admitted (e.g., sinks in patient rooms, medication preparation stations, and nutrition rooms) at hospitals A, B, and C. Commonly used aqueous medical products from all three California hospitals underwent laboratory testing (e.g., chlorhexidine mouthwash, ultrasound gel, endoscopic instrument lubricants, and premoistened bathing cloths). Products used to descale and sanitize the ice machines from hospitals B and D were also tested.

Northern California hospital. The ice machine from hospital A, located in the unit where the cases were identified, was sampled in March 2021 by a private vendor contracted by the health care facility; *B. multivorans* was not isolated. This machine was removed from service in July 2021 and replaced by October 2021; no additional samples could be collected. *B. multivorans* was not isolated from any other environmental samples or aqueous medical products.

Southern California hospitals. At hospital B, *B. multivorans* was isolated in March and July 2022 from ice and water samples and the drain pan of two ice machines located in the ICU (Figure). At hospital C, *B. multivorans* was not isolated from sampled ice machines in July 2022, but a water sample from one of the ice machines had high bacterial concentration, with a heterotrophic plate count† of 102,000 colony forming units/mL, which exceeds

† A measure of the microbial quality of water.

the potable water level recommended by the Environmental Protection Agency.[§] *B. multivorans* was not isolated from any other environmental samples, aqueous medical products, or ice machine descaling and sanitizing products.

Colorado hospital. *B. multivorans* was isolated from six of 10 ice machines that were sampled during July 2023–March 2024 at hospital D but was not isolated from the descaling and sanitizing products.

Genomic Analysis

Random amplified polymorphic DNA analysis and repetitive extragenic palindromic polymerase chain reaction. All available clinical (38) and environmental (three) *B. multivorans* isolates from hospitals A, B, and C underwent random amplified polymorphic DNA (RAPD) analysis and repetitive extragenic palindromic polymerase chain reaction (Rep-PCR) testing at the University of Michigan *B. cepacia* Research Laboratory and Repository (BcRLR).[¶] All 41 isolates from these three California hospitals were genetically closely related (>85% relatedness).

Whole genome sequencing. The Colorado State Public Health Laboratory, in collaboration with the University of Michigan BcRLR, performed whole genome sequencing and phylogenetic comparison of *B. multivorans* clinical and environmental isolates from all four hospitals. Clinical isolates from all 46 patients and four environmental isolates (hospital B = three and hospital D = one) from three of the implicated ice machines revealed that all had the same sequence type (ST659) and were all genetically highly similar (0–14 single nucleotide variant differences across 81% of the selected reference genome).[**]

Public Health Response

During December 2020–February 2021, state public health officials made infection prevention and control recommendations to hospital A, which included avoiding the use of tap water and ice from ice machines during the clinical care of patients. Public health officials made similar recommendations to hospitals B and C during March–August 2022, and to hospital D in July 2023, focused on reducing the risk for tap water and ice exposure during clinical care activities, especially among vulnerable patients, such as those who are immunocompromised or critically ill. All ice machines identified to have *B. multivorans* were removed from service.

In March 2024, CDC issued a national Epidemic Information Exchange notice to identify additional *B. multivorans* infections. An ongoing investigation is being conducted to determine the possible sources of ice machine contamination.

Summary

What is already known about this topic?

During 2021–2022, contaminated ice and water from ice machines were linked to 23 *Burkholderia multivorans* cases at two southern California hospitals.

What is added by this report?

Twenty-three additional, previously unreported *B. multivorans* cases occurred during 2020–2024: 13 at a northern California hospital, eight at a hospital in Colorado, and two additional cases at one of the southern California hospitals. All environmental and clinical isolates were highly genetically similar. The same brand of ice machine and the same filters, descaling, and sanitizing products were used by all four hospitals.

What are the implications for public health practice?

During outbreaks of water-related organisms in health care facilities, health care personnel should consider avoiding the use of tap water, including ice and water from ice machines, for patient care.

Discussion

Epidemiologic and laboratory evidence suggests that contaminated ice and water dispensed from ice machines, all the same brand, were likely sources of exposure among patients identified with *B. multivorans* infections in four hospitals in California and Colorado during September 2020–February 2024. Genomic relatedness of the clinical and environmental *B. multivorans* isolates and identification of the outbreak strain in the same brand of ice machine raises the possibility of a contaminated ice machine component or associated product (e.g., descaling and sanitizing products) leading to contamination of the dispensed ice and water. Differences in the proportion of specimen sources with *B. multivorans* across hospitals suggest various routes of exposure and transmission. For example, the higher proportion of intra-abdominal specimens with *B. multivorans* at hospital D is consistent with the observed practice at this hospital of directly applying refillable ice bags to abdominal surgical wounds and device insertion sites. High bacterial counts, such as that found in water samples from an ice machine at Hospital C, might also indicate risk of transmission of water-associated bacteria to patients.

[§] https://www.epa.gov/ground-water-and-drinking-water/national-primary-drinking-water-regulations

[¶] Methods for RAPD analysis and Rep-PCR as described in https://doi.org/10.1128/jcm.40.9.3300-3307.2002.

[**] The data for the *B. multivorans* isolates have been deposited in the National Center for Biotechnology Information BioProject database with links to BioProject accession numbers PRJNA288601 (https://ncbi.nlm.nih.gov/bioproject/288601), PRJNA991232 (https://ncbi.nlm.nih.gov/bioproject/991232), and PRJNA720893 (https://ncbi.nlm.nih.gov/bioproject/720893).

Limitations

The findings in this report are subject to at least two limitations. First, although *B. multivorans* was not isolated from samples obtained from descaling and sanitizing products used with the ice machines, the tested products might not have represented the same lot numbers as those used at the time of potential patient exposures. Second, specific clinical exposures to tap water and ice are not documented in patient medical records; therefore, it was difficult to confirm when and how patients could have been exposed to ice and water from the contaminated ice machines.

Implications for Public Health Practice

To limit the growth and spread of water-related organisms in water distribution systems, including ice machines, health care facilities should devise and implement a water management program and identify all potential pathways of water transmission to minimize patients' risks for infection (*4*).†† During outbreaks of water-related organisms in health care facilities, these facilities should consider avoiding the use of tap water, including ice and water dispensed from ice machines, for patient care. Health care personnel should notify public health officials of health care–associated outbreaks of *B. multivorans*.

†† https://www.cdc.gov/healthcare-associated-infections/php/toolkit/water-management.html

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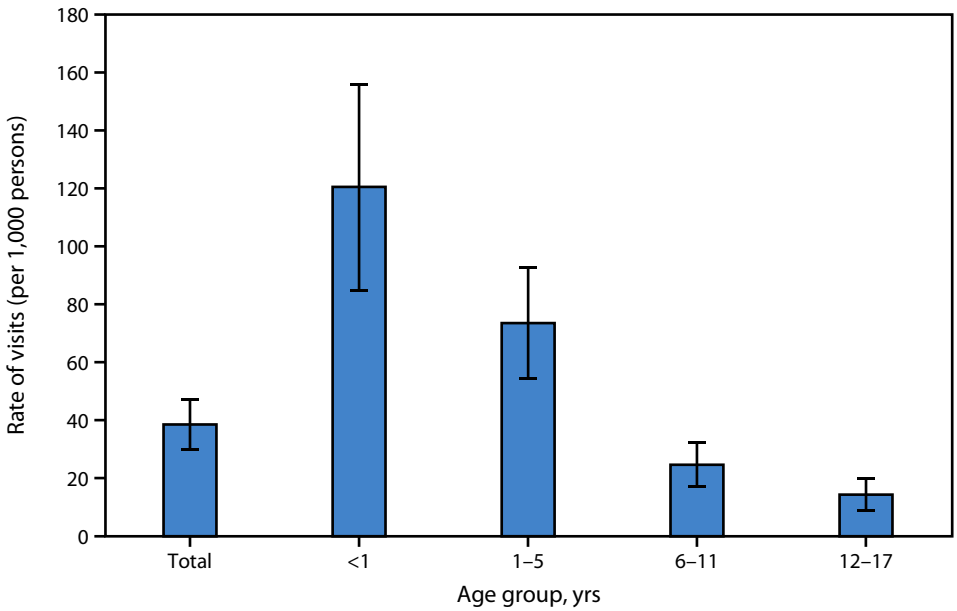
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Rates of Emergency Department Visits* for Children and Adolescents with Acute Upper Respiratory Infection,† by Age Group — United States, 2021–2022



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

† Visits with an acute upper respiratory infection (viral or bacterial) recorded as first listed diagnosis using *International Classification of Diseases, Tenth Revision, Clinical Modification* codes J00–J06.

In 2021–2022, the rate for emergency department (ED) visits for children and adolescents with acute upper respiratory infection was 38.6 per 1,000 persons aged <18 years. The ED visit rate was highest for infants aged <1 year (120.5) and decreased by age, with the lowest rate among adolescents aged 12–17 years (14.4).

Supplementary Table: https://stacks.cdc.gov/view/cdc/162215

Source: National Center for Health Statistics, National Hospital Ambulatory Medical Care Survey, 2021–2022.

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For more information on this topic, CDC recommends the following links: https://www.cdc.gov/respiratory-viruses/about/index.html and https://www.cdc.gov/pneumonia/prevention/index.html.

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