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West Nile Virus and Other Domestic Nationally Notifiable Arboviral Diseases — United States, 2019

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Arthropod-borne viruses (arboviruses) are transmitted to humans primarily through the bites of infected mosquitoes and ticks. West Nile virus (WNV) is the leading cause of domestically acquired arboviral disease in the United States (*1*). Other arboviruses, including La Crosse, Jamestown Canyon, Powassan, eastern equine encephalitis, and St. Louis encephalitis viruses, cause sporadic disease and occasional outbreaks. This report summarizes surveillance data for nationally notifiable domestic arboviruses reported to CDC for 2019. For 2019, 47 states and the District of Columbia (DC) reported 1,173 cases of domestic arboviral disease, including 971 (83%) WNV disease cases. Among the WNV disease cases, 633 (65%) were classified as neuroinvasive disease, for a national incidence of 0.19 cases per 100,000 population, 53% lower than the median annual incidence during 2009–2018. More Powassan and eastern equine encephalitis virus disease cases were reported in 2019 than in any previous year. Health care providers should consider arboviral infections in patients with aseptic meningitis or encephalitis, perform recommended diagnostic testing, and promptly report cases to public health authorities. Because arboviral diseases continue to cause serious illness, and annual incidence of individual viruses continues to vary with sporadic outbreaks, maintaining surveillance is important in directing prevention activities. Prevention depends on community and household efforts to reduce vector populations and personal protective measures to prevent mosquito and tick bites such as use of Environmental Protection Agency–registered insect repellent and wearing protective clothing.*,†

Arboviruses are maintained in transmission cycles between arthropods and vertebrate hosts, including humans and other animals (*2*). Humans primarily become infected when bitten by an infected mosquito or tick. Most human arboviral infections are asymptomatic; symptomatic infections commonly manifest as systemic febrile illness, similar to bacterial or parasitic diseases transmitted by ticks, and less commonly as neuroinvasive disease.

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

* https://www.cdc.gov/ncezid/dvbd/media/stopmosquitoes.html
† https://www.cdc.gov/ticks/avoid/index.html

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Most endemic arboviral diseases are nationally notifiable and reported by state health departments to CDC through ArboNET, the national arboviral surveillance system managed by CDC and state health departments, using standard surveillance case definitions that include clinical and laboratory criteria (*3*). Cases are reported by patient's state and county of residence. Confirmed and probable cases were included for 2019. Cases reported as meningitis, encephalitis, acute flaccid paralysis (AFP), or unspecified neurologic presentation were classified as neuroinvasive disease; the remainder were considered nonneuroinvasive disease. Incidence was calculated using U.S. Census 2019 midyear population estimates and reported neuroinvasive disease cases, which are more reliably diagnosed and reported than nonneuroinvasive disease cases because of the associated morbidity.

A total of 1,173 cases of domestic arboviral disease were reported for 2019; cases were caused by the following viruses: West Nile (971 cases; 83% of all cases), La Crosse (55; 5%), Jamestown Canyon (45; 4%), Powassan (43; 4%), eastern equine encephalitis (38; 3%), St. Louis encephalitis (17; 1%), and unspecified California serogroup (four; <1%). Cases were reported from all states except Delaware, Hawaii, and Vermont, and from 380 (12%) of the 3,142 U.S. counties. Overall, 802 (68%) domestic arboviral disease cases were classified as neuroinvasive.

The 971 WNV disease cases were reported from 285 counties in 43 states and DC; 633 (65%) cases were neuroinvasive, and 794 (82%) patients had illness onset during July–September (Table 1). The median patient age was 60 years (interquartile range [IQR] = 46–70 years); 572 (59%) were male. A total of 662 (68%) patients were hospitalized, and 60 (6%) died.

Among the 633 WNV neuroinvasive disease cases, 361 (57%) were reported as encephalitis, 215 (34%) as meningitis, 16 (3%) as AFP, and 41 (6%) as unspecified neurologic signs or symptoms. A total of 584 (92%) patients with neuroinvasive disease were hospitalized, and 60 (10%) died. The median age of patients who died was 73 years (IQR = 67–82 years). The national incidence of neuroinvasive disease was 0.19 per 100,000 population (Table 2). The highest incidences occurred in Arizona (1.81 per 100,000), New Mexico (1.43), DC (1.28), and Nevada (1.10) (Figure). The largest numbers of neuroinvasive disease cases were reported from California (147), Arizona (132), Colorado (52), and Nevada (34), which together accounted for 58% of all neuroinvasive disease cases. The incidence of WNV neuroinvasive disease increased with age, from 0.01 per 100,000 in children aged <10 years to 0.55 in adults aged ≥70 years. Incidence was higher among males (0.24 per 100,000) than among females (0.14).

Fifty-five La Crosse virus disease cases were reported from 10 states, with the highest number of cases reported from Ohio, Tennessee, and North Carolina (Table 2). The median patient age was 8 years (IQR = 5–12 years), and 51 (93%) were aged <18 years (Table 1). Thirty-three (60%) patients were male. Illness onset dates ranged from June to October,

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TABLE 1. Number and percentage of reported cases of West Nile virus and other arboviral diseases (N = 1,173), by virus type and selected patient characteristics — United States, 2019*

Characteristic	Virus type, no. (%)†					
	West Nile (n = 971)	La Crosse (n = 55)	Jamestown Canyon (n = 45)	Powassan (n = 43)	Eastern equine encephalitis (n = 38)	St. Louis encephalitis (n = 17)
Age group, yrs						
<18	27 (3)	51 (93)	2 (4)	5 (12)	4 (11)	0 (—)
18–59	445 (46)	1 (2)	21 (47)	9 (21)	10 (26)	5 (29)
≥60	499 (51)	3 (5)	22 (49)	29 (67)	24 (63)	12 (71)
Sex						
Male	572 (59)	33 (60)	30 (67)	31 (72)	27 (71)	12 (71)
Female	399 (41)	22 (40)	15 (33)	12 (28)	11 (29)	5 (29)
Period of illness onset						
Jan–Mar	7 (1)	0 (—)	0 (—)	0 (—)	0 (—)	0 (—)
Apr–Jun	105 (11)	6 (11)	9 (20)	17 (40)	1 (3)	3 (18)
Jul–Sep	794 (82)	41 (75)	29 (64)	15 (35)	36 (95)	14 (82)
Oct–Dec	65 (7)	8 (15)	7 (16)	11 (26)	1 (3)	0 (—)
Clinical syndrome						
Nonneuroinvasive	338 (35)	7 (13)	20 (44)	4 (9)	0 (—)	2 (12)
Neuroinvasive	633 (65)	48 (87)	25 (56)	39 (91)	38 (100)	15 (88)
Encephalitis†	361 (57)	37 (77)	14 (56)	29 (74)	36 (95)	9 (60)
Meningitis†	215 (34)	10 (21)	4 (16)	5 (13)	2 (5)	4 (27)
AFP†,§	16 (3)	0 (—)	1 (4)	1 (3)	0 (—)	0 (—)
Unspecified†	41 (6)	1 (2)	6 (24)	4 (10)	0 (—)	2 (13)
Outcome						
Hospitalization	662 (68)	54 (98)	26 (58)	38 (88)	38 (100)	16 (94)
Death	60 (6)	0 (—)	2 (4)	9 (21)	19 (50)	0 (—)

Abbreviation: AFP = acute flaccid paralysis.
* Four unspecified California serogroup virus cases were also reported and are not shown.
† Percentages of cases of encephalitis, meningitis, AFP, and unspecified neurologic presentations are percentages of neuroinvasive cases.
§ Among the 16 West Nile virus disease cases in persons with AFP, 10 (63%) also had encephalitis or meningitis.

with 41 (75%) occurring during July–September. Forty-eight (87%) cases were neuroinvasive, and 54 (98%) patients were hospitalized; none died.

Forty-five Jamestown Canyon virus disease cases were reported from six states, with the highest number of cases reported from Minnesota and Wisconsin (Table 2). A disease case was reported for the first time from Illinois; however, the patient had traveled during the likely period of infection. The median patient age was 59 years (IQR = 31–70 years); 30 (67%) were male (Table 1). Illness onset ranged from April to November, with 29 (64%) cases occurring during July–September. Twenty-five (56%) cases were neuroinvasive, 26 (58%) patients were hospitalized, and two (4%) died, both aged 25–35 years and both with neuroinvasive disease.

Forty-three Powassan virus disease cases were reported from 10 states, with the highest number of cases reported from Massachusetts, Minnesota, and Wisconsin (Table 2). The median patient age was 64 years (IQR = 47–71 years); 31 (72%) were male (Table 1). Illness onset dates ranged from April to December, with 17 (40%) occurring during April–June. Thirty-nine (91%) cases were neuroinvasive. Thirty-eight (88%) patients were hospitalized. Nine (21%) patients died (all with neuroinvasive disease), eight (89%) of whom were aged >60 years.

Thirty-eight cases of eastern equine encephalitis virus disease were reported from 10 states. Twenty-two (58%) cases were reported from Massachusetts (12) and Michigan (10) (Table 2); cases were reported for the first time from Indiana and Tennessee. The median patient age was 64 years (IQR = 54–72 years); 27 (71%) were male. Illness onset dates ranged from June to November, with 36 (95%) occurring during July–September. All cases were neuroinvasive, and all patients were hospitalized. Nineteen (50%) patients died, all of whom were aged >50 years.

Seventeen cases of St. Louis encephalitis virus disease were reported from four states (Table 2). The median patient age was 65 years (IQR = 54–76 years); 12 (71%) were male (Table 1). Illness onset dates ranged from May to September, with 14 (82%) occurring during July–September. Fifteen (88%) cases were neuroinvasive; 16 (94%) patients were hospitalized, and none died.

TABLE 2. Number and rate* of reported cases of arboviral neuroinvasive disease, by virus type, U.S. Census division, and state — United States, 2019

U.S. Census division/ State	Virus type, no. (rate*)					
	West Nile	La Crosse	Jamestown Canyon	Powassan	Eastern equine encephalitis	St. Louis encephalitis
United States	**633 (0.19)**	**48 (0.01)**	**25 (0.01)**	**39 (0.01)**	**38 (0.01)**	**15 (0.00)**
New England	3 (0.02)	1 (0.01)	6 (0.04)	19 (0.13)	19 (0.13)	—†
Connecticut	1 (0.03)	—	—	5 (0.14)	4 (0.11)	—
Maine	—	—	—	2 (0.15)	—	—
Massachusetts	2 (0.03)	—	3 (0.04)	9 (0.13)	12 (0.17)	—
New Hampshire	—	—	3 (0.22)	2 (0.15)	—	—
Rhode Island	—	1 (0.09)	—	1 (0.09)	3 (0.28)	—
Vermont	—	—	—	—	—	—
Middle Atlantic	25 (0.06)	—	—	8 (0.02)	4 (0.01)	—
New Jersey	6 (0.07)	—	—	4 (0.05)	4 (0.05)	—
New York	14 (0.07)	—	—	4 (0.02)	—	—
Pennsylvania	5 (0.04)	—	—	—	—	—
East North Central	40 (0.09)	23 (0.05)	8 (0.02)	5 (0.01)	11 (0.02)	—
Illinois	22 (0.17)	—	1 (0.01)	—	—	—
Indiana	4 (0.06)	—	—	—	1 (0.01)	—
Michigan	11 (0.11)	1 (0.01)	1 (0.01)	—	10 (0.10)	—
Ohio	3 (0.03)	19 (0.16)	—	—	—	—
Wisconsin	—	3 (0.05)	6 (0.10)	5 (0.09)	—	—
West North Central	33 (0.15)	1 (0.00)	11 (0.05)	7 (0.03)	—	—
Iowa	1 (0.03)	—	—	—	—	—
Kansas	7 (0.24)	—	—	—	—	—
Minnesota	2 (0.04)	1 (0.02)	11 (0.20)	6 (0.11)	—	—
Missouri	4 (0.07)	—	—	—	—	—
Nebraska	17 (0.88)	—	—	—	—	—
North Dakota	2 (0.26)	—	—	1 (0.13)	—	—
South Dakota	—	—	—	—	—	—
South Atlantic	33 (0.05)	10 (0.02)	—	—	2 (0.00)	—
Delaware	—	—	—	—	—	—
District of Columbia	9 (1.28)	—	—	—	—	—
Florida	2 (0.01)	—	—	—	—	—
Georgia	9 (0.08)	1 (0.01)	—	—	1 (0.01)	—
Maryland	6 (0.10)	—	—	—	—	—
North Carolina	1 (0.01)	6 (0.06)	—	—	1 (0.01)	—
South Carolina	2 (0.04)	—	—	—	—	—
Virginia	4 (0.05)	—	—	—	—	—
West Virginia	—	3 (0.17)	—	—	—	—

See table footnotes on the next page.

Discussion

As in previous years, WNV was the most common cause of domestic arboviral neuroinvasive disease in 2019. However, WNV neuroinvasive disease incidence (0.19 per 100,000) was 53% lower than the median annual incidence during 2009–2018 (0.40; range = 0.13–0.92) (*4*). The decrease in incidence was most notable in Midwestern and South Central states, particularly Texas, which reported 24 neuroinvasive disease cases, 78% lower than its annual median of 111 (range = 20–844) during 2009–2018 (*4*). Despite overall low WNV disease incidence, multiple states reported more cases than their annual median during 2009–2018, mostly in the Mountain region (*4*).

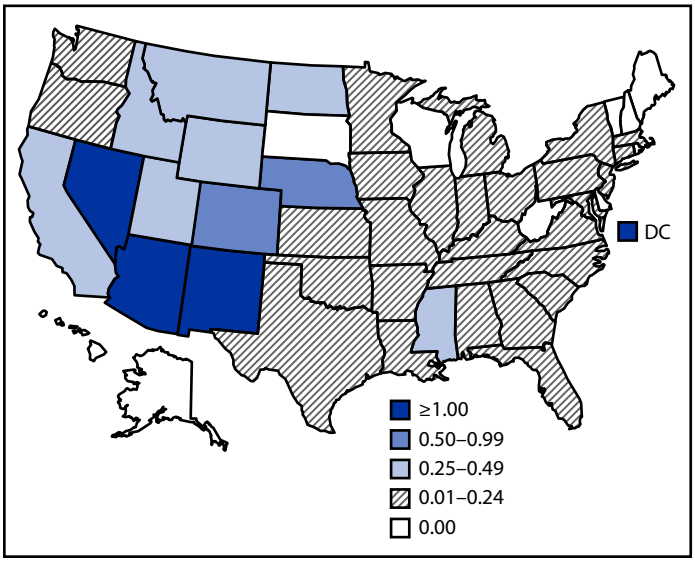
La Crosse virus continued to be the most common cause of neuroinvasive arboviral disease in children (*5*). Jamestown Canyon virus disease incidence has increased over time, with a median of 45 (range = 41–75) cases reported annually during 2017–2019 compared with 11 (range = 0–22) during 2010–2016 (*6*). More cases of Powassan virus disease were reported for 2019 than any previous year, with 43 cases compared with the previous high of 34 cases in 2017 and a median of 15 cases annually during 2010–2018 (*7*). More cases of eastern equine encephalitis virus disease were reported for 2019 (38) than for any previous year; the previous high of 21 cases was reported in 2005, and a median of seven cases was reported each year during 2010–2018 (*8*). Eastern equine encephalitis virus remained the deadliest arbovirus disease, with one half of patients dying. For viruses with higher than average case numbers in 2019, whether the increase reflects an actual increase in disease incidence or increased awareness, surveillance, and testing is unknown.

TABLE 2. (*Continued*) Number and rate* of reported cases of arboviral neuroinvasive disease, by virus type, U.S. Census division, and state — United States, 2019

U.S. Census Division/ State	Virus type, no. (rate*)					
	West Nile	La Crosse	Jamestown Canyon	Powassan	Eastern equine encephalitis	St. Louis encephalitis
East South Central	23 (0.12)	13 (0.07)	—	—	2 (0.01)	—
Alabama	4 (0.08)	—	—	—	1 (0.02)	—
Kentucky	4 (0.09)	1 (0.02)	—	—	—	—
Mississippi	12 (0.40)	—	—	—	—	—
Tennessee	3 (0.04)	12 (0.18)	—	—	1 (0.01)	—
West South Central	48 (0.12)	—	—	—	—	1 (0.00)
Arkansas	7 (0.23)	—	—	—	—	—
Louisiana	11 (0.24)	—	—	—	—	—
Oklahoma	6 (0.15)	—	—	—	—	1 (0.03)
Texas	24 (0.08)	—	—	—	—	—
Mountain	272 (1.09)	—	—	—	—	8 (0.03)
Arizona	132 (1.81)	—	—	—	—	8 (0.11)
Colorado	52 (0.90)	—	—	—	—	—
Idaho	5 (0.28)	—	—	—	—	—
Montana	3 (0.28)	—	—	—	—	—
Nevada	34 (1.10)	—	—	—	—	—
New Mexico	30 (1.43)	—	—	—	—	—
Utah	14 (0.44)	—	—	—	—	—
Wyoming	2 (0.35)	—	—	—	—	—
Pacific	156 (0.29)	—	—	—	—	6 (0.01)
Alaska	—	—	—	—	—	—
California	147 (0.37)	—	—	—	—	6 (0.02)
Hawaii	—	—	—	—	—	—
Oregon	6 (0.14)	—	—	—	—	—
Washington	3 (0.04)	—	—	—	—	—

* Cases per 100,000 population, based on July 1, 2018, U.S. Census population estimates.
† Dashes indicate no cases reported.

FIGURE. Incidence* of reported cases of West Nile virus neuroinvasive disease — United States,† 2019



Abbreviation: DC = District of Columbia.
* Cases per 100,000 population.
† No cases were reported from Alaska or Hawaii.

Summary

What is already known about this topic?

West Nile virus (WNV) is consistently the leading cause of domestically acquired arboviral disease, but other arboviruses cause sporadic cases and outbreaks of neuroinvasive disease, resulting in substantial morbidity and mortality.

What is added by this report?

In 2019, WNV neuroinvasive disease incidence was 53% lower than the median annual incidence during 2009–2018. More Powassan and eastern equine encephalitis virus disease cases were reported than in any previous year.

What are the implications for public health practice?

Health care providers should consider arboviral infections in patients with aseptic meningitis or encephalitis, perform recommended diagnostic testing, and promptly report cases to public health authorities. Surveillance is important to identify outbreaks and guide prevention strategies, which include wearing insect repellent, long pants, and long-sleeved shirts when outdoors.

Although the reported number of cases varies, arboviruses cause substantial morbidity in the United States each year. Cases occur sporadically, with epidemiology varying by virus and geography. Weather, zoonotic host, vector abundance, and human behavior all influence when and where arboviral outbreaks occur, making it difficult to predict locations and timing of cases and underscoring the importance of surveillance in identifying outbreaks and informing prevention efforts.

The findings in this report are subject to at least two limitations. First, arboviral diseases are likely underrecognized and underreported to ArboNET. This is especially true for nonneuroinvasive disease; previous studies estimated that 30 to 70 nonneuroinvasive cases occur for every neuroinvasive WNV disease case reported (*9*). Based on the 633 neuroinvasive WNV disease cases reported for 2019, 18,990 to 44,310 nonneuroinvasive WNV disease cases could have occurred; however, only 338 (1%–2%) were reported. Second, because ArboNET does not require information about clinical signs, symptoms, or laboratory findings, cases might be misclassified.

Health care providers should consider arboviral infections in cases of aseptic meningitis and encephalitis, obtain necessary specimens for laboratory testing, and promptly report cases to public health authorities (*2*,*3*). Understanding the epidemiology, seasonality, and geographic distribution of these arboviruses is important for clinical recognition and differentiation from other neurologic infections. Because human vaccines against domestic arboviruses are not available, prevention depends on community and household efforts to reduce vector populations (e.g., applying insecticides and reducing breeding sites), use of personal protective measures to decrease mosquito and tick exposures (e.g., repellents and protective clothing), and blood donation screening to minimize alternative routes of transmission.

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Alternative Methods for Grouping Race and Ethnicity to Monitor COVID-19 Outcomes and Vaccination Coverage

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Population-based analyses of COVID-19 data by race and ethnicity can identify and monitor disparities in COVID-19 outcomes and vaccination coverage. CDC recommends that information about race and ethnicity be collected to identify disparities and ensure equitable access to protective measures such as vaccines; however, this information is often missing in COVID-19 data reported to CDC. Baseline data collection requirements of the Office of Management and Budget's Standards for the Classification of Federal Data on Race and Ethnicity (Statistical Policy Directive No. 15) include two ethnicity categories and a minimum of five race categories (*1*). Using available COVID-19 case and vaccination data, CDC compared the current method for grouping persons by race and ethnicity, which prioritizes ethnicity (in alignment with the policy directive), with two alternative methods (methods A and B) that used race information when ethnicity information was missing. Method A assumed non-Hispanic ethnicity when ethnicity data were unknown or missing and used the same population groupings (denominators) for rate calculations as the current method (Hispanic persons for the Hispanic group and race category and non-Hispanic persons for the different racial groups). Method B grouped persons into ethnicity and race categories that are not mutually exclusive, unlike the current method and method A. Denominators for rate calculations using method B were Hispanic persons for the Hispanic group and persons of Hispanic or non-Hispanic ethnicity for the different racial groups. Compared with the current method, the alternative methods resulted in higher counts of COVID-19 cases and fully vaccinated persons across race categories (American Indian or Alaska Native [AI/AN], Asian, Black or African American [Black], Native Hawaiian or Other Pacific Islander [NH/PI], and White persons). When method B was used, the largest relative increase in cases (58.5%) was among AI/AN persons and the largest relative increase in the number of those fully vaccinated persons was among NH/PI persons (51.6%). Compared with the current method, method A resulted in higher cumulative incidence and vaccination coverage rates for the five racial groups. Method B resulted in decreasing cumulative incidence rates for two groups (AI/AN and NH/PI persons) and decreasing cumulative vaccination coverage rates for AI/AN persons. The rate ratio for having a case of COVID-19 by racial and ethnic group compared with that for White persons varied by method but was <1 for Asian persons and >1 for other groups across all three methods. The likelihood of being fully vaccinated was highest among NH/PI persons across all three methods. This analysis demonstrates that alternative methods for analyzing race and ethnicity data when data are incomplete can lead to different conclusions about disparities. These methods have limitations, however, and warrant further examination of potential bias and consultation with experts to identify additional methods for analyzing and tracking disparities when race and ethnicity data are incomplete.

To improve monitoring of COVID-19–associated outcomes among racial and ethnic groups, CDC used three methods for grouping persons by race and ethnicity to analyze the following six indicators: 1) COVID-19 case counts, 2) cumulative incidence, 3) rate ratios for COVID-19 infection, 4) number of fully vaccinated persons, 5) cumulative vaccination coverage rates, and 6) rate ratios for being fully vaccinated. The method for grouping race and ethnicity used by CDC (current method) begins by grouping persons with Hispanic ethnicity as Hispanic, regardless of race, then groups persons with reported race and non-Hispanic ethnicity as race category, non-Hispanic (which excludes persons with missing or unknown ethnicity and those with non-Hispanic ethnicity and missing or unknown race). The current method was compared with two alternative methods (methods A and B) that have been used previously (*2*,*3*). Method A first groups persons based on Hispanic ethnicity (as with the current method) and then groups persons with known race and non-Hispanic ethnicity or unknown or missing ethnicity as race category, non-Hispanic (persons with missing or unknown race and missing or unknown or non-Hispanic ethnicity are excluded). Method B groups all persons with Hispanic ethnicity as Hispanic, regardless of race, and persons with reported race and Hispanic, non-Hispanic, unknown, or missing ethnicity are grouped by race category; persons with missing or unknown race and missing or unknown or non-Hispanic ethnicity are excluded. Notably, with method B, the groups are not mutually exclusive (Box).

Daily confirmed COVID-19 cases in the United States during January 1, 2020–May 31, 2021, were obtained from CDC's

BOX. Methods for grouping race and ethnicity* for COVID-19 cases, January 1, 2020–May 31, 2021, and fully vaccinated persons, December 14, 2020–May 31 — United States, 2021

Current method

Race/Ethnicity groups

- American Indian/Alaska Native, non-Hispanic
- Asian, non-Hispanic
- Black or African American, non-Hispanic
- Hispanic
- Native Hawaiian or Other Pacific Islander, non-Hispanic
- White, non-Hispanic

Grouping method

1. Persons with Hispanic ethnicity are grouped as Hispanic, regardless of race.
2. For the remaining records, persons with reported race and non-Hispanic ethnicity, are grouped as race category, non-Hispanic.
3. Persons with missing or unknown ethnicity are excluded even if race is reported, and persons with non-Hispanic ethnicity and missing or unknown race are excluded.

Method A

Race/Ethnicity groups

- American Indian/Alaska Native, non-Hispanic
- Asian, non-Hispanic
- Black or African American, non-Hispanic
- Hispanic
- Native Hawaiian or Other Pacific Islander, non-Hispanic
- White, non-Hispanic

Grouping method

1. Persons with Hispanic ethnicity are grouped as Hispanic, regardless of race.
2. For the remaining records, persons with reported race and non-Hispanic, unknown, or missing ethnicity, are grouped as race category, non-Hispanic.
3. Persons with missing or unknown race and missing or unknown or non-Hispanic ethnicity are excluded.

Method B

Race/Ethnicity groups

- American Indian/Alaska Native
- Asian
- Black
- Hispanic
- Native Hawaiian or Other Pacific Islander
- White

Grouping method

1. For all records, persons with Hispanic ethnicity are grouped as Hispanic, regardless of race.
2. Persons with reported race and ethnicity that is Hispanic, non-Hispanic, unknown, or missing are grouped by race category.
3. The groups are not mutually exclusive.
4. Persons with missing or unknown race and missing or unknown or non-Hispanic ethnicity are excluded.

* Multiracial and other race were excluded from analysis.

case-based surveillance system.* Daily data about COVID-19 vaccine doses administered in the United States during December 14, 2020–May 31, 2021, including full vaccination status, were collected by vaccination providers and reported to CDC by multiple sources.† In the case and vaccination data sent to CDC, race was reported as White, Black, AI/AN, Asian, NH/PI, more than one race, other race, unknown race, or missing race. Ethnicity was reported as Hispanic or Latino (Hispanic), non-Hispanic, unknown ethnicity, or missing ethnicity. COVID-19 incidence and vaccination coverage rates were calculated using the 2019 U.S. Census Bureau's annual resident population estimates.§ The current method and method A used the same population groupings (denominators) for rate calculations (Hispanic persons for the Hispanic group and race category, non-Hispanic persons for the different racial groups). Method B denominators were Hispanic persons for the Hispanic group and persons of Hispanic or non-Hispanic ethnicity for the different racial groups. Rate ratios were used to compare relative differences in COVID-19 incidence and full vaccination coverage rates between racial and ethnic groups. The comparator for the current method and method A was White, non-Hispanic persons and for method B was White persons. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.¶

During January 1, 2020–May 31, 2021, U.S. states and four territories reported 26,724,149 COVID-19 cases to CDC. Among these reports, information on race, ethnicity, or both was missing from 26.7%, 35.2%, and 21.7% of reports received, respectively. During December 14, 2020–May 31, 2021, based on vaccine administration data reported to CDC, 126,692,891 fully COVID-19–vaccinated persons were reported in the United States; information on race, ethnicity, or both was missing from 23.1%, 31.7%, and 19.5% of these reports, respectively.

Summary

What is already known about this topic?

Analyses of race and ethnicity in COVID-19 data to identify and monitor disparities are complicated by missing or unknown data.

What is added by this report?

Methods that use more race information when ethnicity information is missing resulted in higher estimated COVID-19 case counts, incidence, and vaccination coverage for most racial groups studied; however, these methods have limitations and warrant further examination of potential bias.

What are the implications for public health practice?

Ongoing work with experts is needed to identify methods for optimizing race and ethnicity data when data are incomplete. Multiple data sources are needed to monitor disparities and continued efforts are needed to strengthen the reporting of these data, consistent with CDC's Data Modernization Initiative.

Among persons of Hispanic ethnicity, the numbers of COVID-19 cases and persons fully vaccinated, and population incidence and vaccination coverage rates were the same across the three methods for grouping race and ethnicity (Table 1). Methods A and B resulted in more COVID-19 cases and fully vaccinated persons assigned to a racial group compared with the current method because of the inclusion of persons with unknown or missing ethnicity information. Compared with the current method, method A resulted in case counts that were 16.6% to 37.2% higher across race groups, with the largest relative increase in the AI/AN, non-Hispanic group (37.2%). For method B, for which racial and ethnic groups were not mutually exclusive, the percentage increase in case counts compared with the current method ranged from 25.7% to 58.5% among the five race categories. The largest relative increase in case counts was in the AI/AN group (58.5%); case counts in White persons also increased (45.1%). The estimated population incidence of COVID-19 varied depending on the classification method used. Compared with the current method, method A resulted in higher cumulative COVID-19 incidences among the five racial groups, with the largest increase among AI/AN, non-Hispanic persons (37.2%). Method B resulted in increased cumulative incidence among Asian persons (21.8%), Black persons (19.6%) and White persons (14.3%), and slight decreases among AI/AN persons (7.9%) and NH/PI persons (1.0%).

Compared with the current method, method A resulted in higher numbers of fully vaccinated persons across all racial groups, ranging from 17.8% (non-Hispanic Asian) to 37.3% (non-Hispanic NH/PI) higher. Method B resulted in 19.4% to 51.6% higher numbers of fully vaccinated persons across the racial groups, with the largest relative increase among NH/PI persons (51.6%). Full vaccination coverage also varied

* All 50 states, the District of Columbia, New York City, and four U.S. territories (Guam, Northern Mariana Islands, Puerto Rico, and U.S. Virgin Islands) electronically submit standardized information for individual cases of COVID-19 to CDC via a case report form developed for the CDC COVID-19 response (https://www.cdc.gov/coronavirus/2019-ncov/php/reporting-pui.html) or via the CDC National Notifiable Diseases Surveillance System (https://www.cdc.gov/nndss/action/covid-19-response.html).

† COVID-19 vaccine administration data are reported to CDC by multiple entities using immunization information systems, the Vaccine Administration Management System, pharmacy systems, or direct submission of electronic health records. (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/distributing/about-vaccine-data.html). CDC counts persons as being fully vaccinated if they received 2 doses on different days (regardless of time interval) of the 2-dose mRNA vaccine series or received 1 dose of a single-dose vaccine.

§ https://www.census.gov/data/tables/time-series/demo/popest/2010s-national-detail.html

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

TABLE 1. Counts, relative change, and population rates* using three methods for grouping race and ethnicity for COVID-19 cases, January 1, 2020–May 31, 2021 and fully vaccinated persons, December 14, 2020–May 31, 2021 — United States

Race and ethnicity grouping method	No. of COVID-19 cases† (% change§ compared with current method)	No. of cases per 100,000 persons (% change¶ compared with current method)	No. of fully vaccinated persons** (% change§ compared with current method)	No. of fully vaccinated persons per 100,000 (% change¶ compared with current method)
Current method††				
AI/AN, non-Hispanic	163,818 (N/A)	6,728 (N/A)	797,443 (N/A)	32,750 (N/A)
Asian, non-Hispanic	543,027 (N/A)	2,872 (N/A)	5,002,826 (N/A)	26,462 (N/A)
NH/PI, non-Hispanic	50,158 (N/A)	8,417 (N/A)	231,611 (N/A)	38,867 (N/A)
Black, non-Hispanic	1,890,813 (N/A)	4,595 (N/A)	7,215,273 (N/A)	17,535 (N/A)
Hispanic or Latino	4,835,843 (N/A)	7,984 (N/A)	10,897,572 (N/A)	17,991 (N/A)
White, non-Hispanic	8,392,146 (N/A)	4,253 (N/A)	52,872,482 (N/A)	26,797 (N/A)
Total	**15,875,805 (N/A)**	**N/A**	**77,017,207 (N/A)**	**N/A**
Method A§§				
AI/AN, non-Hispanic	224,761 (37.2)	9,231 (37.2)	950,367 (19.2)	39,031 (19.2)
Asian, non-Hispanic	666,250 (22.7)	3,524 (22.7)	5,893,828 (17.8)	31,175 (17.8)
NH/PI, non-Hispanic	58,475 (16.6)	9,813 (16.6)	317,971 (37.3)	53,359 (37.3)
Black, non-Hispanic	2,330,770 (23.3)	5,664 (23.3)	8,575,690 (18.9)	20,841 (18.9)
Hispanic or Latino	4,835,843 (0.0)	7,984 (0.0)	10,897,572 (0.00)	17,991 (0.0)
White, non-Hispanic	10,392,669 (23.8)	5,267 (23.8)	62,750,532 (18.7)	31,803 (18.7)
Total	**18,508,768 (N/A)**	**N/A**	**89,385,960 (N/A)**	**N/A**
Method B¶¶				
AI/AN	259,591 (58.5)	6,198 (-7.9)	1,047,041 (31.3)	25,000 (-23.7)
Asian	682,590 (25.7)	3,500 (21.8)	5,973,946 (19.4)	30,628 (15.7)
NH/PI	67,275 (34.1)	8,337 (-1.0)	351,176 (51.6)	43,520 (12.0)
Black	2,422,392 (28.1)	5,496 (19.6)	8,838,409 (22.5)	20,053 (14.4)
Hispanic or Latino	4,835,843 (0.0)	7,984 (0.0)	10,897,572 (0.00)	17,991 (0.0)
White	12,175,193 (45.1)	4,860 (14.3)	67,307,494 (27.3)	26,867 (0.3)
Total	**20,442,884 (N/A)**	**N/A**	**94,415,638 (N/A)**	**N/A**

Abbreviations: AI/AN = American Indian or Alaska Native; N/A = not applicable; NH/PI = Native Hawaiian or Other Pacific Islander.

* Rates for the full period were calculated using the following equation: (cases/population) x 100,000 persons; (fully vaccinated/population) x 100,000 persons. U.S. Census Bureau 2019 single race population estimates were used.

† As of June 7, 2021 (date accessed) CDC's case-based COVID-19 surveillance system had a total of 26,724,149 reports through May 31, 2021. Persons who were reported as multiracial or other race with non-Hispanic, unknown, or missing ethnicity (1,860,590; 7.0%) were excluded from the analyses.

§ Percentage increase compared with current method calculated as ([value method A or B – value current method]/value current method) x 100.

¶ Percentage difference compared with current method calculated as ([value Method A or B – value current method]/value current method) x 100

** As of June 11, 2021 (date accessed), CDC's vaccine administration surveillance system had a total of 126,692,891 reports through May 31, 2021. Persons who were reported as multiracial or other race with non-Hispanic, unknown, or missing ethnicity (13,859,910; 10.9%).

†† Current method begins by grouping persons with Hispanic ethnicity as Hispanic, regardless of race, then groups persons with reported race and non-Hispanic ethnicity as race category, non-Hispanic; persons with missing or unknown ethnicity and those with non-Hispanic ethnicity and missing or unknown race are excluded.

§§ Method A begins by grouping persons with Hispanic ethnicity as Hispanic, regardless of race, then groups persons with known race and non-Hispanic or unknown or missing ethnicity as race category, non-Hispanic; persons with missing or unknown race and missing or unknown or non-Hispanic ethnicity are excluded.

¶¶ Method B groups all persons with Hispanic ethnicity as Hispanic, regardless of race, and persons with reported race and Hispanic, non-Hispanic, unknown, or missing ethnicity are grouped by race category; persons with missing or unknown race and missing or unknown or non-Hispanic ethnicity are excluded. Groups are not mutually exclusive.

depending on the racial and ethnic classification method used. Compared with the current method, method A resulted in higher numbers of fully vaccinated persons per 100,000 for all racial groups, with the largest increase among non-Hispanic NH/PI persons (37.3%). Method B resulted in coverage increases among all racial groups except AI/AN persons, among whom a 23.7% decrease occurred.

When the current method was used, Hispanic and non-Hispanic NH/PI persons were twice as likely as non-Hispanic White persons to have COVID-19 (Table 2). When method A was used, the rate ratio was highest for non-Hispanic AI/AN (1.76) and non-Hispanic NH/PI (1.84) persons; when method B was used, the rate ratio relative to White persons was highest among Hispanic persons (1.72) and NH/PI persons (1.72). Among Asian persons, the rate ratio for COVID-19 was lower across all three methods (0.66–0.71). NH/PI persons had the highest likelihood of being fully vaccinated when the current method (1.70), method A (1.97), and method B (1.92) were used compared with each method's reference group.

Discussion

Estimation of COVID-19 incidence and vaccination coverage by race and ethnicity is complicated by missing data. Previous studies have proposed methods for classifying race and ethnicity to address such complexities as multirace responses, but these methods do not consider missing data

TABLE 2. Number of COVID-19 cases, age-adjusted incidence, number of persons fully vaccinated, age-adjusted vaccination coverage, and rate ratios (compared with White persons) using three methods for grouping race and ethnicity for COVID-19 cases, January 1, 2020–May 31, 2021 and fully vaccinated persons, December 14, 2020–May 31, 2021 — United States

Race and ethnicity grouping method	No. of COVID-19 cases* (age-adjusted incidence)†	Rate ratio for COVID-19 infection (95% CI)	No. of fully vaccinated persons§ (age-adjusted full vaccination coverage)†	Rate ratio for fully vaccinated persons (95% CI)
Current method¶				
AI/AN, non-Hispanic	163,818 (6,730)	1.59 (1.58–1.60)	797,443 (34,973)	1.41 (1.40–1.41)
Asian, non-Hispanic	543,027 (2,813)	0.67 (0.66–0.67)	5,002,826 (25,625)	1.03 (1.03–1.03)
NH/PI, non-Hispanic	50,158 (8,264)	1.96 (1.94–1.97)	231,611 (42,339)	1.70 (1.70–1.71)
Black, non-Hispanic	1,890,813 (4,616)	1.09 (1.09–1.09)	7,215,273 (19,167)	0.77 (0.77–0.77)
Hispanic or Latino	4,835,843 (8,277)	1.96 (1.96–1.96)	10,897,572 (22,078)	0.89 (0.89–0.89)
White, non-Hispanic	8,392,146 (4,227)	Ref	52,872,482 (24,857)	Ref
Total	**15,875,805**	**N/A**	**77,017,207**	**N/A**
Method A**				
AI/AN, non-Hispanic	224,761 (9,187)	1.76 (1.75–1.76)	950,367 (41,709)	1.41 (1.41–1.42)
Asian, non-Hispanic	666,250 (3,442)	0.66 (0.66–0.66)	5,893,828 (30,204)	1.02 (1.02–1.02)
NH/PI, non-Hispanic	58,475 (9,641)	1.84 (1.83–1.86)	317,971 (58,099)	1.97 (1.96–1.98)
Black, non-Hispanic	2,330,770 (5,659)	1.08 (1.08–1.08)	8,575,690 (22,793)	0.77 (0.77–0.77)
Hispanic or Latino	4,835,843 (8,277)	1.58 (1.58–1.58)	10,897,572 (22,078)	0.75 (0.75–0.75)
White, non-Hispanic	10,392,669 (5,228)	Ref	62,750,532 (29,501)	Ref
Total	**18,508,768**	**N/A**	**89,385,960**	**N/A**
Method B††				
AI/AN	259,591 (6,254)	1.30 (1.29–1.30)	1,047,041 (28,878)	1.11 (1.11–1.11)
Asian	682,590 (3,425)	0.71 (0.71–0.71)	5,973,946 (29,825)	1.14 (1.14–1.14)
NH/PI	67,275 (8,308)	1.72 (1.71–1.73)	351,176 (49,998)	1.92 (1.91–1.92)
Black	2,422,392 (5,517)	1.14 (1.14–1.14)	8,838,409 (22,276)	0.85 (0.85–0.86)
Hispanic	4,835,843 (8,277)	1.72 (1.71–1.72)	10,897,572 (22,078)	0.85 (0.85–0.85)
White	12,175,193 (4,826)	Ref	67,307,494 (26,071)	Ref
Total	**20,442,884**	**N/A**	**94,415,638**	**N/A**

Abbreviations: AI/AN = American Indian or Alaska Native; CI = confidence interval; N/A = not applicable; NH/PI = Native Hawaiian or Other Pacific Islander; Ref = referent.

* As of June 7, 2021 (date accessed), CDC's case-based COVID-19 surveillance system had a total of 26,724,149 reports through May 31, 2021. Persons who were reported as multiracial or other race with non-Hispanic, unknown, or missing ethnicity (1,860,590; 7.0%) were excluded from the analyses.

† Per 100,000 population. Rates were adjusted to the age distribution of the 2019 U.S. Census population estimate.

§ As of June 11, 2021 (date accessed), CDC's vaccine administration surveillance system had a total of 126,692,891 reports through May 31, 2021. Persons who were reported as multiracial or other race with non-Hispanic, unknown, or missing ethnicity (13,859,910; 10.9%) were excluded from the analyses. Texas does not report vaccine counts by race and ethnic group and was excluded.

¶ Current method begins by grouping persons with Hispanic ethnicity as Hispanic, regardless of race, then groups persons with reported race and non-Hispanic ethnicity as race category, non-Hispanic; persons with missing or unknown ethnicity and those with non-Hispanic ethnicity and missing or unknown race are excluded.

** Method A begins by grouping persons with Hispanic ethnicity as Hispanic, regardless of race, then groups persons with known race and non-Hispanic or unknown or missing ethnicity as race category, non-Hispanic; persons with missing or unknown race and missing or unknown or non-Hispanic ethnicity are excluded.

†† Method B groups all persons with Hispanic ethnicity as Hispanic, regardless of race, and persons with reported race and Hispanic, non-Hispanic, unknown, or missing ethnicity are grouped by race category; persons with missing or unknown race and missing or unknown or non-Hispanic ethnicity are excluded. Groups are not mutually exclusive.

in circumstances such as a public health emergency in which real-time monitoring and action are needed to identify and address disparities (*4*,*5*). The alternative methods used in this study (methods A and B) resulted in the analyses of more data by race, which increased estimates of COVID-19 case counts, incidence, and vaccination coverage among most racial groups. The current method, used by CDC, and method A resulted in mutually exclusive racial and ethnic groups. The denominators for rate calculations are either persons reported as Hispanic or persons reported as a race category and non-Hispanic, with an assumption in method A that persons for whom missing ethnicity data were missing are non-Hispanic. Method A is more commonly used when ethnicity is missing from a small percentage of records and other information in the record supports a non-Hispanic designation. When approximately one-third of records are missing ethnicity, as in this report (35% for case and 32% for vaccination coverage data), that assumption might attenuate or amplify disparities for certain groups. With method B, the race and ethnicity groups are not mutually exclusive. This complicates comparisons that use a reference group (often White persons), because the race and ethnicity categories overlap.

The findings in this report are subject to at least four limitations. First, because the analysis did not include persons who identified as multiple races or other race, conclusions cannot be drawn about the use of the alternative methods for grouping and analyzing these racial categories. Second, this report did not explore all possible analytic methods for grouping race and

ethnicity. For example, imputation (i.e., replacing missing data with other values) has been examined as a potential method to improve estimates of COVID-19 racial and ethnic disparities (*6*). Third, data shared with CDC might undercount COVID-19 cases and vaccination coverage and this undercount might differ by race or ethnicity. Finally, although progress has been made to incorporate the Office of Management and Budget standards (such as Statistical Policy Directive No. 15) into the collection and presentation of race and ethnicity data, some data collection efforts still do not fully use this guidance (*7*).

Although race and ethnicity are not the only measures for assessing health disparities, these measures have been integral to CDC's understanding of the health outcomes associated with COVID-19 (*8*–*10*). This analysis demonstrates that alternative methods for analyzing race and ethnicity data when data are incomplete can lead to different interpretations about disparities and highlights the importance of working with experts to identify methods for analyzing and tracking disparities when race and ethnicity data are incomplete. CDC uses multiple data sources to monitor disparities in COVID-19 outcomes and will continue to optimize the available data and work with jurisdictions to strengthen reporting of these data consistent with CDC's COVID-19 Response Health Equity Strategy ** and Data Modernization Initiative.††

** https://www.cdc.gov/coronavirus/2019-ncov/downloads/community/CDC-Strategy.pdf

†† https://www.cdc.gov/surveillance/surveillance-data-strategies/data-IT-transformation.html

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Reduced Risk of Reinfection with SARS-CoV-2 After COVID-19 Vaccination — Kentucky, May–June 2021

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Although laboratory evidence suggests that antibody responses following COVID-19 vaccination provide better neutralization of some circulating variants than does natural infection (*1*,*2*), few real-world epidemiologic studies exist to support the benefit of vaccination for previously infected persons. This report details the findings of a case-control evaluation of the association between vaccination and SARS-CoV-2 reinfection in Kentucky during May–June 2021 among persons previously infected with SARS-CoV-2 in 2020. Kentucky residents who were not vaccinated had 2.34 times the odds of reinfection compared with those who were fully vaccinated (odds ratio [OR] = 2.34; 95% confidence interval [CI] = 1.58–3.47). These findings suggest that among persons with previous SARS-CoV-2 infection, full vaccination provides additional protection against reinfection. To reduce their risk of infection, all eligible persons should be offered vaccination, even if they have been previously infected with SARS-CoV-2.*

Kentucky residents aged ≥18 years with SARS-CoV-2 infection confirmed by positive nucleic acid amplification test (NAAT) or antigen test results† reported in Kentucky's National Electronic Disease Surveillance System (NEDSS) during March–December 2020 were eligible for inclusion. NEDSS data for all Kentucky COVID-19 cases were imported into a REDCap database that contains laboratory test results and case investigation data, including dates of death for deceased patients reported to public health authorities (*3*). The REDCap database was queried to identify previously infected persons, excluding COVID-19 cases resulting in death before May 1, 2021. A case-patient was defined as a Kentucky resident with laboratory-confirmed SARS-CoV-2 infection in 2020 and a subsequent positive NAAT or antigen test result during May 1–June 30, 2021. May and June were selected because of vaccine supply and eligibility requirement considerations; this period was more likely to reflect resident choice to be vaccinated, rather than eligibility to receive vaccine.§ Control participants were Kentucky residents with laboratory-confirmed SARS-CoV-2 infection in 2020 who were not reinfected through June 30, 2021. Case-patients and controls were matched on a 1:2 ratio based on sex, age (within 3 years), and date of initial positive SARS-CoV-2 test (within 1 week). Date of initial positive test result refers to the specimen collection date, if available. The report date in NEDSS was used if specimen collection date was missing. Random matching was performed to select controls when multiple possible controls were available to match per case (*4*).

Vaccination status was determined using data from the Kentucky Immunization Registry (KYIR). Case-patients and controls were matched to the KYIR database using first name, last name, and date of birth. Case-patients were considered fully vaccinated if a single dose of Janssen (Johnson & Johnson) or a second dose of an mRNA vaccine (Pfizer-BioNTech or Moderna) was received ≥14 days before the reinfection date. For controls, the same definition was applied, using the reinfection date of the matched case-patient. Partial vaccination was defined as receipt of ≥1 dose of vaccine, but either the vaccination series was not completed or the final dose was received <14 days before the case-patient's reinfection date. Using conditional logistic regression, ORs and CIs were used to compare no vaccination and partial vaccination with full vaccination among case-patients and controls. SAS (version 9.4; SAS Institute) was used for matching and statistical analyses. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.¶

Overall, 246 case-patients met eligibility requirements and were successfully matched by age, sex, and date of initial infection with 492 controls. Among the population included in the analysis, 60.6% were female, and 204 (82.9%) case-patients were initially infected during October–December 2020

* https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html#CoV-19-vaccination

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

§ May and June were selected for two primary reasons. First, when vaccination supplies were low, some previously infected persons were deferring vaccination for 90 days to allow never-infected persons priority for available vaccine; however, by May 2021, deferral for 90 days was no longer a reason for those infected in 2020 to remain unvaccinated. Second, although vaccination eligibility was initially restricted based on age, comorbidities, and occupation, by April 5, 2021, all Kentucky residents aged ≥16 years became eligible for vaccination (https://chfs.ky.gov/agencies/dph/covid19/Cv19VaccineFAskedQ.pdf). Thus, vaccination status in May or June 2021 might more accurately reflect choice rather than eligibility to be vaccinated.

¶ 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.

Summary

What is already known about this topic?

Reinfection with human coronaviruses, including SARS-CoV-2, the virus that causes COVID-19, has been documented. Currently, limited evidence concerning the protection afforded by vaccination against reinfection with SARS-CoV-2 is available.

What is added by this report?

Among Kentucky residents infected with SARS-CoV-2 in 2020, vaccination status of those reinfected during May–June 2021 was compared with that of residents who were not reinfected. In this case-control study, being unvaccinated was associated with 2.34 times the odds of reinfection compared with being fully vaccinated.

What are the implications for public health practice?

To reduce their likelihood for future infection, all eligible persons should be offered COVID-19 vaccine, even those with previous SARS-CoV-2 infection.

(Table 1). Among case-patients, 20.3% were fully vaccinated compared with 34.3% of controls (Table 2). Kentucky residents with previous infections who were unvaccinated had 2.34 times the odds of reinfection (OR = 2.34; 95% CI = 1.58–3.47) compared with those who were fully vaccinated; partial vaccination was not significantly associated with reinfection (OR = 1.56; 95% CI = 0.81–3.01).

Discussion

This study found that among Kentucky residents who were previously infected with SARS-CoV-2 in 2020, those who were unvaccinated against COVID-19 had significantly higher likelihood of reinfection during May and June 2021. This finding supports the CDC recommendation that all eligible persons be offered COVID-19 vaccination, regardless of previous SARS-CoV-2 infection status.

Reinfection with SARS-CoV-2 has been documented, but the scientific understanding of natural infection-derived immunity is still emerging (*5*). The duration of immunity resulting from natural infection, although not well understood, is suspected to persist for ≥90 days in most persons.** The emergence of new variants might affect the duration of infection-acquired immunity, and laboratory studies have shown that sera from previously infected persons might offer weak or inconsistent responses against several variants of concern (*2,6*). For example, a recent laboratory study found that sera collected from previously infected persons before they were vaccinated provided a relatively weaker, and in some cases absent, neutralization response to the B.1.351 (Beta) variant when compared with the original Wuhan-Hu-1 strain (*1*). Sera from the same persons after vaccination showed a heightened neutralization response to the Beta variant, suggesting that vaccination enhances the immune response even to a variant to which the infected person had not been previously exposed. Although such laboratory evidence continues to suggest that vaccination provides improved neutralization of SARS-CoV-2 variants, limited evidence in real-world settings to date corroborates the findings that vaccination can provide improved protection for previously infected persons. The findings from this study suggest that among previously infected persons, full vaccination is associated with reduced likelihood of reinfection, and, conversely, being unvaccinated is associated with higher likelihood of being reinfected.

The lack of a significant association with partial versus full vaccination should be interpreted with caution given the small numbers of partially vaccinated persons included in the analysis (6.9% of case-patients and 7.9% of controls), which limited statistical power. The lower odds of reinfection among the partially vaccinated group compared with the unvaccinated group is suggestive of a protective effect and consistent with findings from previous studies indicating higher titers after the first mRNA vaccine dose in persons who were previously infected (*7,8*).

The findings in this report are subject to at least five limitations. First, reinfection was not confirmed through whole genome sequencing, which would be necessary to definitively prove that the reinfection was caused from a distinct virus relative to the first infection. Although in some cases the repeat positive test could be indicative of prolonged viral shedding or failure to clear the initial viral infection (*9*), given the time between initial and subsequent positive molecular tests among participants in this study, reinfection is the most likely explanation. Second, persons who have been vaccinated are possibly less likely to get tested. Therefore, the association of reinfection and lack of vaccination might be overestimated. Third, vaccine doses administered at federal or out-of-state sites are not typically entered in KYIR, so vaccination data are possibly missing for some persons in these analyses. In addition, inconsistencies in name and date of birth between KYIR and NEDSS might limit ability to match the two databases. Because case investigations include questions regarding vaccination, and KYIR might be updated during the case investigation process, vaccination data might be more likely to be missing for controls. Thus, the OR might be even more favorable for vaccination. Fourth, although case-patients and controls were matched based on age, sex, and date of initial infection, other unknown confounders might be present. Finally, this is a retrospective study design using data from a single state during a 2-month period; therefore, these findings cannot be used to infer causation. Additional prospective studies with larger populations are warranted to support these findings.

** https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html

TABLE 1. Demographic characteristics of COVID-19 patients with reinfection (case-patients) and COVID-19 patients who were not reinfected (control participants) — Kentucky, May–June 2021

Characteristic	No. (%) Case-patients* (n = 246)	Control participants† (n = 492)
Age group, yrs		
18–29	46 (18.7)	89 (18.1)
30–39	37 (15.0)	83 (16.9)
40–49	43 (17.5)	80 (16.3)
50–59	44 (17.9)	88 (17.9)
60–69	27 (11.0)	51 (10.4)
70–79	28 (11.4)	58 (11.8)
≥80	21 (8.5)	43 (8.7)
Sex		
Female	149 (60.6)	298 (60.6)
Month of initial infection in 2020		
March	0 (0)	3 (0.6)
April	7 (2.8)	11 (2.2)
May	2 (0.8)	2 (0.4)
June	4 (1.6)	11 (2.2)
July	8 (3.3)	17 (3.5)
August	8 (3.3)	13 (2.6)
September	13 (5.3)	22 (4.5)
October	36 (14.6)	78 (15.9)
November	72 (29.3)	141 (28.7)
December	96 (39.0)	194 (39.4)

* Case-patients were eligible for inclusion if initial infection occurred during March–December 2020, and a subsequent positive nucleic acid amplification or antigen test result was received during May–June 2021 (using date of specimen collection). Cases for analyses were restricted to persons aged ≥18 years at time of reinfection.

† Controls were matched by sex, age (within 3 years), and time of initial infection diagnosis (within 7 days).

These findings suggest that among persons with previous SARS-CoV-2 infection, full vaccination provides additional protection against reinfection. Among previously infected Kentucky residents, those who were not vaccinated were more than twice as likely to be reinfected compared with those with full vaccination. All eligible persons should be offered vaccination, including those with previous SARS-CoV-2 infection, to reduce their risk for future infection.

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TABLE 2. Association of SARS-CoV-2 reinfection* with COVID-19 vaccination status — Kentucky, May–June 2021

Vaccination status	No. (%) Case-patients	Control participants	OR (95% CI)†
Not vaccinated	179 (72.8)	284 (57.7)	2.34 (1.58–3.47)
Partially vaccinated¶	17 (6.9)	39 (7.9)	1.56 (0.81–3.01)
Fully vaccinated§	50 (20.3)	169 (34.3)	Ref
Total	**246 (100)**	**492 (100)**	—

Abbreviations: CI = confidence interval; NAAT = nucleic acid amplification test; OR = odds ratio; Ref = referent group.

* All case-patients (reinfected) and control participants (not reinfected) had previous SARS-CoV-2 infection documented by positive NAAT or antigen test results during March–December 2020. Reinfection was defined as receipt of positive NAAT or antigen test results during May 1–June 30, 2021.

† Estimated based on conditional logistic regression.

§ Case-patients were considered partially vaccinated if ≥1 dose of vaccine was received, but the vaccination series was either not completed or the final dose was received <14 days before their reinfection date. For control participants, the same criteria were applied, using the matched case-patient's reinfection date.

¶ Case-patients and control participants were considered fully vaccinated if a complete COVID-19 vaccine series was received ≥14 days before the case-patient's reinfection date.

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Rapid Increase in Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant — Mesa County, Colorado, April–June 2021

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On May 5, 2021, the Colorado Department of Public Health and Environment (CDPHE) identified the first five COVID-19 cases caused by the SARS-CoV-2 B.1.617.2 (Delta) variant in Mesa County in western Colorado (population 154,933, <3% of the state population). All five initial cases were associated with school settings. Through early June, Mesa County experienced a marked increase in the proportion of Delta variant cases identified through sequencing: the 7-day proportion of sequenced specimens identified as B.1.617.2 in Mesa County more than doubled, from 43% for the week ending May 1 to 88% for the week ending June 5. As of June 6, more than one half (51%) of sequenced B.1.617.2 specimens in Colorado were from Mesa County. CDPHE assessed data from surveillance, vaccination, laboratory, and hospital sources to describe the preliminary epidemiology of the Delta variant and calculate crude vaccine effectiveness (VE). Vaccination coverage in early May in Mesa County was lower (36% of eligible residents fully vaccinated) than that in the rest of the state (44%). Compared with that in all other Colorado counties, incidence, intensive care unit (ICU) admissions, and COVID-19 case fatality ratios were significantly higher in Mesa County during the analysis period, April 27–June 6, 2021. In addition, during the same time period, the proportion of COVID-19 cases in persons who were fully vaccinated (vaccine breakthrough cases) was significantly higher in Mesa County compared with that in all other Colorado counties. Estimated crude VE against reported symptomatic infection for a 2-week period ending June 5 was 78% (95% confidence interval [CI] = 71%–84%) for Mesa County and 89% (95% CI = 88%–91%) for other Colorado counties. Vaccination is a critical strategy for preventing infection, serious illness, and death from COVID-19. Enhanced mitigation strategies, including masking in indoor settings irrespective of vaccination status, should be considered in areas with substantial or high case rates.

Whole genome sequencing is performed in the CDPHE laboratory on specimens submitted as part of sentinel surveillance (38 sites across Colorado, including one acute care hospital in Mesa County), as well as for cluster and outbreak response and on suspected variants (reverse transcription–polymerase chain reaction [RT-PCR]–positive specimens with S-gene target failure associated with the B.1.1.7 lineage) (*1*). The Colorado Electronic Disease Reporting System (CEDRS), a surveillance system managed by CDPHE, was used to identify reported confirmed or probable cases of COVID-19 occurring from April 27, the date of illness onset for the first Delta variant case in Mesa County, to June 6, when sequencing identified B.1.617.2 as the dominant variant in Colorado (*2*). The Colorado Immunization Information System (CIIS) was used to verify COVID-19 vaccination status; vaccine breakthrough infections were identified using personally identifying information to match cases in CEDRS to CIIS entries* (*3*). Crude VE against reported symptomatic infection was estimated and compared among Mesa County and all other Colorado counties using a screening method outlined by the World Health Organization† as a rapid tool to assess whether a vaccine is performing as expected (*4*). To better determine settings where the Delta variant was spreading, outbreak data during April 22–June 26 were obtained from the CDPHE outbreak database, which contains information on all reported COVID-19 outbreaks in Colorado and outbreak line lists.§ Residential care facility vaccination data were obtained from

* SARS-CoV-2 RNA or antigen in a respiratory specimen collected from a person ≥14 days after they have completed all recommended doses of the primary series for a Food and Drug Administration–authorized COVID-19 vaccine.

† Crude VE was estimated as (1-[{PCV/(1-PCV)}/{PPV/(1-PPV)}]) following World Health Organization interim guidance on conducting VE evaluations in the setting of new SARS-CoV-2 variants where PCV is the observed percentage of cases in persons who are vaccinated and PPV is the percentage of a comparable group in the population who are vaccinated. The PPV used in the calculations for Mesa County and other Colorado counties was from May 7, 2021, approximately 2 weeks before the anticipated onset for cases included in the PCV estimate. PPV included only vaccine-eligible persons and PCV was limited to symptomatic persons who were vaccine-eligible.

§ An outbreak in a residential care facility (skilled nursing facility, assisted living residence, intermediate care facility, or group home) is defined as the occurrence of two or more confirmed cases of COVID-19 among residents and staff members in a facility within 14 days, or one confirmed case and two or more probable cases of COVID-19 among residents and staff members in a facility within 14 days. Until May 31, 2021, the definition of a school outbreak was defined as two or more confirmed COVID-19 cases among students, teachers, and staff members from separate households within 14 days in a single classroom, cohort, or activity or other close contact in the school setting; or one confirmed case and two or more probable cases of COVID-19 among students, teachers, and staff members from separate households within 14 days in a single classroom, cohort, or activity or other close contact in the school setting. Starting June 1, the definition changed from two or more to five or more cases of COVID-19, of which at least one patient has had a positive molecular amplification test or antigen test, among students, teachers, and staff members from separate households within 14 days in a single classroom, cohort, or activity or other close contact in the school setting.

EMResource, a capacity planning tool used by CDPHE for facility-level reporting of aggregate COVID-19 vaccinations. Incidence of SARS-CoV-2 infection and proportions of outcomes and vaccination rates among patients living in Mesa County and all other Colorado counties were compared and p-values were calculated using chi-square or Fisher's exact tests. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.¶

During April 27–June 6, a total of 1,945 COVID-19 cases were reported in Mesa County through CEDRS (incidence = 1,255 per 100,000). Compared with that in all other Colorado counties, incidence, overall ICU admissions, and overall case fatality ratios were significantly higher in Mesa County (Table). In addition, the proportion of breakthrough cases was significantly higher in Mesa County than in all other Colorado counties. In Mesa County, the proportion of persons aged ≥65 years with COVID-19 who were fully vaccinated (27.5%) was significantly higher than that in all other Colorado counties (17.4%). The crude VE against reported symptomatic infection for a 2-week period ending June 5 was 78% (95% CI = 71%–84%) for Mesa County and 89% (95% CI = 88%–91%) for all other Colorado counties.**

Among 18,475 sequenced specimen results reported in Colorado through June 6, a total of 783 infections with the Delta variant were identified; more than one half (400; 51.1%) of these occurred among Mesa County residents, even though the county accounts for <3% of the state's population. Symptomatic illness was reported in 304 (76.0%) of the 400 Delta variant infections in Mesa County residents and 251 (65.5%) of 383 Delta variant infections in other counties. The 7-day percentage of sequenced sentinel specimens identified as SARS-CoV-2 B.1.617.2 in Mesa County increased from 43% for the week ending May 1 to 88% for the week ending June 5 (Figure). During the 5-week period, 67% (51 of 76) of sentinel surveillance specimens in Mesa County were identified as B.1.617.2 compared with 15% (248 of 1,637) of specimens from all other Colorado counties sequenced over the same time frame.

During April 22–June 26, a total of 37 COVID-19 outbreaks were reported in Mesa County; 13 (35%) in residential care facilities, 11 (30%) in schools, two (5%) in correctional facilities, and 11 (30%) in other settings. Twelve outbreaks, including seven in residential care facilities, had at least one Delta variant case. Average vaccination coverage in these seven residential facilities was 87% among residents (range = 50%–97%) and 50% among staff members (range = 6%–69%); attack rates among residents ranged from 0% to 54.6% (median = 1.2%) and among staff members from 2.2% to 25.5% (median = 10.0%). Five of these seven outbreaks involved at least one case in a fully vaccinated resident or staff member.††

Summary

What is already known about this topic?

The highly transmissible B.1.617.2 (Delta) variant of SARS-CoV-2 has become the predominant circulating U.S. strain.

What is added by this report?

During April–June 2021, COVID-19 cases caused by the Delta variant increased rapidly in Mesa County, Colorado. Compared with that in other Colorado counties, incidence, intensive care unit admissions, COVID-19 case fatality ratios, and the proportion of cases in fully vaccinated persons were significantly higher in Mesa County. Crude vaccine effectiveness against symptomatic infection was estimated to be 78% for Mesa County and 89% for other Colorado counties.

What are the implications for public health practice?

Vaccination is critical for preventing infection, serious illness, and death associated with SARS-CoV-2 infection (including the Delta variant). Multicomponent prevention strategies, such as masking in indoor settings irrespective of vaccination status as well as optimal surveillance testing and infection prevention and control, should be considered in areas of high incidence.

Discussion

The Delta variant is highly transmissible; within 5 weeks of first identification, the Delta variant became the dominant SARS-CoV-2 variant in Mesa County, Colorado and is also now the predominant variant in the United States (*5*). Higher ICU admissions and case fatality ratios in Mesa County compared with those in the rest of the state are consistent with previous reports that infections with the Delta variant might result in more severe outcomes (*6*,*7*). The slightly lower crude VE estimate against symptomatic infection in Mesa County may lend support to previous findings that COVID-19 vaccines provide modestly lower protection against symptomatic infection with the Delta variant (*8*). Alternatively, because the Delta variant was circulating at higher levels in Mesa County than in other Colorado counties, the lower VE in Mesa County might reflect the much higher exposure to circulating virus among vaccinated persons.

The findings in this report are subject to at least four limitations. First, lack of genetic sequencing for all SARS-CoV-2 isolates likely affected estimated rates and proportions; the number of outbreaks involving the Delta variant might be

¶ 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.

** For Mesa County, PPV was 36.2% and PCV was 11.0%. For other Colorado counties, PPV was 44.2% and PCV was 7.9%.

†† A fully vaccinated person is one who has completed all recommended doses of an FDA–authorized COVID-19 vaccine, including Pfizer-BioNTech, Moderna, and Janssen (Johnson & Johnson) ≥14 days before a positive SARS-CoV-2 test result.

TABLE. Age-specific incidence, clinical outcomes, and vaccination status among COVID-19 cases in Mesa and other counties — Colorado, April 27–June 6, 2021

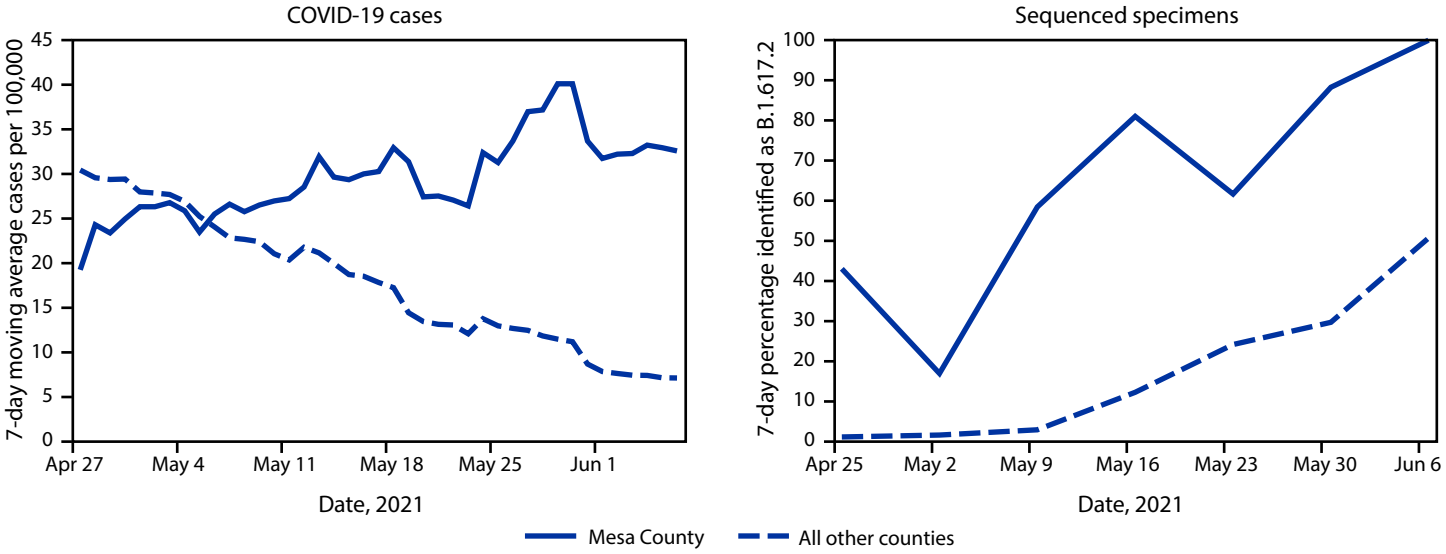
Characteristic	Mesa County	Other Colorado counties	p-value[†]
Total COVID-19 cases, no.	**1,945**	**35,494**	—
Age group, yrs			
0–17	477	7,603	—
18–64	1,246	25,466	—
≥65	222	2,425	—
Overall incidence*	1,255	633	<0.001
Age group, yrs			
0–17	1,408	620	<0.001
18–64	1,377	714	<0.001
≥65	726	297	<0.001
Hospital admission, no./No. (%)	142/1,945 (7.3)	2,448/35,494 (6.9)	0.49
Age group, yrs			
0–17	3/477 (0.6)	97/7,603 (1.3)	0.22
18–64	69/1,246 (5.5)	1,554/25,466 (6.1)	0.42
≥65	70/222 (31.5)	797/2,425 (32.9)	0.69
ICU admission among hospitalized patients, no./No. (%)	49/142 (34.5)	583/2,448 (23.8)	0.004
Age group, yrs			
0–17	1/3 (33.3)	17/97 (17.5)	0.45
18–64	25/69 (36.2)	356/1,554 (22.9)	0.01
≥65	23/70 (32.9)	210/797 (26.4)	0.24
Overall CFR, no./No. (%)	29/1,945 (1.5)	299/35,494 (0.8)	0.003
Age group, yrs			
0–17	1/477 (0.2)	2/7,603 (0.03)	0.16
18–64	7/1,246 (0.6)	101/25,466 (0.4)	0.37
≥65	21/222 (9.5)	196/2,425 (8.1)	0.47
CFR, hospitalized patients, no./No. (%)	22/142 (15.5)	198/2,448 (8.1)	0.002
Age group, yrs			
0–17	1/3 (33.3)	1/97(1.0)	0.06
18–64	5/69 (7.2)	55/1,554 (3.5)	0.11
≥65	16/70 (22.9)	142/797 (17.8)	0.29
Fully vaccinated[§,¶], no./No. (%)	136/1,945 (7.0)	1,715/35,397 (4.8)	<0.001
Age group, yrs			
0–17	2/477 (0.4)	10/7,591 (0.1)	0.16
18–64	73/1,246 (5.9)	1,283/25,381 (5.1)	0.21
≥65	61/222 (27.5)	422/2,425 (17.4)	<0.001

Abbreviations: CFR = case fatality ratio; ICU = intensive care unit.
* Cases per 100,000 population.
† Calculated using chi-square test or Fisher's exact test.
§ A fully vaccinated person is one who has completed all recommended doses of a Food and Drug Administration–authorized COVID-19 vaccine, including Pfizer-BioNTech, Moderna, and Janssen (Johnson & Johnson) ≥14 days before a positive SARS-Co-V-2 test result.
¶ Vaccination status was missing for 97 persons.

underreported for this reason. Second, sentinel surveillance might not provide a fully representative sample of sequence types in Colorado because the specimens originate from hospitals and likely include more specimens from inpatients and emergency department patients compared with specimens from other testing sites. Third, the screening method provides rapid crude VE estimates that do not control for possible effects of confounding or clustering. Some of the differences between VE and severity of illness in Mesa County and that in other counties might be due to differences in the age distribution of patients and the inclusion of cases associated with outbreaks in congregate settings. However, CDPHE estimates that fewer than 10% of cases during the time period occurred in congregate settings. Finally, differences in vaccination coverage in some of these populations might be an additional confounding factor when estimating crude VE at the county and state levels. VE studies with more rigorous methods and the power to estimate protection against severe outcomes are needed to better understand the potential impact of the Delta variant.

Vaccination is a critical strategy for preventing infection, serious illness, and death associated with SARS-CoV-2 (including the Delta variant). Additional targeted prevention strategies (e.g., masking in indoor settings irrespective of vaccination status) and adherence to prevention strategies (e.g., surveillance testing and infection prevention and control procedures) are prudent in areas with high circulation of the Delta variant and in higher risk settings, such as residential care facilities.

FIGURE. Number of COVID-19 cases and proportion of B.1.617.2 (Delta) variant infections in Mesa and other counties — Colorado, April 27–June 6, 2021



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Effectiveness of COVID-19 Vaccines in Preventing Hospitalization Among Adults Aged ≥65 Years — COVID-NET, 13 States, February–April 2021

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Clinical trials of COVID-19 vaccines currently authorized for emergency use in the United States (Pfizer-BioNTech, Moderna, and Janssen [Johnson & Johnson]) indicate that these vaccines have high efficacy against symptomatic disease, including moderate to severe illness (*1*–*3*). In addition to clinical trials, real-world assessments of COVID-19 vaccine effectiveness are critical in guiding vaccine policy and building vaccine confidence, particularly among populations at higher risk for more severe illness from COVID-19, including older adults. To determine the real-world effectiveness of the three currently authorized COVID-19 vaccines among persons aged ≥65 years during February 1–April 30, 2021, data on 7,280 patients from the COVID-19–Associated Hospitalization Surveillance Network (COVID-NET) were analyzed with vaccination coverage data from state immunization information systems (IISs) for the COVID-NET catchment area (approximately 4.8 million persons). Among adults aged 65–74 years, effectiveness of full vaccination in preventing COVID-19–associated hospitalization was 96% (95% confidence interval [CI] = 94%–98%) for Pfizer-BioNTech, 96% (95% CI = 95%–98%) for Moderna, and 84% (95% CI = 64%–93%) for Janssen vaccine products. Effectiveness of full vaccination in preventing COVID-19–associated hospitalization among adults aged ≥75 years was 91% (95% CI = 87%–94%) for Pfizer-BioNTech, 96% (95% CI = 93%–98%) for Moderna, and 85% (95% CI = 72%–92%) for Janssen vaccine products. COVID-19 vaccines currently authorized in the United States are highly effective in preventing COVID-19–associated hospitalizations in older adults. In light of real-world data demonstrating high effectiveness of COVID-19 vaccines among older adults, efforts to increase vaccination coverage in this age group are critical to reducing the risk for COVID-19–related hospitalization.

COVID-NET includes data on laboratory-confirmed COVID-19–associated hospitalizations in 99 U.S. counties in 14 states, representing approximately 10% of the U.S. population.[†] COVID-NET cases were hospitalizations that occurred in residents of a designated COVID-NET catchment area who were admitted within 14 days of a positive SARS-CoV-2 test result. COVID-NET program personnel collected information on COVID-19 vaccination status (vaccine product received, number of doses, and administration dates) from state IISs for all sampled COVID-NET cases.[§] Some sites expanded collection of information on vaccination status to all reported COVID-NET cases, not only sampled cases, which were included for analysis if all cases in a single month had vaccination status available. Data from 13 sites were included for analysis; one site (Iowa) does not have access to the state IIS and cannot collect vaccination data.[¶] Population-level vaccination coverage was determined using deidentified person-level COVID-19 vaccination data reported to CDC by jurisdictions, pharmacies, and federal entities through the IISs,[**] Vaccine Administration Management System,[††] or direct data submission.[§§]

The study was restricted to adults aged ≥65 years and included the period February 1–April 30, 2021. The Janssen vaccine was authorized for use during the study period beginning March 15, 2021.[¶¶] Patients were classified as 1) unvaccinated (no IIS record of vaccination), 2) partially vaccinated (1 dose of Moderna or Pfizer-BioNTech

[*] These authors contributed equally to this report.

[†] https://www.medrxiv.org/content/10.1101/2021.04.21.21255473v1

[§] COVID-NET methodology and sampling scheme: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covid-net/purpose-methods.html

[¶] COVID-NET data included in this analysis were from the following states: California, Colorado, Connecticut, Georgia, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah.

[**] IISs are confidential, computerized, population-based systems that collect and consolidate vaccination data from providers in 64 public health jurisdictions nationwide and can be used to track administered vaccines and measure vaccination coverage. https://www.cdc.gov/vaccines/covid-19/reporting/overview/IT-systems.html

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

[§§] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/distributing/about-vaccine-data.html

[¶¶] Emergency Use Authorization (EUA) for the Janssen (Johnson & Johnson) vaccine was granted by the Food and Drug Administration on February 26, 2021. EUA was granted for the Pfizer-BioNTech vaccine on December 11, 2020, and for the Moderna vaccine on December 18, 2020.

received ≥14 days before hospitalization or 2 doses, with the second dose received <14 days before hospitalization), or 3) fully vaccinated (receipt of both doses of Moderna or Pfizer-BioNTech with second dose received ≥14 days before hospitalization or receipt of a single dose of Janssen ≥14 days before hospitalization). Patients with only 1 dose of any COVID-19 vaccine received <14 days before hospitalization were excluded. Daily county-level coverage data for adults aged 65–74 and ≥75 years in the COVID-NET catchment area were estimated using population denominators from the U.S. Census Bureau; vaccination status was classified as described for hospitalized cases.*** For vaccine records missing county of residence, county of vaccine administration was used.

To estimate vaccine effectiveness and corresponding 95% CIs, methods were adapted based on previously published literature (*4*). Poisson regression was used to compare case counts by vaccination status (outcome) and the proportion of the population vaccinated and unvaccinated (offset).††† Data were stratified by age group because of the potential for confounding by age, and adjusted for COVID-NET site, time (number of weeks since the start of the study period as a categorical covariate), and monthly site-specific sampling frequency.§§§ Vaccine effectiveness was calculated as one minus the exponent of the estimated coefficient of the exposure (vaccination status) variable. For estimating effectiveness of full vaccination, partially vaccinated persons were excluded; for estimating effectiveness of partial vaccination, fully vaccinated persons were excluded. Vaccine product–specific estimates excluded persons who had received other COVID-19 vaccines. To account for the interval between infection and hospitalization, sensitivity analyses were conducted using a reference date 1 week and 2 weeks before admission, rather than admission date, for classification of vaccination status for cases (i.e., adding 7 and 14 days, respectively between last vaccine dose and hospital admission date); the same adjustment was included for population vaccination coverage. Statistical analyses were conducted using SAS software (version 9.4; SAS Institute). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.¶¶¶

During February 1–April 30, 2021, among 7,280 eligible COVID-NET patients, 5,451 (75%) were unvaccinated, 867 (12%) were partially vaccinated, and 394 (5%) were fully vaccinated; 568 (8%) who received a single vaccine dose <14 days before hospitalization were excluded from the analysis (Table). Vaccination coverage in the population increased rapidly during this period among persons aged ≥65 years and varied by age and vaccine product (Figure 1). Among adults aged ≥65 years in the COVID-NET catchment area, full vaccination coverage from any of the three authorized vaccines ranged from 0.7% on February 1, 2021, to 72% on April 30, 2021.

Effectiveness of full vaccination in preventing hospitalization among adults aged 65–74 years was estimated at 96% (95% CI = 94%–98%) for Pfizer-BioNTech, 96% (95% CI = 95%–98%) for Moderna, and 84% (95% CI = 64%–93%) for Janssen vaccine products. Among adults aged ≥75 years, effectiveness of full vaccination was 91% (95% CI = 87%–94%) for Pfizer-BioNTech, 96% (95% CI = 93%–98%) for Moderna, and 85% (95% CI = 72%–92%) for Janssen vaccine products (Figure 2). Effectiveness of partial vaccination among adults aged 65–74 years was 84% (95% CI = 76%–89%) for Pfizer-BioNTech and 91% (95% CI = 87%–93%) for Moderna vaccine products. Among those aged ≥75 years, effectiveness of partial vaccination was 66% (95% CI = 48%–77%) for Pfizer-BioNTech and 82% (95% CI = 76%–86%) for Moderna vaccine products. Sensitivity analyses accounting for interval between infection and hospitalization did not yield notably different vaccine effectiveness estimates, with point estimates varying by <1% for Pfizer-BioNTech and Moderna vaccine models. Point estimates for Janssen COVID-19 vaccine models varied by <10%, with few cases eligible for inclusion and wide CIs.

Discussion

In this analysis of 7,280 laboratory-confirmed COVID-19–associated cases among hospitalized adults aged ≥65 years, all three COVID-19 vaccine products currently authorized for use in the United States had high effectiveness in preventing

*** https://www.cdc.gov/nchs/nvss/bridged_race.htm

††† Population vaccine effectiveness is defined as the reduction in disease risk among vaccinated versus unvaccinated persons in the population. Vaccine effectiveness is typically estimated by examining the proportion of persons with disease among those who are vaccinated and the proportion of persons with disease among those who are unvaccinated. If these numbers are difficult to measure or estimate and only case vaccination information is available, then an alternative approach, called the "screening method," uses estimates of 1) the proportion of persons with disease who are vaccinated and 2) the proportion of persons in the population who are vaccinated. This analysis applied a variation of the screening method through a Poisson regression model, which allows the estimates to account for potential confounding. Specifically, the Poisson regression model uses case counts (both vaccinated and unvaccinated) as the outcome, vaccination status as the exposure variable, and the logarithms of the proportion of vaccinated and unvaccinated persons in the population as offsets. The Poisson model includes the potential confounders time and COVID-NET site as fixed effects because vaccination coverage data are available in each time-by-site stratum. A generalized estimating equation approach with autoregressive correlation structure accommodated daily variations of disease rates and vaccine coverage because this study occurred during a time of very rapid change. Finally, the adjusted vaccine effectiveness estimate was calculated as 1 - exp(β), in which β is the regression coefficient of the vaccination status exposure variable.

§§§ Sampling weights were created based on the probability of selection. Weights were adjusted for nonresponse; adjusted to population catchment totals based on combinations of surveillance site, time period of admission, age, sex, and race/ethnicity via raking procedures; and trimmed to reduce variability.

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

TABLE. Hospitalized COVID-19 patients aged ≥65 years, by vaccination status and age group (N = 6,712)* — COVID-NET,† 13 states, February 1–April 30, 2021

Vaccination status§,¶	No. of cases, by age group (yrs)		
	65–74	≥75	Total (≥65)
All patients (any vaccination status)	3,306	3,406	**6,712**
Unvaccinated patients	2,869	2,582	**5,451**
Vaccinated patients, by vaccine product			
Pfizer-BioNTech			
Partially vaccinated	188	379	**567**
Fully vaccinated	73	185	**258**
Moderna			
Partially vaccinated	104	196	**300**
Fully vaccinated	56	56	**112**
Janssen (Johnson & Johnson)**			
Fully vaccinated	16	8	**24**

Abbreviation: COVID-NET = Coronavirus Disease 2019–Associated Hospitalization Surveillance Network.

* Among 7,280 eligible COVID-NET patients, 568 patients (251 aged 65–74 years and 317 aged ≥75 years) who received only 1 dose of any COVID-19 vaccine <14 days before hospitalization were excluded from analysis.

† COVID-NET data included in this analysis were from the following states: California, Colorado, Connecticut, Georgia, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah.

§ Partially vaccinated patients received 1 dose of Moderna or Pfizer-BioNTech vaccine ≥14 days before hospitalization or 2 doses, with the second dose received <14 days before hospitalization.

¶ Fully vaccinated patients received both doses of Moderna or Pfizer-BioNTech vaccine, with second dose received ≥14 days before hospitalization, or receipt of a single dose of Janssen (Johnson & Johnson) vaccine ≥14 days before hospitalization.

** The Janssen vaccine was authorized for use after the study began; cases were included during March 15–April 30, 2021.

laboratory-confirmed COVID-19–associated hospitalizations. The effectiveness of full vaccination with mRNA vaccines (Pfizer BioNTech and Moderna) was ≥91% and of Janssen was ≥84% among adults aged ≥65 years. These findings are consistent with estimates from other observational studies of the mRNA vaccines and provide an early estimate of the effectiveness of Janssen in preventing COVID-19–associated hospitalization (*1*–*3*,*5*). Although the method used in this analysis does not account for many important potential confounders and results should be interpreted with caution, taken together, these findings provide additional evidence that available vaccines are highly effective in preventing COVID-19–associated hospitalizations and demonstrate that performance of COVID-19 vaccines can be assessed using existing disease surveillance and immunization data.

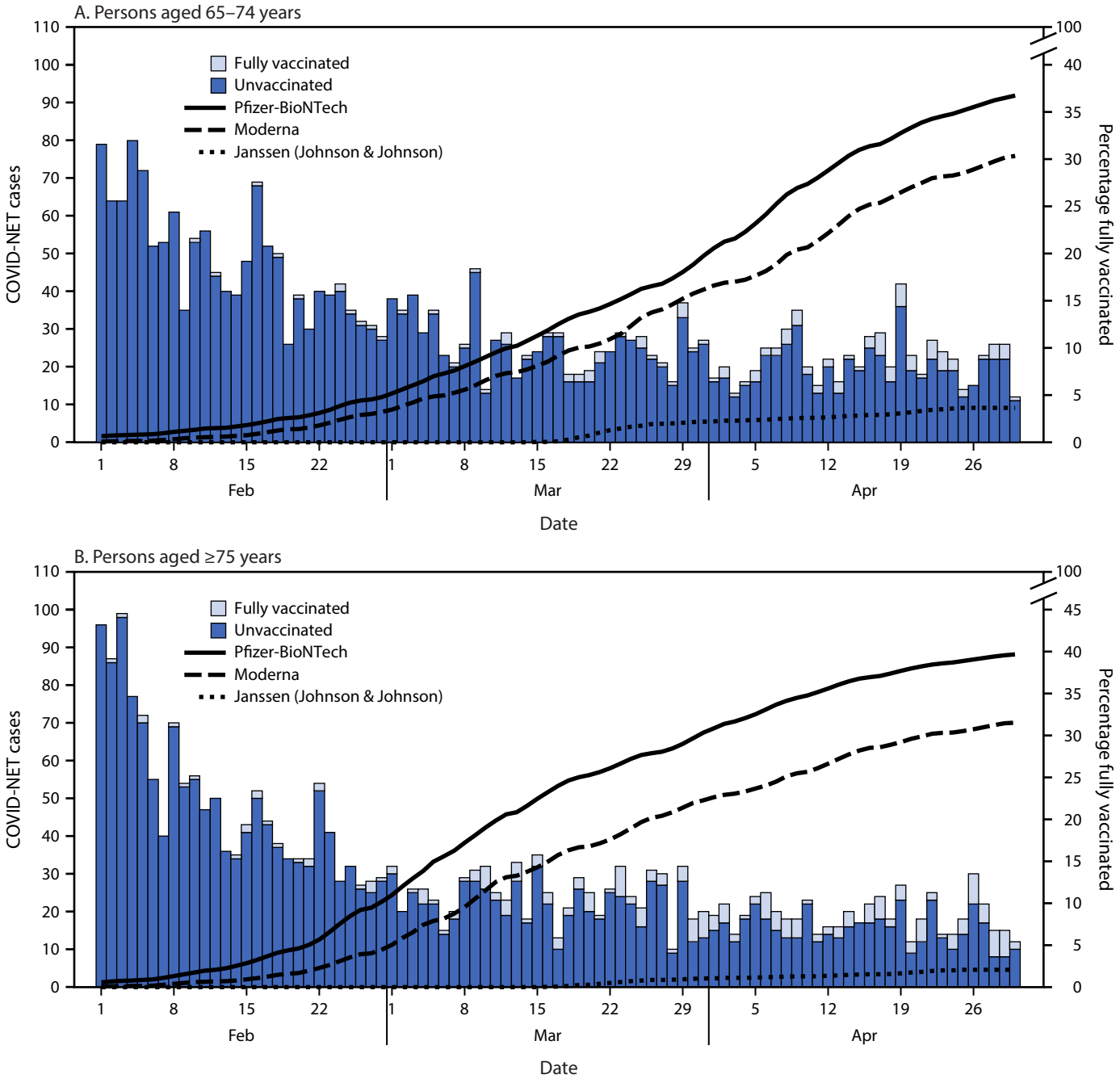
This analysis provides an early estimate of the Janssen vaccine effectiveness in preventing hospitalization in older adults, adding to the limited observational data available assessing Janssen vaccine effectiveness.**** These findings are consistent with clinical trial efficacy data, which found an efficacy of 76.7% for prevention of moderate to severe disease ≥14 days after vaccination (*3*). The relatively few cases and low population vaccination coverage with Janssen in this analysis likely contributed to the wide CIs for the vaccine effectiveness estimate. In addition, given vaccine prioritization for populations at high risk, older adults receiving the Janssen product were more likely to be at lower risk and differ substantially from those receiving products available earlier in the vaccine rollout. Other observational studies have demonstrated variability in the effectiveness of partial vaccination with mRNA vaccines in preventing hospitalization, with point estimates of effectiveness of 64% to 91% (*5*,*6*). Variation in estimates of effectiveness of partial vaccination between Pfizer-BioNTech and Moderna in this analysis might represent confounding from differences among the persons receiving these products. Residents of long-term care facilities (LTCFs) were prioritized early in the vaccine rollout and were more likely to receive Pfizer-BioNTech than Moderna.†††† The underlying risk for severe illness from COVID-19 in this medically fragile population could contribute to lower vaccine effectiveness among LTCF residents than among the general population of older adults and to an apparently lower effectiveness of Pfizer-BioNTech. Moreover, if partial protection increases between the third and fourth week after receipt of the first dose, it is possible that the timing of the second Pfizer-BioNTech and Moderna doses (21 and 28 days after the first dose, respectively) could affect the observed effectiveness of partial vaccination. Therefore, these results should not be interpreted as definitive evidence of a difference in the effectiveness of partial vaccination between the two mRNA vaccines, but rather as an indication that further evaluation is warranted.

The findings in this report are subject to at least four limitations. First, although adjustments were made for time and site, the analysis did not adjust for other potential confounders, such as chronic conditions, because person-level data were not available for the catchment population. In addition, although the analysis was stratified by age and adjusted for time and site, the heterogeneity of disease risk, vaccination coverage within each site, and differences in the populations who received different vaccine products might confound estimates of vaccine effectiveness. Second, the study period for this analysis occurred before the predominance of the B.1.617.2 (Delta) variant; changes in circulating SARS-CoV-2 variants might affect vaccine effectiveness when assessed over time. Third, persons choosing to receive vaccine later in the rollout might have different risk characteristics than do those vaccinated

**** https://www.medrxiv.org/content/10.1101/2021.04.27.21256193v1

†††† Among COVID-NET patients living in LTCFs, more residents received Pfizer-BioNTech vaccine than received Moderna vaccine, consistent with state distribution through the federal Pharmacy Partnership for Long-Term Care Program. https://www.cdc.gov/vaccines/covid-19/long-term-care/pharmacy-partnerships-faqs.html

FIGURE 1. COVID-NET* cases and full vaccination coverage among persons aged 65–74 years (A) and persons aged ≥75 years (B) — 13 states, February 1–April 30, 2021

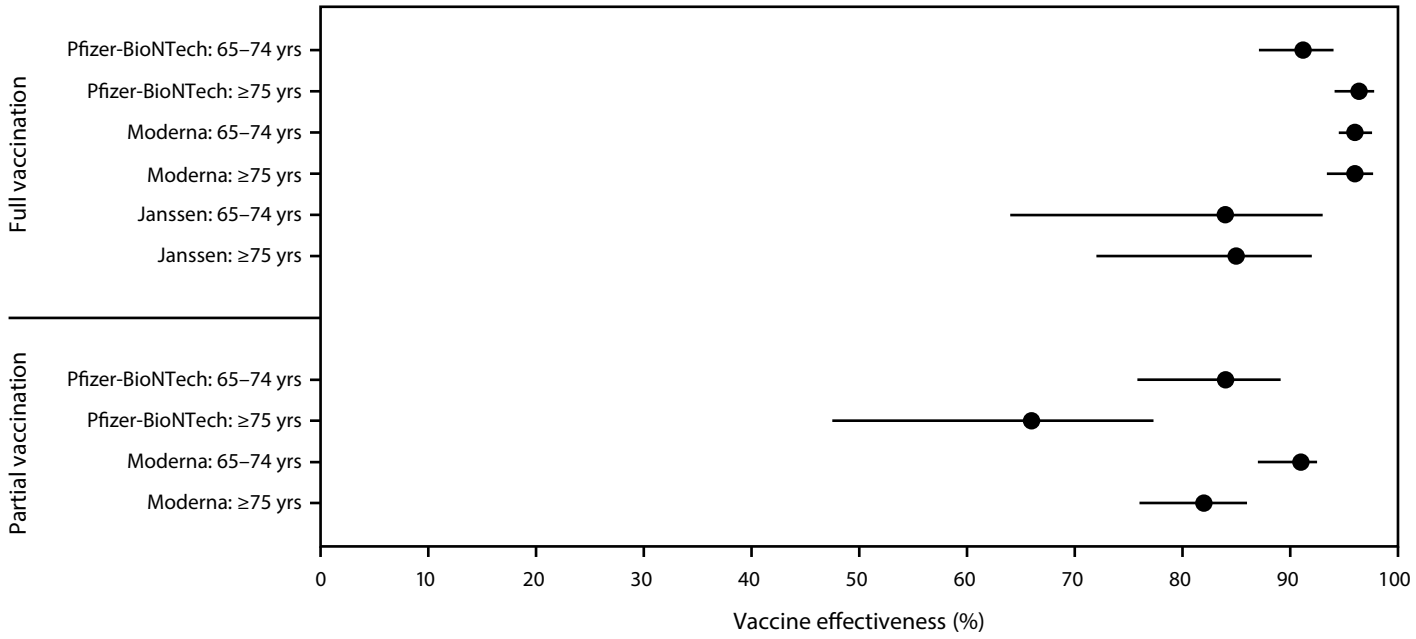


Abbreviation: COVID-NET = Coronavirus Disease 2019–Associated Hospitalization Surveillance Network.
* COVID-NET data included in this analysis were from the following states: California, Colorado, Connecticut, Georgia, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah.

earlier and might have experienced differences in access to vaccine products by time and location. Finally, this analysis was limited to adults aged ≥65 years, and the results are not generalizable to younger age groups.

This analysis found that all COVID-19 vaccines currently authorized in the United States are highly effective in preventing COVID-19–associated hospitalizations in older adults and also demonstrates the utility of this method in generating a

FIGURE 2. Estimates of vaccine effectiveness in preventing COVID-19–associated hospitalization among patients aged ≥65 years for the COVID-NET catchment area, by vaccine product and age group using the screening method — COVID-NET, 13 states,* February 1–April 30, 2021†



Abbreviation: COVID-NET = Coronavirus Disease 2019–Associated Hospitalization Surveillance Network; Janssen = Janssen (Johnson & Johnson).
* COVID-NET data included in this analysis were from the following states: California, Colorado, Connecticut, Georgia, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah.
† Confidence intervals indicated by error bars.

Summary

What is already known about this topic?

Clinical trials of COVID-19 vaccines currently authorized for emergency use in the United States (Pfizer-BioNTech, Moderna, and Janssen [Johnson & Johnson]) have shown high efficacy in preventing symptomatic (including moderate to severe) COVID-19.

What is added by this report?

Among adults aged 65–74 years, effectiveness of full vaccination for preventing hospitalization was 96% for Pfizer-BioNTech, 96% for Moderna, and 84% for Janssen COVID-19 vaccines; among adults aged ≥75 years, effectiveness of full vaccination for preventing hospitalization was 91% for Pfizer-BioNTech, 96% for Moderna, and 85% for Janssen COVID-19 vaccines.

What are the implications for public health practice?

Efforts to increase vaccination coverage are critical to reducing the risk for COVID-19–related hospitalization, particularly in older adults.

relatively rapid assessment of vaccine performance in the setting of high-quality surveillance and vaccine registry data. Efforts to increase vaccination coverage are critical to reducing the risk for COVID-19–related hospitalization, particularly in older adults.

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Use of COVID-19 Vaccines After Reports of Adverse Events Among Adult Recipients of Janssen (Johnson & Johnson) and mRNA COVID-19 Vaccines (Pfizer-BioNTech and Moderna): Update from the Advisory Committee on Immunization Practices — United States, July 2021

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In December 2020, the Food and Drug Administration (FDA) issued Emergency Use Authorizations (EUAs) for Pfizer-BioNTech and Moderna COVID-19 vaccines, and in February 2021, FDA issued an EUA for the Janssen (Johnson & Johnson) COVID-19 vaccine. After each EUA, the Advisory Committee on Immunization Practices (ACIP) issued interim recommendations for vaccine use; currently Pfizer-BioNTech is authorized and recommended for persons aged ≥12 years and Moderna and Janssen for persons aged ≥18 years (*1*–*3*). Both Pfizer-BioNTech and Moderna vaccines, administered as 2-dose series, are mRNA-based COVID-19 vaccines, whereas the Janssen COVID-19 vaccine, administered as a single dose, is a recombinant replication-incompetent adenovirus-vector vaccine. As of July 22, 2021, 187 million persons in the United States had received at least 1 dose of COVID-19 vaccine (*4*); close monitoring of safety surveillance has demonstrated that serious adverse events after COVID-19 vaccination are rare (*5*,*6*). Three medical conditions have been reported in temporal association with receipt of COVID-19 vaccines. Two of these (thrombosis with thrombocytopenia syndrome [TTS], a rare syndrome characterized by venous or arterial thrombosis and thrombocytopenia, and Guillain-Barré syndrome [GBS], a rare autoimmune neurologic disorder characterized by ascending weakness and paralysis) have been reported after Janssen COVID-19 vaccination. One (myocarditis, cardiac inflammation) has been reported after Pfizer-BioNTech COVID-19 vaccination or Moderna COVID-19 vaccination, particularly after the second dose; these were reviewed together and will hereafter be referred to as mRNA COVID-19 vaccination. ACIP has met three times to review the data associated with these reports of serious adverse events and has comprehensively assessed the benefits and risks associated with receipt of these vaccines. During the most recent meeting in July 2021, ACIP determined that, overall, the benefits of COVID-19 vaccination in preventing COVID-19 morbidity and mortality outweigh the risks for these rare serious adverse events in adults aged ≥18 years; this balance of benefits and risks varied by age and sex. ACIP continues to recommend COVID-19 vaccination in all persons aged ≥12 years. CDC and FDA continue to closely monitor reports of serious adverse events and will present any additional data to ACIP for consideration. Information regarding risks and how they vary by age and sex and type of vaccine should be disseminated to providers, vaccine recipients, and the public.

Since June 2020, ACIP has convened 16 public meetings to review data on COVID-19 epidemiology and use of COVID-19 vaccines, most recently on July 22, 2021. The ACIP COVID-19 Vaccines Work Group, comprising experts in infectious diseases, vaccinology, vaccine safety, public health, and ethics, has held weekly meetings since April 2020 to review COVID-19 surveillance data, evidence for vaccine efficacy and safety, and implementation considerations for COVID-19 vaccination programs.

ACIP met to review reports of TTS after Janssen COVID-19 vaccination in April 2021; the committee met again in June 2021 to review reports of myocarditis after mRNA COVID-19 vaccination, particularly after the second dose. At both meetings, ACIP reviewed the individual- and population-level benefits and risks for vaccination and concluded that the benefits of vaccination for individual persons and at the population-level outweigh the risks; details of the findings have been described previously (*7*,*8*). FDA added information about these serious adverse events to the EUA fact sheets*; CDC updated patient and clinician education and communication materials,† and federal agencies continue to closely monitor reports of these serious adverse events.

On July 12, 2021, FDA issued a warning and updated EUA fact sheets after reports of a more than expected number of GBS cases to the Vaccine Adverse Events Reporting System (VAERS) after Janssen COVID-19 vaccination. GBS is a rare neurologic disorder characterized by acute or subacute onset of weakness in limbs or cranial nerve–innervated muscles and by laboratory

* https://www.fda.gov/media/146304/download; https://www.fda.gov/media/146305/download

† https://www.cdc.gov/coronavirus/2019-ncov/vaccines/index.html

findings of increased cerebrospinal fluid protein with normal numbers of cells; the clinical presentation and severity vary (*9*). GBS occurs more commonly in males than in females, and incidence increases with age; 3,000–6,000 GBS cases are reported annually in the United States.[§] Patients might require intensive care unit (ICU) admission and ventilator support; although most patients recover, GBS can result in permanent paralysis or death (*10*).

After the reports of GBS cases after Janssen COVID-19 vaccination, the Work Group met to review clinical trial and postauthorization safety data for GBS. To comprehensively evaluate the benefits and risks associated with COVID-19 vaccination, in addition to reviewing a benefit-risk assessment of GBS after Janssen COVID-19 vaccination, the Work Group also updated benefit-risk assessments of TTS cases after Janssen COVID-19 vaccination and of myocarditis cases after mRNA COVID-19 vaccination in adults aged ≥18 years. The ACIP COVID-19 Vaccines Safety Technical (VaST) Work Group,[¶] comprising independent vaccine safety expert consultants, performed concomitant review of the adverse events information.

On July 22, 2021, ACIP met to review currently available evidence of risks associated with COVID-19 vaccination. The findings from VaST and ACIP COVID-19 Vaccine Work Group assessments, including a summary of the data reviewed, were presented to ACIP during this meeting. ACIP's comprehensive assessment included risks for GBS and TTS after Janssen COVID-19 vaccination and myocarditis after mRNA COVID-19 vaccination in persons aged ≥18 years. To date, there has been no increased risk detected for GBS or TTS after mRNA COVID-19 vaccination, and there has been no increased risk detected for myocarditis after Janssen COVID-19 vaccination. Persons aged <18 years were not included in this assessment because a benefit-risk assessment for persons aged 12–29 years was recently presented to ACIP in June 2021[**]; ongoing safety monitoring continues and can be included in future updates to ACIP (*8*).

To assess the benefit-risk balance of COVID-19 vaccination in adults, ACIP reviewed an assessment comparing the benefits of vaccination (numbers of COVID-19 cases and severe disease outcomes prevented) to the risks (numbers of cases of GBS, TTS, and myocarditis), using methods similar to those described previously.[††] Specifically, the benefits per million vaccine doses administered (i.e., the benefits of being fully vaccinated[§§] in accordance with the FDA EUA) were assessed, including 1) COVID-19 cases prevented, based on rates during the week of June 13–19, 2021[¶¶]; 2) COVID-19 hospitalizations prevented, based on rates during the week of June 19, 2021[***]; and 3) COVID-19 ICU admissions and deaths prevented, based on the proportion of hospitalized patients who were admitted to an ICU or who died.[†††]

The risks assessed for the Janssen COVID-19 vaccination were 1) the number of GBS patients reported to VAERS that occurred within 42 days of Janssen COVID-19 vaccination per million doses administered through June 30, 2021, and 2) the number of patients with TTS reported to VAERS that occurred after Janssen COVID-19 vaccination per million doses through July 8, 2021. The risks for mRNA COVID-19 vaccination were assessed as the number of patients reported to VAERS with myocarditis after receipt of dose 2 of an mRNA COVID-19 vaccine per million doses. Each benefit-risk assessment was stratified by age group (18–29, 30–49, 50–64 and ≥65 years) and sex. The Janssen COVID-19 vaccine analysis assumed 90% vaccine effectiveness[§§§] in preventing severe outcomes and 66% vaccine effectiveness in preventing COVID-19 cases for a 120-day period. The mRNA COVID-19 vaccine analysis assumed 95% vaccine effectiveness[¶¶¶] in preventing severe outcomes and in preventing COVID-19 cases for a 120-day-period. The 120-day period was selected because inputs pertaining to community transmission have increased uncertainty beyond this period, particularly with regard to virus variants in circulation.[****] Using GBS, TTS, and myocarditis cases reported to VAERS with age and sex data available, crude reporting rates[††††] per million vaccine doses administered were calculated, overall and among subgroups, by sex and age using national COVID-19 vaccine administration data. GBS rates from the Vaccine Safety Datalink (VSD),[§§§§] based on cases confirmed by medical record review, were also presented to and reviewed by ACIP.

As of June 30, 2021, approximately 12.6 million doses of Janssen COVID-19 vaccine had been administered in the

[§] https://www.cdc.gov/vaccinesafety/concerns/guillain-barre-syndrome.html
[¶] https://www.cdc.gov/vaccines/acip/work-groups-vast/index.html
[**] https://www.cdc.gov/vaccines/acip/meetings/slides-2021-06.html
[††] https://www.cdc.gov/vaccines/covid-19/info-by-product/janssen/risk-benefit-analysis.html
[§§] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated.html
[¶¶] https://covid.cdc.gov/covid-data-tracker/#demographicsovertime. Data were used for the most recent week not subject to reporting delays before the ACIP meeting.
[***] https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html. Data were used for the most recent week not subject to reporting delays before the ACIP meeting.
[†††] https://gis.cdc.gov/grasp/COVIDNet/COVID19_5.html
[§§§] Vaccine effectiveness for Janssen COVID-19 vaccine based on data from phase 3 clinical trial.
[¶¶¶] Vaccine effectiveness for Pfizer-BioNTech and Moderna COVID-19 vaccines based on data from phase 3 clinical trials.
[****] https://covid.cdc.gov/covid-data-tracker/#variant-proportions
[††††] GBS reporting rates were calculated using unconfirmed cases. TTS reporting rates were calculated using confirmed cases. Myocarditis reporting rates included confirmed cases for aged 18–29 years and unconfirmed cases for aged ≥30 years.
[§§§§] https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vsd/index.html

United States to persons aged ≥18 years. Within VAERS,[¶¶¶¶] 100 reports of GBS after Janssen COVID-19 vaccination were received during February 27–June 30, 2021. The median patient age was 57 years (range = 24–76); 61 (61%) were males, and the median interval from vaccination to symptom onset was 13 days (range = 0–75 days). Ninety-five (95%) patients experiencing GBS were hospitalized, and 10 (10%) were admitted to an ICU. Ninety-eight (98%) of these patients had disease onset within 42 days of vaccination. As of the most recent follow-up,[*****] one patient had died. The GBS reporting rate was 7.8 cases per million Janssen COVID-19 vaccine doses administered. Among subgroups by sex and age, the reporting rate to VAERS was highest among males aged 50–64 years, with 15.6 cases per million Janssen COVID-19 vaccine doses administered (Table 1). VSD has not identified a signal[†††††] for GBS after Janssen COVID-19 vaccination. However, based on medical record–confirmed GBS cases reported during the 21 days[§§§§§] after receipt of Janssen COVID-19 vaccine, the unadjusted GBS rate in VSD was 20.2 per million doses administered (95% confidence interval = 8.1–41.7).[¶¶¶¶¶]

Through July 8, 2021, 38 cases of TTS within 15 days of vaccination and reported to VAERS met the case definition.[******] These 38 reports were confirmed by physician reviewers at CDC and FDA and reviewed with the Clinical Immunization Safety Assessment Project Investigators, who include hematologists. Four of these patients died. The overall TTS reporting rate was 3.0 cases per million doses administered as of July 8, 2021. [††††††] Among subgroups by sex and age, the reporting rate was highest among females aged 30–49 years (8.8 TTS cases per million Janssen COVID-19 vaccine doses administered).

As of June 30, 2021, approximately 141 million second mRNA COVID-19 vaccine doses had been administered in the United States to persons aged ≥18 years. Within VAERS, 497 reports of myocarditis after the second mRNA COVID-19 vaccine dose were received for persons aged ≥18 years. The reporting rate of myocarditis overall among adults was 3.5 cases per million second doses of mRNA COVID-19 vaccine administered. In subgroup analyses by age and sex, the reporting rate was highest among males aged 18–29 years (24.3 cases per million mRNA COVID-19 vaccine second doses administered). Reports of cases in persons aged 18–29 years were individually reviewed and confirmed to meet case definitions, whereas reports of cases in persons aged ≥30 years were received and processed[§§§§§§] but not individually reviewed. There were no confirmed myocarditis-associated deaths.

The estimated benefits (prevention of COVID-19 disease and associated hospitalizations, ICU admissions, and deaths) outweighed the risks (expected cases of GBS, TTS, and myocarditis after vaccination) in all persons aged ≥18 years included in this analysis (Table 2). For example, per million doses of Janssen COVID-19 vaccine administered to males aged 50–64 years, 1,800 hospitalizations, 480 ICU admissions, and 140 deaths attributable to COVID-19 could be prevented, compared with 14–17 GBS cases and 1–2 TTS cases after Janssen COVID-19 vaccination. However, the balance of benefits and risks varied by age and sex because cases of each serious adverse event were primarily identified in specific subgroups of age and sex (primarily males aged 50–64 years for GBS; females aged 30–49 years for TTS; and males aged 18–29 years for myocarditis).

ACIP also reviewed population-level considerations, including that COVID-19 cases are rising in the United States, particularly

TABLE 1. Number of Guillain-Barré syndrome cases* reported to the Vaccine Adverse Events Reporting System within 42 days after Janssen (Johnson & Johnson) COVID-19 vaccination, total Janssen doses administered, and reporting rate per million doses administered, by sex and age group — United States, February–June 2021

Sex/Age group, yrs	GBS cases†	No. of doses administered	GBS cases per million vaccine doses administered
Females			
18–29	1	1,037,996	1.0
30–49	13	1,957,663	6.6
50–64	14	1,888,715	7.4
≥65	9	1,037,996	8.7
Total females	**37**	**5,922,370**	**6.2**
Males			
18–29	3	1,258,963	2.4
30–49	18	2,407,430	7.5
50–64	33	2,115,411	15.6
≥65	7	932,764	7.5
Total males	**61**	**6,714,598**	**9.1**
Total	**98**	**12,636,938**	**7.8**

Abbreviations: GBS = Guillain-Barré syndrome; VAERS = Vaccine Adverse Events Reporting System.
* Unconfirmed cases reported to VAERS.
† 100 cases total were reported to VAERS during this period; the 98 displayed here occurred within 42 days of vaccination and had age and sex information available.

¶¶¶¶ https://vaers.hhs.gov/index.html
***** https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/02-COVID-Alimchandani-508.pdf
††††† The term signal in VSD refers to a prespecified statistical signal signifying risk.
§§§§§ Note that VSD used a risk length of 21 days, compared with VAERS, which used 42 days.
¶¶¶¶¶ https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/03-COVID-Klein-508.pdf
****** https://brightoncollaboration.us/thrombosis-with-thrombocytopenia-syndrome-interim-case-definition/
†††††† Calculations of reporting rates for TTS used denominators of Janssen doses administered through July 8, 2021.

§§§§§§ Processed VAERS reports are those that have been coded using MedDRA, have been deduplicated, and have undergone standard quality assurance and quality control review.

with the predominance of the highly transmissible B.1.617.2 (Delta) variant. More than one half (61%) of U.S. adults aged ≥18 years are fully vaccinated (*4*); however, coverage is lower in some geographic regions. According to a jurisdictional survey conducted on July 16, 2021, most vaccination sites offer more than one type of vaccine and report that Janssen vaccine is used in a variety of populations and settings.¶¶¶¶¶¶

Based on a comprehensive review of existing data, in the context of ongoing transmission of SARS-CoV-2, the virus that causes COVID-19, in the United States as of July 2021, the ACIP concluded that 1) the benefits of vaccinating all recommended age groups with either the Janssen COVID-19 vaccine or mRNA COVID-19 vaccine outweigh the risks for vaccination, including the risks for GBS and TTS after Janssen COVID-19 vaccination, or myocarditis after mRNA COVID-19 vaccination; 2) continuing safety monitoring of serious adverse events after COVID-19 vaccination is critical; and 3) providers and the public should be informed about these potential harms and the use of COVID-19 vaccines. The analysis did not include potential benefits of preventing post–COVID-19 conditions, or likely ongoing benefits beyond the 120-day period; for these reasons, the benefits of COVID-19 vaccination are underestimated.

ACIP members discussed concerns about the clinical severity of the rare risk for GBS and TTS. In addition, they noted the importance of providing options for the type of COVID-19 vaccines offered, especially in the context of the current COVID-19 epidemiology and current vaccine coverage in the United States. ACIP emphasized the importance of informing vaccination providers, and all persons receiving COVID-19 vaccines about the benefits and risks, including the risks after Janssen COVID-19 vaccination for GBS, particularly in males aged 50–64 years, and for TTS among females aged 30–49; and the risk for myocarditis after mRNA COVID-19 vaccination, particularly in males aged 18–29 years. CDC has provided guidance regarding evaluation and management of GBS, TTS, and myocarditis.******* In addition to information about TTS, FDA has added information to the Janssen COVID-19 vaccine

¶¶¶¶¶¶ https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-07/06-COVID-Mbaeyi-508.pdf

******* https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

TABLE 2. Estimated COVID-19 outcomes prevented during 120 days after 1-dose Janssen (Johnson & Johnson) COVID-19 vaccination and 2-dose mRNA (Pfizer-BioNTech or Moderna) COVID-19 vaccination, number of Guillain-Barré syndrome and thrombosis with thrombocytopenia syndrome cases expected per million Janssen vaccine doses administered, and number of myocarditis cases expected per million second mRNA vaccine doses administered, by sex and age group — United States, 2021*

Vaccine	Benefits: COVID-19 outcomes prevented				Harms: adverse events†	
Sex/Age group, yrs	Cases	Hospitalizations	ICU admissions	Deaths	GBS	TTS
Janssen (Johnson & Johnson) COVID-19 vaccine§						
Females						
18–29	8,900	700	50	5	1	4–5
30–49	10,100	900	140	20	6–7	8–10
50–64	12,100	1,600	350	120	7–8	3–4
≥65	29,000	5,900	1,250	840	8–10	0
Males						
18–29	6,600	300	60	3	2	2–3
30–49	7,600	650	150	25	7–8	1–2
50–64	10,100	1,800	480	140	14–17	1–2
≥65	36,600	11,800	3,300	2,300	7–8	0
mRNA (Pfizer-BioNTech or Moderna) COVID-19 vaccine¶					**Myocarditis**	
Females						
18–29	12,800	750	50	5	3–4	
30–49	14,600	950	140	20	1–2	
50–64	17,500	1,700	375	125	1	
≥65	32,000	6,200	1,300	900	<1	
Males						
18–29	9,600	300	60	3	22–27	
30–49	11,000	700	160	25	5–6	
50–64	14,700	1,900	500	150	1	
≥65	52,700	12,500	3,500	2,400	1	

Abbreviations: GBS = Guillain-Barré syndrome; ICU = intensive care unit; TTS = thrombosis with thrombocytopenia syndrome.

* Benefits and harms were calculated using case incidence and hospitalization data for the week ending June 19, 2021, and for harms using cases through June 30 (GBS and myocarditis) and through July 8 (TTS), projected for a 120-day period using methods described here: https://www.cdc.gov/vaccines/covid-19/info-by-product/janssen/risk-benefit-analysis.html

† Estimates for adverse events are based on an estimated risk of cases per million doses administered with a +/- 10% range.

§ Benefits and harms calculated per million doses of Janssen vaccine administered.

¶ Benefits and harms calculated per million second doses of mRNA (Pfizer-BioNTech and Moderna) vaccine administered.

EUA and fact sheets regarding GBS cases that have been reported among vaccine recipients. The vaccine product-specific EUA fact sheet should be provided to all persons before vaccination with any authorized COVID-19 vaccine.

CDC has updated patient education and communication materials[†††††††] reflecting this information; these are important to ensure that vaccine recipients are aware of risks and that they should seek care if they experience concerning symptoms. Persons should be educated about their individual benefits and risks associated with COVID-19 vaccination, and when feasible, provided a choice about which type of COVID-19 vaccine to receive.

Based on ACIP's conclusion regarding the benefit-risk assessment on July 22, 2021, vaccination with any of the available COVID-19 vaccines licensed under the FDA EUAs continues to be recommended for all persons aged ≥18 years. With the Delta variant, this is more urgent than ever. In addition, the Pfizer-BioNTech COVID-19 vaccine continues to be recommended for persons aged ≥12 years.

CDC and FDA will continue to closely monitor reports of serious adverse events and will present any additional data to ACIP for consideration. The benefit-risk analyses for COVID-19 vaccines can be updated to reflect changes in epidemiology of the COVID-19 pandemic and additional information on the risk for serious adverse events after vaccination. ACIP recommendation for use of all COVID-19 vaccines under an EUA are interim and will be updated as additional information becomes available.

Reporting of Vaccine Adverse Events

FDA requires that vaccine providers report to VAERS vaccination administration errors, serious adverse events,[§§§§§§§] cases of multisystem inflammatory syndrome, and cases of COVID-19 that result in hospitalization or death after administration of a COVID-19 vaccine under an EUA. CDC also encourages reporting of any additional clinically significant adverse event, even if it is not clear whether a vaccination caused the event. Information on how to submit a report to VAERS is available at https://vaers.hhs.gov/index.html or 1-800-822-7967. In addition, CDC has developed a voluntary smartphone-based online tool (v-safe) that uses text messaging and online surveys to provide near real-time health check-ins after receipt of a COVID-19 vaccine. In cases of v-safe reports that include possible medically attended health events, CDC's v-safe call center follows up with the vaccine recipient to collect additional information for completion of a VAERS report. Information on v-safe is available at https://www.cdc.gov/vsafe.

Summary

What is already known about this topic?

Rare serious adverse events have been reported after COVID-19 vaccination, including Guillain-Barré syndrome (GBS) and thrombosis with thrombocytopenia syndrome (TTS) after Janssen COVID-19 vaccination and myocarditis after mRNA (Pfizer-BioNTech and Moderna) COVID-19 vaccination.

What is added by this report?

On July 22, 2021, the Advisory Committee on Immunization Practices reviewed updated benefit-risk analyses after Janssen and mRNA COVID-19 vaccination and concluded that the benefits outweigh the risks for rare serious adverse events after COVID-19 vaccination.

What are the implications for public health practice?

Continued COVID-19 vaccination will prevent COVID-19 morbidity and mortality far exceeding GBS, TTS, and myocarditis cases expected. Information about rare adverse events should be disseminated to providers, vaccine recipients, and the public.

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[†††††††] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html

[§§§§§§§] https://vaers.hhs.gov/reportevent.html

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Notes from the Field

Recurrence of a Multistate Outbreak of *Salmonella* Typhimurium Infections Linked to Contact with Hedgehogs — United States and Canada, 2020

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In July 2020, PulseNet, the national molecular subtyping network for enteric disease surveillance, detected a cluster of 17 *Salmonella* Typhimurium infections. The isolates were closely related genetically to each other (four allele differences) by whole genome sequencing (WGS) analysis and related to isolates from two previous outbreaks of *S.* Typhimurium infections linked to pet hedgehogs (*1*,*2*). An investigation was initiated to characterize illnesses and identify the outbreak source.

A case was defined as the isolation of *S.* Typhimurium closely related by WGS to the outbreak strain in a specimen from a patient with illness onset during April–November 2020. State and local officials interviewed patients about hedgehog exposures and purchase information. Animal and environmental sampling of hedgehog enclosures was conducted at some patient residences. Hedgehog purchase locations were contacted in an attempt to identify a possible common source or supplier of hedgehogs. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.*

Forty-nine cases were identified in 25 states, including 14 (29%) in children aged <5 years. Eleven (26%) of 42 patients with available information were hospitalized, and no deaths were reported. Among 36 interviewed patients (or their parents or guardians), 30 (83%) reported hedgehog contact before becoming ill. Seven of 13 patients reported awareness of the risk for *Salmonella* transmission from hedgehogs and other small mammals. Samples collected from hedgehogs in patients' homes in New York and North Dakota and from a hedgehog habitat in California yielded the outbreak strain of *S.* Typhimurium. Isolates were closely related genetically (23 allele differences). The Public Health Agency of Canada identified 31 cases highly related by WGS to U.S. cases, also linked to hedgehog contact (*3*).

Hedgehog purchase locations were available for 20 of the 36 patients interviewed and included U.S. Department of Agriculture–licensed breeders,† unlicensed breeders, pet stores, and online sales (Figure). No common hedgehog supplier was identified as the source for either the U.S. or Canadian outbreaks. Among 27 identified U.S. hedgehog sources, six breeders were interviewed. All six breeders reported that they provide educational information to new owners when they purchase hedgehogs; four of the six provide information on prevention of disease transmission from pets to humans. Five of the six breeders reported that they work with a veterinarian or veterinary clinic; of these, only one breeder reported having a protocol in place for testing hedgehogs for *Salmonella*.

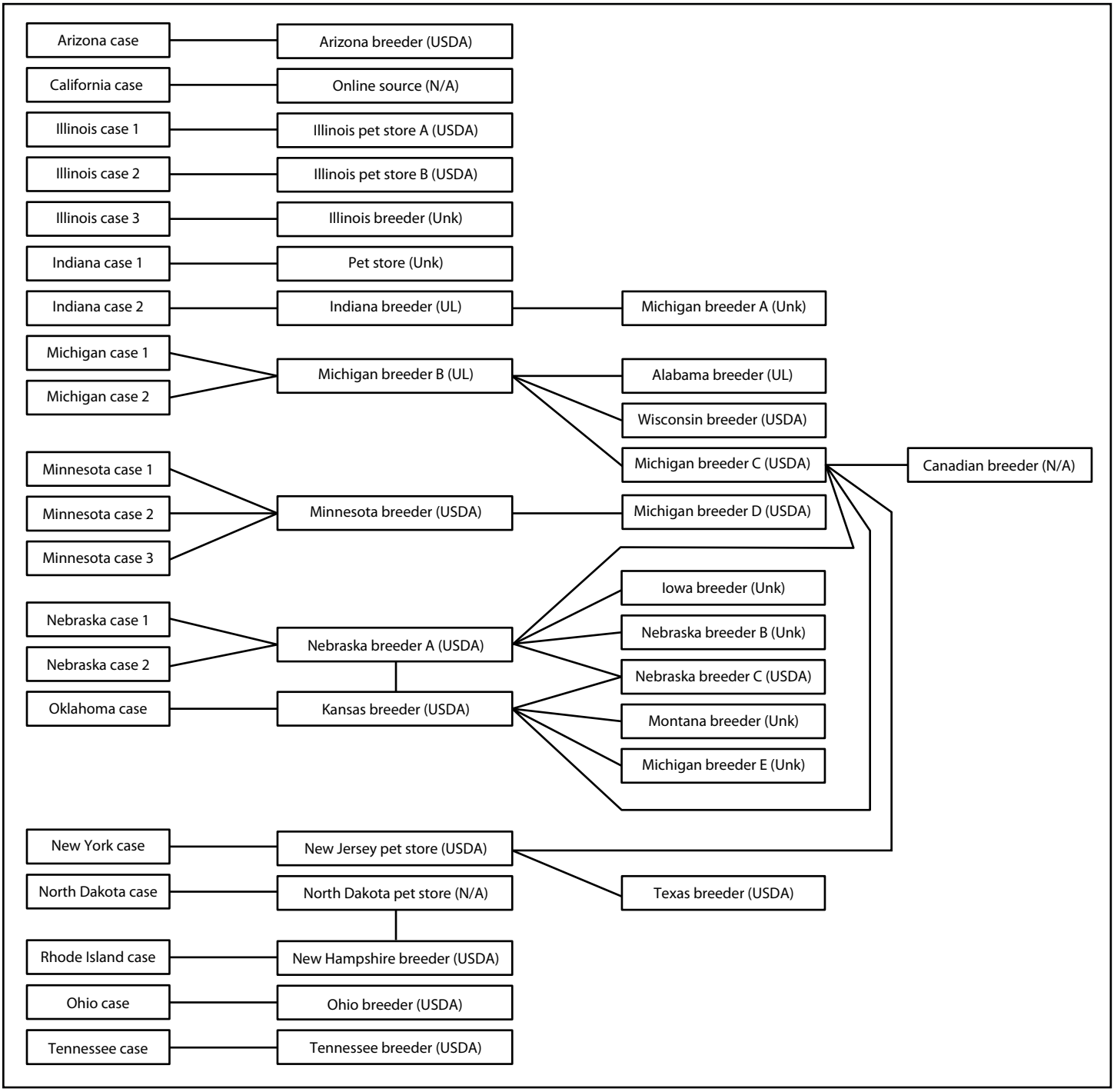
This particular *Salmonella* strain has continued to cause disease despite targeted outreach to hedgehog breeders and industry groups during two previous outbreaks with the strain linked to hedgehogs (*1*,*2*), highlighting that additional efforts are needed to reduce the prevalence and spread of *Salmonella* among hedgehogs and to limit transmission from hedgehogs to humans. CDC recommendations to pet owners during this outbreak focused on handling hedgehogs safely, including proper hand hygiene (*4*). Recommendations to hedgehog breeders included working with veterinarians experienced in reducing *Salmonella* prevalence in animal populations to evaluate sanitation and husbandry practices and monitoring hedgehogs for *Salmonella* through diagnostic testing.

Prevention and control of *Salmonella* in hedgehogs is complicated because of asymptomatic carriage and persistent or intermittent fecal shedding; however, *Salmonella* mitigation is possible through prevention and control measures focused on good sanitation and husbandry practices (*5*,*6*). To prevent future outbreaks linked to contact with pet hedgehogs, breeders and veterinarians need to educate owners on the risk and prevention of *Salmonella* transmission from hedgehogs and advise that hedgehogs might be inappropriate pets for children aged <5 years. The pet industry, veterinarians, and public and animal health officials could collaborate to help prevent disease transmission to humans by establishing and disseminating information on ways to reduce the prevalence of *Salmonella* in hedgehog breeding colonies intended for use in the pet industry.

* 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.

† https://www.aphis.usda.gov/aphis/ourfocus/animalwelfare/ct_awa_regulated_businesses

FIGURE. Traceback* of hedgehogs associated with human *Salmonella* Typhimurium infections from patient to hedgehog source (N = 20) — United States, 2020



Abbreviations: N/A = license status not applicable; UL = unlicensed; Unk = license status unknown; USDA = U.S. Department of Agriculture licensed.

* Traceback for hedgehog distribution from patients back to USDA-licensed hedgehog breeders, unlicensed breeders, pet stores, and online sales. The Michigan, Nebraska, New York, and Oklahoma patients purchased hedgehogs directly from breeders who reported receiving hedgehogs from multiple other breeders. The California patient purchased a hedgehog via an online platform from a seller who had a single hedgehog and did not breed hedgehogs; the source of the seller's hedgehog is unknown. Names and exact locations of the Illinois breeder, Iowa breeder, Michigan breeder, Montana breeder, Nebraska breeder B, and the pet store associated with Indiana case 1 are unknown. The North Dakota patient obtained the hedgehog during an adoption event at a retail pet store chain; information regarding the source of the hedgehog was obtained from the previous owner who surrendered the hedgehog. USDA licensure status: https://www.aphis.usda.gov/aphis/ourfocus/animalwelfare/ct_awa_regulated_businesses

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Erratum

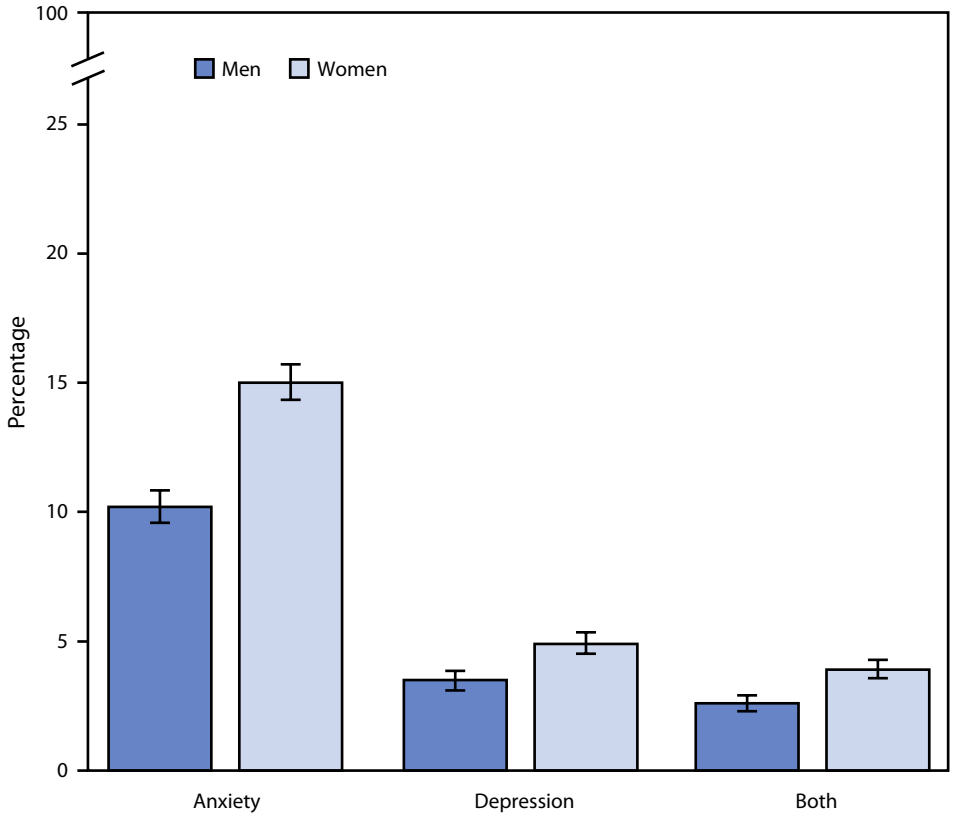
Vol. 70, No. 29

In the report, "Heat-Related Emergency Department Visits During the Northwestern Heat Wave — United States, June 2021," on page 1020, the last sentence of the first paragraph should have read, "The record-breaking heat had the largest impact in Oregon and Washington, especially the Portland metropolitan area, with temperatures reaching 116°F (46.7°C), which is 42°F **(23.3°C)** hotter than the average daily maximum June temperature."

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage* of Adults Aged ≥18 Years Who Daily Experienced Feelings of Anxiety (Feeling Worried, Nervous, or Anxious)† or Depression,§ or Both, by Sex — National Health Interview Survey,¶ United States, 2019



* With 95% confidence intervals indicated by error bars.
† Based on a response to the question, "How often do you feel worried, nervous, or anxious? Would you say daily, weekly, monthly, a few times a year, or never?"
§ Based on a response to the question, "How often do you feel depressed? Would you say daily, weekly, monthly, a few times a year, or never?"
¶ Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population.

In 2019, women were more likely than men to feel worried, nervous, or anxious on a daily basis (15.0% versus 10.2%). Women were also more likely to feel depressed daily (4.9%) compared with men (3.5%). A higher percentage of women than men reported experiencing daily feelings of both anxiety and depression (3.9% versus 2.6%).

Source: National Center for Health Statistics, National Health Interview Survey, 2019. https://www.cdc.gov/nchs/nhis/index.htm

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