# Widespread Hepatitis A Outbreaks Associated with Person-to-Person Transmission — United States, 2016–2020

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Hepatitis A is a vaccine-preventable disease typically acquired through fecal-oral transmission. Hepatitis A virus (HAV) infection rates in the United States declined approximately 97% during 1995–2015 after the introduction and widespread pediatric use of hepatitis A vaccines (*1*). Since 2016, hepatitis A outbreaks have been reported in 37 states, involving approximately 44,650 cases, 27,250 hospitalizations, and 415 deaths as of September 23, 2022 (*2*). A report describing early outbreaks in four states during 2017 noted that most infections occurred among persons reporting injection or noninjection drug use or experiencing homelessness; this finding signaled a shift in HAV infection epidemiology from point-source outbreaks associated with contaminated food to large community outbreaks associated with person-to-person transmission (*3*). CDC analyzed interim data from 33 outbreak-affected states to characterize demographic, risk factor, and clinical outcome data from 37,553 outbreak-associated hepatitis A cases reported during August 1, 2016–December 31, 2020. Among persons with available risk factor or clinical outcome information, 56% reported drug use, 14% reported experiencing homelessness, and 61% had been hospitalized; 380 outbreak-associated deaths were reported. The most effective means to prevent and control hepatitis A outbreaks is through hepatitis A vaccination, particularly for persons at increased risk for HAV infection (*4*). The epidemiologic shifts identified during these outbreaks led to a 2019 recommendation by the Advisory Committee on Immunization Practices (ACIP) for vaccination of persons experiencing homelessness and reinforcement of existing vaccination recommendations for persons who use drugs (*4*). Substantial progress in the prevention and control of hepatitis A has been made; the number of outbreak-affected states has been reduced from 37 to 13 (*2*). Increased hepatitis A vaccination coverage, particularly through implementation of successful, nontraditional vaccination strategies among disproportionately affected populations (*5*), is needed to continue progress in halting current outbreaks and preventing similar outbreaks in the future.

Health departments investigated HAV infections among persons who met the Council of State and Territorial Epidemiologists' hepatitis A case definition[†] using state-specific case investigation forms. Deidentified demographic, risk factor, and clinical outcome data were requested from all states reporting outbreaks for all outbreak-associated cases during August 1, 2016–December 31, 2020. Risk factors

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[†] https://ndc.services.cdc.gov/conditions/hepatitis-a-acute/

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

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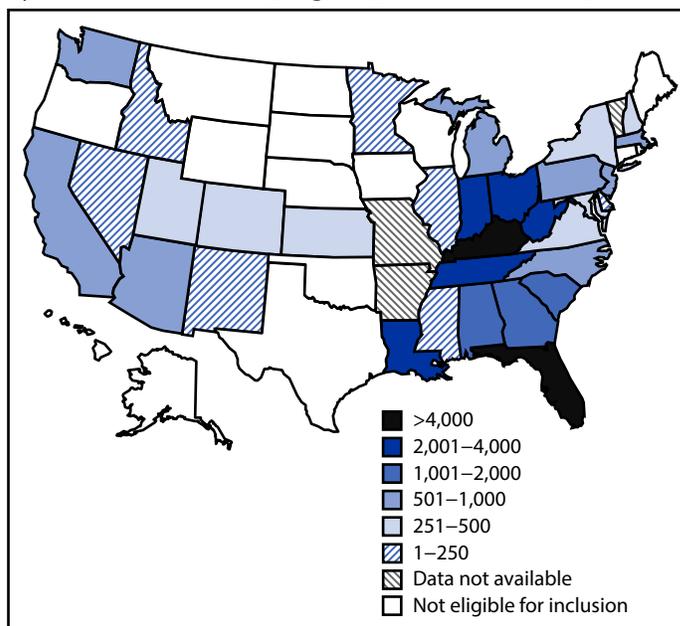[*] These authors contributed equally to this report.

were assessed during the exposure period (15–50 days before symptom onset). States were excluded from variable-specific analysis of any variable with 100% missing data. The analysis was conducted using SAS (version 9.4; SAS Institute). Data collection, which was directly related to disease control, was deemed not to be human subjects research. This activity was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.§

CDC analyzed data from 33 of 36 (92%) outbreak-affected states¶ that were eligible for inclusion** (Figure); these 33 states accounted for approximately 97% of publicly reported hepatitis A outbreak-associated cases at the end of 2020 (4). Among 37,553 reported cases, most were among males (62%), White persons (81%), and those aged 30–49 years (58%) (Table). Median age was 38 years. Among cases with data available, 5% and 30% had evidence of past or current hepatitis B or hepatitis C virus infection, respectively; 61% of persons with hepatitis A were hospitalized, and 1% died. Among persons with outbreak-associated HAV infection and available risk factor

§ 45 C.F.R. part 46.104.
¶ The 33 outbreak-affected states included in the analysis were Alabama, Arizona, California, Colorado, Delaware, Florida, Georgia, Idaho, Illinois, Indiana, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Pennsylvania, South Carolina, Tennessee, Utah, Virginia, Washington, and West Virginia.
** States were eligible for inclusion if, as of the initial request for data in August 2020, they had declared a hepatitis A outbreak associated with person-to-person transmission at any point since August 1, 2016.

information, 56% reported injection or noninjection drug use, 14% reported experiencing homelessness, 12% reported recent incarceration, and 3% reported recent international travel; 5% of males self-identified as men who have sex with men.

**FIGURE. Cumulative outbreak-associated hepatitis A cases reported, by state\* — United States, August 1, 2016–December 31, 2020**



\* States were eligible for inclusion if, as of the initial request for data in August 2020, they had declared a hepatitis A outbreak associated with person-to-person transmission at any point since August 1, 2016.

**TABLE. Characteristics of outbreak-associated hepatitis A cases — United States, August 1, 2016–December 31, 2020**

| Characteristic (no. with available information*) | No. (%) |
|---|---|
| **Total** | **37,553** |
| **Sex (37,553)** | |
| Female | 14,205 (37.8) |
| Male | 23,317 (62.1) |
| Other | 11 (0) |
| Missing | 20 (0.1) |
| **Age group, yrs (37,553)** | |
| 0–9 | 114 (0.3) |
| 10–19 | 395 (1.1) |
| 20–29 | 7,130 (19.0) |
| 30–39 | 13,088 (34.9) |
| 40–49 | 8,583 (22.9) |
| 50–59 | 5,082 (13.5) |
| ≥60 | 3,099 (8.3) |
| Missing | 62 (0.2) |
| **Race[†] (21,952)** | |
| American Indian or Alaska Native | 103 (0.5) |
| Asian or Pacific Islander | 186 (0.8) |
| Black or African American | 1,438 (6.6) |
| White | 17,831 (81.2) |
| Other | 693 (3.2) |
| Missing | 1,701 (7.7) |
| **Hospitalized (37,553)** | |
| Yes | 23,043 (61.4) |
| No | 12,770 (34.0) |
| Missing | 1,740 (4.6) |
| **Death[§] (37,071)** | |
| Yes | 380 (1.0) |
| No | 26,013 (70.2) |
| Missing | 10,678 (28.8) |
| **Any drug use (37,553)** | |
| Yes | 20,991 (55.9) |
| No | 10,268 (27.3) |
| Missing | 6,294 (16.8) |
| **Injection drug use[¶] (22,645)** | |
| Yes | 8,601 (38.0) |
| No | 8,250 (36.4) |
| Missing | 5,794 (25.6) |
| **Noninjection drug use** (22,088)** | |
| Yes | 7,754 (35.1) |
| No | 7,849 (35.5) |
| Missing | 6,485 (29.4) |
| **Homelessness[††] (36,311)** | |
| Yes | 5,008 (13.8) |
| No | 15,383 (42.4) |
| Missing | 15,920 (43.8) |
| **Recent incarceration[§§] (27,404)** | |
| Yes | 3,231 (11.8) |
| No | 14,035 (51.2) |
| Missing | 10,138 (37.0) |
| **Men who have sex with men[¶¶] (20,973)** | |
| Yes | 1,129 (5.4) |
| No | 7,477 (35.7) |
| Missing | 12,367 (59.0) |
| **International travel*** (26,466)** | |
| Yes | 793 (3.0) |
| No | 15,686 (59.3) |
| Missing | 9,987 (37.7) |
| **Hepatitis B coinfection[†††] (20,592)** | |
| Yes | 1,076 (5.2) |
| No | 7,242 (35.2) |
| Missing | 12,274 (59.6) |
| **Hepatitis C coinfection[§§§] (21,357)** | |
| Yes | 6,470 (30.3) |
| No | 5,684 (26.6) |
| Missing | 9,203 (43.1) |

**TABLE (*Continued*). Characteristics of outbreak-associated hepatitis A cases — United States, August 1, 2016–December 31, 2020**

| Characteristic (no. with available information*) | No. (%) |
|---|---|
| **Hepatitis B or hepatitis C coinfection[¶¶¶] (23,937)** | |
| Yes | 7,480 (31.2) |
| No | 7,327 (30.6) |
| Missing | 9,130 (38.1) |

* States were excluded from variable-specific analysis of any variable with 100% missing data. The number with available information was used as the denominator for percent calculations for each characteristic.
† Twenty-seven states contributed data on race (Alabama, California, Colorado, Delaware, Florida, Georgia, Idaho, Illinois, Kansas, Louisiana, Maine, Maryland, Massachusetts, Minnesota, Mississippi, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Pennsylvania, South Carolina, Tennessee, Utah, Virginia, and Washington).
§ Thirty-two states contributed data on death (Alabama, Arizona, California, Colorado, Delaware, Florida, Georgia, Idaho, Illinois, Indiana, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Nevada, New Hampshire, New Jersey, New Mexico, North Carolina, Ohio, Pennsylvania, South Carolina, Tennessee, Utah, Virginia, Washington, and West Virginia).
¶ Twenty-six states contributed data on injection drug use (Alabama, Arizona, California, Colorado, Delaware, Florida, Georgia, Idaho, Illinois, Kansas, Louisiana, Maine, Maryland, Massachusetts, Minnesota, Mississippi, Nevada, New Hampshire, New York, North Carolina, Pennsylvania, Tennessee, Utah, Virginia, Washington, and West Virginia).
** Twenty-four states contributed data on noninjection drug use (Alabama, Arizona, California, Colorado, Delaware, Florida, Georgia, Idaho, Illinois, Kansas, Louisiana, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New York, North Carolina, Pennsylvania, Tennessee, Utah, Virginia, Washington, and West Virginia).
†† Thirty states contributed data on homelessness (Alabama, Arizona, California, Colorado, Delaware, Florida, Georgia, Idaho, Illinois, Indiana, Kansas, Kentucky, Louisiana, Maryland, Massachusetts, Michigan, Mississippi, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, South Carolina, Tennessee, Utah, Virginia, Washington, and West Virginia). Homelessness was categorized to include those meeting the U.S. Department of Housing and Urban Development definition of "Literally Homeless" (https://files.hudexchange.info/resources/documents/HomelessDefinition_RecordkeepingRequirementsandCriteria.pdf) as well as those who were unstably housed (e.g., "couch surfing").
§§ Twenty-five states contributed data on recent incarceration (Alabama, Arizona, California, Colorado, Delaware, Florida, Georgia, Idaho, Indiana, Louisiana, Maryland, Massachusetts, Minnesota, Mississippi, Nevada, New Hampshire, New Jersey, New York, North Carolina, Ohio, Pennsylvania, South Carolina, Tennessee, Utah, and Washington).
¶¶ Restricted to males; 31 states contributed data on men who have sex with men (Arizona, California, Colorado, Delaware, Florida, Georgia, Idaho, Illinois, Indiana, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, Ohio, Pennsylvania, South Carolina, Tennessee, Utah, Virginia, and Washington).
*** Twenty-four states contributed data on international travel (Arizona, California, Delaware, Florida, Georgia, Idaho, Illinois, Indiana, Kentucky, Maine, Maryland, Massachusetts, Michigan, Mississippi, Nevada, New Hampshire, New Mexico, New York, Pennsylvania, South Carolina, Tennessee, Utah, Virginia, and Washington).
††† Nineteen states contributed data on hepatitis B coinfection (California, Delaware, Georgia, Kansas, Kentucky, Louisiana, Maine, Massachusetts, Michigan, Minnesota, New Hampshire, New Jersey, New Mexico, North Carolina, Ohio, Pennsylvania, Utah, Washington, and West Virginia).
§§§ Twenty-one states contributed data on hepatitis C coinfection (California, Colorado, Delaware, Georgia, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, New Hampshire, New Jersey, New Mexico, North Carolina, Ohio, Pennsylvania, Utah, Washington, and West Virginia).
¶¶¶ Twenty-two states contributed data on hepatitis B or hepatitis C coinfection (California, Colorado, Delaware, Georgia, Indiana, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, New Hampshire, New Jersey, New Mexico, North Carolina, Ohio, Pennsylvania, Utah, Washington, and West Virginia).

## Discussion

Since 2016, the United States has experienced widespread hepatitis A outbreaks associated with person-to-person transmission. Interim data from 33 states were analyzed to characterize demographic, risk factor, and clinical outcome data from 37,553 outbreak-associated cases reported during August 1, 2016–December 31, 2020. Cases occurred predominantly among males, White persons, and those aged 30–49 years. The most frequently reported risk factor was drug use.

These outbreaks mark a shift in hepatitis A epidemiology in the United States. Before the introduction of hepatitis A vaccines, HAV transmission was driven largely by spread from asymptomatically infected children, and hepatitis A disproportionately affected racial and ethnic minority populations (6). In these recent hepatitis A outbreaks associated with person-to-person transmission, however, fewer than 1% of cases occurred among persons aged <18 years, and among cases with available race data, more than 80% occurred among White persons. Whereas international travel and exposure to foodborne outbreaks were previously the most frequently reported risk factors (7), drug use (both injection and noninjection) was the predominant risk factor associated with HAV transmission during the 2016–2020 outbreaks. HAV transmission among persons who use drugs occurs through the fecal-oral route (e.g., resulting from lack of sanitation or poor hygiene practices) and might occur percutaneously during injection drug use (3).

Sixty-one percent of persons were hospitalized during the hepatitis A outbreaks associated with person-to-person transmission, which substantially exceeds the proportion of hospitalized cases historically reported in the National Notifiable Diseases Surveillance System (NNDSS); in 2016, 42% of persons with hepatitis A cases reported to NNDSS were hospitalized (8). The older age of patients and corresponding increased likelihood of comorbidities (including coinfection with hepatitis B or hepatitis C virus in nearly one third of cases) likely contributed to the higher prevalence of hospitalization observed in the recent and ongoing hepatitis A outbreaks. Hospitalization and death from HAV infection occur more frequently among adults than among children (9).

The outbreaks described in this report are unprecedented in the hepatitis A vaccine era. National Health and Nutrition Examination Survey data obtained during 2011–2016 indicated that more than 60% of U.S.–born, noninstitutionalized civilian adults in risk groups recommended to receive hepatitis A vaccine by ACIP since 1996 remained susceptible to HAV infection (10). Proactive vaccination of adults at increased risk for HAV infection or adverse consequences of infection is critical to prevent outbreaks and serious illness.

In collaboration with state and local health departments, CDC launched a large-scale, multidisciplinary response in 2017 to control the ongoing outbreaks associated with person-to-person transmission. To provide hepatitis A vaccination to disproportionately affected populations most affected by the outbreaks, health departments developed and implemented nontraditional vaccination and staffing strategies (5). These included holding satellite vaccination clinics (e.g., at correctional facilities, substance use treatment facilities, syringe services programs, and homeless shelters) and broadening the scope of health care professionals approved to administer vaccines. To overcome barriers to vaccination, including mistrust, stigma, and vaccine hesitancy, health departments partnered with organizations that have long-standing, trusted relationships with persons at risk for HAV infection (5). In September 2022, as a result of these intensive and innovative efforts, 24 states have officially declared their outbreaks over, and the remaining 13 states report decreased case counts from the peaks of their outbreaks (2).

The findings in this report are subject to at least five limitations. First, risk factor data were self-reported and subject to recall and social desirability biases. Second, hepatitis A surveillance in the United States is passive; thus, case counts might underestimate the actual number of cases. Third, a substantial proportion of data was missing; caution should be exercised when interpreting results with high rates of missing data. Fourth, ethnicity was not systematically ascertained and could not be included. Finally, states did not use an identical hepatitis A–related death case classification, which might have resulted in differential classification of deaths as being hepatitis A–related.

Hepatitis A epidemiology in the United States has shifted as a result of the ongoing outbreaks associated with person-to-person transmission. Cases occurred almost exclusively among adults, and HAV transmission was driven primarily by close contact among persons who use illicit drugs and persons experiencing homelessness. Improving services for these populations, including access to substance use treatment and sanitation, are important considerations in mitigating HAV transmission. Many adults at increased risk for HAV infection remain vulnerable to infection, despite long-standing vaccination recommendations. Given the high hospitalization rate during these outbreaks and the high level of susceptibility to HAV infection among adults in the United States, efforts are needed to improve awareness of and adherence to ACIP hepatitis A vaccination recommendations. Increased hepatitis A vaccination coverage, through implementation of nontraditional vaccination strategies to reach disproportionately affected populations, along with improved universal and catch-up childhood

## Summary

### What is already known about this topic?

Hepatitis A cases declined substantially in the United States after the introduction of hepatitis A vaccines in 1996.

### What is added by this report?

Hepatitis A epidemiology in the United States has shifted as a result of recent and ongoing outbreaks associated with person-to-person transmission. During August 1, 2016–December 31, 2020, 33 states reported hepatitis A outbreaks involving approximately 37,500 cases. Among cases with available information, 56% of persons reported drug use, 14% reported homelessness, and 61% were hospitalized; 380 outbreak-associated deaths were reported.

### What are the implications for public health practice?

Increased hepatitis A vaccination coverage, through implementation of nontraditional vaccination strategies to reach disproportionately affected populations, along with improved universal and catch-up childhood vaccination, will be necessary to respond to the current hepatitis A outbreaks and prevent similar outbreaks in the future.

vaccination, will be necessary to respond to the current hepatitis A outbreaks and prevent similar outbreaks in the future. Lessons learned during these outbreaks have been reinforced by experiences during the COVID-19 pandemic and other vaccine-preventable disease outbreaks. Disproportionately affected populations often experience stigma, mistrust, and societal barriers that limit adequate access to the health care system. Continued improvements in vaccination infrastructure, immunization information systems, and education and outreach are critically needed to build vaccine confidence and improve vaccine delivery in nontraditional settings.

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# Effectiveness of a Second COVID-19 Vaccine Booster Dose Against Infection, Hospitalization, or Death Among Nursing Home Residents — 19 States, March 29–July 25, 2022

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Nursing home residents continue to experience significant COVID-19 morbidity and mortality (*1*). On March 29, 2022, the Advisory Committee on Immunization Practices (ACIP) recommended a second mRNA COVID-19 vaccine booster dose for adults aged ≥50 years and all immunocompromised persons who had received a first booster ≥4 months earlier.* On September 1, 2022, ACIP voted to recommend bivalent mRNA COVID-19 vaccine boosters for all persons aged ≥12 years who had completed the primary series using monovalent vaccines ≥2 months earlier (*2*). Data on COVID-19 booster dose vaccine effectiveness (VE) in the nursing home population are limited (*3*). For this analysis, academic, federal, and private partners evaluated routine care data collected from 196 U.S. community nursing homes to estimate VE of a second mRNA COVID-19 vaccine booster dose among nursing home residents who had received 3 previous COVID-19 vaccine doses (2 primary series doses and 1 booster dose). Residents who received second mRNA COVID-19 vaccine booster doses during March 29–June 15, 2022, with follow-up through July 25, 2022, were found to have 60-day VE of 25.8% against SARS-CoV-2 (the virus that causes COVID-19 infection), 73.9% against severe COVID-19 outcomes (a combined endpoint of COVID-19–associated hospitalizations or deaths), and 89.6% against COVID-19–associated deaths alone. During this period, subvariants BA.2 and BA.2.12.1 (March–June 2022), and BA.4 and BA.5 (July 2022) of the B.1.1.529 and BA.2 (Omicron) variant were predominant. These findings suggest that among nursing home residents, second mRNA COVID-19 vaccine booster doses provided additional protection over first booster doses against severe COVID-19 outcomes during a time of emerging Omicron variants. Facilities should continue to ensure that nursing home residents remain up to date with COVID-19 vaccination, including bivalent vaccine booster doses, to prevent severe COVID-19 outcomes.

This analysis emulated target trials that compared the effectiveness of a second mRNA booster dose versus non-receipt among recipients of 2 primary doses followed by 1 booster dose. A series of sequential index dates (i.e., trials) were included to assess VE among nursing home residents during March 29–June 15, 2022, with a maximum of 60-days of follow-up through July 25, 2022. The population included nursing home residents from 196 nursing homes in 19 states[†] operated by Genesis HealthCare.[§] Nursing home residents were eligible for study inclusion if they 1) had been present in the nursing home for ≥100 days with <10 days spent out of the facility, 2) had received 3 doses of mRNA COVID-19 vaccine before the index date, and 3) had not received a COVID-19 vaccination in ≥120 days. Nursing home residents were excluded if they had a SARS-CoV-2 infection during the 30 days preceding the index date, had received monoclonal antibodies during the 90 days preceding the index date, or were receiving hospice care.

Nursing home residents who had been vaccinated on each specific index date were assigned to the treatment group, and those who were unvaccinated but eligible were assigned as controls. Vaccination status was determined using residents' immunization record from nursing home electronic health record systems. Nursing home residents who had received 3 previous mRNA COVID-19 vaccine doses, irrespective of timing of vaccination were considered to have received the primary series and first booster vaccination. This analysis employed similar analytic methods to other target trial emulations with mRNA COVID-19 vaccines (*4,5*). Those who had received the second booster dose were matched to controls exactly by facility of residence and index date with 1:1 nearest neighbor matching with a maximum of 0.2 standardized mean difference in propensity score between pairs. If the matched control subsequently received a second booster dose, follow-up ceased for both the control and matched resident in the treatment group at that time. Propensity scores were estimated using logistic regression adjusting for 1) previous COVID-19 infection history (based on *International Classification of Diseases, Tenth Revision, Clinical Modification* diagnosis code U07.1 or SARS-CoV-2 rapid antigen or reverse transcription–polymerase

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* https://www.cdc.gov/media/releases/2022/s0328-covid-19-boosters.html; https://www.cdc.gov/vaccines/acip/recs/grade/covid-19-second-booster-dose-etr.html (Accessed August 31, 2022).

[†] Alabama, Arizona, Colorado, Connecticut, Delaware, Kentucky, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New Mexico, North Carolina, Pennsylvania, Rhode Island, Tennessee, Vermont, Virginia, and West Virginia.

[§] https://www.genesishcc.com/

chain reaction test result), 2) immunosuppressive condition, 3) "do not resuscitate" orders, 4) acute hospitalization during the preceding 90 days, 5) time since last COVID-19 vaccination, 6) length of stay in the nursing home, 7) history of any influenza vaccination during the previous influenza season, 8) age, and 9) number of Charlson index comorbidities (6).

COVID-19 testing followed CDC guidelines for nursing homes, and included testing on admission, readmission, recent exposure, or occurrence of a new symptom. Direct care staff members were tested weekly, and residents could be tested based on recent staff member exposure (7). The four outcomes assessed were 1) any incident SARS-CoV-2 infection, defined as a new positive SARS-CoV-2 rapid antigen or reverse transcription–polymerase chain reaction test result, 2) hospitalization for SARS-CoV-2–related illness (transfer to an acute care hospital within 21 days of a new positive SARS-CoV-2 test result), 3) death occurring within 30 days of a new positive SARS-CoV-2 test result, and 4) severe COVID-19 outcomes (combined endpoint of hospitalization or death). Kaplan-Meier estimators were used to estimate VE as 1 – relative ratio of the cumulative incidence curves between groups at each time point. Observations with missing values were excluded from analysis. Sampling with replacement by matched pair with 500 replications was used to generate 95% CIs. Data were collected from nursing home electronic health record systems. Initial data preparation was conducted using SAS software (version 9.4; SAS Institute) and STATA (version 16; Statacorp). All analyses were performed using R statistical software (version 4.0.1; R Foundation). This activity was deemed not to be human subject research by the Brown University institutional review board and was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.¶

The analysis included 9,527 unique residents across 196 nursing homes (median of 49 residents per facility [IQR = 35–61]). Among these residents, 9,503 (99.7%) served as controls for ≥1 day of follow-up and 3,245 (34.1%) residents received a second booster dose during the study period and were eligible to be included in the treatment group. In the matched analysis, 1,902 residents were matched 1:1 with controls; 1,343 residents

¶ 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.

**TABLE 1. Baseline resident characteristics of matched second booster dose recipients and first booster dose only controls\* — 196 nursing homes, 19 states,[†] March, 29–July 25, 2022**

| Characteristic[§] | No. (%) | | | |
| --- | --- | --- | --- | --- |
| | Total (n = 3,804) | Control\* (n = 1,902) | Second booster dose recipients (n = 1,902) | aSMD |
| Male | 1,350 (35.5) | 663 (34.9) | 687 (36.1) | 0.03 |
| Black or African American | 291 (7.6) | 138 (7.3) | 153 (8.0) | 0.03 |
| Hispanic or Latino | 153 (4.0) | 86 (4.5) | 67 (3.5) | 0.05 |
| Serious mental illness or intellectual disability | 277 (7.3) | 130 (6.8) | 147 (7.7) | 0.03 |
| Needed language translator | 96 (2.5) | 54 (2.8) | 42 (2.2) | 0.04 |
| Current smoker | 86 (2.3) | 30 (1.6) | 56 (2.9) | 0.09 |
| Needed dialysis | 73 (1.9) | 37 (1.9) | 36 (1.9) | <0.01 |
| Received influenza vaccination in previous season | 2,908 (76.4) | 1,418 (74.6) | 1,490 (78.3) | 0.09 |
| Pulmonary disease | 909 (23.9) | 436 (22.9) | 473 (24.9) | 0.05 |
| Diabetes mellitus | 553 (14.5) | 282 (14.8) | 271 (14.2) | 0.02 |
| Immunocompromised | 524 (13.8) | 277 (14.6) | 247 (13.0) | 0.05 |
| COVID-19 history, ever | 2,312 (60.8) | 1,143 (60.1) | 1,169 (61.5) | 0.03 |
| Life expectancy <6 mos | 201 (5.3) | 106 (5.6) | 95 (5.0) | 0.03 |
| Do not resuscitate order | 1,941 (51.0) | 940 (49.4) | 1,001 (52.6) | 0.06 |
| Any hospitalization, previous 90 days | 476 (12.5) | 255 (13.4) | 221 (11.6) | 0.05 |
| Age, yrs, median (IQR) | 78 (69–87) | 78 (69–87) | 78 (69–87) | <0.01 |
| Preindex LOS, days, median (IQR) | 880 (511–1,334) | 878 (517–1,321) | 882 (503–1,345) | <0.01 |
| Time from second dose, days, median (IQR) | 196 (182–212) | 196 (182–211) | 197 (182–213) | 0.01 |
| Charlson chronic conditions, median (IQR)[¶] | 4 (3–6) | 4 (3–6) | 4 (3–6) | 0.03 |
| No. of COVID-19 tests (14 days), mean (SD) | 0.3 (1.1) | 0.3 (1.0) | 0.3 (1.2) | 0.05 |
| No. of COVID-19 tests (90 days), mean (SD) | 2.2 (6.0) | 2.1 (5.9) | 2.3 (6.2) | 0.03 |

**Abbreviations:** aSMD = absolute standardized mean difference; LOS = length of stay; MDS = minimum data set.
\* Controls were nursing home residents who had received 3 previous vaccine doses and who were otherwise eligible for receipt of second booster dose but did not receive a vaccination on a given index date during March 29–June 15, 2022.
† Alabama, Arizona, Colorado, Connecticut, Delaware, Kentucky, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New Mexico, North Carolina, Pennsylvania, Rhode Island, Tennessee, Vermont, Virginia, and West Virginia.
§ All information was extracted from nursing home electronic health records; diagnoses are compiled from *International Classification of Diseases, Tenth Revision, Clinical Modification* codes based on Charlson classifications; and other demographic variables are extracted from nursing home MDS assessments (version 3.0), pharmacy, medical orders, or laboratory records. Serious mental illness or intellectual disability refers to item A1500 on the MDS 3.0.
¶ Total number of Charlson comorbid conditions (e.g., diabetes or congestive heart failure) maximum = 16. A higher number of chronic conditions suggests poor prognosis.

**Summary**

What is already known about this topic?

COVID-19 vaccines have been effective in preventing SARS-CoV-2 infection and associated hospitalizations and deaths among nursing home residents.

What is added by this report?

In a large cohort of nursing home residents, receipt of a second mRNA COVID-19 booster dose during circulation of SARS-CoV-2 Omicron subvariants was 74% effective at 60 days against severe COVID-19–related outcomes (including hospitalization or death) and 90% against death alone compared with receipt of a single booster dose.

What are the implications for public health practice?

Efforts should be made to ensure that nursing home residents remain up to date with recommended booster doses of COVID-19 vaccines.

were excluded because they could not be matched to a control. Residents in the matched group had a mean age of 78 years, a median length of stay of 880 days, a median 196 days since the last COVID-19 vaccination, four Charlson comorbidities, and 35.5% were male. Observed characteristics between matched groups were <0.1 standard mean differences (Table 1). Compared with matched residents, the 1,343 excluded residents were similar, with a mean age of 78 years, a median length of stay of 931 days, a median 202 days since the last COVID-19 vaccination, four Charlson comorbidities, and 35% were male.

Compared with a first booster dose only, 60-day VE of a second mRNA COVID-19 vaccine booster dose was 25.8% (95% CI = 1.2–44.3) against infection, 60.1% (95% CI = –18.8–91.5) against hospitalization, 89.6% (95% CI = 45.0–100.0) against death, and 73.9% (95% CI = 36.1–92.2) against the severe composite outcome of COVID-19–associated hospitalization or death (Table 2).

## Discussion

In this analysis, comparing the relative effectiveness of a second booster dose of COVID-19 mRNA vaccines with a single booster dose among eligible nursing home residents in 19 states, VE of a second booster against the severe composite outcomes of SARS-CoV-2–associated hospitalization or death was 73.9% and 89.6% for death alone. VE against SARS-CoV-2 infection during a period crossing both Omicron subvariants BA.2 and BA.2.12.1 (March–June 2022) and BA.4 and BA.5 (July 2022) predominance was 25.8%.

The findings in this report are subject to at least five limitations. First, the point estimates for the findings in the current study are similar to those estimated in previous studies; however, too few hospitalization events were observed to definitely attribute a reduction to vaccination. A recent study from Israel

**TABLE 2. Estimated vaccine effectiveness\* of a second COVID-19 vaccine booster dose relative to a first booster dose only, for four COVID-19–related outcomes in nursing home residents — 196 nursing homes, 19 states,[†] March, 29–July 25, 2022**

| Outcome | Cumulative incidence[§] | | Risk difference (per 1,000 residents) | Vaccine effectiveness % (95% CI)\*\* |
| | Controls[¶] (n = 1,902) | Second booster dose recipients (n = 1,902) | | |
|---|---|---|---|---|
| SARS-CoV-2 infection[††] | 101 | 75 | −26 | 25.8 (1.2 to 44.3) |
| Hospitalization[§§] | 9 | 3 | −5 | 60.1 (−18.8 to 91.5) |
| Death[¶¶] | 8 | 1 | −7 | 89.6 (45.0 to 100.0) |
| Severe outcomes\*\*\* | 16 | 4 | −12 | 73.9 (36.1 to 92.2) |

\* Through 60 days of follow-up.
[†] Alabama, Arizona, Colorado, Connecticut, Delaware, Kentucky, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New Mexico, North Carolina, Pennsylvania, Rhode Island, Tennessee, Vermont, Virginia, and West Virginia.
[§] Events per 1,000 nursing home residents.
[¶] Nursing home residents who received three previous vaccinations and were otherwise eligible to receive a second booster dose but did not receive a vaccination on a given index date during March 29–June 15, 2022.
\*\* Bootstrapped percentile CIs.
[††] Positive SARS-CoV-2 test result from antigen or reverse transcription–polymerase chain reaction testing.
[§§] Transfer to acute care hospital within 21 days of a positive SARS-CoV-2 test result.
[¶¶] Death within 30 days of a positive SARS-CoV-2 test result.
\*\*\* Death or hospitalization.

provided similar VE estimates during B.1.617.2 (Delta) variant circulation for a second booster dose (34% against infection, 64% for hospitalization, and 72% against death) in a long-term care setting (8). Similarly, a Canadian study reported a 40% relative VE of 4 (versus 3) doses of mRNA COVID-19 vaccine against hospital admission or death among nursing home residents (9) and a U.S study reported 80% VE for a second booster dose (compared with no vaccine) against hospitalization among immunocompetent adults aged ≥50 years during Omicron BA.2 and BA.2.12.1 subvariant predominance (10). However, comparisons with other published studies are challenging because of differences in methods, population health, and virus characteristics, as well as other factors (e.g., time since the last vaccine dose when VE is measured). Unique features of the present analysis compared with previous studies are the focus on the incremental benefit of the second booster dose compared with 1 booster dose (i.e., 4 versus 3 doses) during a period when Omicron BA.2 and BA.2.12.1 and later BA.4 and BA.5 subvariants were the dominant circulating variants; and use of an emulated target trial design, which applied robust matching to compare persons with similar characteristics at time of vaccination. Second, the composite endpoint of death or hospitalization was included because, in the nursing home population, hospitalizing a resident is subject to many considerations beyond acute illness. The overall health and functional

status, life expectancy, resident and family wishes, and general policies of that site are considered. Some residents might have a low likelihood of being hospitalized even with severe COVID-19 illness, which might explain not being able to exclude a null effect for preventing hospitalization alone. Death alone is also problematic because, if residents are hospitalized or transferred, a subsequent death might not be recorded in the nursing home records. Therefore, the composite endpoint of death or hospitalization better described severe outcomes of COVID-19 than did either endpoint alone; however, each outcome was reported separately for interest. Third, the impact of one resident's vaccination on the effectiveness of vaccination for other residents was not accounted for in this study which might underestimate the direct vaccine effect. Fourth, because of the relatively short follow-up time available for observation (60 days) it was not possible to evaluate potential waning of a second booster dose effect. Finally, the comparison of 4 versus 3 doses might also misclassify some persons who received additional doses because of an immunocompromised status as having received a booster dose.

These results indicate that, compared with a single mRNA COVID-19 vaccine booster dose, a second booster dose provided additional protection against COVID-19–associated severe outcomes among nursing home residents during the Omicron period ending with BA. 4 and BA. 5 dominances. The results support the importance of continued efforts to ensure the nursing home population is up to date on recommended COVID-19 vaccine booster doses including the newly authorized bivalent COVID-19 vaccine.

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# Notes from the Field

## Overdose Deaths Involving *Para*-fluorofentanyl — United States, July 2020–June 2021

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Provisional estimates indicate that synthetic opioids, including illicitly manufactured fentanyl (IMF), were involved in approximately two thirds of an estimated 108,174 overdose deaths in the United States during the 12 months ending in April 2022.[*] Previous analyses have identified *para*-fluorofentanyl, a schedule I[†] illicit fentanyl analog, in drug overdose deaths in eight states from late 2020 through June 2021 (*1–3*). Limited data suggest that *para*-fluorofentanyl is likely similar to or slightly less potent than IMF (*3,4*); however, its role in the illicit drug market and its impact on the opioid overdose crisis has not been widely studied. To better understand monthly trends in drug overdose deaths involving *para*-fluorofentanyl in the United States, CDC analyzed overdose death data from the State Unintentional Drug Overdose Reporting System (SUDORS).

SUDORS includes data from death certificates and medical examiner and coroner reports (including enhanced postmortem toxicology testing) on unintentional and undetermined-intent drug overdose deaths. CDC assessed monthly frequencies of overdose deaths during July 2020–June 2021 involving (i.e., listed as a cause of death) *para*-fluorofentanyl, among 42 states[§] and the District of Columbia. *Para*-fluorofentanyl–involved deaths were stratified by jurisdiction and U.S. Census Bureau region.[¶] This

activity was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.[**]

*Para*-fluorofentanyl was involved in 1,658 (2.6%) of 64,915 overdose deaths reported by 43 jurisdictions during July 2020–June 2021. *Para*-fluorofentanyl–involved deaths increased from the first reported occurrences in September 2020 (five deaths) through a peak of 293 deaths in May 2021 (Figure). The number of *para*-fluorofentanyl–involved deaths increased 455.3% from 253 during July–December 2020 to 1,405 during January–June 2021. Deaths involving *para*-fluorofentanyl occurred in 35 jurisdictions and accounted for 3.9%, 2.9%, 1.9%, and 1.1% of overdose deaths in included jurisdictions in the Northeast, South, Midwest, and West U.S. Census Bureau regions, respectively. Six states (Illinois, Maryland, Michigan, New Jersey, Pennsylvania, and Tennessee) reported more than 100 deaths involving *para*-fluorofentanyl. *Para*-fluorofentanyl–involved deaths nearly always co-involved IMF[††]; co-involvement ranged from 100% of deaths in September 2020 to 90.8% in June 2021.

The findings in this report are subject to at least three limitations. First, analyses were limited to 43 jurisdictions and might not be generalizable to the entire United States. Second, although comprehensive postmortem testing protocols recommend IMF testing (*5*), lack of standard testing requirements might lead to an underestimation of *para*-fluorofentanyl involvement in drug overdose deaths. The rise in *para*-flourofentanyl detection could also be caused by increases in testing during the study period. Finally, death certification training and experience vary across and within medical examiner and coroner systems, potentially leading to differences in *para*-fluorofentanyl's inclusion as the cause of death even when it is detected.

The emergence of *para*-fluorofentanyl involvement in deaths in 35 SUDORS-funded jurisdictions supports and furthers evidence of recent increases (*1–3*). Because of high co-involvement with IMF, it is unclear whether the proliferation of *para*-fluorofentanyl reflects a diversification of the illicit drug market (i.e., *para*-fluorofentanyl is being mixed with IMF) or it has emerged as a new stand-alone product. Because data on potency are limited, it is unclear whether *para*-fluorofentanyl

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[*] https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

[†] Schedule I drugs, substances, or chemicals are defined as drugs with no currently accepted medical use and a high potential for abuse. https://www.dea.gov/drug-information/drug-scheduling

[§] Jurisdictions included Alabama, Alaska, Arizona, Arkansas, Colorado, Connecticut, Delaware, District of Columbia, Georgia, Hawaii, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Utah, Vermont, Virginia, Washington, and West Virginia. Alabama, Illinois, Indiana, Louisiana, Missouri, Pennsylvania, and Washington reported deaths from counties that accounted for ≥75% of drug overdose deaths in the state in 2017, per SUDORS funding requirements; all other jurisdictions reported deaths from the full jurisdiction.

[¶] Not all jurisdictions in each region are included in analyses; trend analyses include eight of nine jurisdictions in the Northeast Region (Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, Pennsylvania, Rhode Island, and Vermont); 10 of 12 jurisdictions in the Midwest Region (Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, Ohio, and South Dakota); 15 of 17 jurisdictions in the South Region (Alabama, Arkansas, Delaware, District of Columbia, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, Tennessee, South Carolina, Virginia, and West Virginia); and 10 of 13 jurisdictions in the West Region (Alaska, Arizona, Colorado, Hawaii, Montana, Nevada, New Mexico, Oregon, Utah, and Washington). https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf

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

[††] Fentanyl was classified as likely illicitly manufactured using toxicology, scene, and witness evidence. In the absence of sufficient evidence to classify fentanyl as illicit or prescription (fewer than 12% of deaths involving fentanyl), fentanyl was classified as illicit because most fentanyl overdose deaths involve IMF. All fentanyl analogs were excluded.

**FIGURE. Number of *para*-fluorofentanyl–involved drug overdose deaths and percentage co-involved with illicitly manufactured fentanyl\* — State Unintentional Drug Overdose Reporting System, United States, July 2020–June 2021**
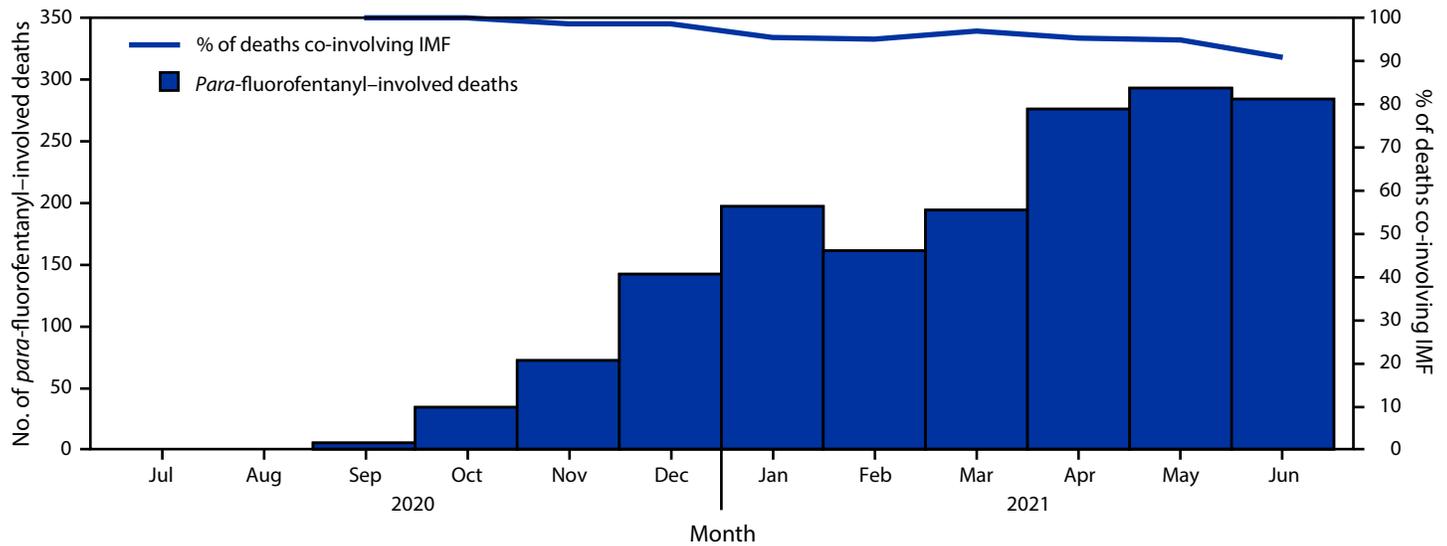


**Abbreviation:** IMF = illicitly manufactured fentanyl.
\* IMF excludes fentanyl analogs.

poses a higher risk than does fentanyl alone; however, access to and timely administration of naloxone to reverse opioid overdoses (*1*), as well as ensuring access to substance use prevention and treatment services, including distribution of fentanyl test strips, is crucial to prevent *para*-fluorofentanyl overdose deaths. In addition, because the illicit drug market continues to evolve rapidly and some jurisdictions might have a lack of or limited testing capabilities, a critical need exists for expanded, enhanced toxicology testing to detect *para*-fluorofentanyl and other emerging drugs.

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# *Vital Signs:* Use of Recommended Health Care Measures to Prevent Selected Complications of Sickle Cell Anemia in Children and Adolescents — Selected U.S. States, 2019

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## Abstract

**Introduction:** Sickle cell disease (SCD), a group of inherited blood cell disorders that primarily affects Black or African American persons, is associated with severe complications and a >20-year reduction in life expectancy. In 2014, an expert panel convened by the National Heart, Lung, and Blood Institute issued recommendations to prevent or reduce complications in children and adolescents with the most severe SCD subtypes, known as sickle cell anemia (SCA); recommendations included 1) annual screening of children and adolescents aged 2–16 years with transcranial Doppler (TCD) ultrasound to identify those at risk for stroke and 2) offering hydroxyurea therapy to children and adolescents aged ≥9 months to reduce the risk for several life-threatening complications.

**Methods:** Data from the IBM MarketScan Multi-State Medicaid Database were analyzed. TCD screening and hydroxyurea use were examined for 3,352 children and adolescents with SCA aged 2–16 years and continuously enrolled in Medicaid during 2019. Percentage change during 2014–2019 and variation by health subgroups were assessed. Analyses were stratified by age.

**Results:** During 2014–2019, TCD screening increased 27% among children and adolescents aged 10–16 years; hydroxyurea use increased 27% among children aged 2–9 years and 23% among children and adolescents aged 10–16 years. However, in 2019, only 47% and 38% of children and adolescents aged 2–9 and 10–16 years, respectively, had received TCD screening and 38% and 53% of children and adolescents aged 2–9 years and 10–16 years, respectively, used hydroxyurea. For both prevention strategies, usage was highest among children and adolescents with high levels of health care utilization and evidence of previous complications indicative of severe disease.

**Conclusion and Implications for Public Health Practice:** Despite increases since 2014, TCD screening and hydroxyurea use remain low among children and adolescents with SCA. Health care providers should implement quality care strategies within their clinics and partner with patients, families, and community-based organizations to address barriers to delivering and receiving recommended care.

## Introduction

Sickle cell disease (SCD), a group of inherited blood disorders characterized by abnormal hemoglobin, reduces life expectancy by >20 years (*1*). SCD primarily affects persons whose ancestors came from Africa, where malaria is endemic, because the carrier state (sickle cell trait, inheritance of a sickle cell gene from only one parent) confers a selective advantage by protecting against the harmful effects of malaria.* Thus, >90%

of the estimated 100,000 persons in the United States with SCD are non-Hispanic Black or African American (Black), and an estimated 3%–9% are Hispanic or Latino (Hispanic) (*2*). In persons with SCD, red blood cells become rigid and deform into a crescent or sickle shape. Sickled cells die early and often become lodged in small blood vessels, compromising blood flow, which can lead to serious health problems. SCD-associated complications include anemia; acute and chronic pain; infections; pneumonia and acute chest syndrome[†]; stroke; and kidney, liver, and heart disease. Despite

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* A more comprehensive summary of the genetics, epidemiology, and health outcomes associated with SCD, the health care needs of persons affected by SCD, and their challenges to receipt of optimal care can be found at National Academies of Sciences, Engineering, and Medicine. 2020. Addressing sickle cell disease: a strategic plan and blueprint for action. Washington, DC: The National Academies Press. https://doi.org/10.17226/25632

† Acute chest syndrome is a severe condition caused by sickling in the small pulmonary blood vessels and characterized by chest pain, cough, fever, hypoxia, and lung infiltrates.

their extensive health care needs, many persons with SCD have difficulty accessing appropriate care and report feeling stigmatized and having their symptoms dismissed when they do seek care (3).

SCD comprises four main genotypes; among these, the hemoglobin SS and hemoglobin Sβ[0]-thalassemia genotypes are the more severe forms and are collectively referred to as sickle cell anemia (SCA). SCA accounts for an estimated 75% of SCD cases in the United States (4). In 2014, an expert panel convened by the National Institutes of Health's National Heart, Lung, and Blood Institute (NHLBI) developed recommendations to prevent or reduce complications of SCD, several of which were specific to children and adolescents with SCA (5). Given that SCA is a common cause of childhood stroke (6), the panel recommended that children and adolescents aged 2–16 years with SCA be screened annually with transcranial Doppler (TCD) ultrasound to identify high cerebral blood velocity, an indicator of elevated stroke risk. Chronic blood transfusion therapy, the recommended intervention, substantially reduces stroke occurrence in children and adolescents identified as being at risk (7). The panel also recommended that children and adolescents aged ≥9 months with SCA (including asymptomatic children) be offered treatment with hydroxyurea, a medication shown to be efficacious in preventing or reducing severe pain episodes, acute chest syndrome, and other SCA-associated complications and increasing patient survival (8). Although the panel chose to recommend offering treatment as a means of opening discussion with families, it emphasized that an established evidence base supported the sustained benefits of hydroxyurea therapy for young persons with SCA without harmful effects on growth, development, female fertility, or increased risks for genetic mutations or cancer (5).

Previous studies documented underutilization of both TCD screening and hydroxyurea (9–11), and barriers to receipt of both interventions have been described (12–15). Barriers to TCD screening include limited radiology visit availability, distance between SCD clinics and radiology centers, providers' lack of familiarity with TCD guidelines (including knowledge gaps among pediatric hematologists, neurologists, and primary care providers who care for children and adolescents with SCA), problems with care coordination (e.g., lack of timely information from radiology centers to providers), and provider concern that TCD screening will not affect outcomes because patients and families are often unable to sustain chronic blood transfusion therapy[§] (12,13). Barriers to

hydroxyurea use include patient and provider uncertainty regarding its effectiveness and fear of adverse effects (including perceived carcinogenesis potential), complexity of treatment regimen (which requires ongoing monitoring and laboratory visits), provider discomfort in managing hydroxyurea therapy, provider concern about lack of patient adherence, and high cost and lack of reimbursement (13–15). Recent studies on use of these prevention strategies are limited. This study examined TCD screening and hydroxyurea use among children and adolescents aged 2–16 years with SCA who were enrolled in Medicaid in 2019 and assessed changes since 2014.

## Methods

This study was conducted using the IBM MarketScan Treatment Pathways online analytic tool with data from the IBM MarketScan Multi-State Medicaid Database from January 1, 2010, to December 13, 2019, which includes medical claims data from approximately 24 million Medicaid enrollees from five to 15 states (the number of states varies by year). SCA was defined using an established algorithm, based on *International Classification of Diseases, Ninth Revision, Clinical Modification* and *International Classification of Diseases, Tenth Revision, Clinical Modification* diagnosis codes, previously validated to identify persons with SCA (16,17) (Supplementary Box, https://stacks.cdc.gov/view/cdc/120746). TCD screening and hydroxyurea use were defined based on procedure and pharmacy codes, respectively. A small proportion (5%) of children and adolescents receiving chronic blood transfusion therapy were excluded from analyses because transfusion therapy might be indicative of previous abnormal TCD results and hydroxyurea and chronic blood transfusion therapy might not be used concurrently. The final analytic sample included 3,352 children and adolescents with SCA who were continuously enrolled in Medicaid in 2019. To assess change over time, a sample of 3,858 children and adolescents continuously enrolled in Medicaid in 2014 were compared with the 2019 sample; the two samples had similar demographic and health profiles (Supplementary Table, https://stacks.cdc.gov/view/cdc/120747).

The proportions of TCD screening and hydroxyurea use and their corresponding 95% CIs were calculated for children and adolescents in 2014 and 2019; percentage change from 2014 to 2019 was also calculated. Differences between years were considered statistically significant if CIs did not overlap. Findings were stratified by age group (2–9 years and 10–16 years) during the respective study year.

In the 2019 sample, TCD screening and hydroxyurea use were examined within health care usage and disease severity subgroups; associations were assessed using prevalence ratios and 95% CIs. Two indicators of severe disease were examined, each defined by whether the child or adolescent had a severe

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[§] Chronic blood transfusion therapy reduces the risk for stroke in children and adolescents with SCA identified to have elevated cerebral blood velocity through TCD screening. However, transfusion therapy is an intensive treatment and frequent transfusions have inherent risks including infection, iron overload, allergic reactions, alloimmunization, and hemolytic transfusion reactions. Therefore, children and adolescents who receive chronic transfusion therapy should be monitored closely and receive regular treatment (chelation therapy) to reduce excess iron buildup in the body.

complication (acute chest syndrome or multiple pain crises) in 2019 or any previous data year (2010–2018) (Supplementary Box, https://stacks.cdc.gov/view/cdc/120746). Data 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.¶

## Results

From 2014 to 2019, TCD screening increased 27% among children and adolescents aged 10–16 years. Among children aged 2–9 years, TCD screening increased 9%, which was not statistically significant. Nonetheless, younger children had higher TCD screening rates than did older children and adolescents in both years; by 2019, proportions of children and adolescents who had received TCD screening were 47% and 38% among those aged 2–9 and 10–16 years, respectively (Figure).

In both age groups, TCD screening varied significantly by health indicators (Table 1). Among children aged 2–9 years, the highest TCD screening rates (>55%) were among children who had a recent hospitalization, 11–20 recent ambulatory care visits, a recent or previous hospitalization for acute chest syndrome, or two or more pain crises requiring hospitalization in the current year or a previous year. Among children and adolescents aged 10–16 years, the highest TCD screening prevalences (43%–48%) were observed among the same subgroups.

From 2014 to 2019, hydroxyurea use increased significantly among children aged 2–9 years (27%) and children and adolescents aged 10–16 years (23%) (Figure). In 2019, hydroxyurea

¶ 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.

use was more prevalent among children and adolescents aged 10–16 years (53%) than among children aged 2–9 years (38%) and also varied significantly by health indicators (Table 2). Moreover, hydroxyurea use exceeded 60% among children and adolescents aged 10–16 years who had had a recent hospitalization, 11–30 recent ambulatory care visits, three or more recent emergency department visits, a recent or previous acute chest syndrome hospitalization, or two or more pain crises requiring hospitalization in the current year or a previous year. Among children aged 2–9 years, the prevalences of hydroxyurea use were highest (47%–58%) in the same subgroups, with one exception: there was little variation in hydroxyurea use by number of emergency department visits.

## Discussion

Although increases in both TCD screening and hydroxyurea use were observed during the 5 years after the NHLBI panel issued their recommendations (5), many children and adolescents with SCA were not receiving these potentially lifesaving interventions in 2019. Usage prevalences of both prevention strategies varied by age, with younger children less likely to use hydroxyurea and older children and adolescents less likely to have an annual TCD screen. Age differences were not explained by health characteristics: age prevalence patterns of both TCD screening and hydroxyurea use were consistent across all health care usage and disease severity subgroups examined. More specific reasons for the age differences cannot be examined with claims data. Usage of both prevention strategies was highest among children and adolescents with documentation of severe disease (i.e., those with manifest health care needs). Nonetheless, even among groups with the highest usage rates

**FIGURE. Percentage of annual transcranial Doppler ultrasound screening (A) and hydroxyurea use (B) among children and adolescents aged 2–16 years with sickle cell anemia\* — selected U.S. states, 2014 and 2019**
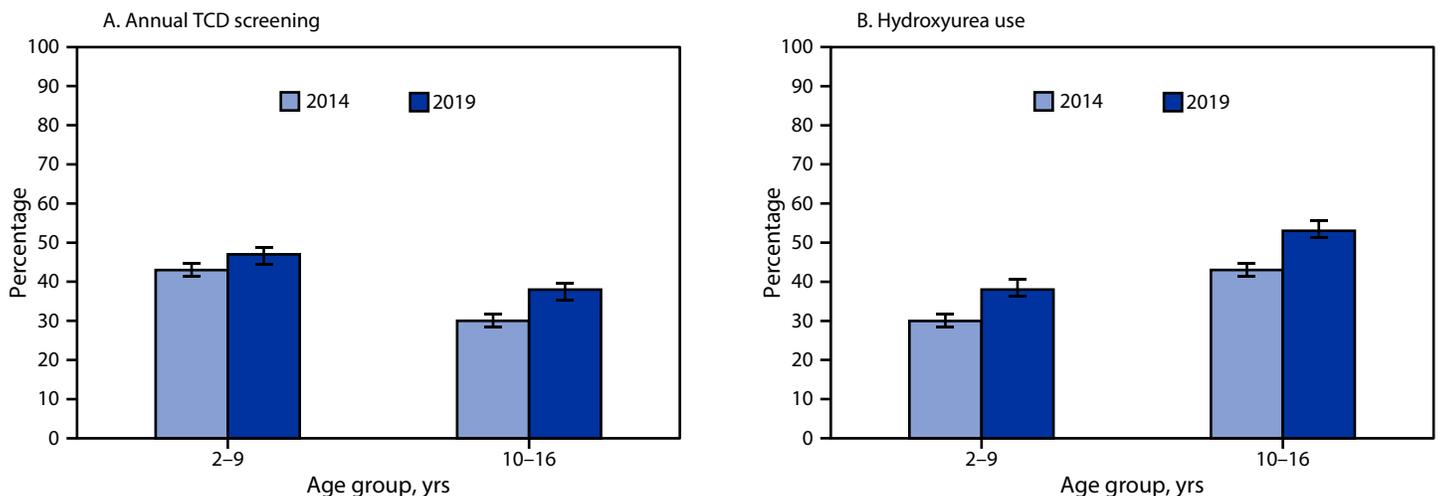


**Abbreviation:** TCD = transcranial Doppler.
\* With 95% CIs indicated by error bars.

**TABLE 1. Transcranial Doppler ultrasound screening among children and adolescents aged 2–16 years with sickle cell anemia continuously enrolled in Medicaid, within health indicator subgroups* — selected U.S. states, 2019**

| | Children and adolescents who received TCD screening | | | |
| --- | --- | --- | --- | --- |
| | Aged 2–9 yrs (n = 1,810) | | Aged 10–16 yrs (n = 1,542) | |
| Health indicator | No. (%) | PR (95% CI) | No. (%) | PR (95% CI) |
| Total | 845 (47) | NA | 581 (38) | NA |
| **Hospitalization during study year** | | | | |
| Yes | 349 (56) | 1.3 (1.2–1.5) | 266 (43) | 1.3 (1.1–1.5) |
| No | 496 (42) | Ref | 315 (34) | Ref |
| **Ambulatory care visits during study year** | | | | |
| 0–10 | 449 (41) | Ref | 271 (32) | Ref |
| 11–20 | 275 (61) | 1.5 (1.3–1.7) | 195 (48) | 1.5 (1.3–1.7) |
| 21–30 | 60 (55) | 1.3 (1.1–1.6) | 51 (41) | 1.3 (1.0–1.6) |
| >30 | 61 (41) | 1.0 (0.8–1.2) | 64 (39) | 1.2 (1.0–1.5) |
| **Emergency department visits during study year** | | | | |
| 0 | 269 (46) | Ref | 212 (36) | Ref |
| 1–2 | 332 (46) | 1.0 (0.9–1.1) | 235 (39) | 1.1 (0.9–1.2) |
| 3–4 | 144 (46) | 1.0 (0.9–1.2) | 79 (38) | 1.0 (0.8–1.3) |
| ≥5 | 100 (54) | 1.2 (1.0–1.4) | 55 (39) | 1.1 (0.9–1.4) |
| **Emergency department reliance** | | | | |
| <20% of noninpatient visits | 594 (51) | Ref | 466 (41) | Ref |
| ≥20% of noninpatient visits | 251 (42) | 0.8 (0.7–0.9) | 115 (30) | 0.7 (0.6–0.9) |
| **One or more hospitalizations for acute chest syndrome in any year (including current)** | | | | |
| Yes | 426 (57) | 1.5 (1.3–1.6) | 359 (45) | 1.5 (1.3–1.8) |
| No | 419 (39) | Ref | 222 (30) | Ref |
| **Largest number of hospitalizations for pain crises in any year (including current)** | | | | |
| 0 | 236 (35) | Ref | 99 (28) | Ref |
| 1 | 292 (46) | 1.3 (1.1–1.5) | 156 (33) | 1.2 (1.0–1.5) |
| 2 | 170 (59) | 1.7 (1.5–1.9) | 135 (45) | 1.6 (1.3–2.0) |
| >2 | 147 (67) | 1.9 (1.7–2.2) | 191 (47) | 1.7 (1.4–2.1) |

**Abbreviations:** NA = not applicable; PR = prevalence ratio; Ref = referent group; TCD = transcranial Doppler ultrasound.
* Children who had no ambulatory care visits and no emergency department visits during 2019 were not included in analyses of emergency department reliance.

**TABLE 2. Hydroxyurea use among children and adolescents aged 2–16 years with sickle cell anemia continuously enrolled in Medicaid, within health indicator subgroups* — selected U.S. states, 2019**

| | Children and adolescents who received hydroxyurea | | | |
| --- | --- | --- | --- | --- |
| | Aged 2–9 yrs (n = 1,810) | | Aged 10–16 yrs (n = 1,542) | |
| Health indicator | No. (%) | PR (95% CI) | No. (%) | PR (95% CI) |
| Total | 693 (38) | NA | 821 (53) | NA |
| **Hospitalization during study year** | | | | |
| Yes | 305 (49) | 1.5 (1.3–1.7) | 415 (68) | 1.6 (1.4–1.7) |
| No | 388 (33) | Ref | 406 (44) | Ref |
| **Ambulatory care visits during study year** | | | | |
| 0–10 | 360 (33) | Ref | 377 (45) | Ref |
| 11–20 | 225 (50) | 1.5 (1.3–1.7) | 271 (66) | 1.5 (1.3–1.6) |
| 21–30 | 54 (49) | 1.5 (1.2–1.8) | 80 (65) | 1.4 (1.2–1.7) |
| >30 | 54 (36) | 1.1 (0.9–1.4) | 93 (56) | 1.3 (1.1–1.5) |
| **Emergency department visits during study year** | | | | |
| 0 | 215 (36) | Ref | 278 (48) | Ref |
| 1–2 | 268 (37) | 1.0 (0.9–1.2) | 316 (52) | 1.1 (1.0–1.2) |
| 3–4 | 131 (42) | 1.1 (1.0–1.4) | 130 (62) | 1.3 (1.1–1.5) |
| ≥5 | 79 (43) | 1.2 (1.0–1.4) | 97 (69) | 1.5 (1.3–1.7) |
| **Emergency department reliance** | | | | |
| <20% of noninpatient visits | 484 (41) | Ref | 622 (55) | Ref |
| ≥20% of noninpatient visits | 208 (34) | 0.8 (0.7–0.9) | 197 (51) | 0.9 (0.8–1.0) |
| **One or more hospitalizations for acute chest syndrome in any year (including current)** | | | | |
| Yes | 348 (47) | 1.5 (1.3–1.6) | 514 (65) | 1.6 (1.4–1.8) |
| No | 345 (33) | Ref | 307 (41) | Ref |
| **Largest number of hospitalizations for pain crises in any year (including current)** | | | | |
| 0 | 177 (26) | Ref | 123 (34) | Ref |
| 1 | 251 (40) | 1.5 (1.3–1.8) | 224 (47) | 1.4 (1.1–1.6) |
| 2 | 137 (48) | 1.8 (1.5–2.1) | 184 (62) | 1.8 (1.5–2.1) |
| >2 | 128 (58) | 2.2 (1.9–2.6) | 290 (71) | 2.1 (1.8–2.4) |

**Abbreviations:** NA = not applicable; PR = prevalence ratio; Ref = referent group.
* Children who had no ambulatory care visits and no emergency department visits during 2019 were not included in analyses of emergency department reliance.

(younger children with an indication of severe disease for TCD screening and older children and adolescents with an indication of severe disease for hydroxyurea) a substantial proportion of children and adolescents for whom these interventions are indicated were not receiving them.

Previous studies document numerous barriers to receipt of both interventions (*12–15*). Promising quality-care initiatives to reduce some barriers have been reported. One SCD center leveraged electronic health records to enhance case management and improve TCD tracking and scheduling and enlisted support specialists to help young children remain relaxed during the procedure; they reported sustained increases in TCD screening, from 63% at baseline to >70% (*18*). A regional collaborative of SCD clinics reported a significant increase in hydroxyurea counseling (from 85% to 98%) after implementation of a program in which clinic staff members and families developed standardized approaches to track preventive care (*19*).

More than 90% of patients with SCD are Black, and 3%–9% are Hispanic (*2*); thus, racism and existing health care disparities compound barriers to care for children with SCA. Interpersonal racism, such as racist connotations, prejudice, discrimination, and bias toward patients with SCA, often results in inadequate care and prolonged suffering (*3*). Structural racism, policies that have led to unequal opportunities in housing, employment, health insurance, and research funding, keep disparities in place and contribute to adverse health outcomes. These challenges are exacerbated by poor access to health care for SCA, given the lack of providers with expertise or facilities with resources to treat SCA. Consequently, SCA patients might delay seeking care, and emergency department visits are common.

Preventing SCA-associated complications requires strategies to reduce racism and disparities. Health care providers can educate themselves, their colleagues, and their institutions about the unique and specific needs of persons with SCA,

**Summary**

What is already known about this topic?

Sickle cell anemia (SCA), which primarily affects Black or African American persons, is associated with severe complications and reduced life expectancy. Among children and adolescents with SCA, transcranial Doppler (TCD) ultrasound screening identifies elevated risk for stroke, and hydroxyurea therapy can reduce the occurrence of several life-threatening complications.

What is added by this report?

During 2019, fewer than one half of Medicaid enrollees aged 2–16 years with SCA had a TCD screen. Fewer than one half of children aged 2–9 years used hydroxyurea and approximately one half of those aged 10–16 years used hydroxyurea.

What are the implications for public health practice?

Health care providers should implement quality care strategies and partner with patients, families, and community-based organizations to address barriers to care.

including how racism impedes optimal health care. They can advocate for and listen to their patients to better understand their needs. Population-based data are also critical to addressing gaps in health care. Data from the Sickle Cell Data Collection program, a state-based tracking system established by CDC in 2015 in California and Georgia, have directly informed health care decision-making. For example, a Georgia Sickle Cell Data Collection assessment that indicated that 10% of children and adolescents with SCD lived a >1-hour drive from any SCD specialty care option led to the opening of new mobile care clinics. Recently, the Sickle Cell Data Collection program expanded to 11 states, which collectively cover approximately 36% of persons with SCD in the United States.

The findings in this report are subject to at least five limitations. First, the sample for this analysis was limited to Medicaid enrollees from selected states; therefore findings are not generalizable to all U.S. children and adolescents with SCA. Nonetheless, previous assessments in two states indicate that most children and adolescents with SCD are covered by Medicaid.** Second, because the MarketScan Medicaid data files do not include information about which states participated each year, it was not possible to assess whether state variability partially explained changes in TCD screening and hydroxyurea use from 2014 to 2019. Third, socioeconomic data, such as income or parents' level of education were also not available. Fourth, the SCA algorithm used in this study (16) maximized case-finding; thus, some children and adolescents with non-SCA genotypes might have been included in this analysis.

** https://www.cdc.gov/ncbddd/hemoglobinopathies/scdc-fact-sheet-medicaid-data.html

However, the algorithm was most precise in classifying children and adolescents with SCA who had a previous severe complication, and the findings for those subgroups indicate that many children and adolescents with overt symptomatology are not receiving TCD screening or hydroxyurea. Finally, because hydroxyurea use was defined by the filling of a single prescription, the findings overestimate ongoing hydroxyurea use.

TCD screening is critical to stroke prevention in children and adolescents with SCA (7); hydroxyurea is efficacious in preventing serious complications (8), and numerous studies demonstrate the safety of its long-term use (20). The findings from this study highlight that health care for children and adolescents with SCA is fragmented. Health system accountability for evidence-based care can be built into electronic health records. Health care providers should implement quality care strategies to maximize TCD screening and hydroxyurea use and partner with patients, families, and community-based organizations to address barriers to care. Given that almost all SCA patients are Black or Hispanic (2), it is important that strategies include proactively addressing both interpersonal and structural racism. Finally, population-based surveillance data for SCA are currently limited to select states; expansion of surveillance coverage would allow CDC to better characterize disease outcomes and health care needs of those with SCA, and SCD overall, across the life span.

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# *Errata*

## Vol. 69, No. SS-7

In the Surveillance Summary "Abortion Surveillance — United States, 2018," on page 15, in Table 2, under the column heading "Abortions obtained by out-of-state residents," the value for New York should have read **4,743 (6.1)**.

## Vol. 70, No. SS-9

In the Surveillance Summary "Abortion Surveillance — United States, 2019," on page 14, in Table 2, under the column heading "Abortions obtained by out-of-state residents," the value for New York should have read **4,166 (5.3)**.

## Vol. 71, No. 21

In the report on page 709, the title should have read "Multistate Outbreak of *Listeria monocytogenes* Infections Linked to **Queso Fresco** — United States, 2021," and in the third paragraph, the fifth sentence should have read, "Consumption of **queso fresco (odds ratio [OR] = 51.2; p = 0.002) and other, similar fresh, soft cheeses (OR = 30.4; p<0.001)** were both statistically significant." On page 710, the first sentence should have read, "Among the eleven patients who completed the Listeria Initiative questionnaire, **seven reported consuming queso fresco; eight reported consuming other, similar fresh, soft cheeses**." In addition, on page 710, in the

first paragraph under "Public Health Response," the second sentence should have read, "Firm A produced or handled **queso fresco and two similar fresh, soft cheeses (requesón and quesillo)** under its own brand name and for private label brands." and the fifth sentence should have read, "Because of cross-contamination concerns, firm A agreed on February 26 to expand the recall to **all types of cheese produced or handled in the facility**." On page 711, in the figure (Figure), the text above the arrow indicating February 11, 2021, should have read, "**Queso fresco and other similar fresh, soft cheeses** statistically significant; MD collects samples." In addition, on pages 709–712, in the summary box and throughout the text, the terms "**queso fresco**," "**soft cheese**," or "**queso fresco and other similar fresh, soft cheeses**" should have been used in place of the term "Hispanic-style cheese."

**FIGURE. Number of persons infected with the outbreak strain of *Listeria monocytogenes*, by date of specimen collection (n = 13) — United States, October 20, 2020–March 17, 2021**
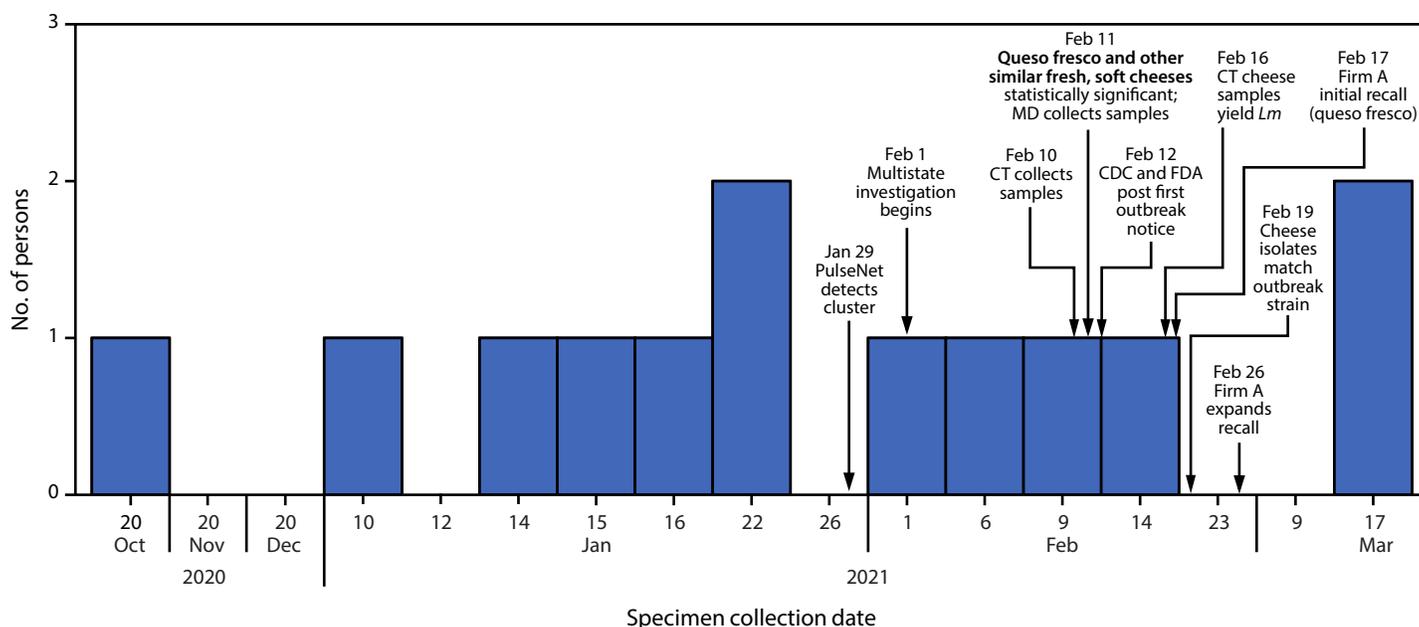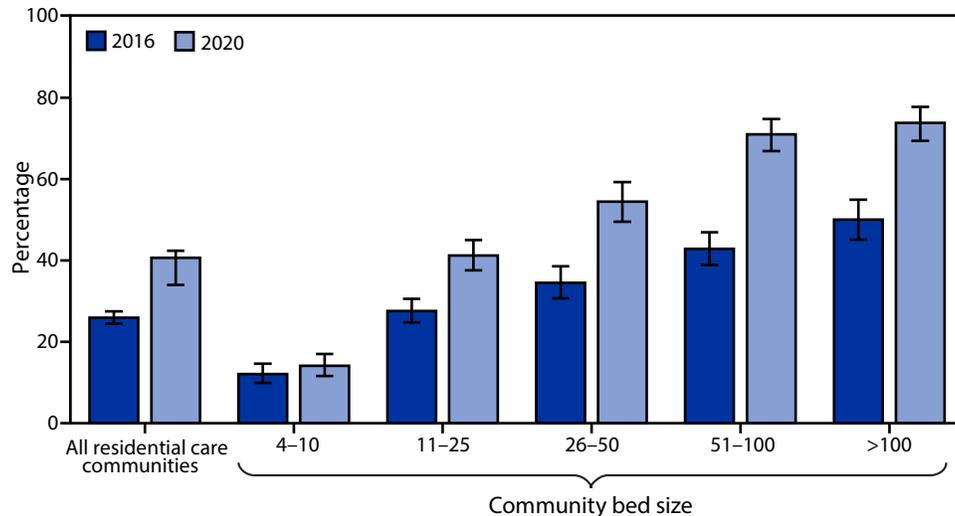


**Abbreviations:** CT = Connecticut; FDA = Food and Drug Administration; *Lm* = *Listeria monocytogenes*; MD = Maryland.

## QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

## Percentage of Residential Care Communities* that Use Electronic Health Records,[†] by Community Bed Size — United States, 2016 and 2020[§]



* Residential care communities are state-regulated, have four or more beds, provide room and board with at least two meals a day, and are staffed around the clock to provide supervision and assistance with personal care and health-related services to adults. Residential care communities licensed to exclusively serve persons who are mentally ill, intellectually disabled, or developmentally disabled were excluded.

[†] Respondents were asked, "An Electronic Health Record is a computerized version of the resident's health and personal information used in the management of the resident's health care. Other than for accounting or billing purposes, does this residential care community use Electronic Health Records?"

[§] Residential care communities with missing data were excluded.

From 2016 to 2020, the percentage of residential care communities using electronic health records increased from 26% to 41%. The percentage using electronic health records increased from 28% to 41% for 11–25 bed communities, 35% to 54% for 26–50 bed communities, 43% to 71% for 51–100 bed communities, and 50% to 74% for more than 100 bed communities. The change (from 12% to 14%) was not significant for 4–10 bed communities.

**Source:** National Post-acute and Long-term Care Study, 2016 and 2020 data. https://www.cdc.gov/nchs/npals/questionnaires.htm

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