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Community Water Fluoridation Levels To Promote Effectiveness and Safety in Oral Health — United States, 2016–2021

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Drinking water fluoridated at the level recommended by the U.S. Public Health Service (USPHS) reduces dental caries (cavities) by approximately 25% in children and adults (*1*). USPHS recommends fluoride levels to achieve oral health benefits and minimize risks associated with excess fluoride exposure. To provide the benefits of community water fluoridation, water systems should target a level of 0.7 mg/L and maintain levels ≥0.6 mg/L (*2*). The Environmental Protection Agency (EPA) sets a safety standard at 2.0 mg/L to prevent mild or moderate dental fluorosis, a condition that causes changes in the appearance of tooth enamel caused by hypermineralization resulting from excess fluoride intake during tooth-forming years (i.e., before age 8 years). During 2016–2021, fluoride measurements for 16.3% of population-weighted monthly fluoride measurements (person-months) reported by community water systems to CDC's Water Fluoridation Reporting System (WFRS) were <0.6 mg/L; only 0.01% of person-months exceeded 2.0 mg/L. More than 80% of population-weighted fluoride measurements from community water systems reporting to WFRS were above 0.6 mg/L. Although 0.7 mg/L is the recommended optimal level, ≥0.6 mg/L is still effective for the prevention of caries. A total of 4,080 community water systems safely fluoridated water 99.99% of the time with levels below the secondary safety standard of 2.0 mg/L. Water systems are encouraged to work with their state programs to report their fluoride data into WFRS and meet USPHS recommendations to provide the full benefit of fluoridation for caries prevention.

Monthly data from WFRS during 2016–2021 were analyzed for water systems that added fluoride (adjusting systems); these systems provide monthly average fluoride levels in mg/L. These monthly average fluoride levels were compared for two goals: prevention and safety. For prevention, reported levels were compared with 0.7 mg/L, the USPHS-recommended optimal fluoride level for preventing caries (*3*). For safety (i.e., to minimize potential fluorosis)* (*4*), reported fluoride levels were compared with the EPA's secondary maximum contaminant level (SMCL), of 2.0 mg/L. All analyses were conducted using SAS (version 9.4; SAS Institute) and R (version 4.1.3; The R Foundation). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.†

Water system populations were obtained from WFRS for each year during 2016–2021 (*5*). These populations are updated periodically by the states directly to WFRS or annually

* EPA also sets a maximum contaminant level (MCL) of 4.0 mg/L to prevent bone disease and mottling of teeth from fluorosis.
† 5 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.

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by CDC from EPA's State Drinking Water Information System. Population-weighted monthly fluoride levels (person-months) were calculated by multiplying each average monthly fluoride level by the size of the population served by each water system.

Data are typically reported to WFRS on a monthly, quarterly, or yearly basis. Participation across states varies based on fluoride-reporting requirements, drinking water or oral health program staffing limitations, and fluoridation program funding status. Among approximately 54,000 water systems in WFRS, a total of 5,888 adjust fluoride levels and serve a population of more than 200 million persons (145 million directly and an additional 55 million through water systems that purchase fluoridated water from adjusted water systems). Among the systems in WFRS, a total of 4,080, serving a population of 124,616,896, provided at least 1 month of data during the study period. Among 7,936,442,898 person-months during 2016–2021, only 796,283 (0.01%) exceeded the SMCL[§]; 16.3% were below 0.6 mg/L, and 83.7% of person-months operated between 0.6 mg/L and 2.0 mg/L with the largest peak in data at the 0.7 mg/L target (Figure).

Discussion

In this examination of the performance of U.S. water systems reporting fluoride levels from the perspectives of preventing caries and supporting established safety standards, the most common person-month fluoride level was the USPHS-recommended level of 0.7 mg/L and fluoride levels rarely exceeded the SMCL (0.01%). SMCL exceedances should be minimized to reduce dental fluorosis. Dental caries are one of the most common preventable chronic diseases among U.S. children: approximately one in four children living below the federal poverty level experiences untreated caries (*6*). Optimal levels of water fluoridation prevent caries by providing frequent and consistent contact with low levels of fluoride, ultimately reducing tooth decay by 25% in children and adults (*7*). Water systems that consistently and optimally fluoridate support the reduction of tooth decay. Suboptimal water systems in which fluoride concentrations are <0.6 mg/L are both ineffective in using resources and in supporting the oral health of their communities. Optimal fluoridation can be maintained with routine maintenance and monitoring, which provide protection from equipment malfunction, disruptions in fluoride supply, and periodic system shutdowns.[¶]

Water fluoridation promotes health equity through its proven effects on decreasing caries, reducing costs to families, and being readily available at the tap. In light of these benefits, Healthy People 2030, an ongoing initiative to improve population health, set the objective to increase the proportion of U.S. residents served by optimally fluoridated water systems

[§] Fluoride levels rarely exceeded the MCL (0.002%).

[¶] https://www.cdc.gov/mmwr/PDF/rr/rr4413.pdf

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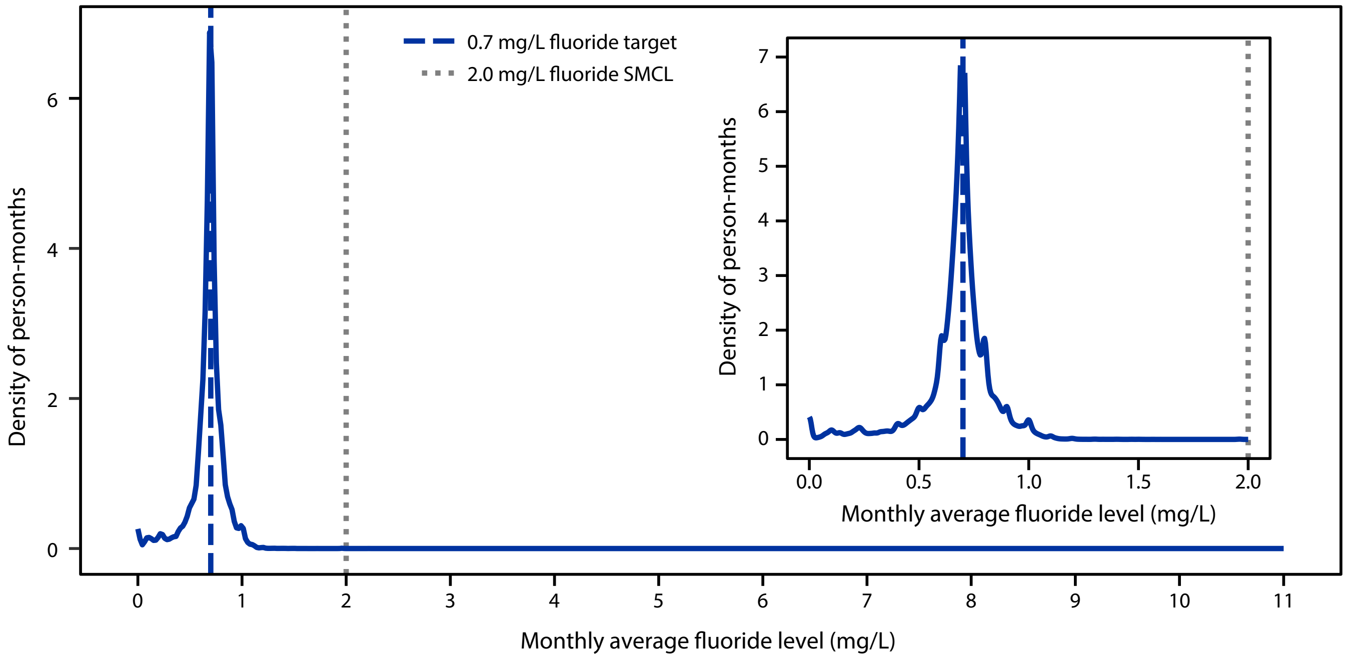
FIGURE. Density estimation of population-weighted monthly average fluoride levels — United States, 2016–2021



Abbreviation: SMCL = secondary maximum contamination level.

to 77.1% from 73.0% in 2018 (*8*). Currently, programs nationwide receive a net savings of $6.5 billion per year by averting direct dental treatment costs (tooth restorations and extractions) and indirect costs (follow-up treatment and losses of productivity) (*9*). After community water fluoridation was discontinued in Juneau, Alaska, for example, a higher number of caries-related procedures among persons aged <18 years was documented, particularly in persons born after cessation of fluoridation, highlighting the long-term oral health benefits of supporting access to fluoridated water (*10*).

Summary

What is already known about this topic?

Community water fluoridation delivers cavity-preventing fluoride to everyone with access. The U.S. government sets optimal fluoridation at 0.7 mg/L and a safety standard at 2.0 mg/L.

What is being added by this report?

During 2016–2021, a total of 4,080 community water systems safely fluoridated water 99.99% of the time, with levels below the secondary safety standard of 2.0 mg/L. However, 16.3% of nearly 8 billion population-weighted monthly fluoride measurements were <0.6 mg/L, placing the prevention of cavities in jeopardy.

What are the implications for public health practice?

Water system managers are encouraged to work with their state programs to report fluoride data to CDC and meet U.S. Public Health Service recommendations to provide the full benefit of cavity prevention through water fluoridation.

The findings in this report are subject to at least two limitations. First, CDC relies on state oral health and drinking water programs to report operational information; 31% of adjusting systems (5,888) did not report any fluoride levels during 2016–2021. Second, population values for all water systems are obtained from EPA's State Drinking Water Information System federal database at the state's discretion; however, additions and deletions of water systems and associated fluoridation status must be received from the state programs. As a result, counts of water system and information might differ from other publicly available community water system databases. Reporting in WFRS might be increased by improving data sharing between state drinking water and oral health programs, especially in states where water system data are entered into WFRS by the oral health program. Methods to increase reporting can include creating a data-sharing memorandum of understanding between the two programs and implementing a state policy that requires water systems to conduct monthly recording and reporting to the state.

Thousands of fluoride-adjusting community water systems reach approximately 200 million persons in the United States. To promote receipt of the full benefits of community water fluoridation, water systems must manage resources to meet the established 0.7 mg/L target consistently, especially those serving communities where fluoride measurements were <0.6 mg/L. CDC carefully and continuously monitors emerging research about the benefits and risks of fluoride exposure so that recommendations are evidence-based. CDC continues to emphasize the importance of community water fluoridation at the recommended level of 0.7 mg/L as the cornerstone of dental caries prevention in the United States.** Water systems are encouraged to work with their state programs to report their fluoride data into WFRS and meet USPHS recommendations to provide the full benefit of fluoride in caries prevention. Maintaining and improving access to optimally fluoridated water remains a vital, safe, and successful method for reducing dental caries and their associated costs for communities and families.

** https://www.cdc.gov/fluoridation/guidelines/cdc-statement-on-community-water-fluoridation.html

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Evaluation of the Cherokee Nation Hepatitis C Virus Elimination Program — Cherokee Nation, Oklahoma, 2015–2020

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Approximately 2.4 million persons in the United States have hepatitis C virus (HCV) infection, and 66,700 acute HCV infection cases were estimated for 2020 (*1*,*2*). American Indian or Alaska Native (AI/AN) persons are disproportionately affected by HCV infection and experienced the highest rates of acute HCV infection (2.1 cases per 100,000 persons) and HCV-associated mortality (10.17 per 100,000 persons) in the United States during 2020 (*1*). During 2015, Cherokee Nation Health Services (CNHS) in Oklahoma implemented an HCV elimination program, which includes universal HCV screening, primary HCV workforce expansion, and harm reduction services (*3*). To assess progress 5 years after program initiation, CNHS analyzed deidentified health record data. During November 1, 2015–October 31, 2020, a total of 1,423 persons received a diagnosis of HCV infection. Among these persons, 1,227 (86.2%) were linked to HCV care, and 871 (61.2%) initiated HCV treatment; 702 (49.3%) returned for their 12-week post treatment completion visit, at which time 698 (49.1%) had achieved laboratory-confirmed sustained virologic response (SVR), defined as undetectable HCV RNA at ≥12 weeks after completion of treatment (SVR12). Although CNHS has linked the majority of persons diagnosed with HCV infection to care, and those who returned for the SVR12 visit had high cure rates (99.4%), treatment initiation was lower than expected. Future activities should prioritize addressing gaps in treatment initiation after linkage to care and confirmation of hepatitis C cure with SVR12 testing.

Cherokee Nation is the largest AI/AN nation in the United States, spanning 14 counties in Oklahoma and including more than 450,000 registered Cherokee citizens (*4*). CNHS is the largest tribally operated health system in the United States, providing health care for over 100,000 AI/AN persons in 11 health care facilities across the reservation (*5*). During 2015, CNHS initiated an HCV elimination program to improve HCV screening, treatment, and cure. CNHS has published cascades of care, which document the progression of persons through the stages of HCV care, from diagnosis to treatment and cure, beginning before and continuing through 22 months after the start of their program (*3*,*6*,*7*). This report describes the most comprehensive CNHS HCV cascade of care, including five years of program data.

To assess progress of the HCV elimination program, CNHS extracted and analyzed deidentified data collected through the CNHS electronic health record system and HCV treatment database. The reported cascade of care is based on a modified version of the Consensus HCV Cascade of Care* (7); treatment completion was not included in the cascade as a distinct stage of care, but completion of HCV treatment among those included in the cascade was assessed. Persons included in this analysis had HCV RNA detected during November 1, 2015–October 31, 2020, and were thought to be alive as of October 31, 2020. Records of persons who received a diagnosis of HCV infection before November 1, 2015, and who had not received treatment as of this date, were also included. SVR12 visit and results were included in the cascade of care when those outcomes occurred by April 30, 2021.

Diagnosis of HCV infection was defined as receipt of a detectable HCV RNA test result. Linkage to HCV care was defined as undergoing an evaluation by a CNHS HCV-trained provider. HCV treatment initiation was defined as documentation 1) by the provider that treatment commenced, or 2) that the prescription was picked up from the pharmacy. The SVR12 visit was defined as documentation that a visit occurred to obtain an HCV RNA result within the study period and ≥12 weeks after the end of treatment. Achieving laboratory-confirmed SVR12 was defined as receipt of an undetectable HCV RNA test result at ≥12 weeks after completion of treatment. Although not included in the cascade of care, treatment completion, defined as documentation by the provider that treatment was completed, or that all prescription refills were picked up from the pharmacy, was assessed. Persons who completed treatment and were assessed for an HCV RNA test result after treatment completion but before the SVR12 due date were not included in the last two stages of the cascade of care (i.e., an SVR12 visit and laboratory-confirmed SVR12).

Sex, age, and presence of advanced liver disease (ascertained using noninvasive liver staging methods, as identified by serologic biomarkers [fibrosis-4 index >3.25†]) were also assessed. Treatments during this period consisted of interferon-free, all oral, direct-acting antivirals).

Progress along each step of the cascade of care was assessed by calculating 1) the proportion of persons who completed each

* The consensus cascade of care definitions recommend that reporting includes the number and percentage of persons 1) ever infected with HCV (reactive HCV antibody test), 2) diagnosed with chronic HCV infection, 3) started on treatment, and 4) achieving SVR12.

† https://www.hcvguidelines.org/treatment-naive/simplified-treatment

step among the population of persons with diagnosed HCV infection, and 2) the proportion of persons at each step who moved to the next step. IBM SPSS Statistics (version 19; IBM Corp.) was used to conduct all analyses. Because this activity was considered a surveillance and public services delivery program, and the data were collected in the context of clinical care,[§] it was deemed exempt from review by the Cherokee Nation Institutional Review Board. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[¶]

Among 1,423 persons who received a diagnosis of HCV infection during November 1, 2015–October 31, 2020, and who had available demographic data, 870 (61.1%) were male, and 545 (38.3%) were female; 351 (24.7%) were aged 31–40 and 370 (26.0%) were aged 51–60 years. A total of 189 (13.3%) persons met criteria for advanced liver disease or cirrhosis (Table).

Among the 1,423 persons with a diagnosis of HCV infection, 1,227 (86.2%) were linked to HCV care, and 871 (71.0%) of those initiated HCV treatment. Among persons who initiated treatment, 702 (80.6%) returned for their SVR12 visit, among whom 698 (99.4%) achieved laboratory-confirmed SVR12 (Figure).

Among the 871 persons who initiated treatment, 800 (91.8%) completed treatment. In addition to the 871 persons who initiated treatment during the study period, another 17 persons initiated and completed HCV treatment after the study period concluded on October 31, 2020; to align with consensus definitions (*7*), these 17 persons were included in the diagnosis and linkage to care levels but excluded from subsequent cascade levels. Among 98 persons who completed treatment but did not return for their SVR12 visit, 40 (40.8%) had evidence of SVR before a 12-week posttreatment visit was due. These results were also not included in the cascade of care.** Eleven of the 98 persons who did not return for an SVR12 visit during the study period had undetectable HCV RNA test results outside of the study period. To align with consensus definitions (*7*), these 11 persons were included in all cascade levels, except the SVR12 visit (Table).

[§] https://www.hhs.gov/ohrp/coded-private-information-or-biospecimens-used-research.html

[¶] 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.

** These persons were excluded because of the possibility that they might have relapsed 12 weeks after treatment discontinuation, when the SVR12 should have occurred. Because they were tested before that date, it is likely they are cured; however, they do not strictly meet the SVR12 definition.

TABLE. Characteristics of persons with hepatitis C virus infection (N = 1,423) and treatment and outcome indicators — Cherokee Nation Health Services Hepatitis C Virus Elimination Program, Oklahoma, November 2015–October 2020

Characteristic	No. (%)
Overall	**1,423 (100.0)**
Sex	
Female	545 (38.3)
Male	870 (61.1)
Unknown	8 (0.6)
Age group, yrs	
≤20	16 (1.1)
21–30	236 (16.6)
31–40	351 (24.7)
41–50	312 (21.9)
51–60	370 (26.0)
61–70	118 (8.3)
71–80	13 (0.9)
Unknown	7 (0.5)
Met criteria for advanced liver disease or cirrhosis (fibrosis-4 index >3.25)	**189 (13.3)**
HCV cascade of care outcomes	
Diagnosis of HCV infection	1,423 (100.0)
Linked to HCV care	1,227 (86.2)
Initiated DAA treatment*	871 (61.2)
Completed DAA treatment	800 (56.2)
Returned for SVR12 visit[†,§]	702 (49.3)
Achieved SVR12 (HCV RNA not detected)	698 (49.1)
Did not achieve SVR12 (HCV RNA detected)[¶]	4 (0.2)

Abbreviations: DAA = direct-acting antiviral; HCV = hepatitis C virus; SVR12 = sustained virologic response ≥12 weeks after HCV treatment completion.

* Does not include 17 persons with HCV infection diagnosed within the study period who initiated and completed treatment after October 31, 2020. Among the 98 persons who completed treatment and did not return for the SVR12 visit, 40 had an undetectable HCV RNA result at treatment completion, and 22 had an undetectable result at their 4-week visit.

[†] Includes six persons who did not complete treatment but who had a 12-week posttreatment visit and had an undetectable HCV RNA result within the study period.

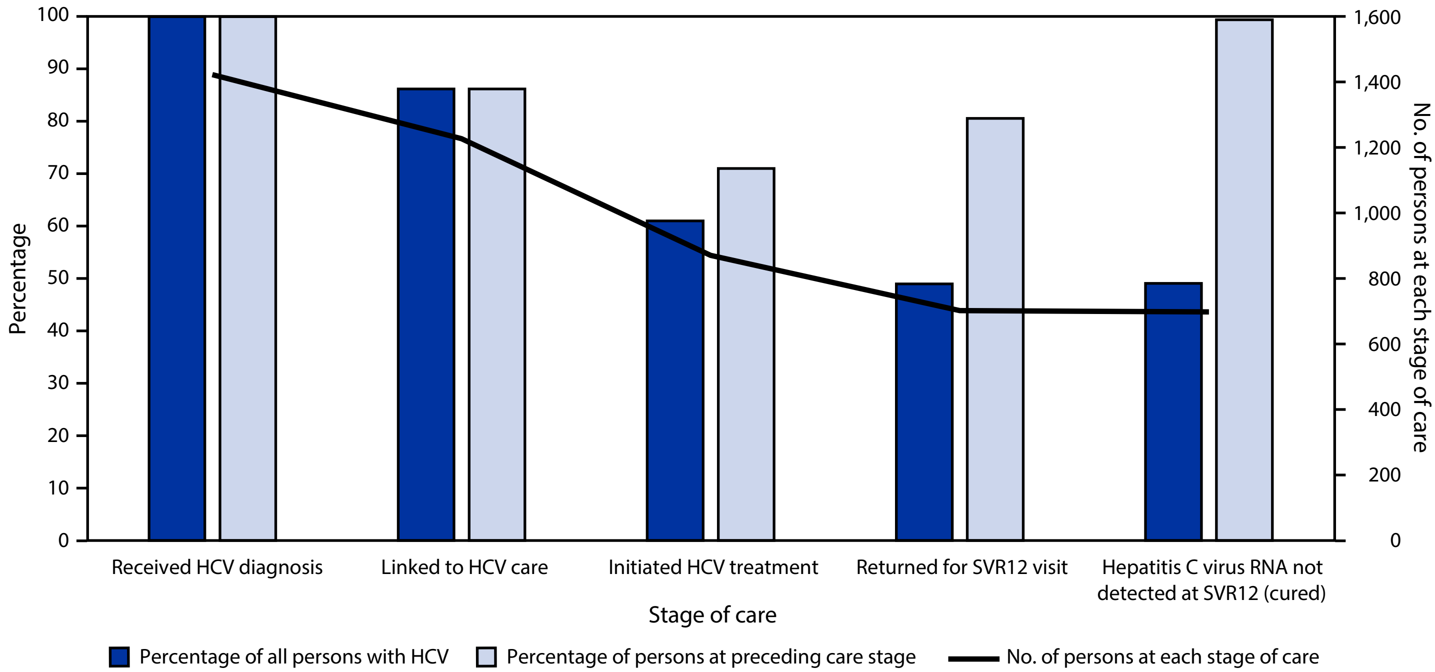
[§] Among the 98 persons who did not return for a 12-week posttreatment result, an additional 11 had an undetectable HCV RNA result after the study period.

[¶] Among the four persons who returned for a 12-week posttreatment visit but did not have an undetectable HCV RNA result, three likely had treatment failure, and one likely had HCV reinfection.

Discussion

These findings align with those published in a 2022 global systematic review of HCV elimination activities (*8*). Five years after implementing the CNHS HCV Elimination Program, approximately 86% of persons who received a diagnosis of HCV infection were linked to care; however, only 61% initiated treatment, 56% completed treatment, and just under 50% achieved SVR12. Among those who initiated treatment and returned for SVR12 visits, 99.4% were cured. Given the high rate of treatment success with direct-acting antivirals, it is likely that the majority of persons who initiated treatment

FIGURE. Cascade of care among persons with hepatitis C virus infection (N = 1,423) — Cherokee Nation Health Services, Oklahoma, November 2015–October 2020



Abbreviations: HCV = hepatitis C virus; SVR12 = sustained virologic response ≥12 weeks after treatment completion.

were also cured (*9*). Thus, although linkage to care has been successful, treatment initiation continues to be a barrier to achieving HCV elimination within the Cherokee Nation.

There are several potential explanations for the gap from HCV treatment evaluation to treatment initiation within the CNHS program. First, Oklahoma Medicaid did not cover hepatitis C treatment for persons with fibrosis scores of F0 or F1 (little to no scarring) until 2018 (*10*). In addition, for all payor types, a previous authorization was required, and although HCV evaluation occurred, several weeks to months might have lapsed before HCV treatment medication became available (*10*). Further, some payors required evaluation by a specialist or that the prescription be written in consultation with a specialist, further delaying treatment initiation (*10*). These delays might have led to some persons falling out of care.

The findings in this report are subject to at least four limitations. First, because this evaluation was conducted among persons served by one Tribal health system, findings might not be generalizable to persons served by other health systems. Second, this evaluation relied on consensus cascade definitions (*7*) that differed from CNHS's previously published cascades of care and, as a result, these findings are not directly comparable. Third, persons included in this study might have received care outside of CNHS, leading to underreporting of true cascade outcomes. Finally, the COVID-19 pandemic overlapped with the final seven months of this evaluation. Although it is impossible to fully ascertain the effects of COVID-19 on the results of this evaluation, the pandemic might have reduced the numbers of persons attending care visits, initiating treatment, and obtaining laboratory tests to monitor viral load, including SVR12. Despite these limitations, these findings are important because of the disproportionate impact of HCV infection and lack of HCV research among AI/AN persons.

To achieve HCV elimination, the reasons for the gaps at each stage of the cascade of care need to be addressed, especially the delay in the acquisition of hepatitis C medications. For CNHS,

Summary

What is already known about this topic?

American Indian and Alaska Native (AI/AN) persons are disproportionately affected by hepatitis C virus (HCV) infection.

What is added by this report?

Five years after implementing a hepatitis C elimination program, Cherokee Nation Health Services (CNHS) had diagnosed hepatitis C in 1,423 persons, 86% of whom were linked to care. Although only 61% initiated treatment, 99% of those who completed treatment were cured. Barriers to HCV treatment initiation include lack of access to direct-acting antivirals at the time of HCV evaluation.

What are the implications for public health practice?

CNHS's Hepatitis C Elimination Program can be used as a model for other health systems serving AI/AN persons; however, barriers to HCV treatment initiation need to be addressed to achieve HCV elimination.

emphasis on treatment initiation should be a priority. Future research should explore barriers to linkage to care, initiating treatment after HCV evaluation, completing treatment, and returning for the SVR12 visit among AI/AN persons, as well as interventions to address these barriers.

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Estimates of SARS-CoV-2 Seroprevalence and Incidence of Primary SARS-CoV-2 Infections Among Blood Donors, by COVID-19 Vaccination Status — United States, April 2021–September 2022

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Changes in testing behaviors and reporting requirements have hampered the ability to estimate the U.S. SARS-CoV-2 incidence (*1*). Hybrid immunity (immunity derived from both previous infection and vaccination) has been reported to provide better protection than that from infection or vaccination alone (*2*). To estimate the incidence of infection and the prevalence of infection- or vaccination-induced antibodies (or both), data from a nationwide, longitudinal cohort of blood donors were analyzed. During the second quarter of 2021 (April–June), an estimated 68.4% of persons aged ≥16 years had infection- or vaccination-induced SARS-CoV-2 antibodies, including 47.5% from vaccination alone, 12.0% from infection alone, and 8.9% from both. By the third quarter of 2022 (July–September), 96.4% had SARS-CoV-2 antibodies from previous infection or vaccination, including 22.6% from infection alone and 26.1% from vaccination alone; 47.7% had hybrid immunity. Prevalence of hybrid immunity was lowest among persons aged ≥65 years (36.9%), the group with the highest risk for severe disease if infected, and was highest among those aged 16–29 years (59.6%). Low prevalence of infection-induced and hybrid immunity among older adults reflects the success of public health infection prevention efforts while also highlighting the importance of older adults staying up to date with recommended COVID-19 vaccination, including at least 1 bivalent dose.*,†

Since July 2020, SARS-CoV-2 seroprevalence in the United States has been estimated by testing blood donations (*3*). CDC, in collaboration with Vitalant, American Red Cross, Creative Testing Solutions, and Westat, established a nationwide cohort of 142,758 blood donors in July 2021; the cohort included persons who had donated blood two or more times in the preceding year.§ All blood donations collected during April–June 2021 were tested for antibodies against the spike (S) and nucleocapsid (N) proteins. Beginning in 2022, up to one blood donation sample per donor was randomly selected each quarter and tested using the Ortho VITROS SARS-CoV-2 Quantitative S immunoglobulin G¶ and total N antibody** tests. Both SARS-CoV-2 infection and COVID-19 vaccination result in production of anti-S antibodies, whereas anti-N antibodies only result from infection. At each donation, blood donors were asked if they had received a COVID-19 vaccine. Using vaccination history and results of antibody testing, the prevalence of the U.S. population aged ≥16 years with vaccine-induced, infection-induced, or hybrid immunity was estimated for four 3-month periods (April–June 2021, January–March 2022, April–June 2022, and July–September 2022); in addition, the proportion of persons who transitioned from one immune status to another by quarter was estimated. Analysis was limited to 72,748 (51.0%) donors for whom it was possible to ascertain immune status during each period using their prior classification (e.g., previously infected or vaccinated), antibody testing results, and their vaccination status at the time of each donation.†† The sample data were weighted to account for selection into the study cohort, for nonresponse during the four analysis periods, and for demographic differences between the blood donor population and the overall U.S. population. The weights were obtained through a combination of stratification and raking, an iterative weighting adjustment procedure (*4*). Rates of infection among those previously uninfected were estimated for each period by determining the percentage of anti-N–negative persons seroconverting to anti-N–positive from one 3-month period included in the study to the next. Estimates were stratified by age group (16–29, 30–49, 50–64, and ≥65 years) and race and ethnicity§§ (Asian, Black or African

* https://www.cdc.gov/coronavirus/2019-ncov/your-health/risks-getting-very-sick.html

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

§ Blood donors who donated at least twice during the year before July 2021 were included in the cohort, because they might represent persons who were more likely to donate frequently. Among donors who donated more than once during a quarter, one sample was selected at random for testing.

¶ https://www.fda.gov/media/150675/download

** https://www.fda.gov/media/151027/download

†† https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing/antibody-tests-guidelines.html

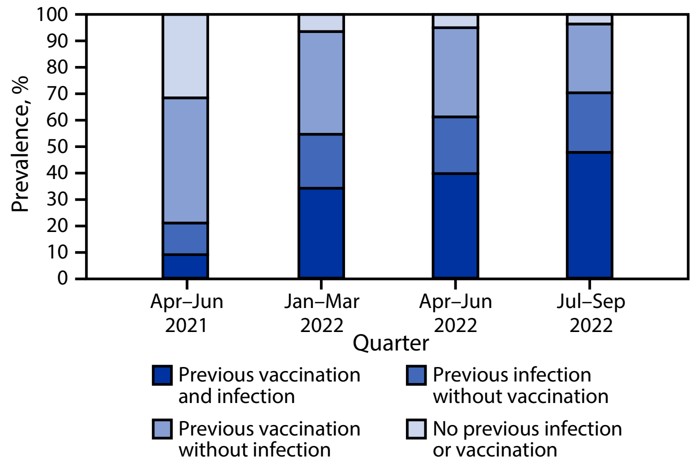
§§ Persons of Hispanic origin might be of any race but are categorized as Hispanic; all racial groups are non-Hispanic.

American [Black], White, Hispanic or Latino [Hispanic], and other). SAS (version 9.4; SAS Institute) was used to compute the final weights, and R (version 4.2.1; R Foundation) was used to calculate all the estimates and create the plots.¶¶ Seroprevalence and infection rates were estimated as weighted means and compared by demographic group and vaccination status using two-sided t-tests with a significance level of α = 0.05. This activity was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.***

During the first quarter examined (April–June 2021), an estimated 68.4% (95% CI = 67.8%–68.9%) of persons aged ≥16 years had SARS-CoV-2 antibodies from previous infection or vaccination, including 47.5% (95% CI = 46.0%–49.0%) from vaccination alone, 12.0% (95% CI = 10.8%–13.5%) from infection alone, and 8.9% (95% CI = 8.7%–9.2%) from both (Figure 1) (Supplementary Figure 1, https://stacks.cdc.gov/view/cdc/128630). During January–March 2022, 93.5% (95% CI = 93.1%–93.9%) of persons aged ≥16 years had antibodies from previous infection or vaccination, including 39.0% (95% CI = 37.4%–40.7%) from vaccination alone, 20.5% (95% CI = 19.2%–22.2%) from infection alone, and 34.1% (95% CI = 32.4%–35.8%) from both. During July–September 2022, 96.4% (95% CI = 96.1%–96.7%) of persons had antibodies from previous infection or vaccination, including 26.1% (95% CI = 25.4%–26.9%) with vaccine-induced immunity alone, 22.6% (95% CI = 21.2%–24.1%) with infection-induced immunity alone, and 47.7% (95% CI = 44.8%–51.2%) with hybrid immunity. During July–September 2022, the prevalence of infection-induced immunity was 85.7% (95% CI = 79.8%–90.2%) among unvaccinated persons and 64.3% (95% CI = 61.9%–66.7%) among vaccinated persons.

During July–September 2022, the lowest prevalence of hybrid immunity, 36.9% (95% CI = 35.8%–38.1%), was observed in persons aged ≥65 years, and the highest, 59.6% (95% CI = 56.7%–62.3%), in adolescents and young adults aged 16–29 years (Figure 2) (Supplementary Figure 2, https://stacks.cdc.gov/view/cdc/128679). During all periods, higher prevalences of hybrid immunity were observed among Black and Hispanic populations than among White and Asian populations (Supplementary Figure 3, https://stacks.cdc.gov/view/cdc/128680).

FIGURE 1. Prevalences of vaccine-induced, infection-induced, and hybrid* immunity† against SARS-CoV-2 among blood donors aged ≥16 years — United States, April 2021–September 2022



* Immunity derived from a combination of vaccination and infection.
† Ascertained by the presence of anti-spike antibodies (present in both COVID-19–vaccinated and SARS-CoV-2–infected persons) and anti-nucleocapsid antibodies (present only in previously infected persons) and self-reported history of vaccination.

Among persons with no previous infection, the incidence of first infections during the study period (i.e., conversion from anti-N–negative to anti-N–positive) was higher among unvaccinated persons (Table). From April–June 2021 through January–March 2022, the incidence of first SARS-CoV-2 infections among unvaccinated persons was 67.0%, compared with 26.3% among vaccinated persons ($p<0.05$). From January–March 2022 through April–June 2022, the incidence among unvaccinated persons was 21.7% and was 13.3% among vaccinated persons. Between April–June 2022 and July–September 2022, the incidence among unvaccinated persons was 28.3%, compared with 22.9% among vaccinated persons ($p<0.05$). Incidence of first SARS-CoV-2 infections was higher among younger than among older persons and was lower among Asian persons than among other racial and ethnic populations, but the differences among groups narrowed over time.

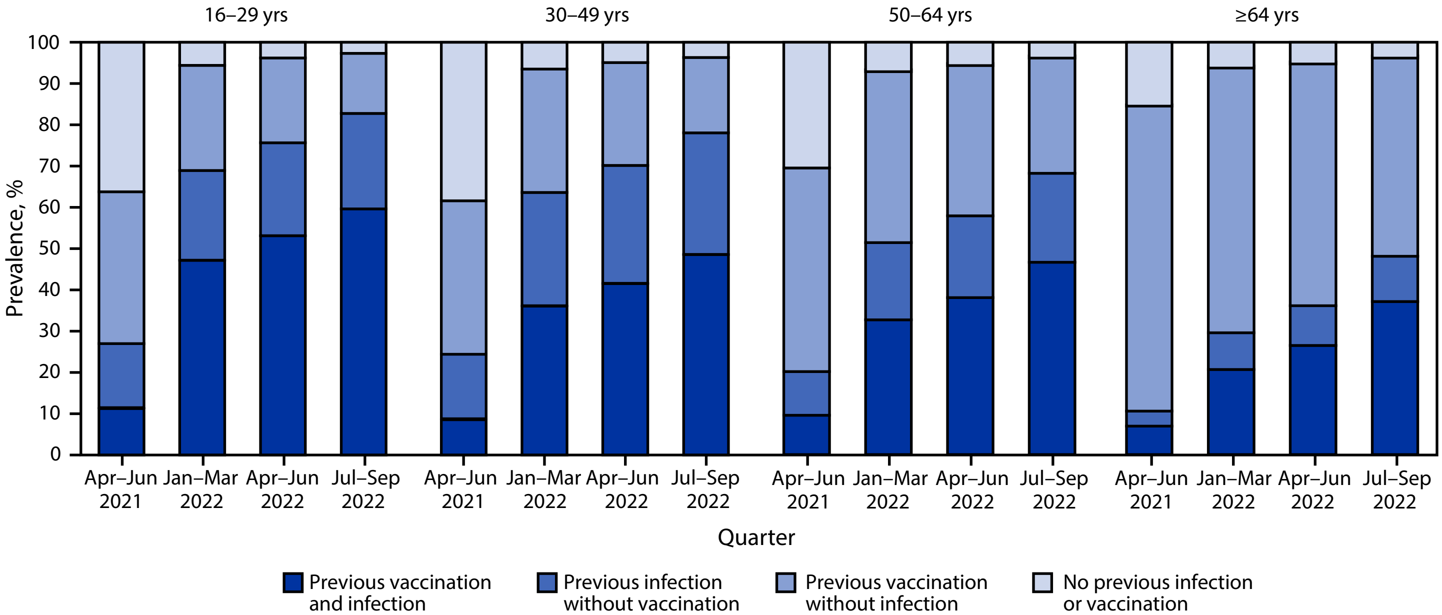
Discussion

Both infection-induced and hybrid immunity increased during the study period. By the third quarter of 2022, approximately two thirds of persons aged ≥16 years had been infected with SARS-CoV-2 and one half of all persons had hybrid immunity. Compared with vaccine effectiveness against any infection and against severe disease or hospitalization, the effectiveness of hybrid immunity against these outcomes has been shown to be higher and wane more slowly (*2*). This

¶¶ Jackknife replication was used to compute replicate weights. Weights were adjusted for nonresponse using adjustment cells created by age category, vaccination and previous infection status, and blood collection organization (Vitalant or American Red Cross). Raking was used to further adjust the weights to account for demographic differences between the blood donor population and U.S. population. The demographic variables used for raking were sex (female and male), age group (16–24, 25–34, 35–44, 45–54, 55–64, and ≥65 years), and race and ethnicity (Asian, Black, White, Hispanic, and other).

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

FIGURE 2. Prevalences of vaccine-induced, infection-induced, and hybrid* immunity† against SARS-CoV-2 among blood donors aged ≥16 years, by age group — United States, April 2021–September 2022



* Immunity derived from a combination of vaccination and infection.

† Ascertained by the presence of anti-spike antibodies (present in both COVID-19–vaccinated and SARS-CoV-2–infected persons) and anti-nucleocapsid antibodies (present only in previously infected persons) and self-reported history of vaccination.

increase in seroprevalence, including hybrid immunity, is likely contributing to lower rates of severe disease and death from COVID-19 in 2022–2023 than during the early pandemic.[†††] The prevalence of hybrid immunity is lowest in adults aged ≥65 years, likely due to higher vaccination coverage and earlier availability of COVID-19 vaccines for this age group, as well as to higher prevalences of behavioral practices to avoid infection (*5*). However, lower prevalences of infection-induced and hybrid immunity could further increase the risk for severe disease in this group, highlighting the importance for adults aged ≥65 years to stay up to date with COVID-19 vaccination and have easy access to antiviral medications.

COVID-19 vaccine efficacy studies have reported reduced effectiveness against SARS-CoV-2 infection during the Omicron-predominant period compared with earlier periods and have shown that protection against infection wanes more rapidly than does protection against severe disease (*6*,*7*). In this study, unvaccinated persons had higher rates of infection (as evidenced by N antibody seroconversion) than did vaccinated persons, indicating that vaccination provides some protection against infection. The differences in incidence could also be due to systematic differences between vaccinated and unvaccinated persons in terms of the prevalence of practicing prevention behaviors such as masking and physical distancing. The relative difference in infection rates narrowed during the most recent months, possibly because of waning of vaccine-induced protection against infection in the setting of increased time after vaccination or immune evasion by the SARS-CoV-2 Omicron variant. The narrowing of difference in infection rates might also be attributable to increasing similarities in behavior among vaccinated and unvaccinated persons during late 2022 (*8*).

The findings in this report are subject to at least six limitations. First, although COVID-19 booster vaccine doses and reinfections can strengthen immunity (*9*,*10*), this analysis did not account for these effects because blood donor vaccination history did not include the number of doses received, and data on reinfections were not captured. Second, immunity wanes over time, but time since vaccination or infection was not included in the analysis (*2*). Third, vaccination status was self-reported, potentially leading to misclassification. Fourth, although the results were adjusted based on differences in blood donor and general population demographics, estimates from blood donors might not be representative of the general population; thus, these results might not be generalizable. Fifth, vaccinated and unvaccinated persons might differ in other ways not captured by this analysis (*8*), nor can causality be inferred from the results on relative infection incidence. Finally, if both vaccination and infection occurred between blood donations included in the study, the order of occurrence could not be determined, and some unvaccinated donors might have been

††† https://covid.cdc.gov/covid-data-tracker/#datatracker-home (Accessed May 25, 2023).

TABLE. Estimated percentage* of persons infected with SARS-CoV-2 for the first time among blood donors, by analysis quarter, sociodemographic characteristics, and vaccination status — United States, April 2021–September 2022

	Period, % (95% CI)		
Characteristic	**Apr–Jun 2021 to Jan–Mar 2022**	**Jan–Mar 2022 to Apr–Jun 2022**	**Apr–Jun 2022 to Jul–Sep 2022**
Overall			
Total	**42.5 (41.8–43.3)**	**14.5 (13.7–15.3)**	**23.6 (22.8–24.5)**
Unvaccinated	67.0 (65.6–68.4)†	21.7 (19.1–24.4)†	28.3 (25.5–31.3)†
Vaccinated	26.3 (25.4–27.1)	13.3 (12.4–14.1)	22.9 (22.1–23.8)
Age group, yrs			
16–29			
Total	**57.4 (54.8–59.9)**	**21.8 (18.6–25.4)**	**29.3 (25.8–33.0)**
Unvaccinated	73.8 (69.5–77.7)	31.5 (21.5–43.7)	29.5 (18.1–44.2)
Vaccinated	41.2 (38.1–44.4)	19.7 (16.6–23.3)	29.2 (25.6–33.1)
30–49			
Total	**51.8 (50.4–53.3)**	**18.0 (16.1–20.0)**	**26.8 (24.9–28.8)**
Unvaccinated	70.6 (68.5–72.5)	23.0 (17.9–28.9)	25.6 (21.3–30.4)
Vaccinated	32.5 (30.6–34.4)	16.9 (15.0–18.9)	27.0 (25.0–29.2)
50–64			
Total	**38.9 (37.3–40.5)**	**13.2 (12.0–14.6)**	**24.1 (22.4–25.9)**
Unvaccinated	61.5 (58.5–64.4)	19.8 (16.0–24.2)	32.0 (27.5–36.9)
Vaccinated	24.6 (23.1–26.3)	12.1 (10.8–13.6)	22.9 (21.2–24.7)
≥65			
Total	**21.0 (20.0–22.2)**	**9.2 (8.4–10.0)**	**18.5 (17.4–19.7)**
Unvaccinated	49.6 (46.3–52.9)	13.7 (11.3–16.5)	27.0 (22.8–31.6)
Vaccinated	15.0 (13.9–16.2)	8.7 (7.9–9.6)	17.8 (16.6–19.0)
Race and ethnicity§			
Asian			
Total	**29.1 (26.0–32.3)**	**8.9 (6.6–11.8)**	**23.2 (19.5–27.5)**
Unvaccinated	53.1 (40.7–65.0)	6.3 (1.9–18.8)	22.1 (8.3–47.0)
Vaccinated	24.7 (21.7–27.9)	9.0 (6.7–12.1)	23.3 (19.5–27.5)
Black or African American			
Total	**42.4 (37.8–47.2)**	**12.9 (9.5–17.4)**	**23.7 (19.4–28.6)**
Unvaccinated	71.6 (61.0–80.3)	14.8 (3.0–49.5)	21.7 (5.0–59.3)
Vaccinated	30.1 (25.9–34.6)	12.8 (9.3–17.3)	23.9 (19.7–28.6)
White			
Total	**43.2 (42.4–43.9)**	**15.3 (14.6–16.1)**	**23.5 (22.8–24.3)**
Unvaccinated	67.4 (66.0–68.8)	22.7 (20.1–25.6)	29.5 (26.6–32.5)
Vaccinated	23.5 (22.9–24.1)	13.8 (13.1–14.6)	22.5 (21.7–23.3)
Hispanic or Latino			
Total	**45.5 (42.9–48.2)**	**14.0 (11.8–16.4)**	**23.4 (20.9–26.1)**
Unvaccinated	64.6 (59.9–69.1)	17.9 (12.2–25.4)	27.2 (18.7–37.9)
Vaccinated	34.5 (31.6–37.5)	13.3 (11.0–16.1)	22.8 (20.3–25.6)
Other and multiple races¶			
Total	**43.4 (38.3–48.7)**	**18.1 (12.7–25.2)**	**27.3 (21.9–33.6)**
Unvaccinated	65.7 (56.5–73.9)	33.4 (15.1–58.7)	21.6 (9.9–40.8)
Vaccinated	28.1 (22.8–34.0)	14.7 (10.4–20.4)	28.3 (22.3–35.2)

* Percentage of uninfected persons (anti-nucleocapsid–negative in the previous 3-month period) seroconverting to anti-nucleocapsid–positive. If both vaccination and infection occurred between donations included in the study, the order could not be determined, and some unvaccinated donors might have been vaccinated before infection and thus misclassified.

† If donors who transitioned from no antibodies to hybrid immunity between April–June 2021 and January–March 2022 were excluded, an estimated 55.5% (95% CI = 53.9%–57.1%) of unvaccinated donors were infected. For other periods, exclusion did not substantially change results. Between January–March and April–June 2022, 0.4% of persons shifted from no antibodies to hybrid immunity. Between April–June and July–September 2022, 0.3% of persons shifted from no antibodies to hybrid immunity.

§ Persons of Hispanic or Latino (Hispanic) origin might be of any race but are categorized as Hispanic; all racial groups are non-Hispanic.

¶ Includes American Indian or Alaska Native and non-Hispanic persons of other races.

Summary

What is already known about this topic?

SARS-CoV-2 hybrid immunity (immunity derived from both previous infection and vaccination) has been reported to provide better protection than that from infection or vaccination alone.

What is added by this report?

By the third quarter of 2022, an estimated 96.4% of persons aged ≥16 years in a longitudinal blood donor cohort had SARS-CoV-2 antibodies from previous infection or vaccination, including 22.6% from infection alone and 26.1% from vaccination alone; 47.7% had hybrid immunity. Hybrid immunity prevalence was lowest among adults aged ≥65 years.

What are the implications for public health practice?

Low prevalence of infection-induced and hybrid immunity among older adults, who are at increased risk for severe disease if infected, reflects the success of public health infection prevention efforts while also highlighting the importance of this group staying up to date with recommended COVID-19 vaccination, including at least 1 bivalent dose.

vaccinated before infection and thus misclassified; in 2022, this was uncommon and occurred in <0.5% of donors during any 3-month period.

This report found that the incidence of first-time SARS-CoV-2 infection was lower among persons who had received COVID-19 vaccine than among unvaccinated persons and that infection-induced and hybrid immunity have increased but remain lowest in adults aged ≥65 years. These adults have consistently had a higher risk for severe disease compared with younger age groups, underscoring the importance of older adults staying up to date with recommended COVID-19 vaccination, including at least 1 bivalent dose.

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Notes from the Field

Pediatric Intracranial Infections — Clark County, Nevada, January–December 2022

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In October 2022, the Southern Nevada Health District (SNHD) was notified of a higher-than-expected number of pediatric patients hospitalized with intracranial abscesses; similar concerns were previously reported nationally (*1*,*2*). This rare infection is associated with significant morbidity (*3*,*4*). When SNHD received the report in October 2022, 14 cases had been diagnosed in the largest pediatric hospital in southern Nevada. SNHD investigated the reported increase to confirm that a cluster had been detected, identify common risk factors for infection, report findings to the community, and recommend measures to prevent future cases.

The observed and expected number of cases were compared to confirm and describe the cluster. Historical median quarterly case numbers with IQRs were obtained from discharge data from all hospitals in Clark County, Nevada during January 2015–December 2021. Persons with primary, secondary, or tertiary discharge diagnoses of intracranial abscess and granuloma (*International Classification of Diseases, Tenth Revision, Clinical Modification* [ICD-10-CM] code G06.0) or extradural and subdural abscess, unspecified (ICD-10-CM code G06.2) during January 2015–December 2022 among persons aged ≤18 years were identified as cases. Because hospital discharge data from the final quarter of 2022 were not available at the time of investigation, cases in 2022 were primarily identified through provider reporting and confirmed by discharge data, if available; for these data, a case was defined as diagnosis of an intraparenchymal abscess, subdural abscess or empyema, epidural abscess or empyema, or evidence of other intracranial extension observed on brain imaging in a person aged ≤18 years without a previous neurosurgical procedure or history of significant head trauma. Detailed medical chart abstraction and semistructured telephone interviews with families affected during 2022 were conducted to ascertain clinical course, risk factors, and exposures. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.*

During 2015–2021 overall, a median of one case per quarter (IQR = 0–2.0) was identified in Clark County. However, during the period preceding the COVID-19 pandemic (2015–2019), the quarterly median was 0.5 cases (IQR = 0–2.0), and during the first 2 years of the pandemic (2020–2021), the median number of quarterly cases reported was 1.5 (IQR = 0–2.5). During 2022, 18 cases were identified (median = five per quarter; IQR = 3.5– 6.0); all occurred after February 2022 (Figure).

Review of medical charts of the 18 cases reported in 2022 found that the median patient age was 12 years (range = 4–15 years) and that all but four cases occurred in males. Children and adolescents were hospitalized for a median of 15 days (range = 9–76 days), and 15 patients required craniotomy for abscess drainage. Sinusitis was diagnosed in 14 patients and mastoiditis in four. No patients received a positive test result for SARS-CoV-2 on admission. No associated deaths were reported.

Telephone interviews were conducted with 14 caregivers as a proxy for the affected child or adolescent, nine of whom reported that the child had cold symptoms, including rhinorrhea, before hospitalization; seven experienced other symptoms, including headache (three), headache with fever (three), and mild head injuries (two).† Eleven caregivers sought care for their child before hospitalization, most often at an emergency department (seven). The median interval from symptom onset to hospitalization was 7 days (range = 2–14 days). Nine interviewees reported that the child had been swimming during the 4 weeks preceding hospitalization, but not at the same pool locations. Five interviewees reported cessation of masking practices after the COVID-19 mask mandate was lifted,§ including three who reported cold symptoms experienced by the affected child before hospitalization.

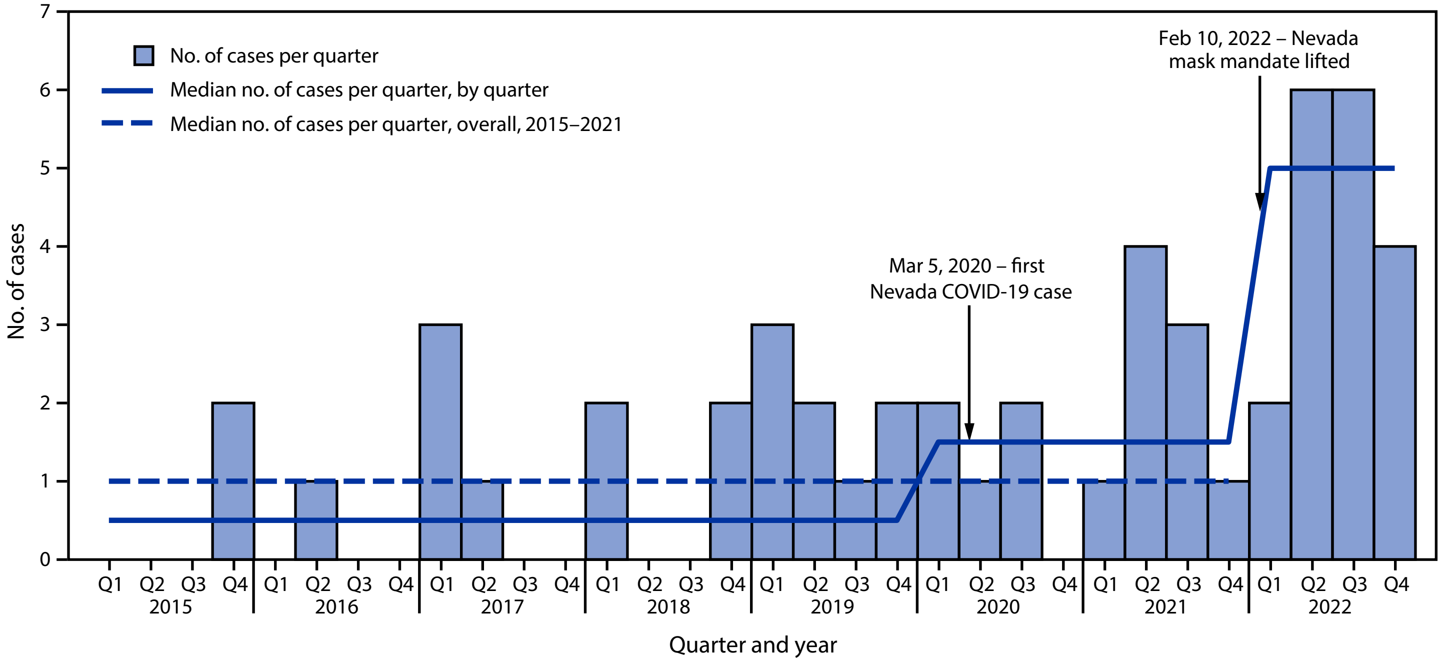
A 2022 investigation of possible increased incidence of pediatric intracranial abscesses identified a higher number of cases in 2022 compared with that reported in 2021 (*2*). Contributing to this increase was a period of elevated cases beginning in mid-2021, which followed a period of consistently low case counts after the onset of the pandemic (*2*). This pattern was also observed in the current investigation. Although this investigation did not identify unexpected risk factors for intracranial abscesses, the substantial increase in cases after the mask mandate in Nevada was lifted might be partially attributable to changes in respiratory pathogen transmission. SNHD released a health advisory notice to pediatric health care providers detailing the investigation findings; surveillance will be continued through 2023 to better monitor trends in incidence of pediatric intracranial infections.

* 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.

† Reported symptoms and injuries are not mutually exclusive.

§ Nevada mask mandate was in effect during July 19, 2021–February 10, 2022, and required use of face masks in indoor public areas including schools.

FIGURE. Number of cases of pediatric intracranial infections and median number of infections per quarter — Clark County, Nevada, 2015–2022



Abbreviation: Q = quarter.

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

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Notes from the Field

Update on Pediatric Intracranial Infections — 19 States and the District of Columbia, January 2016–March 2023

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In May 2022, CDC began an investigation of a possible increase in pediatric intracranial infections, particularly those caused by *Streptococcus* bacteria, during the preceding year (*1*). January 2016–May 2022 data from a large, geographically diverse network of children's hospitals showed altered patterns in pediatric intracranial infections after the onset of the COVID-19 pandemic (*1*). In this update, extended hospitalization data through March 2023 from 37 hospitals in 19 states and the District of Columbia showed a higher-than-expected number of pediatric intracranial infections beginning in August 2021, with a large peak during winter 2022–2023. Pediatric intracranial infections are recognized as a severe complication of viral respiratory infection and sinusitis (*2*), and the winter 2022–2023 peak coincided with spikes in respiratory virus circulation*,† (*3*,*4*). Even during this peak, intracranial infections remained rare. CDC continues to track trends in pediatric intracranial infections and recommends that all persons aged ≤18 years remain current with recommended vaccinations, including influenza and COVID-19.§

To characterize national trends in pediatric intracranial infections, CDC analyzed pediatric hospitalizations for brain abscesses, epidural empyemas, and subdural empyemas reported to the Children's Hospital Association's Pediatric Health Information System (PHIS) by 37 tertiary referral children's hospitals in 19 states and the District of Columbia. The included hospitals consistently reported to PHIS during January 1, 2016–March 31, 2023 (the most recent data available when the analysis was performed).¶ All inpatient encounters with persons aged ≤18 years that had a primary or secondary *International Classification of Diseases, Tenth Revision, Clinical Modification* discharge diagnosis code G06.0 (intracranial abscess and granuloma) or G06.2 (extradural and subdural abscess, unspecified) during the study period were included. Because the study period was extended from that of the earlier report (*1*), the subset of included hospitals differed slightly from that previously analyzed and reported. Data were analyzed in aggregate and by U.S. Census Bureau region (Northeast, Midwest, South, and West) using R software (version 4.0.3; R Foundation) with RStudio (version 1.3.1093; Posit, PBC). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.**

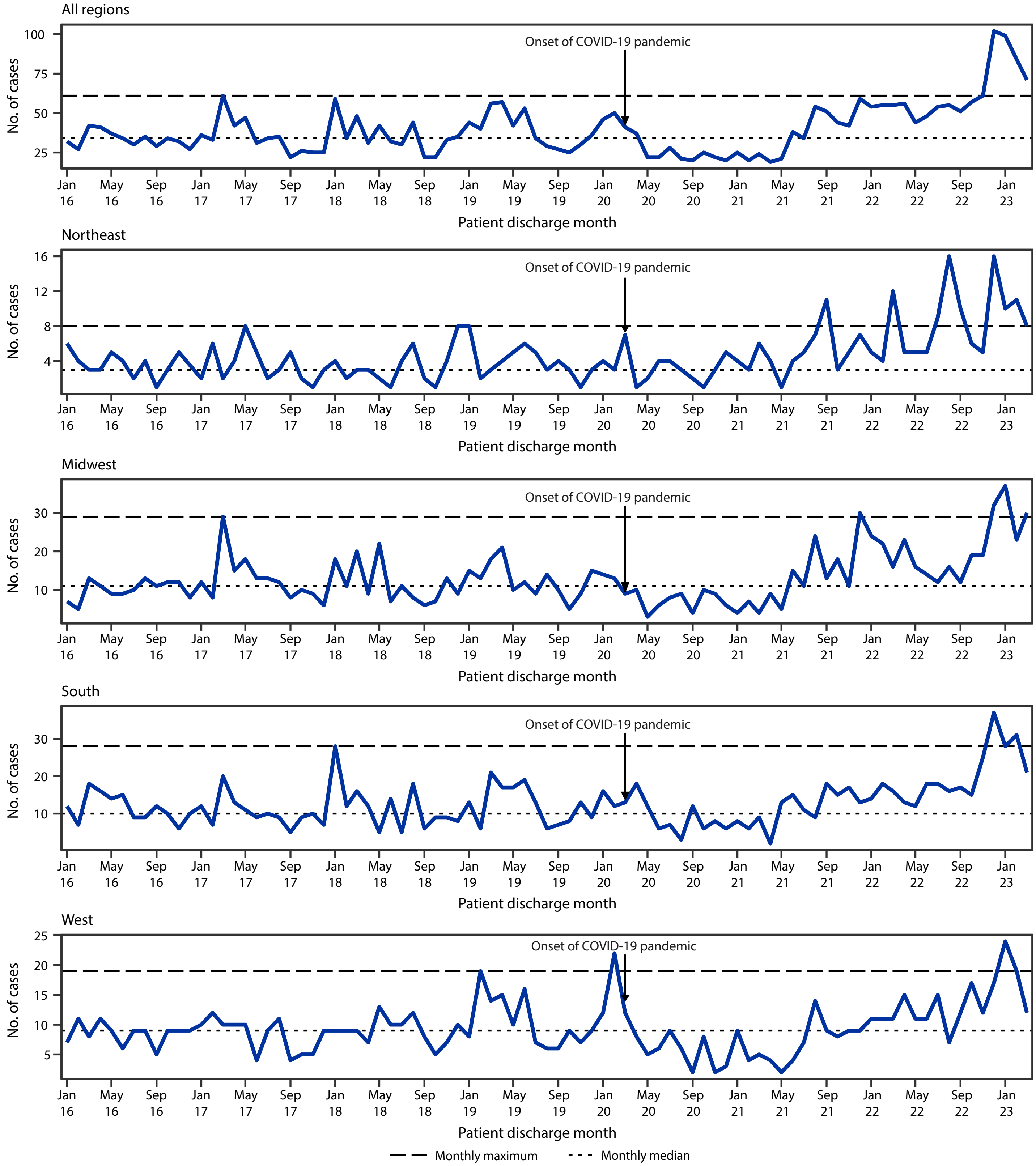
Using pediatric intracranial infection hospitalization data collected during 2016–2019, the monthly median (34; IQR = 29.75–42.00) and maximum (61) number of cases were calculated as a prepandemic baseline (Figure). After the onset of the COVID-19 pandemic in March 2020, monthly intracranial infection case counts remained below the baseline median during May 2020–May 2021. Monthly case counts exceeded the median during August 2021–March 2023†† but did not exceed the baseline maximum until a large peak (102 cases) in December 2022. During January–March 2023, case counts began to decline but remained above the baseline maximum. Although some variability between U.S. Census Bureau regions was observed, overall patterns were generally similar: consistently low case counts after the onset of the pandemic, then a period of increase beginning in mid- to late 2021 followed by a large peak during winter 2022–2023 (Figure). Demographic characteristics of patients (age, race and ethnicity, and sex), measures of severity (length of hospitalization, intensive care unit admission, and in-hospital mortality), and the percentage of patients with a complex chronic condition (*5*) remained approximately stable over the study period and were similar to values reported previously (*1*).

This analysis in a large, geographically diverse network of children's hospitals showed elevations in pediatric intracranial infections beginning in mid-2021 with a large spike in winter 2022–2023, both nationally and by U.S. Census Bureau region. Despite these observed increases, pediatric intracranial infections remain rare. These infections are often preceded by viral respiratory infection and sinusitis, and recent trends might be driven by concurrent, heightened pediatric respiratory pathogen transmission (*3*,*4*). All persons aged ≤18 years

* https://www.cdc.gov/rsv/research/rsv-net/dashboard.html
† https://gis.cdc.gov/GRASP/Fluview/PedFluDeath.html
§ https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html
¶ Population denominators were not available; therefore, analysis was limited to hospitals that reported data for each month during the study period.

** 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.
†† During March 2020–May 2022, as described, the current findings were not identical to those previously reported because of variability in the hospitals included in each analysis. In the current analysis with an extended period of observation, a decline was observed in May 2022, but not to the median value. In the earlier analysis, cases were below the median during April 2020–June 2021, above the median during July 2021–April 2022, and declined to the median in May 2022.

FIGURE. Cases of intracranial infection* among persons aged ≤18 years, by U.S. Census Bureau region — Pediatric Health Information System, 19 states and the District of Columbia, January 2016–March 2023†



* The median and maximum number of cases per month during 2016–2019, by U.S. Census Bureau region.

† Data from 37 children's hospitals in 19 states and the District of Columbia. The number of hospitals that provided data in each U.S. Census Bureau region were as follows: five (Northeast Region), 13 (Midwest Region), 11 (South Region), and eight (West Region).

should be up to date with recommended vaccinations, including influenza and COVID-19. CDC will continue to track trends in pediatric intracranial infections.

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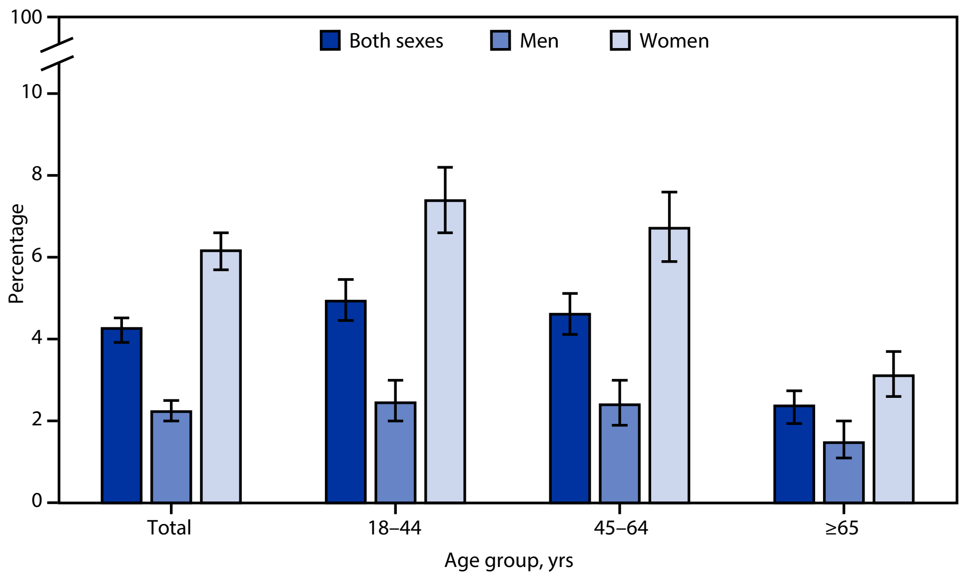
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage* of Adults Aged ≥18 Years Who Have Been Bothered a Lot by Headache or Migraine in the Past 3 Months,† by Sex and Age Group — National Health Interview Survey, 2021§



* With 95% CIs indicated by error bars.
† Based on a response to the question, "In the past 3 months, how often did you have pain? Would you say never, some days, most days, or every day?" Those who responded with "some days," "most days," or "every day" were asked, "Over the past 3 months, how much have you been bothered by headache or migraine? Would you say not at all, a little, a lot, or somewhere in between?"
§ Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population.

In 2021, 4.3% of adults aged ≥18 years reported being bothered a lot by headache or migraine in the past 3 months with the percentage among women (6.2%) higher than that among men (2.2%). Percentages were higher among women than men in all age groups: 7.4% versus 2.5% in adults aged 18–44 years, 6.7% versus 2.4% in those aged 45–64 years, and 3.1% versus 1.5% in those aged ≥65 years. Among men and women, the percentage of those bothered a lot by headache or migraine in the past 3 months was lowest among those aged ≥65 years.

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

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