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Outbreak of Salmonella Newport Infections with Decreased Susceptibility to Azithromycin Linked to Beef Obtained in the United States and Soft Cheese Obtained in Mexico — United States, 2018–2019

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In September 2018, CDC identified Salmonella enterica serotype Newport (Newport) infections that were multidrug resistant (MDR), with decreased susceptibility to azithromycin, a recommended oral treatment agent. Until 2017, decreased susceptibility to azithromycin had occurred in fewer than 0.5% of Salmonella isolates from U.S. residents. This report summarizes the investigation of a multistate MDR Salmonella outbreak conducted by CDC, state and local health departments, and the U.S. Department of Agriculture's Food Safety and Inspection Service. During June 2018-March 2019, 255 cases of infection with the outbreak strain were identified in 32 states; 43% of patients (89 of 206 with information on travel) reported recent travel to Mexico. Infections were linked to consumption of soft cheese obtained in Mexico and beef obtained in the United States. Consumers should avoid eating soft cheese that could be made from unpasteurized milk, regardless of the source of the cheese. When preparing beef, a food thermometer should be used to ensure that appropriate cooking temperatures are reached. When antibiotic treatment is needed for a patient, clinicians should choose antibiotics based on susceptibility testing wherever possible.

Epidemiologic Investigation

In 2018, during an investigation of antibiotic-susceptible Newport infections that led to a U.S. ground beef recall (1), a genetically distinct group of MDR Newport isolates was identified. Isolates were classified as the outbreak strain if they fell within the MDR clade (0–11 alleles by core genome multilocus sequence typing [cgMLST]); isolates were identified using PulseNet, the national subtyping network for foodborne bacterial disease surveillance. A case was defined as isolation of

the outbreak strain from a patient during June 2018–March 2019. After interviews conducted by state and local health departments, some patients were reinterviewed using a standardized hypothesis-generating questionnaire or supplementary questionnaires that included questions about travel and antibiotic treatment. Food exposures were reported for the 7 days before illness onset. Exposures among patients who did not travel internationally were compared with those expected among a nationally representative sample of healthy persons included in the U.S. Foodborne Diseases Active Surveillance Network population survey (2006–2007) (2), after stratification by sex and ethnicity.

During June 2018–March 2019, 255 cases were identified in 32 U.S. states (Figure). Overall, 29% (60/209) of patients for whom information was available were hospitalized, 6% (4/70) were admitted to an intensive care unit, 4% (10/255) had

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Salmonella bacteremia, and two died. The median patient age was 36 years (range = <1–90 years), 58% (145/250) were female, and 65% (143/221) were Hispanic. Overall, 43% (89/206) with information on travel reported visiting Mexico in the 7 days preceding illness onset. Travelers to Mexico mostly reported visiting friends or family (67%, 24/36) and collectively reported visiting 16 of the 32 states within Mexico. Patients who did not visit Mexico were residents of 26 U.S. states.

Among patients who traveled to Mexico with information on food consumption, 87% (41/47) reported eating beef, and 63% (29/46) reported eating soft cheese; among those, 79% (23/29) recalled obtaining the cheese in Mexico (Table 1). Of several types of artisanal cheese reported, the most frequently recalled cheese was queso fresco, a cheese that is typically made with raw, unpasteurized milk from cows or goats (3). Among patients who did not travel to Mexico, 29% (20/70) reported eating Mexican-style soft cheese, and 93% (68/73) reported eating beef (Table 1). The percentage who ate Mexican-style soft cheese was similar to the percentage in the nationally representative sample of healthy persons (p-value = 0.54), whereas the percentage who ate beef was higher than that among healthy persons (p<0.01).

Product and Animal Testing

In September 2018, the outbreak strain was detected in a cecal sample from a steer collected at a slaughter and processing plant in Texas as part of National Antimicrobial Resistance

Monitoring System (NARMS) surveillance (Figure). In October 2018, the outbreak strain was detected in a mixture of queso fresco and Oaxaca soft cheese purchased in a market in Tijuana, Mexico. The cheese had been brought into the United States by a patient who became ill with a strain that was indistinguishable (0 allele difference) from the strain isolated from the cheese. The outbreak strain was detected in beef samples collected in November 2018 and March 2019 at two Texas slaughter and processing facilities. Isolates from the Mexican cheese, the steer cecum, and beef differed by 0–2 alleles from one another and by a minimum of 0–1 alleles from patient isolates (Table 2). Review of patient information did not identify any common suppliers of contaminated beef or cheese.

Antibiotic Resistance

Antibiotic resistance was predicted using whole genome sequencing and confirmed in a subset of isolates by antimicrobial susceptibility testing using broth microdilution; decreased susceptibility to azithromycin was defined as minimum inhibitory concentration ≥32 µg/mL (4). Of 252 isolates with resistance information, 226 (90%) had predicted resistance to trimethoprim-sulfamethoxazole, tetracycline, and chloramphenicol, and decreased susceptibility to azithromycin. In 143 (57%) isolates, there was additional predicted resistance to ampicillin and streptomycin, and nonsusceptibility to ciprofloxacin (defined as minimum inhibitory concentration ≥0.12 µg/mL) (4). All resistance genes were located on an IncR

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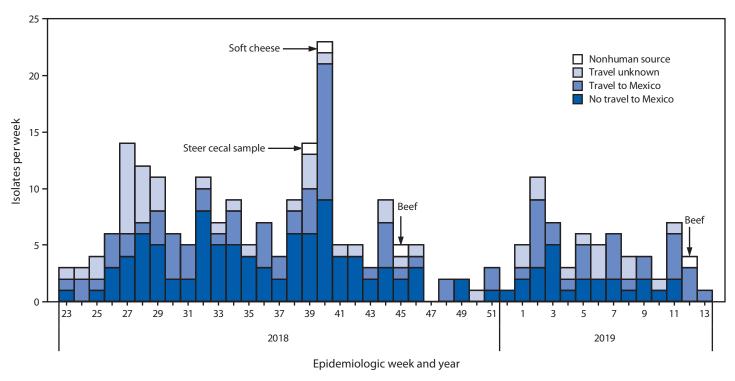
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FIGURE. Identification of isolates of the outbreak strain of Salmonella enterica serotype Newport from infected patients (N = 255), by travel status,* and from nonhuman sources[†] (n = 4), by epidemiologic week and year — United States, June 2018–March 2019



* Defined as reported travel within 7 days before illness onset.

plasmid. Among patients with treatment information, 65/87 (75%) received antibiotic therapy, and 28/86 (33%) received an antibiotic to which the outbreak strain was resistant or showed decreased susceptibility.

Discussion

This investigation identified an MDR strain of Salmonella Newport with decreased susceptibility to azithromycin and nonsusceptibility to ciprofloxacin, two oral agents recommended for treatment of Salmonella infections. The presence of resistance genes on a plasmid is concerning because of the potential for spread to other bacteria (5). The outbreak strain appears to have emerged recently because Newport with decreased susceptibility to azithromycin was not detected in animal, retail meat, or human isolates in NARMS surveillance before 2016 (4). During 2016–2017, two smaller multistate clusters of MDR Newport infections with decreased susceptibility to azithromycin were investigated among U.S. residents; isolates were within 11 alleles of the current outbreak isolates. No source of the infections was identified, but a high percentage of patients reported recent travel to Mexico (Division of Foodborne, Waterborne, and Environmental Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC, unpublished data, 2019). Routine monitoring in 2016 detected an isolate from a sample of beef imported from Mexico that was indistinguishable (0 allele difference) from the outbreak strain isolated from cheese in 2018.

In this MDR outbreak, consumption of cheese and consumption of beef were both associated with illness, indicating that dairy cattle were a likely source of these infections. The detection of the outbreak strain in cheese purchased in Mexico and the high percentage of travelers to Mexico who reported eating Mexican-style soft cheese suggest that soft cheese from Mexico was a source of infection. Mexican-style soft cheese has been previously identified as a source of other *Salmonella* outbreaks (6). The reported consumption of queso fresco, travel to various regions in Mexico, and detection of indistinguishable Newport strains in beef and cheese suggest that contamination of soft cheese resulted from carriage by cattle rather than poor hygiene during cheese production. Dairy cattle often are used as a source of ground beef and have been implicated in previous MDR Newport outbreaks (5).

Among patients who did not travel to Mexico, beef was identified as a source of infection by the close genetic relatedness between isolates from patients and beef samples, and from the higher percentage of patients who ate beef compared with the

[†] Cecal sample and beef samples obtained in the United States; sample of cheese obtained in Mexico by a patient infected with the outbreak strain who consumed this cheese.

TABLE 1. Consumption of beef or Mexican-style soft cheese within 7 days of illness onset among patients (N = 255) with the outbreak strain of *Salmonella enterica* serotype Newport — United States, June 2018–January 2019

_		Patients with known travel statu (n = 206)			
Reported exposure within 7 days of illness onset	No./No. with available information (%)	No. who visited Mexico* (%)	No. who did not visit Mexico* (%)		
Any beef					
No	11/121 (9)	6/47 (13)	5/73 (7)		
Yes	110/121 (91)	41/47 (87)	68/73 (93)		
Source of beef					
United States	55/110 (50)	7/41 (17)	48/68 (71)		
Mexico	18/110 (16) [†]	17/41 (42)	1/68 (1) [†]		
Unknown	38/110 (35)	17/41 (42)	20/68 (29)		
Type of beef					
Other	24/110 (22)	12/41 (29)	12/68 (18)		
Ground	60/110 (55)	18/41 (44)	41/68 (60)		
Unknown	26/110 (24)	11/41 (27)	15/68 (22)		
Any Mexican-style chee	ese				
No	68/118 (58)	17/46 (37)	50/70 (71)		
Yes	50/118 (42)	29/46 (63)	20/70 (29)		
Source of Mexican-style	cheese				
United States	15/50 (30)§	3/29 (10)§	12/20 (60)		
Mexico	29/50 (58)	23/29 (79)	5/20 (25)		
Unknown	7/50 (14)	4/29 (14)	3/20 (15)		

^{*} Of patients with known travel status, 89 had visited Mexico, and 117 had not visited Mexico.

percentage of healthy persons who ate beef. It is also possible that beef was a source of infection among some travelers to Mexico; nearly 90% of them also reported eating beef, and in 2016 the outbreak strain was detected in beef imported from Mexico.

The genetic similarity between isolates from beef in Mexico, beef in the United States, and a steer in the United States strongly suggests that the outbreak strain is present in cattle in both countries. Because use of antibiotics in livestock can cause selection of resistant strains (7), the reported 41% rise in macrolide use in U.S. cattle from 2016 to 2017 (8) might have accelerated carriage of the outbreak strain among U.S. cattle. Avoiding the unnecessary use of antibiotics in cattle, especially those that are important for the treatment of human infections, could help prevent the spread of MDR Newport with decreased susceptibility to azithromycin. Further investigation is warranted to determine the prevalence of Newport with decreased susceptibility to azithromycin in U.S. and Mexican cattle, and to identify measures to prevent transmission among cattle.

Whole genome sequencing was valuable in linking human infections to food sources, distinguishing the MDR outbreak strain from an antibiotic-susceptible strain causing a

TABLE 2. Characteristics of four isolates from nonhuman sources closely related to the outbreak strain of *Salmonella enterica* serotype Newport — United States, June 2018–January 2019

Isolate no.*	Isolation date	Source of isolate	Notes on source	Median no. of alleles different from patient isolates (range)
1	9/6/2018	Steer (cecum)	Texas slaughter and processing facility	3 (1–7)
2	10/05/2018	Cheese [†]	Mixture of Oaxaca and queso fresco	2 (0–5)
3	11/09/2018	Beef trim	Texas slaughter and processing facility	4 (0–8)
4	3/18/2019	Boneless beef	Texas slaughter and processing facility	3 (1–7)

^{*} Isolates were within 0–2 alleles of each other by core genome multilocus sequence typing.

simultaneous outbreak, and predicting antibiotic resistance. In this outbreak, one in three patients received an antibiotic that was likely to have been ineffective. Clinicians should limit use of antibiotics for patients with an acute diarrheal illness to those with clinical indications (9), and antibiotic selection should be based on susceptibility results whenever possible. For empiric treatment of patients with suspected Newport with decreased susceptibility to azithromycin, ceftriaxone or alternative agents should be considered. To prevent infection, consumers should avoid eating soft cheese that could be made with unpasteurized milk, and when preparing beef they should use a thermometer to ensure appropriate cooking temperatures are reached: 145°F (62.8°C) for steaks and roasts followed by a 3-minute rest time, and 160°F (71.1°C) for ground beef or hamburgers (10).

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[†] One patient who did not travel to Mexico reported eating beef obtained in Mexico in addition to beef obtained in the United States

[§] One patient who traveled to Mexico reported eating Mexican-style soft cheese obtained in the United States and also Mexican-style soft cheese obtained in Mexico.

[†] Obtained from the home of a patient who consumed some of it within 7 days before illness onset; the cheese was purchased from a market in Tijuana,

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Summary

What is already known about this topic?

Decreased susceptibility to azithromycin is rare among *Salmonella* serotypes that cause human infections in the United States. If antibiotic treatment is indicated, azithromycin is recommended as an oral therapy.

What is added by this report?

During June 2018–March 2019, an outbreak caused by multi-drug-resistant *Salmonella* Newport with decreased susceptibility to azithromycin led to 255 infections and 60 hospitalizations. Infections were linked to Mexican-style soft cheese obtained in Mexico and beef obtained in the United States.

What are the implications for public health practice?

Whole genome sequencing can be used in *Salmonella* outbreak investigations for rapid prediction of antimicrobial resistance and can link cases to each other and to possible sources of infection.

References

- CDC. Outbreak of Salmonella infections linked to ground beef. Food safety alert. Atlanta, GA: US Department of Health and Human Services, CDC; 2019. https://www.cdc.gov/salmonella/newport-10-18/index.html
- CDC. Foodborne Diseases Active Surveillance Network (FoodNet)
 population survey atlas of exposure, 2006–2007. Atlanta, GA: US
 Department of Health and Human Services, CDC; 2008. https://www.cdc.gov/foodnet/surveys/foodnetexposureatlas0607_508.pdf
- González-Córdova AF, Yescas C, Ortiz-Estrada ÁM, De la Rosa-Alcaraz MLÁ, Hernández-Mendoza A, Vallejo-Cordoba B. Invited review: artisanal Mexican cheeses. J Dairy Sci 2016;99:3250–62. https://doi. org/10.3168/jds.2015-10103

- Food and Drug Administration, CDC, US Department of Agriculture. 2015 NARMS integrated report. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration, CDC; US Department of Agriculture; 2015. https://www.fda.gov/animalveterinary/national-antimicrobial-resistance-monitoring-system/2015narms-integrated-report
- Varma JK, Marcus R, Stenzel SA, et al. Highly resistant Salmonella Newport-MDRAmpC transmitted through the domestic US food supply: a FoodNet case-control study of sporadic Salmonella Newport infections, 2002–2003. J Infect Dis 2006;194:222–30. https://doi. org/10.1086/505084
- Gould LH, Mungai E, Behravesh CB. Outbreaks attributed to cheese: differences between outbreaks caused by unpasteurized and pasteurized dairy products, United States, 1998–2011. Foodborne Pathog Dis 2014;11:545–51. https://doi.org/10.1089/fpd.2013.1650
- Tang KL, Caffrey NP, Nóbrega DB, et al. Restricting the use of antibiotics in food-producing animals and its associations with antibiotic resistance in food-producing animals and human beings: a systematic review and meta-analysis. Lancet Planet Health 2017;1:e316–27. https://doi. org/10.1016/S2542-5196(17)30141-9
- Food and Drug Administration. 2017 summary report on antimicrobials sold or distributed for use in food-producing animals. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2018. https://www.fda.gov/media/119332/download
- 9. Shane AL, Mody RK, Crump JA, et al. 2017 Infectious Diseases Society of America clinical practice guidelines for the diagnosis and management of infectious diarrhea. Clin Infect Dis 2017;65:e45–80. https://doi.org/10.1093/cid/cix669
- 10. US Department of Health and Human Services. FoodSafety:gov. Keep food safe: food safety by type of food. Washington DC: US Department of Health and Human Services; 2019. https://www.foodsafety.gov/keep/types/meat/index.html

National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2018

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The Advisory Committee on Immunization Practices (ACIP) recommends routine vaccination of persons aged 11-12 years to protect against certain diseases, including human papillomavirus (HPV)-associated cancers, meningococcal disease, and pertussis (1). A booster dose of quadrivalent meningococcal conjugate vaccine (MenACWY) is recommended at age 16 years, and serogroup B meningococcal vaccine (MenB) may be administered to persons aged 16-23 years (1). To estimate vaccination coverage among adolescents in the United States, CDC analyzed data from the 2018 National Immunization Survey-Teen (NIS-Teen) which included 18,700 adolescents aged 13–17 years.* During 2017–2018, coverage with ≥1 dose of HPV vaccine increased from 65.5% to 68.1%, and the percentage of adolescents up-to-date[†] with the HPV vaccine series increased from 48.6% to 51.1%, although the increases were only observed among males. Vaccination coverage increases were also observed for ≥1 MenACWY dose (from 85.1% to 86.6%) and ≥2 MenACWY doses (from 44.3% to 50.8%). Coverage with tetanus and reduced diphtheria toxoids and acellular pertussis vaccine (Tdap) remained stable at 89%. Disparities in coverage by metropolitan statistical area (MSA)§ and health insurance status identified in previous years persisted (2). Coverage with ≥1 dose of HPV vaccine was higher among adolescents whose parents reported receiving a provider recommendation; however, prevalence of parents reporting receiving a recommendation for adolescent HPV vaccination varied by state (range = 60%–91%). Supporting providers to give strong recommendations and effectively address parental concerns remains a priority, especially in states and rural areas where provider recommendations were less commonly reported.

NIS-Teen is an annual survey that monitors vaccines received by adolescents aged 13-17 years in the 50 states, the District of Columbia, selected local areas, and U.S. territories. NIS-Teen is conducted among parents and guardians of eligible adolescents identified using a random-digit-dialed sample of cell phone numbers.** During the telephone interview, information is obtained on the sociodemographic characteristics of the teen and household, and contact information and consent to contact the teen's vaccination providers are requested. Vaccination providers identified during the interview are mailed a questionnaire requesting the vaccination history from the teen's medical record. †† Vaccination coverage estimates are based on provider-reported vaccination histories. This report presents vaccination coverage estimates for 18,700 adolescents (8,928 [48%] females and 9,772 [52%] males) aged 13-17 years with adequate provider data. §§ The overall Council of

^{*}Eligible participants were born during January 2000–February 2006. Tdap represents coverage with ≥1 Tdap dose at age ≥10 years. MenACWY represents coverage with the quadrivalent meningococcal conjugate vaccine or meningococcal-unknown type vaccine. ACIP published Category B recommendations for the use of serogroup B meningococcal vaccine (MenB) in October 2015 (https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6441a3.htm), with administration preferred at ages 16–18 years. HPV vaccination coverage represents receipt of any HPV vaccine and does not distinguish among 9-valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV) vaccines. Some adolescents might have received more than the 2 or 3 recommended HPV vaccine doses. Except as noted, coverage estimates for ≥1 and ≥2 varicella vaccine doses were obtained among adolescents with no history of varicella disease. Influenza vaccination coverage data are not included in this report but are available online at https://www.cdc.gov/flu/fluvaxview/index.htm.

[†]Adolescents were considered to be up to date with HPV vaccination if they had received ≥3 doses, or if all of the following applied: 1) they had received 2 doses; 2) the first dose was received before their 15th birthday; and 3) the difference between dates of first and second doses was ≥5 months minus 4 days, the absolute minimum interval between the first and second doses (https://www.cdc.gov/vaccines/programs/iis/cdsi.html).

MSA status was determined based on household reported city and county of residence, and was grouped into three categories: MSA principal city, MSA nonprincipal city, and non-MSA. MSA and principal city were as defined by the U.S. Census Bureau (https://www.census.gov/programs-surveys/metromicro.html). Non-MSA areas include urban populations not located within an MSA as well as completely rural areas.

[¶] Local areas that received federal Section 317 immunization funds were sampled separately: Chicago, Illinois; New York, New York; Philadelphia County, Pennsylvania; Bexar County, Texas; and Houston, Texas. Two local areas were oversampled: Hidalgo County, Texas and Tarrant County, Texas. Only one territory, Guam, was included as an estimation area in 2018.

^{**} All identified cellular-telephone households were eligible for interview. Sampling weights were adjusted for single-frame (cellular telephone), nonresponse, and noncoverage. A description of NIS-Teen single-frame survey methodology and its effect on reported vaccination estimates is available at https://www.cdc.gov/vaccines/imz-managers/coverage/teenvaxview/pubs-presentations/dual-to-single-frame-teen.html.

^{††} For the telephone samples for the states and local areas, the overall Council of American Survey Research Organizations (CASRO) response rate was 23.3%. For adolescents with completed interviews, 48.3% had adequate provider data. For Guam, the CASRO response rate was 22.4%, and 55.0% of adolescents with completed interviews had adequate provider data. In 2017, among completed interviews with adequate provider data, 17% (3,572) were from the landline sample, and 83% (17,377) were from the cell phone sample. The CASRO response rate is the product of three other rates: 1) the resolution rate (the proportion of telephone numbers that can be identified as either for business or residence); 2) the screening rate (the proportion of qualified households that complete the screening process); and 3) the cooperation rate (the proportion of contacted eligible households for which a completed interview is obtained).

^{§§} Adolescents from Guam (309) were excluded from the national estimates.

American Survey Research Organizations response rate was 23.3%, and only 48.3% of adolescents with completed interviews had adequate provider data.

Previously described NIS-Teen methodology, including methods for weighting and synthesizing provider-reported vaccination histories (https://www.cdc.gov/vaccines/imzmanagers/nis/downloads/NIS-TEEN-PUF17-DUG.pdf) was used. Beginning in 2018, NIS-Teen used a single-frame sample of cell phone lines. The landline telephone-sample frame that was used from 2006 through 2017 was dropped because of the declining number of landline-only households in the United States (https://www.cdc.gov/vaccines/imz-managers/coverage/ teenvaxview/pubs-presentations/dual-to-single-frame-teen. html). Data were weighted and analyzed to account for the complex sampling design. T-tests were used to assess vaccination coverage differences by survey year (2018 compared with 2017) and between demographic subgroups. P-values < 0.05 were considered statistically significant. SAS-callable SUDAAN (version 11; SAS Institute) was used to conduct all analyses.

National Vaccination Coverage

In 2018, 51.1% of adolescents aged 13-17 years were up to date with the HPV vaccine series, and 68.1% had received ≥1 dose of HPV vaccine (Table 1) (Figure). During 2017-2018, the increase in HPV vaccination coverage was attributable to increases among males only (increase of 4.4 percentage points in males who were up to date versus 0.6 in females). Coverage with ≥1 MenACWY dose increased by 1.5 percentage points to 86.6%. Among persons aged 17 years, coverage with ≥2 MenACWY doses increased by 6.5 percentage points to 50.8%. Coverage with ≥1 dose of MenB among persons aged 17 years was 17.2% (95% confidence interval = 14.9%-19.9%). No significant increases were observed for coverage with ≥3 hepatitis B doses; ≥2 measles, mumps, and rubella vaccine doses; and ≥1 and ≥2 varicella vaccine doses among adolescents without a history of varicella disease (Table 1).

Vaccination Coverage by Selected Characteristics

Coverage for all measures of HPV and MenACWY vaccination and ≥2 varicella vaccine doses among adolescents without a history of varicella disease were lower among adolescents living in non-MSA areas than in those living in MSA principal cities (Table 2). The largest differences were in HPV up-to-date status (15.4 percentage point difference) and ≥2-dose MenACWY coverage (19.7 percentage point difference). Coverage differences between adolescents living in MSA nonprincipal cities and MSA principal cities were observed for HPV vaccination measures (5.3 and 7.0 percentage point differences for receipt of ≥1 dose and being up-to-date, respectively)

and ≥3 hepatitis B doses (1.7 percentage points). Compared with adolescents with private health insurance, those with Medicaid had higher HPV vaccination coverage (8.8 and 5.5 percentage points higher for receipt of ≥1 dose and being upto-date, respectively) (Table 2). Uninsured adolescents had lower vaccination coverage, with differences ranging from 4.4 percentage points (≥1 varicella vaccine dose) to 18.7 percentage points (≥2 MenACWY doses) lower than did adolescents with private insurance. Vaccination coverage estimates also differed by race/ethnicity (Supplementary Table 1, https:// stacks.cdc.gov/view/cdc/80676); poverty level (Supplementary Table 2, https://stacks.cdc.gov/view/cdc/80677); and jurisdiction (Supplementary Table 3, https://stacks.cdc.gov/view/ cdc/80678). During 2014–2018, ≥1dose-HPV vaccination coverage increased an average of 4.4 percentage points per year nationally. (Supplementary Table 4, https://stacks.cdc. gov/view/cdc/80679).

Provider Recommendation for HPV Vaccination

Overall, 77.5% of parents reported receiving a provider recommendation for adolescent HPV vaccination; prevalence varied by state, ranging from 59.5% in Mississippi to 90.7% in Massachusetts (Supplementary Figure, https://stacks.cdc.gov/view/cdc/80682) (Supplementary Table 5, https://stacks.cdc.gov/view/cdc/80680). Nationally, ≥1-dose HPV vaccination coverage was higher among adolescents whose parents reported receiving a provider recommendation (74.7%) than among those whose parents reported not receiving a provider recommendation (46.7%) (Supplementary Table 5, https://stacks.cdc.gov/view/cdc/80680). Fewer parents living in non-MSA areas reported receiving a provider recommendation than did those living in MSA principal cities (70.3% versus 77.4%) (Supplementary Table 6, https://stacks.cdc.gov/view/cdc/80681).

Discussion

In 2018, U.S. adolescent vaccination coverage with ≥1 and ≥2 doses of MenACWY, ≥1 dose of HPV vaccine and being up-to-date with HPV vaccination continued to improve. Coverage with ≥1 Tdap dose remains high but appears to have stabilized. Although HPV vaccination coverage improved, increases among all adolescents were modest compared with increases in previous years and were observed only among males. Since 2011, ¶ coverage has increased gradually among

⁵⁵ ACIP recommended a 3-dose series of HPV vaccine for girls aged 11 to 12 years in 2006 (https://www.cdc.gov/Mmwr/Preview/Mmwrhtml/rr5602a1. htm) and for boys in 2011 (https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6050a3.htm). In 2016, the recommendation was revised to a 2-dose series for immunocompetent adolescents beginning the series before their 15th birthday with appropriate spacing between doses. All other persons are recommended to complete a 3 dose vaccine series (https://www.cdc.gov/mmwr/volumes/65/wr/mm6549a5.htm).

TABLE 1. Estimated coverage with selected vaccines and doses among adolescents aged 13–17* years, by age at interview — National Immunization Survey–Teen (NIS-Teen), United States, 2018

		Age at i	nterview (yrs), % (9	5% CI)†		Tot	al
	13	14	15	16	17	2018	2017
Vaccine	(n = 3,852)	(n = 3,875)	(n = 3,741)	(n = 3,751)	(n = 3,481)	(n = 18,700)	(n = 20,949)
Tdap§ ≥1 dose	87.1 (85.0–89.0)	87.7 (85.4–89.7)	89.7 (87.8–91.4)	89.0 (87.1–90.6)	91.0 (89.5–92.4) [¶]	88.9 (88.0–89.7)	88.7 (87.8–89.6)
MenACWY**							
≥1 dose	86.3 (84.2-88.1)	86.2 (84.0-88.1)	86.1 (83.7-88.2)	86.3 (84.0-88.3)	88.1 (86.3-89.6)	86.6 (85.6-87.5)††	85.1 (84.2-86.1)
≥2 doses ^{§§}	NA	NA	NA	NA	50.8 (47.7-53.8)	50.8 (47.7–53.8)††	44.3 (41.4–47.2)
HPV ^{¶¶} vaccine							
All adolescents							
UTD***	39.9 (37.0-42.9)	50.3 (47.3-53.2) [¶]	54.0 (51.0-56.9) [¶]	54.5 (51.5-57.5) [¶]	57.5 (54.4-60.5) [¶]	51.1 (49.8–52.5)††	48.6 (47.3-49.9)
≥1 dose	62.6 (59.7–65.4)	66.9 (64.1–69.6) [¶]	69.7 (66.9–72.3) [¶]	71.2 (68.5–73.8) [¶]	70.1 (67.3–72.8) [¶]	68.1 (66.8–69.3)††	65.5 (64.3-66.7)
Females							
UTD	38.9 (35.0-42.9)	52.7 (48.5-56.8) [¶]	54.7 (50.4–59.0) [¶]	57.5 (53.3–61.6) [¶]	66.0 (61.8–70.1) [¶]	53.7 (51.8-55.6)	53.1 (51.2-55.0)
≥1 dose	61.1 (56.9–65.2)	68.6 (64.4–72.5) [¶]	70.7 (66.5–74.5) [¶]	73.5 (69.8–76.8) [¶]	76.3 (72.2–80.0) [¶]	69.9 (68.1–71.6)	68.6 (66.9–70.2)
Males							
UTD	40.9 (36.5-45.3)	47.7 (43.6-51.8)¶	53.2 (49.1–57.3) [¶]	51.8 (47.5–56.1) [¶]	50.0 (45.7–54.3) [¶]	48.7 (46.8–50.6)††	44.3 (42.6-46.0)
≥1 dose	64.0 (59.9–67.9)	65.1 (61.3–68.7)	68.7 (65.0–72.1)	69.2 (65.2–73.0)	64.7 (60.7–68.5)	66.3 (64.6–68.0)††	62.6 (60.9–64.2)
MenB≥1 dose ^{†††}	NA	NA	NA	NA	17.2 (14.9–19.9)	17.2 (14.9–19.9)	14.5 (12.3–17.1)
MMR ≥2 doses	93.5 (92.1–94.7)	93.0 (91.6–94.2)	91.8 (89.9–93.3)	90.5 (88.4–92.2)¶	90.9 (89.2–92.4)¶	91.9 (91.2–92.6)	92.1 (91.3–92.8)
Hepatitis B vaccine ≥3 doses	93.1 (91.5–94.5)	93.0 (91.5–94.3)	91.6 (89.1–93.5)	91.1 (89.3–92.6)	91.8 (90.1–93.2)	92.1 (91.3–92.8)	91.9 (91.1–92.6)
Varicella vaccine							
History of varicella disease ^{§§§}	9.8 (8.1–11.9)	10.3 (8.5–12.4)	11.8 (10.0–13.9)	12.4 (10.7–14.3)	15.0 (13.2–17.1) [¶]	11.9 (11.0–12.7)††	13.2 (12.3–14.2)
No history of varice	lla disease						
≥1 dose vaccine	95.4 (94.2-96.5)	95.4 (94.2-96.3)	94.1 (92.1-95.6)	94.3 (92.7-95.5)	95.2 (93.9-96.3)	94.9 (94.3-95.4)	95.5 (94.8-96.1)
≥2 doses vaccine	92.1 (90.5-93.4)	91.3 (89.6-92.8)	89.8 (87.4-91.8)	86.6 (84.3–88.7) [¶]	87.9 (85.4–90.1) [¶]	89.6 (88.7-90.4)	88.6 (87.6-89.5)
History of varicella or ≥2 vaccine doses	92.9 (91.4–94.1)	92.2 (90.6–93.5)	91.0 (88.9–92.7)	88.3 (86.2–90.1) [¶]	89.7 (87.5–91.6) [¶]	90.8 (90.0–91.6)	90.1 (89.3–90.9)

Abbreviations: CI = confidence interval; HPV = human papillomavirus; MenACWY = quadrivalent meningococcal conjugate vaccine; MenB = serogroup B meningococcal vaccine; MMR = measles, mumps, and rubella vaccine; NA = not applicable; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine; UTD = up-to-date.

females and more rapidly among males. However, only approximately half of adolescents have been fully vaccinated for HPV.

HPV vaccination coverage was higher among adolescents whose parent reported receiving a provider recommendation. Thus, the provider recommendation continues to be a strong predictor of HPV vaccination (3,4). However, even when a provider recommendation was given, only 75% accepted the vaccine, suggesting that there are other reasons adolescents are not being vaccinated. Equipping providers with the tools they need to give strong recommendations

that emphasize the importance of HPV vaccination in preventing cancer and effectively address parental concerns is a priority, especially in states where provider recommendations were less commonly reported. Resources on the importance of HPV vaccination and videos demonstrating how to give a recommendation are available to facilitate discussion between providers, teens, and their parents (https://www.cdc.gov/vaccines/vpd/hpv/hcp/resources.html).

Coverage disparities persisted for some vaccines by MSA status. The disparity in HPV vaccination coverage by MSA

^{*} Adolescents (N = 18,700) in the 2018 NIS-Teen were born January 2000-February 2006.

[†] Estimates with 95% CIs >20 might be unreliable.

[§] Includes percentages receiving Tdap vaccine at age ≥10 years.

Statistically significant difference (p<0.05) in estimated vaccination coverage by age; reference group was adolescents aged 13 years.

^{**} Includes percentages receiving MenACWY or meningococcal-unknown type vaccine.

 $^{^{\}dagger\dagger}$ Statistically significant difference (p<0.05) compared with 2017 NIS-Teen estimates.

^{§§ ≥2} doses of MenACWY or meningococcal-unknown type vaccine. Calculated only among adolescents who were aged 17 years at interview. Does not include adolescents who received 1 dose of MenACWY vaccine at age ≥16 years.

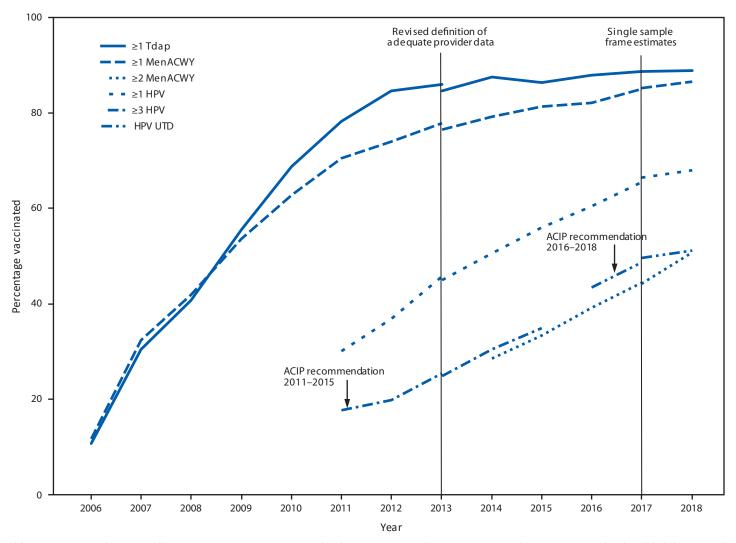
¹¹ HPV vaccine, 9-valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV). Percentages are reported among females and males combined (N = 18,700) and for females only (N = 8,928) and males only (N = 9,772).

^{***} HPV UTD includes those with ≥3 doses, and those with 2 doses when the first HPV vaccine dose was initiated at age <15 years, and there was at least 5 months minus 4 days between the first and second dose. This update to the HPV recommendation occurred in December 2016 (https://www.cdc.gov/mmwr/volumes/65/wr/mm6549a5.htm).

^{††† ≥1} dose of MenB. Calculated only among adolescents aged 17 years at interview. Administered based on individual clinical decision.

^{§§§} By parent/guardian report or provider records.

FIGURE. Estimated vaccination coverage with selected vaccines and doses* among adolescents aged 13–17 years, by survey year and Advisory Committee on Immunization Practices (ACIP) recommendations† — National Immunization Survey–Teen (NIS-Teen), §,¶ United States, 2006–2018



Abbreviations: HPV = human papillomavirus vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine; UTD = up-to-date.

status is not well understood; however, the lower prevalence of provider recommendations in non-MSA areas might be a factor. In one study, parents and guardians in the rural South indicated that they did not have enough information on the vaccine or its purpose (5). Efforts to ensure that rural health care providers have the resources and training necessary to educate parents and guardians about the benefits of HPV vaccination as a cancer prevention tool might increase the number of adolescents protected against diseases caused by HPV.

^{* ≥1} dose Tdap at or after age 10 years; ≥1 dose MenACWY or meningococcal-unknown type vaccine; ≥2 doses MenACWY or meningococcal-unknown type vaccine, calculated only among adolescents aged 17 years at time of interview. Does not include adolescents who received their first and only dose of MenACWY at or after age 16 years; HPV vaccine, nine-valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV). HPV UTD includes those with ≥3 doses and those with 2 doses when the first HPV vaccine dose was initiated before age 15 years and at least 5 months minus 4 days elapsed between the first and second dose.

[†] ACIP revised the recommended HPV vaccination schedule in late 2016. The recommendation changed from a 3-dose to 2-dose series with appropriate spacing between receipt of the first and second dose for immunocompetent adolescents initiating the series before the 15th birthday. Three doses are still recommended for adolescents initiating the series between the ages of 15 and 26 years. Because of the change in recommendation, the graph includes estimates for ≥3 doses HPV from 2011 to 2015 and the HPV UTD estimate from 2016 to 2018. The routine ACIP recommendation for HPV vaccination was made for females in 2006 and for males in 2011. Because HPV vaccination was not recommended for males until 2011, coverage for all adolescents was not measured before that year.

[§] NIS-Teen implemented a revised adequate provider data definition (APD) in 2014 and retrospectively applied the revised APD definition to 2013 data. Estimates using different APD definitions might not be directly comparable.

NIS-Teen moved from a dual landline and cell phone sampling frame to a single cell phone sample frame in 2018, and estimates using 2017 data were calculated two ways, using the dual frame and retrospectively using the single cell phone sampling frame.

TABLE 2. Estimated vaccination coverage with selected vaccines and doses among adolescents* aged 13–17 years by metropolitan statistical area[†] and health insurance status[§] — National Immunization Survey–Teen (NIS-Teen), United States, 2018

		MSA % (95% CI)¶		Health insurance status % (95% CI)¶				
	Non-MSA	MSA nonprincipal city	MSA principal city	Private insurance only	Any Medicaid	Other insurance	Uninsured	
Vaccine	(n = 3,593)	(n = 7,543)	(n = 7,564)	(n = 10,404)	(n = 5,999)	(n = 1,516)	(n = 781)	
Tdap** ≥1 dose	86.8 (84.8–88.5)	89.7 (88.4–90.8)	88.6 (87.1–89.9)	90.1 (89.0–91.2)	88.2 (86.6–89.6)††	85.6 (82.3–88.3)††	85.1 (80.7–88.6)††	
MenACWY ^{§§}								
≥1 dose	79.5 (77.3-81.6)††		86.5 (84.7-88.0)	87.6 (86.4-88.8)	86.5 (84.8-88.0)	84.3 (81.1-87.0)††	78.3 (72.7-83.0)††	
≥2 doses ^{¶¶}	34.6 (28.5–41.2) ^{††}	51.5 (46.7–56.2)	54.3 (49.7–58.9)	52.8 (48.6-56.9)	52.4 (46.9-57.8)	38.6 (30.0-48.0)††	34.1 (21.6–49.4) ^{††}	
HPV*** vaccine								
UTD ^{†††}	40.7 (38.1-43.5)††	49.1 (47.1–51.0)††	56.1 (53.9-58.3)	50.2 (48.4-52.0)	55.7 (53.4–58.1)††	45.1 (40.9–49.3)††	35.5 (30.1–41.4)††	
≥1 dose	59.5 (56.8–62.2) ^{††}	66.6 (64.8–68.4)††	71.9 (69.8–73.9)	65.6 (63.8–67.3)	74.4 (72.3–76.3) ^{††}	62.6 (58.5–66.5)	56.2 (50.1–62.2)††	
MMR ≥2 doses	90.1 (88.1–91.8)	92.3 (91.2–93.2)	92.0 (90.8–93.1)	92.8 (91.9–93.6)	92.0 (90.6–93.1)	90.1 (87.3–92.3)††	84.2 (78.6–88.5)††	
Hepatitis B ≥3 vaccine doses	90.7 (88.8–92.4)	93.1 (92.1–94.0)††	91.4 (89.9–92.6)	93.0 (91.9–93.9)	92.1 (90.8–93.3)	90.5 (87.8–92.6)	84.1 (78.5–88.4)††	
Varicella vaccine								
History of varicella ^{§§§}	15.0 (13.1–17.0)††	10.6 (9.6–11.8)	12.4 (10.9–14.0)	9.8 (8.8–10.9)	13.4 (11.8–15.1)††	13.8 (11.1–17.1)††	20.4 (16.2–25.4)††	
Among adolescents	with no history of v	aricella disease						
≥1 varicella vaccine dose	93.4 (91.5–94.9)	95.0 (94.1–95.8)	95.1 (94.0–96.0)	95.7 (94.9–96.3)	94.4 (93.2–95.4)	93.3 (90.7–95.1)††	91.3 (86.0–94.7)††	
≥2 varicella vaccine doses	86.4 (84.1–88.4)††	89.8 (88.3–91.1)	90.2 (88.8–91.4)	90.5 (89.3–91.7)	89.4 (87.8–90.8)	86.7 (83.4–89.4)††	83.8 (77.6–88.5)††	
History of varicella or ≥2 vaccine doses	88.5 (86.5–90.2)††	90.9 (89.6–92.0)	91.4 (90.1–92.5)	91.5 (90.3–92.5)	90.8 (89.4–92.1)	88.5 (85.6–90.9)††	87.1 (82.0–90.9)	

Abbreviations: CI = confidence interval; HPV = human papillomavirus; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella vaccine; MSA= metropolitan statistical area; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine; UTD = up-to-date.

Vaccination coverage was significantly lower among uninsured adolescents than among those with private insurance. Adolescents without health insurance are eligible to receive vaccines through the Vaccines for Children (VFC) program.***
Lack of parental awareness of (6) and misconceptions about the

program, including that it is only for infants and younger children, might serve as barriers (7). Increasing parental awareness and knowledge of the VFC program should improve vaccination coverage among uninsured adolescents. Providers can assist by ensuring that their health care practice routinely screen patients for eligibility and counsel families about the VFC program.

The findings in this report are subject to at least seven limitations. First, the overall Council of American Survey Research Organizations response rate was low, and fewer than half of adolescents with completed interviews had adequate provider data. Second, bias in estimates might remain even after adjustment for household and provider nonresponse and

^{*} Adolescents (N = 18,700) in the 2018 NIS-Teen were born January 2000–February 2006.

[†] MSA status was determined based on household-reported county of residence, and was grouped into three categories: MSA principal city, MSA nonprincipal city, and non-MSA. MSA and principal city were as defined by the U.S. Census Bureau (https://www.census.gov/programs-surveys/metro-micro.html). Non-MSA areas include urban populations not located within an MSA as well as completely rural areas.

[§] Adolescents' health insurance status was reported by parent or guardian. "Other insurance" includes the Children's Health Insurance Program, military insurance, Indian Health Service, and any other type of health insurance not mentioned elsewhere.

 $[\]P$ Estimates with CIs >20 might be unreliable.

^{**} Includes percentages receiving Tdap vaccine at age ≥10 years.

^{††} Statistically significant difference (p<0.05) in estimated vaccination coverage by MSA or health insurance status. The referent groups were adolescents living in MSA principal city areas and adolescents with private insurance only, respectively.

^{§§} Includes percentages receiving MenACWY and meningococcal-unknown type vaccine.

^{¶¶ ≥2} doses of MenACWY or meningococcal-unknown type vaccine. Calculated only among adolescents aged 17 years at interview. Does not include adolescents who received 1 dose of MenACWY vaccine at age ≥16 years.

^{***} HPV vaccine, nine-valent (9vHPV), quadrivalent (4vHPV), or bivalent (2vHPV) in females and males combined.

^{†††} HPV UTD includes those with ≥3 doses, and those with 2 doses when the first HPV vaccine dose was initiated at age <15 years, and there was at least 5 months minus 4 days between the first and second dose. This update to the HPV recommendation occurred in December 2016 (https://www.cdc.gov/mmwr/volumes/65/wr/mm6549a5.htm).

^{§§§} By parent/guardian report or provider records.

^{***} Children and adolescents aged ≤18 years who are Medicaid-eligible, uninsured, or American Indian/Alaska Native (as defined by the Indian Health Care Improvement Act) are eligible to receive vaccines from providers through the VFC program. Children and adolescents categorized as "underinsured" (because their health plans do not include coverage for recommended vaccinations) are eligible to receive VFC vaccines if they are served by a rural health clinic or federally qualified health center or under an approved deputization agreement. (https://www.cdc.gov/vaccines/programs/vfc/providers/eligibility.html)

Summary

What is already known about this topic?

Vaccines are recommended for adolescents to prevent diphtheria, pertussis, tetanus, meningococcal disease, and cancers caused by human papillomavirus (HPV).

What is added by this report?

In 2018, adolescent vaccination coverage in the United States continued to improve for meningococcal and HPV vaccines (primarily from increases among boys) and remains high for tetanus and reduced diphtheria toxoids and acellular pertussis vaccine. Adolescents whose parents reported having received a provider recommendation were more likely to have received HPV vaccination compared with adolescents whose parents did not report a provider recommendation.

What are the implications for public health care?

Providing parents and guardians with information and strong, high-quality recommendations are valuable tools for improving HPV vaccination and preventing HPV infection and diseases caused by HPV, including cancers.

landline-only and phoneless households.††† Third, changes in estimates of vaccination coverage from 2017 to 2018 should be interpreted with caution, given the transition from dual landline- and cellular- to single-cellular telephone-sampling frame in 2018. Fourth, estimates stratified by jurisdiction might be unreliable because of small sample sizes. Fifth, multiple statistical tests were conducted, and a small number might be significant because of chance alone. Sixth, coverage with ≥2 doses of MenACWY and ≥1 dose of MenB might be underestimated because MenB and second MenACWY dose may be administered at age >17 years (1), and NIS-Teen includes adolescents aged 13–17 years. Finally, the "provider recommendation" variable is based on parental report and thus subject to recall bias.

It is encouraging that HPV vaccination coverage among boys continues to increase; however, the lack of an increase among girls is concerning. In the United States, an estimated 34,800 cases of cancer caused by HPV occur each year; 32,100 (92%), including 59% among women, would be preventable

by the 9-valent HPV vaccine (8). Although, HPV vaccination has resulted in large declines in the prevalence of vaccine type HPV infections among adolescent girls and young adults (9), as well as decreases in cervical precancers (10), continuing to improve HPV vaccination coverage for all adolescents, male and female, will ensure they are protected from HPV infection and diseases caused by HPV, including cancers.

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References

- Robinson CL, Bernstein H, Romero JR, Szilagyi P. Advisory Committee on Immunization Practices recommended immunization schedule for children and adolescents aged 18 years or younger—United States, 2019. MMWR Morb Mortal Wkly Rep 2019;68:112–4. https://doi. org/10.15585/mmwr.mm6805a4
- Walker TY, Elam-Evans LD, Yankey D, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 years—United States, 2017. MMWR Morb Mortal Wkly Rep 2018;67:909–17. https://doi.org/10.15585/mmwr.mm6733a1
- 3. Kornides ML, McRee AL, Gilkey MB. Parents who decline HPV vaccination: who later accepts and why? Acad Pediatr 2018;18(2S):S37–43. https://doi.org/10.1016/j.acap.2017.06.008
- Gilkey MB, Calo WA, Moss JL, Shah PD, Marciniak MW, Brewer NT. Provider communication and HPV vaccination: the impact of recommendation quality. Vaccine 2016;34:1187–92. https://doi. org/10.1016/j.vaccine.2016.01.023
- Boyd ED, Phillips JM, Schoenberger YM, Simpson T. Barriers and facilitators to HPV vaccination among rural Alabama adolescents and their caregivers. Vaccine 2018;36:4126–33. https://doi.org/10.1016/j. vaccine.2018.04.085
- Radecki Breitkopf C, Finney Rutten LJ, Findley V, et al. Awareness and knowledge of human papillomavirus (HPV), HPV-related cancers, and HPV vaccines in an uninsured adult clinic population. Cancer Med 2016;5:3346–52. https://doi.org/10.1002/cam4.933
- Bernstein HH, Bocchini JA Jr; Committee on Infectious Diseases. The need to optimize adolescent immunization. Pediatrics 2017;139:e20164186. https://doi.org/10.1542/peds.2016-4186
- 8. Senkomago V, Henley J, Thomas CC, Mix JM, Markowitz LE, Saraiya M. Human papillomavirus—attributable cancers—United States, 2012–2016. MMWR Morb Mortal Wkly Rep 2019;68:724–8.
- McClung NM, Lewis RM, Gargano JW, Querec T, Unger ER, Markowitz LE. Declines in vaccine-type human papillomavirus prevalence in females across racial/ethnic groups: data from a national survey. J Adolesc Health. In press 2019.
- Gargano JW, Park IU, Griffin MR, et al.; HPV-IMPACT Working Group. Trends in high-grade cervical lesions and cervical cancer screening in 5 states, 2008–2015. Clin Infect Dis 2019;68:1282–91. https://doi. org/10.1093/cid/ciy707

^{†††} In a sensitivity analysis of 2013 estimates using comparisons to vaccination data collected from a sample of National Health Interview Survey (NHIS), respondents indicated that estimated coverage with ≥1 Tdap dose, ≥1 MenACWY dose, and ≥1 HPV dose (females) were within two percentage points of true estimates (https://www.cdc.gov/vaccines/imz-managers/nis/downloads/NIS-TEEN-PUF17-DUG.pdf). These differences were within the margin of plausible error of the model. The model accounted for three types of error: incomplete sample frame (e.g., exclusion of teens in households with no type of telephone service); nonresponse bias; and incomplete ascertainment of vaccination status by NIS-Teen provider record check.

Human Papillomavirus-Attributable Cancers — United States, 2012-2016

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Human papillomavirus (HPV) causes nearly all cervical cancers and some cancers of the vagina, vulva, penis, anus, and oropharynx (1).* Most HPV infections are asymptomatic and clear spontaneously within 1 to 2 years; however, persistent infection with oncogenic HPV types can lead to development of precancer or cancer (2). In the United States, the 9-valent HPV vaccine (9vHPV) is available to protect against oncogenic HPV types 16, 18, 31, 33, 45, 52, and 58 as well as nononcogenic types 6 and 11 that cause genital warts. CDC analyzed data from the U.S. Cancer Statistics (USCS)[†] to assess the incidence of HPV-associated cancers and to estimate the annual number of cancers caused by HPV, overall and by state, during 2012–2016 (3,4). An average of 43,999 HPV-associated cancers were reported annually, and an estimated 34,800 (79%) of those cancers were attributable to HPV. Of these 34,800 cancers, an estimated 32,100 (92%) were attributable to the types targeted by 9vHPV, with 19,000 occurring among females and 13,100 among males. The most common were cervical (9,700) and oropharyngeal cancers (12,600). The number of cancers estimated to be attributable to the types targeted by 9vHPV ranged by state from 40 to 3,270 per year. HPV vaccination is an important strategy that could prevent these cancers, but during 2018, only half of adolescents were up to date on HPV vaccination (5). These surveillance data from population-based cancer registries can be used to inform the planning for, and monitor the long-term impact of, HPV vaccination and cancer screening efforts nationally and within states.

CDC analyzed cancer incidence data from USCS, which includes cancer registry data from CDC's National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results Program. Data from the District of Columbia (DC) and all states met high-quality data criteria for 2012–2016, covering 100% of the U.S. population. Invasive cancer cases were classified by anatomic site using the *International Classification of Diseases for Oncology, Third Edition* (ICD-O–3)§ (Supplementary Table, https://stacks.cdc.gov/view/cdc/80649) and were histologically confirmed. Cancers are not tested for HPV in most cancer registries; therefore, HPV-associated cancers were defined as invasive cancers at anatomic sites with cell types in which HPV DNA frequently is found, including carcinomas of the cervix

HPV-associated cancer incidence rates were calculated using reported cases as the numerator and modification of annual county population estimates as the denominator,** standardized to the 2000 U.S. standard population and expressed as cases per 100,000 persons. The USCS data, including the numbers and rates of HPV-associated cancers, are available to the public through the USCS Data Visualizations Tool.^{††} To estimate the number of HPV-attributable cancers (cancers that are probably caused by HPV), the average annual number of HPV-associated cancers was multiplied by the percentage of each cancer type found to be attributable to HPV in a large U.S. study using HPV genotyping (3). Estimates of HPV-attributable cancers were rounded to the nearest 100 for national data and to the nearest 10 for state-level data. Cancers were grouped as those attributable to the types targeted by 9vHPV, to other HPV types, and HPV-negative cancers (those that occur at anatomic sites in which HPV-associated cancers are often found but do not have detectable HPV DNA). The percentage of HPV-negative cancers was calculated as the difference between the total HPV-associated cancers and the HPV-attributable estimates.

During 2012–2016, an average of 43,999 HPV-associated cancers (12.2 per 100,000 persons) were reported annually, and an estimated 79% (34,800) of these cancers were attributable to HPV (Table 1). Of these cancers, an estimated 32,100 (92%) were attributable to the types targeted by 9vHPV. The largest number were oropharyngeal cancer (12,600), followed by cervical (9,700), anal (6,000), vulvar (2,500), penile (700), and vaginal cancers (600). Among cancers estimated to be attributable to the types targeted by 9vHPV, 19,000 (59%) occurred among females, and 13,100 (41%) occurred among males.

⁽i.e., squamous cell cancers [SCC], adenocarcinomas, and other carcinomas) and SCC of the vulva, vagina, penis, oropharynx, and anus (including rectal SCC) (4). Oropharyngeal SCC included squamous cell cancer types at the base of tongue, pharyngeal tonsils, anterior and posterior tonsillar pillars, glossotonsillar sulci, anterior surface of soft palate and uvula, and lateral and posterior pharyngeal walls. Anal SCC also included rectal SCCs because they are biologically similar and might be misclassified. §

^{*} https://publications.iarc.fr/108.

[†] https://www.cdc.gov/cancer/uscs.

http://www.iacr.com.fr/index.php?option=com_content&view=category&layout=blog&id=100&Itemid=577.

https://journals.lww.com/jlgtd/Fulltext/2019/04001/2019_ASCCP_Oral_ Presentation_Abstracts.2.aspx.

^{**} https://seer.cancer.gov/popdata.

^{††} https://www.cdc.gov/cancer/dataviz, June 2019.

TABLE 1. Average annual number and rate of human papillomavirus (HPV)—associated cancers and estimated percentage and annual number of cancers attributable to HPV, by HPV type, cancer type, and sex — United States,* 2012–2016

	Reported HPV-ass	ociated cancers†	Estimated no.§ (%) of cancers attributable to HPV types¶				
Cancer type	Total no.**	Rate ^{††}	9vHPV-targeted	Other HPV	HPV-negative		
Cervix	12,015	7.2	9,700 (81)	1,200 (10)	1,100 (9)		
Vagina	862	0.4	600 (73)	0 (2)	300 (25)		
Vulva	4,009	2.1	2,500 (63)	300 (6)	1,200 (31)		
Penis	1,303	0.8	700 (57)	100 (6)	500 (37)		
Anus	6,810	1.8	6,000 (88)	200 (3)	600 (9)		
Female	4,539	2.3	4,100 (90)	100 (2)	300 (8)		
Male	2,270	1.3	1,900 (83)	100 (6)	300 (11)		
Oropharynx	19,000	4.9	12,600 (66)	900 (5)	5,500 (29)		
Female	3,460	1.7	2,100 (60)	100 (3)	1,300 (37)		
Male	15,540	8.5	10,500 (68)	800 (5)	4,200 (28)		
Total	43,999	12.2	32,100 (73)	2,700 (6)	9,200 (21)		
Female	24,886	13.7	19,000 (76)	1,700 (7)	4,200 (17)		
Male	19,113	10.6	13,100 (69)	1,000 (5)	5,000 (26)		

Abbreviations: 9vHPV = 9-valent HPV vaccine; ICD-O-3 = International Classification of Diseases for Oncology, Third Edition.

The annual number of cancers estimated to be attributable to the types targeted by 9vHPV ranged by state from 40 (Wyoming) to 3,270 (California) (Table 2). Oropharyngeal cancer was the most common cancer estimated to be attributable to types targeted by 9vHPV in most states, except in Texas, where cervical cancer was most common and in Alaska, DC, New Mexico, and New York, where estimates of oropharyngeal and cervical cancers attributable to the types targeted by 9vHPV were the same.

Discussion

Each year during 2012–2016, an estimated average of 34,800 HPV-attributable cancers were diagnosed in the United States, and 92% (32,100) were attributable to the HPV types targeted by 9vHPV. Previous annual estimates of cancers attributable to the types targeted by 9vHPV were 28,500 for 2008–2012 (4), 30,000 for 2010–2014, §§ and 31,200 for 2011–2015. §§ The higher estimates in more recent years are, in part, due to an

aging and growing population and increases in oropharyngeal, anal, and vulvar cancers (6).

HPV vaccination is an important component of cancer prevention, yet only about half of adolescents are up to date on this vaccine (5). The Advisory Committee on Immunization Practices recommends routine HPV vaccination at age 11-12 years and catch-up HPV vaccination for all persons through age 26 years. Catch-up vaccination is not recommended for all adults aged >26 years because the benefit of HPV vaccination decreases in older age groups; however, vaccination based on shared clinical decision-making can be considered for some persons aged 27-45 years who are not adequately vaccinated (7). In 2018, HPV vaccination coverage varied by state, and no state met the Healthy People 2020 objective for HPV vaccination (receipt of 2 or 3 doses of HPV vaccine by 80% of adolescents aged 13-15 years).*** State efforts to meet the Healthy People 2020 objective for HPV vaccination could reduce geographic disparities in HPVassociated cancer incidence in the future.

^{*} Compiled from population-based cancer registries that participate in the CDC National Program of Cancer Registries, and/or the National Cancer Institute's Surveillance, Epidemiology, and End Results Program and meet the criteria for high data quality for all years during 2012–2016, covering 100% of the U.S. population.

[†] HPV-associated cancers were defined as invasive cancers at anatomic sites with cell types in which HPV DNA frequently is found. All cancers were histologically confirmed. Cervical cancers (ICD-O-3 site codes C53.0–C53.9) are limited to carcinomas (ICD-O-3 histology codes 8010–8671, 8940–8941). Vaginal (ICD-O-3 site code C52.9), vulvar (ICD-O-3 site codes C51.0–C51.9), penile (ICD-O-3 site codes C60.0–60.9), anal (ICD-O-3 site codes C20.9, C21.0–C21.9) and oropharyngeal (ICD-O-3 site codes C01.9, C02.4, C02.8, C05.1, C05.2, C09.0, C09.1, C09.8, C09.9, C10.0, C10.1, C10.2, C10.3, C10.4, C10.8, C10.9, C14.0, C14.2, and C14.8) cancer sites are limited to squamous cell carcinomas (ICD-O-3 histology codes 8050–8084, 8120–8131).

[§] HPV-attributable cancers are cancers that are probably caused by HPV (https://academic.oup.com/jnci/article/107/6/djv086/872092). Estimates for attributable fraction were based on studies that used population-based data from cancer tissue studies to estimate the percentage of those cancers probably caused by HPV. The estimated number of cancers attributable to HPV was calculated by multiplying the number of reported HPV-associated cancer cases by the percentage of each cancer type attributable to HPV. The total of HPV-attributable cancers is the sum of cancers attributable to types included in the 9vHPV and cancers attributable to other HPV types (e.g. 32,100 + 2,700 = 34,800). Estimated counts were rounded to the nearest 100 (counts <100 are not displayed) and might not sum to total because of rounding.

^{¶ &}quot;9vHPV-targeted" types include oncogenic HPV types 16, 18, 31, 33, 45, 52, and 58. "Other HPV" includes other oncogenic HPV types. "HPV-negative" cancers are those that occur at anatomic sites in which HPV-associated cancers are often found, but HPV DNA was not detected.

^{**} The total reported count is the annual count averaged over the 5-year period and might not sum to total because of rounding.

^{††} Rates are per 100,000 persons; age-adjusted to the 2000 U.S. standard population.

^{\$\}forall https://www.cdc.gov/cancer/hpv/pdf/USCS-DataBrief-No1-December2017-508.pdf.

¹⁵ https://www.cdc.gov/cancer/hpv/pdf/USCS-DataBrief-No4-August2018-508.pdf.

^{***} https://www.cdc.gov/vaccines/imz-managers/coverage/teenvaxview/data-reports/hp2020/index.html.

TABLE 2. Estimated annual number of human papillomavirus (HPV)-attributable cancers,* by cancer type,† HPV type,§ and state — United States,¶ 2012–2016

	Estimated no.**								
	All cancers			Oropharyn	x (male an	d female)		Cervix	
State	9vHPV-targeted	Other HPV	HPV-negative	9vHPV-targeted	Other HPV	HPV-negative	9vHPV-targeted	Other HPV	HPV-negative
Alabama	540	40	160	220	10	100	170	20	20
Alaska	60	<10	20	20	<10	10	20	<10	<10
Arizona	530	40	150	220	10	100	160	20	20
Arkansas	360	30	100	140	<10	60	120	10	10
California	3,270	260	870	1,170	80	510	1,120	130	130
Colorado	460	40	130	190	10	80	130	20	20
Connecticut	370	30	110	150	<10	70	100	10	10
Delaware	110	<10	30	40	<10	20	30	<10	<10
District of Columbia	60	<10	10	20	<10	<10	20	<10	<10
Florida	2,690	210	780	1,170	80	520	730	90	90
Georgia	1,050	80	300	400	30	180	320	40	40
Hawaii	120	<10	30	50	<10	20	40	<10	<10
Idaho	150	10	40	60	<10	30	40	<10	<10
Illinois	1,310	100	380	500	30	220	400	50	50
Indiana	740	60	220	300	20	130	210	30	20
Iowa	330	30	100	120	<10	50	90	10	10
Kansas	280	20	80	110	<10	50	80	10	<10
Kentucky	590	50	180	230	10	100	170	20	20
Louisiana	520	40	150	200	10	90	160	20	20
Maine	170	10	60	70	<10	30	30	<10	<10
Maryland	550	40	160	220	10	90	160	20	20
Massachusetts	660	50	210	290	20	130	150	20	20
Michigan	1,000	80	300	410	30	180	260	30	30
Minnesota	470	40	150	200	10	90	120	10	10
Mississippi	350	30	100	130	<10	60	110	10	10
Missouri	710	60	200	290	20	130	200	20	20
Montana	100	<10	30	40	<10	20	30	<10	<10

See table footnotes on next page.

Cervical cancer is the only HPV-associated cancer for which screening is routinely recommended. Recommendations state that women aged 21–65 years be screened regularly for cervical precancers and cancers. Women aged 21–29 years should be screened with the Papanicolaou (Pap) test every 3 years. Women aged 30–65 years can be screened with one of three strategies: the Pap test every 3 years, an HPV test every 5 years, or both a Pap and HPV test every 5 years. Regardless of screening strategy, all abnormal test results require follow-up of abnormal results and appropriate treatment (8). The Healthy People 2020 target for cervical cancer screening coverage is 93%; however, in 2015 only 81% of women aged 21–65 years reported receiving a Pap test within the past 3 years; coverage was lower among Asians, Hispanics, non–U.S. born, and uninsured women. †††

Progression from persistent HPV infection to precancers and eventually invasive cancer occurs over many years, so it might be too soon to see the effects of HPV vaccination on invasive cancers (2). However, several studies have demonstrated the population-level impact of HPV vaccination in the United

Summary

What is already known about this topic?

Human papillomavirus (HPV) causes nearly all cervical cancers and some cancers of the vagina, vulva, penis, anus, and oropharynx. Cervical cancer screening and HPV vaccination can prevent many of these cancers.

What is added by this report?

An average of 34,800 cancers reported annually in the United States during 2012–2016 were attributable to HPV. Of these, 32,100 (92%) cancers were attributable to HPV types targeted by the 9-valent HPV vaccine, ranging by state from 40 to 3,270.

What are the implications for public health practice?

Ongoing surveillance for HPV-associated cancers can inform state-level and national-level HPV vaccination and cervical cancer screening efforts and monitor their long-term impact.

States, including a reduction in the prevalence of vaccine-type HPV infection (9) and rates of high-grade cervical precancers in women aged <25 years (10). Cervical cancer rates declined 1.6% per year during 1999–2015, largely because of screening, although decreases among the youngest age group of women might be due in part to HPV vaccination (6).

^{†††} https://www.healthypeople.gov/2020/topics-objectives/.

TABLE 2. (Continued) Estimated annual number of human papillomavirus (HPV)-attributable cancers,* by cancer type,† HPV type, § and state — United States, ¶ 2012–2016

				Est	imated no.	**			
	A	II cancers	;	Oropharyn	x (male an	d female)		Cervix	
State	9vHPV-targeted	Other HPV	HPV-negative	9vHPV-targeted	Other HPV	HPV-negative	9vHPV-targeted	Other HPV	HPV-negative
Nebraska	170	10	50	60	<10	30	50	<10	<10
Nevada	270	20	70	100	<10	50	90	10	10
New Hampshire	140	10	40	70	<10	30	30	<10	<10
New Jersey	880	70	250	320	20	140	290	30	30
New Mexico	170	10	50	60	<10	30	60	<10	<10
New York	1,980	160	530	660	40	290	660	80	80
North Carolina	1,100	90	330	470	30	210	300	40	30
North Dakota	60	<10	20	30	<10	10	10	<10	<10
Ohio	1,260	100	370	500	30	220	360	40	40
Oklahoma	420	30	120	150	<10	70	130	20	20
Oregon	430	30	120	190	10	80	110	10	10
Pennsylvania	1,410	110	420	550	40	240	400	50	50
Rhode Island	110	<10	30	40	<10	20	30	<10	<10
South Carolina	550	40	170	240	20	100	150	20	20
South Dakota	80	<10	20	30	<10	10	20	<10	<10
Tennessee	780	60	220	310	20	130	230	30	30
Texas	2,310	200	620	830	50	360	890	110	100
Utah	160	10	40	60	<10	30	50	<10	<10
Vermont	60	<10	20	30	<10	10	10	<10	<10
Virginia	760	60	220	310	20	140	210	30	20
Washington	690	50	200	280	20	120	190	20	20
West Virginia	250	20	70	100	<10	40	70	<10	<10
Wisconsin	560	40	170	240	20	100	150	20	20
Wyoming	40	<10	10	20	<10	<10	10	<10	<10

Abbreviations: 9vHPV = 9-valent HPV vaccine; ICD-O-3 = International Classification of Diseases for Oncology, Third Edition.

The findings in this report are subject to at least one limitation. Although population-based cancer registries provide a reliable system for counting invasive cancers, they do not routinely collect or report information on HPV genotype status in cancer tissue; actual counts of HPV-associated cancers can be provided, but for HPV-attributable cancers, only estimates are available. An important strength of this study, however, is the use of high-quality, population-based surveillance data with 100% coverage of the U.S. population, allowing for specific histologic definitions to monitor HPV-associated cancer incidence nationally and in each state.

Among the 43,999 HPV-associated cancers that occur each year in the United States, an estimated 34,800 are attributable to HPV, including 32,100 attributable to HPV types targeted

by 9vHPV. During 2018, only half of adolescents were up to date on HPV vaccination (5). Surveillance for HPV-associated cancers using population-based cancer registries with high-quality data and the assessment of HPV-attributable cancers can be used to monitor the long-term impact of HPV vaccination and current cervical cancer screening strategies in the United States. The examination of state-level data enables states to plan for and monitor the impact of vaccination and cervical cancer screening.

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^{*} HPV-attributable cancers are cancers that are probably caused by HPV (https://academic.oup.com/jnci/article/107/6/djv086/872092). Estimates for attributable fraction were based on studies that used population-based data from cancer tissue studies to estimate the percentage of those cancers probably caused by HPV.

[†] HPV-associated cancers were defined as invasive cancers at anatomic sites with cell types in which HPV DNA frequently is found. All cancers were histologically confirmed. Cervical cancers (ICD-O-3 site codes C53.0–C53.9) are limited to carcinomas (ICD-O-3 histology codes 8010–8671, 8940–8941). Vaginal (ICD-O-3 site code C52.9), vulvar (ICD-O-3 site codes C51.0–C51.9), penile (ICD-O-3 site codes C60.0–60.9), anal (ICD-O-3 site codes C20.9, C21.0–C21.9), and oropharyngeal (ICD-O-3 site codes C01.9, C02.4, C02.8, C05.1, C05.2, C09.0, C09.1, C09.8, C09.9, C10.0, C10.1, C10.2, C10.3, C10.4, C10.8, C10.9, C14.0, C14.2 and C14.8) cancer sites are limited to squamous cell carcinomas (ICD-O-3 histology codes 8050–8084, 8120–8131).

^{§ &}quot;9vHPV-targeted" includes oncogenic HPV types 16, 18, 31, 33, 45, 52, and 58. "Other HPV" includes other oncogenic HPV types. "HPV-negative" cancers are those that occur at anatomic sites in which HPV-associated cancers are often found, but HPV DNA was not detected.

[¶] Compiled from population-based cancer registries that participate in the CDC National Program of Cancer Registries, and/or the National Cancer Institute's Surveillance, Epidemiology, and End Results Program and meet the criteria for high data quality for all years 2012–2016, covering 100% of the U.S. population.

^{**} The estimated number of HPV-attributable cancers was calculated by multiplying the number of HPV-associated cancer cases by the percentage of each cancer type attributable to HPV. The total of HPV attributable cancers was the sum of cancers attributable to types targeted by 9vHPV and other HPV types. HPV-negative counts were the difference of the total count and the HPV-attributable counts. Estimates were rounded to the nearest 10; counts <10 are not displayed.

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References

- Shiels MS, Kreimer AR, Coghill AE, Darragh TM, Devesa SS. Anal cancer incidence in the United States, 1977–2011: distinct patterns by histology and behavior. Cancer Epidemiol Biomarkers Prev 2015;24:1548–56. https://doi.org/10.1158/1055-9965.EPI-15-0044
- Schiffman M, Castle PE, Jeronimo J, Rodriguez AC, Wacholder S. Human papillomavirus and cervical cancer. Lancet 2007;370:890–907. https:// doi.org/10.1016/S0140-6736(07)61416-0
- Saraiya M, Unger ER, Thompson TD, et al.; HPV Typing of Cancers Workgroup. US assessment of HPV types in cancers: implications for current and 9-valent HPV vaccines. J Natl Cancer Inst 2015;107:djv086. https://doi.org/10.1093/jnci/djv086
- Viens LJ, Henley SJ, Watson M, et al. Human papillomavirus—associated cancers—United States, 2008–2012. MMWR Morb Mortal Wkly Rep 2016;65:661–6. https://doi.org/10.15585/mmwr.mm6526a1
- Walker TY, Elam-Evans LD, Yankey D, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 years—United States, 2018. MMWR Morb Mortal Wkly Rep 2019;68:718–23.

- Van Dyne EA, Henley SJ, Saraiya M, Thomas CC, Markowitz LE, Benard VB. Trends in human papillomavirus—associated cancers— United States, 1999–2015. MMWR Morb Mortal Wkly Rep 2018;67:918–24. https://doi.org/10.15585/mmwr.mm6733a2
- Meites E, Szilagyi PG, Chesson HW, Unger ER, Romero JR, Markowitz LE. Human papillomavirus vaccination for adults: updated recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep 2019;68:698–702. https:// doi.org/10.15585/mmwr.mm6832a3
- Curry SJ, Krist AH, Owens DK, et al.; US Preventive Services Task Force. Screening for cervical cancer: US Preventive Services Task Force recommendation statement. JAMA 2018;320:674–86. https://doi. org/10.1001/jama.2018.10897
- 9. Oliver SE, Unger ER, Lewis R, et al. Prevalence of human papillomavirus among females after vaccine introduction—National Health and Nutrition Examination Survey, United States, 2003–2014. J Infect Dis 2017;216:594–603. https://doi.org/10.1093/infdis/jix244
- Gargano JW, Park IU, Griffin MR, et al.; HPV-IMPACT Working Group. Trends in high-grade cervical lesions and cervical cancer screening in 5 states, 2008–2015. Clin Infect Dis 2019;68:1282–91. https://doi. org/10.1093/cid/ciy707

Progress Toward Poliomyelitis Eradication — Afghanistan, January 2018–May 2019

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Since October 2016, Afghanistan and Pakistan have been the only countries with reported cases of wild poliovirus type 1 (WPV1) (1). In Afghanistan, although the number of cases had declined during 2013-2016, the polio eradication program experienced challenges during 2017-2019. This report describes polio eradication activities and progress in Afghanistan during January 2018–May 2019 and updates previous reports (2,3). During May–December 2018, insurgent groups (antigovernment elements) banned house-to-house vaccination in most southern and southeastern provinces, leaving approximately 1 million children inaccessible to oral poliovirus vaccine (OPV) administration. During January-April 2019, vaccination targeting children at designated community sites (site-to-site vaccination) was permitted; however, at the end of April 2019, vaccination campaigns were banned nationally. During 2018, a total of 21 WPV1 cases were reported in Afghanistan, compared with 14 during 2017. During January-May 2019, 10 WPV1 cases were reported (as of May 31), compared with eight during January-May 2018. Sewage sample–testing takes place at 20 sites in the highest-risk areas for poliovirus circulation; 17 have detected WPV1 since January 2017, primarily in the southern and eastern provinces. Continued discussion with antigovernment elements to resume house-to-house campaigns is important to achieving polio eradication in Afghanistan. To increase community support for vaccination, collaboration among humanitarian service agencies to address other urgent health and basic needs is critical.

Immunization Activities

The World Health Organization (WHO) and UNICEF estimated that national routine vaccination coverage of children aged <12 months with the third dose of OPV (OPV3) in Afghanistan was 73% in both 2017 and 2018 (4). Routine immunization services were not generally available in the southern and eastern regions. In both 2017 and 2018, 68% of children aged 6–23 months with nonpolio acute flaccid paralysis (NPAFP) had a history of receipt of 3 OPV doses through routine immunization services, which is a proxy indicator of national OPV3 coverage. The proportion of children aged 6–23 months with NPAFP who never received OPV through routine immunization services or supplementary immunization

activities (SIAs)* (i.e., zero-dose children) was 1% nationally in 2018; the largest percentages of these children were from the southern provinces of Kandahar (26%) and Helmand (15%). Coverage with injectable inactivated poliovirus vaccine (IPV), which was introduced into all OPV-using countries in 2016 in conjunction with the global, synchronized switch from trivalent OPV (containing vaccine virus types 1, 2, and 3) to bivalent OPV (bOPV, containing types 1 and 3), was estimated at 66% in 2018.

During January 2018–May 2019, SIAs targeted children aged <5 years for receipt of monovalent OPV (mOPV1, containing only type 1) or bOPV, including 2 national immunization days (NIDs), 5 subnational immunization days, three responses to WPV1-positive cases, five mop-up SIAs, and one short-interval additional dose campaign (SIAD).† NIDs targeted 9,999,227 children aged <5 years. During SIAs, IPV was administered to 549,557 children aged 4–59 months who lived in very high-risk districts for WPV1 circulation or in areas that had been inaccessible during previous SIAs.

Children missed during SIAs are classified either as inaccessible because of campaign bans or accessible but missed because of campaign quality issues. During the March 2018 NID, according to postcampaign assessments, an estimated 110,591 (1.2%) targeted children were inaccessible for campaigns, and 339,474 (3.6%) were accessible but missed. During the August 2018 NID, which occurred during the May—August 2018 ban on SIAs in areas held by anti-government elements, a total of 1,324,132 (13.2%) targeted children were inaccessible, and 300,471 (3%) were accessible but missed.

The standard SIA approach for polio eradication involves house-to-house OPV vaccination. In November 2018 and January 2019, the polio program gained access for site-to-site campaigns in some areas of the southeastern and southern regions. During the April 2019 NID, the number of missed children among those targeted was reduced to 743,776 (7.4%), including 449,756 (4.5%) who were inaccessible and 294,020

^{*} SIAs are mass house-to-house campaigns targeting children aged <5 years with OPV, regardless of vaccination history.

[†] A mop-up SIA is a door-to-door immunization campaign carried out in specific areas where the virus is known or suspected to be still circulating. A SIAD follows another campaign by <2 weeks.

(2.9%) who were accessible but missed because of campaign quality issues.

Lot quality assurance sampling[§] surveys are used to assess the quality of SIAs in areas where postcampaign monitoring is permitted. Depending on the number of unvaccinated persons in the survey sample, districts were marked as either passed at 90% (estimated coverage ≥90%), passed at 80% (estimated coverage 80%–90%), or failed at <80% (estimated coverage <80%). At the 80% threshold, 8.3% of districts failed in the March 2018 NID, and 3% failed in the August 2018 NID. During the March 2019 NID, 30% of districts failed at the 80% threshold. In March 2019, the passing threshold was raised to 90%. The inability to conduct house-based vaccination campaign evaluations after designated site campaigns resulted in unreliable coverage estimates.

Children aged <5 years are also targeted for vaccination along major travel routes throughout the country, at transit points from inaccessible areas, and at border crossing points with Iran and Pakistan. During January 2018–April 2019, approximately 18,490,713 doses of OPV were administered at transit points and approximately 1,540,171 doses at border crossings.

Poliovirus Surveillance

Acute flaccid paralysis (AFP) surveillance. Detection of ≥2 NPAFP cases per 100,000 persons aged <15 years is considered sufficiently sensitive surveillance to detect a case of polio; to assess quality of case investigation, 80% of AFP cases should have adequate stool specimens collected. The polio surveillance network includes approximately 800 AFP focal points; 2,500 health facilities; and 35,000 reporting community volunteers. In 2018, the national NPAFP rate was 17 per 100,000 persons aged <15 years for areas across all SIA categories (accessible, inaccessible, and partially accessible) (regional range = 11–21) (Table). The percentage of AFP cases with adequate specimens was 94% (≥85% across all SIA access categories) (regional range = 87%–97%).

Environmental surveillance. Supplementary poliovirus surveillance in Afghanistan is conducted monthly through sampling of sewage at 20 sites in nine provinces. WPV1 was detected in two of 184 (1%) specimens tested in 2016, 42 of 316 (13%) specimens tested in 2017, 83 of 336 (25%) specimens tested in 2018, and 25 of 128 specimens (23%) collected in 2019 (as of May 31); all detections of poliovirus in 2019 occurred at sites in Helmand, Kandahar (southern), and Nangarhar (eastern) provinces.

Epidemiology of WPV Cases

During 2018, 21 WPV1 cases were reported from 14 districts in six provinces (Helmand, Kandahar, Kunar, Nangarhar, Nuristan, and Urozgan), compared with 14 WPV1 cases reported from nine districts in five provinces (Helmand, Kandahar, Kunduz, Nangarhar, and Zabul) during 2017. During January-May 2019, 10 cases were reported from nine districts in four provinces (Helmand, Kandahar, Kunar, and Urozgan), compared with eight cases from five districts in three provinces (Kandahar, Kunar, and Nangarhar) during January–May 2018 (Figure 1) (Figure 2). Among the 31 cases reported during January 2018-May 2019, 20 (65%) were among children aged <36 months. Ten (32%) children had never received OPV through routine immunization or SIAs, three (10%) had received 1 or 2 doses, and 18 (58%) had received ≥3 doses each; 21 (68%) of the 31 children had never received OPV through routine immunization, but some had received OPV through SIAs.

Genomic sequence analysis of poliovirus isolates identified multiple episodes of cross-border transmission between Afghanistan and Pakistan during 2018-2019, with sustained local transmission in both countries. Seven (23%) of 31 isolates from patients with AFP and 13 (10%) of 111 isolates from environmental testing identified in Afghanistan had closest genetic links to earlier WPV1 isolates from Pakistan; the remaining WPV1 cases and isolates were most closely linked to cases and isolates from within Afghanistan. During January 2018-May 2019, two genetic clusters (viruses sharing ≥95% sequence identity) were detected among AFP cases. Transmission in the provinces of the eastern and southern regions is largely from independent genetic clusters. During January 2018–May 2019, four orphan viruses** were detected in environmental isolates from Helmand, Kabul, Kandahar (southern), and Nangarhar (eastern) provinces, signaling some AFP surveillance gaps.

S Lot quality assurance sampling is a rapid method used to assess the quality of vaccination activities after SIAs in predefined areas such as health districts (referred to as "lots"), using a small sample size. Lot quality assurance sampling involves dividing the population into lots and ascertaining receipt of vaccination by randomly selected persons within each lot. If the number of unvaccinated persons in the sample exceeds a predetermined value, then the lot is classified as having an unsatisfactory level of vaccination coverage, and mop-up activities are recommended. If the threshold of ≥90% is met (Afghanistan program guidelines have recently increased the threshold from ≥80%), the area or district is classified as having passed, although mop-up activities might still be indicated in certain areas.

Surveillance target is that ≥80% of AFP cases have adequate stool specimens collected. Adequate stool specimens are defined as two stool specimens of sufficient quality for laboratory analysis, collected ≥24 hours apart, both within 14 days of paralysis onset, and arriving in good condition at a World Health Organization–accredited laboratory with reverse cold chain maintained, without leakage or desiccation, and with proper documentation.

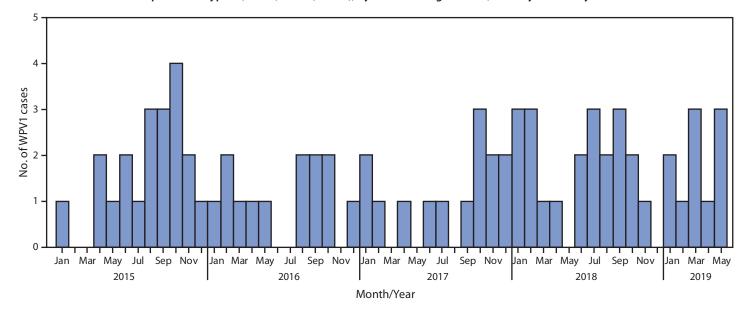
^{**} Orphan viruses are ≥1.5% divergent from their closest genetic match (i.e., ≤98.5% of a match).

TABLE. Acute flaccid paralysis (AFP) surveillance indicators and reported cases of wild poliovirus (WPV), by region and period — Afghanistan, January 2018–May 2019*

		AFP surveillance indi	No. of WPV cases reported			
Region of Afghanistan	No. of AFP cases	Nonpolio AFP rate [†]	% of AFP cases with adequate stool specimens [§]	Jan-May 2018	Jun-Dec 2018	Jan-May 2019
All regions	3,357	17	94	8	13	10
Badakhshan	68	11	96	0	0	0
Central	615	13	97	0	0	0
Eastern	400	20	94	3	3	1
Northeastern	436	19	94	0	0	0
Northern	355	14	93	0	0	0
Southeastern	299	15	96	0	0	0
Southern	592	17	87	5	10	9
Western	592	21	96	0	0	0

^{*} Data current as of May 31, 2019.

FIGURE 1. Number of wild poliovirus type 1 (WPV1) cases (N = 78), by month — Afghanistan, January 2015-May 2019



Discussion

Although the number of WPV1 cases has marginally increased in Afghanistan during 2017–2019 and circulation has remained confined to the southern and eastern regions of the country, the geographic extent of WPV1 circulation has increased at provincial and district levels in 2019. Although the Afghanistan program has succeeded in interrupting internal circulation in certain areas of the country in the past, internal WPV1 circulation has persisted since 2016.

When SIAs are conducted in accessible areas, a small but constant proportion of children continues to be missed because of suboptimal SIA planning, team performance issues, or both. Vaccine refusals and polio campaign fatigue continue in areas where populations without many basic services are still offered monthly polio vaccination. UNICEF has piloted water and sanitation projects in high-refusal areas, but the impact is unclear. Children reported absent during campaigns might represent undeclared caretaker refusals; further investigation might allow identification of underlying reasons that children are not present and help guide remedial action. Extending basic health and public services could improve community trust in such areas.

However, inaccessibility, compounded by the nationwide ban on vaccination campaigns, currently is the most substantial barrier to polio eradication in Afghanistan. Antigovernment elements in southern provinces have frequently banned

[†] Cases per 100,000 persons aged <15 years. Considering underlying rate of nonpolio AFP in population, threshold indicating adequate surveillance is ≥2 nonpolio AFP cases per 100,000 persons aged <15 years.

[§] Surveillance target is that ≥80% of AFP cases have adequate stool specimens collected. Adequate stool specimens are defined as two stool specimens of sufficient quality for laboratory analysis, collected ≥24 hours apart, both within 14 days of paralysis onset, and arriving in good condition at a World Health Organization—accredited laboratory with reverse cold chain maintained, without leakage or desiccation, and with proper documentation.

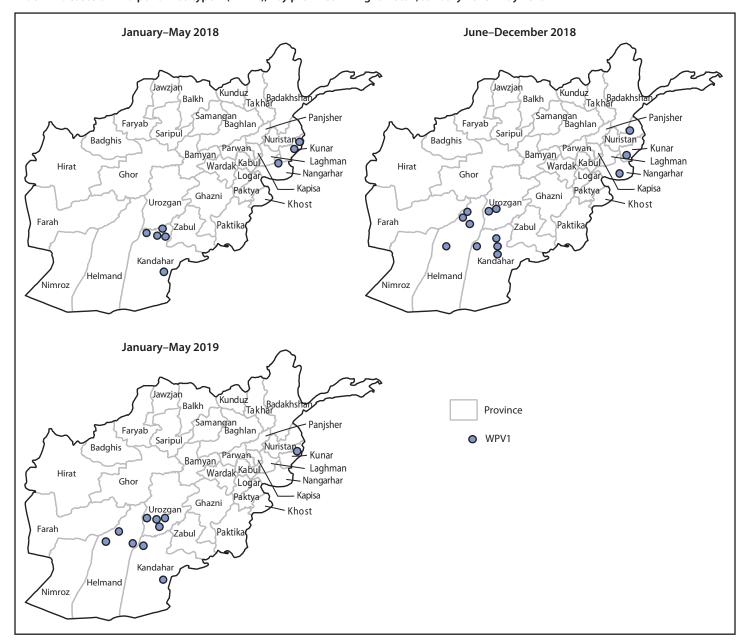


FIGURE 2. Cases of wild poliovirus type 1 (WPV1),* by province — Afghanistan, January 2018-May 2019

house-to-house vaccination in the past, but over many periods, local access was permitted after discussions with local leaders. Antigovernment elements in the eastern provinces have imposed intermittent bans on house-to-house activities since 2016. To date, efforts to resume house-to-house campaigns after the nationwide ban have been unsuccessful; however, resumption of these campaigns is vital to achieving population immunity high enough to interrupt virus transmission, particularly in the southern and eastern provinces.

As long as the ban on vaccination campaigns continues, routine immunization services provide the most critical opportunity for polio vaccination in the country, but these services are extremely limited in many parts of the country. Enhanced efforts by national and international immunization partners can facilitate systematic provision of routine immunization activities through fixed, mobile, and outreach approaches, particularly in the most needed areas.

^{*} Each dot represents one case. Location of dot on map does not represent actual location of case.

Summary

What is already known about this topic?

Wild poliovirus circulation continues in Afghanistan.

What is added by this report?

With bans on house-to-house vaccination campaigns in many provinces since May 2018 and a nationwide ban since April 2019, wild poliovirus circulation has increased during 2018–2019.

What are the implications for public health practice?

Routine immunization systems, which are critically weak in the provinces where wild poliovirus is currently circulating, are vital to polio eradication efforts, particularly until bans on campaigns are lifted. Successful discussions with local leaders have facilitated house-to-house campaigns in the past, and such campaigns are essential to interrupting wild poliovirus virus transmission.

Solutions for improving immunization coverage and providing basic health services, including in areas held by antigovernment elements, are necessary to make substantial progress toward polio eradication in Afghanistan. These solutions will require close partnership from the highest levels of government and all international partners.

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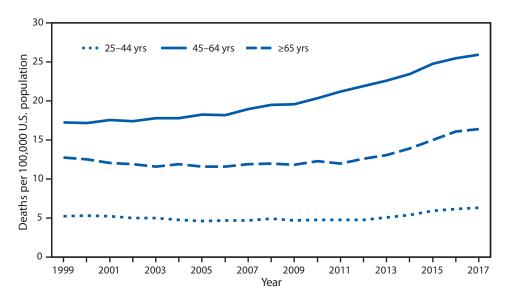
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References

- Greene SA, Ahmed J, Datta SD, et al. Progress toward polio eradication—worldwide, January 2017–March 2019. MMWR Morb Mortal Wkly Rep 2019;68:458–62. https://doi.org/10.15585/mmwr.mm6820a3
- Martinez M, Shukla H, Ahmadzai M, et al. Progress toward poliomyelitis eradication—Afghanistan, January 2017–May 2018. MMWR Morb Mortal Wkly Rep 2018;67:833–7. https://doi.org/10.15585/mmwr. mm6730a6
- 3. Martinez M, Shukla H, Nikulin J, et al. Progress toward poliomyelitis eradication—Afghanistan, January 2016–June 2017. MMWR Morb Mortal Wkly Rep 2017;66:854–8. https://doi.org/10.15585/mmwr. mm6632a5
- 4. World Health Organization. WHO vaccine-preventable diseases: monitoring system. 2019 global summary. Geneva, Switzerland: World Health Organization; 2019. https://apps.who.int/immunization_monitoring/globalsummary/countries?countrycriteria%5Bcountry%5D%5B%5D=AFG

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Rate* of Alcohol-Induced Deaths[†] Among Persons Aged ≥25 Years, by Age Group — National Vital Statistics System, 1999–2017



^{*} Rates are deaths per 100,000 U.S. population.

Rates of alcohol-induced deaths for persons aged 45-64 years increased from 17.3 per 100,000 population in 1999 to 26.0 in 2017. For persons aged 25-44 years, rates declined from 1999 to 2005, were stable from 2005 to 2012, and then increased from 2012 (4.8) to 2017 (6.3). A similar pattern was observed for persons aged ≥ 65 years, with an initial decline, a stable period, and then an increase from 2011 (12.0) to 2017 (16.4).

 $\textbf{Source:} \ \textbf{National Vital Statistics System, Mortality Data, 1999-2017.} \ \textbf{http://www.cdc.gov/nchs/nvss/deaths.htm.}$

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[†] Alcohol-induced deaths include *International Classification of Diseases, Tenth Revision* codes E24.4, alcohol-induced pseudo-Cushing's syndrome; F10, mental and behavioral disorders due to alcohol use; G31.2, degeneration of nervous system due to alcohol; G62.1, alcoholic polyneuropathy; G72.1, alcoholic myopathy; I42.6, alcoholic cardiomyopathy; K29.2, alcoholic gastritis; K70, alcoholic liver disease; K85.2, alcohol-induced acute pancreatitis; K86.0, alcohol-induced chronic pancreatitis; R78.0, finding of alcohol in blood; X45, accidental poisoning by and exposure to alcohol; X65, intentional self-poisoning by and exposure to alcohol, undetermined intent. Alcohol-induced causes exclude unintentional injuries, homicides, and other causes indirectly related to alcohol use, as well as newborn deaths associated with maternal alcohol use.

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