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National Kidney Month — March 2018

Each year, March is designated National Kidney Month to raise awareness about the prevention and early detection of kidney disease. In the United States, kidney diseases are the ninth leading cause of death (*1*). Among U.S. adults aged ≥20 years, 15% (30 million persons) are estimated to have chronic kidney disease. Chronic kidney disease is defined as damaged kidneys or a glomerular filtration rate (i.e., a measure of kidney function) <60 mL/min/1.73 m^2 for >3 months (*2*,*3*). Chronic kidney disease is also estimated to be more common in women than in men (*2*,*3*). However, among persons with moderate to severe chronic kidney disease, awareness of having the disease was lower in women than in men (*3*). Risk factors for chronic kidney disease include diabetes, high blood pressure, cardiovascular disease, and obesity (*2*); controlling diabetes and high blood pressure can delay or prevent chronic kidney disease and improve health outcomes (*2*). CDC supports the Chronic Kidney Disease Surveillance System (https://www.cdc.gov/ckd/surveillance) to document and monitor kidney disease and its risk factors in the U.S. population and to track progress in kidney disease prevention, detection, and management. This week's *MMWR* issue includes a report on acute kidney injury, a risk factor for developing or worsening chronic kidney disease. Information is available about kidney disease prevention and control at https://www.nkdep.nih.gov/ and about diabetes prevention and control at https://www.cdc.gov/diabetes.

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Trends in Hospitalizations for Acute Kidney Injury — United States, 2000–2014

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Acute kidney injury is a sudden decrease in kidney function with or without kidney damage, occurring over a few hours or days. Diabetes, hypertension, and advanced age are primary risk factors for acute kidney injury. It is increasingly recognized as an in-hospital complication of sepsis, heart conditions, and surgery (*1*,*2*). Its most severe stage requires treatment with dialysis. Acute kidney injury is also associated with higher likelihood of long-term care, incidence of chronic kidney disease and hospital mortality, and health care costs (*1*,*2*). Although a number of U.S. studies have indicated an increasing incidence of dialysis-treated acute kidney injury since the late 1990s (*3*), no data are available on national trends in diabetes-related acute

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kidney injury. To estimate diabetes- and nondiabetes-related acute kidney injury trends, CDC analyzed 2000–2014 data from the National Inpatient Sample (NIS) (*4*) and the National Health Interview Survey (NHIS) (*5*). Age-standardized rates of acute kidney injury hospitalizations increased by 139% (from 23.1 to 55.3 per 1,000 persons) among adults with diagnosed diabetes, and by 230% (from 3.5 to 11.7 per 1,000 persons) among those without diabetes. Improving both patient and provider awareness that diabetes, hypertension, and advancing age are frequently associated with acute kidney injury might reduce its occurrence and improve management of the underlying diseases in an aging population.

Using 2000–2014 NIS data, CDC estimated the annual number of hospitalizations with acute kidney injury. NIS contains information from >7 million hospital stays from 44 states each year, estimated to represent >35 million hospitalizations nationally and >95% of the U.S. population (*4*). For this report, acute kidney injury hospitalizations were defined in two ways using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM). All acute kidney injury was defined as the occurrence of at least one diagnostic code 584 (acute renal failure) or the occurrence of at least one procedure code of 39.95 (hemodialysis) or 54.98 (peritoneal dialysis). To exclude hospitalizations among patients with chronic renal failure on long-term dialysis, visits with the following procedural codes were excluded: V45.1 (renal dialysis status), V56.0 (encounter for dialysis and dialysis catheter care), V56.31 (encounter for adequacy testing for hemodialysis), V56.32 (encounter for adequacy testing for peritoneal dialysis), and V56.8 (other dialysis). Dialysis-treated acute kidney injury was defined by a diagnostic code 584 and a procedure code (39.95 or 54.98), also excluding the V-codes specified above. Hospitalizations were considered to be diabetes-related if diabetes (ICD-9-CM code 250) was listed as a diagnosis. The case definition included any hospitalization with a code for acute kidney injury regardless of cause of hospitalization.

NHIS is an annual, in-person household survey of the civilian, noninstitutionalized U.S. population that provides cross-sectional information on the health and use of health care services of the U.S. population. Data from the 2000–2014 NHIS were used to estimate the number of U.S. residents aged ≥20 years with and without diabetes. Diabetes was defined as a "yes" response to the question "Other than during pregnancy, have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?"

All acute kidney injury hospitalizations and dialysis-treated acute kidney injury hospitalizations per 1,000 persons (with and without diabetes) were calculated by dividing the estimated number of acute kidney injury hospitalizations (from NIS) by the estimated population aged ≥20 years with and without diabetes (from NHIS). Trends in all and dialysis-treated acute kidney injury were examined by sex and standardized to the 2000 U.S. standard population. Statistical software was used to obtain point estimates and standard errors based on the Taylor series linearization method and to account for complex sampling designs. Ordinary least squares regression assessed trends over time, reported as p-value for trend with two-sided significance determined as $p<0.05$.

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The total number of hospitalizations with acute kidney injury increased from 953,926 in 2000 to 1,823,054 in 2006 and 3,959,560 in 2014 (Table). Diabetes was an associated comorbidity in 38%, 37%, and 40% of all hospitalizations in these years, respectively. During 2000–2014, the rate of all acute kidney injury hospitalizations among persons with diabetes increased by 139%, from 23.1 to 55.3 per 1,000 persons and by 230% among persons without diabetes, from 3.5 to 11.7 per 1,000 persons (both p<0.001) (Table). Similar patterns were seen for dialysis-treated acute kidney injury, but absolute rates were lower.

The increased rates of acute kidney injury hospitalizations affected both men and women with diabetes. Rates increased 165%, from 23.0 to 60.9 per 1,000 persons (p<0.001) among men and increased 114%, from 23.2 to 49.7 (p<0.001) among women (Figure 1) (Table). Among persons without diabetes, the rate increases were greater (226%, from 4.2 to 13.8 per 1,000 men and 238%, from 2.8 to 9.5 per 1,000 women; p<0.001); however, overall rates were substantially lower (Figure 1) (Table).

Hospitalization rates for dialysis-treated acute kidney injury increased among men and women with diabetes by 68% (from 0.3

TABLE. Age-standardized rate* of hospitalization with acute kidney injury† and dialysis-treated acute kidney injury§ among men and women aged ≥20 years with and without diagnosed diabetes, by sex and diabetes status — United States, 2000, 2006, and 2014

Characteristic	2000	2006	2014¶	Absolute change (95% CI)	Percent change (95% CI)
All persons with diagnosed diabetes					
Weighted no.	11,863,011	17,109,522	21,871,994	—	—
All acute kidney injury (no.)	364,527	666,060	1,571,265	—	—
Hospitalization rate (95% CI)	23.1 (21.5 to 24.8)	28.5 (27.0 to 29.9)	55.3 (54.1 to 56.6)	32.2 (30.1 to 34.3)	139.2 (121.1 to 157.3)
Dialysis-treated acute kidney injury (no.)	4,108	6,300	11,380	—	—
Hospitalization rate (95% CI)	0.3 (0.1 to 0.6)	0.29 (0.1 to 0.5)	0.4 (0.2 to 0.7)	0.1 (0.0 to 0.5)	56.7 (-149.7 to 263.0)
Men with diagnosed diabetes					
Weighted no.	5,907,203	8,203,503	10,907,239	—	—
All acute kidney injury	169,589	334,765	830,155	—	—
Hospitalization rate (95% CI)	23.0 (21.3 to 24.7)	31.5 (29.6 to 32.7)	60.9 (59.6 to 62.2)	37.9 (35.8 to 40.0)	164.6 (144.6 to184.6)
Dialysis-treated acute kidney injury (no.)	2,077	3,425	6,410	—	—
Hospitalization rate (95% CI)	0.3 (0.0 to 0.6)	0.3 (0.1 to 0.6)	0.5 (0.2 to 0.7)	0.2 (0.0 to 0.6)	67.8 (-145.0 to 280.6)
Women with diagnosed diabetes					
Weighted no.	5,955,808	8,906,019	10,964,755	—	—
All acute kidney injury (no.)	194,938	331,295	741,110	—	—
Hospitalization rate (95% CI)	23.2 (21.6 to 24.9)	25.8 (24.4 to 27.1)	49.7 (48.6 to 50.9)	26.5 (24.5 to 28.5)	114.0 (97.8 to 130.3)
Dialysis-treated acute kidney injury (no.)	2,031	2,875	4,970	—	—
Hospitalization rate (95% CI)	0.2 (0.0 to 0.5)	0.2 (0.02 to 0.5)	0.3 (0.1 to 0.6)	0.1 (0.0 to 0.5)	43.6 (-154.8 to 242.0)
All persons without diagnosed diabetes					
Weighted no.	189,675,970	202,950,590	217,677,095	—	—
All acute kidney injury (no.)	589,399	1,156,994	2,388,295	—	—
Hospitalization rate (95% CI)	3.5 (2.4 to 3.7)	6.5 (6.3 to 6.7)	11.7 (11.5 to 11.8)	8.1 (7.9 to 8.3)	230.4 (216.1 to 244.7)
Dialysis-treated acute kidney injury (no.)	8,137	12,219	16,695	—	—
Hospitalization rate (95% CI)	0.1 (0.02 to 0.1)	0.1 (0.04 to 0.1)	0.08 (0.1 to 0.1)	0.03 (0 to 0.07)	64.1 (-37.4 to 165.6)
Men without diagnosed diabetes					
Weighted no.	90,661,859	97,967,409	104,570,034	—	—
All acute kidney injury	316,980	617,208	1,282,955	—	—
Hospitalization rate (95% CI)	4.2 (4.1 to 4.4)	7.7 (7.5 to 8.0)	13.8 (13.6 to 14.0)	9.6 (9.3 to 9.8)	225.5 (212.0 to 239.1)
Dialysis-treated acute kidney injury (no.)	4,791	7,107	9,860	—	—
Hospitalization rate (95% CI)	0.06 (0.03 to 0.1)	0.1 (0.05 to 0.1)	0.1 (0.07 to 0.13)	0.04 (0.0 to 0.08)	61.9 (-29.0 to 152.8)
Women without diagnosed diabetes					
Weighted no.	99,014,111	104,983,181	113,107,061	—	—
All acute kidney injury (no.)	272,419	539,786	1,105,340	—	—
Hospitalization rate (95% CI)	2.8 (2.7 to 2.9)	5.2 (5.0 to 5.4)	9.5 (9.4 to 9.6)	6.7 (6.5 to 6.9)	237.7 (222.2 to 253.2)
Dialysis-treated acute kidney injury (no.)	3,346	5,112	6,835	—	—
Hospitalization rate (95% CI)	0.03 (0.01 to 0.1)	0.1 (0.03 to 0.07)	0.06 (0.01 to 0.08)	0.02 (0.0 to 0.05)	68.0 (-52.8 to 188.8)

Abbreviation: CI = confidence interval.

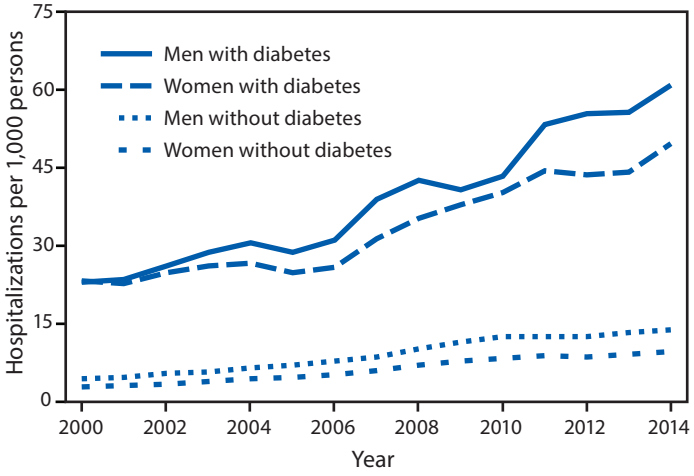
* Rate per 1000 population and age-standardized based on the 2000 U.S. standard population.

† Acute kidney injury identified based on the following *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9 CM) codes: at least one diagnostic code 584 (acute renal failure) or at least one procedure code of 39.95 (hemodialysis) or 54.98 (peritoneal dialysis) and excluding the following codes: V45.1 (renal dialysis status), V56.0 (encounter for dialysis and dialysis catheter care), V56.31 (encounter for adequacy testing for hemodialysis), V56.32 (encounter for adequacy testing for peritoneal dialysis), and V56.8 (other dialysis).

§ Dialysis-treated acute kidney injury identified based on the following ICD-9 CM codes: at least one diagnostic code 584 (acute renal failure) and at least one procedure code of 39.95 (hemodialysis) or 54.98 (peritoneal dialysis), and excluding the following codes: V45.1 (renal dialysis status), V56.0 (encounter for dialysis and dialysis catheter care), V56.31 (encounter for adequacy testing for hemodialysis), V56.32 (encounter for adequacy testing for peritoneal dialysis), and V56.8 (other dialysis).

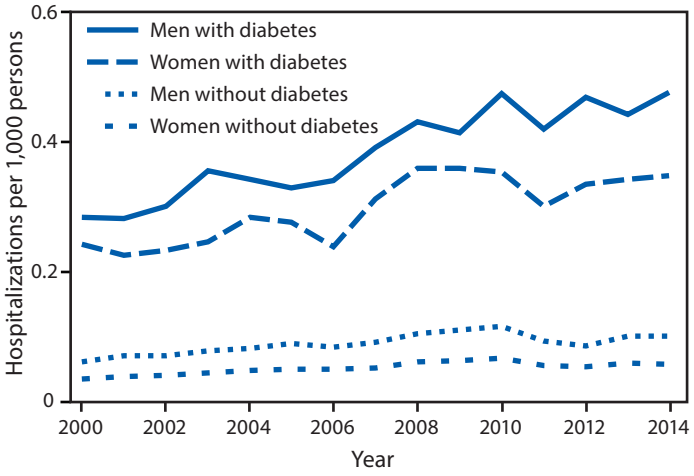
¶ All p-values for trend <0.001.

FIGURE 1. Age-standardized incidence* of hospitalizations with acute kidney injury† among men and women aged ≥20 years with and without diabetes — United States, 2000–2014



* Age-standardized based on the 2000 U.S. standard population.
† Acute kidney injury identified by the following *International Classification of Diseases, Ninth Revision, Clinical Modification* codes: at least one diagnostic code of 584 or at least one procedure code of 39.95 or 54.98 and excluding the following codes: V45.1, V56.0, V56.31, V56.32, and V56.8.

FIGURE 2. Age-standardized incidence* of hospitalizations with dialysis-treated acute kidney injury† among men and women aged ≥20 years with and without diagnosed diabetes — United States, 2000–2014



* Age-standardized based on the 2000 U.S. standard population.
† Acute kidney injury identified by the following *International Classification of Diseases, Ninth Revision, Clinical Modification* codes: at least one diagnostic code of 584 and at least one procedure code of 39.95 or 54.98 and excluding the following codes: V45.1, V56.0, V56.31, V56.32, and V56.8.

to 0.5 per 1,000 men, p<0.001) and 44% (from 0.2 to 0.3 women, p<0.001), respectively (Figure 2) (Table). Among men and women without diabetes, the rates of dialysis-treated acute kidney injury hospitalizations were much lower, but a significant increasing trend was also observed (both p<0.001) (Figure 2) (Table).

Discussion

The present analysis of nationally representative hospitalization data indicates a substantial increase in the rate of hospitalizations for acute kidney injury in men and women in the United States from 2000 to 2014, irrespective of diabetes status. Compared with persons with diabetes, acute kidney injury hospitalization rates among persons without diabetes were much lower, but the observed relative increase was larger (230% versus 139%). However, the absolute changes were much higher in persons with diabetes than in those without diabetes; persons with diabetes are nearly four times more likely to have acute kidney injury hospitalizations than are persons without diabetes. A similar absolute difference was found for dialysis-treated acute kidney injury.

The findings in this report corroborate previous reports from the United States and other countries. In the United States, unadjusted rates of first acute kidney injury hospitalization in the Medicare population with diabetes increased from 29 per 1,000 person-years in 2004 to 51 in 2014 (*2*). Among commercially insured patients aged 22–65 years with diabetes, the rate increased from 9.6 in 2005 to 15 in 2014 (*2*). Similar trends for the overall population (with and without diabetes) were reported for other large health care delivery systems such as Kaiser Permanente of Northern California (*6*). Studies in countries with national health care systems showed that dialysis-treated acute kidney injury increased more than thirteenfold in England during 1998–2013 (*7*), with the steepest increase among patients in intensive care units, and nearly threefold in Denmark during 2000–2012, particularly among elderly patients and those with multiple comorbidities (*8*). This suggests that acute kidney injury is on the rise in many counties, regardless of the health care system.

The increasing rates of acute kidney injury hospitalizations contrast with recently published data for other diabetes-related acute and chronic complications in the United States. A nationwide analysis of trends in five diabetes-related complications, including acute myocardial infarction, stroke, amputations, end-stage renal disease, and deaths from hyperglycemic crisis, indicated that rates of most complications declined during 1990–2010 (*9*). This suggests that increased survival among patients with diabetes, coinciding with a rise in other complications, such as septicemia, shock, congestive heart failure, and liver disease, might be contributing to higher rates of acute kidney injury hospitalizations (*10*).

The findings in this report are subject to at least three limitations. First, NIS data represent the number of acute kidney injury discharge diagnoses per hospital stay, not per patient. Therefore, a patient with multiple admissions during a given year might be counted several times, leading to an overestimate of the acute kidney injury incidence rate. Conversely, using administrative codes to ascertain acute kidney injury likely results in an underestimation of acute kidney injury cases caused by underrecognition and underdiagnosis. Generally, studies using

Summary

What is already known about this topic?

Clinicians increasingly recognize acute kidney injury as an in-hospital complication of sepsis, heart conditions, and surgery. It is associated with higher likelihood of long-term care, increased incidence of chronic kidney disease, increased hospital mortality, and higher health care costs. A number of U.S. studies have indicated an increasing incidence of dialysis-treated acute kidney injury since the late 1990s.

What is added by this report?

Analysis of data from the 2000–2014 National Inpatient Sample and the National Health Interview Surveys indicates a significant absolute and relative increase in hospitalization rates for acute kidney injury among men and women in the United States. Hospitalization for acute kidney injury among persons with diabetes accounted for approximately 40% of all such hospitalizations; absolute increases in hospitalization rates among persons with diabetes were larger than those among persons without diabetes.

What are the implications for public health and health care practice?

Diabetes is a known risk factor for acute kidney injury. The increasing number of persons living with diabetes is likely to also increase the number of persons with acute kidney injury. Improved awareness by health care providers that diabetes, hypertension, and advanced age are important risk factors for acute kidney injury might reduce its occurrence and improve management of the underlying diseases in an aging population.

change in laboratory measures, such as serum creatinine and urinary output, to define acute kidney injury provide much higher estimates of acute kidney injury incidence than those using ICD codes (*3*). Second, trends in hospitalizations with acute kidney injury codes might be influenced by changes in acute kidney injury definition (*11*), increased awareness of acute kidney injury, and changes in clinical practice over time. Data to examine these factors and their influence on hospitalizations with acute kidney injury were not available; however, the observed increases in dialysis-treated acute kidney injury might be less influenced by these factors and suggest a real increase in incidence of acute kidney injury hospitalizations over time. Finally, these data did not permit differentiation between diabetes types and diabetes duration, both of which could affect acute kidney injury hospitalizations.

Acute kidney injury increases the risk of developing or exacerbating underlying chronic kidney disease (gradual loss of kidney function over time). National health (Healthy People 2020; https://www.healthypeople.gov) objectives call for renal evaluation of patients hospitalized for acute kidney injury 6 months after discharge to monitor kidney function and prevent or delay onset of chronic kidney disease. CDC's Chronic Kidney Disease Surveillance System monitors the prevalence of chronic kidney disease and its risk factors (including acute kidney injury) in the U.S. population and tracks progress in its prevention, management, and control.

Improving both patient and provider awareness that diabetes, hypertension, and advancing age are frequently associated with acute kidney injury is important for reversing these trends. Elderly persons have physiologically reduced kidney function and functional reserve with the appearance of global sclerosis, but also more comorbidity than do young adults, all of which heighten older persons' susceptibility to nephrotoxic medicines, dyes used for imaging, and even dehydration, all preventable risks for acute kidney injury. Better recognition of risk factors for acute kidney injury by health care providers might improve the effectiveness of treatment of underlying conditions and prevent or mitigate additional kidney insult to patients, particularly among those hospitalized or in long-term care.

Conflict of Interest

No conflicts of interest were reported.

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Exposure to Electronic Cigarette Advertising Among Middle and High School Students — United States, 2014–2016

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Electronic cigarettes (e-cigarettes) are the most commonly used tobacco product among U.S. middle and high school students (*1*). Exposure to e-cigarette advertisements is associated with higher odds of current e-cigarette use among middle and high school students (*2–4*). To assess patterns of self-reported exposure to four e-cigarette advertising sources (retail stores, the Internet, television, and newspapers and magazines), CDC analyzed data from the 2014, 2015, and 2016 National Youth Tobacco Surveys (NYTSs). Overall, exposure to e-cigarette advertising from at least one source increased each year during 2014–2016 (2014: 68.9%, 18.3 million; 2015: 73.0%, 19.2 million; 2016: 78.2%, 20.5 million). In 2016, exposure was highest for retail stores (68.0%), followed by the Internet (40.6%), television (37.7%), and newspapers and magazines (23.9%). During 2014–2016, youth exposure to e-cigarette advertising increased for retail stores (54.8% to 68.0%), decreased for newspapers and magazines (30.4% to 23.9%), and did not significantly change for the Internet or television. A comprehensive strategy to prevent and reduce youth use of e-cigarettes and other tobacco products includes efforts to reduce youth exposure to e-cigarette advertising from a range of sources, including retail stores, television, the Internet, and print media such as newspapers and magazines (*5*).

Data were analyzed from the 2014, 2015, and 2016 NYTSs, a cross-sectional, paper-and-pencil survey administered to U.S. students in grades 6–12.* NYTS utilizes a three-stage cluster sampling design to generate a nationally representative sample of public and private school students. Sample sizes and response rates for 2014, 2015, and 2016 were 22,007 (73.3%), 17,711 (63.4%), and 20,675 (71.6%), respectively.

Participants were asked "how often do you see advertisements or promotions for electronic cigarettes or e-cigarettes" from the following four sources: 1) "when you are using the Internet"; 2) "when you read newspapers or magazines"; 3) "when you go to a convenience store, supermarket, or gas station"; and 4) "when you watch television or go to the movies." Movies were omitted from the question after 2014. Response options for each question were "I do not [use/visit the source]"; "never"; "rarely"; "sometimes"; "most of the time"; and "always." Consistent with previous research, students who reported "sometimes," "most of the time," or "always" were classified as "exposed" to advertisements from each source; those who selected "never," "rarely," or "I do not [use/visit the source]" were classified as "not exposed" (*6*). The number of exposure sources were summed for each student and reported as the percentage of all students who were exposed to one, two, three, or four sources.

Data were weighted to account for the complex survey design and adjusted for nonresponse. Prevalence estimates and 95% confidence intervals of exposure to each source, and to any source, were computed. Estimates of exposure were assessed overall and by sex, race/ethnicity, school grade, current (past 30-day) use of e-cigarettes, and current (past 30-day) use of any other tobacco product.† Within each year, t-tests were used to assess statistically significant differences between levels of each covariate relative to the referent group ($p<0.05$). Between-year differences in the overall percentage of students exposed to each advertisement source during 2014–2016 were assessed using the Wald F test and posthoc corrections for multiple hypothesis testing ($p<0.0167$).§

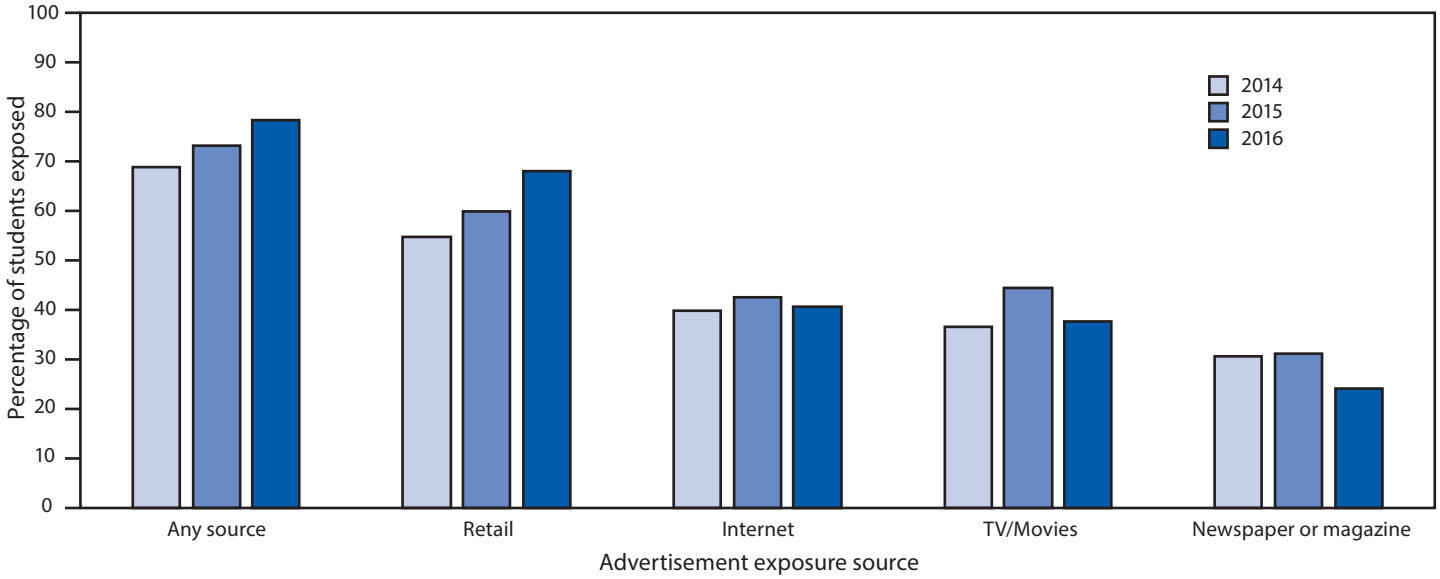
Among U.S. middle and high school students during 2014–2016, exposure to e-cigarette advertisements from any source increased from 68.9% (18.3 million) to 78.2% (20.5 million) (Figure 1) (Table). In 2016, exposure was highest for retail stores (68.0%, 17.7 million), followed by the Internet (40.6%, 10.6 million), television (37.7%, 9.7 million), and newspapers and magazines (23.9%, 6.2 million). In 2016, exposure to advertising from any source was more prevalent among females (79.9%) than males (76.5%); non-Hispanic whites (79.6%) than Hispanics (77.0%) and students of other non-Hispanic races/ethnicities (73.6%); 8th (78.5%), 10th (81.0%), 11th (79.3%), and 12th graders (79.0%) than 6th graders (75.0%); high school students (79.2%) than middle school students (76.9%); current e-cigarette users (82.8%) than nonusers (77.9%); and current users of other tobacco products (82.7%) than nonusers (77.6%). Exposure to each advertising source was higher among current e-cigarette users and other tobacco product users than nonusers during 2014, 2015, and 2016 (Table).

* https://www.cdc.gov/tobacco/data_statistics/surveys/nyts/index.htm.

† Current use of other tobacco products is based on respondents' self-reported use of cigarettes, cigars [includes cigars, cigarillos, and little cigars], smokeless tobacco [includes chewing tobacco/snuff/dip, snus, and dissolvable tobacco], hookah/waterpipe, regular pipe, and/or bidis at least one day in the past 30 days.

§ Statistical tests for differences in e-cigarette advertisement exposure sources by year (2014, 2015, and 2016) were assessed by the Wald F-Test (ANOVA); p-values <0.05 were considered statistically significant. Posthoc comparisons for changes in e-cigarette advertisement exposures between years (2014–2015, 2015–2016, and 2014–2016) were assessed as model-adjusted risk differences from predicted marginals in logistic regression (t-test). A p-value <0.0167, adjusted for multiple comparisons, was considered statistically significant.

FIGURE 1. Percentage* of U.S. middle and high school students exposed to e-cigarette advertisements through any source,† retail stores,§ the Internet,¶ television/movies, and newspapers and magazines†† — National Youth Tobacco Survey, United States, 2014–2016**



* Between-year differences in the percentage of students exposed to each advertisement source during 2014–2016 were assessed using the Wald F test and posthoc corrections for multiple hypothesis testing ($p<0.0167$).
† Statistically significant increases occurred during 2014–2015, 2015–2016, and 2014–2016.
§ Statistically significant increases occurred during 2014–2015, 2015–2016, and 2014–2016.
¶ Statistically significant increase occurred during 2014–2015.
** Statistically significant increase occurred during 2014–2015; statistically significant decrease occurred during 2015–2016. Movies were removed as an exposure source after 2014.
†† Statistically significant decreases occurred during 2015–2016 and 2014–2016.

Overall in 2016, 28.3% of students reported exposure to e-cigarette advertising from one source, 21.2% from two sources, 16.7% from three sources, and 12.0% from four sources (Figure 2). Retail stores were the most common exposure source every year (2014: 54.8%; 2015: 59.9%; 2016: 68.0%), whereas newspapers and magazines were the least common exposure source (2014: 30.4%; 2015: 31.0%; 2016: 23.9%). The Internet was the second most common exposure source in 2014 (39.8%) and 2016 (40.6%); in 2015, television (44.5%) exceeded the Internet (42.6%) as the second most common exposure source.

During 2014–2016, middle and high school students' exposure to e-cigarette advertising significantly increased for retail stores (from 54.8% to 68.0%), significantly decreased for newspapers and magazines (from 30.4% to 23.9%), and did not significantly change for Internet and television.

Discussion

In 2016, an estimated four in five (20.5 million) U.S. youths, including 8.9 million middle school students and 11.5 million high school students, were exposed to e-cigarette advertisements from at least one source, a 13% increase over 2014. Exposure in retail stores increased 24% in 2016 compared with 2014, and was the primary factor responsible for the increases in exposure from any source during 2014–2016. Nearly seven in 10 youths (17.7 million) were exposed to e-cigarette advertising in retail stores in 2016; approximately two in five were exposed on the Internet (10.6 million) or television (9.7 million), and nearly one in four (6.2 million) were exposed in newspapers and magazines. Given the Surgeon General has established that a causal relationship exists between traditional tobacco advertising and youth tobacco product initiation (*7*), and given the association between e-cigarette advertising exposure and e-cigarette use among youths (*2–4*), efforts to reduce youth e-cigarette advertising exposure are an important component of comprehensive youth tobacco prevention efforts (*5*).

During 2014–2016, current users of e-cigarettes and other tobacco products reported higher prevalence of exposure to e-cigarette advertising than nonusers. This is consistent with research documenting an association between e-cigarette advertising exposure and e-cigarette use (*2–4*). However, this relationship might not be limited to e-cigarettes; previous research has demonstrated that among U.S. youths aged 12–17 years, receptivity to e-cigarette marketing is associated with susceptibility to conventional cigarette smoking (*8*). Prevention of youth exposure to e-cigarette advertising might, therefore, be important for prevention of youth use of all tobacco products.

The Surgeon General has concluded that e-cigarette marketing employs strategies similar to conventional cigarette

TABLE. Prevalence of exposure to e-cigarette advertisements* among U.S. youths by sex, race/ethnicity, school level, and use of e-cigarettes and other tobacco products by exposure source — National Youth Tobacco Survey, United States, 2014–2016

Demographic characteristic/Year	% (95% CI)				
	Retail stores	Internet	Television /Movies	Newspapers and magazines	Any source
Overall					
2014	**54.8 (53.6–56.0)**	**39.8 (38.5–41.1)**	**36.5 (35.3–37.7)**	**30.4 (29.3–31.6)**	**68.9 (67.7–70.0)**
2015	**59.9 (58.2–61.7)**	**42.6 (40.8–44.4)**	**44.5 (42.7–46.2)**	**31.0 (29.9–32.2)**	**73.0 (71.3–74.5)**
2016	**68.0 (66.9–69.1)**	**40.6 (39.5–41.8)**	**37.7 (36.1–39.3)**	**23.9 (22.9–24.9)**	**78.2 (77.1–79.1)**
Overall population estimate (in millions)†					
2014	**14.4**	**10.5**	**9.6**	**8.0**	**18.3**
2015	**15.7**	**11.1**	**11.6**	**8.1**	**19.2**
2016	**17.7**	**10.6**	**9.7**	**6.2**	**20.5**
Sex					
Male (referent)					
2014	54.6 (52.9–56.4)	38.5 (37.1–39.8)	36.7 (35.2–38.2)	28.7 (27.6–29.9)	69.0 (67.6–70.3)
2015	58.1 (56.1–60.0)	39.4 (37.6–41.3)	42.9 (40.9–45.0)	28.3 (27.0–29.7)	71.3 (69.3–73.1)
2016	66.3 (64.9–67.7)	37.5 (36.3–38.7)	34.8 (33.2–36.5)	21.8 (20.6–22.9)	76.5 (75.2–77.7)
Female					
2014	54.9 (53.5–56.3)	41.1 (39.4–42.9)§	36.4 (34.8–38.0)	32.1 (30.2–34.1)§	68.8 (67.3–70.3)
2015	62.1 (60.1–64.0)§	46.0 (43.8–48.2)§	46.0 (44.3–47.9)§	33.8 (32.2–35.4)§	74.9 (73.0–76.6)§
2016	69.8 (68.3–71.1)§	43.7 (42.2–45.3)§	40.5 (38.5–42.5)§	26.0 (24.7–27.3)§	79.9 (78.7–81.0)§
Race/Ethnicity					
White, non-Hispanic (referent)					
2014	56.7 (55.0–58.4)	40.2 (38.5–42.0)	35.2 (33.7–36.6)	31.1 (29.7–32.5)	70.4 (68.8–72.0)
2015	63.8 (61.3–66.2)	44.2 (41.8–46.6)	46.0 (43.5–48.4)	33.1 (31.7–34.6)	75.3 (73.2–77.2)
2016	71.3 (69.9–72.8)	41.0 (39.3–42.6)	36.2 (34.1–38.4)	25.1 (23.6–26.6)	79.6 (78.3–80.8)
Black, non-Hispanic					
2014	51.7 (49.4–53.9)¶	41.3 (38.5–44.2)	42.2 (40.0–44.3)¶	32.2 (30.0–34.5)	68.6 (66.3–70.8)
2015	56.7 (54.2–59.1)¶	41.8 (39.2–44.6)	47.1 (44.9–49.3)	27.9 (25.6–30.3)¶	72.8 (70.6–75.0)¶
2016	63.6 (61.5–65.7)¶	39.7 (37.3–42.2)	43.8 (41.3–46.3)¶	21.0 (19.4–22.7)¶	78.5 (76.4–80.5)
Hispanic					
2014	55.6 (53.8–57.4)	39.4 (37.8–41.1)	37.4 (35.6–39.4)¶	29.2 (27.1–31.3)	68.9 (67.2–70.6)
2015	55.8 (53.7–57.9)¶	40.4 (38.3–42.6)¶	42.2 (40.1–44.3)¶	29.4 (27.8–31.1)¶	70.5 (68.4–72.6)¶
2016	65.9 (64.4–67.5)¶	41.9 (40.2–43.6)	39.1 (37.1–41.2)¶	23.4 (22.0–24.9)	77.0 (75.3–78.6)¶
Other, non-Hispanic					
2014	44.4 (39.2–49.7)¶	32.6 (28.3–37.2)¶	29.9 (26.1–33.9)¶	25.3 (22.1–28.7)¶	58.3 (52.4–63.9)¶
2015	51.1 (47.5–54.7)¶	39.3 (35.1–43.6)¶	35.6 (32.8–38.5)¶	26.6 (23.3–30.2)¶	63.8 (59.7–67.6)¶
2016	62.6 (58.6–66.4)¶	37.0 (33.5–40.6)	31.9 (27.5–36.6)	22.9 (20.1–25.8)	73.6 (70.0–76.9)¶
Grade level					
6th grade (referent)					
2014	50.6 (47.2–54.0)	32.8 (30.8–34.8)	31.8 (29.4–34.3)	24.1 (22.1–26.2)	64.7 (61.9–67.3)
2015	52.7 (49.2–56.2)	35.5 (31.9–39.4)	40.8 (37.5–44.2)	24.4 (22.1–26.9)	66.7 (62.7–70.4)
2016	62.9 (60.0–65.8)	38.4 (35.4–41.5)	34.4 (31.3–37.5)	17.2 (15.5–19.2)	75.0 (72.4–77.4)
7th grade					
2014	55.0 (51.7–58.3)	36.7 (34.4–39.0)**	35.6 (32.8–38.5)**	25.9 (24.0–28.0)	67.8 (65.1–70.3)
2015	60.3 (57.5–63.1)**	40.3 (37.5–43.1)**	44.2 (41.1–47.4)**	27.4 (24.5–30.4)	72.6 (69.8–75.3)**
2016	66.2 (63.5–68.7)**	41.4 (38.7–44.2)	36.9 (34.0–39.9)	21.0 (19.2–22.9)**	77.3 (75.1–79.4)
8th grade					
2014	52.6 (48.9–56.3)	37.6 (34.7–40.5)**	34.6 (32.2–37.1)**	25.0 (21.5–28.9)	66.6 (63.4–69.6)
2015	59.7 (56.4–63.0)**	41.2 (37.4–45.1)**	43.5 (39.7–47.3)	29.6 (27.1–32.2)**	73.9 (70.7–76.9)**
2016	67.8 (65.1–70.3)**	38.5 (35.8–41.3)	36.6 (33.7–39.7)	22.0 (19.9–24.3)**	78.5 (76.4–80.4)**
9th grade					
2014	54.7 (52.1–57.2)	39.2 (37.0–41.4)**	37.2 (34.9–39.7)**	32.0 (30.1–34.0)**	68.7 (65.9–71.4)
2015	60.4 (57.8–62.8)**	45.4 (42.8–48.0)**	46.6 (44.3–49.0)**	32.2 (30.1–34.3)**	74.8 (72.8–76.7)**
2016	68.0 (65.5–70.5)**	39.5 (37.3–41.8)	37.4 (34.6–40.3)	23.7 (21.9–25.5)**	77.6 (75.4–79.7)

See table footnotes on next page.

TABLE. (*Continued*) Prevalence of exposure to e-cigarette advertisements* among U.S. youths by sex, race/ethnicity, school level, and use of e-cigarettes and other tobacco products by exposure source — National Youth Tobacco Survey, United States, 2014–2016

	% (95% CI)				
Demographic characteristic/year	Retail stores	Internet	Television /Movies	Newspapers and magazines	Any source
10th grade					
2014	56.2 (53.6–58.8)**	43.4 (40.9–45.8)**	38.9 (36.5–41.3)**	34.0 (31.6–36.5)**	71.3 (68.8–73.7)**
2015	60.2 (57.5–62.8)**	43.8 (40.6–47.0)**	43.7 (41.2–46.3)	32.4 (30.0–34.9)**	72.5 (70.0–74.9)**
2016	71.6 (69.4–73.8)**	44.0 (41.6–46.4)**	39.8 (37.3–42.4)**	27.8 (25.5–30.2)**	81.0 (78.9–82.9)**
11th grade					
2014	57.8 (54.9–60.6)**	45.5 (43.3–47.6)**	39.9 (37.1–42.7)**	35.9 (33.7–38.1)**	71.8 (69.3–74.1)**
2015	63.1 (58.9–67.2)**	45.8 (42.9–48.7)**	45.9 (42.8–49.0)**	35.5 (32.7–38.4)**	74.1 (70.8–77.1)**
2016	69.8 (67.4–72.1)**	41.6 (39.2–44.0)	40.4 (37.4–43.4)**	26.9 (24.6–29.4)**	79.3 (77.3–81.3)**
12th grade					
2014	56.8 (54.2–59.3)**	44.1 (41.7–46.6)**	37.8 (34.5–41.3)**	37.1 (34.7–39.5)**	71.9 (69.6–74.1)**
2015	64.4 (61.2–67.5)**	46.8 (43.3–50.3)**	46.8 (44.3–49.3)**	36.9 (34.8–39.1)**	77.0 (74.4–79.4)**
2016	70.8 (67.9–73.5)**	41.3 (38.3–44.2)	38.7 (35.3–42.2)	29.6 (27.7–31.6)	79.0 (76.5–81.3)**
School level					
Middle school (referent)					
2014	52.8 (50.9–54.7)	35.8 (34.2–37.4)	34.1 (32.3–35.8)	25.0 (23.8–26.3)	66.4 (64.9–67.9)
2015	57.6 (55.1–60.1)	39.0 (36.3–41.8)	42.8 (40.0–45.7)	27.1 (25.5–28.9)	71.1 (68.4–73.6)
2016	65.6 (63.9–67.3)	39.5 (37.7–41.3)	36.0 (33.9–38.1)	20.1 (18.9–21.4)	76.9 (75.2–78.5)
High school					
2014	56.3 (54.7–57.9)††	42.9 (41.4–44.4)††	38.4 (36.8–40.1)††	34.6 (33.3–36.0)††	70.9 (69.3–72.4)††
2015	61.9 (60.1–63.7)††	45.4 (43.8–47.0)††	45.7 (44.2–47.3)††	34.1 (32.9–35.4)††	74.5 (73.1–75.9)††
2016	70.0 (68.4–71.6)††	41.6 (40.2–42.9)	39.0 (36.9–41.2)††	26.9 (25.8–28.0)††	79.2 (77.8–80.6)††
Current (past 30-day) use of e-cigarettes					
Current nonuser (referent)					
2014	53.1 (51.9–54.4)	38.3 (37.0–39.5)	35.5 (34.3–36.8)	29.3 (28.3–30.4)	67.4 (66.3–68.6)
2015	59.0 (57.1–60.8)	40.9 (39.0–42.7)	43.8 (41.9–45.8)	29.7 (28.5–30.9)	71.9 (70.1–73.6)
2016	67.7 (66.6–68.7)	40.0 (38.8–41.2)	37.2 (35.6–38.9)	23.5 (22.5–24.6)	77.9 (76.8–78.9)
Current user					
2014	70.5 (67.3–73.6)§§	55.2 (52.4–57.9)§§	46.2 (43.6–48.8)§§	41.9 (38.6–45.3)§§	82.6 (80.4–84.7)§§
2015	68.4 (64.8–71.8)§§	56.8 (53.7–59.8)§§	49.1 (46.5–51.7)§§	41.3 (38.6–44.0)§§	81.8 (79.3–84.1)§§
2016	74.3 (70.7–77.6)§§	47.1 (43.4–50.8)§§	42.2 (39.1–45.4)§§	28.3 (24.8–32.0)§§	82.8 (79.8–85.5)§§
Current (past 30-day) use, other tobacco product¶¶					
Current nonuser (referent)					
2014	53.0 (51.8–54.2)	38.1 (36.8–39.5)	35.3 (34.0–36.6)	28.8 (27.7–29.9)	67.3 (66.1–68.4)
2015	59.0 (57.2–60.8)	41.2 (39.3–43.2)	43.7 (41.9–45.6)	29.7 (28.5–30.9)	72.1 (70.4–73.8)
2016	67.5 (66.4–68.6)	40.1 (39.0–41.3)	36.8 (35.2–38.5)	23.4 (22.3–24.5)	77.6 (76.6–78.6)
Current user					
2014	66.0 (63.6–68.4)§§	50.2 (47.5–53.0)§§	44.2 (42.1–46.4)§§	40.8 (38.3–43.3)§§	79.0 (77.0–80.9)§§
2015	66.4 (63.6–69.0)§§	51.8 (48.8–54.7)§§	49.2 (46.8–51.7)§§	40.0 (37.8–42.3)§§	78.6 (76.0–81.0)§§
2016	72.6 (69.4–75.6)§§	44.7 (41.9–47.6)§§	44.8 (41.6–48.0)§§	28.3 (25.8–30.9)§§	82.7 (79.7–85.4)§§

Abbreviation: CI = confidence interval.

* Exposure to each e-cigarette advertisement source was assessed by the following questions: Retail Stores: "When you go to a convenience store, super market, or gas station, how often do you see ads or promotions for e-cigarettes?"; Internet: "When you are using the internet, how often do you see ads or promotions for e-cigarettes?"; Television (TV)/Movies: In 2014, Television/movie exposure was assessed by the question "When you watch TV or go to the movies, how often do you see ads or promotions for e-cigarettes?" In 2015–2016, only TV exposures were assessed: "When you watch TV, how often do you see ads or promotions for e-cigarettes?"; and Newspaper and Magazines: "When you read newspapers or magazines, how often do you see ads or promotions for e-cigarettes?" For all questions, response options included "Never, Rarely, Sometimes, Most of the time, or Always." A "not applicable" (N/A) response was also included to capture respondents who did not use each advertising source. Respondents were categorized as "Exposed" if they reported seeing ads or promotions "sometimes," "most of the time," or "always." Respondents were categorized as "Unexposed" if they reported seeing ads or promotions "never," or "rarely." Individuals who reported N/A were included in the analysis in the "Unexposed" group. A composite measure of any advertisement exposure (any source) is assessed based on exposure to retail, internet, television/movies, and print ad exposures.

† Population estimates rounded down to the nearest 0.1 million.

§ Significantly different from males at p<0.05 based on paired t-test.

¶ Significantly different from non-Hispanic white at p<0.05 based on paired t-test.

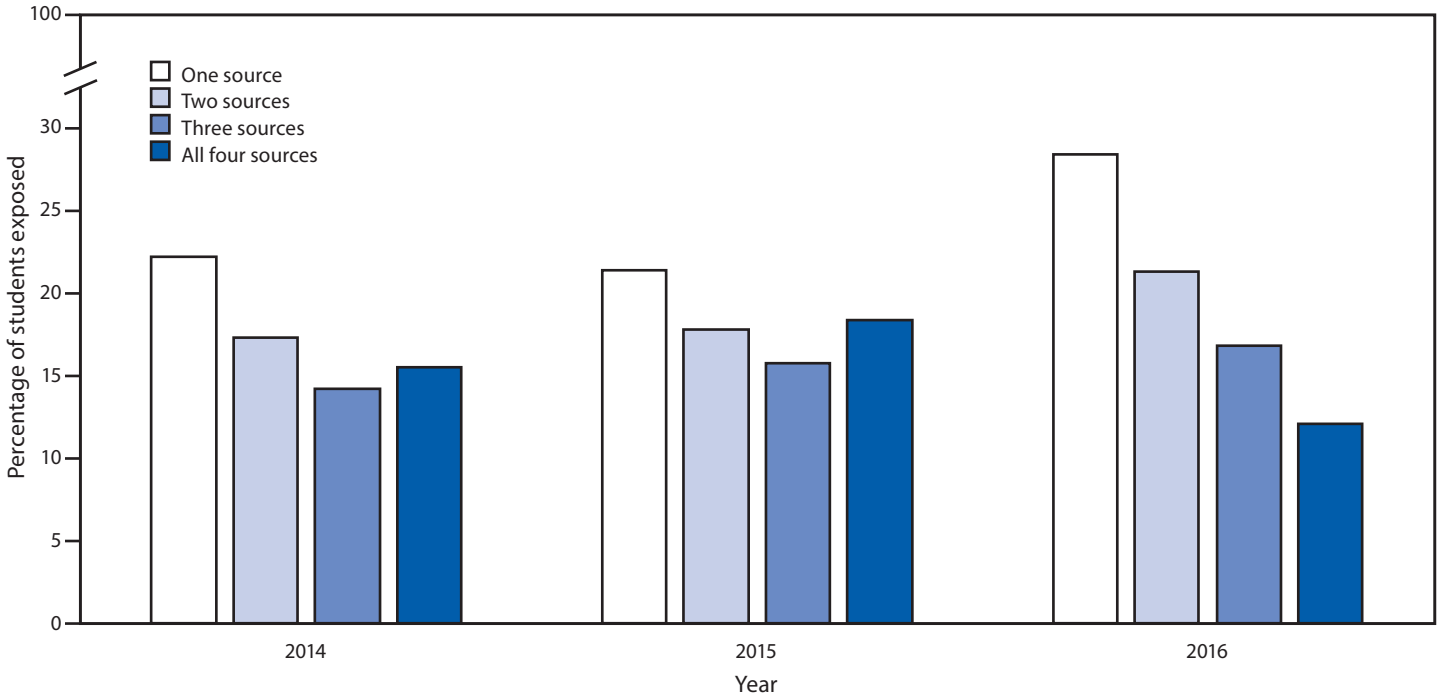
** Significantly different from 6th grade at p<0.05 based on paired t-test.

†† Significantly different from middle school at p<0.05 based on paired t-test.

§§ Significantly different from noncurrent users at p<0.05 based on paired t-test.

¶¶ Based on respondents' use of cigarettes, cigars, smokeless tobacco (includes chewing tobacco/snuff/dip, snus, and dissolvable tobacco), hookah/waterpipe, regular pipe, and/or bidis on at least one day during the past 30 days.

FIGURE 2. Percentage of U.S. middle and high school students who were exposed to e-cigarette advertising, by number of exposure sources*—National Youth Tobacco Survey, United States, 2014–2016



* The four exposure sources were retail stores, the Internet, television/movies, and newspapers and magazines. Movies were removed as an advertising source after 2014.

advertising tactics that have been proven to appeal to youths, such as themes of romance, freedom, and rebellion; celebrity endorsements; and health claims (*5*,*7*). Exposure to e-cigarette advertising might reduce youths' perception of harm associated with e-cigarettes and increase their beliefs that e-cigarettes can be used where smoking is prohibited (*8*). Product design features might also influence use. For example, JUUL, the top-selling U.S. e-cigarette brand,¶ is an e-cigarette shaped like a USB flash drive that has a high nicotine concentration (*9*). According to news reports and social media posts, students are using JUUL in school classrooms and bathrooms (*9*).**,†† In addition, e-cigarettes are marketed and promoted using strategies that are not legally permissible for conventional cigarettes, including television, sports, and music event sponsorships, in-store self-service displays, and advertisements placed outside of brick-and-mortar businesses at children's eye level (*5*,*10*).

As of August 2016, the Food and Drug Administration enforces restrictions on e-cigarette sales to minors, including those over the Internet.§§ Additional actions to reduce youths' tobacco access and advertising exposure could include requiring that e-cigarettes are sold in adult-only facilities, limiting tobacco outlet density or proximity to schools, prohibiting self-service displays, and requiring face-to-face transactions for all e-cigarette purchases (*6*). Additional potential strategies include regulation of advertising with demonstrated youth appeal or broad youth reach at retail stores, on television, online, and in print media; and high-impact tobacco education campaigns that warn youths about the dangers of any tobacco product use, including e-cigarettes (*5*,*6*).

The findings in this study are subject to at least four limitations. First, self-reports of advertising exposure might be subject to reporting bias. Moreover, current e-cigarette users might be more likely to recall exposure than nonusers. Second, the NYTS might not be representative of all U.S. youths, because it does not capture those who are homeschooled, have dropped out of school, or are in detention centers. However, data from the Current Population Survey indicate that 98.5%, 98.0%, and 93.0% of U.S. youths aged 10–13, 14–15, and 16–17 years, respectively, were enrolled in a traditional school in 2016.¶¶ Third, advertising exposure might be underestimated because exposure from other potential sources such as sporting events, radio, billboards, or movies was not assessed. Finally, the removal of movies as a source of exposure after 2014 limited the comparability of television e-cigarette advertisements between years. However, this change likely resulted in an underestimation of exposure in 2015 and 2016.

¶ Wells Fargo Securities, LLC. Nielsen: Tobacco 'All Channel' Report Ending 2.24.18.
** https://www.reddit.com/r/juul/comments/61is7i/whats_juul_in_school/.
†† https://www.youtube.com/watch?v=CIYQtVsOELY.
§§ https://www.fda.gov/downloads/TobaccoProducts/GuidanceComplianceRegulatoryInformation/Retail/UCM520813.pdf.

¶¶ https://www.census.gov/data/tables/2016/demo/school-enrollment/2016-cps.html.

Summary

What is already known about this topic?

E-cigarettes are the most commonly used tobacco product among U.S. middle and high school students. E-cigarette advertising is associated with e-cigarette use among youths, and employs themes and strategies that are similar to conventional cigarette advertising tactics that have been proven to appeal to youths.

What is added by this report?

In 2016, an estimated 4 in 5 (20.5 million) U.S. middle and high school students were exposed to e-cigarette advertisements from at least one source, a significant increase over 2014 and 2015. Nearly seven in 10 youths (17.7 million) were exposed to e-cigarette advertising in retail stores in 2016, while approximately two in five were exposed on the Internet or on television, and nearly one in four were exposed through newspapers and magazines.

What are the implications for public health practice?

As part of comprehensive youth tobacco prevention efforts, approaches to reduce youth access to e-cigarettes and exposure to advertising could include regulation of youth-oriented marketing, restrictions on youth access to tobacco products in retail settings, and high-impact youth-focused tobacco education campaigns.

Exposure to e-cigarette advertisements increased among U.S. middle and high school students during 2014–2016. As part of comprehensive youth tobacco prevention efforts, approaches to reduce youth access to e-cigarettes and exposure to e-cigarette advertising could include regulation of youth-oriented marketing, restrictions on youth access to tobacco products in retail settings, and high-impact youth-focused tobacco education campaigns (*5*). These approaches, coupled with comprehensive state tobacco control programs, have the potential to prevent and reduce youth use of all tobacco products, including e-cigarettes (*5*).

Conflict of Interest

No conflicts of interest were reported.

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Vaccine-Derived Poliovirus Outbreaks and Events — Three Provinces, Democratic Republic of the Congo, 2017

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The last confirmed wild poliovirus (WPV) case in Democratic Republic of the Congo (DRC) had paralysis onset in December 2011 (*1*). DRC has had cases of vaccine-derived polioviruses (VDPVs) documented since 2004 (Table 1) (*1–6*). After an outbreak of 30 circulating VDPV type 2 (cVDPV2) cases during 2011–2012, only five VDPV2 cases were reported during 2013–2016 (Table 1) (*1–6*). VDPVs can emerge from oral poliovirus vaccine (OPV types 1, 2, or 3; Sabin) polioviruses that have genetically mutated resulting in reversion to neurovirulence. This process occurs during extensive person-to-person transmission in populations with low immunity or after extended replication in the intestines of immune-deficient persons following vaccination (*1–6*). During 2017 (as of March 8, 2018), 25 VDPV cases were reported in three provinces in DRC: in Tanganyika province, an emergence with one VDPV2 case (pending final classification) in Kabalo health zone and an emergence with one ambiguous VDPV type 1 (aVDPV1) case in Ankoro health zone; in Maniema province, an emergence with two cVDPV2 cases; and in Haut Lomami province, an emergence with 20 cVDPV2 cases that originated in Haut Lomami province and later spread to Tanganyika province (hereafter referred to as the Haut Lomami outbreak area) and an emergence with one aVDPV type 2 (aVDPV2) case in Lwamba health zone (Table 1) (Figure) (*6*). Outbreak response supplementary immunization activities (SIAs) were conducted during June–December 2017 (Table 2) (*6*). Because of limitations in surveillance and suboptimal SIA quality and geographic scope, cVDPV2 circulation is likely continuing in 2018, requiring additional SIAs. DRC health officials and Global Polio Eradication Initiative (GPEI) partners are increasing human and financial resources to improve all aspects of outbreak response.

Vaccine-Derived Polioviruses

VDPVs are classified as circulating (cVDPVs) when there is evidence of community transmission; immunodeficiency-associated VDPVs (iVDPVs) when isolated from persons with primary immunodeficiency (representing a potential risk for outbreaks in areas of low poliovirus immunity*); or ambiguous (aVDPVs) when the identity is uncertain (i.e., when investigations have not indicated ongoing transmission and the virus is not an iVDPV, including isolates identified from environmental surveillance) (*7*). VDPV types 1 or 3 are polioviruses that are >1% divergent (i.e., ≥10 nucleotide differences in the genetic sequence) from the corresponding OPV strain in the complete viral protein 1 (VP1) genomic coding region (*1–7*). VDPV2s are >0.6% divergent (i.e., ≥6 nucleotide differences in the genetic sequence) (*1–7*).

* https://www.ncbi.nlm.nih.gov/pubmed/19090774.

Trivalent OPV to Bivalent OPV Switch

The 2014 World Health Assembly endorsed a strategy to reduce the risks associated with OPV polioviruses (i.e., the occurrence of vaccine-associated paralytic polio or VDPV cases) (*5*). The type 2 component of trivalent OPV (tOPV, types 1-, 2-, and 3-containing) was responsible for most cVDPV cases occurring after 2006 (*1,4–6*). Considering that WPV type 2 was declared eradicated in 2015 and in accordance with the Polio Eradication and Endgame Strategic Plan 2013–2018, all countries ceased using any type 2–containing OPV as of May 1, 2016 (*5,6*). A globally synchronized switch from tOPV to bivalent OPV (bOPV, type 1- and 3-containing) occurred in all OPV-using countries, including DRC (*5,6*). A single dose of inactivated polio vaccine (IPV) was introduced into routine immunization to mitigate the risks for an immunity gap to type 2 poliovirus (*5*).

Monovalent type 2 OPV (mOPV2) is held in a global stockpile for response to poliovirus type 2 outbreaks after the switch (*8*). The World Health Organization (WHO) Director General approves release of mOPV2 based on recommendations from the Advisory Group on mOPV2 Provision (Advisory Group) (*8*).

Vaccine-Derived Polioviruses in Democratic Republic of the Congo

During 2004–2017 (as of March 8, 2018), 11 of DRC's 26 provinces reported 118 cases of acute flaccid paralysis (AFP) with VDPVs isolated in stool samples (Table 1) (*1–6*). Until 2017, when the VDPV1 case in Tanganyika province was reported, all VDPVs had been type 2 (*1–6*). During 2004–2017, 63 (53%) of the 118 AFP cases with VDPV were reported in Haut Lomami province; those 63 VDPV cases were reported from eight of the province's 16 health zones, with 34 (54%) cases from just two health zones, Kinkondja and Malemba-Nkulu (*1–6*).

TABLE 1. Number of acute flaccid paralysis (AFP) cases with any vaccine-derived poliovirus (VDPV) in stool samples, by year of paralysis onset and province — Democratic Republic of the Congo, 2004–2017*,†

Province	Year												
	2004	2005	2007	2008	2009	2010	2011	2012	2014	2015	2016	2017	Total
Bas Uele	—§	—	—	—	—	1	—	—	—	—	—	—	**1**
Equateur	—	—	—	—	—	1	—	—	—	—	—	—	**1**
Haut Katanga	—	—	—	—	—	—	—	—	—	1	—	—	**1**
Haut Lomami	—	7	—	16	2	—	13	17	—	—	—	8	**63**
Kasai	—	—	—	—	2	3	—	—	—	—	—	—	**5**
Maindombe	—	2	—	—	1	—	—	—	—	1	—	—	**4**
Maniema	1	—	—	1	—	10	—	—	—	—	—	2	**14**
Mongala	—	—	—	—	1	2	—	—	—	—	1	—	**4**
Sud Kivu	—	—	1	—	—	—	—		—	—	—	—	**1**
Tanganyika	—	—	—	1	1	—	—	—	1	—	—	15	**18**
Tshopo	—	—	1	1	1	2	—	—	—	—	1	—	**6**
National	1	9	2	19	8	19	13	17	1	2	2	25	**118**

* As of March 8, 2018.
† No AFP cases with paralysis onset in 2006 or 2013 had VDPV isolated from their stool sample.
§ Dashes indicate no cases.

Historically, the routine immunization program in DRC has not met global standards (*1*,*6*,*9*,*10*). Since 1996, regular preventive and outbreak response OPV SIAs have been conducted to enhance population immunity. WHO and United Nations Children's Fund estimates of national coverage with the third dose of OPV (OPV3) in the first year of life remained <50% until 2004; coverage estimates increased to 78% by 2011 (*9*). Estimates based on vaccine doses administered and coverage survey results indicate that national OPV3 coverage has never exceeded 80% (*6*,*9*,*10*). The most recent (2013–2014) DRC Demographic and Health Survey identified subnational areas where estimated OPV3 coverage remained <60% (*10*). Introduction of IPV into the routine program in 2015 (before the tOPV to bOPV switch) has had minimal impact in building type 2 poliovirus immunity; estimated national IPV coverage was 48% in 2015 and 70% in 2016 (*9*). Thus, many areas within DRC have been and remain susceptible to the emergence of VDPVs, especially after periods of reduced numbers of OPV SIAs.

Where conducted in response to VDPVs detected before 2017, SIAs were able to interrupt transmission (*1*). No previous VDPV transmission spread nationally from the location of emergence or reappeared after apparent interruption (*1*–*5*). The 2017 cVDPV2 transmission is ongoing (*6*).

Tanganyika aVDPV1 Event, 2017

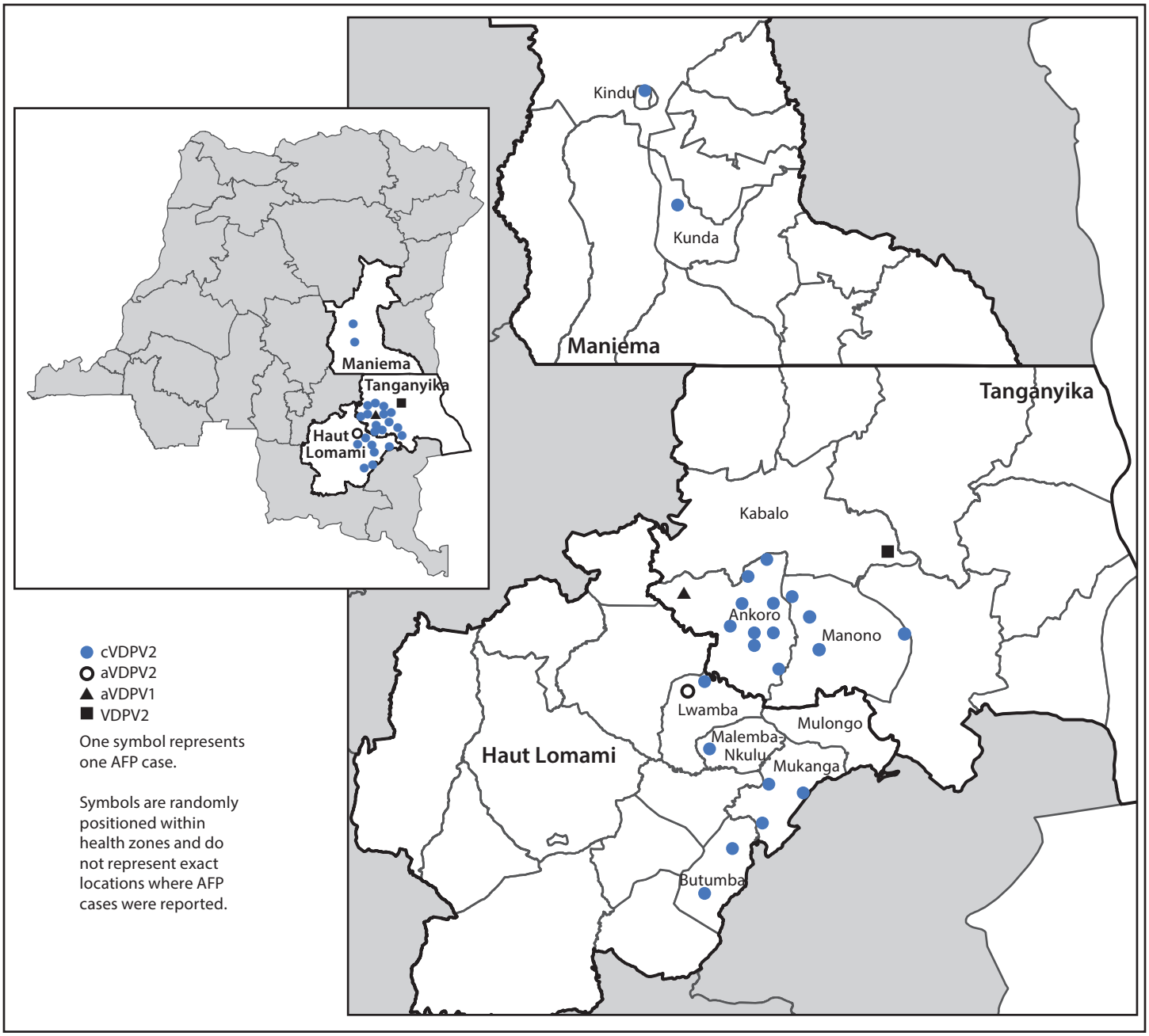
DRC's single case of VDPV1 was reported in April 2017 (Figure) (*6*). The patient had paralysis onset on April 1 in Tanganyika's Ankoro health zone. The VDPV1 from this case had 25 nucleotide differences in the VP1 region from Sabin virus type 1, suggesting prolonged undetected replication. No additional VDPV1 viruses have been isolated, and the patient is not known to have an immunodeficiency; thus, to date, the case has been classified as an aVDPV1, and the occurrence is classified as a VDPV1 event per WHO's standard operating procedures (*7*,*8*). During April 9–11, before confirmation of the case, a previously planned National Immunization Day with bOPV targeting children aged <5 years was conducted in DRC (Table 2). All health zones included in the Tanganyika clustered lot quality assurance sampling (LQAS) surveys passed the criteria for acceptable SIA performance at the 80% threshold (*8*). Clustered LQAS is a survey methodology for rapidly assessing the quality of vaccination coverage in a predefined geographic area (i.e., a "lot"); if less than nine unvaccinated children are observed in a lot of 60 children, SIA performance is said to be acceptable at the 80% threshold.† No additional SIAs with a type 1-containing OPV were conducted in Tanganyika province in 2017. According to the standard operating procedures, SIAs are not required for an aVDPV1 event, although enhanced surveillance and AFP case contact investigations are recommended (*8*).

Maniema cVDPV2 Outbreak, 2017

The first cVDPV2 patient in Maniema province had paralysis onset on March 26, 2017, in Kindu health zone (Figure) (*6*). The second case, occurring in a child residing in Kunda health zone, had paralysis onset on April 18 (*6*). No additional cases have been reported to date. Genetic analyses of the cVDPV2 viruses isolated from these cases indicated that the VP1 region sequences were identical, differing from the Sabin type 2 vaccine strain at the same 7 nucleotide positions in the VP1 region and that divergence from Sabin occurred at approximately the time of the tOPV-bOPV switch (May 2016).

† http://polioeradication.org/wp-content/uploads/2016/09/Assessing-Vaccination-Coverage-Levels-Using-Clustered-LQAS_Apr2012_EN.pdf.

FIGURE. Geographic distribution of reported cases of vaccine-derived poliovirus (VDPV),* by province and health zone — Democratic Republic of the Congo, 2017†



Abbreviations: AFP = acute flaccid paralysis; aVDPV1/aVDPV2 = ambiguous VDPV types 1 or 2; cVDPV2 = circulating VDPV type 2; VDPV2 = VDPV type 2.
* The VDPV2 case is still pending final classification.
† As of March 8, 2018.

The Advisory Group approved the release of mOPV2 for two SIAs targeting 276,076 children aged <5 years in eight health zones surrounding and including Kindu and Kunda in June and July (Table 2) (*6*). Results of the clustered LQAS conducted after the two SIAs indicated that Kunda health zone did not meet the criteria for acceptable SIA performance at the 80% threshold. In September, a mop-up campaign targeting 57,339 children was conducted in Kunda; clustered LQAS results indicated acceptable performance (Table 2) (*6*). After the mop-up campaign, the Advisory Group reviewed an assessment of the risk for continued viral transmission in Maniema and concluded that no additional mOPV2 SIAs were advised.

TABLE 2. Polio supplementary immunization activities (SIAs) conducted in Haut Lomami, Maniema, and Tanganyika provinces, by vaccine-derived poliovirus outbreak or event — Democratic Republic of the Congo, 2017*

Outbreak/Event	Province	Health zones with confirmed VDPV case(s)	SIA start date (oral poliovirus vaccine used), by month in 2017						
			Apr† (bOPV)	Jun (mOPV2)	Jul (mOPV2)	Sep§ (mOPV2)	Oct¶ (bOPV)	Nov** (mOPV2)	Dec** (mOPV2)
Tanganyika aVDPV1/VDPV2	Tanganyika	Ankoro	Apr 9	—††	—	—	—	Nov 30	Dec 16
		Kabalo	Apr 9	—	—	—	—	—	—
Haut Lomami Area cVDPV2/aVDPV2	Tanganyika	Ankoro	Apr 9	—	—	—	—	Nov 30	Dec 16
		Manono	Apr 9	—	—	—	—	Nov 30	Dec 16
	Haut Lomami	Butumba	Apr 9	Jun 6	Jul 13	—	—	Nov 30	Dec 16
		Mukanga	Apr 9	Jun 6	Jul 13	Sep 14	Oct 12	Nov 30	Dec 16
		Malemba-Nkulu	Apr 9	Jun 6	Jul 13	—	Oct 12	Nov 30	Dec 16
		Lwamba	Apr 9	Jun 6	Jul 13	—	Oct 12	Nov 30	Dec 16
Maniema cVDPV2	Maniema	Kindu	Apr 9	Jun 6	Jul 20	—	—	—	—
		Kunda	Apr 9	Jun 6	Jul 20	Sep 14	—	—	—

Abbreviations: aVDPV1/aVDPV2 = ambiguous VDPV types 1 or 2; bOPV = bivalent oral poliovirus vaccine containing types 1 and 3; cVDPV2 = circulating VDPV type 2; VDPV2 = VDPV type 2; mOPV2 = monovalent oral poliovirus vaccine containing type 2.

* As of March 8, 2018.

† The April 2017 bOPV SIA was a National Immunization Day planned prior the occurrence of these VDPV cases and was not conducted as event response.

§ The September 14, 2017 SIA was considered a mop-up and was only conducted in two health zones with VDPV cases.

¶ The October 12, 2017 bOPV SIA was conducted as part of a previously planned Local Immunization Day and was not conducted as part of outbreak response.

** The November 30, 2017 and December 16, 2017 mOPV2 SIAs were conducted in response to the cVDPV2 outbreak in the Haut Lomami area and were not related to the aVDPV1 event. The SIAs were conducted before the confirmation of the aVDPV2 in Lwamba health zone and the VDPV2 (pending classification) in Kabalo health zone.

†† Dashes indicate that no SIA was held during the month indicated.

Haut Lomami Area cVDPV2 Outbreak and aVDPV2 Event, 2017

The first patient in the cVDPV2 outbreak in the Haut Lomami outbreak area had paralysis onset on February 20, 2017 in Malemba-Nkulu health zone (Figure) (*6*). The cVDPV2 had 15 nucleotide differences from Sabin type 2 vaccine strain in the VP1 region, indicating more than 1 year of undetected circulation and therefore originating before the tOPV-bOPV switch. Six additional cVDPV2 cases with paralysis onset between March 8 and July 27 were reported in Butumba (two), Lwamba (one), and Mukanga (three) health zones. These four health zones are geographically contiguous and within Haut Lomami province (Figure) (*6*).

The Advisory Group recommended mOPV2 for two SIAs targeting 513,820 children aged <5 years in 12 health zones (in three provinces: Haut Lomami, Lualaba, and Haut Katanga), including and surrounding the health zones where cases were reported (6). The SIAs were conducted in June and July (Table 2) (*6*). Results of clustered LQAS indicated that acceptable SIA performance in Mitwaba health zone (Haut Katanga province) was not achieved. In addition, the cVDPV2 cases in Mukanga were confirmed after the July SIA. Consequently, in September, a mop-up campaign targeting 66,006 children was conducted in Mitwaba and Mukanga with acceptable performance, based on the clustered LQAS (Table 2) (*6*). Considering the cases in Mukanga health zone with confirmation after the July SIA, the Advisory Group approved mOPV2 for two additional SIAs in the 12 health zones where the first two were conducted. Included in these SIAs were eight additional health zones (including Ankoro and Manono in Tanganyika province) contiguous with the 12 and identified as being at high risk for virus circulation because of population movement to and from the outbreak health zones, low vaccination coverage, the presence of populations that refuse vaccination, and poor AFP surveillance performance.

Just after the Advisory Group's approval in October 2017, the first of 13 additional, genetically linked cVDPV2 cases were confirmed in Ankoro and Manono health zones in Tanganyika province, with paralysis onset from September 14 to December 22, 2017 (Figure). In-depth genomic sequence analyses of all viral isolates from the cVDPV2 outbreak to date indicate that transmission had already extended into Tanganyika before the first outbreak response efforts were conducted in Haut Lomami province during June–September 2017; however, AFP surveillance in Tanganyika did not detect the transmission until months later. (Figure) (Table 2). The approved SIAs were conducted in December and targeted 850,002 children (Table 2). The clustered LQAS results revealing unacceptable SIA quality at the 80% threshold in numerous health zones and the paralysis onset of new cVDPV2 cases in late December 2017 indicate a need for additional SIAs in 2018.

After the December 2017 SIAs, two new VDPV2 emergences were confirmed in Haut Lomami and Tanganyika provinces. The first was in an AFP case with paralysis onset 15 November 2017 in Lwamba health zone (Haut Lomami province); this case has been classified as an aVDPV2 and the occurrence a VDPV2 event (Figure) (*8*). The second was in an AFP case in Kabalo health zone (Tanganyika province) with paralysis

onset 29 December 2017; the final classification for this case is pending completion of the investigation (Figure).

Discussion

The emergence and circulation of VDPVs during many years and over a broad geographical area is evidence of widespread suboptimal poliovirus immunity in major portions of DRC (*1*–*6*). National OPV3 coverage estimates have never exceeded 80%, and lower coverage exists in certain subnational areas (*1*,*6*,*9*,*10*). Even with preventive and outbreak response SIAs, many children remain unvaccinated or insufficiently vaccinated.

Longstanding circumstances within Haut Lomami, Maniema, Tanganyika, and other eastern provinces, including insufficient human resources, insecurity, poor roads, lack of transport and cold chain equipment, riverine and other difficult-to-reach communities, and communities historically refusing vaccination have posed challenges to routine immunization, SIA implementation, and AFP surveillance and have resulted in susceptibility to the emergence of VDPVs[§] (*10*).

No additional cases of cVDPV2 in Maniema or VDPV1 in Tanganyika have been reported since April 2017; however, 2017 key AFP surveillance performance indicators did not meet GPEI standards in either province. The cVDPV2 transmission that spread from the administrative boundaries of Haut Lomami province to Tanganyika province had delayed detection because of surveillance gaps; thus, the initial response SIAS (June–September 2017) were of insufficient geographic scope to confine the outbreak (*6*). An external outbreak response assessment conducted in late 2017 concluded that polio immunity is inadequate to interrupt VDPV transmission in the affected areas and that AFP surveillance lacks the sensitivity to detect all remaining transmission (CDC and GPEI, unpublished data, 2017).

GPEI partners are intensifying outbreak response efforts in the Haut Lomami outbreak area and Maniema province. To achieve this, an additional surge in human and financial resources is planned. More consultants and GPEI staff will be deployed to the operational level to assist with implementation of tailored strategies to overcome the above-mentioned challenges. Planning for future SIAs will account for local circumstances, appropriate resources will be requested, and supervision will be enhanced. Intensified active AFP case search, systematic stool sample collection from AFP case contacts, and the use of telephones for "real-time" surveillance reporting will likely increase surveillance sensitivity. Environmental surveillance (i.e., wastewater collection for poliovirus testing) was established in late 2017 in Kindu (Maniema province) and in Lubumbashi (Haut Katanga province adjacent to Haut Lomami) and will continue. The risk for VDPV emergence in DRC will remain until population immunity is increased and maintained. The immediate goal is to interrupt VDPV transmission in the outbreak areas so that efforts can be turned toward improving polio vaccination and surveillance in other high risk areas in DRC.

[§] https://academic.oup.com/jid/article/210/suppl_1/S50/2194000.

Summary

What is already known about this topic?

Democratic Republic of the Congo has had cases of polio caused by vaccine-derived polioviruses (VDPVs) documented since 2004. The emergence of these VDPVs, which cause paralysis similar to wild polioviruses, can occur where population immunity to poliovirus is suboptimal. After an outbreak of 30 circulating VDPV type 2 (cVDPV2) cases during 2011–2012, only five VDPV2 cases were reported during 2013–2016.

What is added by this report?

In 2017 (as of March 8, 2018), 25 cases of VDPV were reported from three provinces, Haut Lomami, Maniema, and Tanganyika. Among the 25 VDPV cases, 22 were classified as cVDPV2, with 20 associated with an emergence that started in Haut Lomami province and spread to Tanganyika province and two associated with a separate emergence in Maniema province. Despite response efforts, transmission of these VDPVs has not yet been interrupted.

What are the implications for public health practice?

Risk for VDPV emergence in DRC will remain unless population immunity to poliovirus is increased and maintained. Efforts are being made as part of the current VDPV outbreak response to overcome long-standing constraints to polio vaccination. Such efforts will be extended to other regions of the country once transmission in the current outbreak areas is interrupted.

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Conflict of Interest

No conflicts of interest were reported.

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Morbidity and Mortality Weekly Report

Emergence of Monkeypox — West and Central Africa, 1970–2017

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The recent apparent increase in human monkeypox cases across a wide geographic area, the potential for further spread, and the lack of reliable surveillance have raised the level of concern for this emerging zoonosis. In November 2017, the World Health Organization (WHO), in collaboration with CDC, hosted an informal consultation on monkeypox with researchers, global health partners, ministries of health, and orthopoxvirus experts to review and discuss human monkeypox in African countries where cases have been recently detected and also identify components of surveillance and response that need improvement. Endemic human monkeypox has been reported from more countries in the past decade than during the previous 40 years. Since 2016, confirmed cases of monkeypox have occurred in Central African Republic, Democratic Republic of the Congo, Liberia, Nigeria, Republic of the Congo, and Sierra Leone and in captive chimpanzees in Cameroon. Many countries with endemic monkeypox lack recent experience and specific knowledge about the disease to detect cases, treat patients, and prevent further spread of the virus. Specific improvements in surveillance capacity, laboratory diagnostics, and infection control measures are needed to launch an efficient response. Further, gaps in knowledge about the epidemiology and ecology of the virus need to be addressed to design, recommend, and implement needed prevention and control measures.

Monkeypox Cases in West Africa and Central Africa

Since the global eradication of smallpox, monkeypox has emerged as the most prevalent orthopoxvirus infection in humans (*1*). The majority of documented human monkeypox cases have occurred in Democratic Republic of the Congo (DRC), where it was first recognized as a human disease in 1970; however, during the last decade, the number of cases in other west and central African countries have been increasing; many of these countries had not reported a case for several decades (Table) (Figure). Since 2016, monkeypox cases have been reported and confirmed from Central African Republic (19 cases), DRC (>1,000 reported per year), Liberia (two), Nigeria (>80), Republic of the Congo (88), and Sierra Leone (one) (Table); an outbreak in captive chimpanzees occurred in Cameroon. With 80 confirmed cases, Nigeria is currently experiencing the largest documented outbreak of human monkeypox in West Africa. The emergence of cases is a concern for global health security.

Monkeypox is a zoonotic orthopoxvirus with a similar disease presentation to smallpox in humans, with the additional distinguishing symptom of lymphdenopathy. After an initial febrile prodrome, a centrifugally distributed maculopapular rash develops, with lesions often present on the palms of the hands and soles of the feet. The infection can last up to 4 weeks, until crusts separate and a fresh layer of skin is formed. Sequelae include secondary bacterial infections, respiratory distress, bronchopneumonia, gastrointestinal involvement, dehydration, encephalitis, and ocular infections, which can result in permanent corneal scarring. No specific treatment for a monkeypox virus infection currently exists, and patients are managed with supportive care and symptomatic treatment. In persons who have not been vaccinated against smallpox, which offers cross-protection, the case fatality rate is 11%. Human-to-human transmission occurs via respiratory droplets and contact with lesions that contain the virus (*1*).

Monkeypox primarily occurs in the rain forests in West Africa and Central Africa. Although antibodies have been detected in a range of small mammal species (*2*), the reservoir species of monkeypox remains unknown, and the virus has been isolated only twice from wild animals, once from a rope squirrel (*Funisciurus anerythrus*) in DRC and once from a sooty mangabey (*Cercocebus atys*) in Côte d'Ivoire. Contact with the animal reservoir/reservoirs, including contact with live or dead animals, often through the hunting and preparation of bushmeat as food, is a presumed driver of monkeypox infection. Closer contact between humans and animals through deforestation, demographic changes, climate change, hunting, and population movement might account for the recent increase in reported cases and expansion of geographic range. Civil war and population displacement can force inhabitants to seek alternative sources of protein, including the consumption of monkeys, squirrels, and other rodents.

Vaccination against smallpox is known to be cross-protective against the other orthopoxviruses, including monkeypox. Following the eradication of smallpox in 1980 and the cessation of smallpox vaccination in the early 1980s, waning vaccine-induced population immunity and lack of protection among younger age groups might have contributed to the resurgence of the disease (*3*).

Monkeypox virus has two recognized clades: West African and Congo Basin. Differences in epidemiologic and clinical features between viral isolates support the distinction between

TABLE. Reported cases of monkeypox in humans and animals, by country — Africa,* 1970–2018

Country	Year	Location	No. of cases†	No. of deaths
Cameroon§	1979	Mfou District	1	0
	1989	Nkoteng	1	0
Central African Republic	1984	Sangha Administrative Region	6	0
	2001	—	4	—
	2010	—	2	0
	2015	Mbomou Prefecture, Bakouma and Bangassou subprefectures	12	3
	2016	Haute-Kotto Health District, Yalinga	11	1
	2017	Mbaiki Health District	2	0
	2017	Ouango Health Districts	6	0
Côte d'Ivoire¶	1971	Abengourou	1	0
	1981	—	1	—
Democratic Republic of the Congo	1970–2017	Multiple provinces	>1,000/year**	—
Gabon	1987	Region between Lambarene and N'Djole	5	2
Liberia	1970	Grand Geddah	4	0
	2017	Rivercess and Maryland counties	2	0
Nigeria	1971	Aba State	2	0
	1978	Oyo State	1	0
	2017–2018	Multiple states	89††	6††
Republic of the Congo	2003	Likouala Region	11	1
	2009	Likouala Region	2	0
	2017	Likouala Region	88	6
Sierra Leone	1970	Aguebu	1	0
	2014	Bo	1	1
	2017	Pujehan District	1	0
Sudan§§,¶¶	2005	Unity State	19	0

* The United States experienced a monkeypox outbreak in 2003 with 47 confirmed and probable cases, attributed to a shipment of wild animals from West Africa to the United States.
† Includes laboratory-confirmed cases and suspected cases that had an epidemiologic (close contact), spatial, or temporal link to a laboratory-confirmed case.
§ Outbreaks have occurred twice (2014 and 2016) in captive chimpanzee groups.
¶ Monkeypox virus was isolated from a wild caught sooty mangabey (*Cercocebus atys*).
** Democratic Republic of the Congo has reported >1,000 suspected cases each year since 2005.
†† As of February 25, 2018; laboratory-confirmed cases only.
§§ The presence of Monkeypox virus in Sudan was attributed to movement of the virus from Democratic Republic of the Congo.
¶¶ The cases occurred in an area that is now part of South Sudan.

these two clades (*4*). Advances in the use of DNA sequencing to understand viral strains and populations will be valuable for interpreting transmission events and confirming the existence of endemic variants (*5*,*6*). Further studies are needed to understand temporal and spatial genetic differences in viral strains.

Discussion

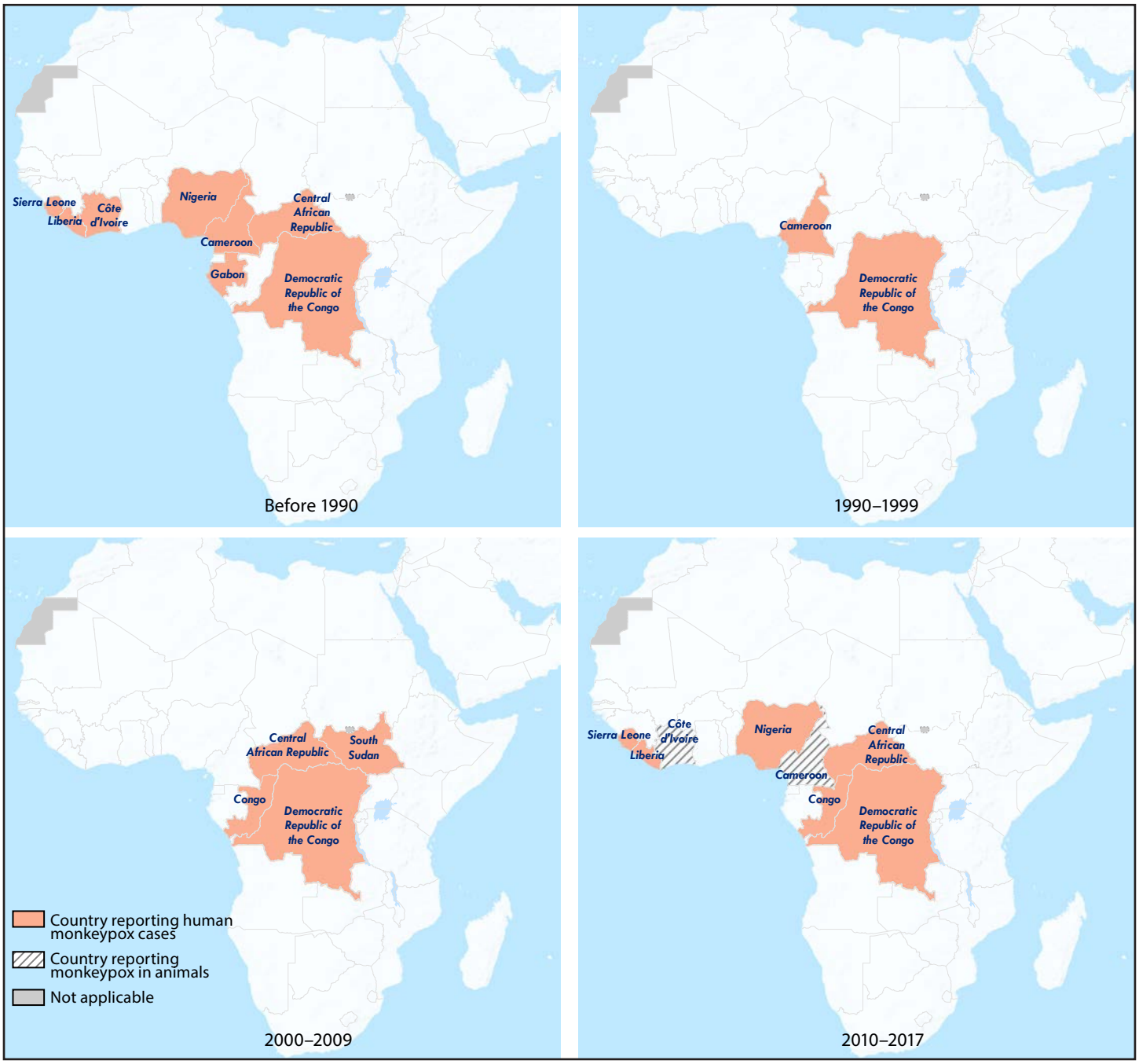
Monkeypox presents challenges for public health officials and health care personnel in terms of surveillance and laboratory capacities, and management and treatment of disease. Overall, surveillance in West Africa has improved as a result of recommendations from the Joint External Evaluations* and the Global Health Security Agenda assessments after the 2014–2016 Ebola virus disease epidemic. However, health care providers in many countries lack knowledge and experience in the recognition, diagnosis, and treatment of monkeypox, and implementation of public health measures that are needed to stop further spread. The establishment of appropriate disease surveillance systems requires initial and long-term financial and human resource investments. Monkeypox is not currently a disease for which mandatory reporting is required through the Integrated Disease Surveillance and Response system across Africa.† DRC has implemented mandatory reporting of the disease, which has improved systematic reporting. Although notifications occur regularly, investigations with diagnostic specimens and implementation of control measures, including contact tracing and strict patient isolation, are less rigorously applied. Because monkeypox is a viral zoonosis, coordination of interventions between the human and animal (wildlife) health sectors is necessary, including routine sharing of information.

Laboratory confirmation of infection is critical, because human monkeypox closely resembles several other febrile rash illnesses including smallpox and varicella. The appropriate specimens for identification of the virus in active cases of monkeypox are swabs or crusts of lesions, in contrast to blood, serum, and sputum specimens collected by clinicians and laboratory technicians for diagnosis of many other diseases, and specimens must be accompanied by detailed clinical information for appropriate interpretation of laboratory results.

* http://www.who.int/ihr/procedures/mission-reports-africa/en/.

† http://www.afro.who.int/publications/technical-guidelines-integrated-disease-surveillance-and-response-african-region-0.

FIGURE. Countries reporting monkeypox cases in humans and animals — West and Central Africa, 1970–2017*



* Current as of February 25, 2018.

Implementation of monkeypox-specific case investigation forms, and training health care workers in their use, can support appropriate case investigation and confirmation (*7*). The most efficient means of laboratory confirmation is through molecular assays, which will require strengthening of national laboratory capacity in countries with endemic disease. Regional and global reference laboratory systems need to be established to support diagnostic assay quality assurance and confirmation, and appropriate storage and safe transport of specimens in areas with limited infrastructure will require innovative solutions.

Monkeypox cases frequently occur in forested rural areas, which often have limited access to health services. The provision of clinical supportive care and treatment for complications such as ocular and secondary infections, respiratory involvement, and fluid imbalance, can be challenging because of resource and specialized care limitations (*7*,*8*).

Summary

What is already known about this topic?

Human monkeypox is a viral zoonosis that occurs in West Africa and Central Africa. Most cases are reported from Democratic Republic of the Congo. The disease causes significant morbidity and mortality, and no specific treatment exists.

What is added by this report?

Nigeria is currently experiencing the largest documented outbreak of human monkeypox in West Africa. During the past decade, more human monkeypox cases have been reported in countries that have not reported disease in several decades. Since 2016, cases have been confirmed in Central African Republic (19 cases), Democratic Republic of the Congo (>1,000 reported per year), Liberia (two), Nigeria (>80), Republic of the Congo (88), and Sierra Leone (one). The reemergence of monkeypox is a global health security concern.

What are the implications for public health practice?

A recent meeting of experts and representatives from affected countries identified challenges and proposed actions to improve response actions and surveillance. The World Health Organization and CDC are developing updated guidance and regional trainings to improve capacity for laboratory-based surveillance, detection, and prevention of monkeypox, improved patient care, and outbreak response.

Although infection prevention and control techniques and supplies are often lacking in rural areas, measures such as contact precautions, appropriate disinfection, and limited contact with patients can be implemented at health care facilities and patient homes. Patients and their families might also face stigma in their communities because of lack of knowledge about the disease and fear that cases might represent an epidemic such as Ebola, and rumors can cause panic; however, psychosocial support for patients and their families is often not prioritized. Education and risk communication for affected families and communities are important components of a public health response that addresses potentially risky behaviors, such as hunting and consumption of bushmeat and contact with ill persons. Engaging communities in developing feasible interventions and encouraging needed health-seeking behavior is important. If resources are available, contacts could be followed to limit further community exposures and halt subsequent chains of transmission. Information on final outcomes and long-term sequelae need to be better documented to improve understanding of the disease course (*8*).

Better collaboration between human and animal health personnel is needed to understand the impact of monkeypox among humans and animals and the mechanisms of animal-to-human transmission and to implement adequate prevention and response measures. Developing integrated, regional plans and ensuring cross-border coordination among countries that share geographically contiguous risk zones are needed to stop the spread of disease.

The 2018 list of priority diseases for the WHO Research and Development Blueprint identified monkeypox as an emerging disease requiring rapid evaluation of available potential countermeasures (*9*). In this regard, vaccines and medical therapeutics developed for smallpox could be validated for use against human monkeypox in clinical studies through operational research in countries with endemic disease to optimize their potential impact.

The increase in number of monkeypox cases being reported from countries in Africa that have not reported cases in several decades and the myriad factors that affect monkeypox transmission highlight the need to update knowledge about the disease and strengthen preparedness efforts. To address gaps in knowledge and expertise in areas with endemic disease, a number of areas of work are being prioritized by WHO in collaboration with CDC. To improve understanding of mechanisms of virus transmission, both zoonotic and interhuman, national disease surveillance systems need to be strengthened for humans, as well as for wildlife, using community-based event reporting. In countries with endemic disease, this includes the reporting of all suspected cases through the Integrated Disease Surveillance and Response system, collection of relevant disease-specific data to support laboratory diagnostic and epidemiological interpretation, and follow-up of confirmed cases.

Improvements in laboratory capacity require training in laboratory procedures, the types of specimens to collect, and safe specimen collection, storage, and transportation. Improvements in the capacity to detect monkeypox virus have been found to increase zoonotic disease detection and response, as seen during the Ebola virus disease response in Tshuapa Province of DRC (*10*). Regional trainings to increase national-level expertise and the sharing of country-level experiences will have the potential to build a network for exchange of best practices and technical support. Global health security will benefit from additional efforts to build regional-level capacity.

Including local-level training in national response and surveillance plans is important to ensure that health care workers and surveillance staff members in regions with endemic disease are equipped to detect and manage cases. In all these endeavors, WHO and orthopoxvirus reference centers such as CDC, Institut Pasteur Dakar (Senegal), and Institut National de Recherche Biomedicale (DRC) are working to provide guidance and technical support for the required public health actions.

As with all zoonotic diseases, a comprehensive One Health[§] approach is necessary for disease detection and response,

[§] https://www.cdc.gov/onehealth/index.html.

including wildlife surveillance and investigations into the animal reservoir/reservoirs, which require dedicated resources. Multicountry collaborations are important for sharing experiences, developing stronger national and regional capacities, and alerting neighboring countries of cases of monkeypox in humans and animals. Unlike smallpox, a human disease with no animal reservoir that was eradicated through vaccination campaigns, monkeypox has an animal reservoir/reservoirs. Insights into the animal reservoir and ecological niche will enable monitoring the virus's movements outside the natural ecological setting. Improving understanding of monkeypox will aid in developing innovative solutions to mitigate further spread of the virus. Furthermore, improved detection and response capacity for monkeypox will enhance capacity for responding to other zoonoses and orthopoxvirus events at regional and national levels.

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Conflict of Interest

No conflicts of interest were reported.

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Notes from the Field

False-Negative Hepatitis B Surface Antigen Test Results in a Hemodialysis Patient — Nebraska, 2017

Blake Hendrickson, MPH[1]; Saleem Kamili, PhD[2]; Tim Timmons[3]; Peter C. Iwen, PhD[4]; Caitlin Pedati, MD[1]; Thomas Safranek, MD[1]

In March 2017, the Nebraska Department of Health and Human Services (NDHHS) was contacted by a hemodialysis clinic regarding a patient who had tested negative for hepatitis B virus (HBV) surface antigen (HBsAg) after vaccination in 2010 and who later tested positive for HBsAg. A public health investigation subsequently determined that the false-negative results were caused by a surface antigen mutation. Notably, several commercial HBsAg testing kits cannot detect this mutant virus, making it a challenging pathogen for public health surveillance and intervention efforts (*1*).

When the patient started dialysis in 2010, there was no evidence that the patient had ever been tested for HBV. The patient's vaccination status was also unknown, and 4 doses of HBV vaccine were administered at 0, 1, 2, and 6 months, as recommended for hemodialysis patients (*2*). Postvaccination testing in 2010 was positive for hepatitis B surface antibody (anti-HBs = 82 mIU/mL), indicating immunity to HBV. Postvaccination HBsAg testing performed with a Food and Drug Administration (FDA)–approved assay at Laboratory A was negative. As recommended for patients with demonstrated immunity, only anti-HBs was monitored routinely from 2010 to 2016 to ensure continued protection (anti-HBs >10 mIU/mL) (*2*). In 2016, the patient was hospitalized for acute shortness of breath, and an HBsAg test performed as part of a routine evaluation at laboratory B was positive, indicating a current infection with HBV. The positive result was confirmed by additional testing at commercial and public health laboratories (Table). Insufficient data were available to determine whether the patient acquired HBV infection before or after vaccination.

Specific precautions for HBV-positive patients in a dialysis center include receiving dialysis in a separate room and being assigned separate staff members and equipment (*2*). These control measures were not implemented during 2010–2016 because the index patient had not had a positive HBsAg test result. After the positive HBsAg results were reported, an epidemiologic investigation was initiated by NDHHS and the Lincoln-Lancaster County Health Department to determine the cause of the false-negative test results and to identify any HBV transmission.

A blood sample was collected in April 2017 and sent to the Division of Viral Hepatitis Laboratory Branch at CDC to confirm the HBV diagnosis. CDC testing found high HBV DNA levels (14,200,000 IU/mL), evidence of immunity (anti-HBs = 114 mIU/mL), and HBsAg positivity by one assay and negativity by another assay (Table). Sequencing the S gene of HBV DNA identified an sG145R surface antigen mutation. This mutation is associated with false-negative results, which explains the failure of multiple tests to identify the patient as being HBsAg-positive (*1*).

The epidemiologic investigation identified 45 recent dialysis contacts and 10 close family contacts who were at risk for infection. None of the contacts had prior evidence of HBV infection, all were screened by tests capable of detecting this mutant virus (using a suitable HBsAg assay or by HBV DNA), and all test results were negative, indicating no evidence of HBV transmission, despite the potential exposures to the HBV-infected patient. Family members without evidence of prior HBV vaccination were also advised to complete the HBV vaccination series.

A subsequent survey of laboratories that reported HBsAg results to NDHHS in the previous year identified nine of 23 laboratories using tests that are not known to detect common HBsAg mutations. This included both local hospitals and large national reference laboratories.

The prevalence of sG145R mutations and other HBsAg mutants associated with false-negative test results is not known. However, some studies suggest that mutant strains are found in 6%–12% of chronic HBV carriers (*3*). In addition to issues with diagnostic detection, some mutants are also not recognized and neutralized by protective antibodies induced by current HBV vaccines and HBV immune globulin therapy (*3*).

This case highlights a unique challenge associated with detecting HBV infections when a surface antigen mutation is present. In recent years, some manufacturers have adapted their testing assays to better identify sG145R and other HBsAg mutations. It is important that laboratories use FDA-approved assays that have the ability to detect HBsAg mutants, which was not done in this case at Laboratory A. The clinical and public health community also must be aware of these testing limitations so that discordant results can be identified for correct diagnosis and care of HBV-infected persons and to minimize the spread of these mutant viruses.

TABLE. HBsAg lab results for the case patient by facility and testing instrument

Date collected	Laboratory facility	Testing instrument	Result
November 11, 2010	A*	Advia Centaur XPT	Negative
December 8, 2016	A*	Advia Centaur XPT	Negative†
December 9, 2016	B*	Advia Centaur XP	Positive
December 14, 2016	C*	Advia Centaur XP	Positive
January 5, 2017	A*	Advia Centaur XPT	Negative†
February 2, 2017	A*	Advia Centaur XPT	Negative†
March 2, 2017	A*	Advia Centaur XPT	Negative†
March 2, 2017	C*	Advia Centaur XP	Positive
May 7, 2017	CDC	Vitros Eci	Negative†
May 7, 2017	CDC	Abbott ARCHITECT	Positive
May 23, 2017	NPHL	Advia Centaur XP	Positive
July 25, 2017	D*	ETI-MAK-2 PLUS	Positive
July 25, 2017	E*	Vitros 3600	Negative†

Abbreviation: NPHL = Nebraska Public Health Lab.
* Deidentified commercial laboratory.
† False-negative result.

Conflict of Interest

No conflicts of interest were reported.

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Notes from the Field

Assessing Rabies Risk After a Mass Bat Exposure at a Research Facility in a National Park — Wyoming, 2017

Andrea Cote, DVM[1,2]; Sarah Anne J. Guagliardo, PhD[1,3]; Cuc H. Tran, PhD[3]; Maria A. Said, MD[4]; Veronica Pickens[5]; Karl Musgrave, DVM[2]; Ryan Wallace, DVM[3]

On August 2, 2017, the Wyoming Department of Health (WDH) was notified by local public health nursing of a group of 20 persons who had slept in a national park research facility and reported contact with bats and bat excrement. Four of the 20 persons had already received rabies postexposure prophylaxis (PEP)* when WDH notified the National Park Service (NPS) and requested assistance from CDC for a mass bat exposure investigation of the remaining 16 persons. Rabies is a fatal, viral zoonotic disease causing an estimated 59,000 human deaths annually worldwide. Transmission from animals to humans mainly occurs through bites; however, scratches or mucous membrane contact with saliva also present transmission risks (*1*–*3*). Although human rabies in the United States is rare, most human cases result from bat exposures; 75% of infected patients become ill within 3 months of exposure (*3*). Bat infestation of human habitations increases the risk for bat contact. Infestations can expose numerous persons to rabies and are referred to as mass bat exposures.

Review of facility records identified 172 persons from 11 research groups who had slept at the research facility, with 73% of persons sleeping in one of two buildings possibly infested with bats since both buildings opened for the summer season on May 19, 2017, and closed August 2, 2017, to overnight guests. The facility director provided investigators with contact information for group leaders, who then provided contact information for potentially exposed persons. Persons resided in 29 states, the District of Columbia, one U.S. territory, and four non-U.S. residents were from four countries. Investigators from WDH, CDC, NPS, and public health professionals in other local, state, and international jurisdictions attempted to contact all potentially exposed persons by telephone, e-mail, and through social media. All persons who completed a risk assessment were contacted 1–2 weeks later to complete a follow-up assessment regarding receipt of PEP and to answer additional questions. Rabies risk assessments and follow-up assessments were conducted by telephone and e-mail.

A risk assessment tool adapted from a previous mass bat exposure investigation (*4*) was used to determine each person's risk for rabies virus exposure. The assessment was modified with additional questions to create three risk categories based on bat contact, sightings, and whether the bedroom door was open or closed while the person was sleeping. Persons were categorized as having no risk (no direct bat contact, no bats observed, and door closed while sleeping), low risk (no direct bat contact, no bats observed, and door open while sleeping), or high risk for bat exposure (direct contact with a bat or lack of knowledge of possible bat contact while sleeping because of medications, deep sleep, or alcohol consumption).

By February 8, 2018, risk assessments had been completed for 165 (95.9%) of 172 potentially exposed U.S. residents, with the remaining persons considered lost to follow-up. Among those assessed, 123 (74.5%) persons were classified as having no exposure risk, 21 (12.7%) a low exposure risk, and 21 (12.7%) a high exposure risk. Although all persons were encouraged to consult with a health care provider if they had concerns about exposure, persons classified as having a high exposure risk were counseled regarding potential rabies virus exposure and strongly encouraged to receive PEP. All information collected from the risk assessments was shared with the appropriate public health officials. All 165 U.S. residents who stayed at the research facility and completed a risk assessment were contacted for a follow-up assessment; 79 (47.9%) completed the follow-up assessment. Among these persons, 21 (26.6%) reported receiving PEP, including five of 56 (8.9%) with no exposure risk, seven of 14 (50%) with low exposure risk, and nine of nine (100%) with high exposure risk. It is possible, however, that additional persons declining participation in the follow-up assessment might have received PEP.

As one of the largest documented mass bat exposures in U.S. history, this investigation required extensive coordination among local, state, and federal agencies, in addition to foreign governments. Public health responses to mass bat exposures vary by jurisdiction, but all work to ensure risk assessments are performed to ascertain possible rabies virus exposures that might require PEP, while also ensuring that nonexposed persons do not undergo unnecessary and costly treatment (*5*). The immediate public health response to this situation was to close the buildings to overnight guests to prevent potential rabies virus exposure to additional persons. The research facility director coordinated with a bat exclusion

* https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5902a1.htm.

company to remediate and exclude areas of possible bat entry. Mass bat exposures can occur in any public building, yet no formal guidance exists for PEP administration in the context of mass bat exposures (*5*). The standardized risk assessment† developed for this investigation might help guide future mass bat exposure responses to identify rabies risk among persons with potential exposures, and therefore reduce unnecessary administration of PEP.

† The bat exposure assessment questionnaire for adults included the following 11 questions: "1. What dates did you sleep at the [Building A], if any? What dates did you sleep at the [Building B]?"; "2. Prior to going to sleep, did you check your room for bats? Did you see any bats in the room?"; "3. Did you sleep with the bedroom door closed?"; "4. Did you sleep under a bed net?"; "5. Where did you see a bat while at the [facility] or during your trip to [park/location]? A. in a sleeping room, B. not in a sleeping room, C. outside, D. other location, E. no bat seen. Did you hear of any bats seen inside cabins or quarters other than in [Buildings A and B]? If a bat was seen, ask to describe the dates and circumstances of each sighting. If a bat was seen, was the bat (if more than one bat was seen, collect information for each incident in the space above): A. healthy, flying normally, B. injured or apparently sick, C. dead, D. unknown"; "6. What contact did you have with a bat? Specifically, any of the following: A. bitten, B. scratched, C. touched. If yes, please describe your contact (ask specifically about touching of head/mouth/teeth and whether or not gloves were worn)"; "7. Were you asleep and then awoke to find a bat in your room during your stay? Do you recall seeing a bat swoop down or make contact with any other person while they were sleeping? If yes, do you recall the names of any other people the bat may have had contact with? (List their name and contact information)"; "8. Were you on any medications during your stay, including over the counter medications that may have made you drowsy or less likely to feel contact with a bat? If yes, please list the medications"; "9. Do you have any of the following conditions that may decrease your awareness of a bat bite? A. deep sleeper or other condition that may make them less likely to awaken if bitten by a bat, B. drug or alcohol use during your stay, C. do you normally sleep with bare skin exposed (particularly arms or legs), D. other (please list)"; "10. Have you ever been vaccinated against rabies? If yes, in what year did you receive vaccination? If yes, how many doses of vaccine did you receive?"; and "11. Are you willing to speak with us at a different time regarding possible bat sightings?"

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Conflict of Interest

No conflicts of interest were reported.

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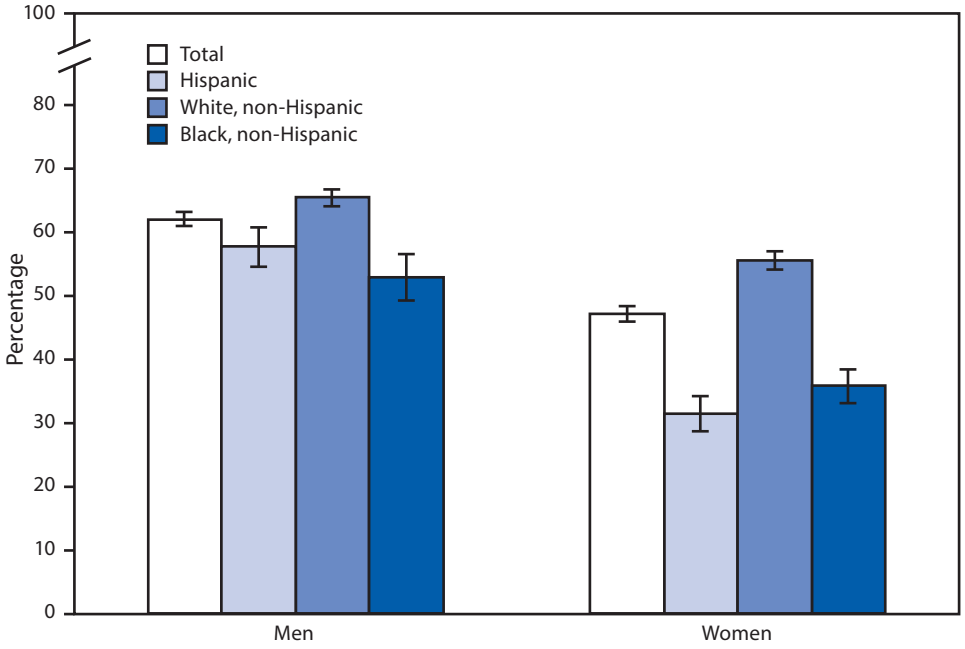
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Age-Adjusted Percentages* of Adults Aged ≥18 Years Who Are Current Regular Drinkers of Alcohol,† by Sex, Race, and Hispanic Origin§ — National Health Interview Survey, 2016¶



* With 95% confidence intervals indicated with error bars.
† Current regular drinkers are defined as having had at least 12 drinks in the past year. This is derived from the following questions: "In any one year, have you had at least 12 drinks of any type of alcoholic beverage?"; "In your entire life, have you had at least 12 drinks of any type of alcoholic beverage?"; and "In the past year, how often did you drink any type of alcoholic beverage?"
§ Categories shown are for Hispanic adults, who may be of any race or combination of races, and non-Hispanic adults who selected one racial group. Not all race groups are shown. Total bars are based on all adults aged ≥18 years.
¶ Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population, are shown for sample adults aged ≥18 years, and are age-adjusted using the projected 2000 U.S. population as the standard population and using four age groups: 18–44, 45–64, 65–74, and ≥75 years.

In 2016, men aged ≥18 years were more likely than women to be current regular drinkers of alcohol (62.1% versus 47.2%). Non-Hispanic white men (65.5%) were more likely to be current regular drinkers than Hispanic men (57.8%) and non-Hispanic black men (52.9%). Non-Hispanic white women (55.6%) were more likely to be current regular drinkers than non-Hispanic black women (35.9%) and Hispanic women (31.5%).

Source: Tables of summary health statistics for US adults, National Health Interview Survey, 2016. https://www.cdc.gov/nchs/nhis/SHS/tables.htm.

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