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National Diabetes Month — November 2017

November is National Diabetes Month. Approximately 114 million U.S. persons are living with diabetes (30 million) or prediabetes (84 million) (*1*). Persons with prediabetes are at increased risk for developing type 2 diabetes, heart disease, and stroke (*1*). Type 2 diabetes can be prevented through lifestyle changes (e.g., weight loss, healthy eating, and increased physical activity) (*1*,*2*). Persons with diabetes can take steps to control the disease and prevent complications (*1*,*3*). This issue of *MMWR* includes a report on diabetes-related kidney failure.

Working with partners, CDC plays an important role in preventing or delaying the onset of type 2 diabetes, preventing complications of diabetes, and improving health and quality of life for persons with diabetes. The National Diabetes Statistics Report, 2017 (*1*) provides the latest statistics about diabetes. With the Ad Council, the American Diabetes Association, and the American Medical Association, CDC has developed public service announcements to encourage persons to take the prediabetes risk test (https://DoIHavePrediabetes.org). CDC also joined forces with CBS Television Stations in a television and digital miniseries, "Your Health with Joan Lunden and CDC," to provide information about diabetes prevention and control (https://www.cdc.gov/diabetestv/index.html). More information is available at https://www.cdc.gov/diabetes.

References

1. CDC. National diabetes statistics report, 2017. Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https://www.cdc.gov/diabetes/data/statistics/statistics-report.html
2. Knowler WC, Barrett-Connor E, Fowler SE, et al.; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393–403. https://doi.org/10.1056/NEJMoa012512
3. Venkat Narayan KM, Williams D, Gregg EW, Cowie C, eds. Diabetes public health: from data to policy. New York, NY: Oxford University Press; 2011.

Incidence of End-Stage Renal Disease Attributed to Diabetes Among Persons with Diagnosed Diabetes — United States and Puerto Rico, 2000–2014

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During 2014, 120,000 persons in the United States and Puerto Rico began treatment for end-stage renal disease (ESRD) (i.e., kidney failure requiring dialysis or transplantation) (*1*). Among these persons, 44% (approximately 53,000 persons) had diabetes listed as the primary cause of ESRD

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(ESRD-D) (*1*). Although the number of persons initiating ESRD-D treatment each year has increased since 1980 (*1*,*2*), the ESRD-D incidence rate among persons with diagnosed diabetes has declined since the mid-1990s (*2*,*3*). To determine whether ESRD-D incidence has continued to decline in the United States overall and in each state, the District of Columbia (DC), and Puerto Rico, CDC analyzed 2000–2014 data from the U.S. Renal Data System and the Behavioral Risk Factor Surveillance System. During that period, the age-standardized ESRD-D incidence among persons with diagnosed diabetes declined from 260.2 to 173.9 per 100,000 diabetic population (33%), and declined significantly in most states, DC, and Puerto Rico. No state experienced an increase in ESRD-D incidence rates. Continued awareness of risk factors for kidney failure and interventions to improve diabetes care might sustain and improve these trends.

The U.S. Renal Data System collects, analyzes, and distributes ESRD clinical and claims data to the Centers for Medicare & Medicaid Services (CMS) (*1*). In addition to demographic information, the U.S. Renal Data System includes the date patients were first treated and the primary cause of ESRD from the CMS Medical Evidence Report that health care providers are required by law to complete for each new patient with ESRD (*1*). For this analysis, the number of persons aged ≥18 years initiating ESRD treatment (i.e., dialysis or transplantation) who had diabetes listed as the primary cause of ESRD in each state, DC, and Puerto Rico during 2000–2014 were obtained from the U.S. Renal Data System. Throughout the period, 44%–45% of the new ESRD cases were ESRD-D (*1*).

The Behavioral Risk Factor Surveillance System (BRFSS) conducts state-based, random-digit–dialed telephone surveys in the 50 states, DC, and Puerto Rico and other U.S. territories. BRFSS respondents were classified as having diagnosed diabetes if they answered "yes" to the question, "Has a doctor ever told you that you have diabetes?" Women who were told that they had diabetes only during pregnancy were classified as not having diabetes. BRFSS data were weighted to estimate the number of noninstitutionalized persons aged ≥18 years with diagnosed diabetes in each state, DC, and Puerto Rico. In 2011, BRFSS changed sampling and weighting methodology and added cell phone respondents; however, these changes did not appear to affect overall estimates of self-reported diabetes (*4*). In 2014, the median BRFSS response rate for all states and territories was 40.5% (cell phone) and 48.7% (landline).*

ESRD-D incidence was calculated by dividing the number of persons initiating ESRD-D treatment by the estimated number of persons with diagnosed diabetes in each state, DC, and Puerto Rico. Data were analyzed using statistical software to estimate standard errors and calculate 95% confidence intervals (CIs), and were age-standardized by the direct method based on the 2000 U.S. standard population. Joinpoint regression was used for trend analyses (*5*). Joinpoint regression uses permutation tests to determine whether the rate of change for each trend

* https://www.cdc.gov/brfss/annual_data/2014/pdf/2014_dqr.pdf.

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segment is significantly different from zero (p value <0.05) to identify points (i.e., joinpoints) where linear trends change significantly in direction or magnitude (e.g., zero joinpoints indicates a straight line). In the final model, each trend segment is described by an annual percentage change and the trend for the entire study period is described by the average annual percentage change (AAPC), both with 95% CIs. Alaska, Vermont, and Wyoming were excluded from the trend analysis because of the small annual number (<50) of new ESRD-D cases identified during the study period.

During 2000–2014, the total number of adults aged ≥18 years in the United States, DC, and Puerto Rico who began ESRD-D treatment each year increased from 42,236 (state range = 32–5,117) to 53,382 (state range = 47–7,228) (AAPC = 1.5% per year [95% CI = 1.2%–1.8%], p<0.001) (Figure 1). From 2000 to 2014, among 47 states, DC, and Puerto Rico, the age-standardized ESRD-D incidence decreased 33% (AAPC = 2.8% per year [95% CI = -3.3% to -2.3%], p<0.001), from 260.2 (state range = 171.2–569.6) to 173.9 (state range = 81.7–363.6) per 100,000 persons with diabetes (Table) (Figure 1). During 2000–2014, rates declined significantly in most states, DC, and Puerto Rico (Table) (Figure 2). In Kansas and Utah, rates declined and then leveled off. From 2000 to 2014, rates did not decline significantly in California, Hawaii, Mississippi, or Montana (Table). In 2000, the rate was ≥217.5 per 100,000 persons with diabetes in 41 states, DC, and Puerto Rico, and the rate was not <164.5 in any state; in 2014, the rate was ≥217.5 in five states and DC, and was <164.5 in 24 states (Table) (Figure 2).

Discussion

ESRD is a costly and disabling condition that often results in premature death (*1*). During 2000–2014, the overall age-standardized incidence of ESRD-D among adults with diagnosed diabetes decreased by 33%. Rates declined significantly in most states, DC, and Puerto Rico. In 2014, the highest rates were in DC and Hawaii. Continued awareness and interventions to reduce the prevalence of risk factors for kidney failure, improve diabetes care, and reduce the incidence of type 2 diabetes might sustain these positive trends.

The 33% decline in ESRD-D incidence from 2000 to 2014 reported here is similar to the 28% decline reported using 2000–2010 nationally representative surveillance data (*3*). Reasons for the decline in ESRD-D incidence cannot be determined from surveillance data. However, reasons for the decline might include reductions in risk factors for kidney failure (e.g., hyperglycemia and hypertension) in the diabetic population or better treatment of kidney disease, including the use of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers, which slow the decline in kidney function in addition to lowering blood pressure, thus delaying the onset of ESRD-D (*6*).

Although ESRD-D incidence rates are declining, the number of patients with newly diagnosed ESRD-D is likely to increase as the number of persons with diabetes increases (*2*). Furthermore, one in three adults with diabetes is estimated to have chronic kidney disease (i.e., kidney damage or reduced kidney function); however, most persons with chronic kidney disease are unaware that they have it (*7*). Early detection and better management of chronic kidney disease in persons with diabetes can slow its progression to ESRD, prevent complications, and improve cardiovascular outcomes (*7*). Testing for urine albumin, which is an early marker of kidney disease, is recommended for all patients with diabetes, and treatment with angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers is indicated for persons with diabetes and hypertension (*8*). Effective interventions to improve blood glucose levels and blood pressure control might prevent or delay the onset of kidney disease (*7*) in adults with diabetes. To support primary prevention, effective community-based approaches to prevent obesity and increase physical activity, along with type 2 diabetes prevention programs targeted to populations at high risk, might reduce the incidence of type 2 diabetes, and consequently, diabetic kidney disease (*9*).

The findings in this report are subject to at least four limitations. First, data on ESRD treatment were based on reports to CMS; patients whose treatment was not reported to CMS (e.g., persons who refused treatment or who died from ESRD before receiving treatment) were not included and might result in an underestimation of incidence. Second, revised diagnostic criteria for diabetes in 1997 might have led to the detection of more persons with diabetes earlier in the disease process (persons who have not had diabetes long enough to develop ESRD-D) (*8*) and might result in an underestimation of incidence. Third, the estimated population with diagnosed diabetes was based on self-reports. Although self-report of diabetes is highly accurate (persons with diagnosed diabetes are likely to report having diabetes) (*10*), the total number of adults with diabetes is underestimated, which thus results in an overestimation of ESRD-D incidence. Finally, BRFSS survey methods changed in 2011 potentially confounding interpretation of trends. However, using different surveillance data to estimate the U.S. diabetic population yielded a similar overall decline in ESRD-D incidence rates (*3*).

CDC works with public and private partners to reduce the incidence of type 2 diabetes and to improve outcomes for persons with diabetes. In 2013, CDC assisted state health departments in implementing diabetes self-management education and training programs and strategies to increase use of diabetes self-management education and training by persons

TABLE. Age-standardized incidence* of end-stage renal disease attributed to diabetes (ESRD-D) among adults aged ≥18 years with diagnosed diabetes, by state and territory† — U. S. states, the District of Columbia, and Puerto Rico, 2000–2014

	Rate			Trend analysis	
State/Territory	2000	2014	% Change	AAPC (95% CI)	p value
Alabama	294.7	176.3	-40	-2.7 (-3.8 to -1.5)	<0.001
Arizona	405.7	196.2	-52	-4.3 (-5.7 to -3.0)	<0.001
Arkansas	249.5	155.3	-38	-3.3 (-4.7 to -1.9)	<0.001
California	227.2	188.3	-17	-1.4 (-2.8 to 0.1)	0.06
Colorado	290.5	142.3	-51	-4.5 (-6.1 to -2.9)	<0.001
Connecticut	289.8	131.5	-55	-4.2 (-5.7 to -2.6)	<0.001
Delaware	315.4	135.8	-57	-4.0 (-5.6 to -2.4)	<0.001
District of Columbia	569.6	304.8	-46	-2.9 (-5.2 to -0.5)	0.02
Florida	248.6	142.4	-43	-2.9 (-4.0 to -1.8)	<0.001
Georgia	288.5	166.3	-42	-3.8 (-5.2 to -2.4)	<0.001
Hawaii	557.8	363.6	-35	-1.6 (-3.5 to 0.2)	0.08
Idaho	247.9	166.7	-33	-4.8 (-8.4 to -1.2)	0.01
Illinois	276.8	187.5	-32	-3.0 (-4.4 to -1.6)	<0.001
Indiana	279.7	180.8	-35	-2.3 (-3.5 to -1.2)	<0.001
Iowa	217.4	128.0	-41	-4.7 (-6.7 to -2.7)	<0.001
Kansas§	273.3	143.1	-48	-3.7 (-5.1 to -2.3)	<0.001
Kentucky	254.7	143.5	-44	-2.5 (-3.6 to -1.5)	<0.001
Louisiana	337.9	219.8	-35	-4.2 (-5.5 to -2.8)	<0.001
Maine	224.7	114.3	-49	-6.0 (-8.4 to -3.6)	<0.001
Maryland	255.1	160.8	-37	-4.8 (-6.1 to -3.5)	<0.001
Massachusetts	202.9	101.5	-50	-4.9 (-5.8 to -4.0)	<0.001
Michigan	237.2	215.9	-9	-3.1 (-4.2 to -2.0)	<0.001
Minnesota	291.0	123.0	-58	-4.7 (-5.7 to -3.7)	<0.001
Mississippi	287.1	219.3	-24	-1.0 (-2.4 to 0.5)	0.19
Missouri	263.9	150.7	-43	-3.2 (-4.5 to -2.0)	<0.001
Montana	230.0	138.2	-40	-2.2 (-4.5 to 0.2)	0.07
Nebraska	280.5	106.1	-62	-5.4 (-7.2 to -3.5)	<0.001
Nevada	222.1	166.2	-25	-4.1 (-5.6 to -2.5)	<0.001
New Hampshire	350.8	81.7	-77	-4.6 (-7.1 to -2.0)	0.002
New Jersey	292.0	189.6	-35	-2.5 (-3.4 to -1.6)	<0.001
New Mexico	358.2	210.1	-41	-4.5 (-5.8 to -3.2)	<0.001
New York	243.2	155.5	-36	-3.3 (-4.4 to -2.2)	<0.001
North Carolina	304.9	177.3	-42	-3.8 (-4.6 to -2.9)	<0.001
North Dakota	235.6	186.4	-21	-3.0 (-5.0 to -1.0)	0.007
Ohio	299.7	164.4	-45	-3.0 (-4.3 to -1.6)	<0.001
Oklahoma	341.0	190.8	-44	-4.3 (-5.5 to -3.0)	<0.001
Oregon	171.2	148.3	-13	-2.4 (-4.4 to -0.4)	0.02
Pennsylvania	245.6	159.9	-35	-3.0 (-3.9 to -2.0)	<0.001
Rhode Island	176.2	136.8	-22	-4.3 (-7.2 to -1.3)	0.01
South Carolina	298.1	202.7	-32	-3.4 (-5.2 to -1.6)	0.001
South Dakota	265.8	227.1	-15	-3.4 (-4.8 to -1.9)	<0.001
Tennessee	250.5	145.3	-42	-3.0 (-4.1 to -1.9)	<0.001
Texas	342.5	220.9	-36	-2.3 (-3.7 to -0.9)	0.003
Utah¶	205.2	156.2	-24	-3.7 (-6.5 to -0.8)	0.01
Virginia	265.7	196.5	-26	-4.3 (-5.9 to -2.7)	<0.001
Washington	176.1	145.0	-18	-1.8 (-2.6 to -0.9)	<0.001
West Virginia	330.6	178.2	-46	-2.7 (-4.4 to -0.9)	0.006
Wisconsin	232.7	174.7	-25	-3.6 (-5.1 to-2.1)	<0.001
United States	**260.6**	**173.4**	**-33**	**-2.8 (-3.3 to -2.3)**	**<0.001**
Puerto Rico	240.8	207.8	-14	-1.5 (-2.4 to -0.7)	0.002
Total	**260.2**	**173.9**	**-33**	**-2.8 (-3.3 to -2.3)**	**<0.001**

Abbreviations: AAPC = average annual percentage change; APC = annual percentage change; CI = confidence interval.

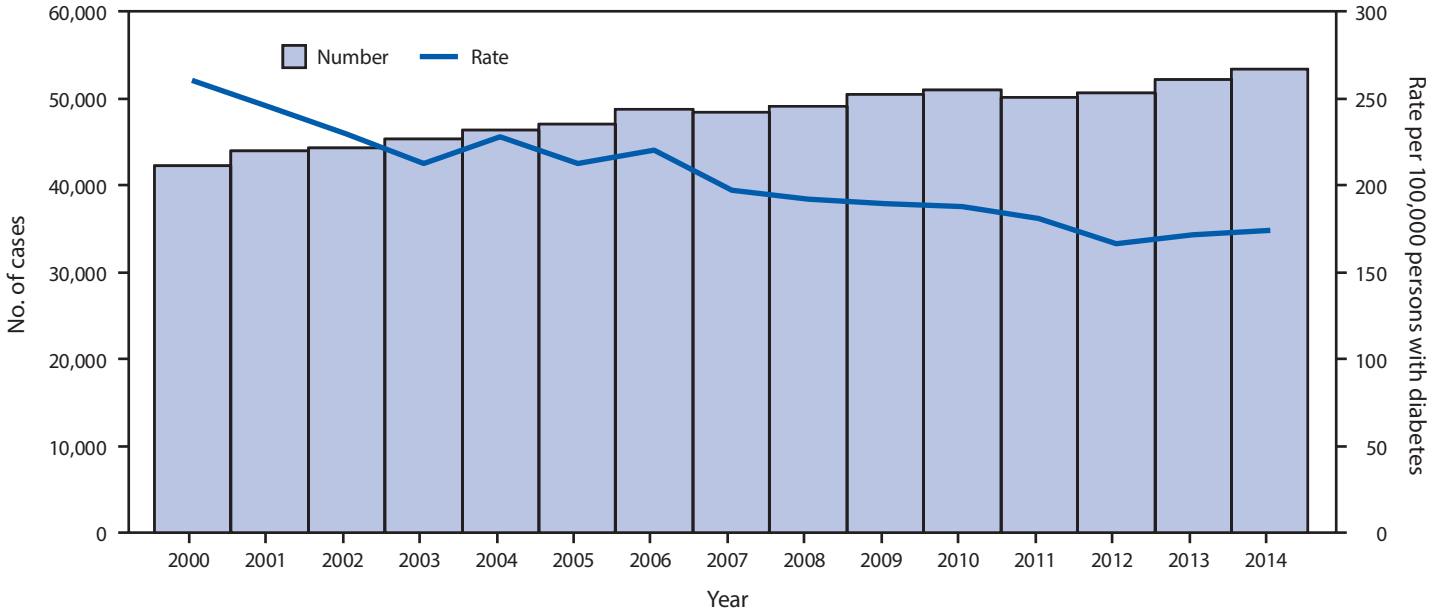
* Rate per 100,000 persons with diabetes and age-standardized based on the 2000 U.S. standard population.

† Alaska, Vermont, and Wyoming were excluded because of the small annual number (<50) of new ESRD-D cases during the study period.

§ Rates declined from 2000 to 2011 (APC = -6.0% per year [95% CI: -7.1% to -4.9%], p<0.001), and then leveled off from 2011 to 2014 (APC = 5.2% per year [-1.4% to 12.2%], p = 0.11).

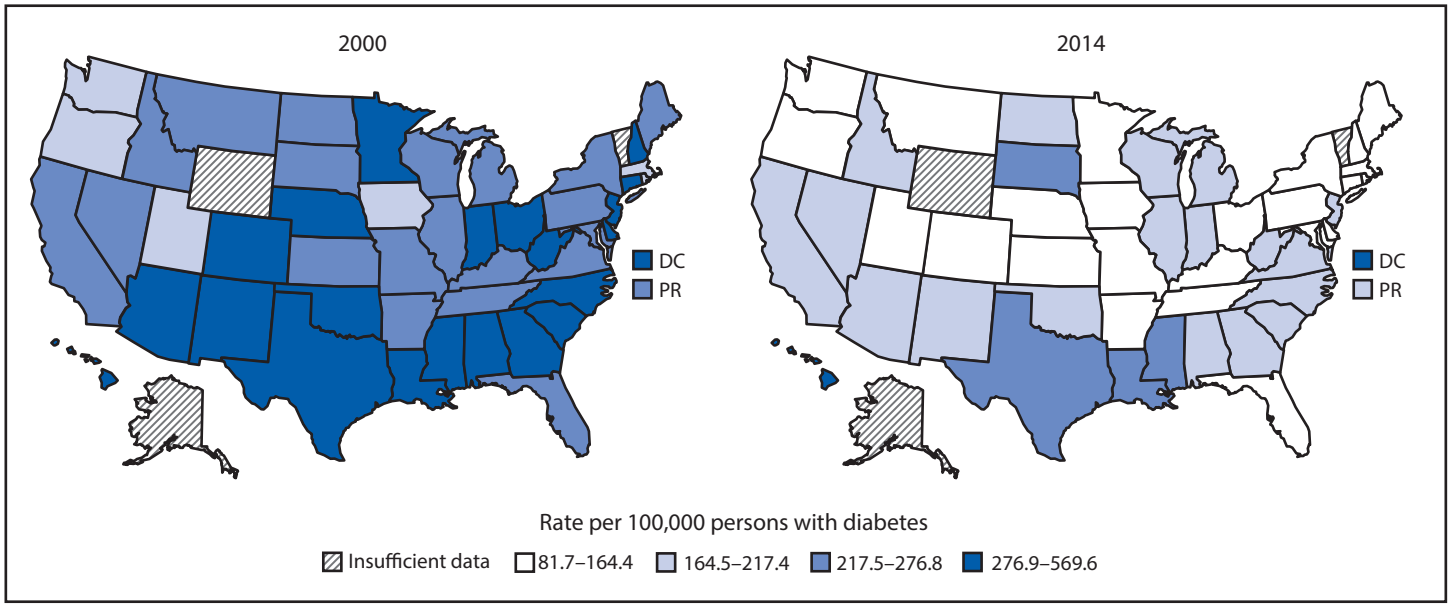
¶ Rates declined from 2000 to 2012 (APC = -5.6% per year [95% CI: -7.4% to -3.8%], p<0.001), and then leveled off from 2012 to 2014 (APC = 8.4% per year [-11.7% to 33.0%), p = 0.40).

FIGURE 1. Number and rate* of adults aged ≥18 years who began treatment for end-stage renal disease attributed to diabetes (ESRD-D) — U. S. states, the District of Columbia, and Puerto Rico, 2000–2014†



* Rate per 100,000 persons with diabetes and age-standardized based on the 2000 U.S. standard population, excluding Alaska, Vermont, and Wyoming because of the small annual number (<50) of new ESRD-D cases during the study period.
† In 2011, the Behavioral Risk Factor Surveillance System (BRFSS) survey changed sampling and weighting methodology and added cell phone respondents; however, this change did not appear to affect overall estimates of self-reported diabetes. BRFSS estimates of the population with self-reported diabetes were used to calculate ESRD-D incidence rates.

FIGURE 2. Age-standardized incidence* of end-stage renal disease attributed to diabetes (ESRD-D) among adults aged ≥18 years with diagnosed diabetes, by state† — U. S. states, the District of Columbia, and Puerto Rico, 2000 and 2014§



Abbreviations: DC = District of Columbia; PR = Puerto Rico.
* Rate per 100,000 persons with diabetes and age-standardized based on the 2000 U.S. standard population.
† Alaska, Vermont, and Wyoming were excluded because of the small annual number (<50) of new ESRD-D cases.
§ Legend categories were created using ranks based on the combined 2000 and 2014 rates.

Summary

What is already known about this topic?

The incidence of end-stage renal disease attributed to diabetes (ESRD-D) in the U.S. population with diagnosed diabetes began to decline in the mid-1990s.

What is added by this report?

During 2000–2014, the age-standardized incidence of ESRD-D has continued to decline significantly in the United States and in most states, the District of Columbia, and Puerto Rico. No state experienced an increase in rates.

What are the implications for public health practice?

Continued awareness of diabetes and interventions to reduce the prevalence of risk factors for kidney failure, improve diabetes care, and prevent type 2 diabetes might sustain the decline in ESRD-D incidence rates in the population with diagnosed diabetes.

with diabetes. Diabetes self-management education and training is an important component of integrated diabetes care, teaching patients about diabetes and strategies they can use to manage their disease. CDC's National Diabetes Prevention Program (https://www.cdc.gov/diabetes/prevention) supports the nationwide implementation of evidence-based, structured lifestyle programs to prevent or delay the onset of type 2 diabetes among persons with prediabetes (persons who have blood glucose levels that are elevated, but not high enough to be diagnosed as diabetes). CDC's U.S. Diabetes Surveillance System (https://www.cdc.gov/diabetes/data) monitors diabetes and its risk factors and complications, including ESRD-D, to assess progress in diabetes prevention and control (*2*). CDC's Chronic Kidney Disease Surveillance System (https://www.cdc.gov/ckd/surveillance) monitors the prevalence of chronic kidney disease (i.e., before ESRD) and its risk factors in the U.S. population and tracks progress in chronic kidney disease prevention, management, and control.

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Conflict of Interest

No conflicts of interest were reported.

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References

1. United States Renal Data System (USRDS). 2017 USRDS annual data report: epidemiology of kidney disease in the United States. Bethesda, MD: US Department of Health and Human Services, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2016. https://www.usrds.org/adr.aspx
2. CDC. U.S. Diabetes Surveillance System. Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https://gis.cdc.gov/grasp/diabetes/DiabetesAtlas.html
3. Gregg EW, Li Y, Wang J, et al. Changes in diabetes-related complications in the United States, 1990–2010. N Engl J Med 2014;370:1514–23. https://doi.org/10.1056/NEJMoa1310799
4. CDC. Surveillance Resource Center: methodologic changes in the Behavioral Risk Factor Surveillance System in 2011 and potential effects on prevalence estimates. Atlanta, GA: US Department of Health and Human Services, CDC; 2013. https://www.cdc.gov/surveillancepractice/reports/brfss/brfss.html
5. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med 2000;19:335–51. https://doi.org/10.1002/(SICI)1097-0258(20000215)19:3<335::AID-SIM336>3.0.CO;2-Z
6. Afkarian M, Zelnick LR, Hall YN, et al. Clinical manifestations of kidney disease among US adults with diabetes, 1988–2014. JAMA 2016;316:602–10. https://doi.org/10.1001/jama.2016.10924
7. CDC. National chronic kidney disease fact sheet, 2017. Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https://www.cdc.gov/diabetes/pubs/pdf/kidney_factsheet.pdf
8. American Diabetes Association. Standard of medical care in diabetes—2017. Diabetes Care 2017;40(Suppl 1):S75–98.
9. Albright AL, Gregg EW; National Diabetes Prevention Program. Preventing type 2 diabetes in communities across the U.S.: the National Diabetes Prevention Program. Am J Prev Med 2013;44(Suppl 4):S346–51. https://doi.org/10.1016/j.amepre.2012.12.009
10. Saydah SH, Geiss LS, Tierney E, Benjamin SM, Engelgau M, Brancati F. Review of the performance of methods to identify diabetes cases among vital statistics, administrative, and survey data. Ann Epidemiol 2004;14:507–16. https://doi.org/10.1016/j.annepidem.2003.09.016

Vaccination Coverage Among Children Aged 19–35 Months — United States, 2016

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Vaccination is the most effective intervention to reduce morbidity and mortality from vaccine-preventable diseases in young children (*1*). Data from the 2016 National Immunization Survey-Child (NIS-Child) were used to assess coverage with recommended vaccines (*2*) among children aged 19–35 months in the United States. Coverage remained ≥90% for ≥3 doses of poliovirus vaccine (91.9%), ≥1 dose of measles, mumps, and rubella vaccine (MMR) (91.1%), ≥1 dose of varicella vaccine (90.6%), and ≥3 doses of hepatitis B vaccine (HepB) (90.5%). Coverage in 2016 was approximately 1–2 percentage points lower than in 2015 for ≥3 doses of diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP), ≥3 doses of poliovirus vaccine, the primary *Haemophilus influenzae* type b (Hib) series, ≥3 HepB doses, and ≥3 and ≥4 doses of pneumococcal conjugate vaccine (PCV), with no changes for other vaccines. More direct evaluation of trends by month and year of birth (*3*) found no change in coverage by age 2 years among children included in combined data from the 2015 and 2016 NIS-Child (born January 2012 through January 2015). The observed decreases in annual estimates might result from random differences in vaccination coverage by age 19 months between children sampled in 2016 and those sampled in 2015, among those birth cohorts eligible to be sampled in both survey years. For most vaccines, 2016 coverage was lower among non-Hispanic black* (black) children than among non-Hispanic white (white) children, and for children living below the federal poverty level† compared with those living at or above the poverty level. Vaccination coverage was generally lower among children insured by Medicaid (2.5–12.0 percentage points), and was much lower among uninsured children (12.4–24.9 percentage points), than among children with private insurance. The Vaccines for Children§ (VFC) program was designed to increase access to vaccines among children who might not otherwise be vaccinated because of inability to pay. Greater awareness and facilitating use of VFC might be helpful in reducing these disparities. Efforts should also be focused on minimizing breaks in continuity of health insurance and eliminating missed opportunities to vaccinate children during visits to health care providers. Despite the observed disparities and small changes in coverage from 2015, vaccination coverage among children aged 19–35 months remained high and stable in 2016.

The NIS-Child uses a random-digit–dialing sample of landline and cellular telephone numbers to contact parents or guardians of children aged 19–35 months in the 50 states, the District of Columbia, selected local areas, and U.S. territories.¶ Parents/guardians are interviewed by telephone to collect sociodemographic and health insurance information for age-eligible children in the household. With consent of parent or guardian, a survey is mailed to all identified vaccination providers to collect dates and types of all vaccines administered to the child. Vaccination coverage estimates use only provider-reported vaccination data. NIS-Child methodology, including weighting procedures, has been described previously.** The household interview response rate†† was 33.9% from the combined landline/cell phone sample. Among households with completed interviews, 54.6% had adequate vaccination data from providers,§§ yielding 14,988 children available for determination of national coverage estimates for 2016. Logistic

* Child's race/ethnicity was reported by his/her parent or guardian. Children categorized in this report as white, black, American Indian/Alaska native, Asian, native Hawaiian/other Pacific Islander, or multiple races were identified as non-Hispanic by the parent or guardian. Children identified as being of multiple races had more than one race category designated. Children identified as Hispanic might be of any race.

† Poverty level uses income and family size to categorize households into those 1) at or above the poverty level, and 2) below the poverty level. Poverty level was based on 2015 U.S. Census poverty thresholds (https://www.census.gov/data/tables/time-series/demo/income-poverty/historical-poverty-thresholds.html).

§ https://www.cdc.gov/vaccines/programs/vfc/index.html.

¶ Estimates for states, selected local areas, and territories are available online at https://www.cdc.gov/vaccines/imz-managers/coverage/childvaxview/data-reports/index.html. The local areas sampled separately for the 2016 NIS-Child included areas that receive federal Section 317 immunization funds and are included in the NIS-Child sample every year (Chicago, Illinois; New York, New York; Philadelphia County, Pennsylvania; Bexar County, Texas; and Houston, Texas) and two additional sample areas (El Paso County, Texas and Dallas County, Texas). The 2016 NIS-Child was also conducted in Guam, Puerto Rico, and the U.S. Virgin Islands. This report includes national estimates, excluding the territories.

** Further details regarding the statistical methodology of NIS-Child are available in the NIS-Child Data User's Guide 2015, which is available at https://www.cdc.gov/vaccines/imz-managers/nis/datasets.html.

†† The Council of American Survey Research Organizations (CASRO) household response rate is calculated as the product of the resolution rate (percentage of the total telephone numbers called that were classified as nonworking, nonresidential, or residential), screening completion rate (percentage of known households that were successfully screened for the presence of age-eligible children), and the interview completion rate (percentage of households with one or more age-eligible children that completed the household survey). The CASRO household response rate is equivalent to the American Association for Public Opinion Research type 3 response rate http://www.aapor.org/AAPOR_Main/media/publications/Standard-Definitions20169theditionfinal.pdf.

§§ Children with receipt of at least one vaccination reported by a provider and those who received no vaccinations were considered to have adequate provider data.

regression was used to assess the association of race/ethnicity with vaccination coverage, adjusting for poverty status. T-tests on weighted data were used to evaluate differences in coverage estimates by demographic characteristics; differences were considered to be statistically significant for p-values <0.05. Trends in vaccination coverage by ages 19, 24, and 35 months were evaluated by month and year of birth using weighted linear regression (*3*). Linear trends were estimated using combined data from 2015 and 2016 NIS-Child (births from January 2012 through January 2015), and an expanded analysis of the 2012–2016 data (births from January 2009 through January 2015). Results by age 24 months (2 years) most closely approximate the average age at vaccination assessment in the annual NIS-Child sample (28 months).

2016 Vaccination Coverage

Coverage remained ≥90% for ≥3 doses of poliovirus vaccine (91.9%), ≥1 dose MMR (91.1%), ≥1 dose of varicella vaccine (90.6%), and ≥3 doses of HepB (90.5%) (Table 1). Coverage was lowest for ≥2 doses of hepatitis A vaccine (HepA) (60.6%), the combined 7-vaccine series (70.7%),¶¶ the HepB birth dose (71.1%), and a completed series of rotavirus vaccine (74.1%). Only 0.8% of children received no vaccinations.

Vaccination Coverage by Race/Ethnicity, Poverty Status, and Type of Health Insurance

Compared with white children, black children had lower coverage with ≥3 and ≥4 doses of DTaP, the primary and full series of Hib, ≥3 and ≥4 doses of PCV, ≥2 doses of HepA, the completed rotavirus vaccine series, and the 7-vaccine series (Table 2). For ≥3 doses of DTaP, the primary series of Hib, and ≥3 doses of PCV, these disparities were not statistically significant after adjustment for poverty status; however, for the remaining vaccines, racial/ethnic disparities persisted only among children living at or above poverty (data not shown). For example, coverage with ≥4 doses of DTaP was similar for white and black children below poverty (75.6% and 76.6%, respectively); among children living at or above poverty, coverage rates among white and black children were 86.8% and 77.2%, respectively. Among children at or above poverty, a higher proportion of black children than white children (25.8% of black children compared with 10.4% of white children) were living just above the poverty level (up to 138% of poverty). The proportion of white children living in households with an income to poverty ratio of ≥4 was twice that of black children (41.5% and 20.4%, respectively). Rotavirus vaccination coverage was lower among Hispanic (73.0%) than among white (77.3%) children.

For most vaccines, coverage among children living below the federal poverty level was lower than coverage among those living at or above the federal poverty level (Table 2). The largest gaps were for rotavirus vaccine (12.7 percentage points), ≥4 PCV doses (7.4 percentage points), the 7-vaccine series (6.5 percentage points), and the full series of Hib (6.2 percentage points). HepB birth dose coverage was higher among children living below the poverty level.

Vaccination coverage varied widely by health insurance status, with highest coverage (other than for the HepB birth dose) among children with private insurance, and lowest among uninsured children (Table 2). Compared with children who had private insurance, percentage point differences for children insured by Medicaid ranged from -2.5 for ≥3 doses of poliovirus vaccine and ≥1 dose of varicella to -12.0 for rotavirus vaccination, and for uninsured children, ranged from -12.4 for ≥3 doses of HepB to -24.9 for ≥4 doses of PCV. A higher percentage of uninsured children had received no vaccinations (3.4%) compared with those insured by Medicaid (0.8%) or private insurance (0.6%).

Trends in Vaccination Coverage

Coverage in 2016 was statistically significantly lower than in 2015 by 1.3 to 2.3 percentage points for ≥3 doses of DTaP, ≥3 doses of poliovirus vaccine, the primary series of Hib, ≥3 doses of HepB, and ≥3 and ≥4 doses of PCV (Table 1). Analysis of trends in coverage by age 2 years, by month and year of birth (*3*), indicated that coverage among children included in combined data from the 2015 and 2016 NIS-Child (born January 2012 through January 2015) did not change for any vaccination. When expanded to children included in the 2012–2016 NIS-Child (children born January 2009 through January 2015), coverage did not change for ≥4 doses of DTaP, ≥1 dose of MMR, the full series of Hib, ≥1 dose of varicella, and ≥4 doses of PCV (Figure). Coverage over 12 consecutive birth months declined by 0.3 percentage points for ≥3 doses of poliovirus vaccine and increased for ≥3 doses of HepB (0.6 percentage points) and ≥2 doses of HepA (1.7 percentage points). Rotavirus vaccination coverage by age 19 months also increased by 1.4 percentage points per 12 birth months. No differences in 2015 and 2016 survey respondent characteristics, changes in survey operations, or errors in processing of survey data were identified.

Discussion

Coverage with recommended vaccines for children aged 19–35 months continues to be high and stable but remains

¶¶ The combined 7-vaccine series (4:3:1:3*:3:1:4) includes ≥4 doses of DTaP; ≥3 doses of poliovirus vaccine; ≥1 dose of measles-containing vaccine; ≥3 or ≥4 doses of Hib (depending upon product type of vaccine); ≥3 doses of HepB; ≥1 dose of varicella vaccine; and ≥4 doses of PCV.

TABLE 1. Estimated vaccination coverage among children aged 19–35 months, by selected vaccines and doses — National Immunization Survey-Child, United States, 2012–2016*

Vaccine/Dose	2012 % (95% CI)	2013 % (95% CI)	2014 % (95% CI)	2015 % (95% CI)	2016 % (95% CI)
DTaP†					
≥3 doses	94.3 (93.6–95.0)§	94.1 (93.2–95.0)	94.7 (94.0–95.4)	95.0 (94.4–95.5)	93.7 (92.8–94.5)§
≥4 doses	82.5 (81.3–83.7)§	83.1 (81.8–84.3)	84.2 (83.0–85.4)	84.6 (83.5–85.7)	83.4 (82.1–84.6)
Poliovirus (≥3 doses)	92.8 (92.0–93.5)§	92.7 (91.6–93.6)	93.3 (92.5–94.1)	93.7 (93.0–94.3)	91.9 (90.9–92.9)§
MMR (≥1 dose)¶	90.8 (89.9–91.6)	91.9 (90.9–92.7)	91.5 (90.6–92.4)	91.9 (91.0–92.7)	91.1 (90.1–92.0)
Hib					
Primary series**	93.3 (92.5–94.0)	93.7 (92.7–94.5)	93.3 (92.5–94.1)	94.3 (93.7–94.9)	92.8 (91.8–93.6)§
Full series**	80.9 (79.7–82.1)	82.0 (80.7–83.3)	82.0 (80.7–83.2)	82.7 (81.5–83.8)	81.8 (80.5–83.0)
HepB					
≥3 doses	89.7 (88.8–90.5)§	90.8 (89.7–91.7)	91.6 (90.7–92.4)	92.6 (91.9–93.3)	90.5 (89.3–91.5)§
Birth dose††	71.6 (70.2–73.0)§	74.2 (72.8–75.7)§	72.4 (70.9–73.9)	72.4 (71.0–73.7)	71.1 (69.5–72.7)
Varicella (≥1 dose)¶	90.2 (89.4–91.1)	91.2 (90.2–92.1)	91.0 (90.1–91.9)	91.8 (91.0–92.5)	90.6 (89.6–91.5)
PCV					
≥3 doses	92.3 (91.5–93.1)§	92.4 (91.4–93.3)	92.6 (91.8–93.4)	93.3 (92.5–94.0)	91.8 (90.8–92.7)§
≥4 doses	81.9 (80.7–83.0)§	82.0 (80.6–83.3)	82.9 (81.6–84.2)	84.1 (83.0–85.2)	81.8 (80.4–83.1)§
HepA					
≥1 dose	81.5 (80.4–82.6)	83.1 (81.9–84.3)§	85.1 (84.0–86.2)§	85.8 (84.7–86.8)	86.1 (84.9–87.2)
≥2 doses	53.0 (51.6–54.5)	54.7 (53.1–56.3)	57.5 (55.9–59.1)§	59.6 (58.1–61.0)	60.6 (59.1–62.2)
Rotavirus§§	68.6 (67.2–69.9)	72.6 (71.1–74.0)§	71.7 (70.1–73.2)	73.2 (71.8–74.6)	74.1 (72.6–75.5)
Combined series¶¶	68.4 (66.9–69.7)	70.4 (68.8–71.9)	71.6 (70.2–73.1)	72.2 (70.9–73.6)	70.7 (69.2–72.2)
No vaccinations	0.8 (0.6–1.1)	0.7 (0.5–1.1)	0.8 (0.6–1.0)	0.8 (0.6–1.0)	0.8 (0.6–1.0)

Abbreviations: CI = confidence interval; DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; HepA = hepatitis A vaccine; HepB = hepatitis B vaccine; Hib = *Haemophilus influenzae* type b vaccine; MMR = measles, mumps, and rubella vaccine; PCV = pneumococcal conjugate vaccine.

* For 2012, children born January 2009–May 2011; for 2013, children born January 2010–May 2012; for 2014, children born January 2011–May 2013; for 2015, children born January 2012–May 2014; and for 2016, children born January 2013–May 2015.

† Includes children who might have been vaccinated with diphtheria and tetanus toxoids, or diphtheria and tetanus toxoids and pertussis vaccine.

§ Statistically significant ($p<0.05$) change in coverage compared with previous year.

¶ Includes children who may have been vaccinated with measles, mumps, rubella, and varicella vaccine.

** Hib primary series: receipt of ≥2 or ≥3 doses, depending on product type received; full series: primary series and booster dose includes receipt of ≥3 or ≥4 doses, depending on product type received.

†† One dose HepB administered from birth through age 3 days.

§§ Includes ≥2 doses of Rotarix monovalent rotavirus vaccine (RV1), or ≥3 doses of RotaTeq pentavalent rotavirus vaccine (RV5).

¶¶ The combined 7-vaccine series (4:3:1:3*:3:1:4) includes ≥4 doses of DTaP, ≥3 doses of poliovirus vaccine, ≥1 dose of measles-containing vaccine, the full series of Hib (≥3 or ≥4 doses, depending on product type of vaccine), ≥3 doses of hepatitis B vaccine, ≥1 dose of varicella vaccine, and ≥4 doses of PCV.

below 90% for vaccines that require booster doses during the second year of life (≥4 doses of DTaP and PCV as well as Hib full series) and for other recommended vaccines (HepB birth dose, rotavirus, and HepA). Disparities in coverage persisted for black children and those living below the poverty level, and coverage was generally lower for children who were uninsured or covered by Medicaid than among those with private insurance. These disparities indicate that improvements are needed in access to and delivery of age-appropriate immunization to all children, regardless of insurance or financial status (i.e., "the immunization safety net").

Health insurance and poverty status are interrelated factors associated with lower vaccination coverage in young children. Compared with children who had only private insurance, those with Medicaid had lower coverage, and those who were uninsured had much lower coverage, for most vaccines. Uninsured children, who account for 3.0% of the 2016 NIS-Child weighted sample, are eligible for the VFC program, which was designed to increase access to vaccination among children through age 18 years who might not otherwise be vaccinated because of inability to pay. Some families might not be aware of the VFC program, be unable to afford fees associated with visits to a vaccine provider, or might need assistance locating a physician who participates in the VFC program. Children living below poverty and up to a certain percentage above the poverty level are eligible for Medicaid (42.5% of 2016 NIS-Child population met the minimum Medicaid eligibility level of 138%) and are entitled to VFC vaccines. Barriers to health care access and use among the publicly insured include language barriers, lack of trust in providers, transportation problems, inconvenient office hours, and other provider- and system-level factors (*4*). Medicaid patients also tend to experience more breaks in insurance coverage than do privately insured children, and discontinuities in insurance coverage have been associated with lower vaccination coverage (*5*). NIS-Child establishes insurance status at the time of interview,

TABLE 2. Estimated vaccination coverage among children aged 19–35 months, by selected vaccines and doses, race/ethnicity,* poverty level,† and health insurance status§ — National Immunization Survey-Child, United States, 2016¶

	Race/Ethnicity							Poverty level		Health insurance status			
Vaccine/ Dose	White, non-Hispanic (Referent) (n = 8,794) % (95% CI)	Black, non-Hispanic (n = 1,307) % (95% CI)	Hispanic (n = 2,727) % (95% CI)	American Indian/ Alaska Native, non-Hispanic (n = 214) % (95% CI)	Asian, non-Hispanic (n = 731) % (95% CI)	Native Hawaiian or other Pacific Islander, non-Hispanic (n = 104) % (95% CI)	Multiple races, non-Hispanic (n = 1,111) % (95% CI)	At or above poverty (Referent) (n = 11,062) % (95% CI)	Below poverty (n = 3,366) % (95% CI)	Private only, (Referent) (n = 8,284) % (95% CI)	Any Medicaid (n = 5,757) % (95% CI)	Other insurance (n = 567) % (95% CI)	Uninsured (n = 380) % (95% CI)
DTaP**													
≥3 doses	94.6 (93.7–95.3)	90.8 (87.7–93.2)††	93.3 (90.6–95.2)	93.6 (87.4–96.9)	96.6 (92.8–98.4)	91.4 (82.6–96.0)	92.8 (88.9–95.4)	94.7 (93.7–95.6)	91.7 (89.8–93.3)††	95.9 (95.1–96.7)	92.5 (90.9–93.8)††	93.2 (87.0–96.6)	80.2 (72.6–86.2)††
≥4 doses	84.8 (83.4–86.2)	76.8 (72.5–80.7)††	83.3 (80.0–86.2)	83.5 (75.7–89.2)	86.4 (80.3–90.8)	83.2 (72.2–90.4)	83.6 (79.2–87.2)	85.1 (83.5–86.6)	79.2 (76.7–81.5)††	87.3 (85.6–88.9)	81.2 (79.2–83.0)††	79.7 (69.9–87.0)	63.2 (54.6–71.0)††
Polio (≥3 doses)	92.5 (91.3–93.6)	90.3 (87.2–92.7)	91.7 (88.8–93.9)	92.4 (85.8–96.1)	94.7 (90.8–97.0)	91.3 (82.5–95.9)	89.4 (84.2–93.1)	92.5 (91.2–93.7)	90.6 (88.6–92.3)	93.6 (92.2–94.7)	91.1 (89.4–92.9)††	92.8 (86.7–96.3)	79.4 (71.8–85.4)††
MMR§§ (≥1 dose)	91.6 (90.4–92.7)	89.4 (86.4–91.9)	90.6 (88.0–92.7)	91.3 (83.2–95.7)	93.6 (89.7–96.2)	86.1 (75.1–92.7)	91.0 (87.1–93.8)	92.1 (91.0–93.2)	89.0 (86.7–90.0)††	93.1 (91.8–94.2)	90.1 (88.4–91.5)††	91.7 (86.0–95.3)	77.3 (69.5–83.5)††
Hib													
Primary series¶¶	93.8 (92.9–94.6)	90.2 (86.8–92.8)††	92.3 (89.6–94.3)	92.6 (85.9–96.3)	95.0 (91.4–97.2)	91.4 (82.6–96.0)	91.0 (86.8–93.9)	94.0 (92.9–94.9)	90.5 (88.4–92.2)††	95.4 (94.4–96.1)	91.2 (89.5–92.7)††	92.9 (86.8–96.3)	78.1 (70.1–84.3)††
Full series¶¶	83.0 (81.7–84.4)	75.6 (71.6–79.2)††	82.1 (78.6–85.1)	82.9 (74.9–88.8)	83.5 (77.2–88.4)	—***	83.0 (78.6–86.7)	83.6 (82.1–85.0)	77.4 (74.8–79.9)††	85.5 (83.7–87.1)	79.6 (77.5–81.5)††	82.6 (76.2–87.5)	61.5 (52.7–69.6)††
HepB													
≥3 doses	91.3 (90.0–92.4)	90.0 (86.9–92.5)	89.1 (85.7–91.8)	91.0 (83.4–95.3)	93.8 (89.9–96.3)	86.0 (75.0–92.6)	88.8 (83.9–92.4)	90.5 (89.0–91.8)	90.5 (88.3–92.4)	91.2 (89.6–92.6)	90.4 (88.6–92.0)	92.4 (86.3–95.9)	78.8 (71.1–84.9)††
Birth dose†††	68.6 (66.7–70.4)	74.0 (69.9–77.8)††	73.4 (68.9–77.4)††	75.0 (64.6–83.1)	73.8 (66.1–80.2)	—***	70.7 (64.3–76.3)	70.1 (68.1–72.0)	74.9 (71.8–77.7)††	68.0 (65.8–70.2)	74.3 (71.6–76.8)††	73.7 (67.4–79.2)	63.9 (55.1–71.8)
Varicella§§ (≥1 dose)	90.8 (89.6–91.9)	89.9 (86.9–92.3)	90.2 (87.4–92.4)	90.9 (82.9–95.4)	94.2 (90.2–96.6)††	86.7 (75.8–93.1)	89.3 (85.0–92.5)	91.2 (89.9–92.3)	89.3 (87.3–91.0)	92.3 (91.0–93.5)	89.8 (88.2–91.3)††	91.0 (85.2–94.7)	75.9 (68.1–82.3)††
PCV													
≥3 doses	93.1 (92.1–94.0)	88.3 (84.9–91.1)††	92.2 (89.5–94.3)	92.2 (85.5–95.9)	89.8 (83.7–93.8)	89.1 (79.0–94.7)	90.7 (86.4–93.7)	93.0 (91.8–94.1)	89.9 (87.8–91.7)††	94.0 (92.8–95.1)	90.4 (88.7–91.9)††	93.8 (87.9–96.9)	79.2 (71.5–85.2)††
≥4 doses	84.1 (82.6–85.5)	74.5 (70.0–78.5)††	81.4 (77.9–84.4)	80.1 (71.3–86.7)	81.0 (72.9–87.1)	82.9 (71.9–90.2)	82.9 (78.4–86.6)	84.2 (82.6–85.8)	76.8 (74.1–79.4)††	86.9 (85.1–88.5)	78.4 (76.2–80.5)††	79.2 (69.2–86.5)	62.0 (53.2–70.0)††
HepA (≥2 doses)	60.0 (58.1–61.9)	53.9 (49.6–58.1)††	63.6 (59.7–67.2)	69.8 (60.1–78.0)††	69.7 (63.6–75.3)††	—***	57.4 (51.7–62.9)	61.9 (60.0–63.8)	56.9 (53.9–59.9)††	62.7 (60.6–64.8)	60.0 (57.5–62.4)	59.1 (50.4–67.3)	42.6 (33.5–52.3)††
Rotavirus§§§	77.3 (75.6–78.8)	67.2 (62.9–71.3)††	73.0 (69.0–76.5)††	—***	71.8 (63.6–78.7)	—***	73.4 (68.2–78.1)	78.2 (76.4–79.9)	65.5 (62.4–68.5)††	80.7 (78.7–82.6)	68.7 (66.3–71.0)††	72.8 (63.4–80.5)	59.9 (51.2–68.0)††
Combined series¶¶¶	72.2 (70.4–73.9)	64.1 (59.6–68.3)††	71.0 (67.1–74.6)	68.5 (58.2–77.2)	72.3 (64.6–78.9)	—***	71.5 (66.1–76.3)	72.5 (70.7–74.3)	66.0 (63.0–68.9)††	74.9 (72.8–76.9)	68.1 (65.7–70.3)††	69.5 (60.4–77.3)	51.0 (41.9–60.0)††

Abbreviations: CI = confidence interval; DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; HepA = hepatitis A vaccine; HepB = hepatitis B vaccine; Hib = *Haemophilus influenzae* type b vaccine; MMR = measles, mumps, and rubella vaccine; PCV = pneumococcal conjugate vaccine.

* Children's race/ethnicity was reported by parent or guardian. Children identified in this report as white, black, Asian, American Indian/Alaska Native, Native Hawaiian or other Pacific Islander, or multiple races were reported by the parent or guardian as non-Hispanic. Children identified as being of multiple races had more than one race category selected. Children identified as Hispanic might be of any race.

† Children were classified as below poverty if their total family income was less than the poverty threshold specified for the applicable family size and number of children aged <18 years. Children with total family income at or above the poverty threshold specified for the applicable family size and number of children aged <18 years were classified as at or above poverty. A total of 560 children with adequate provider data and missing data on income were excluded from the analysis. Poverty level was based on 2015 U.S. Census poverty thresholds (https://www.census.gov/data/tables/time-series/demo/income-poverty/historical-poverty-thresholds.html).

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

¶ Children in the 2016 National Immunization Survey-Child were born January 2013–May 2015.

** Includes children who might have been vaccinated with diphtheria and tetanus toxoids, or diphtheria and tetanus toxoids, and pertussis vaccine.

†† Statistically significant ($p<0.05$) difference from the referent group.

§§ Includes children who may have been vaccinated with measles, mumps, rubella, and varicella vaccine.

¶¶ Hib primary series: receipt of ≥2 or ≥3 doses, depending on product type received; full series: primary series and booster dose includes receipt of ≥3 or ≥4 doses, depending on product type received.

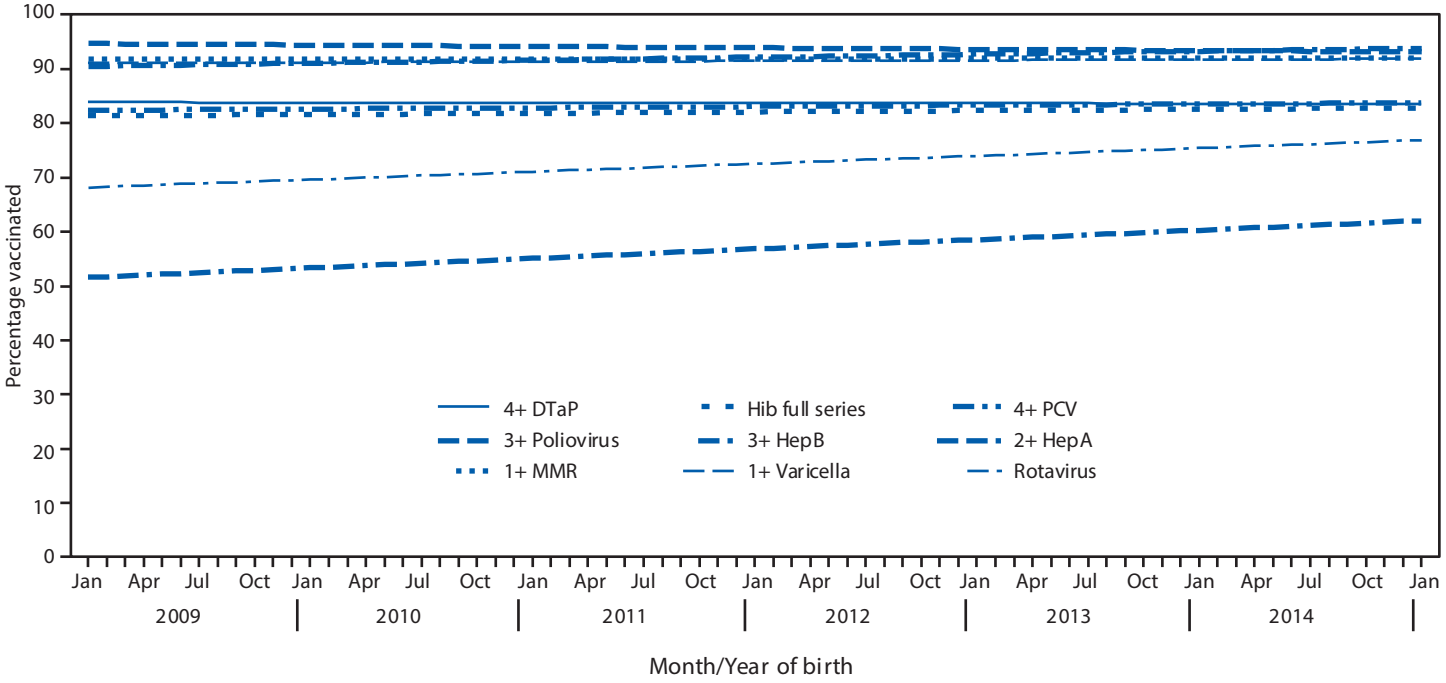
*** Estimate not available because the 95% CI was ≥20.

††† One dose HepB administered from birth through age 3 days.

§§§ Includes ≥2 or ≥3 doses, depending on product type of vaccine received (≥2 doses for Rotarix [RV1], or ≥3 doses for RotaTeq [RV5]).

¶¶¶ The combined seven vaccine series (4:3:1:3*:3:1:4) includes ≥4 doses of DTaP, ≥3 doses of poliovirus vaccine, ≥1 dose of measles-containing vaccine, the full series of Hib (≥3 or ≥4 doses, depending on product type of vaccine), ≥3 doses of HepB, ≥1 dose of varicella vaccine, and ≥4 doses of PCV.

FIGURE. Estimated linear trend in coverage with selected vaccines* by age 24 months,† by month and year of birth§ — National Immunization Survey-Child, United States, 2012–2016



Abbreviations: DTaP = diphtheria and tetanus toxoids and acellular pertussis vaccine; HepA = hepatitis A vaccine; HepB = hepatitis B vaccine; Hib = *Haemophilus influenzae* type b vaccine; MMR = measles, mumps, and rubella vaccine; PCV = pneumococcal conjugate vaccine.

* Hib full series: receipt of ≥3 or ≥4 doses, depending on product type received (primary series and booster dose). Rotavirus includes ≥2 or ≥3 doses, depending on product type of vaccine received (≥2 doses for Rotarix [RV1], or ≥3 doses for RotaTeq [RV5]).

† Except for rotavirus, vaccination coverage was assessed before the child reached age 24 months. The Kaplan-Meier method was used to account for censoring of vaccination status for children assessed before age 24 months. Rotavirus vaccination was assessed before the child reached age 19 months and might include some vaccinations reported as received after the maximum recommended age of 8 months, zero days.

§ Estimated linear relationship between month and year of birth and vaccination coverage, based on weighted linear regression analysis using the inverse of the estimated variance of each point estimate to construct the weights. Estimated percentage point change over 12 consecutive birth months: 4+ DTaP -0.05 (-0.4, 0.3); 3+ Poliovirus -0.3 (-0.5, -0.006); 1+ MMR 0.05 (-0.2, 0.3); Hib full series 0.2 (-0.1, 0.6); 3+ HepB 0.6 (0.3, 0.9); 1+ Varicella 0.1 (-0.1, 0.4); 4+ PCV 0.2 (-0.1, 0.6); 2+ HepA 1.7 (1.2, 2.3); Rotavirus 1.4 (1.0, 1.9).

not necessarily at the time of recommended vaccination, with enrollment in insurance sometimes occurring after the time window for receipt of certain vaccines. CDC has undertaken a number of activities designed to elucidate potential barriers to early childhood vaccination from the perspective of the state immunization programs and health care providers enrolled in the VFC program. There are also plans to assess parental experience with and barriers to accessing vaccination services.

Lower vaccination coverage among black children than among white children has been explained by differences in poverty status in past years (*6*), but in 2016, racial disparities were found among children living at or above the poverty level for some vaccines. This might reflect incomplete control for poverty status, because black children living above poverty could still live in lower income households, on average, than do white children. In the 2016 NIS-Child, the proportion of white children living in households with an income to poverty ratio of ≥4 was twice that of black children.

During routine checks for accuracy of the 2016 NIS-Child data, statistically significant differences were observed in vaccination coverage by age 19 months estimated from the 2016 compared with the 2015 surveys, among birth cohorts eligible to be included in both survey years (*3,7*). These differences were observed for 9 of the 15 vaccine doses evaluated and might indicate a systematic change in bias of the survey from 2015 to 2016. However, no differences were found in survey respondent characteristics and survey operations, and no errors were identified in processing of survey data; thus, it is possible that these differences might be attributable to random variation.

The observed vaccination coverage differences among birth cohorts eligible for both survey years contributed to drops in annual estimates of vaccination coverage using the entire sample of survey respondents from 2015 to 2016, but do not provide evidence for change in vaccination coverage over time (*3*). When trends were assessed more directly by month and year of birth from January 2012 through January 2015 (*3*), coverage by age 2 years was stable for all vaccines. When trends

Summary

What is already known about this topic?

Vaccination is an effective method for reducing the impact of many diseases among young children in the United States. For over 20 years, the National Immunization Survey-Child has gathered data on children aged 19–35 months to assess coverage with the vaccines recommended by the Advisory Committee on Immunization Practices (ACIP).

What is added by this report?

Coverage with most recommended vaccines remained stable and high in 2016; coverage was ≥90% for polio, measles, mumps, and rubella, varicella, and hepatitis B vaccines, and lowest (61%–74%) for hepatitis A, the birth dose of hepatitis B, and rotavirus vaccines, and the combined 7-vaccine series. For most vaccines, coverage was lower among black children, children living below the federal poverty level, and children who were uninsured or covered by Medicaid compared with white children, children living at or above the federal poverty level, and children with private insurance.

What are the implications for public health practice?

Continued collaboration between CDC and state immunization programs to further elucidate and address disparities in coverage by poverty status should provide valuable information while strategies needed for improving access to and delivery of age-appropriate immunization are identified. Health care providers can increase vaccination coverage using evidence-based strategies such as provider reminders, standing orders to provide vaccination whenever appropriate, and immunization information systems.

were assessed over a longer range of births, from January 2009 through January 2015, coverage was stable for most vaccines; for other vaccines, estimated change over twelve monthly birth cohorts was within one percentage point, and increased by 1–2 percentage points for rotavirus vaccination and ≥2 doses of HepA. Further evaluations of methods for assessing trends in survey accuracy and vaccination coverage using NIS-Child data are needed. Improved data quality of immunization information systems (IIS) will facilitate their use as another data source for population-based coverage assessment (*8*).

The findings in this report are subject to at least three limitations that have been previously described, including exclusion of households without telephones, nonresponse bias, and incomplete vaccination histories reported by providers (*6*). Total survey error has been evaluated in a sensitivity analysis accounting for these errors. Analyses of 2012 and 2013 data revealed that NIS-Child might have underestimated true vaccination coverage in those years by ≤4 percentage points for MMR, ≤5 percentage points for ≥4 doses of DTaP, and 5 percentage points for a 6-vaccine series that excluded PCV (*9*,*10*). Changes in annual vaccination coverage estimates should be interpreted with caution (*3*), particularly when they are smaller than the survey margin of error.

These data indicate that the immunization safety net is not reaching all children early in life. Coverage could be increased with implementation of evidence-based interventions, such as provider reminders to eliminate missed opportunities to vaccinate, standing orders to provide vaccination whenever appropriate, and use of IIS to track vaccination administration.*** In addition to maintaining the strong U.S. immunization program, innovative approaches are needed to identify children not reached by the current safety net, including using local level IIS data. Continued vaccination coverage assessment using the NIS-Child will guide efforts to improve vaccination coverage. Data completeness and functionality of IIS have improved in recent years (*8*); however, additional progress is needed to maximize IIS utility for vaccination coverage assessments at state and local levels.

***https://www.thecommunityguide.org/topic/vaccination.

Conflict of interest

No conflicts of interest were reported.

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References

1. Zhou F, Shefer A, Wenger J, et al. Economic evaluation of the routine childhood immunization program in the United States, 2009. Pediatrics 2014;133:577–85. https://doi.org/10.1542/peds.2013-0698
2. Robinson CL; Advisory Committee on Immunization Practices (ACIP), ACIP Child/Adolescent Immunization Work Group. Advisory Committee on Immunization Practices recommended immunization schedules for persons aged 0 through 18 years—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:86–7. https://doi.org/10.15585/mmwr.mm6504a4
3. CDC. Evaluating vaccination coverage trends with the National Immunization Survey-Child (NIS-Child), 2012–2016, United States. Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https://www.cdc.gov/vaccines/imz-managers/coverage/childvaxview/pubs-presentations/NIS-vax-trends-2012-2016.html
4. Allen EM, Call KT, Beebe TJ, McAlpine DD, Johnson PJ. Barriers to care and health care utilization among the publicly insured. Med Care 2017;55:207–14. https://doi.org/10.1097/MLR.0000000000000644
5. Smith PJ, Stevenson J, Chu SY. Associations between childhood vaccination coverage, insurance type, and breaks in health insurance coverage. Pediatrics 2006;117:1972–8. https://doi.org/10.1542/peds.2005-2414
6. Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Dietz V. Vaccination coverage among children aged 19–35 months—United States, 2015. MMWR Morb Mortal Wkly Rep 2016;65:1065–71. https://doi.org/10.15585/mmwr.mm6539a4

7. Yankey D, Hill HA, Elam-Evans LD, et al. Estimating change in telephone survey bias in an era of declining response rates and transition to wireless telephones—evidence from the National Immunization Survey (NIS), 1995–2013. Presented at the 2015 American Association for Public Opinion Research 70th Annual Conference, Hollywood, FL; May 14–17, 2015.
8. Murthy N, Rodgers L, Pabst L, Fiebelkorn AP, Ng T. Progress in childhood vaccination data in immunization information systems—United States, 2013–2016. MMWR Morb Mortal Wkly Rep 2017;66:1178–81.
9. Wolter KM, Pineau VJ, Skalland B, et al. Total survey error assessment for sociodemographic subgroups in the 2012 U.S. National Immunization Survey. In: Biemer PP, de Leeuw E, Eckman S, Edwards B, Kreuter F, Lyberg LE, eds. Total survey error in practice. New York, NY: John Wiley and Sons; 2017.
10. Skalland B, Wolter K, Ma Q, et al. A total survey error framework and assessment for the 2013 National Immunization Survey. Presented at the International Total Survey Error Workshop, Sydney, Australia; October, 2016.

Progress in Childhood Vaccination Data in Immunization Information Systems — United States, 2013–2016

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In 2016, 55 jurisdictions in 49 states and six cities in the United States* used immunization information systems (IISs) to collect and manage immunization data and support vaccination providers and immunization programs. To monitor progress toward achieving IIS program goals, CDC surveys jurisdictions through an annual self-administered IIS Annual Report (IISAR). Data from the 2013–2016 IISARs were analyzed to assess progress made in four priority areas: 1) data completeness, 2) bidirectional exchange of data with electronic health record systems, 3) clinical decision support for immunizations, and 4) ability to generate childhood vaccination coverage estimates. IIS participation among children aged 4 months through 5 years increased from 90% in 2013 to 94% in 2016, and 33 jurisdictions reported ≥95% of children aged 4 months through 5 years participating in their IIS in 2016. Bidirectional messaging capacity in IISs increased from 25 jurisdictions in 2013 to 37 in 2016. In 2016, nearly all jurisdictions (52 of 55) could provide automated provider-level coverage reports, and 32 jurisdictions reported that their IISs could send vaccine forecasts to providers via Health Level 7 (HL7) messaging, up from 17 in 2013. Incremental progress was made in each area since 2013, but continued effort is needed to implement these critical functionalities among all IISs. Success in these priority areas, as defined by the IIS Functional Standards (*1*), bolsters clinicians' and public health practitioners' ability to attain high vaccination coverage in pediatric populations, and prepares IISs to develop more advanced functionalities to support state/local immunization services. Success in these priority areas also supports the achievement of federal immunization objectives, including the use of IISs as supplemental sampling frames for vaccination coverage surveys like the National Immunization Survey (NIS)-Child, reducing data collection costs, and supporting increased precision of state-level estimates.

IISs, also known as immunization registries, are confidential, computerized, population-based systems that collect and consolidate vaccination data from providers in a jurisdiction (*2*). IISs increase vaccination rates and reduce vaccine-preventable diseases by enabling effective interventions (e.g., client reminder and recall, provider assessment and feedback), tracking patient immunizations, estimating vaccination coverage, and facilitating vaccine management and accountability (*3*). For IISs to support real-time immunization efforts both at the population level and at the point of clinical care, these systems need to capture complete childhood immunization data. To promote IIS functionality and data quality, CDC and external partners, including state/local immunization programs and IIS vendors, developed 27 Functional Standards to guide IIS development from 2013 to 2017 (*1*). CDC monitors progress toward these Functional Standards through a self-administered survey known as the IIS Annual Report (IISAR). During 2016–2017, CDC issued guidance to jurisdictions identifying four priority areas (covering multiple Functional Standards) that immunization programs should focus on before developing other IIS functionalities. The four priority areas are: 1) data completeness for children aged 0–6 years (Functional Standard 1.1, 3.1); 2) bidirectional information exchange with electronic health record systems (1.4, 1.5); 3) pediatric clinical decision support for immunizations (1.2), and 4) ability to generate jurisdictional and provider-level childhood vaccination coverage estimates (5.2). This report assesses progress toward achieving success in these four priority areas from 2013 to 2016, using data from the 2013–2016 IISARs. IISAR is a secure web-based survey instrument distributed annually to state, local, and territorial immunization programs by CDC. Immunization programs self-report their IIS's progress toward meeting the Functional Standards during the previous calendar year.

Data completeness comprises four measures: birth record capture, child participation, provider participation, and IIS coverage estimate comparison to NIS-Child. These measures represent the ability of an IIS to capture the population within the jurisdiction as well as all vaccinations administered. Birth record capture is defined as the ability of an IIS to create patient records for all children who are born in a jurisdiction. Child participation is defined as the number of children aged 4 months through 5 years with ≥2 vaccinations recorded in the IIS, divided by the total U.S. Census–based population estimate for the same age group in that jurisdiction. Provider participation is defined as the number of vaccination provider sites enrolled in an IIS that reported ≥1 vaccine doses to the IIS within the last 6 months of the preceding calendar year. IIS participation among the >40,000 provider sites served by

*Excluding the U.S. territories.

the publicly funded Vaccines for Children (VFC) program[†] was analyzed. The comparison of IIS coverage estimates with estimates from NIS-Child measures an IIS's success in capturing complete population and vaccination information within a jurisdiction.[§]

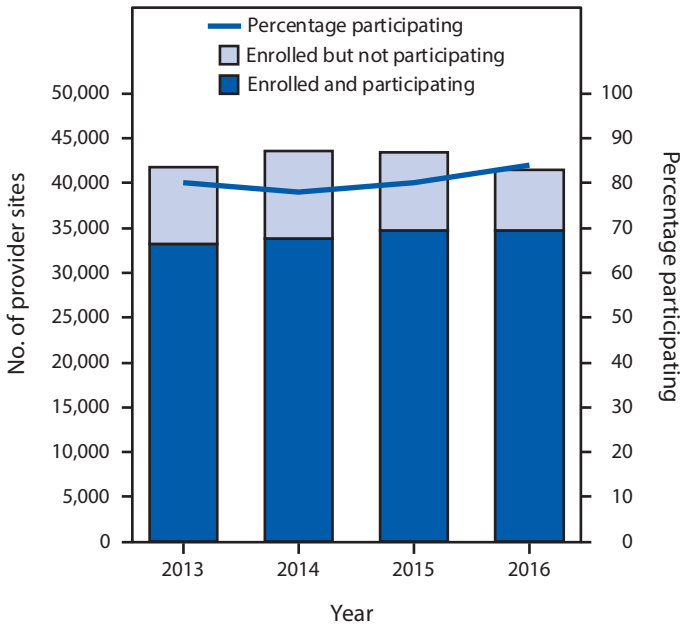
Across all IIS jurisdictions, 106%[¶] of U.S. births were captured in IIS in 2016, an increase from 102% in 2013. Childhood IIS participation increased from 90% in 2013 to 94% in 2016, which approaches the *Healthy People 2020* objective of ≥95% child IIS participation. Among the 55 jurisdictions, 33 (60%) reported that ≥95% of children aged 4 months through 5 years in their geographic area participated in their IIS in 2016, compared with 24 (44%) in 2013. In 2016, provider participation was 85% among VFC provider sites enrolled in an IIS. The number of VFC provider sites enrolled in an IIS decreased from 41,710 in 2014 to 41,393 in 2016. Among these enrolled sites, the number of VFC provider sites participating in an IIS increased slightly from 33,266 in 2013 to 34,662 in 2016 (Figure 1).

For the combined 7-vaccine series,[**] the number of jurisdictions with IIS estimates within 10 percentage points of the corresponding NIS-Child coverage estimates increased from 17 in 2013 to 25 in 2016 (Figure 2). In 2016, 30 IISs had 7-vaccine series coverage estimates that were at least 10 percentage points lower than the corresponding NIS-Child estimate.

Bidirectional information exchange allows providers to submit immunization data directly from electronic health records (EHRs) to IISs, and to request and receive immunization information from IISs into EHRs for the patients they serve. HL7 messaging is a nationally recognized platform-independent standard that supports the bidirectional exchange of health-related information, including immunization-related messaging. In 2016, 91% of jurisdictions had an IIS that used HL7 version 2.5.1 to receive vaccination histories from providers and returned acknowledgment messages, compared with 87% in 2013. Furthermore, in 2016, 67% of jurisdictions had an IIS that received requests for vaccination histories and returned responses to those requests, compared with 45% in 2013 (Figure 3). Finally, in 2016, 78% of jurisdictions had an IIS that could transmit immunization data using Simple Object Access Protocol, the CDC-endorsed transport standard for the exchange of immunization information, compared with 75% of jurisdictions reporting this capability in 2013 (*4*).

Clinical Decision Support (CDS) functionalities enable providers to evaluate the validity of vaccine doses administered to patients and forecast future vaccines that will be needed, based on recommendations developed by the Advisory Committee on Immunization Practices. From 2013 to 2016, all jurisdictions' IISs had CDS capabilities that were available to providers through the IIS's user interface. In 2016, 58% (32 of 55) of jurisdictions reported sending a vaccine forecast to another system via HL7 messaging. This is an 87% increase from 2013, when 31% (17 of 55) of jurisdictions reported performing this task.

FIGURE 1. Number and percentage of Vaccines for Children program provider sites enrolled and participating* in an Immunization Information System (IIS), by year — IIS Annual Report, United States, 2013–2016



* Participation is defined as having submitted information to the IIS about administering ≥1 vaccine dose in the last 6 months of the preceding calendar year. Provider sites must be enrolled in an IIS to participate in the IIS.

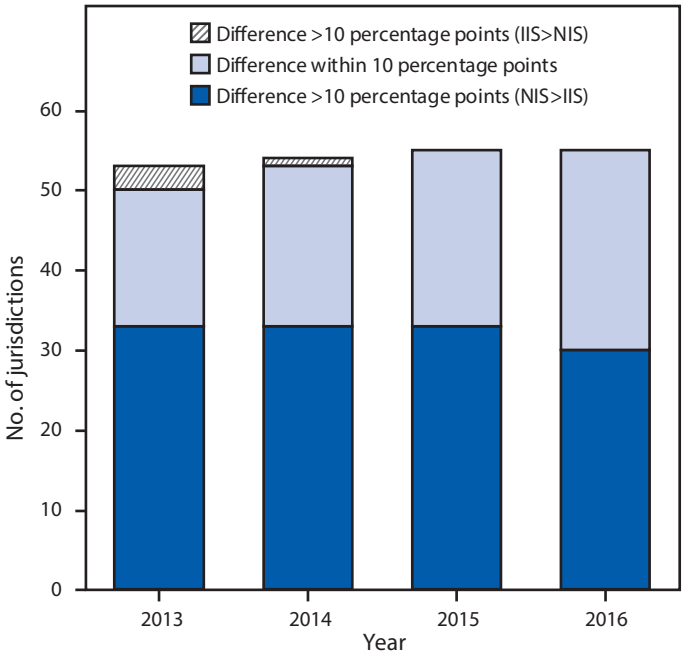
[†] The Vaccines for Children program provides vaccines at no cost to eligible children, including those whose parents or guardians might not be able to afford vaccines. https://www.cdc.gov/vaccines/programs/vfc/index.html.

[§] NIS-Child is a nationally representative survey that estimates vaccination coverage among children aged 19–35 months using provider-reported vaccination data. Many factors can potentially affect the calculated percentage point differences between IIS and NIS-Child estimates, including possible errors in IIS vaccination and population calculations, errors in NIS-Child (such as random error, selection bias, and underascertainment of vaccination status), variability in data completeness in individual IIS, and other methodological differences between NIS-Child and IISs. Despite these limitations, the NIS-Child is well established as a reliable indicator of childhood vaccination rates, and serves as a useful holistic benchmark for assessing an IIS' performance in capturing recorded doses administered within its jurisdiction.

[¶] Comparisons were made with U.S. Census estimates for children aged <1 year in 2016. Birth record capture percentages often exceed 100% because of newborn data being recorded in more than one IIS (e.g., a child who is born in 1 state but who is a resident in a different state might be recorded in both IISs), and because of incomplete inactivation of records of children who move out of a jurisdiction.

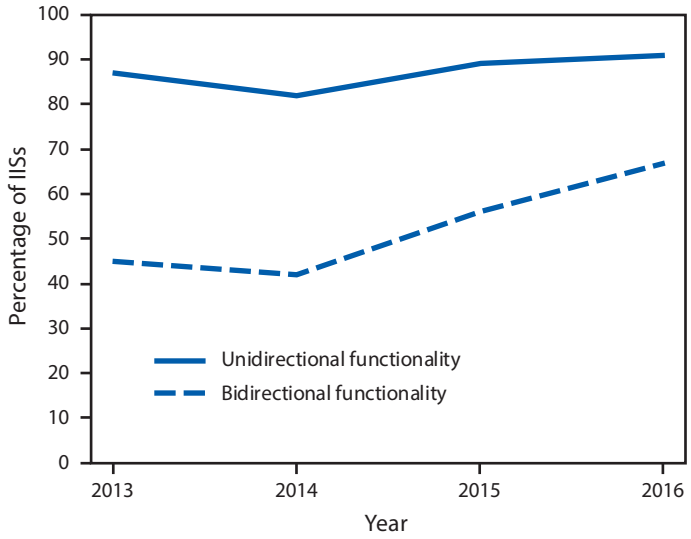
[**] ≥4 doses of diphtheria and tetanus toxoids and acellular pertussis vaccine; ≥3 doses of poliovirus vaccine; ≥1 dose of measles-containing vaccine; *Haemophilus influenzae* type B vaccine full series; ≥3 doses of Hepatitis B vaccine; ≥1 doses of varicella vaccine; and ≥4 doses of pneumococcal conjugate vaccine.

FIGURE 2. Percentage point differences between National Immunization Survey (NIS)-Child and Immunization Information Systems (IISs) for combined 7-vaccine series* completion — IIS Annual Report, United States, 2013–2016



* ≥4 doses of diphtheria and tetanus toxoids and acellular pertussis vaccine; ≥3 doses of poliovirus vaccine; ≥1 doses of measles-containing vaccine; *Haemophilus influenzae* type B vaccine full series; ≥3 doses of hepatitis B vaccine; ≥1 dose of varicella vaccine; and ≥4 doses of pneumococcal conjugate vaccine.

FIGURE 3. Percentage of Immunization Information Systems (IISs) with unidirectional and bidirectional information exchange functionality* — United States, 2013–2016



* Unidirectional functionality is defined as the ability to receive vaccination histories (message type: VXU) from providers and return acknowledgment messages (message type: ACK), and bidirectional functionality is defined as the ability to receive requests for vaccination histories (message type: QBP) and return responses to those requests (message type: RSP). Achievement of unidirectional functionality is a prerequisite to achieving bidirectional functionality. https://www.cdc.gov/vaccines/programs/iis/technical-guidance/downloads/hl7guide-1-5-2014-11.pdf.

IISs can be used to generate coverage estimates for childhood vaccinations at the jurisdictional level (e.g., state, postal code, or county) and at the provider level to identify vulnerable subpopulations. In 2016, 89% of jurisdictions (49 of 55) provided a predefined, automatic report on immunization coverage by geography. This is 11% higher than in 2013, when 80% of jurisdictions provided these reports. In 2016, 95% of jurisdictions (52 of 55) provided a predefined, automatic report on immunization coverage by provider site. This is 7% higher than in 2013, when 89% of jurisdictions reported providing these reports.

Discussion

Since 2013, incremental progress was noted in each of the four priority areas for immunization programs that were assessed. Notably, the increased number of jurisdictions that had IIS estimates that were within 10 percentage points of the corresponding NIS-Child coverage estimate suggests that more jurisdictions have IISs with more complete data, or at least that the IIS and NIS are similar in their ability to estimate vaccination coverage for that jurisdiction's population. Jurisdictions with IIS coverage estimates that were at least 10 percentage points lower than the corresponding NIS-Child estimate might have less complete IIS data, particularly at sites with the largest IIS–NIS discrepancies.

By prioritizing resources to the identified priority areas, jurisdictions can make substantial progress in this important subset of activities rather than incremental progress across all Functional Standards. Improvements in priority areas can also support a broader range of immunization services; for example, improved data completeness for children aged <6 years would strengthen immunization delivery for this population (Functional Standard 1.1–1.3) and increase VFC program accountability (2.1–2.6). In addition, as IISs identify more children and record all doses administered within their jurisdiction, IIS-based vaccination coverage estimates will be able to supplement estimates from surveys like the NIS-Child (*5*). IISs are integral components of routine clinical practice and public health surveillance for immunization. Availability of more complete IIS data also offer many benefits to health care providers and public health practitioners, including consolidating patients' vaccination histories, identifying undervaccinated subgroups, and forecasting the needs of individual patients for recommended vaccines (*3*).

Summary

What is already known about this topic?

In 2012, 86% of U.S. children aged 4 months through 5 years (19.5 million) had ≥2 doses recorded in immunization information systems (IISs).

What is added by this report?

From 2013 to 2016, the percentage of children with ≥2 immunizations recorded in IISs increased from 90% to 94%, approaching the Healthy People 2020 objective of ≥95%. However, variability in IIS pediatric data quality persists: 30 of 55 IISs produced 7-vaccine series coverage rates that were at least 10 percentage points lower than the corresponding National Immunization Survey-Child coverage rate in 2016, suggesting incompleteness of IIS data. Across all IISs, there was progress in achieving bidirectional information exchange with electronic health record systems, pediatric clinical decision support for immunizations, and the ability to generate jurisdictional and provider-level childhood vaccination coverage estimates.

What are the implications for public health practice?

To realize the full benefits of IISs, immunization programs need to implement strategies that prioritize and align resources to achieve functionality and high data quality in four focus areas: 1) pediatric data completeness, 2) bidirectional data exchange with electronic health record systems, 3) clinical decision support for immunizations, and 4) ability to generate childhood vaccination coverage estimates. Strategies such as implementing best practices, adhering to national standards, and incorporating independent third-party assessments can reduce variability across IISs, and support IIS' full potential to facilitate complete vaccination of U.S. children against vaccine-preventable diseases.

Standards and best practices exist that can guide IIS development and maintenance activities, including the IIS Functional Standards (*1*), national standards for the electronic exchange of immunization information,[††] CDS resources,[§§] and data quality best practices.[¶¶] Alignment with these standards and best practices reduces variability across IISs and helps IISs use resources more efficiently to provide the most value for immunization programs, providers, patients, and parents. Continuously monitoring the progress of each IIS can also help jurisdictions identify areas for improvement. Such monitoring is done using the IISAR or other tools, such as an initiative to assess, measure, and validate IISs that was recently developed by the American Immunization Registry Association (*6*).

The findings in this report are subject to at least three limitations. First, results were self-reported and might be subject to response bias. Second, only a subset of the Functional Standards pertaining to the four priority areas was analyzed in this report; this evaluation was not a comprehensive analysis of the progress made in all Functional Standards. Finally, reported capacity of a functionality does not necessarily indicate active utilization of that functionality.

This was the first systematic assessment of progress in four priority areas that are foundational for IISs. Incorporating strategies such as prioritizing activities, aligning resources, implementing best practices, adhering to national standards, and implementing independent third-party assessments can promote consistency across jurisdictions, encourage program accountability, ensure quality standards, and help IISs more rapidly attain their full potential to facilitate complete vaccination of U.S. children against vaccine-preventable diseases.

Conflict of Interest

No conflicts of interest were reported.

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References

1. CDC. Immunization information system (IIS) functional standards. Atlanta, GA: US Department of Health and Human Services, CDC; 2012. https://www.cdc.gov/vaccines/programs/iis/func-stds.html
2. CDC. Progress in immunization information systems—United States, 2012. MMWR Morb Mortal Wkly Rep 2013;62:1005–8.
3. Groom H, Hopkins DP, Pabst LJ, et al.; Community Preventive Services Task Force. Immunization information systems to increase vaccination rates: a community guide systematic review. J Public Health Manag Pract 2015;21:227–48. https://doi.org/10.1097/PHH.0000000000000069
4. CDC. Transport (SOAP). Atlanta, GA: US Department of Health and Human Services, CDC; 2016. https://www.cdc.gov/vaccines/programs/iis/technical-guidance/soap/services.html
5. Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kang Y. Vaccination coverage among children aged 19–35 months—United States. MMWR Morb Mortal Wkly Rep 2017;66:1171–7.
6. American Immunization Registry Association. Summary and environmental scan of assessment and certification models. Washington, DC: American Immunization Registry Association; 2015. http://www.immregistries.org/resources/other-aira-resources/Summary_and_Environmental_Scan_of_Assessment,_Certification_Models_-_Final.pdf

[††] IIS HL7 Implementation: https://www.cdc.gov/vaccines/programs/iis/technical-guidance/hl7.html; IIS Transport (SOAP): https://www.cdc.gov/vaccines/programs/iis/technical-guidance/soap/services.html.

[§§] IIS Clinical Decision Support for Immunization (CDSi): https://www.cdc.gov/vaccines/programs/iis/cdsi.html.

[¶¶] American Immunization Registry Association: Data Quality Assurance in IIS: http://www.aira.browsermedia.com/resources/AIRA-MIROW_DQA_Selected_Aspects_best_practice_guide_05-17-2013.pdf; American Immunization Registry Association: Data Visualization Guide: http://repository.immregistries.org/files/resources/58a601d626d7a/aira_data_validation_guide.pdf; IIS Deduplication: https://www.cdc.gov/vaccines/programs/iis/technical-guidance/deduplication.html.

Harmful Algal Bloom–Associated Illnesses in Humans and Dogs Identified Through a Pilot Surveillance System — New York, 2015

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Cyanobacteria, also known as blue-green algae, are photosynthetic, aquatic organisms found in fresh, brackish, and marine water around the world (*1*). Rapid proliferation and accumulation of potentially toxin-producing cyanobacteria characterize one type of harmful algal bloom (HAB). HABs have the potential to cause illness in humans and animals (*2*,*3*); however, the epidemiology of these illnesses has not been well characterized. Statewide in 2015, a total of 139 HABs were identified in New York, 97 (70%) of which were confirmed through laboratory analysis; 77 independent beach closures were ordered at 37 beaches on 20 different bodies of water. To better characterize HAB-associated illnesses, during June–September 2015, the New York State Department of Health (NYSDOH) implemented a pilot surveillance system in 16 New York counties. Activities included the collection of data from environmental HAB reports, illness reports, poison control centers, and syndromic surveillance, and increased outreach to the public, health care providers, and veterinarians. During June–September, 51 HAB-associated illnesses were reported, including 35 that met the CDC case definitions*; 32 of the cases occurred in humans and three in dogs. In previous years, New York never had more than 10 HAB-associated illnesses reported statewide. The pilot surveillance results from 16 counties during a 4-month period suggest that HAB-associated illnesses might be more common than previously reported.

Exposure to HABs through contact, inhalation, or ingestion of contaminated water can cause illness in humans and animals (*2*,*3*). Signs and symptoms associated with HAB exposure have occurred from exposure to cyanobacteria in situations in which toxins were not detected (*4*,*5*). Symptoms associated with HAB exposure can include skin reactions, eye irritation, ear irritation, liver damage, and gastrointestinal, respiratory, and neurologic signs and symptoms (*1*–*3*).

"One Health" is a concept that encompasses the interrelatedness of human and animal health and the environment and recognizes that health outcomes might be optimized through multidisciplinary collaboration. The application of a One Health approach to HABs might result in the development of improved public health prevention and response efforts (*6*,*7*). To better understand the occurrence of HABs and the epidemiology of cyanobacteria HAB-associated illnesses NYSDOH implemented a pilot surveillance system in 2015, applying a One Health approach in a subset of counties overseen by local health departments (LHDs).

NYSDOH selected 16 (26%) of 62 New York counties for participation in the pilot surveillance system based on the likelihood of an HAB occurrence within their jurisdiction and the LHDs' interest in participation. Public health workers from each participating county attended a training webinar and received an electronic package of surveillance tools, including health outreach documents for the general public, health care providers, and veterinarians; human and animal illness questionnaires; and illness reporting forms adapted from CDC's One Health Harmful Algal Bloom System materials (*8*). During June–September 2015, HAB-associated human and animal illnesses and environmental HAB occurrences reported by LHDs and the New York State Department of Environmental Conservation (NYSDEC) were submitted to NYSDOH.

NYSDEC was the main source of information regarding environmental HAB occurrence, location, and laboratory confirmation. A program within NYSDEC evaluates bodies of water for HABs in response to reports of possible HABs from the public, various park staffs, and lake associations. NYSDEC notified NYSDOH of any possible or laboratory-confirmed HABs within 24 hours so that a response (e.g., closing the beach) could be implemented promptly. NYSDEC also notified the relevant LHDs and lake associations, when applicable.

When there is visual evidence of an HAB (e.g., visible scum or discolored water consistent with an HAB) at a regulated bathing beach in New York, the jurisdiction with authority over the beach requires it to be closed to swimming, wading, and other water contact. Visual evidence, as opposed to toxin monitoring, is used to trigger beach closures because of the risk for illness from both toxin-producing and nontoxin-producing

* Suspected human and animal cases required exposure to water, algae, seafood, or dietary harmful algal bloom (HAB) sources; signs or symptoms following an HAB exposure; and a public health assessment of whether the illness was likely HAB-related. For animals, assessments also could have been completed by qualified nonpublic health entities that were identified by state or federal agency partners. Probable human and animal cases met the suspected case definition and, in addition, were required to have a professional medical diagnosis or have been supported by either observational or HAB environmental laboratory data. Confirmed human and animal cases met the suspected case definition and were required to have HAB clinical laboratory data plus either 1) a professional medical diagnosis or rule-out of other causes of illness; or 2) a professional medical diagnosis, rule-out of other causes of illness, and HAB environmental laboratory data. https://www.cdc.gov/habs/pdf/ohhabs-case-and-event-definitions-table-3-14-17.pdf.

HABs and the variability in the location and length of HAB occurrences. In such instances, water contact was prohibited until the HAB was no longer visible in the beach area for at least 1 day, and testing with commercially available algal toxin-detecting test strips had determined that concentrations of cyanobacterial toxins were below the recommended guidance value of 10 μg/L (*9*). Using the combination of visualization and test strip approach allows for more immediate protective measures than laboratory confirmation of HABs, which might take several days to complete. Visual evidence in water bodies other than bathing beaches is also used as a trigger for LHDs to alert the public via social media, websites, press releases, and advisory signs.

As part of the pilot surveillance system, outreach materials were disseminated through NYSDOH and NYSDEC websites, a veterinary magazine, and presentations and flyers at various meetings involving lake and water quality associations. Outreach materials encouraged members of the public who had a suspected exposure to report symptoms to their LHD. Additional surveillance activities were implemented by NYSDOH when an HAB was identified that posed a substantial public health concern affecting drinking water or recreational water activities. Such surveillance activities included 1) monitoring hospital syndromic surveillance data for patients who displayed symptoms consistent with HAB exposure, 2) providing educational materials to health care providers and veterinarians near the sites of HABs, and 3) coordinating with poison control centers to notify NYSDOH if suspected HAB exposure calls were received.

HAB-associated illnesses were voluntarily reported to NYSDOH through participating counties, NYSDEC, the New York State Office of Parks, Recreation and Historic Preservation, and a veterinary office. Each report of illness was investigated using a questionnaire administered by either the LHD or NYSDOH and assessed using the CDC case definitions for HAB-associated illness. Case definitions are specific to animals and humans and take into consideration information such as environmental or visual evidence of an HAB, confirmation via toxin-detecting test strips, or laboratory confirmation (i.e., via microscopy, enzyme-linked immunosorbent assay, liquid chromatography mass spectrometry, or density of blue green chlorophyll) along with clinical evidence of HAB exposure (e.g., consistency of symptoms and onset of illness after exposure). During June–September 2015, NYSDOH received 51 HAB-associated illness reports from the pilot surveillance system, 35 (68.8%) of which met the CDC case definitions, including 32 in humans and three in dogs. Among those patients with such data available, median age of the humans was 24 years (2–63 years) and median age of the dogs was 7 years (2–12 years); 18 (56%) of the humans and one of the dogs were female. One (3%) of the 32 human cases was classified as confirmed, 20 (57%) as probable, and 11 (31%) as suspected. All three canine cases were classified as probable.

Among cases that occurred in humans, skin problems were reported by 22 (69%) patients (Table). No hospitalizations or deaths were reported among humans. All human cases were associated with exposure to HABs in recreational water. Recreational activities included swimming (28 patients; 88%); wakeboarding, jet skiing, waterskiing or tubing (seven; 22%); boating (seven; 22%); wading (six; 19%); and using personal watercraft (four; 13%). All three affected dogs had gastrointestinal symptoms, and two were hospitalized; the third dog's symptoms resolved without intervention, and none of the dogs died. One dog was associated with human cases. The dogs were exposed to HABs in recreational water and, according to their owners, might have ingested water or algae.

Discussion

HAB-associated illness reports made to NYSDOH before 2015 never exceeded 10 statewide in any given year, whereas 51 illness reports were made through a pilot surveillance system in 16 New York counties during June–September 2015. Of the 51 reports identified through the pilot surveillance system, 35 were considered cases of HAB-associated illness that met the CDC case definition, suggesting that such illnesses might be underreported.

The findings in this report are subject to at least three limitations. First, self-reported illnesses and exposures can be subject to inaccuracy and bias. Second, surveillance for HAB-associated illnesses is difficult because HAB–associated signs and symptoms are nonspecific (e.g., skin rash, nausea, or diarrhea); the frequent lack of data showing these illnesses are causally linked to HAB exposure leads to a case definition with low specificity. Finally, all of the pilot counties had experienced at least one HAB in a water body in the previous season. Therefore, the pilot counties might represent communities more aware of HABs and their potential health effects.

Developing partnerships with local, state, and federal partners using a One Health approach assisted NYSDOH in successfully implementing a pilot surveillance system through identification of environmental HAB events, illness identification and reporting, and outreach to the public, lake associations, physicians, and veterinarians. NYSDEC's HAB monitoring program supported NYSDOH efforts to implement an HAB-associated illness surveillance system through the identification of HABs and public outreach. Collaboration with other organizations, such as lake associations, medical and veterinary organizations, and poison control centers, might have helped to establish reporting of HAB-associated illnesses. Tools are available online to guide

TABLE. Illness outcomes and number of commonly reported symptoms for harmful algal bloom–associated illnesses in humans (N = 32) and dogs (N = 3),* identified through a pilot surveillance system — New York, June–September 2015

Outcome/Symptom	No. of human cases	No. of canine cases
Illness outcome		
Outpatient care†	17	0
Hospitalized	0	2
Commonly reported symptoms§		
Skin problems (e.g., rash)	22	0
Respiratory (e.g., cough or dry cough)	16	0
Gastrointestinal (e.g., abdominal pain, diarrhea, nausea, vomiting)	15	3
Other symptoms (e.g., chills, muscle aches, or watery eyes)	13	0
Fatigue/General weakness	11	2
Sore throat	11	0
Neuroglogic (e.g., headache or seizure)	6	2
Exposure type/Setting§		
Swimming	28	3
Boating	7	0
Wading	6	3
Personal watercraft (e.g., kayak or canoe)	4	0
Tubing/Waterskiing	2	—
Jet skiing	1	—
Drinking untreated water	0	3

* Among 32 human cases, 11 were suspected, 20 were probable, and one was confirmed. All three canine cases were probable. https://www.cdc.gov/habs/pdf/ohhabs-case-and-event-definitions-table-3-14-17.pdf.
† Includes reported visit to an emergency department, urgent care clinic, or primary care.
§ Categories are not mutually exclusive. Patients could have multiple symptoms and exposures.

the implementation of HAB-associated illness surveillance or to develop prevention and response efforts for other state and local health departments (*8*).

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Conflict of Interest

No conflicts of interest were reported.

[1]New York State Department of Health; [2]CDC/CSTE Applied Epidemiology Fellowship Program; [3]New York State Department of Environmental Conservation.

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Summary

What is already known about this topic?

Recreational water exposure to excessive growths of cyanobacteria, called harmful algal blooms (HABs), can result in adverse health effects in humans and animals. Although HAB-associated illnesses and outbreaks have been documented in recent years, the extent and severity of these illnesses have not been well described.

What is added by this report?

In 2015, New York implemented a pilot cyanobacteria HAB-associated illness surveillance system in 16 counties. During June–September, 51 human and canine HAB-associated illnesses were reported, including 35 that met the CDC case definition.

What are the implications for public health practice?

HAB-associated illnesses might be more common than has been previously reported. Establishing working relationships with local health departments, environmental agencies, medical and veterinary organizations, poison control centers, and lake associations can provide important partnerships for public health response to HABs.

References

1. CDC. Harmful algal bloom (HAB)–associated illness: general information. Atlanta, GA: US Department of Health and Human Services, CDC; 2016. https://www.cdc.gov/habs/general.html
2. Manganelli M, Scardala S, Stefanelli M, et al. Emerging health issues of cyanobacterial blooms. Ann Ist Super Sanita 2012;48:415–28. https://doi.org/10.4415/ANN_12_04_09
3. Backer LC, Manassaram-Baptiste D, LePrell R, Bolton B. Cyanobacteria and algae blooms: review of health and environmental data from the Harmful Algal Bloom-Related Illness Surveillance System (HABISS) 2007–2011. Toxins (Basel) 2015;7:1048–64. https://doi.org/10.3390/toxins7041048
4. Bernstein JA, Ghosh D, Levin LS, et al. Cyanobacteria: an unrecognized ubiquitous sensitizing allergen? Allergy Asthma Proc 2011;32:106–10. https://doi.org/10.2500/aap.2011.32.3434
5. Pilotto L, Hobson P, Burch MD, Ranmuthugala G, Attewell R, Weightman W. Acute skin irritant effects of cyanobacteria (blue-green algae) in healthy volunteers. Aust N Z J Public Health 2004;28:220–4. https://doi.org/10.1111/j.1467-842X.2004.tb00699.x
6. Backer LC, Miller M. Sentinel animals in a One Health approach to harmful cyanobacterial and algal blooms. Vet Sci 2016;3:8. https://doi.org/10.3390/vetsci3020008
7. Hilborn ED, Beasley VR. One Health and cyanobacteria in freshwater systems: animal illnesses and deaths are sentinel events for human health risks. Toxins (Basel) 2015;7:1374–95. https://doi.org/10.3390/toxins7041374
8. CDC. One Health Harmful Algal Bloom System (OHHABS). Atlanta, GA: US Department of Health and Human Services, CDC; 2016. https://www.cdc.gov/habs/ohhabs.html
9. US Environmental Protection Agency. Guidelines and recommendations. Washington, DC: US Environmental Protection Agency; 2016. https://www.epa.gov/nutrient-policy-data/guidelines-and-recommendations

Update on Vaccine-Derived Polioviruses — Worldwide, January 2016–June 2017

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In 1988, the World Health Assembly launched the Global Polio Eradication Initiative (GPEI) (*1*). Among the three wild poliovirus (WPV) serotypes, only type 1 (WPV1) has been detected since 2012. Since 2014, detection of WPV1 has been limited to three countries, with 37 cases in 2016 and 11 cases in 2017 as of September 27. The >99.99% decline worldwide in polio cases since the launch of the GPEI is attributable to the extensive use of the live, attenuated oral poliovirus vaccine (OPV) in mass vaccination campaigns and comprehensive national routine immunization programs. Despite its well-established safety record, OPV use can be associated with rare emergence of genetically divergent vaccine-derived polioviruses (VDPVs) whose genetic drift from the parental OPV strains indicates prolonged replication or circulation (*2*). VDPVs can also emerge among persons with primary immunodeficiencies (PIDs). Immunodeficiency-associated VDPVs (iVDPVs) can replicate for years in some persons with PIDs. In addition, circulating vaccine-derived polioviruses (cVDPVs) can emerge very rarely among immunologically normal vaccine recipients and their contacts in areas with inadequate OPV coverage and can cause outbreaks of paralytic polio. This report updates previous summaries regarding VDPVs (*3*). During January 2016–June 2017, new cVDPV outbreaks were identified, including two in the Democratic Republic of the Congo (DRC) (eight cases), and another in Syria (35 cases), whereas the circulation of cVDPV type 2 (cVDPV2) in Nigeria resulted in cVDPV2 detection linked to a previous emergence. The last confirmed case from the 2015–2016 cVDPV type 1 (cVDPV1) outbreak in Laos occurred in January 2016. Fourteen newly identified persons in 10 countries were found to excrete iVDPVs, and three previously reported patients in the United Kingdom and Iran (*3*) were still excreting type 2 iVDPV (iVDPV2) during the reporting period. Ambiguous VDPVs (aVDPVs), isolates that cannot be classified definitively, were found among immunocompetent persons and environmental samples in 10 countries. Cessation of all OPV use after certification of polio eradication will eliminate the risk for new VDPV infections.

WPV type 2 (WPV2) was last detected in 1999 and global WPV2 eradication was declared in September 2015; WPV type 3 has not been detected since 2012. Since August 2014, residual endemic WPV1 transmission has been detected only in Afghanistan, Pakistan, and Nigeria, mostly in inaccessible areas. In response to the emergence of multiple cVDPV2 outbreaks, the World Health Organization (WHO) coordinated the synchronized withdrawal of the type 2 component (OPV2; Sabin type 2) from trivalent OPV (tOPV; Sabin types 1, 2, and 3) (*4*). In April 2016, all OPV-using countries switched to bivalent OPV (bOPV; Sabin types 1 and 3). Since the switch, the number of isolated Sabin 2 strains from both acute flaccid paralysis and environmental surveillance systems has steadily declined (*5*). To monitor the disappearance of Sabin 2 strains and to ensure identification of type 2 VDPVs (VDPV2s), as of August 1, 2016, all poliovirus type 2 (PV2) isolates are referred for genetic sequencing.

Properties and Virologic Characterization of VDPVs

Poliovirus isolates are grouped into three categories: WPV, vaccine-related poliovirus (VRPV), and VDPV. VRPVs have limited divergence in the capsid protein (VP1) nucleotide sequences from the corresponding OPV strain (poliovirus type 1 and 3 [PV1 and PV3]: ≤1% divergent; poliovirus type 2: ≤0.6% divergent) (*3*). VDPVs are >1% divergent (for PV1 and PV3) or >0.6% divergent (for PV2) in VP1 nucleotide sequences from the corresponding OPV strain (*3*). VDPVs are further classified as 1) cVDPVs, when evidence of person-to-person transmission in the community exists; 2) iVDPVs, when they are isolated from persons with PIDs; and 3) aVDPVs, when they are clinical isolates from persons with no known immunodeficiency and no evidence of transmission, or they are sewage isolates that are unrelated to other known VDPVs and whose source is unknown (*2*). GPEI guidelines about reporting and classification of VDPVs were last updated in August 2016 (http://polioeradication.org/wp-content/uploads/2016/09/Reporting-and-Classification-of-VDPVs_Aug2016_EN.pdf).

All poliovirus isolates are characterized by laboratories of the Global Polio Laboratory Network. VDPV screening is conducted using real-time reverse transcription–polymerase chain reaction (RT-PCR) nucleic acid amplification, targeted to nucleotide substitutions that frequently revert to the parental WPV sequence during replication of OPV in the human intestine (*6*). Starting August 1, 2016, the use of the VDPV2 screening assay was discontinued and all PV2 isolates are sequenced. Potential VDPVs identified by real-time RT-PCR screening are sequenced in the VP1 region for definitive analysis.

Detection of cVDPVs

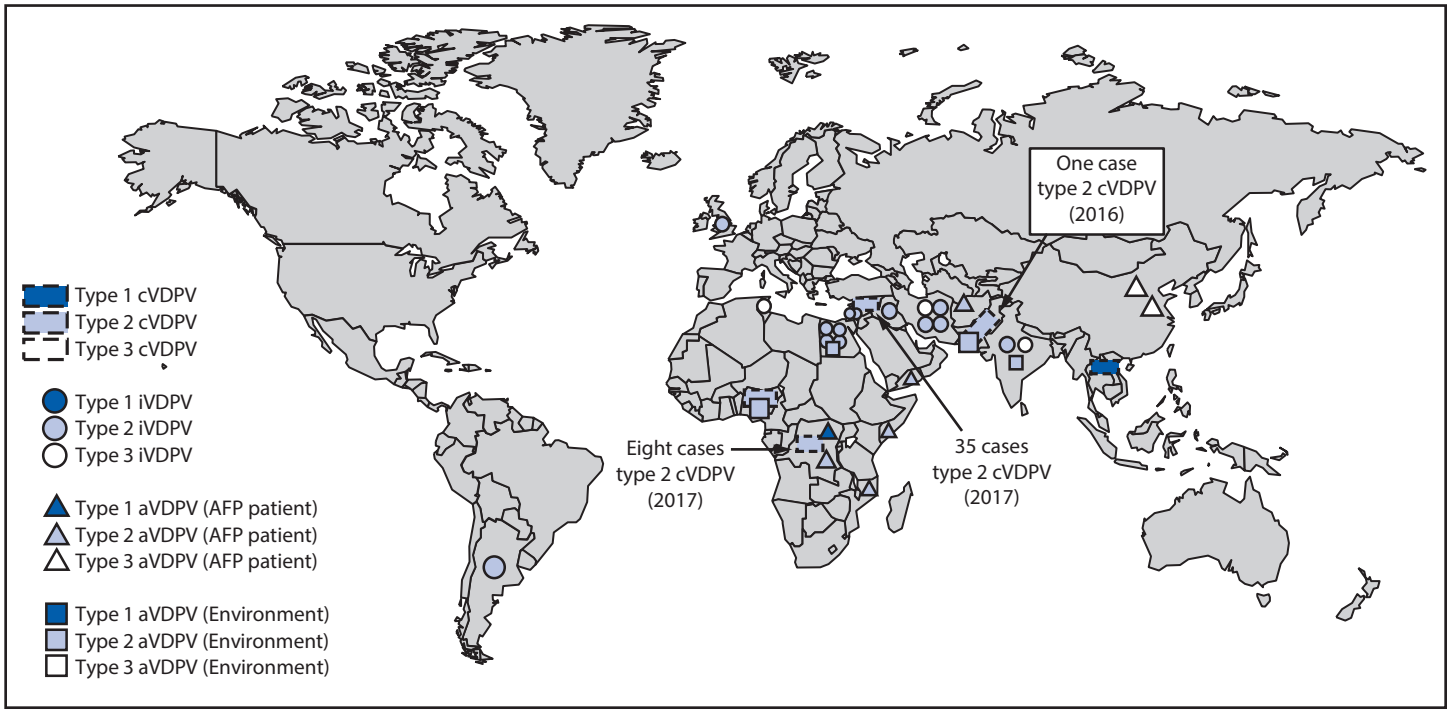
During January 2016–June 2017, the number of countries with detected cVDPV circulation decreased from seven to five since the previous reporting period (*3*) (Figure 1); all except one (cVDPV1 in Laos) reported cVDPV2 circulation (Table). No additional cases have been identified from previously reported VDPV outbreaks in Guinea (cVDPV2), Madagascar (cVDPV1), Myanmar (cVDPV2), Ukraine (cVDPV1), Pakistan (cVDPV2) and Nigeria (cVDPV2). Cases continued to be identified from the previously reported distinct cVDPV2 outbreak in Nigeria (*7*) and the previously reported cVDPV1 outbreak in Laos (*3*). New outbreaks were reported in DRC (two cVDPV2 emergences; one with six cases and one with two cases), Nigeria (cVDPV2, one case), Pakistan (cVDPV2, one case), and Syria (cVDPV2, 35 cases) (Table). Detection of the new cVDPV2 outbreaks occurred after the global tOPV to bOPV switch (April 2016). During January 2016–June 2017, among 48 cVDPV cases, 45 (93%) were cVDPV2 (Table) (Figure 2). Selected cVDPVs from the reporting period are described below.

Democratic Republic of the Congo. Circulating VDPV2s were isolated from eight acute flaccid paralysis (AFP) patients and one contact during February–June 2017. cVDPV2s represented two distinct emergences (0.7%–2.1% VP1 nucleotide divergence from parental Sabin 2 strain): one circulating in Haut Lomami province (six cases; latest case onset June 26, 2017)* and one circulating in Maniema province (isolated from two patients and one contact; latest case onset April 18, 2017). Reported OPV coverage was low (74%); two monovalent OPV type 2 (mOPV2) mass vaccination campaigns were conducted during July 13–29, 2017 and mop-up vaccination campaigns were conducted during September 17–20, 2017.

Nigeria. During the reporting period, cVDPV2s (with 3.5%–4.1% VP1 nucleotide divergence from a cVDPV2 emergence originating in Chad in 2012) were found only in the northern state of Borno. The cVDPV2s were isolated in districts of Borno proximal to inaccessible areas, one from an environmental sample collected on April 23, 2016 in Maiduguri, and one from a contact sample collected on August 26, 2016 in Monguno, after detection of a WPV1 case in the same area. An independent cVDPV2 emergence (with 1.3%–1.8% VP1 nucleotide divergence) was reported in Sokoto with virus detected from a patient with onset of AFP October 28, 2016 and a nonhousehold contact sample collected on November 24, 2016. Estimated divergence of the

* As of September 15, one new cVDPV2 was isolated from an AFP case detected in Haut Lomami province with onset date August 9, 2017.

FIGURE 1. Vaccine-derived polioviruses (VDPVs) detected, by serotype and VDPV classification* — worldwide, January 2016–June 2017



Abbreviations: AFP = Acute flaccid paralysis; aVDPV = ambiguous VDPV; cVDPV = circulating VDPV; iVDPV = immunodeficiency-associated VDPV.
* Spread of cVDPVs followed the elimination of the corresponding serotype of indigenous wild poliovirus, but with continued introduction of oral poliovirus vaccine into communities with growing immunity gaps. All of the cVDPV outbreaks were detected first by the laboratory, using sequence data and evolutionary analyses.

TABLE. Vaccine-derived polioviruses (VDPVs) detected, by classification and other selected characteristics — worldwide, January 2016–June 2017

Category	Country	Year(s) detected*	Source†	Serotype	No. of isolates§ January 2016–June 2017			Capsid protein VP1 divergence from Sabin OPV strain (%)¶	Coverage with 3 doses of OPV (%)**	Estimated duration of VDPV replication†† (yrs)	Current status (date of last outbreak case, patient isolate, or environmental sample)
					No. of cases	No. of contacts	Non-AFP source				
cVDPV	Democratic Republic of the Congo	2017	Outbreak	2	6	0	0	2.1	74	1.9	06/26/17
	Democratic Republic of the Congo	2017	Outbreak	2	2	1	0	0.7	74	0.6	04/18/17
	Laos	2015–16	Outbreak	1	3	4	0	2.3–3.9	83	3.5	02/06/16
	Nigeria	2016	Outbreak	2	1	1	0	1.3–1.8	49	1.6	11/24/16
	Nigeria	2013–16	Outbreak–importation	2	0	1	1	3.5–4.1	49	3.7	08/26/16
	Pakistan	2016	Outbreak	2	1	0	4	1.0–2.0	72	1.8	12/28/16
	Syria	2017	Outbreak	2	35	27	0	2.3–3.1	48	2.8	06/30/17
Total cVDPV	—§§	—§§	—§§	—§§	**48**	**34**	**5**	—§§	—§§	—§§	—§§
iVDPV	Argentina	2016	Non-AFP AGG	2	1	0	0	0.9	87	0.8	10/22/16
	Egypt	2016	Non-AFP SCID	2	0	0	1	2.0	95	1.8	05/21/16
	Egypt	2016	Non-AFP SCID	2	0	0	1	0.6	95	0.5	07/17/16
	Egypt	2017	AFP patient	2	1	0	0	1.9	95	1.7	02/13/17
	India	2016	AFP patient XLA	2	1	0	0	0.7	86	0.6	03/08/16
	India	2015–2016	Non-AFP SCID	3	0	0	1	4.5–10.2	86	9	08/04/16
	Iran	2016	AFP patient	2	1	0	0	0.6	99	0.5	11/26/16
	Iran	2015–2016	Non-AFP PID	2	0	0	1	1.5	99	1.4	02/18/16
	Iran	2015–2017	Non-AFP PID	2	0	0	1	2.5	99	2.3	02/12/17
	Iran	2015–2016	Non-AFP PID	3	0	0	1	2.6	99	2.4	08/07/16
	Iraq	2016	AFP patient	2	1	0	0	0.7	68	0.6	02/02/16
	Israel	2017	Non-AFP PID	2	0	0	1	2.4	94	2.2	01/23/17
	Nigeria	2016	AFP patient	2	1	0	0	0.9	49	0.8	05/14/16
	Pakistan	2016	AFP patient	2	1	0	0	1.1	72	1	09/07/16
	Tunisia	2016–2017	AFP patient XLA	3	1	0	0	1.2	98	1.1	01/11/17
	United Kingdom	2015–2017	Non-AFP PID	2	0	0	1	17.94	94	>30	05/11/17
	West Bank and Gaza Strip	2016–2017	Non-AFP SCID	2	0	0	1	1.0	94	0.9	02/08/17
Total iVDPV	—§§	—§§	—§§	—§§	**8**	**0**	**9**	—§§	—§§	—§§	—§§
aVDPV	Afghanistan	2016	AFP patient	2	1	0	0	1.0	60	0.9	09/10/16
	China	2016	AFP patient	3	1	0	0	1.2	99	1	08/16/16
	China	2017	AFP patient	3	1	0	0	1.1	99	1	02/19/16
	Democratic Republic of the Congo	2016	AFP patient	2	2	0	0	0.6–1.7	74	0.5–1.5	03/15/16
	Democratic Republic of the Congo	2017	AFP patient	1	1	0	0	2.7	74	2.5	04/01/17
	Egypt	2016	Environmental sample	2	0	0	1	0.6	95	0.5	03/15/16
	India	2016–2017	Environmental sample	2	0	0	7	0.7–1.5	86	0.6–1.4	03/29/17
	Mozambique	2016	AFP patient	2	1	1	0	1.3	80	1.1	11/30/16
	Nigeria	2017	Non-AFP	2	0	1	0	0.7	49	0.7	03/02/17
	Nigeria	2017	Environmental sample	2	0	0	11	0.6–1.1	49	0.5–1	04/17/17
	Pakistan	2016–2017	Environmental sample	2	0	0	8	0.6–1.3	72	0.5–1.1	05/29/17
	Russian Federation	2016	AFP patient	2	1	1	0	1.1–1.4	97	1–1.2	12/08/16
	Somalia	2016	AFP patient	2	1	0	0	1.1	47	1	10/27/16
	Yemen	2016	AFP patient	2	1¶¶	1¶¶	0	0.8–0.9	65	0.9	06/20/16
Total aVDPV	—§§	—§§	—§§	—§§	**10**	**4**	**27**	—§§	—§§	—§§	—§§

Abbreviations: AFP = acute flaccid paralysis; AGG = agammaglobulinemia; aVDPV = ambiguous VDPV; cVDPV = circulating VDPV; IPV = inactivated poliovirus vaccine; iVDPV = immunodeficiency-associated VDPV; OPV = oral poliovirus vaccine; PID = primary immunodeficiency; SCID = severe combined immunodeficiency; XLA = X-linked agammaglobulinemia.

* Total years detected for previously reported cVDPV outbreaks (Nigeria).

† Outbreaks list total cases clearly associated with cVDPVs. Some VDPV case isolates from outbreak periods might be listed as aVDPVs.

§ Total cases for VDPV-positive specimens from AFP cases and total VDPV-positive samples for environmental (sewage) samples.

¶ Percentage of divergence is estimated from the number of nucleotide differences in the VP1 region from the corresponding parental OPV strain.

** Coverage with 3 doses of OPV, based on 2016 data from the World Health Organization (WHO) Vaccine Preventable Diseases Monitoring System (2016 global summary) and WHO-United Nations Children's Fund coverage estimates, http://www.who.int/gho/immunization/poliomyelitis/en/. National data might not reflect weaknesses at subnational levels.

†† Duration of cVDPV circulation was estimated from extent of VP1 nucleotide divergence from the corresponding Sabin OPV strain; duration of iVDPV replication was estimated from clinical record by assuming that exposure was from initial receipt of OPV; duration of aVDPV replication was estimated from sequence data.

§§ Not cumulative data.

¶¶ Two genetically linked isolates were classified as aVDPVs according to the VDPV guidelines (http://polioeradication.org/wp-content/uploads/2016/09/Reporting-and-Classification-of-VDPVs_Aug2016_EN.pdf), which require detection for >2 months.

cVDPV2s in Sokoto from Sabin 2 indicate OPV2 origin at least 6 months before the tOPV to bOPV switch in April 2016.

Pakistan. During October 2016–December 2016, a new cVDPV2 emergence was reported in Quetta, the provincial capital of Baluchistan. Five cVDPV2s (with 1.0%–2.0% VP1 nucleotide divergence) were detected, four from sewage samples collected in two distinct environmental sites during three consecutive months (most recent sample date December 28, 2016) and one from an AFP patient with paralysis onset on December 17, 2016.

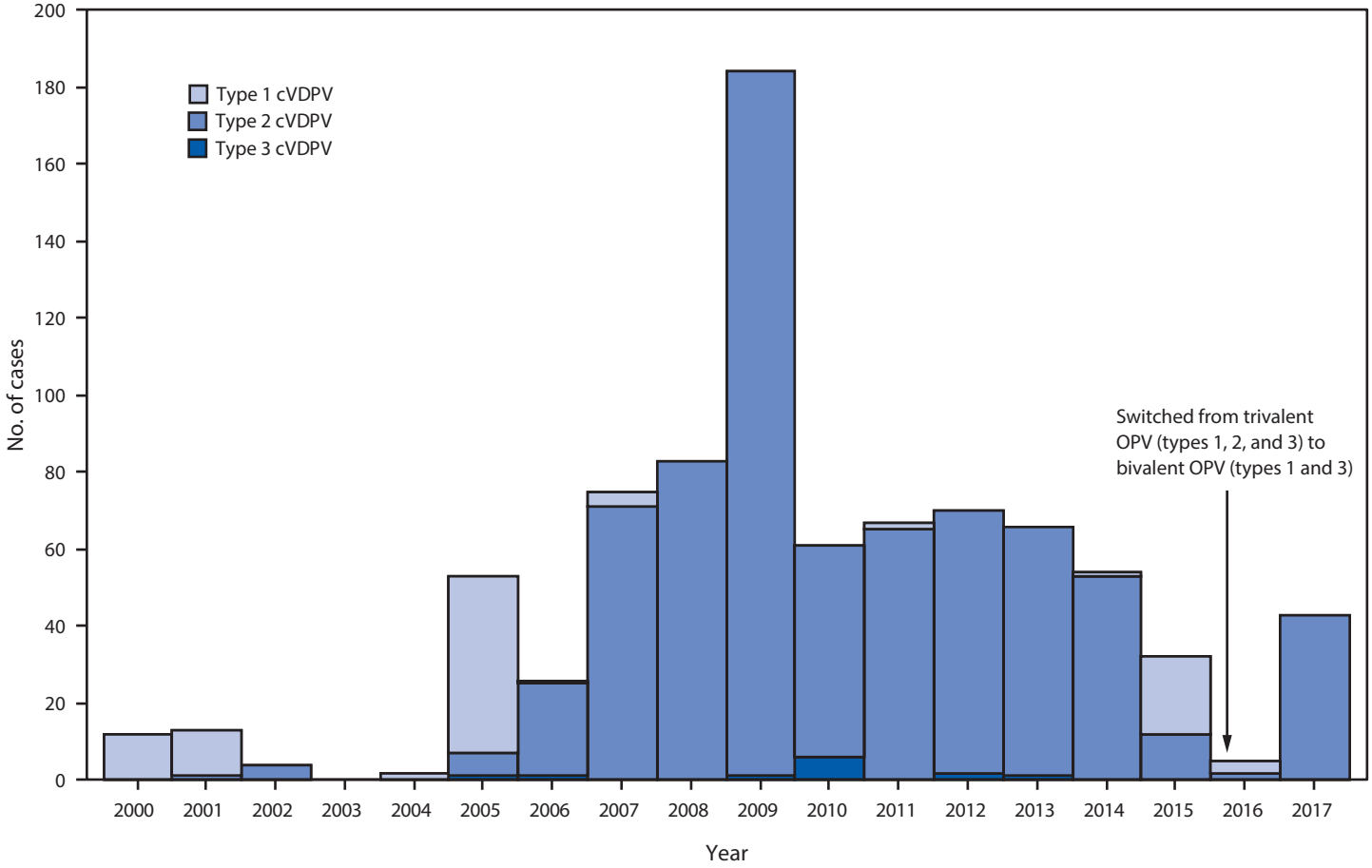
Syria. Syria is facing a humanitarian crisis because of armed conflict, and during March 2017–June 2017, cVDPV2s were isolated from 35 AFP patients and 27 contacts in two governorates (Deir ez-Zor and Raqqa).[†] The outbreak was associated with an emergence first observed in a child aged 22 months with onset of paralysis on March 3, 2017. Among 32 AFP cases, 29 (90%) were identified in the Mayadeen district of Deir Ez-Zor governorate. The extent of VP1 nucleotide divergence from the parental Sabin 2 strain among all cVDPV2s was 2.3%–3.1% VP1 nucleotide divergence. Reported OPV coverage was low (48%) and in response to the outbreak, mOPV2 mass vaccination campaigns were conducted during July (Deir Ez-Zor) and August (Raqqa), reaching an estimated 350,000 children.

[†] As of September 15, four new cVDPV2s were isolated from four AFP cases detected in Deir ez-Zor (three cases) and Homs (one case) governorates. The total number of AFP cases is 39. The onset date of the latest AFP case was July 13, 2017.

Detection of iVDPVs

During January 2016–June 2017, 17 iVDPV infections were reported from 11 countries (Table), including 14 that were newly detected iVDPV infections. During this reporting period, with the exception of three type 3 iVDPVs (iVDPV3), all were type 2. Since introduction of OPV, the cumulative serotype distribution shows that iVDPV2 are the most common (69%), followed by type 3 (14%) type 1 (12%) and heterotypic mixtures (i.e.,

FIGURE 2. Circulating vaccine-derived poliovirus (cVDPV) cases detected, by serotype — worldwide, January 2000–June 2017*,†



Abbreviation: OPV = oral poliovirus vaccine.
* Data available by August 25, 2017.
† In April 2016, all OPV-using countries switched from trivalent OPV (types 1, 2, and 3) to bivalent OPV (types 1 and 3).

types 1 and 2 or types 2 and 3) (5%). Selected iVDPVs from the reporting period are described below.

Egypt. A boy aged 11 months infected with iVDPV2 developed AFP in February 2017. In addition, three patients with PID who did not have AFP were newly identified as infected with iVDPV2s.

India. A girl aged 65 months with agammaglobulinemia was infected with iVDPV2 and developed AFP in February 2016. An iVDPV3 infection in a patient with severe combined immunodeficiency without AFP was first detected in January 2015; the last sample from this patient that was positive for iVDPV3 was collected in August 2016. Samples collected since October 2016 were negative for type 3 VDPVs (VDPV3).

Iran. A boy aged 14 months with PID, who received his fourth OPV dose in September 2016, and was infected with an iVDPV2, developed AFP in November 2016.

Iraq. A girl aged 7 months with PID and infected with iVDPV2 developed AFP in February 2016.

Pakistan. An iVDPV2 was isolated from a boy aged 7 months with PID after onset of AFP in February 2016.

Tunisia. A girl aged 6 months with PID and infected with iVDPV3 developed AFP in November 2016. The last VDPV-positive specimen was collected in January 2017.

Detection of aVDPVs

During January 2016–June 2017, aVDPVs were isolated in 11 countries (Table). The most divergent aVDPV (2.7% VP1 divergence) was isolated from an AFP patient in DRC. This represented an emergence independent of cVDPV2 circulating in the country during the same period. Detection of aVDPVs in settings with <60% polio vaccination coverage might indicate a risk for cVDPV emergence and further spread as well as potential gaps in surveillance. Selected aVDPVs from the reporting period are described below.

Afghanistan. A type 2 aVDPV (aVDPV2), with 1.0% VP1 divergence, was isolated in a girl aged 30 months who developed AFP in September 2016.

China. Two type 3 aVDPVs (aVDPV3s), with 1.1%–1.2% VP1 divergence, were isolated from two AFP patients in Henan and Inner Mongolia provinces with onset dates in February 2017 and August 2016, respectively.

DRC. Two aVDPV2s, with 0.6%–1.7% VP1 divergence, were isolated from AFP patients in two different provinces during January–March 2016. An aVDPV1 (with 2.7% VP1 divergence) was isolated in a boy aged 32 months who developed AFP in April 2017.

India. Seven aVDPV2s, with 0.7%–1.5% VP1 divergence, were isolated from environmental samples collected in three different cities (four collection sites in Delhi, one in Kolkata, and two in Hyderabad) during the reporting period.

Nigeria. Twelve aVDPV2s (11 from sewage samples and one from a contact, and all with 0.6%–1.1% VP1 divergence) were isolated in Bauchi (one), Gombe (two), Katsina (one), and Sokoto (eight) states during the reporting period.

Pakistan. Eight aVDPV2s, with 0.6%–1.3 VP1 divergence, were detected in environmental samples collected in Quetta (six), Pishin (one), and Hyderabad (one) during June 2016–May 2017.

Yemen. Two aVDPV2s, with 0.8%–0.9% VP1 divergence, were detected, one from an AFP patient with onset date June 11, 2016, and one from a contact sample collected June 20, 2016.

Discussion

The number of reported cVDPV outbreaks has decreased from nine to seven since the January 2015–May 2016 reporting period (*3*); however, the total number of reported cVDPV cases in these outbreaks has increased. Control and interruption of cVDPV2 outbreaks in areas at high risk for cVDPV emergence is partly attributable to steadily improving quality of supplementary immunization activities[§] and increased access to unimmunized children. For example, the large cVDPV2 outbreaks reported in Nigeria, Chad, and Pakistan during the last 5 years were interrupted; however, residual detection of cVDPV2s at the subnational level is indicative of persistent pockets of underimmunized children in mostly inaccessible areas (*7*). The new cVDPV2 outbreaks in DRC and Syria highlight the importance of maintaining high levels of poliovirus immunity, as well as sensitive AFP surveillance.

Expanded environmental surveillance in countries at high risk for poliovirus (PV) importation or VDPV emergence has increased the sensitivity of poliovirus detection and has played a critical role in monitoring residual PV2 excretion after OPV2 cessation. Despite the logistical and technical challenges of detecting and sequencing polioviruses from sewage samples, environmental surveillance remains critical in not only increasing the sensitivity of both WPV and VDPV detection, but also accelerating the GPEI response (*8*).

During the reporting period, VDPV2s were detected both before and after the global withdrawal of OPV2 in April 2016. During the preswitch period (January 2016–April 2016), emergence of cVDPV2 in countries with low routine vaccination coverage underscored the risks of widening immunization gaps to PV2; detection of highly divergent cVDPV2s from sewage samples collected in the state capital adjacent to inaccessible areas of northeast Nigeria also indicated virus circulation that

[§] Supplementary immunization activities are mass vaccination campaigns conducted in a short period (days to weeks) during which a dose of OPV is administered to all children aged <5 years, regardless of previous vaccination history. Campaigns can be conducted nationally or in portions of a country.

Summary

What is already known about this topic?

Vaccine-derived polioviruses (VDPVs), strains that are genetically divergent from the oral poliovirus vaccine (OPV) viruses, fall into three categories: 1) circulating VDPVs (cVDPVs) from outbreaks, 2) immunodeficiency-associated VDPVs (iVDPVs) from patients with primary immunodeficiency diseases (PIDs), and 3) ambiguous VDPVs (aVDPVs), which cannot be more definitively identified. cVDPVs are biologically equivalent to wild polioviruses, emerge in settings of low population immunity, and can sustain long-term circulation. Because >94% of cVDPVs since 2006 and 69% of iVDPVs since OPV introduction are type 2, the World Health Organization coordinated worldwide replacement of trivalent OPV (tOPV, types 1, 2, and 3) with bivalent OPV (bOPV, types 1 and 3) in April 2016.

What is added by this report?

During 2017, new cVDPV outbreaks were detected in the Democratic Republic of the Congo (two emergences) and Syria (one emergence). Residual circulation of a previous cVDPV2 emergence in Nigeria was detected in 2016 and low-level detection of new emergences in Nigeria and Pakistan occurred during 2016. Fourteen newly identified persons in 10 countries were found to excrete iVDPVs.

What are the implications for public health practice?

The goal of the Global Polio Eradication Initiative is the cessation of all poliovirus circulation. The risk for VDPV emergence will continue as long as OPV is used. The switch from tOPV to bOPV in April 2016 was the first step toward phasing out the use of all OPV, setting the stage for a subsequent total worldwide shift from OPV to IPV.

was missed by AFP surveillance. cVDPV2 outbreaks detected after the switch in both Syria and DRC highlighted the risks associated with chronically low tOPV vaccination coverage before the switch. Outbreak response to VDPV2 transmission after OPV2 cessation requires use of mOPV2; the scope and intensity of mOPV2 vaccination campaigns in outbreak areas is assessed by the mOPV2 Advisory Group, which advises the WHO Director General on release of mOPV2. Response to the cVDPV2 outbreak in Syria included two mOPV2 mass vaccination campaigns targeting >300,000 children aged <5 years, followed by inactivated polio vaccine (IPV) vaccination campaigns targeting >100,000 children aged 2–24 months, including populations at high risk in adjacent areas and countries.

In April 2016, all 155 OPV-using countries and territories switched from tOPV to bOPV; the number of countries reporting PV2 detection decreased 83%, from 42 before the switch to seven after the switch (January–March 2017) (*5*). The GPEI and Global Polio Laboratory Network have continued to strengthen AFP and poliovirus surveillance. In addition, the increase in the number of environmental surveillance sites has enhanced PV detection (*9*). Routine immunization services also are being strengthened, and most countries incorporated at least 1 dose of IPV into routine childhood immunization schedules in 2016. Augmented surveillance for VDPV infections among patients with PID (*10*) has increased the number of known iVDPV excretors. Continued progress in development of antivirals is needed to eliminate virus shedding in persons with chronic iVDPV infections.

During the last 5 years, the number of WPV cases (>400 in 2013; 12 in 2017) was lower than the estimated number (250–500) of global vaccine-associated paralytic poliomyelitis cases.[¶] The ultimate goal of the polio endgame strategic plan is the global cessation of all OPV use after the end of all WPV circulation, which started with cessation of OPV with a type 2 component. Cessation of all OPV use after certification of polio eradication will eliminate the risk for cVDPV outbreaks, and new iVDPV and aVDPV infections.

[¶] Vaccine-associated paralytic polio is a rare (1 in 2.7 million administered doses of OPV) occurrence of paralysis that usually occurs with the first OPV dose; no risk for spreading to others exists. Additional information is available at http://www.who.int/immunization/diseases/poliomyelitis/endgame_objective2/oral_polio_vaccine/VAPPandcVDPVFactSheet-Feb2015.pdf.

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Conflict of interest

No conflicts of interest were reported.

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References

1. Morales M, Tangermann RH, Wassilak SG. Progress toward polio eradication—worldwide, 2015–2016. MMWR Morb Mortal Wkly Rep 2016;65:470–3. https://doi.org/10.15585/mmwr.mm6518a4
2. Burns CC, Diop OM, Sutter RW, Kew OM. Vaccine-derived polioviruses. J Infect Dis 2014;210(Suppl 1):S283–93. https://doi.org/10.1093/infdis/jiu295

3. Jorba J, Diop OM, Iber J, Sutter RW, Wassilak SG, Burns CC. Update on vaccine-derived polioviruses—worldwide, January 2015–May 2016. MMWR Morb Mortal Wkly Rep 2016;65:763–9. https://doi.org/10.15585/mmwr.mm6530a3
4. Hampton LM, Farrell M, Ramirez-Gonzalez A, et al.; Immunization Systems Management Group of the Global Polio Eradication Initiative. Cessation of trivalent oral poliovirus vaccine and introduction of inactivated poliovirus vaccine—worldwide, 2016. MMWR Morb Mortal Wkly Rep 2016;65:934–8. https://doi.org/10.15585/mmwr.mm6535a3
5. Diop OM, Asghar H, Gavrilin E, et al. Virologic monitoring of poliovirus type 2 after oral poliovirus vaccine type 2 withdrawal in April 2016—worldwide, 2016–2017. MMWR Morb Mortal Wkly Rep 2017;66:538–42. https://doi.org/10.15585/mmwr.mm6620a4
6. Burns CC, Kilpatrick DR, Iber JC, Chen Q, Kew OM. Molecular properties of poliovirus isolates: nucleotide sequence analysis, typing by PCR and real-time RT-PCR. Methods Mol Biol 2016;1387:177–212. https://doi.org/10.1007/978-1-4939-3292-4_9
7. Etsano A, Damisa E, Shuaib F, et al. Environmental isolation of circulating vaccine-derived poliovirus after interruption of wild poliovirus transmission—Nigeria, 2016. MMWR Morb Mortal Wkly Rep 2016;65:770–3. https://doi.org/10.15585/mmwr.mm6530a4
8. Cowger TL, Burns CC, Sharif S, et al. The role of supplementary environmental surveillance to complement acute flaccid paralysis surveillance for wild poliovirus in Pakistan—2011–2013. PLoS One 2017;12:e0180608. https://doi.org/10.1371/journal.pone.0180608
9. Maes EF, Diop OM, Jorba J, Chavan S, Tangermann RH, Wassilak SG. Surveillance systems to track progress toward polio eradication—worldwide, 2015–2016. MMWR Morb Mortal Wkly Rep 2017;66:359–65. https://doi.org/10.15585/mmwr.mm6613a3
10. Aghamohammadi A, Abolhassani H, Kutukculer N, et al.; JMF Centers Network Investigators and Study Collaborators. Patients with primary immunodeficiencies are a reservoir of poliovirus and a risk to polio eradication. Front Immunol 2017;8:685. https://doi.org/10.3389/fimmu.2017.00685

Implementation of Rotavirus Surveillance and Vaccine Introduction — World Health Organization African Region, 2007–2016

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Rotavirus is a leading cause of severe pediatric diarrhea globally, estimated to have caused 120,000 deaths among children aged <5 years in sub-Saharan Africa in 2013 (*1*). In 2009, the World Health Organization (WHO) recommended rotavirus vaccination for all infants worldwide (*2*). Two rotavirus vaccines are currently licensed globally: the monovalent Rotarix vaccine (RV1, GlaxoSmithKline; 2-dose series) and the pentavalent RotaTeq vaccine (RV5, Merck; 3-dose series). This report describes progress of rotavirus vaccine introduction (*3*), coverage (using estimates from WHO and the United Nations Children's Fund [UNICEF]) (*4*), and impact on pediatric diarrhea hospitalizations in the WHO African Region. By December 2016, 31 (66%) of 47 countries in the WHO African Region had introduced rotavirus vaccine, including 26 that introduced RV1 and five that introduced RV5. Among these countries, rotavirus vaccination coverage (completed series) was 77%, according to WHO/UNICEF population-weighted estimates. In 12 countries with surveillance data available before and after vaccine introduction, the proportion of pediatric diarrhea hospitalizations that were rotavirus-positive declined 33%, from 39% preintroduction to 26% following rotavirus vaccine introduction. These results support introduction of rotavirus vaccine in the remaining countries in the region and continuation of rotavirus surveillance to monitor impact.

The status of rotavirus vaccine introduction and 2016 WHO/UNICEF estimates of national vaccination coverage were obtained from the WHO repository (*3*,*4*). Among African Region countries that have introduced rotavirus vaccine into their national Expanded Programs on Immunization, most recommend that rotavirus doses coincide with administration of the infant doses of diphtheria and tetanus toxoids and pertussis (DTP) vaccine (at ages 6 and 10 weeks for RV1 and at ages 6, 10, and 14 weeks for RV5); most countries are using RV1 (*5*). Because the WHO/UNICEF estimates do not include a coverage estimate for the first dose of rotavirus vaccine or the second dose of DTP vaccine, rotavirus vaccination coverage (completed series of either 2 RV1 or 3 RV5 doses) was compared with first-dose and third-dose coverage for DTP. Countries that have introduced rotavirus vaccine were grouped by year of vaccine introduction for analysis.

Rotavirus surveillance data were collected through sentinel hospitals participating in the African Rotavirus Surveillance Network (ARSN), which was established in four countries in 2006 and had expanded to 29 countries by 2016 (Figure) (*6*). Surveillance staff members at sentinel sites in ARSN enroll children aged <5 years who are hospitalized for acute diarrhea (≥3 looser than normal stools in a 24-hour period before hospitalization, with duration of illness ≤7 days before hospitalization) and collect a stool specimen, which is tested for rotavirus using an enzyme immunoassay. Countries were included in this analysis if their sites collected and tested at least 80 specimens over at least 11 months in a given year. The percentage of tested specimens that were positive for rotavirus was calculated in the vaccine preintroduction and postintroduction periods, by country. The year of rotavirus vaccine introduction was considered a transition period and was excluded from calculations.

FIGURE. Rotavirus vaccine introduction status — World Health Organization (WHO) African Region, 2016

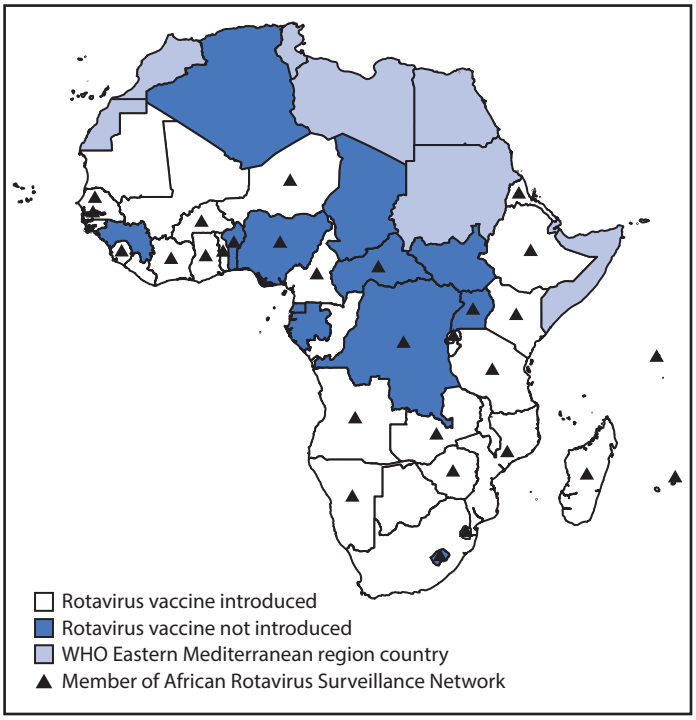

TABLE 1. Percentage coverage with first and third DTP vaccine doses and completed rotavirus (RV) vaccination series — World Health Organization African Region, 2016

Country	Year RV vaccine introduced	RV vaccine type	Coverage (%)			Percentage-point difference in coverage	
			DTP1	DTP3	RV (completed series)	DTP1 versus completed RV	DTP3 versus completed RV
Countries introducing RV vaccine 2009–2013*	—	—	**93**	**88**	**82**	**11**	**6**
South Africa	2009	RV1	78	66	73	5	-7
Botswana	2012	RV1	98	95	95	3	0
Ghana	2012	RV1	94	93	94	0	-1
Malawi	2012	RV1	89	84	81	8	3
Rwanda†	2012	RV5	99	98	98	1	0
Tanzania	2012	RV1	99	97	96	3	1
Burkina Faso	2013	RV5	95	91	91	4	0
Burundi	2013	RV1	97	94	96	1	-2
Ethiopia	2013	RV1	86	77	63	23	14
Gambia†	2013	RV5	99	95	95	4	0
Zambia	2013	RV1	99	91	90	9	1
Countries introducing RV vaccine 2014*	—	—	**89**	**79**	**73**	**16**	**6**
Angola	2014	RV1	79	64	53	26	11
Cameroon	2014	RV1	92	85	80	12	5
Republic of the Congo	2014	RV1	85	80	80	5	0
Eritrea	2014	RV1	97	95	96	1	-1
Kenya	2014	RV1	96	89	74	22	15
Madagascar	2014	RV1	84	77	78	6	-1
Mali	2014	RV5	86	68	60	26	8
Mauritania	2014	RV1	87	73	73	14	0
Namibia	2014	RV1	98	92	86	12	6
Niger	2014	RV1	87	67	61	26	6
Senegal	2014	RV1	96	93	93	3	0
Sierra Leone	2014	RV1	97	84	95	2	-11
Togo	2014	RV1	93	89	90	3	-1
Zimbabwe	2014	RV1	94	90	91	3	-1
Countries introducing RV vaccine 2015–2016*	—	—	**92**	**81**	**73**	**19**	**8**
Guinea-Bissau	2015	RV1	95	87	61	34	26
Mauritius	2015	RV1	97	96	92	5	4
Mozambique	2015	RV1	90	80	76	14	4
Swaziland	2015	RV1	96	90	95	1	-5
Liberia	2016	RV1	99	79	48	51	31
Sao Tome and Principe	2016	RV5	97	96	24	73	72

Abbreviations: DTP = diphtheria and tetanus toxoids and pertussis; DTP1 = first dose of DTP vaccine; DTP3 = third dose of DTP vaccine; RV1 = monovalent RV vaccine (Rotarix); RV5 = pentavalent RV vaccine (RotaTeq).
* Summary data for introduction period are population-weighted averages.
† Country initially introduced RV5, but switched to RV1 in 2017.

Overall, 31 (66%) countries in the region had introduced rotavirus vaccine into their national immunization schedules by December 2016, with 26 introducing RV1 and five introducing RV5 (Table 1). Among all countries, completed series rotavirus vaccination coverage was 77% (population-weighted average); national coverage ranged from 24% (Sao Tome and Principe, 2016 introduction) to 98% (Rwanda, 2012 introduction). When grouping by year of vaccine introduction, the highest overall population-weighted coverage (82%) was in countries that introduced the vaccine before 2014. These same countries also had the smallest average percentage-point difference between completed rotavirus vaccination coverage and DTP1 coverage (overall, 11 percentage points less than DTP1).

Surveillance data were available for 12 and 18 countries during the vaccine preintroduction and postintroduction periods, respectively (Table 2). The average percentage of tested stool specimens that were positive for rotavirus during the vaccine preintroduction period was 41%, ranging from 20% (Ethiopia) to 51% (Togo). During the vaccine postintroduction period, the average percentage of rotavirus-positive specimens was 24%, ranging from 12% (Madagascar) to 41% (Mauritius). In the 12 countries with both vaccine preintroduction and postintroduction data, rotavirus positivity declined by 33%

TABLE 2. Rotavirus (RV) stool specimen surveillance results, by country and vaccine introduction status — World Health Organization African Region, 2008–2015

Country	Year RV vaccine introduced	Vaccine preintroduction period			Vaccine postintroduction period			% decline in RV positivity*
		Years included	RV specimens tested	No (%) positive	Years Included	RV specimens tested	No. (%) positive	
Countries introducing 2012–2013	—	—	**9,916**	**3,685 (37)**	—	**20,389**	**5,544 (27)**	**27%**
Ghana	2012	2008, 2010–2011	2,374	1,161 (49)	2013–2016	1,494	405 (27)	45%
Rwanda	2012	2011	240	121 (50)	2013–2015	2,237	447 (20)	60%
Tanzania	2012	2009–2010	852	308 (36)	2013–2016	8,615	2,186 (25)	30%
Zambia	2012	2007–2011	4,519	1,700 (38)	2013–2016	5,227	1,700 (33)	14%
Burkina Faso	2013	NS	NS	NS	2014–2016	1,889	615 (33)	NS
Ethiopia	2013	2008–2012	1,931	395 (20)	2014–2016	822	165 (20)	2%
Gambia	2013	NS	NS	NS	2014	105	26 (25)	NS
Countries introducing 2014	—	—	**14,062**	**5,628 (40)**	—	**6,704**	**1,552 (23)**	**42%**
Angola	2014	NS	NS	NS	2015	229	41 (18)	NS
Cameroon	2014	2008–2013	3,449	1,398 (41)	2015–2016	973	197 (20)	50%
Kenya	2014	2007–2013	4,406	1546 (35)	2015–2016	688	158 (23)	35%
Madagascar	2014	NS	NS	NS	2015–2016	451	56 (12)	NS
Niger	2014	NS	NS	NS	2016	168	22 (13)	NS
Senegal	2014	2011–2013	374	159 (43)	2015–2016	235	38 (16)	62%
Togo	2014	2008, 2010–2013	1,028	526 (51)	2015–2016	319	119 (37)	27%
Zimbabwe	2014	2008–2009, 2011–2013	4,805	1,999 (42)	2015–2016	3,641	921 (25)	39%
Countries Introducing 2015	—	—	**1,319**	**626 (47)**	—	**1,081**	**330 (31)**	**36%**
Mauritius	2015	2010–2014	1,203	578 (48)	2016	570	235 (41)	14%
Mozambique	2015	NS	NS	NS	2016	420	68 (16)	NS
Swaziland	2015	2013	116	48 (41)	2016	91	27 (30)	28%

Abbreviations: NS = No surveillance data available (surveillance not started or data do not meet analysis criteria); RV = rotavirus vaccine.
* Calculated only for countries with data on rotavirus vaccine preintroduction and postintroduction. Percentage declines might not correspond to preintroduction and postintroduction percentages because of rounding.

overall (range = 2%–62%), from 39% in the preintroduction period to 26% in the postintroduction period (p<0.001); in these countries, the overall population-weighted 2016 completed rotavirus vaccination series coverage was 82%. In 2016, the overall percentage of positive rotavirus stool specimens was 26% in countries that had introduced the vaccine in 2015 or earlier, and 43% in countries that had not yet introduced the vaccine (p<0.001).

Discussion

Countries in the WHO African Region have made significant progress in the introduction of rotavirus vaccines, with 31 (66%) of 47 member countries having introduced rotavirus vaccine into their national schedules by December 2016. In 2016, the overall completed series rotavirus vaccination coverage in these countries was 77%, which was lower than coverage for DTP1 and DTP3. Some of this difference might be attributable to challenges that are common to new vaccine introduction (e.g., it can take time for all vaccination clinics to have reliable cold chain space and a steady stock of a new vaccine). In addition, challenges specific to the recording and reporting of coverage for new vaccines include mid-year introductions, unavailability of updated data tools, and inadequate orientation of health workers on use of vaccine tally sheets. Another factor specific to rotavirus is the issue of age restrictions. Because of concerns about a potential increased risk for intussusception in older infants who receive the vaccine, WHO initially recommended that rotavirus vaccination be administered only to children aged ≤32 weeks (*2*). In 2013, WHO recommended lifting these restrictions based on new data and a risk-benefit analysis (*7*); however, some countries, or some health workers, might still be administering rotavirus vaccine with age restrictions. Additional research is needed to better understand the impact of lifting age restrictions on coverage, and the difference between rotavirus and DTP vaccination coverage.

Surveillance data from ARSN indicate that, among countries with data available both preceding and following rotavirus vaccine introduction, the proportion of rotavirus-positive hospitalizations for diarrhea among children aged <5 years declined 33% following rotavirus vaccine introduction; overall declines were especially notable in countries that had introduced rotavirus vaccine before 2015. These results are particularly encouraging given rotavirus vaccines' lower efficacy

Summary

What is already known about this topic?

Rotavirus is a leading cause of severe pediatric diarrhea worldwide, and a disproportionate number of deaths occur in countries in the World Health Organization (WHO) African Region. WHO recommends rotavirus vaccination for all infants worldwide.

What is added by this report?

As of December 2016, 31 of 47 (66%) countries in the WHO African Region had introduced rotavirus vaccination into their national schedules. Among these countries, the overall coverage for the completed series of rotavirus vaccination was 77% in 2016. In 12 countries with available sentinel hospital surveillance data before and after rotavirus vaccine introduction, the proportion of pediatric diarrhea hospitalizations that were rotavirus-positive declined 33%, from 39% to 26%.

What are the implications for public health practice?

Continued commitment to improving rotavirus vaccination coverage in the WHO African Region should contribute to reducing the morbidity and mortality associated with this disease. Maintaining and enhancing the existing surveillance network will be critical to the ability to measure vaccine impact.

in low-income settings (50%–64% efficacy) than in high-income and middle-income settings (85%–100% efficacy) (*8*), which had raised concerns about the public health impact of their introduction. However, consistent with recent global analyses demonstrating substantial rotavirus vaccine impact across country income strata (*9*), the present analysis suggests that rotavirus vaccination has had a meaningful impact on rotavirus disease in Africa.

Sixteen countries in the WHO African Region had not yet introduced rotavirus vaccine as of December 2016; 10 are eligible for Gavi financial support, four of which have received approval. Apart from funding, other factors can affect rotavirus vaccine introduction and subsequent coverage. Coverage with routinely recommended vaccines, as a marker of immunization system function, highlights several countries in the region where the immunization infrastructure needs strengthening. Armed conflict and natural disasters, experienced by several countries in the region, can further stress immunization services. Even under routine circumstances, cold chain management, vaccine transportation, and human resource constraints can negatively affect vaccination coverage; these challenges might be experienced most acutely in countries with large rural populations.

The findings in this report are subject to at least five limitations. First, UNICEF/WHO coverage estimates are based on the best estimates of a combination of administrative data and survey data, each of which might be subject to overreporting or underreporting. Other factors potentially causing a discrepancy between rotavirus coverage and DTP coverage include the inability to compare the final dose of RV1 to the second dose of DTP, and the lack of data on coverage with the first dose of rotavirus vaccines. Second, although protocols for rotavirus surveillance are standardized across the entire network, there are a limited number of surveillance sites in each country; these might not be representative of pediatric diarrheal illness across the country and might provide an incomplete picture of impact. Third, immunization and surveillance data quality vary among countries. Fourth, not all sites have been able to conduct continuous rotavirus disease surveillance, and data were not included in these results if analysis criteria were not met. Finally, rotavirus surveillance data are not available for all countries before introduction, limiting the ability to assess vaccine impact in countries without vaccine preintroduction data or those that are not part of the ARSN.

Overall, substantial progress has been made in the introduction of rotavirus vaccine and surveillance for rotavirus disease in countries in the WHO African Region. In countries where rotavirus vaccine has been introduced, a substantial decline in the percentage of rotavirus-associated pediatric diarrhea hospitalizations was observed. As rotavirus vaccination coverage increases, an even greater decline might be expected; however, continuous surveillance is a critical component of measuring vaccine impact. Financial support from Gavi, the Vaccine Alliance, has played a key role in rotavirus vaccine introduction and rotavirus surveillance in the region (*10*). Nonetheless, Gavi support will not continue indefinitely; as their economies improve, countries will graduate from Gavi support and begin to finance the total cost of the vaccine. Maintaining surveillance for rotavirus disease will provide important data necessary to promoting continued investment in rotavirus vaccination. Rotavirus vaccination is a critical element in reducing child deaths from diarrhea and contributing to the improvement of child health globally.

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Conflict of Interest

No conflicts of interest were reported.

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References

1. Tate JE, Burton AH, Boschi-Pinto C, Parashar UD; World Health Organization–Coordinated Global Rotavirus Surveillance Network. Global, regional, and national estimates of rotavirus mortality in children <5 years of age, 2000–2013. Clin Infect Dis 2016;62(Suppl 2):S96–105. https://doi.org/10.1093/cid/civ1013
2. World Health Organization. Rotavirus vaccines: an update. Wkly Epidemiol Rec 2009;84:533–40.
3. World Health Organization. Immunization vaccines and biologicals database, September 2016. Geneva, Switzerland: World Health Organization; 2016. http://www.who.int/immunization/monitoring_surveillance/data/en/
4. World Health Organization (WHO). WHO/UNICEF estimates of national immunization coverage. Geneva, Switzerland: World Health Organization/United Nations Children's Fund; 2016. http://www.who.int/immunization/monitoring_surveillance/routine/coverage/en/index4.html
5. World Health Organization (WHO). WHO vaccine-preventable diseases: monitoring system. 2017 global summary. Geneva, Switzerland: World Health Organization; 2017. http://apps.who.int/immunization_monitoring/globalsummary/schedules
6. Mwenda JM, Tate JE, Parashar UD, et al. African rotavirus surveillance network: a brief overview. Pediatr Infect Dis J 2014;33(Suppl 1):S6–8. https://doi.org/10.1097/INF.0000000000000174
7. World Health Organization. Rotavirus vaccines. WHO position paper—January 2013. Wkly Epidemiol Rec 2013;88:49–64.
8. Soares-Weiser K, Maclehose H, Bergman H, et al. Vaccines for preventing rotavirus diarrhoea: vaccines in use. Cochrane Database Syst Rev 2012;11:CD008521.
9. Burnett E, Jonesteller CL, Tate JE, Yen C, Parashar UD. Global impact of rotavirus vaccination on childhood hospitalizations and mortality from diarrhea. J Infect Dis 2017;215:1666–72. https://doi.org/10.1093/infdis/jix186
10. Gavi, the Vaccine Alliance. Countries approved for support. Geneva, Switzerland, Gavi; 2017. http://www.gavi.org/results/countries-approved-for-support/

Deaths Involving Fentanyl, Fentanyl Analogs, and U-47700 — 10 States, July–December 2016

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On October 27, 2017, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

Preliminary estimates of U.S. drug overdose deaths exceeded 60,000 in 2016 and were partially driven by a fivefold increase in overdose deaths involving synthetic opioids (excluding methadone), from 3,105 in 2013 to approximately 20,000 in 2016 (*1*,*2*). Illicitly manufactured fentanyl, a synthetic opioid 50–100 times more potent than morphine, is primarily responsible for this rapid increase (*3*,*4*). In addition, fentanyl analogs such as acetylfentanyl, furanylfentanyl, and carfentanil are being detected increasingly in overdose deaths (*5*,*6*) and the illicit opioid drug supply (*7*). Carfentanil is estimated to be 10,000 times more potent than morphine (*8*). Estimates of the potency of acetylfentanyl and furanylfentanyl vary but suggest that they are less potent than fentanyl (*9*). Estimates of relative potency have some uncertainty because illicit fentanyl analog potency has not been evaluated in humans. This report describes opioid overdose deaths during July–December 2016 that tested positive for fentanyl, fentanyl analogs, or U-47700, an illicit synthetic opioid, in 10 states participating in CDC's Enhanced State Opioid Overdose Surveillance (ESOOS) program.* Fentanyl analogs are similar in chemical structure to fentanyl but not routinely detected because specialized toxicology testing is required. Fentanyl was detected in at least half of opioid overdose deaths in seven of 10 states, and 57% of fentanyl-involved deaths also tested positive for other illicit drugs, such as heroin. Fentanyl analogs were present in >10% of opioid overdose deaths in four states, with carfentanil, furanylfentanyl, and acetylfentanyl identified most frequently. Expanded surveillance for opioid overdoses, including testing for fentanyl and fentanyl analogs, assists in tracking the rapidly changing illicit opioid market and informing innovative interventions designed to reduce opioid overdose deaths.

The 10 states† reporting data abstracted information from preliminary death certificates and medical examiner/coroner reports on unintentional and undetermined opioid overdose deaths using standard definitions for variables. Data were entered into the State Unintentional Drug Overdose Reporting System (SUDORS), the component of ESOOS designed for tracking fatal opioid overdoses.§ For each death, available data on demographic characteristics, circumstances of the overdose collected from death scene investigations (e.g., evidence of illicit drug use), and results of forensic toxicology testing were entered into SUDORS. Opioid overdose deaths occurring during July–December 2016 with positive test results for fentanyl, fentanyl analogs, and U-47700 in 10 states are described, and key demographic and overdose circumstance factors are stratified by substance. Full toxicology findings of decedents were reviewed, including the presence of heroin, cocaine, and methamphetamine. Because heroin involvement in overdose deaths is difficult to distinguish from prescription morphine, deaths in which heroin was confirmed by toxicologic findings were combined with deaths in which heroin was suspected because morphine was detected and death scene evidence suggested heroin use.¶ The use of medical examiner/coroner reports, previously unavailable across states, provides unique insights into specific substances and circumstances associated with overdoses, which can inform interventions.

Fentanyl was detected in 56.3% of 5,152 opioid overdose deaths in the 10 states during July–December 2016 (Figure). Among these 2,903 fentanyl-positive deaths, fentanyl was determined to be a cause of death by the medical examiner or

* CDC's Enhanced State Opioid Overdose Surveillance program funded 12 states through a competitive application process in fiscal year 2016. Data were available for this report for 10 of the 12 states. https://www.cdc.gov/drugoverdose/foa/state-opioid-mm.html.

† Maine, Massachusetts, Missouri (data available for 22 counties), New Hampshire, New Mexico, Ohio, Oklahoma, Rhode Island, West Virginia, and Wisconsin

§ State Unintentional Drug Overdose Reporting System (SUDORS) estimates of opioid-involved overdose deaths might differ from those of the National Vital Statistics System because SUDORS uses preliminary death certificate data and collects additional information from medical examiner and coroner reports, which are abstracted within 8 months of death. In SUDORS, an opioid-involved overdose death either was identified through review of the medical examiner/coroner report or had *International Classification of Disease, Tenth Revision* (ICD-10) underlying cause-of-death codes X40–44 (unintentional) or Y10–Y14 (undetermined) and multiple cause-of-death codes T40.0, T40.1, T40.2, T40.3, T40.4, or T40.6 on the death certificate. Data for this report were downloaded on September 5, 2017.

¶ A confirmed heroin death is defined as a death that tested positive for the heroin metabolite 6-acetylmorphine. The heroin metabolite 6-acetylmorphine, however, rapidly metabolizes to morphine, and thus a death involving heroin might only test positive for morphine, which is also present in deaths involving prescription morphine. A suspected heroin death is one in which testing for morphine is positive and the decedent also has a history of heroin use or death scene evidence indicating illicit drug use or injection in the absence of any evidence of prescription drug use or use of prescription morphine. https://www.ncbi.nlm.nih.gov/pubmed/25041514.

coroner in nearly all (97.1%) of the deaths. Northeastern states (Maine, Massachusetts, New Hampshire, and Rhode Island) and Missouri** reported the highest percentages of opioid overdose deaths involving fentanyl (approximately 60%–90%), followed by Midwestern and Southern states (Ohio, West Virginia, and Wisconsin), where approximately 30%–55% of decedents tested positive for fentanyl. New Mexico and Oklahoma reported the lowest percentage of fentanyl-involved deaths (approximately 15%–25%). In contrast, states detecting any fentanyl analogs in >10% of opioid overdose deaths were spread across the Northeast (Maine, 28.6%, New Hampshire, 12.2%), Midwest (Ohio, 26.0%), and South (West Virginia, 20.1%) (Figure) (Table 1).

Fentanyl analogs were present in 720 (14.0%) opioid overdose deaths, with the most common being carfentanil (389 deaths, 7.6%), furanylfentanyl (182, 3.5%), and acetylfentanyl (147, 2.9%) (Table 1). Fentanyl analogs contributed to death in 535 of the 573 (93.4%) decedents. Cause of death was not available for fentanyl analogs in 147 deaths.†† Five or more deaths involving carfentanil occurred in two states (Ohio and West Virginia), furanylfentanyl in five states (Maine, Massachusetts, Ohio, West Virginia, and Wisconsin), and acetylfentanyl in seven states (Maine, Massachusetts, New Hampshire, New Mexico, Ohio, West Virginia, and Wisconsin). U-47700 was present in 0.8% of deaths and found in five or more deaths only in Ohio, West Virginia, and Wisconsin (Table 1). Demographic characteristics of decedents were similar among overdose deaths involving fentanyl analogs and fentanyl (Table 2). Most were male (71.7% fentanyl and 72.2% fentanyl analogs), non-Hispanic white (81.3% fentanyl and 83.6% fentanyl analogs), and aged 25–44 years (58.4% fentanyl and 60.0% fentanyl analogs) (Table 2).

Other illicit drugs co-occurred in 57.0% and 51.3% of deaths involving fentanyl and fentanyl analogs, respectively, with cocaine and confirmed or suspected heroin detected in a substantial percentage of deaths (Table 2). Nearly half (45.8%) of deaths involving fentanyl analogs tested positive for two or more analogs or fentanyl, or both. Specifically, 30.9%, 51.1%, and 97.3% of deaths involving carfentanil, furanylfentanyl, and acetylfentanyl, respectively, tested positive for fentanyl or additional fentanyl analogs. Forensic investigations found evidence of injection drug use in 46.8% and 42.1% of overdose deaths involving fentanyl and fentanyl analogs, respectively. Approximately one in five deaths involving fentanyl and fentanyl analogs had no evidence of injection drug use but did have evidence of other routes of administration. Among these deaths, snorting (52.4% fentanyl and 68.8% fentanyl analogs) and ingestion (38.2% fentanyl and 29.7% fentanyl analogs) were most common. Although rare, transdermal administration was found among deaths involving fentanyl (1.2%), likely indicating pharmaceutical fentanyl (Table 2). More than one third of deaths had no evidence of route of administration.

** Illicitly manufactured fentanyl is more easily mixed with white powder heroin, which is primarily sold east of the Mississippi River, than with black tar heroin. Although white powder heroin dominates the heroin market in the Northeast, the heroin market in Missouri includes both white powder heroin and black tar heroin. This might, in part, explain the high percentage of fentanyl overdoses documented in the state. Additional information available at https://www.justice.gov/archive/ndic/dmas/Midwest_DMA-2011(U).pdf.

†† Data on whether fentanyl analogs contributed to the death in which they were detected was not available for 20.4% of deaths with fentanyl analogs. As new fentanyl analogs emerged, they were captured as free text (without the option to indicate whether they contributed to the death) until being added to the menu of substances in the toxicology portion of SUDORS.

FIGURE. Percentage of opioid overdose deaths testing positive for fentanyl and fentanyl analogs, by state — 10 states, July–December 2016

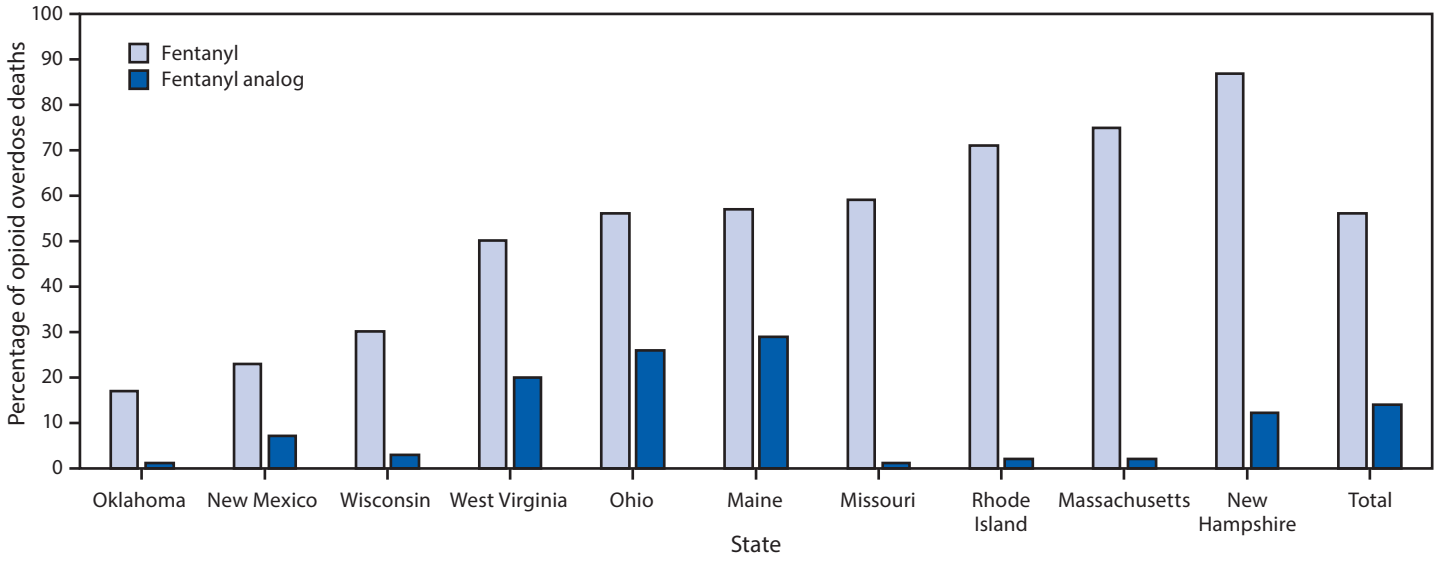

TABLE 1. Number and percentage of opioid overdose decedents testing positive for fentanyl analogs and U-47700 — 10 states, July–December 2016

State	Total opioid overdose deaths	Any fentanyl analog present* No. (%)	Fentanyl analogs				U-47700 synthetic opioid No. (%)
			Carfentanil No. (%)	Furanylfentanyl No. (%)	Acetylfentanyl No. (%)	Other† No. (%)	
Total§	**5,152**	**720 (14.0)**	**389 (7.6)**	**182 (3.5)**	**147 (2.9)**	**74 (1.4)**	**40 (0.8)**
Maine	**154**	**44 (28.6)**	0	25 (16.2)	17 (11.0)	5 (3.3)	—
Massachusetts	**1,071**	**17 (1.6)**	0	10 (0.9)	—¶	—	—
New Hampshire	**131**	**16 (12.2)**	0	—	13 (9.9)	0	—
New Mexico	**166**	**11 (6.6)**	0	—	7 (4.2)	0	—
Ohio	**2,043**	**531 (26.0)**	354 (17.3)	85 (4.2)	91 (4.5)	40 (2.0)	15 (0.7)
West Virginia	**393**	**79 (20.1)**	35 (8.9)	44 (11.2)	6 (1.5)	23 (5.9)	7 (1.8)
Wisconsin	**413**	**14 (3.4)**	0	6 (1.5)	5 (1.2)	—	5 (1.2)
Other three states**	**781**	**8 (1.0)**	0	—	—	—	—

* Individual fentanyl analog deaths might sum to a number greater than the number of deaths with any fentanyl analog present because more than one fentanyl analog could be present in an opioid overdose death.
† Includes 3-methylfentanyl, acrylfentanyl, butyrylfentanyl, para-fluorofentanyl (or 4-fluorofentanyl), para-fluorobutyrylfentanyl (or 4-fluorobutyrylfentanyl), and para-fluoroisobutyrylfentanyl (or 4-fluoroisobutyrylfentanyl).
§ Data from 10 states included in the total numbers; individual states presented if five or more deaths tested positive for any fentanyl analog.
¶ Five or more deaths tested positive for acetylfentanyl in Massachusetts, but the number was suppressed to prevent calculation of number for other states, which was less than five.
** Missouri (22 counties), Oklahoma, and Rhode Island.

Discussion

This analysis of opioid overdose deaths in 10 states participating in the ESOOS program found that illicitly manufactured fentanyl is a key factor driving opioid overdose deaths and that fentanyl analogs are increasingly contributing to a complex illicit opioid market with significant public health implications. Previous reports have indicated that use of illicitly manufactured fentanyl mixed with heroin, with and without users' knowledge, is driving many fentanyl overdoses, particularly east of the Mississippi River (*3*,*4*). Consistent with these findings, at least half of opioid overdose deaths in six of the seven participating states east of the Mississippi tested positive for fentanyl. Over half the overdose deaths involving fentanyl and fentanyl analogs tested positive for confirmed or suspected heroin (the most commonly detected illicit substance), cocaine, or methamphetamine. This supports findings from other reports indicating that fentanyl and fentanyl analogs are commonly used with or mixed with heroin or cocaine (*3*,*4*). Nearly half of overdose deaths involving fentanyl and fentanyl analogs, however, did not test positive for other illicit opioids, suggesting that fentanyl and fentanyl analogs might be emerging as unique illicit products.

Fentanyl and fentanyl analogs are highly potent and fast-acting synthetic compounds that can trigger rapid progression to loss of consciousness and death and thus might require immediate treatment and high doses of naloxone (*5*). Because of the potency of fentanyl and fentanyl analogs and the rapid onset of action, these drugs were determined by medical examiners and coroners to play a causal role in almost all fatal opioid overdoses in which they were detected. Injection, the most commonly reported route of administration in fatal overdoses, exacerbates these risks because of rapid absorption and high bioavailability. The high potency of fentanyl and fentanyl analogs, however, can result in overdose even when administered via other routes. Nearly one in five deaths involving fentanyl and fentanyl analogs had evidence of snorting, ingestion, or smoking, with no evidence of injection. Multiple overdose outbreaks and law enforcement drug product submissions across the country have reported counterfeit prescription pills laced with fentanyl and fentanyl analogs (*10*).

With few exceptions, fentanyl analogs are illicitly manufactured, because they do not have a legitimate medical use in humans.§§ The detection of fentanyl analogs in >10% of opioid overdoses in four states raises the concern that fentanyl analogs have become a part of illicit opioid markets in multiple states. The fentanyl analogs most commonly detected were carfentanil, furanylfentanyl, and acetylfentanyl. Carfentanil, which is intended for sedation of large animals, is much more potent than fentanyl, whereas furanylfentanyl and acetylfentanyl are less potent (*9*). Carfentanil contributed to approximately 350 overdose deaths in Ohio, but was detected in only one other state (West Virginia). Because of its extreme potency, even limited circulation of carfentanil could markedly increase the number of fatal overdoses. Recent data suggest that carfentanil deaths are occurring in multiple other states, including Kentucky, which reported 10 overdose deaths involving carfentanil in the second half of 2016 (Kentucky Department of Public Health, unpublished data, 2017) and New Hampshire, which reported 10 deaths in 2017.¶¶ Forty-six percent of

§§ The three fentanyl analogs with legitimate human medical use are remifentanil, alfentanil, and sufentanil; none of the SUDORS deaths was positive for these substances. Carfentanil is used exclusively in large animal veterinary medicine.
¶¶ Additional information is available at https://www.dhhs.nh.gov/dcbcs/bdas/documents/dmi-august-2017.pdf.

TABLE 2. Demographic characteristics and overdose circumstance factors for decedents in opioid overdose deaths involving fentanyl, fentanyl analogs, and U-47700, by substance — 10 states, July–December 2016

			Fentanyl analogs				U-47700 synthetic opioid (N = 40)
	Fentanyl (N = 2,903)	Any fentanyl analog* (N = 720)	Carfentanil (N = 389)	Furanylfentanyl (N = 182)	Acetylfentanyl (N = 147)	Other† (N = 74)	
Characteristic	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**
Age group (yrs)§							
15–24	276 (9.5)	63 (8.8)	31 (8.0)	—¶	15 (10.2)	—	—
25–34	926 (31.9)	220 (30.6)	124 (31.9)	50 (27.5)	46 (31.3)	27 (36.5)	19 (47.5)
35–44	768 (26.5)	212 (29.4)	103 (26.5)	61 (33.5)	48 (32.7)	22 (29.7)	6 (15.0)
45–54	540 (18.6)	133 (18.5)	73 (18.8)	32 (17.6)	26 (17.7)	9 (12.2)	6 (15.0)
55–64	343 (11.8)	77 (10.7)	50 (12.9)	18 (9.9)	—	8 (10.8)	—
≥65	47 (1.6)	15 (2.1)	8 (2.1)	—	—	—	0
Median age (IQR) in yrs	37 (29–48)	38 (30–48)	39 (30–49)	38 (31–47)	36 (30–45)	36 (29–46)	32 (27–43)
Sex							
Male	2,080 (71.7)	520 (72.2)	276 (71.0)	134 (73.6)	111 (75.5)	49 (66.2)	32 (80.0)
Female	820 (28.2)	200 (27.8)	113 (29.0)	48 (26.4)	36 (24.5)	25 (33.8)	8 (20.0)
Race and Hispanic origin							
White, non-Hispanic	2,360 (81.3)	602 (83.6)	340 (87.4)	148 (81.3)	120 (81.6)	62 (83.8)	36 (90.0)
Black, non-Hispanic	274 (9.4)	75 (10.4)	42 (10.8)	17 (9.3)	9 (6.1)	9 (12.2)	—
Other, non-Hispanic	37 (1.3)	9 (1.3)	—	—	—	—	—
Hispanic	189 (6.5)	20 (2.8)	—	—	—	—	0
Other fentanyl(s) present							
Fentanyl or other fentanyl analog	n/a	330 (45.8)	120 (30.9)	93 (51.1)	143 (97.3)	46 (62.2)	24 (60.0)
Fentanyl	n/a	299 (41.5)	105 (27.0)	62 (34.1)	139 (94.6)	31 (41.9)	16 (40.0)
1 fentanyl analog present**	263 (9.1)	653 (90.7)	352 (90.5)	129 (70.9)	129 (87.8)	43 (58.1)	12 (30.0)
≥2 fentanyl analogs present	36 (1.2)	67 (9.3)	37 (9.5)	53 (29.1)	18 (12.2)	31 (41.9)	6 (15.0)
4-ANPP††	60 (2.1)	82 (11.4)	—	77 (42.3)	—	13 (17.6)	8 (20.0)
Other illicit drugs present							
Any illicit drugs	1,656 (57.0)	369 (51.3)	190 (48.8)	91 (50.0)	91 (61.9)	42 (56.8)	15 (37.5)
Suspected/Confirmed heroin§§	1,132 (39.0)	250 (34.7)	123 (31.6)	60 (33.0)	75 (51.0)	26 (35.1)	11 (27.5)
Cocaine	1,011 (34.8)	202 (28.1)	99 (25.4)	52 (28.6)	43 (29.3)	26 (35.1)	7 (17.5)
Methamphetamine	167 (5.8)	64 (8.9)	43 (11.1)	12 (6.6)	10 (6.8)	—	—
Evidence of injection	1,358 (46.8)	303 (42.1)	151 (38.8)	76 (41.8)	81 (55.1)	35 (47.3)	19 (47.5)
No evidence of injection but evidence of other route¶¶	532 (18.3)	138 (19.2)	85 (21.9)	33 (18.1)	19 (12.9)	10 (13.5)	11 (27.5)
Evidence of snorting	279 (52.4)	95 (68.8)	57 (67.1)	21 (63.6)	15 (78.9)	9 (90.0)	8 (72.7)
Evidence of ingestion	203 (38.2)	41 (29.7)	27 (31.8)	8 (24.2)	7 (36.8)	—	—
Evidence of smoking	95 (17.9)	25 (18.1)	16 (18.8)	7 (21.2)	—	—	—
Evidence of transdermal	35 (6.6)	—	—	0	—	0	0
Evidence of sublingual	6 (1.1)	—	—	0	0	0	0
No evidence of route	1,013 (34.9)	279 (38.8)	153 (39.3)	73 (40.1)	47 (32.0)	29 (39.2)	10 (25.0)

Abbreviation: n/a = not applicable.

* Individual fentanyl analog deaths might sum to a number greater than the number of deaths with any fentanyl analog present because more than one fentanyl analog could be present in an opioid overdose death.

† Includes 3-methylfentanyl, acrylfentanyl, butyrylfentanyl, para-fluorofentanyl (or 4-fluorofentanyl), para-fluorobutyrylfentanyl (or 4-fluorobutyrylfentanyl), and para-fluoroisobutyrylfentanyl (or 4-fluoroisobutyrylfentanyl).

§ Fewer than five persons aged ≤14 years died of an overdose that tested positive for a fentanyl analog.

¶ Data suppressed because fewer than five deaths, or suppressed to prohibit calculation of other suppressed cell.

** For fentanyl analogs, indicates no other analog present.

†† Despropionylfentanyl is a fentanyl compound that can serve as a marker for illicitly manufactured fentanyl and fentanyl analogs because it is both a precursor and a metabolite of these illicit products (but not pharmaceutical fentanyl), while having low metabolic activity that does not contribute to overdose toxicity. Despropionylfentanyl is also known as 4-anilino-N-phenethylpiperidine, or 4-ANPP.

§§ Includes decedents testing positive for heroin metabolite 6-acetylmorphine, plus decedents testing positive for morphine where there was a history of heroin use, death scene evidence of illicit drug use, or evidence of injection, and no scene evidence of prescription drug use or other evidence of prescription morphine.

¶¶ Percentage of deaths with evidence of routes of administration other than injection calculated out of the number of deaths in this row.

SUDORS opioid overdose deaths involving fentanyl analogs tested positive for fentanyl or an additional fentanyl analog, ranging from 31% for carfentanil to 97% for acetylfentanyl. The increased mixing or co-use of fentanyl, heroin, cocaine, and varying fentanyl analogs might contribute to increased risk for overdose because persons misusing opioids and other drugs are exposed to drug products with substantially varied potency.

The findings in this report are subject to at least five limitations. First, results are limited to 10 states and therefore might not be generalizable. Second, the presence of fentanyl analogs is underestimated because commonly used toxicologic testing does not include fentanyl analogs, some fentanyl analogs are difficult to detect (*9*), and specialized testing for fentanyl analogs varied across states and over time. Third, the route of fentanyl and fentanyl analog administration must be interpreted cautiously because the data do not link specific drugs to routes of administration and thus the precise route of administration of fentanyl or fentanyl analogs cannot be determined in overdose deaths involving multiple substances (e.g., heroin and cocaine) and routes (e.g., injection and snorting). Fourth, the combination of deaths with toxicologic confirmation of heroin with those with detection of morphine and death scene evidence suggesting heroin use might have resulted in misclassification of some deaths. Finally, fentanyl source could not be definitively determined; however, only a small percentage of fentanyl deaths had evidence consistent with prescription fentanyl (e.g., transdermal use versus injection).

Illicitly manufactured fentanyl is now a major driver of opioid overdose deaths in multiple states, with a variety of fentanyl analogs increasingly involved, if not solely implicated, in these deaths. This finding raises concern that in the near future, fentanyl analog overdose deaths might mirror the rapidly rising trajectory of fentanyl overdose deaths that began in 2013 and become a major factor in opioid overdose deaths. In response to this concern, CDC expanded ESOOS to 32 states and the District of Columbia in 2017 and added funding for all 33 recipients to improve forensic toxicologic testing of opioid overdose deaths to include capacity to test for a wider range of fentanyl analogs.*** Increased implementation of evidence-based efforts targeting persons at high risk for illicit opioid use, including increased access to medication-assisted treatment, increased availability of naloxone in sufficient doses, and other innovative intervention programs targeting this group, is needed to address a large and growing percentage of opioid overdose deaths involving fentanyl and fentanyl analogs.

*** https://www.cdc.gov/drugoverdose/foa/state-opioid-mm.html.

Summary

What is already known about this topic?

Sharp increases in opioid overdose deaths since 2013 are partly explained by the introduction of illicitly manufactured fentanyl into the heroin market. Outbreaks related to fentanyl analogs also have occurred. One fentanyl analog, carfentanil, is estimated to be 10,000 times more potent than morphine. Fentanyl analogs are not routinely detected because specialized toxicology testing is required.

What is added by this report?

This is the first report using toxicologic and death scene evidence across multiple states to characterize opioid overdose deaths. Fentanyl was involved in >50% of opioid overdose deaths, and >50% of deaths testing positive for fentanyl and fentanyl analogs also tested positive for other illicit drugs. Approximately 700 deaths tested positive for fentanyl analogs, with the most common being carfentanil, furanylfentanyl, and acetylfentanyl.

What are the implications for public health practice?

Increasing mixing or co-use of fentanyl, heroin, cocaine, and fentanyl analogs might contribute to increased overdose risk, because users are exposed to drug products that vary substantially in potency and that include some extremely potent products. Surveillance for opioid overdoses needs to expand to track the rapidly changing illicit opioid market. In fall 2017, CDC funded 33 jurisdictions to expand forensic toxicology testing. Increased implementation of evidence-based efforts targeting persons at high risk for using illicit opioids, including increased access to medication-assisted treatment and increased availability of naloxone, and innovative interventions are needed.

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Conflict of Interest

No conflicts of interest were reported.

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References

1. Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in drug and opioid overdose deaths—United States, 2000–2014. MMWR Morb Mortal Wkly Rep 2016;64:1378–82. https://doi.org/10.15585/mmwr.mm6450a3
2. CDC. Provisional counts of drug overdose deaths, as of 8/6/2017. Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https://www.cdc.gov/nchs/data/health_policy/monthly-drug-overdose-death-estimates.pdf
3. O'Donnell JK, Gladden RM, Seth P. Trends in deaths involving heroin and synthetic opioids excluding methadone, and law enforcement drug product reports, by census region—United States, 2006–2015. MMWR Morb Mortal Wkly Rep 2017;66:897–903. https://doi.org/10.15585/mmwr.mm6634a2
4. Drug Enforcement Administration. 2017 national drug threat assessment summary. Washington, DC: US Department of Justice, Drug Enforcement Administration; 2017. https://www.dea.gov/docs/DIR-040-17_2017-NDTA.pdf
5. Daniulaityte R, Juhascik MP, Strayer KE, et al. Overdose deaths related to fentanyl and its analogs—Ohio, January–February 2017. MMWR Morb Mortal Wkly Rep 2017;66:904–8. https://doi.org/10.15585/mmwr.mm6634a3
6. Massey J, Kilkenny M, Batdorf S, et al. Opioid overdose outbreak—West Virginia, August 2016. MMWR Morb Mortal Wkly Rep 2017;66:975–80. https://doi.org/10.15585/mmwr.mm6637a3
7. Drug Enforcement Administration, Diversion Control Division. National Forensic Laboratory Information System: 2016 annual report. Springfield, VA: Drug Enforcement Administration; 2017. https://www.nflis.deadiversion.usdoj.gov/DesktopModules/ReportDownloads/Reports/NFLIS2016AR.pdf
8. Suzuki J, El-Haddad S. A review: fentanyl and non-pharmaceutical fentanyls. Drug Alcohol Depend 2017;171:107–16. https://doi.org/10.1016/j.drugalcdep.2016.11.033
9. Schueler H. Emerging synthetic fentanyl analogs. Acad Forensic Pathol 2017;7:36–40. https://doi.org/10.23907/2017.004
10. Drug Enforcement Administration. Intelligence brief: counterfeit prescription pills containing fentanyls: a global threat. July 2016. https://www.dea.gov/docs/Counterfeit%20Prescription%20Pills.pdf

Announcement

Community Preventive Services Task Force Recommendation for Interventions Including Activity Monitors to Increase Physical Activity in Adults with Overweight or Obesity

The Community Preventive Services Task Force (CPSTF) recommends interventions that include activity monitors to increase physical activity in adults with overweight or obesity. "Physical Activity: Interventions Including Activity Monitors for Adults with Overweight or Obesity" is available at https://www.thecommunityguide.org/findings/physical-activity-interventions-including-activity-monitors-adults-overweight-obesity.

Established in 1996 by the U.S. Department of Health and Human Services, the CPSTF is an independent, nonfederal panel of public health and prevention experts whose members are appointed by the director of CDC. The CPSTF provides information for a wide range of persons who make decisions about programs, services, and other interventions to improve population health. Although CDC provides administrative, scientific, and technical support for the CPSTF, the recommendations developed are those of the task force and do not undergo review or approval by CDC.

Notice to Readers

New Web Location for Weekly and Annual NNDSS Data

To improve the usability, availability, quality, and timeliness of surveillance data as part of the CDC Surveillance Strategy (*1*), CDC will provide users a convenient way to access notifiable infectious and noninfectious disease data through the National Notifiable Diseases Surveillance System (NNDSS) website.

CDC has redesigned the data and statistics section of the NNDSS website to be a one-stop shop for users to find both detailed information about the notifiable disease data and links to the weekly and annual data. Although these data will no longer be published in their current format in *MMWR*, users can easily access the information on the NNDSS website. To ease the transition, *MMWR* also will link users from its website to the new location on the NNDSS website.

Weekly Reporting

CDC expects to transition the reporting of NNDSS weekly data in January 2018. The redesigned NNDSS Data and Statistics website at https://wwwn.cdc.gov/nndss/data-and-statistics.html will contain links to infectious disease data tables that are available in HTML, text, and PDF formats and hosted on the CDC WONDER platform (*2*). The figure comparing selected notifiable diseases with historical data from the current *MMWR* weekly also will be available. In addition, the website will provide NNDSS documentation, including how the data are collected and reported, publication criteria, notes about interpreting data, and the list of notifiable conditions by year.

Annual Reporting

CDC is transitioning the reporting of NNDSS annual data on November 3, 2017. The NNDSS Data and Statistics website is available at https://wwwn.cdc.gov/nndss/data-and-statistics.html and includes links to infectious disease data tables that are available in HTML, text, and PDF formats and hosted on the CDC WONDER platform. The website also provides links to noninfectious conditions and disease outbreak surveillance reports published by CDC programs and hosted on the CDC WONDER platform. In addition, the website provides the following resources: documentation for NNDSS infectious diseases and noninfectious conditions and disease outbreaks, including how the data are collected, reported, and finalized; publication criteria; notes about interpreting data; and the list of notifiable conditions by year.

Consolidating the notifiable disease data on the NNDSS website is part of the NNDSS Modernization Initiative (NMI) strategy to streamline NNDSS and access to data for users; NMI is a component of the CDC Surveillance Strategy. This consolidation of information also is in response to the recommendations of a CDC-wide workgroup, consisting of representatives from the CDC Excellence in Science Committee, the Surveillance Science Advisory Group, and *MMWR*, to make more data available online and to allow *MMWR* to focus on publishing scientific and actionable surveillance reports.

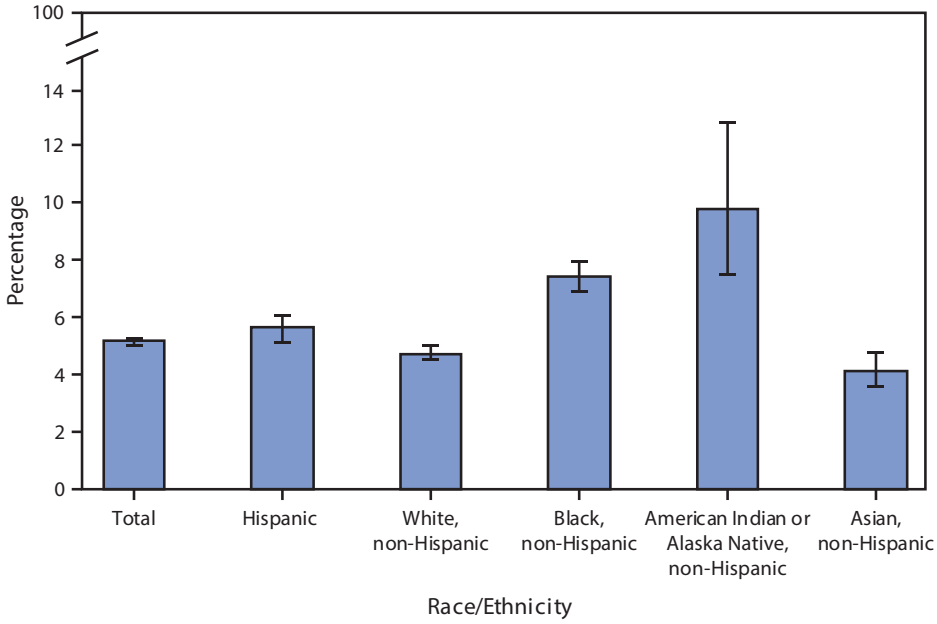
References

1. Richards CL, Iademarco MF, Anderson TC. A new strategy for public health surveillance at CDC: improving national surveillance activities and outcomes. Public Health Rep 2014;129:472–6. https://doi.org/10.1177/003335491412900603
2. CDC. CDC WONDER. Atlanta, GA: US Department of Health and Human Services, CDC; 2017. https://wonder.cdc.gov/

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Age-Adjusted Percentage* of Adults Aged ≥45 Years Who Were Limited in Any Way Because of Difficulty Remembering or Periods of Confusion,† by Race/Ethnicity§ — United States, 2014–2016¶



* With 95% confidence intervals shown with error bars. Estimates are age-adjusted to the projected 2000 U.S. population as the standard population using three age groups: 45–49, 50–64, and ≥65 years.

† Based on a positive response to the survey question, "Are you/Is anyone in the family limited in any way because of difficulty remembering or because you/they experience periods of confusion?" Responses may be self-reported or reported by a knowledgeable family member. Information is obtained on each family member with the condition/limitation and included in the estimate of total prevalence.

§ 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 bar is based on all adults aged ≥45 years.

¶ Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population and are derived from the National Health Interview Survey Family Component.

Overall, 5.1% of adults aged ≥45 years were limited in any way because of difficulty remembering or periods of confusion. The percentage of adults experiencing this limitation was highest among non-Hispanic American Indian/Alaska Native adults (9.8%) and non-Hispanic black adults (7.4%), followed by Hispanic adults (5.6%), non-Hispanic white adults (4.7%), and non-Hispanic Asian adults (4.1%).

Source: National Health Interview Survey, 2014–2016 data. https://www.cdc.gov/nchs/nhis.htm.

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