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Hepatitis Awareness Month and Testing Day — May 2016

This month marks the 21st Hepatitis Awareness Month and the 5th observance of May 19 as National Hepatitis Testing Day in the United States. Approximately 90% of U.S. deaths from viral hepatitis are caused by infection with hepatitis C virus (HCV). In 2013, for the first time, deaths associated with HCV infection surpassed the total number of deaths from 60 other nationally notifiable infectious diseases (*1*). In 2014, the HCV-related incidence rate and mortality rate among American Indian/Alaska Native (AI/AN) populations were approximately twofold greater than the comparable rates for the general population (*2*).

This issue of *MMWR* includes two reports describing actions in AI communities to improve access to HCV testing, care, and curative treatment. The first report evaluates a tribal HCV testing policy established by the Cherokee Nation (CN). Findings indicated that, during 2012–2015, first-time testing for HCV increased fivefold, and HCV treatment more than doubled among CN members. The second report examines the impact of an Indian Health Service (IHS) program to promote implementation of the CDC recommendation for one-time HCV testing for persons in the 1945–1965 birth cohort. As a result, during 2012–2015, HCV testing increased fourfold among those in the birth cohort across IHS clinics in 34 states. Data from both reports reveal that strategies such as provider education, clinical decision tools, and telehealth models of care can expand access to HCV testing and treatment, helping to eliminate hepatitis C as a health disparity for AI/AN populations.

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Identification and Clinical Management of Persons with Chronic Hepatitis C Virus Infection — Cherokee Nation, 2012–2015

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An estimated 3.5 million persons in the United States are living with hepatitis C virus (HCV) infection, resulting in approximately 20,000 deaths each year, primarily from cirrhosis or hepatocellular carcinoma (*1*,*2*). American Indian/Alaska Native (AI/AN) populations have the highest incidence of acute

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HCV infection among all U.S. racial/ethnic groups and are at greater risk for HCV-related mortality compared with the general population (*3*). In 2013, new antiviral drugs became available that make possible 8–12 week treatment regimens with fewer adverse events and are able to achieve sustained virologic response (SVR) in >90% of treated patients (*4*), equivalent to a cure of HCV infection. Also of note, HCV testing recommendations were expanded in 2012 by CDC and in 2013 by the U.S. Preventive Services Task Force to include one-time testing of persons born during 1945–1965 (the "baby boomer" cohort) in addition to anyone at increased risk for HCV infection (*5*,*6*). Given the availability of new HCV drugs, expanded testing recommendations, and high incidence of HCV infection in AI/AN populations, in October 2012, Cherokee Nation Health Services (CNHS) implemented a tribal HCV testing policy.* As part of the policy, CNHS added a reminder in the electronic health record (EHR) for clinical decision support and provided HCV education to primary care clinicians. From October 2012 to July 2015, among 92,012 persons with at least one CNHS clinic encounter, the cumulative number who received HCV screening for the first time increased from 3,337 (3.6%) to 16,772 (18.2%). The largest percentage of HCV screening was among persons born during 1945–1965. Of 715 persons who tested positive for HCV antibodies, 488 (68.3%) were tested for HCV RNA; among those 488 persons, 388 (79.5%) were RNA positive and were thus confirmed to have chronic HCV infection. Treatment was initiated for 223 (57.5%) of the 388 with chronic infection; 201 (90.1%) completed treatment, of whom 180 (89.6%) achieved SVR. CNHS has successfully increased HCV testing and treatment and is now collaborating with CDC and other external partners to develop an HCV elimination program for the Cherokee Nation that might serve as a model for similar settings.

The Cherokee Nation is a federally recognized government of more than 317,000 sovereign Cherokee persons in the United States. CNHS is an independent network that includes one hospital and eight clinics with a centralized EHR system providing care to approximately 131,000 AI/ANs (87% Cherokee and 13% other federally recognized tribes) in 14 counties of primarily rural northeastern Oklahoma.

During October 2012–2015, an infectious diseases specialist serving CNHS provided in-person hepatitis C training to clinicians and allied health professionals in each health care facility. Fifteen workshops were organized with a total of 291 participants. In response to the expanded national HCV testing recommendations, CNHS collaborated with the Indian Health Service (IHS) to design and implement an EHR reminder to test patients born during 1945–1965. Beginning in August 2013, the EHR reminder was added on a rolling basis depending on local priorities and capacity, reaching all primary care clinics by January 2014. The EHR prompt targeted any person born during 1945–1965

* A Cherokee translation of this report will be available in June in the hepatitis C awareness section at http://cherokeepublichealth.org/. The title of this report translates as follows: **ᎪᏟᏍᏁᏗ ᎠᏄ ᎠᏕᏫᏂᏓᏍᏗ ᎥᏳᎩ ᎤᏁᏜᎢ ᏴᏫ ᎪᎯᎩ ᏠᏁᎨᎢ ᎤᏬᏍᏆᎢ ᎥᏳᎩ** (HCV) **ᏚᎾᏓᏂᏩᎯᏍᏗᏜᎢ ᎥᏓᎾᏂ ᏣᎳᎩᎯ ᎠᏰᎵ**, 2012–2015.

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who had at least one medical visit in the preceding 3 years and no documented HCV antibody test in the medical record.

In conjunction with expanded testing, CNHS increased capacity to provide care for HCV-infected patients as well as to decrease patients' waiting and travel time for evaluation. The Extension for Community Healthcare Outcomes (ECHO) telehealth program (*7,8*) was implemented in July 2014 to increase primary care provider capacity to care for HCV-infected patients. ECHO implementation enabled expansion of HCV care and treatment services from one clinic with one health care provider with expertise in HCV care to five clinics staffed by seven HCV-trained health care providers, including three physicians, two nurse practitioners, and two pharmacists. In January 2014, an HCV registry was established to monitor clinical care for HCV RNA-positive patients who initiated antiviral treatment. The registry is maintained by the infectious diseases clinic of CNHS. In October 2015, public health nurses began outreach activities for HCV-infected patients, including home visits.

To evaluate the impact of the new testing and care and treatment strategies, de-identified data from the CNHS centralized EHR system and the HCV registry were extracted and analyzed. HCV testing coverage was calculated as the proportion of patients with at least one clinical encounter with CNHS during October 2012–July 2015 who received one or more HCV antibody tests during that period. Progression along the steps of the cascade of care was examined by two methods: 1) the percentage of persons with HCV antibodies who completed each step, and 2) the percentage of persons at each step who moved to the next step. SVR was defined as undetectable HCV RNA obtained at least 12 weeks after the end of treatment. Advanced liver disease was determined based on noninvasive liver staging methods as identified by serologic biomarkers (fibrosis-4 index >3.25) (*9*).

During October 2012–July 2015, a total of 92,012 patients aged ≥20 years had at least one medical encounter with CNHS. Among these patients, 90% were residents of the 14-county CNHS tribal jurisdictional area, 56% were female, and 29.4% were born during 1945–1965. The cumulative proportion of the population tested for HCV antibodies increased fivefold, from 3.6% to 18.2%, and did not differ by sex. By July 2015, the largest cumulative percentage of persons tested (39.5%) were in the baby boomer cohort (1945–1954 and 1955–1964), representing a sixfold increase (Figure 1).

Among the 16,772 patients tested for HCV antibody, 715 (4.3%) were antibody-positive. Among the HCV antibody-positive patients, 488 (68.3%) had a confirmatory HCV RNA test performed, of whom 388 (79.5%) were found to be chronically infected (HCV RNA-positive). More than half (57.5%) of persons with chronic HCV infection initiated treatment, of whom 89.6% achieved SVR (Figure 2).

FIGURE 1. Cumulative percentage of persons who received one or more hepatitis C virus antibody tests, by birth cohort — Cherokee Nation Health Services, October 2012–July 2015

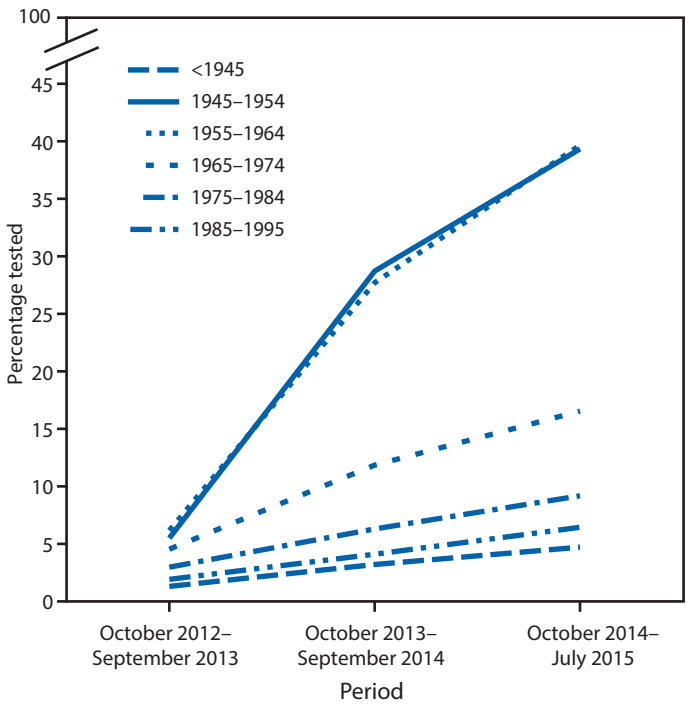
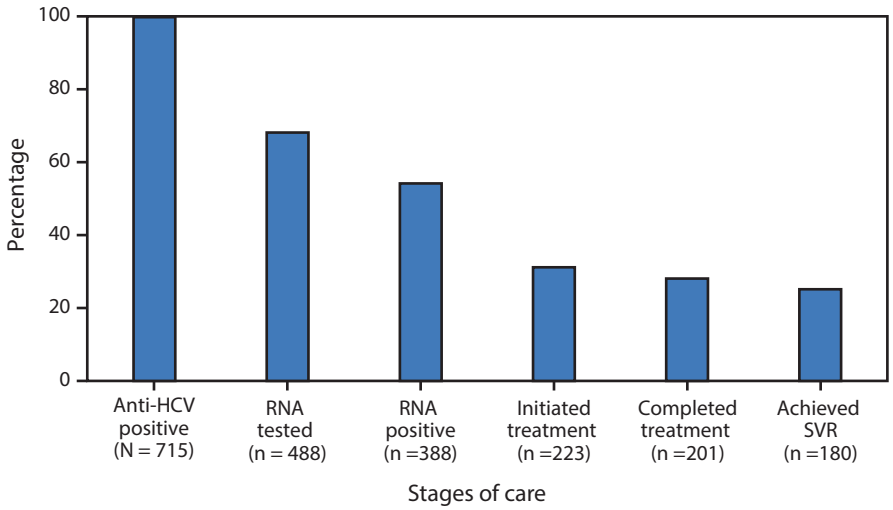


FIGURE 2. Percentages for 715 hepatitis C virus (HCV) antibody-positive patients, showing cascade of care — Cherokee Nation Health Services, October 2012–July 2015

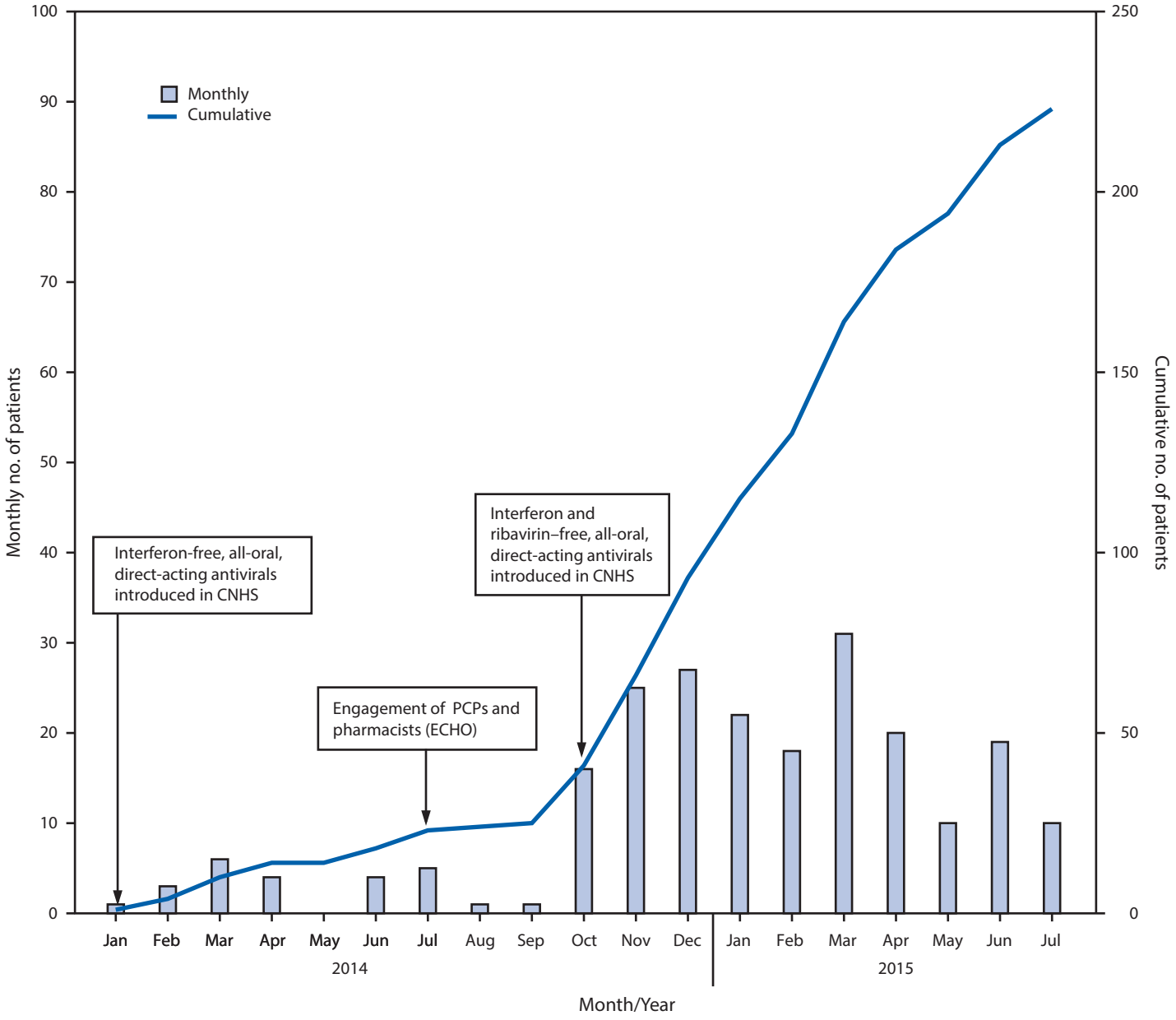


Abbreviation: SVR = sustained virologic response.

Among the 223 patients initiating treatment, HCV genotype 1 (GT1) was the most common infection (157 patients, 70.4%), followed by GT2 (35 patients, 15.7%), GT3 (30 patients, 13.5%) and GT4 (one patient, 0.5%). Among the 134 patients in the baby boomer birth cohort, 50 (37.3%) were found to have advanced liver disease. Among the 86 patients with chronic HCV infection born after 1965, 23 (26.7%) had evidence of advanced liver disease. Seven patients who initiated treatment failed to complete treatment because of noncompliance (four), psychiatric complications (two), and pregnancy (one). Twenty-one patients were lost to follow up (including one who died) before testing for SVR.

As direct, oral, interferon-free antiviral agents became available and clinic capacity improved, the number of patients treated for chronic HCV infection increased over time. More than 15 patients (range = 16–31) initiated treatment in eight of the 19 months (Figure 3).

FIGURE 3. Number of patients with hepatitis C virus (HCV) infection who tested RNA positive and initiated all-oral, anti-HCV therapy, by month and cumulative total — Cherokee Nation Health Services (CNHS), January 2014–July 2015



Abbreviations: ECHO = Extension for Community Healthcare Outcomes; PCPs = primary care providers.

Summary

What is already known about this topic?

Hepatitis C virus (HCV) infection, the most common bloodborne infection in the United States, is the leading cause of liver-related mortality and disproportionally affects the American Indian/Alaska Native (AI/AN) populations. New all-oral HCV therapies can halt disease progression and provide a cure, but increased testing is needed to identify persons living with chronic HCV infection because more than half of infected persons are unaware of their infection.

What is added by this report?

Beginning in October 2012, Cherokee Nation Health Services (CNHS) implemented measures to improve HCV testing and care among the AI/AN population in northeastern Oklahoma. During October 2012–July 2015, the percentage of all persons tested for the first time increased fivefold. HCV treatment was initiated for more than half of the approximately 400 patients identified with chronic HCV infection, 90% of whom completed treatment and were cured.

What are the implications for public health practice?

CNHS successfully increased HCV testing and treatment and is now collaborating with external partners to develop an HCV elimination program for the Cherokee Nation that might serve as a model for similar settings.

Discussion

HCV antibody testing by CNHS increased fivefold over the approximately 33-month evaluation period. As of July 2015, testing coverage among persons in the baby boomer birth cohort was nearly 40%. The substantial increase in the number of tests ordered among persons born during 1945–1965 likely resulted from implementation of the EHR reminder in August 2013. Although the EHR reminder specifically targeted the baby boomer birth cohort, HCV testing also increased among other birth cohorts during this period, although to a lesser degree. Increased testing in younger populations could have resulted from enhanced primary care provider education and more awareness of HCV-related risk factors. Over the entire 33-month period, only 57.5% of eligible patients initiated treatment; however, the number of patients initiating treatment increased substantially over time. The increase occurred during a period when interferon-free oral, anti-HCV agents became available and followed implementation of the ECHO program and enhanced primary care education and training in July 2014.

The increase in HCV testing and case finding increased the need for HCV RNA confirmatory testing and linkage to care. Approximately 30% of patients found to be HCV antibody–positive had not received a confirmatory HCV RNA test. Furthermore, among patients identified with chronic HCV infection, 32% had advanced liver disease and needed immediate treatment. There is a clear need for increased health care capacity to identify and treat persons with chronic HCV infection to prevent further morbidity and mortality. Thus, the role of primary care providers has been critical in addressing the clinical needs of the growing volume of patients identified with HCV infection. Another important component of increasing capacity has been the work of public health nurses in outreach activities for patients infected with HCV, including making home visits and drawing blood for further testing (i.e., for HCV RNA), if needed. CNHS has posted fliers in clinic waiting areas to prompt patients who might already know they are HCV antibody–positive to contact one of the clinics that provides HCV care. The Cherokee Nation is systematically continuing to identify and treat chronic HCV infection, and expanding clinical capacity to meet patient needs by leveraging telehealth within its primary care delivery system. The Cherokee Nation has declared October 30 as CNHS HCV Awareness Day.

The findings in this report are subject to at least four limitations. First, the results are not generalizable to other populations because they were specific to the AI/AN community managed in a specific tribal health care system. Second, the data were observational, and the outcomes cannot be directly attributed to the interventions. Third, the availability of three new oral antiviral regimens during this period (sofosbuvir in January 2014, sofosbuvir/ledipasvir in October 2014, and ombitasvir/paritaprevir/ritonavir/dasabuvir in December 2014) might have contributed to the observed increase in antiviral treatments in addition to the reported increase in clinical capacity. Finally, the cascade of care does not include a population-based estimate of the number of HCV cases because these data are not yet available.

In response to findings of the expanded CNHS testing initiative, in October 2015, with the assistance of CDC and other partners, the Cherokee Nation launched The Path Toward Elimination of HCV program. The Cherokee Nation is committed to implementing a comprehensive program with goals for eliminating HCV as a health disparity for the population. The program includes expansion of a clinical phase to implement broad-based HCV testing, care, and treatment activities in CNHS with the goal of treating 85% of CNHS patients with HCV infection over a 3-year period. As a first step, tribal HCV screening policy was expanded to include persons aged 20–69 years. In addition, CNHS is striving to increase clinical capacity to 20 providers and eight pharmacists trained as HCV care providers. A second phase will be a community-based effort to implement interventions as necessary to interrupt HCV transmission, focused primarily on persons who inject drugs.

Currently CNHS is collaborating with the Cherokee Nation Tribal Council, Cherokee Nation Public Health, CDC, the University of Oklahoma Health Sciences Center, Yale School of Public Health, Oklahoma State Department of Health, Gilead Foundation, and community-based organizations to develop

effective strategies and programs to prevent, test, treat, and cure HCV infection. Cherokee Nation's HCV elimination program is the first of its kind in the United States. The National Academies of Science, Engineering, and Medicine currently is examining the feasibility of eliminating hepatitis C in the United States and developing recommendations for specific actions to hasten the end of HCV transmission and disease (*10*).

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Birth Cohort Testing for Hepatitis C Virus — Indian Health Service 2012–2015

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Hepatitis C virus (HCV) infection is a substantial and largely unrecognized public health problem. An estimated 3.5 million persons in the United States are currently living with HCV infection, at least half of whom are unaware of their infection (*1*–*3*). Persons born during 1945–1965 (the "baby boomer" birth cohort) have a sixfold higher prevalence (2.6%) than adults of other ages, and represent 81% of all persons chronically infected with HCV (*4*). Therefore, in addition to recommending testing for all persons at risk for HCV infection, CDC and the U.S. Preventive Services Task Force (USPSTF) recommend one-time HCV testing for the birth cohort (*5*,*6*). Compared with the national average, American Indian/Alaska Native (AI/AN) persons have approximately twofold the rate of acute HCV incidence and HCV associated mortality *(2).* In June 2012, the Indian Health Service (IHS) implemented HCV testing in the 1945–1965 birth cohort and created a nationally standardized performance measure to monitor implementation of the recommendation. As of June 2015, the proportion of the birth cohort screened for HCV increased from a baseline of 7.9% (14,402/182,503) to 32.5% (68,514/211,014) among the AI/AN population served by IHS nationwide; provider training and the use of clinical decision tools were associated with increases in HCV testing. With this fourfold increase in testing in just 3 years, IHS needs to prepare for the challenges associated with increased identification of persons living with HCV infection.

IHS provides care to approximately 1.9 million AI/AN members of 566 federally recognized tribes through a large network of health care facilities. IHS operates 46 hospitals, 344 health centers, and 230 village clinics and health stations in 35 states.* Among hospitals and health clinics, 77% (300/390) are tribally operated, and the remainder are federally operated. Most facilities provide primary care in remote and rural settings.

An estimated 85% of IHS facilities use a common electronic health record (EHR), which routinely provides data to monitor a set of preventive health performance measures through the electronic Clinical Reporting System (CRS). In 2011, annual† HCV antibody testing of the birth cohort was added as a performance measure to establish a baseline in anticipation of the release of expanded CDC recommendations for HCV testing in August 2012. HCV testing coverage is measured as the proportion of the total health care users within the population (i.e., AI/AN residents of a defined catchment community with at least one clinical visit in the past 3 years) born during 1945–1965 with at least one documented HCV antibody test and no previous recorded diagnosis of HCV infection. Persons with current HCV infection were identified using *International Classification of Disease* (ICD) codes. HCV antibody testing was ascertained using Current Procedural Terminology (CPT), Logical Observation Identifiers Names and Codes, or local facility taxonomies.§ Nationally, CRS reports HCV antibody tests performed in patients in all federal and tribal facilities by sex and age. Data from federally operated IHS facilities were further stratified by facility, sex, and age; because of current data sharing agreements, such stratification was not performed on data from tribal facilities. No patient-level data are shared on the CRS platform. Results from HCV antibody tests are not available in aggregate, and thus, are not reported here.

Because IHS facilities are decentralized, implementation of HCV testing for persons in the birth cohort is a local decision based on capacity and priorities. With the publication of HCV screening recommendations by CDC in August 2012, support for HCV testing was integrated into existing programs using methods and strategies that have been documented as successful in IHS facilities (e.g., EHR clinical decision support tools, local testing policies, and nursing collaborative agreements to order laboratory tests for indicated testing procedures) (*7*). Based on best practices identified nationally, regionally, and locally, IHS also implemented clinical trainings and obtained telehealth support. Provider training and other technical assistance were offered to all facilities; however, their use was optional.

During 2012–2015, the unique birth cohort patients tested for HCV antibody in combined federal and tribal IHS facilities increased fourfold from 14,402 (7.9%) to 68,514 (32.5%) (Table 1). HCV testing was higher among females across all years (Table 1). The 62 federally operated service units¶ accounted for 53% (112,319/211,014) of the total IHS birth cohort population eligible for testing in 2015; facilities in the

*An IHS health station is an ambulatory care facility (fixed or mobile) that is geographically separate from an inpatient hospital or health center, provides one or more clinical services, and is operated <40 hours per week.

†The IHS CRS data year is July–June. All annual data cited in this report for 2012–2015 represents the data report period of July 2011–June 2015.

§HCV purpose of visit codes defined as ICD-9 codes 070.41, 070.44, 070.51, 070.54, 070.70 through 070.71, V02.62; ICD-10: B17.10, B17.11, B18.2, B19.20, and B19.21. HCV antibody test is determined by CPT 86803.

¶The 90 federally operated physical health care facilities are grouped into 62 federally operated service units for purposes of administration and data. For example, a service unit might consist of a hospital plus two nearby clinics.

TABLE 1. Hepatitis C virus antibody testing (cumulative) among persons born during 1945–1965, by total eligible population and sex — Indian Health Service, 2012–2015

Year (total eligible population)	No. tested (% coverage)	No. male (%)	No. female (%)
2012 (N = 182,503)	14,402 (7.9)	5,617 (6.8)	8,785 (8.7)
2013 (N = 195,623)	20,419 (10.4)	7,591 (8.7)	12,828 (11.9)
2014 (N = 214,340)	52,971 (24.7)	20,859 (21.8)	32,112 (27.0)
2015 (N = 211,014)	68,514 (32.5)	27,636 (29.3)	40,878 (35.0)

TABLE 2. Hepatitis C virus antibody testing (cumulative) among persons born during 1945–1965, by Indian Health Service federally operated facilities and region,* 2015

Region	No. of facilities	Total eligible population	No. tested (% coverage)	Coverage range among facilities
Northern plains	21	31,206	9,927 (31.8)	18.4%–66.6%
Southern plains	12	9,579	3,009 (31.4)	6.5%–70.5%
Southwest	21	64,120	26,424 (41.2)	1.9%–69.4%
East	3	602	188 (31.2)	15.6%–44.7%
Pacific coast	6	6,812	2,444 (35.9)	21.3%–75.1%
Total	**62**	**112,319**	**41,992 (37.4)**	**1.9%–75.1%**

* *Northern plains*: Iowa, Minnesota, Montana, Nebraska, South Dakota; *Southern plains*: Oklahoma, Texas; *Southwest*: Arizona, Colorado, New Mexico, Nevada, Utah; *East*: Maine, Massachusetts, North Carolina; *Pacific coast*: Idaho, Oregon, Washington.

Southwest region, which is the most populous among the federally operated facilities, had the highest testing rates (Table 2).

By June 2015, the proportion of the birth cohort tested by geographic regions varied from 31.2% to 41.2%. However, there was much greater variation in birth cohort testing observed by facility, ranging from 1.9% to 75.1%. The average testing coverage of the birth cohort among federal facilities in the top testing quartile was 58.5% (17,288/29,606); 14 (93%) of the 15 facilities had deployed the HCV clinical decision support testing reminder as of June 2015. Among the bottom quartile of federal facilities, none had implemented a clinical decision tool; average testing coverage of the birth cohort was 16.4% (2,781/17,128).

Discussion

IHS expansion of HCV testing of the birth cohort has been highly successful, resulting in a fourfold increase in testing overall. Substantial increases were observed nationwide, with wide variability at the facility level. Testing rates in all regions were higher for women, possibly attributable to higher rates of health care utilization and therefore more opportunities to screen.

Reductions in HCV-associated morbidity and mortality are only possible through follow-up of persons found to be seropositive, including confirmation of HCV viremia, genotyping, and liver disease staging/assessment for treatment. To increase the likelihood of successful treatment outcomes, it is also critical that persons living with HCV receive counseling and are linked to behavioral health interventions, including those aimed at reducing alcohol use when appropriate. Compared with other racial/ethnic populations, alcohol-related death rates are higher among AI/ANs, placing these persons at increased risk for progression of HCV-associated morbidity and liver disease (*8*). Other cofactors affecting disease progression (e.g., human immunodeficiency virus) must also be considered as part of routine clinical follow-up care for HCV infection.

Follow-up HCV care and treatment services for persons tested and found to be living with HCV infection have been implemented in several IHS facilities, including some that are located in remote settings with limited referral options. These care and treatment programs are led by a variety of primary care providers (e.g., physicians, nurses, and pharmacists), generally in collaboration with a specialist through telehealth programs that have proven to be effective (e.g., Extension for Community Healthcare Outreach programs) (*9*).

Although IHS has had success in increasing HCV testing, challenges remain. Clinical capacity remains a substantial barrier to providing the care and treatment necessary for cure. Despite the availability of highly effective and safe HCV therapies that can reach sustained virologic response (cure) within 12 weeks, some primary care providers remain hesitant to provide treatment because they associate HCV medications with previously used interferon-based treatment regimens that were complicated, lengthy, and poorly tolerated. Furthermore, the cost of the new HCV drugs can be prohibitive; currently, the vast majority of IHS patients obtain HCV medication at no cost through state Medicaid and pharmaceutical manufacturer patient assistance programs. It is unclear if this approach will be sustainable as a larger number of AI/AN persons with HCV infection are identified and linked to care.

The findings in this report are subject to at least four limitations. First, HCV seroprevalence could not be estimated at a national level due to lack of laboratory test results or other standardized and reliable indicators of infection. However, work is underway to identify and standardize data sources to obtain accurate national estimates; preliminary data suggest estimates of HCV antibody or RNA positivity range from 2% to 10% based on ICD codes. Second, migration of approximately 15% of facilities to private sector electronic health records that do not interface with IHS electronic systems are not included in this analysis. Third, improvements in HCV testing cannot be attributed to any specific intervention strategies using observational data. However, the higher rates of HCV testing observed among the facilities that implemented an EHR decision tool compared with those that did not suggest that such tools substantially contributed to higher testing rates. Finally, provider training and other technical assistance

Summary

What is already known about this topic?

Hepatitis C virus (HCV) is an increasing cause of morbidity and mortality in the United States, and disproportionally affects American Indians/Alaska Natives. Curative HCV therapies provide an opportunity to reduce the prevalence of HCV infection in the United States. Adults born during 1945–1965 (birth cohort) account for approximately 75% of the estimated 3.5 million persons with HCV infections in the United States and are recommended to receive one-time testing for HCV.

What is added by this report?

In June 2012, the Indian Health Service (IHS) implemented national recommendations for one-time HCV testing in the birth cohort. During 2012–2015 HCV testing coverage in the American Indian/Alaska Native birth cohort increased from 7.9% to 32.5% in IHS facilities serving largely remote and rural populations across 35 states. Testing coverage in individual IHS facilities ranged from 1.9% to 75.1%; the largest increase occurred among facilities that deployed an electronic clinical decision support tool for HCV testing.

What are the implications for public health practice?

Identifying persons with HCV infection in American Indian/Alaska Native populations is a priority. Implementation of clinical decision tools should be considered to improve testing and detection; clinical capacity should be adequate to provide the follow-up care and treatment necessary for cure.

could not be quantified systematically, because response and implementation varied widely among IHS facilities. Additional investigation is needed to better understand why some facilities have adopted testing more readily than others and to determine the extent to which use of clinical decision tool reminders contributed to higher coverage rates.

HCV-related morbidity and mortality are now largely preventable, and IHS is committed to ensuring that HCV infections are diagnosed, and that persons with HCV infection in AI/AN communities receive timely access to care and treatment. Successful implementation of HCV testing of the birth cohort as recommended by CDC and USPSTF has been demonstrated in IHS facilities providing health care services in largely remote and rural sites and might represent best practices for health networks operating in similar settings. Next steps include estimating seroprevalence of and confirmation of HCV infection in preparation to scale up the capacity to care for AI/AN living with current infection. IHS will also continue to develop strategies to overcome anticipated future cost-associated barriers to HCV treatment and cure.

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Progress Toward Polio Eradication — Worldwide, 2015–2016

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In 1988, the World Health Assembly resolved to eradicate poliomyelitis. Wild poliovirus (WPV) transmission persists in only two countries (Afghanistan and Pakistan) after the removal of Nigeria from the list of countries with endemic polio in September 2015.* Indigenous WPV type 2 has not been detected since 1999 and was declared eradicated by the Global Commission for the Certification of Poliomyelitis Eradication in September 2015.† Since November 2012, when the last case of WPV type 3 was detected in Nigeria, WPV type 1 has been the sole circulating type of WPV (*1*). This report summarizes global progress toward polio eradication during 2015–2016 and updates previous reports (*2*). In 2015, 74 WPV cases were reported in two countries (Afghanistan and Pakistan), a decrease of 79% from the 359 WPV cases reported in 2014 in nine countries; 12 WPV cases have been reported in 2016 (to date), compared with 23 during the same period in 2015 (*3*). Paralytic polio caused by circulating vaccine-derived poliovirus (cVDPV) remains a risk in areas with low oral poliovirus vaccine (OPV) coverage. Seven countries, including Pakistan, reported 32 cVDPV cases in 2015 (*4*). In four of these countries, ≥6 months have passed since the most recent case or isolate. One country (Laos) with VDPV transmission in 2015 has reported three additional cVDPV cases in 2016 to date. Encouraging progress toward polio eradication has been made over the last year; however, interruption of WPV transmission will require focus on reaching and vaccinating every missed child through high quality supplementary immunization activities (SIAs) and cross-border coordination between Afghanistan and Pakistan (*5*,*6*).

Routine Poliovirus Vaccination Coverage

Estimated global coverage among infants aged ≤1 year with 3 doses of OPV (OPV3) through routine immunization was 88% in 2014 (the most recent year for which complete data are available). WHO and the United Nations Children's Fund estimate that OPV3 coverage by WHO region was 80% in the African Region, 86% in the Eastern Mediterranean Region, 95% in the European Region, 90% in the Region of the Americas, 90% in the South-East Asia Region, and 87% in the Western Pacific Region; considerable inter- and intra-country variability exists. National OPV3 coverage was 75% in Afghanistan and 72% in Pakistan; coverage is estimated to be substantially lower in areas with WPV transmission (*5*–*7*).

* http://www.who.int/mediacentre/news/releases/2015/nigeria-polio/en/.

† http://www.polioeradication.org/mediaroom/newsstories/Global-eradication-of-wild-poliovirus-type-2-declared/tabid/526/news/1289/Default.aspx.

Supplementary Immunization Activities (SIAs)

In 2015, approximately 2 billion OPV doses were administered during 231 SIAs in five WHO regions (Table 1), including 1.2 billion doses administered during national immunization days, 770 million during subnational immunization days, 11 million during child health days, and 22 million during large-scale door-to-door SIAs ("mop-up" activities) in areas where poliovirus was known or suspected to be circulating. Approximately 1.2 billion of the administered doses were trivalent (tOPV, containing OPV types 1, 2, and 3), 843 million were bivalent (bOPV, containing types 1 and 3), and 5 million were monovalent type 1 OPV doses.

Poliovirus Surveillance

Polio cases caused by either WPV or cVDPV are detected through surveillance for acute flaccid paralysis (AFP) and subsequent stool specimen testing at WHO-accredited laboratories in the Global Polio Laboratory Network. The main indicators of adequate surveillance include 1) an annual nonpolio AFP rate of ≥1 case per 100,000 population aged <15 years for countries in WHO regions certified as polio free, or a rate of ≥2 for all other countries and 2) adequate stool specimens collected from ≥80% of reported AFP cases.§ In 2015, both performance indicators were met nationally in six (75%; Afghanistan, Guinea, Myanmar, Nigeria, Pakistan, and Ukraine) of the eight countries reporting WPV and cVDPV cases during 2015–2016. Although Afghanistan and Pakistan both met these AFP surveillance indicators, evidence suggests ongoing gaps in AFP surveillance quality, based on review of case epidemiology, results of environmental sampling, and subnational indicators (*8*).

§ Adequate stool specimens require two stool specimens collected ≥24 hours apart, within 14 days of paralysis onset, with arrival at a WHO-accredited laboratory in good condition.

TABLE 1. Number of supplementary immunization activities (SIAs) conducted and number of oral poliovirus vaccine (OPV) doses administered, by World Health Organization (WHO) region — worldwide, 2014–2015

WHO region	2014		2015	
	SIAs	OPV doses	SIAs	OPV doses
African	142	775,972,255	117	766,000,000
Region of the Americas	0	0	0	0
Eastern Mediterranean	183	639,908,596	101	495,000,000
European	8	6,351,137	3	8,000,000
South-East Asia	6	800,605,667	8	756,000,000
Western Pacific	2	32,827,615	2	210,000
Overall	**341**	**2,255,655,270**	**231**	**2,025,210,000**

Reported Poliovirus Cases

Countries reporting WPV cases. In 2015, a total of 74 WPV cases were identified (Figure); 54 (73%) were detected in Pakistan, and 20 (27%) were detected in Afghanistan. No WPV cases were identified in countries outside of Pakistan and Afghanistan during 2015–2016 (to date). During January 1–May 4, 2016, the low transmission season for polio, 12 cases were reported worldwide; eight were detected in Pakistan and four in Afghanistan (Table 2).

Afghanistan reported 20 cases in 16 districts in 2015, compared with 28 cases in 19 districts in 2014, representing a 29% reduction in the number of cases reported. In 2015, 40% of cases were reported from Nangarhar province in the eastern region. During January 1–May 4, 2016, four WPV cases were detected (three in Kunar province in the eastern region and one in Helmand province), compared with one case detected during the same period in 2015.

Pakistan reported an 82% decrease in the number of WPV cases reported, from 306 cases in 44 districts in 2014 to 54 cases in 23 districts in 2015. During January 1–May 4, 2016, eight WPV cases were reported, compared with 22 cases during the same time period in 2015, representing a 64% decrease. All five regions reporting WPV in Pakistan reported a decreased number of cases in 2015; the decrease was largest (91% reduction in cases) in the Federally Administered Tribal Areas.

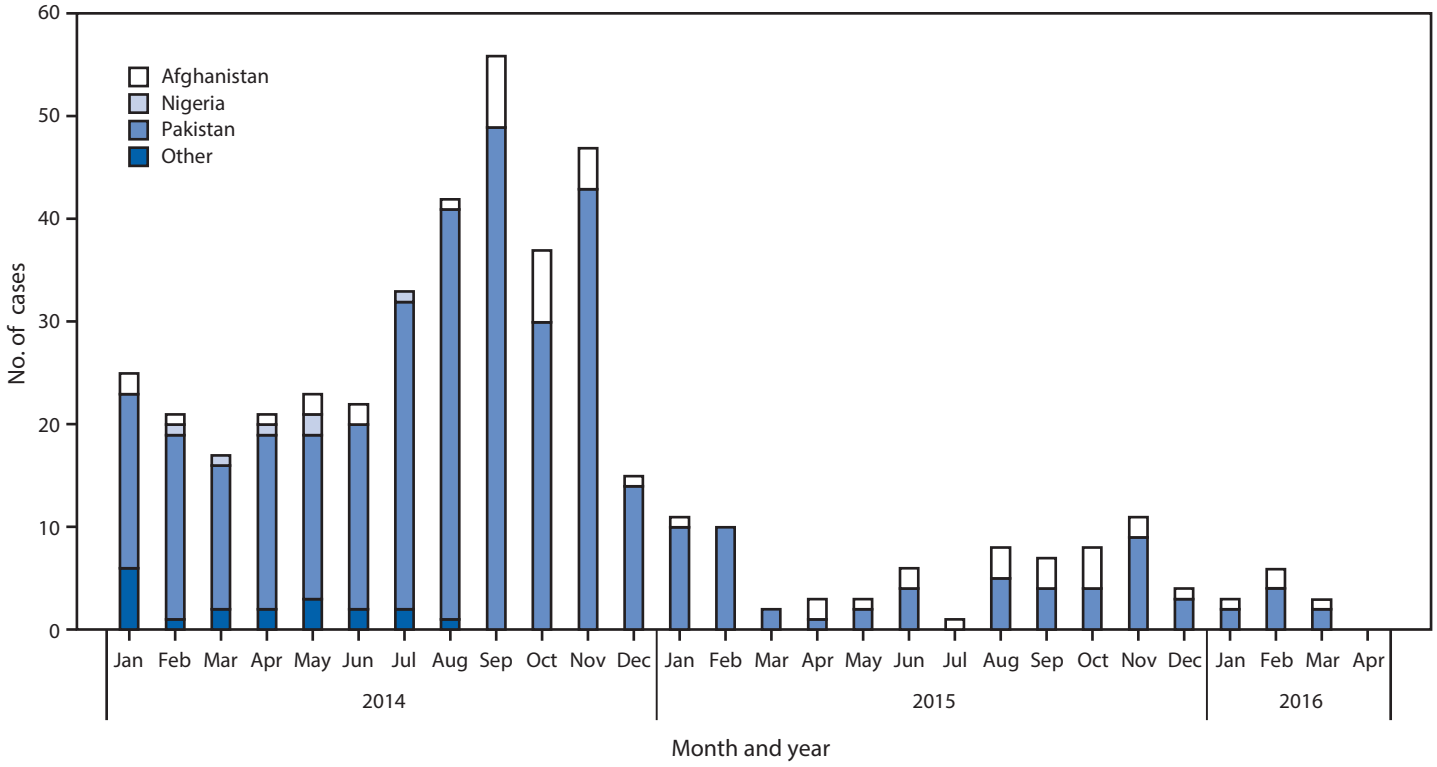
TABLE 2. Number of reported poliovirus cases, by country — worldwide, January 1, 2014–May 4, 2016

	2014 (January–December)		2015 (January 1–May 4)		2016 (January 1–May 4)	
Country	WPV	cVDPV	WPV	cVDPV	WPV	cVDPV
Countries with endemic polio						
Afghanistan	20	0	1	0	4	0
Pakistan	54	2	22	1	8	0
Total	**74**	**2**	**23**	**1**	**12**	**0**
Other countries with reported cVDPV cases						
Guinea	0	7	0	0	0	0
Laos	0	8	0	0	0	3
Madagascar	0	10	0	0	0	0
Myanmar	0	2	0	0	0	0
Nigeria	0	1	0	0	0	0
Ukraine	0	2	0	0	0	0
Total	**0**	**30**	**0**	**0**	**0**	**3**
Overall	**74**	**32**	**23**	**1**	**12**	**3**

Abbreviations: cVDPV = circulating vaccine-derived poliovirus; WPV = wild poliovirus.

Countries reporting cVDPV cases. In 2015, a total of 32 cVDPV cases were reported from seven countries. Outbreaks of cVDPV type 1 (cVDPV1) occurred in Laos (eight cases), Madagascar (10 cases), and Ukraine (two cases), and outbreaks of cVDPV type 2 (cVDPV2) occurred in Guinea (seven cases), Myanmar (two cases), Nigeria (one case), and Pakistan (two cases).

FIGURE. Number of cases of wild poliovirus worldwide — January 1, 2014–May 4, 2016*



* Other countries include Cameroon (n = 5), Equatorial Guinea (n = 5), Ethiopia (n = 1), Iraq (n = 2), Somalia (n = 5), and Syria (n = 1).

Four of the seven countries with cVDPV cases in 2015 had continued transmission from cVDPV cases in 2014, including Guinea (one case), Madagascar (one case), Nigeria (30 cases), and Pakistan (21 cases). Countries reporting cVDPV cases in 2015 with ≥6 months since the most recent case include Pakistan (most recent case February 9, 2015), Ukraine (July 7, 2015), Madagascar (August 22, 2015), and Myanmar (October 5, 2015). Laos reported three additional cVDPV1 cases in 2016 (to date), for a total of 11 cases during the outbreak; to date, no cVDPV2 cases have been reported in 2016. However, an environmental sample collected in Borno State, Nigeria, in March 2016 recently tested positive for cVDPV2 and is linked to prior circulation.

Discussion

Substantial gains toward polio eradication were made in 2015, with a 79% decrease in the number of polio cases reported worldwide compared with the number of cases reported in 2014. The removal of Nigeria from the list of countries with endemic polio in 2015 creates the opportunity for the African Region to join the Region of the Americas and the South-East Asia, Western Pacific, and European regions, as the fifth of six WHO regions to be certified free of indigenous WPV. Certification will occur after a minimum of 3 years of sensitive AFP surveillance. In addition, the Global Commission for the Certification of Poliomyelitis Eradication's declaration of the eradication of WPV type 2 in 2015, and the absence of reported circulation of WPV type 3 since 2012, allows focus on WPV type 1 as the sole circulating type of WPV in the world, endemic only in Afghanistan and Pakistan. WHO considers the continued transmission of WPV type 1 between both countries to constitute a public health emergency of international concern under the 2005 International Health Regulations.[¶] Continued focus on identifying groups of children who missed polio vaccination through routine immunization or SIAs, improving SIA quality, and increasing AFP surveillance sensitivity in these countries is needed to stop transmission.

In 2015, Afghanistan had a major reduction in WPV cases. The majority of cases were reported from Nangarhar province in eastern Afghanistan, which borders Pakistan, and were genetically linked to cases in Pakistan, emphasizing the need for continued improvement of cross-border coordination and SIA synchronization. Although some children are missed during SIAs in Afghanistan because of inaccessibility and security concerns, the majority are missed during SIAs because of managerial issues, including inadequate microplanning and campaign implementation. The southern region, although accessible for program implementation, has very limited access for supervision and monitoring. Innovative approaches, such as the 4th-day revisit strategy during campaigns, the use of permanent vaccination teams dedicated to regular house-to-house visits, and vaccination at transit points leading in and out of insecure areas need to continue to be regularly used to reach all missed children (*5*). The recent establishment of emergency operations centers at the national level and in three critical regions enhances the country's capacity to plan and implement polio eradication activities.

Progress in Pakistan accounted for most of the sharp decline in the number of polio cases during 2015–2016. The substantial gains made are, at least in part, attributable to the establishment of a cohesive national emergency operations center that implemented a rigorous National Polio Eradication Emergency Action Plan (*6*). However, operational problems with vaccination of all children during SIAs, program accountability at all levels, and ongoing movement of unvaccinated children across the Afghanistan-Pakistan border remain challenges facing the polio program in Pakistan.

Although no WPV cases were detected in countries without endemic WPV circulation, seven countries reported cVDPV outbreaks during 2015–2016, demonstrating the risk for VDPV emergence associated with low OPV coverage. In each of these countries, certain factors, such as the concurrent Ebola epidemic in Guinea and instability in vaccine procurement

Summary

What is already known about this topic?

Wild poliovirus (WPV) transmission is now endemic in only Afghanistan and Pakistan. During 2014–2015, outbreaks of WPV in five countries without endemic polio were successfully ended, and Nigeria was removed from the list of countries with endemic polio transmission.

What is added by this report?

WPV transmission has continued in Afghanistan and Pakistan during 2016; compared with transmission in 2015, the number of WPV cases decreased. Circulating vaccine-derived poliovirus remains a risk in areas with low oral poliovirus vaccine (OPV) coverage, with five countries reporting ongoing outbreaks during 2015–2016. In April 2016, 154 countries and territories discontinued use of type 2 Sabin vaccine by simultaneously switching from trivalent OPV (containing types 1, 2, and 3) to bivalent OPV (containing types 1 and 3) for routine and supplementary immunization.

What are the implications for public health practice?

With progress made toward interruption of WPV transmission in Afghanistan and Pakistan, the world is closer than ever to the eradication of polio. To stop transmission, continued cooperation between the two countries is needed, with a focus on identifying groups of missed children, improving quality of supplementary immunization activities, and increasing the sensitivity of acute flaccid paralysis surveillance.

[¶] http://www.who.int/mediacentre/news/statements/2016/8th-IHR-emergency-committee-polio/en/.

and public trust in Ukraine, diminished the quality of routine immunization services and allowed the emergence and spread of the outbreaks. Approximately 95% of cVDPV cases since 2006 have been caused by cVDPV2 (*9*). Therefore, with certification of the eradication of WPV type 2, in April 2016, 154 of 155 planned countries and territories** discontinued use of type 2 Sabin vaccine by switching from tOPV to bOPV for routine and supplementary immunization during a globally synchronized initiative that spanned 2 weeks, from April 17–May 1, 2016 (*9*). The global switch from tOPV to bOPV will markedly reduce the risk associated with type 2 cVDPV emergence and transmission; however, the global community must continue to support strong routine immunization service delivery to curb the risk for type 1 or type 3 cVDPV outbreaks or transmission after WPV importation from countries with endemic poliovirus transmission.

With progress made during 2015–2016 toward interruption of WPV transmission in Afghanistan and Pakistan, the world is closer than ever to the eradication of polio. Continued cooperation between the two countries is needed for this goal to be reached. In addition, the greater worldwide community needs to remain vigilant in implementing the Global Polio Eradication Initiative's Polio Eradication and Endgame Strategic Plan for 2013–2018 to end WPV and VDPV transmission (*10*).

** http://www.polioeradication.org/mediaroom/newsstories/The-Global-Switch-As-It-Happens/tabid/526/news/1373/Default.aspx.

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Interim Guidance for Zika Virus Testing of Urine — United States, 2016

On May 10, 2016, this report was posted as an MMWR *Early Release on the* MMWR *website (http://www.cdc.gov/mmwr).*

Diagnostic testing for Zika virus infection can be accomplished using molecular and serologic methods. Real-time reverse transcription–polymerase chain reaction (rRT-PCR) is the preferred test for Zika virus infection because it can be performed rapidly and is highly specific (*1,2*). However, in most patients, Zika virus RNA is unlikely to be detected in serum after the first week of illness (*2,3*). Recent reports using adaptations of previously published methods (*2,4*) suggest that Zika virus RNA can be detected in urine for at least 2 weeks after onset of symptoms (*3,5–7*). Currently, the CDC Trioplex rRT-PCR assay is the only diagnostic tool authorized by the Food and Drug Administration for Zika virus testing of urine (*1*). Other laboratory-developed tests will need in-house validations to adequately characterize the performance of the assay and meet Clinical Laboratory Improvement Amendments requirements. Further investigation is needed to determine the sensitivity and utility of Zika virus rRT-PCR on urine specimens collected ≥14 days after onset of symptoms.

On the basis of the newly available data, CDC recommends that Zika virus rRT-PCR be performed on urine collected <14 days after onset of symptoms in patients with suspected Zika virus disease. Zika virus rRT-PCR testing of urine should be performed in conjunction with serum testing if using specimens collected <7 days after symptom onset (*8*). A positive result in either specimen type provides evidence of Zika virus infection. Procedures for the collection and submission of body fluids, including urine specimens, have been described previously (*9*). CDC recommendations for Zika virus testing of serum and other clinical specimens remain unchanged at this time (*8*). CDC will continue to review and update guidance for Zika virus testing as new data become available.

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Comparison of Test Results for Zika Virus RNA in Urine, Serum, and Saliva Specimens from Persons with Travel-Associated Zika Virus Disease — Florida, 2016

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In May 2015, Zika virus was reported to be circulating in Brazil. This was the first identified introduction of the virus in the Region of the Americas. Since that time, Zika virus has rapidly spread throughout the region. As of April 20, 2016, the Florida Department of Health Bureau of Public Health Laboratories (BPHL) has tested specimens from 913 persons who met state criteria for Zika virus testing. Among these 913 persons, 91 met confirmed or probable Zika virus disease case criteria and all cases were travel-associated (*1*). On the basis of previous small case studies reporting real time reverse-transcription polymerase chain reaction (RT-PCR) detection of Zika virus RNA in urine, saliva, and semen (*2*–*6*), the Florida Department of Health collected multiple specimen types from persons with suspected Zika virus disease. Test results were evaluated by specimen type and number of days after symptom onset to determine the most sensitive and efficient testing algorithm for acute Zika virus disease. Urine specimens were collected from 70 patients with suspected Zika virus disease from zero to 20 days after symptom onset. Of these, 65 (93%) tested positive for Zika virus RNA by RT-PCR. Results for 95% (52/55) of urine specimens collected from persons within 5 days of symptom onset tested positive by RT-PCR; only 56% (31/55) of serum specimens collected on the same date tested positive by RT-PCR. Results for 82% (9/11) of urine specimens collected >5 days after symptom onset tested positive by RT-PCR; none of the RT-PCR tests for serum specimens were positive. No cases had results that were exclusively positive by RT-PCR testing of saliva. BPHL testing results suggest urine might be the preferred specimen type to identify acute Zika virus disease.

Criteria for Zika virus testing included persons who experienced two or more of the following symptoms: rash, fever, arthralgia or conjunctivitis during or within 2 weeks of return from an area with Zika virus activity, or who had an epidemiologic link to a Zika virus–infected traveler (sexual partner, household member, etc.). RT-PCR was routinely performed on urine, serum, or saliva specimens collected within 21 days of symptom onset. Clinicians were informed that only the serum RT-PCR and antibody tests were to be used for diagnostic purposes. Urine and saliva RT-PCR tests were only used for surveillance purposes. Serologic testing was performed on all serum specimens included in this analysis. The probable case definition criteria for Zika virus disease, based on serology, required Zika virus–specific IgM antibodies and no dengue virus–specific IgM antibodies detected in serum or cerebrospinal fluid.

Zika virus RT-PCR was performed at BPHL using a laboratory-developed test based on a previously published protocol using two RT-PCR targets (*7*) (this is not the CDC Trioplex rRT-PCR assay authorized for emergency use by the Food and Drug Administration (*8*)). Specimens were tested in a primary assay, in duplicate in the same run, with a primer and probe set that detects all known genotypes of Zika virus, ZIKV 1086/1162c/1107FAM (later renamed ZIKV 1087/1163c/1108FAM). If detected in at least one of the duplicates, the same extract was tested with a secondary assay, in duplicate in the same run, with a primer and probe set that detects the Asian genotype currently circulating in the Western Hemisphere, ZIKV 4481/4552c/4507cFAM (unpublished Zika real time RT-PCR protocol, RS Lanciotti, Division of Vector-Borne Infectious Diseases, CDC, Fort Collins, Colorado, updated January 14, 2016).

Specimens reported as positive had cycle threshold (Ct) values ≤38 for at least one of the replicates in both the primary and secondary RT-PCR assays. Specimens reported as equivocal had a Ct value ≤38 in the primary assay, but not the secondary assay. For the purpose of this analysis, equivocal specimens were considered as negative. Specimens reported as negative had Ct values >38 in the primary assay and were not tested further. Zika virus and dengue virus IgM antibody testing was performed at BPHL using a laboratory-developed IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA) based on a CDC flavivirus MAC-ELISA protocol (*9*). In March 2016, BPHL transitioned to the Food and Drug Administration's Emergency Use Authorization Zika MAC-ELISA developed by CDC (*8*). Zika virus antigen and positive control material were provided by CDC. A positive/negative (P/N) ratio was calculated from results of the MAC-ELISA for each specimen tested and was interpreted as the following: P/N ratios <2 were reported as negative, P/N ratios 2–<3 were reported as equivocal, and P/N ratios ≥3 were reported as presumptive positive, as defined in the emergency use authorization.

As of April 20, 2016, 91 cases of travel-associated Zika virus disease had been reported in Florida. Urine specimens were collected from a total of 70 persons with Zika virus disease, and in 65 (93%) of the cases, the urine specimen was positive by RT-PCR (Figure). The five specimens that were negative by RT-PCR testing were collected on days 2, 5, 5, 7, and 14 after symptom onset. Viral RNA was detectable in urine as early as the 1st day of symptoms and as late as 20 days after onset of symptoms. Ten of 12 urine specimens (83%) collected 7–20 days after symptom onset were positive. Among 62 of the 65 cases with positive urine specimens by RT-PCR testing, both primer and probe sets were positive in duplicate reactions. For two of the three remaining cases, a saliva specimen also tested positive by RT-PCR.

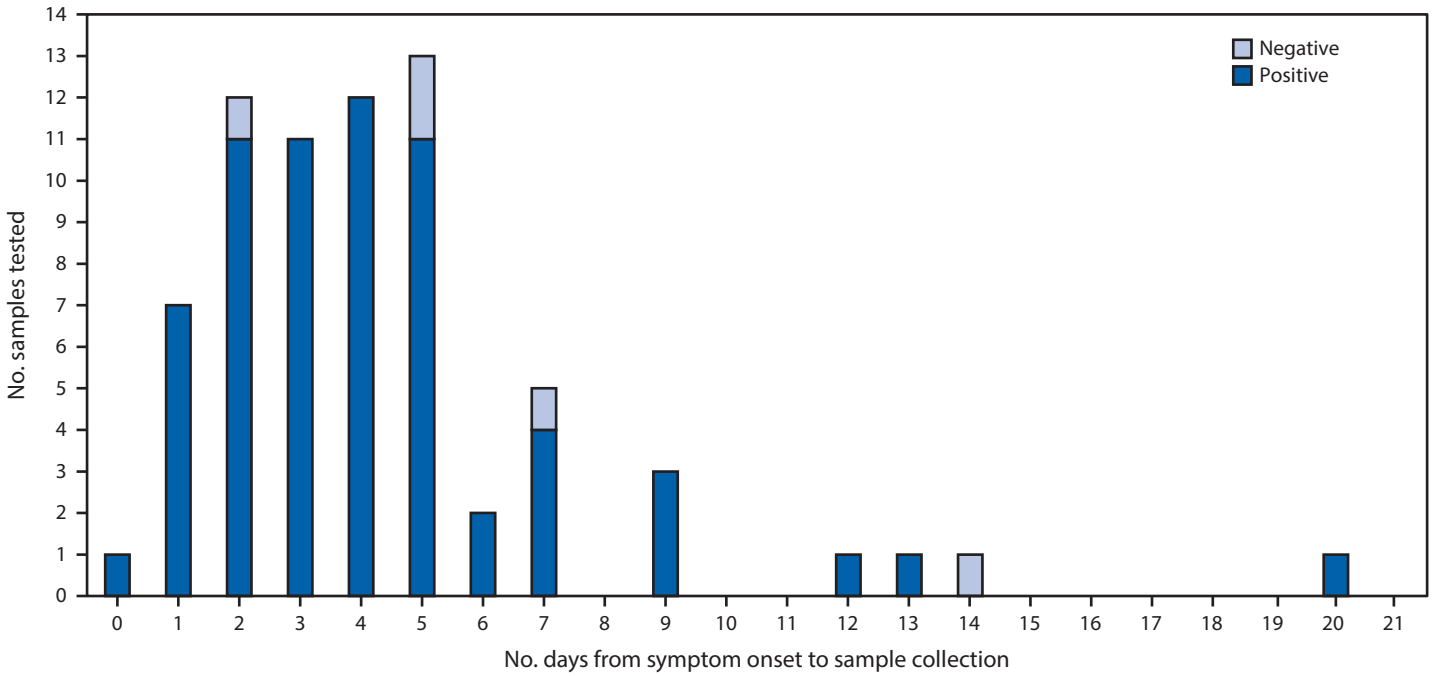
In 66 cases, persons had urine and serum specimens collected on the same day. The majority of these persons were female (64%), white (77%), and Hispanic (71%), with a median age of 46 years (range = 23–76 years). In two cases, female patients were pregnant. Approximately twice as many persons had RT-PCR positive test results for Zika virus RNA in urine specimens compared with serum specimens, 61 persons (92%) versus 31 (47%), respectively. One person had positive test results in serum alone (2 days after symptom onset) and 31 persons had positive test results only for urine specimens.

Among the 55 persons with urine and serum specimens collected within the first 5 days of symptom onset, 52 (95%) had urine specimens that tested positive for Zika virus RNA by RT-PCR testing and 31 (56%) had serum specimens that tested positive (Table 1). Forty percent (22/55) of the serum specimens had detectable Zika virus IgM antibodies, including two specimens collected 1 day after symptom onset. Among the 11 cases with specimens collected >5 days after symptom onset, nine persons (82%) had urine specimens that tested positive by RT-PCR; none had serum specimens that tested positive (Table 1).

Three specimen types collected on the same day were available for 53 of the 66 cases and were tested by RT-PCR: 92% of urine specimens, 81% of saliva specimens, and 51% of serum specimens tested positive. Viral RNA was detected in saliva as early as 1 day and as late as 20 days after symptom onset (Table 2). All cases with saliva specimens that tested positive for Zika virus RNA by RT-PCR testing also had at least one other specimen type that tested positive by RT-PCR testing.

Of the 66 serum specimens that also had paired urine specimens, five (8%) tested positive for both Zika virus RNA and IgM antibody (the five specimens were collected 1, 2, 3, 5, and 5 days after symptom onset) (Table 1). Among the 31 cases in which urine specimens tested positive by RT-PCR, but serum specimens tested negative, Zika virus IgM antibody was detected in serum

FIGURE. Results of RT-PCR testing for Zika virus RNA in urine specimens of 70 persons with travel-associated Zika virus disease, by number of days after onset of symptoms — Florida, 2016*



Abbreviation: RT-PCR = reverse transcription-polymerase chain reaction.

* Four persons included in figure did not contribute to the 66 persons with urine and serum specimens collected on the same day; each of these four persons had Zika virus RNA detected in their urine specimens, which were collected on days 3, 7, 12, and 13, respectively.

TABLE 1. Results of Zika virus IgM antibody testing of serum specimens and RT-PCR testing of serum and urine specimens for Zika virus RNA, by days after symptom onset for 66 persons with travel-associated Zika virus disease — Florida, 2016

Days after onset	Serum IgM No. positive/No. tested (%)	Serum RT-PCR No. positive/No. tested (%)	Urine RT-PCR No. positive/No. tested (%)
0	0/1 (0)	0/1 (0)	1/1 (100)
1	2/7 (29)	6/7 (85)	7/7 (100)
2	3/12 (25)	8/12 (67)	11/12 (92)
3	5/10 (50)	4/10 (40)	10/10 (100)
4	3/12 (25)	8/12 (67)	12/12 (100)
5	9/13 (69)	5/13 (38)	11/13 (85)
6	2/2 (100)	0/2 (0)	2/2 (100)
7	4/4 (100)	0/4 (0)	3/4 (75)
9	2/3 (67)	0/3 (0)	3/3 (100)
14	1/1 (100)	0/1 (0)	0/1 (0)
20	1/1 (100)	0/1 (0)	1/1 (100)
Range of days			
0–5	22/55 (40)	31/55 (56)*	52/55 (95)*
6–10	8/9 (89)	0/9 (0)*	8/9 (89)*
11–15	1/1 (100)	0/1 (0)	0/1 (0)
16–20	1/1 (100)	0/1 (0)	1/1 (100)

Abbreviations: IgM = immunoglobulin M; RT-PCR = real time reverse-transcription polymerase chain reaction.
* Statistically significant difference in proportion RT-PCR positive in serum specimens versus urine specimens, by exact McNemar's test (0–5 days, p<0.001; 6–10 days, p<0.01).

in 23 (74%). Of the remaining eight cases in which neither IgM antibodies nor viral RNA were detected in serum, Zika virus RNA was detected in saliva as well as urine in five cases (the five cases had all three specimens collected on days 2, 3, 4, 5, and 9 after symptom onset, respectively), and in three cases (serum and urine specimens collected days 0, 2, and 3, respectively) saliva specimens were not collected for testing. Overall, Zika virus IgM antibodies were detectable in the serum specimens from 48% of the 66 cases. Four of the 66 cases had serum and urine specimens that tested negative by RT-PCR testing, but positive (serum specimens only) by IgM antibody testing (specimens collected 5, 5, 7, and 14 days after symptom onset, respectively).

Discussion

Results of testing conducted at BPHL suggest that urine might be the preferred specimen type to identify acute Zika virus disease. Rates of detection from urine were higher than from serum, even during the first few days after symptom onset and continuing after day five, when no serum specimens tested in this evaluation had detectable RNA. Assays used for diagnostic purposes need to be validated for the specific specimen type being tested. The ability to confirm that a recent illness is caused by Zika virus and not another flavivirus by detection of Zika virus RNA in a clinical specimen is important, given the limitations in interpretation of results from serology testing in persons who have had previous flavivirus infection or vaccination. Among pregnant women, this ability to confirm Zika virus is important because close monitoring during pregnancy is recommended for women with confirmed Zika virus disease. The ease of collection of urine specimens is an additional advantage. This report also demonstrates that saliva specimens (another specimen that is easily obtained) can also yield a higher rate of RNA detection than serum even during the first 5 days; the detection rate in saliva also approaches the detection rate in urine. However, no cases were identified through saliva testing alone.

The findings in this report are subject to at least four limitations. First, eight patients from the group with serum and urine tested by RT-PCR who had RNA detected in their urine specimen but not in their serum specimen did not have Zika virus IgM antibodies detected in their serum to provide an independent confirmation of Zika virus infection. However, five of these eight patients had a saliva specimen available, and all five had viral RNA detected in

Summary

What is already known about this topic?

Limited data suggest Zika virus is excreted in multiple body fluids, including urine and saliva. Urine and saliva might be appropriate specimens for evaluating Zika virus disease.

What is added by this report?

A comparison of reverse-transcription polymerase chain reaction (RT-PCR) test results for urine and serum specimens from 66 persons with Zika virus disease with both specimens collected on the same date indicated that approximately twice as many urine specimens (61) than serum specimens (31) tested positive. No results from RT-PCR testing of serum specimens were positive >5 days after symptom onset; results from testing nine of 11 urine specimens were positive. A further comparison of 53 persons with Zika virus disease with urine, saliva, and serum specimens collected on the same date found positive results from testing in 49 (92%) urine specimens, 43 (81%) saliva specimens, and 27 (51%) serum specimens.

What are the implications for public health practice?

These results suggest urine might be a useful specimen for identifying acute Zika virus disease.

TABLE 2. Results of RT-PCR testing of urine, saliva, and serum specimens for Zika virus RNA, by days after symptom onset for 53 travel-associated cases of Zika virus disease — Florida, 2016

Days after onset	Urine No. positive/No. tested (%)	Saliva No. positive/No. tested (%)	Serum No. positive/No. tested (%)
1	7/7 (100)	7/7 (100)	6/7 (86)
2	9/9 (100)	9/9 (100)	6/9 (67)
3	9/9 (100)	8/9 (89)	4/9 (44)
4	9/9 (100)	8/9 (89)	7/9 (78)
5	10/12 (83)	9/12 (75)	4/12 (33)
6	1/1 (100)	0/1 (0)	0/1 (0)
7	2/3 (67)	0/3 (0)	0/3 (0)
9	1/1 (100)	1/1 (100)	0/1 (0)
14	0/1 (0)	0/1 (0)	0/1 (0)
20	1/1 (100)	1/1 (100)	0/1 (0)

Abbreviation: RT-PCR = real time reverse-transcription polymerase chain reaction.

saliva. The lack of IgM antibodies in some of the cases might be explained by the early timing of the serum collection; Zika virus IgM antibody might be detectable in serum specimens collected as early as 4–5 days after symptom onset, and is usually present by 7 days after symptom onset (*7*). However, convalescent serum specimens were not obtained to help confirm Zika virus disease by serology. Second, only five urine specimens came from patients >7 days after symptom onset; therefore the RNA detection rate in urine specimens from this period is not well characterized. However, the limited data available demonstrate that testing of some specimens can have positive results as far out as 20 days. Third, date of symptom onset can be difficult to ascertain, particularly in symptoms with mild symptoms. Therefore, the absolute rate of RNA detection for a particular day after symptom onset might be imprecise, but the relative detection rate across specimen types should not be impacted by this limitation. Finally, real-time RT-PCR results should be carefully interpreted to account for the possibility of false-negative and false-positive results, particularly at the lower limits of detection of the assay, when reproducibility is low and results are not confirmed with both primer/probe sets in replicate tests.

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Morbidity and Mortality Weekly Report

Reduced Incidence of Chikungunya Virus Infection in Communities with Ongoing *Aedes Aegypti* Mosquito Trap Intervention Studies — Salinas and Guayama, Puerto Rico, November 2015–February 2016

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Aedes species mosquitoes transmit chikungunya virus, as well as dengue and Zika viruses, and bite most often during the day.* Infectious mosquito bites frequently occur in and around homes (*1*,*2*). Caribbean countries first reported local transmission of chikungunya virus in December 2013, and soon after, chikungunya virus spread throughout the Americas (*3*). Puerto Rico reported its first laboratory-positive chikungunya case in May 2014 (*4*), and subsequently identified approximately 29,000 suspected cases throughout the island by the end of 2015.† Because conventional vector control approaches often fail to result in effective and sustainable prevention of infection with viruses transmitted by *Aedes* mosquitoes (*5*), and to improve surveillance of mosquito population densities, CDC developed an Autocidal Gravid Ovitrap (AGO) (*6*) to attract and capture the female *Aedes aegypti* mosquitoes responsible for transmission of infectious agents to humans (Figure). The AGO trap is a simple, low-cost device that requires no use of pesticides and no servicing for an extended period of time (*6*).

Since 2012, four communities in two municipalities in southern Puerto Rico, Salinas and Guayama, have participated in an ongoing field trial of AGO traps to control *Ae. aegypti* mosquitoes. Two intervention communities used three AGO traps per home for vector control whereas the other two, nonintervention communities, used only surveillance traps to monitor mosquito population densities. With AGO control traps placed around approximately 85% of homes in intervention communities in addition to randomly distributed surveillance traps, captures of adult *Ae. aegypti* mosquitos in the intervention communities decreased (*6*–*8*). From June 2014 to December 2014, after the identification of the first laboratory-positive chikungunya case, the average densities of *Ae. aegypti* female mosquitoes were 1.1 and 11.6 per surveillance trap per week in communities with and without AGO control traps, respectively (CDC, unpublished data), and this approximately tenfold difference in mosquito densities between the nonintervention and intervention areas remained relatively constant throughout 2015.

AGO traps have remained in place in the same configuration in the four communities from the start of the field trial to the present. Therefore, the introduction of chikungunya virus into the previously unexposed population of Puerto Rico provided a unique opportunity to assess whether the lower mosquito densities observed in areas with AGO traps were associated with reduced incidence of chikungunya virus infection through a serosurvey in these communities. A CDC Institutional Review Board approved a serosurvey for this purpose.

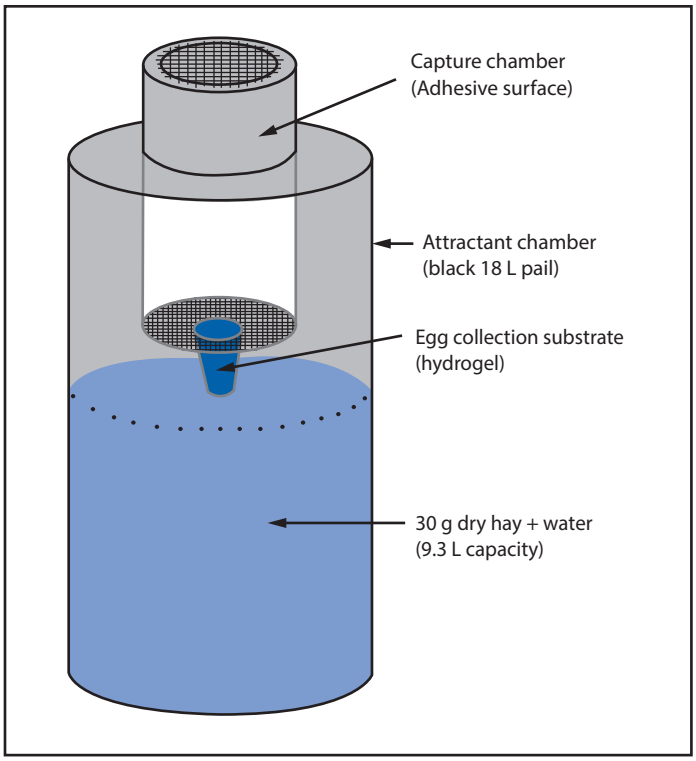
Stratified random sampling targeted 620 households from intervention and nonintervention communities, representing 28.5% of residents of the communities participating in the AGO field trial. Field personnel visited the selected households up to three times each to recruit household members for participation in the study. All residents of the selected households except children aged <5 years were eligible to participate. Participating household members provided a blood specimen and completed a questionnaire on household characteristics, demographics, history of recent illnesses, and personal mosquito bite prevention practices. Serum specimens were tested by immunoglobulin G (IgG) enzyme-linked immunosorbent assay (*9*) to detect evidence of chikungunya virus infection. The prevalence of chikungunya virus IgG antibody after the introduction of chikungunya virus in a population without previous chikungunya virus exposure provides a valid estimate of chikungunya virus incidence in residents of these communities.

This report contains preliminary results from data collected during November 2015–February 2016. In the sampling frame, 377 of 620 houses were occupied with a household member responding to field personnel visits. Of the 377 responding households from the two intervention and two nonintervention communities, 233 households (62%) participated in the study, and 327 (64%) of 511 eligible household members agreed to participate. The proportion of female participants (63%) and mean age of participants (53 years) were somewhat greater than those measures for all eligible household members (55%; 49 years). The female/male distribution and mean age of participants from intervention communities were not significantly different from those of participants from nonintervention communities. After

* http://www.cdc.gov/dengue/.

† Puerto Rico Department of Health. Chikungunya Weekly Report, 2014. http://www.salud.gov.pr/Estadisticas-Registros-y-Publicaciones/Pages/Chikungunya.aspx.

FIGURE. Diagram of an Autocidal Gravid Ovitrap used to attract and capture female *Aedes aegypti* mosquitoes — Salinas and Guayama, Puerto Rico



adjustment for sample design, the proportion of chikungunya virus IgG antibody among participants from the two intervention communities was one half that of participants from intervention communities (risk ratio = 0.52, 95% confidence interval = 0.38–0.71) (Table).

Lower incidence of chikungunya virus infection in the intervention compared with nonintervention communities occurred in the context of tenfold lower mosquito densities in the intervention areas with AGO traps. These preliminary findings suggest AGO traps might reduce virus transmission by reducing mosquito density. Additional data and statistical analyses are ongoing to account for nonresponse, adjust for age of participants and community characteristics, and evaluate associations between behaviors and chikungunya virus incidence. CDC produces AGO traps in limited numbers. To increase the availability of AGO traps for surveillance and for further studies of their use in control of *Ae. aegypti* mosquitoes in other settings and on a larger scale, efforts are under way for private sector companies to mass produce AGO traps of similar quality with comparable adult female *Ae. aegypti* mosquito capture rates.

TABLE. Crude prevalence of chikungunya virus IgG antibody among residents of four communities participating in vector control studies, community type — Salinas and Guayama, Puerto Rico, November 2015–February 2016

Community type	Participants	Anti-CHIKV IgG positive participants (%)
Nonintervention communities (no AGO traps)	152	69 (45.4)
Community A	103	42 (40.8)
Community B	49	27 (55.1)
Intervention communities (AGO traps present)	175	40 (22.9)
Community C	101	19 (18.8)
Community D	74	21 (28.4)

Abbreviations: AGO = Autocidal Gravid Ovitrap; CHIKV = chikungunya virus; IgG = immunoglobulin G.

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Notes from the Field

Probable Mucormycosis Among Adult Solid Organ Transplant Recipients at an Acute Care Hospital — Pennsylvania, 2014–2015

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On September 17, 2015, the Pennsylvania Department of Health (PADOH) notified CDC of a cluster of three potentially health care–associated mucormycete infections that occurred among solid organ transplant recipients during a 12-month period at hospital A. On September 18, hospital B reported that it had identified an additional transplant recipient with mucormycosis. Hospitals A and B are part of the same health care system and are connected by a pedestrian bridge. PADOH requested CDC's assistance with an on-site investigation, which started on September 22, to identify possible sources of infection and prevent additional infections.

Mucormycosis is a severe, often fatal infection caused by a group of angioinvasive molds. Outbreaks of health care–associated mucormycosis have been identified, most commonly in persons with marked immunosuppression, such as bone marrow and solid organ transplant recipients (*1*,*2*). Sources of these outbreaks are difficult to determine given that mucormycetes are ubiquitous environmental organisms. Past outbreaks have been associated with contaminated medical supplies and hospital construction projects (*3*,*4*). Performing an Infection Control Risk Assessment (ICRA) before and during construction or renovation projects is an important measure that can reduce the risk for health care–associated mucormycosis (*4*,*5*). An ICRA is a multidisciplinary approach used to mitigate environmental sources of microbes and to prevent infectious hazards through use of built environment design, ventilation and infrastructure support, and control measures implemented during construction or renovation (*6*).

A probable health care–associated case of mucormycosis was defined as identification of a mucormycete by culture or molecular testing in a diagnostic specimen from a person who had a history of solid organ transplantation, and admission to hospital A or B during May 2014–September 2015 for ≥14 days, within the 30 days before diagnosis. The period for cases was expanded beyond the 12-month period of infections to account for exposure time during hospitalization. Suspected cases were similarly defined as identification of a mucormycete in a diagnostic specimen by histopathology only or association with a hospital stay of 7–13 days before diagnosis. No infections were considered confirmed health care–associated cases because of uncertainties regarding the incubation period of mucormycosis (*3*).

The initial three cases were classified as probable and the fourth case as suspected. All four patients underwent solid organ transplantation during the same admission as their mucormycosis diagnosis and were receiving immunosuppressive medications as well as voriconazole for antifungal prophylaxis. The three probable cases were in patients who were primary heart (two cases) and lung transplant (one case) recipients who underwent transplantation 31–93 days before mucormycosis diagnosis. The suspected case occurred in a patient who had been admitted for a second liver transplant and was taking immunosuppressive medications at home; mucormycosis was diagnosed in this patient 13 days after admission, although signs compatible with invasive fungal infection started earlier in the admission. At least two different mucormycete species were isolated from the four patients. Three of the four patients had died before the arrival of the PADOH/CDC team.

The three patients with probable health care–associated mucormycosis all received care in the same room (room A) of the 20-bed cardiothoracic intensive care unit (CTICU) in hospital A for 14–58 days between their transplantations and mucormycosis diagnoses. Room A was the only negative-pressure isolation room in the CTICU and was adjacent to a door leading to a carpeted hallway and family room. Frequent use of this door by personnel and visitors might have disturbed airflow, allowing dust and mold spores, if present, to enter the room. None of the patients had a clinical indication requiring negative-pressure isolation. The patient with suspected health care–associated mucormycosis did not spend any time in room A of the CTICU or a negative-pressure room.

Before the PADOH/CDC on-site investigation had begun, hospital A had closed and deconstructed the CTICU for renovation. A mucormycete genetically unrelated to the patient isolates was recovered from one air sample from room A that hospital A obtained before the renovation work began. Multiple construction and demolition projects were occurring at or near hospitals A and B during the period when this cluster occurred. However, the hospital system reported performing ICRAs for these projects. No common construction-related exposure shared by the four patients was identified.

Although voriconazole is a commonly used antifungal prophylactic agent among transplant recipients in the United

States, it is ineffective against mucormycetes (*3*). Before the PADOH/CDC investigation, the hospital system changed the antifungal prophylactic agent used for transplant recipients to isavuconazole, a mucormycete-active prophylactic agent.

Hospitals A and B are no longer using negative-pressure rooms to house solid organ transplant patients who are without a clinical indication. Caring for immunosuppressed patients in negative-pressure environments has been previously identified as a risk factor for invasive mold infections, possibly related to the potential to concentrate dust and mold spores in these rooms (*7*). Negative-pressure rooms are recommended for isolation of patients with a suspected or confirmed airborne infectious disease; this investigation highlights how unnecessary placement of immunocompromised patients in negative-pressure rooms could result in net harm and therefore should be avoided.

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Announcement

National Stroke Awareness Month — May 2016

May is National Stroke Awareness Month, an observance that raises awareness of the signs and symptoms of stroke and encourages persons to act FAST (Face drooping, Arm weakness, Speech difficulty, Time to call 911) if someone is having a stroke. Stroke is the fifth leading cause of death in the United States and a leading cause of severe disability (*1*,*2*). In the United States, one person dies from stroke every 4 minutes (*2*).

Stroke can happen at any age, but increasingly younger persons are having strokes. About one in seven strokes occur in adolescents and young adults, aged 15–49 years (*3*). Certain groups of persons are more likely to have a stroke at younger ages. Several risk factors for stroke, such as stress, anxiety, and depression, are more common in women than men (*4*). African Americans aged <45 years have approximately twice the risk for stroke, compared with whites in that age group (*5*).

Stroke is preventable and treatable. Controlling blood pressure and living a healthy lifestyle (e.g., exercising; eating more fruits and vegetables and foods low in sodium or salt; and avoiding smoking) can reduce your chances of having a stroke.

CDC promotes stroke awareness through several initiatives. On May 17, CDC is hosting a Public Health Grand Rounds webcast on stroke that offers continuing education credits for public health professionals and health care providers. The Million Hearts initiative (http://millionhearts.hhs.gov/index.html), led by CDC and the Centers for Medicare & Medicaid Services, also promotes stroke prevention. More information about stroke prevention is available online from CDC's Division for Heart Disease and Stroke Prevention (http://www.cdc.gov/stroke/).

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Errata

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In the report, "*Mycobacterium abscessus* Infections Among Patients of a Pediatric Dentistry Practice — Georgia, 2015," on page 355, the first sentence should have read, "All water samples from the seven dental stations had bacterial counts above the **CDC** recommended ≤500 colony-forming units (CFU)/mL (average = 91,333 CFU/mL); *M. abscessus* was isolated from all water samples **(*3*)**."

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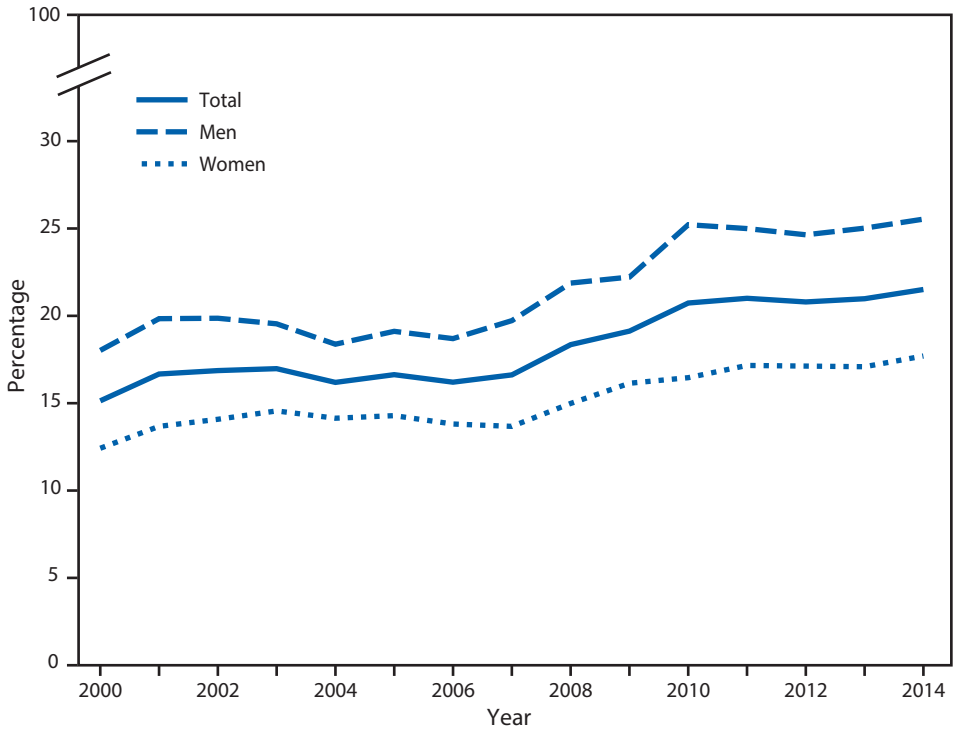
In the report, "Reduced Incidence of Chikungunya Virus Infection in Communities with Ongoing *Aedes Aegypti* Mosquito Trap Intervention Studies — Salinas and Guayama, Puerto Rico, November 2015–February 2016," the last sentence of the fifth paragraph should have read, "After adjustment for sample design, the proportion of chikungunya virus IgG antibody among participants from the two intervention communities was one half that of participants from **nonintervention** communities (risk ratio = 0.52, 95% confidence interval = 0.38–0.71) (Table)." The report was first published online as an Early Release on May 10, 2016, and is now contained in this regular May 13 issue.

In the report, "Interim Guidance for Zika Virus Testing of Urine — United States, 2016," the second sentence of the second paragraph should have read, "**Zika virus rRT-PCR testing of urine should be performed in conjunction with serum testing (*8*).**" The report was first published online as an Early Release on May 10, 2016, and is now contained in this regular May 13 issue.

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage of U.S. Adults Who Met the 2008 Federal Physical Activity Guidelines for Aerobic and Strengthening Activity,* by Sex — National Health Interview Survey,† 2000–2014



* Based on self-reports of frequency and duration of light-moderate and vigorous leisure-time aerobic physical activity and frequency of leisure-time strengthening activity at levels consistent with federal physical activity guidelines for adults (http://health.gov/paguidelines/guidelines/).

† Estimates are based on household interviews of a sample of the noninstitutionalized U.S. civilian population aged ≥18 years and are derived from the National Health Interview Survey sample adult component.

The percentage of U.S. adults who met the 2008 federal physical activity guidelines for Americans increased from 15.1% in 2000 to 21.5% in 2014. Most of the increase occurred from 2006 to 2010 for men and from 2007 to 2011 for women. During all years, men were more likely than women to meet the physical activity guidelines. In 2014, 25.5% of men and 17.7% of women met the guidelines.

Source: National Health Interview Survey, 2000–2014 data. http://www.cdc.gov/nchs/nhis.htm.

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