

Increased Gonorrhea Cases — Utah, 2009–2014

Joanna Watson, DPhil^{1,2}; Jerry Carlile, MSPH²; Angela Dunn, MD^{1,2}; Megan Evans²; Erin Fratto, MS²; Joel Hartsell, MPH²; Lynn Meinor²; Matthew Mietchen, MPH²; Allyn Nakashima, MD²

Gonorrhea (caused by infection with *Neisseria gonorrhoeae*) is the second most commonly reported notifiable disease in the United States (1). Left untreated, gonorrhea is associated with serious long-term adverse health effects, including pelvic inflammatory disease, ectopic pregnancy, and infertility. Infection also facilitates transmission of human immunodeficiency virus (2,3). Effective gonorrhea control relies upon early detection and effective antimicrobial treatment. To assess gonorrhea rate trends in Utah, the Utah Department of Health (UDOH) analyzed Utah National Electronic Disease Surveillance System (UT-NEDSS) data for the state during 2009–2014. After declining during 2009–2011, the statewide gonorrhea rate increased fivefold to 49 cases per 100,000 population in 2014. During 2009–2014, the proportion of cases among women increased from 21% to 39% (decreasing among males from 79% to 61%). Among male patients, the proportion who identified as men who have sex with men (MSM) decreased from 67% to 42%. These demographic changes suggest that increased heterosexual transmission of gonorrhea in Utah might be occurring. Health departments need to work with providers to ensure populations at high risk are being screened and properly treated for gonorrhea. Clinicians need to be aware of increases in the risk for infection among women and non-MSM males when making screening and testing decisions and educate their patients regarding gonorrhea transmission and prevention practices.

All cases of gonorrhea reported in Utah during 2009–2014 were included in the analysis. Data reported to UT-NEDSS were obtained from laboratory reports and local health department (LHD) case investigations. The majority of LHDs in Utah attempted to interview all gonorrhea patients. During interviews, LHD personnel obtained demographic information and details of sexual contacts (including, for male patients, sex of sex partner) during the 3 months preceding the diagnosis. LHDs obtained information about diagnosing provider type and treatment from laboratory reports or directly from providers.

For each year during 2009–2014, gonorrhea reporting rates (per 100,000 population overall and by sex, age group, and race/ethnicity) were calculated by dividing the number of laboratory-confirmed gonorrhea cases reported to UDOH by U.S. Census Bureau estimates of the Utah population for that year. Proportions were calculated for the following patient

INSIDE

- 894 CDC Grand Rounds: Preventing Suicide Through a Comprehensive Public Health Approach
- 898 Current Cigarette Smoking, Access, and Purchases from Retail Outlets Among Students Aged 13–15 Years — Global Youth Tobacco Survey, 45 Countries, 2013 and 2014
- 902 Epidemiology of Varicella During the 2-Dose Varicella Vaccination Program — United States, 2005–2014
- 906 Carbapenem-Resistant Enterobacteriaceae Transmission in Health Care Facilities — Wisconsin, February–May 2015
- 910 Guillain-Barré Syndrome During Ongoing Zika Virus Transmission — Puerto Rico, January 1–July 31, 2016
- 915 Likely Sexual Transmission of Zika Virus from a Man with No Symptoms of Infection — Maryland, 2016
- 917 Hearing Loss in Infants with Microcephaly and Evidence of Congenital Zika Virus Infection — Brazil, November 2015–May 2016
- 920 Notes from the Field: Cluster of Lymphogranuloma Venereum Cases Among Men Who Have Sex with Men — Michigan, August 2015–April 2016
- 922 QuickStats

Continuing Education examination available at http://www.cdc.gov/mmwr/cme/conted_info.html#weekly.



characteristics: sex of partner(s) (for men), diagnosis provider, whether the patient was interviewed by LHD, and whether the patient was treated.

During 2009–2011, the gonorrhea rate in Utah decreased from 12 to 10 cases per 100,000 population, before increasing in 2012, 2013, and 2014, to 17, 33, and 49 cases per 100,000, respectively (Table 1). During 2011–2014, the rate was higher among men (range = 14.9–59.2) than among women (range = 4.7–38.5); however, the percentage increase observed during 2011–2014 was substantially greater among women (715%) than among men (297%).

During 2009–2014, rates in Utah were consistently highest among persons aged 20–24 years and 25–29 years. However, the percentage of cases reported among persons in those two age groups combined (20–29 years) decreased each year, from 58% in 2009 to 49% in 2014. Throughout 2009–2014, the gonorrhea rate was highest among non-Hispanic blacks; however, the absolute number of cases was highest among non-Hispanic whites, who accounted for approximately 80% of Utah's population (Table 1).

The percentage of patients interviewed by LHDs each year ranged from 75% to 86%, and approximately 96% of patients had been treated for gonorrhea. During 2009–2014, the proportion of male gonorrhea patients self-reporting as MSM decreased 38%, from 66.8% to 41.7% (Table 2) (Figure). The proportion of male gonorrhea patients self-identifying as MSM differed markedly among racial/ethnic populations. During 2014, approximately 51% of non-Hispanic white men,

26% of Hispanic men, and 19% of non-Hispanic black men self-reported as MSM (Table 2).

The proportion of cases diagnosed at a sexually transmitted disease (STD) clinic decreased from 38% during 2009 to 20% during 2014. MSM were substantially more likely to have received a diagnosis at an STD clinic than both non-MSM men and women for all years during 2009–2014 (Table 2).

Discussion

The national gonorrhea rate declined approximately 74% during 1975–1997 (1). After 1997, the rate fluctuated, but continued to decrease, reaching an all-time low during 2009. The national rate increased each year during 2009–2012, and after decreasing slightly during 2013, increased again during 2014 (the most recent year for which national data are available) (1). During 2013, the national gonorrhea rate was higher among men than among women for the first time since 2000, and remained higher during 2014. In contrast, during 2000–2014, rates were consistently higher among men than among women in the West census region, including Utah (1). Higher gonorrhea rates among men than women indicate substantial transmission among MSM. However, other factors (e.g., screening or partner notification practices) also can affect the male-to-female case ratio. Although not all states collect such information for gonorrhea cases, in Utah, information on the sex of sex partner(s) is collected for male patients, and until 2012, indicated that the majority of gonorrhea cases in males were among MSM.

The *MMWR* series of publications is published by the Center for Surveillance, Epidemiology, and Laboratory Services, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30329-4027.

Suggested citation: [Author names; first three, then et al., if more than six.] [Report title]. *MMWR Morb Mortal Wkly Rep* 2016;65:[inclusive page numbers].

Centers for Disease Control and Prevention

Thomas R. Frieden, MD, MPH, *Director*
 Harold W. Jaffe, MD, MA, *Associate Director for Science*
 Joanne Cono, MD, ScM, *Director, Office of Science Quality*
 Chesley L. Richards, MD, MPH, *Deputy Director for Public Health Scientific Services*
 Michael F. Iademarco, MD, MPH, *Director, Center for Surveillance, Epidemiology, and Laboratory Services*

MMWR Editorial and Production Staff (Weekly)

Sonja A. Rasmussen, MD, MS, *Editor-in-Chief*
 Charlotte K. Kent, PhD, MPH, *Executive Editor*
 Jacqueline Gindler, MD, *Editor*
 Teresa F. Rutledge, *Managing Editor*
 Douglas W. Weatherwax, *Lead Technical Writer-Editor*
 Soumya Dunworth, PhD, Teresa M. Hood, MS,
Technical Writer-Editors

Martha F. Boyd, *Lead Visual Information Specialist*
 Maureen A. Leahy, Julia C. Martinroe,
 Stephen R. Spriggs, Moua Yang, Tong Yang,
Visual Information Specialists
 Quang M. Doan, MBA, Phyllis H. King, Terraye M. Starr,
Information Technology Specialists

MMWR Editorial Board

Timothy F. Jones, MD, *Chairman*
 Matthew L. Boulton, MD, MPH
 Virginia A. Caine, MD
 Katherine Lyon Daniel, PhD
 Jonathan E. Fielding, MD, MPH, MBA
 David W. Fleming, MD

William E. Halperin, MD, DrPH, MPH
 King K. Holmes, MD, PhD
 Robin Ikeda, MD, MPH
 Rima F. Khabbaz, MD
 Phyllis Meadows, PhD, MSN, RN
 Jewel Mullen, MD, MPH, MPA

Jeff Niederdeppe, PhD
 Patricia Quinlisk, MD, MPH
 Patrick L. Remington, MD, MPH
 Carlos Roig, MS, MA
 William L. Roper, MD, MPH
 William Schaffner, MD

TABLE 1. Number and rate* of gonorrhea cases, by sex, age group, and race/ethnicity — Utah National Electronic Disease Surveillance System, 2009–2014

Characteristic	2009	2010	2011	2012	2013	2014
	No. (Rate)	No. (Rate)	No. (Rate)	No. (Rate)	No. (Rate)	No. (Rate)
Total	341 (12.3)	310 (11.0)	277 (9.7)	480 (16.5)	951 (32.8)	1,442 (48.9)
Sex						
Male	271 (19.8)	235 (16.9)	211 (14.9)	348 (24.2)	578 (39.7)	878 (59.2)
Female	70 (5.2)	75 (5.4)	66 (4.7)	132 (9.3)	373 (25.9)	564 (38.5)
Age group (yrs)						
15–19	50 (22.7)	47 (21.3)	38 (17.4)	55 (25.1)	87 (39.1)	149 (65.5)
20–24	94 (41.3)	100 (43.8)	81 (34.7)	118 (48.8)	240 (97.6)	392 (156.5)
25–29	103 (45.0)	64 (27.7)	69 (30.6)	88 (40.4)	212 (95.6)	321 (148.4)
30–34	31 (14.6)	41 (18.8)	39 (17.4)	84 (37.0)	153 (66.2)	253 (109.2)
35–39	18 (10.3)	26 (14.6)	25 (13.7)	45 (23.5)	96 (49.3)	149 (72.8)
40–44	14 (9.3)	18 (11.6)	11 (6.8)	31 (18.7)	54 (32.1)	66 (37.9)
Race/Ethnicity						
White, non-Hispanic	236 (10.7)	254 (11.4)	206 (9.1)	315 (13.8)	667 (28.8)	930 (38.9)
Black, non-Hispanic	26 (100.4)	9 (33.9)	20 (73.1)	57 (198.5)	71 (237.4)	99 (322.4)
Hispanic	60 (17.3)	34 (9.4)	41 (11.1)	83 (22.0)	171 (44.1)	319 (80.5)
Asian	4 (7.5)	2 (3.6)	2 (3.5)	3 (5.0)	13 (20.6)	21 (32.8)
Native Hawaiian/Pacific Islander	3 (12.8)	3 (12.3)	3 (12.2)	5 (19.7)	7 (26.8)	18 (67.8)
American Indian/Alaska Native	2 (7.3)	6 (22.1)	5 (18.3)	14 (50.9)	20 (71.2)	15 (52.6)
Multiple race	1 (2.2)	0 (0)	0 (0)	1 (2.0)	2 (3.7)	5 (9.2)

* Per 100,000 population using U.S. Census Bureau estimates.

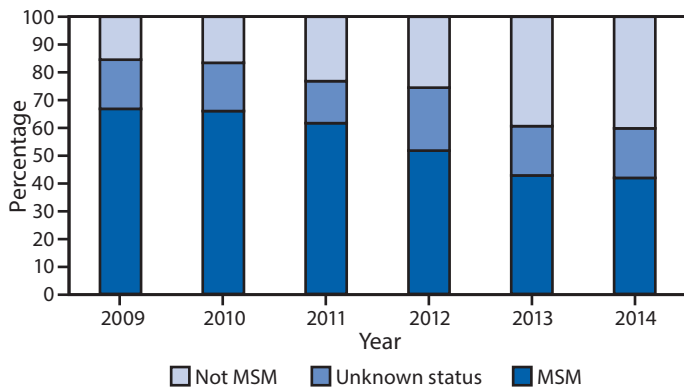
TABLE 2. Selected characteristics of reported gonorrhea cases obtained from local health department investigations, including patient interviews — Utah, 2009–2014

Characteristic	2009	2010	2011	2012	2013	2014	Total
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
MSM (% of male patients)							
Yes	181 (66.8)	155 (66.0)	130 (61.6)	180 (51.7)	247 (42.7)	366 (41.7)	1,259 (49.9)
No	42 (15.5)	39 (16.6)	49 (23.2)	89 (25.6)	227 (39.2)	352 (40.1)	798 (31.7)
Unknown	48 (17.7)	41 (17.5)	32 (15.2)	79 (22.7)	104 (18.0)	160 (18.2)	464 (18.4)
MSM (% of white male patients)							
Yes	146 (74.1)	131 (66.8)	112 (67.9)	145 (62.5)	205 (49.8)	284 (50.8)	1,023 (58.1)
No	16 (8.1)	30 (15.3)	28 (17.0)	46 (19.8)	133 (32.3)	176 (31.5)	429 (24.4)
Unknown	35 (17.8)	35 (17.9)	25 (15.2)	41 (17.7)	74 (18.0)	99 (17.7)	309 (17.5)
MSM (% of black male patients)							
Yes	10 (47.6)	2 (33.3)	3 (25.0)	5 (10.9)	4 (10.0)	15 (19.0)	39 (19.1)
No	8 (38.1)	3 (50.0)	9 (75.0)	24 (52.2)	25 (62.5)	49 (62.0)	118 (57.8)
Unknown	3 (14.3)	1 (16.7)	0 (0.0)	17 (37.0)	11 (27.5)	15 (19.0)	47 (23.0)
MSM (% of Hispanic male patients)							
Yes	19 (50.0)	20 (71.4)	15 (51.7)	24 (43.6)	27 (26.0)	49 (25.8)	154 (34.7)
No	15 (39.5)	3 (10.7)	8 (27.6)	17 (30.9)	62 (59.6)	112 (58.9)	217 (48.9)
Unknown	4 (10.5)	5 (17.9)	6 (20.7)	14 (25.5)	15 (14.4)	29 (15.3)	73 (16.4)
Diagnosing provider (MSM only)							
STD clinics	109 (60.2)	88 (56.8)	74 (56.9)	94 (52.2)	135 (54.7)	174 (47.5)	674 (53.5)
Other or unknown*	72 (39.8)	67 (43.2)	56 (43.1)	86 (47.8)	112 (45.3)	192 (52.5)	585 (46.5)
Diagnosing provider (non-MSM male only)							
STD clinics	15 (35.7)	2 (5.1)	9 (18.4)	22 (24.7)	51 (22.6)	70 (19.8)	169 (21.2)
Other or unknown*	27 (64.3)	37 (94.9)	40 (81.6)	67 (75.3)	176 (77.4)	282 (80.2)	629 (78.8)
Diagnosing provider (female only)							
STD clinics	3 (4.3)	3 (4.0)	5 (7.6)	17 (12.9)	44 (11.5)	42 (7.4)	114 (8.9)
Other or unknown*	67 (95.7)	72 (96.0)	61 (92.4)	115 (87.1)	329 (88.5)	522 (92.6)	1,166 (91.1)

Abbreviations: MSM = men who have sex with men; STD = sexually transmitted disease.

* Includes emergency department or urgent care, family planning or Planned Parenthood Association of Utah, prenatal or obstetrics, private physician or health maintenance organization, corrections facility, other unspecified providers, and unknown providers. Unknown ranges were 0%–3% among men and 0%–1.5% among women.

FIGURE. Percentage of male gonorrhea patients who self-reported as men who have sex with men (MSM) — Utah, 2009–2014



Since 2011, the gonorrhea rate in Utah has increased substantially, with a much larger percentage increase among women than among men. The proportion of male patients self-reporting as MSM has decreased each year since 2009, indicating an expansion of heterosexual transmission of gonorrhea in Utah.

These data indicate that, in Utah, MSM were more likely to have received a diagnosis of gonorrhea from an STD clinic than women and non-MSM men, whereas the proportion of cases diagnosed at STD clinics decreased during 2009–2014. Research conducted in California found that gonorrhea patients who received a diagnosis at STD clinics were more likely to receive treatment that adhered to CDC treatment guidelines than were patients who received a diagnosis in other clinical settings (4). The increase in both proportion and number of gonorrhea cases diagnosed outside of STD clinics underscores the importance of providing education to clinicians regarding local epidemiology of gonorrhea infection, treatment options, and availability of treatment methods, such as expedited partner therapy (5) (prescribing treatment for heterosexual sex partners of gonorrhea patients without physical examination, where legally permitted) (6). Expedited partner therapy for heterosexual sex partners of gonorrhea patients has been available since 2009 in Utah, where it is recommended only in cases where other management strategies are impractical or unsuccessful.

Reviewing public health intervention strategies based on changes in disease epidemiology also provides an opportunity to consider introduction of innovative methods for identifying and providing testing services to persons at high risk. Examples of methods used successfully elsewhere are computerized interviews self-administered to emergency department attendees to ascertain STD testing needs (7), and an Internet-based program to facilitate home STD testing using self-collected vaginal, urethral, and rectal swabs (8).

Summary

What is already known about this topic?

Until 2013, national gonorrhea rates among women were slightly higher than rates among men. The reported gonorrhea rate has increased each year since 2009, with the exception of a slight decrease during 2013. In contrast to national rates, multiple Western states have consistently reported substantially higher gonorrhea rates among men than among women, indicating high transmission levels among men who have sex with men (MSM). However, MSM status of patients is not always ascertained.

What is added by this report?

During 2009–2011, the gonorrhea rate in Utah decreased from 13 to 10 cases per 100,000 population, then increased to 17 cases in 2012, and 49 cases in 2014. The rate continued to be higher among men than among women; however, the increase was larger among women. Utah has collected reliable data regarding the sex of male gonorrhea patients' sex partners since 2009. The proportion of gonorrhea patients in Utah who self-reported as MSM decreased from 67% in 2009 to 42% in 2014. The proportion of gonorrhea patients in Utah who described themselves as MSM differed substantially by race/ethnicity.

What are the implications for public health practice?

Changes in case population demographics in Utah are indicative of an expansion in gonorrhea transmission to new sexual networks, with increased heterosexual transmission. This information will help to guide targeting of gonorrhea testing, treatment, and public health interventions.

In response to the increase in gonorrhea in Utah, UDOH formed a collaborative workgroup with multiple Utah LHDs. To gain a fuller understanding of the increase and the demographic changes associated with it, the workgroup developed a supplemental survey that was added to gonorrhea case investigation interviews during May–August 2014. The survey addressed the following topics: symptoms before diagnosis; health insurance; student status; places where patients met sex partners; sex with anonymous partners; drug and alcohol use; incarceration (of patient or partners); and gender (male, female, or transgender) of patients' sex partners. The survey findings will be used to guide a case-control study to identify risk factors for gonorrhea infection among adult Utah residents.

The findings in this report are subject to at least two limitations. First, reporting of all gonorrhea cases to public health officials is unlikely for a number of reasons, including underreporting by laboratories and providers, failure of infected persons to access care, and misdiagnosis. However, no substantial changes in gonorrhea testing or reporting methods were identified during 2009–2014; therefore, these factors are unlikely to account for the reported increase in diagnoses and reporting. Second, case interview data are missing for 14%–24% of patients, because of LHDs' inability to contact

the patient, not attempting to contact the patient, or patients declining to be interviewed.

Because of increasing numbers of gonorrhea cases in Utah, identifying populations at high risk is important to develop effective public health interventions. With likely increased heterosexual transmission and changes in the way patients are accessing services in Utah, health departments need to work with providers to ensure populations at high risk are being screened and properly treated for gonorrhea. In areas of the United States where gonorrhea has historically been associated with MSM, the public needs to be made aware of the potential for transmission into previously unaffected sexual networks, and the importance of STD testing for populations at risk needs to be reinforced. Clinicians need to be aware of changes in the risk for infection among women and non-MSM males when making screening and testing decisions and recommendations and educate their patients regarding gonorrhea transmission and prevention practices. Analysis of existing data and collection of additional data by other jurisdictions with substantial gonorrhea transmission among MSM might provide important information about whether similar demographic changes in reported gonorrhea cases are occurring in these areas as well.

Acknowledgments

Utah local health departments; Sarah Kidd, MD, Monica Patton, MD, Emily Weston, MPH, Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC.

¹Epidemic Intelligence Service, CDC; ²Utah Department of Health.

Corresponding author: Joanna Watson, wq6@cdc.gov, 509-354-8063.

References

1. CDC. 2014 Sexually transmitted diseases surveillance: gonorrhea. Atlanta, GA: US Department of Health and Human Services, CDC; 2015. <http://www.cdc.gov/std/stats14/gonorrhea.htm>
2. Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection. *Sex Transm Infect* 1999;75:3–17. <http://dx.doi.org/10.1136/sti.75.1.3>
3. Walker CK, Sweet RL. Gonorrhea infection in women: prevalence, effects, screening, and management. *Int J Womens Health* 2011;3:197–206.
4. Lechtenberg RJ, Samuel MC, Bernstein KT, Lahiff M, Olson N, Bauer HM. Variation in adherence to the treatment guidelines for *Neisseria gonorrhoeae* by clinical practice setting, California, 2009 to 2011. *Sex Transm Dis* 2014;41:338–44. <http://dx.doi.org/10.1097/OLQ.0000000000000113>
5. CDC. Guidance on the use of expedited partner therapy in the treatment of gonorrhea. Atlanta, GA: US Department of Health and Human Services, CDC; 2015. <http://www.cdc.gov/std/ept/gc-guidance.htm>
6. CDC. Legal status of expedited partner therapy (EPT). Atlanta, GA: US Department of Health and Human Services, CDC; 2016. <http://www.cdc.gov/std/ept/legal/>
7. Ahmad FA, Jeffe DB, Plax K, et al. Computerized self-interviews improve *Chlamydia* and gonorrhea testing among youth in the emergency department. *Ann Emerg Med* 2014;64:376–84. <http://dx.doi.org/10.1016/j.annemergmed.2014.01.031>
8. Gaydos CA, Barnes M, Jett-Goheen M, et al. Characteristics and predictors of women who obtain rescreening for sexually transmitted infections using the www.iwantthekit.org screening programme. *Int J STD AIDS* 2013;24:736–44.

CDC Grand Rounds: Preventing Suicide Through a Comprehensive Public Health Approach

Corinne David-Ferdon, PhD¹; Alex E. Crosby, MD¹; Eric D. Caine, MD²; Jarrod Hindman, MS³; Jerry Reed, PhD^{2,4}; John Iskander MD⁵

Suicide in the United States is a major public health problem with approximately 42,000 reported suicides in 2014 among persons aged ≥ 10 years (1). The overall suicide rate is increasing, with a 27% increase from 2000 (12.1 per 100,000 population) to 2014 (15.4 per 100,000) (Figure 1). Males, youths and young adults, and certain racial/ethnic groups have historically had higher rates of suicide. In 2014, suicide rates were approximately four times higher among males (24.3 per 100,000) than females (6.8 per 100,000), and suicide was the second leading cause of death among youths and young adults aged 10–34 years (1). Among persons aged 10–24 years, the 2014 suicide rate among non-Hispanic American Indian/Alaska Natives was 20.2 per 100,000, 1.9 times higher than non-Hispanic whites (10.5 per 100,000), 3.5 times higher than non-Hispanic blacks (5.8 per 100,000), and 3.7 times higher than Hispanics (5.5 per 100,000) (1). Adults aged 35–64 years are an emerging group at risk, with suicide rates increasing 33% since 2000 and accounting for the largest proportion of suicides (1).

Suicide data severely underestimate the extent of the problem, with many more persons experiencing suicidal thoughts and making suicide plans and nonfatal suicide attempts. For example, among adults aged ≥ 18 years in 2014, for every one adult who died by suicide there were nine adults treated in hospital emergency departments for self-inflicted injuries, 27 who reported making a suicide attempt, and 227 who reported seriously considering suicide (Figure 2). Self-reports by youths also have shown a high prevalence of suicide risk behaviors. According to CDC's 2015 Youth Risk Behavior Survey, 17.7% of students in grades 9–12 reported seriously considering suicide, and 8.6% reported attempting suicide during the 12 months before the survey (2). The percentages of students who reported seriously considering suicide and students who reported making a plan for attempting suicide increased significantly during 2009–2015 (2).

This is another in a series of occasional MMWR reports titled CDC Grand Rounds. These reports are based on grand rounds presentations at CDC on high-profile issues in public health science, practice, and policy. Information about CDC Grand Rounds is available at <http://www.cdc.gov/cdcgrandrounds>.

Suicide Prevention Needs a Public Health Approach

Suicide prevention has been based on a mental health treatment approach because clinical conditions (e.g., depression, anxiety, psychosis, or alcohol and substance dependence) are apparent among many who kill themselves (3). However, this approach only reaches small segments of the population who have identified risk factors and who can surmount treatment barriers, such as stigma and limited availability of or access to services (4). This orientation is also too limiting because most persons with mental health problems do not engage in suicidal behavior or die by suicide. First-time suicide attempts can be fatal, and suicide warning signs (e.g., depression, increased use of drugs or alcohol, or mood changes) can be common symptoms among nonsuicidal persons and not predictive of future suicide attempts or suicide. Thus, a treatment-only approach to prevention has limited impact on national rates of suicide and nonfatal suicidal risk behavior (5).

A public health approach adds a complementary, wider, and prevention-oriented focus that increases attention to the many factors across the lifespan that contribute to circumstances that promote suicidal thinking and suicide attempts. This approach offers opportunities to foster protective factors throughout a person's life, supporting ongoing prevention well before the prospect of suicide is imminent. CDC's National Violent Death Reporting System (NVDRS) currently operates in 32 states and pools data from multiple sources (e.g., death certificates, coroners/medical examiners, and law enforcement) to better describe the who, when, where, and how of violent deaths and precipitating life circumstances. These data highlight suicide prevention opportunities (6). NVDRS data show that most suicides have multiple precipitating conditions, such as depression, intimate partner problems, physical health conditions, financial challenges, and legal problems (7). Suicide risk factors also include personal or family experiences of violence (e.g., child abuse and neglect or family history of suicide) and broader community conditions, such as high crime rates, easy access by persons at risk to lethal means (e.g., large amounts of medication or unlocked firearm), and limited access to health and social services (7,8). NVDRS data underscore that mental health treatment should not be the only prevention strategy; approximately 70% of suicide decedents were not receiving mental health services at the time of their death, and approximately 80% did not have

FIGURE 1. Suicide rates per 100,000 persons, by age group (years) — United States, 2000–2014

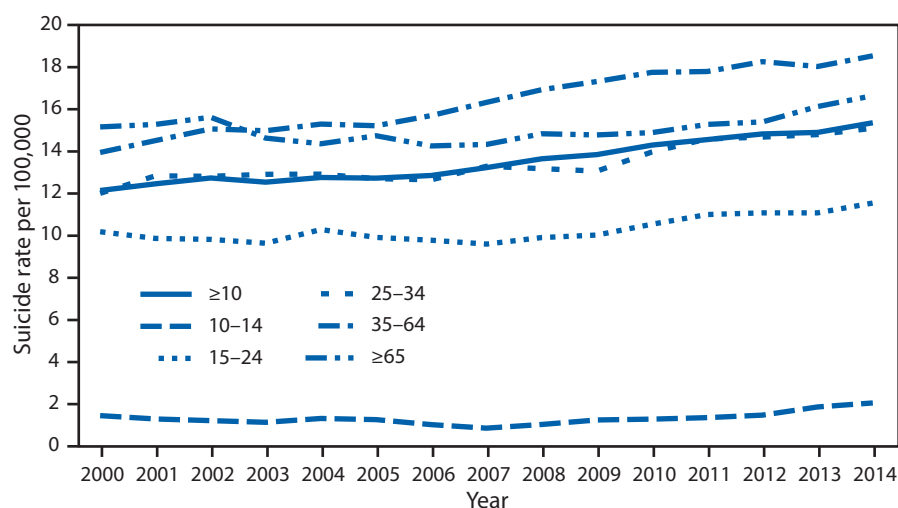
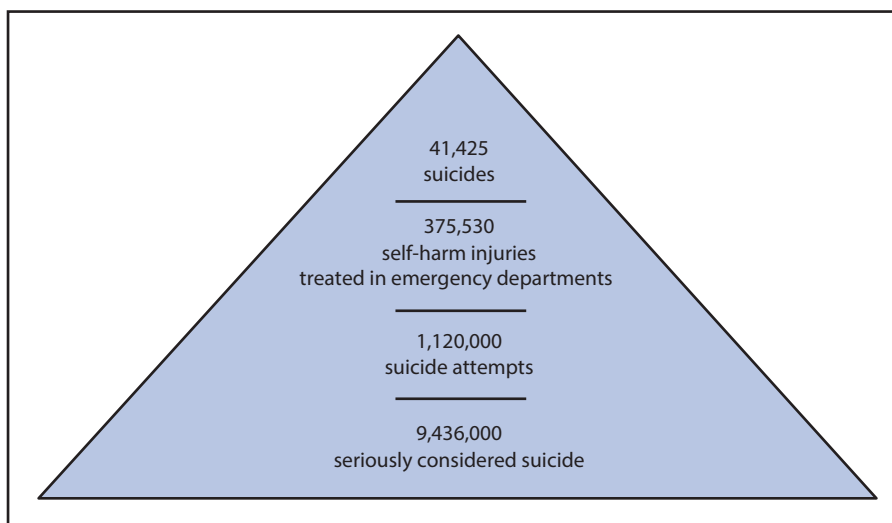


FIGURE 2. Reported number of adults aged ≥18 years who died by suicide,* had self-harm injuries treated in emergency departments,† attempted suicide,‡ or seriously considered suicide§ — United States, 2014



* National Vital Statistics System.

† National Electronic Injury Surveillance System—All Injury Program.

§ National Survey on Drug Use and Health.

a known history of previous suicide attempts (7). Public health approaches, in contrast to clinical service delivery, can reach more persons and address many of the community-level factors that increase the potential for suicide, other forms of violence, and other health risk behaviors (e.g., drug and alcohol abuse). With its emphasis on a science-driven approach, the public health sector has the skills and expertise to collect and analyze relevant data, select and implement comprehensive prevention strategies, organize and integrate efforts involving diverse partners, and conduct rigorous and ongoing evaluation of interventions to successfully prevent complex adverse health events, such as suicide.

Promising Suicide Prevention Approaches

As recognized by the “National Strategy for Suicide Prevention: Goals and Objectives for Action, 2012,” a comprehensive and coordinated prevention approach is needed (5). Promising models are available. For example, when fully implemented, the United States Air Force Suicide Prevention Program had 11 components that together increased community awareness of suicide, provided personnel training, encouraged help-seeking and help-accepting, enhanced confidentiality policies, sought to change social norms (e.g., reducing stigma for seeking mental health care), and created organizational accountability for implementing the program. This comprehensive approach was associated with substantial reductions in suicide rates (33%), homicide (51%), accidental death (18%), and severe family violence (54%) (9). Together for Life, a multicomponent suicide prevention program targeted to Montreal police, includes a publicity campaign directed at officers, training of all units and supervisors on suicide risk and how to give support, and a telephone helpline. The program was associated with a 79% reduction in suicide rates over 12 years while police in a comparison group experienced no statistically significant changes (10).

Prevention strategies at earlier stages of life also have shown promise. The Good Behavior Game is a classroom-based behavior management strategy for elementary schools that teaches youth to better control their emotions and work well with others through classroom rules, team activities, and positive reinforcement of appropriate behavior. This program has demonstrated reductions in antisocial behavior, smoking, and drug and alcohol use, as well as significant decreases in suicidal ideation and suicide attempts throughout childhood, adolescence, and young adulthood (11). Sources of Strength is a school-based program designed to reach all students regardless of their risk. Program components build connections between trained peer leaders and trusted adults who work together to seek to increase students’ acceptance of help-seeking, healthy coping, and communication with adults while reducing the acceptability of suicidal and other harmful behaviors. Program benefits include increases in

referrals for assistance, acceptability of help-seeking and help-accepting, and enhanced perceptions of adult support, including among students with a history of suicidal ideation (12).

Increasing suicide rates demonstrate the need for more research to develop and implement prevention strategies that reach vulnerable groups. The National Action Alliance for Suicide Prevention, a public-private partnership of more than 200 organizations, systematically examined the state of the science to identify research gaps (13). One area identified as in need of more research is prevention approaches for adults aged 35–64 years. Consistent with this prioritized research agenda, CDC is rigorously testing innovative suicide prevention strategies (e.g., online, primary care-based settings) for middle-aged men.

A public health approach to suicide prevention is growing. The CDC-funded Injury Control Research Center for Suicide Prevention (ICRC-S) (<http://suicideprevention-icrc-s.org/>) is a collaboration of the University of Rochester Medical Center and the Education Development Center and draws on public health approaches to inform prevention activities at the state, regional, and national levels. ICRC-S is enhancing access to data to inform prevention planning, systematically defining and addressing challenges to preventing suicide among middle-aged adults, examining issues (e.g., intimate partner violence, substance use, and economic challenges) that contribute to suicide, and using social media methods to define and reach groups at risk. The Colorado Department of Public Health & Environment is using a public health approach to advance both research and practice to reach vulnerable groups, guided by its statewide public and private Suicide Prevention Commission and collaboration with ICRC-S and other national organizations. Activities include implementation and evaluation of online resources to engage men in help-seeking for suicide and mental health difficulties (<http://mantherapy.org/>), education of emergency department clinicians regarding counseling caregivers of youths following a suicide attempt about reducing youths' access to lethal means (e.g., medication), and primary prevention with all youths regardless of known risk by prioritizing the Sources of Strength program in Colorado schools.

Increasing Awareness of Suicide Prevention Opportunities

Increasing communication about suicide and its risk factors, decreasing the stigma associated with seeking help from others, and strengthening access to support services to address emotional, interpersonal, and financial stressors are important prevention opportunities. The safe and appropriate discussion of suicide by traditional and online media can support prevention. Research-informed guidelines for reporting on suicide developed by partners in the United States and the

World Health Organization are designed to reduce the possibility of suicide contagion, provide hope, and raise awareness (Box). An evaluation of Austrian guidelines focused on subway suicides found a change in reporting practices (e.g., headlines and reports not sensationalized and reports not published on the front page) was associated with a 75% decrease in subway suicides and decreases were maintained over time (14).

Rapid access to trained crisis support personnel also can provide opportunities to substantially reduce persons' depression, suicidal thinking, and overwhelmed feelings (15). The National Suicide Prevention Lifeline (1-800-273-TALK) connects callers (1.5 million in 2015) with counselors in their local area through a network of 160 community crisis centers and offers specialized support to veterans, Spanish speakers, and online users (<http://www.suicidepreventionlifeline.org/>). National reductions in suicide are possible by using surveillance data (e.g., NVDRS) to increase awareness, inform strategic interventions, and implement and sustain effective prevention. Expanded partnerships among CDC's ICRCs and state health departments are an important public health strategy to implement and evaluate comprehensive prevention strategies that

BOX. Examples of guidelines for media and online reporting on suicide

- Inform audience without using sensationalized headlines and language.
- Minimize prominence by avoiding prominent placement and repetition of stories.
- Avoid providing detailed information about the method, location of suicide, and information a person might have left in a note.
- Exercise caution when using photographs or video footage by avoiding images of method, location, grieving family and friends, memorials, and funerals.
- Inform that most, but not all, persons who die by suicide exhibit warning signs and provide examples of warning signs (e.g., talking about wanting to die, increased use of drugs or alcohol, or mood changes).
- Report on suicide as a public health issue rather than in a style similar to reporting crimes.
- Provide advice from suicide prevention experts rather than first responders.
- Provide information about where to seek help.
- Use terms, such as “died by suicide” or “killed him/herself” rather than referring to suicide as “successful” or “unsuccessful.”

Sources: <http://reportingsuicide.org/> and http://www.who.int/mental_health/prevention/suicide/resource_media.pdf.

reduce risk factors, increase interventions for suicidal behavior, and reduce access to lethal means by persons at greatest risk for suicide. By bringing together a public and mental health approach to suicide prevention, suicides can be prevented.

¹Division of Violence Prevention, National Center for Injury Prevention and Control, CDC; ²Injury Control Research Center for Suicide Prevention, University of Rochester Medical Center, New York; ³Colorado Department of Public Health & Environment; ⁴Suicide Prevention Resource Center and Education Development Center, Massachusetts; ⁵Office of the Director, CDC.

Corresponding author: Corinne David-Ferdon, cferdon@cdc.gov, 770-488-0542.

References

1. CDC. Web-Based Injury Statistics Query and Reporting System (WISQARS). Atlanta, GA: US Department of Health and Human Services, CDC; 2016. <http://www.cdc.gov/injury/wisqars/index.html>
2. CDC. High school YRBS: youth online. Atlanta, GA: US Department of Health and Human Services, CDC; 2016. <https://nccd.cdc.gov/Youthonline/App/Default.aspx>
3. Harris EC, Barraclough B. Suicide as an outcome for mental disorders. A meta-analysis. *Br J Psychiatry* 1997;170:205–28. <http://dx.doi.org/10.1192/bjp.170.3.205>
4. New Freedom Commission on Mental Health. Achieving the promise: transforming mental health care in America. Final report. Rockville, MD: US Department of Health and Human Services; 2003. <http://govinfo.library.unt.edu/mentalhealthcommission/reports/FinalReport/downloads/downloads.html>
5. US Surgeon General and the National Action Alliance for Suicide Prevention. National strategy for suicide prevention: goals and objectives for action. Washington, DC: US Department of Health and Human Services, US Surgeon General and the National Action Alliance for Suicide Prevention; 2012. <http://www.surgeongeneral.gov/library/reports/national-strategy-suicide-prevention/index.html>
6. Blair JM, Fowler KA, Jack SPD, Crosby AE. The National Violent Death Reporting System: overview and future directions. *Inj Prev* 2016;22(Suppl 1):i6–11. <http://dx.doi.org/10.1136/injuryprev-2015-041819>
7. Lyons BH, Fowler KA, Jack SP, Betz CJ, Blair JM. Surveillance for violent deaths—National Violent Death Reporting System, 17 states, 2013. *MMWR Surveill Summ* 2016;65(No. SS-10). <http://dx.doi.org/10.15585/mmwr.ss6510a1>
8. Caine ED. Forging an agenda for suicide prevention in the United States. *Am J Pub Health* 2013;103:822–9. <http://dx.doi.org/10.2105/AJPH.2012.301078>
9. Knox KL, Litts DA, Talcott GW, Feig JC, Caine ED. Risk of suicide and related adverse outcomes after exposure to a suicide prevention programme in the US Air Force: cohort study. *BMJ* 2003;327:1376–80. <http://dx.doi.org/10.1136/bmj.327.7428.1376>
10. Mishara BL, Martin N. Effects of a comprehensive police suicide prevention program. *Crisis* 2012;33:162–8. <http://dx.doi.org/10.1027/0227-5910/a000125>
11. Center for the Study and Prevention of Violence. Blueprints for healthy youth development. Boulder, CO: University of Colorado Boulder, Institute of Behavioral Science, Center for the Study and Prevention of Violence; 2016. <http://www.blueprintsprograms.com/>
12. Wyman PA, Brown CH, LoMurray M, et al. An outcome evaluation of the Sources of Strength suicide prevention program delivered by adolescent peer leaders in high schools. *Am J Public Health* 2010;100:1653–61. <http://dx.doi.org/10.2105/AJPH.2009.190025>
13. National Action Alliance for Suicide Prevention, Research Prioritization Task Force. A prioritized research agenda for suicide prevention: an action plan to save lives. Rockville, MD: National Action Alliance for Suicide Prevention, Research Prioritization Task Force; 2014. <http://actionallianceforsuicideprevention.org/task-force/research-prioritization>
14. Sonneck G, Etzersdorfer E, Nagel-Kuess S. Imitative suicide on the Viennese subway. *Soc Sci Med* 1994;38:453–7. [http://dx.doi.org/10.1016/0277-9536\(94\)90447-2](http://dx.doi.org/10.1016/0277-9536(94)90447-2)
15. Gould MS, Cross W, Pisani AR, Munfakh JL, Kleinman M. Impact of applied suicide intervention skills training on the National Suicide Prevention Lifeline. *Suicide Life Threat Behav* 2013;43:676–91. <http://dx.doi.org/10.1111/sltb.12049>

Current Cigarette Smoking, Access, and Purchases from Retail Outlets Among Students Aged 13–15 Years — Global Youth Tobacco Survey, 45 Countries, 2013 and 2014

Denise D'Angelo, MPH¹; Indu B. Ahluwalia, PhD¹; Eugene Pun, MPH¹; Shaoman Yin, PhD²; Krishna Palipudi, PhD¹; Lazarous Mbulo, PhD¹

Tobacco use is a leading preventable cause of morbidity and mortality, with nearly 6 million deaths caused by tobacco use worldwide every year (1). Cigarette smoking is the most common form of tobacco use in most countries, and the majority of adult smokers initiate smoking before age 18 years (2,3). Limiting access to cigarettes among youths is an effective strategy to curb the tobacco epidemic by preventing smoking initiation and reducing the number of new smokers (3,4). CDC used the Global Youth Tobacco Survey (GYTS) data from 45 countries to examine the prevalence of current cigarette smoking, purchase of cigarettes from retail outlets, and type of cigarette purchases made among school students aged 13–15 years. The results are presented by the six World Health Organization (WHO) regions: African Region (AFR); Eastern Mediterranean Region (EMR); European Region (EUR); Region of the Americas (AMR); South-East Asian Region (SEAR); and Western Pacific Region (WPR). Across all 45 countries, the median overall current cigarette smoking prevalence among students aged 13–15 years was 6.8% (range = 1.7% [Kazakhstan]–28.9% [Timor-Leste]); the median prevalence among boys was 9.7% (2.0% [Kazakhstan]–53.5% [Timor-Leste]), and among girls was 3.5% (0.0% [Bangladesh]–26.3% [Italy]). The proportion of current cigarette smokers aged 13–15 years who reported purchasing cigarettes from a retail outlet such as a store, street vendor, or kiosk during the past 30 days ranged from 14.9% [Latvia] to 95.1% [Montenegro], and in approximately half the countries, exceeded 50%. In the majority of countries assessed in AFR and SEAR, approximately 40% of cigarette smokers aged 13–15 years reported purchasing individual cigarettes. Approximately half of smokers in all but one country assessed in EUR reported purchasing cigarettes in packs. These findings could be used by countries to inform tobacco control strategies in the retail environment to reduce and prevent marketing and sales of tobacco products to youths (5).

GYTS is a nationally representative school-based, paper-and-pencil, cross-sectional survey of students in school grades associated with ages 13–15 years. GYTS uses a standardized methodology*

*The Global Youth Tobacco Survey uses a two-stage sample design to select schools with a probability of selection proportional to enrollment size. The classes within selected schools are chosen randomly and all students in selected classes are eligible to participate in the survey.

that allows cross-country comparisons (6). Forty-five countries in which the GYTS is implemented had data available for 2013 or 2014 and were included in this report. Current cigarette smoking was defined as a report by a student that they had smoked cigarettes on at least 1 day in the past 30 days. Among current cigarette smokers, cigarette purchasing from a retail outlet was defined for the majority of countries as a report of having purchased them from a store or shop, a street vendor, or a kiosk in response to the question: “The last time you smoked cigarettes during the past 30 days, how did you get them?” Past 30-day purchase of cigarettes in packs or as individual sticks was also assessed among current cigarette smokers. Data were weighted for each country to yield nationally representative estimates. Country-specific prevalence estimates with corresponding 95% confidence intervals were calculated, overall and by sex. Estimates based on sample sizes <35 or relative standard error >30% are not shown. A Wilcoxon rank sum test was used to compare the median prevalence estimates between boys and girls in each country. Overall sample sizes ranged from 526 (San Marino [EUR]) to 9,694 (Bosnia and Herzegovina [EUR]). Response rates ranged from 61.5% (Pakistan [EMR]) to 100% (Bangladesh [SEAR]).

Cigarette smoking prevalences among youths aged 13–15 years by WHO region ranged from 2.3% (Mozambique) to 11.2% (Zimbabwe) in AFR, from 3.3% (Pakistan) to 11.4% (Jordan) in EMR, from 1.7% (Kazakhstan) to 23.4% (Italy) in EUR, from 3.8% (Bahamas) to 7.8% (Belize) in AMR, from 2.1% (Bangladesh) to 28.9% (Timor-Leste) in SEAR, and from 2.5% (Vietnam) to 11.0% (Northern Mariana Islands) in WPR. Across all countries, the median overall current cigarette smoking prevalence was 6.8% (range = 1.7% [Kazakhstan]–28.9% [Timor-Leste]); the median prevalence among boys was 9.7% (2.0% [Kazakhstan]–53.5% [Timor-Leste]), and among girls was 3.5% (0% [Bangladesh]–26.3% [Italy]) (Table).

In 26 of the 45 countries, approximately half of current cigarette smokers aged 13–15 years reported purchasing cigarettes from a retail outlet in the past 30 days (Figure); this proportion ranged from 14.9% in Latvia to 95.1% in Montenegro. The proportion of current cigarette smokers who reported buying cigarettes in packs ranged from 15.2% in Bangladesh to 89.8% in Serbia, and the proportion of who reported buying cigarettes as individual sticks ranged from 3.6% in Greece to 84.8% in Bangladesh (Table).

TABLE. Prevalence of current cigarette smoking and proportion of current smokers who purchased cigarettes in packs or individually among students aged 13–15 years — 45 countries, Global Youth Tobacco Survey, 2013–2014

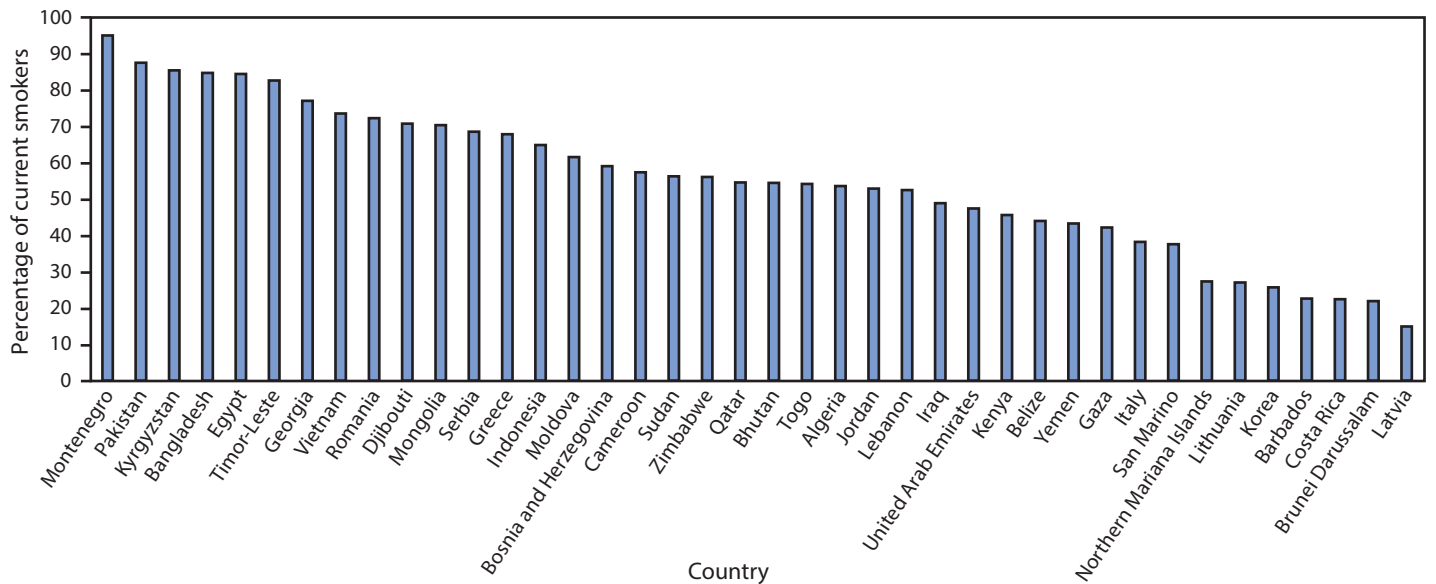
WHO Region/Country (survey year)	Current cigarette smokers				Cigarette purchases among current smokers	
	Unweighted sample size	Total % (95% CI)	Male % (95% CI)	Female % (95% CI)	Pack % (95% CI)	Individual cigarettes % (95% CI)
African Region						
Algeria (2013)	3,921	5.7 (4.6–7.0)	12.2 (9.8–15.2)	0.8 (0.4–1.6)	30.0 (20.4–41.9)	59.7 (50.3–68.4)
Cameroon (2014)	1,772	5.7 (3.4–9.4)	8.3 (5.0–13.4)	2.5 (1.4–4.3)	30.8 (20.1–43.9)	44.8 (27.9–62.9)
Gabon (2014)	760	5.2 (3.9–6.8)	6.1 (4.5–8.3)	4.0 (2.2–6.9)	—*	—*
Kenya (2013)	1,270	4.9 (3.2–7.6)	7.4 (4.5–11.7)	2.6 (1.3–3.9)	19.2 (8.8–37.0)	51.0 (30.2–71.4)
Mozambique (2013)	2,804	2.3 (1.6–3.4)	2.1 (1.2–3.5)	2.3 (1.4–3.8)	—*	—*
Senegal (2013)	751	4.5 (2.6–7.7)	4.7 (2.6–8.5)	3.1 (1.2–7.6)	—*	—*
Togo (2013)	2,740	4.8 (3.5–6.6)	7.4 (5.3–10.3)	1.2 (0.7–2.0)	33.2 (18.8–51.6)	45.0 (31.1–59.7)
Zimbabwe (2014)	4,438	11.2 (6.9–17.8)	11.3 (6.9–17.9)	8.9 (5.2–14.8)	23.1 (14.6–34.6)	22.6 (17.3–28.9)
Eastern Mediterranean Region						
Djibouti (2013)	1,190	6.6 (4.5–9.6)	8.0 (5.3–11.8)	4.2 (2.1–8.4)	40.9 (28.8–54.3)	38.6 (25.6–53.4)
Egypt (2014)	1,973	4.8 (2.7–8.6)	8.3 (3.9–16.5)	0.8 (0.3–2.0)	30.9 (10.7–62.5)	69.1 (37.5–89.3)
Gaza (2013)	1,476	6.5 (4.4–9.6)	9.7 (6.8–13.6)	3.5 (2.5–4.9)	34.0 (18.7–53.7)	43.8 (26.8–62.4)
Iraq (2014)	1,181	5.7 (3.7–8.7)	7.8 (4.4–13.7)	3.6 (2.4–5.3)	63.2 (56.8–69.2)	19.6 (10.8–32.9)
Jordan (2014)	1,779	11.4 (8.0–15.9)	17.3 (13.0–22.6)	5.4 (3.3–8.8)	41.1 (28.3–55.2)	42.8 (33.5–52.5)
Lebanon (2013)	1,126	11.3 (7.8–16.0)	18.8 (12.8–26.6)	5.1 (2.9–8.8)	79.4 (66.7–88.1)	7.0 (2.6–17.6)
Pakistan (2013)	5,393	3.3 (2.3–4.7)	4.8 (3.2–6.9)	0.9 (0.5–2.0)	39.9 (25.2–56.7)	35.2 (21.2–52.3)
Qatar (2013)	1,627	9.8 (6.7–14.0)	14.9 (11.3–19.6)	4.7 (3.0–7.3)	56.5 (42.0–70.0)	15.0 (6.2–31.8)
Sudan (2014)	1,304	4.5 (3.2–6.4)	6.2 (4.2–9.0)	2.2 (1.3–3.7)	—*	—*
United Arab Emirates (2013)	3,291	6.2 (4.5–8.6)	9.7 (6.9–13.4)	2.7 (1.6–4.6)	66.9 (57.6–75.1)	13.9 (8.9–21.0)
Yemen (2014)	1,529	6.8 (4.3–10.6)	9.2 (5.2–15.8)	2.5 (1.3–4.8)	27.4 (9.6–57.3)	61.5 (32.6–84.1)
European Region						
Bosnia and Herzegovina (2013)	9,694	11.2 (9.5–13.2)	13.4 (11.0–16.1)	8.8 (7.0–11.2)	85.5 (81.7–88.7)	4.1 (2.7–6.3)
Georgia (2014)	923	7.0 (4.4–11.1)	9.9 (6.0–15.8)	3.8 (1.8–7.6)	—*	—*
Greece (2013)	3,988	10.1 (8.3–12.2)	10.3 (8.4–12.6)	9.9 (8.0–12.2)	68.2 (62.2–73.7)	3.6 (1.7–7.4)
Italy (2014)	1,399	23.4 (20.8–26.4)	20.6 (16.6–25.3)	26.3 (22.3–30.8)	n/a [†]	n/a [†]
Kazakhstan (2014)	1,685	1.7 (1.1–2.5)	2.0 (1.1–3.7)	1.3 (0.8–2.2)	—*	—*
Kyrgyzstan (2014)	3,358	2.4 (1.6–3.5)	4.0 (2.7–5.8)	0.9 (0.4–1.8)	47.6 (29.5–66.4)	40.9 (24.7–59.3)
Latvia (2014)	3,891	16.8 (15.1–18.5)	16.9 (14.7–19.3)	16.5 (14.3–19.0)	62.5 (58.6–66.3)	13.6 (9.6–18.9)
Lithuania (2014)	2,936	19.4 (17.0–22.2)	20.0 (16.9–23.6)	19.0 (16.4–21.8)	79.8 (73.5–84.9)	11.6 (8.2–16.3)
Moldova (2013)	3,379	7.2 (5.3–9.7)	11.0 (7.9–15.2)	3.2 (2.1–5.1)	81.7 (72.7–88.2)	10.6 (6.4–17.0)
Montenegro (2014)	3,573	6.9 (3.4–13.5)	10.8 (4.6–23.3)	2.8 (1.7–4.5)	85.4 (67.1–94.4)	5.5 (1.9–14.9)
Romania (2013)	3,216	9.4 (7.8–11.3)	10.1 (8.2–12.4)	8.5 (6.6–10.9)	50.7 (42.0–59.3)	44.4 (36.1–53.0)
San Marino (2014)	526	12.9 (12.3–13.5)	11.7 (10.9–12.6)	14.1 (13.3–15.0)	—*	—*
Serbia (2013)	2,964	13.0 (10.5–16.1)	12.7 (10.3–15.5)	13.3 (9.8–17.8)	89.8 (86.1–92.6)	4.2 (2.5–7.0)
Region of the Americas						
Bahamas (2013)	984	3.8 (2.5–5.8)	4.6 (2.6–8.1)	2.6 (1.4–4.6)	—*	—*
Barbados (2013)	1,266	7.0 (5.6–8.8)	8.8 (6.7–11.6)	5.0 (3.5–7.1)	31.6 (19.5–46.7)	26.3 (17.6–37.3)
Belize (2014)	1,228	7.8 (6.1–9.9)	10.4 (8.0–13.4)	5.4 (3.7–7.8)	28.0 (20.2–37.4)	50.9 (38.2–63.5)
Costa Rica (2013)	2,110	5.0 (3.8–6.6)	5.7 (4.2–7.6)	4.3 (2.8–6.6)	48.1 (30.6–66.1)	29.5 (7.6–45.0)
South-East Asia Region						
Bangladesh (2013)	3,072	2.1 (0.9–4.9)	3.4 (1.5–7.1)	0.0	15.2 (4.5–40.4)	84.8 (59.6–95.5)
Bhutan (2013)	1,318	14.0 (11.8–16.4)	23.1 (19.0–27.6)	6.6 (4.8–9.0)	29.0 (21.6–37.6)	53.1 (42.5–63.3)
Timor-Leste (2013)	1,381	28.9 (22.1–36.9)	53.5 (38.5–68.0)	11.0 (7.6–15.7)	31.7 (17.8–49.7)	44.8 (34.8–55.3)
Indonesia (2014)	4,144	18.3 (13.9–23.6)	33.9 (26.1–42.7)	2.5 (1.4–4.3)	24.6 (18.1–32.5)	74.3 (66.9–80.5)
Western Pacific Region						
Brunei Darussalam (2013)	887	8.5 (5.0–13.9)	13.4 (7.3–23.3)	3.4 (1.6–7.2)	—*	—*
Korea (2013)	3,385	5.2 (4.2–6.3)	7.5 (5.8–9.7)	2.6 (1.9–3.5)	82.9 (75.7–88.2)	13.4 (9.2–19.2)
Mongolia (2014)	5,973	3.9 (3.2–4.9)	5.9 (4.6–7.5)	1.9 (1.2–3.1)	38.4 (28.8–49.1)	57.1 (46.2–67.3)
Northern Mariana Islands (2014)	1,661	11.0 (10.1–11.9)	13.4 (12.3–14.5)	8.5 (7.2–10.1)	64.8 (60.3–69.1)	18.2 (14.9–22.1)
Vietnam (2014)	3,404	2.5 (1.7–3.7)	4.9 (3.3–7.0)	0.2 (0.1–0.8)	33.2 (20.3–49.3)	55.7 (40.8–69.6)

Abbreviations: CI = Confidence Interval; WHO = World Health Organization.

* Data suppressed because sample size <35.

† Italy did not ask this question.

FIGURE. Proportion of current cigarette smokers aged 13–15 years who purchased cigarettes from a retail outlet* in the past 30 days — Global Youth Tobacco Survey, 45 countries,† 2013–2014



* Retail outlets include store, shop, street vendor, and kiosk. Additional outlets in selected countries are truck stop (Zimbabwe); pharmacy and school canteen (Pakistan); cafeteria (Qatar); gas station and cafeteria (United Arab Emirates); supermarket (Bosnia and Herzegovina and Kazakhstan); small shop and bazaar (Kyrgyzstan); bar, cafe, and restaurant (Moldova); suppliers' house (Brunei Darussalam).

† Data from Bahamas, Gabon, Kazakhstan, Mozambique, and Senegal are suppressed because sample size <35.

Discussion

The overall prevalence of cigarette smoking among students aged 13–15 years in the 45 countries included in this report ranged from 1.7% (Kazakhstan) to 28.9% (Timor-Leste). Median smoking prevalence was higher among boys than girls. Prevalence also varied among the countries assessed. Reducing youths' access to tobacco products at retail outlets is an effective strategy to reduce smoking by youths (3,4). The WHO Framework Convention on Tobacco Control (FCTC) is the first international treaty negotiated under the auspices of WHO, developed in response to the globalization of the tobacco epidemic. Demand reduction measures outlined in FCTC have the potential to protect youths from tobacco use and include tobacco tax increases (Article 6) and bans on tobacco advertising, promotions, and sponsorship (Article 13) (7). In addition, supply reduction measures such as addressing illicit trade of tobacco products (Article 15) and prohibition of sale of tobacco products to and by minors (Article 16), also have the potential to reduce the number of youths who smoke (7).

Forty-three of 45 countries that conducted GYTS in 2013 and 2014 have ratified the FCTC. However, varying levels of tobacco control policy implementation and other country-specific factors can influence cigarette smoking prevalence and access by youths to cigarettes from retail outlets (7,8). Challenges in fully implementing Article 16 might include tobacco industry attempts to undermine access laws that aim

Summary

What is already known about this topic?

Cigarette smoking is the most common form of tobacco use in most countries, and the majority of adult smokers initiate smoking before age 18 years.

What is added by this report?

Global Youth Tobacco Survey data from 45 countries in 2013 and 2014 identified sex and cross-country differences in prevalence of cigarette smoking among students aged 13–15 years. In most countries, approximately half of youths reported access to cigarettes from a store, street vendor, or kiosk. In the majority of countries assessed in the African and South-East Asia regions, approximately 40% of smokers aged 13–15 years reported purchasing individual cigarettes.

What are the implications for public health practice?

Tobacco control and prevention policies aimed at youth-oriented marketing and sales of tobacco products to youth can help to reduce youths' initiation and use of tobacco products and reverse the global tobacco epidemic.

to reduce use of tobacco among minors, opposition from retailers, poor enforcement, and availability of cigarettes at alternate outlets that are not regulated in some countries (9). The availability of cigarettes for purchase as single sticks, which was common in some countries, makes purchasing less expensive and more attainable for youths, who are generally sensitive to prices (10).

The variations in the prevalence of cigarette smoking by youths observed by country and by sex might reflect differences in social norms, customs, and adult tobacco use patterns that influence adolescent tobacco use (2), and underscore the potential impact of full implementation of evidence-based interventions outlined in the WHO MPOWER package.[†] The MPOWER package outlines policies aimed at reversing the global tobacco epidemic, including implementing and enforcing comprehensive smoke-free laws, increasing access to cessation services, warning about the dangers of tobacco use with antismoking media campaigns, and raising taxes to increase the price of tobacco products.

The findings in this report are subject to at least four limitations. First, data were self-reported by students, which might result in misreporting of smoking behavior or tobacco purchasing patterns. Second, students who do not purchase cigarettes themselves might acquire them from other sources such as friends or family. Third, the data presented represent only youths who are enrolled in school, which might limit generalizability to all youths in these countries. Finally, only a limited number of countries were assessed from each WHO region; therefore, the findings in this report do not represent the respective WHO regions overall.

Tobacco prevention and control interventions that restrict youths' access to tobacco products and reduce exposure to youth-oriented tobacco product promotions can reduce tobacco use among youths. Implementing evidence-based measures from FCTC Article 16, in conjunction with evidence-based strategies outlined in WHO's MPOWER package, are critical to reducing the estimated 1 billion tobacco-related deaths projected worldwide this century (1).

[†] http://www.who.int/tobacco/mpower/mpower_report_full_2008.pdf.

Acknowledgments

Linda Anton, Global Youth Tobacco Survey Collaborating Group; World Health Organization collaborators.

¹Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, CDC; ²CDC Foundation, Atlanta, Georgia.

Corresponding author: Denise D'Angelo, DDAngelo@cdc.gov, 770-488-6288.

References

1. World Health Organization. WHO global report: mortality attributable to tobacco, 2012. http://apps.who.int/iris/bitstream/10665/44815/1/9789241564434_eng.pdf
2. CDC Foundation. Global Adult Tobacco Survey (GATS) atlas, 2015. Atlanta, GA: CDC Foundation; 2016. http://www.cdc.gov/tobacco/global/gtss/tobacco_atlas
3. US Department of Health and Human Services. Preventing tobacco use among youth and young adults: a report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, CDC; 2012. <http://www.surgeongeneral.gov/library/reports/preventing-youth-tobacco-use/full-report.pdf>
4. DiFranza JR. Which interventions against the sale of tobacco to minors can be expected to reduce smoking? *Tob Control* 2012;21:436–42. <http://dx.doi.org/10.1136/tobaccocontrol-2011-050145>
5. Center for Public Health Systems Science. Point-of-sale strategies: a tobacco control guide. St. Louis, MO: Washington University in St. Louis, Center for Public Health Systems Science, George Warren Brown School of Social Work and the Tobacco Control Legal Consortium; 2014.
6. CDC; Global Youth Tobacco Survey Collaborative Group. Global Youth Tobacco Survey (GYTS): core questionnaire and optional questions, version 1.0. Atlanta, GA: US Department of Health and Human Services, CDC; 2012.
7. World Health Organization. WHO framework convention on tobacco control. Geneva, Switzerland: World Health Organization; 2005. http://www.who.int/tobacco/framework/WHO_FCTC_english.pdf
8. World Health Organization. 2015. Parties to the WHO framework convention on tobacco control. Geneva, Switzerland: World Health Organization; 2015. http://www.who.int/fctc/signatories_parties/en/
9. Nagler RH, Viswanath K. Implementation and research priorities for FCTC Articles 13 and 16: tobacco advertising, promotion, and sponsorship and sales to and by minors. *Nicotine Tob Res* 2013;15:832–46. <http://dx.doi.org/10.1093/ntr/nts331>
10. Linetzky B, Mejia R, Ferrante D, De Maio FG, Diez Roux AV. Socioeconomic status and tobacco consumption among adolescents: a multilevel analysis of Argentina's Global Youth Tobacco Survey. *Nicotine Tob Res* 2012;14:1092–9. <http://dx.doi.org/10.1093/ntr/nts004>

Epidemiology of Varicella During the 2-Dose Varicella Vaccination Program — United States, 2005–2014

Adriana S. Lopez, MHS¹; John Zhang, PhD¹; Mona Marin, MD¹

Before availability of varicella vaccine in the United States, an estimated 4 million varicella cases, 11,000–13,500 varicella-related hospitalizations, and 100–150 varicella-related deaths occurred annually. The varicella vaccination program was implemented in the United States in 1996 as a 1-dose routine childhood program. Based on data from two varicella active surveillance sites, the varicella vaccination program led to 90% decline in incidence over the next decade (1). However, because of continued varicella outbreaks, a routine 2-dose schedule (at ages 12–15 months and 4–6 years) was recommended and has been in place since 2006 (2). The declines in incidence (1,3–6) made it feasible for states to implement varicella case-based surveillance and to report varicella data to CDC through the National Notifiable Diseases Surveillance System (NNDSS). State data have become the primary source for monitoring trends in varicella incidence nationally (7). Using NNDSS data, CDC previously reported nationwide declines in varicella incidence of 72% from the end of the 1-dose to the early years of the 2-dose varicella vaccination program (2006–2010) (7). This report updates varicella incidence trends to include the most recent years in the 2-dose varicella vaccination program. Between the period 2005–2006 (before the 2-dose recommendation) and 2013–2014, overall varicella incidence declined 84.6%, with the largest declines reported in children aged 5–9 years (89.3%) and 10–14 years (84.8%). The availability of varicella-specific data varied over time. During the last 2 years examined (2013 and 2014), completeness of reporting of two critical variables monitored by CDC, vaccination status (receipt of at least 1 dose of varicella vaccine) of cases and severity of disease based on number of lesions, were 54.2% and 39.1%, respectively. State and local health departments, in collaboration with CDC, should continue working to improve reporting of cases and completeness of critical varicella-specific variables to better monitor impact of the varicella vaccination program.

Demographic, clinical, and epidemiologic data from varicella cases reported through passive surveillance from state and local health departments are electronically transmitted to CDC via NNDSS. CDC analyzed data from all states and the District of Columbia (DC) that reported varicella cases, starting with the year the state first reported varicella cases to CDC. For this report, DC is counted as a state. An earlier report had calculated varicella incidence using ad hoc inclusion criteria of adequate (incidence of ≥ 1 case per 100,000 population) and

consistent (≥ 3 consecutive years) reporting (7); in this analysis these criteria were also examined.

Nationwide age-specific and overall varicella incidence rates from passive surveillance data were calculated for each year from 2005 to 2014 by dividing the aggregate number of confirmed and probable* varicella cases from reporting states by the aggregate population of the same states using U.S. Census data (<https://www.census.gov/popest/data/historical/index.html>). To examine trends between the end of the 1-dose varicella vaccination program and the most recent years of the 2-dose program, incidence rates were averaged for 2005–2006 and 2013–2014 to account for year-to-year variability.

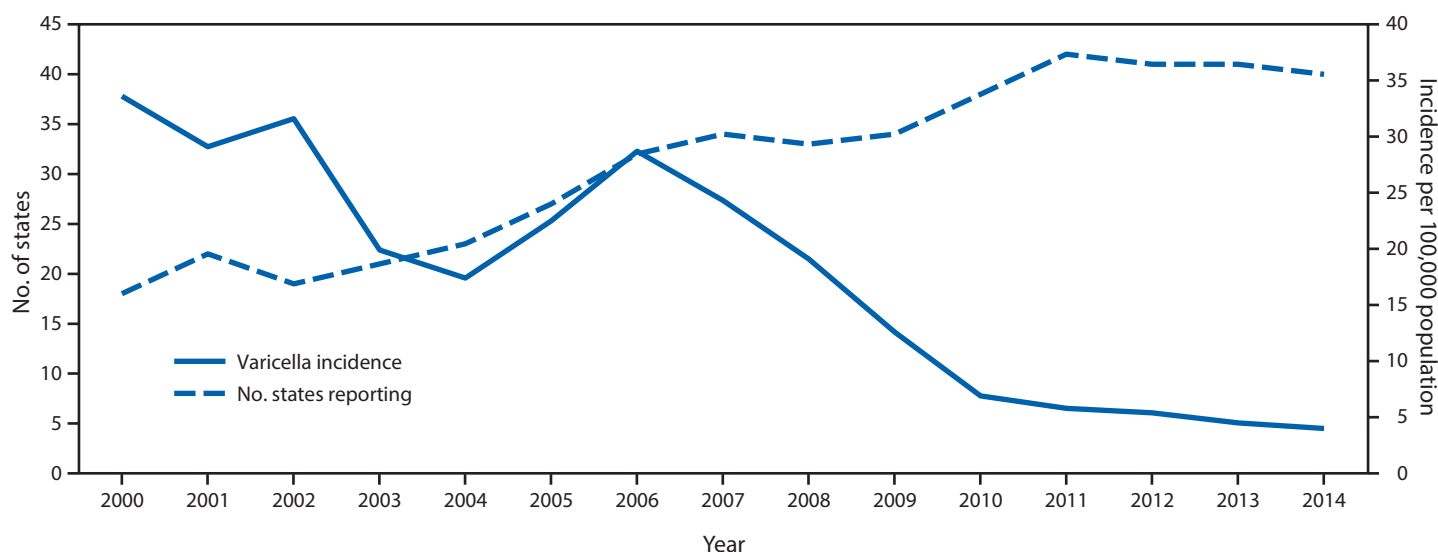
To evaluate changes in varicella incidence since the varicella vaccination program was introduced, incidence trends from 1993 to 2014, which include data from before the start of the U.S. varicella vaccination program, were analyzed for four states (Illinois, Michigan, Texas, and West Virginia) that have reported varicella cases to CDC every year since before implementation of the varicella vaccination program. Poisson regression was used to assess all trends over time.

Provisional varicella-specific case-based data from 2013 and 2014 were analyzed to assess critical variables monitored by CDC: vaccination status of cases, disease severity (based on number of lesions),[†] hospitalization, and association with outbreaks (defined variably by states as three or more cases or as five or more cases).

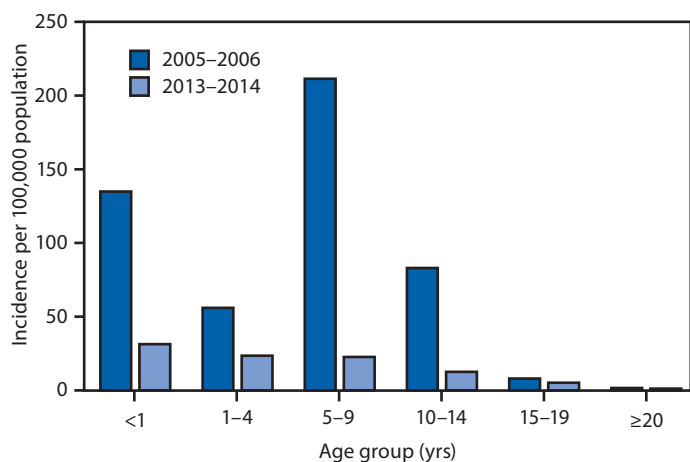
During 2005–2014, the number of states reporting varicella data to CDC through NNDSS increased 48.1%, from 27 in 2005 to 40 in 2014 (Figure 1). Among the 40 states reporting data in 2014, 38 have implemented case-based varicella surveillance. The average annual varicella incidence declined significantly (84.6%) from 25.4 per 100,000 population during 2005–2006 to 3.9 per 100,000 population during 2013–2014 ($p < 0.001$) (Figure 1). Statistically significant declines in incidence were reported for all age groups during this time (Figure 2), with the largest declines among children

* A confirmed case of varicella is an illness with acute onset of diffuse (generalized) maculopapulovesicular rash without other apparent cause that is laboratory confirmed or that meets the clinical case definition and is epidemiologically linked to a confirmed or a probable case. A probable case of varicella meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to another probable or confirmed case.

[†] Varicella disease is classified as mild (<50 lesions), mild/moderate (50–249 lesions), moderate (250–499 lesions), or severe (≥ 500 lesions or any complications such as bacterial superinfection, varicella pneumonitis, encephalitis, hospitalization, or death). <http://www.cdc.gov/vaccines/pubs/surv-manual/chpt17-varicella.html>.

FIGURE 1. Overall varicella incidence per 100,000 population* and number of states reporting varicella cases to CDC — United States, 2000–2014

* Varicella incidence declined 84.6% from 2005–2006 (the end of the 1-dose varicella vaccination program) to 2013–2014 (the most recent years of data available for the 2-dose varicella vaccination program). During the same interval, the number of states reporting varicella cases through the National Notifiable Diseases Surveillance System (NNDSS) increased from 27 to 40. NNDSS data were used to calculate national incidence starting in 2000 because before this year, data were too sparse to calculate national estimates.

FIGURE 2. Reported varicella incidence,* by age group† — United States, 2005–2006 compared with 2013–2014

* 25 states provided age data during 2005–2006, and 37 states reported data during 2013–2014.

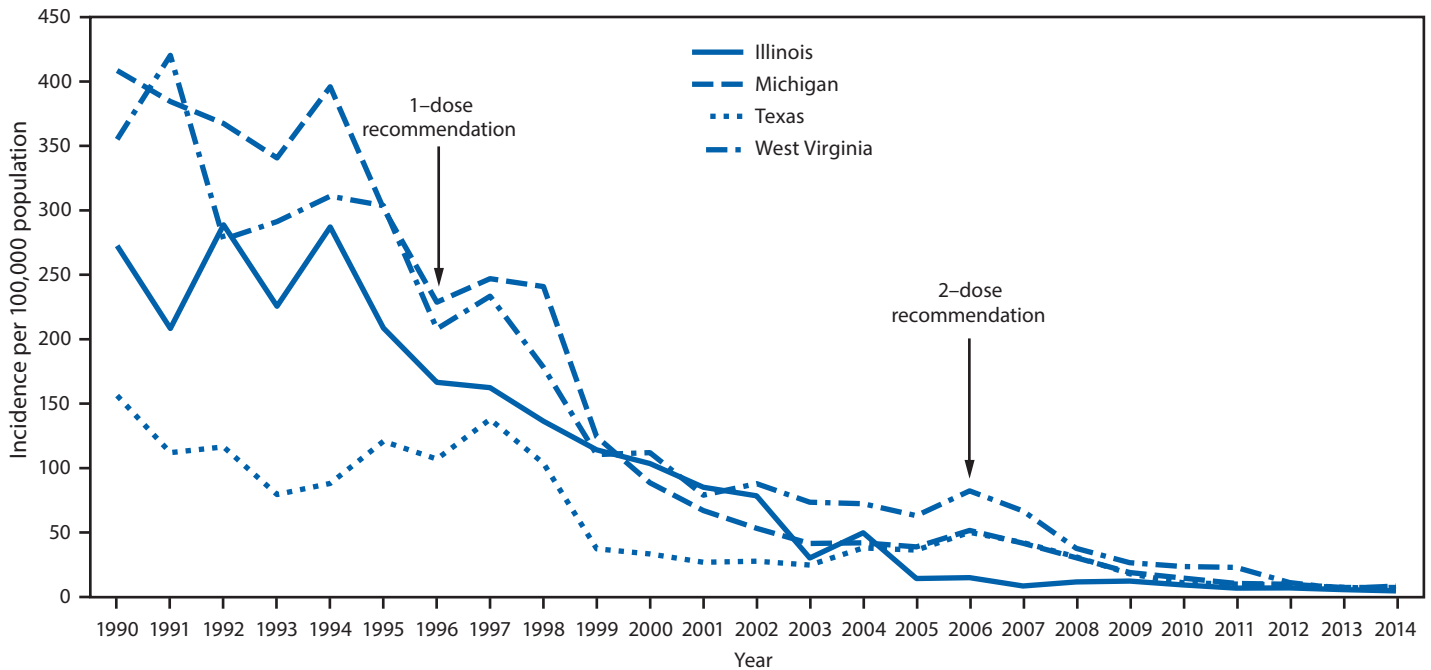
† Percentage declines for each age group are as follows: <1 year, 76.8%; 1–4 years, 58.0%; 5–9 years, 89.3%; 10–14 years, 84.8%; 15–19 years, 35.0%; ≥20 years, 25.0%. Percentage declines were statistically significant ($p < 0.001$) overall and for all age groups.

aged 5–9 years (89.3%) and 10–14 years (84.8%). Fewer states contributed adequate (incidence ≥ 1 case per 100,000 population) and consistent (≥ 3 consecutive years) data (26 in 2005 and 35 in 2014); however, the decline in varicella incidence, when restricted to these states, was similar (80.2%) to that in all reporting states and decreased from 27.3 cases per 100,000 population during 2005–2006 to 5.4 per 100,000 during 2013–2014 ($p < 0.001$).

In the four states (Illinois, Michigan, Texas, and West Virginia) that have been reporting varicella cases annually since before implementation of the varicella vaccination program, incidence declined an average of 97.4% from 1993–1995 to 2013–2014 (range = 92.9%–97.9%) (Figure 3).

During 2013–2014, completeness of varicella-specific data from states that reported to NNDSS varied. Data on vaccination status of varicella patients was available for 12,784 (59.8%) cases; 7,000 (54.8%) of those cases occurred in persons who had received at least 1 dose of varicella vaccine. Among these reports, the number of doses received was reported for 2,266 (32.4%) patients, including 921 (39.0%) persons who had received 1 dose of varicella vaccine, 1,331 (56.4%) who had received 2 doses, and 14 (0.6%) who were reported to have received 3 doses. A total of 3,715 (17.4%) reports included information about hospitalization. Among these reports, 81 (2.2%) indicated that the patient was hospitalized. Reports from 17 (22.4%) of 76 hospitalized patients with information on vaccination status indicated receipt of varicella vaccine, and 13 vaccinated hospitalized patients had information on number of doses. Eight patients had received 1 dose, and five had received 2 doses. Among the 8,358 (39.1%) case reports with data on the number of skin lesions, 4,269 (51.1%) were considered to have had mild disease and 4,089 (48.9%) had moderate to severe disease. Mild disease occurred significantly more frequently among vaccinated patients (76.8%) than among unvaccinated patients (23.2%) ($p < 0.001$). Information on outbreak association of cases was available for 13,826 (64.6%)

FIGURE 3. Varicella incidence per 100,000 population* in states that have reported varicella cases to CDC annually since before implementation of the varicella vaccination program — Illinois, Michigan, Texas, and West Virginia, 1990–2014



* Varicella incidence declined 97.4% overall from 1993–1995 to 2013–2014 (range = 92.9%–97.9%) in the four states (Illinois, Michigan, Texas, and West Virginia) that have reported varicella cases to CDC every year since before implementation of the varicella vaccination program.

reports, among which 2,279 (16.5%) cases were associated with an outbreak. Laboratory testing data were reported for 2,240 (24.6%) of 9,104 cases for which information about varicella testing was available; among these, 1,842 (82.2%) were positive by either polymerase chain reaction, direct fluorescent antibody testing, immunoglobulin M by enzyme-linked immunosorbent assay, or viral culture.

Discussion

Previous reports have documented significant declines in varicella incidence in the United States since the varicella vaccination program was implemented in 1996 through the early years of the 2-dose program (1,3–8). During 1995–2010, data to assess impact of the varicella vaccination program were obtained from a varicella active surveillance project, which was discontinued in 2010 (3). Since 2000, more states are reporting to NNDSS; these data can now be used to assess impact of the program (7). NNDSS data documented an 85% decline in varicella incidence from the 2-year period 2005–2006 (the end of the 1-dose varicella vaccination program) through 2013–2014, and a 97% decline since the varicella vaccination program was implemented. Since recommendation of the second varicella vaccine dose, the largest declines in incidence have occurred in the age groups more likely to have received the second dose (children and adolescents aged 5–14 years).

During 2013–2014, 55% of all reported varicella cases occurred in persons who had received varicella vaccine; this finding is not unexpected in a highly vaccinated population, in which overall incidence declines, but among cases that still occur, a high percentage will be among vaccinated persons.

As varicella incidence continues to decline, more states are able to conduct case-based surveillance. Almost 80% of states are reporting case-based varicella data to CDC for use in national surveillance. However, the completeness of reported data varies, and data from critical variables are missing for approximately 40% of cases. Continued efforts by states to improve reporting and completeness of reported data will be valuable for accurately describing trends and epidemiology of varicella disease.

Although incidence rates were slightly higher when only states with adequate and consistent reporting (7) were included in trend analyses, the percentage declines between 2005–2006 and 2013–2014 were similar. Therefore, removing the adequacy and consistency of reporting criteria for calculating incidence allows for the inclusion of more states to provide a better representation of varicella incidence nationwide.

Varicella surveillance data can also provide information about characteristics of cases that result in severe outcomes such as hospitalization and death. Analyses of administrative (hospital discharge, medical claims, and vital statistics) data

Summary**What is already known about this topic?**

The introduction of a routine childhood dose of varicella vaccine in the United States in 1996 led to an approximate 90% decline in varicella incidence. However, because of continued outbreaks, a second routine childhood dose of varicella vaccine was introduced in 2006. Declines in incidence have continued during the early years since implementation of the 2-dose vaccination recommendation and have made it feasible for more states to conduct varicella case-based surveillance, such that state data reported to CDC through the National Notifiable Diseases Surveillance System (NNDSS) are now used to monitor trends in varicella incidence.

What is added by this report?

Among all states that reported varicella data to NNDSS, there was an 85% decline in varicella incidence from 2005–2006 (the end of the 1-dose varicella vaccination program) to 2013–2014. The largest declines occurred among children and adolescents aged 5–14 years (those age groups likely to receive a second dose). Although the number of states reporting varicella data to CDC has increased over time, >40% of reported cases are missing data for varicella-specific variables important for monitoring the varicella vaccination program.

What are the implications for public health practice?

Further reduction in the number of varicella cases will provide states with increased opportunities for enhancing varicella surveillance and improving completeness of reporting to monitor impact of the vaccination program. These efforts will improve the accuracy of national data, provide important information for further assessment of varicella vaccination, and inform vaccination policy.

have demonstrated significant declines in hospitalizations (86%–93%) and deaths (87%) among all age groups since implementation of the varicella vaccination program (9,10). However, it is important to understand why severe outcomes still occur and whether these outcomes are occurring among vaccinated persons. Improvements in completeness of NNDSS data will permit evaluation of severe outcomes by vaccination status.

The findings in this report are subject to at least three limitations. First, because data are passively reported and case ascertainment is likely incomplete, varicella cases might be missed, resulting in an underestimate of incidence. Conversely, because varicella disease in vaccinated persons is mild and atypical (fewer lesions and predominantly maculopapular rash) and increasingly challenging to diagnose clinically, nonvaricella cases might be misclassified, resulting in possible overestimates of incidence. Second, laboratory testing is still not routinely done for varicella diagnosis; only 25% of reported cases had available information about testing, although some states might not receive laboratory data if results are negative. Finally, approximately 40% of data for important varicella-specific

variables were missing; therefore, the reported findings describing patient characteristics should be interpreted with caution.

With the reduction in the number of varicella cases, states have increased opportunities for improving varicella surveillance to better monitor impact of the vaccination program. Starting in 2015, 48 jurisdictions have been funded through CDC's Epidemiology and Laboratory Capacity program to add a vaccine preventable disease surveillance coordinator to help enhance varicella surveillance. Jurisdictions with varicella case-based surveillance are working to improve reporting of cases and completeness of reporting. In addition, CDC will receive data on varicella outbreaks from all funded jurisdictions, to allow better assessment of impact of the second dose on varicella outbreaks. These efforts will improve the accuracy of national data, provide important information for further assessment of varicella vaccination, and inform vaccination policy.

¹Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, CDC.

Corresponding author: Adriana S. Lopez, MHS, alopez@cdc.gov, 404-639-8369.

References

1. Guris D, Jumaan AO, Mascola L, et al. Changing varicella epidemiology in active surveillance sites—United States, 1995–2005. *J Infect Dis* 2008;197(Suppl 2):S71–5. <http://dx.doi.org/10.1086/522156>
2. Marin M, Güris D, Chaves SS, Schmid S, Seward JF; Advisory Committee on Immunization Practices. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2007;56(No. RR-4).
3. Bialek SR, Perella D, Zhang J, et al. Impact of a routine two-dose varicella vaccination program on varicella epidemiology. *Pediatrics* 2013;132:e1134–40. <http://dx.doi.org/10.1542/peds.2013-0863>
4. Daly ER, Anderson L, Dreisig J, Dionne-Odom J. Decrease in varicella incidence after implementation of the 2-dose recommendation for varicella vaccine in New Hampshire. *Pediatr Infect Dis J* 2013;32:981–3. <http://dx.doi.org/10.1097/INF.0b013e318293308e>
5. Sosa LE, Hadler JL. Epidemiology of varicella in Connecticut, 2001–2005. *J Infect Dis* 2008;197(Suppl 2):S90–3. <http://dx.doi.org/10.1086/522128>
6. Mullins J, Kudish K, Sosa L, Hadler J. Continuing decline in varicella incidence after the 2-Dose Vaccination Recommendation—Connecticut, 2009–2014. *Open Forum Infect Dis* 2015;2:ofv150. <http://dx.doi.org/10.1093/ofid/ofv150>
7. CDC. Evolution of varicella surveillance—selected states, 2000–2010. *MMWR Morb Mortal Wkly Rep* 2012;61:609–12.
8. Leung J, Lopez AS, Blostein J, et al. Impact of the US two-dose varicella vaccination program on the epidemiology of varicella outbreaks: data from nine states, 2005–2012. *Pediatr Infect Dis J* 2015;34:1105–9. <http://dx.doi.org/10.1097/INF.0000000000000821>
9. Leung J, Harpaz R. Impact of the maturing varicella vaccination program on varicella and related outcomes in the United States: 1994–2012. *J Pediatric Infect Dis Soc* 2015;pii044 Epub August 12, 2016. <http://dx.doi.org/10.1093/jpids/piv044>
10. Leung J, Bialek SR, Marin M. Trends in varicella mortality in the United States: Data from vital statistics and the national surveillance system. *Hum Vaccin Immunother* 2015;11:662–8. <http://dx.doi.org/10.1080/21645515.2015.1008880>

Carbapenem-Resistant Enterobacteriaceae Transmission in Health Care Facilities — Wisconsin, February–May 2015

Lina I. Elbadawi, MD^{1,2}; Gwen Borlaug, MPH²; Kristin M. Gundlach³; Timothy Monson, MS³; David Warshauer, PhD³; Maroya S Walters, PhD⁴; Alexander Kallen, MD⁴; Christopher A. Gulvik, PhD⁴; Jeffrey P. Davis, MD²

Carbapenem-resistant Enterobacteriaceae (CRE) are multi-drug-resistant gram-negative bacilli that can cause infections associated with high case fatality rates, and are emerging as epidemiologically important health care-associated pathogens in the United States (1). Prevention of CRE transmission in health care settings is dependent on recognition of cases, isolation of colonized and infected patients, effective use of infection control measures, and the correct use of antibiotics. The use of molecular technologies, including polymerase chain reaction (PCR) testing, pulsed-field gel electrophoresis (PFGE), and whole genome sequencing (WGS), can lead to detection of transmission events and interruption of transmission. In Wisconsin, acute care and critical access hospitals report laboratory-identified CRE to the Wisconsin Division of Public Health (WDPH), and clinical laboratories submit CRE isolates to the Wisconsin State Laboratory of Hygiene (WSLH) for molecular testing. During February–May 2015, a total of 49 CRE isolates from 46 patients were submitted to WSLH. On June 8, WSLH informed WDPH of five carbapenemase-producing CRE isolates with closely related PFGE patterns identified among four inpatients at two hospitals in southeastern Wisconsin. An investigation revealed a high degree of genetic relatedness among the patients' isolates, but did not identify the mechanism of transmission between the two facilities. No breaches in recommended practices were identified; after reviewing respiratory care procedures, no further cases were identified. Routine hospital- and laboratory-based surveillance can detect and prevent health care transmission of CRE.

Since December 1, 2011, WDPH, under its authority in the Department of Health Services Administrative Code Chapter 145, has required all 138 Wisconsin acute care and critical access hospitals to report laboratory-identified CRE, using the multidrug-resistant organism and *Clostridium difficile* infection module of the National Healthcare Safety Network (2). The WSLH laboratory-based CRE surveillance program requests all clinical microbiology laboratories to submit carbapenem-nonsusceptible Enterobacteriaceae isolates to WSLH for PCR testing to determine the presence of genes encoding carbapenemase, including KPC, NDM, IMP, VIM, and OXA-48. All CRE isolates determined by PCR testing to have a carbapenemase gene are subtyped by PFGE testing to detect clusters; CRE isolates with PFGE patterns that are indistinguishable or closely related (1–2 band difference) are reported to WDPH's health

care-associated–infection prevention program for epidemiologic follow-up. WSLH's use of WGS to detect single nucleotide polymorphisms (SNPs) of enteric bacterial pathogens and subsequent expansion of WGS to nonenteric bacteria has further enhanced the capability of WSLH to make genetic comparisons of CRE isolates of interest (3).

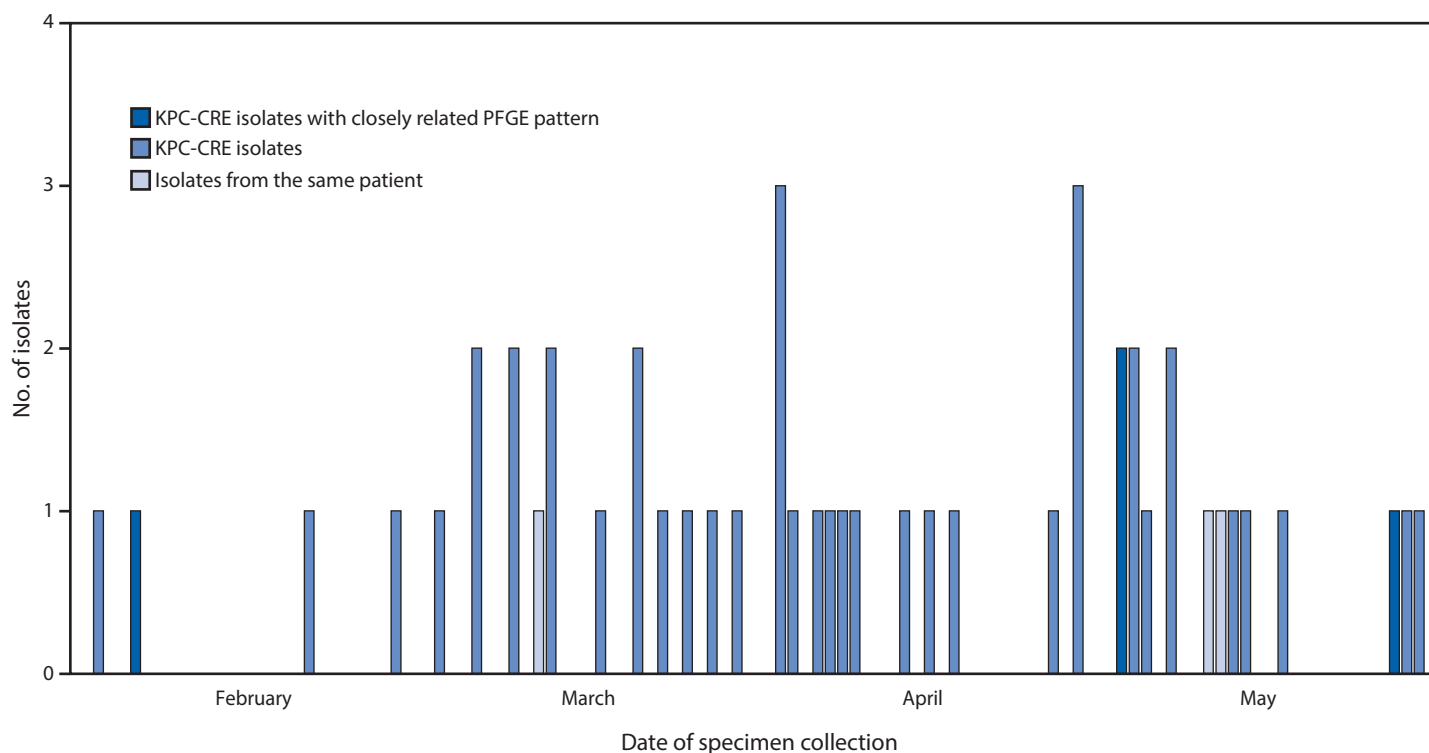
During February–May 2015, a total of 49 CRE isolates from 46 patients that met the National Healthcare Safety Network case definition for laboratory-identified CRE events (2) were submitted to WSLH (Figure 1). On June 8, 2015, WSLH notified WDPH that five carbapenemase-producing CRE isolates with closely related PFGE patterns had been identified among four inpatients at two hospitals in southeastern Wisconsin. A subsequent investigation included analysis of routine PFGE subtyping to detect clusters among all carbapenemase-producing CRE isolates submitted to WSLH and identify possible transmission events not recognized by hospital personnel. WSLH performed WGS on the five-cluster KPC-CRE isolates to characterize further the genetic relatedness. Interpretation of WGS was done at CDC using Lyve-SET, analysis software that identifies high quality SNPs (hqSNPs; sites with at least 10X coverage and 75% consensus)* (4). The bootstrap statistical method (resampling with replacement) was used to assess phylogenetic variation among genes in the WGS.

To determine hospital care points common to the four patients and possible modes of CRE transmission, WDPH personnel developed an instrument for epidemiologic data collection and conducted medical record reviews, site visits (October 28 and November 9, 2015), a review of respiratory care protocols, and interviews with infection prevention staff members, primary care providers, and patients (when available). During July 15–August 12, 2015, active surveillance was conducted in the respiratory units of concern at the two hospitals to determine whether ongoing transmission of KPC-CRE was occurring. Surveillance rectal swabs were collected once weekly among all patients hospitalized in the two respiratory units and submitted to WSLH for CRE culture.

Among the 49 isolates submitted during February–May 2015 (Figure 1), one cluster of five KPC-CRE isolates with two closely related PFGE patterns was detected among

* 10X coverage means each position must have at least 10 Illumina reads map to it; 75% consensus means that the identity of each position must be $\geq 75\%$ of a single nucleotide (<https://github.com/lskatz/lyve-SET>).

FIGURE 1. Number of laboratory-confirmed carbapenem-resistant Enterobacteriaceae (CRE) isolates,* by date of specimen collection — Wisconsin, February–May 2015



Abbreviation: PFGE = pulsed-field gel electrophoresis.

* N = 49 isolates from 46 unique patients.

four inpatients (patients A–D) at two hospitals (hospital 1 and hospital 2) in southeastern Wisconsin: one isolate each from patients A, B, and D, and two isolates from patient C (Figure 2). The remaining 44 isolates, which included 20 KPC-CRE isolates, had unique PFGE patterns that did not match one another or the cluster patterns.

Isolates obtained from patients A and B (hospital 1) differed by two hqSNPs; no hqSNP differences were detected among isolates from patients C and D (hospital 2). Isolates from patients A and B each differed from isolates from patients C and D by only one hqSNP (Figure 3), indicating a high degree of sequence relatedness among all five KPC-CRE isolates. This is consistent with the occurrence of one or more intrafacility transmission events in hospital 1 and hospital 2.

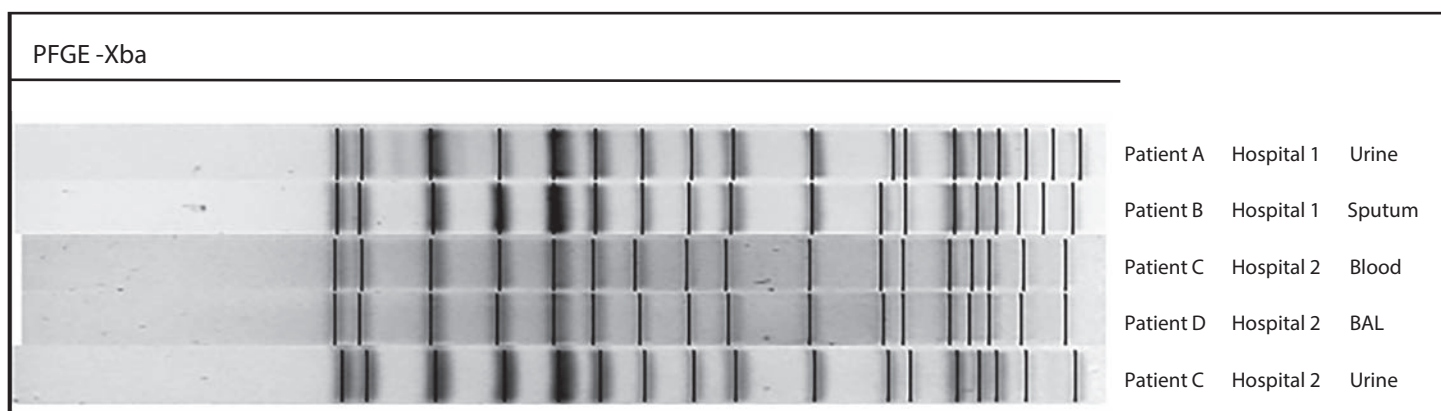
Median age of the four patients was 65 years (range = 52–75 years), all were non-Hispanic whites, and two were women; median hospitalization length was 83 days (range = 65–103 days). Illnesses diagnosed among the patients at admission included postviral ascending weakness consistent with Guillain-Barré syndrome, cerebrovascular accident, pneumonia, and bacteremia during and after chemotherapy, radiation, and surgical resection of a glioblastoma. All four patients had been intubated and undergone a tracheostomy and had previous percutaneous

endoscopic gastrostomy performed. However, none of these procedures had occurred at the same facility. None of the patients had undergone a gastrointestinal procedure that placed them at high risk for exposure to CRE (e.g., endoscopic retrograde cholangiopancreatography) (5).

Patient A was hospitalized during December 11, 2014–January 22, 2015, and patient B was hospitalized during March 20–April 26, 2015, in the same respiratory unit of hospital 1, but 57 days apart. Patient C was hospitalized during March 2–May 8, 2015, in hospital 2's medical respiratory intensive care unit, and patient D was hospitalized during February 26–April 6, 2015, on the orthopedic surgical floor and was subsequently hospitalized in the medical respiratory intensive care unit during June 2–June 16, 2015, 25 days after patient C was discharged. On March 22, 2015, patients C and D had a 24-hour period of overlap in hospital 2's medical respiratory intensive care unit, when patient D was moved from the orthopedic surgical floor for acute respiratory management. Although patients A–D were not transferred between hospitals 1 and 2, patient transfers between these two facilities are common.

A total of 122 rectal swabs were collected among 83 patients hospitalized in the two respiratory units during

FIGURE 2. Pulsed-field gel electrophoresis (PFGE) subtyping comparison of five KPC-producing *Klesbsiella pneumoniae* isolates digested with XbaI — Wisconsin, February–May 2015



Abbreviation: BAL = bronchoalveolar lavage.

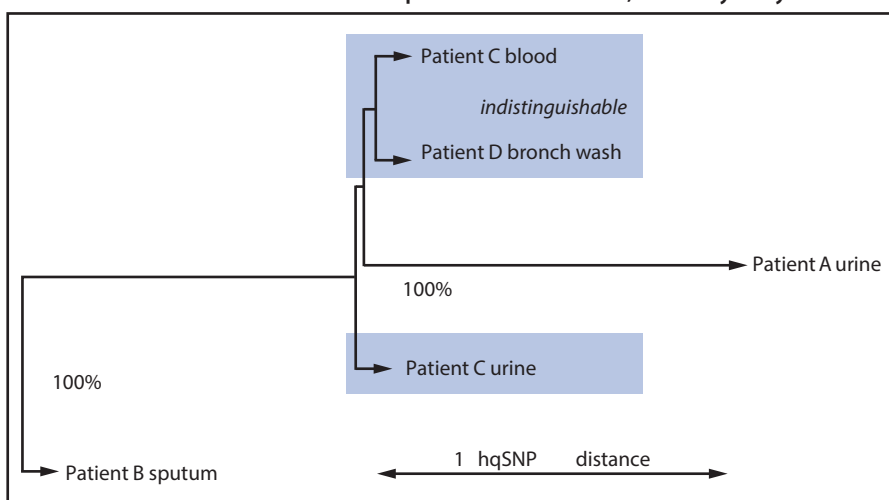
July 15–August 12 (the active surveillance period). During this period, a patient with previously known KPC-CRE infection (Patient E) was transferred from hospital 2 to hospital 1. Other than a specimen isolate from patient E, which did not match the cluster isolates, no KPC-CRE isolates were recovered in culture and no evidence of further CRE transmission was detected.

WDPH personnel conducted site visits and reviewed infection prevention protocols and policies for care of the ventilator circuit with infection prevention personnel at both facilities. These reviews were based on CDC Guidelines for Preventing Health-Care–Associated Pneumonia (6). No breaches in recommended practices were identified; however, infection prevention personnel could not describe respiratory personnel hand hygiene practices after handling of the circuit tubing. Thus, WDPH personnel recommended a facility compliance check of those practices. Public health actions to prevent future transmission of CRE at these hospitals included WDPH personnel working with infection prevention staff members regarding infection prevention measures related to ventilator care. No subsequent clusters of KPC-CREs have been reported from hospitals 1 and 2.

Discussion

Although the precise mechanism of CRE transmission was not determined, WDPH personnel used the detection of the KPC-CRE cluster to raise awareness among the hospitals' infection prevention staff members regarding the possibility of intrafacility CRE transmission events among their patients.

FIGURE 3. Maximum likelihood phylogenetic tree* of five carbapenem-resistant Enterobacteriaceae isolates from four patients — Wisconsin, February–May 2015†,§



Abbreviations: bronch = bronchoalveolar; hqSNP = high quality single nucleotide polymorphism.

* 100 bootstraps performed; bootstraps with <50% confidence are not labeled at their nodes.

† The three isolates in shaded areas were indistinguishable from one another (i.e., 0 hqSNPs apart).

§ To focus on the five outbreak leaves, the two unrelated control isolates used to root the phylogeny are not illustrated.

The circumstances provided an opportunity for review of facility infection prevention practices and respiratory care processes critical to prevention of health care–associated pneumonia. After addressing these concerns, no evidence of further transmission of these closely related strains of KPC-CRE at these facilities was found.

The investigation demonstrated the importance of routine hospital- and laboratory-based surveillance for the detection of health care–related transmission of CRE. The use of molecular subtyping methods (e.g., PFGE and WGS) to determine genetic relatedness of the bacterial isolates was particularly valuable. Matching PFGE patterns among isolates and subsequent WGS analysis of KPC-CRE led to focused

Summary**What is already known about this topic?**

Carbapenem-resistant Enterobacteriaceae (CRE) are multidrug-resistant gram-negative bacilli that can cause infections associated with high case fatality rates, and are emerging as epidemiologically important health care–associated pathogens in the United States. Prevention of CRE transmission in health care settings is dependent on recognition of cases, isolation of colonized and infected patients, effective use of infection control measures, and the correct use of antibiotics.

What is added by this report?

Through the Wisconsin State Laboratory of Hygiene laboratory-based CRE surveillance program, which requests all clinical microbiology laboratories to submit carbapenem-nonsusceptible Enterobacteriaceae isolates for molecular testing by one or more methods (e.g., polymerase chain reaction [PCR], pulsed-field gel electrophoresis [PFGE], and whole genome sequencing [WGS]), a cluster of CRE infections among four hospital inpatients at two southeastern Wisconsin hospitals was discovered. At the time, personnel at the two implicated hospitals were not previously aware of the possibility of transmission of CRE among their patients.

What are the implications for public health practice?

The use of molecular technologies, including PCR testing, PFGE, and WGS, can lead to detection of transmission events and interruption of transmission by uncommon and multidrug-resistant organisms. Public health and other programs that include antibiotic stewardship and antimicrobial resistance monitoring might benefit from data generated by molecular testing of multidrug-resistant organisms to enhance detection of intra- and interfacility transmission events.

epidemiologic investigations, subsequent cluster identification, and opportunities to provide infection prevention education to staff members at the involved hospitals.

Although routine use of PFGE and subsequent WGS in this investigation represents a novel application of technology to detect CRE transmission, the burden of resources might preclude similar use in states with medium-to-high prevalences of CRE. However, the increasing availability of WGS might improve utility of this approach in the future. In Wisconsin, a state with relatively low CRE prevalence since the inception of statewide CRE surveillance during December 2011–April 2016, PFGE has been conducted on 225 CRE isolates (average = ~50 per year). Five clusters have been detected, and attendant public health–related responses likely prevented further transmission and case occurrences in health care facilities.

This report is subject to at least one limitation. PFGE patterns can be remarkably similar among certain CRE in the absence of any epidemiologic link. This is especially true of ST258 CR-producing *Klebsiella pneumoniae* (7). Therefore,

PFGE data must be considered with epidemiologic data to determine potential transmission events.

Multidrug-resistant organisms, in particular CRE, have the capability of spreading undetected, with the possibility of devastating outbreaks in health care settings (8). Routine hospital- and laboratory-based surveillance for the detection of CRE and the use of molecular techniques to characterize isolates can detect and reduce occurrence of multidrug-resistant infections through interventions designed to interrupt transmission. Timely access to technology and results can facilitate rapid implementation of effective interventions (9).

Acknowledgments

Infection prevention, nursing, and respiratory staff members from hospital 1 and hospital 2, southeastern Wisconsin.

¹Epidemic Intelligence Service, Division of Scientific Education and Professional Development, CDC; ²Bureau of Communicable Diseases, Wisconsin Division of Public Health; ³Wisconsin State Laboratory of Hygiene, ⁴Division of Healthcare Quality Promotion, CDC.

Corresponding author: Lina I. Elbadawi, lebadawi@cdc.gov, 608-266-0392.

References

1. CDC. Vital signs: carbapenem-resistant Enterobacteriaceae. *MMWR Morb Mortal Wkly Rep* 2013;62:165–70.
2. CDC. Multidrug-resistant organism & *Clostridium difficile* infection (MDRO/CDI) module. Atlanta, GA: US Department of Health and Human Services, CDC; 2016. http://www.cdc.gov/nhsn/pdfs/pscmanual/12pscmdro_cdadcurrent.pdf
3. Marsh JW, Krauland MG, Nelson JS, et al. Genomic epidemiology of an endoscope-associated outbreak of *Klebsiella pneumoniae* carbapenemase (KPC)-producing *K. pneumoniae*. *PLoS One* 2015;10:e0144310. <http://dx.doi.org/10.1371/journal.pone.0144310>
4. Katz LS, Petkau A, Beaulaurier J, et al. Evolutionary dynamics of *Vibrio cholerae* O1 following a single-source introduction to Haiti. *MBio* 2013;4:e00398–13. <http://dx.doi.org/10.1128/mBio.00398-13>
5. Epstein L, Hunter JC, Arwady MA, et al. New Delhi metallo- β -lactamase-producing carbapenem-resistant *Escherichia coli* associated with exposure to duodenoscopes. *JAMA* 2014;312:1447–55. <http://dx.doi.org/10.1001/jama.2014.12720>
6. Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R; CDC; Healthcare Infection Control Practices Advisory Committee. Guidelines for preventing health-care–associated pneumonia, 2003: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. *MMWR Recomm Rep* 2004;53(No. RR-3).
7. Navon-Venezia S, Leavitt A, Schwaber MJ, et al.; Israeli KPC Kpn Study Group. First report on a hyperepidemic clone of KPC-3-producing *Klebsiella pneumoniae* in Israel genetically related to a strain causing outbreaks in the United States. *Antimicrob Agents Chemother* 2009;53:818–20. <http://dx.doi.org/10.1128/AAC.00987-08>
8. Bush K. Bench-to bedside review: the role of beta-lactamases in antibiotic-resistant Gram-negative infections. *Crit Care* 2010;14:224. <http://dx.doi.org/10.1186/cc8892>
9. Ben-David D, Maor Y, Keller N, et al. Potential role of active surveillance in the control of a hospital-wide outbreak of carbapenem-resistant *Klebsiella pneumoniae* infection. *Infect Control Hosp Epidemiol* 2010;31:620–6. <http://dx.doi.org/10.1086/652528>

Guillain-Barré Syndrome During Ongoing Zika Virus Transmission — Puerto Rico, January 1–July 31, 2016

Emilio Dirlikov, PhD^{1,2}; Chelsea G. Major, MPH^{3,4}; Marrielle Mayshack^{1,4}; Nicole Medina, MPH³; Desiree Matos³; Kyle R. Ryff, MPH¹; Jomil Torres-Aponte, MS¹; Rebecca Alkis⁵; Jorge Munoz-Jordan, PhD³; Candimar Colon-Sanchez, MS³; Jorge L. Salinas, MD²; Daniel M. Pastula, MD^{3,6}; Myriam Garcia, MT^{7,8}; Marangely Olivero Segarra, MS^{7,8}; Graciela Malave, MT^{7,8}; Dana L. Thomas, MD⁹; Gloria M. Rodríguez-Vega, MD¹⁰; Carlos A. Luciano, MD¹¹; James Sejvar, MD¹²; Tyler M. Sharp, PhD³; Brenda Rivera-Garcia, DVM¹

On August 26, 2016, this report was posted as an MMWR Early Release on the MMWR website (<http://www.cdc.gov/mmwr>).

Guillain-Barré syndrome (GBS) is a postinfectious autoimmune disorder characterized by bilateral flaccid limb weakness attributable to peripheral nerve damage (1). Increased GBS incidence has been reported in countries with local transmission of Zika virus, a flavivirus transmitted primarily by certain *Aedes* species mosquitoes (2). In Puerto Rico, three arthropod-borne viruses (arboviruses) are currently circulating: Zika, dengue, and chikungunya. The first locally acquired Zika virus infection in Puerto Rico was reported in December 2015 (3). In February 2016, the Puerto Rico Department of Health (PRDH), with assistance from CDC, implemented the GBS Passive Surveillance System (GBPSS) to identify new cases of suspected GBS (4). Fifty-six suspected cases of GBS with onset of neurologic signs during January 1–July 31, 2016, were identified. Thirty-four (61%) patients had evidence of Zika virus or flavivirus infection; the median age of these patients was 55 years (range = 21–88 years), and 20 (59%) patients were female. These 34 patients were residents of seven of eight PRDH public health regions. All 34 patients were hospitalized and treated with intravenous immunoglobulin G (IVIg), the standard treatment for GBS; 21 (62%) required intensive care unit admission, including 12 (35%) who required endotracheal intubation and mechanical ventilation. One patient died of septic shock after treatment for GBS. Additionally, 26 cases of neurologic conditions other than GBS were reported through GBPSS, including seven (27%) in patients with evidence of Zika virus or flavivirus infection. Residents of and travelers to Puerto Rico and countries with active Zika virus transmission should follow recommendations for prevention of Zika virus infections.* Persons with signs or symptoms consistent with GBS should promptly seek medical attention. Health care providers in areas with ongoing local transmission seeing patients with neurologic illnesses should consider GBS and report suspected cases to public health authorities.

* <http://www.cdc.gov/zika/prevention/>.

Epidemiologic Surveillance for GBS

In February 2016, as part of the ongoing response to local Zika virus transmission (3–5), PRDH implemented GBPSS with CDC assistance. Health care providers throughout the island are requested to report all patients with suspected GBS to PRDH by submitting a case report form[†] along with patient specimens (serum, urine, cerebrospinal fluid [CSF], and saliva). Reporting of patients with other neurologic disorders and a suspected antecedent arboviral infection is also encouraged. All submitted specimens are tested at CDC Dengue Branch (San Juan, Puerto Rico) or PRDH Biological and Chemical Emergencies Laboratory using a Triplex reverse transcription–polymerase chain reaction (RT-PCR) assay to detect nucleic acid from Zika, dengue, and chikungunya viruses.[§] Serum and CSF specimens are also tested by immunoglobulin M (IgM) enzyme-linked immunosorbent assay (ELISA) for all three viruses. Persons with Zika virus nucleic acid detected by RT-PCR in any specimen are considered to have confirmed Zika virus infection. Persons with negative results for Zika virus by RT-PCR in all specimens tested are considered to have presumptive recent infection with a single arbovirus when results are positive for that virus by IgM ELISA, and presumptive flavivirus infection if they test positive for both Zika virus and dengue virus by IgM ELISA. Neurologic diagnosis for GBS cases with evidence of arboviral infection was confirmed by chart review using the Brighton Collaboration criteria, a set of standardized diagnostic criteria based on clinical presentation, CSF laboratory results, and electrophysiologic findings (6). Chart reviews are performed after hospital discharge, >28 days after onset of neurologic signs for persons who remain hospitalized, or death.

Fifty-six suspected cases of GBS with onset of neurologic signs during January 1–July 31, 2016, were identified, including one case identified before implementation of GBPSS and

[†] The GBS case report form is available in both Spanish (<http://www.salud.gov.pr/Sobre-tu-Salud/Documents/Español.pdf>) and English (<http://www.salud.gov.pr/Sobre-tu-Salud/Documents/ingl%c3%a9s.pdf>).

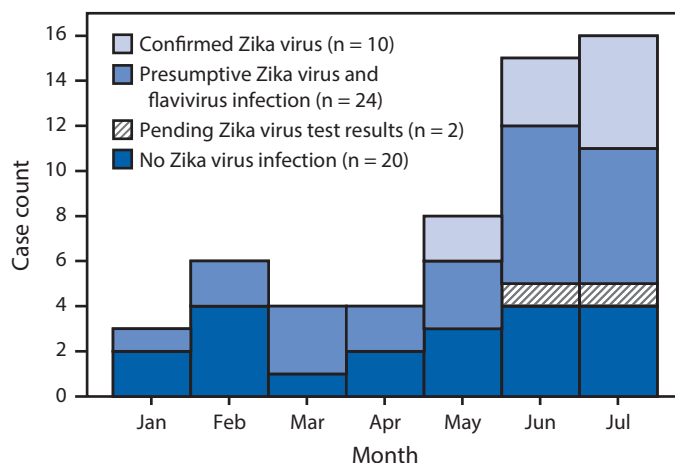
[§] <http://www.fda.gov/20EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm485199.htm>.

two cases identified during a mid-year assessment of the surveillance system. Among identified suspected cases of GBS, 20 patients (37%) had no evidence of Zika virus infection, two (4%) patients had pending laboratory test results, and 34 (61%) patients had any evidence of Zika virus or flavivirus infection. Among these 34 patients, 10 (18%) had confirmed Zika virus infection, 16 (29%) had presumptive Zika virus infection, and eight (14%) had presumptive flavivirus infection. Additionally, one (2%) patient had equivocal results for both Zika and dengue virus by IgM ELISA, and three (5%) had equivocal results for chikungunya virus by IgM ELISA.

During January–July 2016, the median monthly case count of persons with suspected GBS and no evidence of Zika virus infection or pending laboratory results, by month of onset of neurologic signs, was three (range = 1–5). Overall, the number of persons with suspected GBS and evidence of Zika virus or flavivirus infection was 2.5 times greater than the number of persons with suspected GBS and no evidence of Zika virus infection, with an increasing number of cases occurring each month beginning in April (Figure 1). The 34 patients with suspected GBS and evidence of Zika virus or flavivirus infection were residents of seven of eight PRDH health regions (Figure 2); the median age of these patients was 55 years (range = 21–88 years), and 20 (59%) of the 34 patients were female.

Charts have been reviewed for 32 of these 34 patients; GBS was confirmed for all 32. Acute illness during the preceding 2 months was recorded in the medical charts of 30 (94%) patients (Table). The most frequently reported symptoms associated with the reported antecedent acute illness were rash (n = 18, 53%), fever (n = 12, 35%), and diarrhea (n = 7, 21%). Median interval from antecedent acute illness to onset of neurologic signs was 5 days (range = 0–17 days). All 34 patients were hospitalized after onset of neurologic signs, and among patients who were discharged (n = 28) or had died (n = 1) as of August 18, median duration of hospitalization was 12 days (range = 6–47 days). Among the 32 patients with completed chart reviews, the most common recorded clinical neurologic signs and symptoms were hyporeflexia or areflexia (n = 31, 97%), leg weakness (n = 31, 97%), leg paresthesia (n = 24, 75%), arm weakness (n = 24, 75%), facial weakness (n = 20, 63%), arm numbness (n = 19, 59%), and dysphagia (n = 19, 59%). All 25 patients who underwent lumbar punctures had cytoalbuminologic dissociation (increased CSF protein concentration and total CSF white blood cell count <50 cells/ μ l), which is frequently observed in patients with GBS. Five patients had electrophysiologic testing, which indicated the acute inflammatory demyelinating polyneuropathy subtype of GBS in all five. All 34 patients were treated with IVIg. As of August 18, 21 (62%) of 34 patients had been admitted to intensive care units, and 12 (35%) required mechanical ventilation.

FIGURE 1. Reported cases of confirmed and suspected Guillain-Barré syndrome (n = 56), by Zika virus laboratory result and month of onset of neurologic signs — Puerto Rico, January 1–July 31, 2016



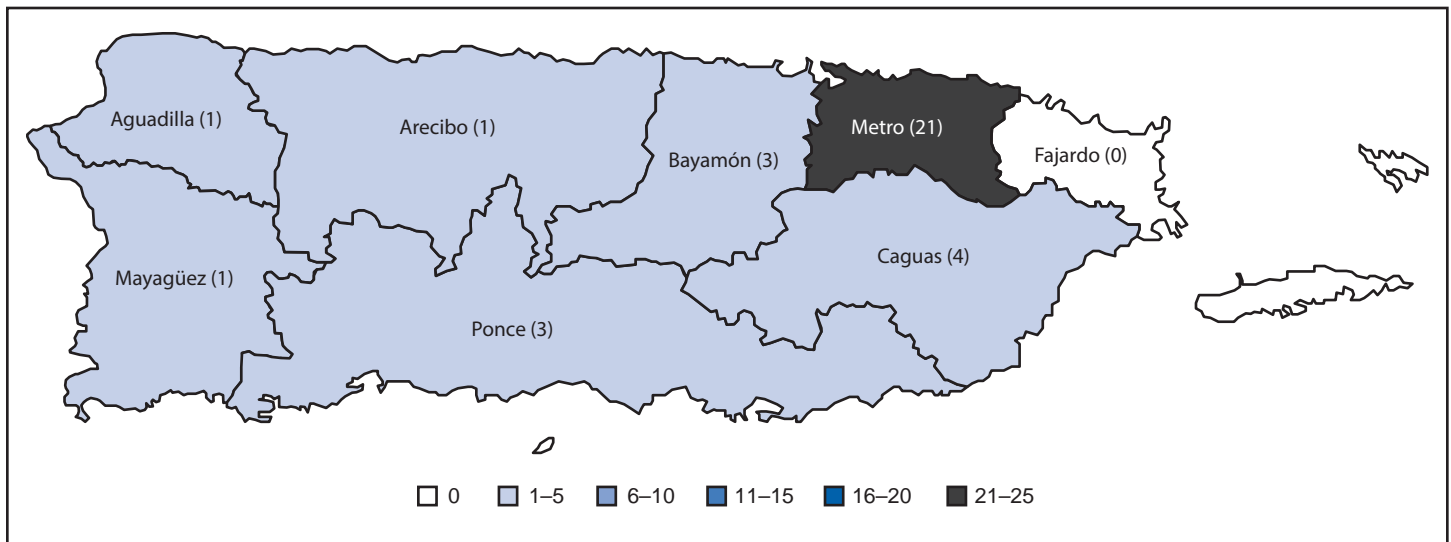
As of August 18, five (15%) patients remained hospitalized, 15 (44%) were discharged home, and 13 (38%) were transferred to a rehabilitation or skilled nursing facility. One patient (3%) with presumptive flavivirus infection died of septic shock, despite treatment with broad-spectrum antibiotics.

Additionally, 26 cases of neurologic disorders other than GBS were reported to PRDH via GBPSS; seven (27%) patients had evidence of recent Zika virus or flavivirus infection. The neurologic disorders among these seven patients include three cases of encephalitis (one patient had confirmed Zika virus infection, one had presumptive Zika virus infection, and one had presumptive flavivirus infection); two cases of myelitis, both in patients with confirmed Zika virus infection; one case of acute neurologic deficit, in a patient with confirmed Zika virus infection; and one case of postinfectious papilledema, in a patient with presumptive Zika virus infection.

Surveillance System Assessment

During July 2016, the surveillance system's completeness in ascertaining suspected cases of GBS was assessed. Thirty-two (46%) of 70 total hospitals on the island were contacted. Hospital staff members from medical records or infection control departments were asked to provide a list of patients who had been hospitalized during January–June 2016, and who had an *International Classification of Disease, 10th revision* code for GBS (G61.0) in their medical record. Unreported cases of possible GBS were defined as patients who were hospitalized after GBPSS was initiated in mid-February, had hospital stays >3 days, and were not reported to GBPSS. Patients with an alternative final diagnosis were excluded. Twenty-six (81%) of the 32 contacted hospitals responded, including 13 of the 16 hospitals that reported at least one suspected case of GBS and

FIGURE 2. Reported cases of confirmed and suspected Guillain-Barré syndrome in persons with evidence of Zika virus or flavivirus infection, by public health region of residence — Puerto Rico, January 1–July 31, 2016 (N = 34)



13 hospitals from a purposive sample of 16 hospitals selected randomly among the remaining hospitals on the island after stratifying by hospital size and region.

Two cases of possible GBS that had not been reported directly to GBPSS were identified. Both had specimens submitted to PRDH's Passive Arboviral Diseases Surveillance System shortly before onset of their neurologic illness, which confirmed Zika virus infection.[‡] The patients were hospitalized for GBS in May and June respectively, and GBS diagnosis was confirmed by chart review.

Discussion

Because of the increased incidence of GBS reported in countries affected by Zika virus (7), PRDH implemented GBPSS soon after reporting the first case of Zika virus disease (4). Timely reporting has allowed for identification of ten cases of GBS with Zika virus infection confirmed by RT-PCR. Before this report, only individual cases of confirmed Zika virus infection in patients with GBS have been described (8). Cases of GBS with evidence of flavivirus infection are expected to be attributable to Zika virus, the predominant flavivirus currently circulating in Puerto Rico; during November 1, 2015–July 7, 2016, PRDH identified 5,582 confirmed and presumptive Zika virus cases compared with only 136 cases of dengue virus infections (5). Although fatalities among GBS patients are rare (1), the potential severity and burden of GBS on the health care system are highlighted by the death described here and

by the large proportion of patients that required intensive care services, including mechanical ventilation.

Consistent with the global epidemiology of GBS, the median age of patients with suspected GBS and evidence of Zika virus or flavivirus infection was >50 years (9). Although GBS generally occurs somewhat more frequently in men than in women (9), the majority of patients described in this report were females. Analyses to explore the unexpected distribution of cases by sex are planned, including an apparent predominance of women in Puerto Rico with Zika virus infections. Although provider outreach activities and GBS case clustering might partially explain increased monthly case counts during April–July, an increased number of cases is consistent with ongoing Zika virus transmission. In French Polynesia, where a Zika virus disease outbreak occurred during 2013–2014, an increase in the number of GBS patients was reported (7). In contrast to French Polynesia, where electrophysiologic studies (when performed) identified the acute motor axonal neuropathy subtype of GBS (7), in Puerto Rico, the acute inflammatory demyelinating polyneuropathy subtype of GBS was identified in all five GBS cases with evidence of Zika virus or flavivirus infection who had electrophysiologic studies performed. Consistent with other reports that have found a range of neurologic conditions potentially associated with Zika virus infection (10), 27% of the 26 patients with neurologic conditions other than GBS identified through the GBPSS had evidence of Zika virus or flavivirus infection.

Residents of and travelers to Puerto Rico and countries with ongoing Zika virus transmission should follow recommendations for prevention of Zika virus infections. Given

[‡]PRDH and CDC Dengue Branch incorporated Zika virus case reporting and diagnostic testing into existing dengue and chikungunya virus surveillance systems and developed a laboratory-based Passive Arboviral Diseases Surveillance System.

TABLE. Characteristics, interpretation of laboratory results, confirmation of neurologic diagnosis, and course of illness in patients with Guillain-Barré syndrome (GBS)* and evidence of Zika virus or flavivirus infection (N = 34) — Puerto Rico, January 1–July 31, 2016

Characteristic	Median (range)
Age (yrs)	55 (21–88)
Sex	No. (%) of patients
Female	20 (59)
Interpretation of laboratory results	
Confirmed Zika virus infection	10 (29)
Presumptive Zika virus infection	16 (47)
Presumptive flavivirus infection	8 (24)
Confirmation of neurologic diagnosis via chart review	
Patient charts reviewed	32 (94)
Patients with confirmed GBS diagnosis	32 (94)
Patients pending chart review	2 (6)
Course of illness	
Duration (days) (N = 32*)	Median (range)
Antecedent acute illness to neurologic symptom onset	5 (0–17)
Hospitalization [†]	12 (6–47)
Antecedent illness (N = 32*)	No. (%) of patients
Acute antecedent illness [§]	30 (94)
Rash	18 (56)
Fever	12 (38)
Diarrhea	7 (22)
Signs and symptoms of neurologic illness (N = 32*)	
Hyporeflexia or areflexia	31 (97)
Leg weakness	31 (97)
Leg paresthesia	24 (75)
Arm weakness	24 (75)
Face weakness	20 (63)
Arm paresthesia	19 (59)
Dysphagia	19 (59)
Cytoalbuminologic dissociation (N = 25) [¶]	25 (100)
Electrophysiologic findings (N = 5)**	
Acute inflammatory demyelinating polyneuropathy subtype	5 (100)
Medical interventions	
Admitted to hospital	34 (100)
Intravenous immunoglobulin G	34 (100)
Admitted to intensive care unit	21 (62)
Mechanical ventilation	12 (35)
Clinical outcome (N = 29)[†]	
Discharged home	15 (52)
Discharged to rehabilitation center or skilled nursing facility	13 (45)
Died	1 (3)

* Data for 32 confirmed cases of GBS gathered via patient chart review. Because of chart review criteria, chart review is pending for two suspected cases of GBS with evidence of Zika virus or flavivirus infection.

[†] Does not include five patients still hospitalized as of August 18, 2016.

[§] Defined as antecedent illness in the two months preceding onset of neurologic signs, as recorded in the medical record.

[¶] Refers to increased cerebrospinal fluid protein concentration and cerebrospinal fluid total white cell count <50 cells/ μ l. Lumbar punctures were performed and cerebrospinal fluid results were available for 25 patients.

** Electrophysiologic studies available for five patients.

Summary

What is already known about this topic?

Guillain-Barré syndrome (GBS) is an uncommon autoimmune disorder characterized by varying degrees of weakness, sensory abnormalities, and autonomic dysfunction due to peripheral nerve or nerve root damage. Countries affected by Zika virus have reported increased numbers of cases of GBS. After identification of local transmission of Zika virus in Puerto Rico in December 2015, the Puerto Rico Department of Health implemented the GBS Passive Surveillance System in February 2016.

What is added by this report?

Among 56 patients with suspected GBS who had onset of neurologic symptoms during January 1–July 31, 2016, evidence of Zika or other flavivirus infection was present in 34 (61%), including 10 (18%) with confirmed Zika virus infection. The median age of the 34 patients was 55 years, and 59% were female. Thirty (88%) patients reported an acute illness before developing neurologic symptoms, with median time to onset of neurologic symptoms of 5 days. One patient died from septic shock after treatment for GBS. Additionally, evidence of Zika virus or flavivirus infection was detected in seven patients with neurologic disorders other than GBS.

What are the implications for public health practice?

Persons with signs or symptoms consistent with GBS should promptly seek medical attention. Health care providers who evaluate patients with neurologic illnesses should consider GBS and report suspected cases to public health authorities. Residents of and travelers to Puerto Rico are advised to follow existing recommendations for prevention of Zika virus infection.

the potential increase in GBS incidence during ongoing Zika virus transmission, health care providers in areas with ongoing local transmission should be familiar with the clinical features of GBS to ensure timely patient diagnosis and treatment. Patients with signs and symptoms consistent with GBS should seek medical attention, regardless of antecedent illness. Health care providers should report suspected cases of GBS and other neurologic conditions to public health authorities.**

** <http://www.salud.gov.pr/Sobre-tu-Salud/Pages/ProfesionalesdeSalud.aspx#gbszika>.

Acknowledgments

Norma Diaz Paris, Juan B. Méndez, Anibal Cruz Sanchez, Jazmín Román, María V. Ramos, Zobeida Santiago, Laura Castro, Central and Regional Offices of Epidemiology and Research, Puerto Rico Department of Health; Cesar A. Virgen, MD, University of California San Diego; Elba V. Caraballo, PhD, Koraly Torres Alicea, Damaris Laboy Fernández, Janice Perez, MPH, Vera Soltero, JD, MPH, Division of Vector-Borne Diseases, CDC; Tyler Chavers, Emory University, Atlanta, Georgia; Yvette Lopez Vazquez, San Juan Bautista School of Medicine, Puerto Rico; Brenda Deliz, MD, University of Puerto Rico; University District Hospital, Puerto Rico; Hospital Pediátrico Universitario, Puerto Rico; HIMA-San Pablo, Caguas and Bayamón, Puerto Rico; University of Puerto Rico Hospital — Dr. Federico Trilla; Municipal Hospital of San Juan, Puerto Rico; Hospital Auxilio Mutuo, Puerto Rico; Veterans Association Hospital of San Juan, Puerto Rico; Hospital Damas, Puerto Rico; Manatí Medical Center, Puerto Rico; Mayagüez Medical Center, Puerto Rico; Doctor's Center Hospital, Bayamón and Manatí, Puerto Rico; HealthSouth Rehabilitation Center, San Juan, Puerto Rico; Hospital Oriente, Puerto Rico; Hospital Pavia, Arecibo, Santurce, Hato Rey, and Yauco, Puerto Rico; Ryder Memorial Hospital, Puerto Rico.

¹Office of Epidemiology and Research, Puerto Rico Department of Health; ²Epidemic Intelligence Service, Division of Scientific Education and Professional Development, CDC; ³Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC; ⁴Office for State, Tribal, Local, and Territorial Support, CDC; ⁵Emory University, Atlanta, Georgia; ⁶Department of Neurology and Division of Infectious Diseases, University of Colorado Denver; ⁷Biological and Chemical Emergencies Laboratory, Office of Public Health Preparedness and Response, Puerto Rico Department of Health; ⁸Public Health Laboratory, Puerto Rico Department of Health; ⁹Division of State and Local Readiness, Office of Public Health Preparedness and Response, CDC; ¹⁰HIMA-San Pablo, Caguas, Puerto Rico; ¹¹University of Puerto Rico; ¹²Office of Infectious Disease, National Center for Emerging and Zoonotic Infectious Diseases, CDC.

Corresponding author: Emilio Dirlikov, GBS@salud.pr.gov, 787-706-4358.

References

1. Yuki N, Hartung H-P. Guillain-Barré syndrome. *N Engl J Med* 2012;366:2294–304. <http://dx.doi.org/10.1056/NEJMra1114525>
2. Petersen LR, Jamieson DJ, Honein MA. Zika virus. *N Engl J Med* 2016;375:294–5.
3. Thomas DL, Sharp TM, Torres J, et al. Local transmission of Zika virus—Puerto Rico, November 23, 2015–January 28, 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:154–8. <http://dx.doi.org/10.15585/mmwr.mm6506e2>
4. Dirlikov E, Ryff KR, Torres-Aponte J, et al. Update: ongoing Zika virus transmission—Puerto Rico, November 1, 2015–April 14, 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:451–5. <http://dx.doi.org/10.15585/mmwr.mm6517e2>
5. Adams L, Bello-Pagan M, Lozier M, et al. Update: ongoing Zika virus transmission—Puerto Rico, November 1, 2015–July 7, 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:774–9. <http://dx.doi.org/10.15585/mmwr.mm6530e1>
6. Sejvar JJ, Kohl KS, Gidudu J, et al.; Brighton Collaboration GBS Working Group. Guillain-Barré syndrome and Fisher syndrome: case definitions and guidelines for collection, analysis, and presentation of immunization safety data. *Vaccine* 2011;29:599–612. <http://dx.doi.org/10.1016/j.vaccine.2010.06.003>
7. Cao-Lormeau VM, Blake A, Mons S, et al. Guillain-Barré syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. *Lancet* 2016;387:1531–9. [http://dx.doi.org/10.1016/S0140-6736\(16\)00562-6](http://dx.doi.org/10.1016/S0140-6736(16)00562-6)
8. Siu R, Bukhari W, Todd A, Gunn W, Huang QS, Timmings P. Acute Zika infection with concurrent onset of Guillain-Barré syndrome. *Neurology* 2016. Epub July 27, 2016. <http://dx.doi.org/10.1212/WNL.0000000000003038>
9. Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis. *Neuroepidemiology* 2011;36:123–33. <http://dx.doi.org/10.1159/000324710>
10. Araujo AQ, Silva MT, Araujo AP. Zika virus-associated neurological disorders: a review. *Brain* 2016;139:2122–30. <http://dx.doi.org/10.1093/brain/aww158>

Likely Sexual Transmission of Zika Virus from a Man with No Symptoms of Infection — Maryland, 2016

Richard B. Brooks, MD^{1,2}; Maria Paz Carlos, PhD³; Robert A. Myers, PhD³; Mary Grace White, MPH⁴; Tanya Bobo-Lenoci, MS⁴; Debra Aplan, MSN⁵; David Blythe, MD²; Katherine A. Feldman, DVM²

On August 26, 2016, this report was posted as an MMWR Early Release on the MMWR website (<http://www.cdc.gov/mmwr>).

In June 2016, the Maryland Department of Health and Mental Hygiene (DHMH) was notified of a nonpregnant woman who sought treatment for a subjective fever and an itchy rash, which was described as maculopapular by her provider. Laboratory testing at the Maryland DHMH Laboratories Administration confirmed Zika virus infection. Case investigation revealed that the woman had not traveled to a region with ongoing transmission of Zika virus, but did have sexual contact with a male partner who had recently traveled to the Dominican Republic. The male partner reported exposure to mosquitoes while traveling, but no symptoms consistent with Zika virus infection either before or after returning to the United States. The woman reported no other sex partners during the 14 days before onset of her symptoms and no receipt of blood products or organ transplants.

The couple reported having had condomless vaginal intercourse twice after the man's return from the Dominican Republic and before the woman's symptom onset, approximately 10 days (day 10) and 14 days (day 14) after the man's return. The man also reported that he received fellatio from the woman during their sexual encounter on day 14. On day 16 (2 and 6 days after the episodes of condomless vaginal intercourse) the woman developed symptoms of Zika virus infection, including fever and rash. On day 19 (3 days after symptom onset) she sought medical care; the provider suspected Zika virus infection, and serum and urine specimens were collected. Flavivirus and chikungunya virus tests were performed at the Maryland DHMH Laboratories Administration. Zika virus RNA was detected in urine, but not in serum, by real-time reverse transcription–polymerase chain reaction (rRT-PCR) using a test based on an assay developed at CDC (1). Serum rRT-PCR testing for dengue virus and chikungunya virus was negative. Serologic testing was negative for Zika virus immunoglobulin M (IgM) antibodies using the CDC Zika IgM antibody capture enzyme-linked immunosorbent assay (Zika MAC-ELISA) and negative for dengue virus and chikungunya virus IgM antibodies using InBios ELISA kits (InBios International, Inc., Seattle, Washington). Confirmatory serologic testing at the CDC Arbovirus Diagnostic Laboratory was equivocal for Zika virus IgM antibodies using the Zika MAC-ELISA. Plaque-reduction neutralization tests (PRNTs)

performed at the CDC Arbovirus Diagnostic Laboratory confirmed a recent Zika virus infection. Convalescent serologic testing performed at the Maryland DHMH Laboratories Administration on day 56 (40 days after symptom onset) was equivocal for Zika virus IgM antibodies using the CDC Zika MAC-ELISA and negative for dengue virus and chikungunya virus IgM antibodies using InBios ELISA kits. PRNTs performed at the CDC Arbovirus Diagnostic Laboratory confirmed a recent, unspecified flavivirus infection.

The woman's male sex partner was interviewed on day 26 after his return to the United States. He reported that he had no symptoms consistent with Zika virus infection (i.e., fever, rash, conjunctivitis, or arthralgias) either during his travel or since his return, and he did not have any of the following other symptoms: myalgias, chills, eye pain, oral ulcers, genital ulcers, anal ulcers, hematospermia, hematuria, dysuria, and prostate pain. He reported feeling tired, which he attributed to having recently traveled. Serum, plasma, and urine specimens were collected from him on day 29, at which time he reported no new symptoms. Zika virus rRT-PCR testing performed at the Maryland DHMH Laboratories Administration was negative on serum and plasma and equivocal on urine. Serologic testing was positive for Zika virus IgM antibodies using the CDC Zika MAC-ELISA and positive for dengue virus IgM antibodies using an InBios ELISA kit. PRNTs performed at the CDC Arbovirus Diagnostic Laboratory confirmed a recent, unspecified flavivirus infection. Semen collected on day 31 had no detectable Zika virus RNA by rRT-PCR testing performed at the Maryland DHMH Laboratories Administration.

To date, only one other case has been reported in which a man without symptoms might have sexually transmitted Zika virus to his female partner (2). However, in that reported case, both the man and the woman had traveled to a country with ongoing Zika virus transmission where they were likely exposed to mosquitoes. In that case, although the detection of Zika virus RNA in the woman's serum and urine by rRT-PCR 39 days after return from travel suggested sexual transmission from her male partner, it could not be ruled out that she had been infected from a mosquito bite during travel and had a longer than average incubation period or a prolonged period of viremia. No cases of sexual transmission of Zika virus from an asymptomatic man returning from travel to an area with active Zika transmission to his female sex partner who did

not travel have been reported. Absence of Zika virus symptoms in persons returning from areas with ongoing Zika virus transmission might not preclude sexual transmission of Zika virus to their sex partners. Ongoing surveillance is needed to determine the risk for sexual transmission of Zika virus infection from asymptomatic persons. The findings in this report indicate that it might be appropriate to consider persons who have condomless sex with partners returning from areas with ongoing Zika virus transmission as exposed to Zika virus, regardless of whether the returning traveler reports symptoms of Zika virus infection. Providers should request Zika virus testing for any patients with illness compatible with Zika virus disease who have had sexual exposure without barrier devices to prevent infections to a partner who traveled to an area with active Zika virus transmission (3). Such patients should also be reported to local or state health departments (4,5).

Current recommendations for the prevention of sexual transmission of Zika virus in returning travelers differ depending on whether the returning traveler is symptomatic and on whether the couple is planning to become pregnant (3,6). Couples in areas without active Zika transmission with circumstances in which one partner traveled to an area with active Zika virus transmission but did not develop symptoms of Zika virus disease should wait at least 8 weeks after the partner who traveled returned from the Zika-affected area before attempting conception, regardless of the sex of the traveler. Men with a diagnosis of Zika virus infection should wait at least 6 months before attempting conception, and women with a diagnosis of Zika virus infection should wait at least 8 weeks before attempting conception. Health care providers should counsel couples that correct and consistent use of condoms reduces the risk for sexually transmitted diseases and discuss the use of the most effective contraceptive methods that can be used correctly and consistently (6). Couples who do not desire pregnancy should consider abstaining from sex or using

the most effective contraceptive methods that can be used correctly and consistently in addition to barrier methods, such as condoms, which reduce the risk for sexual transmission of Zika virus and other sexually transmitted infections (3). As more is learned about the incidence and duration of seminal shedding of Zika virus in infected men, recommendations to prevent sexual transmission of Zika virus will be updated if needed.

¹Epidemic Intelligence Service, Division of Scientific Education and Professional Development, CDC; ²Prevention and Health Promotion Administration, Maryland Department of Health and Mental Hygiene; ³Maryland Department of Health and Mental Hygiene Laboratories Administration; ⁴Baltimore City Health Department, Maryland; ⁵Montgomery County Department of Health and Human Services, Maryland

Corresponding author: Richard B. Brooks, richard.brooks@maryland.gov, 410-767-7395.

References

1. Lanciotti RS, Kosoy OL, Laven JJ, et al. Genetic and serologic properties of Zika virus associated with an epidemic, Yap State, Micronesia, 2007. *Emerg Infect Dis* 2008;14:1232–9. <http://dx.doi.org/10.3201/eid1408.080287>
2. Fréour T, Mirallié S, Hubert B, et al. Sexual transmission of Zika virus in an entirely asymptomatic couple returning from a Zika epidemic area, France, April 2016. *Euro Surveill* 2016;21:30254. <http://dx.doi.org/10.2807/1560-7917.ES.2016.21.23.30254>
3. Brooks JT, Friedman A, Kachur RE, LaFlam M, Peters PJ, Jamieson DJ. Update: interim guidance for prevention of sexual transmission of Zika virus—United States, July 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:745–7. <http://dx.doi.org/10.15585/mmwr.mm6529e2>
4. Oster AM, Russell K, Stryker JE, et al. Update: interim guidance for prevention of sexual transmission of Zika virus—United States, 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:323–5. <http://dx.doi.org/10.15585/mmwr.mm6512e3>
5. Davidson A, Slavinski S, Komoto K, Rakeman J, Weiss D. Suspected female-to-male sexual transmission of Zika virus—New York City, 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:716–7. <http://dx.doi.org/10.15585/mmwr.mm6528e2>
6. Petersen EE, Polen KN, Meaney-Delman D, et al. Update: interim guidance for health care providers caring for women of reproductive age with possible Zika virus exposure—United States, 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:315–22. <http://dx.doi.org/10.15585/mmwr.mm6512e2>

Hearing Loss in Infants with Microcephaly and Evidence of Congenital Zika Virus Infection — Brazil, November 2015–May 2016

Mariana C. Leal, PhD^{1,2}; Lilian F. Muniz, PhD²; Tamires S.A. Ferreira, MD¹; Cristiane M. Santos, MD¹; Luciana C. Almeida²; Vanessa Van Der Linden, MD^{3,4}; Regina C.F. Ramos, MD⁵; Laura C. Rodrigues, PhD⁵; Silvio S. Caldas Neto, PhD²

On August 30, 2016, this report was posted as an MMWR Early Release on the MMWR website (<http://www.cdc.gov/mmwr>).

Congenital infection with Zika virus causes microcephaly and other brain abnormalities (1). Hearing loss associated with other congenital viral infections is well described; however, little is known about hearing loss in infants with congenital Zika virus infection. A retrospective assessment of a series of 70 infants aged 0–10 months with microcephaly and laboratory evidence of Zika virus infection was conducted by the Hospital Agamenon Magalhães in Brazil and partners. The infants were enrolled during November 2015–May 2016 and had screening and diagnostic hearing tests. Five (7%) infants had sensorineural hearing loss, all of whom had severe microcephaly; however, one child was tested after receiving treatment with an ototoxic antibiotic. If this child is excluded, the prevalence of sensorineural hearing loss was 5.8% (four of 69), which is similar to that seen in association with other congenital viral infections. Additional information is needed to understand the prevalence and spectrum of hearing loss in children with congenital Zika virus infection; all infants born to women with evidence of Zika virus infection during pregnancy should have their hearing tested, including infants who appear normal at birth.

The most well-described feature of congenital Zika syndrome is microcephaly (2,3). Clinical aspects appear to be predominantly neurologic, with neuroimaging showing calcifications between cortical and subcortical zones, cortical development errors, and pachygyria/agyria (2–4). In addition to the neurologic manifestations, ophthalmic (5) and orthopedic (1) lesions have been described as a component of the syndrome. A single study in Brazil investigated auditory function among 23 neonates with microcephaly and presumed congenital Zika virus infection, using otoacoustic emissions testing without a confirmatory examination, and found 9% with auditory deficits (4). In all of the studies described, Zika virus infection was a diagnosis of exclusion because, at the time, specific testing for Zika virus was not readily available. Hearing loss is a well established feature of other congenital infections, including cytomegalovirus (CMV), rubella, toxoplasmosis, herpes simplex, and syphilis. In these syndromes, the hearing loss is sensorineural, usually bilateral, and severe or profound; it is often undetectable at birth, and sometimes it is progressive or fluctuating (6,7).

During November 2015–May 2016, as part of the protocol for evaluation of children who were born with microcephaly during the Zika virus disease epidemic, 150 children were referred to Hospital Agamenon Magalhães, a reference center for diagnosis of hearing loss and hearing rehabilitation in Pernambuco, Brazil; the 23 children previously evaluated in Pernambuco (4) were not part of this cohort. This report is a retrospective analysis of hearing assessments in 70 infants aged 0–10 months with microcephaly and laboratory evidence of Zika virus infection evaluated during that time. Zika virus–associated microcephaly was defined as head circumference ≤ 32 cm for term newborns (gestational age at birth 37 weeks to 41 weeks and 6 days), or at least two standard deviations below the mean for gestational age and sex using the Fenton curve for preterm newborns (8), with the characteristic radiologic findings from cranial computerized tomography or magnetic resonance imaging, and laboratory confirmation of Zika virus by a positive Zika virus-specific immunoglobulin M (IgM) capture enzyme-linked immunosorbent assay (ELISA) performed on cerebrospinal fluid (9).^{*} Other infectious causes of congenital sensorineural hearing loss, including CMV, toxoplasmosis, herpes simplex, and syphilis, were excluded by serologic testing of infants and their mothers. Information was collected concerning the presence and timing of rash during pregnancy and on maternal or perinatal risk factors for congenital hearing loss, such as alcohol consumption, familial hearing loss, ototoxic drug exposure, birth trauma, and postnatal infections. The degree of microcephaly was evaluated, with severe microcephaly defined as head circumference at birth of at least three standard deviations below the mean for gestational age and sex.

Auditory evaluation was carried out by screening and diagnostic tests as recommended by the American Academy of Pediatrics' Joint Committee on Infant Hearing (10). The screening test consisted of measurement of the short latency auditory brainstem response (ABR) to click stimuli, and was considered to be normal when wave V (the fifth and most prominent and consistent wave) was identified in two consecutive averaged waveforms at 35 decibels normal hearing level (dB nHL). If the first screening test was not normal, it was repeated approximately 1 month later. If the second test also indicated hearing loss, a diagnostic confirmatory

^{*} Used in accordance with the CDC emergency use authorization protocol.

frequency-specific ABR was conducted, in which the stimuli were tone bursts at frequencies of 500 and 2,000 Hz. The diagnosis of hearing loss was confirmed if hearing thresholds exceeded 25 dB nHL. No behavioral auditory testing was performed. Conductive hearing loss was not considered to be related to Zika virus infection because the hearing impairment caused by congenital viral infections is sensorineural. All children considered normal on hearing evaluation will be regularly assessed for evidence of late-onset hearing impairment. Associations between sensorineural hearing loss and presence of maternal rash during pregnancy, timing of maternal rash during pregnancy, and severe microcephaly were analyzed using contingency tables and tested using Fisher's exact test, with statistical significance defined as $p < 0.05$. Although all investigations were carried out as part of routine clinical care, and human subjects review was not required, the protocol was submitted for ethical review and approved by Hospital Agamenon Magalhães.

The mean age at the first auditory testing was 114 ± 59.1 days (range = 16–315 days, median = 97 days). Among all 70 infants, 16 (22.8%) failed the first screening test in at least one ear; among these, eight failed the repeat test and were evaluated by frequency-specific ABR. The diagnosis of hearing impairment was confirmed by ABR in seven (10%) children, including two with conductive hearing loss and five with sensorineural hearing loss. Sensorineural hearing loss was bilateral in three children and unilateral in two. One child with bilateral profound sensorineural hearing loss had been treated for sepsis with intravenous amikacin, an antibiotic with known ototoxicity, before the first test. A second child with bilateral profound sensorineural hearing loss had a twin brother with normal head circumference and cerebrospinal fluid negative for Zika-specific IgM. A third infant with sensorineural hearing loss had moderate impairment on the left and profound impairment on the right. One of the two infants with unilateral sensorineural hearing loss had mild impairment, and the other had profound impairment.

Information on presence of rash during pregnancy was obtained from 63 mothers, 54 (86%) of whom reported a rash during pregnancy (Table). Among these 54 mothers, 41 (76%) experienced the rash during the first trimester. The mothers of four infants with confirmed sensorineural hearing loss, including the one infant treated with amikacin, reported having had a rash during the first 3 months of pregnancy; the mother of the fifth infant with confirmed sensorineural hearing loss reported having had a rash in the fourth month of pregnancy. Timing of maternal rash during pregnancy did not differ between infants with and without sensorineural hearing loss ($p = 0.64$). Information needed to determine the degree

TABLE. Number of infants with microcephaly and laboratory evidence of congenital Zika virus infection (N = 70), by hearing test status, and selected characteristics — Brazil, November 2015–May 2016

Characteristic (number with information available)	No hearing loss or conductive hearing loss		Sensorineural hearing loss	
	(n = 65)	No. (%)	(n = 5)	No. (%)
Gestational age at birth	(n = 59)		(n = 5)	
37–41 weeks (term)	50	(85)	5	(100)
<37 weeks (preterm)	8	(14)	0	(—)
≥42 weeks (postterm)	1	(2)	0	(—)
Self-reported rash during pregnancy	(n = 58)		(n = 5)	
Yes	49	(84)	5	(100)
No	9	(16)	0	(—)
Timing of rash during pregnancy	(n = 49)		(n = 5)	
First trimester	37	(76)	4	(80)
Second trimester	10	(20)	1	(20)
Third trimester	2	(4)	0	(—)
Infant sex	(n = 65)		(n = 5)	
Male	36	(55)	3	(60)
Female	29	(45)	2	(40)
Degree of microcephaly	(n = 60)		(n = 5)	
Severe (>3 SD below mean for gestational age)	39	(65)	4	(100)
Other (≤3 SD below mean for gestational age)	21	(35)	0	(—)
Age at testing (days)	(n = 70)		(n = 5)	
Mean	114		105	
Median	98		60	
SD	59		57	
Range	16–315		36–171	

Abbreviation: SD = standard deviation.

of microcephaly was available for 65 (93%) infants, among whom 44 (68%) had severe microcephaly; all five children with sensorineural hearing loss were in this group; however, no significant association was detected between the presence of sensorineural hearing loss and severe microcephaly ($p = 0.55$).

Discussion

In this report of complete auditory function evaluation in a series of 70 children with microcephaly and laboratory evidence of congenital Zika virus infection, five (7.1%) infants had sensorineural hearing loss. The hearing loss varied in severity and laterality, which has been reported in hearing loss associated with other congenital infections (6,7). If the one infant with bilateral profound sensorineural hearing loss who had been treated with amikacin (a known ototoxic antibiotic) before the hearing testing is excluded, the proportion of infants with sensorineural hearing loss was 5.8% (four of 69). This proportion, although lower than the 9% reported from a small sample of newborns with microcephaly associated with presumed Zika-virus infection tested by otoacoustic emissions (4), is within the range (6%–65%) reported for other congenital viral infections (6,7). In the majority of cases of hearing loss associated with congenital viral infection, the damage to the auditory system is within the cochlea (7). It is likely that

Summary**What is already known about this topic?**

Congenital Zika virus infection is characterized by microcephaly and other abnormalities of the brain and eye; orthopedic lesions have also been documented. While the full clinical spectrum of the syndrome is not yet known, the neurologic damage and corresponding radiologic brain imaging have been well described. Other congenital infections can cause hearing loss, which is diagnosed at birth or during later follow-up; however, few data exist regarding hearing loss associated with confirmed congenital Zika virus infection.

What is added by this study?

Congenital infection with Zika virus appears to be associated with sensorineural hearing loss. Among 70 children with microcephaly and laboratory evidence of congenital Zika virus infection, four of 69 (5.8%) were found to have sensorineural hearing loss without other potential cause.

What are the implications for public health practice?

Congenital infection with Zika virus should be considered a risk factor for hearing loss. Children with evidence of congenital Zika virus infection who have normal initial screening tests should receive regular follow-up, because onset of hearing loss associated with other congenital viral infections can be delayed and the loss can be progressive.

similar lesions account for the hearing deficit in children with congenital Zika virus infection, although histologic studies are needed to confirm this. However, a concomitant central origin cannot be discounted, and behavioral auditory evaluation might provide additional information.

The findings in this report are subject to at least two limitations. First, auditory behavioral tests, in which an infant's responses (e.g., quieting, eye-widening, or startle) to various calibrated sounds are recorded, and which can complement the hearing evaluation and provide information about processing of auditory signals, were not used. Second, this series includes only children with microcephaly. It is possible that the full spectrum of congenital Zika virus infection includes children without microcephaly, but with auditory deficits, as occurs in congenital rubella and CMV infections, in which children born with no apparent structural anomaly can be found to have hearing loss at birth or later in life.

Although no statistically significant associations of hearing loss with timing of rash during pregnancy and degree of microcephaly were detected, sensorineural auditory impairment occurred predominantly in infants whose mothers had a rash illness during the first trimester of pregnancy, and all the infants with sensorineural hearing loss had severe microcephaly. Therefore, severe microcephaly in infants with evidence of congenital Zika virus infection should be considered a risk factor for auditory impairment.

The prevalence of progressive hearing loss associated with congenital Zika virus infection is not known. To elucidate the full spectrum of hearing loss in infants with congenital Zika virus infection, testing and follow-up of all children born to women who had Zika virus infection during pregnancy, including infants with no apparent anomalies at birth, is needed. Sensorineural hearing loss should be considered part of the spectrum of clinical findings associated with congenital Zika virus infection, and congenital Zika virus infection should be considered a risk factor for hearing loss in auditory screening programs. Children with evidence of congenital Zika virus infection who have normal initial screening tests should receive regular follow-up, because onset of hearing loss could be delayed and the loss could be progressive.

Acknowledgments

Marli Tenório, MD, Ernesto Marques, MD, Virology and Experimental Therapy Department, Oswaldo Cruz Foundation, Pernambuco, Brazil.

¹Hospital Agamenon Magalhães; ²Federal University of Pernambuco; ³Association for Assistance of Disabled Children; ⁴Oswaldo Cruz University Hospital; ⁵London School of Hygiene and Tropical Medicine.

Corresponding author: Mariana C. Leal, marianacleal@hotmail.com.

References

1. Rasmussen SA, Jamieson DJ, Honein MA, Petersen LR. Zika virus and birth defects—reviewing the evidence for causality. *N Engl J Med* 2016;374:1981–7.
2. Schuler-Faccini L, Ribeiro EM, Feitosa IML, et al. Possible association between Zika virus infection and microcephaly. *MMWR Morb Mortal Wkly Rep* 2016;65:59–62. <http://dx.doi.org/10.15585/mmwr.mm6503e2>
3. Aragão MFV, Van der Linden V, Brainer-Lima AM, et al. Clinical features and neuroimaging (CT and MRI) findings in presumed Zika virus related congenital infection and microcephaly: retrospective case series study. *BMJ* 2016;353:i1901. <http://www.bmj.com/content/353/bmj.i1901>
4. Microcephaly Epidemic Group. Microcephaly in infants, Pernambuco State, Brazil, 2015. *Emerg Infect Dis* 2016;22:1090–3. http://wwwnc.cdc.gov/eid/article/22/6/16-0062_article
5. Ventura CV, Maia M, Bravo Filho V, Gois AL, Belfort R Jr. Zika virus in Brazil and macular atrophy in a child with microcephaly. *Lancet* 2016;387:228. [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(16\)00006-4/abstract](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)00006-4/abstract)
6. Goderis J, De Leenheer E, Smets K, Hoecke HV, Keymeulen A, Dhooget I. Hearing loss and congenital CMV infection: a systematic review. *Pediatrics* 2014;134:972–82. <http://pediatrics.aappublications.org/content/134/5/972>
7. Cohen BE, Durstenfeld A, Roehm PC. Viral causes of hearing loss: a review for hearing health professionals. *Trends Hear* 2014;18. pii: 2331216514541361
8. Brazilian Ministry of Health. Protocol for monitoring and response to microcephaly occurrence relating to ZikaV infection [Portuguese]. <http://www.combateaedes.saude.gov.br/images/sala-de-situacao/Microcefalia-Protocolo-de-vigilancia-e-resposta-10mar2016-18h.pdf>
9. Cordeiro MT, Pena LJ, Brito CA, Gil LH, Marques ET. Positive IgM for Zika virus in the cerebrospinal fluid of 30 neonates with microcephaly in Brazil. *Lancet* 2016;387:1811–2.
10. American Academy of Pediatrics, Joint Committee on Infant Hearing. Year 2007 position statement: principles and guidelines for early hearing detection and intervention programs. *Pediatrics* 2007;120:898–921.

Notes from the Field

Cluster of Lymphogranuloma Venereum Cases Among Men Who Have Sex with Men — Michigan, August 2015–April 2016

Alex de Voux, PhD^{1, 2}; James B. Kent, MS³;
Kathryn Macomber, MPH³; Karen Krzanowski, MA, MPH⁴;
Dawn Jackson⁴; Tayneata Starr⁴; Sandra Johnson⁴;
Deborah Richmond, MSN⁵; Lawrence R. Crane, MD⁵;
Jonathan Cohn, MD⁵; Christopher Finch⁵; Jevon McFadden, MD⁶;
Allan Pillay, PhD²; Cheng Chen, PhD²; Laurie Anderson²;
Ellen N. Kersh, PhD²

Lymphogranuloma venereum (LGV) is a sexually transmitted disease (STD) caused by infection with invasive *Chlamydia trachomatis* serovars L1–L3 (1). LGV is characterized by inguinal and/or femoral lymphadenopathy, typically following a transient, self-limited genital ulcer or papule that might go unnoticed. Rectal infection can result in proctocolitis that can present with mucoid and/or hemorrhagic rectal discharge, anal pain, constipation, fever, and tenesmus, and signs of granulomas and/or ulcerations on anoscopy (1,2). LGV can be an invasive, systemic infection, and if it is not treated early, LGV proctocolitis can lead to chronic colorectal fistulas and strictures (2). In Europe, outbreaks of LGV have been reported among men who have sex with men (MSM), often in association with human immunodeficiency virus (HIV) coinfection (3–5). The prevalence of LGV in the United States is unknown (1), because diagnostic tests to differentiate LGV from non-LGV *Chlamydia trachomatis* are not widely available (6), and providers might not know that they should report cases that are presumptively treated.

On August 12, 2015, a patient attending a clinic in Michigan for HIV care, who had clinical symptoms compatible with LGV, was reported to the Michigan Department of Health and Human Services (MDHHS). The patient was a black MSM with HIV infection, who had an inguinal node and an open, nonhealing penile ulcer; a swab of the ulcer was positive for *Chlamydia trachomatis*. Before this case, the last reported case of LGV in Michigan was in 2005. In September 2015, three additional patients with symptoms and clinical findings compatible with LGV were reported in Michigan, and on September 22, MDHHS initiated an outbreak investigation. A case definition was developed (Box), and two health alerts were issued, urging providers to consider LGV as a diagnosis in patients with lymphadenopathy or proctocolitis of unclear etiology and to report suspected cases to MDHHS. MDHHS also investigated sexual partners of diagnosed patients. CDC was notified on September 23, and offered a laboratory-developed molecular test for LGV-specific strains (6).

BOX. Case definition of lymphogranuloma venereum (LGV) included in Michigan Health Alert Network sent out on October 22, 2015

Suspected case

- A clinically compatible illness in a person with one or more signs or symptoms compatible with LGV (proctocolitis, inguinal/femoral lymphadenopathy, or genital or rectal ulcers), and
- A sexual partner of a person meeting the probable or confirmed case definition.

Probable case, either or both of the following:

- A patient meeting the suspected case definition, in whom other causes of LGV-like symptoms (e.g., syphilis, gonorrhea, and herpes simplex virus) have been ruled out, and a positive *Chlamydia trachomatis* from culture or nucleic acid amplification test (NAAT) from a body site associated with symptoms.
- Sexual partner of a person meeting the probable or confirmed case definition and a positive *C. trachomatis* from culture or NAAT.

Confirmed case

- A probable case with laboratory confirmation for *C. trachomatis* genotypes L1, L2, or L3 by genetic analysis (LGV-specific polymerase chain reaction or sequencing).

During August 12, 2015–April 30, 2016, MDHHS received 38 reports of LGV all among MSM who were HIV-infected.

Among these 38 reports, 21 (55%) were confirmed by CDC, based on 19 positive rectal swab specimens and two positive swabs from penile lesions. Eleven probable and six suspected cases were also identified. Among the 21 confirmed cases, one was Hispanic white, and 20 were black. The median age was 29 years (range = 19–60 years). The median CD4 count was 483 cells/ml (range = 270–1,271 cells/ml); HIV RNA was undetectable (<20 copies/ml) in 12 patients and in the remaining nine patients, the median was 7,030 copies/ml. Among all 38 confirmed, probable, and suspected cases, six (16%) were in persons with newly diagnosed HIV infection. Four (11%) patients had hepatitis C infection, six (16%) had syphilis, three (8%) had asymptomatic oropharyngeal gonorrhea, and five (13%) had asymptomatic rectal gonorrhea. Proctitis was present in 19 (50%) patients. All patients were treated according to CDC recommendations (2) with 100 mg doxycycline twice daily for 21 days.

LGV should be considered in the differential diagnosis of lymphadenopathy or proctocolitis with no other etiology, especially among HIV-infected MSM. Among patients with symptoms or signs suggestive of LGV, presumptive treatment should be offered at the initial health care visit. All confirmed, probable, and suspected cases of LGV should be reported to the local health department. Sexual contacts of LGV cases should be examined, tested for *Chlamydia trachomatis* at the anatomic sites of exposure and, if no symptoms or signs are present, treated presumptively with 100 mg doxycycline twice daily for 1 week (2). Additional information is available at <http://www.cdc.gov/std/tg2015/lgv.htm>.

¹Epidemic Intelligence Service, Division of Scientific Education and Professional Development, CDC; ²Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC; ³Michigan Department of Health & Human Services, Division of Communicable Diseases; ⁴Michigan Department of Health & Human Services, Division of HIV and STD Programs; ⁵Wayne State University School of Medicine, Detroit, Michigan; ⁶Career Epidemiology Field Officer Program, Office of Public Health Preparedness and Response, CDC.

Corresponding author: Alex de Voux, AdeVoux@cdc.gov, 404-639-1203.

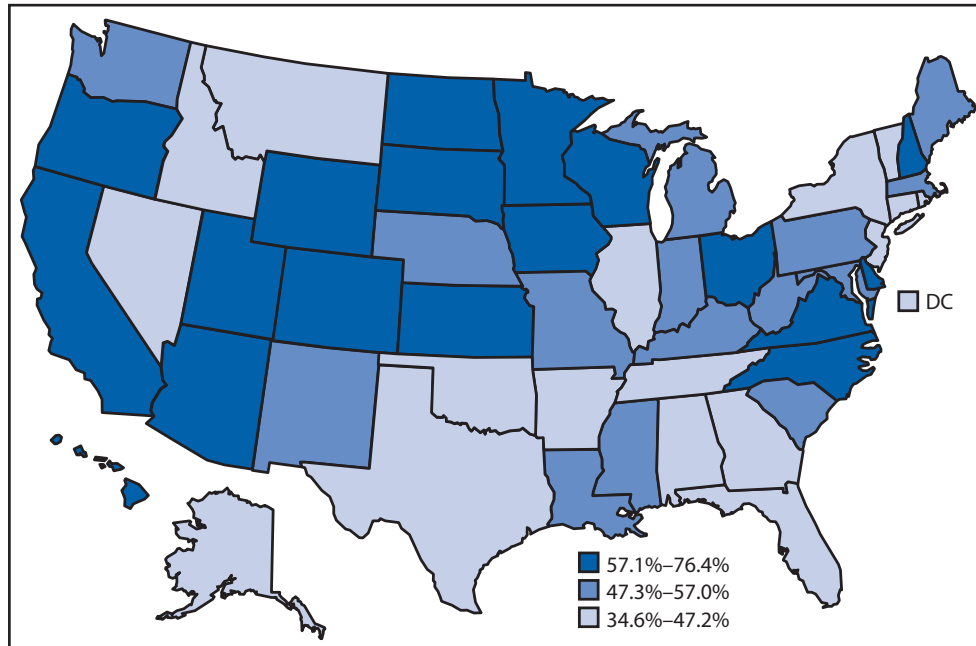
References

1. Perine P, Stamm W. Lymphogranuloma venereum. In: Holmes KK, Sparling P, Mardh P, et al., eds. Sexually transmitted diseases. 3rd ed. New York: McGraw-Hill Health Professions Division; 1999: 423–32.
2. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep* 2015;64(No. RR-3).
3. van de Laar MJW, Gotz HM, de Zwart O, et al. Lymphogranuloma venereum among men who have sex with men—Netherlands, 2003–2004. *MMWR Morb Mortal Wkly Rep* 2004;53:985–8.
4. Childs T, Simms I, Alexander S, Eastick K, Hughes G, Field N. Rapid increase in lymphogranuloma venereum in men who have sex with men, United Kingdom, 2003 to September 2015. *Euro Surveill* 2015;20:30076. <http://dx.doi.org/10.2807/1560-7917.ES.2015.20.48.30076>
5. Saxon C, Hughes G, Ison C; UK LGV Case-Finding Group. Asymptomatic lymphogranuloma venereum in men who have sex with men, United Kingdom. *Emerg Infect Dis* 2016;22:112–6. <http://dx.doi.org/10.3201/EID2201.141867>
6. Chen C-Y, Chi KH, Alexander S, Ison CA, Ballard RC. A real-time quadruplex PCR assay for the diagnosis of rectal lymphogranuloma venereum and non-lymphogranuloma venereum *Chlamydia trachomatis* infections. *Sex Transm Infect* 2008;84:273–6. <http://dx.doi.org/10.1136/sti.2007.029058>

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage of Physicians Who Have Electronic Access to Patient Health Information from Outside Their Medical Practice,^{*,†} by State — United States, 2015



* Physicians were defined as having patient health information electronically available at the point of care if they answered "often," "sometimes," or "rarely" to the question, "When treating patients seen by other providers outside your medical organization, how often do you or your staff have clinical information from those outside encounters electronically available at the point of care? Electronically available does not include scanned or PDF documents." Overall, 50.3% of U.S. physicians reported having this type of electronic health information exchange.

† A sample survey of office-based physicians.

In 2015, approximately half (50.3%) of the physicians in the United States had information from other providers outside of their practice electronically available at the point of care. There was wide variation by state, ranging from 34.6% in Idaho to 76.4% in South Dakota. Sixteen states and the District of Columbia were in the range with the lowest percentage of physicians with electronic access to more comprehensive patient information (34.6%–47.2%). Another 16 states were in the middle range (47.3%–57.0%). The 18 states with the highest percentage of physicians having such information electronically available were in the top range (57.1%–76.4%).

Source: National Electronic Health Records Survey (NEHRS), 2015. Survey data available through the NCHS Research Data Center at <http://www.cdc.gov/rdc/leftbrch/whatnew.htm>.

Reported by: Eric W Jamoom, PhD, ejamoom@cdc.gov, 301-458-4798; Ninee Yang, PhD.

Morbidity and Mortality Weekly Report

The *Morbidity and Mortality Weekly Report (MMWR)* Series is prepared by the Centers for Disease Control and Prevention (CDC) and is available free of charge in electronic format. To receive an electronic copy each week, visit *MMWR*'s free subscription page at <http://www.cdc.gov/mmwr/mmwrsubscribe.html>. Paper copy subscriptions are available through the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402; telephone 202-512-1800.

Readers who have difficulty accessing this PDF file may access the HTML file at <http://www.cdc.gov/mmwr/index2016.html>. Address all inquiries about the *MMWR* Series, including material to be considered for publication, to Executive Editor, *MMWR* Series, Mailstop E-90, CDC, 1600 Clifton Rd., N.E., Atlanta, GA 30329-4027 or to mmwrq@cdc.gov.

All material in the *MMWR* Series is in the public domain and may be used and reprinted without permission; citation as to source, however, is appreciated.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

References to non-CDC sites on the Internet are provided as a service to *MMWR* readers and do not constitute or imply endorsement of these organizations or their programs by CDC or the U.S. Department of Health and Human Services. CDC is not responsible for the content of these sites. URL addresses listed in *MMWR* were current as of the date of publication.

ISSN: 0149-2195 (Print)