Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 65 / No. 6
February 19, 2016

# Prevalence of Healthy Sleep Duration among Adults — United States, 2014

Yong Liu, MD[1]; Anne G. Wheaton, PhD[1]; Daniel P. Chapman, PhD[1]; Timothy J. Cunningham, ScD[1]; Hua Lu, MS[1]; Janet B. Croft, PhD[1]

To promote optimal health and well-being, adults aged 18–60 years are recommended to sleep at least 7 hours each night (*1*). Sleeping <7 hours per night is associated with increased risk for obesity, diabetes, high blood pressure, coronary heart disease, stroke, frequent mental distress, and all-cause mortality (*2–4*). Insufficient sleep impairs cognitive performance, which can increase the likelihood of motor vehicle and other transportation accidents, industrial accidents, medical errors, and loss of work productivity that could affect the wider community (*5*). CDC analyzed data from the 2014 Behavioral Risk Factor Surveillance System (BRFSS) to determine the prevalence of a healthy sleep duration (≥7 hours) among 444,306 adult respondents in all 50 states and the District of Columbia. A total of 65.2% of respondents reported a healthy sleep duration; the age-adjusted prevalence of healthy sleep was lower among non-Hispanic blacks, American Indians/Alaska Natives, Native Hawaiians/Pacific Islanders, and multiracial respondents, compared with non-Hispanic whites, Hispanics, and Asians. State-based estimates of healthy sleep duration prevalence ranged from 56.1% in Hawaii to 71.6% in South Dakota. Geographic clustering of the lowest prevalence of healthy sleep duration was observed in the southeastern United States and in states along the Appalachian Mountains, and the highest prevalence was observed in the Great Plains states. More than one third of U.S. respondents reported typically sleeping <7 hours in a 24-hour period, suggesting an ongoing need for public awareness and public education about sleep health; worksite shift policies that ensure healthy sleep duration for shift workers, particularly medical professionals, emergency response personnel, and transportation industry personnel; and opportunities for health care providers to discuss the importance of healthy sleep duration with patients and address reasons for poor sleep health.

BRFSS* is a state-based, random-digit–dialed telephone survey of the noninstitutionalized U.S. population aged ≥18 years. BRFSS is conducted collaboratively by state health departments and CDC (*6*) among both landline and cell phone respondents, and data are weighted to state population estimates. Response rates for BRFSS are calculated using standards set by the American Association of Public Opinion Research Response Rate Formula #4.† The response rate is defined as the number of respondents who completed the survey as a proportion of all eligible and likely eligible persons. The median response rate for all states and territories in 2014 was 47.0% and ranged from 25.1% to 60.1%.

Survey respondents in 2014 were asked, "On average, how many hours of sleep do you get in a 24-hour period?" Hours of

*2014 BRFSS Summary Data Quality Report (http://www.cdc.gov/brfss/annual_data/2014/pdf/2014_DQR.pdf).

†http://www.aapor.org/Standards-Ethics/Standard-Definitions-(1).aspx.

## INSIDE





**U.S. Department of Health and Human Services**
Centers for Disease Control and Prevention

sleep were recorded in whole numbers by rounding 30 minutes or more up to the next whole hour and dropping 29 or fewer minutes. The age-adjusted prevalence and 95% confidence interval (CI) of the recommended healthy sleep duration (≥7 hours) was calculated by state and selected characteristics, and adjusted to the 2000 projected U.S. population aged ≥18 years. For comparisons of prevalence between subgroups, statistical significance ($p<0.05$) was determined by t-tests. All indicated differences between subgroups are statistically significant. Statistical software programs that account for the complex sampling design of the BRFSS were used for the analysis.

Among 444,306 respondents, 11.8% reported a sleep duration ≤5 hours, 23.0% reported 6 hours, 29.5% reported 7 hours, 27.7% reported 8 hours, 4.4% reported 9 hours, and 3.6% reported ≥10 hours. Overall, 65.2% reported the recommended healthy sleep duration (age-adjusted prevalence = 64.9%) (Table 1). The age-specific prevalence of sleeping ≥7 hours was highest among respondents aged ≥65 years (73.7%) compared with other age groups. The age-adjusted prevalence of healthy sleep duration was lower among Native Hawaiians/Pacific Islanders (53.7%), non-Hispanic blacks (54.2%), multiracial non-Hispanics (53.6%), and American Indians/Alaska Natives (59.6%) compared with non-Hispanic whites (66.8%), Hispanics (65.5%), and Asians (62.5%). Respondents who indicated they were unable to work or unemployed had lower age-adjusted healthy sleep duration prevalences (51.0% and 60.2%, respectively) than did employed respondents (64.9%). The prevalence of healthy sleep duration was highest among respondents with a college degree or higher (71.5%). The prevalence was higher among married respondents (67.4%) compared with those who were divorced, widowed, or separated (55.7%), or never married (62.3%).

Prevalence of healthy sleep duration varied among states and ranged from 56.1% in Hawaii to 71.6% in South Dakota (Table 2). Most of the Great Plains states were in the upper quintile for healthy sleep duration; states in the southeastern United States and along the Appalachian Mountains tended to be in the lower quintiles (Figure).

## Discussion

This is the first published report to document state-based estimates of self-reported healthy sleep duration for all 50 states and the District of Columbia. On average, 65.2% of adult respondents reported a healthy sleep duration. The geographic distribution pattern of low healthy sleep duration prevalence is consistent with 2008 state prevalence patterns of perceived insufficient rest or sleep among U.S. adults (*7*). The lower healthy sleep duration prevalence in the BRFSS among non-Hispanic black adults relative to non-Hispanic whites is consistent with a previous nationwide 2007–2010 comparison from the National Health and Nutrition Examination Survey (NHANES) (*8*). The results also suggest that employment and higher education might be determinants of healthy sleep.

A lower prevalence of healthy sleep duration was observed in the southeastern United States and in states along the Appalachian Mountains. This distribution is similar to geographic variations in prevalence estimates for obesity (*9*) and diabetes (*9*) and death rates

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].

**TABLE 1. Age-specific and age-adjusted* percentage of adults who reported ≥7 hours sleep per 24-hour period, by selected characteristics — Behavioral Risk Factor Surveillance System, United States, 2014**

| Characteristic | No.† | % (95% CI)§ |
|---|---|---|
| **Total** | **444,306** | **NA** |
| Unadjusted | NA | 65.2 (64.9–65.5) |
| Age-adjusted | NA | 64.9 (64.6–65.2) |
| **Age group (yrs)** | | |
| 18–24 | 23,234 | 67.8 (66.8–68.7) |
| 25–34 | 42,084 | 62.1 (61.3–62.9) |
| 35–44 | 52,385 | 61.7 (60.9–62.5) |
| 45–64 | 173,357 | 62.7 (62.2–63.1) |
| ≥65 | 153,246 | 73.7 (73.2–74.2) |
| **Sex*** | | |
| Male | 185,796 | 64.6 (64.2–65.0) |
| Female | 258,510 | 65.2 (64.8–65.7) |
| **Race/Ethnicity*** | | |
| White, non-Hispanic | 348,988 | 66.8 (66.4–67.1) |
| Black, non-Hispanic | 33,535 | 54.2 (53.3–55.2) |
| Hispanic | 29,044 | 65.5 (64.5–66.4) |
| American Indian/Alaska Native | 6,862 | 59.6 (57.1–62.1) |
| Asian | 8,313 | 62.5 (60.2–64.7) |
| Native Hawaiian/Pacific Islander | 797 | 53.7 (47.2–60.0) |
| Multiracial, non-Hispanic | 8,241 | 53.6 (51.5–55.7) |
| Other, non-Hispanic | 1,943 | 62.0 (58.1–65.8) |
| **Employment status*** | | |
| Employed | 220,751 | 64.9 (64.4–65.3) |
| Unemployed | 19,300 | 60.2 (58.8–61.6) |
| Retired | 130,478 | 60.9 (54.4–67.1) |
| Unable to work | 31,953 | 51.0 (49.4–52.5) |
| Homemaker/student | 37,393 | 69.5 (68.5–70.5) |
| **Education level*** | | |
| Less than high school diploma | 33,833 | 62.5 (61.5–63.5) |
| High school diploma | 125,462 | 62.4 (61.8–63.0) |
| Some college | 120,814 | 62.4 (61.8–62.9) |
| College graduate or higher | 161,088 | 71.5 (71.0–71.9) |
| **Marital status*** | | |
| Married | 238,262 | 67.4 (66.9–67.9) |
| Divorced, widowed, separated | 126,519 | 55.7 (54.5–56.9) |
| Never married | 65,232 | 62.3 (61.5–63.2) |
| Member of unmarried couple | 11,152 | 65.2 (63.3–67.1) |

**Abbreviations:** CI = confidence interval; NA = not applicable.
* Age-adjusted to the 2000 projected U.S. population aged ≥18 years, except for age groups.
† Unweighted sample of respondents. Categories might not sum to sample total because of missing responses.
§ Weighted percentage and 95% CI.

**TABLE 2. Age-adjusted* percentage of adults who reported ≥7 hours sleep per 24-hour period, by state — Behavioral Risk Factor Surveillance System, United States, 2014**

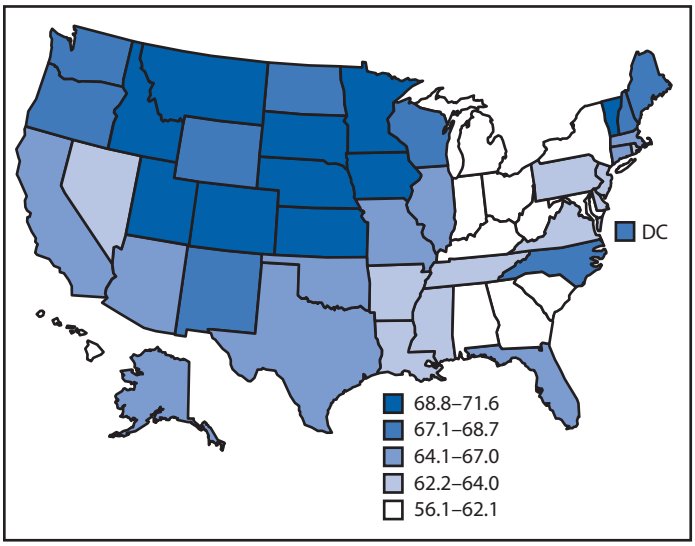
| State | No.† | % (95% CI)§ |
|---|---|---|
| Alabama | 8,335 | 61.2 (59.6–62.8) |
| Alaska | 4,286 | 65.0 (62.9–67.0) |
| Arizona | 14,437 | 66.7 (65.3–68.0) |
| Arkansas | 5,067 | 62.6 (60.3–64.9) |
| California | 8,660 | 66.4 (65.1–67.7) |
| Colorado | 13,043 | 71.5 (70.5–72.5) |
| Connecticut | 7,707 | 64.8 (63.2–66.5) |
| Delaware | 4,153 | 62.4 (60.0–64.6) |
| District of Columbia | 3,866 | 67.8 (65.4–70.2) |
| Florida | 9,565 | 64.2 (62.7–65.7) |
| Georgia | 6,164 | 61.3 (59.5–63.0) |
| Hawaii | 7,110 | 56.1 (54.3–57.8) |
| Idaho | 5,380 | 69.4 (67.4–71.2) |
| Illinois | 5,023 | 65.6 (63.7–67.4) |
| Indiana | 11,239 | 61.5 (60.2–62.8) |
| Iowa | 7,976 | 69.0 (67.5–70.4) |
| Kansas | 13,442 | 69.1 (68.1–70.1) |
| Kentucky | 10,890 | 60.3 (58.7–61.9) |
| Louisiana | 6,608 | 63.7 (62.2–65.2) |
| Maine | 8,980 | 67.1 (65.6–68.6) |
| Maryland | 12,171 | 61.1 (59.4–62.8) |
| Massachusetts | 15,072 | 65.5 (64.2–66.8) |
| Michigan | 8,275 | 61.3 (59.8–62.8) |
| Minnesota | 16,049 | 70.8 (69.9–71.7) |
| Mississippi | 4,043 | 63.0 (60.8–65.2) |
| Missouri | 6,888 | 66.0 (64.2–67.8) |
| Montana | 7,306 | 69.3 (67.5–71.0) |
| Nebraska | 22,007 | 69.6 (68.5–70.7) |
| Nevada | 3,649 | 63.8 (61.3–66.3) |
| New Hampshire | 6,022 | 67.5 (65.7–69.4) |
| New Jersey | 12,617 | 62.8 (61.5–64.2) |
| New Mexico | 8,737 | 68.0 (66.3–69.5) |
| New York | 6,641 | 61.6 (60.1–63.2) |
| North Carolina | 7,034 | 67.6 (66.2–68.9) |
| North Dakota | 7,635 | 68.2 (66.4–70.0) |
| Ohio | 10,712 | 62.1 (60.5–63.6) |
| Oklahoma | 8,237 | 64.3 (62.9–65.7) |
| Oregon | 5,099 | 68.3 (66.4–70.1) |
| Pennsylvania | 10,707 | 62.5 (61.1–64.0) |
| Rhode Island | 6,243 | 63.3 (61.4–65.1) |
| South Carolina | 10,636 | 61.5 (60.2–62.9) |
| South Dakota | 7,270 | 71.6 (69.6–73.5) |
| Tennessee | 4,966 | 62.9 (60.7–65.0) |
| Texas | 14,950 | 67.0 (65.7–68.3) |
| Utah | 14,719 | 69.2 (68.3–70.1) |
| Vermont | 6,357 | 69.0 (67.4–70.4) |
| Virginia | 9,225 | 64.0 (62.6–65.3) |
| Washington | 9,874 | 68.2 (66.8–69.6) |
| West Virginia | 6,050 | 61.6 (60.0–63.2) |
| Wisconsin | 6,955 | 67.8 (66.1–69.5) |
| Wyoming | 6,229 | 68.7 (66.5–70.8) |
| **Median (50 states and DC)** | **444,306** | **64.9 (64.6–65.2)** |

**Abbreviations:** CI = confidence interval; DC = District of Columbia.
* Age-adjusted to the 2000 projected U.S. population aged ≥18 years.
† Unweighted sample of respondents.
§ Weighted percentage and 95% CI.

from heart disease§ and stroke.¶ Short sleep duration (<7 hours per night) and other indicators of poor sleep health are associated with greater insulin resistance, metabolic abnormalities, and weight gain (*5*), which might then result in diabetes and adverse cardiovascular outcomes. A sleep duration of ≥7 hours is associated with lower prevalence estimates of cigarette smoking, leisure-time physical inactivity, and obesity compared with a short sleep duration.** Although unhealthy adults with chronic conditions might sleep longer (*2*,*3*), little empirical evidence exists to indicate that long sleep duration (≥9 hour per night) causes adverse conditions among healthy adults exists (*1*).

§ National map of heart disease death rates by county (http://www.cdc.gov/dhdsp/maps/national_maps/hd_all.htm).
¶ National map of stroke death rates by county (http://www.cdc.gov/dhdsp/maps/national_maps/stroke_all.htm).
** http://www.cdc.gov/nchs/data/hestat/sleep04-06/sleep04-06.htm.

**FIGURE. Age-adjusted percentage of adults who reported ≥7 hours of sleep per 24-hour period, by state — Behavioral Risk Factor Surveillance System, United States, 2014**




**Summary**

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

Short sleep duration (<7 hours per night) is associated with greater likelihoods of obesity, high blood pressure, diabetes, coronary heart disease, stroke, frequent mental distress, and death.

**What is added by this report?**

The first state-specific estimates of the prevalence of a ≥7 hour sleep duration in a 24-hour period show geographic clustering of lower prevalence estimates for this duration of sleep in the southeastern United States and in states along the Appalachian Mountains, which are regions with the highest burdens of obesity and other chronic conditions. Non-Hispanic black, American Indian/Alaska Native, and Native Hawaiian/Pacific Islander, and multiracial populations report a lower prevalence of ≥7 hours sleep compared with the rest of the U.S. adult population.

**What are the implications for public health practice?**

The determination that more than a third of U.S. adults report sleeping <7 hours and findings of geographic and sociodemographic variations in low prevalence of healthy sleep duration suggest opportunities for promoting sleep health. These opportunities include sleep health education, reducing racial/ethnic and economic disparities, changes in work shift policies, and routine medical assessment of patients' sleep concerns in health care systems.

The findings in this report are subject to at least two limitations. First, sleep duration was obtained by self-report and was not corroborated by actigraphy (sensor-measurement of motor activity), polysomnography (sleep study), other objective measures, or sleep journals. The overall estimate of 65.2% in the 2014 BRFSS adult population is slightly higher than the population estimate of 60.1% from the 2007–2008 NHANES (*2*) and slightly lower than the prevalence of 71.6% reported from the 2008–2010 National Health Interview Survey (NHIS).[††] Some variation might be a result of the different wording used by the different surveys. Although BRFSS and NHIS both asked about typical sleep duration in a 24-hour period, NHANES asked how much sleep respondents typically get "at night on weekdays or workdays." Finally, institutionalized respondents were not assessed in the present investigation, NHANES, or NHIS; if institutionalized persons are more likely to have shorter sleep durations because of chronic physical or mental conditions, then the prevalence of ≥7 hours might be overestimated in the BRFSS population. However, the relationships of healthy sleep with sociodemographic characteristics, risk factors, and outcomes are consistent with the other studies despite variations in definitions of healthy or optimal sleep.

Based on recent recommendations for healthy sleep duration (*1*), these findings suggest that, although almost two thirds of U.S. adults sleep ≥7 hours in a 24-hour period, an estimated 83.6 million U.S. adults sleep <7 hours. Therefore, clinicians might find routine discussion of sleep health with their patients as well as pursuit of explanations for poor sleep health an important component of providing health care. Healthy sleep duration in adults can be promoted by sleep health education and behavior changes, such as setting a pattern of going to bed at the same time each night and rising at the same time each morning; making sure that the bedroom environment is quiet, dark, relaxing, and neither too hot nor too cold; turning off or removing televisions, computers, mobile devices, and distracting or light-emitting electronic devices from the bedroom; and avoiding large meals, nicotine, alcohol, and caffeine before bedtime.[§§] Insomnia symptoms, such as trouble falling or staying asleep can usually be resolved with improved sleep habits or psychological or behavioral therapies (*10*). At present, no professional sleep organizations have issued consensus statements or recommendations about the efficacy or safety of either over-the-counter or prescription sleep aids for improving sleep duration in the general adult population. In addition, strategies to reduce risks associated with shift work and long work hours include designing better work schedules.[§§] Evaluation and monitoring of sleep might also be an important function of health care professionals, including sleep specialists (*5*). Keeping a 10-day sleep journal or diary about sleep times, napping, and behaviors that affect sleep, such as exercise, alcohol use, and caffeine consumption, might be helpful before discussing sleep problems with a physician.[¶¶]

[††] http://www.cdc.gov/nchs/data/series/sr_10/sr10_257.pdf.

[§§] National Institute of Occupational Safety and Health: review of the evidence about risks associated with shift work and long workhours and strategies to reduce these risks, including suggestions for designing better work schedules (http://www.cdc.gov/niosh/docs/2015-115).

[¶¶] http://www.cdc.gov/sleep.

[1]Division of Population Health, National Center for Chronic Disease Prevention and Health Promotion, CDC.

Corresponding author: Anne G. Wheaton, AWheaton@cdc.gov, 770-488-5362.

## References

1. Watson NF, Badr MS, Belenky G, et al.; Consensus Conference Panel. Joint consensus statement of the American Academy of Sleep Medicine and Sleep Research Society on the recommended amount of sleep for a healthy adult: methodology and discussion. Sleep 2015;38:1161–83.
2. Grandner MA, Chakravorty S, Perlis ML, Oliver L, Gurubhagavatula I. Habitual sleep duration associated with self-reported and objectively determined cardiometabolic risk factors. Sleep Med 2014;15:42–50. http://dx.doi.org/10.1016/j.sleep.2013.09.012.
3. Liu Y, Wheaton AG, Chapman DP, Croft JB. Sleep duration and chronic diseases among US adults age 45 years and older: evidence from the 2010 Behavioral Risk Factor Surveillance System. Sleep 2013;36:1421–7.
4. Gallicchio L, Kalesan B. Sleep duration and mortality: a systematic review and meta-analysis. J Sleep Res 2009;18:148–58. http://dx.doi.org/10.1111/j.1365-2869.2008.00732.x.
5. Institute of Medicine of the National Academies. Sleep disorders and sleep deprivation: an unmet public health problem. Washington, DC: The National Academies Press; 2006. http://iom.nationalacademies.org/Reports/2006/Sleep-Disorders-and-Sleep-Deprivation-An-Unmet-Public-Health-Problem.aspx.
6. Mokdad AH, Stroup DF, Giles WH; Behavioral Risk Factor Surveillance Team. Public health surveillance for behavioral risk factors in a changing environment. Recommendations from the Behavioral Risk Factor Surveillance Team. MMWR Recomm Rep 2003;52(No. RR-9).
7. CDC. Perceived insufficient rest or sleep among adults—United States, 2008. MMWR Morb Mortal Wkly Rep 2009;58:1175–9.
8. CDC. QuickStats: Sleep duration among adults aged ≥20 years, by race/ethnicity—National Health and Nutrition Examination Survey, United States, 2007–2010. MMWR Morb Mortal Wkly Rep 2013;62:755.
9. CDC. Estimated county-level prevalence of diabetes and obesity—United States, 2007. MMWR Morb Mortal Wkly Rep 2009;58:1259–63.
10. Schutte-Rodin S, Broch L, Buysse D, Dorsey C, Sateia M. Clinical guideline for the evaluation and management of chronic insomnia in adults. J Clin Sleep Med 2008;4:487–504.

# Cluster of HIV Infections Attributed to Unsafe Injection Practices — Cambodia, December 1, 2014–February 28, 2015

Mean Chhi Vun[1]; Romeo R. Galang[2]; Masami Fujita[3]; William Killam[4]; Runa Gokhale[2]; John Pitman[5]; Dejana Selenic[5]; Sovatha Mam[1]; Chandara Mom[1]; Didier Fontenille[6]; Francois Rouet[6]; Saphonn Vonthanak[7]; Roka Cluster Investigation Team

In December 2014, local health authorities in Battambang province in northwest Cambodia reported 30 cases of human immunodeficiency virus (HIV) infection in a rural commune (district subdivision) where only four cases had been reported during the preceding year. The majority of cases occurred in residents of Roka commune. The Cambodian National Center for HIV/AIDS (acquired immunodeficiency syndrome), Dermatology and Sexually Transmitted Diseases (NCHADS) investigated the outbreak in collaboration with the University of Health Sciences in Phnom Penh and members of the Roka Cluster Investigation Team. By February 28, 2015, NCHADS had confirmed 242 cases of HIV infection among the 8,893 commune residents, an infection rate of 2.7%. Molecular investigation of the HIV strains present in this outbreak indicated that the majority of cases were linked to a single HIV strain that spread quickly within this community. An NCHADS case-control study identified medical injections and infusions as the most likely modes of transmission. In response to this outbreak, the Government of Cambodia has taken measures to encourage safe injection practices by licensed medical professionals, ban unlicensed medical practitioners, increase local capacity for HIV testing and counseling, and expand access to HIV treatment in Battambang province. Measures to reduce the demand for unnecessary medical injections and the provision of unsafe injections are needed. Estimates of national HIV incidence and prevalence might need to be adjusted to account for unsafe injection as a risk exposure.

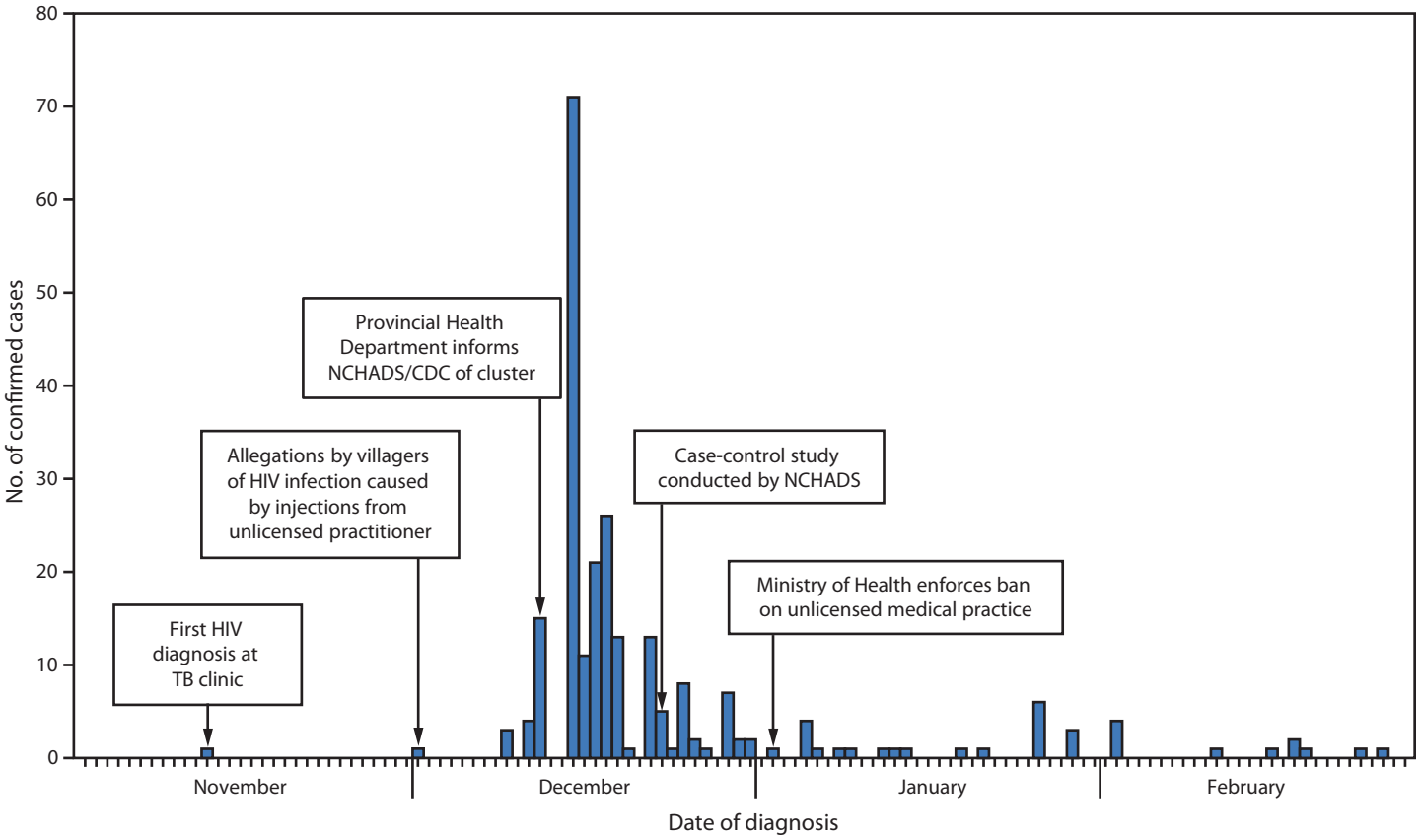
The Roka Cluster Investigation Team initiated an investigation to confirm cases, identify risk factors, and recommend control strategies. Data from antiretroviral therapy (ART) sites and registers of community-based HIV/AIDS care programs were reviewed to exclude persons with existing HIV diagnoses. Specimens that had tested HIV-positive by HIV rapid test kit were laboratory confirmed using an enzyme immunoassay (Serodia, Fujirebio Diagnostics, Japan). Specimens were also tested for antibody to hepatitis C (anti-HCV) and hepatitis B surface antigen (HBsAg). A case-control study was undertaken to identify risk factors associated with HIV infection. Controls were selected from commune residents who tested HIV-negative at the time of the study and were matched by age, sex, and place of residence. To describe the number and size of HIV infection clusters among the outbreak cases, phylogenetic analysis was performed on blood specimens from case patients by the Institut Pasteur du Cambodge. Limiting-antigen (LAg) Avidity assay testing was performed to identify recent infection.

The index patient was a resident of Roka commune with tuberculosis, aged 74 years, who received a diagnosis of HIV infection on November 12, 2014. (Figure) Two of the index patient's family members also tested positive for HIV during the same period. The family alleged that the infections were linked to medical injections received from an unlicensed health practitioner. These allegations triggered a surge in demand for HIV testing by other commune residents. During November 2014–February 2015, a total of 2,045 commune residents underwent HIV testing. Overall, 242 confirmed HIV cases were identified, including 52 (22%) in children aged <14 years, and 51 (21%) in adults aged >60 years. One hundred fifty cases (62%) were in females. Four women aged >60 years and one girl aged 7 months died after their HIV diagnoses; the causes of death are unknown. As of January 19, among 102 patient specimens tested, 72 (70.6%) were positive for anti-HCV, and eight (7.8%) were positive for HBsAg. Current national data are not available for comparison; however, population prevalence of anti-HCV and HBsAg in the neighboring province of Siem Riep are estimated at 5.8% and 4.6%, respectively (*1*). An investigation of the provincial blood transfusion center ruled out blood transfusion as a source of infection in this cluster. Preliminary results from the case-control study indicated that cases were nearly five times as likely as controls to have received an intravenous or intramuscular injection, and four times as likely as controls to have received an intravenous infusion during the preceding 6 months.

Phylogenetic analyses of the C2-V3 region of the HIV-1 gp120 gene, and related protease and reverse transcriptase genes demonstrated clustering of HIV viral strains among the outbreak cases and similarity between strains identified in the outbreak and other strains in Southeast Asia. Preliminary incidence assay results (Sedia LAg Avidity enzyme immunoassay, Sedia Biosciences Corporation, Portland, Oregon) suggested that 30% of infections in this outbreak could be classified as having occurred within the 130 days preceding specimen collection.

Concurrent to the case-control study, NCHADS implemented confirmatory HIV testing, conducted community outreach, and supported the scale-up of voluntary HIV testing and counseling in the commune and in the provincial capital (Battambang City). ART services were established at the Roka

**FIGURE. Number of persons (N = 242) infected with human immunodeficiency virus, by date of diagnosis — Roka Commune, Cambodia, November 9, 2014–February 28, 2015**




**Abbreviations:** HIV = human immunodeficiency virus; NCHADS = National Center for HIV/AIDS, Dermatology and Sexually Transmitted Diseases; TB = tuberculosis.

village health center, complementing existing ART services at the Battambang regional hospital. By January 16, 2015, a total of 207 patients, including 179 adults and 28 children (86% of the 242 identified patients with HIV) had initiated ART; the remaining patients were registered in pre-ART care.

A majority of the confirmed cases in this outbreak were from a population not associated with commercial sex work, men who have sex with men (MSM), or injection drug use, the primary risk factors driving Cambodia's HIV epidemic (*2*). The clustering of HIV cases across age groups and other evidence indicating high demand for medical injections in Cambodia further support the likelihood of transmission via injection, intravenous infusion, or other invasive medical procedures (*3*).

## Discussion

Cambodia has successfully reduced national HIV incidence and contained HIV prevalence among commercial sex workers, MSM, and persons who inject drugs. However, this outbreak highlights the risk for HIV transmission in the general population through unsafe medical injections (*2*). HIV transmission by unsafe medical injections has not historically been prioritized in Cambodia's national HIV prevention strategy, which has focused on transmission associated with sex and injection drug use, and, to a lesser extent, blood safety.

Demand for medical injections among Cambodian adults is high, averaging 2.6 injections per person per year, compared with countries such as Vietnam (1.5 injections per person per year), India (2.0), and Nepal (1.2) (*4*). On average, women in Cambodia receive more injections per year (3.3 per person per year, weighted 95% confidence intervals [CI] = 3.1–3.6) than men (1.9, 95% CI = 1.7–2.2), but in some provinces, women receive as many as 5.9 injections per year on average (*5*). The proportion of injections administered with reused equipment in this cluster is unknown; however, a 2013 study estimated 5.5% reuse in the Western Pacific region (*4*). Analyses of Cambodia's 2005 Demographic Health Survey data indicate that 14,618 HIV-negative persons received an average of 2.0 (95% CI = 1.8–2.1) medical injections per person per year, whereas 84 HIV-positive persons received an average of 7.2 (95% CI = 2.6–11.8) medical injections per person per year. Despite this substantial difference, it is not known whether HIV infection resulted from medical injections, or whether

persons living with HIV receive more medical injections because they are sicker. Furthermore, a portion of the association among HIV-infected persons might be confounded by injections received for other sexually transmitted infections (*6*).

The per-act risk for HIV transmission from unsafe medical injections has been estimated among select populations and within nosocomial outbreak settings globally. The risks for transmission among persons who inject drugs and share needles and among health care workers with occupational exposure through percutaneous needle-stick injuries were estimated at 63 and 23 per 10,000 acts, respectively (*7*); however the authors reported wide confidence intervals because of a lack of uniformity in these exposures. A recent outbreak of HIV infections among persons who inject drugs in a rural community in the United States also illustrated the explosive outbreak potential when HIV is introduced into settings where contaminated needles are shared (*8*).

Nosocomial HIV outbreaks, as recently demonstrated in Kyrgyzstan, have demonstrated the potential for overuse of medical injections to cause outbreaks in low-risk populations in countries with HIV epidemics that are concentrated in certain high-risk groups (*9*). In these nosocomial outbreaks, HIV transmission risk per injection with HIV-contaminated equipment has been estimated to be as high as 2%–7% (*7*,*10*). In 2004, it was estimated that 1%–5% of new HIV infections in sub-Saharan Africa might be associated with unsafe medical injections (*6*).

The findings in this report are subject to at least three limitations. First, case identification might be limited to persons who sought HIV testing because of perceived risk of infection related to an unlicensed practitioner rather than with an unsafe injection, leading to a possible underestimation of the total number of cases. Second, findings from the case-control study support an association between medical injection and HIV infection; however, a causal relationship could not be established. Finally, the type and frequency of procedures and the type of equipment used are unknown, limiting ability to identify specific practices (e.g., contamination of multidose medication vials, and sharing of needle or infusion equipment) associated with HIV infection.

The Cambodian government has issued guidance to local health departments to increase enforcement of medical licensing regulations and holds monthly meetings to monitor progress toward this goal. Planning is underway to expand HIV surveillance and evaluate medical injection risk factors elsewhere in Cambodia. Future interventions will seek to reduce public demand for medical injections nationally, and raise health care worker awareness about infection control as well as noninjectable alternatives.

Cambodia's current national HIV prevalence and incidence estimates are based on models that do not include risk factors associated with unsafe injections or blood transfusion. Given the high prevalence of medical injection use in Cambodia, the contribution of medical injection overuse to Cambodia's national HIV burden might be higher than estimated. Efforts should be made to educate health care workers and communities at large on safe injection practices to reduce the demand for unnecessary medical injections and increase injection safety. National HIV prevention strategies should be expanded to monitor unsafe injections as a mode of transmission. Globally, a need exists for tools to estimate HIV risk in low-prevalence countries where substantial proportions of the population are regularly exposed to unnecessary and potentially unsafe injections.

**Summary**

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

Unsafe medical injection practices have been reported in Cambodia during the last decade. Current national human immunodeficiency virus (HIV) prevalence estimates do not include HIV transmission risk associated with unsafe injection or blood transfusion. HIV testing and surveillance in Cambodia are focused on high risk groups, including men who have sex with men, persons who inject drugs, and commercial sex workers.

**What is added by this report?**

The largest cluster of new HIV infections ever attributed to unsafe injections among a general population was reported in a rural area of Cambodia; 2.7% of residents were infected. The outbreak was detected after increased demand for HIV testing by residents who perceived themselves to be at risk after exposure to an unlicensed provider of injections and intravenous infusions.

**What are the implications for public health practice?**

HIV prevention strategies that target specific populations often do not consider the risk for HIV transmission via unsafe injections in the general population. Further studies are needed to clarify HIV prevalence in general populations where HIV risk perception is low; quantify the risk for other bloodborne infections (e.g., hepatitis C) via unsafe injections; understand public demand for medical injections; and improve health care workers' injection practices in the public and private sectors. Measures to reduce both the demand for unnecessary medical injections and the provision of unsafe injections are needed.

## Acknowledgments

Students, faculty, staff members, Cambodia University of Health Sciences; FHI 360, North Carolina; ARV Users Association, Cambodia; AIDS Healthcare Foundation, the Netherlands; Khmer Soviet Friendship Hospital, Cambodia; Dr. Dora Warren, CDC Cambodia Country Director (2009–2015).

[1]Cambodia National Center for HIV/AIDS, Dermatology and STD; [2]Epidemic Intelligence Service, CDC; [3]World Health Organization, Cambodia; [4]Division of Global HIV/AIDS, CDC, Phnom Penh, Cambodia; [5]Division of Global HIV/AIDS, CDC; [6]Institut Pasteur du Cambodge, Phnom Penh, Cambodia; [7]Cambodia University of Health Sciences.

Corresponding author: Romeo R. Galang, RGalang@cdc.gov, 404-639-6387.

## References


1. Yamada H, Fujimoto M, Svay S, et al. Seroprevalence, genotypic distribution and potential risk factors of hepatitis B and C virus infections among adults in Siem Reap, Cambodia. Hepatol Res 2015;45:480–7. http://dx.doi.org/10.1111/hepr.12367.
2. National AIDS Authority. Cambodia country progress report: monitoring progress towards the targets of the 2011 UN Political Declaration on HIV and AIDS. Phnom Penh, Cambodia: National AIDS Authority; 2014. http://www.unaids.org/sites/default/files/country/documents//KHM_narrative_report_2014.pdf.
3. Vong S, Perz JF, Sok S, et al. Rapid assessment of injection practices in Cambodia, 2002. BMC Public Health 2005;5:56–62. http://dx.doi.org/10.1186/1471-2458-5-56.
4. Pépin J, Abou Chakra CN, Pépin E, Nault V. Evolution of the global use of unsafe medical injections, 2000–2010. PLoS One 2013;8:e80948. http://dx.doi.org/10.1371/journal.pone.0080948.
5. National Institute of Statistics; Directorate General for Health; ICF Macro. Cambodia demographic and health survey 2010. Phnom Penh, Cambodia: National Institute of Statistics, Directorate for General Health; Calverton, Maryland: ICF Macro; 2011. http://dhsprogram.com/pubs/pdf/FR249/FR249.pdf.
6. Schmid GP, Buvé A, Mugyenyi P, et al. Transmission of HIV-1 infection in sub-Saharan Africa and effect of elimination of unsafe injections. Lancet 2004;363:482–8. http://dx.doi.org/10.1016/S0140-6736(04)15497-4.
7. Patel P, Borkowf CB, Brooks JT, Lasry A, Lansky A, Mermin J. Estimating per-act HIV transmission risk: a systematic review. AIDS 2014;28:1509–19. http://dx.doi.org/10.1097/QAD.0000000000000298.
8. Conrad C, Bradley HM, Broz D, et al. Community outbreak of HIV infection linked to injection drug use of oxymorphone—Indiana, 2015. MMWR Morb Mortal Wkly Rep 2015;64:443–4.
9. Utyasheva L. Kyrgyzstan: nine health care workers guilty of negligence causing HIV transmission among children. HIV AIDS Policy Law Rev 2008;13:48–9.
10. Gisselquist D, Upham G, Potterat JJ. Efficiency of human immunodeficiency virus transmission through injections and other medical procedures: evidence, estimates, and unfinished business. Infect Control Hosp Epidemiol 2006;27:944–52. http://dx.doi.org/10.1086/506408.

# Update: Influenza Activity — United States, October 4, 2015–February 6, 2016

Kate Russell, MD[1,2]; Lenee Blanton, MPH[2]; Krista Kniss, MPH[2]; Desiree Mustaquim, MPH[2]; Sophie Smith, MPH[2]; Jessica Cohen, MPH[2,3]; Shikha Garg, MD[2]; Brendan Flannery, PhD[2]; Alicia M. Fry, MD[2]; Lisa A. Grohskopf, MD[2]; Joseph Bresee, MD[2]; Teresa Wallis, MS[2]; Wendy Sessions, MPH[2]; Rebecca Garten, PhD[2]; Xiyan Xu, MD[2]; Anwar Isa Abd Elal[2]; Larisa Gubareva, PhD[2]; John Barnes, PhD[2]; David E. Wentworth, PhD[2]; Erin Burns, MA[2]; Jacqueline Katz, PhD[2]; Daniel Jernigan, MD[2]; Lynnette Brammer, MPH[2]

From October through mid-December 2015, influenza activity remained low in most regions of the United States. Activity began to increase in late December 2015 and continued to increase slowly through early February 2016. Influenza A viruses have been most frequently identified, with influenza A (H3N2) viruses predominating during October until early December, and influenza A (H1N1)pdm09 viruses predominating from mid-December until early February. Most of the influenza viruses characterized during that time are antigenically similar to vaccine virus strains recommended for inclusion in the 2015–16 Northern Hemisphere vaccines. This report summarizes U.S. influenza activity* during October 4, 2015–February 6, 2016, and updates the previous summary (*1*).

## Viral Surveillance

World Health Organization (WHO) and National Respiratory and Enteric Virus Surveillance System (NREVSS) laboratories include both public health and clinical laboratories throughout the United States and contribute to virologic surveillance for influenza. Clinical laboratories test respiratory specimens for diagnostic purposes, whereas public health laboratories primarily test specimens for surveillance purposes. Because of differences in these testing practices, virologic data for clinical and public health laboratories is being presented separately beginning with the 2015–16 influenza season.

During October 4, 2015–February 6, 2016, clinical laboratories in the United States tested 279,056 respiratory specimens for influenza viruses, of which 7,966 (2.9%) were positive (Figure 1). During the week ending February 6 (week 5), 17,175 specimens were tested, of which 1,563 (9.1%) were positive for influenza. Among these, 1,135 (73%) were positive for influenza A viruses and 428 (27%) were positive for influenza B viruses.

Public health laboratories tested 26,287 respiratory specimens for influenza during October 4, 2015–February 6, 2016. Of the 3,529 specimens that were positive for influenza, 2,664 (75%) were positive for influenza A viruses and 865 (25%) were positive for influenza B viruses. Among the 2,536 (95%) influenza A viruses subtyped, 1,698 (67%) were influenza A (H1N1)pdm09, and 838 (33%) were influenza A (H3N2) viruses. Among the influenza B viruses, 495 (57%) had lineage determined: 372 (75%) belonged to the B/Yamagata lineage, and 123 (25%) belonged to the B/Victoria lineage. Since October 4, 2015, influenza-positive tests have been reported from all 50 states, the District of Columbia, and Puerto Rico, representing all U.S. Department of Health and Human Services regions.†

Since October 4, age has been reported for 3,059 patients with influenza-positive tests (87%), including 387 (13%) children aged 0–4 years, 958 (31%) persons aged 5–24 years, 1,294 (42%) persons aged 25–64 years, and 420 (14%) persons aged ≥65 years. Cumulatively, influenza A (H3N2) viruses were predominant among persons aged ≥65 years, whereas influenza A (H1N1)pdm09 viruses predominated among other age groups. During January 3, 2016–February 6, 2016, influenza A (H1N1)pdm09 viruses have been the predominant viruses detected among all age groups. The greatest number of influenza B viruses were reported in persons aged 5–24 years.

## Novel Influenza A Viruses

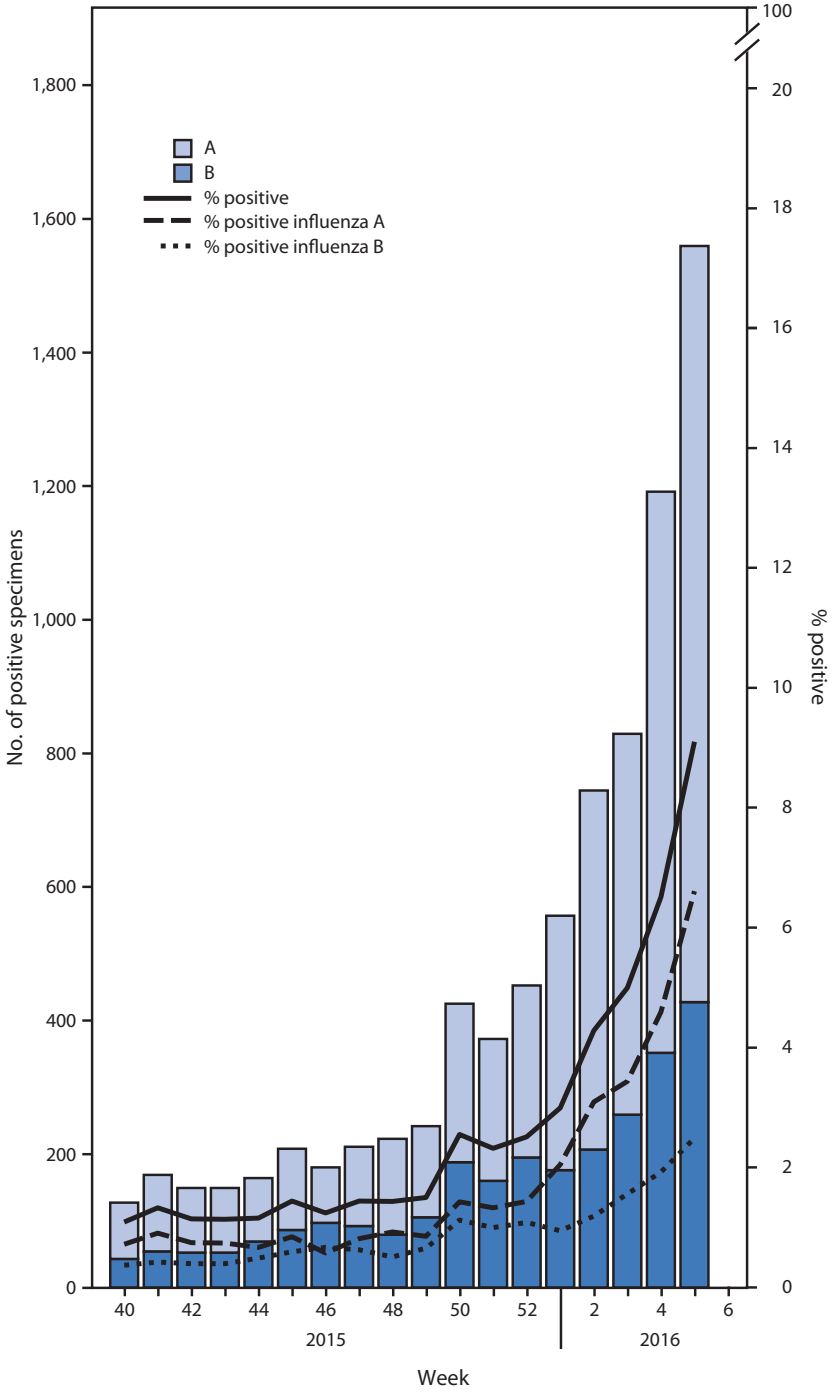
One human infection with a novel influenza A virus was reported to CDC during the week ending January 2, 2016, (week 52) from the state of New Jersey. The patient was infected with an influenza A (H3N2) variant§ (H3N2v) virus. The

* The CDC influenza surveillance system collects five categories of information from nine data sources: 1) viral surveillance (U.S. World Health Organization collaborating laboratories, the National Respiratory and Enteric Virus Surveillance System, and novel influenza A virus case reporting); 2) outpatient illness surveillance (U.S. Outpatient Influenza-Like Illness Surveillance Network); 3) mortality (the National Center for Health Statistics Mortality Surveillance System, 122 Cities Mortality Reporting System, and influenza-associated pediatric mortality reports); 4) hospitalizations (FluSurv-NET, which includes the Emerging Infections Program and surveillance in three additional states); and 5) summary of the geographic spread of influenza (state and territorial epidemiologist reports).

† The 10 regions include the following jurisdictions: Region 1: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont; Region 2: New Jersey, New York, Puerto Rico, and the U.S. Virgin Islands; Region 3: Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia; Region 4: Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee; Region 5: Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin; Region 6: Arkansas, Louisiana, New Mexico, Oklahoma, and Texas; Region 7: Iowa, Kansas, Missouri, and Nebraska; Region 8: Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming; Region 9: Arizona, California, Hawaii, Nevada, American Samoa, Commonwealth of the Northern Mariana Islands, Federated States of Micronesia, Guam, Marshall Islands, and Republic of Palau; Region 10: Alaska, Idaho, Oregon, and Washington.

§ Influenza viruses that circulate in swine are called swine influenza viruses when isolated from swine, but are called variant influenza viruses when isolated from humans. Seasonal influenza viruses that circulate worldwide in human populations have important antigenic and genetic differences from influenza viruses circulating in swine.

**FIGURE 1. Number* and percentage of respiratory specimens testing positive for influenza reported by clinical laboratories, by influenza virus type and surveillance week — United States, October 4, 2015–February 6, 2016**




* 2,966 (2.9%) of 279,056 tested were positive during October 4, 2015–February 6, 2016.

patient reported having no direct contact with swine, but during the week before symptom onset had visited a farm where swine were present. The patient was not hospitalized and fully recovered. There was no evidence of human-to-human transmission.

## Antigenic and Genetic Characterization of Influenza Viruses

The 93 public health laboratories participating as WHO collaborating laboratories in the United States are requested to submit a subset of their influenza virus-positive respiratory specimens to CDC for further characterization. CDC characterizes influenza viruses through one or more laboratory tests including genome sequencing, hemagglutination inhibition (HI), or neutralization assays. These data are used to monitor circulating influenza viruses for early identification of viruses that are antigenically different from the recommended influenza vaccine reference viruses. Most viruses analyzed are propagated in mammalian cell cultures because viruses propagated in tissue culture better represent viruses in circulation, and isolation rates of human influenza viruses are higher in mammalian cell cultures than in eggs, which is the matrix used for production of the majority of influenza vaccines (*2*,*3*). In addition, viruses are more likely to undergo adaptive changes when propagated in eggs. Antigenic and genetic characterization of circulating viruses is performed using both mammalian cell- and egg-propagated reference viruses.

Data obtained from antigenic characterization continue to play an important role in the assessment of the similarity between reference viruses and circulating viruses. Although vaccine effectiveness field studies must be conducted to determine how well the vaccine is working, these laboratory data are used to evaluate whether changes in the virus that could affect vaccine effectiveness might have occurred. Beginning with the 2014–15 season, a proportion of influenza A (H3N2) viruses have not yielded sufficient hemagglutination titers for antigenic characterization by HI. For nearly all viruses characterized at CDC laboratories, next generation sequencing is performed to determine the genetic identity of circulating viruses. For the subset of viruses that do not yield sufficient hemagglutination titers, antigenic properties are inferred using results obtained from viruses within the same genetic group as those that have been characterized antigenically.

Since October 1, 2015, CDC has antigenically or genetically characterized 483 viruses from the United States

(180 influenza A (H1N1)pdm09, 216 influenza A (H3N2), 52 influenza B/Yamagata lineage, and 35 influenza B/Victoria lineage). All 180 influenza A (H1N1)pdm09 viruses were antigenically characterized as A/California/7/2009-like, the influenza A (H1N1) component of 2015–16 Northern Hemisphere vaccines. Although all recent influenza A(H1N1)pdm09 viruses belong to hemagglutinin (HA) genetic group 6B, two genetic subgroups have emerged. To date, however, both genetic subgroups remain antigenically similar to the A/California/7/2009 virus. All 216 influenza A (H3N2) viruses were sequenced and belonged to genetic groups for which a majority of viruses antigenically characterized were antigenically like[¶] A/Switzerland/9715293/2013, the influenza A (H3N2) reference virus representing the A(H3N2) component of the 2015–16 Northern Hemisphere vaccine. A subset of 105 influenza A (H3N2) viruses also were antigenically characterized; 98 of 105 (93%) influenza A (H3N2) viruses were A/Switzerland/9715293/2013-like by HI or neutralization testing. All 52 of the B/Yamagata-lineage were antigenically characterized as B/Phuket/3073/2013-like, the influenza B component of the 2015–16 Northern Hemisphere trivalent and quadrivalent influenza vaccines. All 35 influenza B viruses belonging to the B/Victoria-lineage were antigenically characterized as B/Brisbane/60/2008-like, an influenza B component of the 2015–16 Northern Hemisphere quadrivalent influenza vaccines.

## Antiviral Resistance of Influenza Viruses

Since October 4, 2015, a total of 699 influenza viruses (301 influenza A (H1N1)pdm09 viruses, 246 influenza A (H3N2) viruses, and 152 influenza B viruses) have been examined for antiviral resistance by the WHO Collaborating Center for Surveillance, Epidemiology, and Control of Influenza at CDC. All 152 influenza B viruses and 246 influenza A (H3N2) viruses tested were sensitive to oseltamivir and peramivir. Among 301 influenza A (H1N1)pdm09 viruses tested for resistance, two (0.7%) were found to be resistant to both oseltamivir and peramivir. All 301 influenza A (H1N1)pdm09 viruses tested were sensitive to zanamivir. High levels of resistance to the adamantanes (amantadine and rimantadine) persist among influenza A (H1N1)pdm09 and (H3N2) viruses. Adamantane drugs are not recommended for use against influenza at this time.

## Outpatient Illness Surveillance

Since October 4, 2015, the weekly percentage of outpatient visits for influenza-like illness (ILI)[**] reported by approximately 2,000 U.S. Outpatient ILI Surveillance Network (ILINet) providers in 50 states, New York City, Chicago, the U.S. Virgin Islands, Puerto Rico, and the District of Columbia that constitute ILINet has ranged from 1.3%–2.5%. The percentage exceeded the national baseline[††] of 2.1% for 2 consecutive weeks, from the week ending December 26, 2015–January 2, 2016 (weeks 51 and 52) (Figure 2). The increase in percentage of patient visits for ILI during those 2 weeks might be influenced in part by a reduction in routine health care visits during the winter holiday season, as has occurred during previous influenza seasons. The percentage was at or above the national baseline for 4 consecutive weeks, from the week ending January 16, 2016–February 6, 2016 (weeks 2–5). During the 1997–1998 through 2014–15 influenza seasons, excluding the 2009 pandemic, peak weekly percentages of outpatient visits for ILI ranged from 2.4%–7.7% and remained above baseline levels for an average of 13 weeks (range = 1–19 weeks). For the week ending February 6, 2016 (week 5), the percentage of outpatient visits for ILI was 2.4%, and seven U.S. Department of Health and Human Services regions (1, 2, 3, 4, 6, 8, and 10) reported ILI activity at or above region-specific baseline levels.

Data collected in ILINet are used to produce a measure of ILI activity[§§] by jurisdiction. During the week ending February 6, 2016 (week 5), Puerto Rico and one state (Arizona) experienced high ILI activity. Two states (Arkansas and Connecticut) experienced moderate ILI activity. New York City and eight states (Florida, Illinois, Massachusetts, New Mexico, Oklahoma, Oregon, Texas, and Utah) experienced low ILI activity. Minimal ILI activity was experienced in 38 states (Alabama, Alaska, California, Delaware, Georgia, Hawaii, Idaho, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New York, North Carolina, North Dakota, Ohio, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Vermont, Virginia, Washington, West Virginia, Wisconsin, and Wyoming). The District of Columbia and one state (Colorado) had insufficient data to report.

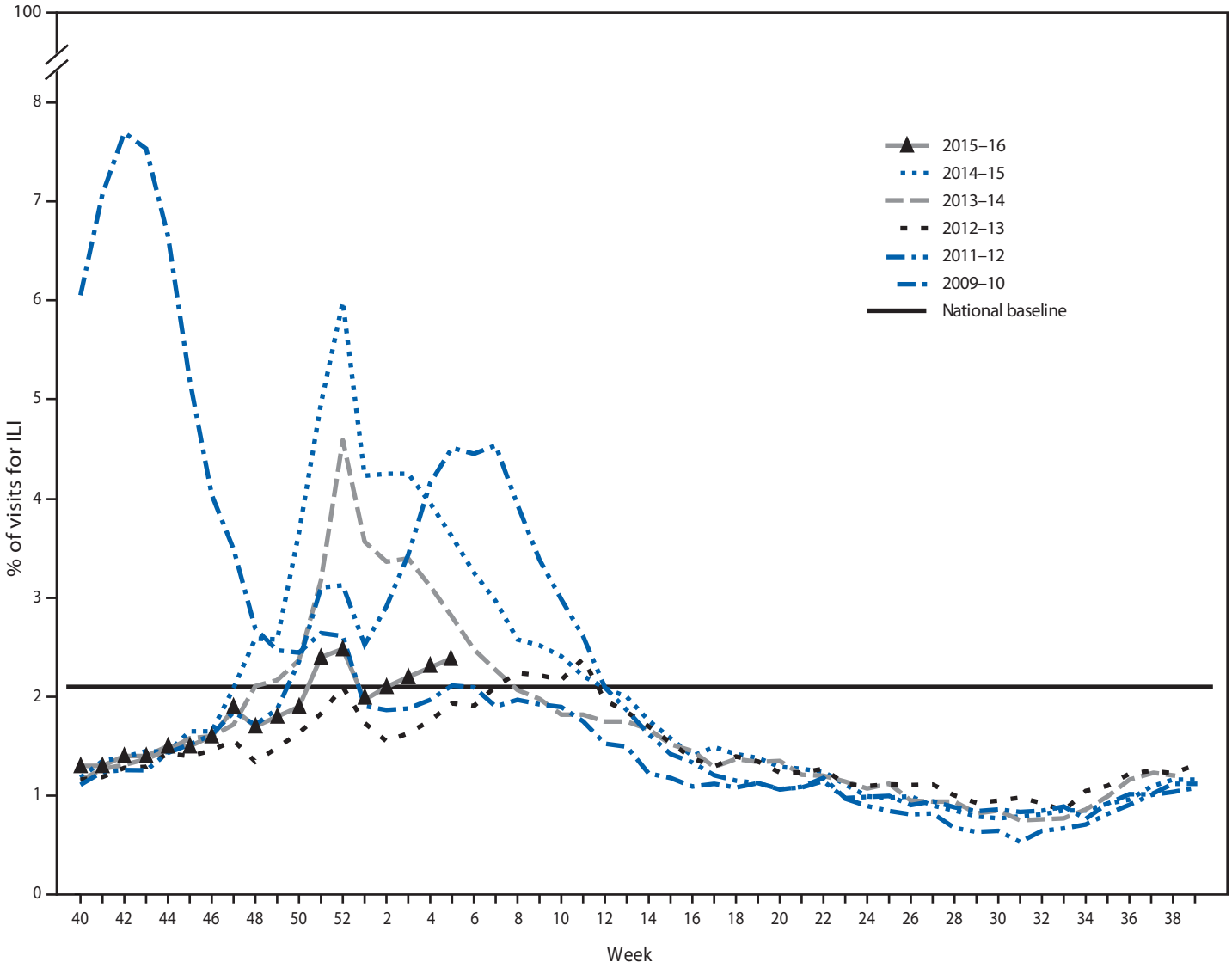
[¶] A virus is considered "reference virus-like" if its hemagglutination inhibition (HI) or neutralization focus reduction (FRA) titer is within 4-fold of the homologous HI/FRA titer of the reference strain. A virus is considered as low to the reference virus if there is ≥8-fold or greater reduction in the HI or FRA titer when compared with the homologous HI or FRA titer of the reference strain.

[**] Defined as a fever ≥100°F (≥37.8°C), oral or equivalent, and cough and/or sore throat, without a known cause other than influenza.

[††] The national and regional baselines are the mean percentage of visits for ILI during noninfluenza weeks for the previous three seasons plus two standard deviations. Noninfluenza weeks are defined as periods of ≥2 consecutive weeks in which each week accounted for <2% of the season's total number of specimens that tested positive for influenza. National and regional percentages of patient visits for ILI are weighted on the basis of state population. Use of the national baseline for regional data is not appropriate.

[§§] Activity levels are based on the percentage of outpatient visits in a jurisdiction attributed to ILI and are compared with the average percentage of ILI visits that occur during weeks with little or no influenza virus circulation. Activity levels range from minimal, corresponding to ILI activity from outpatient clinics at or below the average, to high, corresponding to ILI activity from outpatient clinics much higher than the average. Because the clinical definition of ILI is nonspecific, not all ILI is caused by influenza; however, when combined with laboratory data, the information on ILI activity provides a clearer picture of influenza activity in the United States.

**FIGURE 2. Percentage of visits for influenza-like illness (ILI)* reported to the CDC, by surveillance week — Outpatient Influenza-Like Illness Surveillance Network, United States, 2015–16 influenza season and selected previous influenza seasons**




* Defined as fever (≥100°F [≥37.8°C]), oral or equivalent, and cough and/or sore throat, without a known cause other than influenza.

## Geographic Spread of Influenza

For the week ending February 6 (week 5), Puerto Rico and seven states (Arizona, California, Connecticut, Iowa, Kentucky, Massachusetts, and New York) reported widespread activity.¶¶ Guam and 17 states (Florida, Indiana, Maine, Maryland, Michigan, Minnesota, Nevada, New Hampshire, New Jersey, New Mexico, North Dakota, Pennsylvania, Rhode Island, Texas, Utah, Vermont, and Washington) reported regional activity. Sixteen states (Alabama, Arkansas, Colorado, Idaho, Illinois, Kansas, Montana, North Carolina, Ohio, Oklahoma, Oregon, South Carolina, Tennessee, Virginia, Wisconsin, and Wyoming) reported local activity and the District of Columbia and nine states (Alaska, Delaware, Georgia, Hawaii, Louisiana, Missouri, Nebraska, South Dakota, and West Virginia) reported sporadic activity. No activity was reported in one state (Mississippi) and the U.S. Virgin Islands did not report. During the previous five influenza seasons, the peak number of jurisdictions reporting

¶¶ Levels of activity are 1) no activity; 2) sporadic: isolated laboratory-confirmed influenza cases or a laboratory-confirmed outbreak in one institution, with no increase in activity; 3) local: increased ILI, or two or more institutional outbreaks (ILI or laboratory-confirmed influenza) in one region of the state, with recent laboratory evidence of influenza in that region; virus activity no greater than sporadic in other regions; 4) regional: increased ILI activity or institutional outbreaks (ILI or laboratory-confirmed influenza) in more than two, but less than half of the regions in the state with recent laboratory evidence of influenza in those regions; and 5) widespread: increased ILI activity or institutional outbreaks (ILI or laboratory-confirmed influenza) in at least half the regions in the state, with recent laboratory evidence of influenza in the state.

widespread activity during each season has ranged from 20 in the 2011–12 season to 49 in the 2010–11 season.

## Influenza-Associated Hospitalizations

CDC monitors hospitalizations associated with laboratory-confirmed influenza infection in adults and children through the Influenza Hospitalization Surveillance Network (FluSurv-NET),*** which covers approximately 27 million persons, 9% of the U.S. population. During October 4, 2015–February 6, 2016, a total of 896 laboratory-confirmed influenza-associated hospitalizations were reported, with a cumulative incidence for all age groups of 3.2 per 100,000. Persons aged ≥65 years had the highest rate of influenza-associated hospitalization and accounted for approximately 40% of reported influenza-associated hospitalizations. The cumulative hospitalizations rate (per 100,000 population) during October 4, 2015–February 6, 2016, was 4.5 among children aged <5 years, 1.1 among children and adolescents aged 5–17 years, 1.5 among adults aged 18–49 years, 4.1 among adults aged 50–64 years and 10.2 among adults aged ≥65 years. During the past three influenza seasons (2012–13 through 2014–15), end-of-season age-specific cumulative hospitalization rates have ranged from 47.3–67.0 per 100,000 population for persons aged 0–4 years, 9.4–16.6 for persons aged 5–17 years, 16.1–21.4 for persons aged 18–49 years, 40.9–53.7 for persons aged 50–64 years, and 84.7–308.5 for persons aged ≥65 years. Among all hospitalizations reported during October 4, 2015–February 6, 2016, a total of 624 (70%) were associated with influenza A, 242 (27%) with influenza B, 20 (2.2%) with influenza A and B co-infection, and 10 (1.1%) had no virus type information. Among 189 patients with influenza A subtype information, 160 (85%) were A(H1N1)pdm09 virus and 29 (15%) were A(H3N2) virus.

Complete medical chart abstraction data were available for 349 (39%) hospitalized patients with laboratory-confirmed influenza as of February 6, 2016. Among these, 91% of hospitalized adults had at least one underlying medical condition that placed them at high risk for influenza-associated complications.††† The most commonly reported medical conditions were cardiovascular disease (39%), metabolic disorders (38%), and obesity (36%). Forty seven percent of hospitalized children had at least one underlying medical condition, the most commonly reported being asthma (19%) and neurologic disorders (17%). Among 29 hospitalized women of childbearing age (15–44 years), 7 (24%) were pregnant.

## Pneumonia and Influenza-Associated Mortality

Pneumonia and influenza (P&I)-associated deaths are tracked through two systems, the National Center for Health Statistics (NCHS) Mortality Surveillance System, which reports the week the death occurred, and the 122 Cities Mortality Reporting System, which reports the week that the death certificate was registered. Because of these differences in reporting, the two data sources produce different percentages. Beginning with the 2015–16 influenza season, the NCHS Mortality Surveillance System has been the principal component of U.S. Mortality Surveillance System.

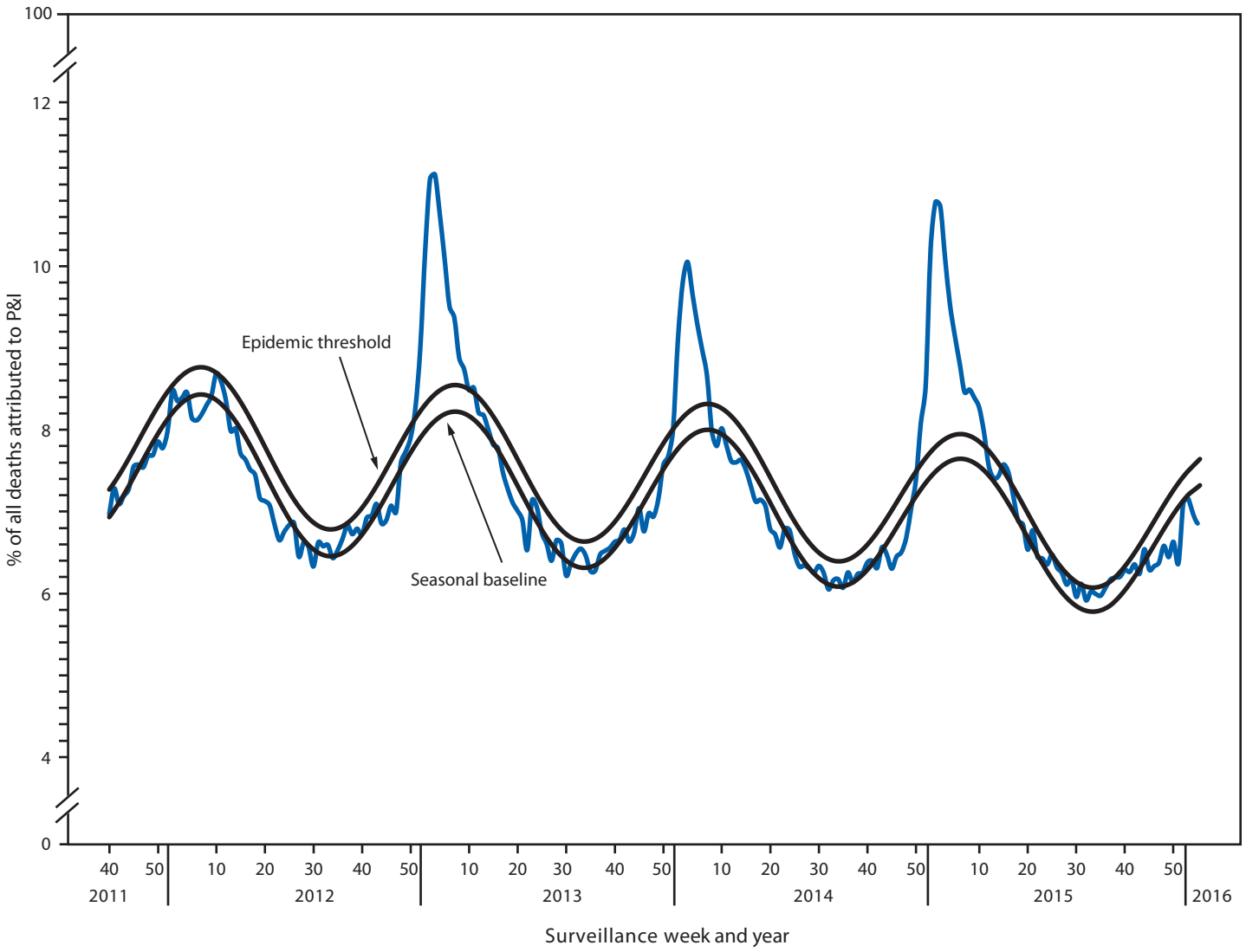
For the week ending January 23, 2016 (week 3), 6.9% (1,861 of 27,158) of all U.S. deaths were classified as resulting from P&I as reported by NCHS (Figure 3). This percentage is below the epidemic threshold of 7.6% for week 3.§§§ Since October 4, 2015 the percentage of deaths attributable to P&I ranged from 6.2% to 7.2% and has not exceeded the epidemic

*** FluSurv-NET conducts population-based surveillance for laboratory-confirmed influenza-associated hospitalizations in children and adolescents aged <18 years (since the 2003–04 influenza season) and adults aged ≥18 years (since the 2005–06 influenza season). The FluSurv-NET covers approximately 70 counties in the 10 Emerging Infections Program states (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee) and additional Influenza Hospitalization Surveillance Project (IHSP) states. IHSP began during the 2009–10 season to enhance surveillance during the 2009 H1N1 pandemic. IHSP sites included Iowa, Idaho, Michigan, Oklahoma, and South Dakota during the 2009–10 season; Idaho, Michigan, Ohio, Oklahoma, Rhode Island, and Utah during the 2010–11 season; Michigan, Ohio, Rhode Island, and Utah during the 2011–12 season; and Iowa, Michigan, Ohio, Rhode Island, and Utah during the 2012–13 season; and Michigan, Ohio, and Utah during the 2013–14, 2014–15, and 2015–16 seasons. Cumulative unadjusted incidence rates are calculated using CDC's National Center for Health Statistics population estimates for the counties included in the surveillance catchment area. Laboratory confirmation is dependent on clinician-ordered influenza testing, and testing for influenza often is underutilized because of the poor reliability of rapid test results and greater reliance on clinical diagnosis for influenza. As a consequence, cases identified as part of influenza hospitalization surveillance likely are an underestimation of the actual number of persons hospitalized with influenza.

††† Persons at higher risk include children aged <5 years (especially those aged <2 years); adults aged ≥65 years; persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematologic (including sickle cell disease), metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle, such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury); persons with immunosuppression, including that caused by medications or by human immunodeficiency virus infection; women who are pregnant or postpartum (within 2 weeks after delivery); persons aged ≤18 years who are receiving long-term aspirin therapy; American Indians/Alaska Natives; persons who are morbidly obese (i.e., body mass index ≥40); and residents of nursing homes and other chronic care facilities.

§§§ The seasonal baseline proportion of P&I deaths is projected using a robust regression procedure, in which a periodic regression model is applied to the observed percentage of deaths from P&I that were reported by the National Center for Health Statistics Mortality Surveillance System and the 122 Cities Mortality Reporting System during the preceding 5 years. The epidemic threshold is set at 1.645 standard deviations above the seasonal baseline. Users of the data should not expect the NCHS mortality surveillance data and the 122 Cities Mortality Reporting System to produce the same percentages, and the percent P&I deaths from each system should be compared with the corresponding system specific baselines and thresholds.

**FIGURE 3. Percentage of all deaths attributable to pneumonia and influenza (P&I), by surveillance week and year* — National Center for Health Statistics Mortality Surveillance System, United States, 2012–2016**




* Data as of February 6, 2016.

threshold this season. During the past five influenza seasons, peak weekly percentages of deaths attributable to P&I have ranged from 8.7% during the 2011–12 season to 11.1% during the 2012–13 season.

Since October 4, 2015, the weekly percentage of deaths attributed to P&I as reported in the 122 Cities Mortality Reporting System has not exceeded the epidemic threshold for ≥2 weeks, ranging from 5.2%–7.7%. For the week ending February 6, 2016 (week 5), the weekly percentage of deaths attributable to P&I was 6.2%, below the epidemic threshold of 6.9% for week 5. During the past five influenza seasons, peak weekly percentages of deaths attributable to P&I have ranged from 7.8% during the 2011–12 season to 9.9% during the 2012–13 season.

## Influenza-Associated Pediatric Mortality

As of February 6, 2016 (week 5), 11 influenza-associated pediatric deaths that occurred during the 2015–16 season have been reported to CDC. Of these, one death was associated with an influenza A (H3N2) virus, three were associated with an influenza A (H1N1)pdm09 virus, three were associated with an influenza A virus for which no subtyping was performed, and four were associated with an influenza B virus. Since influenza-associated pediatric mortality became nationally notifiable in 2004, the total number of influenza-associated pediatric deaths has ranged from 37–171 per season, excluding the 2009 pandemic, during which 358 pediatric deaths were reported to CDC during April 15, 2009–October 2, 2010.

## Discussion

Timing of influenza activity in the United States can be variable but most often peaks during January–March (*4*). During the three most recent influenza seasons, 2012–13, 2013–14, and 2014–15, activity began relatively early, and peaked in late December and early January. The current season activity began to increase in mid-December, a more typical influenza activity pattern. Activity has continued to increase through February 6, 2016. It is not possible to predict when influenza activity will peak but influenza activity will likely continue to increase and remain elevated for several weeks. Influenza A (H3N2), influenza A (H1N1)pdm09, and influenza B viruses have cocirculated this season. During the weeks ending October 10, 2015–December 5, 2015 (weeks 40 through 48), influenza A (H3N2) was the most common virus identified. However, beginning with week 49, influenza A (H1N1)pdm09 has been the most common. CDC has received reports of severe respiratory illness among young- to middle-aged adults with influenza A (H1N1)pdm09 (*5*). This has also been observed during previous seasons when influenza A (H1N1)pdm09 predominated (*6*).

Although vaccine effectiveness estimates are not yet available for the 2015–16 Northern Hemisphere vaccine, laboratory data to date have indicated similarity between circulating viruses and recommended vaccine components. Vaccination remains the best way to prevent influenza infection and associated complications (*4*). Health care providers should continue to offer and encourage vaccination for unvaccinated persons aged ≥6 months throughout the influenza season.

Although influenza vaccination is the best way to prevent influenza, antiviral medications are an important adjunct for reducing the health impact of influenza. Treatment with influenza antiviral medications as early as possible is recommended for patients with confirmed or suspected influenza who have severe, complicated, or progressive illness; who require hospitalization; or who are at high risk for influenza-related complications (*7*,*8*). Antiviral treatment should not be withheld from high-risk or severely ill patients with suspected influenza infection pending confirmatory influenza text results or based on illness onset (*7*). Treatment is most effective when given early in the illness; providers should not delay treatment while waiting for test results and should not rely on insensitive assays such as rapid antigen detection influenza diagnostic tests to determine treatment (*7*,*8*).

Influenza surveillance reports for the United States are posted online weekly (http://www.cdc.gov/flu/weekly). Additional information regarding influenza viruses, influenza surveillance, influenza vaccine, influenza antiviral medications, and novel influenza A infections in humans is online (http://www.cdc.gov/flu).

**Summary**

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

CDC collects, compiles, and analyzes data on influenza activity year-round in the United States. Timing of influenza activity and predominant circulating influenza viruses vary by season.

**What is added by this report?**

Influenza activity remained low in the United States through early December and began to increase slowly in mid-December. Influenza A and B viruses have been reported. Influenza A (H3N2) viruses predominated from October to mid-December, and influenza A (H1N1)pdm09 viruses have predominated from mid-December to February. To date, the majority of influenza viruses that have been antigenically or genetically characterized are similar to components of the 2015–16 Northern Hemisphere vaccine.

**What are the implications for public health practice?**

Vaccination is the primary method to prevent influenza illness and its complications. Health care providers should continue to recommend influenza vaccination to all unvaccinated persons aged ≥6 months now and throughout the influenza season. As an adjunct to vaccine, treatment with influenza antiviral medications is recommended for patients with confirmed or suspected influenza who have severe, complicated, or progressive illness; who require hospitalization; or who are at high risk for influenza-related complications. Antivirals can lessen severity and duration of illness and can reduce severe outcomes of influenza. Antiviral medications work best when administered early in the course of influenza-like illness.

## Acknowledgments

State, county, city, and territorial health departments and public health laboratories; U.S. World Health Organization collaborating laboratories; National Respiratory and Enteric Virus Surveillance System laboratories; U.S. Outpatient Influenza-Like Illness Surveillance Network sites; FluSurv-NET; National Center for Health Statistics, CDC; 122 Cities Mortality Reporting System; World Health Organization, FluNet; Angie Foust, Elisabeth Blanchard, Priya Budhathoki, Thomas Rowe, Lizheng Guo, Ewelina Lyszkowicz, Shoshona Le, Malania Wilson, Juliana DaSilva, Alma Trujillo, Michael Hillman, Thomas Stark, Samuel Shepard, Sujatha Seenu, Ha Nguyen, Vasiliy Mishin, Margaret Okomo-Adhiambo, Michelle Adamczyk, Juan De la Cruz, Influenza Division, National Center for Immunization and Respiratory Diseases, CDC.

[1]Epidemic Intelligence Service, CDC; [2]Influenza Division, National Center for Immunization and Respiratory Diseases, CDC; [3]Atlanta Research and Education Foundation, Georgia.

Corresponding author: Kate Russell, KERussell@cdc.gov, 404-639-3747.

## References


1. Smith S, Blanton L, Kniss K, et al. Update: influenza activity—United States. MMWR Morb Mortal Wkly Rep 2015;64:1342–8. http://dx.doi.org/10.15585/mmwr.mm6448a4.
2. Schild GC, Oxford JS, de Jong JC, Webster RG. Evidence for host-cell selection of influenza virus antigenic variants. Nature 1983;303:706–9. http://dx.doi.org/10.1038/303706a0.
3. Katz JM, Wang M, Webster RG. Direct sequencing of the HA gene of influenza (H3N2) virus in original clinical samples reveals sequence identity with mammalian cell-grown virus. J Virol 1990;64:1808–11.
4. Fiore AE, Uyeki TM, Broder K, et al. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. MMWR Recomm Rep 2010;59(No. RR-8).
5. CDC. Health Alert Network No. 387—Flu season begins: severe influenza illness reported. Atlanta, GA: US Department of Health and Human Services, CDC; 2016. http://emergency.cdc.gov/han/han00387.asp.
6. Epperson S, Blanton L, Kniss K, et al. Influenza activity—United States, 2013–14 season and composition of the 2014–15 influenza vaccines. MMWR Morb Mortal Wkly Rep 2014;63:483–90.
7. Fiore AE, Fry A, Shay D, Gubareva L, Bresee JS, Uyeki TM. Antiviral agents for the treatment and chemoprophylaxis of influenza—recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep 2011;60(No. RR-1).
8. Dobson J, Whitley RJ, Pocock S, Monto AS. Oseltamivir treatment for influenza in adults: a meta-analysis of randomised controlled trials. Lancet 2015;385:1729–37. http://dx.doi.org/10.1016/S0140-6736(14)62449-1.

# Local Transmission of Zika Virus — Puerto Rico, November 23, 2015–January 28, 2016

Dana L. Thomas, MD[1,2]; Tyler M. Sharp, PhD[3]; Jomil Torres, MS[1]; Paige A. Armstrong, MD[4]; Jorge Munoz-Jordan, PhD[3]; Kyle R. Ryff, MPH[1]; Alma Martinez-Quiñones, MPH[5]; José Arias-Berríos, MD[6]; Marrielle Mayshack[1,7]; Glenn J. Garayalde, MD[8]; Sonia Saavedra, MD, PhD[8]; Carlos A. Luciano, MD[6]; Miguel Valencia-Prado[5]; Steve Waterman, MD[3]; Brenda Rivera-García, DVM[1]

*On February 12, 2016, this report was posted as an MMWR Early Release on the MMWR website (http://www.cdc.gov/mmwr).*

Zika virus, a mosquito-borne flavivirus, spread to the Region of the Americas (Americas) in mid-2015, and appears to be related to congenital microcephaly and Guillain-Barré syndrome (*1*,*2*). On February 1, 2016, the World Health Organization (WHO) declared the occurrence of microcephaly cases in association with Zika virus infection to be a Public Health Emergency of International Concern.* On December 31, 2015, Puerto Rico Department of Health (PRDH) reported the first locally acquired (index) case of Zika virus disease in a jurisdiction of the United States in a patient from southeastern Puerto Rico. During November 23, 2015–January 28, 2016, passive and enhanced surveillance for Zika virus disease identified 30 laboratory-confirmed cases. Most (93%) patients resided in eastern Puerto Rico or the San Juan metropolitan area. The most frequently reported signs and symptoms were rash (77%), myalgia (77%), arthralgia (73%), and fever (73%). Three (10%) patients were hospitalized. One case occurred in a patient hospitalized for Guillain-Barré syndrome, and one occurred in a pregnant woman. Because the most common mosquito vector of Zika virus, *Aedes aegypti*, is present throughout Puerto Rico, Zika virus is expected to continue to spread across the island. The public health response in Puerto Rico is being coordinated by PRDH with assistance from CDC. Clinicians in Puerto Rico should report all cases of microcephaly, Guillain-Barré syndrome, and suspected Zika virus disease to PRDH. Other adverse reproductive outcomes, including fetal demise associated with Zika virus infection, should be reported to PRDH. To avoid infection with Zika virus, residents of and visitors to Puerto Rico, particularly pregnant women, should strictly follow steps to avoid mosquito bites, including wearing pants and long-sleeved shirts, using permethrin-treated clothing and gear, using an Environmental Protection Agency (EPA)-registered insect repellent, and ensuring that windows and doors have intact screens.

In November 2015, PRDH, with assistance from CDC, initiated surveillance for Zika virus disease in Puerto Rico by modifying the existing Passive Dengue Surveillance System (*3*) to include suspected Zika virus disease. Patients in whom a clinician suspected Zika virus disease were reported by sending a serum specimen with a modified dengue case investigation form.† In January 2016, PRDH initiated enhanced surveillance for Zika virus disease by performing Zika virus testing on specimens submitted during November 2015–January 2016 that had tested negative for dengue or chikungunya.

Specimens collected within 7 days of illness onset were tested by reverse transcription-polymerase chain reaction (RT-PCR) with updated primers to detect Zika virus RNA. Specimens collected ≥4 days after illness onset were tested by immunoglobulin M (IgM) capture enzyme-linked immunosorbent assay (ELISA) to detect serologic evidence of recent Zika virus infection. Laboratory-confirmed Zika virus disease cases were defined as detection of either Zika virus RNA by RT-PCR, or anti-Zika virus IgM antibody by ELISA with a simultaneous negative anti-dengue virus IgM antibody test.

## Epidemiology and Laboratory Investigations

During November 23, 2015–January 28, 2016, a total of 155 suspected Zika virus disease cases were identified in Puerto Rico, including 82 reported through passive surveillance, and 73 specimens tested through the enhanced surveillance protocol. Overall, 30 (19%) cases had laboratory confirmation of Zika virus disease. Among these cases, one (3%) patient had reported illness onset in November 2015 (the index patient), eight (27%) in December 2015, and 21 (70%) in January 2016. One patient with illness onset in late December reported travel to the Dominican Republic within 14 days of illness onset.

After identification of the index case, two cases were detected during the first 2 weeks of December; six cases per week were reported during the 2nd and 3rd weeks of 2016 (Figure 1). Patients resided in municipalities throughout eastern Puerto Rico and the San Juan metropolitan area, and one each resided in Ponce and Guánica (Figure 2). The most frequently reported symptoms were rash, myalgia, arthralgia, and fever (Table). Fever, rash, arthralgia, and conjunctivitis were reported in seven (23%) patients. Coinfection with influenza B virus was reported in one patient. Three (10%) patients were hospitalized: the index patient, one patient with Guillain-Barré

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

† http://www.cdc.gov/dengue/resources/denguecasereports/dcif_english.pdf.

syndrome, and another patient who was hospitalized because of thrombocytopenia and clinical suspicion of dengue.

**Index case.** The first case of Zika virus disease identified in Puerto Rico occurred in a man aged 80 years from southeastern Puerto Rico with multiple chronic medical conditions, who reported onset of symptoms on November 23, 2015. Eight days after illness onset, he was evaluated in a hospital emergency department for progressive weakness after several days of watery, nonbloody diarrhea, recent episodes of falling, shoulder pain, chills, malaise, and abdominal pain. He did not report myalgia, headache, or retro-orbital pain. He was febrile, tachycardic, tachypneic, and hypotensive, with bilateral erythematous sclera. Laboratory results revealed leukocytosis with a predominance of neutrophils; hemoconcentration; thrombocytopenia; elevated serum transaminases, blood urea nitrogen, and creatinine; hyponatremia; and hypoglycemia. He received a diagnosis of sepsis, was admitted to the intensive care unit for fluid resuscitation and monitoring, and was treated with broad spectrum antibiotics. Diagnostic considerations included leptospirosis and dengue. He experienced respiratory decompensation requiring intubation and 5 days of mechanical ventilation. He was hospitalized for 2 weeks, during which time he underwent an extensive evaluation. Blood and stool cultures were negative, as were serologic tests for human immunodeficiency virus, *Leptospira*, and Strongyloides. Schistosoma immunoglobulin G titers were elevated, for which praziquantel was administered. On December 2, serum was collected for dengue and chikungunya diagnostic testing, and was positive for anti-dengue virus IgM, negative for anti-chikungunya virus IgM, and negative for detection of dengue virus and chikungunya virus RNA. Because a hospital-based enhanced surveillance protocol was in place for detection of Zika virus, the same serum specimen was tested for Zika virus infection by RT-PCR with a positive result. Confirmatory molecular diagnostic testing was performed at CDC. Detection of anti-dengue virus IgM antibody likely was a result of cross-reactive anti-Zika virus IgM antibody. Although no pathogen other than Zika virus was identified, the patient's clinical course suggests that he also had an occult bacterial infection.

## Selected Additional Patients' Characteristics

**Case A.** On January 13, 2016, a man aged 37 years developed a rash, which resolved over the next 2 days; the next day, he noted paresthesias in his hands and feet, followed by progressive weakness in bulbar and limb muscles and uncontrolled fluctuating hypertension consistent with dysautonomia. On medical evaluation he had bilateral facial weakness, weakness in the upper and lower limbs, and areflexia, and was hospitalized for ascending paralysis. Cerebrospinal fluid protein was elevated, and electrodiagnostic studies showed evidence of a demyelinating polyneuropathy, consistent with the acute inflammatory demyelinating polyneuropathy variant of Guillain-Barré syndrome. The patient responded to treatment with intravenous immunoglobulin. A serum specimen collected 15 days after illness onset, and before administration of intravenous immunoglobulin, was positive for anti-Zika virus IgM antibody, negative for anti-dengue IgM antibody, and negative for Zika, dengue, and chikungunya virus RNA by RT-PCR. A urine specimen collected 19 days after illness onset was also negative for Zika virus RNA by RT-PCR. This is the only patient in Puerto Rico with Guillain-Barré syndrome and confirmed Zika virus disease identified to date.

**Case B.** On January 22, 2016, RT-PCR–confirmed Zika virus disease was diagnosed in a woman in her first trimester of pregnancy; she had sought care because of a 2-day history of nonfebrile eye, body, and joint pain; petechial rash; conjunctivitis; and nausea. Her obstetrician provided counseling regarding risks to her fetus and recommended clinical follow-up, according to CDC interim guidelines (*4*).

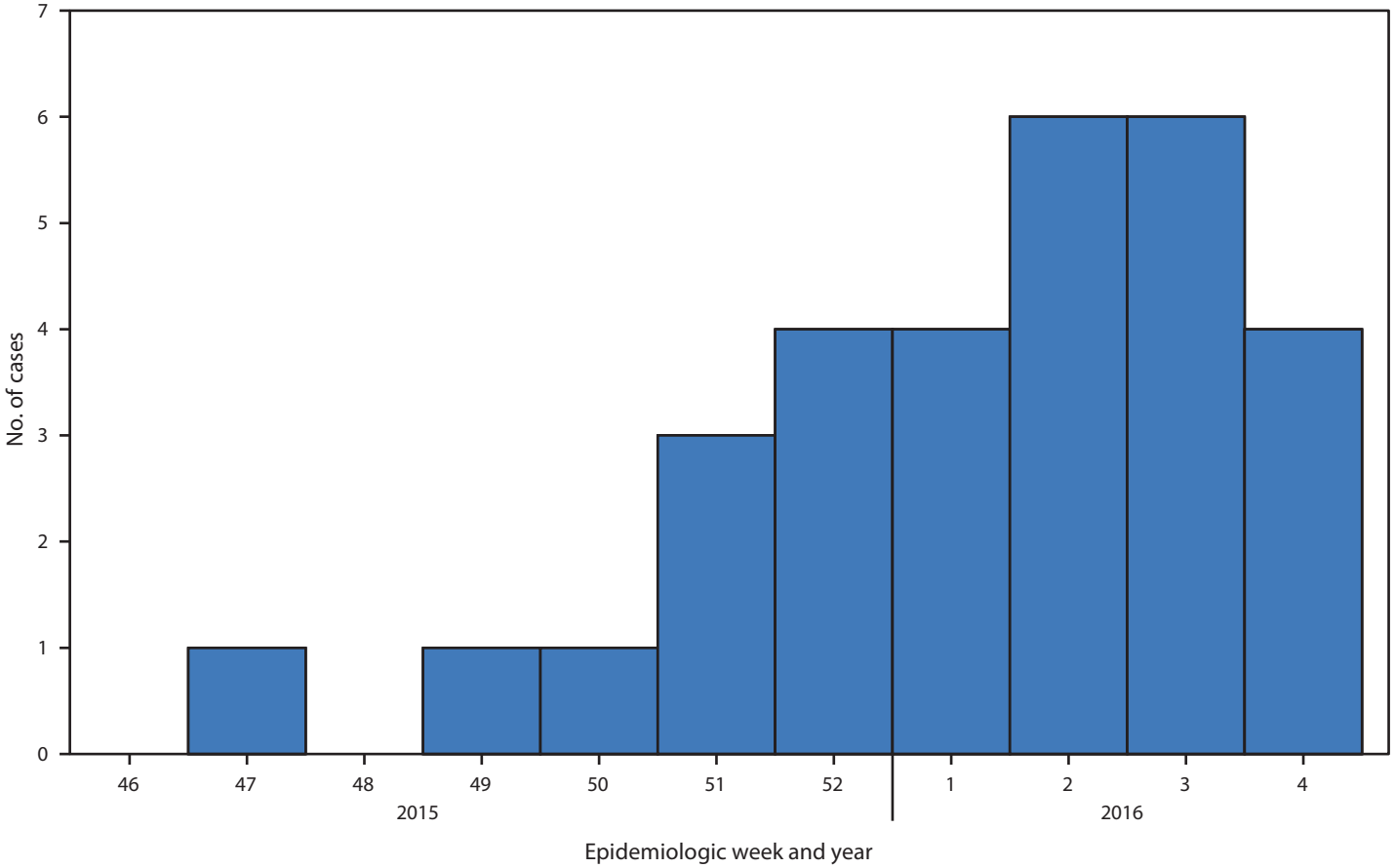
## Public Health Response

The public health response has focused on educating clinicians and the public, establishing laboratory capacity, improving epidemiologic capacity for detecting and monitoring all laboratory-confirmed cases of Zika virus disease in pregnant women, and reducing risk for infection to women who are pregnant. Community cleanup campaigns are being organized throughout the island to remove standing water from containers where *Aedes aegypti* mosquitos might breed. Additional approaches to effective and sustainable mosquito control are being considered.

No cases of microcephaly potentially associated with Zika virus infection have been reported to PRDH. Because microcephaly was not previously captured through routine surveillance, retrospective medical record review of live births during 2013–2015 will be conducted to define the baseline annual incidence of congenital microcephaly among live births, as defined by head circumference below the third percentile for sex and gestational age (*5*). The Puerto Rico Birth Defects Surveillance and Prevention System (BDSPS) case definition has been modified to capture microcephaly cases not associated with another major birth defect of the central nervous system. Clinicians in Puerto Rico have been advised to report all cases of congenital microcephaly to the BDSPS. PRDH, with assistance from CDC, will maintain a registry of all pregnant women with laboratory-confirmed Zika virus infection, who will be followed throughout their pregnancy.

Guillain-Barré syndrome is not a reportable condition in the United States, including Puerto Rico. In conjunction with neurologists in Puerto Rico, a Guillain-Barré syndrome surveillance

**FIGURE 1. Zika virus disease cases* (N = 30), by week of onset of patient's illness — Puerto Rico, November 23, 2015–January 28, 2016**




* All cases laboratory-confirmed, Dengue Branch, CDC.

system is being established to identify cases of clinically diagnosed Guillain-Barré syndrome. After identification of a case of clinically confirmed Guillain-Barré syndrome, testing for arboviral and other infections will be performed. Cases of Guillain-Barré syndrome will be further investigated to define the association between Zika virus infection and Guillain-Barré syndrome.

Because of reports of detection of Zika virus RNA in saliva and urine (*6*,*7*), as well as reports of sexual transmission of Zika virus (*8*,*9*), patients with laboratory-confirmed Zika virus infection will be followed to determine the persistence of Zika virus RNA, as well as the presence of infectious virus in saliva, urine, and semen.

## Discussion

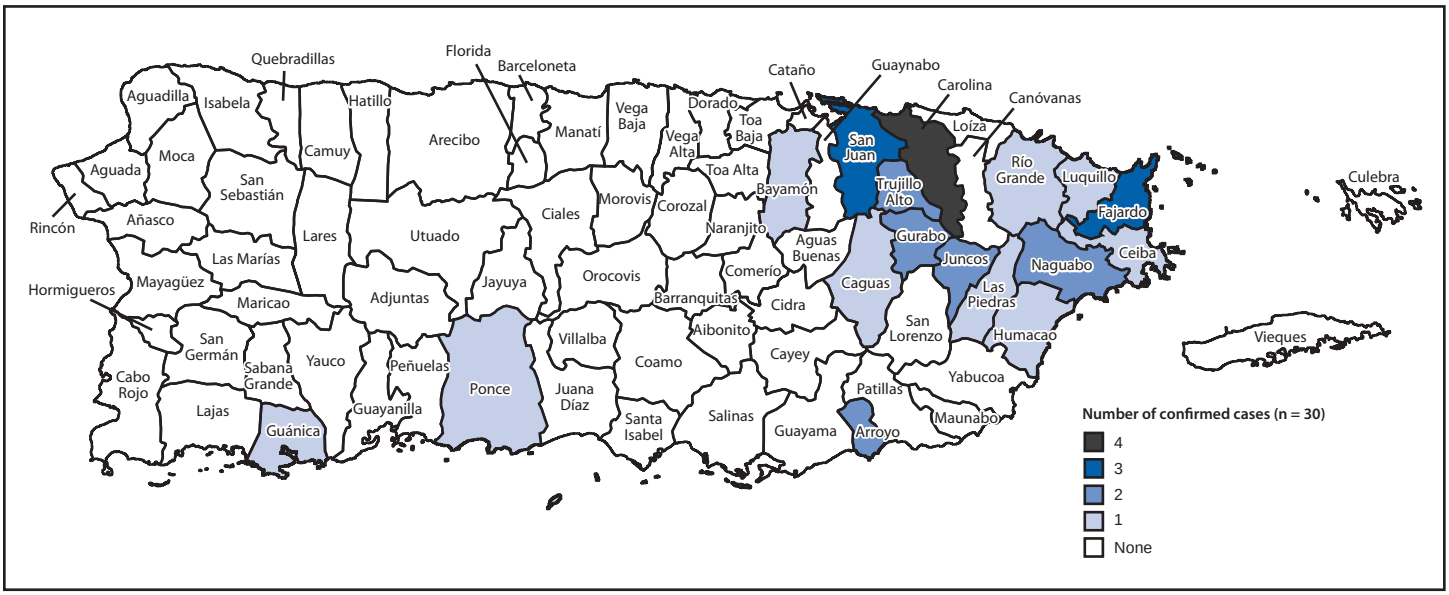
In May 2015, WHO reported the first local transmission of Zika virus in the Americas in Brazil (*10*). As of February 3, 2016, local transmission of Zika virus has been reported in 26 countries and territories in the Caribbean and South and Central America.[§]

[§] http://www.cdc.gov/zika/geo/index.html.

The cases described in this report are the first documented local transmission of Zika virus in a jurisdiction of the United States. *Aedes aegypti*, the most common mosquito vector of Zika virus worldwide, is present throughout Puerto Rico. Therefore, Zika virus is expected to continue to spread throughout the territory, and the 3.5 million residents of Puerto Rico, including approximately 43,000 pregnant women per year, are at risk for Zika virus infection.

Approximately 80% of Zika virus infections are asymptomatic (*11*). The most common symptoms reported by patients in Puerto Rico with laboratory-confirmed Zika virus disease were rash, body and joint pain, and fever. Approximately 25% of patients reported all of the signs and symptoms most commonly associated with Zika virus disease: fever, rash, arthralgia, and conjunctivitis (*11*). This suggests a variable clinical presentation in patients with Zika virus disease. Whether these signs and symptoms are reflective of all persons with symptomatic Zika virus infection, or represent patients with more severe disease, is unknown, as these patients had all sought medical care. This bias might be reflected in the observed rate of patient hospitalization, which was higher than expected on the

**FIGURE 2. Municipality of residence of persons with Zika virus disease*,† — Puerto Rico, November 23, 2015–January 28, 2016§**




* All cases laboratory-confirmed, Dengue Branch, CDC.
† Total number of cases = 30; 1 case not shown because location unknown; 1 case in Juncos was travel-associated.
§ Data current as of February 11, 2016.

basis of previous reports (*11*). Because symptomatic persons with less severe Zika virus disease might not have sought care, the cases reported here might underestimate the incidence of symptomatic Zika virus infection in Puerto Rico.

Clinicians in Puerto Rico should report all patients with fever, joint pain, rash, or conjunctivitis to PRDH as a suspected case of Zika virus disease if another etiology has not been identified. All patients with suspected dengue, chikungunya, or Zika virus disease from whom a specimen has been collected during the first 6 days of illness will be tested by PRDH with an assay currently under development at CDC that simultaneously tests for Zika, chikungunya, and dengue virus RNA. Because of possible complications associated with dengue, including increased vascular permeability that might lead to shock and hemorrhage, patients with suspected Zika, dengue, or chikungunya should be managed as dengue patients¶ until another diagnosis is established. Clinicians in Puerto Rico should also be aware of currently ongoing influenza virus transmission at epidemic levels,** and consider influenza in the differential diagnosis when evaluating patients with acute febrile illness. Current case counts of laboratory-confirmed Zika virus disease cases are available online.††

Currently, no medication or vaccine is available to treat or prevent Zika virus disease. To prevent infection, persons residing in affected areas or traveling to areas of active Zika virus transmission should strictly follow steps to avoid mosquito bites. Men who reside in or have traveled to an area of active Zika virus transmission who have a pregnant partner should abstain from sexual activity or consistently and correctly use condoms during sex, and men who reside in or have traveled to an area of active Zika virus transmission who are concerned about sexual transmission of Zika virus might consider abstaining from sexual activity or using condoms consistently and correctly during sex.§§ Mosquito-bite prevention includes using air conditioning or window and door screens when indoors, wearing long sleeves and pants, using permethrin-treated clothing and gear, and using insect repellents. When used according to the product label, EPA-registered insect repellents are safe for pregnant women.¶¶ Residents of Puerto Rico should cover, empty, or discard water containers that might serve as mosquito breeding sites (e.g., tires, plastic containers, and water cisterns). PRDH, CDC, and other partner organizations are urgently implementing broader plans for mosquito control and reduction of risk for Zika virus infection among pregnant women.

¶ Dengue clinical case management online training course (http://www.cdc.gov/dengue/training/cme.html).
** http://www.salud.gov.pr/Estadisticas-Registros-y-Publicaciones/Pages/Influenza.aspx.
†† http://www.salud.gov.pr/Estadisticas-Registros-y-Publicaciones/Pages/Informe-Arboviral.aspx.
§§ http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e1er.htm?s_cid=mm6505e1.htm_w.
¶¶ http://www.cdc.gov/Features/stopmosquitoes/index.html.

**TABLE. Demographic characteristics, clinical course, and signs and symptoms in 30 patients with Zika virus disease identified by the Puerto Rico Department of Health — Puerto Rico, November 23, 2015–January 28, 2016**

| Characteristic | Patients | |
|---|---|---|
| | Age/Illness onset (range) | No. (%) |
| Median age (yrs) | 40 (10–80) | |
| Median time from illness onset to specimen collection (days) | 3 (0–15) | |
| History of recent travel* | | 1 (3) |
| Female | | 18 (60) |
| Pregnant | | 1 (3) |
| Hospitalized | | 3 (10) |
| **Signs and symptoms†** | | |
| Rash | | 23 (77) |
| Myalgia | | 23 (77) |
| Arthralgia | | 22 (73) |
| Fever | | 22 (73) |
| Eye pain | | 20 (67) |
| Chills | | 20 (67) |
| Headache | | 19 (63) |
| Sore throat | | 12 (40) |
| Petechiae | | 10 (33) |
| Conjunctivitis | | 8 (27) |
| Diarrhea | | 7 (23) |
| Nausea/Vomiting | | 5 (17) |

* Travel outside of Puerto Rico and the United States in the 14 days before illness onset.
† Signs and symptoms were reported by the patients' clinician.

[1]Office of Epidemiology, Puerto Rico Department of Health; [2]Division of State Laboratory Readiness, Office of Public Health Preparedness and Response, CDC; [3]Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC; [4]Epidemic Intelligence Service, CDC; [5]Puerto Rico Birth Defects Surveillance and Prevention System, Puerto Rico Department of Health; [6]Department of Neurology, University of Puerto Rico School of Medicine; [7]Office for State, Tribal, Local and Territorial Support, CDC; [8]Veterans' Affairs Caribbean Healthcare System.

Corresponding author: Dana Thomas, Zika@salud.gov.pr, 787-265-2929.

## References

1. Pan American Health Organization. Epidemiological alert: neurological syndrome, congenital malformations, and Zika virus infection. Implications for public health in the Americas. Washington, DC: World Health Organization, Pan American Health Organization; 2015. http://www.paho.org/hq/index.php?option=com_docman&task=doc_download&Itemid=&gid=32405&lang=en.
2. European Centres for Disease Control and Prevention. Zika virus epidemic in the Americas: potential association with microcephaly and Guillain-Barré syndrome. Stockholm, Sweden: European Centre for Disease Prevention and Control; 2015. http://ecdc.europa.eu/en/publications/Publications/zika-virus-rapid-risk-assessment-8-february-2016.pdf.
3. Noyd DH, Sharp TM. Recent advances in dengue: relevance to Puerto Rico. P R Health Sci J 2015;34:65–70.
4. Petersen EE, Staples JE, Meaney-Delman D, et al. Interim guidelines for pregnant women during a Zika virus outbreak—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:30–3. http://dx.doi.org/10.15585/mmwr.mm6502e1.
5. Staples JE, Dziuban EJ, Fischer M, et al. Interim guidelines for the evaluation and testing of infants with possible congenital Zika virus infection—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:63–7. http://dx.doi.org/10.15585/mmwr.mm6503e3.
6. Musso D, Roche C, Nhan TX, Robin E, Teissier A, Cao-Lormeau VM. Detection of Zika virus in saliva. J Clin Virol 2015;68:53–5. http://dx.doi.org/10.1016/j.jcv.2015.04.021.
7. Gourinat AC, O'Connor O, Calvez E, Goarant C, Dupont-Rouzeyrol M. Detection of Zika virus in urine. Emerg Infect Dis 2015;21:84–6. http://dx.doi.org/10.3201/eid2101.140894.
8. Foy BD, Kobylinski KC, Foy JLC, et al. Probable non-vector-borne transmission of Zika virus, Colorado, USA. Emerg Infect Dis 2011;17:880–2. http://dx.doi.org/10.3201/eid1705.101939.
9. Musso D, Roche C, Robin E, Nhan T, Teissier A, Cao-Lormeau VM. Potential sexual transmission of Zika virus. Emerg Infect Dis 2015;21:359–61. http://dx.doi.org/10.3201/eid2102.141363.
10. Zanluca C, de Melo VC, Mosimann AL, Dos Santos GI, Dos Santos CN, Luz K. First report of autochthonous transmission of Zika virus in Brazil. Mem Inst Oswaldo Cruz 2015;110:569–72. http://dx.doi.org/10.1590/0074-02760150192.
11. Duffy MR, Chen TH, Hancock WT, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. N Engl J Med 2009;360:2536–43. http://dx.doi.org/10.1056/NEJMoa0805715.

**Summary**

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

Zika virus emerged in the Region of the Americas in mid-2015, and since then outbreaks have occurred in multiple South American and Caribbean countries and territories. Zika virus infection appears to be related to increased risk for fetal microcephaly and Guillain-Barré syndrome.

**What is added by this report?**

The first locally acquired case of Zika virus disease in Puerto Rico was identified in early December 2015. During the subsequent months, 29 additional laboratory-confirmed cases have been detected, including in one pregnant woman and in a man with Guillain-Barré syndrome.

**What are the implications for public health practice?**

Clinicians in Puerto Rico and other clinicians evaluating patients with recent travel to Puerto Rico should report all cases of suspected Zika virus disease to public health authorities. Residents of and visitors to Puerto Rico should strictly follow steps to avoid mosquito bites including using air conditioning or window and door screens when indoors, wearing long sleeves and pants, using permethrin-treated clothing and gear, and using insect repellents. When used according to the product label, Environmental Protection Agency-registered insect repellents are safe for pregnant women.

# Notes from the Field

## Evidence of Zika Virus Infection in Brain and Placental Tissues from Two Congenitally Infected Newborns and Two Fetal Losses — Brazil, 2015

Roosecelis Brasil Martines, MD, PhD[1]; Julu Bhatnagar, PhD[1]; M. Kelly Keating, DVM[1]; Luciana Silva-Flannery, PhD[1]; Atis Muehlenbachs, MD, PhD[1]; Joy Gary, DVM, PhD[1]; Cynthia Goldsmith, MS[1]; Gillian Hale, MD[1]; Jana Ritter, DVM[1]; Dominique Rollin, MD[1]; Wun-Ju Shieh, MD, PhD[1]; Kleber G. Luz, MD, PhD[2]; Ana Maria de Oliveira Ramos, MD, PhD[3]; Helaine Pompeia Freire Davi, MD, PhD[4]; Wanderson Kleber de Oliveria, MD[5]; Robert Lanciotti, PhD[6]; Amy Lambert, PhD[6]; Sherif Zaki, MD, PhD[1]

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

Zika virus is a mosquito-borne flavivirus that is related to dengue virus and transmitted primarily by *Aedes aegypti* mosquitoes, with humans acting as the principal amplifying host during outbreaks. Zika virus was first reported in Brazil in May 2015 (*1*). By February 9, 2016, local transmission of infection had been reported in 26 countries or territories in the Americas.* Infection is usually asymptomatic, and, when symptoms are present, typically results in mild and self-limited illness with symptoms including fever, rash, arthralgia, and conjunctivitis. However, a surge in the number of children born with microcephaly was noted in regions of Brazil with a high prevalence of suspected Zika virus disease cases. More than 4,700 suspected cases of microcephaly were reported from mid-2015 through January 2016, although additional investigations might eventually result in a revised lower number (*2*). In response, the Brazil Ministry of Health established a task force to further investigate possible connections between the virus and brain anomalies in infants (*3*).

Since November 2015, CDC has been developing assays for Zika virus testing in formalin-fixed, paraffin-embedded (FFPE) tissue samples. In December 2015, FFPE tissues samples from two newborns (born at 36 and 38 weeks gestation) with microcephaly who died within 20 hours of birth and two miscarriages (fetal losses at 11 and 13 weeks) were submitted to CDC, from the state of Rio Grande do Norte in Brazil, for histopathologic evaluation and laboratory testing for suspected Zika virus infection. All four mothers had clinical signs of Zika virus infection, including fever and rash, during the first trimester of pregnancy, but did not have clinical signs of active infection at the time of delivery or miscarriage. The mothers were not tested for antibodies to Zika virus. Samples included brain and other autopsy tissues from the two newborns, a placenta from one of the newborns, and products of conception from the two miscarriages.

FFPE tissues were tested by Zika virus reverse transcription-polymerase chain reaction (RT-PCR) targeting the nonstructural protein 5 and envelope genes using general methods for RT-PCR (*4*), and by immunohistochemistry using a mouse polyclonal anti-Zika virus antibody, using methods previously described (*5*). Specific specimens from all four cases were positive by RT-PCR, and sequence analysis provided further evidence of Zika virus infection, revealing highest identities with Zika virus strains isolated from Brazil during 2015. In the newborns, only brain tissue was positive by RT-PCR assays. Specimens from two of the four cases were positive by immunohistochemistry: viral antigen was noted in mononuclear cells (presumed to be glial cells and neurons within the brain) of one newborn, and within the chorionic villi from one of the miscarriages. Testing for dengue virus was negative by RT-PCR in specimens from all cases.

For both newborns, significant histopathologic changes were limited to the brain, and included parenchymal calcification, microglial nodules, gliosis, and cell degeneration and necrosis. Other autopsy tissues and placenta had no significant findings. Tests for toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and HIV were negative in the two mothers who experienced miscarriages. Placental tissue from one miscarriage showed heterogeneous chorionic villi with calcification, fibrosis, perivillous fibrin deposition, and patchy intervillositis and focal villitis, while tissue from the other miscarriage had sparsely sampled normal-appearing chorionic villi.

This report describes evidence of a link between Zika virus infection and microcephaly and fetal demise through detection of viral RNA and antigens in brain tissues from infants with microcephaly and placental tissues from early miscarriages. Histopathologic findings indicate the presence of Zika virus in fetal tissues. These findings also suggest brain and early gestational placental tissue might be the preferred tissues for postmortem viral diagnosis. Nonfrozen, formalin-fixed specimens or FFPE blocks are the preferred sample type for histopathologic evaluation and immunohistochemistry, and RT-PCR can be performed on either fresh frozen or formalin-fixed specimens. To better understand the pathogenesis of Zika virus infection and associated congenital anomalies and fetal death, it is necessary to evaluate autopsy and placental tissues from additional cases, and to determine the effect of gestational age during maternal illness on fetal outcomes.

* Updated information about local transmission of Zika virus is available online (http://www.cdc.gov/zika/geo/index.html).

[1]Infectious Diseases Pathology Branch, Division of High-Consequence Pathogens and Pathology, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), CDC; [2]Department of Infectious Diseases, Federal University of Rio Grande do Norte, Natal, RN, Brazil; [3]Department of Pathology, Federal University of Rio Grande do Norte, Natal, Brazil; [4]Service for Ascertaining Death in the State of Rio Grande do Norte (SVO/RN), Natal/RN, Brazil; [5]Ministry of Health, Brazil; [6]Arboviral Diseases Branch, Division of Vector-Borne Diseases, NCEZID, CDC.

Corresponding author: Roosecelis Brasil Martines, RBrasilMartines@cdc.gov, 404-639-3886.

## References

1. Zanluca C, de Melo VC, Mosimann ALP, Dos Santos GI, Dos Santos CN, Luz K. First report of autochthonous transmission of Zika virus in Brazil. Mem Inst Oswaldo Cruz 2015;110:569–72. http://dx.doi.org/10.1590/0074-02760150192.
2. Victoria CG, Schuler-Faccini L, Matijasevich A, Ribeiro E, Pessoa A, Barros FC. Microcephaly in Brazil: how to interpret reported numbers? Lancet 2016. Epub February 5, 2016. http://dx.doi.org/10.1016/S0140-6736(16)00273-7.
3. Schuler-Faccini L, Ribeiro EM, Feitosa IML, et al.; Brazilian Medical Genetics Society–Zika Embryopathy Task Force. Possible association between Zika virus infection and microcephaly—Brazil, 2015. MMWR Morb Mortal Wkly Rep 2016;65:59–62. http://dx.doi.org/10.15585/mmwr.mm6503e2.
4. Bhatnagar J, Blau DM, Shieh WJ, et al. Molecular detection and typing of dengue viruses from archived tissues of fatal cases by rt-PCR and sequencing: diagnostic and epidemiologic implications. Am J Trop Med Hyg 2012;86:335–40. http://dx.doi.org/10.4269/ajtmh.2012.11-0346.
5. Shieh WJ, Blau DM, Denison AM, et al. 2009 pandemic influenza A (H1N1): pathology and pathogenesis of 100 fatal cases in the United States. Am J Pathol 2010;177:166–75. http://dx.doi.org/10.2353/ajpath.2010.100115.

# Notes from the Field

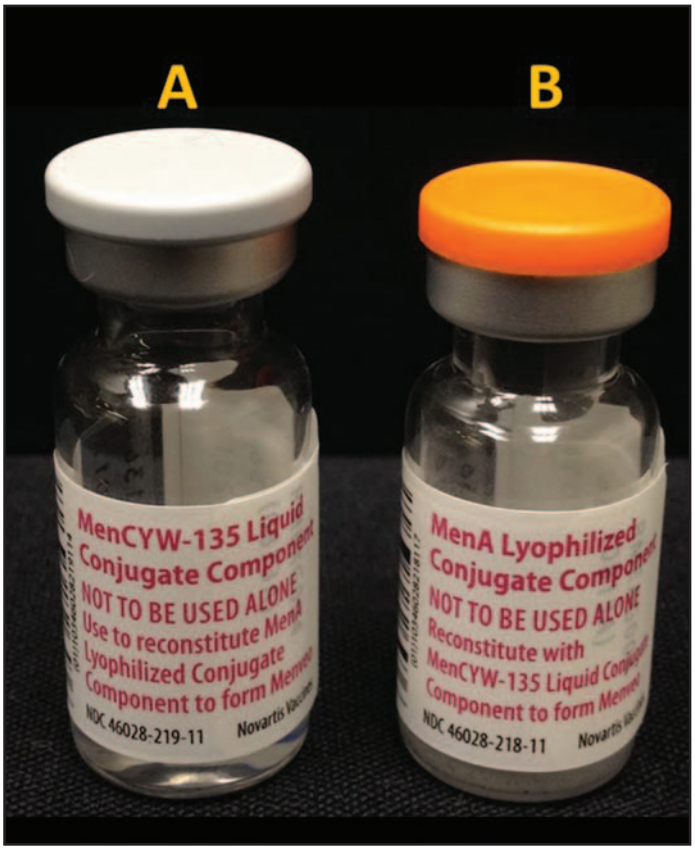
## Administration Error Involving a Meningococcal Conjugate Vaccine — United States, March 1, 2010–September 22, 2015

John R. Su, MD[1]; Elaine R. Miller, MPH[1]; Jonathan Duffy, MD[1]; Bethany M. Baer, MD[2]; Maria V. Cano, MD[1]

Menveo (GlaxoSmithKline, previously Novartis AG) is a conjugate vaccine that was recommended in October 2010 for routine use in adolescents (preferably aged 11 or 12 years, with a booster at 16 years), and among persons aged 2 through 54 years with certain immunosuppressive conditions, to prevent invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y, and W-135 (*1*). These recommendations have since been updated (*2*). Menveo is supplied in two vials that must be combined before administration. The MenA lyophilized (freeze-dried) component must be reconstituted with the MenCYW-135 liquid component (Figure). To administer the vaccine, the liquid component is drawn into a syringe, and used to reconstitute the lyophilized component. The resulting solution is administered by intramuscular injection. Failure to prepare Menveo as directed by the manufacturer's instructions can lead to lack of protection against the intended pathogens (*N. meningitidis* serogroups A, C, Y, and/or W-135) (*3*). Recently, an immunization provider administered only the lyophilized component of Menveo, subsequently administered a properly prepared dose of Menveo to the same patient, and asked CDC if this practice was safe. This question prompted CDC to search the Vaccine Adverse Event Reporting System (VAERS) database for reports during March 1, 2010–September 22, 2015, of only one component of Menveo being administered. Additionally, to more broadly identify disproportional reporting of adverse events in general following Menveo immunization compared with other vaccines in VAERS (including errors in vaccine preparation and administration), the Food and Drug Administration performed data mining with empiric Bayesian methods (*4*).

There were 390 reports of administration of only one component of Menveo to a total of 407 recipients. A total of 269 (66%) recipients received only the liquid MenCYW-135 component, and 138 recipients received only the lyophilized MenA component, reconstituted in sterile water, saline, a different liquid vaccine (hepatitis B vaccine in two cases, and diphtheria-tetanus-acellular pertussis [DTaP] vaccine in one case), or an unspecified diluent. Six reports described clusters of events; five described administration of only the liquid MenCYW-135 component to a total of 21 recipients, and one described administration of only the lyophilized MenA component to two recipients. Among 314 recipients whose sex was reported, 160 (51%) were male. The median age of 293 recipients with known age was 15 years (range = 0–65 years); 87% were aged 11–20 years. Among all 407 recipients, 346 (85%) experienced no adverse event; the reported adverse events included redness, fever, and pain. Medical Dictionary for Regulatory Activities (MedDRA) preferred terms* that were reported at least twice as frequently as expected for Menveo (compared with all other vaccines) were all associated with administration of only one component of Menveo.

**FIGURE. Labels for the two components of Menveo conjugate meningococcal vaccine, liquid MenCYW-135 (A) and lyophilized MenA (B), both indicating that neither component is to be used alone**




Vaccination providers should follow the instructions provided with Menveo (including vaccine labeling, packaging, and product insert) regarding proper administration. Vaccines

* MedDRA (http://www.meddra.org/how-to-use/support-documentation/english) provides a standardized vocabulary of medical terminology to facilitate sharing of regulatory information. MedDRA terms are hierarchical, from very specific low-level terms that are grouped into "preferred terms," to broad groups of terms regarding organ systems. For this analysis, preferred terms were the most appropriate level of specificity for data mining.

requiring reconstitution should only be reconstituted with the specific diluent supplied by the manufacturer for that vaccine (*3*,*5*). A recipient who receives an improperly prepared dose of Menveo should receive a repeat dose of meningococcal conjugate vaccine prepared according to manufacturer instructions; this repeat dose can be administered at any time (*3*).

As a passive surveillance system, VAERS might capture only a fraction of events where only one component of Menveo is administered; therefore, these errors might be more common than VAERS data indicate. Administration of only one vaccine component is not unique to Menveo. Similar errors have been reported for Pentacel, another vaccine packaged as separate liquid (DTaP and inactivated poliovirus vaccine) and lyophilized (*Haemophilus influenzae* type b) components that must be combined before administration. By carefully following instructions included with the vaccine, administration errors with Menveo and similarly packaged vaccines can be prevented. Some reports to VAERS noted that the errors in administering Menveo were detected by routine processes as part of quality assurance. Strategies to prevent errors in vaccine administration are available from CDC (*5*).

[1]Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, CDC, [2]Office of Biostatistics and Epidemiology, Center for Biologics Evaluation and Research, Food and Drug Administration.

Corresponding author: John R. Su, ezu2@cdc.gov, 404-498-0698.

## References

1. CDC. Updated recommendations for use of meningococcal conjugate vaccines—Advisory Committee on Immunization Practices (ACIP), 2010. MMWR Morb Mortal Wkly Rep 2011;60:72–6.
2. Advisory Committee on Immunizaton Practices. Current meningococcal vaccine recommendations. Atlanta, GA: US Department of Health and Human Services, Advisory Committee on Immunizaton Practices; 2015. http://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/mening.html.
3. Meningococcal disease. Chapter 14. In: Hamborsky J, Kroger A, Wolfe S, eds. Epidemiology and prevention of vaccine-preventable diseases. 13th ed. Washington DC: Public Health Foundation; 2015. http://www.cdc.gov/vaccines/pubs/pinkbook/mening.html.
4. DuMouchel W. Bayesian data mining in large frequency tables, with an application to the FDA spontaneous reporting system. Am Stat 1999;53:177–90.
5. Vaccine administration. Chapter 6. In: Hamborsky J, Kroger A, Wolfe S, eds. Epidemiology and prevention of vaccine-preventable diseases. 13th ed. Washington DC: Public Health Foundation; 2015. http://www.cdc.gov/vaccines/pubs/pinkbook/vac-admin.html.

# Notes from the Field

## Nosocomial Outbreak of Middle East Respiratory Syndrome in a Large Tertiary Care Hospital — Riyadh, Saudi Arabia, 2015

Hanan H. Balkhy, MD[1]; Thamer H. Alenazi, MD[1]; Majid M. Alshamrani, MD[1]; Henry Baffoe-Bonnie, MD[1]; Hail M. Al-Abdely, MD[3]; Aiman El-Saed, MD, PhD[1]; Hussain A. Al Arbash, MD[4]; Zayid K. Al Mayahi, MD[4]; Abdullah M. Assiri, MD[5]; Abdulaziz bin Saeed, MD[5]

Since the first diagnosis of Middle East respiratory syndrome (MERS) caused by the MERS coronavirus (MERS-CoV) in the Kingdom of Saudi Arabia in 2012, sporadic cases and clusters have occurred throughout the country (*1*). During June–August, 2015, a large MERS outbreak occurred at King Abulaziz Medical City, a 1,200-bed tertiary-care hospital that includes a 150-bed emergency department that registers 250,000 visits per year.

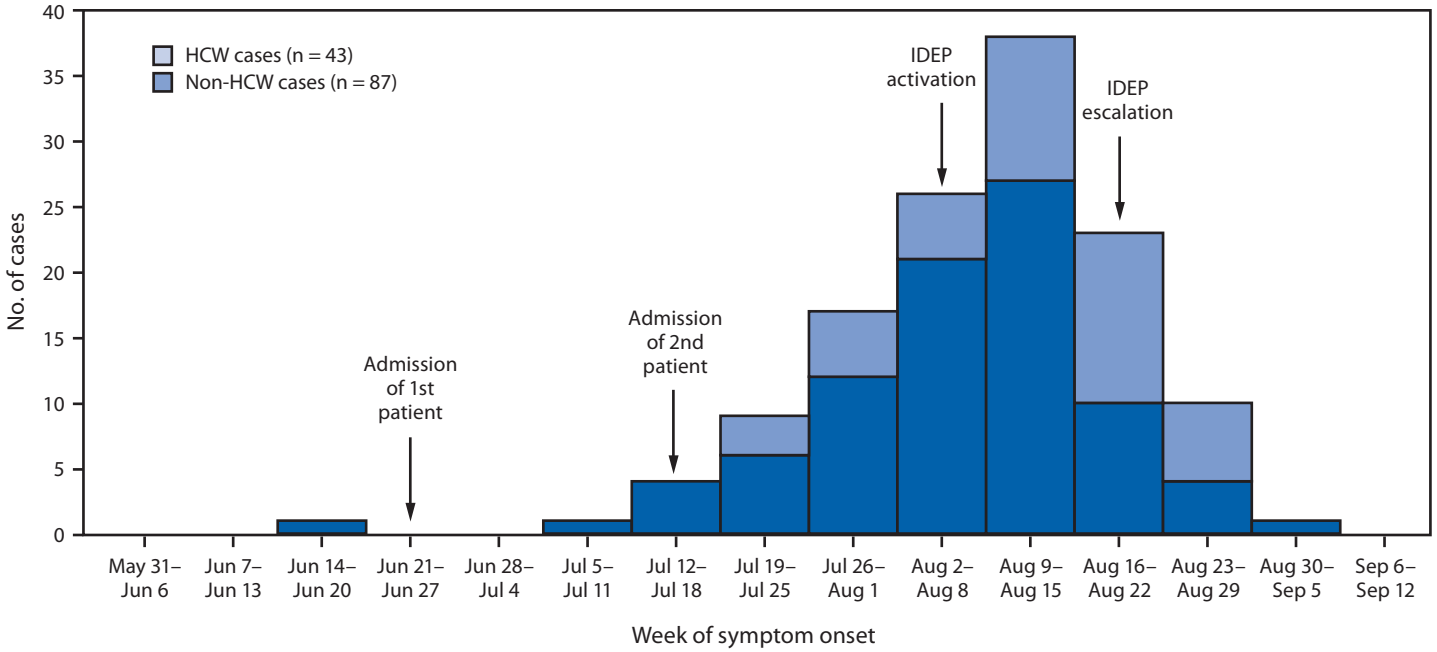
In late June 2015, approximately 3 months after the last previously recognized MERS case in the hospital, a man aged 67 years with multiple comorbidities (diabetes, hypertension, congestive heart failure, and a history of coronary artery bypass graft surgery) and a 10-day history of fever and cough was evaluated in the emergency department (Figure). The patient had no identified exposure to camels. A nasopharyngeal swab from the patient tested positive for MERS-CoV by reverse transcription-polymerase chain reaction (RT-PCR) (*2*). The patient was admitted and died in the hospital after 31 days. Although this patient's hospitalization overlapped with the onset of subsequent hospital-associated MERS cases, no direct links between this first case and any of the subsequent cases were identified.

Approximately 3 weeks after the first patient's admission, a second patient, a man aged 56 years, with multiple comorbidities (diabetes with hypothyroidism, coronary artery disease, and hypertension with a history of coronary artery bypass surgery) and a history of camel exposure was evaluated in the emergency department for fever, cough, and shortness of breath. His nasopharyngeal specimen tested positive for MERS-CoV by RT-PCR. Three additional cases of MERS were epidemiologically linked to this patient's illness during his first week of hospitalization, including infections in two health care workers from the emergency department. An outbreak investigation was conducted by the hospital's infection control program to identify risk factors for infection and to develop and implement control measures. A suspected MERS case was defined as the occurrence of respiratory symptoms in a person with or without documented exposure to a patient with confirmed or probable MERS infection, but without confirmation by laboratory test results. A probable case was the occurrence of respiratory symptoms in a person with history of exposure to a patient with confirmed or probable MERS infection, but with inconclusive laboratory results (such as positive results by PCR on only one of the two genomic targets). A confirmed case was a suspected or probable case that was subsequently confirmed by a positive RT-PCR test for MERS-CoV. Contacts of persons with confirmed and probable cases were screened and persons with suspected cases were tested.

A total of 130 MERS cases were detected at King Abulaziz Medical City during late June–late August. Among these cases, 81 (62%) were confirmed and 49 (38%) were probable, including 43 (33%) cases in health care workers; 20 of these 43 cases (47%) occurred in emergency department health care workers, and 23 (53%) were in health care workers from other areas of the hospital. The majority of confirmed cases were linked to the emergency department. The median age of MERS patients who were health care workers was 37 years, and 77% were female; among MERS patients who were not health care workers, the median age was 66 years, and 65% were male. Signs and symptoms included fever and one or more respiratory symptoms, primarily cough and shortness of breath. Twenty-one (16%) asymptomatic cases were detected during contact screening, including infection in 18 health care workers. Overall, 96 (74%) MERS patients required hospitalization, including 63 (66%) who required intensive care management; 34 (26%) patients were isolated at home. Among all 130 cases, 51 (53%) died; no deaths occurred among health care workers.

On August 2, a preexisting Infectious Disease Epidemic Plan (IDEP), established by the hospital outbreak committee and based on CDC and World Health Organization guidelines (*3*,*4*), was activated (Figure). The plan included strict enforcement of infection control measures, including hand hygiene, airborne and contact isolation for confirmed and probable cases, and droplet and contact isolation for suspected cases. Measures were taken to house suspected patients and confirmed/probable patients on separate wards. Because cases continued to be identified despite the hospital's status of being in level II IDEP, on August 18, the plan was escalated to the highest level, IDEP level III, which included closure of the emergency department, postponement of elective surgical procedures, and suspension of all outpatient appointments and visits. Complete evacuation of the emergency department was achieved on August 22, and was associated with a rapid decline in the number of new cases. Onset of symptoms in the last infected patient was August 28. On September 28, the end

**FIGURE. Number of cases of Middle East Respiratory Syndrome (N = 130), by week of symptom onset and health care worker (HCW) status — King Abdulaziz Medical City, Riyadh, Saudi Arabia, June–August, 2015**




**Abbreviation:** IDEP = infectious disease epidemic plan.

of outbreak was declared after the completion of two 14-day incubation periods without further identification of new cases.

This large MERS outbreak in a major tertiary-care hospital in Riyadh was thought to be related to emergency department overcrowding, uncontrolled patient movement, and high visitor traffic. The outbreak required institution of multiple measures to interrupt transmission, including almost complete shutdown of the hospital. Primary MERS cases have been linked to patients with camel exposure in previously described outbreaks (*5*) and exposure to camels was confirmed in three patients during the early stages of this outbreak. Escalation of the outbreak, however, was clearly linked to extended health care–related person-to-person transmission. In addition to the community transmission, four generations of hospital transmission were believed to have occurred during the outbreak. Although data are still limited, this occurrence is considered a more intense transmission than has been previously described in similar outbreaks (*6*). Although the outbreak was associated with considerable patient mortality, no deaths occurred among health care workers, who were younger, healthier, and had fewer comorbidities compared with patients who were not health care workers. Early recognition of cases and rapid implementation of infection control guidance is necessary to prevent health care facility-associated outbreaks of MERS-CoV.

[1]King Abdulaziz Medical City; Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia; [1]King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Jeddah, Saudi Arabia; [3]Ministry of Health, Riyadh, Saudi Arabia; [4]Field Epidemiology Training Program, Ministry of Health, Riyadh, Saudi Arabia; [5]King Fahad Medical City, Ministry of Health, Riyadh, Saudi Arabia.

Corresponding author: Hanan Balkhy, MD, 966-1-801-1111-43720, balkhyh@ngha.med.sa.

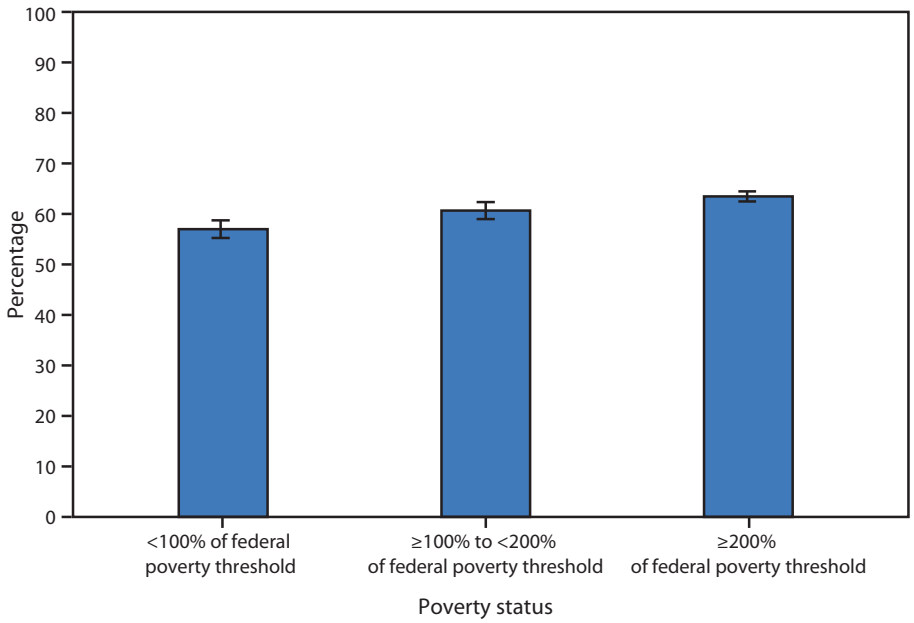
## References

1. Alameer K, Abukhzam B, Khan W, El-Saed A, Balkhy H. Middle East respiratory syndrome coronavirus (MERS-Cov) screening of exposed healthcare workers in a tertiary care hospital in Saudi Arabia. Antimicrob Resist Infect Control 2015;4(Suppl 1):O57. http://dx.doi.org/10.1186/2047-2994-4-S1-O57.
2. World Health Organization. Laboratory testing for Middle East respiratory syndrome coronavirus. Interim guidance. Geneva, Switzerland: World Health Organization; 2015. http://apps.who.int/iris/bitstream/10665/176982/1/WHO_MERS_LAB_15.1_eng.pdf?ua=1.
3. CDC. Interim infection prevention and control recommendations for hospitalized patients with Middle East respiratory syndrome coronavirus (MERS-CoV). Atlanta, GA: US Department of Health and Human Services, CDC; 2015. http://www.cdc.gov/coronavirus/mers/infection-prevention-control.html#infection-prevention.
4. World Health Organization. Infection prevention and control of epidemic- and pandemic-prone acute respiratory diseases in health care. Geneva, Switzerland: World Health Organization, 2007. http://apps.who.int/iris/bitstream/10665/69707/1/WHO_CDS_EPR_2007.6_eng.pdf?ua=1.
5. Alraddadi BM, Watson JT, Almarashi A, et al. Risk factors for primary Middle East respiratory syndrome coronavirus illness in humans, Saudi Arabia, 2014. Emerg Infect Dis 2016;22:49–55. http://dx.doi.org/10.3201/eid2201.151340.
6. Fagbo SF, Skakni L, Chu DKW, et al. Molecular epidemiology of hospital outbreak of Middle East respiratory syndrome, Riyadh, Saudi Arabia, 2014. Emerg Infect Dis 2015;21:1981–8. http://dx.doi.org/10.3201/eid2111.150944.

# QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

## Percentage* of Adults† Who Were Prescribed Medication by a Doctor or Other Health Care Professional During the Past 12 Months,§ by Poverty Status¶ — National Health Interview Survey, United States, 2014**




* Percentages shown with 95% confidence intervals as error bars.
† Aged ≥18 years.
§ Based on the response of "yes" to the survey question, "During the past 12 months, were you prescribed medication by a doctor or other health professional?"
¶ Poverty status is based on family income and family size using the annually updated U.S. Census Bureau poverty thresholds. Family income was imputed when missing.
** Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population and are derived from the National Health Interview Survey sample adult component.

In 2014, the percentage of adults who were prescribed medication by a doctor or other health care professional during the past 12 months increased as income increased. Among adults aged ≥18 years, 57% of those with family incomes <100% of the federal poverty threshold were prescribed medication in the past 12 months, compared with 60.7% of those with incomes 100%–200% of the federal poverty threshold and 63.5% of those with incomes ≥200% of the federal poverty threshold.

**Source:** National Health Interview Survey, 2014 data (http://www.cdc.gov/nchs/nhis.htm).

**Reported by:** Lindsey I. Black, MPH, lblack1@cdc.gov, 301-458-4548; Patricia Barnes, MA.

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.



ISSN: 0149-2195 (Print)