

Interim Estimates of 2013–14 Seasonal Influenza Vaccine Effectiveness — United States, February 2014

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In the United States, annual vaccination against seasonal influenza is recommended for all persons aged ≥ 6 months (1). Each season since 2004–05, CDC has estimated the effectiveness of seasonal influenza vaccine to prevent influenza-associated, medically attended acute respiratory illness (ARI). This report uses data from 2,319 children and adults enrolled in the U.S. Influenza Vaccine Effectiveness (Flu VE) Network during December 2, 2013–January 23, 2014, to estimate an interim adjusted effectiveness of seasonal influenza vaccine for preventing laboratory-confirmed influenza virus infection associated with medically attended ARI. During this period, overall vaccine effectiveness (VE) (adjusted for study site, age, sex, race/ethnicity, self-rated health, and days from illness onset to enrollment) against influenza A and B virus infection associated with medically attended ARI was 61%. The influenza A (H1N1)_{pdm09} (pH1N1) virus that emerged to cause a pandemic in 2009 accounted for 98% of influenza viruses detected. VE was estimated to be 62% against pH1N1 virus infections and was similar across age groups. As of February 8, 2014, influenza activity remained elevated in the United States, the proportion of persons seeing their health-care provider for influenza-like illness was lower than in early January but remained above the national baseline, and activity still might be increasing in some parts of the country (2). CDC and the Advisory Committee on Immunization Practices routinely recommend that annual influenza vaccination efforts continue as long as influenza viruses are circulating (1). Persons aged ≥ 6 months who have not yet been vaccinated this season should be vaccinated. Antiviral medications are

an important second line of defense to treat influenza illness and should be used as recommended (3) among suspected or confirmed influenza patients, regardless of patient vaccination status. Early antiviral treatment is recommended for persons with suspected influenza with severe or progressive illness (e.g., hospitalized persons) and those at high risk for complications from influenza, no matter how severe the illness.

Methods used by the U.S. Flu VE Network have been published previously (4). At five study sites, patients aged ≥ 6 months seeking outpatient medical care for an ARI with

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cough, within 7 days of illness onset, were enrolled.* Study enrollment began after laboratory-confirmed cases of influenza were identified through local surveillance for ≥ 2 consecutive weeks. Trained study staff members reviewed appointment schedules and lists of symptoms to identify patients with ARI and approached eligible patients (or parents/guardians) to complete a brief screening survey. Patients were eligible for enrollment if they 1) were aged ≥ 6 months on September 1, 2013, and thus were eligible for vaccination; 2) reported an ARI with cough and onset ≤ 7 days earlier; and 3) had not been treated with influenza antiviral medication (e.g., oseltamivir) during this illness. Consenting participants completed an enrollment interview. Respiratory specimens were collected from each patient using nasal and oropharyngeal swabs, which were placed together in a single cryovial with viral transport medium. Only nasal swabs were collected for patients aged < 2 years. Specimens were tested at U.S. Flu VE Network laboratories using CDC's real-time reverse transcription polymerase chain reaction (rRT-PCR) protocol for detection and

*The U.S. Flu VE Network sites and the date enrollment began were as follows: Group Health Cooperative (Seattle, Washington) (December 9, 2013); the Marshfield Clinic Research Foundation (Marshfield, Wisconsin) (December 23, 2013); the University of Michigan School of Public Health (the University of Michigan School of Public Health, partnered with the University of Michigan Health System, Ann Arbor, and the Henry Ford Health System, Detroit, Michigan [December 9, 2013]); the University of Pittsburgh Schools of the Health Sciences and UPMC (Pittsburgh, Pennsylvania) (December 2, 2013); and Baylor Scott and White Health, Texas A&M University Health Sciences Center College of Medicine (Temple, Texas) (December 10, 2013).

identification of influenza viruses. Participants were considered vaccinated if they received ≥ 1 dose of any seasonal influenza vaccine ≥ 14 days before illness onset, according to medical records and registries (at Wisconsin and Washington sites) or medical records and self-report (at Michigan, Pennsylvania, and Texas sites). VE was estimated as $100\% \times (1 - \text{odds ratio})$ comparing odds of vaccination among influenza-positive versus influenza-negative participants. Estimates were adjusted for study site, age, sex, race/ethnicity, self-rated health, and days from illness onset to enrollment using logistic regression. Interim VE estimates for the 2013–14 season were based on patients enrolled through January 23, 2014.

Of the 2,319 children and adults with ARI enrolled at the five study sites during December 2, 2013–January 23, 2014, a total of 784 (34%) tested positive for influenza virus by rRT-PCR (Figure); 778 (99%) of these viruses were influenza A, and six (1%) were influenza B (Table 1). Among 755 subtyped influenza A viruses, 742 (98%) were pH1N1 viruses. The proportion of patients with influenza differed by study site, age, race/ethnicity, and interval from onset to enrollment (Table 1). The proportion vaccinated was 38% to 48% across sites and also differed by age, race/ethnicity, and interval from onset to enrollment.

The proportion vaccinated with 2013–14 seasonal influenza vaccine was 29% among influenza cases compared with 50% among influenza-negative controls (Table 2). After adjusting for study site, age, sex, race/ethnicity, self-rated health, and days from illness onset to enrollment, VE against medically attended

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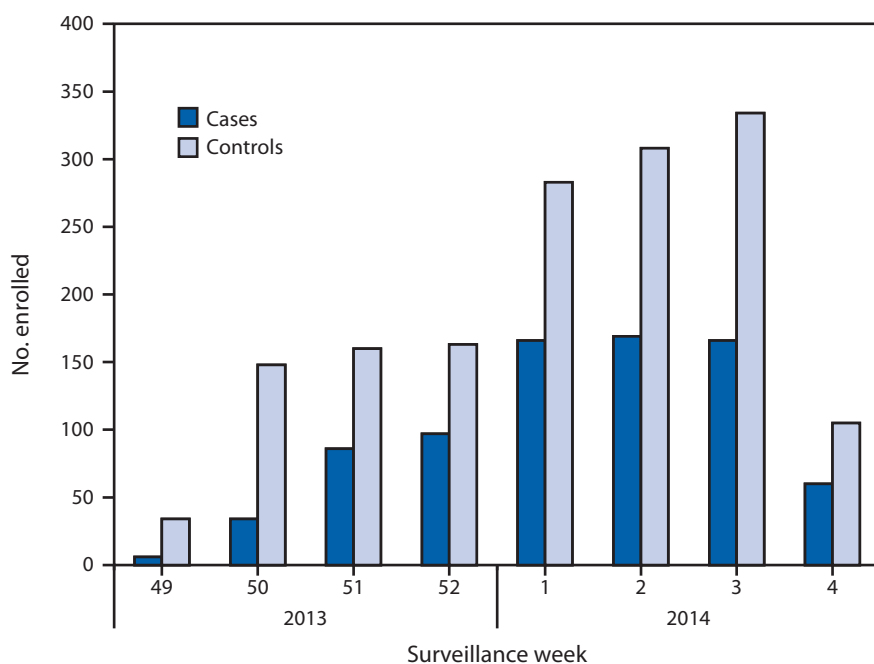
ARI attributable to influenza was 61% (95% confidence interval [CI] = 52%–68%). The adjusted VE for all ages against medically attended ARI caused by pH1N1 virus infection was 62% (CI = 53%–69%). Similar VE against pH1N1 was observed for all age groups.

Editorial Note

Interim results for the 2013–14 season indicate that vaccination has reduced the risk for influenza-associated medical visits by approximately 60%, demonstrating the benefits of influenza vaccination during the current season. Influenza activity is likely to continue for several more weeks in the United States. Vaccination efforts should continue as long as influenza viruses are circulating. Persons aged ≥ 6 months who have not yet received the 2013–14 influenza vaccine should be vaccinated. As of February 8, 2014, approximately 134 million doses of influenza vaccine had been distributed in the United States for the 2013–14 season, from approximately 138–145 million doses that were anticipated to be available for the U.S. market. Because some vaccine providers might have exhausted their vaccine supplies at this time, persons seeking vaccination might need to call more than one provider to locate vaccine.[†]

These age-adjusted interim VE estimates for the 2013–14 influenza vaccine suggest continued effectiveness in preventing outpatient medical visits associated with pH1N1 virus infection. The 2009 influenza pandemic viruses have continued to circulate each season since the 2009 pandemic, but the 2013–14 influenza season is the first season since 2009–10 during which the pH1N1 viruses have predominated; as of February 8, 2014, pH1N1 viruses accounted for nearly 96% of subtyped influenza A viruses reported to CDC (2). Interim VE estimates for 2013 influenza vaccine for prevention of pH1N1-associated outpatient ARI visits were similar to VE estimates for monovalent pandemic and seasonal influenza vaccines for prevention of outpatient medical visits associated with pH1N1 virus infection during previous influenza seasons (4–7) and are consistent with recent interim estimates from Canada (8). Nationally, more than 99% of pH1N1 viruses tested by CDC this season, including 40 viruses from U.S. Flu VE Network sites, have been antigenically similar to A/California/7/2009, the pH1N1 component of 2013–14 influenza vaccines. In addition, deep sequencing analysis of

FIGURE. Numbers of influenza-positive, medically attended, acute respiratory illness cases and influenza-negative, acute respiratory illness controls, by week of illness onset — U.S. Influenza Vaccine Effectiveness Network, United States, December 2, 2013–January 23, 2014*



* Week 4 only includes patients with completed laboratory tests and thus does not reflect all enrolled patients during that week across study sites.

43 pH1N1 virus specimens from the Wisconsin site showed genetic similarity to other recent pH1N1 viruses that have been tested and found to be antigenically similar to the recommended vaccine virus (Thomas C. Friedrich, PhD, School of Veterinary Medicine, University of Wisconsin-Madison, unpublished data, 2014).

These interim estimates suggest similar preventive benefits against pH1N1 influenza virus infections across age groups. During the pandemic, young adults, children, pregnant women, and persons with medical conditions (including morbid obesity) that placed them at high risk for influenza-related complications[§] experienced high rates of severe illness and influenza-associated hospitalization. Although

[§] Persons at higher risk include 1) children aged <2 years; 2) adults aged ≥ 65 years; 3) persons with chronic pulmonary conditions (including asthma); cardiovascular disease (except hypertension alone); renal, hepatic, or 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); 4) persons with immunosuppression, including that caused by medications or by human immunodeficiency virus infection; 5) women who are pregnant or postpartum (within 2 weeks after delivery); 6) persons aged ≤ 18 years who are receiving long-term aspirin therapy; 7) American Indians/Alaska Natives; 8) persons who are morbidly obese (i.e., body mass index ≥ 40); and 9) residents of nursing homes and other chronic-care facilities.

[†] An influenza vaccine locator tool is available at <http://flushot.healthmap.org/?address>.

TABLE 1. Selected characteristics for enrolled patients with medically attended, acute respiratory illness, by influenza test result status and seasonal influenza vaccination status — U.S. Influenza Vaccine Effectiveness Network, United States, December 2, 2013–January 23, 2014

Characteristic	Test result status				p-value [†]	Vaccination status			
	Influenza-positive		Influenza-negative			Vaccinated*			p-value
	No.	(%)	No.	(%)	No.	Total	(%)		
Overall	784	(34)	1,535	(66)		999	2,319	(43)	
Study site					<0.001				0.03
Michigan	110	(24)	342	(76)		195	452	(43)	
Pennsylvania	196	(36)	354	(64)		209	550	(38)	
Texas	129	(34)	250	(66)		165	379	(44)	
Washington	131	(28)	341	(72)		228	472	(48)	
Wisconsin	218	(47)	248	(53)		202	466	(43)	
Sex					0.06				0.16
Male	343	(36)	608	(64)		393	951	(41)	
Female	441	(32)	927	(68)		606	1,368	(44)	
Age group					<0.001				<0.001
6 mos–8 yrs	120	(24)	378	(76)		236	498	(47)	
9–17 yrs	52	(26)	150	(74)		61	202	(30)	
18–49 yrs	360	(40)	536	(60)		280	896	(31)	
50–64 yrs	195	(41)	286	(59)		241	481	(50)	
≥65 yrs	57	(24)	185	(76)		181	242	(75)	
Race/Ethnicity[‡]					0.001				0.001
White	626	(36)	1,113	(64)		769	1,739	(44)	
Black	61	(29)	153	(71)		64	214	(30)	
Other race	44	(23)	145	(77)		88	189	(47)	
Hispanic	52	(30)	121	(70)		76	173	(44)	
Self-rated health status[¶]					0.72				0.29
Fair or poor	57	(34)	112	(66)		82	169	(49)	
Good	165	(31)	363	(69)		241	528	(46)	
Very good	315	(35)	590	(65)		378	905	(42)	
Excellent	246	(34)	469	(66)		298	715	(42)	
Illness onset to enrollment (days)					<0.001				0.01
<3	360	(45)	447	(55)		316	807	(39)	
3–4	264	(31)	583	(69)		372	847	(44)	
5–7	160	(24)	505	(76)		311	665	(47)	
Influenza test result									
Negative	—	—	1,535	—		769	1,535	(50)	
Influenza B–positive	6	—	—	—		4	6	(67)	
Influenza A–positive	778	—	—	—		221	778	(28)	
A (H1N1)pdm09	742	—	—	—		207	742	(28)	
A (H3N2)	13	—	—	—		4	13	(31)	
A subtype pending	23	—	—	—		10	23	(43)	

* Defined as having received ≥1 dose of vaccine ≥14 days before illness onset. According to medical record, to date, 93% of participants had been vaccinated with inactivated influenza vaccines. A total of 56 participants who received the vaccine ≤13 days before illness onset were excluded from the study sample.

† The chi-square statistic was used to assess differences between the numbers of persons with influenza-negative and influenza-positive test results, in the distribution of enrolled patient and illness characteristics, and in differences between groups in the percentage vaccinated.

‡ Enrollees were categorized into one of four mutually exclusive racial/ethnic populations: white, black, other race, and Hispanic. Persons identified as Hispanic might be of any race. Persons identified as white, black, or other race are non-Hispanic. The overall prevalences calculated included data from all racial/ethnic groups, not just the four included in this analysis. Race/ethnicity data were missing for four enrollees.

¶ Data on self-rated health status were missing for two enrollees.

influenza-associated hospitalization rates during the 2013–14 season have been highest among children aged <5 years and persons aged 50–64 and ≥65 years, as of February 8, 2014, approximately 60% of reported influenza-related hospitalizations have occurred in persons aged 18–64 years, and 22% of reported influenza-related hospitalizations among women of childbearing age (15–44 years) have occurred in pregnant women (2). Interim results indicate significant protection from vaccination among adults aged 18–64 years. However, early

estimates for the 2013–14 season[¶] indicated that as of mid-November, only 34% of adults aged 18–64 years had received influenza vaccine this season, compared with 41% of children (aged 6 months–17 years) and 62% of adults aged ≥65 years. Among pregnant women, early estimates for the 2013–14 season indicated that only 41% had been vaccinated by mid-November. A study of pregnant women showed that vaccination during the 2010–11 and 2011–12 seasons significantly

¶ Influenza vaccination coverage estimates for the 2013–14 season are available at <http://www.cdc.gov/flu/fluview/index.htm>.

TABLE 2. Number and percentage receiving 2013–14 seasonal influenza vaccine among 2,319 outpatients with acute respiratory illness and cough, by influenza test result status, age group, and vaccine effectiveness* against all influenza A and B and against influenza A (H1N1)pdm09 — U.S. Influenza Vaccine Effectiveness Network, United States, December 2, 2013–January 23, 2014

Influenza type/Age group	Influenza-positive			Influenza-negative			Vaccine effectiveness			
	No. vaccinated	Total	(%)	No. vaccinated	Total	(%)	Unadjusted		Adjusted	
							(%)	(95% CI)	(%)	(95% CI)
Influenza A and B										
Overall	225	784	(29)	774	1,535	(50)	(60)	(52–67)	(61)	(52–68)
Age group										
6 mos–17 yrs	41	172	(24)	256	528	(48)	(67)	(51–78)	(67)	(51–78)
18–49 yrs	76	360	(21)	204	536	(38)	(56)	(41–68)	(60)	(44–71)
50–64 yrs	73	195	(37)	168	286	(59)	(58)	(39–71)	(60)	(39–73)
≥65 yrs	35	57	(61)	146	185	(79)	(58)	(19–78)	(52)	(2–77)
Influenza A (H1N1)pdm09										
Overall	207	742	(28)	774	1,535	(50)	(62)	(54–69)	(62)	(53–69)
Age group										
6 mos–17 yrs	40	168	(24)	256	528	(48)	(67)	(51–78)	(67)	(51–78)
18–49 yrs	70	339	(21)	204	536	(38)	(58)	(42–69)	(61)	(45–72)
50–64 yrs	67	184	(36)	168	286	(59)	(60)	(41–73)	(62)	(42–75)
≥65 yrs	30	51	(59)	146	185	(79)	(62)	(26–80)	(56)	(7–79)

Abbreviation: CI = confidence interval.

* Vaccine effectiveness was estimated as $100\% \times (1 - \text{odds ratio} [\text{ratio of odds of being vaccinated among outpatients with influenza-positive test results to the odds of being vaccinated among outpatients with influenza-negative test results}])$; odds ratios were estimated using logistic regression.

reduced influenza-associated medical visits (9). Final 2013–14 influenza season vaccination coverage estimates will be available after the end of the season.

As of February 8, 2014, influenza activity remained elevated nationally and widespread across most of the country. These VE estimates imply that some vaccinated persons will become infected with influenza. Clinicians should maintain a high index of suspicion for influenza infection among persons with ARI while influenza activity is ongoing. Early antiviral treatment can reduce influenza-associated illness severity and complications (3). Early antiviral treatment is recommended for persons with suspected influenza with severe or progressive illness (e.g., hospitalized persons) and those at high risk for complications from influenza,** no matter how severe the illness. Antiviral medications should be used as recommended for treatment in patients with suspected influenza, regardless of vaccination status. The decision to initiate antiviral treatment should not wait for laboratory confirmation of influenza and should not be dependent on insensitive assays, such as rapid influenza diagnostic tests.

The findings in this report are subject to at least four limitations. First, vaccination status included self-report at three of five sites; dates of vaccination were available only for persons with documented vaccination obtained from medical records or immunization registries. Verification of vaccination status at all sites will be available for end-of-season VE estimates, which might differ from interim estimates. Second, information from medical records and immunization registries is needed to evaluate

VE for fully versus partially vaccinated children (certain children aged <9 years require 2 vaccine doses) and by vaccine type (e.g., inactivated compared with live attenuated), as well as to evaluate the effects of prior season vaccination; end-of-season analysis of VE for the two most common vaccine types and effects of partial or prior season vaccination is planned. Third, the observational study design has greater potential for confounding and bias than do randomized clinical trials. However, a recent study found that the study design used by the U.S. Flu VE Network produced unbiased VE estimates when applied to analysis of data from randomized placebo-controlled trials (10). In this interim report, adjustment for age, study site, and potential confounding factors identified in previous studies resulted in adjusted estimates that were similar to crude estimates, although final estimates will adjust for additional potential confounders, such as chronic medical conditions, for which information was not available for interim estimates. Finally, end-of-season VE estimates could change as additional patient data become available or if there is a change in circulating viruses late in the season. Also, the VE estimates in this report are limited to the prevention of outpatient medical visits, rather than more severe illness outcomes, such as hospitalization or death; additional studies to measure VE against more severe outcomes are warranted.

Annual vaccination against circulating influenza viruses remains the best strategy for preventing illness from influenza. This report highlights the value of seasonal influenza vaccination and supports ongoing vaccination efforts for all persons aged ≥6 months. Antiviral medications continue to be an important adjunct in the treatment and control of influenza and should be used as recommended, regardless of patient vaccination status.

** A complete summary of guidance for antiviral use is available at <http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>.

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What is already known on this topic?

The influenza A (H1N1)pdm09 (pH1N1) virus that emerged to cause a pandemic in 2009 has continued to circulate in the United States and has been included as the H1N1 component of all seasonal influenza vaccines since the pandemic. Annual vaccination provides the best protection against circulating influenza viruses and is recommended for all persons aged ≥6 months. Estimates of seasonal influenza vaccine effectiveness (VE) for preventing medically attended illness caused by pH1N1 influenza viruses have ranged from 50% to 80% in previous seasons.

What is added by this report?

Based on data from 2,319 children and adults with acute respiratory illness enrolled in the U.S. Influenza Vaccine Effectiveness Network during December 2, 2013–January 23, 2014, the overall VE (adjusted for study site, age, sex, race/ethnicity, self-rated health, and days from illness onset to enrollment) for all ages against influenza A and B virus infection associated with medically attended acute respiratory illness was 61% (95% confidence interval = 52%–68%). Against the predominant influenza pH1N1 virus, VE for all ages was 62%, with similar protection from medically attended illness across age groups.

What are the implications for public health practice?

The 2013–14 seasonal influenza vaccine provides substantial protection against pH1N1 influenza virus, which has been the predominant influenza virus this season. Persons aged ≥6 months who have not yet received the 2013–14 influenza vaccine should be vaccinated. Evidence of protection offered by the 2013–14 influenza vaccine supports the public health benefit of the recent expansion of annual seasonal influenza vaccination to all persons aged ≥6 months.

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Influenza-Associated Intensive-Care Unit Admissions and Deaths — California, September 29, 2013–January 18, 2014

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The California Department of Public Health (CDPH) conducts surveillance on severe influenza illness among California residents aged <65 years. Severe cases are defined as those resulting in admission to an intensive care unit (ICU) or death; reporting of ICU cases is voluntary, and reporting of fatal cases is mandatory. This report describes the epidemiologic, laboratory, and clinical characteristics of ICU and fatal influenza cases with symptom onset on or after September 29, 2013, and reported by January 18, 2014 of the 2013–14 influenza season. At the time of this report, local health jurisdictions (LHJs) in California had reported 94 deaths and 311 ICU admissions of patients with a positive influenza test result. The 405 reports of severe cases (i.e., fatal and ICU cases combined) were more than in any season since the 2009 pandemic caused by the influenza A (H1N1)pdm09 (pH1N1) virus. The pH1N1 virus is the predominant circulating influenza virus this season. Of 405 ICU and fatal influenza cases, 266 (66%) occurred among patients aged 41–64 years; 39 (10%) severe influenza illnesses occurred among children aged <18 years. Only six (21%) of 28 patients with fatal illness whose vaccination status was known had received 2013–14 seasonal influenza vaccine ≥ 2 weeks before symptom onset. Of 80 patients who died for whom sufficient information was available, 74 (93%) had underlying medical conditions known to increase the risk for severe influenza, as defined by the Advisory Committee on Immunization Practices (ACIP). Of 47 hospitalized patients with fatal illness and known symptom onset and antiviral therapy dates, only eight (17%) received neuraminidase inhibitors within 48 hours of symptom onset. This report supports previous recommendations that vaccination is important to prevent influenza virus infections that can result in ICU admission or death, particularly in high-risk populations, and that empiric antiviral treatment should be promptly initiated when influenza virus infection is suspected in hospitalized patients, despite negative results from rapid diagnostic tests.

During the 2009 influenza pandemic, LHJs in California were required to report severe cases of influenza to CDPH. Severe case reporting was voluntary after the pandemic until August 2011, when influenza-associated deaths among persons aged <65 years were made reportable. ICU cases among patients aged <65 years remained voluntarily reportable to

the state; 57 of 61 LHJs report such cases in real time.* For this report, a fatal case was defined as a death occurring in a California resident aged <65 years who had a positive test for influenza and clinical signs and symptoms compatible with influenza with onset on or after September 29, 2013, and reported by January 18, 2014. An ICU case met the same definition as a fatal case, but occurred in a patient hospitalized in an ICU who had not died by January 18, 2014.

Acceptable laboratory confirmation methods for influenza included testing respiratory specimens by reverse transcription–polymerase chain reaction (RT-PCR), direct-fluorescent antibody staining, viral culture, or rapid influenza diagnostic tests. Cases were reported by providers, hospitals, medical examiners, and coroners to LHJs, which then reported cases to CDPH. CDPH sought and abstracted data from autopsy and medical records for fatal cases and reviewed available data for all severe cases for the 2013–14 season received through January 18, 2014. Data reviewed included patient demographics, clinical course and treatment, underlying medical conditions, influenza vaccination status, and laboratory testing. Comparisons with previous influenza seasons were made by using CDPH influenza data from the period 2009–2013. Population estimates were derived from the California Department of Finance for relative risk (RR) calculations comparing the group aged 41–64 years with younger age groups in aggregate.

Epidemiologic Characteristics

As of January 18, 2014, 405 ICU and fatal influenza cases had been reported from 41 (67%) of 61 LHJs[†] in California;

*The detailed timeline for changes to severe influenza reporting requirements beginning with the 2009 pandemic is as follows: Pediatric influenza deaths were reportable across the entire period. At the initial wave of the 2009 pandemic, case report forms were required for all probable and confirmed cases of pH1N1 virus infection, regardless of severity. On August 12, 2009, cases for hospitalized patients could be reported to the state as weekly aggregate numbers; individual case report forms were still required for ICU and fatal cases. On August 10, 2010, the 2009 influenza A (H1N1) pandemic was declared over, and the strain was no longer reportable as a novel influenza strain; ICU and fatal cases were voluntarily reportable and reporting of pediatric deaths resumed as prior to the pandemic. In August 2011, all influenza-related deaths among persons aged <65 years were made reportable to CDPH and reporting of ICU cases among persons aged <65 years remained voluntary.

[†]Three large California LHJs do not typically report ICU cases to CDPH in real time, and one LHJ does not report ICU cases; thus, only fatal cases from those populations are fully represented in this analysis.

symptom onset dates were October 20, 2013–January 15, 2014. The largest number of severe cases (103) by week of symptom onset occurred during the week ending January 11, 2014. These represent the highest cumulative number of severe cases at this point in the influenza season and the highest number of new cases in a single week since the 2009 H1N1 pandemic (Figure 1).

Three fatal influenza cases and 36 ICU cases were among children aged <18 years, including one fatal case and 24 ICU cases among those aged <5 years (Table). Among the 94 fatal cases and 311 ICU cases, 72 (77%) and 195 (63%) were among persons aged 41–64 years, respectively (Figure 2). These are higher proportions than in any season for which data were compared (2009 pandemic to present; $p < 0.03$). Persons in the 41–64 years age group had six times the risk for death (RR = 6.0; 95% confidence interval [CI] = 3.7–9.6) and almost four times the risk for ICU admission (RR = 3.8; CI = 3.1–4.7) versus those aged ≤ 40 years. Of 25 pediatric ICU and fatal cases, the proportion (6%) among children aged 0–4 years is the lowest observed per season since the 2009 pandemic ($p < 0.03$).

Laboratory Characteristics

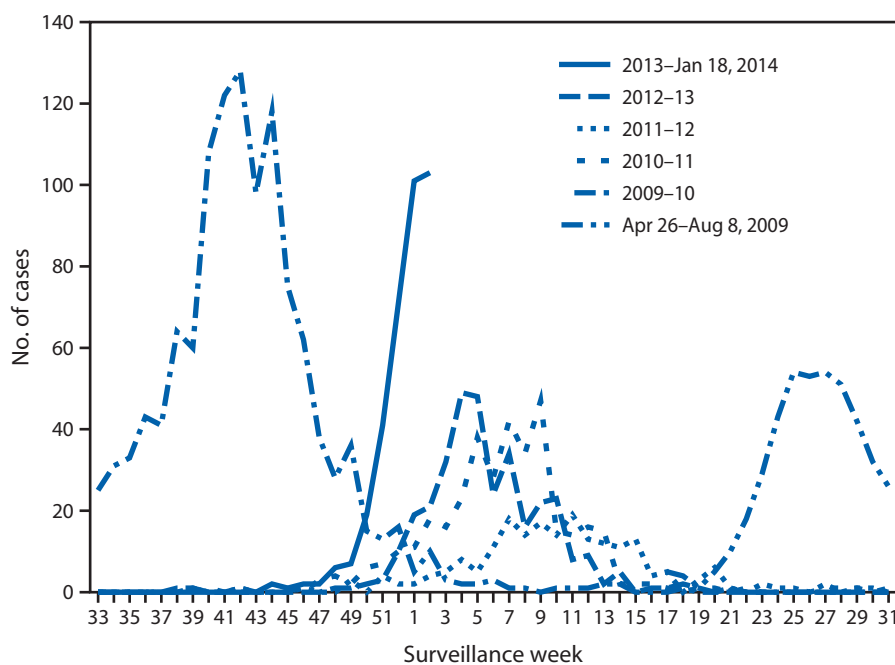
All 94 fatal cases were associated with influenza A virus; subtyping was performed on respiratory specimens from 77 (82%) patients, and all specimens were identified as pH1N1 virus. Of 311 ICU cases, 303 (97%) tested positive for influenza A virus, and eight (3%) tested positive for influenza B virus. Of ICU cases testing positive for influenza A, 165 (54%) were subtyped, and all were identified as pH1N1 virus.

Results of rapid influenza diagnostic tests[§] were reported in medical records of 24 (26%) of the 94 fatal cases. Ten were negative results, indicating a false-negative rate of 42%, compared with RT-PCR.

Clinical Characteristics

Of the 94 patients who died, 80 (85%) had sufficient medical history reported to determine whether they had pre-existing conditions that put them at high risk for influenza complications as defined by ACIP (1). A comorbid condition

FIGURE 1. Number of cases of severe influenza,* by week of symptom onset — California, April 26, 2009–January 11, 2014[†]



* Severe cases of influenza are defined as influenza infections resulting in intensive care unit (ICU) admission or death.

[†] ICU cases from three large local health jurisdictions have not been fully reported yet for the 2013–14 influenza season; for comparability, their ICU data are excluded from all years in this figure. Only cases occurring through January 11, 2014, are included because reporting for the cases with onset in the week ending January 18, 2014 was incomplete at the time of this report.

predisposing to severe influenza was identified in 74 (93%) of these 80 patients with fatal illness. One fatal case occurred in a pregnant woman who had other preexisting medical conditions. The most commonly noted ACIP comorbid conditions were diabetes mellitus (20 cases [25%]), chronic obstructive pulmonary disease (16 [20%]), asthma (11 [14%]), and morbid obesity (body mass index ≥ 40) (11 [14%]). Of the six patients with no known comorbid condition predisposing them to complications from influenza, as defined by ACIP, three (50%) were obese, with body mass indices of 30–39.

Only six (21%) of 28 decedents whose vaccination status was known had documentation of receipt of 2013–14 seasonal influenza vaccine ≥ 2 weeks before symptom onset. Ten (11%) of the 94 patients who died were not hospitalized. Hospitalized patients who died were admitted to the ICU a median of 6 days after symptom onset (range = 0–56 days) and spent a median of 5 days in the ICU (range = 0–22 days). Of 65 fatal cases among persons for whom clinical information was available, 60 (92%) patients underwent endotracheal intubation and received mechanical ventilation.

In 80 fatal cases for which antiviral treatment information was available, neuraminidase inhibitors (e.g., oral oseltamivir or inhaled zanamivir) were prescribed for 62 (78%), with

[§] Additional information available at <http://www.cdc.gov/flu/professionals/diagnosis/rapidlab.htm>.

TABLE. Characteristics of influenza cases resulting in intensive-care unit (ICU) admission or death — California, September 29, 2013–January 18, 2014

Characteristic	Deaths		ICU admissions	
	No.	(%*)	No.	(%*)
Overall	94	(100)	311	(100)
Sex				
Male	46	(49)	172	(55)
Female	48	(51)	139	(45)
Age group (yrs)				
0–4	1	(1)	24	(8)
5–17	2	(2)	12	(4)
18–40	19	(20)	70	(23)
41–64	72	(77)	195	(63)
Unknown	0	—	10	(3)
Race				
American Indian	0	—	1	(0.3)
Asian	4	(4)	12	(4)
Black	6	(6)	16	(5)
Pacific Islander	0	—	2	(0.6)
White	64	(68)	162	(52)
Other	0	—	2	(0.6)
Unknown	20	(21)	116	(37)
Ethnicity				
Hispanic	30	(32)	57	(18)
Non-Hispanic	44	(47)	138	(44)
Unknown	20	(21)	116	(37)
Preexisting medical condition				N/A
ACIP-influenza: Yes	74	(79)		
ACIP-influenza: No	6	(6)		
ACIP-influenza: Unknown	14	(15)		
Obesity level				N/A
BMI ≥40 (morbidly obese)	11	(12)		
BMI 30–39 (obese)	16	(17)		
BMI <30	29	(31)		
Unknown BMI	38	(40)		
Influenza type				
Influenza A	94	(100)	303	(97)
Influenza B	0	—	8	(3)
Influenza subtype				
A (H1N1)pdm09	77	(82)	165	(53)
Pending or unknown	17	(18)	146	(47)
Patient received antiviral therapy (n = 80)				N/A
Yes	62	(78)		
No	18	(23)		
Antiviral start date on or before date of admission (n = 58)				N/A
Yes	27	(46)		
No	31	(54)		
Antiviral therapy started ≤48 hours after symptom onset (n = 47)				N/A
Yes	8	(17)		
No	39	(83)		
2013–14 influenza vaccination status[†]				N/A
Yes	6	(6)		
No	22	(23)		
Unknown or not reported in medical record	66	(70)		
Rapid influenza antigen diagnostic test				N/A
Positive	14	(15)		
Negative	10	(11)		
Not performed or not reported in medical record	70	(74)		

Abbreviations: ACIP = Advisory Committee on Immunization Practices; BMI = body mass index; weight (kg) / (height [m])²; N/A = not available.

* Percentages might not sum to 100% because of rounding.

[†] ≥2 weeks before symptom onset.

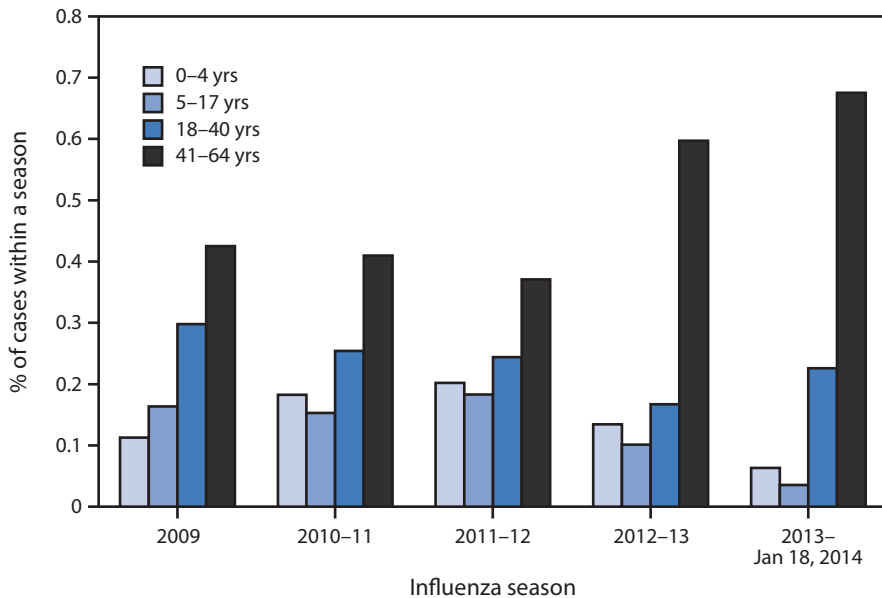
57 (92%) of these patients receiving oral oseltamivir. Of 58 fatal cases with known dates of antiviral therapy, 27 patients (46%) received antiviral treatment on or before their hospital admission date. Of 47 patients with fatal illness and known symptom onset and antiviral therapy dates, eight (17%) received neuraminidase inhibitors within 48 hours of symptom onset.

Editorial Note

Surveillance for severe influenza can support an assessment of the severity of influenza seasons, identify populations most affected, and identify emerging influenza viruses that can cause substantial morbidity and mortality. Surveillance for severe influenza (i.e., fatal and ICU cases) also enabled CDPH to identify unusual characteristics of influenza activity early in the 2013–14 influenza season. In contrast with previous seasons, a higher proportion of severe cases in the current season in California were reported among adults aged 41–64 years, and a lower proportion among children aged 0–4 years. In addition, severe cases were being reported in higher numbers and earlier in the season than in any season since 2009. The majority of patients with fatal illness tested positive for pH1N1 virus, suffered from comorbid conditions predisposing them to severe influenza complications, and had not received 2013–14 seasonal influenza vaccine.

The proportion of severe cases among children is the lowest observed since the 2009 pandemic, when data collection for all severe cases in persons aged <65 years began, although high rates of hospitalization were observed among this age group in 2009 (2). These data from the 2013–14 influenza season demonstrate that patients aged 41–64 years were at relatively higher risk for influenza than in previous recent influenza seasons. The reason for this difference is unknown and might include virologic factors or a relative lack of population immunity in this age group because of low rates of either vaccination or prior exposure. The difference might also reflect bias resulting from reporting changes across time. National hospitalization rates for

FIGURE 2. Percentage of severe* influenza cases, by age group, across influenza seasons — California, 2009–January 18, 2014



* Severe cases of influenza are defined as influenza infections resulting in intensive-care unit admission or death.

What is already known on this topic?

The influenza A (H1N1)pdm09 virus has been the predominant circulating virus in the United States throughout the ongoing 2013–14 influenza season, resulting in high proportions of intensive-care unit (ICU) admissions and deaths among adults aged <65 years.

What is added by this report?

The 2013–14 influenza season in California has resulted in more ICU admissions and deaths associated with influenza virus infection than in any season since the 2009 H1N1 pandemic. Of fatal and ICU cases with laboratory-confirmed influenza occurring in persons aged <65 years, those aged 41–64 years with underlying medical conditions predisposing them to influenza complications have been disproportionately affected. Influenza vaccination and antiviral treatment have been underutilized in observed cases with overreliance on rapid diagnostic tests with poor sensitivity.

What are the implications for public health practice?

Early recognition of influenza illness and initiation of empiric antiviral treatment as soon as possible is recommended for persons with preexisting conditions that place them at high risk for influenza complications. Negative rapid influenza diagnostic test results should not be used to make clinical decisions on patients with influenza-like illness. Vaccination remains a critical public health tool in preventing severe influenza resulting in ICU admission or death.

laboratory-confirmed influenza for this season also are following an unusual age distribution, with 61% of hospitalizations occurring among persons aged 18–64 years (3).

The majority of fatal cases reviewed occurred among persons who had underlying conditions predisposing them to severe influenza and who had no record of having received 2013–14 influenza vaccine. Clinicians should make influenza vaccination a priority for all patients, and early diagnosis and treatment of influenza-like illness should be a priority in the care of patients with preexisting conditions recognized by ACIP as increasing the risk for influenza complications (4).

This review of severe cases has highlighted potential gaps in clinical care of critically ill patients with suspected influenza. These data support previous findings that rapid influenza diagnostic tests have inadequate sensitivity in identifying influenza virus infection compared with RT-PCR (5,6). Additionally, even when RT-PCR is used, clinicians should consider

testing lower respiratory tract samples (e.g., bronchoalveolar lavage or endotracheal aspirate) among undiagnosed critically ill patients because upper respiratory samples can test negative among patients with severe lower respiratory tract disease (7).

Approximately 54% of hospitalized patients with fatal illness did not receive antiviral treatment at hospital presentation. Neuraminidase inhibitors have an excellent safety profile and empiric treatment with a neuraminidase inhibitor should be initiated as soon as possible for any hospitalized patient with suspected influenza (8). For outpatients with high-risk conditions and persons with progressive disease who are not being admitted, antiviral treatment is also recommended (9).[‡] Observational studies have also reported modest clinical benefits when antiviral treatment is started late in the course of illness, which indicates that even patients admitted late in the course of illness should receive antiviral treatment (10). Either oral oseltamivir or inhaled zanamivir are recommended for treatment of suspected or confirmed influenza (<http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>). Inhaled zanamivir should not be used for patients who are severely ill with influenza or intubated. For severely ill patients with influenza who cannot receive oral oseltamivir or inhaled zanamivir, intravenous zanamivir, an investigational drug, can be considered.** Oseltamivir resistance is low among circulating influenza viruses in the United States.

[‡] Additional information available at <http://www.cdc.gov/flu/professionals/antivirals/antiviral-agents-flu.htm>.

** Additional information available at <http://www.cdc.gov/flu/professionals/antivirals/intravenous-antivirals.htm>.

The findings in this report are subject to at least four limitations. First, because the analysis is limited to fatal cases among persons aged <65 years reported per state regulation, data on persons aged ≥65 years, who typically are at highest risk for severe influenza infections and death, are not included. Second, this midseason analysis might have resulted in underestimation of cumulative cases as well as morbidity and mortality rates when calculated across the season. Third, because reporting of ICU cases is voluntary, ascertainment of such cases might not be complete. Finally, the representativeness of the data might be limited by delayed reporting from some LHJs. The interpretations in this report might change as additional data become available.

Because weeks or months still remain in the 2013–14 influenza season, vaccination is still recommended, and persons who are in a group at higher risk for influenza complications, including adults aged <65 years with underlying medical conditions, are recommended to receive influenza vaccination as soon as possible. In the event of illness, persons at higher risk for influenza complications, whether vaccinated or not, should seek medical care promptly for assessment and potential early antiviral treatment.

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Update: Influenza Activity — United States, September 29, 2013–February 8, 2014

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Influenza activity in the United States began to increase in mid-November and remained elevated through February 8, 2014. During that time, influenza A (H1N1)pdm09 (pH1N1) viruses predominated overall, while few B and A (H3N2) viruses were detected. This report summarizes U.S. influenza activity* during September 29, 2013–February 8, 2014, and updates the previous summary (*J*).[†]

Viral Surveillance

During September 29, 2013–February 8, 2014, approximately 140 World Health Organization (WHO) and National Respiratory and Enteric Virus Surveillance System collaborating laboratories in the United States tested 189,123 respiratory specimens for influenza viruses; 36,619 (19%) were positive (Figure 1). Of these, 35,365 (97%) were influenza A viruses, and 1,254 (3.4%) were influenza B viruses. Of the 35,365 influenza A viruses, 23,111 (65%) were subtyped; 845 (3.7%) of these were influenza A (H3) viruses, one was H3N2v, and 22,265 (96%) were pH1N1. Since September 29, 2013, influenza-positive tests have been reported from all 50 states, the District of Columbia, and Puerto Rico, representing all 10 U.S. Department of Health and Human Services regions.[§] The

percentage of specimens testing positive for influenza increased through the week ending December 28, 2013 (week 52), when 31% tested positive, and decreased subsequently. In the week ending February 8, 2014 (week 6), 17% of specimens tested positive. Since the start of the influenza season, through February 8, 2014, pH1N1 viruses predominated in the United States overall; influenza A (H3N2) and B viruses were identified infrequently.

Antigenic Characterization

WHO collaborating laboratories in the United States are requested to submit a subset of their influenza-positive respiratory specimens to CDC for further antigenic characterization. CDC has antigenically characterized 1,046 influenza viruses collected by U.S. laboratories during the 2013–14 season, including 920 pH1N1 viruses, 86 influenza A (H3N2) viruses, and 40 influenza B viruses. Of the 920 pH1N1 viruses, 919 were characterized as A/California/7/2009-like, which is the influenza A (H1N1) component of the 2013–14 Northern Hemisphere vaccine. All influenza A (H3N2) viruses were antigenically like A/Texas/50/2012, which is the influenza A (H3N2) component of the 2013–14 Northern Hemisphere vaccine. Of the 40 influenza B viruses tested, 21 (52.5%) belong to the B/Yamagata lineage and were characterized as B/Massachusetts/2/2012-like, which is included as an influenza B component in the 2013–14 Northern Hemisphere trivalent and quadrivalent influenza vaccines. The remaining 19 (47.5%) influenza B viruses tested belong to the B/Victoria lineage and were characterized as B/Brisbane/60/2008-like, which is included as an influenza B component in the 2013–14 Northern Hemisphere quadrivalent influenza vaccine.

Antiviral Resistance of Influenza Viruses

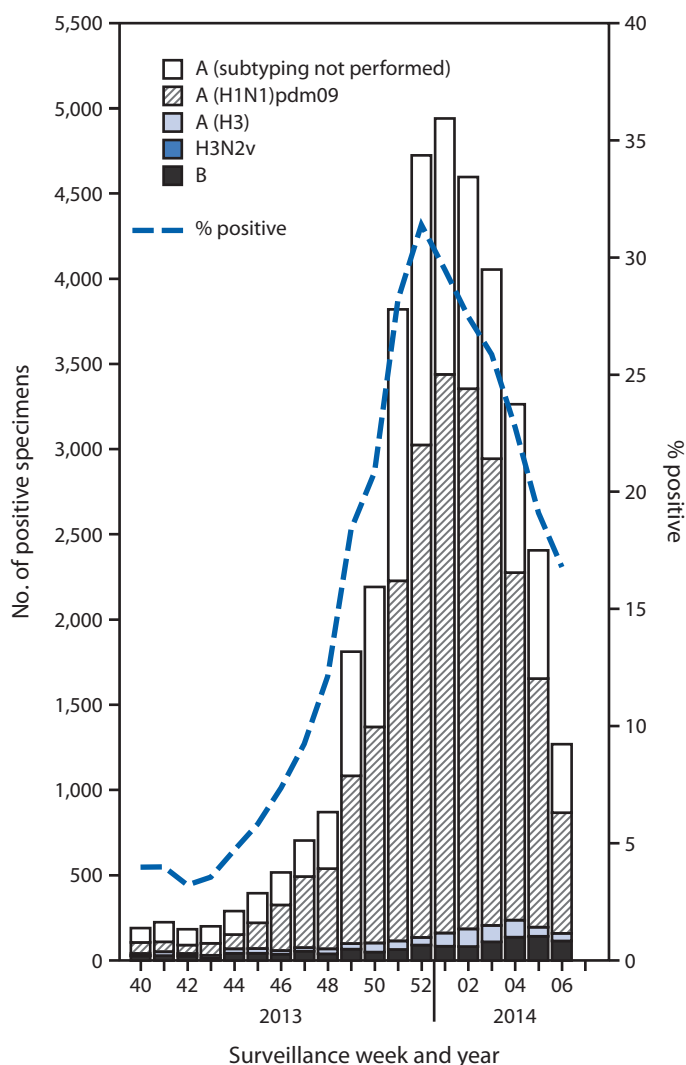
Testing of pH1N1, influenza A (H3N2), and influenza B virus isolates for resistance to neuraminidase inhibitors (oseltamivir and zanamivir) is performed at CDC and public health laboratories using a functional assay. Additional pH1N1 and influenza A (H3N2) clinical samples are tested for mutations of the virus known to confer oseltamivir resistance. Since October 1, 2013, a total of 3,314 influenza viruses have been tested for antiviral resistance,

*The CDC influenza surveillance system collects five categories of information from eight data sources: 1) viral surveillance (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 (122 Cities Mortality Reporting System and influenza-associated pediatric mortality reports); 4) hospitalizations (Influenza Hospitalization Surveillance Network [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).

[†]Data reported as of February 14, 2014.

[§]*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, the 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.

FIGURE 1. Number* and percentage of respiratory specimens testing positive for influenza, by type, surveillance week, and year — U.S. World Health Organization and National Respiratory and Enteric Virus Surveillance System collaborating laboratories, United States, 2013–14 influenza season†



* N = 36,619.

† Data reported as of February 14, 2014.

including 3,109 pH1N1 viruses, 151 influenza A (H3N2) viruses, and 54 influenza B viruses. Of the 3,109 pH1N1 viruses tested, 25 (0.8%) were resistant to oseltamivir. Of the 1,120 pH1N1 viruses tested for resistance to zanamivir, all (including all oseltamivir-resistant viruses tested) were sensitive to zanamivir. All influenza A (H3N2) and influenza B viruses tested were sensitive to both oseltamivir and zanamivir.

Outpatient Illness Surveillance

Since September 29, 2013, the weekly percentage of outpatient visits for influenza-like illness (ILI)[§] reported by approximately

[§] Defined as a fever ($\geq 100^{\circ}\text{F}$ [$\geq 37.8^{\circ}\text{C}$]), oral or equivalent, and cough and/or sore throat, without a known cause other than influenza.

2,000 U.S. Outpatient ILI Surveillance Network (ILINet) providers in all 50 states, New York City, Chicago, the U.S. Virgin Islands, Puerto Rico, and the District of Columbia, which comprise ILINet, has ranged from 1.2% to 4.6% and was at or above the national baseline** of 2.0% from the week ending November 30, 2013 (week 48) to February 8, 2014 (week 6) (Figure 2). Peak weekly percentages of outpatient visits for ILI ranged from 2.4% to 7.6% from the 1997–98 through 2012–13 seasons, excluding the 2009 pandemic. For the week ending February 8, 2014 (week 6), all 10 regions reported ILI activity above their region-specific baseline levels. This is the 14th week this season during which one or more region-specific baselines were exceeded. Data collected in ILINet are used to produce a measure of ILI activity^{††} by jurisdiction. During week 6, six states (Arkansas, Connecticut, Kansas, New York, Oklahoma, and Texas) experienced high ILI activity, seven states experienced moderate ILI activity (Alabama, Delaware, Hawaii, Louisiana, Maryland, New Jersey, and Virginia), and 19 states and New York City (Arizona, California, Colorado, Florida, Kentucky, Massachusetts, Minnesota, Mississippi, Missouri, Nebraska, New Mexico, Nevada, North Carolina, Pennsylvania, Rhode Island, South Dakota, Utah, Washington, and Wisconsin) experienced low ILI activity. ILI activity was minimal in 18 states, and data were insufficient to calculate an ILI activity level for the District of Columbia.

Geographic Spread of Influenza Activity

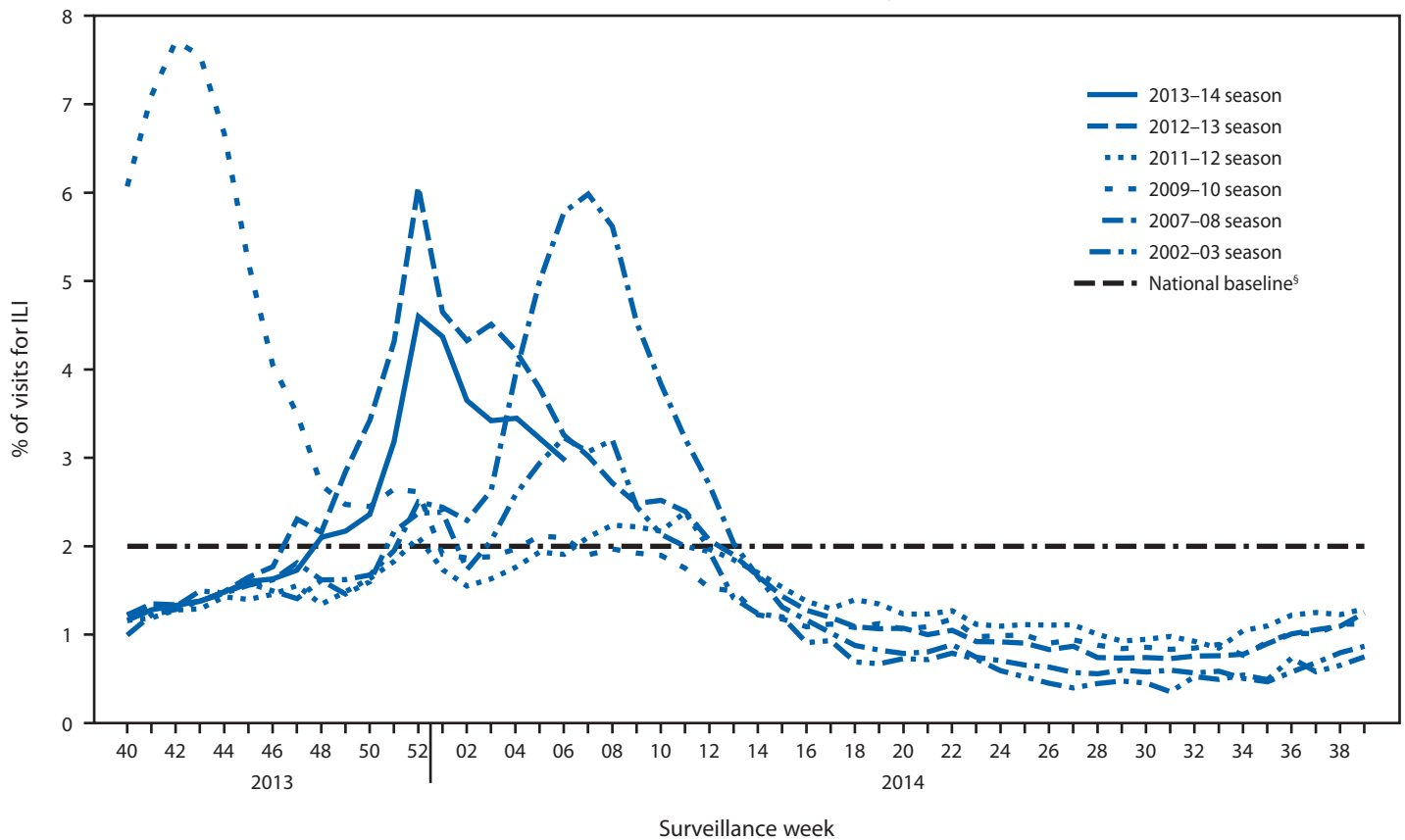
For the week ending February 8, 2014 (week 6), the geographic spread of influenza^{§§} was reported as widespread in 24

** The national and regional baselines are the mean percentage of visits for ILI during weeks with little or no influenza virus circulation (noninfluenza weeks) for the previous three seasons plus two standard deviations. A noninfluenza week is 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, which would correspond to ILI activity from outpatient clinics being at or below the average, to high, which would correspond to ILI activity from outpatient clinics being much higher than the average. Because the clinical definition of ILI is very 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.

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

FIGURE 2. Percentage of all outpatient visits that are for influenza-like illness (ILI)* reported to CDC, by surveillance week — Outpatient Influenza-Like Illness Surveillance Network, United States, September 29, 2013–February 8, 2014, and selected previous influenza seasons†



* Defined as a fever ($\geq 100^{\circ}\text{F}$ [$\geq 37.8^{\circ}\text{C}$]), oral or equivalent, and cough and/or sore throat, without a known cause other than influenza.

† Data reported as of February 14, 2014.

‡ The national baseline is the mean percentage of visits for ILI during weeks with little or no influenza virus circulation (noninfluenza weeks) for the previous three seasons plus two standard deviations. A noninfluenza week is 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.

states (Arizona, Arkansas, California, Connecticut, Delaware, Florida, Illinois, Indiana, Maine, Maryland, Massachusetts, Missouri, New Hampshire, New Jersey, New York, North Carolina, Ohio, Oklahoma, Pennsylvania, Rhode Island, South Carolina, Vermont, Virginia, and Utah), regional in 20 states (Alabama, Alaska, Colorado, Idaho, Iowa, Kansas, Kentucky, Louisiana, Montana, Michigan, Minnesota, Nebraska, Nevada, North Dakota, Oregon, South Dakota, Tennessee, Texas, Washington, and Wisconsin), and local in five states (Georgia, Mississippi, New Mexico, West Virginia, and Wyoming), Guam, and the District of Columbia. Sporadic influenza activity was reported by one state (Hawaii) and Puerto Rico. No influenza activity was reported by the U.S. Virgin Islands.

Influenza-Associated Hospitalizations

CDC monitors hospitalizations associated with laboratory-confirmed influenza in adults and children through the Influenza

Hospitalization Surveillance Network (FluSurv-Net),^{§§} which

^{§§} FluSurv-NET conducts population-based surveillance for laboratory-confirmed influenza-associated hospitalizations among children aged < 18 years (since the 2003–04 influenza season) and adults aged ≥ 18 years (since the 2005–06 influenza season). 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 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; Iowa, Michigan, Ohio, Rhode Island, and Utah during the 2012–13 season; and Michigan, Ohio, and Utah during the 2013–14 season. 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 influenza diagnostic test results and greater reliance on clinical diagnosis for influenza. As a consequence, the number of cases identified as part of influenza hospitalization surveillance likely is an underestimation of the actual number of persons hospitalized with influenza.

covers approximately 27 million persons, 8.5% of the U.S. population. From October 1, 2013 through February 8, 2014 (week 6), a total of 6,655 laboratory-confirmed influenza-associated hospitalizations were reported. This yields a rate of 24.6 hospitalizations per 100,000 population (Figure 3). Persons aged ≥ 65 years had the highest influenza-associated hospitalization rate (50.9 per 100,000), followed by those aged 50–64 years (38.7 per 100,000), 0–4 years (35.9 per 100,000), 18–49 years (16.8 per 100,000), and 5–17 years (6.6 per 100,000). Of the 6,655 influenza-associated hospitalizations that have been reported, 9.4% were reported in persons aged 0–4 years, 4.5% in those aged 5–17 years, 61.2% in those aged 18–64 years, and 24.8% in those aged ≥ 65 years (Figure 4). Among cases, 6,328 (95%) were associated with influenza A virus infection, 253 (3.8%) were associated with influenza B, 21 (0.3%) were associated with influenza A and B coinfections, and 53 (0.8%) had no virus type information. Among those with influenza A subtype information, 39 (1.4%) were associated with influenza A (H3), and 2,766 (98.6%) were pH1N1.

The frequency distribution of chronic underlying medical conditions among hospitalized patients is based on a subset (approximately 30%) of cases with complete medical chart abstraction and may change as new data become available. Among hospitalized adults, 15% had no identified chronic underlying medical conditions, compared with 43% percent of hospitalized children. The most commonly reported chronic underlying medical conditions in adults were obesity (43%), metabolic disorders (33%), cardiovascular disease (29%), and chronic lung disease (excluding asthma) (27%). In children (persons aged < 18 years), the most commonly reported chronic underlying medical conditions were asthma (24%), neurologic disorders (13%), obesity (10%), and chronic lung disease (excluding asthma) (8%). Among 301 hospitalized women of childbearing age (15–44 years), 65 (22%) were pregnant.

Pneumonia and Influenza-Associated Mortality

During the week ending February 8, 2014 (week 6), pneumonia and influenza (P&I) was reported as an underlying or contributing cause for 8.4% (1,023 of 12,180) of all deaths reported to the 122 Cities Mortality Reporting System. This percentage is above the epidemic threshold*** of 7.3% for that week. Since September 29, 2013, the weekly percentage of deaths attributed to P&I ranged from 5.3% to 8.7%. The

*** 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 122 Cities Mortality Reporting System during the preceding 5 years. The epidemic threshold is set at 1.645 standard deviations above the seasonal baseline.

What is already known on this topic?

CDC collects, compiles, and analyzes data on influenza activity year-round in the United States, which show that the timing and severity of circulating influenza viruses can vary by geographic location and between influenza seasons. Although influenza causes serious illness and death every season, populations most affected at any point during a season can vary geographically, by age group, and by other characteristics.

What is added by this report?

Influenza activity in the United States began to increase in mid-November and remained elevated through February 8, 2014. During September 29, 2013–February 8, 2014, influenza A (H1N1)pdm09 viruses were identified most frequently, but a small number of influenza B and influenza A (H3N2) viruses also were reported. This season has been more severe for young and middle-aged adults than in the most recent seasons. The second highest hospitalization rates have occurred in patients aged 50–64 years this season, and more than half of influenza-associated hospitalizations occurred in adults aged 18–64 years.

What are the implications for public health practice?

Vaccination remains the most effective method to prevent influenza and its complications and is important for persons of all ages, not just the very young and old. Health-care providers should recommend and offer vaccine to all unvaccinated persons aged ≥ 6 months now and throughout the influenza season. Treatment with neuraminidase inhibitor antiviral medications can reduce severe outcomes of influenza, especially when initiated early, in patients with confirmed or suspected influenza.

percentage first exceeded the epidemic threshold during the week ending January 11, 2014 (week 2) and remained elevated through the week ending February 8, 2014 (week 6). Peak weekly percentages of deaths attributable to P&I in the previous five seasons ranged from 7.9% during the 2008–09 and 2011–12 seasons to 9.9% during the 2012–13 season.

Among 14,628 P&I deaths reported through the 122 Cities Mortality Reporting System from September 29, 2013 to February 8, 2014, a total of 571 (3.9%) were influenza-associated (i.e., they had influenza listed on the death certificate as an underlying or contributing cause of death), of which 352 (62%) were in persons aged 25–64 years, 194 (34%) in persons aged ≥ 65 years, and 25 (4%) in persons aged 0–24 years (Figure 4).

Influenza-Associated Pediatric Mortality

As of February 8, 2014 (week 6), 50 influenza-associated pediatric deaths that occurred in the 2013–14 season were reported to CDC: one was associated with an influenza B virus, 29 with pH1N1 viruses, 17 with an influenza A virus for which no subtyping was performed, one with an

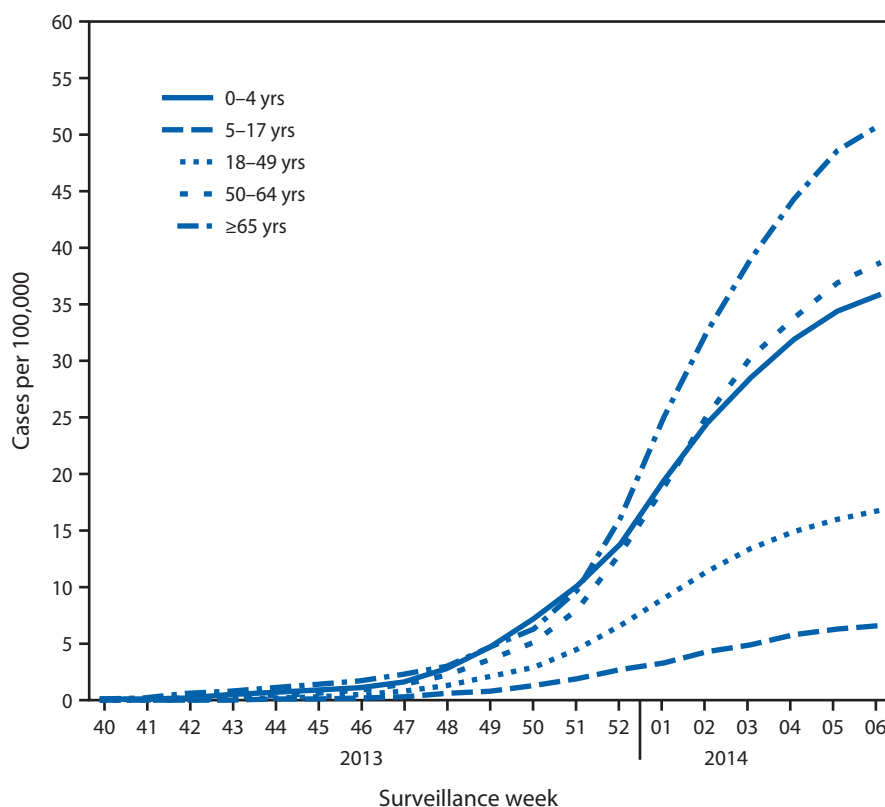
influenza A and influenza B virus coinfection, and two with an influenza virus for which the type was not determined. Since influenza-associated pediatric mortality became a nationally notifiable condition in 2004, the total number of influenza-associated pediatric deaths has ranged from 35 to 171 per season, excluding the 2009 pandemic, when 348 pediatric deaths were reported to CDC during April 15, 2009–October 2, 2010.

Editorial Note

Influenza activity in the United States began to increase in mid-November and remained elevated and widespread as of February 8, 2014. During September 29, 2013–February 8, 2014, pH1N1 accounted for the majority of circulating influenza viruses, but influenza A (H3N2) and influenza B viruses also were identified. This season, influenza activity first increased in the southern states. By the end of December 2013, high influenza activity was seen throughout the United States. During the first 4 weeks of 2014, influenza activity decreased in the southeast and south central areas of the United States but began increasing in the west and northeast areas. Elevated influenza activity in parts of the United States is expected for several more weeks.

Surveillance data from previous influenza seasons have shown that the epidemiology of influenza is related to the circulating subtype, which can vary by season. This is the first season that pH1N1 has been the predominant influenza virus circulating in the United States since this subtype emerged in 2009. Although illness was seen in all age groups during the 2009 pandemic, persons aged 50–64 years had the highest influenza-associated death rate and second highest influenza-associated hospitalization rate among all age groups (2). Preliminary surveillance data for the 2013–14 influenza season suggest that although overall disease prevalence is lower than during the 2009 pandemic, persons aged 18–64 years are again at relatively high risk for severe illness from influenza this season. As of February 8, 2014, persons aged 18–64 years represented 4,077 (61%) of influenza-associated hospitalizations reported by FluSurv-NET. In contrast, during the past three seasons in which H3N2 or B influenza viruses predominated, persons aged 18–64 years accounted for only 35% (2012–13), 40% (2011–12), and 43% (2010–11) of all influenza-associated hospitalizations reported by FluSurv-NET (Figure 4). For the 2013–14 season, cumulative influenza-associated hospitalization rates for persons aged 18–49 years (16.8 per 100,000) and 50–64

FIGURE 3. Rates of hospitalization for laboratory-confirmed influenza, by age group and surveillance week — FluSurv-NET,* 2013–14†



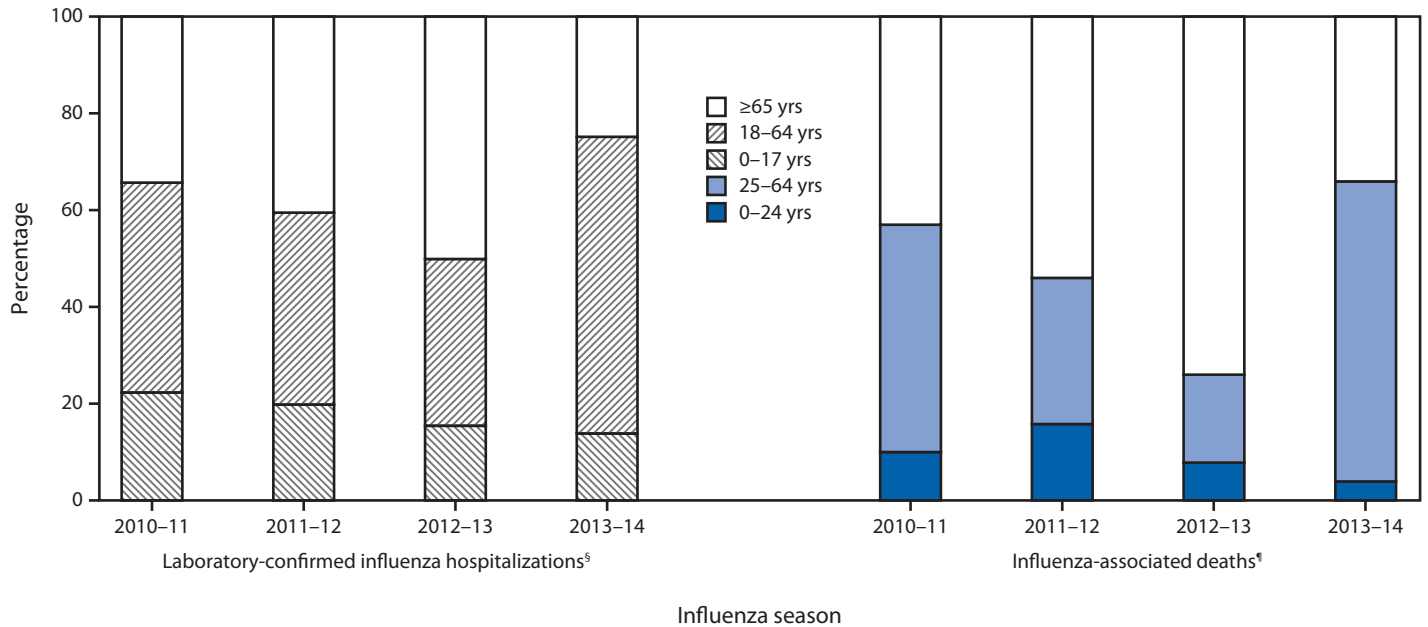
* FluSurv-NET conducts population-based surveillance for laboratory-confirmed influenza-associated hospitalizations in children aged <18 years (since the 2003–04 influenza season) and adults aged ≥18 years (since the 2005–06 influenza season). The FluSurv-NET covers approximately 80 counties in the 10 Emerging Infections Program states (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee) and additional Influenza Hospitalization Surveillance Project states (Michigan, Ohio, and Utah).

† Data reported as of February 14, 2014.

years (38.7 per 100,000) in FluSurv-NET have already surpassed the end-of-season rates from three of the previous four seasons (3).

During the three previous influenza seasons, the total number of P&I deaths reported through the 122 Cities Mortality Reporting System ranged from 37,444 to 41,708, of which <1% to 2% were deaths for which influenza was listed on the death certificate as an underlying or contributing cause of death. Although the age distribution of pneumonia deaths this season is similar to previous seasons, the age distribution of influenza deaths has changed. The number of influenza deaths during the current season (through February 8, 2014) among persons aged 25–64 years (352) exceeds the 138 deaths reported for that age group for the entire 2012–13 influenza surveillance season (September 30, 2012–September 28, 2013). This age group has accounted for approximately 62% of all influenza-associated deaths already this season, compared with 47% in 2010–11, 30% in 2011–12, and 18% in 2012–13 (Figure 4).

FIGURE 4. Percentage of laboratory-confirmed influenza hospitalizations and influenza-associated deaths, by age group* and influenza seasons† — FluSurv-NET and 122 U.S. Cities Mortality Reporting System, United States, 2010–14 influenza seasons



* For laboratory-confirmed influenza hospitalizations, age groups are 0–17 years, 18–64 years, and ≥65 years; for influenza-associated deaths, age groups are 0–24 years, 25–64 years, and ≥65 years.

† Influenza A (H3N2) was the predominant virus circulating during the three previous seasons, while influenza A (H1N1)pdm09 has been the predominant virus circulating during the 2013–14 influenza season. For the 2013–14 season, all values presented are early estimates or data through week 6 of the influenza season; for previous seasons, data shown are end-of-season values.

[§] Totals were 6,307 for the 2010–11 season, 2,409 for the 2011–12 season, 12,371 for the 2012–13 season, and 6,655 through February 8, 2014, for the 2013–14 season.

[¶] Totals were 406 for the 2010–11 season, 122 for the 2011–12 season, 753 for the 2012–13 season, and 571 through February 8, 2014, for the 2013–14 season.

The more severe impact of pH1N1 on adults aged 18–64 years seen this season and during the pandemic is thought to result from at least two factors. First, persons in this age group likely lack the cross-protective immunity to pH1N1 seen in adults aged ≥65 years, which was likely acquired from past infection with antigenically related viruses (4). Second, preliminary vaccination coverage estimates for this season indicate that by early November 2013, adults aged 18–64 years had been vaccinated against influenza at a rate substantially lower (33.9%; 95% confidence interval [CI] = 31.9%–35.9%) than those aged 6 months–17 years (41.1%; 95% CI = 38.8%–43.4%) and ≥65 years (61.8%; 95% CI = 57.9%–65.7%) (5). In previous years, adults aged 18–64 years also have been less likely to receive influenza vaccine, compared with persons in other age groups (5). Although some persons infected with pH1N1 during the 2009 pandemic might retain some residual immunity, this protection has likely declined over time. Furthermore, seroprevalence studies showed that only a minority (approximately 35% of all ages combined) were seropositive for pH1N1 after the 2009 pandemic, with even smaller percentages (26%) among those aged 25–64 years (6).

Surveillance data available from the 2013–14 season are a reminder that, although some age groups are at increased risk of influenza complications every year (e.g., adults aged ≥65 years), influenza can cause severe illness in persons of any age, even in adults aged 18–64 years. Vaccination is the primary means to prevent influenza and its complications and is recommended annually for all persons aged ≥6 months. Data from the current and two previous influenza seasons suggest that vaccination reduced the risk for medical visits associated with influenza by 47%–61% (7,8). Health-care providers should continue to recommend and offer influenza vaccine for the remainder of the season to all unvaccinated persons aged ≥6 months.

Early and aggressive treatment of influenza with neuraminidase inhibitor antiviral drugs should be used when indicated, and data from this season show that pH1N1 remains susceptible to these agents. Currently circulating influenza A virus strains have shown resistance to amantadine and rimantadine, also known as adamantanes; therefore, adamantanes are not recommended for antiviral treatment or chemoprophylaxis of currently circulating influenza A virus strains (9).

Antiviral treatment is recommended as early as possible (ideally within 48 hours of illness onset) for patients with severe illness (e.g., patients hospitalized with influenza) or patients at high risk for serious influenza complications, including children aged <2 years, adults aged ≥65 years, and persons with certain underlying medical conditions (10).^{†††} If treatment can be initiated within 48 hours of illness onset, antiviral medications also may be considered for outpatients with suspected or confirmed influenza who are not known to be at increased risk for developing severe illness (10).

Influenza surveillance reports for the United States are posted online weekly and are available at <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 available at <http://www.cdc.gov/flu>.

^{†††} Persons at higher risk include 1) children aged <2 years; 2) adults aged ≥65 years; 3) persons with chronic pulmonary conditions (including asthma); cardiovascular disease (except hypertension alone); renal, hepatic, hematologic (including sickle cell disease); metabolic disorders (including diabetes mellitus); or neurologic and neurodevelopmental 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); 4) persons with immunosuppression, including that caused by medications or by human immunodeficiency virus infection; 5) women who are pregnant or postpartum (within 2 weeks after delivery); 6) persons aged ≤18 years who are receiving long-term aspirin therapy; 7) American Indians/Alaska Natives; 8) persons who are morbidly obese (body mass index ≥40); and 9) residents of nursing homes and other chronic-care facilities.

Acknowledgments

State, local, and territorial health departments and public health laboratories. US WHO collaborating laboratories. National Respiratory and Enteric Virus Surveillance System laboratories. US Outpatient Influenza-Like Illness Surveillance Network. Influenza Hospitalization Surveillance Network. Influenza-Associated Pediatric Mortality Surveillance System. 122 Cities Mortality Reporting System.

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Declines in Student Obesity Prevalence Associated with a Prevention Initiative — King County, Washington, 2012

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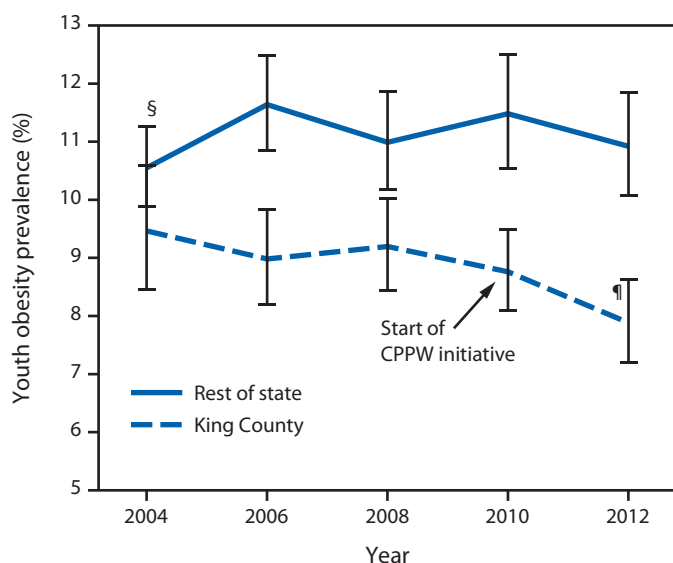
The United States has invested heavily, through public and private sector initiatives, in actions to prevent youth obesity by promoting healthy eating and physical activity. This report documents recent trends in youth obesity in King County, Washington, which implemented a Communities Putting Prevention to Work (CPPW) obesity prevention initiative during 2010–2012, including a school-based component. Similar large-scale obesity prevention initiatives did not occur elsewhere in Washington. Beginning in 2004, the Washington State Department of Health began monitoring youth obesity through the biennially administered Washington State Healthy Youth Survey (HYS). Based on data from this survey, neither King County nor the rest of Washington showed statistically significant changes in obesity prevalence in 2006, 2008, and 2010, relative to 2004. In 2012, however, King County youth obesity prevalence showed a statistically significant decrease, while no change occurred in the remainder of the state. Within King County, CPPW was implemented only in low-income school districts to address geographic inequities in obesity rates. Analysis within King County comparing CPPW and non-CPPW school districts before and after the intervention (2010 versus 2012) revealed a statistically significant decline in obesity prevalence in CPPW schools yet no change in non-CPPW schools. This decline in CPPW schools was significantly different than in non-CPPW schools. These findings suggest that school-based policy, systems, and environment changes might help reduce youth obesity, warranting further evaluation of short- and long-term impacts on population health.

The analysis used data from the HYS (1), a school-based survey analogous to the Youth Risk Behavior Survey, conducted each even-numbered year during 2004–2012. The Washington State Department of Health used self-reported height and weight data from the survey (asked only of respondents in grades 8, 10, and 12) to calculate body mass index (BMI), then used standard BMI-for-age charts to classify each respondent as obese or not obese. Obesity was defined as a BMI equal to or greater than the 95th percentile for children of same age and sex in year 2000 national growth charts (2). Survey response rates for grades 8, 10, and 12 combined from 2004 to 2012 ranged from 63% to 71% (approximately 34,000 respondents per survey year) and 61% to 67% (approximately 18,500 respondents per survey year) for King County and the rest of Washington, respectively. Data were weighted to be representative of school enrollment by year, grade, and sex.

The 2004–2012 obesity trend among students (grades 8, 10, 12 combined) in King County was compared with the trend in the rest of Washington. Within King County, the 2010 to 2012 change in obesity prevalence in school districts that received CPPW interventions was compared with non-CPPW districts. For comparison of King County with the rest of Washington, logistic regression analysis was used to assess the significance of obesity trends from 2004 to 2012, and the statistical interaction of geography and year was used to test for a significant difference in trends. For comparison of CPPW with non-CPPW school districts, the aim was to assess the impact of the intervention. Logistic regression analysis was used to estimate the 2010 to 2012 change in the odds of obesity for each group, and the statistical interaction of group and year was used to test for a significant difference in the change in the odds of obesity across groups. For the King County versus rest of Washington analysis, race/ethnicity, maternal education, and sex were evaluated as potential confounders by 1) assessing associations with year and obesity (chi-squared test; $p < 0.05$ identifies potential confounder) and 2) for those associated with both, including these in logistic regression models to compare crude and adjusted trends ($\geq 10\%$ change in crude estimate identifies confounder). Two-tailed p -values < 0.05 were considered to indicate significance in all statistical tests.

Among students in both King County and the rest of Washington State, no statistically significant changes were observed in the prevalence of obesity from the baseline 2004 HYS survey through 2010. In 2012, for the first time, obesity prevalence in King County showed a statistically significant decrease, from 9.5% in 2004 to 7.9% in 2012, with the odds of a student being obese in 2012 being 10% less than in 2004 (odds ratio [OR] = 0.90; 95% confidence interval [CI] = 0.82–0.98). In contrast, among students in the rest of Washington, obesity prevalence was stable from 2004 to 2012 (Figure 1, Table 1). The difference in the change over time in obesity prevalence between King County and the rest of Washington was significant (King County students saw greater reduction; p -value for interaction = 0.02). No evidence of confounding was identified; neither maternal education nor sex distributions changed over time in these populations, and although race/ethnicity distributions did change over time, obesity trends adjusted for race/ethnicity were similar ($< 10\%$ change) to crude trends.

FIGURE 1. Prevalence of youth* obesity in King County, Washington, compared with the rest of the state, 2004–2012[†]



Abbreviation: CPPW = Communities Putting Prevention to Work.
 * Students in grades 8, 10, and 12 are combined.
[†] Data are weighted to be representative of school enrollment by year, grade, and sex.
[§] 95% confidence interval.
[¶] Obesity trend for 2004–2012 shows statistically significant decline ($p < 0.05$).

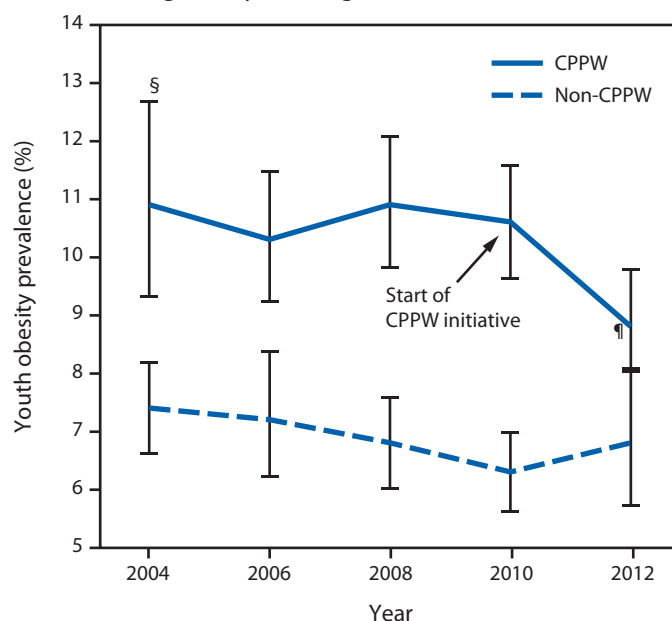
TABLE 1. Prevalence of youth* obesity in King County compared with the rest of Washington state, 2004–2012[†]

Year	King County		Rest of state	
	Prevalence (%)	(95% CI)	Prevalence (%)	(95% CI)
2004	9.5	(8.4–10.6)	10.6	(9.9–11.3)
2006	9.0	(8.2–9.9)	11.6	(10.8–12.5)
2008	9.2	(8.4–10.0)	11.0	(10.2–11.9)
2010	8.8	(8.1–9.5)	11.5	(10.5–12.5)
2012	7.9 [§]	(7.2–8.7)	10.9	(10.1–11.9)

Abbreviation: CI = confidence interval.
 * Students in grades 8, 10, and 12 are combined.
[†] Data are weighted to be representative of school enrollment by year, grade, and sex.
[§] Obesity trend for 2004–2012 shows statistically significant decline ($p < 0.05$).

The CPPW initiative was implemented in 2010. CPPW students represented 57% of King County students, were more likely than non-CPPW students to be eligible for free and reduced price lunch (44% versus 17%), and had higher baseline obesity prevalence (Figure 2, Table 2). Among students in King County’s non-CPPW school districts, obesity prevalence was stable from 2010 to 2012 (OR = 0.95; CI = 0.87–1.04). Among students in CPPW school districts, prevalence decreased significantly from 2010 to 2012, from 10.6% to 8.8%, and the odds of a student being obese in 2012 were 9.3% less than in 2010 (OR = 0.91; CI = 0.84–0.98) (Figure 2). These changes were temporally associated with

FIGURE 2. Prevalence of youth* obesity, by school district participation in the Communities Putting Prevention to Work (CPPW) initiative — King County, Washington, 2004–2012[†]



* Students in grades 8, 10, and 12 are combined.
[†] Data are weighted to be representative of school enrollment by year, grade, and sex.
[§] 95% confidence interval.
[¶] Change in obesity since 2010 statistically significant ($p < 0.05$).

TABLE 2. Prevalence of youth* obesity, by school district participation in the Communities Putting Prevention to Work (CPPW) initiative — Washington state, 2004–2012[†]

Year	CPPW districts		Non-CPPW districts	
	Prevalence (%)	(95% CI)	Prevalence (%)	(95% CI)
2004	10.9	(9.3–12.7)	7.4	(6.6–8.2)
2006	10.3	(9.2–11.5)	7.2	(6.2–8.4)
2008	10.9	(9.8–12.1)	6.8	(6.0–7.6)
2010	10.6	(9.6–11.6)	6.3	(5.6–7.0)
2012	8.8 [§]	(8.0–9.8)	6.8	(5.7–8.1)

Abbreviation: CI = confidence interval.
 * Students in grades 8, 10, and 12 are combined.
[†] Data are weighted to be representative of school enrollment by year, grade, and sex.
[§] Change in obesity since 2010 is statistically significant ($p < 0.05$).

school-based CPPW interventions. Comparing CPPW and non-CPPW students, the 2010 to 2012 change in obesity was significantly different (CPPW districts saw greater reduction; $p = 0.045$ for interaction term). Before the CPPW intervention in 2010, obesity prevalence was stable in the CPPW districts, whereas it declined in the non-CPPW districts.

Editorial Note

This report demonstrates a temporal and spatial association between declines in self-reported youth obesity and

implementation of a CPPW project during 2010–2012. King County CPPW focused its efforts on low-income school districts and communities because community health assessment data indicated that the prevalences of obesity, poor nutrition, and physical inactivity were disproportionately high relative to higher-income communities. Although data were available only for students in grades 8, 10, and 12, CPPW school district interventions reached all students (grades K through 12) and included implementation of nutrition standards for school meals, student-led healthy eating and active living promotional campaigns, farm-to-school initiatives, high-quality physical education, nutrition and culinary training for school cafeteria staff, and participation in community health coalitions (3). Youth obesity prevalence monitored from 2004 first showed a statistically significant decline in King County in 2012 after implementation of CPPW but not in the rest of Washington, where no comparable initiatives took place, and within King County in CPPW school districts but not in non-CPPW districts. In CPPW school districts, obesity prevalence dropped by 17%, and a student's odds of being obese fell by 9.3% from 2010 to 2012 (OR = 0.91), whereas obesity prevalence in non-CPPW school districts remained stable during this period.

These decreases in youth obesity prevalence are consistent with trends reported from other metropolitan sites that also have implemented robust obesity prevention initiatives (4). This report extends these observations by demonstrating both a temporal association with CPPW implementation and a spatial association with the location of CPPW investment.

The findings in this report are subject to at least five limitations. First, weight and height were self-reported; thus, the findings are subject to recall and response bias. Additionally, self-reported weight and height tend to underestimate BMI (5); however, it is unlikely that the degree of underestimation would change during the study period, and thus, this would not affect analysis of temporal trends. Second, it was not possible to fully control for factors that could confound obesity trends, such as differential changes over time in household income. Third, the limited number of time points and sample size precluded a more robust use of time-series analytic methods and stratified or multivariate analyses to assess interactions and address confounding. Fourth, this is a preliminary finding describing a short-term trend. Finally, this is an observational study; the findings cannot be used to establish causality. If in fact CPPW did in part reduce youth obesity prevalence, other factors also might have contributed to the decreases in King County and CPPW school districts obesity rates, such as non-CPPW community-level healthy eating and active living programs and secular population-wide obesity trends.

CDC has prioritized obesity prevention as one of its 10 “winnable battles.”* CPPW was a targeted CDC intervention to prevent obesity by promoting healthy eating and physical activity.

* Information available at <http://www.cdc.gov/winnablebattles/obesity/index.html>.

What is already known on this topic?

Early signs of declines in youth obesity have been reported from localities and states that have implemented robust obesity prevention initiatives.

What is added by this report?

By 2012, for the first time, self-reported youth obesity prevalence in King County, Washington, saw a statistically significant decrease from its 2004 baseline prevalence, from 9.5% in 2004 to 7.9% in 2012, after a Communities Putting Prevention to Work project was implemented in the county's low-income school districts from 2010 to 2012.

What are the implications for public health practice?

School-based policy, systems, and environment changes might be important elements of a comprehensive obesity prevention strategy.

These findings suggest that focused and comprehensive policy, systems, and environment change interventions can reduce obesity in youth. Future analysis of HYS data, as they become available, will support assessment of CPPW's longer-term impacts on youth obesity. Continued community-level interventions paired with robust epidemiologic, cost and process evaluations might prevent obesity, provide the opportunity to learn more about how these comprehensive interventions work, and identify which elements are most cost-effective in reducing obesity and improving population health across various settings (6,7).

Acknowledgments

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Follow-Up of Infants Diagnosed with HIV — Early Infant Diagnosis Program, Francistown, Botswana, 2005–2012

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The 2011 prevalence of human immunodeficiency virus (HIV) among pregnant women in Botswana was 30.4%. High coverage rates of HIV testing and antiretroviral prophylaxis have reduced the rate of mother-to-child transmission of HIV in Botswana from as high as 40% with no prophylaxis to <4% in 2011. In June 2005, the national Early Infant Diagnosis (EID) Program began testing HIV-exposed infants (i.e., those born to HIV-infected mothers) for HIV using polymerase chain reaction (PCR) at 6 weeks postpartum (1). During 2005–2012, follow-up of all HIV-infected infants diagnosed in all 13 postnatal care facilities in Francistown, Botswana, was conducted to ascertain patient outcomes. A total of 202 infants were diagnosed with HIV. As of September 2013, 82 (41%) children were alive and on antiretroviral therapy (ART), 79 (39%) had died, and 41 (20%) were either lost to follow-up, had transferred, or their mothers declined ART. Despite success in preventing mother-to-child transmission in Botswana, results of the EID program highlight the need for early diagnosis of HIV-infected infants, prompt initiation of ART, and retention in care.

The Botswana Prevention of Mother-to-Child Transmission (PMTCT) Program began nationwide in November 2001. Health care, including antenatal care, PMTCT services, and ART is free for Botswana citizens. Over 95% of pregnant women in Botswana register for antenatal care, and nearly all women are offered PMTCT services. Infants of HIV-positive women are tested at age 6 weeks or at first health-care contact thereafter to diagnose infections that occur during pregnancy or delivery using PCR testing on dried blood spot specimens. Breastfed infants are retested 6 weeks after breastfeeding cessation to diagnose HIV infections that might have been transmitted through breast milk. In 2011, 98% of women who received antenatal care were tested for HIV, 93% of HIV-positive pregnant women received antiretroviral prophylaxis to prevent mother-to-child transmission, and the rate of HIV infection among infants aged <18 months tested by PCR was <4% (Botswana Ministry of Health, unpublished data, 2013).

HIV-infected infants from all 13 postnatal care facilities that collect dried blood spots for EID testing were identified by PCR at Nyangabgwe HIV Reference Laboratory in

Francistown, Botswana, during June 2005–December 2012. Reporting of HIV test results and referrals to treatment was determined from clinic infant testing registers. Dates for ART evaluation and initiation for infected infants were determined from the electronic register at the Infectious Disease Care Clinic in Francistown, the primary referral point for all pediatric HIV patients. Patient identifiers including first name, last name, date of birth, and sex were used to link infants across different databases. Clinical records were reviewed for patient outcomes through September 2013.

PMTCT identified a total of 10,923 HIV-exposed infants. Of these, 7,772 (71%) were tested for HIV, and 202 (2.6%) were diagnosed with HIV infection. Of the 202 HIV-infected infants, the mothers of 153 (75%) had post-HIV test counseling, and 123 (60%) infants had received ART (Figure). The median time from birth to EID testing was 9 weeks (interquartile range [IQR] = 6–23 weeks), from dried blood spot specimen collection to post-test counseling was 4 weeks (IQR = 3–7 weeks), and from post-test counseling to ART initiation was 3 weeks (IQR = 1–9 weeks). The median time from birth to ART initiation was 23 weeks (IQR = 15–48 weeks).

Through September 2013, a total of 82 (41%) children were alive and on ART (Figure). Of the 79 (39%) HIV-infected children who died, 56 died before receiving ART, and 23 died after being started on ART. Measured in person-years, the overall mortality rate for the 202 HIV-infected infants was 12.7 per 100 person-years (95% confidence interval [CI] = 10.0–16.1). The mortality rate among HIV-infected patients not receiving ART was 75.2 per 100 person-years (CI = 56.1–100.7), and the rate among patients receiving ART was 4.6 per 100 person-years (CI = 3.0–7.0). The mortality rate ratio comparing those who did not receive ART with those who received ART was 16.5 (CI = 9.8–27.7).

Fifty of the 79 patients who died had a documented cause of death. The leading causes of death were pneumonia (25 patients), gastroenteritis (nine), and sepsis (three). A total of 24 (12%) infants were lost to follow-up and 16 (8%) transferred out of the catchment area. One (0.5%) family declined ART for its infant.

Editorial Note

Effective pediatric HIV treatment requires early diagnosis, prompt initiation of ART, and frequent monitoring to ensure retention and quality care. ART initiation in the first 3 months of life can reduce mortality by 76% (2). Without ART, 52% of perinatally HIV-infected infants and 26% of postnatally HIV-infected infants will die within 12 months (3).

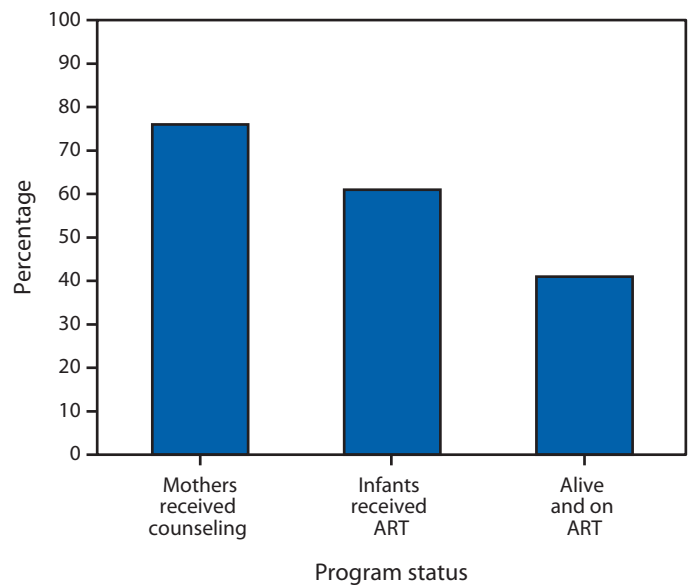
Despite being among the most successful PMTCT programs in sub-Saharan Africa, the scale-up of EID in Botswana reveals several challenges in treating pediatric HIV. Almost one third of HIV-exposed infants in Francistown were not tested by the EID program. One important barrier to EID testing is that new mothers in Botswana traditionally move to their home villages after delivery, making it difficult to locate HIV-exposed infants. Other issues that might inhibit enrollment in care include fear of disclosure of their HIV status and possible stigmatization, lack of parental understanding of the need to enroll the infant in care, long wait times at clinics, and lack of transportation (4).

The results in Botswana were similar to those observed in other sub-Saharan countries. EID program data in several African countries show the estimated completion rate from HIV testing to initiation of ART ranged from 0.5% to 52.8% (5). In Tanzania, 88% of 4,292 HIV-exposed infants were tested through the EID programs in three districts; 69% of HIV infants diagnosed with HIV were enrolled in care, and 39% of infants who had received ART were retained in care (6). In a large referral hospital in South Africa, 72% of 838 HIV-exposed infants were tested through the EID program, and 67% of mothers received the HIV test results (7). Of the 38 infants diagnosed with HIV in South Africa, 61% received ART, and 34% were retained in care at 68 weeks (7).

In Botswana, lack of coordination across HIV services resulted in delays between HIV testing, post-test counseling, and ART initiation. Overall, the median time from birth to ART initiation was >5 months, including 1 month between HIV diagnosis and post-test counseling of mothers. The use of mobile phone technology has reduced the turn-around time for return of EID results to health-care providers in Zambia (8). In Botswana, electronic registries for PMTCT services and ART are being introduced in clinics to facilitate better coordination between the programs and improve outcomes for the mother and infant.

Death rates in Botswana were significantly higher among infants who did not receive ART compared with those who did. However, 19% of the 123 infants who did receive ART died by the end of the follow-up period. Pneumonia and diarrhea were the most common causes of death among HIV-infected children in the study in Francistown and also are leading causes of death among all children in Botswana aged <5 years.

FIGURE. Percentage of infants diagnosed with HIV (N = 202*) whose mothers received post-HIV test counseling, percentage who received ART, and percentage who were alive and on ART through September 2013 — Early Infant Diagnosis Program, Francistown, Botswana, 2005–2012



Abbreviations: HIV = human immunodeficiency virus; ART = antiretroviral therapy.
* A total of 10,923 infants in the program were exposed to HIV (i.e., born to HIV-infected mothers); 7,772 were tested for HIV infection, and 202 were diagnosed with HIV infection.

Botswana recently introduced vaccines against pneumococcal pneumonia and rotavirus to help prevent pneumonia and diarrhea in children. Breastfeeding has been shown to reduce overall child mortality and is recommended by the World Health Organization for HIV-infected mothers who are receiving ART (9). However, most HIV-exposed infants are fed formula that is provided for free by the government of Botswana.

The findings in this report are subject to at least four limitations. First, poor documentation at the 13 postnatal care facilities caused some discrepancies in data collected. For example, there were instances where infants were started on ART, but there was no documentation that their mothers were ever counseled after their infants were tested for HIV. Second, data were collected in Francistown and might not be representative of the rest of Botswana. Third, outcome data were not available for 20% of HIV-infected infants who were lost to follow-up or transferred. Finally, existing information management systems were not able to provide complete data on services received by infants who were examined outside of Francistown. This might have resulted in an underestimate of the percentage of HIV-exposed infants tested in the EID program.

Strategies for increasing EID testing coverage, prompt referral of HIV-diagnosed infants for ART, and retention in care are needed to ensure the survival of children who are born

What is already known on this topic?

Despite high rates of human immunodeficiency virus (HIV) testing and antiretroviral prophylaxis for HIV-infected pregnant women in Botswana, up to 4% of their infants are born HIV-infected. Without antiretroviral therapy (ART), half of HIV-infected infants will die in the first year of life. Delays in HIV screening, return of test results, referral, and initiation of ART, and loss to follow-up increase infant mortality.

What is added by this report?

The Botswana Early Infant Diagnosis (EID) Program was introduced in 2005 to screen infants for HIV beginning at age 6 weeks. In Francistown, Botswana, during 2005–2012, 71% of infants born to HIV-infected women were screened for HIV. As of September 2013, among the 202 HIV-infected infants identified by the EID program, 41% were alive and on ART, 39% had died, and 20% were lost to follow-up, had transferred, or the family had declined therapy.

What are the implications for public health practice?

Even in a successful program to prevent mother-to-child transmission, survival of HIV-infected infants is poor without early diagnosis, rapid initiation of treatment, and retention in care. Strategies to overcome educational, cultural, and structural barriers are needed to improve patient outcomes in the EID program.

with HIV. These strategies include strengthening the referral system to reduce the time at each step of the route from prenatal and postnatal care to EID testing and pediatric treatment. In addition, program challenges such as educational, cultural, and structural barriers among mothers also must be addressed as part of a comprehensive EID strategy.

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Notes from the Field

Varicella-Associated Death of a Vaccinated Child with Leukemia — California, 2012

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Varicella, a contagious viral disease, is typically self-limited but can result in serious complications, especially among persons who are immunocompromised (1). On April 10, 2012, a girl aged 4 years with acute lymphoblastic leukemia (ALL) was exposed to a mildly ill cousin who developed a varicella rash 2 days later. The episode was reported to the child's oncologist after 13 days. The girl was prescribed 7 days of oral acyclovir for prophylaxis and concurrently began her scheduled chemotherapy, which included a 5-day course of dexamethasone (prednisone equivalent dose of 23 mg/day). Twenty-two days after her varicella exposure, the girl was taken to an emergency department for fever and abdominal pain. She was treated symptomatically; her caretakers were instructed to discontinue chemotherapy and to follow up with her oncologist. Two days later, the girl returned to the emergency department with a generalized rash. She was hospitalized and treated with intravenous acyclovir and antibiotics. However, she developed multiorgan failure and died on May 7. Varicella was confirmed by polymerase chain reaction testing, and no alternative diagnoses were found for her acute illness.

The patient had received her first dose of varicella vaccine (Varivax) in March 2009. She was diagnosed with ALL in March 2011. At that time, she was varicella-zoster virus (VZV) immunoglobulin G (IgG)-positive.

To date, there have been five deaths, including this death, reported to CDC among U.S. children who had received 1 dose of varicella vaccine. Four of these deaths occurred among children being treated with immunosuppressive medications; high-dose corticosteroids were a component of their treatments. This patient's fatal varicella likely was the result of profound immunosuppression, resulting in part from the chemotherapy and corticosteroid treatment (2).

At the time of her ALL diagnosis, this patient had evidence of immunity to varicella (1) based on detection of VZV IgG; postexposure treatment with varicella zoster immune globulin (VariZIG) was not indicated by existing Advisory Committee on Immunization Practices (ACIP) recommendations (3). However, detection of VZV IgG after 1 dose of varicella vaccine might not correspond to adequate protection in immunocompromised persons (1). Because of challenges in assessing protection against varicella in immunocompromised patients, postexposure VariZIG for selected VZV-seropositive persons, such as hematopoietic-cell transplantation recipients, has been recommended by some experts, although this is not an ACIP recommendation (4). Clinicians may consider use of postexposure prophylaxis among profoundly immunocompromised patients on an individual basis.

Varicella vaccination has led to significant declines in varicella disease in the United States (1). Eligible persons without evidence of immunity to varicella should receive 2 doses of varicella vaccine (1). Live-attenuated varicella vaccine is contraindicated for immunocompromised persons, but the vaccination program offers protection to these vulnerable persons through herd effects. To provide more targeted herd protection for immunocompromised children, varicella vaccination of their household contacts is recommended (1).

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Announcements

World Encephalitis Day — February 22, 2014

Encephalitis, inflammation of the brain, is caused by several different infectious and noninfectious entities. Encephalitis can be an uncommon complication of a common infection, such as infection with a herpes virus or with any of several vaccine-preventable disease viruses, or a predictable presentation of a rare pathogen, such as the amoeba, *Naegleria fowleri*.

The epidemiology of encephalitis is influenced by many factors, including vaccine availability, global travel, and environmental alterations, such as climate change (1). Some encephalitis etiologies, such as the measles, mumps, rubella, and varicella viruses, have been virtually eliminated in certain settings through vaccination. However, other encephalitis pathogens have emerged or reemerged, including West Nile virus, Nipah virus, European tickborne encephalitis virus, enterovirus 71, and the amoeba, *Balamuthia mandrillaris*.

Determining the cause of encephalitis can be difficult in part because of its nonspecific clinical presentation and the large number of causative agents. Despite exhaustive testing, an etiology is only identified in 40%–80% of cases (2). Moreover, autoimmune and infectious encephalitides are clinically indistinguishable (3).

The overall case-fatality rate of encephalitis is 5%–30%, but individual outcomes are highly dependent on the underlying cause and host factors, and survivors are often left permanently disabled. For instance, rabies is almost universally fatal, whereas encephalitis from enterovirus infection generally has better outcomes. Encephalitis also has substantial health-care costs given its severity as well as complexity of diagnosis and treatment (2).

Despite these challenges, progress is being made. World Encephalitis Day will be observed on February 22, 2014, to draw attention to encephalitis and invigorate global prevention efforts (4–6).

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Smartphone Application Available for Preventing Group B *Streptococcus* Infections

Despite more than a decade of prevention efforts and updated prevention guidelines published in 2010, group B *Streptococcus* (GBS) remains the leading cause of early onset neonatal sepsis in the United States (1). A free smartphone application, Prevent Group B Strep, is available from CDC to improve maternal and neonatal management of GBS disease prevention at the point-of-care.

Developed for obstetric and neonatal providers, the GBS prevention application features patient-specific and scenario-specific guidance consistent with the 2010 guidelines for the prevention of perinatal GBS disease (1). The application generates customized user guidance, such as when intrapartum antibiotics are indicated and which antibiotic regimens are appropriate for penicillin-allergic women, based on patient characteristics.

CDC, in collaboration with the American College of Obstetricians and Gynecologists, American Academy of Pediatrics, American College of Nurse-Midwives, and American Academy of Family Physicians, developed the GBS prevention application to improve implementation of evidence-based guidelines and prevent cases of GBS disease. The application is available for Apple iPhone/iPad and Google Android devices. The GBS prevention application and additional information are available at <http://www.cdc.gov/groupbstrep/guidelines/prevention-app.html>.

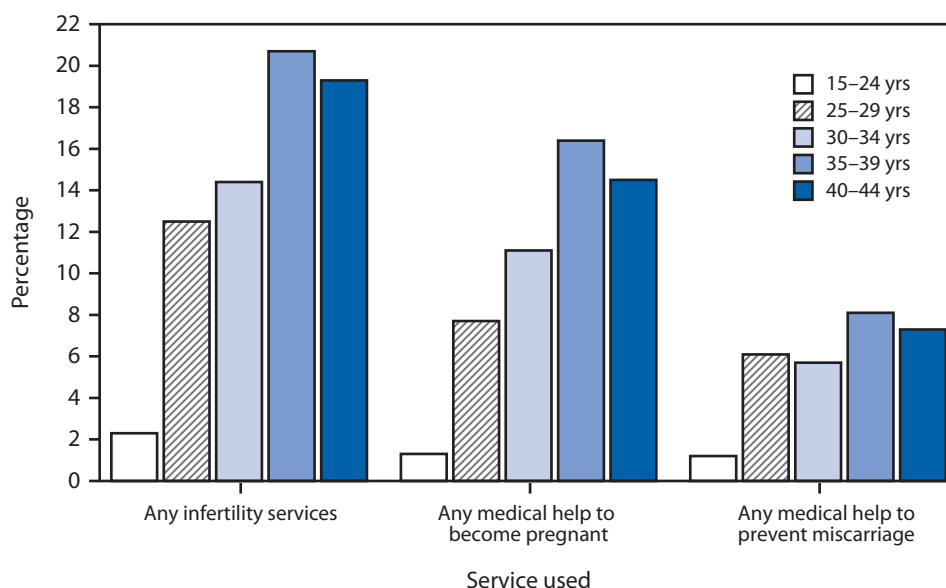
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QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage of Females Aged 15–44 Years Ever Using Infertility Services,* by Age Group — National Survey of Family Growth, United States, 2006–2010



* Infertility services include medical help to become pregnant or to prevent miscarriage; both types of medical help could be reported.

During 2006–2010, among females aged 15–44 years, the percentage of those who ever used infertility services increased through age 34 years, leveling off for women aged 35–44 years. Approximately one fifth of women aged 35–39 years and 40–44 years had ever used infertility services, either to become pregnant or to prevent a miscarriage, compared with 2.3% among females aged 15–24 years. Use of medical help to become pregnant ranged from 1.2% for females aged 15–24 years to 16.4% for women aged 35–39 years. Use of medical help to prevent miscarriage showed a similar but less steep increase with age.

Source: Chandra A, Copen CE, Stephen EH. Infertility service use in the United States: data from the National Survey of Family Growth, 1982–2010. Natl Health Stat Rep 2014(73).

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