

Fatal Hemophagocytic Lymphohistiocytosis Associated with Locally Acquired Dengue Virus Infection — New Mexico and Texas, 2012

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Dengue is caused by infection with any of four mosquito-transmitted dengue viruses (DENV-1–4) and is characterized by fever, headache, myalgia, and leukopenia (1). Hemophagocytic lymphohistiocytosis (HLH) is a potentially fatal hyperinflammatory syndrome that can be familial or acquired, and is characterized by persistent fever, pancytopenia, hepatosplenomegaly, and increased serum ferritin (2). Acquired HLH is most frequently associated with Epstein Barr virus infection but also has been associated with dengue (3). This report describes a fatal case of acquired HLH that was apparently triggered by infection with DENV-3. The patient developed an acute febrile illness in August 2012 during a 1-month vacation in New Mexico. After returning to her home in Texas, she was initially diagnosed with West Nile virus (WNV) infection, developed pancytopenia, liver failure, and disseminated intravascular coagulopathy, and died. DENV-3 was detected in a premortem bone marrow biopsy in which erythrophagocytosis was evident. This case underscores the need for clinicians in the United States to be vigilant for dengue and request diagnostic testing for suspected cases, which should be reported to public health authorities.

Case Investigation

On September 2, 2012, a woman aged 63 years went to an outpatient clinic in central Texas with a 7-day history of fatigue, anorexia, headache, hematuria, and leg pain (Figure 1). She had a history of Crohn's disease treated with mercaptopurine and mesalamine, hysterectomy because of uterine cancer, thyroidectomy, hypertension treated with lisinopril, coronary artery disease, hyperlipidemia, chronic renal disease with microhematuria, obesity, and depression treated with fluoxetine. Upon examination, the patient was febrile, hypotensive, and

had low oxygen saturation ($\text{SaO}_2 = 92\%$ [normal = $\geq 95\%$]). Laboratory values revealed leukopenia (white blood cell count = $3,600/\text{mm}^3$ [normal = $3,800\text{--}10,600/\text{mm}^3$]) (Figure 2, top panel). She was diagnosed with dehydration, given 1 L of intravenous normal saline, and instructed to see her primary care physician if her symptoms did not resolve.

On September 4, the patient went to her primary care physician and reported fatigue, anorexia, headache, leg cramps, fever, and chills. She did not have respiratory, gastrointestinal, or urinary symptoms. Physical examination revealed hypotension and fever. Lisinopril was discontinued, serum was drawn for typhus and WNV serology, and doxycycline was prescribed. A weakly positive anti-WNV immunoglobulin M (IgM) diagnostic test result was received on September 10, and the patient was prescribed bed rest for 2 weeks. Doxycycline was discontinued because of negative typhus serology.

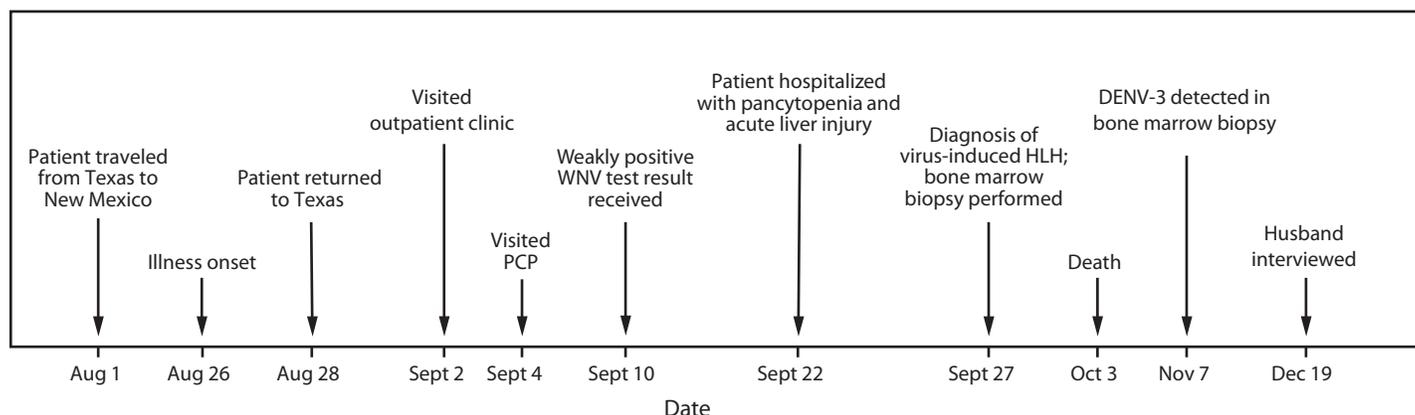
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FIGURE 1. Timeline of events surrounding the illness of a woman with fatal dengue-associated hemophagocytic lymphohistiocytosis — New Mexico and Texas, 2012



Abbreviations: PCP = primary care physician; WNV = West Nile virus; HLH = hemophagocytic lymphohistiocytosis; DENV-3 = dengue virus-type 3.

On September 22, the woman sought care at a regional emergency department because of persistent fatigue, fever, and chills. At triage, the patient was hypotensive, tachycardic, afebrile, and had low oxygen saturation ($\text{SaO}_2 = 90\%$). Icteric sclerae were noted on physical examination. Laboratory results revealed thrombocytopenia (platelet count = $94,000/\text{mm}^3$ [normal = $140,000\text{--}400,000/\text{mm}^3$]) and anemia (hemoglobin = 11.3 g/dL [normal = $12.0\text{--}16.0\text{ g/dL}$]) (Figure 2, top panel). Results also revealed acute liver injury (aspartate aminotransferase = 662 IU/L [normal = $10\text{--}42\text{ IU/L}$]); total bilirubin = 6.5 mg/dL [normal $0.2\text{--}1.2\text{ mg/dL}$]) (Figure 2, bottom

panel). She was transferred to a tertiary care hospital for inpatient management. At admission, the patient reported extreme fatigue, difficulty walking, shortness of breath without cough, anorexia, fever, chills, and dark urine. She continued to be hypotensive and was given 1 L of intravenous normal saline. Mercaptopurine and mesalamine were discontinued. Diagnostic testing was negative for infection with hepatitis A, B, and C viruses.

On hospital day 2, the patient continued to be afebrile, hypotensive, and tachycardic with no adenopathy or organomegaly. Abdominal ultrasound revealed diffuse fatty infiltration of the

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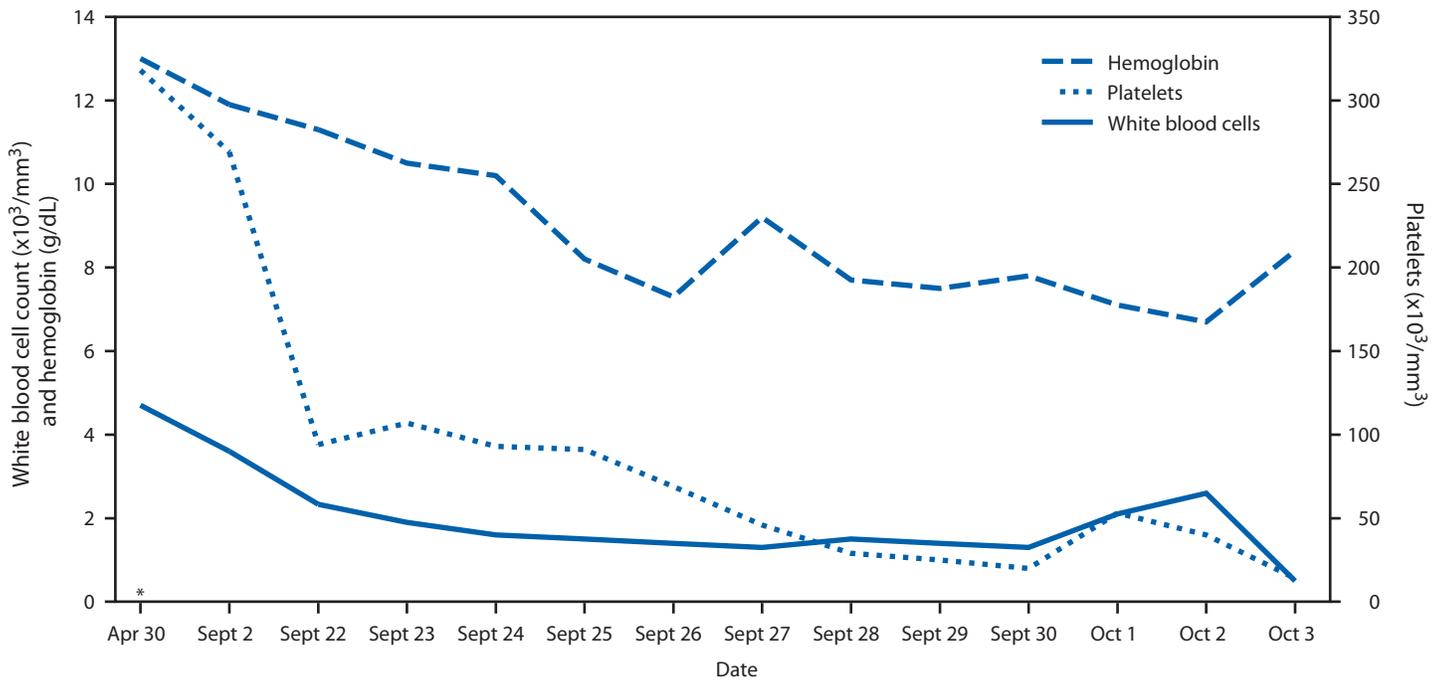
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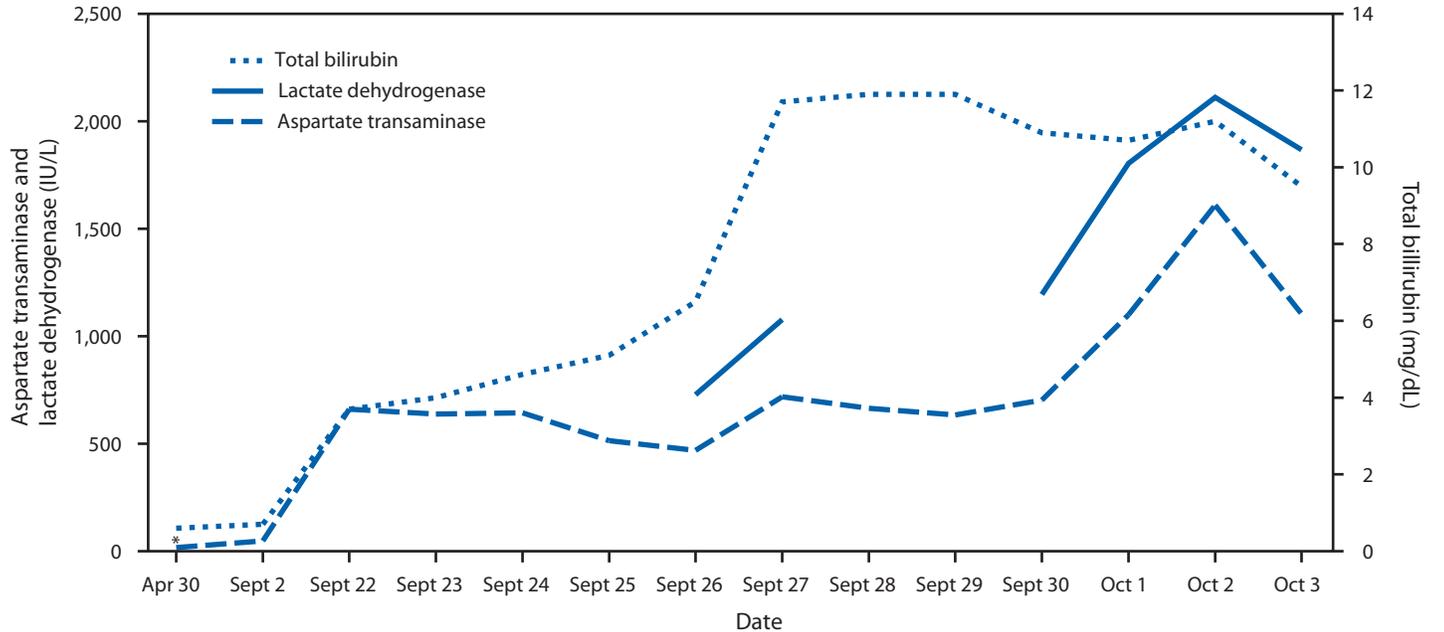
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FIGURE 2. Key laboratory values from hematology and liver chemistry panels for a woman with fatal dengue-associated hemophagocytic lymphohistiocytosis — New Mexico and Texas, 2012

Hematology panel



Liver chemistry panel



* Laboratory values collected during routine physical examination, before illness onset.

liver. Tests to detect antinuclear antibodies were negative. On hospital day 3 she developed bibasilar posterior respiratory crackles and was transferred to the intensive care unit for placement of a central venous catheter. On hospital day 4 she developed pitting pedal edema, wheezing with productive cough, and bleeding from the site of central venous catheter insertion. Serum ferritin was increased ($>7,500$ ng/mL [normal range = 7–282 ng/mL]) as was partial thromboplastin time (>250 seconds [normal range = 25.1–36.5 seconds]). Serum fibrinogen was decreased (<60 mg/dL [normal range = 200–393 mg/dL]). On September 26 (hospital day 5), the patient had fever, tachypnea, neutropenia (absolute neutrophil count = $900/\text{mm}^3$ [normal = $1,500$ – $8,000/\text{mm}^3$]), and elevated liver enzymes (lactate dehydrogenase = 727 IU/L [normal = 91 – 180 IU/L]). Chest radiography revealed infiltrates with an opacity in the lower lobe of the left lung. Titers taken to detect antinuclear antibodies and rheumatoid factor were positive, a presumptive diagnosis of virus-induced HLH was made, and a bone marrow biopsy and aspiration was performed.

Over the next 7 days, the patient developed bilateral pleural effusions, splenomegaly, anasarca, hemoptysis, and watery diarrhea with blood. A core needle liver biopsy on September 27 (hospital day 6) revealed fulminant hepatitis suggestive of a viral process with no overt hepatocyte necrosis. Serum specimens were collected on hospital day 7 for *Rickettsia* and repeat WNV serology, which were negative and weakly positive, respectively. Although the result of reverse transcription–polymerase chain reaction (RT-PCR) testing to detect WNV nucleic acid was negative on the same day, interferon therapy was initiated because of the possibility of WNV-induced hepatitis. Hemodialysis was initiated on hospital day 10 because of kidney failure, and the following day the patient developed respiratory distress and was intubated.

The patient received a diagnosis of severe metabolic acidosis and volume overload on hospital day 11, and soon after became encephalopathic and unresponsive. Palliative care was initiated, and the previously collected liver and bone marrow biopsies were sent to CDC for confirmation of WNV infection. On October 3, the patient died. She had been administered a total of 27 units of blood products during hospital days 4–12 because of bleeding. Retrospective medical record review confirmed that the case met the HLH clinical case definition (2).

The liver biopsy showed extensive liver damage, including marked steatosis and ballooning degeneration with neutrophilic and histiocytic aggregates and portal lymphocytic infiltrates. Macrophages with intracellular erythrocytes were noted in the bone marrow biopsy (Figure 3). RNA was extracted from the bone marrow aspirate and tested by RT-PCR assays specific for WNV and flaviviruses; the assay results were negative and positive, respectively. Sequencing of the flavivirus-specific PCR

FIGURE 3. Stars indicate erythrocytes phagocytized by a macrophage in a hematoxylin and eosin–stained section of bone marrow biopsy from a patient with fatal dengue-associated hemophagocytic lymphohistiocytosis — New Mexico and Texas, 2012



* Scale bar represents 10 micrometers.

product on November 7 revealed 98% nucleotide identity with DENV-3, which was confirmed with DENV-type specific RT-PCR. Anti-DENV immunohistochemistry was negative in both the liver and bone marrow biopsies. Special stains for acid-fast bacilli, fungi, and bacteria and immunohistochemistry for *Coxiella burnetii* on the liver biopsy were negative. No premortem or postmortem blood specimens were available for diagnostic testing.

Epidemiologic Investigation

Interview of the patient's husband on December 19 revealed that the vacationing couple had traveled from Texas on August 1 to Santa Fe, New Mexico, where they went for regular walks and frequently spent evenings on their patio. The patient and her husband visited an international fair featuring American Indian arts and crafts during August 18–19. In part because of the patient's illness, the couple returned to Texas on August 28. The patient had not been outside the continental United States since May 2012, when she visited France. She had previously visited several locations in the tropics, and lived in Bermuda for 1 year in the early 1970s.

Four other persons traveled to Santa Fe with the couple, none of whom reported fever in the 2 weeks before or after the patient's illness onset. All five of her travel companions provided a serum specimen for detection of anti-DENV IgM and IgG antibodies, and none had evidence of recent or past DENV infection, respectively.

Eighteen persons from Texas donated blood that was given to the patient before the bone marrow biopsy was performed on September 27. Of 17 donors who were contacted, none

reported fever in the 2 weeks before or 1 week after donating blood. Fourteen donors provided a serum specimen for diagnostic testing, and none had evidence of recent or past DENV infection.

Editorial Note

This is the third locally acquired dengue-related death documented in the 50 United States; all three occurred in the past 10 years and were geographically associated with Texas (4,5). Dengue is endemic throughout the tropics, and recent estimates suggest that 390 million DENV infections occurred worldwide in 2010 (6). The majority of dengue cases reported in the 50 United States are travel associated (7). However, because approximately 80% of all laboratory-positive dengue cases tested at private laboratories during 2008–2011 were not reported to public health authorities (CDC Dengue Branch, unpublished data, 2014), the actual incidence of dengue in the United States is unknown.

HLH was recently estimated to have a prevalence of 1 per 100,000 children in Texas and a survival rate of 67% (8). Familial HLH typically manifests early in life and is invariably fatal without treatment, including chemotherapy and immunotherapy followed by hematopoietic stem cell transplantation (2). HLH in adolescents and adults is more often acquired following infection or malignancy and can be successfully treated with therapy against the trigger and corticosteroids (2). Crohn's disease and immunosuppression are associated with an increased risk for developing HLH (2,9) and might have contributed to development of HLH in the patient described in this report. Also consistent with HLH, the patient had elevated transaminases, bilirubin, and lactate dehydrogenase (2) and all the known risk factors for death in adult HLH patients, including age >30 years, jaundice, disseminated intravascular coagulopathy, and absence of lymphadenopathy (10). HLH is a rare complication of dengue (3), with only 27 cases documented since 1966, including eight (30%) fatal cases. Clinicians in areas with endemic dengue should be aware of dengue-associated HLH because the clinical similarity of severe dengue and HLH might contribute to underrecognition of HLH.

Approximately 95% of persons with dengue will experience an acute febrile illness without clinically significant hemorrhage or plasma leakage (1). Because of nonspecific signs and symptoms, such cases can be misdiagnosed as influenza, WNV infection, or another common acute febrile illness. Although the patient described in this report initially received a diagnosis of WNV infection because of a weakly positive serologic test result, the result likely was produced by crossreactive anti-DENV IgM antibody. Clinicians should be aware of this possible crossreaction when evaluating patients with

What is already known on this topic?

Dengue is a potentially fatal acute febrile illness caused by infection with any of four mosquito-transmitted dengue viruses and is endemic throughout the tropics; most reported cases in the 50 United States are in travelers. Hemophagocytic lymphohistiocytosis (HLH) is a potentially fatal clinical syndrome that can be acquired following dengue virus infection.

What is added by this report?

The case described in this report represents the third locally acquired dengue-related death in the 50 United States and the first dengue-associated HLH case documented in the country.

What are the implications for public health practice?

Clinicians and public health professionals in the United States should be vigilant for and report cases of travel-associated and locally acquired dengue and request that both molecular and serologic diagnostics be performed in suspected cases. Clinicians in areas with endemic dengue should be aware of HLH as a potential complication of dengue and of the recommended HLH treatment regimen.

suspected WNV infection, especially those with recent travel to the tropics. Physicians and public health professionals in the United States should be vigilant for dengue, particularly in the context of ongoing WNV outbreaks and where competent DENV vectors (e.g., *Aedes aegypti* and *Aedes albopictus* mosquitos) are present.

Although the location where the patient became infected with DENV-3 could not be conclusively identified, there are several possible scenarios. The DENV incubation period ranges from 3 to 10 days (1), and the patient was in Santa Fe for 26 days (August 1–26) before illness onset. Although competent mosquito vectors of DENV are not known to establish stable populations at elevations above approximately 5,577 feet (1,700 meters) (1), and Santa Fe sits at an elevation of 7,260 feet (2,213 meters), an imported mosquito might have survived in the warmer August climate, fed on a DENV-infected person, and subsequently infected the patient. Alternatively, infection via contaminated blood products is a rare route of DENV transmission, and this route of transmission could not be ruled out because four blood donors did not provide a serum specimen for testing. Finally, it is possible that the patient's initial illness was caused by an unidentified agent, and she was infected with DENV-3 while en route to or in Texas, after which she developed HLH caused by infection with the unidentified agent and/or DENV-3.

Clinicians in the United States should be aware of dengue and request diagnostic testing that includes both molecular and serologic diagnostics for patients with dengue-like symptoms. Competent DENV vectors are present in most states, and importation of DENV via travelers has resulted

in recent dengue outbreaks in Florida, Hawaii, and Texas. All suspected dengue cases should be reported to state and local health departments.

Persons living in or traveling to areas where a risk for dengue exists should avoid mosquito bites by using insect repellent, staying in residences with air conditioning or intact mosquito screens on windows and doors, and emptying or covering all water containers that can serve as mosquito breeding sites.* A world map showing locations of current reports of dengue activity is available online from CDC.†

* Additional information available at <http://www.cdc.gov/dengue/prevention>.

† Available at <http://www.cdc.gov/dengue>.

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Prevalence and Indicators of Viral Suppression Among Persons with Diagnosed HIV Infection Retained in Care — Georgia, 2010

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Advances in treatment have led to dramatic improvements in the health of persons infected with human immunodeficiency virus (HIV). Moreover, treatment can reduce HIV transmission because suppressed levels of circulating virus makes HIV-infected persons less infectious (1). Until recently, antiretroviral therapy (ART) was recommended only for HIV patients with advanced disease (stages 2 and 3), and was optional for patients with early disease (stage 1). In March 2012, national HIV treatment guidelines were changed to recommend ART at all disease stages (1). To establish a baseline for care and treatment outcomes among persons with HIV, the Georgia Department of Public Health (DPH) examined whether viral suppression among HIV patients in Georgia varied by disease stage at diagnosis before implementation of the new guidelines. Disease stage at diagnosis was assessed as an indicator of viral suppression several months after diagnosis, adjusting for age, sex, and race/ethnicity among patients who were reported to DPH with HIV infections newly diagnosed during 2010 and retained in care. This report describes the results of that analysis, which indicated that disease stage at diagnosis was a significant indicator of viral suppression; viral suppression was significantly less frequent among persons with earlier disease stage at diagnosis. Compared with viral suppression among 80.5% of persons with stage 3 HIV disease, only 72.3% with stage 2 disease (prevalence ratio [PR] = 0.9; 95% confidence interval [CI] = 0.8–1.0) and 64.5% with stage 1 disease (PR = 0.8; CI = 0.7–0.9) met criteria for viral suppression, likely resulting from lack of initiating treatment or inadequate adherence to treatment regimens, as suggested in previous studies (1,2). These data can serve as a baseline to determine the impact of the guideline change in the future, and can be used to emphasize the importance of implementing the guidelines by expanding treatment to persons at all disease stages to reach the goal of viral suppression for all persons with HIV, thus closing the gap in viral suppression among persons diagnosed at disease stages 1 and 2. Health-care providers and community-based organizations should inform patients of the recommendation for ART initiation at all disease stages.

Georgia state law* requires that health-care providers report cases of HIV infection and that laboratories report test results

indicative of HIV infection (including positive Western blots, all viral loads, CD4+ counts, and viral nucleotide sequence results) to DPH. Prevalence of viral suppression was determined among Georgia patients aged ≥13 years who had HIV infection newly diagnosed during 2010 and who were retained in care by using the last viral load reported at 4–15 months after diagnosis. Patients were considered retained in care if they had at least two laboratory reports containing a CD4+ or viral load >3 months apart during the 4–15 months after diagnosis. Patients who were retained in care and died ≤15 months after diagnosis were included, and 16 patients with no record of their sex at birth were excluded from the analysis.

Viral suppression was defined as a viral load <200 copies/mL as measured using the last viral load reported at 4–15 months after diagnosis. Disease stage at diagnosis was determined by using the first recorded CD4+ count (or percentage of total lymphocytes if CD4+ count was unavailable) ≤3 months after diagnosis and was defined as stage 1 (≥500 cells/μL or ≥29%), stage 2 (200–499 cells/μL or 14%–28%), or stage 3 (<200 cells/μL or <14%). Transmission categories (i.e., male-to-male sexual contact, injection drug use, male-to-male sexual contact and injection drug use, heterosexual contact, and other/unknown) were assigned by reviewing each patient's HIV infection risk factors and using a hierarchy of risks previously described to determine the most likely route of HIV transmission (3). Missing transmission category data were estimated by using a multiple imputation method, as previously described (3). Because transmission category was not a significant effect modifier or confounder of the association between viral suppression and any other variable, it was excluded from the final model. PRs for viral suppression and 95% CIs were estimated by using log-binomial regression; sex, race/ethnicity, age at diagnosis, and disease stage at diagnosis were included in the model.

During 2010, a total of 2,921 new HIV infections were diagnosed among persons in Georgia aged ≥13 years, 1,340 (45.9%) patients were retained in care, and 958 (32.8%) met criteria for viral suppression. The analysis presented in this report examines the cross-section of the newly diagnosed population that is retained in care. Among those retained in care, the majority were black (53.7%), and 27.3% were aged 25–34 years; 22.9% were aged 35–44 years, and 21.6% were aged 45–54 years. Male-to-male sexual contact (61.7% of men) and heterosexual contact (67.9% of women) were the most

*Reporting disease; confidentiality; reporting required of pharmacists; immunity from liability as to information supplied; notification of potential bioterrorism, O.C.G.A. §31-12-2(b) (2010).

commonly reported transmission categories among men and women, respectively (Table 1).

Among the 1,340 persons retained in care, 958 (71.5%) met criteria for viral suppression ≤ 15 months after diagnosis. Blacks (63.3%) and persons aged 13–24 years (56.5%) had the lowest prevalence of meeting criteria for viral suppression. A lower percentage of persons with stage 1 disease at diagnosis (64.5%) met criteria for viral suppression than those with stage 2 (72.3%), stage 3 (80.5%), or unknown disease stage (66.3%) at diagnosis. By transmission category, the lowest percentage of viral suppression was among men with infection attributed to male-to-male sexual contact and injection drug use (65.3%) and women with heterosexual contact (67.9%) (Table 1).

Race/ethnicity, age, and disease stage at diagnosis were statistically significant indicators of viral suppression ≤ 15 months after diagnosis: black persons (PR = 0.9; CI = 0.8–0.9), persons aged 13–24 years (PR = 0.8; CI = 0.7–0.9), and persons diagnosed at

disease stage 1 (PR = 0.8; CI = 0.7–0.9) and stage 2 (PR = 0.9; CI = 0.8–1.0) had a lower prevalence of viral suppression, compared with white persons, persons aged ≥ 55 years, and persons diagnosed at disease stage 3, respectively (Table 2).

Editorial Note

Efforts are ongoing on national and local levels to promote HIV testing, identify those with acute infection, link and retain persons living with HIV infection in medical care, and achieve higher rates of viral suppression. Monitoring these steps throughout HIV diagnosis and treatment, known as the HIV care continuum, can be used to assess progress toward these goals and target the groups most in need (4,5). Published national statistics[†] from 18 states and the District of Columbia indicate 50.9% retained in care, and 43.4% virally suppressed;

[†] Available at http://www.cdc.gov/hiv/pdf/2011_monitoring_hiv_indicators_hssr_final.pdf.

TABLE 1. Prevalence of viral suppression among persons aged ≥ 13 years who had HIV infection diagnosed in 2010 and were retained in care* (N = 1,340), by selected characteristics — Georgia[†]

Characteristic	Persons with diagnosed HIV		Viral suppression	
	No.	%	No.	%
Overall	1,340	100.0	958	71.5
Race/Ethnicity				
Black	720	53.7	456	63.3
White	149	11.1	116	78.2
Hispanic	78	5.8	61	77.9
Other/Unknown	393	29.3	325	82.7
Age group (yrs)[§]				
13–24	255	19.0	144	56.5
25–34	366	27.3	258	70.5
35–44	307	22.9	229	74.6
45–54	290	21.6	228	78.6
≥ 55	122	9.0	99	81.2
Disease stage at diagnosis[¶]				
1	211	15.8	136	64.5
2	336	25.1	243	72.3
3	375	28.0	302	80.5
Unknown	418	31.2	277	66.3
Transmission category^{**}				
Male	1,033	77.1 (100.0)	740	71.6
Male-to-male sexual contact	638	47.6 (61.7)	418	65.5
Injection drug use	30	2.3 (3.0)	20	65.3
Male-to-male sexual contact and injection drug use	15	1.1 (1.5)	10	66.7
Heterosexual contact	46	3.4 (4.4)	35	77.4
Other/Unknown ^{††}	304	22.7 (29.4)	257	84.5
Female	307	22.9 (100.0)	218	71.0
Injection drug use	43	3.2 (13.4)	33	78.6
Heterosexual contact	208	15.6 (67.9)	142	67.9
Other/Unknown ^{††}	56	4.2 (18.3)	43	76.8

* Retained in care defined as having at least two laboratory tests (CD4+ or viral load) at least 3 months apart during 4–15 months after diagnosis.

[†] Among persons residing in Georgia and having a positive Western Blot or viral load based on surveillance data reported during 2010. Viral suppression defined as viral load < 200 on the basis of most recent test during 4–15 months after diagnosis. Only includes persons with their sex recorded at birth.

[§] Age based on the person's age at year's end 2010.

[¶] Based on first recorded CD4+ cell count ≤ 3 months after diagnosis. Defined as stage 1: CD4+ count ≥ 500 cells/ μ L or CD4+ percentage of total lymphocytes ≥ 29 ; stage 2: CD4+ count of 200–499 cells/ μ L or CD4+ percentage of total lymphocytes of 14–28; and stage 3: CD4+ count of < 200 cells/ μ L or CD4+ percentage of total lymphocytes of < 14 .

^{**} Data by transmission category have been statistically adjusted to account for missing transmission category. Nested percentages indicate percentages among newly diagnosed persons of specified sex.

^{††} Includes hemophilia, blood transfusion, perinatal exposure, or risk factor unknown or not indicated.

however, these proportions are among persons living with HIV and are not directly comparable to the Georgia proportions, which represent only those persons with newly diagnosed HIV.

Disease stage at diagnosis has not been studied as an indicator of viral suppression. In this study, prevalence of viral suppression ≤ 15 months after diagnosis was significantly lower among those with stage 1 and 2 disease at diagnosis, compared with stage 3. Because 1) national HIV treatment guidelines were changed to recommend ART at all disease stages after this study's analysis period, and 2) a recent survey of clinicians at HIV treatment centers in two states, conducted before guideline changes, revealed that only 14% would initiate ART regardless of CD4+ count (6), the lower prevalence of viral suppression among patients with an earlier disease stage at diagnosis likely resulted, in part, from fewer patients starting ART during early stages of disease. At the time of the study, the guidelines recommended treatment for persons with stage 2 disease, and the results indicate that recommended treatment for these persons was not fully implemented. Adherence to medication regimens might also be better among persons with more advanced disease, compared with those with subclinical disease (1,2). Similar to other recent studies, this report also found lack of viral suppression occurring more commonly among young persons and blacks (7–9). In addition to closing these gaps, an opportunity exists for improving viral suppression among those diagnosed at an early disease stage as guidelines for wider initiation of ART are implemented.

The findings in this report are subject to at least three limitations. First, data might have been incomplete as a result of underreporting, laboratory tests performed in other jurisdictions that might not be reported to DPH, incomplete report forms, patients lost to follow-up, or patients accessing HIV treatment outside Georgia. Second, the definition of “retained in care” might exclude patients who were tested outside the specified timeframe but are retained in care and patients who might receive care without laboratory tests. Finally, it was not possible to assess ART use or adherence.

Early diagnosis of HIV infection allows for timely interventions to achieve viral suppression, which benefits patients by improving their health status and the community by reducing HIV transmission (1). However, this study found that, even among persons retained in care, earlier diagnosis correlates with lower viral suppression. Not only were persons with stage 1 disease at diagnosis less likely to have viral suppression than those at stage 3 (as would be expected because ART was not recommended for stage 1 disease in 2010), but patients with stage 2 disease were less likely to have viral suppression than those with stage 3 disease, even though ART was recommended for both stages. It is now recommended that persons

TABLE 2. Indicators of viral suppression among persons aged ≥ 13 years who had HIV infection diagnosed in 2010 and were retained in care* (N = 1,340), by selected characteristics — Georgia[†]

Characteristic	Prevalence ratio	(95% CI)	p value
Race/Ethnicity			
Black	0.9	(0.8–0.9)	<0.01
White (reference group)	1.0		
Hispanic	1.0	(0.9–1.2)	0.70
Other/Unknown	1.1	(1.0–1.2)	0.07
Age group (yrs)[§]			
13–24	0.8	(0.7–0.9)	<0.01
25–34	0.9	(0.7–1.0)	0.17
35–44	0.9	(0.8–1.0)	0.23
45–54	0.9	(0.9–1.1)	0.33
≥ 55 (reference group)	1.0		
Disease stage at diagnosis[¶]			
1	0.8	(0.7–0.9)	<0.01
2	0.9	(0.8–1.0)	0.02
3 (reference group)	1.0		
Unknown	0.8	(0.8–0.9)	<0.01
Sex			
Male	1.0		
Female	1.0	(0.9–1.1)	0.97

Abbreviation: CI = confidence interval.

* Retained in care defined as having at least two laboratory tests (CD4+ or viral load) at least 3 months apart during 4–15 months after diagnosis.

[†] Among persons residing in Georgia and having a positive Western Blot or viral load based on surveillance data reported during 2010. Viral suppression defined as viral load < 200 on the basis of most recent test during 4–15 months after diagnosis. Only includes persons with their sex recorded at birth.

[§] Age based on the person's age at year's end 2010.

[¶] Based on first recorded CD4+ cell count ≤ 3 months after diagnosis. Defined as stage 1: CD4+ count ≥ 500 cells/ μ L or CD4+ percentage of total lymphocytes ≥ 29 ; stage 2: CD4+ count of 200–499 cells/ μ L or CD4+ percentage of total lymphocytes of 14–28; and stage 3: CD4+ count of < 200 cells/ μ L or CD4+ percentage of total lymphocytes of < 14 .

diagnosed with early disease are initiated on ART; as new guidelines are implemented, the prevalence of viral suppression should increase among this population from the baseline rate found by this study. These findings can be used to emphasize the importance of implementing the guidelines by expanding treatment to persons at all disease stages to close the gap in viral suppression among persons diagnosed at disease stages 1 and 2, and of assessing the impact of the new treatment guidelines; if no improvements in viral suppression among persons with stage 1 and 2 disease are observed in 2013, additional studies could determine if prescribing practices have not changed, or if there are other reasons for the poor suppression. All state or local health departments should monitor the continuum of care for persons living with HIV in their jurisdiction to determine care and treatment needs and evaluate public health interventions and implementation of treatment guidelines. Health-care providers and community-based organizations should implement the new treatment guidelines by initiating ART at all disease stages and inform patients about the benefits of earlier initiation of, and adherence to, ART for viral suppression at all disease stages.

What is already known on this topic?

Efforts are ongoing on national and local levels to promote testing for human immunodeficiency virus (HIV) infection, identify those with acute infection, link and retain persons living with HIV in medical care, and achieve higher rates of viral suppression. Disparities in adherence and viral suppression have been examined previously; however, disease stage at diagnosis has not been assessed as an indicator of viral suppression.

What is added by this report?

In a multivariate analysis of patients with newly diagnosed HIV infection in Georgia during 2010, disease stage at diagnosis was a statistically significant indicator of viral suppression among those retained in care, with the prevalence of viral suppression decreasing with earlier disease stage at diagnosis; fewer persons with stage 1 disease (prevalence ratio = 0.8; 95% confidence interval = 0.7–0.9) and stage 2 disease (prevalence ratio = 0.9; 95% confidence interval = 0.8–1.0) achieved viral suppression, compared with persons with stage 3 disease at diagnosis.

What are the implications for public health practice?

It is now recommended that persons diagnosed with early disease are initiated on antiretroviral therapy. As new HIV treatment guidelines are implemented, the prevalence of viral suppression should increase among this population from the baseline rate found by this study. These findings can be used to emphasize the importance of implementing and assessing the impact of the new guidelines. If no improvements in viral suppression among persons with stage 1 disease are observed in 2013, additional studies could determine if prescribing practices have not changed or if there are other reasons for the poor suppression.

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Trends in Uninsured Clients Visiting Health Centers Funded by the Title X Family Planning Program — Massachusetts, 2005–2012

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In 2006, Massachusetts passed legislation that broadened access to health insurance for its residents. The percentage of the state population that had health insurance (obtained through either private insurance or publicly funded programs) subsequently increased, reaching 97% in 2011, leaving only 3% uninsured, compared with approximately 9%–20% uninsured among nonelderly residents in 2006 (*1*). Given such high rates of insurance coverage, questions arise about the need for categorical public health programs designed to serve clients without health insurance. This report describes trends in the percentage of uninsured clients seen at community-based organizations in Massachusetts that received federal funding for one such program, the Title X family planning program. Title X program data from 2005–2012 indicate that client volume remained high throughout the period, and that the percentage of clients who were uninsured declined, from 59% in 2005 to 36% in 2012. Across years, young adults aged 20–29 years and persons whose incomes were 101%–250% of the federal poverty level were more likely to be uninsured than were persons in other age and income groups. After health-care reform, publicly funded family planning services in Massachusetts saw continued demand from uninsured and insured clients. Family planning services in other states implementing health-care reform might have a similar experience, and public health agencies are encouraged to track such trends to monitor the demand for such services and inform budget planning and resource allocation.

Annual program monitoring data for 2005–2012 were obtained from organizations funded by Title X in Massachusetts. The Title X Family Planning Annual Report (FPAR) data system collects information annually from all entities that receive grants from the Title X appropriation. FPAR includes data on the number and percentage of all family planning clients who did and did not have health insurance that covered a broad set of primary care benefits at the time of their last visit. In this definition, coverage for only limited primary care services, such as that obtained through some Medicaid family planning expansion programs, would not be considered insurance coverage. Also, for this report, the term “health insurance” is used to include coverage obtained through either private insurance companies or publicly funded programs such as Medicaid.

In Massachusetts, health centers obtained health insurance information directly from clients and entered it into a

centralized regional data system, either directly or by exporting from electronic systems. The Title X Region One office received and processed that information. Data for clients whose insurance status was unknown ($\leq 3\%$ of total clients across all years) are not presented. FPAR also includes data on self-reported income and age of clients. The regional system stores records of each clinic visit, allowing cross-tabulation of these variables.

Of the six health-care organizations in Massachusetts that directly received grants under the Title X program at any time during 2005–2012, five were funded in any one of those years, and four were funded continuously (Figure 1). In one region of the state, the grantee changed in 2010 from one organization to another (B and F). Each organization oversaw a network of health centers, ranging from five (grantee F) to 51 clinical locations (grantee E). The health centers offered family planning and other preventive services, such as cervical and breast cancer screening, screening for hypertension, and sexually transmitted disease and human immunodeficiency virus testing.

Of the five grantees in 2012, three (A, C, and D) were relatively small, not-for-profit agencies that focused on reproductive health either exclusively or as part of a mix of health and social services. One (F) was a nonprofit reproductive health organization affiliated with a national network, which became a Title X grantee in 2010. The last was a social services agency that offered family planning services through a network of community health centers and other health-care providers in the greater Boston area (E). Together they served low-income clients across the state.

During 2012, the health-care organizations saw 66,227 family planning clients, which was 90% of their 2005 client volume. Grantees varied in client volume, with the number of unduplicated clients served ranging from 9,037 to 29,921 in 2012. Of the four organizations that were continuously funded during this period, one saw a 1% increase in clients, whereas the others experienced decreases of 6%, 7%, and 30%.

From 2005 to 2012, the percentage of clients served by Title X–funded organizations in Massachusetts who were uninsured declined from 59% to 36% (Figure 1). Each of the grantees reported decreases in the percentage of family planning clients without health insurance in this period. In 2005, the percentage of clients who reported not having health insurance ranged from 77% (A) to 46% (E). By 2012, those without health insurance ranged from 52% (A) to 24% (E).

All age groups experienced similar decreases in the percentage of persons who reported they had no health insurance (Figure 2). In each year examined, adults aged 20–29 years comprised 43%–46% of all clients seen by these health centers. They also were the most likely to be uninsured throughout the period. However, they showed the greatest decrease in the percentage lacking insurance (65% uninsured in 2005, 39% in 2012), followed by teens (56% uninsured in 2005; 31% in 2012).

The percentage without insurance declined in all income groups (Figure 3). Throughout the period, however, clients with incomes of 101%–138% and 139%–250% of the federal poverty level (FPL) had the highest percentages without insurance (46% and 43%, respectively, in 2012).

Editorial Note

The results of this study indicate that in the 6 years following health-care reform in Massachusetts, publicly funded providers continued to be used as providers of choice for many clients with health-care coverage and remained as a “safety net” for uninsured persons in need of family planning services. For these family planning providers, implementation of state health-care reform coincided with significant decreases in the percent of their clients without insurance, although that proportion remained significantly higher than in the general population. The proportion of uninsured clients at safety-net family planning providers dropped significantly within 2 years of reform. However, it then began to level off, remaining over 23% for each health-care organization 6 years after reform. Community health centers and the substance abuse treatment sector in Massachusetts experienced similar shifts (2,3). Conservative estimates from other federal programs such as the Breast and Cervical Cancer Screening Program indicate that large numbers of women will continue to qualify for those subsidized services after insurance expansion (4).

The continued provision of safety-net family planning services is important not just for

FIGURE 1. Percentage of family planning clients without health insurance among Title X-funded health centers, by grantee — U.S. Department of Health and Human Services Region One Family Planning Annual Report, Massachusetts, 2005–2012

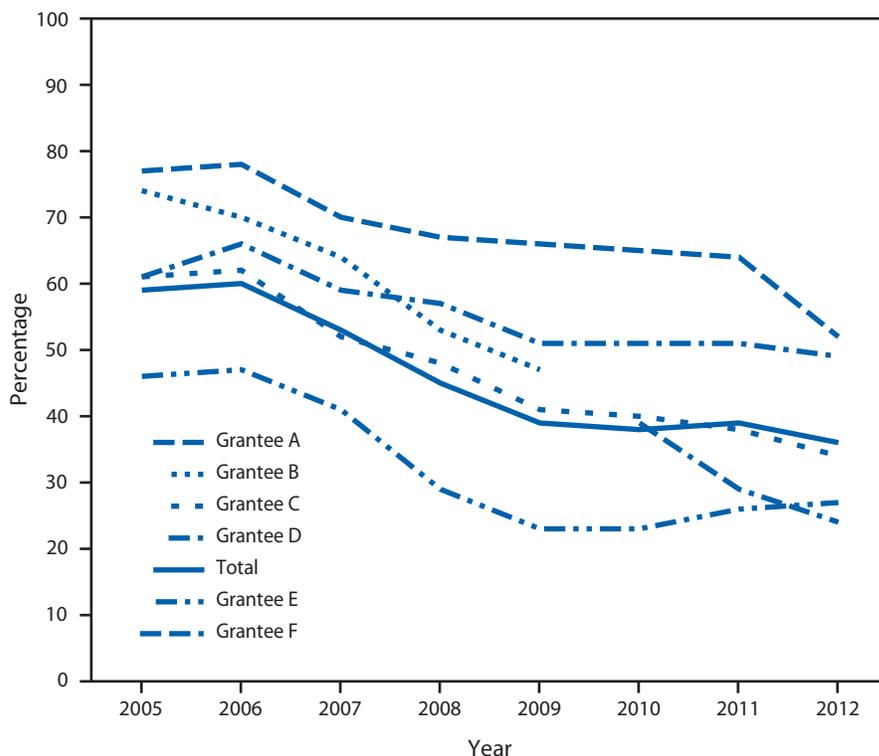


FIGURE 2. Percentage of Title X clients without health insurance, by age group — U.S. Department of Health and Human Services Region One Family Planning Annual Report, Massachusetts, 2005–2012

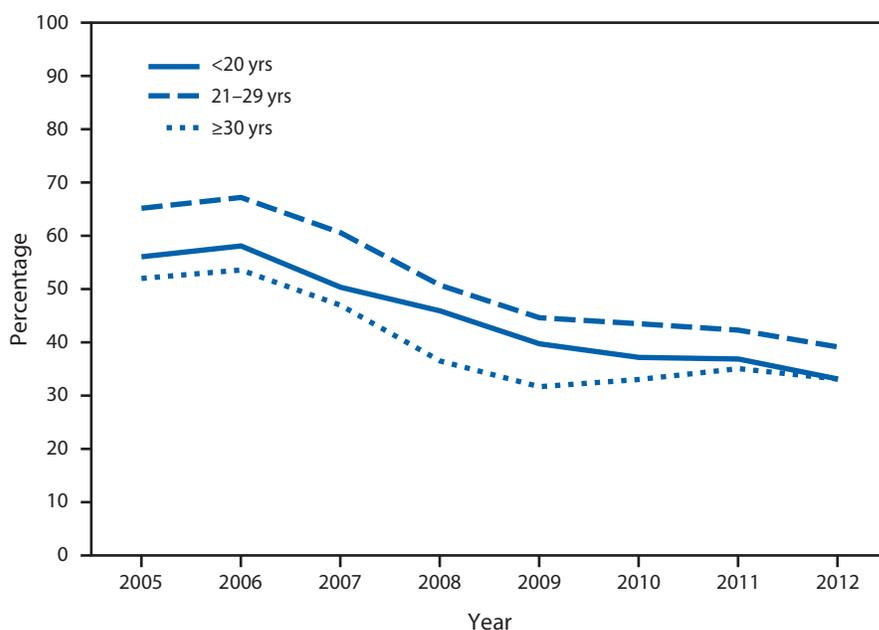
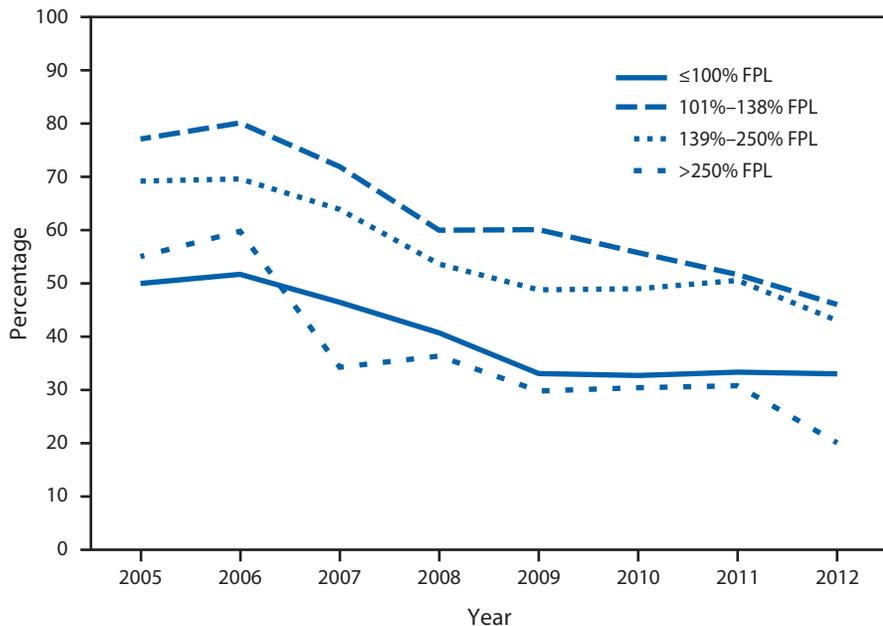


FIGURE 3. Percentage of Title X clients without health insurance, by federal poverty level (FPL) — U.S. Department of Health and Human Services Region One Family Planning Annual Report, Massachusetts, 2005–2012



the individual clients accessing services at these organizations but for broader health equity goals as well. Adults aged 20–29 years experience the most unintended pregnancies of any age group in the United States (5), and these clients constitute a large proportion of clients seen by these health centers. Yet insurance coverage among these young adults lagged behind that of other age groups. Within this client population, near-poor clients (clients whose incomes were above 100% FPL but below 250% FPL) were most likely to be uninsured. The Title X program was designed to serve poor and near-poor clients, the same population typically served by means-tested Medicaid family planning expansion programs (6). This analysis indicates that these income groups might still need access to supportive and safety-net services, even after health-care reform.

Research explaining these trends is sparse and raises questions about why so many clients at Title X–funded health centers lacked health insurance years after reform. Young adults are known to be among those groups with the lowest insurance coverage in Massachusetts and might opt to remain without insurance (7). Newly covered persons might experience difficulty maintaining enrollment in health insurance plans because of strict eligibility rules and changing life circumstances. Those persons might seek services at safety-net providers during periods when they are without health-care coverage (8). Others might not use their insurance as intended because they do not understand its family planning coverage, they seek a service

that is not covered by their insurance, or they cannot afford the copayments (3,8).

There is also a role for safety-net providers to serve those who are insured, many of whom might prefer those providers (9). Insured adolescents and young adults might seek subsidized family planning services because they want to keep their visits out of health insurance records and confidential from parents (9,10). Other newly insured clients might not be able to access new primary care providers offered in their insurance networks in a timely way, and thus will continue to seek services from safety-net providers (2,10). As the proportion of clients with insurance who use safety-net providers increases, organizations such as these will have to consider how to rapidly forge new relationships with private insurers and expand their third-party billing capacity.

The findings in this report are subject to at least three limitations. First, FPAR data on insurance, age, and income are self-reported and prone to response bias. Second, the analysis examined trends associated with, but not necessarily caused by, the timing of health-care reform in Massachusetts. Finally, the health-care context in Massachusetts is exceptional in many ways and limits the generalizability of these findings to other states.

Anticipating the effects of health reform in other contexts is difficult. In other states, the percentage of uninsured family planning clients seen at Title X–funded organizations might be significantly higher after a similar period of reform. That might occur in states with 1) higher baseline percentages of uninsured persons, 2) more undocumented immigrants, 3) less expansive public insurance options, 4) less state support for family planning, or 5) a less developed system of community health centers. In other states, the percentage of uninsured clients might be lower, depending on the status of these and other factors. Nevertheless, the experience of Massachusetts highlights the benefit of carefully monitoring the use of publicly funded family planning services in the years following implementation of health reform, and to continue to provide those services, as needed. Additional research and evaluation is critical to better understand the factors affecting trends among uninsured clients that Title X–funded providers, and other safety-net providers, will continue to see as health insurance coverage expands across the United States.

What is known about this topic?

In Massachusetts, health-care reform enacted in 2006 made health-care insurance coverage nearly universal. How health-care service use will change when insurance coverage expands is unclear, particularly for health-care providers who serve as a safety-net for uninsured clients.

What is added by this report?

Data provided by health-care providers funded through the federal Title X family planning program in Massachusetts demonstrate that the percentage of clients who were uninsured decreased significantly during the 6 years since enactment, but the demand for safety-net family planning providers has continued.

What are the implications for public health practice?

Ongoing monitoring of the use of publicly funded family planning services is needed after expansion of enrollment in health insurance.

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Notes from the Field

Increase in Reported Legionellosis — Milwaukee, Wisconsin, June–September 2013

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In early July 2013, the City of Milwaukee Health Department (MHD) was notified by the Wisconsin Division of Public Health of an increase in reported cases of legionellosis in southeastern Wisconsin. Legionellosis is a reportable disease to state and local public health authorities in Wisconsin. During June 1–September 30, 2013, a total of 58 clinically diagnosed cases of Legionnaires' disease, confirmed by laboratory testing, were reported in Milwaukee County, more than twice the number of total annual case reports in each of the previous 5 years. Forty-five (78%) of these cases were reported in the city of Milwaukee. The median age of county patients was 53 years (range = 29–77 years); all but one was hospitalized, and no deaths were reported. MHD received one report of a death attributed to legionellosis in the county during this period.

Environmental sampling for detection of *Legionella* was initiated by MHD at 11 sites within the city of Milwaukee, including select commercial building cooling towers; a large, decorative, outdoor water fountain; a public swimming pool/waterpark with spray features; and two residences of homebound patients. Thirty-nine swab and bulk water specimens were collected. Samples taken from three different cooling towers were positive for *Legionella pneumophila* serogroup 1, but were not genetically matched. Pulsed-field gel electrophoresis performed by the Wisconsin State Laboratory of Hygiene and MHD on nine lower-respiratory specimens from confirmed cases and tests by the MHD laboratory at the 11 environmental sites revealed six distinct strains of *L. pneumophila*. No strains found in the patients were related to the strains found in environmental samples.

Mapping of county cases using spatial analysis software showed that 31 (53%) patients reported home addresses within 3 miles of one or more of the three *Legionella*-positive towers. In comparison, approximately 40% of the county's residents live within 3 miles of one or more of the three geographically separate towers. Although a relative risk of 1.6 indicated

increased risk for *Legionella* exposure within a 3-mile radius of a tower, the association was not statistically significant (95% confidence interval = 0.9–2.7).

To address the risk for *Legionella* exposure, MHD met with regional cooling tower contractors and consultants. Gaps were identified in seasonal cooling tower maintenance and operation caused by unseasonably cool June weather followed by extremely hot weather in early July 2013. This resulted in a delayed start of building air conditioning operation after a prolonged period of tower disuse. In response, MHD distributed the CDC Procedure for Cleaning Towers Infected with *Legionella** to local building maintenance organizations, realty management groups, and heating, ventilation, and air conditioning professional organizations.

The increase in legionellosis in the city of Milwaukee during June–September 2013 suggests that cases were community-acquired from multiple environmental sources, possibly including contaminated cooling towers. Multiple physician alerts issued by MHD and DPH in July 2013 led to an increase in testing for *Legionella* by providers. Consequently, heightened clinician and laboratory surveillance might have contributed to a portion of the recorded increase in legionellosis. This investigation underscores the need for local public health authorities to be prepared to rapidly enhance surveillance, deliver appropriate public risk messaging, and coordinate with the private sector to mitigate environmental transmission of *Legionella* within a community.

* Available at <http://city.milwaukee.gov/imagelibrary/groups/healthauthors/dcp/pdfs/cdcprocedureforcleaningtowerle.pdf>.

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Errata

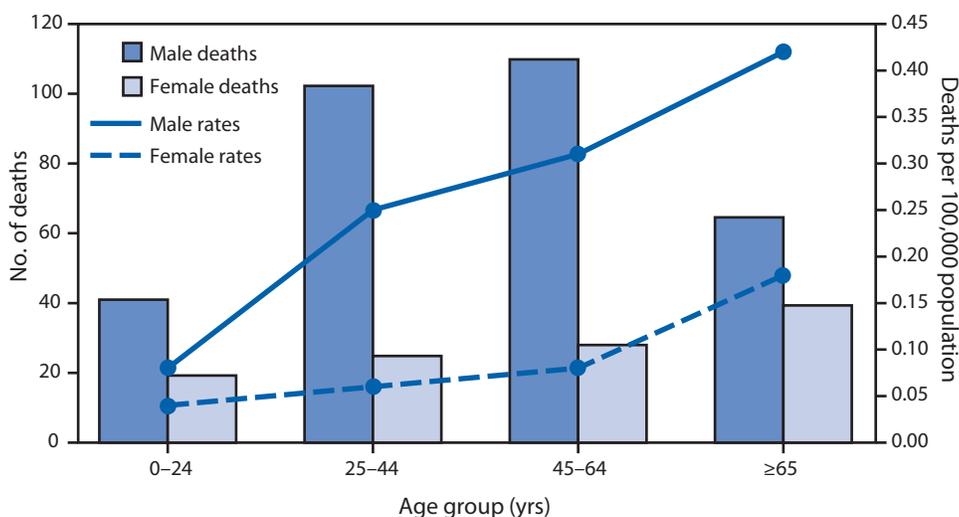
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In the report, “Seasonal Influenza Vaccination Coverage Among Women Who Delivered a Live-Born Infant — 21 States and New York City, 2009–10 and 2010–11 Influenza Seasons,” errors occurred in Table 1 on page 1002. For West Virginia, in the three columns for the 2009–10 season, the cells for number, prevalence, and 95% confidence interval should read **1,121**, **44.2**, and **(40.6–47.8)**, respectively, and for the last cell in the West Virginia row (“Change between 2009–10 and 2010–11 seasons (%)”), the percentage should read **11.4**. In the row labelled “Median,” in the last cell, the percentage should read **11.6**.

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Average Annual Number of Deaths and Death Rates from Unintentional, Non-Fire-Related Carbon Monoxide Poisoning,*† by Sex and Age Group — United States, 1999–2010



* Unintentional, non-fire-related carbon monoxide poisoning is defined both as 1) accidental poisoning by and exposure to gases or vapors (code X47) listed as the underlying cause, and 2) toxic effect of carbon monoxide (code T58) listed as the contributing cause, according to the *International Classification of Diseases, 10th Revision*. All deaths caused by intentional exposure (X67), exposure of undetermined intent (Y17), or fire-related exposure to carbon monoxide (codes X00–X09, X76, X97, and Y26) were excluded.

† Deaths are 12-year annual averages, and death rates are per 100,000 12-year annual average population.

During 1999–2010, a total of 5,149 deaths from unintentional carbon monoxide poisoning occurred in the United States, an average of 430 deaths per year. The average annual death rate from carbon monoxide poisoning for males (0.22 per 100,000 population) was more than three times higher than that for females (0.07). The death rates were highest among those aged ≥65 years for males (0.42) and females (0.18). The rates were the lowest for males (0.08) and females (0.04) aged <25 years.

Source: National Vital Statistics System. Mortality public use data files, 1999–2010. Available at http://www.cdc.gov/nchs/data_access/vitalstatsonline.htm.

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