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Update: Noncongenital Zika Virus Disease Cases — 50 U.S. States and the District of Columbia, 2016

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Zika virus is a flavivirus primarily transmitted to humans by *Aedes aegypti* mosquitoes (*1*). Zika virus infections also have been documented through intrauterine transmission resulting in congenital infection; intrapartum transmission from a viremic mother to her newborn; sexual transmission; blood transfusion; and laboratory exposure (*1–3*). Most Zika virus infections are asymptomatic or result in mild clinical illness, characterized by acute onset of fever, maculopapular rash, arthralgia, or nonpurulent conjunctivitis; Guillain-Barré syndrome, meningoencephalitis, and severe thrombocytopenia rarely have been associated with Zika virus infection (*1*). However, congenital Zika virus infection can result in fetal loss, microcephaly, and other birth defects (*1*,*2*). In 2016, a total of 5,168 noncongenital Zika virus disease cases were reported from U.S. states and the District of Columbia. Most cases (4,897, 95%) were in travelers returning from Zika virus-affected areas. A total of 224 (4%) cases were acquired through presumed local mosquitoborne transmission, and 47 (1%) were acquired by other routes. It is important that providers in the United States continue to test symptomatic patients who live in or recently traveled to areas with ongoing Zika virus transmission or had unprotected sex with someone who lives in or traveled to those areas. All pregnant women and their partners should take measures to prevent Zika virus infection during pregnancy. A list of affected areas and specific recommendations on how to prevent Zika virus infection during pregnancy are available at https://www.cdc.gov/pregnancy/zika/protect-yourself.html.

Before 2015, local transmission of Zika virus had been reported in Africa, Southeast Asia, and the Pacific Islands (*1*). In 2015, local mosquitoborne transmission of Zika virus was first identified in Brazil and subsequently spread throughout the Region of the Americas. To date, 48 countries and territories in the Americas have had confirmed mosquitoborne transmission of Zika virus (*4*). In the United States, Zika virus disease and congenital Zika virus infection became nationally notifiable conditions in February 2016, when the Council of State and Territorial Epidemiologists (CSTE) approved interim case definitions (*5*). In June 2016, CSTE approved revisions to the laboratory criteria and the addition of asymptomatic Zika virus infections to the case definitions (*6*). States were asked to reclassify their Zika virus disease cases according to the revised definitions. This report describes confirmed and probable cases of noncongenital Zika virus disease with illness onset during 2016, reported from U.S. states and the District of Columbia to ArboNET, the national arboviral surveillance system. Cases were classified as confirmed or probable according to clinical,

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epidemiologic, and laboratory-testing criteria. Asymptomatic noncongenital Zika virus infections and all congenital Zika virus infections were excluded from this summary. More information on reported congenital infections is available at https://www.cdc.gov/zika/reporting/pregnancy-outcomes.html.

A total of 5,168 noncongenital Zika virus disease cases with symptom onset during January 1–December 31, 2016, were reported to ArboNET (Figure 1). The number of reported cases peaked in July and declined rapidly after August. Although cases were reported from 49 states and the District of Columbia, approximately half (48%) were reported from three states (Florida [1,107; 21%], New York [1,002; 19%], and California [421; 8%]) (Figure 2).

The median age of patients with Zika virus disease was 37 years (range = 10 months–89 years), with 4,118 (80%) aged 20–59 years (Table). Overall, 3,310 (64%) cases occurred in females, and a higher proportion of female patients (24%) were aged 20–29 years compared with male patients (16%). Among the 3,310 Zika virus disease cases that occurred in females, 469 (14%) were in pregnant women.

Guillain-Barré syndrome was reported in 15 (0.3%) cases; the median age of these patients was 61 years (range = 27–81 years). Overall, 153 (3%) patients were hospitalized (Table); the median age of hospitalized patients was 41 years (range = 1–89 years). Among the 111 females hospitalized with Zika virus disease, 25 (23%) were pregnant. One hospitalized male patient died (*7*).

Among all 5,168 reported cases, 4,897 (95%) occurred in travelers returning from areas with Zika virus transmission (Table). The most common travel destination among the 3,891 (79%) cases for which this information was available was the Caribbean (2,389; 61%), followed by Central America (766; 20%), North America (521; 13%), South America (195; 5%), and Southeast Asia and the Pacific Islands (20; <1%).

Presumed local mosquitoborne transmission was the source of infection for 224 (4%) Zika virus disease patients, including 218 in Florida and six in Texas (Figure 1). The first autochthonous, mosquitoborne cases in the continental United States occurred in Florida in June 2016; local transmission peaked in August and then sharply declined. The patients with locally transmitted disease in Texas all had reported onset in November and December. The median age of patients with local mosquitoborne disease was 37 years (range = 7–81 years) and 103 (46%) were female.

Forty-seven (1%) cases were acquired through other routes, including sexual transmission (45), laboratory transmission (one), and person-to-person through an unknown route (one) (Table). The median age of patients with reported sexually transmitted Zika virus disease was 29 years (range = 18–61 years) and 43 (96%) were female.

Discussion

From 2007 to 2014, only 14 travel-associated cases of Zika virus disease were recognized in the United States (*1*,*8*). Following the introduction and spread of Zika virus in the

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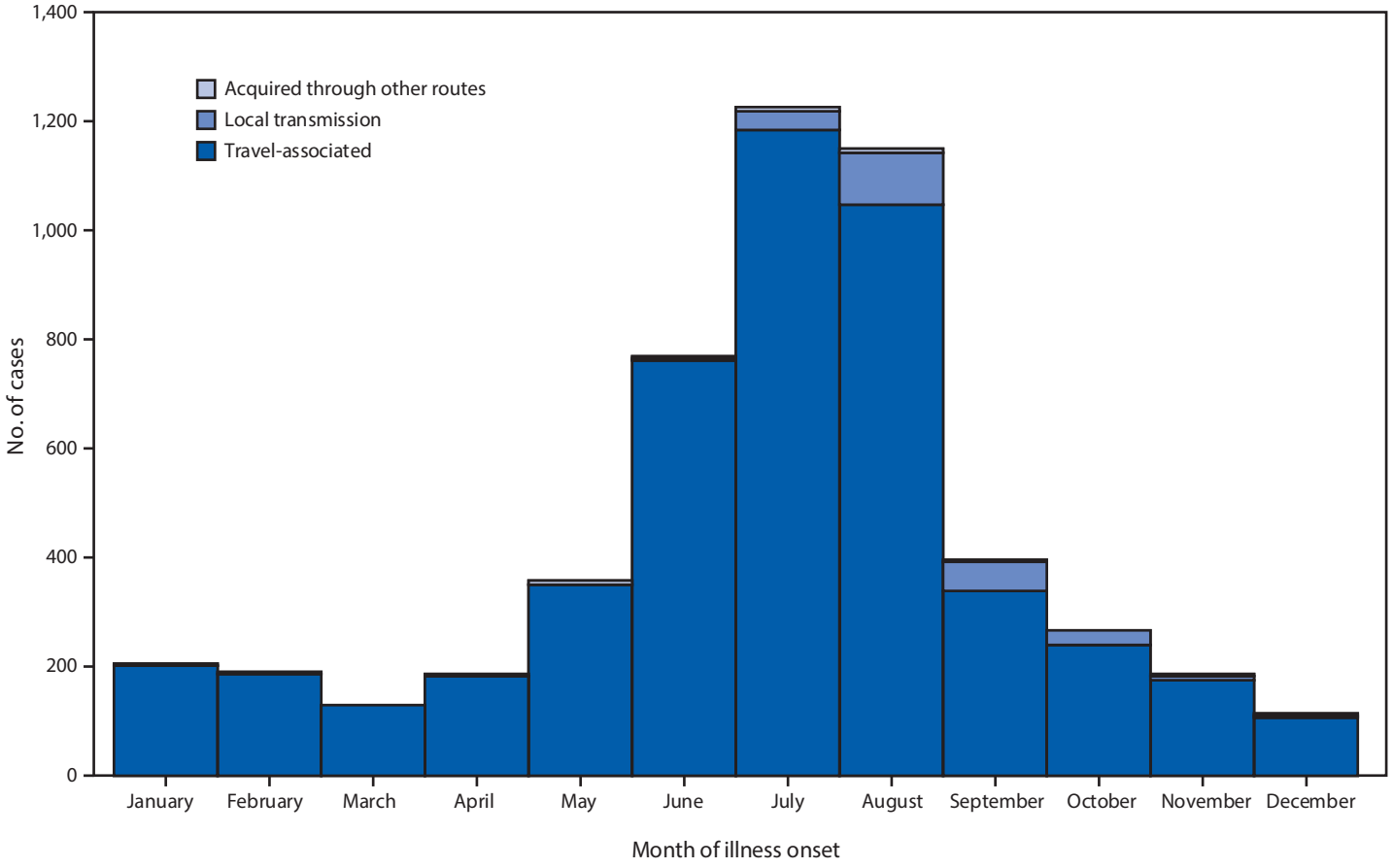
FIGURE 1. Noncongenital Zika virus disease cases (N = 5,168),* by month of illness onset — 50 U.S. states and the District of Columbia, January 1–December 31, 2016



* Other routes include 47 reported cases that were transmitted through sexual contact (45), laboratory exposure (one), and person-to-person through an unknown route (one).

Americas in 2015, the number of travel-associated cases in U.S. states increased, with 4,897 cases reported in 2016. The number of reported travel-associated cases in the United States peaked during July 2016 and declined during the second half of the year. An additional 224 cases attributable to local mosquitoborne transmission were reported during 2016 and were geographically limited to small areas in Florida and Texas.

Similar to the U.S. experience with both dengue and chikungunya, also transmitted by *Aedes aegypti*, most Zika virus disease cases occurred among travelers recently returning from locations outside the continental United States (*9*). The geographic and seasonal pattern of reported local mosquitoborne Zika virus transmission in the United States was also similar to prior local transmission of chikungunya and dengue viruses. Despite the presence of *Aedes aegypti* in multiple states, other environmental conditions (e.g., use of air conditioning and window screens, temperate climate, lower human population density, and reduced mosquito habitat) likely limited the transmission risk in U.S. states. If Zika virus disease trends continue to follow these historical mosquitoborne disease patterns, cases among travelers will continue to occur, but at lower levels, and limited local transmission with sporadic cases or clusters is possible. During the first 8 months of 2017, the number of reported cases (331) was markedly lower than the number reported during the same time frame in 2016 (4,205). Current data are available at https://www.cdc.gov/zika/reporting/case-counts.html.

The demographic characteristics of Zika virus disease cases reported by U.S. states in 2016 are similar to those described in an earlier report summarizing data from the first 6 months of 2016 (*7*). Overall, 64% of cases reported in 2016 occurred in females, and a higher percentage of the female patients were aged 20–29 years. These findings are likely driven by increased testing of women of childbearing age because of concerns about possible congenital infection. This hypothesis is supported by the local mosquitoborne disease data where more active surveillance and testing was performed and cases were more equally distributed between males and females. Other

FIGURE 2. Number of confirmed and probable Zika virus disease cases, by state of residence — 50 U.S. states and the District of Columbia, January 1–December 31, 2016

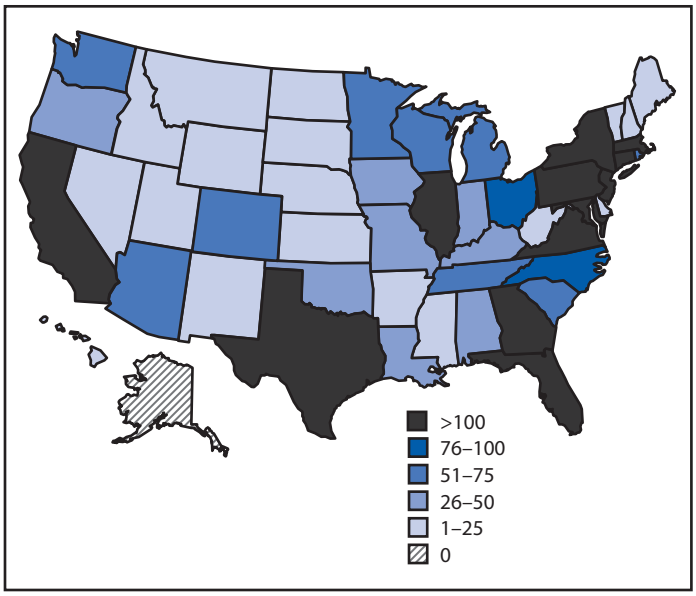


TABLE. Characteristics of confirmed and probable noncongenital cases of Zika virus disease — 50 U.S. states and the District of Columbia, January 1–December 31, 2016

Characteristic	No. (%) Female (n = 3,310)	Male (n = 1,858)	Total (N = 5,168)
Age group (yrs)			
0–9	60 (2)	33 (2)	**93 (2)**
10–19	249 (8)	155 (8)	**404 (8)**
20–29	794 (24)	298 (16)	**1,092 (21)**
30–39	771 (24)	440 (24)	**1,211 (23)**
40–49	600 (18)	387 (21)	**987 (19)**
50–59	499 (15)	329 (18)	**828 (16)**
≥60	335 (10)	214 (12)	**549 (11)**
Unknown	2 (<1)	2 (<1)	**4 (<1)**
Transmission mode			
Travel-associated	3,163 (96)	1,734 (93)	**4,897 (95)**
Local mosquitoborne	103 (3)	121 (7)	**224 (4)**
Other*	44 (1)	3 (<1)	**47 (1)**
Clinical outcome			
Hospitalized	111 (3)	42 (2)	**153 (3)**
Died	0 (0)	1 (<1)	**1 (<1)**

* Includes sexual transmission (45), laboratory exposure (one), and person-to-person through an unknown route (one).

factors also might have contributed to the higher proportion of reported female travel-associated cases (e.g., differential health care–seeking, mosquito exposure, or sexual transmission).

The findings in this report are subject to at least three limitations. First, the case numbers are likely an underestimate because most cases are mild, which might result in persons not seeking health care or clinicians not ordering diagnostic tests. Second, because ArboNET cases from early 2016 had to be reclassified to reflect the June 2016 case definition changes, some cases might have not been correctly recategorized. Finally, a number of different diagnostic tests are in use and might vary in diagnostic accuracy. For this reason, false positive or false negative test results might result in cases being missed or incorrectly diagnosed and reported.

This report did not include data from the U.S. territories; Puerto Rico, U.S. Virgin Islands and American Samoa experienced large outbreaks of Zika virus in 2016 that were the result of local mosquitoborne transmission. Because the epidemiology of Zika virus was very different in U.S. states as compared to U.S. territories, this report focuses on cases reported from U.S. states only.

CDC continues to recommend that health care providers test patients with a clinically compatible illness who live in or recently traveled to areas with ongoing Zika virus transmission or had unprotected sex with someone who lives in or traveled to those areas (https://www.cdc.gov/zika/hc-providers/testing-guidance.html). In July 2017, new guidance was released for providers caring for pregnant women with possible Zika virus exposure to reflect the lower positive predictive value of diagnostic testing in the setting of decreasing prevalence of disease and the difficulty in determining the timing of infection based on serologic testing as the outbreak continued (*2*). All pregnant women should be asked about possible Zika virus exposure before and during the pregnancy at every prenatal care visit to guide appropriate diagnostic testing and clinical care. Interim guidance for the evaluation of infants with possible congenital Zika virus exposure has been published (*10*). CDC continues to recommend that pregnant women avoid travel to areas with risk for Zika virus transmission, and all pregnant women and their partners should take measures to prevent Zika virus infection during pregnancy.

Timely identification and investigation of cases, especially in areas with *Aedes aegypti* mosquitoes, will reduce the risk for local mosquitoborne transmission in the continental United States. Although the risk for travel-associated Zika virus disease appears to be decreasing, all persons should continue to take precautions when traveling to areas with a risk for Zika virus transmission, including using strategies to prevent mosquito bites and sexual transmission. Additional information is available at https://www.cdc.gov/zika/.

Summary

What is already known about this topic?

Zika virus disease is an arboviral disease usually causing mild illness; however, congenital infection is associated with microcephaly and other birth defects. Although most cases in residents of U.S. states were travel-associated, local transmission has been reported.

What is added by this report?

In 2016, a total of 5,168 confirmed or probable cases of noncongenital Zika virus disease with symptom onset during January 1–December 31, 2016, were reported to ArboNET from U.S. states and the District of Columbia. Most (95%) cases were travel-associated. Locally acquired disease accounted for 4% of cases, with transmission occurring in Florida (218) and Texas (six). Forty-seven cases (1%) were acquired through other routes, including sexual transmission (45), laboratory transmission (one), and person-to-person through an unknown route (one).

What are the implications for public health practice?

CDC recommends that health care providers continue to test patients with a clinically compatible illness who live in or recently traveled to areas with ongoing Zika virus transmission or had unprotected sex with someone who lives in or traveled to those areas (https://www.cdc.gov/zika/hc-providers/testing-guidance.html). Although the risk for travel-associated Zika virus disease appears to be decreasing, it is important that persons traveling to areas with a risk for Zika virus transmission continue to take precautions, including using strategies to prevent mosquito bites and sexual transmission.

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Conflict of Interest

No conflicts of interest were reported.

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Dental Personnel Treated for Idiopathic Pulmonary Fibrosis at a Tertiary Care Center — Virginia, 2000–2015

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In April 2016, a Virginia dentist who had recently received a diagnosis of idiopathic pulmonary fibrosis (IPF) and was undergoing treatment at a specialty clinic at a Virginia tertiary care center contacted CDC to report concerns that IPF had been diagnosed in multiple Virginia dentists who had sought treatment at the same specialty clinic. IPF is a chronic, progressive lung disease of unknown cause and associated with a poor prognosis (*1*). Although IPF has been associated with certain occupations (*2*), no published data exist regarding IPF in dentists. The medical records for all 894 patients treated for IPF at the Virginia tertiary care center during September 1996–June 2017 were reviewed for evidence that the patient had worked as a dentist, dental hygienist, or dental technician; among these patients, eight (0.9%) were identified as dentists and one (0.1%) as a dental technician, and each had sought treatment during 2000–2015. Seven of these nine patients had died. A questionnaire was administered to one of the living patients, who reported polishing dental appliances and preparing amalgams and impressions without respiratory protection. Substances used during these tasks contained silica, polyvinyl siloxane, alginate, and other compounds with known or potential respiratory toxicity. Although no clear etiologies for this cluster exist, occupational exposures possibly contributed. This cluster of IPF cases reinforces the need to understand further the unique occupational exposures of dental personnel and the association between these exposures and the risk for developing IPF so that appropriate strategies can be developed for the prevention of potentially harmful exposures.

IPF is a form of chronic, progressive fibrosing interstitial pneumonia of unknown cause. IPF is associated with histopathologic and radiologic patterns of usual interstitial pneumonia in the absence of other known causes of interstitial lung disease (*1*) and is characterized by unexplained slowly progressive dyspnea that can be accompanied by a nonproductive cough (*2*). Available treatment options for IPF include pharmacotherapy (i.e., pirfenidone and nintedanib) and lung transplantation (*2*). The estimated median survival after diagnosis is 3–5 years (*2*). Although the etiology of IPF is unknown, exposures that have been suggested as contributing factors include viral infections, cigarette smoking, and occupations where exposure to dust, wood dust, and metal dust are common (*2*). In the United States, on the basis of the case definitions used by separate studies to analyze data collected during 1988–2005, the estimated annual incidence of IPF varied from 6.8 to 17.4 per 100,000 population, and the estimated prevalence varied from 14.0 to 63.0 per 100,000 population (*3*) and increased with increasing age (*2*). No published data could be found regarding dental personnel and IPF.

In June 2017, the electronic medical records of all 894 patients with a diagnosis of IPF treated at the Virginia specialty clinic during September 1996–June 2017 were reviewed to identify patients having the occupation of dentist, dental hygienist, or dental technician. Available electronic medical records of patients identified as having one of these occupations were reviewed, pertinent data were abstracted, and an attempt was made to interview living patients to ascertain symptoms and occupational and nonoccupational exposures, after obtaining informed consent. This study received approval from the Inova Fairfax Hospital Institutional Review Board.

Among 894 patients treated for IPF at the tertiary care center, nine (1%) were identified as dental personnel, including eight dentists and one dental technician. All patients were male and were treated during 2000–2015. Five were white, one was black, and the race of three was unknown. At the time of pulmonary consultation, the median patient age was 64 years (range = 49–81 years) (Table). States of residence included Virginia (five), Maryland (three), and Georgia (one). Seven of the nine patients had died; among these, the median survival time from consultation was 3 years (range = 1–7 years). Among eight patients tested at the time of pulmonary consultation, pulmonary function tests demonstrated three patients had normal spirometry, two of whom also had documented normal lung volumes, and five patients had restrictive spirometry and low lung volumes, interpreted as lung restriction. Each of the five patients with restriction had low predicted values for diffusing capacity of the lungs for carbon monoxide (D_{LCO}) (median = 47% [range = 19%–55%]). Pulmonary function test results were not available for one patient. One of the living patients who did not complete an interview underwent a lung transplant 3 years after diagnosis. No tissue specimens were available for analysis.

Three patients were former smokers, one had never smoked, and smoking history was unknown for five (Table). A telephone interview was conducted with the patient who had contacted CDC; it was not possible to complete an interview with the other living patient. The interviewed patient, who

TABLE. Selected characteristics of nine male dental personnel treated for idiopathic pulmonary fibrosis at time of first pulmonary consultation at a tertiary care center — Virginia, 2000–2015

Age (yrs)	Symptoms	Tobacco use	Pulmonary function*,†	Computed tomography finding	Clinical follow-up
49	NA	NA	Moderate restriction	Extensive basilar honeycombing	Died 1 year after initial consultation
50	Cough, phlegm, SOB	NA	Severe restriction	Extensive honeycombing and traction bronchiectasis	Alive. Underwent lung transplant 3 years after diagnosis.
58	DOE	Former	Mild restriction	Basilar subpleural fibrosis, diffuse peripheral septal thickening with cystic changes	Died 7 years after initial consultation
63	SOB	Former	Normal§	Advanced fibrosis, honeycombing, bullous and cystic lesions	Died 3 years after initial consultation
64	NA	NA	NA	Peripheral reticular infiltrates	Died 3 years after initial consultation
66	NA	NA	Restriction¶	Bibasilar infiltrates, bibasilar honeycombing	Died 6 years after initial consultation
70	DOE, decreased exercise tolerance	Former	Normal	NA	Died 4 years after initial consultation
70	Cough, throat clearing, SOB	Never	Mild restriction	NA	Alive
81	NA	NA	Normal	Mild to moderate subpleural fibrosis with bibasilar honeycombing	Died 2 years after initial consultation

Abbreviations: DOE = dyspnea on exertion; NA = not available; SOB = shortness of breath.
* Interpretation conducted by investigators and based on spirometry and measurement of total lung capacity, when available.
† Severity classified using criteria established by the American Thoracic Society/European Respiratory Society Task Force (http://www.thoracic.org/statements/resources/pft/pft5.pdf).
§ Only spirometry results available.
¶ Severity cannot be classified because forced expiratory volume in 1 second not available.

had never smoked, reported not wearing a National Institute for Occupational Safety and Health-certified respirator during dental activities throughout his 40-year dental practice; he wore a surgical mask for the last 20 years of his dental practice. He reported performing polishing of dental appliances, preparing amalgams and impressions, and developing x-rays using film developing solutions. He also reported work-related exposure to dust while working as a street sweeper for 3 months before entering dental school and environmental exposure to dust from coral beaches for approximately 15 years while intermittently visiting the Caribbean region as a practicing dentist.

Discussion

During September 1996–June 2017, nine (1%) of 894 patients treated for IPF at a single tertiary care center in Virginia were identified as dental personnel. Each patient presented for care during 2000–2015. Seven of the patients had died. This is the first known described cluster of IPF occurring among dental personnel. Although no clear etiology exists for this cluster, it is possible that occupational exposures contributed to the development of IPF.

During 2016, dentists accounted for an estimated 0.038% of U.S. residents (*4*), yet represented 0.893% of patients undergoing treatment for IPF at one tertiary care center, nearly a 23-fold difference. Dental personnel are exposed to infectious agents, chemicals, airborne particulates, ionizing radiation, and other potentially hazardous materials (*5*). Inhalational exposures experienced by dentists likely increase their risk for certain work-related respiratory diseases. For example, cases of dental technicians with pneumoconiosis, a restrictive occupational lung disease resulting from inhalation of dust, have been identified after exposure to either silica or cobalt-chromium-molybdenum-based dental prostheses (*6*,*7*). A case of pneumoconiosis was identified postmortem in an elderly dentist who died from respiratory failure (*8*). Examination of lung tissue at autopsy using scanning electron microscopy revealed particles consistent with alginate impression powders used during the dentist's practice. Nine cases of silicosis were recognized among dental laboratory technicians exposed to crystalline silica in five states during 1994–2000 (*9*). Asbestos-related lung disease, attributed to manipulating wet asbestos-containing paper during preparation of molds in casting operations, has also been identified in dentists (*10*). The one living patient in this cluster who was interviewed reported occupational exposures to silica and other materials used in dental practice, but also other work-related and environmental exposures to dust.

IPF has not been previously described among dental personnel. However, a query of the National Occupational Respiratory Mortality System for 4 separate years (1999, 2003, 2004, and 2007) for "other interstitial pulmonary diseases with fibrosis"* (which would include IPF) listed as the underlying or contributing cause of death revealed 35 decedents categorized as

* *International Classification of Diseases, Tenth Revision* (ICD-10) code J84.1.

Summary

What is already known about this topic?

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive lung disease of unknown cause and is associated with a poor prognosis. IPF has been associated with certain occupations; however, no published data exist regarding IPF in dental personnel.

What is added by this report?

A unique cluster of nine cases of IPF was identified among dental personnel treated at a tertiary care center in Virginia during 2000–2015. No clear etiology has been identified, but occupational exposures are possible.

What are the implications for public health practice?

During 2016, approximately 650,000 dental personnel were estimated to be employed in the United States, including 122,330 dentists. This cluster of IPF cases reinforces the need to understand further the occupational exposures of dental personnel and the association between these exposures and the risk for developing IPF so that strategies can be developed for prevention of potentially harmful exposures.

having worked in the "office of dentists" and 19 categorized as having the occupation "dentist," with proportionate mortality ratios of 1.52 (95% confidence interval [CI] = 1.05–2.11) and 1.67 (95% CI = 1.01–2.61), respectively (Respiratory Health Division, CDC, unpublished data, 2017). These findings suggest that a higher rate of IPF might occur among dental personnel than among the general population.

The living patient who was interviewed reported occupational exposures to known respiratory hazards (e.g., silica) yet did not wear National Institute for Occupational Safety and Health-certified respiratory protection. It is possible other patients in this case series had similar experiences. Dental personnel who perform tasks that result in occupational exposures to known respiratory hazards should wear adequate respiratory protection if other controls (e.g., improved ventilation) are not practical or effective (https://www.osha.gov/SLTC/respiratoryprotection/index.html). If respiratory protection is used, a written respiratory protection program should be implemented as required by the Occupational Safety and Health Administration Respiratory Protection Standard, including training, fit testing, and maintenance and use requirements (https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_id=12716&p_table=STANDARDS).

The findings in this report are subject to at least four limitations. First, in this analysis, only patients undergoing treatment at a single tertiary care center specializing in IPF treatment were identified, which might have led to an overrepresentation of dentists, given their comparatively high socioeconomic status. Conversely, dental personnel in Virginia and the surrounding region undergoing IPF treatment at other facilities during this same time frame were not identified, thereby potentially underrepresenting the magnitude of this cluster. Second, only one patient completed an interview, limiting the ability to explore past occupational exposures. Third, multiple patients had reported exposures that occurred outside of work and that are known risk factors for IPF, including tobacco smoke and dust (*2*). Finally, no biopsy specimens were available for examination to assess histological commonalities among the patients.

This investigation revealed the first described cluster of dental personnel with diagnosed IPF. The eight dentists identified in this cluster exceeded the number of expected cases, consistent with National Occupational Respiratory Mortality System data regarding IPF mortality and the proportion of U.S. residents who are dentists. Dentists and other dental personnel experience unique occupational exposures, including exposure to infectious organisms, dusts, gases, and fumes. It is possible that occupational exposures contributed to this cluster. After this analysis, another IPF case was diagnosed in a dentist treated at this specialty clinic. Further investigation of the risk for dental personnel and IPF is warranted to develop strategies for prevention of potentially harmful exposures.

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Conflict of Interest

No conflicts of interest were reported.

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Update: Dura Mater Graft–Associated Creutzfeldt-Jakob Disease — Japan, 1975–2017

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Creutzfeldt-Jakob disease (CJD) is a fatal neurodegenerative disorder that, according to the most well-accepted hypothesis (*1*), is caused by replicating, transmissible, abnormal forms of a host-encoded prion protein (prions). Most CJD cases occur spontaneously (sporadic CJD) or are inherited (genetic CJD). Iatrogenic CJD can occur after exposure to prion-contaminated instruments or products in medical/surgical settings. Cadaveric dura mater graft–associated CJD (dCJD) accounts for a common form of iatrogenic CJD. This report summarizes the epidemiologic features of 154 cases of dCJD identified in Japan during 1975–2017; these cases account for >60% of dCJD cases reported worldwide (*1*,*2*). The unusually high prevalence of dCJD in Japan was first reported in 1997 (*3*). In 2008, a single brand of graft (Lyodura [B. Braun Melsungen AG, Melsungen, Germany]), frequently used as a patch in neurosurgical procedures, was identified as the probable vehicle of transmission (*4*). No international recall of the implicated Lyodura occurred, the product had a relatively long shelf life, and the grafts were used frequently in Japanese patients with non–life-threatening conditions (*4*,*5*). Since 2008, additional cases have been ascertained, reflecting the identification of previously missed cases and the occurrence of new cases with longer latency periods (interval from exposure to symptom onset) for dCJD (up to 30 years), underscoring the importance of maintaining surveillance for dCJD.

In 1996, after the first report of variant CJD (the human prion disease caused by the agent of bovine spongiform encepathalopathy ["mad cow disease"]) in the United Kingdom (*6*), the nongovernmental Japanese CJD Surveillance Committee (J-CJDSC), with support from the Japanese Ministry of Health, Labour, and Welfare, conducted a preliminary nationwide mail survey to identify cases of human prion disease in Japan; since 1999, J-CJDSC has maintained a national CJD registry (*7*). J-CJDSC members investigate each reported suspected CJD case in cooperation with CJD specialists in each prefecture. The methods for identifying dCJD cases in Japan have been described previously (*5*,*7*,*8*). All identified CJD cases, including cases of dCJD, are entered into the J-CJDSC database, which contains demographic and clinical information, including a detailed history of any surgical procedures and international travel and CJD laboratory test results (including cerebrospinal fluid analyses and genetic testing) (*7*).

Among 829 identified physician-diagnosed cases of CJD during 1979–May 1996, a total of 43 (5%) patients had received a dura mater graft as part of a surgical procedure (typically a patch during neurosurgery); 41 (95%) of these dCJD patients had received a Lyodura graft (*3*). A 1987 U.S. investigation of a dCJD case found that Lyodura produced before May 1987 carried an unusually high risk for dCJD because of the contamination-prone method of production (*9*,*10*); after that report, the manufacturer reported revising its collection and processing procedures to reduce the CJD transmission risk.

By 2008, a total of 132 dCJD cases had been reported in Japan, and among 120 (91%), Lyodura was identified as the probable vehicle of transmission; the graft brand for the other 12 dCJD patients was unknown (*4*). By the end of 2017, the J-CJDSC database included 154 patients with dCJD, including an additional 22 patients identified since the last report (*4*).

Among 154 dCJD patients, receipt of a Lyodura graft was documented in 140 (91%); the brand of dural graft received by 14 patients was not identified. The most common medical conditions for which patients received the cadaveric dura mater grafts were brain tumors (including meningioma) (69; 45%), facial palsy or trigeminal neuralgia (26; 17%), and brain hemorrhage (25; 16%). Less common conditions included intracranial aneurysm (10; 6%), unspecified anomalies (eight; 5%), intracranial hematoma (seven; 5%), trauma (seven; 5%), and other (two; 1%). The median age at symptom onset among dCJD patients was 58 years (range = 15–81 years; mean = 56 years); 89 (58%) patients were female. All patients had received their dura mater graft during 1975–1993 (Figure 1) (Figure 2), and dates of illness onset ranged from 1985 to 2016.

Although the shelf life of Lyodura established by the manufacturer was 5 years, three dCJD patients had surgical procedures in 1993, at least 6 years after the company had changed their collection and processing procedures. J-CJDSC determined that all three patients had received a Lyodura graft, and that at least one of the grafts was processed before 1987, and had therefore expired (the processing date of the second and third patients' grafts are unknown). Eleven (7%) dCJD patients identified by J-CJDSC received grafts during 1988–1993 (Figure 2), including eight during 1988–1991,

FIGURE 1. Number of cases (N = 154) of dura mater graft–associated Creutzfeldt-Jakob disease (dCJD), by year of neurosurgical procedure and year of symptom onset — Japan, 1975–2017

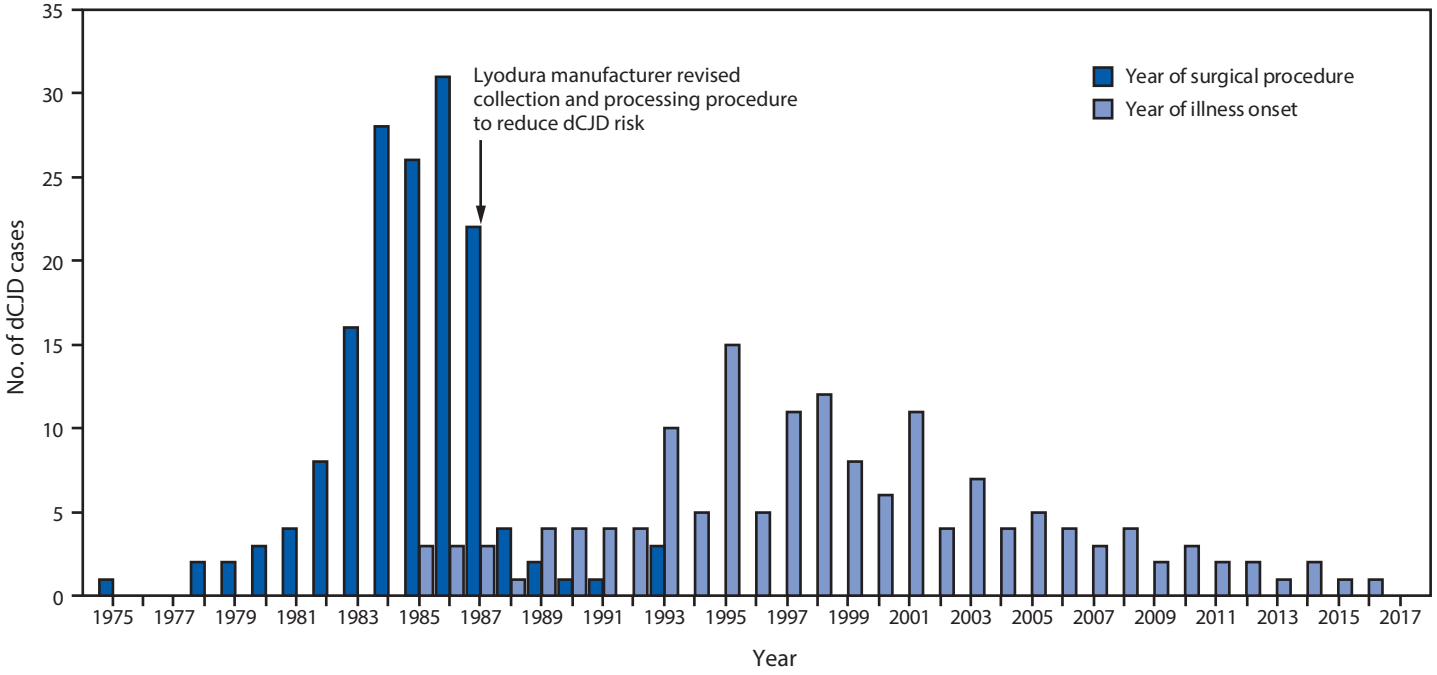
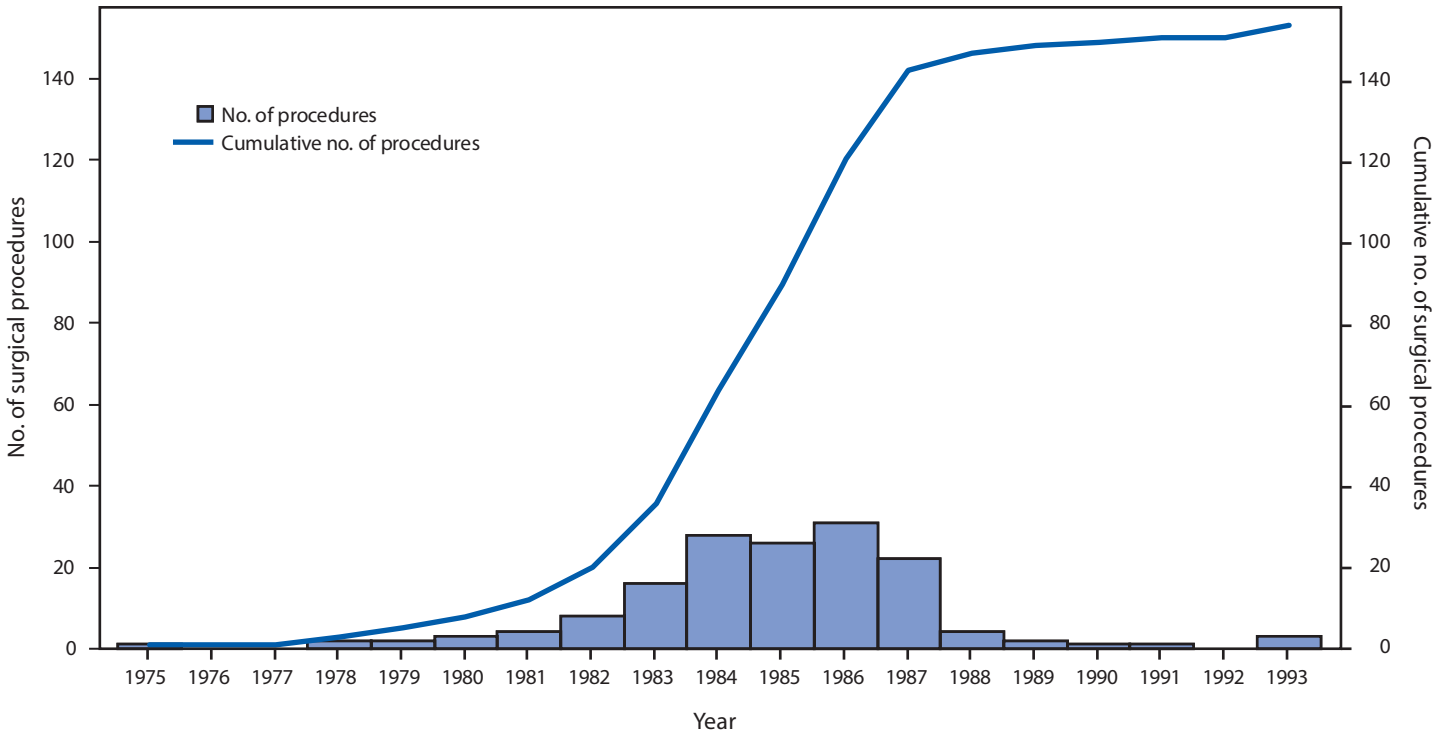


FIGURE 2. Number of surgical procedures linked to cases of dura mater graft–associated Creutzfeldt-Jakob Disease (dCJD),* by year of surgical procedure — Japan, 1975–1993†



* Among 154 dura mater graft procedures, the brand was documented as Lyodura in 140 (91%).
† The manufacturer of Lyodura reported that it revised its collection and processing procedures in May 1987 to reduce the risk for CJD contamination; the recommended shelf life for Lyodura was 5 years.

indicating that they might have received unexpired Lyodura produced before the company changed its processing procedures in 1987. In 1997, a case occurred in a patient with a history of two neurosurgical procedures in 1991. Investigation by J-CJDSC revealed that the patient had received a graft produced before 1987 during the first procedure. None of the dCJD cases identified to date received a dural graft after 1993.

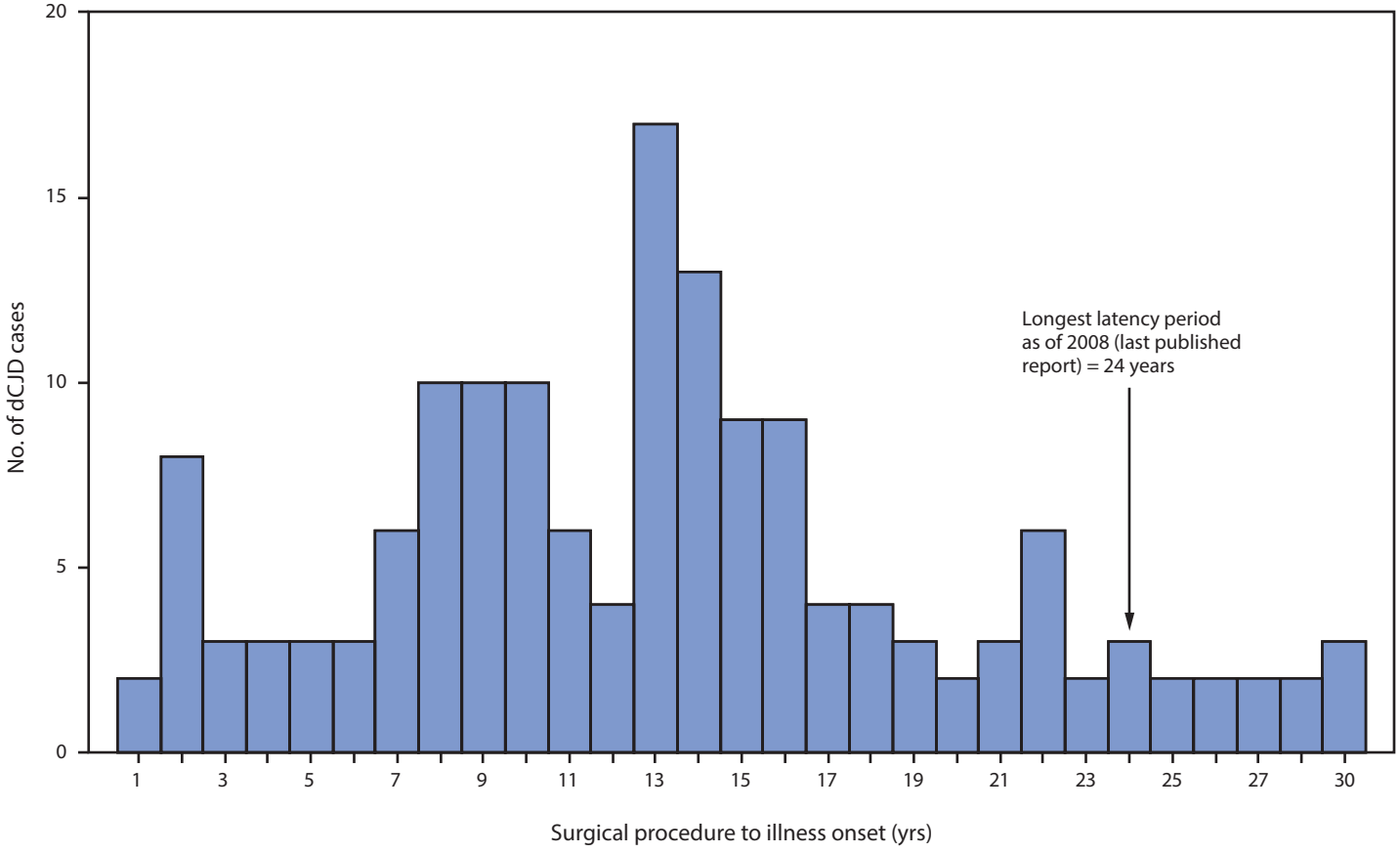
In Japan, it is estimated that 20,000 persons received a Lyodura graft each year during 1983–1987, approximately 50 times more than the estimated number of U.S. recipients (*4*). During this period, 123 Japanese patients who subsequently developed dCJD had surgical procedures, including 114 (93%) who had documentation of receipt of a Lyodura graft (the graft brand of the other nine patients was unknown), indicating that the risk for developing dCJD within 30 years of receiving a Lyodura graft in Japan was at least one per 877 (i.e., 114 dCJD cases per 100,000 Lyodura graft recipients). In this analysis, both the median and mean intervals from receipt of dural graft to illness onset (latency period) were 13 years (range = 1–30 years) (Figure 3). Since the update in 2008, 11 of the 22 newly reported dCJD cases have had latency periods exceeding 24 years, the longest interval reported in 2008 (*4*) (Figure 3). In three of these 11 cases, the latency period was 30 years, the longest reported to date.

Discussion

A comprehensive 2012 global summary of dCJD cases by country (*2*) reported that 142 (62%) of 228 cases of dCJD described worldwide occurred in Japan, and that at least one dCJD case was reported from 20 other countries. In the United States, four cases attributed to dura mater grafts have been identified; three were linked to a Lyodura graft produced before 1987, and one to a different commercially produced cadaveric dura mater graft. Lyodura grafts produced before 1987 were widely distributed to many countries, but most frequently to Japan.

During the U.S. investigation of the first Lyodura-associated CJD case in 1987 (*9*,*10*), investigators learned that the company mixed dura from multiple donors during batch processing of single lots and sterilized the grafts with gamma irradiation,

FIGURE 3. Interval from surgical procedure to illness onset* among 154 cases of dura mater graft–associated Creutzfeldt-Jakob disease (dCJD) — Japan, 1975–2017



* Median = 13 years; range = 1–30 years.

a procedure that does not inactivate prions (*10*). A Lyodura representative also reported that the company did not maintain records identifying donors, so they could not be traced. Lyodura was only available to U.S. hospitals by mail if ordered from a non-U.S. distributor because the manufacturer did not produce the product for distribution in the United States.

Owing to Lyodura's 5-year shelf life, it is likely that the eight dCJD patients in Japan who received Lyodura during 1988–1991 received grafts produced before the company changed its processing procedures in 1987. In addition, the three patients who received a graft in 1993 all received Lyodura grafts, one of which was documented to be an expired graft processed before 1987.

Age at onset of dCJD depends on the patient's age at receipt of a dural graft and the latency period. Although the latency period varies among patients, currently available data indicate that the upper limit is at least 30 years, which is longer than has been reported previously (*4*). The most recently diagnosed case, for example, occurred in a patient who received Lyodura during surgery for a craniopharyngioma in 1985 at age 27 years and developed dCJD 30 years later in 2015.

The findings in this report are subject to at least four limitations related to ascertainment of dCJD cases. First, because it is possible that dCJD patients with an unknown brand of dural graft did, in fact, receive Lyodura, it is likely that one dCJD case per 877 Lyodura recipients is an underestimate of the proportion of dCJD patients with Lyodura-related CJD. Second, the risk for a Lyodura-related CJD infection among dural graft recipients is unknown because many infected patients likely died from other causes before developing CJD. Third, additional dCJD cases related to receipt of Lyodura might still occur. The increased use of Lyodura in Japan is the most likely reason for the unusually high number of dCJD cases in Japan (*4*), although only estimates of the numbers of recipients in Japan and other countries, including the United States, are available. Finally, the medical conditions for which dura mater grafts were used in Japan differed from those in other countries (*5*): patients with dCJD in Japan more frequently received dura mater grafts for non–life-threatening conditions than did patients in other countries (*5*).

The cases described in this report indicate that recipients of prion-contaminated grafts could remain at risk for CJD for at least 30 years after receiving grafts. Given the known potential for even longer latency periods for prion diseases, this outbreak is expected to continue. The dCJD cases underscore the importance of establishing measures to eliminate or greatly reduce the possibility of CJD transmissions (e.g., strict donor screening, appropriate record keeping, prevention of cross-contaminations, and ideally, the use of validated sterilization methods) whenever human tissues, particularly of cadaveric origin, might be used to treat other patients. In addition, a system of human disease surveillance to detect the possible emergence of new sources of prion disease transmissions is needed. Furthermore, physicians maintaining a high index of suspicion for unusual prion disease cases, as well as a system of human disease surveillance to detect the emergence of new sources of prion disease transmissions, is needed to enable the prevention of infections Finally, maintaining surveillance for CJD in Japan is important to better assess the impact of the outbreak of dCJD and to identify additional cases.

Summary

What is already known about this topic?

During 1975–2008, a total of 132 cases of dura mater graft-associated Creutzfeldt-Jakob disease (dCJD), a fatal neurodegenerative disease caused by replicating, transmissible prion proteins, had been identified in Japan and accounted for >60% of patients worldwide with dCJD. This relatively high number of cases was most likely related to the increased use in Japan of the primary vehicle of transmission, Lyodura brand cadaveric grafts produced before May 1987, when the manufacturer changed its production process to reduce the risk for prion transmission.

What is added by this report?

During 2008–2017, an additional 22 dCJD patients, with onset from 1985 through 2016, were identified in Japan, resulting in 154 dCJD patients in Japan. No new dCJD patient whose surgery occurred after 1993 has been identified. However, the latency period is now known to be at least 30 years and because of the known potential for even longer latency periods for prion diseases, this outbreak is likely to continue.

What are the implications for public health practice?

The dCJD outbreak underscores the importance of strict screening of donors, appropriate record keeping, avoidance of comingling of grafts, and ideally, the use of validated sterilization procedures whenever dura mater grafts are manufactured. The long latency (decades) of human prion diseases can pose challenges to the detection of new sources of infection and highlights the need to recognize prion disease outbreaks and implement preventive measures as early as possible.

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Ministry of Health, Labour and Welfare, Japan.

Conflict of Interest

No conflicts of interest were reported.

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Vital Signs: Trends in Emergency Department Visits for Suspected Opioid Overdoses — United States, July 2016–September 2017

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On March 6, 2018, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

Abstract

Introduction: From 2015 to 2016, opioid overdose deaths increased 27.7%, indicating a worsening of the opioid overdose epidemic and highlighting the importance of rapid data collection, analysis, and dissemination.

Methods: Emergency department (ED) syndromic and hospital billing data on opioid-involved overdoses during July 2016–September 2017 were examined. Temporal trends in opioid overdoses from 52 jurisdictions in 45 states were analyzed at the regional level and by demographic characteristics. To assess trends based on urban development, data from 16 states were analyzed by state and urbanization level.

Results: From July 2016 through September 2017, a total of 142,557 ED visits (15.7 per 10,000 visits) from 52 jurisdictions in 45 states were suspected opioid-involved overdoses. This rate increased on average by 5.6% per quarter. Rates increased across demographic groups and all five U.S. regions, with largest increases in the Southwest, Midwest, and West (approximately 7%–11% per quarter). In 16 states, 119,198 ED visits (26.7 per 10,000 visits) were suspected opioid-involved overdoses. Ten states (Delaware, Illinois, Indiana, Maine, Missouri, Nevada, North Carolina, Ohio, Pennsylvania, and Wisconsin) experienced significant quarterly rate increases from third quarter 2016 to third quarter 2017, and in one state (Kentucky), rates decreased significantly. The highest rate increases occurred in large central metropolitan areas.

Conclusions and Implications for Public Health Practice: With continued increases in opioid overdoses, availability of timely data is important to inform actions taken by EDs and public health practitioners. Increases in opioid overdoses varied by region and urbanization level, indicating a need for localized responses. Educating ED physicians and staff members about appropriate services for immediate care and treatment and implementing a post-overdose protocol that includes naloxone provision and linking persons into treatment could assist EDs with preventing overdose.

Introduction

The opioid overdose epidemic continues to worsen in the United States. In 2016, a total of 63,632 drug overdose deaths occurred, a 21.4% increase from 2015 (*1*,*2*). Nearly two thirds (66.4%) of drug overdose deaths in 2016 involved prescription opioids, illicit opioids, or both, an increase of 27.7% from 2015 (*2*). Heroin and synthetic opioids (e.g., fentanyl) are driving increases in opioid-involved deaths (*2*–*4*). Tracking opioid overdoses is important to informing targeted interventions; however, timely national data on opioid overdoses evaluated in emergency departments (EDs) have been unavailable. Hospital billing data from 2014 indicate that approximately 92,000 ED visits occurred for unintentional, nonfatal opioid overdoses (*5*), but the time lag poses challenges to monitoring and response. ED syndromic data are important for tracking public health outbreaks (*6*) and can potentially identify changes in opioid overdoses quickly. Compared with billing data, syndromic data are collected in near real-time and can be viewed within 24–48 hours of an ED visit. ED syndromic data can serve as an early warning system to alert communities to a rise in opioid overdoses. Given the rapid availability of ED syndromic data, spikes in ED overdose trends are important to monitor and can potentially predict future fatal overdose trends and inform a more localized response. In addition, persons who experience an overdose are more likely to have a subsequent overdose (*7*); thus, EDs provide a crucial opportunity to link patients to treatment to avoid repeat overdoses. This report examines changes in opioid overdoses seen in the ED according to regional, state, and urbanization levels, to identify and track opioid overdoses and inform response efforts and recommendations for ED physicians and staff members.

Methods

ED visits* from CDC's National Syndromic Surveillance Program (NSSP)† and Enhanced State Opioid Overdose Surveillance (ESOOS)§ program were analyzed to track trends in suspected unintentional or undetermined¶ opioid overdoses (opioid overdoses) by quarter and U.S. region (Northeast, Southeast, Southwest, West, and Midwest)** during July 2016–September 2017. NSSP receives demographic and chief complaint data and *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) diagnostic codes for approximately 60% of ED visits†† in the United States (*8*,*9*). Only visits involving patients aged ≥11 years were analyzed because they account for the majority of overdoses (*2*). NSSP ED data were analyzed using the Electronic Surveillance System for the Early Notification of Community-based Epidemics (ESSENCE) software. ED visits with ICD-10-CM diagnosis codes T40.0–T40.4, T40.6, T40.69, F11.12, F11.22, or F11.92; or chief complaint text indicating opioid use, "opioid," and a word or abbreviation indicating an overdose (e.g., "OD") were classified as suspected opioid overdoses.§§ To account for changes occurring across time and region, quarterly trends for the percentage of ED visits involving suspected opioid overdoses (ED visits involving opioid overdoses divided by total ED visits and multiplied by 10,000) were analyzed and stratified by sex, age group, and U.S. region. Quarterly rate changes were calculated for all quarters. Yearly change, controlling for seasonal effects, was estimated as the change from third quarter 2016 to third quarter 2017. Significance testing was conducted using chi-square tests. Average linear quarterly percentage change was calculated for each strata using a joinpoint regression program.¶¶

Whereas NSSP includes syndromic data from a large number of states, the lowest level of aggregation is at the regional level, without additional approval from each state.*** Hence, ESOOS syndromic and hospital billing data were analyzed at the state and county level to identify suspected opioid overdoses during July 2016–September 2017 in 16 funded states (Delaware, Illinois, Indiana, Kentucky, Maine, Massachusetts, Missouri, New Hampshire, New Mexico, Nevada, North Carolina, Ohio, Pennsylvania, Rhode Island, West Virginia, and Wisconsin), providing a more localized view. Three states used the NSSP suspected opioid overdose definition and 13 states developed their own definitions to capture the specific text and diagnoses used in their hospitals. Quarterly percentage change in rates are presented by state and county urbanization level††† and analyzed as described.

* Emergency department visits are determined by considering facilities that are categorized as "emergency" and for patients who are deemed "emergency" status and excludes patients designated as only inpatient or only outpatient.

† NSSP's BioSense platform launched in 2003 to establish a national public health surveillance system for early detection and assessment of potential bioterrorism-related illness. It has expanded to track infectious diseases and injuries. https://www.cdc.gov/nssp/biosense/index.html.

§ Enhanced State Opioid Overdose Surveillance (ESOOS) (#CDC-RFA-CE16-1608) started in 2016 and now funds 32 states and the District of Columbia to increase the timeliness of all suspected nonfatal drug, opioid, and heroin opioid overdose reporting (e.g., emergency department); increase the timeliness and comprehensiveness of fatal opioid overdose reporting and associated risk factors; and disseminate findings to stakeholders working to prevent or respond to opioid-involved overdoses. https://www.cdc.gov/drugoverdose/foa/state-opioid-mm.html.

¶ Analyses were intended to include nonfatal opioid overdose visits with unintentional and undetermined intents. ED visits resulting in death were not excluded, but accounted for only 1% of total opioid overdose ED visits in ESSENCE during the study period (data not shown). Though not explicitly excluded, *International Classification of Diseases, Tenth Revision, Clinical Modification* diagnosis codes or chief complaint text fields that mention intentional or assault-related opioid overdoses were not included because trends in unintentional overdoses are expected to differ from intentional overdoses. In addition, intentional opioid overdose is not as common as unintentional overdose. During 2006–2011, 26.5% of opioid overdoses were intentional; whereas, 53.5% and 20.0% were for unintentional and undetermined intents, respectively.

** Listed are the states within regions that currently share data with NSSP and had data available for the timeframe in this study. The Northeast region includes HHS Regions 1 (Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont), 2 (New Jersey and New York), and 3 (District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia); the Southeast region includes HHS Region 4 (Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee); the Southwest region includes HHS Region 6 (Arkansas, Louisiana, New Mexico, and Texas); the Midwest region includes HHS Regions 5 (Indiana, Illinois, Michigan, Minnesota, Ohio, and Wisconsin) and 7 (Iowa, Kansas, Missouri, and Nebraska); and the West region includes HHS Regions 8 (Colorado, Montana, North Dakota, and Utah), 9 (Arizona, California, and Nevada) and 10 (Alaska, Idaho, Oregon, and Washington). Some of the states listed above do not provide data for the entire state; for example, Texas (Region 6) has data from 50 counties; Iowa (Region 7) has data from one county; Colorado (Region 8) has data from three counties; and California (Region 9) has data from seven counties.

†† A 3–4 week delay usually occurs in the submission of discharge diagnosis codes that might affect the ability of the state case definitions to detect overdoses when free text information is unavailable or sparse. In addition, availability and completeness of data vary across the approximately 2,500 EDs with chief complaint text and discharge diagnosis codes missing in 15% and 46% of ED visits in NSSP, respectively.

§§ Additional information on the development of the opioid overdose case definition is available upon request to the corresponding author.

¶¶ https://surveillance.cancer.gov/joinpoint/.

*** State and local health departments using NSSP have access to their own detailed data (i.e., case-level data) and aggregate national and regional data and can share their detailed data with any other jurisdiction or CDC. CDC has access to all of the detailed data for operations and management purposes. In addition, for surveillance purposes, CDC can run queries against a subset of data elements and generate and report regional and national results. With approval, CDC also conducts collaborative analyses with jurisdictions and can access their detailed data. With ESOOS, states could allow CDC access to their data in NSSP for analysis in ESSENCE, or they could provide data (either syndromic or hospital billing) in different formats.

††† The six classification levels for counties were 1) large central metro: part of a metropolitan statistical area with ≥1 million population and covers a principal city; 2) large fringe metro: part of a metropolitan statistical area with ≥1 million population but does not cover a principal city; 3) medium metro: part of a metropolitan statistical area with ≥250,000 but <1 million population; 4) small metro: part of a metropolitan statistical area with <250,000 population; 5) micropolitan (nonmetro): part of a micropolitan statistical area (has an urban cluster of ≥10,000 but <50,000 population); and 6) noncore (nonmetro): not part of a metropolitan or micropolitan statistical area.

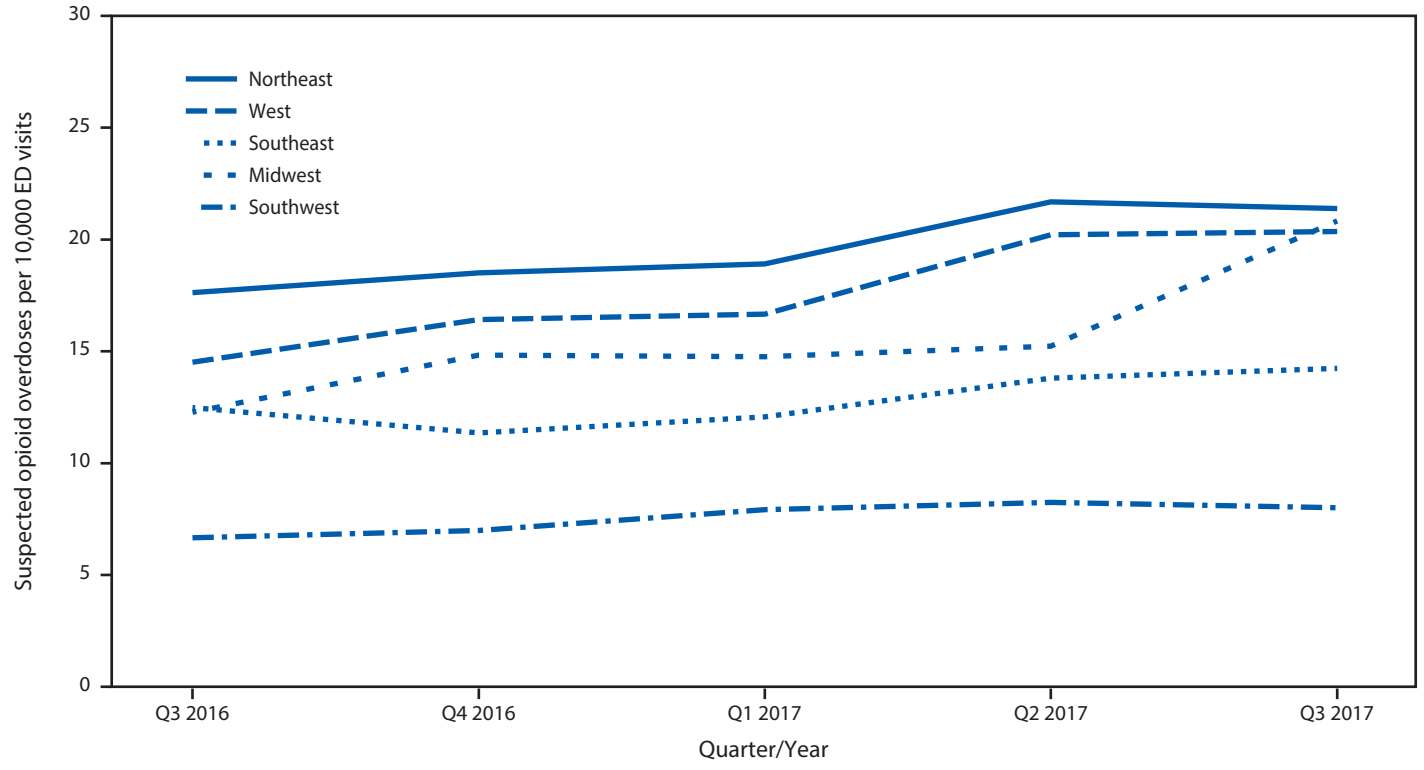
Results

Among approximately 91 million ED visits captured in NSSP during July 2016–September 2017, a total of 142,557 (15.7 per 10,000 visits) were suspected opioid overdoses. Opioid overdose ED visits in NSSP increased 29.7% from third quarter 2016 (July–September) to third quarter 2017; all five U.S. regions experienced prevalence increases (Figure 1), with the largest in the Midwest (69.7%), followed by the West (40.3%), Northeast (21.3%), Southwest (20.2%), and Southeast (14.0%) (Table 1). Substantial increases occurred among all demographic groups during the same period, including males (30.2%), females (24.0%), and persons aged 25–34 years (30.7%), 35–54 years (36.3%), and ≥55 years (31.9%). Most regions, age groups, and both sexes also experienced significant positive linear trends across all five quarters.

Among approximately 45 million ED visits reported by the 16 ESOOS states from July 2016 through September 2017, a total of 119,198 (26.7 per 10,000 visits) were suspected opioid overdoses. Opioid overdose ED visits increased 34.5% from third quarter 2016 to third quarter 2017 (Table 2). Ten states experienced significant increases in prevalence during this period, although substantial variation was observed among states in the same region. For example, in the Northeast, significant increases occurred in Delaware (105.0%), Pennsylvania (80.6%), and Maine (34.0%), but other states, including Massachusetts, New Hampshire, and Rhode Island experienced nonsignificant (<10%) decreases. In the Southeast, a significant increase (31.1%) occurred in North Carolina, a significant decrease (15.0%) occurred in Kentucky, and a small, nonsignificant decrease (5.3%) was observed in West Virginia. In the West, a significant increase (17.9%) occurred in Nevada. All states in the Midwest reported significant increases, including Wisconsin (108.6%), Illinois (65.5%), Indiana (35.1%), Ohio (27.7%), and Missouri (21.4%).

All urbanization levels experienced large and significant increases in ED opioid overdose visits from third quarter 2016

FIGURE 1. Quarterly rate* of suspected opioid overdose, by U.S. region† — 52 jurisdictions in 45 states, National Syndromic Surveillance Program, July 2016–September 2017§



Abbreviation: ED = emergency department.

* Per 10,000 ED visits.

† *Northeast Region:* HHS Region 1 (Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont), Region 2 (New Jersey and New York), and Region 3 (District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia); *Southeast Region:* HHS Region 4 (Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee); *Southwest Region:* HHS Region 6 (Arkansas, Louisiana, New Mexico, and Texas); *Midwest Region:* HHS Region 5 (Indiana, Illinois, Michigan, Minnesota, Ohio, and Wisconsin) and Region 7 (Iowa, Kansas, Missouri, and Nebraska); *West Region:* HHS Region 8 (Colorado, Montana, North Dakota, and Utah), Region 9 (Arizona, California, and Nevada) and Region 10 (Alaska, Idaho, Oregon, and Washington).

§ Data current as of December 13, 2017.

TABLE 1. Change in quarterly rates*,† for suspected opioid overdose, by U.S. region,§ sex, and age group — 52 jurisdictions in 45 states, National Syndromic Surveillance Program, July 2016–September 2017¶

Characteristic	% Change					Average quarterly % change (95% CI)
	Q3 2016–Q4 2016	Q4 2016–Q1 2017	Q1 2017–Q2 2017	Q2 2017–Q3 2017	Q3 2016–Q3 2017	
Overall	**3.89**	**2.43**	**13.15**	**7.68**	**29.65****	**5.6 (1.8 to 9.5)****
U.S. Region						
Northeast	5.01	2.17	14.67	-1.40	21.30**	4.7 (-2.4 to 12.2)
Southeast	-9.08	6.32	14.29	3.21	14.03**	5.5 (0.6 to 10.6)**
Southwest	4.85	13.35	4.12	-2.87	20.19**	11.4 (1.1 to 22.9)**
Midwest	20.84	-0.48	3.19	36.73	69.67**	9.2 (4.1 to 14.6)**
West	13.11	1.50	21.28	0.75	40.28**	6.9 (3.4 to 10.5)**
Sex						
Male	6.21	2.62	10.66	7.96	30.21**	6.8 (4.4 to 9.2)**
Female	1.93	2.01	11.90	6.57	23.99**	5.8 (2.3 to 9.4)**
Age group (yrs)						
15–24	-1.11	-2.69	9.46	1.87	7.31**	2.1 (-1.6 to 5.9)
25–34	5.63	3.65	10.23	8.28	30.67**	6.9 (4.7 to 9.1)**
35–54	6.17	3.72	11.81	10.70	36.28**	8.0 (5.0 to 11.0)**
≥55	9.33	1.03	12.50	6.17	31.93**	7.1 (4.3 to 9.9)**

Abbreviation: CI = confidence interval.

* Per 10,000 emergency department visits.

† Using the indicator counts and denominators, a rate of ED visits for each quarter was created using the count of suspected opioid overdose ED visits divided by the total number of ED visits for each quarter. Percentage change in rates subtracted the prior quarter from the current quarter then divided by the prior quarter multiplied by 100%.

§ The Northeast region includes HHS Regions 1 (Maine, Massachusetts, New Hampshire, Rhode Island and Vermont), 2 (New Jersey and New York), and 3 (District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia); the Southeast region includes HHS Region 4 (Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee); the Southwest region includes HHS Region 6 (Arkansas, Louisiana, New Mexico, and Texas); the Midwest region includes HHS Regions 5 (Indiana, Illinois, Michigan, Minnesota, Ohio, and Wisconsin) and 7 (Iowa, Kansas, Missouri, and Nebraska); and the West region includes HHS Regions 8 (Colorado, Montana, North Dakota, and Utah), 9 (Arizona, California, and Nevada), and 10 (Alaska, Idaho, Oregon, and Washington).

¶ Data current as of December 13, 2017.

** Statistically significant ($p<0.05$).

to third quarter 2017, including large central metropolitan (54.1%), medium metropolitan (42.6%), small metropolitan (36.9%), micropolitan (23.6%), large fringe metropolitan (21.1%), and noncore (20.6%) areas. Large central metropolitan areas experienced significant linear increases (Figure 2).

Discussion

Despite data from the 2016 National Survey on Drug Use and Health indicating that heroin use and opioid misuse might be stabilizing (*10*), this analysis suggests that prevalence of suspected opioid overdose ED visits substantially increased in NSSP (29.7%) and ESOOS (34.5%) states from third quarter 2016 to third quarter 2017. Increases in ESOOS states were greater than those in NSSP states, which is likely driven by the higher mortality burden of drug overdose in ESOOS states (*2*). The increases occurred in most demographic groups and U.S. regions and suggest a worsening of the epidemic into late 2017 in several states, possibly related to the wide variation in the availability and potency of illicit drug products (e.g., fentanyl sold as or mixed into heroin) that increase overdose risk and drive increases in mortality (*3*,*4*,*11*). Enhanced prevention and treatment efforts in the ED and access to evidence-based opioid use disorder treatment, including medication-assisted treatment and harm reduction services, are needed (*12*).

The sharp increases and variation across localities indicate that real-time data are needed to better detect and respond to overdose spikes and to facilitate response coordination for regional or multiple state outbreaks. Enhanced data sharing among contiguous localities is needed because regional variation in drug products often cross state or county borders (*11*). Increases in the Midwest in NSSP and all five Midwestern ESOOS states (Illinois, Indiana, Missouri, Ohio, and Wisconsin) are consistent with opioid overdose death trends (*2*). However, increases in prevalence of ED visits for suspected opioid overdoses in the Southwest and West and decreases in the Southeast (Kentucky and West Virginia) were unanticipated and might foreshadow changes in opioid overdose death trends in 2017. The significant decreases in Kentucky might be explained by fluctuations in drug supply and warrant confirmation. In the Northeast, several states reported small decreases (Massachusetts, New Hampshire, and Rhode Island) or large increases (Delaware, Maine, and Pennsylvania) that are consistent with early 2017 drug overdose death reports from these states,§§§ possibly related

§§§ Additional information is available on estimates of drug overdose deaths in 2017 compared with 2016 in Massachusetts (https://www.mass.gov/files/documents/2017/11/15/2017-annual-update-action-items-gov-working-group.pdf), New Hampshire (https://www.dhhs.nh.gov/dcbcs/bdas/documents/dmi-october-2017.pdf), Maine (http://www.maine.gov/ag/news/article.shtml?id=765461) and Rhode Island (http://www.health.ri.gov/data/drugoverdoses/) as well as Delaware, Maine, and Pennsylvania (https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm).

TABLE 2. Change in quarterly and annual rates*,† for suspected opioid overdose, by state — 16 states,§ Enhanced State Opioid Overdose Surveillance program, July 2016–September 2017¶

Region/State	% Change					Average quarterly % change (95% CI)
	Q3 2016–Q4 2016	Q4 2016–Q1 2017	Q1 2017–Q2 2017	Q2 2017–Q3 2017	Q3 2016–Q3 2017	
Overall	**8.91**	**9.09**	**13.06**	**0.12**	**34.49****	**8.4 (4.8 to 12.0)****
Northeast						
Delaware	8.77	10.95	43.00	18.76	104.95**	20.9 (10.5 to 32.2)**
Maine	2.57	-8.13	29.45	9.81	33.95**	7.9 (-2.4 to 19.3)
Massachusetts	-8.48	-11.48	3.11	18.97	-0.62	-1.0 (-11.4 to 10.6)
New Hampshire	-4.33	-17.91	29.67	-8.76	-7.09	-0.8 (-12 to 11.7)
Pennsylvania	29.79	17.51	25.89	-5.94	80.59**	17.0 (5.6 to 29.7)**
Rhode Island	2.80	4.54	5.44	-11.91	-0.18	0.9 (-5.0 to 7.2)
Southeast						
Kentucky	-26.94	40.45	3.52	-20.02	-15.04**	0.5 (-16.3 to 20.6)
North Carolina	-0.43	3.28	15.20	10.63	31.05**	7.4 (1.8 to 13.4)**
West Virginia	43.31	-16.64	4.02	-23.77	-5.28	-2.5 (-19.3 to 17.9)
Southwest						
New Mexico	26.11	1.51	-5.01	-10.93	8.30	1.2 (-10.4 to 14.4)
Midwest						
Illinois	23.13	1.48	2.82	28.80	65.47**	11.1 (2.7 to 20.1)**
Indiana	-10.15	11.20	10.45	22.43	35.11**	8.4 (-1.9 to 19.8)
Missouri	4.77	-1.77	9.54	7.67	21.38**	4.7 (1.2 to 8.3)**
Ohio	22.74	25.67	21.67	-31.94	27.74**	9.6 (-12.2 to 36.7)
Wisconsin	17.12	67.28	3.22	3.14	108.58**	22.3 (4.2 to 43.7)**
West						
Nevada	13.69	-9.46	11.37	2.82	17.88**	3.4 (-2.3 to 9.5)

Abbreviation: CI = confidence interval.

* Per 10,000 emergency department visits.

† Using the indicator counts and denominators, a rate of ED visits for each quarter was created using the count of suspected opioid overdose ED visits divided by the total number of ED visits for each quarter. Percentage change in rates subtracted the prior quarter from the current quarter then divided by the prior quarter multiplied by 100%.

§ Delaware, Illinois, Indiana, Kentucky, Maine, Massachusetts, Missouri, Nevada, New Hampshire, New Mexico, North Carolina, Ohio, Pennsylvania, Rhode Island, West Virginia, and Wisconsin.

¶ Data current as of January 8, 2018.

** Statistically significant (p<0.05).

to implementation of interventions including expansion of access to medication-assisted treatment.¶¶¶

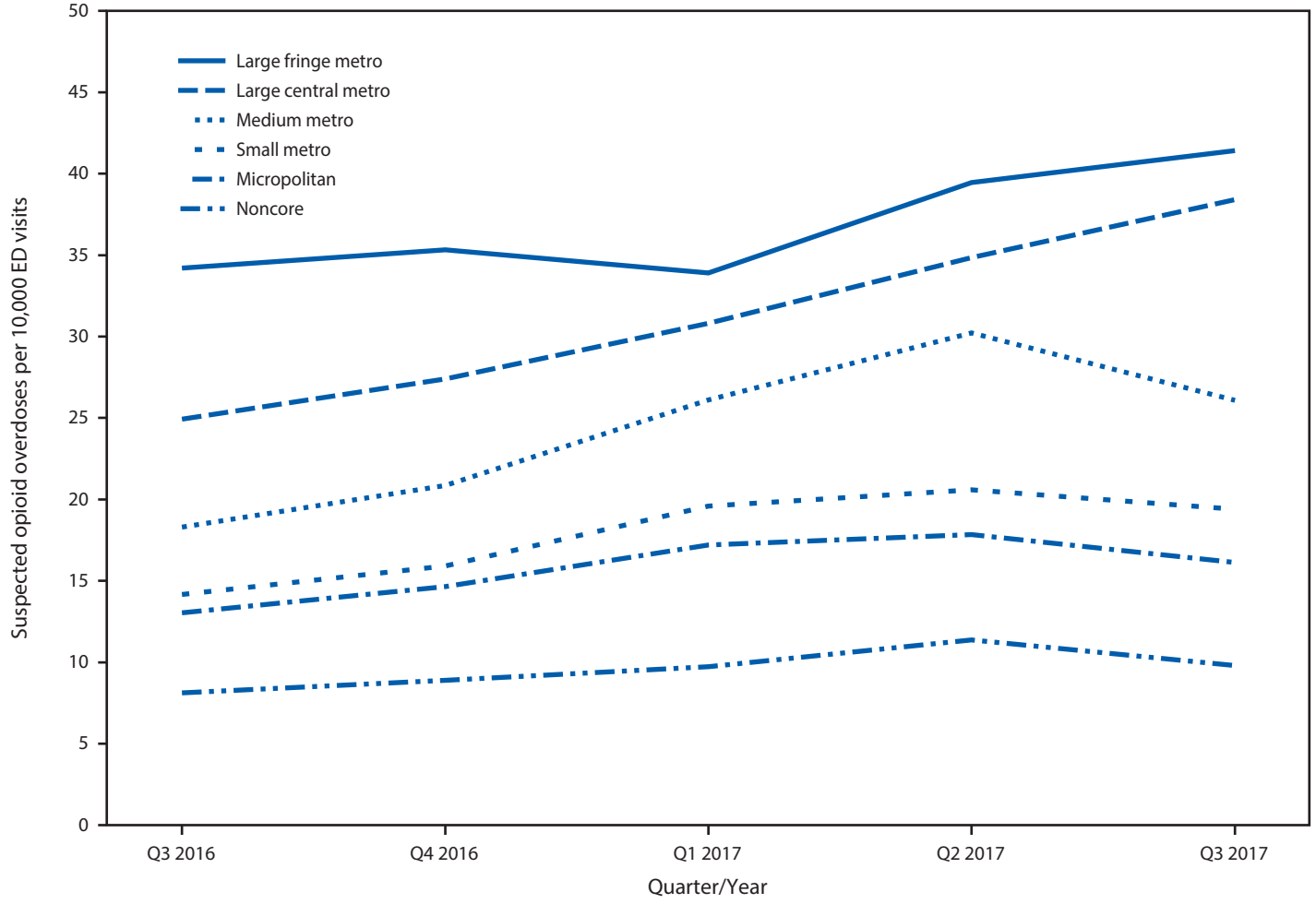
The increases in opioid overdose rates in ESOOS metropolitan counties, specifically in large central (54.1%), medium (42.6%), and small metropolitan (36.9%) counties from third quarter 2016 to third quarter 2017 are consistent with previous reports indicating that heroin overdose hospitalizations, ED visits, and deaths were highest in metropolitan areas (*2*–*5*). Two of the three areas with highest rates of heroin overdose deaths, large central metropolitan and medium metropolitan areas (*2*), reported the sharpest increases in opioid overdose ED visits, highlighting the need for targeted efforts to reduce the prevalence of opioid overdose in these areas and slow or reverse increases in overdoses driven by changes in the illicit opioid drug market. The magnitude of opioid pain reliever misuse and heroin use, however, only varies slightly across urbanization levels, and all urbanization levels report increases in ED visits for opioid overdoses (*5*). Thus, generalized public health interventions tailored to each community context are necessary.

The findings in this report are subject to at least three limitations. First, NSSP and ESOOS case definitions might underestimate or overestimate opioid overdoses based on coding differences in hospitals, the availability of ICD-10-CM diagnostic codes, and the quality of chief complaint data (*13*). Consequently, analyses focused on comparison of trends by region and state, not of absolute rates. Findings should be verified against other data sources, and trends are expected to change slightly as visit data are updated. Second, hospital participation in NSSP varied across quarters; therefore, results could be related to changes in hospital participation. Finally, findings are not generalizable to areas not participating in NSSP or ESOOS.

With the rapidly evolving opioid overdose epidemic, ED data can serve as an early warning system, alerting communities to changes in prevalence of overdoses and permitting a timely, informed, and localized response that could facilitate a more rapid and coordinated response including targeting of resources

¶¶¶ Additional information is available on Rhode Island's plan on addiction and overdose (http://www.health.ri.gov/news/temp/RhodeIslandsStrategicPlanOnAddictionAndOverdose.pdf), State of Rhode Island Executive Order 17-07 (http://www.governor.ri.gov/documents/orders/ExecOrder-17-07-07122017.pdf) and Commonwealth of Massachusetts governor's working group on opioid overdose: action items (https://www.mass.gov/files/documents/2017/11/15/2017-annual-update-action-items-gov-working-group.pdf).

FIGURE 2. Quarterly rate* of suspected opioid overdose, by level of county urbanization†,§ — 16 states,¶ Enhanced State Opioid Overdose Surveillance program, July 2016–September 2017**



Abbreviation: ED = emergency department.

* Per 10,000 ED visits.

† The six classification levels for counties were 1) large central metro: part of a metropolitan statistical area with ≥1 million population and covers a principal city; 2) large fringe metro: part of a metropolitan statistical area with ≥1 million population but does not cover a principal city; 3) medium metro: part of a metropolitan statistical area with ≥250,000 but <1 million population; 4) small metro: part of a metropolitan statistical area with <250,000 population; 5) micropolitan (nonmetro): part of a micropolitan statistical area (has an urban cluster of ≥10,000 but <50,000 population); and 6) noncore (nonmetro): not part of a metropolitan or micropolitan statistical area.

§ The average linear quarterly percentage change (QPC) was significant for large central metro (average QPC = 11.7, 95% confidence interval [CI] = 10.7 to 12.7, p<.001). QPCs for large fringe metro (average QPC = 5.1, 95% CI = -0.3 to 10.7); medium metro (average QPC = 11.4, 95% CI = -1.3 to 25.8); small metro (average QPC = 9.3, 95% CI = -0.1 to 19.5); micropolitan (average QPC = 6.4, 95% CI = -3.1 to 16.9); and noncore (average QPC = 6.4, 95% CI = -2.8 to 16.5) were not significant.

¶ Delaware, Illinois, Indiana, Kentucky, Maine, Massachusetts, Missouri, New Hampshire, New Mexico, Nevada, North Carolina, Ohio, Pennsylvania, Rhode Island, West Virginia, and Wisconsin.

** Data current as of January 8, 2018.

(e.g., increase naloxone supply to affected areas), and issuance of emergency health alerts or advisories. EDs also can serve as a point of intervention for persons who experience an overdose and are at higher risk for a subsequent overdose. Educating ED physicians and staff members about appropriate services for immediate care and treatment and post-overdose protocols are important to preventing future overdoses among their patients. ED physicians could assess history of prescription drug use during care by accessing data from prescription drug monitoring programs and provide education to patients. Post-overdose protocols can help prevent subsequent overdose by providing naloxone and connecting patients with case management services or peer navigators to help link them into treatment and harm reduction services, including syringe services programs (*12*). Opioid overdoses continue to increase in most jurisdictions, and rapid response efforts and a multisectoral approach are needed to reduce and prevent overdoses and their associated morbidity and mortality.

Key Points

- During July 2016–September 2017, emergency department (ED) visits among those aged ≥11 years for opioid overdoses in the United States increased 29.7% overall and 34.5% in 16 states with high prevalence of overdose mortality. Significant rate increases were found in five Midwest region states (largest in Wisconsin [109%]) and in three Northeast region states (largest in Delaware [105%]); nonsignificant decreases (<10%) were found in three Northeast states. In the Southeast, rates increased in North Carolina (31%) and decreased in Kentucky (15.0%).
- Every demographic group reported substantial rate increases, including males (30%) and females (24%) and persons in all age groups (25–34 [31%]; 35–54 [36%], and ≥55 [32%] years).
- The highest opioid overdose rate increases occurred in large central metropolitan areas (a population of ≥1 million and covering a principal city).
- ED syndromic data can serve as an early warning system to alert communities of changes in opioid overdoses because of the rapid availability of this data (i.e., can be viewed within 24–48 hours of an ED visit).
- Treatment in EDs for drug overdose provides opportunities for intervention and prevention, which require coordination among all involved health care providers and agencies.
- Additional information is available at https://www.cdc.gov/vitalsigns/.

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Conflict of Interest

No conflicts of interest were reported.

[1]Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, CDC; [2]Division of Health Informatics and Surveillance, Center for Surveillance, Epidemiology, and Laboratory Services, CDC.

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Notes from the Field

Brucella abortus Vaccine Strain RB51 Infection and Exposures Associated with Raw Milk Consumption — Wise County, Texas, 2017

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In July 2017, the Texas Department of State Health Services (DSHS) Region 2/3 office reported a human case of brucellosis associated with the consumption of raw (unpasteurized) cow's milk purchased from a dairy in Paradise, Texas. CDC's Bacterial Special Pathogens Branch (BSPB) confirmed the isolate as *Brucella abortus* vaccine strain RB51 (RB51).

Brucellosis is a zoonotic bacterial disease that affects humans and many animal species. In humans, the disease is characterized by fever and nonspecific influenza-like symptoms that frequently include myalgia, arthralgia, and night sweats. Without appropriate treatment, brucellosis can become chronic, and life-threatening complications can arise. Human brucellosis transmitted by cattle was once common in the United States. Control strategies have focused on elimination of brucellosis through vaccination and surveillance of cattle herds, in addition to milk pasteurization. Because of these measures, domestically acquired human cases are now rare (*1*).

RB51, a live-attenuated vaccine used to prevent *B. abortus* infection in cattle, has been documented to cause human disease, most commonly through occupational exposures such as needle sticks (*2*). Importantly, unlike wild strains of *B. abortus,* RB51 does not stimulate an antibody response detectable by routine serological assays, requiring culture for confirmation. Additionally, RB51 is resistant to rifampin, a common treatment choice for human brucellosis (*2,3*). This case represents the first documented instance of human brucellosis caused by RB51 through consumption of raw milk acquired in the United States.

Following isolation of RB51 from the patient's blood, bulk milk tank samples from the farm tested positive for RB51 by polymerase chain reaction and bacterial culture. Culture of individual milk samples from all 43 cows in the herd identified two RB51 culture-positive cows. Subsequent whole genome sequencing indicated genetic relatedness between the cow and human isolate.

In Texas, farm sales of raw milk products to the public are legal with a "Grade 'A' Raw for Retail" license, regulated by the DSHS Milk and Dairy Group. By the end of August, through correspondence with the dairy, DSHS had identified approximately 800 persons who might have visited the farm during June 1–August 7. On September 1, Texas DSHS and BSPB began notification calls to these households, recommending that all exposed persons (i.e., those who consumed raw milk products from the farm during June 1–August 7) seek medical attention and begin 3 weeks of postexposure prophylaxis, even if asymptomatic (*4*).

Contact information was available for 582 households. The notification was issued successfully to 397 (68.2%) households. Among these notified households, 324 (81.6%) identified at least one exposed household member. Contacted persons referred 34 additional potentially exposed households, including households from seven other states.* A nationwide press release and Health Alert Network Health Advisory were issued in September to facilitate further identification of exposed persons (*5*).

To date, there are no other confirmed cases associated with this investigation. CDC and Texas DSHS continue measures to increase awareness among health care providers and the public regarding unique challenges associated with treatment and diagnosis of RB51 in humans and the risks of consuming raw milk.

* Alabama, Arkansas, California, North Dakota, Ohio, Oklahoma, and Tennessee.

Conflict of Interest

No conflicts of interest were reported.

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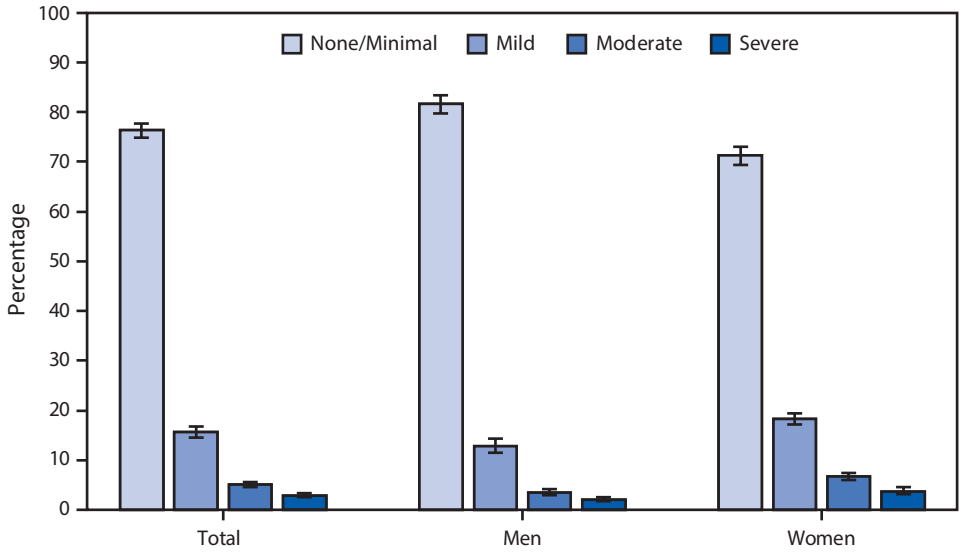
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage* of Adults Aged ≥20 Years Reporting Depressive Symptoms† in the Past 2 Weeks, by Sex — National Health and Nutrition Examination Survey, United States, 2013–2016



* With 95% confidence intervals indicated with error bars.
† Depression symptom categories were determined based on responses to the Patient Health Questionnaire (PHQ-9) screening instrument. For questions about frequency of symptoms, the response categories, "not at all," "several days," "more than half the days," and "nearly every day," were scored as 0 to 3 with a total score of 0 to 27. Depression scores have been categorized as the following: 0–4 as none or minimal depression, 5–9 as mild, 10–14 as moderate, 15–19 as moderately severe, and 20–27 as severe. For this analysis, scores of ≥15 were termed "severe" depressive symptoms.

During 2013–2016, 76.3% of adults aged ≥20 years had no or minimal depressive symptoms, 15.6% had mild symptoms, 5.1% had moderate symptoms, and 2.9% had severe depressive symptoms. A lower percentage of women than men had no or minimal depressive symptoms (71.3% versus 81.6%), but a higher percentage of women than men had mild (18.3% versus 12.8%), moderate (6.7% versus 3.4%), or severe (3.7% versus 2.1%) symptoms.

Source: NCHS Data Brief No. 303. https://www.cdc.gov/nchs/data/databriefs/db303.pdf.

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