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West Nile Virus and Other Domestic Nationally Notifiable Arboviral Diseases — United States, 2018

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Arthropodborne viruses (arboviruses) are transmitted to humans primarily through the bites of infected mosquitoes and ticks. West Nile virus (WNV) is the leading cause of domestically acquired arboviral disease in the continental United States (*1*). Other arboviruses, including eastern equine encephalitis, Jamestown Canyon, La Crosse, Powassan, and St. Louis encephalitis viruses, cause sporadic cases of disease and occasional outbreaks. This report summarizes surveillance data reported to CDC for 2018 on nationally notifiable arboviruses. It excludes dengue, chikungunya, and Zika viruses because they are primarily nondomestic viruses typically acquired through travel. In 2018, 48 states and the District of Columbia (DC) reported 2,813 cases of domestic arboviral disease, including 2,647 (94%) WNV disease cases. Of the WNV disease cases, 1,658 (63%) were classified as neuroinvasive disease (e.g., meningitis, encephalitis, and acute flaccid paralysis), for a national incidence of 0.51 cases of WNV neuroinvasive disease per 100,000 population. Because arboviral diseases continue to cause serious illness and have no definitive treatment, maintaining surveillance is important to direct and promote prevention activities. Health care providers should consider arboviral infections in patients with aseptic meningitis or encephalitis, perform appropriate diagnostic testing, and report cases to public health authorities.

Arboviruses are maintained in a transmission cycle between arthropods and vertebrate hosts, including humans and other animals (*2*). Humans primarily become infected when bitten by an infected mosquito (West Nile, La Crosse, Jamestown Canyon, St Louis encephalitis, and eastern equine encephalitis viruses) or tick (Powassan virus). Most human infections are asymptomatic; symptomatic infections commonly manifest as a systemic febrile illness and less commonly as neuroinvasive disease.

Most endemic arboviral diseases are nationally notifiable and are reported by state health departments to CDC through ArboNET, the national arbovirus surveillance system, using standard surveillance case definitions that include clinical and laboratory criteria (*3*). Cases are reported by the patient's state of residence. Confirmed and probable cases were included in this analysis. Cases reported as acute flaccid paralysis, encephalitis, meningitis, or an unspecified neurologic presentation were classified as neuroinvasive disease; cases with more than one neuroinvasive presentation were counted once according to the order specified above. Other clinical presentations were considered nonneuroinvasive disease. Incidence rates were calculated using neuroinvasive disease cases and the U.S. Census 2018 midyear population estimates.

A total of 2,813 cases of domestic arboviral disease were reported to CDC for 2018. Cases were caused by WNV (2,647 cases, 94%), La Crosse virus (86), Jamestown Canyon virus (41), Powassan virus (21), St. Louis encephalitis virus (eight), eastern equine encephalitis virus (six), and unspecified California serogroup virus (four). Cases were reported from

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all states except Hawaii and New Hampshire. Of the 3,142 U.S. counties, 858 (27%) reported one or more arboviral disease cases.

Overall, 2,647 WNV disease cases were reported from 787 counties in 48 states and DC. Of these, 1,658 (63%) cases were neuroinvasive and 2,435 (92%) patients had illness onset during July–September (Table 1). In 2018, WNV disease was reported for the first time from a resident of Alaska; however, the patient's likely location of infection was reported as a state with previously documented transmission. Two WNV disease cases were reported in solid organ transplant recipients with a common donor, and subsequent investigation demonstrated transmission via organ transplantation. The median age of patients with WNV disease was 59 years (interquartile range [IQR] = 44–70); 1,638 (62%) were male. A total of 1,774 (67%) patients were hospitalized, and 167 (6%) died. The median age of patients who died was 74 years (IQR = 67–82).

Among the 1,658 WNV neuroinvasive cases, 908 (55%) were reported as encephalitis, 542 (33%) as meningitis, 70 (4%) as acute flaccid paralysis, and 138 (8%) as an unspecified neurologic presentation. Of the 70 patients with acute flaccid paralysis, 25 (36%) also had encephalitis or meningitis. Among patients with neuroinvasive disease, 1,541 (93%) were hospitalized and 165 (10%) died. The incidence of WNV neuroinvasive disease in the United States was 0.51 per 100,000 population (Table 2). The highest incidence rates occurred in North Dakota (7.89 per 100,000), Nebraska (6.43), South Dakota (5.33), Montana (2.35), and Iowa (1.87) (Figure). The largest number of cases were reported from California (154), Illinois (126), Nebraska (124), Texas (108), and Pennsylvania (95), which together accounted for nearly 37% of neuroinvasive disease cases. The incidence of WNV neuroinvasive disease increased with age group, from 0.03 per 100,000 in children aged <10 years to 1.66 in adults aged ≥70 years. Incidence was higher among males (0.65 per 100,000) than among females (0.36 per 100,000).

La Crosse virus disease cases (86) were reported from seven states, primarily in the East North Central and South Atlantic divisions (Table 2). La Crosse virus disease was reported for the first time in a Rhode Island resident; however, the patient's likely location of infection was reported as a state with previously documented transmission. The median age of patients was 8 years (IQR = 5–12), and 81 (94%) were aged <18 years (Table 1). Illness onset dates ranged from May through October, with 61 (71%) reporting onset during July–September. Eighty-three (97%) cases were neuroinvasive, and 82 (95%) patients were hospitalized; no cases were fatal.

Jamestown Canyon virus disease cases (41) were reported from eight states, primarily in the East North Central and West North Central divisions (Table 2). Jamestown Canyon virus disease cases were reported for the first time from Connecticut and Michigan. The median age of patients was 53 years (IQR = 40–65), and 35 (85%) were male (Table 1). Illness onset ranged from April through November, with 26 (63%) reporting onset during July–September. Twenty-five (61%) cases were neuroinvasive, 30 (73%) patients were hospitalized,

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TABLE 1. Selected characteristics of reported cases of West Nile virus and other arboviral diseases, by virus type — United States, 2018

Characteristic	Virus, no. (%)					
	West Nile* (N = 2,647)	La Crosse (N = 86)	Jamestown Canyon (N = 41)	Powassan (N = 21)	St. Louis encephalitis (N = 8)	Eastern equine encephalitis (N = 6)
Age group (yrs)						
<18	58 (2)	81 (94)	1 (2)	1 (5)	0 (0)	0 (0)
18–59	1,281 (48)	4 (5)	25 (61)	6 (29)	3 (38)	2 (33)
≥60	1,308 (49)	1 (1)	15 (37)	14 (67)	5 (63)	4 (67)
Sex						
Male	1,638 (62)	43 (50)	35 (85)	14 (67)	4 (50)	3 (50)
Female	1,009 (38)	43 (50)	6 (15)	7 (33)	4 (50)	3 (50)
Period of illness onset						
January–March	4 (<1)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)
April–June	37 (1)	10 (12)	9 (22)	11 (52)	0 (0)	2 (33)
July–September	2,435 (92)	61 (71)	26 (63)	5 (24)	4 (50)	4 (67)
October–December	170 (6)	15 (17)	6 (15)	4 (19)	4 (50)	0 (0)
Clinical syndrome						
Nonneuroinvasive	989 (37)	3 (3)	16 (39)	0 (0)	3 (38)	0 (0)
Neuroinvasive	1,658 (63)	83 (97)	25 (61)	21 (100)	5 (62)	6 (100)
Encephalitis	908 (34)	70 (81)	11 (27)	15 (71)	3 (38)	6 (100)
Meningitis	542 (20)	13 (15)	7 (17)	5 (24)	1 (13)	0 (0)
Acute flaccid paralysis	70 (3)	0 (0)	4 (10)	0 (0)	0 (0)	0 (0)
Unspecified	138 (5)	0 (0)	3 (7)	1 (5)	1 (13)	0 (0)
Outcome						
Hospitalization	1,774 (67)	82 (95)	30 (73)	21 (100)	5 (63)	5 (83)
Death	167 (6)	0 (0)	1 (2)	3 (14)	1 (13)	1 (17)

* Date of illness onset missing for one case of West Nile virus.

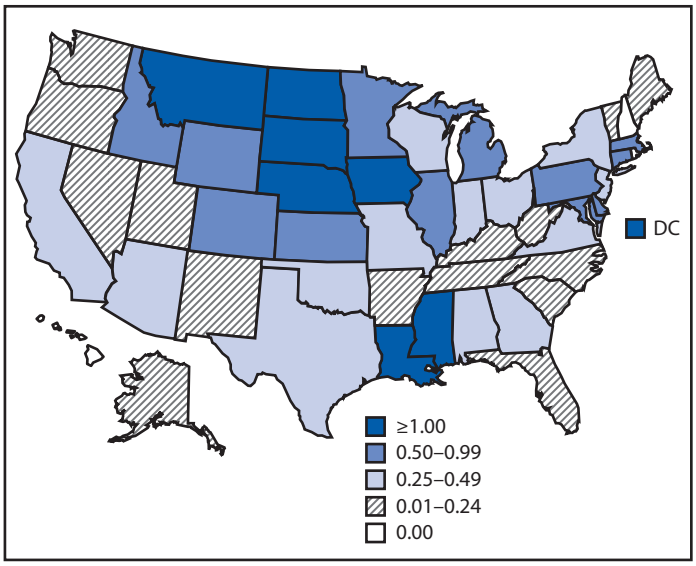
and one (2%) patient with neuroinvasive disease died. The incidence of Jamestown Canyon virus neuroinvasive disease was highest in Wisconsin (0.22 per 100,000).

Powassan virus disease cases (21) were reported from eight states, primarily in the New England and Middle Atlantic divisions (Table 2). Powassan virus disease was reported for the first time from Indiana; however, transfusion of a blood product originating from a viremic donor in Wisconsin was the likely source of infection. The median age of patients was 67 years (IQR = 53–74), and 14 (67%) were male (Table 1). Illness onset dates ranged from March through December, with 11 (52%) reporting onset during April–June. All 21 cases were neuroinvasive and resulted in hospitalization, including one (5%) pediatric case. Three (14%) patients died; all were aged >60 years.

Eight cases of St. Louis encephalitis virus disease were reported from four states (California, Georgia, Pennsylvania, and Wisconsin) (Table 2). The median age of patients was 68 years (IQR = 50–76), and four were male (Table 1). Illness onset dates ranged from July through October, with four patients reporting onset in October. Five cases were neuroinvasive, and all five patients were hospitalized; one patient died.

Six cases of eastern equine encephalitis virus disease were reported from four states (Florida, Georgia, Michigan, and Pennsylvania) (Table 2). The median age of patients was 64 years (IQR = 58–71), and three were male. Illness onset dates ranged from May through September, with four patients reporting onset during July–September. All cases were neuroinvasive, and five patients were hospitalized; one patient died.

FIGURE. Incidence* of reported cases of West Nile virus neuroinvasive disease — United States, 2018



Abbreviation: DC = District of Columbia.
* Cases per 100,000 population.

TABLE 2. Number and rate* of reported cases of arboviral neuroinvasive disease, by virus type, U.S. Census division, and state — United States, 2018

U.S. Census division/ State	Virus, no. (rate)					
	West Nile	La Crosse	Jamestown Canyon	Powassan	St. Louis encephalitis	Eastern equine encephalitis
United States	**1,658 (0.51)**	**83 (0.03)**	**25 (0.01)**	**21 (0.01)**	**5 (<0.01)**	**6 (<0.01)**
New England	**62 (0.42)**	**1 (<0.01)**	**3 (0.02)**	**8 (0.05)**	—†	—
Connecticut	18 (0.50)	—	1 (0.03)	2 (0.06)	—	—
Maine	1 (0.07)	—	1 (0.07)	—	—	—
Massachusetts	42 (0.61)	—	1 (0.01)	6 (0.09)	—	—
New Hampshire	—	—	—	—	—	—
Rhode Island	—	1§ (0.09)	—	—	—	—
Vermont	1 (0.16)	—	—	—	—	—
Middle Atlantic	**216 (0.52)**	**—**	**—**	**6 (0.01)**	**—**	**1 (<0.01)**
New Jersey	44 (0.49)	—	—	1 (0.01)	—	—
New York	77 (0.39)	—	—	4 (0.02)	—	—
Pennsylvania	95 (0.74)	—	—	1 (<0.01)	—	1 (<0.01)
East North Central	**306 (0.65)**	**38 (0.08)**	**14 (0.03)**	**4 (<0.01)**	**1 (<0.01)**	**1 (<0.01)**
Illinois	126 (0.99)	—	—	—	—	—
Indiana	26 (0.39)	—	—	1¶ (0.01)	—	—
Michigan	80 (0.80)	—	1 (0.01)	—	—	1 (0.01)
Ohio	45 (0.38)	38 (0.33)	—	—	—	—
Wisconsin	29 (0.50)	—	13 (0.22)	3 (0.05)	1 (0.02)	—
West North Central	**364 (1.70)**	**—**	**7 (0.03)**	**3 (0.01)**	**—**	**—**
Iowa	59 (1.87)	—	—	—	—	—
Kansas	23 (0.79)	—	—	—	—	—
Minnesota	34 (0.61)	—	7 (0.12)	3 (0.05)	—	—
Missouri	17 (0.28)	—	—	—	—	—
Nebraska	124 (6.43)	—	—	—	—	—
North Dakota	60 (7.89)	—	—	—	—	—
South Dakota	47 (5.33)	—	—	—	—	—
South Atlantic	**172 (0.26)**	**31 (0.05)**	**—**	**—**	**—**	**4 (<0.01)**
Delaware	8 (0.83)	—	—	—	—	—
District of Columbia	7 (1.00)	—	—	—	—	—
Florida	30 (0.14)	—	—	—	—	3 (0.01)
Georgia	30 (0.29)	—	—	—	—	1 (<0.01)
Maryland	35 (0.58)	—	—	—	—	—
North Carolina	10 (0.10)	24 (0.23)	—	—	—	—
South Carolina	12 (0.24)	—	—	—	—	—
Virginia	38 (0.45)	2 (0.02)	—	—	—	—
West Virginia	2 (0.11)	5 (0.28)	—	—	—	—
East South Central	**67 (0.35)**	**12 (0.06)**	**1 (<0.01)**	**—**	**—**	**—**
Alabama	16 (0.33)	—	—	—	—	—
Kentucky	9 (0.20)	—	—	—	—	—
Mississippi	31 (1.04)	—	—	—	—	—
Tennessee	11 (0.16)	12 (0.18)	1 (0.01)	—	—	—
West South Central	**182 (0.45)**	**1 (<0.01)**	**—**	**—**	**—**	**—**
Arkansas	6 (0.20)	—	—	—	—	—
Louisiana	56 (1.20)	—	—	—	—	—
Oklahoma	12 (0.30)	—	—	—	—	—
Texas	108 (0.38)	1 (<0.01)	—	—	—	—
Mountain	**130 (0.53)**	**—**	**—**	**—**	**—**	**—**
Arizona	25 (0.35)	—	—	—	—	—
Colorado	52 (0.91)	—	—	—	—	—
Idaho	10 (0.57)	—	—	—	—	—
Montana	25 (2.35)	—	—	—	—	—
Nevada	3 (0.10)	—	—	—	—	—
New Mexico	5 (0.24)	—	—	—	—	—
Utah	7 (0.22)	—	—	—	—	—
Wyoming	3 (0.52)	—	—	—	—	—
Pacific	**159 (0.30)**	**—**	**—**	**—**	**4 (<0.01)**	**—**
Alaska	1§ (0.14)	—	—	—	—	—
California	154 (0.39)	—	—	—	4 (0.01)	—
Hawaii	—	—	—	—	—	—
Oregon	2 (0.05)	—	—	—	—	—
Washington	2 (0.03)	—	—	—	—	—

* Per 100,000 population, based on July 1, 2018, U.S. Census population estimates.
† Dashes indicate none reported.
§ Patient reported travel to a state with a history of the virus.
¶ Patient acquired infection through blood transfusion.

Discussion

As in previous years, WNV was the most common cause of neuroinvasive arboviral disease in the United States, accounting for 92% of reported neuroinvasive disease cases. The incidence of WNV neuroinvasive disease in 2018 (0.51 per 100,000) was nearly 25% higher than the median incidence of 0.41 during 2008–2017 (range = 0.13 [2009]–0.92 [2012]) (*4*). Multiple western states with historically large numbers of cases (e.g., Arizona and California) reported below average incidences in 2018, and multiple northeastern states (e.g., New Jersey, New York, and Pennsylvania) experienced higher incidences than usual.

More La Crosse virus disease cases were reported in 2018 than in any year since 2011 (*5*), and La Crosse virus continued to be the most common cause of neuroinvasive arboviral disease in children (*6*). Arboviruses were an ongoing concern for blood and tissue safety, because the first documented case of Powassan virus transmission via blood transfusion was reported (*7*), and two WNV disease cases in solid organ recipients from a single donor were the first transplant-transmitted cases reported since 2013 (*8*). Fewer cases of Jamestown Canyon virus disease were reported in 2018 than in 2017; however, the number of cases reported was still higher than that in other years before 2017 (*9*). Although increased activity of the virus cannot be ruled out, the recent increase in cases might be attributable to a known increase in awareness and testing, particularly in the upper Midwest. The epidemiology of eastern equine encephalitis and St. Louis encephalitis cases was consistent with previous years.

Although the reported number of cases varies annually, arboviruses continue to cause substantial morbidity in the United States. Cases occur sporadically, and the epidemiology varies by virus and geography. Approximately 93% of arboviral disease cases occurred during April–September in 2018, which is consistent with the peak season in past years. Weather, zoonotic host, vector abundance, and human behavior all influence when and where arboviral disease outbreaks occur. These factors make it difficult to predict locations and timing of future cases and highlight the importance of surveillance in identifying outbreaks and informing public health prevention efforts.

The findings in this report are subject to at least two limitations. First, ArboNET is a passive surveillance system that underreports the actual incidence of disease. Detection and reporting of neuroinvasive disease are considered more consistent and complete than that of nonneuroinvasive disease. Previous studies have estimated that between 30 and 70 nonneuroinvasive disease cases occur for every case of WNV neuroinvasive disease reported (*10*). Based on the number of neuroinvasive disease cases reported for 2018, between 49,740 and 116,060 nonneuroinvasive disease cases of WNV would have been expected to occur; however, only 989 (1%–2%) were reported. Second, because ArboNET does not require information about clinical signs and symptoms or laboratory findings, cases might be misclassified.

Health care providers should consider arboviral infections in the differential diagnosis of aseptic meningitis or encephalitis, obtain appropriate specimens for laboratory testing, and promptly report cases to public health authorities (*2*,*3*). Understanding the epidemiology, seasonality, and geographic distribution of these arboviruses is important for clinical recognition and differentiation from other neurologic infections. Because human vaccines against domestic arboviruses are not available, prevention depends on community and household efforts to reduce vector populations, personal protective measures to decrease mosquito and tick exposures, and blood donation screening to minimize alternative routes of transmission.

Summary

What is already known about this topic?

West Nile virus (WNV) is consistently the leading cause of domestically acquired arboviral disease, but other arboviruses cause sporadic cases and outbreaks of neuroinvasive disease.

What is added by this report?

WNV neuroinvasive disease incidence was nearly 25% higher in 2018 than the median incidence during 2008–2017. WNV transmission via organ transplantation was reported for the first time since 2013. The first documented case of Powassan virus transmission via blood transfusion was reported.

What are the implications for public health practice?

Health care providers should consider arboviral infections in patients with aseptic meningitis or encephalitis, perform appropriate diagnostic testing, and report cases to public health authorities. Surveillance helps to identify outbreaks and guide prevention strategies.

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Vital Signs: Pharmacy-Based Naloxone Dispensing — United States, 2012–2018

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Abstract

Background: The CDC Guideline for Prescribing Opioids for Chronic Pain recommends considering prescribing naloxone when factors that increase risk for overdose are present (e.g., history of overdose or substance use disorder, opioid dosages ≥50 morphine milligram equivalents per day [high-dose], and concurrent use of benzodiazepines). In light of the high numbers of drug overdose deaths involving opioids, 36% of which in 2017 involved prescription opioids, improving access to naloxone is a public health priority. CDC examined trends and characteristics of naloxone dispensing from retail pharmacies at the national and county levels in the United States.

Methods: CDC analyzed 2012–2018 retail pharmacy data from IQVIA, a health care, data science, and technology company, to assess U.S. naloxone dispensing by U.S. Census region, urban/rural status, prescriber specialty, and recipient characteristics, including age group, sex, out-of-pocket costs, and method of payment. Factors associated with naloxone dispensing at the county level also were examined.

Results: The number of naloxone prescriptions dispensed from retail pharmacies increased substantially from 2012 to 2018, including a 106% increase from 2017 to 2018 alone. Nationally, in 2018, one naloxone prescription was dispensed for every 69 high-dose opioid prescriptions. Substantial regional variation in naloxone dispensing was found, including a twenty-fivefold variation across counties, with lowest rates in the most rural counties. A wide variation was also noted by prescriber specialty. Compared with naloxone prescriptions paid for with Medicaid and commercial insurance, a larger percentage of prescriptions paid for with Medicare required out-of-pocket costs.

Conclusion: Despite substantial increases in naloxone dispensing, the rate of naloxone prescriptions dispensed per high-dose opioid prescription remains low, and overall naloxone dispensing varies substantially across the country. Naloxone distribution is an important component of the public health response to the opioid overdose epidemic. Health care providers can prescribe or dispense naloxone when overdose risk factors are present and counsel patients on how to use it. Efforts to improve naloxone access and distribution work most effectively with efforts to improve opioid prescribing, implement other harm-reduction strategies, promote linkage to medications for opioid use disorder treatment, and enhance public health and public safety partnerships.

Introduction

Among the 70,237 drug overdose deaths in the United States in 2017 (the last year for which complete data are available), a total of 47,600 (67.8%) involved opioids (*1*). Millions of Americans are at increased risk for an opioid overdose, including persons who use illicit opioids, those who use or misuse prescription opioids, and those with an opioid use disorder (*2*). A population particularly at risk includes persons who use illicit drugs (e.g., cocaine and methamphetamine) that might be mixed with illicit opioids (*3*). The CDC Guideline for Prescribing Opioids for Chronic Pain recommends considering prescribing naloxone when factors that increase risk for overdose are present (e.g., history of overdose or substance use disorder, opioid dosages ≥50 morphine milligram equivalents [MME] per day [high-dose], and concurrent use of benzodiazepines) (*4*). Given that approximately two thirds of overdose deaths involved opioids, 36% of which in 2017 were prescription opioids (*1*), the distribution of naloxone to reverse an overdose is an important element of the public health response to the opioid overdose epidemic (*5*).

For decades, emergency medical service (EMS) providers, first responders, and emergency department clinicians have administered naloxone in cases of suspected drug overdose, and community-based organizations have offered naloxone through education and distribution programs. Recent efforts have focused on expanding naloxone access through clinician

Summary

What is already known about this topic?

In 2017, 47,600 persons died from drug overdoses involving opioids. Naloxone, a drug that can temporarily reverse the effects of opioids, can help prevent overdose deaths.

What is added by this report?

Naloxone dispensing from retail pharmacies increased from 2012 to 2018, with substantial increases in recent years. Despite increases, in 2018, only one naloxone prescription was dispensed for every 69 high-dose opioid prescriptions. The lowest rates of naloxone dispensing were observed in the most rural counties.

What are the implications for public health practice?

Additional efforts are needed to improve naloxone access at the local level, including prescribing and pharmacy dispensing. Distribution of naloxone is a critical component of the public health response to the opioid overdose epidemic.

prescribing and pharmacy dispensing. All 50 states and the District of Columbia have enacted laws permitting pharmacy-based naloxone dispensing (*6*). Laws allowing providers to prescribe naloxone to any persons in a position to assist another with an overdose (i.e., third-party prescriptions) and standing orders for pharmacists to dispense naloxone have been associated with increases in naloxone dispensing from retail pharmacies (*7*). Several states have mandated that clinicians coprescribe naloxone when overdose risk factors (e.g., high opioid dosages) are present, a recommendation for consideration in the CDC Guideline for Prescribing Opioids for Chronic Pain (*4*); such laws have been associated with substantial increases in naloxone dispensing (*8*). Many of these states have only recently implemented these laws; thus, sufficient time has not passed to examine their full impact at the state or county level.

Recent analyses examining the extent and characteristics of pharmacy-based naloxone dispensing are lacking. Also unknown is the extent to which naloxone dispensing varies by county and by other factors (e.g., prescriber specialty and patient insurance coverage). Understanding variation could help identify the need for tailored approaches to improve prescribing and dispensing, similar to those that have been indicated for opioid prescribing (*9*). To address this gap and to inform future overdose prevention and response efforts, CDC examined trends in, and characteristics of, naloxone dispensing from retail pharmacies at the national and county levels in the United States.

Methods

Data on naloxone dispensing came from IQVIA, which maintains information on prescriptions from approximately 50,400 retail pharmacies, representing 92% of all prescriptions in the United States. Changes in naloxone dispensing from 2012 to 2018 were examined nationally, by U.S. Census region, and by county urban/rural status (i.e., metropolitan, micropolitan, and rural) (*10*). Annual dispensing rates were calculated by dividing the number of naloxone prescriptions by U.S. Census population estimates per 100,000 persons. CDC analyzed naloxone dispensing in 2018 by age group, sex, out-of-pocket costs, and method of payment.

To assess naloxone dispensing relative to high-dose opioid dispensing, CDC calculated the number of naloxone prescriptions dispensed per 100 high-dose (≥50 MME per day) opioid prescriptions, overall, and by prescriber specialty, U.S. Census region, and urban/rural status in 2017 and 2018, as well as the number of prescriptions and unique patients to whom naloxone and high-dose opioids were dispensed.

CDC also examined naloxone prescriptions at the county level from 2,881 (91.7%) U.S. counties in 2018. Multivariable logistic regression models were fit to identify county-level factors associated with being a high-dispensing (top quartile per 100,000 population) and low-dispensing (bottom quartile) county. The following county-level characteristics were obtained from the American Community Survey: percentage male, non-Hispanic white, disabled, and without a high school diploma, insurance status, unemployment rate, and poverty rate. Urban/rural status* was obtained from CDC's National Center for Health Statistics. High-dose opioid dispensing rates were calculated; drug overdose death rates were obtained from the National Vital Statistics System. Potential buprenorphine treatment capacity was calculated using data from the Substance Abuse and Mental Health Services Administration by determining the maximum number of patients who could be treated by providers with buprenorphine-prescribing waivers per 1,000 residents. Analyses were conducted using Stata (version 14.2; StataCorp).

Results

Naloxone dispensing from retail pharmacies increased substantially from 2012 to 2018, from 1,282 prescriptions (0.4 per 100,000) in 2012 to 556,847 (170.2) in 2018 (Table 1). Substantial increases occurred across all U.S. Census regions and urban/rural categories. In 2018, dispensing rates were highest among micropolitan counties (206.3 per 100,000) and in the South (195.0) and lowest in rural counties (147.4) and in the Midwest (139.9).

* 2013 National Center for Health Statistics Urban-Rural Classification Scheme for Counties was used for the creation of the county type variables. https://www.cdc.gov/nchs/data_access/urban_rural.htm. The three classification levels for counties were 1) metropolitan: part of a metropolitan statistical area; 2) micropolitan: part of a micropolitan statistical area (has an urban cluster of ≥10,000 but <50,000 population); and 3) noncore (i.e., rural): not part of a metropolitan or micropolitan statistical area.

TABLE 1. Estimated annual number of naloxone prescriptions dispensed and rate* of naloxone dispensing from retail pharmacies — United States, 2012–2018

Characteristic	No. of prescriptions (rate)						
	2012	2013	2014	2015	2016	2017†	2018†
All	**1,282 (0.4)**	**1,597 (0.5)**	**6,588 (2.1)**	**26,231 (8.2)**	**134,109 (41.5)**	**270,710 (83.3)**	**556,847 (170.2)**
County urbanization level§							
Metropolitan	938 (0.4)	1,237 (0.5)	5,944 (2.2)	22,953 (8.3)	119,005 (42.9)	230,514 (82.4)	472,848 (169.1)
Micropolitan	223 (0.8)	255 (0.9)	416 (1.5)	2,630 (9.7)	11,466 (42.1)	27,893 (102.3)	56,247 (206.3)
Rural	121 (0.6)	105 (0.6)	227 (1.2)	647 (3.4)	3,637 (19.3)	12,303 (65.4)	27,752 (147.4)
U.S. Census region¶							
Northeast	165 (0.3)	276 (0.5)	1,568 (2.8)	7,052 (12.6)	32,032 (57.1)	53,259 (95.0)	96,773 (172.5)
Midwest	359 (0.5)	359 (0.5)	1,099 (1.6)	2,949 (4.3)	14,984 (22.0)	39,902 (58.5)	95,555 (139.9)
South	456 (0.4)	361 (0.3)	2,376 (2.0)	11,384 (9.4)	58,307 (47.6)	128,117 (103.7)	243,277 (195.0)
West	302 (0.4)	602 (0.8)	1,545 (2.1)	4,846 (6.4)	28,786 (37.6)	49,432 (63.9)	121,243 (155.5)

Source: IQVIA Xponent 2012–2018; data were extracted in 2019. The data reflect approximately 92% of all prescriptions from retail pharmacies and are projected nationally.
* Per 100,000 population.
† Starting with 2017 data, IQVIA changed the frame of measurement from number of prescriptions "dispensed to bin" to number of prescriptions "sold to the patient." To do this, IQVIA eliminated the effects of voided and reversed prescriptions (prescriptions that were never received by the patient), resulting in a downward shift in naloxone prescriptions dispensed of 19.5% for 2017 and 18.9% for 2018.
§ 2013 National Center for Health Statistics Urban-Rural Classification Scheme for Counties was used for the creation of the county type variables. https://www.cdc.gov/nchs/data_access/urban_rural.htm. The three classification levels for counties were 1) metropolitan: part of a metropolitan statistical area; 2) micropolitan: part of a micropolitan statistical area (has an urban cluster of ≥10,000 but <50,000 population); and 3) noncore (i.e., rural): not part of a metropolitan or micropolitan statistical area.
¶ *Northeast:* Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont. *Midwest:* Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin. *South:* Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia. *West:* Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.

In 2018, naloxone dispensing rates were higher for female recipients (187.7 per 100,000) than for male recipients (151.6) and higher for persons aged 60–64 years (362.8) than for any other age group (Supplementary Figure 1, https://stacks.cdc.gov/view/cdc/79933). In 2018, the largest percentage of dispensed naloxone prescriptions were to persons with commercial insurance (51.1%), followed by Medicare (35.9%), Medicaid (10.7%), and self-pay (2.4%). Overall, 42.3% of prescriptions did not require out-of-pocket costs; among the remainder, 24.5% required out-of-pocket costs of <$10.00, 21.9% required out-of-pocket costs of $10.01–$50.00, and 5.8% required out-of-pocket costs >$50.00. Among prescriptions paid for by Medicare, 71.1% required out-of-pocket costs; among prescriptions paid for by Medicaid, 43.8% required out-of-pocket costs; among prescriptions paid for by commercial insurance, 41.5% required out-of-pocket costs; 31.0% of self-pay prescriptions had out-of-pocket costs >$50.00 (Supplementary Figure 2, https://stacks.cdc.gov/view/cdc/79934).

From 2017 to 2018, the number of high-dose opioid prescriptions decreased 21%, from 48.6 million to 38.4 million, and the number of naloxone prescriptions increased 106%, from 270,710 to 556,847 (Table 2). In 2018, an estimated 9 million patients were dispensed a high-dose opioid prescription, and 406,203 were dispensed naloxone. The rate of naloxone prescriptions per 100 high-dose opioid prescriptions increased 150% from 2017 (0.6) to 2018 (1.5), varying widely by prescriber specialty. In 2018, among specialty groups with the most high-dose opioid prescriptions, the rate of naloxone prescriptions per 100 high-dose opioid prescriptions was lowest among surgeons (0.2), pain medicine physicians (1.3), physician assistants (1.3), primary care physicians (1.5), and nurse practitioners (2.3). Among all specialty groups, psychiatrists had the highest rate of naloxone prescriptions dispensed for every 100 high-dose opioid prescriptions (12.9), followed by addiction medicine specialists (12.2) and pediatricians (10.4).

Across U.S. counties, the rate of naloxone prescriptions dispensed varied substantially, from an average of 16.2 per 100,000 population in the lowest quartile to 410.0 in the highest quartile (Figure). The rate of naloxone prescriptions per 100 high-dose opioid prescriptions also varied across counties, from an average of 0.2 in the lowest quartile to 2.9 in the highest quartile (Figure). In 2018, the rate of naloxone prescriptions per 100 high-dose opioid prescriptions ranged from 1.5 in metropolitan counties and 1.6 in the Northeast to 1.2 in rural counties and 1.3 in the Midwest; the largest increase in 2018 was in the Midwest (Table 2). In 2018, 236 counties (8.3% of counties with available data), dispensed high-dose opioid prescriptions but did not dispense any naloxone prescriptions.

After adjusting for all county characteristics in the multivariable logistic regression models, high naloxone-dispensing counties had higher high-dose opioid dispensing rates, higher drug overdose deaths rates, higher potential buprenorphine treatment capacity, lower percentages of non-Hispanic white residents, higher disability prevalence, and higher rates of Medicaid enrollment (Table 3).

Compared with metropolitan counties, micropolitan and rural counties had lower odds of being a high-dispensing county.

Discussion

Naloxone dispensing from retail pharmacies increased substantially from 2012 to 2018. Although naloxone dispensing doubled from 2017 to 2018, dispensing rates remained low, and although high-dose opioid dispensing decreased by 21%, it still remained high. Missed opportunities remain to implement strategies to provide naloxone to patients at risk for overdose. The release of the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain has been associated with accelerated declines in high-dose opioid dispensing (*11*). Additional efforts to implement the guideline recommendations have the potential to improve naloxone dispensing. Nationally, in 2018, only one naloxone prescription was dispensed for every 69 high-dose

TABLE 2. High-dose opioid* and naloxone prescriptions dispensed by prescriber specialty, county urbanization level, and U.S. Census region — United States, 2017–2018

	2017			2018					
Characteristic	High-dose opioid prescriptions No. (%)	Naloxone prescriptions No. (%)	Naloxone prescriptions per 100 high-dose opioid prescriptions	High-dose opioid prescriptions No. (%)	% Change from 2017	Naloxone prescriptions No. (%)	% Change from 2017	Naloxone prescriptions per 100 high-dose opioid prescriptions	% Change from 2017
All	**48,607,464 (100.00)**	**270,710 (100.00)**	**0.56**	**38,399,208 (100.00)**	**−21**	**556,847 (100.00)**	**106**	**1.45**	**150**
Prescriber specialty									
Primary care†	11,361,552 (29.03)	63,336 (29.32)	0.56	9,032,155 (29.45)	−21	133,612 (29.58)	111	1.48	150
Pain medicine§	7,113,086 (18.17)	40,192 (18.61)	0.57	5,995,058 (19.54)	−16	76,751 (16.99)	91	1.28	117
Surgery	6,356,264 (16.24)	3,072 (1.42)	0.05	4,415,915 (14.40)	−31	8,252 (1.83)	169	0.19	300
Nurse practitioner	4,104,420 (10.49)	43,189 (20.00)	1.05	3,606,936 (11.76)	−12	83,941 (18.58)	94	2.33	109
Physician assistant	3,813,215 (9.74)	22,408 (10.38)	0.59	3,063,470 (9.99)	−20	39,282 (8.70)	75	1.28	117
Other¶	1,984,141 (5.07)	9,878 (4.57)	0.50	1,637,893 (5.34)	−17	28,749 (6.36)	191	1.76	260
Medical subspecialties**	1,079,412 (2.76)	5,821 (2.70)	0.54	843,779 (2.75)	−22	20,646 (4.57)	255	2.45	380
Dentistry††	1,252,860 (3.20)	270 (0.13)	0.02	739,038 (2.41)	−41	549 (0.12)	103	0.07	400
Obstetrics/Gynecology	848,538 (2.17)	4,014 (1.86)	0.47	554,218 (1.81)	−35	17,286 (3.83)	331	3.12	520
Emergency medicine	920,683 (2.35)	8,656 (4.01)	0.94	544,236 (1.77)	−41	15,312 (3.38)	77	2.81	211
Pediatrics	176,639 (0.45)	6,068 (2.81)	3.44	144,933 (0.47)	−18	15,056 (3.33)	148	10.39	206
Psychiatry	109,084 (0.28)	7,986 (3.70)	7.32	81,274 (0.26)	−25	10,487 (2.32)	31	12.90	77
Addiction medicine	17,632 (0.05)	1,090 (0.50)	6.18	14,826 (0.05)	−16	1,810 (0.40)	66	12.21	97
County urbanization level§§									
Metropolitan	40,506,108 (83.33)	230,514 (85.15)	0.57	31,922,158 (83.13)	−21	472,848 (84.92)	105	1.48	150
Micropolitan	5,230,850 (10.76)	27,893 (10.30)	0.53	4,156,759 (10.83)	−21	56,247 (10.10)	102	1.35	180
Rural	2,870,505 (5.91)	12,303 (4.54)	0.43	2,320,289 (6.04)	−19	27,752 (4.98)	126	1.20	200
U.S. Census region¶¶									
Northeast	7,595,881 (15.63)	53,259 (19.67)	0.70	6,088,692 (15.86)	−20	96,773 (17.38)	82	1.59	129
Midwest	9,489,742 (19.52)	39,902 (14.74)	0.42	7,219,882 (18.80)	−24	95,555 (17.16)	139	1.32	225
South	20,627,124 (42.44)	128,117 (47.33)	0.62	16,528,879 (43.04)	−20	243,277 (43.69)	90	1.47	150
West	10,894,718 (22.41)	49,432 (18.26)	0.45	8,561,754 (22.30)	−21	121,243 (21.77)	145	1.42	180

Sources: IQVIA Real World Data Longitudinal Prescriptions (LRx) 2017–2018 (prescriber specialty); data were extracted in 2019. IQVIA Xponent 2017–2018 (county urbanization level and U.S. Census region); data were extracted in 2019. The data reflect approximately 92% of all prescriptions from retail pharmacies. Data from Xponent are projected nationally. Number of prescriptions by specialty does not sum to the total because the data are not projected.

* High-dose opioid prescriptions are defined as ≥50 morphine milligram equivalents per day.

† Primary care includes family practice, general practice, and internal medicine.

§ Pain medicine includes anesthesiology, pain medicine, and physical medicine and rehabilitation.

¶ Other includes clinical pharmacology, dermatology, dermatopathology, genetics, hospice and palliative medicine, medical microbiology, naturopathic doctor, neurology, neurophysiology, nuclear medicine, nutrition, occupational medicine, optometry, otology, pathology, pharmacist, podiatry, psychology, radiology, sports medicine, unspecified, and other. Pharmacists are included among other specialties given their limited ability to prescribe opioids.

** Medical subspecialties include allergy, cardiology, cardiovascular, diabetes, endocrinology, gastroenterology, hematology, hepatology, hospitalist, immunology, infectious disease, nephrology, oncology, pulmonary disease, and rheumatology.

†† Includes dentists, endodontics, orthodontics, pedodontics, periodontics, and prosthodontics. Oral and maxillofacial surgery are classified as surgery.

§§ 2013 National Center for Health Statistics Urban-Rural Classification Scheme for Counties was used for the creation of the county type variables. https://www.cdc.gov/nchs/data_access/urban_rural.htm. The three classification levels for counties were 1) metropolitan: part of a metropolitan statistical area; 2) micropolitan: part of a micropolitan statistical area (has an urban cluster of ≥10,000 but <50,000 population); and 3) noncore (i.e., rural): not part of a metropolitan or micropolitan statistical area.

¶¶ *Northeast:* Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont. *Midwest:* Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin. *South:* Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia. *West:* Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming.

FIGURE. Naloxone prescriptions, by county — United States, 2018

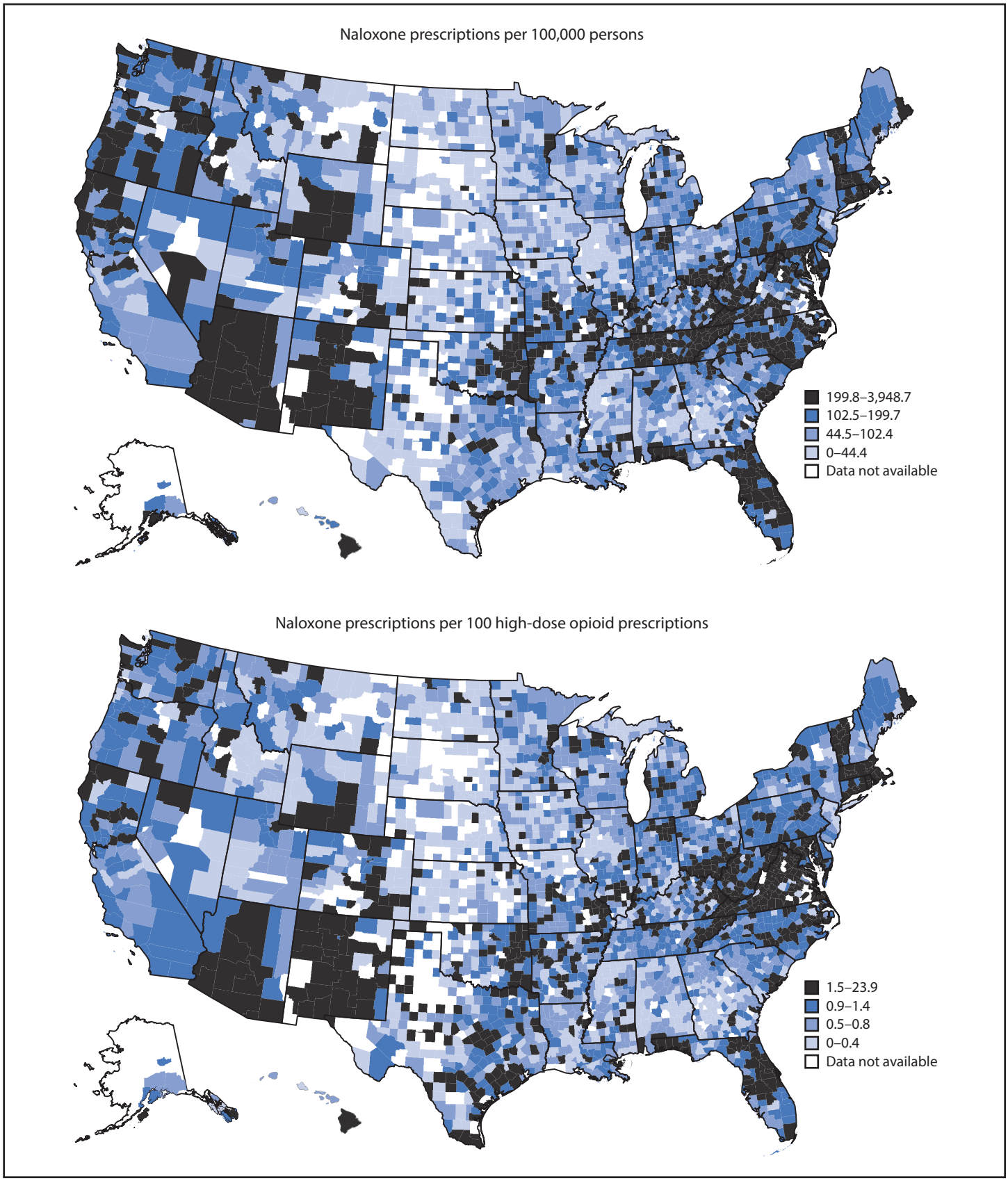

TABLE 3. County characteristics associated with high- and low-level naloxone dispensing rates — United States, 2018

	High-dispensing counties†		Low-dispensing counties†	
Characteristic*	**OR**	**p-value**	**OR**	**p-value**
High-dose opioid dispensing rate (2018)§	1.13	<0.001	0.84	<0.001
Drug overdose death rate (2017)	1.02	<0.001	0.97	<0.001
Potential buprenorphine treatment capacity	1.02	0.028	0.95	0.001
Male (%)	0.96	0.175	1.02	0.519
Non-Hispanic white (%)	0.99	0.009	1.01	0.019
Disabled (%)	1.10	<0.001	0.93	0.001
Insurance status (%)				
Uninsured	1.01	0.755	1.02	0.304
Medicare	0.99	0.667	1.06	<0.001
Medicaid	1.04	0.004	0.96	0.004
Unemployment rate	0.96	0.367	1.01	0.852
No high school diploma (%)	0.98	0.157	1.01	0.501
Income below the Federal Poverty Level (%)	0.98	0.273	1.03	0.048
County urbanization level¶				
Metropolitan	Referent	N/A	Referent	N/A
Micropolitan	0.70	0.011	1.12	0.465
Rural	0.46	<0.001	2.61	<0.001

Abbreviations: N/A = not applicable; OR = odds ratio.
Source: IQVIA Xponent 2018; data were extracted in 2019.
* IQVIA Xponent 2018 (high-dose opioid dispensing rate); American Community Survey (percentage male, percentage non-Hispanic white, percentage disabled, insurance status, unemployment rate, percentage without a high school diploma, poverty rate); National Center for Health Statistics (urban/rural status); National Vital Statistics System (drug overdose death rates); and Substance Abuse and Mental Health Services Administration (potential buprenorphine opioid use disorder treatment capacity). Results are from multivariable logistic regression models that include 2881 U.S. counties.
† According to 2018 naloxone dispensing rates, high-dispensing counties are in the top quartile (199.8–3,948.7 per 100,000), and low-dispensing counties are in the bottom quartile (0–44.4 per 100,000).
§ High-dose opioid prescriptions are defined as ≥50 morphine milligram equivalents per day.
¶ 2013 National Center for Health Statistics Urban-Rural Classification Scheme for Counties was used for the creation of the county type variables. https://www.cdc.gov/nchs/data_access/urban_rural.htm. The three classification levels for counties were 1) metropolitan: part of a metropolitan statistical area; 2) micropolitan: part of a micropolitan statistical area (has an urban cluster of ≥10,000 but <50,000 population); and 3) noncore (i.e., rural): not part of a metropolitan or micropolitan statistical area.

opioid prescriptions; receipt of a high-dose opioid prescription is a risk factor for overdose. If each provider had considered offering naloxone to every patient receiving a high-dose opioid prescription, as recommended in the CDC guideline, nearly 9 million naloxone prescriptions could have been dispensed, approximately 16 times the 557,000 recorded in 2018. In addition, in one in 12 counties, high-dose opioids were dispensed, but naloxone was not dispensed from a pharmacy. Further, there was a twenty-fivefold variation in naloxone dispensing across counties, with rural counties and the Midwest experiencing the lowest rates despite laws permitting pharmacy-based naloxone dispensing in all 50 states and the District of Columbia (*6*). Naloxone access laws that grant direct authority to pharmacists to dispense naloxone have been associated with reduced fatal opioid overdoses (*12*).

Counties with the greatest need for overdose reversal, (e.g., those with high rates of drug overdose death and high-dose opioid dispensing) tend to have a higher rate of pharmacy-based naloxone dispensing. The highest county-level naloxone dispensing rates were observed in some of the states hit hardest by opioid overdose mortality (e.g., Florida and Massachusetts) and in states that have implemented requirements for naloxone coprescribing (e.g., Arizona and Virginia). Improved access to naloxone holds promise for opioid overdose reversals and the opportunity to link survivors to treatment to prevent a future overdose.

Variation in pharmacy naloxone dispensing rates cannot be fully explained by factors linked to the need for naloxone. Many states have only recently implemented laws requiring coprescription; thus, sufficient time has not passed to examine their full impact. Compared with metropolitan counties, rural counties had a higher likelihood of having low rates of naloxone dispensing, even when controlling for other relevant factors. This is concerning given slower EMS response times and underuse of naloxone by EMS in rural areas relative to the overdose prevalence, which are potentially attributable to resource, certification, and practice constraints (*13*). Harm-reduction programs are more limited in rural areas, and a smaller proportion of rural programs distribute naloxone (*14*). Thus, pharmacy naloxone dispensing holds great promise for positive impact in rural communities.

Clinicians have reported a lack of knowledge and low levels of self-efficacy in counseling patients about overdose and naloxone (*15*). Factors that increase risk for overdose include a history of overdose or substance use disorder, opioid dosages ≥50 MME per day, and concurrent use of benzodiazepines, all

of which are indications for prescribing naloxone that providers should consider (*4*). Efforts such as academic detailing, virtual mentoring, and electronic health record alerts can further educate and prompt clinicians about naloxone prescribing (*16*–*18*). Specialties that prescribe higher numbers of high-dose opioids and serve patients at risk for overdose, but were found in the current analysis to have markedly lower rates of naloxone prescriptions dispensed per high-dose opioid prescription (e.g., primary care providers, nurse practitioners, and physician assistants), as well as pain medicine specialists and surgeons, could particularly benefit.

In addition to overcoming prescribing and dispensing barriers, out-of-pocket costs and the rising cost of naloxone present challenges (*19*). Persons without insurance have the highest out-of-pocket costs, with ≥30% of naloxone prescriptions requiring out-of-pocket costs >$50 in 2018. In contrast, approximately one half of prescriptions received by patients with commercial insurance or Medicaid had no out-of-pocket costs, and fewer than one in 10 patients paid >$50. Although naloxone prescriptions among Medicare Part D patients have been increasing, recent research indicates that only a small minority of patients at high risk for overdose in Medicare Part D in 2017 received naloxone (*20*). In this study, patients covered by Medicare paid more, with more than two thirds of prescriptions requiring out-of-pocket costs. In April 2019, the Centers for Medicare and Medicaid Services encouraged Medicare Part D plan sponsors to lower cost-sharing for naloxone (*21*).

The findings in this report are subject to at least five limitations. First, prescriptions reflect those dispensed by pharmacies through either standing orders or clinician prescription; distribution through other channels was not recorded. Second, this analysis was not able to distinguish between prescriptions dispensed under a standing order and those prescribed directly to a patient by a clinician or dispensed to family and friends through third-party authority. Third, available data do not permit assessment of patient factors that might indicate overdose risk and naloxone need; comparing the number of high-dose opioid prescriptions with naloxone prescriptions is an approximation. Fourth, county-level analyses were aggregated by the county where naloxone was dispensed; persons who received these prescriptions and lived in a different county from the pharmacy were not part of the population denominator for the county in which naloxone was dispensed. Finally, the analyses were unable to examine, and findings might not reflect, the impact of recent state policies (e.g., laws requiring coprescription of naloxone).

Comprehensively addressing the opioid overdose epidemic will require efforts to improve naloxone access and distribution in tandem with efforts to prevent initiation of opioid misuse, improve opioid prescribing, implement harm reduction strategies, promote linkage to medications for opioid use disorder treatment, and enhance public health and public safety partnerships. Distribution of naloxone is a critical component of the public health response to the opioid overdose epidemic. Last year, the U.S. Surgeon General called for heightened awareness and availability of naloxone to reverse the effects of opioid overdose, and the U.S. Department of Health and Human Services issued guidance on populations at risk for opioid overdose and thus candidates for naloxone prescribing; pharmacies are a critical venue to help realize expanded access to naloxone (*22*,*23*).

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Notes from the Field

Unintentional Fentanyl Overdoses Among Persons Who Thought They Were Snorting Cocaine — Fresno, California, January 7, 2019

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On January 7, 2019, three patients arrived at the Community Regional Medical Center emergency department in Fresno, California, after snorting (i.e., nasally insufflating) white powder they thought was cocaine. One (patient A) was in cardiac arrest, and two (patients B and C) had opioid toxidrome (miosis, respiratory depression, and depressed mental status) (Table). After spontaneous circulation was reestablished in patient A, he was admitted to the intensive care unit, where he was pronounced brain-dead 3 days later. Patients B and C responded to naloxone, but repeated dosing was required to maintain respiratory status. Routine urine drug screens, which do not include testing for synthetic opioids such as fentanyl, were negative for opioids for all three patients. This finding, in combination with opioid toxidrome requiring repeated doses of naloxone, caused the medical toxicology team to be suspicious of an unintentional synthetic opioid exposure, and they notified the Fresno County Department of Public Health (FCDPH). After discussion with law enforcement the following day, a fourth patient (patient D) was identified in neighboring Madera County. Patient D was in cardiac arrest when emergency medical services arrived, and she was pronounced dead at the scene. Blood and urine specimens for patients A, B, and C were analyzed using liquid chromatography quadrupole time-of-flight mass spectrometry* for 13 fentanyl analogs and metabolites,† one novel synthetic opioid (U-47700), and 157 other drugs and metabolites. Results confirmed fentanyl without fentanyl analogs or other novel synthetic opioids.

After notification of the initial three cases, a multiagency response was implemented by FCDPH; Fresno County Sheriff-Coroner's Office; Fresno Police Department; Fresno County Department of Behavioral Health; Community Regional Medical Center; University of San Francisco-Fresno; and the Drug Enforcement Administration. Initial actions included 1) disseminating a news release targeting the media and other emergency departments; 2) holding a multiagency press conference; 3) conducting media interviews; 4) informing law enforcement, prehospital providers, and the public about naloxone distribution and use; 5) educating persons on the proper disposal of old or new but unused medications through the Fresno County Department of Behavioral Health/California Health Collaborative drop-off containers§; and 6) publicizing the California Central Valley Opioid Safety Coalition webpage,¶ which provides information about naloxone and substance use disorders.

On January 12, 2019, a similar drug overdose incident was reported in Chico, California, in which postmortem toxicology testing for one person confirmed fentanyl (*1*). Fourteen other persons at the same event were hospitalized with opioid toxidrome and later released. They reported thinking they were snorting cocaine,** but confirmatory toxicology results are unavailable. Fresno, Madera, and Chico are located along the same state highway (CA-99) corridor.

Death rates involving cocaine increased by approximately one third during 2016–2017. In 2017, nearly three fourths of cocaine deaths also involved opioids, with the arrival of synthetic opioids driving much of this increase (*2*). Mixing of drugs is a phenomenon being detected at a national level, with some variation across regions (*2*). There have been other reports of outbreaks caused by fentanyl disguised as cocaine among opioid-naïve populations in New Haven, Connecticut, and Philadelphia, Pennsylvania (*3*,*4*). These reports indicate similar exposures to low serum fentanyl concentrations (*3*,*4*) and also describe the need for multiple naloxone doses for effective reversal. In British Columbia, Canada, furanyl fentanyl caused an outbreak in patients who thought they were smoking crack cocaine (*5*). Fentanyl is likely underdetected because it is not routinely included on hospital urine immunoassays and it is useful to know the limitations of an institution's screening techniques. Targeted and untargeted analyses are necessary to detect fentanyl, fentanyl analogs, and other novel synthetic opioids (*6*). Traditional toxicology testing is targeted at specific known drugs, whereas liquid chromatography quadrupole time-of-flight mass spectrometry analysis can either detect an unexpected drug from patient or drug product specimens or match an unknown molecular weight on the spectra with a specific chemical formula to identify a novel drug.

*Analysis conducted at the University of California San Francisco Clinical Laboratory, Zuckerberg San Francisco General Hospital.

†Fentanyl, norfentanyl (metabolite), butyryl fentanyl, acetylfentanyl, 3-methylfentanyl, beta-hydroxythiofentanyl, furanyl fentanyl, para-fluorofentanyl, fluorobutyryl fentanyl, carfentanil, acrylfentanyl, tetrahydrofuranfentanyl, cyclopropyl fentanyl.

§https://healthcollaborative.org/lock-it-up-project/.

¶http://centralvalleyopioidsafety.org/.

**http://actionnewsnow.com/content/news/Overdose-Victim-Family-Members-Speak-Out-About-Incident--504403741.html.

TABLE. Demographic characteristics, naloxone administration characteristics, toxicology results,* and outcomes of four patients with fentanyl overdoses — Fresno and Madera Counties, California, January 7, 2019

Characteristic	Patient A	Patient B	Patient C	Patient D
Age group (yrs)	30–39	20–29	20–29	30–39
Sex	Male	Male	Male	Female
Provider/Route and naloxone dose (mg)				
EMS/Intranasal	N/A	3.0	2.0	N/A
ED/Intravenous	N/A	1.0	0.4, 1.0	N/A
Outcome	ICU, brain death 3 days later	TU, discharge on day 2	TU, discharge on day 2	Pronounced dead at scene
Serum drug levels (ng/mL)	fentanyl 2.5; norfentanyl 0.4	fentanyl 5.3; norfentanyl 0.6	fentanyl 4.3; norfentanyl <0	N/A
Other substances detected in serum	Cotinine	Methamphetamine, amphetamine, cotinine	none	Fentanyl, norfentanyl†

Abbreviations: ED = emergency department; EMS = emergency medical services; ICU = intensive care unit; N/A = not applicable; TU = telemetry unit.
* Except for patient D, testing was performed on blood specimens obtained upon initial hospital evaluation; for patient D, testing was performed on postmortem blood specimen. Testing for patients A, B, and C was done at the University of California San Francisco Clinical Laboratory, Zuckerberg San Francisco General Hospital using liquid chromatography quadrupole time-of-flight mass spectrometry.
† Included as other because quantitative levels could not be determined.

In the days following the multiagency press conference, FCDPH disseminated a California Health Alert Network message to approximately 700 Fresno County providers about free online medication-assisted treatment waiver training and encouraged use of the Controlled Substance Utilization Review and Evaluation System prescription drug–monitoring program for opioid users.†† Local emergency departments continued to focus on referring persons using drugs other than opioids (e.g., cocaine) to substance use disorder treatment as indicated. FCDPH continues to monitor potential fentanyl overdose cases and work with the Fresno County Department of Behavioral Health, medical providers, and the Fresno County Sheriff-Coroner's Office to educate and warn the public about the risks of street drugs. On January 24, a suspect was charged with two counts of distributing fentanyl resulting in death, related to the overdoses in Fresno and Madera counties described in this report.§§ This multiagency response was key to disseminating information to the public and other health providers about the outbreak and about naloxone distribution and use. Efforts to better understand the nature of substance use and co-involvement of different drug classes is needed for tailored prevention and response strategies.

†† https://oag.ca.gov/cures.
§§ https://www.dea.gov/press-releases/2019/01/25/fresno-man-charged-two-counts-distributing-fentanyl-resulting-death.

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All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

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Erratum

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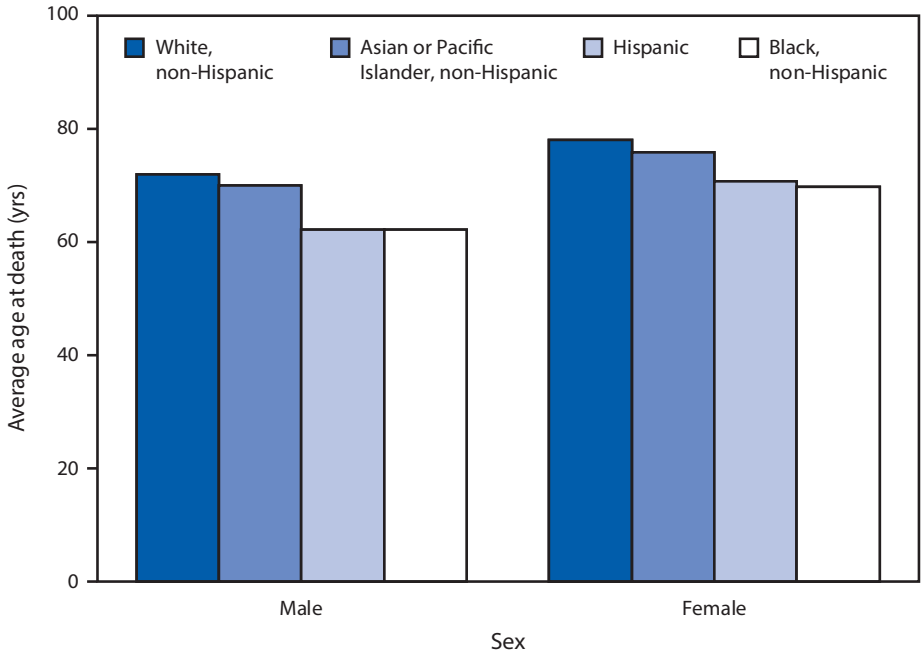
In the report "*Vital Signs*: Surveillance for Acute Flaccid Myelitis — United States, 2018," on page 609, in the first paragraph of the Results section, the fourth sentence should have read "Patients with illnesses classified as non-AFM were significantly older than were patients with confirmed AFM (median = **8.8** years [range = 1 month–78.1 years]; p<0.001) (Table 1)."

On page 611, in Table 1, for "Laboratory finding; Spine MRI performed," the number of confirmed cases should have been "**233/233 (100)**," and the P-value should have been "**0.10**." In addition, for "Timing of preceding illness to onset of limb weakness, median days (range, IQR); Any respiratory illness," the interquartile range (IQR) for noncases should have been "6.5 (0–28, **4–11.5**)."

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Average Age at Death*,† by Race/Hispanic Origin and Sex — National Vital Statistics System, United States, 2017



* The average age at death is the sum of age at death for all deaths from each group divided by the total number of deaths from that group.
† Records with age not stated were not included.

In 2017, in the United States, the average age at death among males was highest for non-Hispanic whites (72.0 years), followed by non-Hispanic Asians or Pacific Islanders (70.0), Hispanics (62.2), and non-Hispanic blacks (62.1). Among females, the average age at death was highest for non-Hispanic whites (78.1 years), followed by non-Hispanic Asians or Pacific Islanders (75.8), Hispanics (70.7), and non-Hispanic blacks (69.7).

Source: National Vital Statistics System. Underlying cause of death data, 1999–2017. https://wonder.cdc.gov/ucd-icd10.html.

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