

Opioid Prescribing Rates in Nonmetropolitan and Metropolitan Counties Among Primary Care Providers Using an Electronic Health Record System — United States, 2014–2017

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Drug overdose is the leading cause of unintentional injury-associated death in the United States. Among 70,237 fatal drug overdoses in 2017, prescription opioids were involved in 17,029 (24.2%) (1). Higher rates of opioid-related deaths have been recorded in nonmetropolitan (rural) areas (2). In 2017, 14 rural counties were among the 15 counties with the highest opioid prescribing rates.* Higher opioid prescribing rates put patients at risk for addiction and overdose (3). Using deidentified data from the Athenahealth electronic health record (EHR) system, opioid prescribing rates among 31,422 primary care providers[†] in the United States were analyzed to evaluate trends from January 2014 to March 2017. This analysis assessed how prescribing practices varied among six urban-rural classification categories of counties, before and after the March 2016 release of CDC's *Guideline for Prescribing Opioids for Chronic Pain* (Guideline) (4). Patients in non-core (the most rural) counties had an 87% higher chance of receiving an opioid prescription compared with persons in large central metropolitan counties during the study period. Across all six county groups, the odds of receiving an opioid prescription decreased significantly after March 2016. This decrease followed a flat trend during the preceding period in micropolitan and large central metropolitan county groups; in contrast, the decrease continued previous downward trends in the other four county groups. Data from EHRs can effectively supplement traditional surveillance methods for monitoring

trends in opioid prescribing and other areas of public health importance, with minimal lag time under ideal conditions. As less densely populated areas appear to indicate both substantial progress in decreasing opioid prescribing and ongoing need for reduction, community health care practices and intervention programs must continue to be tailored to community characteristics.

Athenahealth is a commercial vendor and developer of cloud-based practice management and EHR systems for physician practices and hospitals. Approximately 100,000 health providers, serving about 86 million patients in the United States, use Athenahealth's applications. This retrospective study used deidentified Athenahealth EHR prescription data from 31,422 primary health care providers serving approximately 17 million

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Continuing Education examination available at https://www.cdc.gov/mmwr/cme/conted_info.html#weekly.

* U.S. Opioid Prescribing Rate Maps. <https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html>.

[†] Primary care providers in an ambulatory setting; limited to family medicine, family practice, or general practice, or providers who have an internal medicine specialty with no subspecialty. Nurse practitioners and physician assistants are included among primary care providers.



patients. Patient-level data were aggregated by week over the 166 weeks from January 5, 2014, through March 11, 2017. For each week during which a patient had at least one Athenahealth record, that patient contributed one patient-week to this analysis. For each patient-week, it was noted whether primary care providers using Athenahealth's EHR system prescribed one or more opioids (Supplementary Table 1, <https://stacks.cdc.gov/view/cdc/61743>).[§] Percentage of patient-weeks during which an opioid prescription was written was considered equivalent to the percentage of patients receiving an opioid prescription during that time.

For comparisons over time, data were divided into three periods. Period 1 comprises 52 weeks from January 5, 2014, through January 3, 2015; period 2 includes the next 63 weeks, ending March 19, 2016; and period 3 covers the final 51 weeks, through March 11, 2017. The first cutpoint allows comparisons between the first and second years' data, and the second cutpoint supports comparisons before and after the publication of the CDC Guideline. For comparison by population density, data were stratified by providers' counties according to

[§] Short and long acting opioid drugs in this study included buprenorphine, butorphanol, codeine, dihydrocodeine, fentanyl, hydrocodone, hydromorphone, levorphanol, meperidine, methadone, morphine, naltrexone, nalbuphine, naloxone, oxycodone, oxymorphone, pentazocine, propoxyphene, tapentadol, and tramadol. The study does not count cough and cold medications containing opioids.

CDC's National Center for Health Statistics urban-rural classification scheme.[¶] From most to least densely populated, the six categories include large central metropolitan, large fringe metropolitan, medium metropolitan, small metropolitan, micropolitan, and noncore counties.

This analysis includes three components. First, the period-specific percentage of patients with opioid prescriptions was estimated empirically and with seasonal adjustment using logistic regression. Second, smooth temporal trends were statistically separated from annual seasonal components using locally weighted regression (5). Third, to quantify the period-specific annual rate of increase or decrease in prescribing rates, a second logistic regression model estimated the seasonally adjusted annual percent change (APC) in the odds of receiving an opioid prescription. Statistical software was used for all analyses; statistical tests and confidence intervals (CIs) are presented as simultaneous procedures adjusted for multiple comparisons.

Overall, 128,194,491 patient-weeks of data are included in the analysis; at least one opioid was prescribed during 8,810,237 (6.9%) of these patient-weeks, decreasing from 7.4% during period 1 to 6.4% during period 3 (Table 1) (Supplementary Table 2, <https://stacks.cdc.gov/view/cdc/61744>). Buprenorphine prescribed for pain and opioid use disorder treatment represented only 0.02% of all opioid

[¶] https://www.cdc.gov/nchs/data_access/urban_rural.htm; https://www.cdc.gov/nchs/data/series/sr_02/sr02_166.pdf.

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TABLE 1. Number and percentage of patient-weeks with at least one opioid prescription — Athenahealth, United States, January 2014–March 2017

Urban-rural category*	No. of patient-weeks	No. receiving opioid prescription	Percentage receiving opioid prescription			
			Overall	Period 1†	Period 2†	Period 3†
Noncore	8,979,403	864,364	9.6	10.3	9.9	9.0
Micropolitan	16,342,824	1,532,747	9.4	9.4	9.6	9.1
Small metro	18,860,569	1,443,246	7.7	8.0	7.7	7.4
Medium metro	32,045,592	2,158,111	6.7	7.3	6.9	6.2
Large fringe metro	31,430,958	1,753,802	5.6	6.4	5.8	5.0
Large central metro	20,535,145	1,057,967	5.2	5.4	5.2	5.0
All counties	128,194,491	8,810,237	6.9	7.4	7.0	6.4

* National Center for Health Statistics urban-rural classification scheme for counties. https://www.cdc.gov/nchs/data_access/urban_rural.htm.

† Period 1: January 5, 2014–January 3, 2015; period 2: January 4, 2015–March 19, 2016; period 3: March 20, 2016–March 11, 2017. Period-specific percentages are based on raw counts rather than statistical models.

prescriptions. By county classification, the overall percentage of patients with opioid prescriptions ranged from 5.2% in large central metropolitan counties to 9.6% in noncore counties during the study period. Patients in noncore counties had an 87% higher chance of receiving an opioid prescription than did patients in large central metropolitan areas during the study period.

The lowest period-specific percentages of patient-weeks with an opioid prescription occurred in large central metropolitan counties (5.0%–5.4%) ($p < 0.001$, multiplicity-adjusted Wald tests), except during period 3, when percentages in large metropolitan counties (5.0%) were the same as those in large fringe metropolitan counties (5.0%) (Supplementary Table 2, <https://stacks.cdc.gov/view/cdc/61744>). In contrast, the highest period-specific percentages (9.0%–10.3%) were in noncore counties ($p < 0.02$), except in period 3, when percentages in noncore counties (9.0%) were similar to those in micropolitan counties (9.1%). Across metropolitan and nonmetropolitan categories, all percentages of weeks with an opioid prescription during period 2 were significantly different from those

in period 1, and percentages in period 3 differed significantly from those in period 2 ($p < 0.003$).

Visual inspection of the prescribing trends by urban-rural status and by period revealed patterns in both the raw (Supplementary Figure 1, <https://stacks.cdc.gov/view/cdc/61741>) and seasonally adjusted (Supplementary Figure 2, <https://stacks.cdc.gov/view/cdc/61742>) data. During period 1, before release of the CDC Guideline, the odds of receiving an opioid prescription increased 6.4% per year in noncore counties (95% multiplicity-adjusted Wald CI = 2.1–10.8), and 9.7% per year in micropolitan counties (95% CI = 6.5–13.0) (Table 2) (Figure). During period 3, after release of the CDC Guideline, the odds of receiving an opioid prescription decreased significantly in all county groups. Comparing trends between periods, the APC increased in large central metropolitan counties in period 2 compared with period 1 ($p < 0.001$) and decreased between periods 2 and 3 ($p < 0.001$). In the other five urban-rural categories, the APC decreased in period 2 compared with period 1 ($p < 0.02$); among these five groups, only micropolitan counties experienced a significant decrease in APC between periods 2 and 3 ($p < 0.001$).

TABLE 2. Annual percent change (APC) in odds of receiving at least one opioid prescription — Athenahealth, United States, January 2014–March 2017

Urban-rural category*	Period 1†	Period 2†	Period 3†	p-value (direction of change)§	
	APC (95% CI)	APC (95% CI)	APC (95% CI)	Period 1 versus period 2	Period 2 versus period 3
Noncore	6.4 (2.1 to 10.8) [¶]	-10.1 (-12.2 to -8.0) [¶]	-7.5 (-10.7 to -4.2) [¶]	<0.001 (decrease)	0.713 (—)
Micropolitan	9.7 (6.5 to 13.0) [¶]	-0.8 (-2.6 to 0.9)	-13.3 (-15.6 to -10.9) [¶]	<0.001 (decrease)	<0.001 (decrease)
Small metro	0.2 (-2.8 to 3.2)	-4.5 (-6.2 to -2.7) [¶]	-5.8 (-8.4 to -3.2) [¶]	0.013 (decrease)	0.977 (—)
Medium metro	-2.5 (-4.8 to -0.1)**	-8.7 (-10.1 to -7.4) [¶]	-9.2 (-11.2 to -7.2) [¶]	<0.001 (decrease)	0.999 (—)
Large fringe metro	-2.0 (-4.7 to 0.8)	-14.9 (-16.2 to -13.5) [¶]	-13.1 (-15.1 to -10.9) [¶]	<0.001 (decrease)	0.616 (—)
Large central metro	-9.9 (-13.2 to -6.4) [¶]	1.8 (-0.3 to 3.9)	-11.7 (-14.3 to -8.9) [¶]	<0.001 (increase)	<0.001 (decrease)
All counties	-1.4 (-10.6 to 8.8)	-8.2 (-13.3 to -2.7)^{††}	-10.4 (-17.9 to -2.2)^{††}	0.371 (—)	0.856 (—)

Abbreviation: CI = confidence interval.

* National Center for Health Statistics urban-rural classification scheme for counties. https://www.cdc.gov/nchs/data_access/urban_rural.htm.

† Period 1: January 5, 2014–January 3, 2015; period 2: January 4, 2015–March 19, 2016; period 3: March 20, 2016–March 11, 2017.

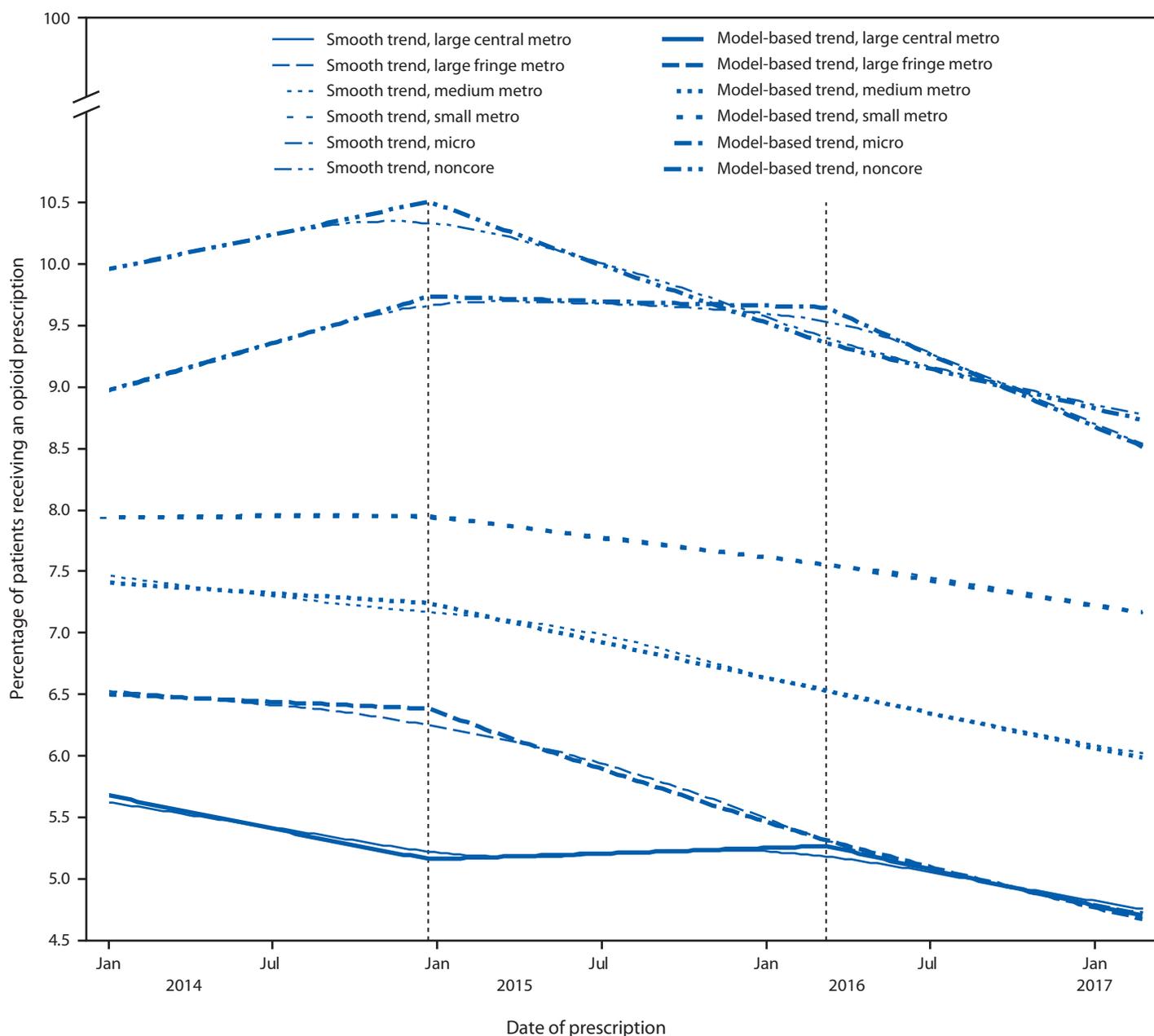
§ p-values from multiplicity-adjusted Wald tests; (—) indicates a nonsignificant difference ($p > 0.05$) between APCs in adjacent periods.

[¶] $p < 0.001$.

** $p < 0.05$.

†† $p < 0.01$.

FIGURE. Model-based trends in percentage of patient-weeks with at least one opioid prescription, by urban-rural category — Athenahealth, United States, January 2014–March 2017



Discussion

Throughout the analysis period, opioid prescribing rates by primary care providers were significantly higher in nonmetropolitan counties than in metropolitan counties. Whereas the prescribing rate increased from January 2014 through January 2015 (period 1) in both micropolitan and noncore counties, those trends halted, and rates became flat or declined through mid-March 2016 (period 2). Trends in all other urban-rural categories were flat or decreasing over the same two periods. The odds of a patient receiving an opioid prescription decreased

in all urban-rural county groups after the March 2016 publication of the CDC Guideline. Those trends represented significant decreases in the micropolitan and large central metropolitan categories. In the other four county groups, however, the significant decreases after March 2016 represented a continuation of previously decreasing trends.

Higher odds of opioid prescribing in nonmetropolitan counties might be attributed in part to prescription drug use and misuse at an earlier age as well as higher prevalences of chronic pain among persons living in rural areas (6,7). Nonmetropolitan

counties also tend to have larger populations of older adults who have higher prevalences of conditions associated with pain (6). Opioid prescribing in rural (nonmetropolitan) areas is strongly influenced by providers' individual relationships with their patients (8), and can be inconsistent with opioid prescribing guidelines. As well, access to medication-assisted treatment facilities and alternative therapies are limited in rural areas (8). Variations in the implementation of state-run prescription drug monitoring programs and state-based laws (9), such as the regulation of pain-management clinics, might also differ in urban and rural communities.

Despite reductions in opioid prescribing in recent years (1), opioid-involved overdose death rates have increased, largely driven by heroin and illicitly manufactured fentanyl (2). Many persons who self-report heroin use have a history of misusing prescription opioids (10). Addressing prescription opioid use is an important step in curbing opioid-involved overdose deaths. Interventions such as using Prescription Drug Monitoring Programs and practices that align with evidence-based adoption of the CDC Guideline can improve prescribing decisions.** The Guideline can help providers and patients weigh the benefits and risks of prescribing opioids according to best available evidence and individual patient needs (4). This study demonstrates that data from EHRs can effectively supplement traditional surveillance methods for monitoring trends in opioid prescribing and other areas of public health importance. The lag between the collection of the data and this analysis could potentially be reduced to a matter of weeks with optimized workflows.

The findings in this report are subject to at least three limitations. First, the conclusions drawn from the records provided by Athenahealth might not be generalizable to all patients in primary care. Second, although the data include all patients with an opioid prescription, they do not include other characteristics of each prescription, including indication (e.g., chronic versus acute pain or opioid use disorder treated with buprenorphine [although this drug accounted for a small fraction of all opioids prescribed]) and whether prescriptions were filled and taken as prescribed. Finally, this analysis does not account for differing demographic profiles across counties, such as age distributions and payer types, which could be confounded by population density in its association with opioid prescribing rates.

The percentage of patients who received an opioid prescription was lower in more densely populated counties than among less populated rural counties; however, all areas, including rural counties, experienced substantial decreases in prescribing

Summary

What is already known about this topic?

Opioid prescribing rates vary by county urbanization level and are declining overall.

What is added by this report?

Analysis of patient opioid prescription data from a national electronic health record vendor during 2014–2017 found that the percentage of patients prescribed an opioid was higher in rural than in urban areas. Significant decreases in opioid prescribing occurred across all urban-rural categories after the March 2016 release of the CDC *Guideline for Prescribing Opioids for Chronic Pain*.

What are the implications for public health practice?

As less densely populated areas indicate both progress in decreasing opioid prescribing and need for ongoing reduction, tailoring community health care practices and intervention programs to community characteristics will remain important.

over time. As less densely populated areas appear to indicate both substantial progress in decreasing opioid prescribing and ongoing need for reduction, community health care practices and intervention programs must continue to be tailored to community characteristics.

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Gastroschisis Trends and Ecologic Link to Opioid Prescription Rates — United States, 2006–2015

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Prevalence of gastroschisis, a serious birth defect of the abdominal wall resulting in some of the abdominal contents extending outside the body at birth, has been increasing worldwide (1,2). Gastroschisis requires surgical repair after birth and is associated with digestive and feeding complications during infancy, which can affect development. Recent data from 14 U.S. states indicated an increasing prevalence of gastroschisis from 1995 to 2012 (1). Young maternal age has been strongly associated with gastroschisis, but research suggests that risk factors such as smoking, genitourinary infections, and prescription opioid use also might be associated (3–5). Data from 20 population-based state surveillance programs were pooled and analyzed to assess age-specific gastroschisis prevalence during two 5-year periods, 2006–2010 and 2011–2015, and an ecologic approach was used to compare annual gastroschisis prevalence by annual opioid prescription rate categories. Gastroschisis prevalence increased only slightly (10%) from 2006–2010 to 2011–2015 (prevalence ratio = 1.1, 95% confidence interval [CI] = 1.0–1.1), with the highest prevalence among mothers aged <20 years. During 2006–2015, the prevalence of gastroschisis was 1.6 times higher in counties with high opioid prescription rates (5.1 per 10,000 live births; CI = 4.9–5.3) and 1.4 times higher where opioid prescription rates were medium (4.6 per 10,000 live births; CI = 4.4–4.8) compared with areas with low prescription rates (3.2 per 10,000 live births; CI = 3.1–3.4). Public health research is needed to understand factors contributing to the association between young maternal age and gastroschisis and assess the effect of prescription opioid use during pregnancy on this pregnancy outcome.

CDC requested annual data from U.S. population-based birth defects surveillance programs to assess the prevalence of gastroschisis during 2006–2015. The case definition for gastroschisis was based on the *British Pediatric Association Classification of Diseases* code (756.71), the *International Classification of Diseases, Ninth Revision, Clinical Modification* code (756.79 before October 1, 2009, and 756.73 thereafter because 756.79 was a shared code with omphalocele), or the *International Classification of Diseases, Tenth Revision, Clinical Modification* code (Q79.3 after October 1, 2015). Gastroschisis

cases included all pregnancy outcomes (i.e., live births, fetal deaths, terminations, and unspecified nonlive births). The total number of live births in the same catchment area were used as denominators.

Twenty states* provided data on gastroschisis by year, maternal age group, and maternal race/ethnicity. Births from these 20 state surveillance programs accounted for approximately 47% of all U.S. births. To provide a sufficient number of subjects for each comparison category, birth years were pooled into two 5-year periods (2006–2010 and 2011–2015). For each year during 2006–2015, IQVIA Xponent† provided CDC with county-specific opioid prescription rate categories (low = <57.2 opioid prescriptions per 100 persons per year; medium = 57.2–82.3; high = 82.4–112.5; and very high = >112.5) (6). The IQVIA county-specific opioid prescription rates were calculated by dividing the number of opioid prescriptions in each county by the U.S. Census county-level population estimates for each year. CDC provided these county opioid prescription levels to each participating birth defects surveillance program, which used them to ascertain the total number of gastroschisis cases and total number of live births each year in the state’s counties with low, medium, high, and very high opioid prescribing rates. Because gastroschisis prevalence was not found to be significantly different in areas where opioid prescribing rates were high and very high, these two categories were combined and are referred to as high for the remainder of this report. Surveillance programs aggregated gastroschisis data by year and opioid prescribing level; county-specific gastroschisis information on individual cases was not reported to CDC.

Prevalence of gastroschisis was calculated as number of gastroschisis cases (among all birth outcomes) divided by the total

*The 20 states that provided data on gastroschisis and the years for which data were provided were Arizona, CDC/Georgia (Metropolitan Atlanta Congenital Defects Program), Illinois, Kansas, Kentucky, Louisiana (2010–2015), Massachusetts, Minnesota, Nebraska, New Jersey, New York, North Carolina, Ohio (2010–2015), Rhode Island, South Carolina (2010–2015), Tennessee (2010–2015), Texas, Utah, Vermont (2009–2015), and Virginia. Data were provided from 2006 to 2015 unless otherwise noted.

†The IQVIA Xponent provides estimates of the number of opioid prescriptions dispensed in the United States based on a sample of approximately 59,000 pharmacies, which represent 88% of all prescriptions in the United States.

number of live births, and is presented as prevalence per 10,000 live births for each year and each 5-year period, by maternal age group and race/ethnicity. Exact Poisson methodology was used to calculate CIs (7). Statistical software was used for all analyses, including to generate prevalence ratios (PRs) for each maternal age and race/ethnicity category and overall. Linear trends in gastroschisis prevalence by maternal age from 2006 to 2015 were examined using the Cochran-Armitage test. In the ecologic analysis, PRs were calculated by dividing the prevalence of gastroschisis in areas with high and medium prescription rates by those with low rates for each calendar year and over the entire study period.

During 2006–2010, among 8,342,741 live births, 3,489 gastroschisis cases (4.2 per 10,000 live births; CI = 4.0–4.3)

were reported; during 2011–2015, among 9,359,005 live births, 4,166 (4.5 per 10,000 live births; CI = 4.3–4.6) were reported (PR = 1.1, CI = 1.0–1.1) (Table). Gastroschisis prevalence was higher among infants born to non-Hispanic white mothers and Hispanic mothers than among those born to non-Hispanic black mothers in most maternal age categories (<20, 20–24, and 25–29 years). From 2006 to 2015, a linear increase in the prevalence of gastroschisis was observed in three of the four maternal age categories (Figure 1). Although gastroschisis prevalence was highest among infants born to mothers aged <20 years in each year, there was no significant linear increase.

During 2006–2015, prevalences of gastroschisis in areas where opioid prescription rates were high (5.1 per 10,000 live

TABLE. Gastroschisis cases, gastroschisis prevalence, and prevalence ratio (PR), by maternal age group and race/ethnicity for two periods — 20 U.S. states, 2006–2015*

Maternal age group (yrs), [†] race/ethnicity	2006–2010		2011–2015		2006–2015		PR [¶] (95% CI)
	No. of cases	Prevalence [§] (95% CI)	No. of cases	Prevalence [§] (95% CI)	No. of cases	Prevalence [§] (95% CI)	
<20 yrs							
White, non-Hispanic	461	17.1 (15.6–18.7)	420	17.2 (15.6–18.9)	881	17.1 (16.0–18.3)	1.0 (0.9–1.1)
Black, non-Hispanic	172	9.0 (7.7–10.5)	148	9.4 (8.0–11.1)	320	9.2 (8.2–10.3)	1.0 (0.8–1.3)
Hispanic	489	14.7 (13.4–16.1)	425	17.5 (15.9–19.2)	914	15.9 (14.9–16.9)	1.2 (1.0–1.4)**
A/PI or AI/AN, non-Hispanic	48	26.0 (19.2–34.5)	36	25.6 (18.0–35.5)	84	25.8 (20.6–32.0)	1.0 (0.6–1.5)
Total^{††}	1,194	14.5 (13.7–15.3)	1,055	15.7 (14.8–16.7)	2,249	15.0 (14.4–15.7)	1.1 (1.0–1.2)
20–24 yrs							
White, non-Hispanic	676	7.9 (7.3–8.5)	998	10.4 (9.8–11.1)	1,674	9.2 (8.8–9.7)	1.3 (1.2–1.5)**
Black, non-Hispanic	169	4.4 (3.8–5.2)	246	5.4 (4.8–6.1)	415	5.0 (4.5–5.5)	1.2 (1.0–1.5)
Hispanic	457	7.0 (6.4–7.7)	507	8.7 (8.0–9.5)	964	7.8 (7.4–8.4)	1.2 (1.1–1.4)**
A/PI or AI/AN, non-Hispanic	52	7.6 (5.7–10.0)	56	8.2 (6.2–10.7)	108	7.9 (6.5–9.6)	1.1 (0.7–1.6)
Total^{††}	1,389	7.0 (6.6–7.4)	1,859	8.9 (8.5–9.3)	3,248	8.0 (7.7–8.2)	1.3 (1.2–1.4)**
25–29 yrs							
White, non-Hispanic	298	2.5 (2.2–2.8)	495	3.4 (3.1–3.7)	793	3.0 (2.8–3.2)	1.4 (1.2–1.6)**
Black, non-Hispanic	51	1.6 (1.2–2.1)	89	2.3 (1.8–2.8)	140	2.0 (1.7–2.3)	1.4 (1.0–2.0)
Hispanic	153	2.5 (2.1–2.9)	188	3.2 (2.8–3.7)	341	2.8 (2.5–3.2)	1.3 (1.0–1.6)**
A/PI or AI/AN, non-Hispanic	18	1.2 (0.7–1.9)	38	2.3 (1.6–3.1)	56	1.8 (1.3–2.3)	1.9 (1.1–3.3)**
Total^{††}	536	2.3 (2.1–2.5)	828	3.1 (2.9–3.4)	1,364	2.8 (2.6–2.9)	1.3 (1.2–1.5)**
≥30 yrs							
White, non-Hispanic	147	0.8 (0.7–0.9)	242	1.1 (0.9–1.2)	389	0.9 (0.9–1.0)	1.3 (1.1–1.6)**
Black, non-Hispanic	28	0.8 (0.5–1.1)	46	1.0 (0.7–1.3)	74	0.9 (0.7–1.1)	1.2 (0.8–2.0)
Hispanic	51	0.7 (0.6–1.0)	83	1.1 (0.9–1.3)	134	0.9 (0.8–1.1)	1.5 (1.0–2.1)**
A/PI or AI/AN, non-Hispanic	14	0.5 (0.3–0.9)	21	0.6 (0.4–0.9)	35	0.6 (0.4–0.8)	1.2 (0.6–2.3)
Total^{††}	249	0.8 (0.7–0.9)	404	1.0 (0.9–1.1)	653	0.9 (0.8–1.0)	1.3 (1.1–1.6)**
All ages							
White, non-Hispanic	1,616	3.9 (3.7–4.1)	2,161	4.4 (4.2–4.6)	3,777	4.2 (4.0–4.3)	1.1 (1.1–1.2)**
Black, non-Hispanic	432	3.5 (3.1–3.8)	532	3.6 (3.3–3.9)	964	3.5 (3.3–3.8)	1.0 (0.9–1.2)
Hispanic	1,183	5.2 (4.9–5.5)	1,207	5.5 (5.2–5.9)	2,390	5.4 (5.1–5.6)	1.1 (1.0–1.2)**
A/PI or AI/AN, non-Hispanic	132	2.6 (2.2–3.1)	152	2.6 (2.2–3.0)	284	2.6 (2.3–2.9)	1.0 (0.8–1.2)
Total^{††}	3,489	4.2 (4.0–4.3)	4,166	4.5 (4.3–4.6)	7,655	4.3 (4.2–4.4)	1.1 (1.0–1.1)**

Abbreviations: A/PI = Asian/Pacific Islander; AI/AN = American Indian/Alaska Native; CI = confidence interval.

* States contributing to the table: Arizona, CDC/Georgia (Metropolitan Atlanta Congenital Defects Program), Illinois, Kansas, Kentucky, Louisiana (2010–2015), Massachusetts, Minnesota, Nebraska, New Jersey, New York, North Carolina, Ohio (2010–2015), Rhode Island, South Carolina (2010–2015), Tennessee (2010–2015), Texas, Utah, Vermont (2009–2015), and Virginia. Data were provided from 2006 to 2015 unless otherwise noted.

[†] Cases missing information on maternal age are not included in this table.

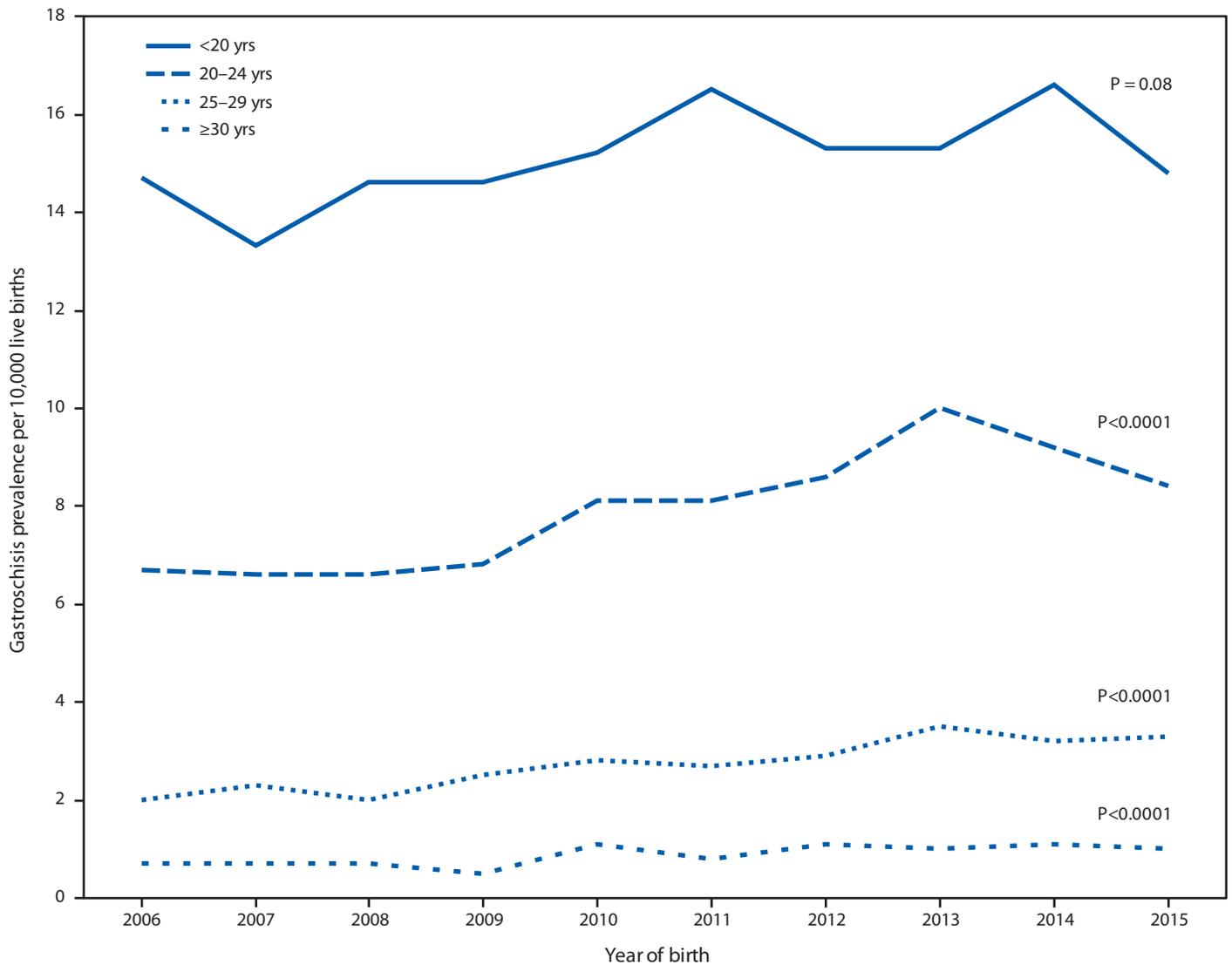
[§] Prevalence per 10,000 live births.

[¶] Unrounded prevalence for 2011–2015 divided by the unrounded prevalence for 2006–2010.

** Denotes a statistically significant confidence interval.

^{††} Total includes non-Hispanic white, non-Hispanic black, Hispanic, non-Hispanic A/PI, non-Hispanic AI/AN, and other/unknown maternal race/ethnicity.

FIGURE 1. Trends in gastroschisis prevalence, by maternal age group — 20 states, 2006–2015*

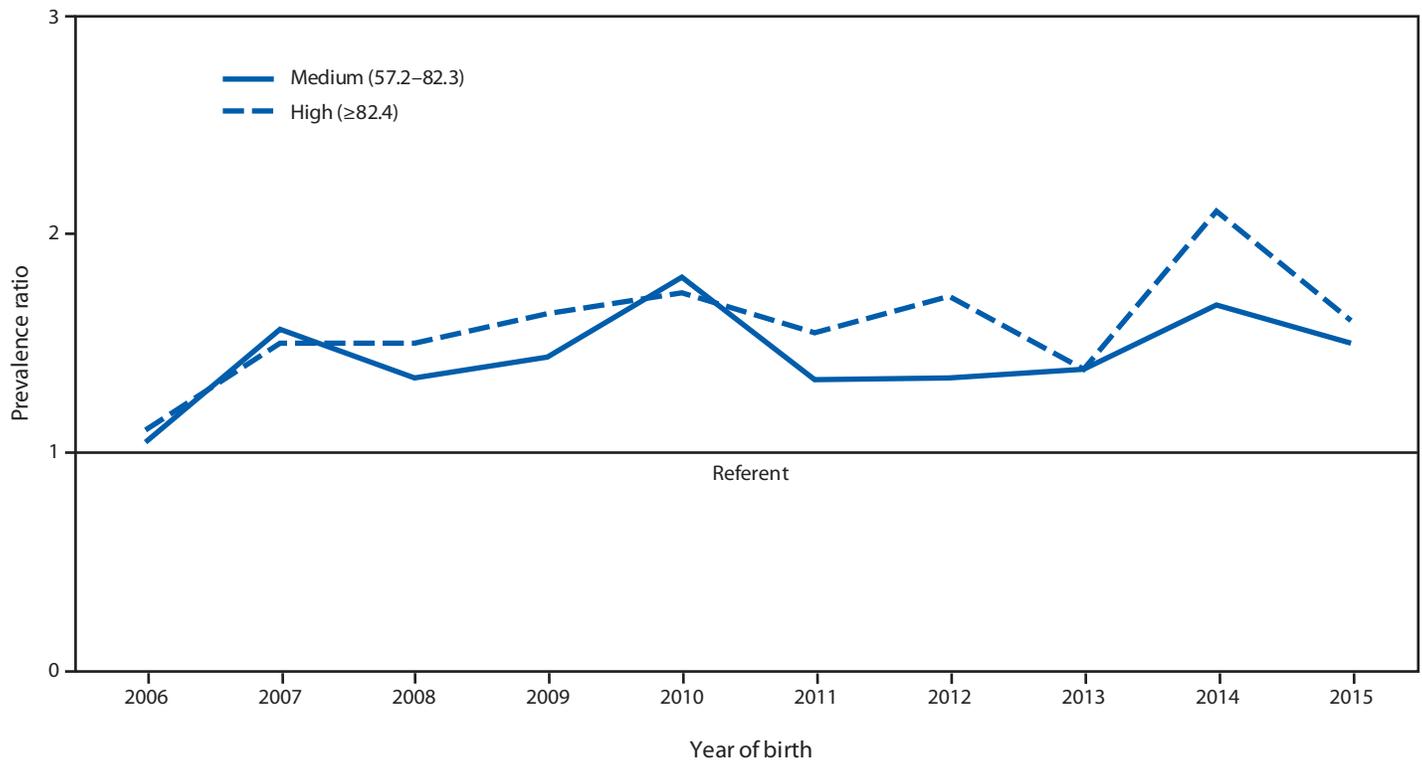


* States contributing to the figure: Arizona, CDC/Georgia (Metropolitan Atlanta Congenital Defects Program), Illinois, Kansas, Kentucky, Louisiana (2010–2015), Massachusetts, Minnesota, Nebraska, New Jersey, New York, North Carolina, Ohio (2010–2015), Rhode Island, South Carolina (2010–2015), Tennessee (2010–2015), Texas, Utah, Vermont (2009–2015), and Virginia. Data were provided from 2006 to 2015 unless otherwise noted.

births; CI = 4.9–5.3) and medium (4.6 per 10,000 live births; CI = 4.4–4.8) were 1.6 and 1.4 times higher, respectively, than were those in areas where opioid prescription rates were low (3.2 per 10,000 live births; CI = 3.1–3.4). PRs fluctuated over time, but stayed above 1.0 for each included study year (Figure 2). Within maternal age strata, higher gastroschisis PRs for high versus low opioid prescription rates were observed among mothers aged ≥ 25 years (<20 years: PR = 1.1, CI = 1.0–1.2; 20–24 years: 1.2, CI = 1.1–1.4; 25–29 years: 1.6, CI = 1.4–1.8; ≥ 30 years: 1.6, CI = 1.3–1.9).

Discussion

In the 20 states included in this report, gastroschisis prevalence increased slightly during 2011–2015 compared with that during 2006–2010. Although gastroschisis is more prevalent in infants born to mothers aged <20 years, the largest increases in prevalence occurred among mothers aged 20–24 years, 25–29 years, and ≥ 30 years. These findings do not entirely align with 1995–2012 data from 14 U.S. states (1), during which the greatest increase occurred among women aged <20 years. The current analysis includes data from more states, as well as more recent data, but there is no clear explanation for the slower rise in prevalence among the youngest group,

FIGURE 2. Trends in gastroschisis prevalence ratio, by year* and annual opioid prescription rate category† — 20 U.S. states, 2006–2015[§]

* Overall prevalence ratio for medium opioid prescription rate category and high opioid prescription rate category versus low opioid prescription rate category for each year of the study period 2006–2015.

† Opioid prescription rate categories include medium: 57.2–82.3 prescriptions per 100 persons and high: ≥82.4 prescriptions per 100 persons. The low opioid prescription rate category (<57.2 prescriptions per 100 persons) was used as the reference group.

[§] States contributing to the figure: Arizona, CDC/Georgia (Metropolitan Atlanta Congenital Defects Program), Illinois, Kansas, Kentucky, Louisiana (2010–2015), Massachusetts, Minnesota, Nebraska, New Jersey, New York, North Carolina, Ohio (2010–2015), Rhode Island, South Carolina (2010–2015), Tennessee (2010–2015), Texas, Utah, Vermont (2009–2015), and Virginia. Data were provided from 2006 to 2015 unless otherwise noted.

compared with that described in the earlier analysis. In most age categories, gastroschisis prevalence was higher among non-Hispanic white mothers and Hispanic mothers than among non-Hispanic black mothers, which is consistent with previous U.S. and international reports (1,2).

Possible causes for the increase in gastroschisis prevalence reported both in the United States and worldwide are not well understood (1,2). In the ecologic analysis, gastroschisis prevalence was higher in areas with high and medium opioid prescription rates, compared with that in areas with low rates. This ecologic analysis supports the findings from a large case-control study, which suggested that self-reported prescription opioid use in the first trimester was associated with gastroschisis (3). There have not been any observations published on animal models for this association. In a study exploring cumulative exposures among mothers of gastroschisis patients, the effect of a combined set of stressors, including prescription opioid use, was higher among older mothers (4), which is consistent with the finding in the ecologic analysis that the association between opioid prescription rates and gastroschisis appeared

to be more pronounced in mothers aged ≥25 years. The findings from different study designs have disparate strengths and weaknesses. The current ecologic design lacks patient-level data on exposure, but does provide information on population-level exposures and all cases of gastroschisis in each catchment area. The case-control studies have patient-level exposure data, but rely on maternal self-report and are limited to information from those mothers who voluntarily participated in the research studies. Together, these findings provide compelling evidence of the need to better understand the potential contribution of opioid exposure in the etiology of gastroschisis as well as the possible role opioids have played in the observed increases in gastroschisis.

The findings in this report are subject to at least three limitations. First, the ecologic analysis does not allow for inferring causality from the increased prevalence of gastroschisis in areas where opioid prescription rates were medium and high compared with those where opioid prescription rates were low because it could not link opioid prescriptions to individual mothers or examine timing of opioid use during pregnancy.

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Summary

What is already known about this topic?

Gastroschisis prevalence has increased worldwide. A previous U.S. report found that gastroschisis increased during 1995–2012, with the greatest increase among mothers aged <20 years.

What is added by this report?

During 2011–2015, gastroschisis prevalence was 4.5 per 10,000 live births, which was 10% higher than the prevalence during 2006–2010. An ecologic analysis found a higher prevalence of gastroschisis in areas where opioid prescriptions rates were high, supporting epidemiologic data suggesting an association between opioid use during pregnancy and gastroschisis.

What are the implications for public health practice?

Further public health research on gastroschisis is needed to gain insight into etiology, including the possible role of opioid exposure during pregnancy on birth defects.

Second, county-specific opioid prescription rate data limited to women could not be obtained, and the data did not include illicit opioid drugs, buprenorphine formulations used to treat opioid use disorder, or methadone dispensed through opioid treatment programs. However, previous research indicates that women are more likely than are men to be prescribed opioids and to report having received their opioids through prescription (8). Finally, this ecologic analysis did not account for county-level or patient-level confounders; it is possible that other county-level differences, in, for instance, socioeconomic status, average age at childbirth, age distribution, or differing demographics (e.g., older population with higher levels of chronic pain or use of prescription opioids), could have influenced these results. Future investigations using surveillance or case-control data will seek to examine patient-level data to account for these potential confounders as well as illicit opioid use, maternal smoking, and other polysubstance use.

The updated gastroschisis prevalence trends can be used to guide future basic science, public health, and clinical research on gastroschisis. Given that the majority of infants with gastroschisis are born to mothers aged <25 years, continued research is needed to focus on possible causal factors in the unique association between young maternal age and gastroschisis. The findings from the ecologic analysis can be used to prioritize basic science, public health, and clinical research on opioid exposure during pregnancy and its potential impact on birth defects. Having a better understanding of all possible effects of opioid use during pregnancy can help provide evidence-based information to health care providers and women about the potential risks to the developing fetus.[§]

[§]<http://www.pediatrics.org/cgi/doi/10.1542/peds.2018-3801>.

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Overdose Deaths Involving Fentanyl and Fentanyl Analogs — New York City, 2000–2017

Cody Colon-Berezin, MSPH¹; Michelle L. Nolan, MPH¹; Jaclyn Blachman-Forshay, MPH¹; Denise Paone, EdD¹

Unintentional drug overdose deaths have climbed to record high levels, claiming approximately 70,000 lives in the United States in 2017 alone (1). The emergence of illicitly manufactured fentanyl* (a synthetic, short-acting opioid with 50–100 times the potency of morphine) mixed into heroin, cocaine, and counterfeit pills, with or without the users' knowledge, has increased the risk for fatal overdose (2,3). The New York City (NYC) Department of Health and Mental Hygiene (DOHMH) conducts routine overdose mortality surveillance by linking death certificates with toxicology findings from the NYC Office of the Chief Medical Examiner (OCME). A 55% increase in the rate of fatal drug overdose in NYC was observed from 2015 to 2017, resulting in the highest number of overdose deaths recorded since systematic reporting began in 2000. Toxicology data indicate that this unprecedented increase in overdose deaths is attributable to fentanyl. Early identification of increased fentanyl involvement enabled DOHMH to respond rapidly to the opioid overdose epidemic by increasing awareness of the risks associated with fentanyl and developing effective risk reduction messaging. These results strongly suggest that, wherever possible, jurisdictions should consider integrating toxicology findings into routine overdose surveillance and work with local medical examiners or coroners to include fentanyl in the literal text on death certificates.

Since 2013, illicitly manufactured fentanyl has been involved in a growing number of overdose deaths nationally (3,4) and in NYC and has been represented increasingly in seizures of synthetic opioids (5,6). The increased presence of fentanyl in the illicit drug market has implications for overdose prevention efforts; however, national reporting on the presence of fentanyl in overdose deaths is limited by the lack of standardized toxicology testing for fentanyl and the inconsistent listing of fentanyl as a cause of death on death certificates, resulting in underreporting of fentanyl involvement in fatal overdoses. Nationally, reporting on drugs involved in overdose deaths relies on death certificate data; despite local efforts to improve drug reporting on death certificates, at least 15% of overdose deaths do not specify any drugs (7). Thus, drug-specific data continue to be underreported, making it difficult to quantify the role of fentanyl in increasing overdose death rates.

*In this report, "fentanyl" refers to both the pharmacologic compound and any of its analogs.

For this analysis, DOHMH defined a death as an unintentional drug overdose if the medical examiner determined the manner of death to be accidental and the underlying or multiple-cause code was assigned an *International Classification of Diseases, Tenth Revision* code of X40–X44 (accidental overdose of drugs), F11–F16, or F18–F19 (excluding F-codes with 0.2 or 0.6 third digit).[†] Toxicology findings were abstracted from OCME files and were used to classify overdose deaths according to the substances involved. Although OCME conducted fentanyl testing of all overdose cases during 2000–2012, universal testing for fentanyl was suspended during late 2013–July 2016, and the proportion of deaths tested during this time is unknown. However, despite inconsistent testing, in 2015 the proportion of all overdose deaths where fentanyl was detected exceeded that during the period of known universal fentanyl testing.

Unintentional drug overdose deaths were dichotomized according to whether or not any fentanyl was detected. The proportions of overdose deaths that involved fentanyl, overall and by other drug type involved, were calculated. Age-adjusted person-time rates were calculated by year using 2000–2016[§] NYC population estimates adjusted to the U.S. Census 2000 projected population. Changes in rates were tested using z-tests and 95% confidence intervals; comparisons were based on the gamma confidence interval distribution.

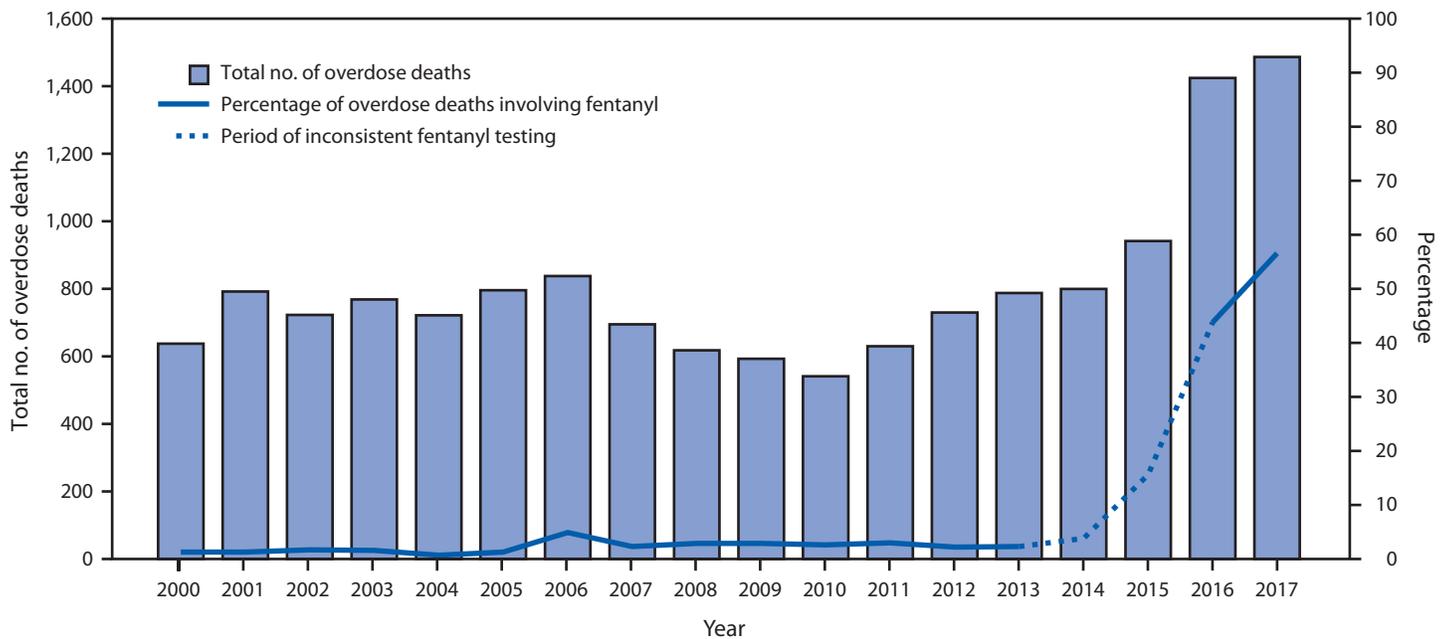
Among 10,673 fatal overdoses in NYC during 2000–2014, a total of 7,822 (73%) involved an opioid. Fentanyl was determined to be involved in 246 of these deaths (i.e., 2% of all overdose deaths or 3% of deaths involving an opioid) (Figure). Beginning in 2015, the percentage of fentanyl-involved overdose deaths increased sharply; in 2016, 624 (44%) of 1,425 drug overdose deaths involved fentanyl, and in 2017, 842 (57%) of 1,487 overdose deaths involved fentanyl.

From 2014 to 2017, the rate of fentanyl-involved overdose deaths in NYC increased almost 3,000%, from 0.4 per 100,000 to 12.1. This trend is driving the overall increase in the rate

[†] Disorders related to the use of opioids; cannabis; sedatives, hypnotics, or anxiolytics; cocaine; stimulants, hallucinogens; inhalants; or other psychoactive substances (excluding F-codes with 0.2 or 0.6 as the third digit, which specify a substance dependence or amnesic syndrome, respectively). DOHMH performs a secondary review on OCME case that have been assigned an X or F code because some F-coded cases involve acute drug intoxication. This review also facilitates reporting of toxicology involved.

[§] DOHMH population estimates are modified from U.S. Census Bureau intercensal estimates.

FIGURE. Number of overdose deaths and percentage of overdose deaths involving fentanyl* — New York City, 2000–2017



* Universal testing for fentanyl was stopped sometime during 2013 and restarted on July 1, 2016; fentanyl data during 2013–2016 were obtained from the Office of the Chief Medical Examiner but are known to be incomplete.

of overdose deaths in NYC, which rose 81% during the same period, from 11.7 per 100,000 in 2014 to 21.2 in 2017, the highest rate since tracking of overdose deaths using this methodology began in 2000. In 2017, 531 (69%) heroin-involved deaths and 387 (53%) cocaine-involved overdose deaths also involved fentanyl (Table). Fentanyl also was involved in 146 (39%) deaths that involved cocaine but not heroin.

Discussion

DOHMH first detected an increase in fentanyl-involved overdose deaths in October 2015. Universal testing for the presence of fentanyl by OCME was suspended from 2013 through mid-2016, which made interpreting the significance of the observed increase a challenge. Working with DOHMH, OCME reinstated universal testing for fentanyl by July 1, 2016. Despite the absence of systematic testing, DOHMH released a health advisory[‡] in April 2016 confirming an increase in the rate of fentanyl-involved deaths, compared with previous periods of known universal testing (2000–2012). By the end of 2017, NYC recorded the highest number (1,487) and rate (21.2 per 100,000) of overdose deaths since tracking of overdose deaths using this methodology began in 2000 (8). From 2012, the last year of universal testing for fentanyl, to 2017, the first full year of resumed universal testing, the percentage

of overdose deaths involving fentanyl increased from 2% (16 of 730) to 57% (842 of 1,487), suggesting that fentanyl was driving the observed increase in drug overdose deaths.

Without monthly surveillance of overdose deaths, timely detection of the emergent spike in fentanyl-involved deaths would not have been possible. The subsequent implementation of routine, comprehensive toxicology testing was critical to prospectively quantifying the extent of fentanyl's presence in fatal overdoses. Whereas the use of toxicology data are central to overdose reporting in NYC, not all jurisdictions have the capacity to conduct toxicology testing on all suspected overdose cases or to abstract this information from medical examiner files. Health authorities without the capacity to abstract and report toxicology data can work with medical examiners to ensure drug-specific language is included in the cause of death fields on death certificates, which can improve the completeness of overdose reporting and tracking nationally. DOHMH has worked closely with OCME to ensure that suspected overdose cases are routinely tested for fentanyl, and that specific drugs (i.e., “fentanyl,” instead of “opioid”) involved in overdose deaths are listed in the literal text on death certificates, thus improving the quality of NYC overdose data (9).

The emergence of fentanyl as a factor in approximately half of the overdose deaths in NYC by 2016 necessitated novel and rapid strategies for disseminating information on reducing harms. After releasing routine health advisory notices in April

[‡] <https://www1.nyc.gov/assets/doh/downloads/pdf/han/advisory/fentanyl-overdose.pdf>.

TABLE. Drug overdose deaths involving fentanyl, by selected drug(s) of involvement — New York City, 2017

Drugs	No. of overdose deaths	No. of overdose deaths with fentanyl detected (%)
Total	1,487	842 (57)
Heroin*	771	531 (69)
Cocaine*	732	387 (53)
Cocaine without heroin	379	146 (39)

* Drug categories are not mutually exclusive; includes deaths involving both heroin and cocaine.

and again in October 2016** to clinicians and health care providers citywide, DOHMH determined that more targeted communication concerning the risks associated with fentanyl was warranted. DOHMH conducted neighborhood-level outreach to syringe services programs and other programs that work with persons who inject drugs, advising them to 1) avoid using alone; 2) start with a small amount; 3) carry naloxone; and 4) avoid mixing drugs. Rapid responders were deployed to neighborhoods with higher rates of fentanyl-involved deaths to distribute educational flyers and fact sheets. This strategy was crucial to promoting public awareness of fentanyl in a timely manner.

As states expand overdose prevention efforts, the experience of NYC illustrates the importance of robust overdose surveillance, particularly in jurisdictions experiencing large increases in overdose deaths (10). Because of the high risk for overdose associated with using fentanyl, timely detection of fentanyl-involved deaths at the local level is critical (10). Incorporating systematic testing for fentanyl into overdose death investigations could provide vital information on underlying mortality causes and facilitate implementation of targeted overdose prevention education.

The findings in this report are subject to at least two limitations. First, universal testing for fentanyl was performed on all suspected overdose cases during 2000–2012 but was suspended late in 2013. In response to the detected increase in fentanyl involvement, OCME resumed universal testing for fentanyl on July 1, 2016. Therefore, fentanyl-involved overdose deaths might be underrepresented in the data during 2013–2016. Second, whereas fentanyl analogs clearly are illicitly manufactured, DOHMH is not able to distinguish deaths attributable to illicit fentanyl from those involving pharmaceutical fentanyl. However, analysis of NYC and national Prescription Drug Monitoring Program data indicate that while fentanyl seizures by law enforcement have risen sharply, rates of fentanyl prescription have remained stable (4). It is therefore likely that illicitly manufactured fentanyl, not pharmaceutical fentanyl, is driving NYC's increase in drug overdose mortality.

** <https://www1.nyc.gov/assets/doh/downloads/pdf/han/advisory/fentanyl-advisory.pdf>.

Summary

What is already known about this topic?

During 1999–2017, the rate of drug overdose deaths nationally approximately tripled; approximately 70,000 overdose deaths occurred nationally in 2017, with nearly 68% involving an opioid.

What is added by this report?

Using toxicology data, New York City identified fentanyl in 2% of drug overdose deaths during 2000–2012. By 2017, fentanyl was involved in 57% of all drug overdose deaths in New York City.

What are the implications for public health practice?

Universal fentanyl testing by local medical examiners and inclusion of drug-specific language on death certificates can aid surveillance and address the role of fentanyl in drug overdoses. Community-level educational outreach is indicated when an increase in fentanyl involvement is detected.

The trends seen in NYC reflect the broader impact of fentanyl on rates of overdose deaths across the country, with the rate of overdose deaths involving synthetic opioids increasing by approximately 45% nationally from 2016 to 2017 (1). Addressing the fentanyl-driven overdose epidemic requires the coordinated efforts of public health authorities and medical examiners to systematically identify and list fentanyl in fatal overdose cases, to the extent possible. Access to drug-specific data can help target interventions and monitor their effectiveness. These measures will help direct the distribution of resources and the implementation of critical public health responses.

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Notes from the Field

Fentanyl Drug Submissions — United States, 2010–2017

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Julie O'Donnell, PhD¹; Puja Seth, PhD¹

In 2017, the United States recorded 70,237 drug overdose deaths; among these, 47,600 (67.8%) involved an opioid, and 28,466 (40.5%) involved a synthetic opioid other than methadone (e.g., fentanyl and tramadol) (1). During 2013–2017, sustained growth in the availability of illicitly manufactured fentanyl (IMF) drove large increases in overdose deaths involving a synthetic opioid other than methadone (1). Specifically, the number of drug products obtained by law enforcement that were submitted for laboratory testing and tested positive for fentanyl (fentanyl submissions) increased rapidly, especially in the Midwest and Northeast U.S. Census regions.* Fentanyl, a synthetic opioid that is 50–100 times more potent than morphine, is legally available by prescription for pain treatment[†]; IMF is sold unadulterated (e.g., as a powder, pressed into counterfeit pills) or mixed with or sold as heroin or cocaine (2).^{§,¶}

Preliminary data** from laboratories participating in the Drug Enforcement Administration's National Forensic Laboratory Information System^{††} were analyzed to compare

the numbers and rates^{§§} of U.S. fentanyl submissions^{¶¶} between consecutive half year periods (January–June and July–December) during 2010–2017. After increasing an average of 87% (range = 10%–317%) during each consecutive half year period beginning in the first half of 2013, the number of fentanyl submissions between the first and second halves of 2017 declined 2% (from 29,344 to 28,826) (Figure). The rate declined from 9.03 per 100,000 residents during the first half of 2017 to 8.83 during the second half, suggesting that the rate of increase in the number of fentanyl submissions might be stabilizing for the first time in 4 years.

Ohio, Pennsylvania, and Massachusetts, the three states with the largest numbers of fentanyl submissions during January–June, 2017 (accounting for 48% of all fentanyl submissions) experienced an average 13% decline during July–December, 2017. Submissions declined 9% in Ohio (from 6,208 to 5,631), 16% in Pennsylvania (from 4,421 to 3,730), and 15% in Massachusetts (from 3,511 to 2,974). In contrast, the number of fentanyl submissions increased 8% in the South*** (from 5,883 to 6,341) and 36% in the West (from 547 to 743) during the same period. The largest increases occurred in South Carolina (216 to 428; 98% increase), Florida (674 to 850; 26%), and Virginia (942 to 1,097; 16%) in the South, and in California (269 to 386; 43%) and Arizona (137 to 226; 65%) in the West.

Preliminary stabilization in fentanyl submissions (a proxy for IMF availability because the majority of fentanyl submissions

* <https://www.nflis.deadiversion.usdoj.gov/DesktopModules/ReportDownloads/Reports/NFLISFentanylBrief2017.pdf>.

† <https://www.cdc.gov/drugoverdose/opioids/fentanyl.html>.

§ <https://emergency.cdc.gov/han/han00413.asp>.

¶ <https://www.dea.gov/documents/2018/10/02/2018-national-drug-threat-assessment-ndta>.

** Reported numbers of drug submissions are preliminary because of delays in testing drug products. Effects of these delays are greatest in the most recent periods. As such, numbers of fentanyl submissions in 2017, and especially in the second half of 2017, might increase slightly when the Drug Enforcement Administration releases updated 2017 data from the National Forensic Laboratory Information System.

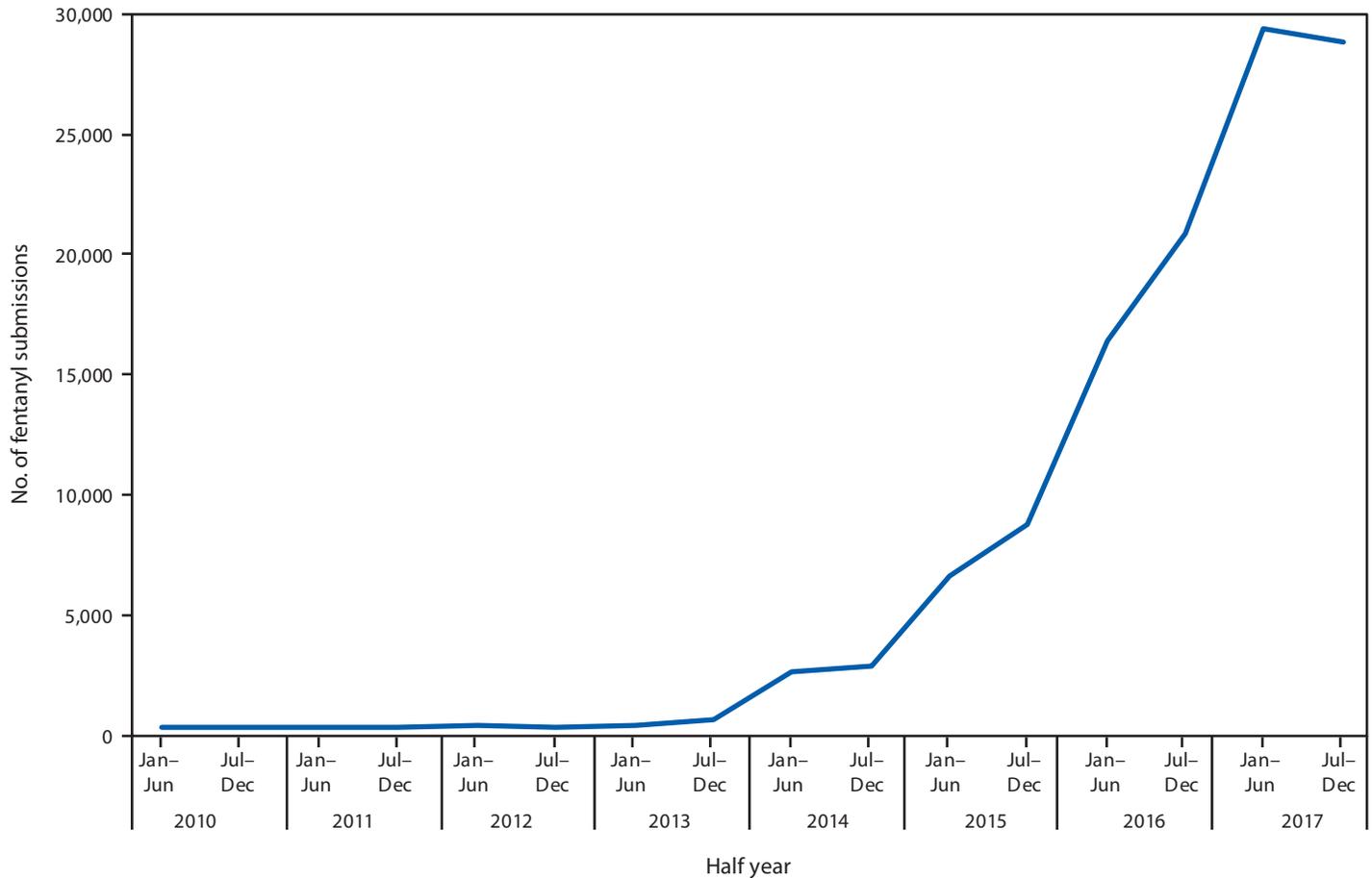
†† The National Forensic Laboratory Information System currently collects data from laboratories that perform analyses of approximately 98% of the U.S. drug caseload and includes 50 state systems and 101 local or municipal laboratory systems. State and local enforcement and prosecution policies vary and might affect the extent to which drug products are submitted for analysis. Also, laboratory policies for analyzing drug evidence vary. For instance, many laboratories do not analyze drug evidence if the criminal case involving the drug evidence was dismissed from court or if the drug evidence was not linked to a defendant. <https://www.nflis.deadiversion.usdoj.gov/DesktopModules/ReportDownloads/Reports/NFLIS-Drug-AR2017.pdf>.

§§ Rates were calculated using the estimated monthly U.S. resident population on April 1, 2017 (325,132,603 persons for January–June, 2017) and on October 1, 2017 (326,392,644 persons for July–December, 2017) obtained from the U.S. Census fact finder website on January 11, 2019. https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=PEP_2017_PEPMONTHN&prodType=table.

¶¶ Among fentanyl submissions, prescription fentanyl versus illicitly manufactured fentanyl cannot be distinguished in data from the National Forensic Laboratory Information System.

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

FIGURE. Number of fentanyl submissions identified by participating federal, state, and local laboratories, by half year — National Forensic Laboratory Information System, United States, 2010–2017*[†]



* Trend does not control for changes in the National Forensic Laboratory Information System participation rate (percentage of the national drug caseload represented by laboratories that have joined the system), which varied from 88% in 2010 to 98% in 2017 (midyear estimate).

[†] Drug Enforcement Administration, Diversion Control Division (2018). Drug Enforcement Administration National Forensic Laboratory Information System. For CDC *Morbidity and Mortality Weekly Report: Numbers of Fentanyl Drug Submissions in the United States — 2010–2017* (Data set). Retrieved from <https://www.nflis.deadiversion.usdoj.gov/>. Data for the period January–June, 2010 to July–December, 2014 retrieved on July 3, 2017; data for the period January–June, 2015 to July–December, 2017 retrieved on June 16, 2018.

are IMF)^{†††} observed nationwide in 2017 appears to be driven by reduced numbers in certain states with high numbers of submissions (e.g., Ohio, Pennsylvania, and Massachusetts). These states were among the first to report sharp increases in the number of fentanyl submissions and overdose deaths during 2013–2014 (3). A previous report found that changes in fentanyl submissions and overdose deaths were positively correlated (3); consistent with this, the preliminary decline in fentanyl submissions coincided with a slowing of the increase in the number of overdose deaths involving synthetic opioids other than methadone in late 2017.^{§§§} The number of overdose deaths involving synthetic opioids other than methadone increased 4% (from 13,986 to 14,480) between the first and

second halves of 2017 compared with an average increase of 34% (range = 7%–69%) during consecutive half year periods beginning in the first half of 2013.^{¶¶¶}

Although these findings are encouraging, they should be interpreted with caution. The reported trend is based on a narrow temporal sample and might not persist, and although numbers of fentanyl submissions might have peaked in early states with high submissions, increases have been reported in other states in the South and West. Even if the observed trend in fentanyl submissions is sustained, increased availability of other emerging synthetic opioids (e.g., fentanyl analogs) might continue to drive up the number of opioid overdose deaths (4,5). Targeting persons at high risk for illicit opioid overdose,

^{†††} <https://www.dea.gov/sites/default/files/2018-07/PRB-DIB-003-18.pdf>.

^{§§§} <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>.

^{¶¶¶} <https://wonder.cdc.gov>.

including broadly distributing naloxone and expanding efforts to provide linkage to care, are effective and important public health strategies that might mitigate the U.S. opioid overdose epidemic (3).

Acknowledgments

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Notes from the Field

Typhoid Fever Outbreak — Harare, Zimbabwe, October 2017–February 2018

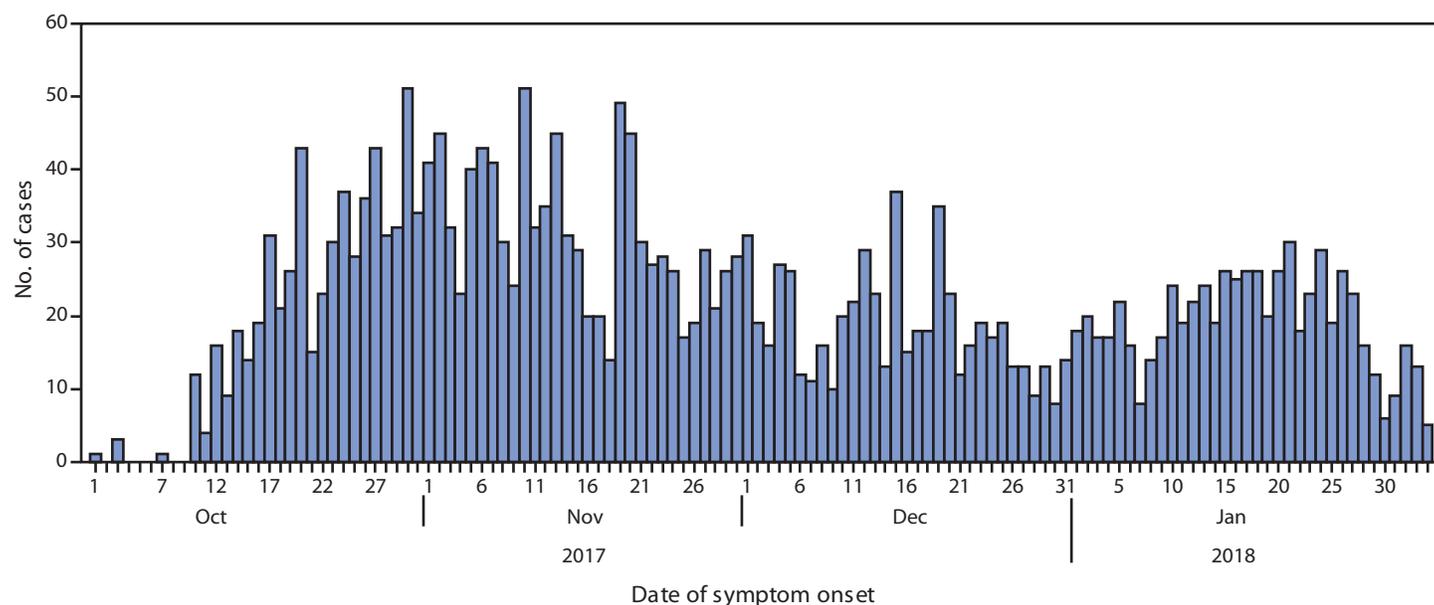
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On October 16, 2017, the Harare City Health Department (HCHD) in Zimbabwe identified a suspected typhoid fever (typhoid) case in a resident of Harare's Mbare suburb. Typhoid is a potentially fatal illness caused by *Salmonella enterica* serovar Typhi (Typhi). HCHD initiated an investigation and identified a cluster of 17 suspected typhoid cases, defined as the occurrence of fever and at least one of the following symptoms: headache, malaise, abdominal discomfort, vomiting, diarrhea, cough, or constipation. A confirmed case had Typhi isolated from blood, stool, or rectal swab culture (1).

As of February 24, 2018 (the most recent publicly available data), 3,187 suspected and 191 confirmed cases were identified (Figure), with no reported deaths among confirmed cases. Among suspected cases, 1,696 (53%) patients were male, and median age was 17 years (range = 1 month–90 years). In addition to clusters in Mbare, clusters were detected in Harare's western suburbs, including Kuwadzana, where high rates of ciprofloxacin-resistant Typhi were identified.

Previous typhoid outbreaks in Harare have been associated with municipal water shortages and increased use of contaminated boreholes and shallow wells (2–5). In January 2018, CDC collaborated with HCHD to standardize the collection, analysis, and interpretation of water quality data from wells, boreholes, and municipal taps. HCHD and partners paired this approach with efforts to improve water, sanitation, and hygiene (WASH) through assessing and repairing boreholes (particularly those with in-line chlorinators in affected areas); attending to burst sewers; conducting water sampling of municipal and borehole water; and educating local residents about typhoid. At the request of HCHD, a CDC team also conducted a review of case management and clinical outcomes among suspected typhoid patients admitted to Harare's designated typhoid treatment center during October 1–December 31, 2017. Among 583 patients admitted with a diagnosis of suspected typhoid, complications occurred in 79 (14%), the most common being acute kidney injury (26), anemia (10), peritonitis (nine), and electrolyte abnormalities (nine). One patient experienced intestinal perforation. Five patients with suspected typhoid died; however, because these cases were not culture-confirmed, they were not reported as typhoid-related deaths. Cultures were processed for 286 (49%) inpatients; 74 (26%) yielded Typhi. Fifteen (33%) of 46 isolates from hospitalized patients were ciprofloxacin-resistant. Complication rates were higher (19%) and median illness duration was longer (9 days) among patients with ciprofloxacin-resistant isolates than among those

FIGURE. Suspected cases of typhoid fever (N = 3,187), by date of symptom onset — Harare, Zimbabwe, October 1, 2017–February 24, 2018



with nonresistant isolates (9%; 7 days), but the differences were not statistically significant.

CDC laboratorians collaborated with Zimbabwe laboratory staff members to design a reporting protocol for laboratory results and ensure that accurate results of antimicrobial susceptibility testing was included in all reports. The standardized collection and analysis of clinical and laboratory information during an outbreak in which an unusual regional antibiotic resistance pattern featured prominently prompted public health officials to recommend third-generation cephalosporins as first-line treatment for patients residing in areas with high rates of ciprofloxacin resistance (1).

The combination of poor water quality and sanitation and urban overcrowding continues to be a persistent driver of seasonal outbreaks of waterborne diseases in Harare. Although localized WASH interventions, such as those described here, serve to disrupt local transmission, comprehensive measures will be needed to improve the water treatment and delivery system in Harare. One such measure that was informed by the epidemiologic data is a Gavi-funded* vaccination campaign using typhoid conjugate vaccine scheduled for January–February 2019, targeting 350,000 persons; this is the first use of typhoid conjugate vaccine and the first outbreak response vaccination campaign in Africa. The goal of this effort will be to disrupt transmission, thereby providing time for implementation of sustainable and widespread WASH interventions.

*<https://www.gavi.org/library/news/statements/2018/new-typhoid-vaccine-to-receive-gavi-support/>.

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Notes from the Field

Tuberculosis Control in the Aftermath of Hurricane Maria — Puerto Rico, 2017

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On September 20, 2017, Hurricane Maria made landfall in Puerto Rico as a Category 4 storm, with sustained winds of 130–156 miles per hour, and 15–40 inches of rain causing catastrophic flash floods. The storm destroyed electricity and communication systems, left large areas without water service, and caused widespread damage to critical infrastructure, transportation, health care, and agriculture. On the sixth day after the event, 58 (84%) of 69 hospitals on the island had no electric power or fuel for generators (1). The devastation led to declaration of a major disaster, just 10 days after a similar declaration for Hurricane Irma, a Category 5 storm that left 1 million Puerto Ricans without electricity after its center passed approximately 57 miles north of Puerto Rico (2,3). Although the island's entire population was affected by Hurricane Maria, the poorer, more remote, and economically disadvantaged communities, as well as those with larger numbers of bedridden and elderly persons, fared worse (4) because they had less access to already depleted health care services, more fragile homes, and no alternative means for electricity generation.

The Puerto Rico Department of Health Tuberculosis Control Program (PRTB) conducts tuberculosis (TB) surveillance and control activities through six regional clinics, directed by a central office in San Juan. PRTB uses directly observed therapy as the standard of care to ensure adherence to treatment. Beginning in mid-2016, PRTB had transitioned some patients from self-administered or directly observed therapy to video-observed therapy (vDOT) using a smartphone. However, the widespread and extended interruption in power and wireless communication made vDOT unavailable after the hurricane.

In anticipation of the hurricane, as specified in its preparedness plan, PRTB provided all patients receiving treatment for active TB with a 1-month supply of anti-TB medications before the hurricane and encouraged patients to tell health officers at shelters about their diagnosis if they had to be relocated from their homes. The Puerto Rico Department of Health recommended that shelters implement screening procedures for infectious diseases, such as rabies, TB, leptospirosis, and others, at the time of entry. PRTB resumed minimal operations on the fifth day after Hurricane Maria passed, with few staff

members able to report for duty, and prioritized contacting patients receiving treatment for active TB. Among 27 high-priority patients with active TB, 19 (70%) were accounted for within 15 working days and all 27 (100%) within 21 working days after the hurricane. Consistent with lessons learned after Hurricane Katrina, all patients with active TB received a 1-month supply of medication (5); therefore, no patients experienced an interruption in treatment, nor were any lost to follow-up because of the hurricane. PRTB notified two U.S. state health departments about noninfectious patients moving to their states; both patients were able to continue their treatment without interruption.

The PRTB laboratory was severely damaged. To maintain TB surveillance capacity, PRTB received assistance from CDC's Division of Tuberculosis Elimination, Laboratory Branch, the Association of Public Health Laboratories (APHL), three state APHL laboratories (Florida, Georgia, and Virginia), and the CDC Foundation to transport and test clinical specimens for *Mycobacterium tuberculosis*. The first package of *M. tuberculosis* specimens was sent on October 17, 4 weeks after the disaster (6), and the process continued until local laboratory testing resumed in July 2018.

This natural disaster led PRTB to strengthen its preparedness plan. Although PRTB patients fared better than did patients with acute and chronic conditions in terms of access to medications (7), PRTB identified that it is imperative to ensure that a minimum 2-month supply inventory of TB medication be available in each regional clinic to be able to anticipate postdisaster needs and delay of external aid in similar disasters (5). In addition, and complementary to the PRTB response plan, each regional clinic needs to develop its own emergency response plan, identifying resources, availability of health services and transportation, and potential needs, taking into consideration social and economic circumstances of its patients.

The unprecedented destruction in Puerto Rico caused by Hurricane Maria challenged TB control, but PRTB's limited personnel, in collaboration with partners, were able to maintain treatment and access to TB laboratory services. In addition, this multiagency collaboration, along with the successful preparedness plan, mitigated the impact on TB public health service delivery despite major societal and infrastructure disruption associated with possibly the worst natural disaster ever to hit the island.

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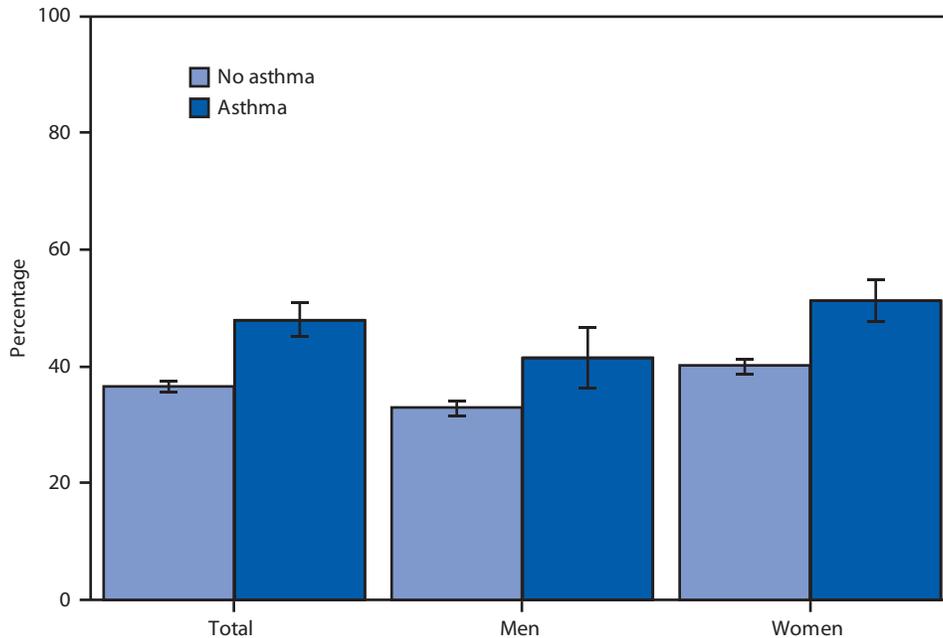
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QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage* of Adults Aged 18–64 Years Who Had an Influenza Vaccination[†] in the Past 12 Months, by Sex and Current Asthma Status[§] — National Health Interview Survey,[¶] 2017



* With 95% confidence intervals indicated by error bars.

[†] Based on a response to the question “During the past 12 months, have you had a flu vaccination?” Annual calendar year estimates of immunizations differ from seasonal influenza immunization totals, which reflect vaccinations obtained during the influenza season.

[§] Asthma status is determined by positive responses to the questions “Have you ever been told by a doctor or health professional that you had asthma?” and “Do you still have asthma?”

[¶] Estimates are based on household interviews of a sample of the noninstitutionalized U.S. civilian population aged 18–64 years and are derived from the National Health Interview Survey Sample Adult component.

In 2017, adults aged 18–64 years with current asthma were more likely to have had an influenza vaccination in the past 12 months (47.9%) than those without asthma (36.4%). Regardless of asthma status, women were more likely than men to have had an influenza vaccination in the past 12 months. Women aged 18–64 years with current asthma (51.3%) were more likely to have had an influenza vaccination than men with current asthma in this age group (41.6%). Among adults aged 18–64 years without asthma, women also were more likely to have had an influenza vaccination (40.0%) than were men (32.8%).

Source: National Health Interview Survey, 2017. <https://www.cdc.gov/nchs/nhis.htm>.

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