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Characteristics of Initial Prescription Episodes and Likelihood of Long-Term Opioid Use — United States, 2006–2015

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Because long-term opioid use often begins with treatment of acute pain (*1*), in March 2016, the CDC Guideline for Prescribing Opioids for Chronic Pain included recommendations for the duration of opioid therapy for acute pain and the type of opioid to select when therapy is initiated (*2*). However, data quantifying the transition from acute to chronic opioid use are lacking. Patient records from the IMS Lifelink+ database were analyzed to characterize the first episode of opioid use among commercially insured, opioid-naïve, cancer-free adults and quantify the increase in probability of long-term use of opioids with each additional day supplied, day of therapy, or incremental increase in cumulative dose. The largest increments in probability of continued use were observed after the fifth and thirty-first days on therapy; the second prescription; 700 morphine milligram equivalents cumulative dose; and first prescriptions with 10- and 30-day supplies. By providing quantitative evidence on risk for long-term use based on initial prescribing characteristics, these findings might inform opioid prescribing practices.

A random 10% sample of patient records during 2006–2015 was drawn from the IMS Lifelink+ database, which includes commercial health plan information from a large number of managed care plans and is representative of the U.S. commercially insured population (*3*). The data are provided in a deidentified format and the institutional review board at the authors' institution deemed the study was not human subject research. Records were selected of patients aged ≥18 years who had at least one opioid prescription during June 1, 2006–September 1, 2015, and ≥6 months of continuous enrollment without an opioid prescription before their first opioid prescription. Patients excluded were those who had any cancer (other than nonmelanoma skin cancer) or a substance abuse disorder diagnosis in the 6 months preceding their first opioid prescription, or whose first prescription was for any buprenorphine formulation indicated for treatment of substance abuse.

Patients were followed from the date of their first prescription until loss of enrollment, study end date, or discontinuation of opioids, which was defined as ≥180 days without opioid use. The duration of use and number of prescriptions and cumulative dose (expressed in morphine milligram equivalents*) for the first episode of opioid use (defined as continuous use of opioids with a gap of no greater than 30 days) were calculated. The number of days' supply and average daily dose in morphine milligram equivalents for the first prescription were also calculated. The first opioid prescription was categorized

* Morphine milligram equivalents is a conversion factor to convert different opioids into an equivalent dose of morphine. http://www.pdmpassist.org/pdf/BJA_performance_measure_aid_MME_conversion.pdf.

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into six mutually exclusive categories: long-acting; oxycodone short-acting; hydrocodone short-acting; other Schedule II short-acting; Schedule III–IV and nalbuphine; and tramadol.[†]

The Kaplan-Meier statistic was used to estimate median time to discontinuation of opioid use; probability of continued opioid use at 1 year and 3 years for different treatment duration thresholds (daily for 1–40 days and weekly for 1–26 weeks); number of prescriptions (1–15); and cumulative dose of the first episode of opioid use (50–2000 morphine milligram equivalents). Similarly, the relationship between the number of days' supply, choice of first opioid prescription, and probability of continued opioid use at 1 and 3 years was also examined. Sensitivity analyses were conducted by modifying the discontinuation definition from ≥180 opioid-free days to ≥90 opioid-free days, changing the allowable gap in the first episode of opioid use from 30 days to 7 days, and excluding patients whose average daily dose of the first prescription exceeded 90 morphine milligram equivalents.

A total of 1,294,247 patients met the inclusion criteria, including 33,548 (2.6%) who continued opioid therapy for ≥1 year. Patients who continued opioid therapy for ≥1 year were more likely to be older, female, have a pain diagnosis before opioid initiation, initiated on higher doses of opioids, and publically or self-insured, compared with patients who discontinued opioid use in <365 days (Table). Among persons prescribed at least 1 day of opioids, the probability of continued opioid use at 1 year was 6.0% and at 3 years was 2.9% (supplemental figure 1; https://stacks.cdc.gov/view/cdc/44182) (supplemental figure 2; https://stacks.cdc.gov/view/cdc/44550) with a median time to discontinuation of 7 days (supplemental figure 3; https://stacks.cdc.gov/view/cdc/44551). Approximately 70% of patients have an initial duration of opioids of ≤7 days and 7.3% were initially prescribed opioids for ≥31 days. The largest incremental increases in the probability of continued opioid pain reliever use were observed when the first prescription supply exceeded 10 or 30 days (Figure 1), when a patient received a third prescription (Figure 2), or when the cumulative dose was ≥700 morphine milligram equivalents (supplemental figure 4; https://stacks.cdc.gov/view/cdc/44552). Substantial increases in probabilities of continued opioid use occurred when the initial duration reached 6 and 31 days (supplemental figure 2; https://stacks.cdc.gov/view/cdc/44550); the findings of the sensitivity analyses were similar (supplemental figures 5–10; https://stacks.cdc.gov/view/cdc/44183).

The highest probabilities of continued opioid use at 1 and 3 years were observed among patients who initiated treatment with a long-acting opioid (27.3% at 1 year; 20.5% at 3 years), followed by those whose initial treatment was with tramadol

[†] The six mutually exclusive categories are 1) long-acting: buprenorphine, fentanyl, morphine, oxycodone, oxymorphone, and tapentadol; 2) other Schedule II short-acting: fentanyl, hydromorphone, levorphanol, meperidine, methadone, morphine, oxymorphone and tapentadol; 3) oxycodone short-acting; 4) hydrocodone short-acting; 5) Schedule III–IV and nalbuphine: codeine, dihydrocodeine, butorphanol, nalbuphine, pentazocine and propoxyphene; 6) tramadol.

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TABLE. Characteristics of incident opioid users and patients who continued opioid use for ≥365 days (1 year) and ≥1,095 days (3 years) — United States, 2006–2015

Characteristic	All incident opioid users (N = 1,294,247)		Patients who continued opioid therapy for ≥365 days (n = 33,548)		Patients who continued opioid therapy for ≥1,095 days (n = 6,441)	
	Mean (SD)	95% CI	Mean (SD)	95% CI	Mean (SD)	95% CI
Duration of first episode of opioid use	14.81 (65.00)	14.70–14.92	183.28 (343.27)	179.61–186.96	362.40 (593.26)	347.91–376.90
Enrollment duration (yrs)	2.48 (2.04)	2.47–2.48	3.30 (1.83)	2.47–2.48	4.98 (1.48)	4.94–5.02
Age (yrs)	44.52 (14.56)	44.50–44.54	49.58 (13.45)	49.44–49.72	50.52 (12.68)	50.21–50.83
	No. (%)	95% CI	No. (%)	95% CI	No. (%)	95% CI
Female	698,950 (54.00)	53.92–54.09	18,768 (55.94)	55.41–56.47	3,500 (54.34)	53.12–55.55
Treatment indication						
Back pain	226,681 (17.51)	17.45–17.58	10,396 (30.99)	30.50–31.49	2,137 (33.18)	32.04–34.34
Neck pain	90,352 (6.98)	6.94–7.03	3,824 (11.40)	11.06–11.74	775 (12.03)	11.26–12.85
Head pain	30,123 (2.33)	2.30–2.35	1,495 (4.46)	4.24–4.68	306 (4.75)	4.26–5.30
Joint pain	389,700 (30.11)	30.03–30.19	14,862 (44.30)	43.77–44.83	2,968 (46.08)	44.87–47.30
Patient region						
South	476,565 (36.74)	36.64–36.83	13,437 (40.05)	39.53–40.53	2,449 (38.02)	36.84–39.21
Midwest	376,520 (29.09)	29.01–29.17	9,566 (28.51)	28.03–29.00	1,973 (30.63)	29.52–31.77
East	279,595 (21.60)	21.53–21.67	6,153 (18.34)	17.93–18.76	1,234 (19.16)	18.22–20.14
West	142,698 (11.03)	10.97–11.08	3,640 (10.85)	10.52–11.19	574 (8.91)	8.24–9.63
Missing/Other	19,869 (1.54)	1.51–1.56	752 (2.24)	2.09–2.41	211 (3.28)	2.87–3.74
Payer type						
Commercial	866,815 (66.97)	66.89–67.06	20,920 (62.36)	61.84–62.88	3,910 (60.70)	38.11–40.49
Medicaid/State CHIP	14,855 (1.15)	1.13–1.17	864 (2.58)	2.42–2.76	154 (2.39)	2.05–2.79
Medicare	16,951 (1.31)	1.29–1.33	1,160 (3.46)	3.27–3.66	257 (3.96)	3.52–4.48
Self-insured	387,122 (29.91)	29.83–29.99	10,471 (31.21)	30.72–31.71	2,089 (32.43)	31.30–33.59
RX only/Unknown	8,504 (0.66)	0.64–0.67	130 (0.39)	0.33–0.46	32 (0.50)	0.35–0.70
Prescription characteristic						
First prescription ≥90 MME*	89,438 (6.91)	6.87–6.95	2,613 (7.79)	7.51–8.08	545 (8.46)	7.81–9.17
First prescription ≥120 MME*	22,895 (1.77)	1.75–1.79	1,075 (3.20)	3.02–3.40	244 (3.79)	3.35–4.28
First long-acting opioid prescription†	6,588 (0.51)	0.50–0.52	905 (2.70)	2.53–2.88	226 (3.51)	3.09–3.99

Abbreviations: CHIP = Children's Health Insurance Plan; CI = confidence interval; MME = morphine milligram equivalents; RX = prescription; SD = standard deviation.

* Average daily dose was calculated as total strength of the prescription expressed in MME divided by the days' supply of the first prescription. If a patient had multiple prescriptions on the first day, the daily dose in MME for all the prescriptions on the index date were summed and divided by the days' supply of the longest lasting prescription.

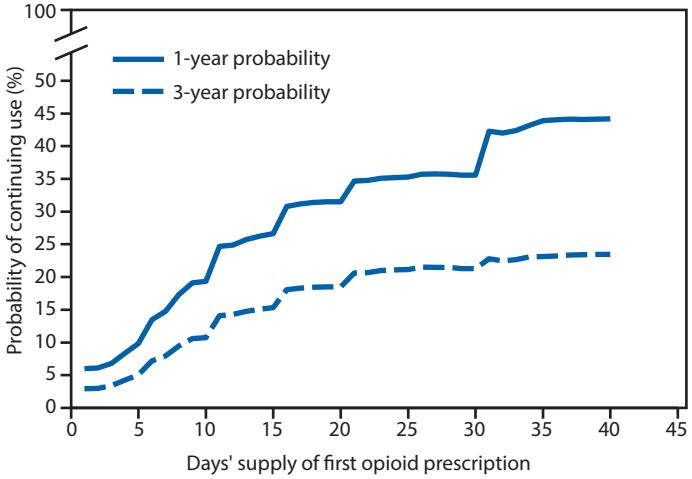
† The first prescription was categorized into six mutually exclusive categories and, in case of multiple prescriptions, on the index date using the following hierarchy to assign category: 1) long-acting; 2) other Schedule II short-acting; 3) Oxycodone short-acting; 4) Hydrocodone short-acting; 5) Schedule III-IV and Nalbuphine; or 6) tramadol.

(13.7% at 1 year; 6.8% at 3 years) or a Schedule II short-acting opioid other than hydrocodone or oxycodone (8.9% at 1 year; 5.3% at 3 years) (supplemental table; https://stacks.cdc.gov/view/cdc/44181). The probabilities of continued opioid use at 1 and 3 years for persons starting on hydrocodone short acting (5.1% at 1 year; 2.4% at 3 years), oxycodone short-acting (4.7% at 1 year; 2.3% at 3 years), or Schedule III–IV (5.0% at 1 year; 2.2% at 3 years) opioids were similar (supplemental table; https://stacks.cdc.gov/view/cdc/44181).

Discussion

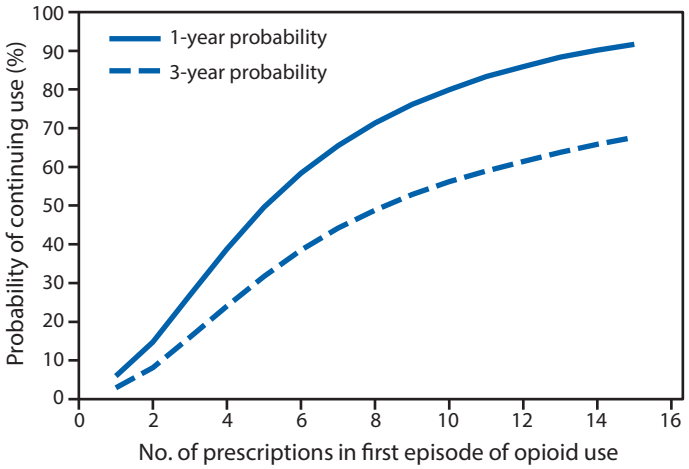
The probability of long-term opioid use increases most sharply in the first days of therapy, particularly after 5 days or 1 month of opioids have been prescribed, and levels off after approximately 12 weeks of therapy. The rate of long-term use was relatively low (6.0% on opioids 1 year later) for persons with at least 1 day of opioid therapy, but increased to 13.5% for persons whose first episode of use was for ≥8 days and to 29.9% when the first episode of use was for ≥31 days. Although ≥31 days of initial opioid prescriptions are not common, approximately 7% do exceed a 1-month supply. Discussions with patients about the long-term use of opioids to manage pain should occur early in the opioid prescribing process, perhaps as early as the first refill, because approximately 1 in 7 persons who received a refill or had a second opioid prescription authorized were on opioids 1 year later. As expected, patients initiated on long-acting opioids had the highest probabilities of long-term use. However, the finding that patients initiated with tramadol had the next highest probability of long-term use was unexpected; because of tramadol's minimal affinity for the μ-opioid receptor, it is deemed a relatively safe opioid agonist with lower abuse potential than other opioids (*4*). However, a report by the Substance Abuse and Mental Health Services Administration determined that emergency department visits associated with tramadol-related adverse events increased by 145% during 2005–2011 (*5*). Long-term

FIGURE 1. One- and 3-year probabilities of continued opioid use among opioid-naïve patients, by number of days' supply* of the first opioid prescription — United States, 2006–2015



* Days' supply of the first prescription is expressed in days (1–40) in 1-day increments. If a patient had multiple prescriptions on the first day, the prescription with the longest days' supply was considered the first prescription.

FIGURE 2. One- and 3-year probabilities of continued opioid use among opioid-naïve patients, by number of prescriptions* in the first episode of opioid use — United States, 2006–2015



* Number of prescriptions is expressed as 1–15, in increments of one prescription.

data on tramadol for pain management are sparse, with only one trial exceeding 12 weeks in duration (*6*). Despite this, among patients initiated with tramadol, >64% of patients who continued opioid use beyond 1 year were still on tramadol, suggesting that tramadol might be prescribed intentionally for chronic pain management. A 2016 study in Oregon (*7*), which did not include tramadol (a predictor of long-term use according to current data), reported similar findings: opioid naïve patients aged <45 years who received two prescription fills (versus one) or a cumulative dose of 400–799 (versus <120) morphine milligram equivalents in their first month of therapy were 2.3 and 3.0 times as likely to be chronic opioid users, respectively. However, that analysis only examined opioid use in the first month after initiation of opioid therapy to characterize risks for long-term use and did not account for the actual duration of therapy.

The findings in this report are subject to at least five limitations. First, although the cumulative dose of the first episode of opioid use is described, the likelihood of long-term use when the prescriber was titrating the dose was not determined. Rather, the total cumulative dose was calculated, which might have been increasing or decreasing over time. Second, the extent to which chronic opioid use was intentional versus the outgrowth of acute use is not known. Less than 1% of patients in this analysis were prescribed Schedule II long-acting opioids at the outset, so intentional chronic opioid prescribing might be uncommon; however, approximately 10% of patients were prescribed tramadol, which might indicate intentional chronic opioid prescribing. Third, information on pain intensity or duration were not available, and the etiology of pain, which might influence the duration of opioid use, was not considered in the analysis. Fourth, the frequency of prescriptions having certain days' supplied (e.g., prescriptions with a 7-day supply would be more frequently observed than those with an 11- or 13-day supply) was not considered. The variability in the relationships between days' supply, the cumulative dose, and duration of first episode and the probability of long-term use could be affected. Finally, prescriptions that were either paid for out-of-pocket or obtained illicitly were not included in the analysis.

Transitions from acute to long-term therapy can begin to occur quickly: the chances of chronic use begin to increase after the third day supplied and rise rapidly thereafter. Consistent with CDC guidelines, treatment of acute pain with opioids should be for the shortest durations possible. Prescribing <7 days (ideally ≤3 days) of medication when initiating opioids could mitigate the chances of unintentional chronic use. When initiating opioids, caution should be exercised when prescribing >1 week of opioids or when authorizing a refill or a second opioid prescription because these actions approximately double the chances of use 1 year later. In addition, prescribers should discuss the long-term plan for pain management with patients for whom they are prescribing either Schedule II long-acting opioids or tramadol.

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Summary

What is already known about this topic?

Based on the CDC Guideline for Prescribing Opioids for Chronic Pain, literature supporting long-term opioid therapy for pain is limited; research suggests an increased risk for harms with long-term opioid use. Early opioid prescribing patterns for opioid-naïve patients have been found to be associated with the likelihood of long-term use.

What is added by this report?

In a representative sample of opioid naïve, cancer-free adults who received a prescription for opioid pain relievers, the likelihood of chronic opioid use increased with each additional day of medication supplied starting with the third day, with the sharpest increases in chronic opioid use observed after the fifth and thirty-first day on therapy, a second prescription or refill, 700 morphine milligram equivalents cumulative dose, and an initial 10- or 30-day supply. The highest probability of continued opioid use at 1 and 3 years was observed among patients who started on a long-acting opioid followed by patients who started on tramadol.

What are the implications for public health practice?

Awareness among prescribers, pharmacists, and persons managing pharmacy benefits that authorization of a second opioid prescription doubles the risk for opioid use 1 year later might deter overprescribing of opioids. Knowledge that the risks for chronic opioid use increase with each additional day supplied might help clinicians evaluate their initial opioid prescribing decisions and potentially reduce the risk for long-term opioid use. Discussions with patients about the long-term use of opioids to manage pain should occur early in the opioid prescribing process.

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Trends in Suicide by Level of Urbanization — United States, 1999–2015

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Suicide is a major and continuing public health concern in the United States. During 1999–2015, approximately 600,000 U.S. residents died by suicide, with the highest annual rate occurring in 2015 (*1*). Annual county-level mortality data from the National Vital Statistics System (NVSS) and annual county-level population data from the U.S. Census Bureau were used to analyze suicide rate trends during 1999–2015, with special emphasis on comparing more urban and less urban areas. U.S. counties were grouped by level of urbanization using a six-level classification scheme. To evaluate rate trends, joinpoint regression methodology was applied to the time-series data for each level of urbanization. Suicide rates significantly increased over the study period for all county groupings and accelerated significantly in 2007–2008 for the medium metro, small metro, and non-metro groupings. Understanding suicide trends by urbanization level can help identify geographic areas of highest risk and focus prevention efforts. Communities can benefit from implementing policies, programs, and practices based on the best available evidence regarding suicide prevention and key risk factors. Many approaches are applicable regardless of urbanization level, whereas certain strategies might be particularly relevant in less urban areas affected by difficult economic conditions, limited access to helping services, and social isolation.

NVSS county-level mortality data for 1999–2015 were used to identify suicides among U.S. residents (excluding those aged <10 years because intent for self-harm typically is not attributed to young children) based on the *International Classification of Diseases, 10th Revision* (ICD-10) underlying cause codes X60–X84, Y87.0, and U03. Annual suicide counts were tabulated for county groupings defined according to a six-level urbanization classification scheme employed in the CDC WONDER reporting application (*2*). This classification scheme represents the level of urbanization as of 2006, selected to coincide with the middle of the study period. From most urban to least urban, the county classifications are large central metro, large fringe metro, medium metro, small metro, micropolitan (i.e., town/city; non-metro), and non-core (i.e., rural; non-metro).* Tabulated counts were combined with U.S. Census Bureau annual county-level population estimates to calculate annual suicide rates (per 100,000 residents aged ≥10 years). Rates were age-adjusted to the year 2000 U.S. standard.

Trends were evaluated by applying joinpoint regression methodology† to the annual suicide rate time series for each county grouping. This modeling approach simultaneously identifies statistically significant trends as well as shifts in trends that occur within a time series. Based on the results of the modeling process, the study frame was subsequently divided into an earlier 9-year period (1999–2007) and a later 8-year period (2008–2015) for purposes of examining changes in suicide rates by other factors, including sex, age group, race/ethnicity, and method of suicide.

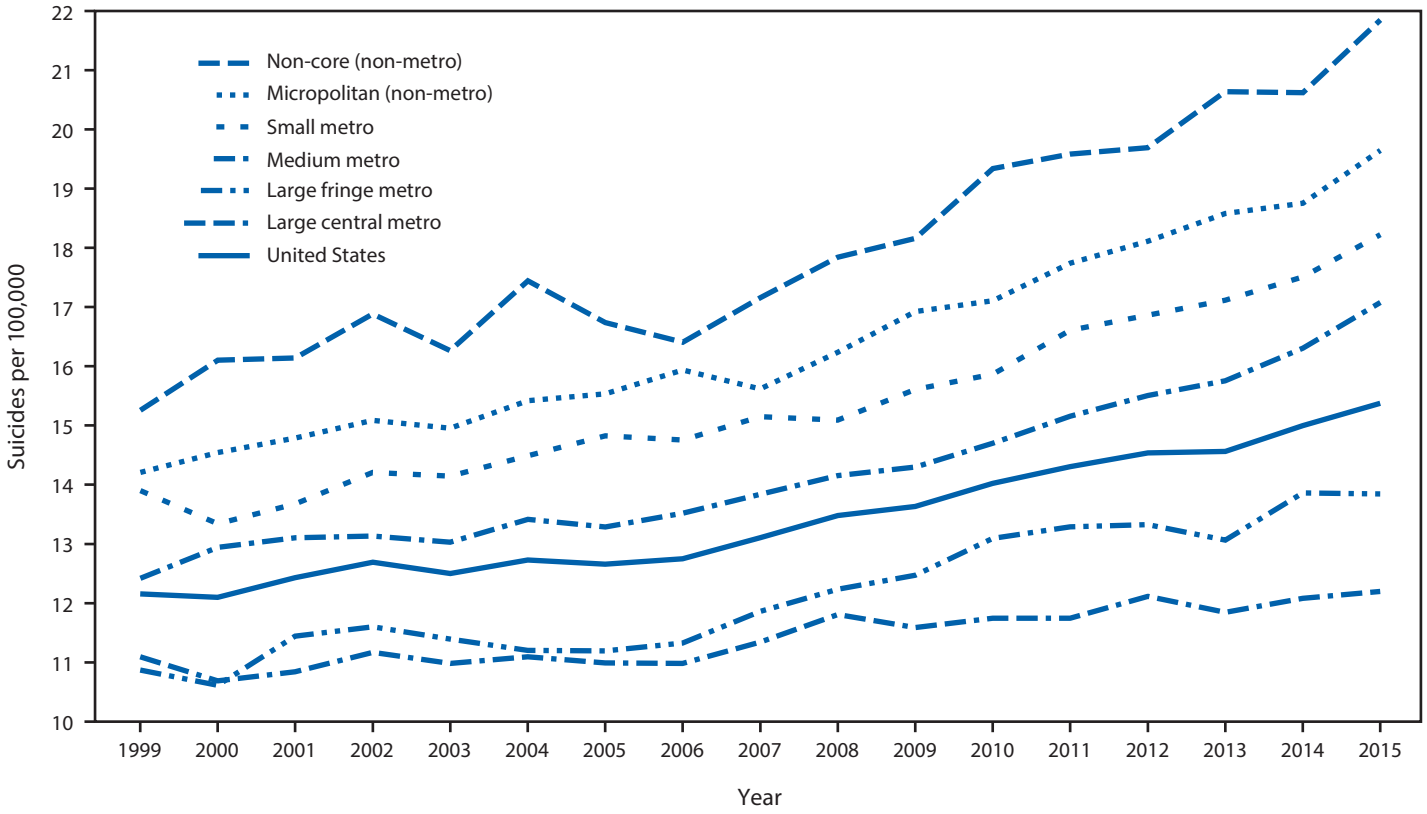
Increases in annual suicide rates over the study period occurred among all six county urbanization classifications (Figure). Rates at the beginning of the study period were lowest for the more urban counties and highest for the less urban counties, a gap that widened over time. The joinpoint regression results supported the same general conclusions, but further suggested that the gap in rates widened most conspicuously after 2007–2008 (Table 1) (Table 2). For the large central metro and large fringe metro county groupings, the joinpoint modeling process identified continuous and statistically significant rate increases over the entire study period (Table 1). For the medium metro, small metro, micropolitan, and non-core county groupings, statistically significant rate increases were also identified over the earlier part of the study period; modeled rate increases for these four county groupings accelerated significantly in 2007–2008 (Table 2).

During both 1999–2007 and 2008–2015, overall rates of suicide among males were approximately four times those among females; rates increased across the two periods for both males (from 21.1 per 100,000 to 23.3) and females (from 5.0 to 6.2) (Table 3). By age group, the highest rates were among persons aged 35–64 years and ≥75 years; the 35–64 year age group also showed the largest rate increase (from 14.9 to 17.9). By race/ethnicity, non-Hispanic whites and American Indian/Alaska Natives had the highest rates of suicide, with rates for both groups showing notable increases across periods (from 14.9 to 18.1 and from 15.8 to 20.0, respectively). Rates among non-Hispanic blacks and Asian/Pacific Islanders and among Hispanics were much lower, and showed comparatively modest increases across periods. Rates increased across periods for

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

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

FIGURE. Suicide rates* by level of county urbanization† — United States, 1999–2015



* Per 100,000 residents aged ≥10 years, age-adjusted to the year 2000 U.S. standard.

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

both non-firearm and firearm suicide, with a greater increase in the rate of non-firearm suicide, particularly from suffocation (which includes hanging).

Discussion

After declining since 1986, the U.S. suicide rate increased during 2000–2015 (*3*). This study provides added support to previous findings that a geographic disparity in suicide rates exists in the United States, with higher rates in less urban areas and lower rates in more urban areas (*4*) and extends these findings to characterize suicide trends by urbanization level over time. Specifically, the current study found that suicide rates across all urbanization levels increased during the period 1999–2015, the gap in rates between less urban and more urban areas widened over time, and rates in medium metro, small metro, and non-metro areas increased at a more rapid pace beginning in 2007–2008.

Geographic disparities in suicide rates might be associated with suicide risk factors known to be highly prevalent in less urban areas, such as limited access to mental health care, made worse by shortages in behavioral health care providers in these areas (*5*), and greater social isolation (*5,6*). Such disparities might also reflect the influence of the opioid overdose epidemic. This epidemic is known to have disproportionately affected less urban areas during the earlier part of the study period (*7*), and opioid misuse is associated with increased risk for suicide (*8*). That increases in suicide rates outside large metro areas accelerated in 2007–2008 might reflect the influence of the economic recession of 2007–2009, which had a disproportionate impact and involved longer recovery times in less urban areas (*9*). The potential cumulative burden of suicide risk factors in less urban areas might affect not only individuals but relationships, families, and communities as well, suggesting the need for comprehensive suicide prevention measures. Given the disparate nature of suicide risk factors beyond mental health factors alone (e.g., social isolation, financial hardship, and access to lethal means), and the far-reaching emotional and economic consequences of suicide on families and communities, implementing such measures calls for a broad public health approach at the individual, community, and societal levels.

TABLE 1. Trends in suicide rates by large county level of urbanization* — United States, 1999–2015

County urbanization level	No. of counties	No. of suicides	Overall annual suicide rate increase†	p-value	Joinpoint year
Large central metro	63	150,636	0.09	<0.01	—
Large fringe metro	352	133,479	0.20	<0.01	—

* Counties or county-equivalents; a small number of counties were combined into multicounty groupings. The six classification levels for counties were 1) large central metro: part of a metropolitan statistical area with ≥1 million population and covers a principal city; 2) large fringe metro: part of a metropolitan statistical area with ≥1 million population but does not cover a principal city; 3) medium metro: part of a metropolitan statistical area with ≥250,000 but <1 million population; 4) small metro: part of a metropolitan statistical area with <250,000 population; 5) micropolitan (non-metro): part of a micropolitan statistical area (has an urban cluster of ≥10,000 but <50,000 population); and 6) non-core (non-metro): not part of a metropolitan or micropolitan statistical area.
† Per 100,000 residents aged ≥10 years, age-adjusted to the year 2000 U.S. standard.

TABLE 2. Trends in suicide rates by medium and small county level of urbanization* — United States, 1999–2015

County urbanization level	No. of counties	No. of suicides	Initial annual suicide rate increase†	p-value	Joinpoint year	Annual suicide rate increase† after joinpoint year	p-value for difference
Medium metro	331	126,447	0.14	<0.01	2008	0.41	<0.01
Small metro	339	64,739	0.19	<0.01	2008	0.41	<0.01
Micropolitan (non-metro)	694	75,002	0.19	<0.01	2007	0.45	<0.01
Non-core (non-metro)	1,355	52,075	0.18	<0.05	2007	0.55	<0.01

* Counties or county-equivalents; a small number of counties were combined into multicounty groupings. The six classification levels for counties were 1) large central metro: part of a metropolitan statistical area with ≥1 million population and covers a principal city; 2) large fringe metro: part of a metropolitan statistical area with ≥1 million population but does not cover a principal city; 3) medium metro: part of a metropolitan statistical area with ≥250,000 but <1 million population; 4) small metro: part of a metropolitan statistical area with <250,000 population; 5) micropolitan (non-metro): part of a micropolitan statistical area (has an urban cluster of ≥10,000 but <50,000 population); and 6) non-core (non-metro): not part of a metropolitan or micropolitan statistical area.
† Per 100,000 residents aged ≥10 years, age-adjusted to the year 2000 U.S. standard.

Just as suicide is not caused by a single factor, research suggests that suicide prevention cannot be achieved with a single strategy. Suicide prevention efforts might be most effective when multiple strategies operating across the range of contexts in which persons live and work are combined (*10*). Many prevention strategies and approaches might be broadly applicable for all communities regardless of size, whereas others might be particularly relevant for less urban areas. For example, all communities might benefit from strategies that enhance coping and problem-solving skills, strengthen economic support during times of financial hardship, and identify and support persons at risk for suicide (e.g., through gatekeeper training, crisis intervention, and effective treatments). Reducing access to lethal means among persons at risk, improving organizational policies and culture to promote positive social norms such as help-seeking, supporting surviving friends and family members, and promoting safe messaging and news reporting about suicide to prevent suicide contagion are additional strategies that might benefit all communities (*10*). On the other hand, residents in less urban areas might benefit particularly from prevention strategies that address provider shortages, for example, through programs that incentivize mental health clinicians to work in underserved areas, or through the provision of treatment via telephone, video, and web-based technologies. Less urban areas also might benefit from suicide prevention strategies that promote social connectedness through community engagement activities that

Summary

What is already known about this topic?

The U.S. suicide rate has been increasing since 2000. Rates in less urban areas have been higher than rates in more urban areas, with some evidence of a growing difference.

What is added by this report?

During 1999–2015, suicide rates increased across all levels of urbanization, with the gap in rates between less urban and more urban areas widening over time, most conspicuously over the later part of this period. Geographic disparities in suicide rates might reflect suicide risk factors known to be prevalent in less urban areas, such as limited access to mental health care, social isolation, and the opioid overdose epidemic, because opioid misuse is associated with increased risk for suicide. That the gap in rates began to widen more noticeably after 2007–2008 might reflect the influence of the economic recession, which disproportionately affected less urban areas.

What are the implications for public health practice?

There is a growing need for comprehensive suicide prevention employing a broad public health approach. This might include strategies applicable for all communities (e.g., strengthening economic support during times of financial hardship and teaching coping and problem-solving skills) along with strategies that address subsets of the population at increased risk, such as rural communities (e.g., programs that address provider shortages and promote social connectedness). CDC's technical package of multisector policies, programs, and practices serves as a resource for states and communities to guide decision-making based on the best available evidence for preventing suicide.

TABLE 3. Average annual suicide rates,* overall and by sex, age group, race/ethnicity, and suicide method — United States, 1999–2007 and 2008–2015

Characteristic	Period	
	1999–2007	2008–2015
Overall†	**12.6**	**14.4**
Sex†		
Male	21.1	23.3
Female	5.0	6.2
Age group (yrs)		
10–19	4.3	4.9
20–34	12.6	14.1
35–64	14.9	17.9
65–74	12.7	14.4
≥75	17.2	17.0
Race/Ethnicity†,§		
White, non-Hispanic	14.9	18.1
Black, non-Hispanic	6.3	6.5
American Indian/Alaska Native, non-Hispanic	15.8	20.0
Asian/Pacific Islander, non-Hispanic	6.5	7.0
Hispanic	6.7	6.8
Method†		
Firearm	6.7	7.2
Non-firearm	5.9	7.2
Suffocation (including hanging)	2.7	3.7
Poisoning	2.2	2.4
Drug	1.6	1.9
Non-drug	0.6	0.5
Other non-firearm	1.0	1.1

* Per 100,000 residents aged ≥10 years.
† Age-adjusted to the year 2000 U.S. standard.
§ Hispanic persons might be of any race.

provide residents with the opportunity to interact with each other and to become familiar with supportive organizations and resources (*10*).

The findings in this report are subject to at least two limitations. First, a small fraction of suicide records (<0.4%) were excluded from the analysis because of missing ethnicity data, resulting in a slight downward bias on some rate estimates. Second, individual counties were considered to embody the same level of urbanization throughout the 1999–2015 study period; the year 2006 urbanization classification scheme does not reflect changes in county composition over time. However, an earlier comparison of the year 2006 classification scheme with an updated 2013 classification scheme indicates that >90% of counties retained the same status and that when a change in classification occurred, it typically involved a shift to an adjacent level of urbanization; the potential influence of the constant classification scheme should therefore be relatively minimal.

The current study highlights higher rates of suicide in areas with lower levels of urbanization, and demonstrates a growing disparity between rates in less urban and more urban areas of the United States. Suicide is preventable, and evidence-based strategies to prevent suicide in both less urban and more urban areas exist. Resources such as CDC's *Preventing Suicide: a Technical Package of Policies, Programs, and Practices* (*10*) and the National Violent Death Reporting System can help states and communities prioritize prevention efforts and address persistent upward trends in suicide rates.

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Mercury Spill Responses — Five States, 2012–2015

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Despite measures to educate the public about the dangers of elemental mercury, spills continue to occur in homes, schools, health care facilities, and other settings, endangering the public's health and requiring costly cleanup. Mercury is most efficiently absorbed by the lungs, and exposure to high levels of mercury vapor after a release can cause cough, sore throat, shortness of breath, nausea, vomiting, diarrhea, headaches, and visual disturbances (*1*). Children and fetuses are most susceptible to the adverse effects of mercury vapor exposure. Because their organ systems are still developing, children have increased respiratory rates, and they are closer to the ground where mercury vapors are most highly concentrated (*2*). To summarize key features of recent mercury spills and lessons learned, five state health departments involved in the cleanup (Iowa, Michigan, Missouri, North Carolina, and Wisconsin) compiled data from various sources on nonthermometer mercury spills from 2012 to 2015. The most common sites of contamination were residences, schools and school buses, health care facilities, and commercial and industrial facilities. Children aged <18 years were present in about one third of the spills, with approximately one in seven incidents resulting in symptoms consistent with acute mercury exposure. To protect the public's health after a mercury spill, it is important that local, state, and federal agencies communicate and coordinate effectively to ensure a quick response, and to minimize the spread of contamination. To reduce the number of mercury spills that occur in the United States, public health officials should increase awareness about exchange programs for mercury-containing items and educate school and health care workers about sources of mercury and how to dispose of them properly.

State and local health departments routinely evaluate the cleanup of homes and schools where mercury spills have occurred to ensure that mercury vapor concentrations are reduced to safe levels. Cleanup of elemental mercury is challenging because it is dense and breaks into tiny beads when spilled. Elemental mercury also adheres to surfaces such as shoes, which can promote the spread of contamination, further complicating collection and removal. The Agency for Toxic Substances and Disease Registry (ATSDR) has developed recommended mercury vapor action levels or ranges for different settings to assist health departments with reoccupancy decisions. For residential settings, the ATSDR mercury vapor action level is 1 $\mu g/m^3$; however, concentrations of 1–3 $\mu g/m^3$ are considered acceptable for schools because of the reduced exposure duration (*3*). During 2012–2015, questions related to cleanup of elemental mercury remained the most common type of environmental inquiry received by U.S. poison centers, accounting for 17,498 encounters (including 5,786 for mercury thermometers) and 23% of all environmental inquiries (*4–7*). During this period, 11,777 encounters involved elemental mercury exposures, with approximately 93% resulting from unintentional releases and 28% occurring in children aged ≤12 years (*4–7*).

After reports that several state health departments responded to significant mercury spills, in March 2015, the Council of State and Territorial Epidemiologists (CSTE) convened a workgroup to compile mercury spill data to increase awareness of the frequency and hazards of mercury spills. Staff members from five state health departments (Iowa, Michigan, Missouri, North Carolina, and Wisconsin) participated in the workgroup and compiled nonthermometer mercury spill data during 2012–2015 from various sources, including internal records, state agencies of emergency management, environmental quality and natural resources, the ATSDR National Toxic Substance Incidents Program, and U.S. Environmental Protection Agency (EPA) on-scene coordinators. Frequency analyses were conducted to summarize key features of the spills, including location and amount, and whether the spill resulted in an official evacuation, children were present, or the spill resulted in symptoms consistent with acute mercury exposure (either medically documented or self-reported). Case studies were collected from each state.

Five state health departments were involved in the cleanup of 64 nonthermometer mercury spills during 2012–2015 (Table 1). The most common sites of contamination were residences (44%), schools and school buses (20%), health care facilities (17%) and commercial and industrial facilities (17%). Approximately 42% of these mercury spills were estimated to involve <0.5 pound (i.e., 1 tablespoon) of mercury, 33% involved >0.5 pound, and 25% involved an unknown amount. A quarter of the mercury spills resulted in an official evacuation, and children aged <18 years were present in at least 35% of the events. Fourteen percent of mercury spills resulted in symptoms consistent with acute mercury exposure, including cough, sore throat, shortness of breath, nausea, vomiting, diarrhea, headaches, and visual disturbances.

Five cases that occurred during 2012–2014 illustrate the variety of mercury spills to which state health departments were asked to respond.

TABLE 1. Summary of mercury spill data from five state health departments,* 2012—2015

Characteristic	No. (%) of spills
Total spills	**64 (100)**
Location of spill†	
Residence	28 (44)
School/School bus	13 (20)
Health care facility	11 (17)
Other commercial/ industrial facility	11 (17)
Water treatment plant	3 (5)
Rest area/ Parking lot/ Street	3 (5)
Penitentiary	1 (2)
Amount spilled (pounds)	
<0.5	27 (42)
0.5–1	9 (14)
>1–5	8 (13)
>5	4 (6)
Unknown	16 (25)
Official evacuation	
Yes	16 (25)
No	48 (75)
Potentially exposed children aged <18 years	
0	32 (50)
1–5	17 (27)
>5	5 (8)
Unknown	10 (16)
Potentially exposed adults aged ≥18 years	
0	17 (27)
1–5	26 (41)
>5	11 (17)
Unknown	10 (16)
Persons with acute symptoms	
0	54 (84)
1–5	9 (14)
Unknown	1 (2)

* Iowa, Michigan, Missouri, North Carolina, and Wisconsin.
† Some incidents involved multiple locations.

Armstrong, Iowa (2012). A person carried a jar containing approximately 12 pounds of mercury into a bar, where it accidentally spilled. Extensive mercury contamination was found in the bar and in the home of one of the bar patrons. Cleanup in the bar required removing the tile floor, sealing the subfloor, and superheating the indoor air with forced ventilation. Remediation of the home involved extensive cleaning and removal of contaminated items as hazardous waste, including a vacuum cleaner, washer, and clothes dryer. After cleanup of these locations by EPA contractors, mercury vapor monitoring was conducted under typical conditions to confirm that both locations were safe for re-entry. Although the cleanup took one week to complete, no adverse health effects were reported because quick action by responders limited mercury vapor exposure.

Lenoir, North Carolina (2012). A student brought a test tube containing mercury to an elementary school. The test tube was dropped in a classroom, spilling approximately 0.5 pounds of mercury. Five exposed students (aged 10–12 years) were taken to a hospital, decontaminated, and released. Multiple federal, state, and local agencies were involved in the response and assessment. Cleanup operations and environmental monitoring were conducted by an environmental contractor and EPA. The school was closed for 2 days before it was cleared for reoccupancy.

Kansas City, Missouri (2013). A resident hired a professional clock company to move his antique grandfather clock up a set of stairs. The clock had an estimated 15 pounds of mercury contained in the pendulum. During the move, nearly 2 pounds of mercury were spilled throughout the apartment building. Cleanup of this spill took approximately 2 weeks and resulted in the disposal of the pendulum and the mercury remaining inside it. No adverse health effects were reported among those living at the home.

Delton, Michigan (2014). A man attempted to extract gold from jewelry by combining it with elemental mercury and heating the mixture. He was severely poisoned from inhaling very high concentrations of mercury vapors. Multiple federal, state, and local agencies were involved in the cleanup of the home and the medical care of the patient, who survived, but required extensive medical treatment. The home was eventually demolished.

Bloomer, Wisconsin (2014). An old mercury-containing boiler was being removed from a home and approximately 3.5 pounds of mercury were released in the basement, garage, and driveway. The state health department provided cleanup guidance and a mercury vapor monitor to assist on-site agencies in overseeing cleanup of this large spill. Professional cleanup of the basement, garage, and driveway required the use of powdered sulfur and a specialized mercury vacuum. The washer and clothes dryer were also contaminated and were discarded as hazardous waste. No adverse health effects were reported by persons living in the home.

Discussion

As health officials began to understand and appreciate the adverse health effects that exposure to mercury can cause in humans, state and federal agencies began to institute laws and regulations to reduce and control the use, release, and disposal of elemental mercury (*8*).* These regulations have been effective at reducing environmental contamination from industrial and commercial sources; however, numerous stores of elemental mercury still exist in smaller quantities in residences, schools, and health care facilities. Mercury spills can be expensive to clean up to levels considered safe for long-term occupancy, with the cost varying based on the location and extent of contamination. During 2012–2015, EPA reported

* https://noharm-uscanada.org/issues/us-canada/laws-and-resolutions.

Summary

What is already known about this topic?

Exposure to elemental mercury vapor can cause adverse health effects, especially in children and fetuses. Government agencies and other organizations have tried numerous ways to educate the public about the hazards of elemental mercury and encourage the safe disposal of mercury-containing products.

What is added by this report?

Despite measures to educate the public on the dangers of mercury, mercury spills continue to occur in homes, schools, health care facilities, and other settings, requiring costly cleanup to prevent human exposures to harmful levels of mercury vapor. State and local health departments routinely guide the cleanup of buildings where mercury spills have occurred to ensure that mercury vapor concentrations are reduced to safe levels. Illustrative cases of nonthermometer mercury spills in five states are presented, which highlight the extensive use of resources required for remediation, as well as the potential for severe adverse health effects.

What are the implications for public health practice?

To protect the public's health after a mercury spill, it is important that local, state, and federal agencies communicate and coordinate effectively to ensure a rapid response and minimize the spread of contamination. Increasing awareness of exchange programs for mercury-containing items and education of school and health care workers about appropriate disposal might reduce the number of mercury spills that occur in the United States.

responding to 225 chemical-release incidents in which mercury was listed as the primary contaminant of concern; the average cost of cleanup to those incidents ranged from approximately $30,000 to $75,000 for each year from 2012 to 2015, and the highest cleanup cost during this time period was $913,915 in 2013 (EPA, unpublished data, December 2015).

Government agencies, academic institutions, and health care and environmental organizations have developed numerous strategies to educate the public about the hazards of elemental mercury and encourage the safe disposal of mercury-containing products (Table 2). For example, ATSDR developed a web-based mercury spill prevention initiative for schools, called "Don't Mess with Mercury" (http://www.atsdr.cdc.gov/dontmesswithmercury/index.html). The website targets middle schools, providing videos, a game, and lesson plans. EPA has also developed fact sheets with best practices for the removal of mercury-containing devices from residential buildings and health care facilities (*9*,*10*). Despite these efforts, however, mercury spills in these settings continue to occur, requiring costly cleanup to prevent exposures to harmful levels of mercury vapor.

Many states have enacted laws against the use of mercury in schools and health care facilities, and instituted bans and phaseouts for the sale of mercury-containing products.*

TABLE 2. Common sources of mercury in homes, schools and health care facilities — United States, 2001–2017

Source	Approximate amount (pounds)	Approximate amount (grams)
Compact fluorescent lightbulbs*	0.00001	0.004
Thermostats (tilt switches)†	0.0001–0.0100	0.05–5
Thermometers§	0.001–0.020	0.5–10
Float switches†	0.0002–0.1500	0.1–70
Blood pressure monitors§	0.15–0.20	70–90
Manometers¶,**	0.07–0.75	30–340
Gas pressure regulators (residential) ††	≤0.3	≤140
Esophageal dilators§	≤1.0	≤450
Barometers§	≤1.8	≤800
Boiler heating systems††	≤3.5	≤1600
Grandfather clocks (pendulum)§§	≤15.0	≤6800

* https://www.epa.gov/cfl/what-are-connections-between-mercury-and-cfls.
† http://www.newmoa.org/prevention/mercury/imerc/factsheets/switches_relays_2014.pdf.
§ https://www3.epa.gov/region9/waste/p2/projects/hospital/mercury.pdf.
¶ http://www.newmoa.org/prevention/mercury/imerc/factsheets/measuring_devices.cfm.
** http://www.epa.ohio.gov/portals/41/p2/mercury_pbt/manometer_web.pdf.
†† https://www.epa.gov/sites/production/files/2015-10/documents/before_you_tear_it_down.pdf.
§§ https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5623a2.htm.

However, many mercury-containing items remain in schools, health care facilities, and homes. Incentivizing persons to relinquish mercury and mercury-containing items through exchange programs (e.g., mercury thermometers for digital thermometers) has been successful in reducing the potential for residential mercury spills, but more awareness of these programs is needed. Although health care workers are aware of the hazards of elemental mercury exposure, they might not be aware of potential mercury sources in health care facilities. Educational programs at schools and hospital grand rounds could help inform school and health care workers about these potential mercury sources and how to dispose of them properly. Although there might be a cost associated with disposing of mercury-containing items properly, that cost is typically far less than the costs incurred to clean up a spill.

The findings in this report are subject to at least three limitations. First, only five states contributed data for this analysis, so the characteristics of mercury spills described in this report might not be representative of all mercury spills that occur in the United States. Second, these data were compiled from many different data sources, so the level of detail available about the spills varied considerably. Third, because the role of state health departments in mercury spill response varies by state, some state health departments responded to mercury spills more frequently than others, and not all mercury spills that occurred are captured in this report.

When mercury spills do occur, a quick and coordinated response is necessary to ensure the protection of public health and proper remediation. When a spill occurs, health

departments, local or regional hazardous materials responders, state health and environmental agencies, regional EPA offices, poison control centers, and health care providers should be immediately informed.

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Investigation of *Salmonella* Enteritidis Outbreak Associated with Truffle Oil — District of Columbia, 2015

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On September 8, 2015, the District of Columbia Department of Health (DCDOH) received a call from a person who reported experiencing gastrointestinal illness after eating at a District of Columbia (DC) restaurant with multiple locations throughout the United States (restaurant A). Later the same day, a local emergency department notified DCDOH to report four persons with gastrointestinal illness, all of whom had eaten at restaurant A during August 30–September 5. Two patients had laboratory-confirmed *Salmonella* group D by stool culture. On the evening of September 9, a local newspaper article highlighted a possible outbreak associated with restaurant A. Investigation of the outbreak by DCDOH identified 159 patrons who were residents of 11 states and DC with gastrointestinal illness after eating at restaurant A during July 1–September 10. A case-control study was conducted, which suggested truffle oil–containing food items as a possible source of *Salmonella enterica* serotype Enteritidis infection. Although several violations were noted during the restaurant inspections, the environmental, laboratory, and traceback investigations did not confirm the contamination source. Because of concern about the outbreak, the restaurant's license was suspended during September 10–15. The collaboration and cooperation of the public, media, health care providers, and local, state, and federal public health officials facilitated recognition of this outbreak involving a pathogen commonly implicated in foodborne illness.

Epidemiologic Investigation

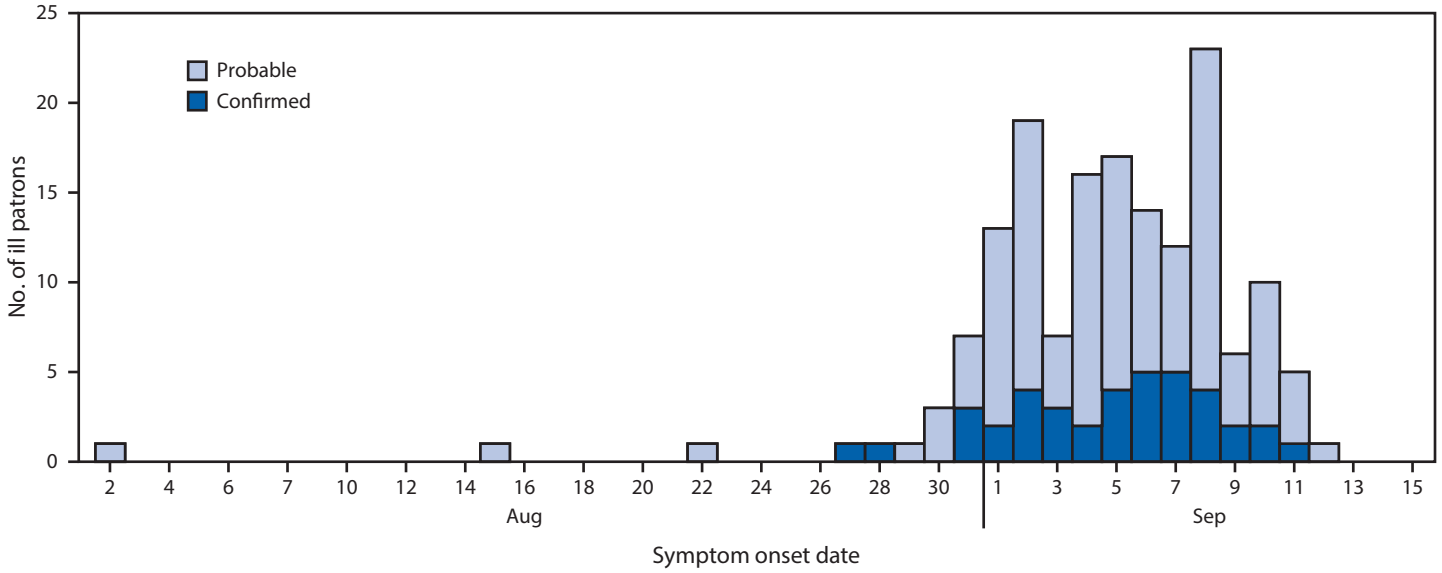
To identify food items associated with gastrointestinal illness, DCDOH initiated a case-control study; a case was defined as the occurrence of gastrointestinal illness in a person beginning ≤7 days after eating at restaurant A during July 1–September 10, 2015. Cases were categorized as confirmed (*Salmonella* group D isolated from a clinical specimen by culture) or probable (linked epidemiologically, but without laboratory confirmation of *Salmonella*). Case-patients were identified on the basis of laboratory reports confirming *Salmonella*, self-report (i.e., contacted DCDOH directly), notifications from health care providers, and referrals from other restaurant patrons. Control subjects ate at restaurant A during July 1–September 10, 2015, but did not report gastrointestinal illness. Control subjects were identified through case-patients or self-reported to DCDOH. Case-patients and control subjects were interviewed using the DCDOH foodborne investigation questionnaire and were asked to review restaurant A's online menu and list all food items ordered, shared, or tasted. Sociodemographic and clinical information (e.g., symptoms, doctor visits) was also collected.

During September 9–October 28, 2015, DCDOH identified 277 patrons who ate at restaurant A, among whom 254 (92%) were interviewed directly or through a proxy and included in the analysis. Among the 254 interviewees were 159 (63%) case-patients (40 confirmed and 119 probable) and 95 (37%) control subjects. The majority (90%) of illness onset dates occurred during August 31–September 10 (Figure). Case-patients included DC residents and residents of 11 states, many of whom were visiting DC during the Labor Day weekend. No significant differences were noted between case-patients and control subjects in terms of age, sex, race/ethnicity, and place of residence (Table 1). Among the 153 case-patients for whom symptom information was available, 143 (93%) reported diarrhea, 128 (84%) abdominal cramps, 105 (69%) chills, 103 (67%) headache, 100 (65%) nausea, and 82 (54%) fever.

Food items consumed by 155 probable and confirmed case-patients and 88 control subjects were compared. Six food items were significantly associated with case status (Table 2), three of which (beef carpaccio, truffle mushroom croquette, and truffle risotto) contained truffle oil. When all truffle oil–containing items were combined into a single variable, including the three that were individually significant, consumption of a truffle oil–containing item was reported by 89% of case-patients compared with 57% of control subjects ($p<0.001$).

DCDOH interviewed six of seven restaurant A employees who reported illness to their manager from late August through early September, the period when most patron illnesses occurred. Two employees sought medical care; one submitted a stool sample for laboratory testing and was confirmed to have a *Salmonella* Enteritidis infection. This employee, who reported eating a truffle oil–containing item that was not offered on the menu in addition to other restaurant A food items, was not involved in food preparation.

FIGURE. Date of onset* of gastrointestinal illness among 159 case-patients who ate at restaurant A, by case status — Washington, DC, August 2–September 12, 2015†,§,¶



* Symptom onset date was missing for six case-patients (five probable, one confirmed).
† One case-patient reported eating at restaurant A twice on the same day and is considered as one entry.
§ One case-patient reported two meal occasions at restaurant A (classified as probable on one occasion and as confirmed for another meal occasion) and is counted as two separate entries.
¶ Two case-patients reported two meal occasions, but reported illness on only one occasion.

Environmental and Laboratory Investigations

On September 9, a routine restaurant inspection was performed in response to the complaint received the previous day. Although multiple food safety violations were noted, the inspection findings did not warrant restaurant closure. On September 10, a second inspection was conducted as part of the outbreak investigation. Food samples collected on September 9 and 10, and environmental samples collected on September 11 were tested for *Salmonella*. Truffle fries sampled from the deep fryer and uncooked truffle mushroom croquettes were among the samples collected on September 10; a truffle oil sample was collected on September 14. DC Public Health Laboratory (DCPHL) and state public health laboratories performed pulsed-field gel electrophoresis (PFGE) testing on isolates from clinical specimens and uploaded pattern results into PulseNet (*1*). The outbreak cluster code was assigned using clinical samples from two initial hospitalized patients.

DCPHL tested the truffle fries, which screened positive for *Salmonella* by using polymerase chain reaction (PCR), but *Salmonella* was not isolated during confirmatory testing. All other food and environmental samples were negative for *Salmonella*. Among persons who reported illness, 41 (40 patrons and one employee; 26%) had stool samples collected. All 41 had the outbreak *Salmonella* Enteritidis strain (PFGE X*ba*I pattern JEGX01.0008).

Traceback Investigation

DCDOH issued a nationwide call for cases through CDC's Epidemic Information Exchange on September 10. Approximately 1 week later, the Los Angeles County Department of Public Health notified DCDOH of a possible outbreak associated with the same restaurant chain at a Los Angeles restaurant. On October 1, the Food and Drug Administration and the New York State Department of Agriculture and Markets inspected the New York-based commissary that prepared and distributed food items to both restaurant locations. Distributed food items to both restaurants were similar and included truffle oil, dried mushrooms, and croquette mix. Food items were unavailable for testing because the commissary had voluntarily ceased operations on September 13. Analysis of 102 subsamples of environmental sponges from food preparation areas using the VIDAS Enzyme Linked Fluorescent Assay did not detect *Salmonella* species. Shipment records for black trumpet mushrooms, cremini mushrooms, truffle oil, and food items prepared at the commissary using these ingredients were reviewed. The records for the implicated truffle oil shipped during August 1–September 15 yielded no significant findings. Truffle oil was regularly shipped to all restaurant A locations across the United States, including locations without any reported illnesses.

TABLE 1. Demographic characteristics of restaurant A patrons (n = 254) during July–September 2015, by case status — Washington, DC, 2015*,†,§

Characteristic	Case-patients (n = 159)¶		Control subjects (n = 95)	
	Mean (SD)	Range	Mean (SD)	Range
Age (yrs)	36.6 (11.9)	9–72	38.9 (13.3)	14–80
	No. (%)		No. (%)	
Female	106 (67)		57 (66)	
White, non-Hispanic	98 (74)		37 (79)	
DC resident**	57 (38)		27 (40)	
Visited doctor	78 (52)		0 (0)	
Hospitalized	9 (12)		0 (0)	
Died	0 (0)		0 (0)	

Abbreviation: SD = standard deviation.

* Number of persons with missing information: sex (nine), race (74), age (59), state of residence (36), doctor visits (10), hospitalization (19).

† Seven patrons reported dining at restaurant A on multiple occasions during July–September. Four case-patients reported illness within 7 days after at least one meal occasion, and three control subjects did not report illness on any meal occasion.

§ Excludes 21 patrons for whom symptom onset date, meal date, or symptom status were missing and two patrons who were confirmed to be infected with a pathogen other than Salmonella group D.

¶ Includes 40 confirmed and 119 probable case-patients.

** Case-patients who ate at restaurant A included residents from 11 states and Washington, DC: Washington, DC (57), Virginia (41), Maryland (36), New York (five), Pennsylvania (four), California (two), Alabama (one), Arizona (one), Illinois (one), Kentucky (one), Massachusetts (one), and Michigan (one).

TABLE 2. Selected foods consumed among patrons (n = 243) who reported eating at restaurant A during July–September 2015, by case status — Washington, DC, 2015*,†,§,¶

Food item	Case-patients (n = 155) No. (%)	Control subjects (n = 88) No. (%)	p value
Burrata crostini	39 (26)	9 (10)	<0.01
Beef carpaccio**	12 (8)	1 (1)	0.04
Branzino	16 (11)	2 (2)	0.02
Lamb chops	14 (9)	1 (1)	0.01
Truffle mushroom croquette**	90 (59)	28 (33)	<0.001
Truffle risotto**	32 (21)	8 (9)	0.02
Any truffle oil–containing item	134 (89)	45 (57)	<0.001

* Four case-patients and three control subjects reported multiple meals during this time period. Two of the four case-patients reported illness on a single occasion and were considered control subjects for the other meal occasion.

† Excludes four case-patients and seven control subjects for whom information concerning foods consumed at restaurant A was missing.

§ Number of patrons with missing information: burrata crostini (14), beef carpaccio (12), branzino (16), lamb chops (16), truffle mushroom croquette (12), truffle risotto (16), and truffle oil–containing item (22).

¶ Lists only food items that were significant at p<0.05 by using Pearson's chi-squared test or Fisher's exact test.

** Truffle oil–containing item.

Public Health Response

DCDOH issued a summary suspension of restaurant A's license on September 10 because of increasing concern about a potential outbreak. Restaurant A removed truffle oil–containing food items from the menu and was required to address food safety risk factor violations before its license was restored. After reopening on September 16, 2015, restaurant A was required to undergo periodic inspections. No additional *Salmonella* Enteritidis cases have been reported since restaurant A reopened.

Discussion

Gastrointestinal illness was reported in 159 persons from 11 states and DC after eating at restaurant A during July–September, 2015. All confirmed *Salmonella* Enteritidis cases had indistinguishable PFGE patterns. The case-control study results indicated truffle oil as a likely source of infection. Approximately 90% of case-patients reported that they ate a truffle oil–containing item.

Although *Salmonella* Enteritidis is most commonly associated with poultry and eggs (*2*,*3*), the strain identified in this outbreak was also associated with consuming Turkish pine nuts in a 2011 multistate outbreak (*4*). Whole genome sequencing conducted by CDC identified significant differences between this *Salmonella* Enteritidis strain and the one implicated in the 2011 pine nut outbreak. Previous reports indicate that *Salmonella* Enteritidis has the capacity to thrive in low-water activity foods (e.g., nuts and oils) (*5*), including peanut oil (*6*).

The findings in this report are subject to at least three limitations. First, attributing an outbreak to a single food vehicle is a recognized challenge in foodborne outbreak investigations (*2*). In this situation, food and environmental samples were collected after restaurant A had begun disposing of food items and addressing potential sources of contamination, and the commissary inspection occurred after its closure. Second, the truffle oil sampled on September 14 was unlikely to have been consumed by case-patients, because the latest meal date for case-patients was September 9. Finally, because of failure to isolate the organism in culture from food samples, it could not be established whether the PCR-detected *Salmonella* in the truffle fries led to actual illness or matched the outbreak strain. Despite these limitations, the epidemiologic evidence strongly suggested that truffle oil was the likely source of the outbreak.

Recognition of this multistate outbreak associated with truffle oil might have easily gone unnoticed; restaurant patrons and emergency department staff played a significant role in its timely recognition. The PFGE pattern associated with this outbreak is the eighth most common in the PulseNet database. Assigning a specific cluster code for this suspected outbreak at the time isolates from the hospitalized cases were added to PulseNet was difficult because uploads for the pattern code had not exceeded normal thresholds. Close collaboration between DCDOH epidemiologists and DCPHL ultimately led to a cluster code assignment, which facilitated case identification in residents of other states. Results from the routine inspection conducted after the initial complaint did not alone

Summary

What is already known about this topic?

Salmonella enterica is a common foodborne pathogen, causing an estimated 1 million cases of foodborne illness each year. *Salmonella* Enteriditis is the most common serotype and has frequently been associated with infections attributed to poultry and eggs.

What is added by this report?

During July–September 2015, a total of 159 patrons reported gastrointestinal illness after eating at a single District of Columbia restaurant. Forty-one persons (40 restaurant patrons and one employee) were infected with an indistinguishable *Salmonella* Enteritidis strain on the basis of pulsed-field gel electrophoresis (*Xba*I pattern JEGX01.0008). Results from a case-control study using restaurant patron data identified a novel food vehicle, truffle oil, as the likely source of *Salmonella* Enteritidis infection in this outbreak. Approximately 89% of case-patients reported eating truffle oil–containing items, compared with 57% of patrons who did not report gastrointestinal illness ($p<0.001$).

What are the implications for public health practice?

Public health officials and consumers should be aware that truffle oil has been implicated as the likely source of a *Salmonella* Enteritidis outbreak and could possibly harbor this pathogen. Timely engagement of the public, health care providers, and local and federal public health officials, is particularly critical for early recognition of outbreaks involving common foodborne pathogens, such as *Salmonella* Enteritidis.

warrant restaurant closure; however, increasing concern about a potential outbreak, based on multiple complaints of illness, prompted DCDOH to suspend the restaurant's license a day later. This timely public health response likely prevented additional illnesses, because 9% of case-patients reported eating at restaurant A the day before the closure. The engagement of the public, media, health care providers, and local, state, and federal public health officials facilitated recognition of an outbreak involving a *Salmonella* serotype that is a common source of foodborne illness.

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Notes from the Field

Investigation of Patients Testing Positive for Yellow Fever Viral RNA After Vaccination During a Mass Yellow Fever Vaccination Campaign — Angola, 2016

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The yellow fever outbreak declared in Angola in January 2016 soon became the largest recorded yellow fever outbreak in the country's history. In response, the Angola Ministry of Health, supported by the World Health Organization (WHO), conducted mass yellow fever vaccination campaigns beginning in February 2016 for all persons aged ≥6 months. By June 2016, a total of 11.6 million yellow fever vaccine doses had been distributed among a national population of 25 million. Because of the urgency of distributing vaccine to stop the outbreak, surveillance for cases of yellow fever after vaccination and serious adverse events after immunization (AEFIs) was not implemented. However, CDC and the Angola Field Epidemiology and Laboratory Training Program conducted an investigation of patients with a history of yellow fever vaccination and symptoms of yellow fever disease whose specimens tested positive for yellow fever viral RNA by reverse transcription–polymerase chain reaction (RT-PCR) to assess whether such cases could represent vaccine failure or AEFIs.

Although no yellow fever vaccine efficacy studies have been conducted, the vaccine is reliably immunogenic; worldwide, only five postvaccine yellow fever cases have been described (*1*). Neutralizing antibodies develop by day 10 after vaccination in 80% of yellow fever vaccinees (*1*). Primary yellow fever vaccine recipients have self-limited, vaccine-derived, physiologic viremia, typically during days 3–4, although this postvaccination viremia can last as long as 2 weeks. Thus, the detection of yellow fever viral RNA by RT-PCR testing before postvaccination day 3 or after day 13 could represent wild-type infection (acquired either before vaccination or later if there is vaccine failure) or yellow fever vaccine-associated viscerotropic disease (YEL-AVD), a rare but serious AEFI in which the vaccine-derived virus proliferates in multiple organs after primary vaccination. The symptoms of YEL-AVD are similar to those of naturally acquired yellow fever, typically beginning by postvaccination day 10; vaccine-derived viremia can persist beyond day 13. The risk for YEL-AVD is 0.3–0.4 cases per 100,000 yellow fever vaccine doses distributed among U.S. travelers; however, risk estimates in the context of mass vaccination campaigns in Africa are limited (*2*). Therefore, symptom onset within 10 days after vaccination and viremia on or after day 3 could represent YEL-AVD, physiologic viremia, or yellow fever after vaccine failure.

National epidemiologic and linked laboratory data, including RT-PCR results, were reviewed to identify all suspected yellow fever cases (defined in the outbreak as the occurrence of fever and jaundice) in persons who also had a history of yellow fever vaccination and who received a positive RT-PCR test result during January 1–May 11, 2016. Vaccination was recorded in the database based on self-report or presentation of a WHO vaccination card. Database records of yellow fever vaccination among patients who received positive RT-PCR test results were confirmed through review of original suspected yellow fever case surveillance forms and patient medical records and through telephone interviews with patients or their families. The intervals from vaccination date to symptom onset date and from vaccination date to sample collection date were calculated. The uniformity of distribution of vaccination date was assessed using Chi-square goodness-of-fit testing.

Among 2,907 suspected cases of yellow fever, 459 (16%) patients had documentation of receipt of yellow fever vaccine. Among these, 376 (82%) also had documented RT-PCR results, including 51 (14%) who received positive RT-PCR test results. Among these 51 patients, 50 had surveillance forms, and seven had medical records for review; 20 patients or their families could be contacted to confirm vaccination. Among the 51 patients who received positive RT-PCR test results, symptom onset occurred after vaccination in 32 (63%). Among the remaining 19, five were excluded because they had not been vaccinated, eight because their symptoms preceded vaccination, and six because they had no documented vaccination date.

Among the 32 patients who received positive RT-PCR test results after vaccination, 24 (75%) were male, the mean age was 20 years (standard deviation = 12 years), and 13 (41%) died. Eighteen (56%) received positive test results for yellow fever viral RNA after postvaccination day 13, and 11 (34%) received positive test results during days 0–13; the sample collection date was missing for three patients. Symptom onset occurred during postvaccination days 0–10 in 17 (53%) patients, and after day 10 in 15 (47%). Distribution of vaccination dates was uniform, implying no clustering by date. Information about location of vaccination was not available to assess clustering by place.

Insufficient clinical and laboratory information was available to determine which of the 32 patients who received positive RT-PCR test results had wild-type infection (either

before vaccination or as a result of vaccine failure) or physiologic viremia after vaccination. A lack of supplementary information also precluded determining whether any of these 32 patients met diagnostic criteria for YEL-AVD (*2*). Although nucleotide sequencing can distinguish wild-type from vaccine-derived yellow fever viremia, and viral RNA quantification can aid in the diagnosis of YEL-AVD, additional testing on specimens from five of these patients performed at a reference laboratory found no detectable viral RNA, thus precluding viral RNA sequencing.

After this investigation, the Angola Ministry of Health modified the suspected yellow fever case surveillance form to include the location of vaccination and instructions to send specimens from patients who develop symptoms and receive positive RT-PCR test results after vaccination for specialized testing. In addition, personnel from the Angola Ministry of Health and WHO investigate such cases, gathering comprehensive clinical and laboratory data, to improve surveillance for both yellow fever after vaccination and serious AEFIs.

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Announcement

World Water Day — March 22, 2017

World Water Day is sponsored by the United Nations and observed each year on March 22. This year, World Water Day focuses on wastewater, which includes sewage, storm water, and discarded water used in the community (*1*). Many developing countries have inadequate wastewater management strategies because they lack resources, infrastructure, available technology, or space. Untreated wastewater in these countries is often disposed of directly into rivers, lakes, or oceans, polluting the environment and increasing the risk for disease transmission (*2*).

The World Health Organization's Sustainable Development Goal 6 aims in part to improve access to sanitation facilities (*3*), an important first step in proper wastewater management. As of 2015, approximately 2.4 billion persons worldwide lacked improved sanitation facilities (i.e., facilities designed to ensure users will not come into contact with human waste), and 946 million persons practiced open defecation (*4*). In countries that have sanitation facilities, waste streams must be collected and properly treated before being disposed into the environment. Although 68% of the global population now uses an improved sanitation facility, worldwide only 20% of wastewater receives proper treatment (*4*,*5*).

Through the CDC Innovation Fund, CDC is collaborating with Sanivation (http://www.sanivation.com), a startup company, on a novel approach to improving access to sanitation facilities and wastewater management strategies in Kenya. Company representatives install toilet facilities in Kenyan households and make twice-weekly visits to collect waste from toilets. Sanivation treats the collected waste with solar thermal energy and blends it with carbonized agricultural waste to produce low-cost charcoal briquettes for cooking fuel and heating homes.

Additional information about World Water Day is available at http://www.unwater.org/worldwaterday. Additional information about CDC's initiatives to improve global access to water and sanitation is available at https://www.cdc.gov/healthywater/global.

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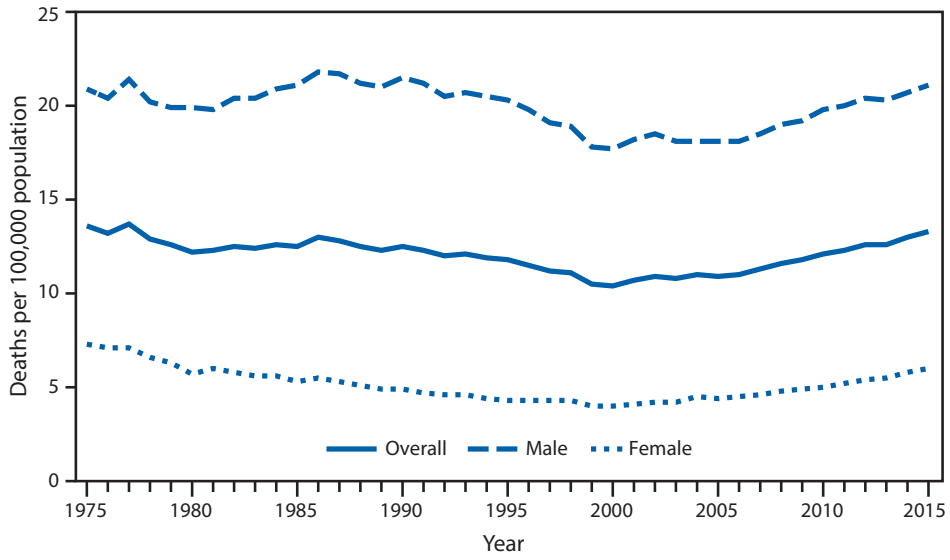
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Age-Adjusted Rate* for Suicide,† by Sex — National Vital Statistics System, United States, 1975–2015



* Age adjusted rates are suicide deaths per 100,000 standard population.
† Suicides are identified using *International Classification of Diseases (ICD), 8th Revision* codes E950–E959 for 1975–1978; *ICD, 9th Revision* codes E950–E959 for 1979–1998; and *ICD, 10th Revision* codes U03, X60–X84, and Y87.0 for 1999–2015.

There was an overall decline of 24% in the age-adjusted suicide rate from 1977 (13.7 per 100,000) to 2000 (10.4). The rate increased in most years from 2000 to 2015. The 2015 suicide rate (13.3) was 28% higher than in 2000. The rates for males and females followed the overall pattern; however, the rate for males was approximately 3–5 times higher than the rate for females throughout the study period.

Source: CDC. National Vital Statistics System. Mortality data. https://www.cdc.gov/nchs/nvss/deaths.htm.

Reported by: Sally C. Curtin, MA, sac2@cdc.gov, 301-458-4142; Holly Hedegaard, MD; Margaret Warner, PhD.

For more information on this topic, CDC recommends the following link: https://www.cdc.gov/violenceprevention/suicide/index.html.

The *Morbidity and Mortality Weekly Report (MMWR)* Series is prepared by the Centers for Disease Control and Prevention (CDC) and is available free of charge in electronic format. To receive an electronic copy each week, visit *MMWR*'s free subscription page at *https://www.cdc.gov/mmwr/mmwrsubscribe.html*. Paper copy subscriptions are available through the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402; telephone 202-512-1800.

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