

Regional Differences in the Drugs Most Frequently Involved in Drug Overdose Deaths: United States, 2017

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Abstract

Objective—This report describes regional differences in the specific drugs most frequently involved in drug overdose deaths in the United States in 2017.

Methods—Data from the 2017 National Vital Statistics System—Mortality files were linked to electronic files containing literal text information from death certificates. Drug overdose deaths were identified using *International Classification of Diseases, 10th Revision* underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Drug mentions were identified using established methods for searching the literal text from death certificates. Deaths were assigned to 1 of 10 U.S. Department of Health and Human Services (HHS) regions based on the decedent's state of residence. The number and age-adjusted death rate was determined for the 10 drugs most frequently involved in drug overdose deaths in 2017, both nationally and for each HHS region. Deaths involving more than one drug were counted in all relevant drug categories (i.e., the same death could be counted in more than one drug category).

Results—Among drug overdose deaths in 2017 that mentioned at least 1 specific drug on the death certificate, the 10 drugs most frequently involved included fentanyl, heroin, cocaine, methamphetamine, alprazolam, oxycodone, morphine, methadone, hydrocodone, and diphenhydramine. Regionally, 6 drugs (alprazolam, cocaine, fentanyl, heroin, methadone, and oxycodone) were found among the 10 most frequently involved drugs in all 10 HHS regions, although the relative ranking varied by region. Age-adjusted rates of drug overdose deaths involving fentanyl or deaths involving cocaine were higher in the regions east of the Mississippi River, while age-adjusted rates for drug overdose deaths involving methamphetamine were higher in

the West. The regional patterns observed did not change after adjustment for differences in the specificity of drug reporting.

Conclusions—The drugs most frequently involved in drug overdose deaths in 2017 varied by HHS region. Understanding the regional differences can help inform local prevention and policy efforts.

Keywords: fentanyl • heroin • cocaine • methamphetamine • National Vital Statistics System

Introduction

Deaths from drug overdose remain a significant public health concern in the United States. For 1999 through 2017, the age-adjusted rate of drug overdose deaths more than tripled, from 6.1 per 100,000 to 21.7 per 100,000 (1).

Recent studies suggest that the type of drugs involved in overdose deaths varied across the country (2,3). As in other reports of drug overdose mortality (1–5), these studies used National Vital Statistics System—Mortality (NVSS–M) data, coded using the *International Classification of Diseases, 10th Revision* (ICD–10). ICD–10 is the classification system used in the United States to categorize the underlying and multiple causes of death (6). One limitation of the ICD–10 classification system is that, with a few exceptions, ICD–10 codes reflect broad categories of drugs rather than unique specific drugs. The broad drug categorizations used in ICD–10 make it difficult to use ICD–10-coded data to monitor trends and identify regional differences in the specific drugs most frequently involved in drug overdose deaths.

To address the limitations of using ICD–10-coded mortality data, the National Center for Health Statistics (NCHS) and



the U.S. Food and Drug Administration (FDA) collaboratively developed methods that involve searching the literal text from death certificates to identify mentions of specific drugs and other substances, as well as contextual terms that help identify involvement of the drugs or substances in the death (7). Death certificate literal text is the written information provided by the medical certifier, usually a coroner or medical examiner in the case of drug overdose deaths, that describes the cause of death and other factors or circumstances contributing to the death (8). The literal text information is captured in three fields of the U.S. standard death certificate: the causes of death from Part I, significant conditions contributing to death from Part II, and a description of how the injury occurred (9).

The literal text analysis methods have been used to identify the specific drugs most frequently involved in drug overdose deaths in 2010 through 2016 (10,11) and to describe patterns in drug overdose deaths involving fentanyl (12). This report examines regional differences in drug overdose deaths using the literal text analysis methodology to identify the specific drugs most frequently involved in drug overdose deaths in 2017.

Methods

Data source and study population

This descriptive study used NVSS–M data from 2017. NVSS–M data contain cause-of-death, demographic, and geographic information obtained from death certificates (13). The study population included decedents who were U.S. residents and had an underlying cause of death of drug overdose, as identified by ICD–10 codes: X40–X44 (unintentional), X60–X64 (suicide or intentional self-harm), X85 (homicide), and Y10–Y14 (undetermined intent). Among the drug overdose deaths in 2017, 87% were unintentional, 7% were suicides, 5% were of undetermined intent, and less than 1% were homicides (1). The underlying cause-of-death codes reflect deaths resulting from acute intoxication from drugs (i.e., drug overdose). Deaths from chronic exposure to drugs (e.g., liver toxicity) or adverse effects experienced from therapeutic or prophylactic dosages of drugs were not included. Use of this code set (X40–X44, X60–X64, X85, and Y10–Y14) is consistent with other NCHS publications on drug overdose deaths and facilitates comparison with other analyses using the ICD–10-coded data (1,14).

NVSS–M files were supplemented with literal text data, also obtained from death certificates (7). The identification of drug mentions and contextual information about the involvement of the drug in the death (described below) is based on information provided in three fields of the death certificate: the causes of death from Part I, significant conditions contributing to death from Part II, and a description of how the injury occurred.

Identifying drug mentions and involvement of the drug in the death

The method for searching literal text information to characterize the drugs involved in deaths has been described in detail elsewhere (7,10–12). Briefly, the method involves searching

the literal text for mentions of drugs and other substances, as well as terms that provide context about the involvement of the drug in the death (i.e., whether the drug contributed to the death). The drugs or substances mentioned in a literal text field are assumed to be involved in the death unless the contextual information indicates otherwise. Software programs, referred to as the drug mention with involvement (DMI) programs, were developed using SAS version 9.4 to automate the process of searching the literal text (7).

Principal variants

The DMI programs identify mentions of drugs and other substances using various search terms, including generic drug names, brand names, common usage or street names, abbreviations, metabolites, misspellings, and other variations. Each search term is mapped to a “principal variant,” the overarching label assigned to a drug, a drug class, or exposure not otherwise specified. For example, terms such as “COCAIEN,” “COCAINE CRACK,” “COCAINE HYDROCHLORIDE,” and “COCAINETOXICITY” are all mapped to the principal variant “COCAINE.” In general, the principal variant is the generic drug name. Some search terms—mostly for combination drug products—are mapped to two or more principal variants. Use of principal variants makes it possible to generate aggregate counts for all search terms that refer to the same drug or substance. Principal variants also are categorized according to whether they referred to specific drugs or substances (e.g., methadone), classes of drugs or substances (e.g., opioids), or nonspecific references to exposures to drugs (e.g., words such as “DRUG,” “MULTIDRUG,” or “POLYPHARMACY”). The DMI search terms and principal variants table is provided in an accompanying CSV file (https://ftp.cdc.gov/pub/Health_Statistics/NCHS/Publications/NVSR/68_12/).

Referent drug groups

The term “referent drug group” in the tables and figures in this report generally refers to a single principal variant for the drug of interest. However, some of the referent drug groups comprise two or more principal variants, generally reflecting a drug and its metabolites. For example, the principal variant HYDROCODONE and the principal variant NORHYDROCODONE (a metabolite of hydrocodone) were grouped together to create the referent drug group of HYDROCODONE. The referent drug group FENTANYL included fentanyl as well as fentanyl metabolites, precursors, and analogs. The grouping of principal variants into referent drug groups was based on expertise from FDA and NCHS. The referent drug groups table, which contains a list of search terms and the principal variants included in each referent drug group, is provided in an accompanying CSV file (https://ftp.cdc.gov/pub/Health_Statistics/NCHS/Publications/NVSR/68_12/).

Analysis

The deaths were categorized by the decedent’s jurisdiction of residence using the 10 U.S. Department of Health and Human Services (HHS) public health regions (15). As shown in [Figure 1](#),

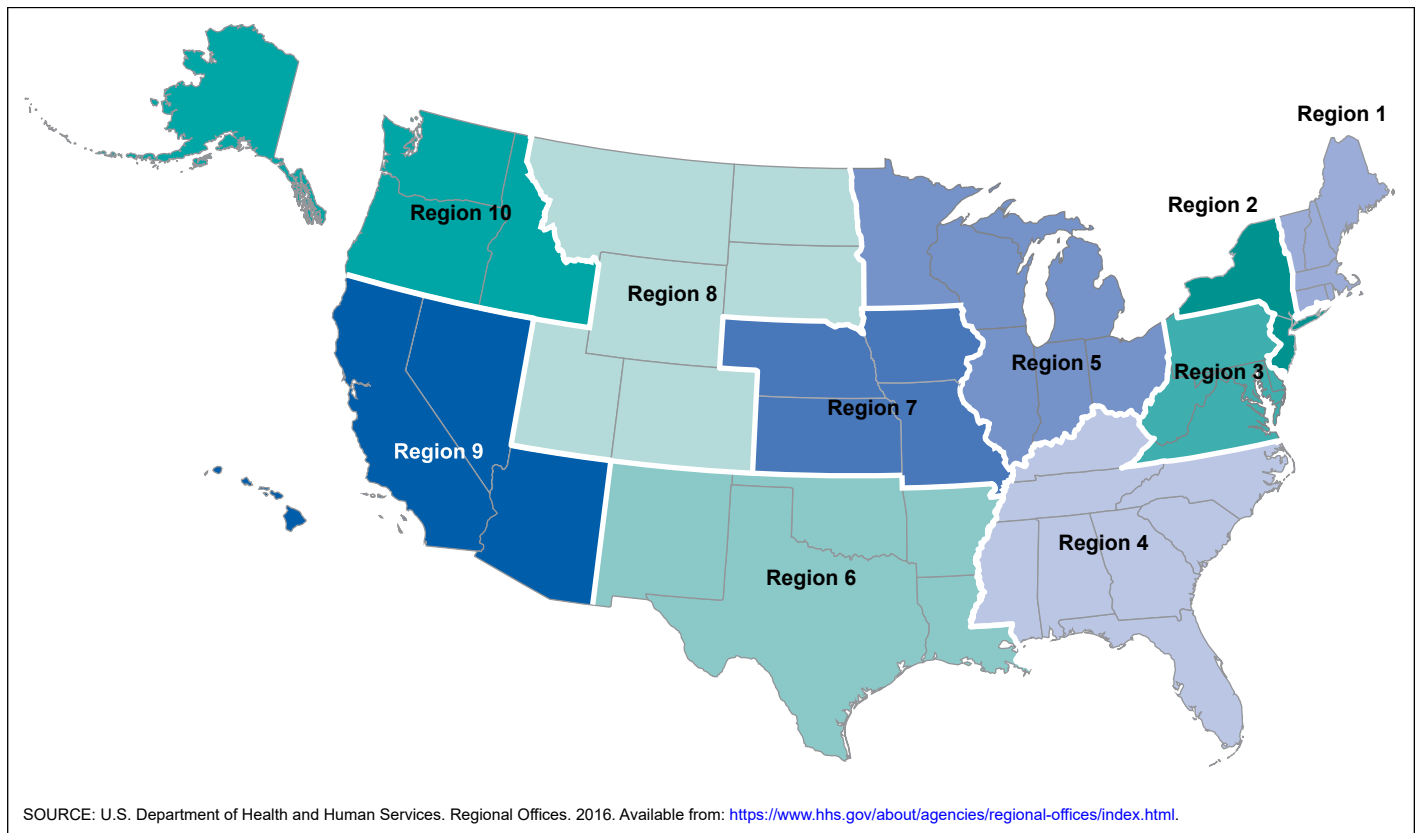


Figure 1. U.S. Department of Health and Human Services regions

these regions are: Region 1 (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont), Region 2 (New Jersey, New York, and New York City), Region 3 (Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia), Region 4 (Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee), Region 5 (Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin), Region 6 (Arkansas, Louisiana, New Mexico, Oklahoma, and Texas), Region 7 (Iowa, Kansas, Missouri, and Nebraska), Region 8 (Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming), Region 9 (Arizona, California, Hawaii, and Nevada), and Region 10 (Alaska, Idaho, Oregon, and Washington).

The referent drug groups most frequently involved in drug overdose deaths in 2017 were identified nationally and by HHS region. Deaths involving more than one referent drug group (e.g., a death involving both heroin and cocaine) were included in totals for all applicable referent drug groups (e.g., the same death is included in counts of heroin deaths and in counts of cocaine deaths); therefore, referent drug group counts are not mutually exclusive and should not be summated. Numbers and age-adjusted rates for deaths involving the most frequent referent drug groups are reported nationally (top 15) and for each of the 10 HHS regions (top 10) due to smaller numbers. Age-adjusted death rates were calculated using the direct method and the 2000 U.S. standard population (13). Comparisons of rates between regions were tested for statistical significance using methods described elsewhere (13). A statement that a given death rate is higher or lower than another rate indicates that the difference in

rates was statistically significant at an alpha level of 0.05.

The numbers and rates of drug-specific overdose deaths shown in the tables and figures should be considered the minimum number or rate for that referent drug group, because there could be additional deaths in which the drug was involved but the drug was not reported in the literal text on the death certificate. Additionally, the numbers and rates may differ from those obtained using ICD-10-coded data.

Assessing the effect of regional differences in specificity of drug reporting

The ICD-10 multiple cause codes T36–T50.8 provide information on the types of drugs or drug classes involved in the death. The percentage of deaths with an underlying cause of X40–X44, X60–X64, X85, and Y10–Y14 that also have any multiple cause code of T36–T50.8 is an indication of the specificity of reporting of drugs or drug classes in drug overdose deaths. This measure was used to assess possible differences in reporting of specific drugs or drug classes among the 10 HHS regions. In 2017, the percentage of drug overdose deaths with a multiple-cause code of T36–T50.8 was 87.6% nationally. The reporting of at least one specific drug or drug class among drug overdose deaths varied by HHS region (Region 1, 98.9%; Region 2, 90.5%; Region 3, 75.4%; Region 4, 88.0%; Region 5, 91.8%; Region 6, 82.9%; Region 7, 88.1%; Region 8, 89.2%; Region 9, 88.3%; and Region 10, 93.3%).

This difference in reporting of specific drugs and drug classes by region could potentially influence the numbers and

rates for drug overdose deaths involving specific drugs. To assess the possible influence of differences in reporting, an adjustment analysis was conducted. In this analysis, an adjustment factor was applied to each age-adjusted rate for drug overdose deaths involving specific drugs. The adjustment factor assumed that the specificity of drug reporting was constant across the HHS regions at the rate for Region 1 (98.9%), the region with the highest reporting of specific drugs or drug classes. A description of the methodology and the results from the adjustment analysis are provided in the [Technical Notes](#). The findings reported in the Results reflect values using unadjusted numbers and rates. Differences in the findings using the adjusted rates compared with the unadjusted rates are described in the [Technical Notes](#).

Results

[Table A](#) shows the relative ranking of the 15 drugs most frequently involved in drug overdose deaths in the United States in 2017. The top 15 drugs belonged to several drug classes: opioids (fentanyl, heroin, hydrocodone, methadone, morphine, oxycodone, and tramadol), benzodiazepines (alprazolam, clonazepam, and diazepam), stimulants (amphetamine, cocaine, and methamphetamine), an antihistamine (diphenhydramine) and an anticonvulsant (gabapentin). Nationally, 38.9% of drug overdose deaths involved fentanyl (including fentanyl metabolites, precursors, and analogs), 22.8% involved heroin, 21.3% involved cocaine, and 13.3% involved methamphetamine. Alprazolam, oxycodone, and morphine were each involved in 6.9%–9.5% of the drug overdose deaths in 2017, while methadone, hydrocodone, diphenhydramine, clonazepam, diazepam, gabapentin, amphetamine, and tramadol were each involved in less than 5.0%. (Note: Because deaths involving

more than one referent drug group were counted in all relevant categories, referent drug group counts are not mutually exclusive and should not be summated.)

In 2017, the age-adjusted mortality rate for drug overdose deaths involving fentanyl was 8.7 per 100,000, 5.0 for heroin, 4.6 for cocaine, and 2.9 for methamphetamine.

[Table B](#) shows the relative ranking of the 10 drugs most frequently involved in drug overdose deaths by HHS region. The number of deaths involving each drug should be interpreted in light of regional differences in the specificity of reporting of drug information. Although the most frequent drugs varied by region, several similarities were observed:

- Alprazolam, cocaine, fentanyl, heroin, methadone, and oxycodone ranked among the top 10 for all HHS regions.
- Morphine ranked among the top 10 in all regions except Region 1.
- Hydrocodone and methamphetamine ranked among the top 10 in all regions except Regions 1 and 2.
- Diphenhydramine ranked among the top 10 in all regions except Regions 3 and 4.

Four drugs ranked among the top 10 most frequent drugs involved in drug overdose deaths in three or fewer regions: diazepam in Regions 1–3; clonazepam in Regions 1 and 2; buprenorphine in Region 1, and gabapentin in Region 4.

Fentanyl was the drug most frequently involved in drug overdose deaths in Regions 1–5 and 7. Methamphetamine was the drug most frequently involved in Regions 6 and 8–10. For all regions, heroin ranked as the second or third most frequently involved drug. Cocaine ranked as the second or third most frequently involved drug in Regions 1–6, but ranked fourth to sixth in Regions 7–10.

Table A. Drugs most frequently involved in drug overdose deaths: United States, 2017

Rank ²	Referent drug group	United States (<i>n</i> = 70,237, 21.7) ¹		
		Number of deaths	Percent ³	Age-adjusted rate ⁴
1	Fentanyl	27,299	38.9	8.7
2	Heroin	15,982	22.8	5.0
3	Cocaine	14,948	21.3	4.6
4	Methamphetamine	9,356	13.3	2.9
5	Alprazolam	6,647	9.5	2.1
6	Oxycodone	6,053	8.6	1.8
7	Morphine	4,874	6.9	1.5
8	Methadone	3,286	4.7	1.0
9	Hydrocodone	3,072	4.4	0.9
10	Diphenhydramine	2,286	3.3	0.7
11	Clonazepam	2,055	2.9	0.6
12	Diazepam	2,025	2.9	0.6
13	Gabapentin	1,848	2.6	0.6
14	Amphetamine	1,581	2.3	0.5
15	Tramadol	1,333	1.9	0.4

¹Number and age-adjusted rate (deaths per 100,000 standard population) for all drug overdose deaths. Age-adjusted death rates were calculated using the direct method and adjusted to the 2000 standard population.

²Drugs were ranked by number of deaths. Ranks were not tested for statistical significance.

³Percentage of drug overdose deaths that involve the referent drug group.

⁴Age-adjusted death rates (deaths per 100,000 standard population) were calculated using the direct method and adjusted to the 2000 standard population.

NOTES: Drug overdose deaths were identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to the referent drug group. Deaths involving more than one referent drug group (e.g., a death involving both heroin and cocaine) were counted in both totals. To avoid counting the same death multiple times, the numbers for drug-specific deaths should not be summated.

SOURCE: NCHS National Vital Statistics System, Mortality files linked with death certificate literal text, 2017.

Figures 2–5 show the age-adjusted rates of drug overdose deaths involving selected drugs by region. The selected drugs include the top four drugs seen nationally (fentanyl, heroin, cocaine, and methamphetamine). The age-adjusted rates of drug overdose deaths involving fentanyl were above 9.0 per 100,000 in Regions 1–5 (east of the Mississippi River), ranging from 9.1 in Region 4 to 22.5 in Region 1, and below 6.0 per 100,000 in Regions 6–10 (west of the Mississippi River), ranging from 1.5 in Regions 6 and 9 to 5.5 in Region 7 (Table B, Figure 2). A similar regional pattern was seen for cocaine, with rates above 5.0 per 10,000 in Regions 1–5, ranging from 5.3 in Region 4 to 9.5 in Region 1, and rates below 3.0 per 100,000 in Regions 6–10, ranging from 1.3 in Regions 7, 9, and 10 to 2.3 in Region 6 (Table B, Figure 4). For heroin, age-adjusted rates were 7.5 per 100,000 or above in Regions 1–3 and 5 (Northeast and Great Lakes states), and 4.0 per 100,000 or below in all other regions (Table B, Figure 3). Age-adjusted rates for drug overdose deaths involving methamphetamine were below 2.0 per 100,000 in Regions 1–3 (Northeast), between 2.0 and 4.0 in Regions 4–7 (South and Midwest), and above 4.0 in Regions 8–10 (West) (Table B, Table, and Figure 5).

Discussion

Drugs most frequently involved

Nine of the top 10 drugs most frequently involved in drug overdose deaths in 2017 were the same as those previously reported in 2011–2016 (11). They include the opioids fentanyl, heroin, hydrocodone, methadone, morphine, and oxycodone; the benzodiazepine alprazolam; and the stimulants cocaine and methamphetamine. Diazepam, which ranked among the top 10 in 2011–2016 (11), ranked 12th in 2017, with diphenhydramine and clonazepam ranking 10th and 11th in 2017, respectively.

In 2017, the drug most frequently involved in drug overdose deaths in the United States was fentanyl. Fentanyl also ranked as the most frequently involved drug in overdose deaths in 2016 (11). In 2016, approximately 29% of all drug overdose deaths in the United States (18,335 of 63,632 deaths) involved fentanyl, resulting in an age-adjusted death rate of 5.9 per 100,000 (11). In 2017, approximately 39% of all drug overdose deaths (27,299 of 70,237 deaths) involved fentanyl, for an age-adjusted rate of 8.7 per 100,000.

Regionally, six drugs (alprazolam, cocaine, fentanyl, heroin, methadone, and oxycodone) were found among the top 10 most frequently involved drugs in all 10 HHS regions, although the relative ranking varied by region. Fentanyl was the drug most frequently involved in drug overdose deaths in HHS Regions 1–5 and 7, while methamphetamine was the drug most frequently involved in Regions 6 and 8–10. The age-adjusted rates of drug

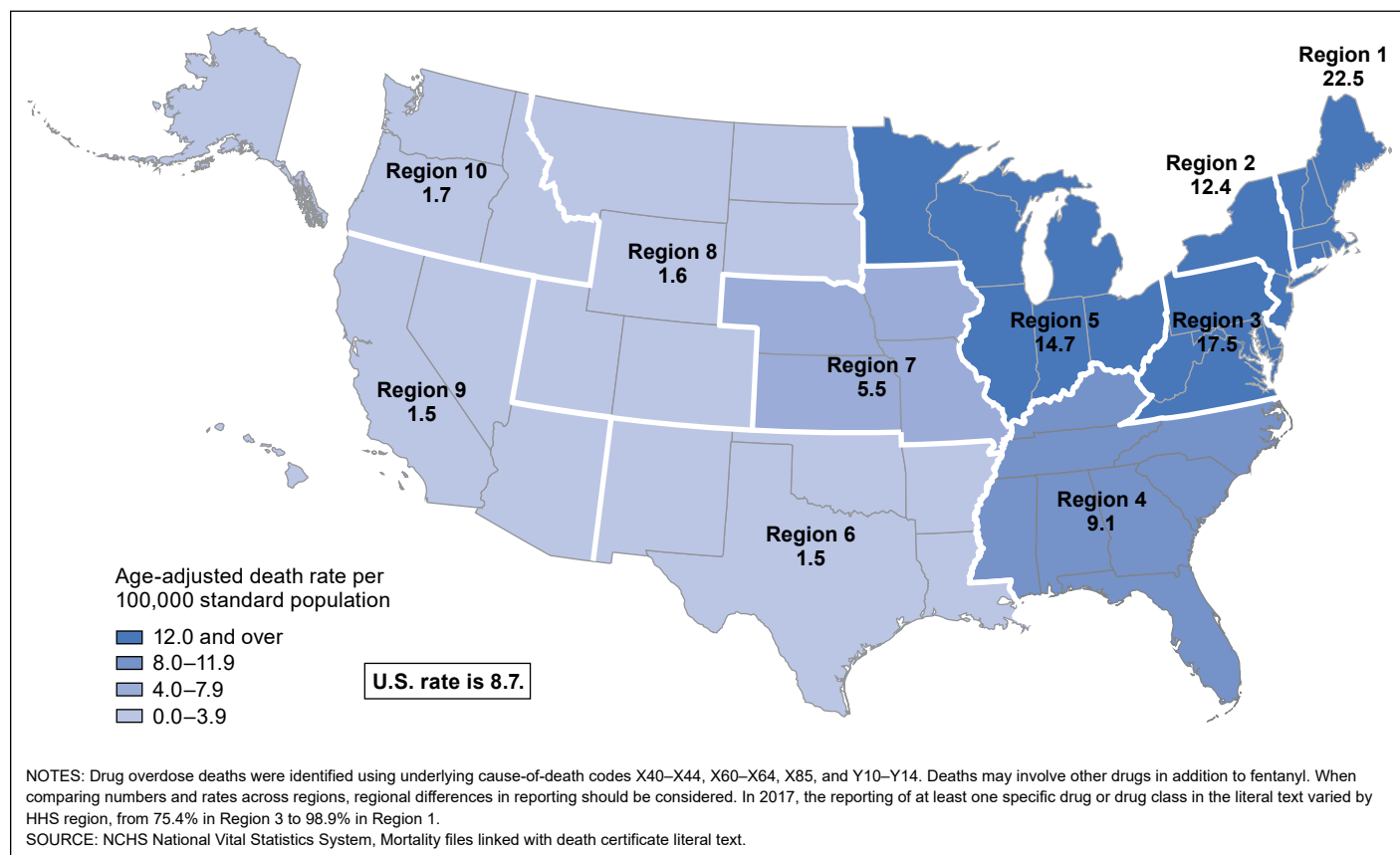


Figure 2. Age-adjusted rate of drug overdose deaths involving fentanyl, by region: 2017

Table B. Drugs most frequently involved in drug overdose deaths, by U.S. Department of Health and Human Services region: 2017

Region 1 ¹ —CT, ME, MA, NH, RI, and VT					Region 2 ¹ —NJ, NY, and NYC				
Rank ²	Referent drug group	Number of deaths	Percent ³	Age-adjusted rate ⁴	Rank ²	Referent drug group	Number of deaths	Percent ³	Age-adjusted rate ⁴
...	All drugs	4,585	100.0	31.8	...	All drugs	6,606	100.0	22.7
1	Fentanyl	3,158	68.9	22.5	1	Fentanyl	3,548	53.7	12.4
2	Cocaine	1,347	29.4	9.5	2	Heroin	2,491	37.7	8.6
3	Heroin	1,070	23.3	7.5	3	Cocaine	1,947	29.5	6.7
4	Oxycodone	361	7.9	2.4	4	Alprazolam	802	12.1	2.8
5	Alprazolam	354	7.7	2.5	5	Oxycodone	599	9.1	2.0
6	Clonazepam	281	6.1	1.9	6	Morphine	377	5.7	1.3
7	Methadone	277	6.0	1.9	7	Methadone	375	5.7	1.2
8	Diphenhydramine	181	3.9	1.2	8	Clonazepam	275	4.2	1.0
9	Buprenorphine	159	3.5	1.1	9	Diphenhydramine	225	3.4	0.8
10	Diazepam	157	3.4	1.0	10	Diazepam	224	3.4	0.7
Region 3 ¹ —DE, DC, MD, PA, VA, and WV					Region 4 ¹ —AL, FL, GA, KY, MS, NC, SC, and TN				
Rank ²	Referent drug group	Number of deaths	Percent ³	Age-adjusted rate ⁴	Rank ²	Referent drug group	Number of deaths	Percent ³	Age-adjusted rate ⁴
...	All drugs	10,764	100.0	35.4	...	All drugs	14,578	100.0	22.7
1	Fentanyl	5,223	48.5	17.5	1	Fentanyl	5,597	38.4	9.1
2	Heroin	2,473	23.0	8.2	2	Cocaine	3,353	23.0	5.3
3	Cocaine	2,403	22.3	7.9	3	Heroin	2,499	17.1	4.0
4	Morphine	827	7.7	2.7	4	Alprazolam	2,007	13.8	3.1
5	Oxycodone	724	6.7	2.3	5	Methamphetamine	1,774	12.2	2.9
6	Alprazolam	634	5.9	2.1	6	Oxycodone	1,651	11.3	2.5
7	Methamphetamine	478	4.4	1.7	7	Morphine	1,278	8.8	2.0
8	Methadone	474	4.4	1.5	8	Hydrocodone	758	5.2	1.1
9	Diazepam	236	2.2	0.8	9	Gabapentin	748	5.1	1.2
10	Hydrocodone	233	2.2	0.7	10	Methadone	577	4.0	0.9
Region 5 ¹ —IL, IN, MI, MN, OH, and WI					Region 6 ¹ —AR, LA, NM, OK, and TX				
Rank ²	Referent drug group	Number of deaths	Percent ³	Age-adjusted rate ⁴	Rank ²	Referent drug group	Number of deaths	Percent ³	Age-adjusted rate ⁴
...	All drugs	14,345	100.0	28.2	...	All drugs	5,811	100.0	13.9
1	Fentanyl	7,287	50.8	14.7	1	Methamphetamine	1,245	21.4	3.0
2	Heroin	3,942	27.5	7.8	2	Cocaine	997	17.2	2.3
3	Cocaine	3,678	25.6	7.3	3	Heroin	989	17.0	2.4
4	Alprazolam	1,237	8.6	2.5	4	Alprazolam	633	10.9	1.6
5	Methamphetamine	1,224	8.5	2.5	5	Fentanyl	606	10.4	1.5
6	Morphine	894	6.2	1.8	6	Hydrocodone	461	7.9	1.1
7	Oxycodone	868	6.1	1.6	7	Oxycodone	451	7.8	1.1
8	Hydrocodone	720	5.0	1.4	8	Morphine	297	5.1	0.7
9	Methadone	581	4.1	1.1	9	Diphenhydramine	260	4.5	0.6
10	Diphenhydramine	450	3.1	0.9	10	Methadone	232	4.0	0.6

See footnotes at end of table.

Table B. Drugs most frequently involved in drug overdose deaths, by U.S. Department of Health and Human Services region: 2017—Con.

Region 7 ¹ — IA, KS, MO, and NE					Region 8 ¹ — CO, MT, ND, SD, UT, and WY				
Rank ²	Referent drug group	Number of deaths	Percent ³	Age-adjusted rate ⁴	Rank ²	Referent drug group	Number of deaths	Percent ³	Age-adjusted rate ⁴
...	All drugs	2,193	100.0	16.3	...	All drugs	1,994	100.0	16.7
1	Fentanyl	717	32.7	5.5	1	Methamphetamine	572	28.7	4.9
2	Methamphetamine	447	20.4	3.4	2	Heroin	423	21.2	3.6
3	Heroin	394	18.0	3.0	3	Oxycodone	324	16.2	2.7
4	Oxycodone	204	9.3	1.5	4	Morphine	204	10.2	1.7
5	Cocaine	182	8.3	1.3	5	Cocaine	187	9.4	1.6
6	Alprazolam	151	6.9	1.0	6	Fentanyl	185	9.3	1.6
7	Morphine	116	5.3	0.8	7	Alprazolam	164	8.2	1.4
8	Hydrocodone	101	4.6	0.7	8	Diphenhydramine	129	6.5	1.1
9	Diphenhydramine	87	4.0	0.6	9	Methadone	117	5.9	1.0
10	Methadone	74	3.4	0.6	10	Hydrocodone	113	5.7	0.9

Region 9 ¹ — AZ, CA, HI, and NV					Region 10 ¹ — AK, ID, OR, and WA				
Rank ²	Referent drug group	Number of deaths	Percent ³	Age-adjusted rate ⁴	Rank ²	Referent drug group	Number of deaths	Percent ³	Age-adjusted rate ⁴
...	All drugs	7,279	100.0	13.7	...	All drugs	2,082	100.0	14.5
1	Methamphetamine	2,741	37.7	5.2	1	Methamphetamine	683	32.8	4.8
2	Heroin	1,178	16.2	2.2	2	Heroin	523	25.1	3.7
3	Fentanyl	744	10.2	1.5	3	Fentanyl	234	11.2	1.7
4	Cocaine	672	9.2	1.3	4	Oxycodone	220	10.6	1.5
5	Oxycodone	651	8.9	1.2	5	Methadone	183	8.8	1.2
6	Morphine	572	7.9	1.1	6	Cocaine	182	8.7	1.3
7	Alprazolam	531	7.3	1.0	7	Morphine	160	7.7	1.1
8	Methadone	396	5.4	0.7	8	Alprazolam	134	6.4	1.0
9	Hydrocodone	389	5.3	0.7	9	Hydrocodone	120	5.8	0.8
10	Diphenhydramine	258	3.5	0.5	10	Diphenhydramine	104	5.0	0.8

... Category not applicable.

¹U.S. Department of Health and Human Services (HHS) regions: Region 1 (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont), Region 2 (New Jersey, New York, and New York City), Region 3 (Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia), Region 4 (Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee), Region 5 (Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin), Region 6 (Arkansas, Louisiana, New Mexico, Oklahoma, and Texas), Region 7 (Iowa, Kansas, Missouri, and Nebraska), Region 8 (Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming), Region 9 (Arizona, California, Hawaii, and Nevada), and Region 10 (Alaska, Idaho, Oregon, and Washington).

²Drugs were ranked by number of deaths. Ranks were not tested for statistical significance.

³Percentage of drug overdose deaths in the region that involve the referent drug group.

⁴Age-adjusted death rates (deaths per 100,000 standard population) were calculated using the direct method and adjusted to the 2000 standard population.

NOTES: Drug overdose deaths were identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to the referent drug group. Deaths involving more than one referent drug group (e.g., a death involving both heroin and cocaine) were counted in both totals. To avoid counting the same death multiple times, the numbers and percentages for drug-specific deaths should not be summated. Caution should be used when comparing numbers and rates across regions. The reporting of at least one specific drug in the literal text varied by region (Region 1, 98.9%; Region 2, 90.5%; Region 3, 75.4%; Region 4, 88.0%; Region 5, 91.8%; Region 6, 82.9%; Region 7, 88.1%; Region 8, 89.2%; Region 9, 88.3%; Region 10, 93.3%).

SOURCE: NCHS National Vital Statistics System, Mortality files linked with death certificate literal text, 2017.

overdose deaths involving fentanyl were above 9.0 per 100,000 in Regions 1–5 (east of the Mississippi River) and below 6.0 per 100,000 in Regions 6–10 (west of the Mississippi River). A similar regional pattern was seen for cocaine, with rates above 5.0 per 100,000 in Regions 1–5 and below 3.0 per 100,000 in Regions 6–10. Age-adjusted rates for drug overdose deaths involving heroin were above 7.5 per 100,000 in Regions 1–3 and 5. For drug overdose deaths involving methamphetamine, age-adjusted rates were above 4.0 per 100,000 in Regions 8–10 (western United States).

These regional differences in the drugs most frequently involved in drug overdose deaths mirror findings from studies and data sources related to drug use. For example, a recent report identified higher rates of heroin-related overdose hospitalizations in the Northeast census region compared with other areas of the

country (16). The Northeast census region encompasses the same states as HHS regions 1 and 2 but also includes Pennsylvania. In this study, HHS Regions 1 and 2 were among the regions with the highest rates of drug overdose deaths involving heroin. The National Forensic Laboratory Information System (NFLIS), a program of the Drug Enforcement Administration, Diversion Control Division, systematically collects drug identification results from drug cases submitted to and analyzed by federal, state, and local forensic laboratories (17). The 2017 annual report from NFLIS includes national and regional estimates for the 25 most frequently identified drugs in seizure data. In 2017, the percentage of seizures testing positive for methamphetamine were higher in the West census region (46.2%) than in the Northeast census region (2.5%). The percentage of seizures testing positive for fentanyl and for cocaine in the Northeast

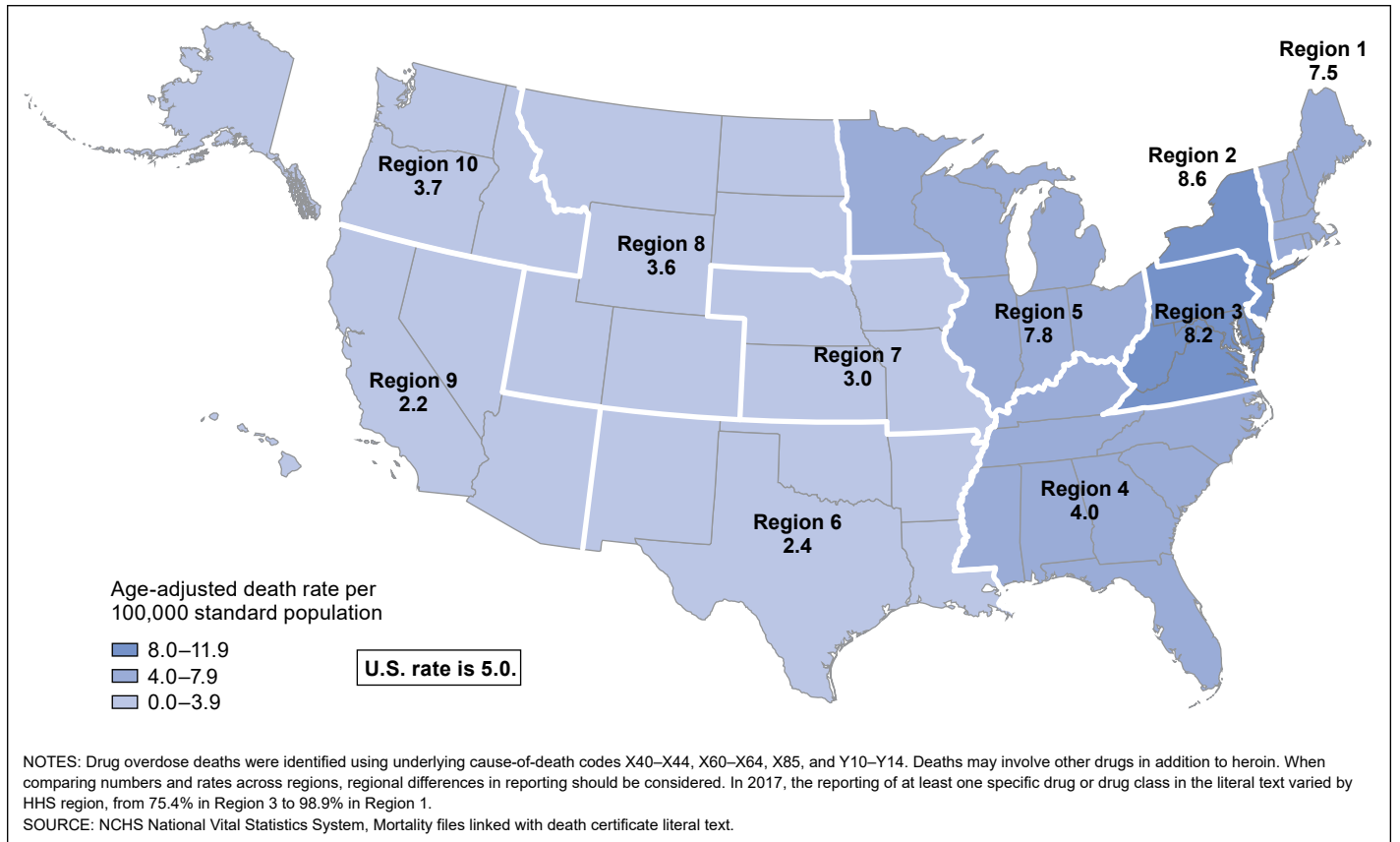


Figure 3. Age-adjusted rate of drug overdose deaths involving heroin, by region: 2017

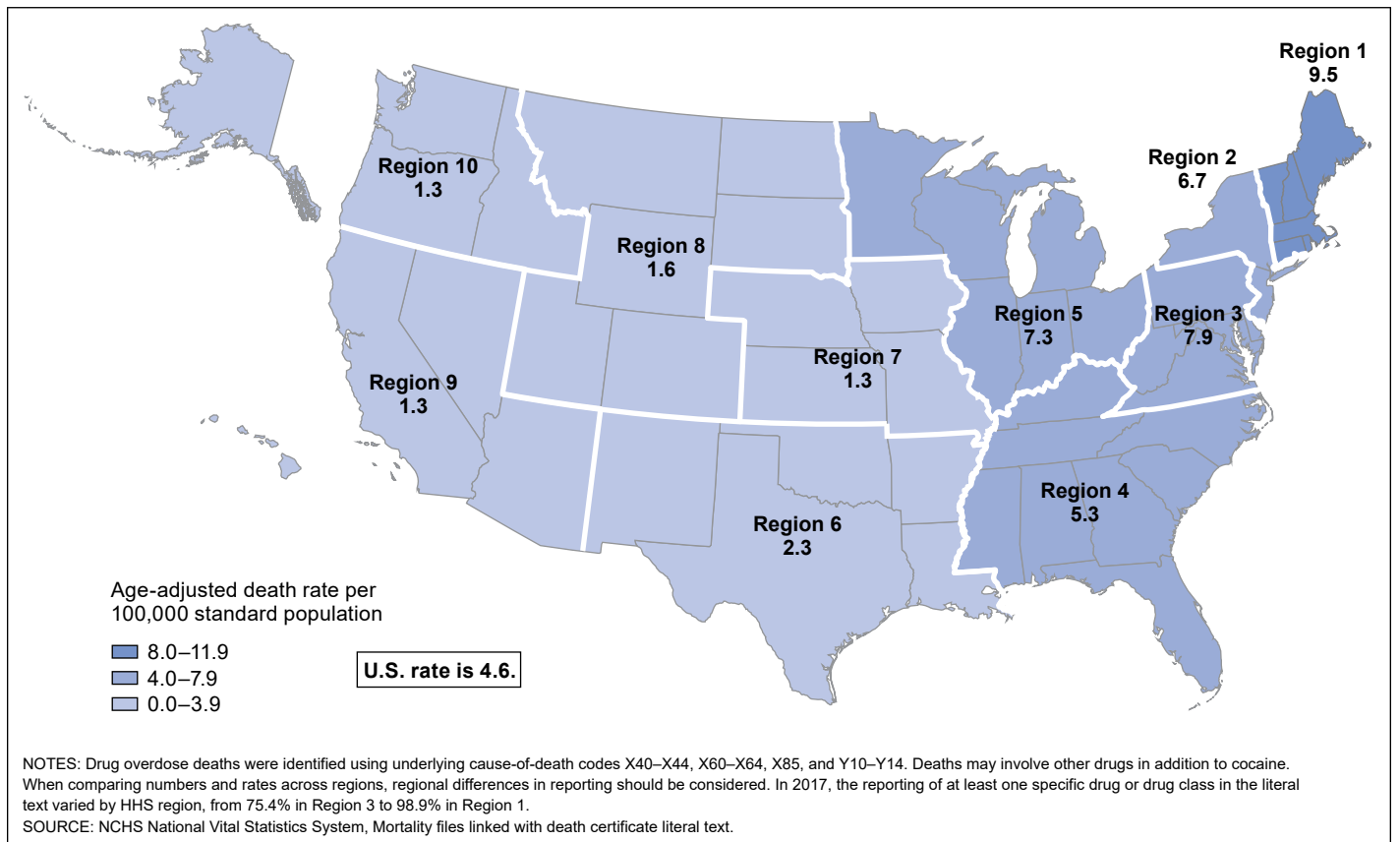


Figure 4. Age-adjusted rate of drug overdose deaths involving cocaine, by region: 2017

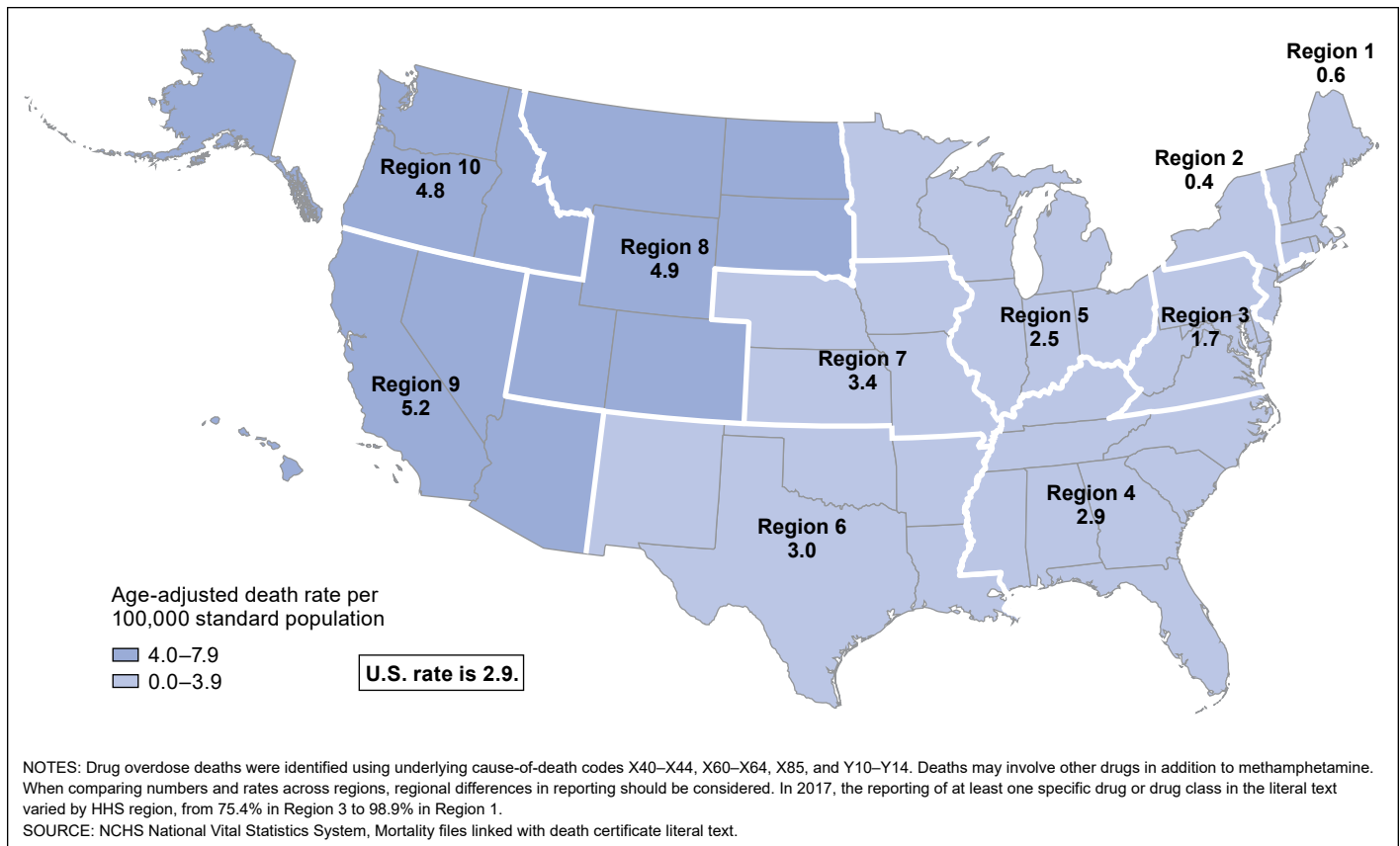


Figure 5. Age-adjusted rate of drug overdose deaths involving methamphetamine, by region: 2017

census region (8.9% and 20.7%, respectively) were higher than in the West census region (0.5% and 7.1%) (17). In this study, HHS Regions 8–10 (western United States) had higher rates of drug overdose deaths involving methamphetamine, and Regions 1–2 (northeastern United States) were among the regions with higher rates of drug overdose deaths involving fentanyl or cocaine.

Data considerations and study limitations

Methods based on literal text analysis are dependent on the quality and completeness of the information provided, which may vary from jurisdiction to jurisdiction due to differences in death investigation and reporting practices or other differences in the medicolegal death investigation systems across the United States (18–21). Regional differences in the quality and completeness of death investigation and reporting must be kept in mind when reviewing the findings. Issues that contribute to variation in literal text information on drug overdose deaths have been discussed in detail elsewhere (10,18,19). Briefly, these include several factors:

- *Variation in death investigation practice and reporting*—This includes whether toxicological laboratory testing is performed to determine the type(s) of drugs present. The substances tested for and the circumstances under which the tests are performed may vary by jurisdiction, decedent, and over time. Depending on such factors as office staffing and personnel, caseload, budget, and availability of specific

toxicology tests, routine toxicological analysis can range from no testing at all, to urine screening with no further confirmation, to complete quantification of all potential toxins involved (21).

- *Interpretation of toxicology results*—Interpretation of findings depends on which tests are ordered, the characteristics of the causative agent(s), the characteristics of the metabolites, and other evidence gathered during the investigation and physical examination of the body (22,23).
- *Attribution to a specific drug*—Some drugs have the same metabolites or are metabolites of other drugs, potentially resulting in misattribution of the specific class of drugs involved in the death (22,24).
- *Determination of which drugs to report on the death certificate*—Decision-making about which drugs to report on the death certificate can vary by medical certifier. Some medical certifiers focus on a single lethal drug rather than listing multiple drugs involved in the death, while others may list multiple drugs because they believe the drugs to be of equal lethality or that the interaction of all drugs mentioned is important. Some certifiers may not want to impose an order when listing the drugs that were present. Others have noted that space limitations in the software programs they use to complete electronic death registration limit their ability to include all drugs that contributed to the death (25).

These and other factors may contribute to the variation in the completeness and accuracy of the information on the death certificate about the specific drugs involved in the death.

The methods used in this study are dependent on the information provided in the literal text on the death certificate. Nationally, in 2017, at least one specific drug or drug class was reported on the death certificate for 87.6% of drug overdose deaths. Regionally, the percentage of drug overdose deaths with at least one specific drug or drug class reported in the death certificate literal text ranged from 75.4% of deaths in Region 3 to 98.9% of deaths in Region 1. To address the variation in reporting by region, an adjustment analysis was conducted that estimated drug-specific overdose mortality rates assuming 1) consistent reporting across regions and 2) the same regional distribution of deaths by specific drug for deaths that identified one or more specific drugs as for deaths that did not identify a specific drug (Technical Notes). Although the range of values observed using the adjusted rates differed from those using the unadjusted rates, the overall regional patterns remained the same. Nevertheless, the variation in the specificity of drug reporting by region must be considered when reviewing the results.

Finally, previous reports have shown that drug overdose deaths frequently involve multiple drugs (10,11). For deaths in which multiple drugs are involved, the contribution of each drug to the death cannot be determined from the literal text analysis. This limitation in identifying the specific contribution of any given drug to the death should also be considered.

Conclusion

Information from the literal text on death certificates can be used to identify regional differences in the drugs most frequently involved in drug overdose deaths. In this study using data from 2017, distinct patterns emerged with higher rates of drug overdose deaths involving fentanyl, involving cocaine, and involving heroin in the eastern areas of the United States, and higher rates of drug overdose deaths involving methamphetamine in the West. Understanding these regional differences in the drugs most frequently involved in drug overdose deaths may help inform prevention and policy efforts.

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Detailed Table

Age-adjusted rates per 100,000 for drug overdose deaths involving selected opioids and stimulants: United States and by U.S. Department of Health and Human Services region, 2017 12

Table. Age-adjusted rates per 100,000 for drug overdose deaths involving selected opioids and stimulants: United States and by U.S. Department of Health and Human Services region, 2017

Location	Referent drug group			
	Fentanyl	Heroin	Cocaine	Methamphetamine
United States	8.7	5.0	4.6	2.9
Region 1	22.5	7.5	9.5	0.6
Region 2	12.4	8.6	6.7	0.4
Region 3	17.5	8.2	7.9	1.7
Region 4	9.1	4.0	5.3	2.9
Region 5	14.7	7.8	7.3	2.5
Region 6	1.5	2.4	2.3	3.0
Region 7	5.5	3.0	1.3	3.4
Region 8	1.6	3.6	1.6	4.9
Region 9	1.5	2.2	1.3	5.2
Region 10	1.7	3.7	1.3	4.8

NOTES: Drug overdose deaths were identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Deaths may involve other drugs in addition to the referent drug. Deaths involving more than one drug (e.g., a death involving both heroin and cocaine) are counted in both totals. Caution should be used when comparing rates across regions. In 2017, the reporting of at least one specific drug or drug class in the literal text varied from 76.8% in Region 3 to 99.2% in Region 1.

SOURCE: NCHS, National Vital Statistics System, Mortality files linked with death certificate literal text.

Technical Notes

Assessment of regional differences in drug-specific rates using an adjustment factor to account for differences in reporting

The multiple cause-of-death codes T36–T50.8 from the *International Classification of Diseases, 10th Revision*, provide information on the types of drugs or drug classes involved in the death. The percentage of deaths with an underlying cause of X40–X44, X60–X64, X85, and Y10–Y14 that also have any multiple-cause code of T36–T50.8 indicates the specificity used in reporting drugs or drug classes in drug overdose deaths. In 2017, 87.6% of drug overdose deaths in the United States had a multiple cause-of-death code of T36–T50.8. The reporting of at least one specific drug or drug class among drug overdose deaths varied by U.S. Department of Health and Human Services (HHS) region (Region 1, 98.9%; Region 2, 90.5%; Region 3, 75.4%; Region 4, 88.0%; Region 5, 91.8%; Region 6, 82.9%; Region 7, 88.1%; Region 8, 89.2%; Region 9, 88.3%; and Region 10, 93.3%).

The differences in reporting of specific drugs or drug classes by HHS region could potentially influence the number and rates of drug overdose deaths for specific drugs (Table B, Figures 2–5). To account for variation in regional reporting, an adjustment analysis was conducted. In this analysis, an adjustment factor was applied to the age-adjusted mortality rate for drug overdose deaths involving the top 10 drugs in each HHS region. The adjustment factor was determined based on two assumptions: 1) the percentage of deaths with one or more drugs or drug classes specified in each HHS region is the same as the percentage in Region 1 (98.9%), the region with the highest drug-specific reporting, and 2) the regional distribution of deaths by specific drug was the same for deaths that did not identify a specific drug as for deaths that identified one or more specific drugs. The adjustment factor was used to estimate what the drug-specific death rates would have been if the percentage of deaths with one or more specific drugs or drug classes had been uniform among all HHS regions at the level of the region with the most complete reporting.

The adjustment factor for each region was calculated by dividing 98.9 (the drug specificity reporting percentage in Region 1) by the drug specificity reporting percentage in each of the remaining regions. For example, the drug specificity reporting percentage in Region 4 is 88.0%. The adjustment factor for Region 4 is 98.9 divided by 88.0, which equals 1.12. To calculate the adjusted rates for Region 4, the unadjusted rate for each specific referent drug group in the region was multiplied by 1.12.

Although methamphetamine did not appear among the top 10 drugs in Regions 1 and 2, the adjustment analysis was also conducted for drug overdose deaths involving methamphetamine in these regions, so that the rates for Regions 1 and 2 could be included in Figure 5.

The following Table shows the age-adjusted mortality rates for the drugs most frequently involved in drug overdose deaths for each HHS region before and after adjusting for regional variation in reporting. Based on the adjusted rates, the range of

rates reported in the Results were slightly modified, although the overall regional patterns remained the same:

- The adjusted rates of drug overdose deaths involving fentanyl were greater than 10.0 per 100,000 in Regions 1–5, ranging from 10.23 in Region 4 to 22.92 in Region 3. The rates in Regions 6–10 ranged from 1.65 in Region 9 to 6.21 in Region 7.
- The adjusted rates of drug overdose deaths involving cocaine were greater than 5.0 per 100,000 in Regions 1–5, ranging from 5.92 in Region 4 to 10.34 in Region 3. Rates in Regions 6–10 ranged from 1.36 in Region 10 to 2.78 in Region 6.
- The adjusted rates of drug overdose deaths involving heroin were above 7.0 per 100,000 in Regions 1–3 and 5 and below 5.0 per 100,000 in all other regions.
- The age-adjusted rates for drug overdose deaths involving methamphetamine were below 2.0 per 100,000 in Regions 1 and 2, between 2.0 and 4.0 in Regions 3–7, and above 5.0 in Regions 8–10.

Table. Rates of drug overdose deaths involving specific drugs, adjusted for regional differences in specificity of drug reporting, by U.S. Department of Health and Human Services region: United States, 2017

Region 1 ¹ —CT, ME, MA, NH, RI, and VT			Region 2 ¹ —NJ, NY, and NYC		
Drug specificity = 98.9%, adjustment factor = 1.00			Drug specificity = 90.5%, adjustment factor = 1.09		
Referent drug group	Unadjusted rate	Adjusted rate	Referent drug group	Unadjusted rate	Adjusted rate
Fentanyl	22.47	22.47	Fentanyl	12.38	13.53
Cocaine	9.47	9.47	Heroin	8.64	9.44
Heroin	7.54	7.54	Cocaine	6.71	7.34
Oxycodone	2.36	2.36	Alprazolam	2.80	3.06
Alprazolam	2.49	2.49	Oxycodone	1.99	2.18
Clonazepam	1.94	1.94	Morphine	1.28	1.40
Methadone	1.91	1.91	Methadone	1.22	1.34
Diphenhydramine	1.22	1.22	Clonazepam	0.95	1.04
Buprenorphine	1.12	1.12	Diphenhydramine	0.77	0.84
Diazepam	1.02	1.02	Diazepam	0.74	0.81
Methamphetamine	0.57	0.57	Methamphetamine	0.42	0.46
Region 3 ¹ —DE, DC, MD, PA, VA, and WV			Region 4 ¹ —AL, FL, GA, KY, MS, NC, SC, and TN		
Drug specificity = 75.4%, adjustment factor = 1.31			Drug specificity = 88.0%, adjustment factor = 1.12		
Referent drug group	Unadjusted rate	Adjusted rate	Referent drug group	Unadjusted rate	Adjusted rate
Fentanyl	17.47	22.92	Fentanyl	9.10	10.23
Heroin	8.24	10.81	Cocaine	5.27	5.92
Cocaine	7.88	10.34	Heroin	4.04	4.54
Morphine	2.67	3.51	Alprazolam	3.14	3.53
Oxycodone	2.32	3.05	Methamphetamine	2.87	3.23
Alprazolam	2.12	2.78	Oxycodone	2.49	2.80
Methamphetamine	1.67	2.19	Morphine	2.00	2.25
Methadone	1.52	1.99	Hydrocodone	1.12	1.26
Diazepam	0.75	0.99	Gabapentin	1.15	1.29
Hydrocodone	0.72	0.95	Methadone	0.89	1.00
Region 5 ¹ —IL, IN, MI, MN, OH, and WI			Region 6 ¹ —AR, LA, NM, OK, and TX		
Drug specificity = 91.8%, adjustment factor = 1.08			Drug specificity = 82.9%, adjustment factor = 1.19		
Referent drug group	Unadjusted rate	Adjusted rate	Referent drug group	Unadjusted rate	Adjusted rate
Fentanyl	14.65	15.78	Methamphetamine	3.04	3.63
Heroin	7.82	8.43	Cocaine	2.33	2.78
Cocaine	7.25	7.81	Heroin	2.41	2.88
Alprazolam	2.47	2.67	Alprazolam	1.55	1.84
Methamphetamine	2.51	2.70	Fentanyl	1.48	1.76
Morphine	1.75	1.88	Hydrocodone	1.10	1.32
Oxycodone	1.64	1.77	Oxycodone	1.10	1.32
Hydrocodone	1.36	1.46	Morphine	0.70	0.83
Methadone	1.12	1.21	Diphenhydramine	0.62	0.74
Diphenhydramine	0.88	0.95	Methadone	0.56	0.67
Region 7 ¹ —IA, KS, MO, and NE			Region 8 ¹ —CO, MT, ND, SD, UT, and WY		
Drug specificity = 88.1%, adjustment factor = 1.12			Drug specificity = 89.2%, adjustment factor = 1.11		
Referent drug group	Unadjusted rate	Adjusted rate	Referent drug group	Unadjusted rate	Adjusted rate
Fentanyl	5.53	6.21	Methamphetamine	4.85	5.38
Methamphetamine	3.41	3.83	Heroin	3.57	3.96
Heroin	3.02	3.39	Oxycodone	2.72	3.02
Oxycodone	1.46	1.64	Morphine	1.67	1.85
Cocaine	1.30	1.46	Cocaine	1.59	1.76
Alprazolam	1.05	1.17	Fentanyl	1.60	1.78
Morphine	0.83	0.94	Alprazolam	1.38	1.54
Hydrocodone	0.70	0.79	Diphenhydramine	1.07	1.18
Diphenhydramine	0.62	0.70	Methadone	0.98	1.08
Methadone	0.56	0.63	Hydrocodone	0.94	1.05

See footnotes at end of table.

Table. Rates of drug overdose deaths involving specific drugs, adjusted for regional differences in specificity of drug reporting, by U.S. Department of Health and Human Services region: United States, 2017—Con.

Region 9 ¹ —AZ, CA, HI, and NV			Region 10 ¹ —AK, ID, OR, and WA		
Drug specificity = 88.3%, adjustment factor = 1.12			Drug specificity = 93.3%, adjustment factor = 1.06		
Referent drug group	Unadjusted rate	Adjusted rate	Referent drug group	Unadjusted rate	Adjusted rate
Methamphetamine	5.16	5.78	Methamphetamine	4.83	5.13
Heroin	2.25	2.52	Heroin	3.70	3.92
Fentanyl	1.47	1.65	Fentanyl	1.69	1.79
Cocaine	1.26	1.41	Oxycodone	1.51	1.60
Oxycodone	1.24	1.39	Methadone	1.24	1.31
Morphine	1.06	1.18	Cocaine	1.28	1.36
Alprazolam	1.03	1.15	Morphine	1.11	1.18
Methadone	0.72	0.81	Alprazolam	0.95	1.01
Hydrocodone	0.72	0.80	Hydrocodone	0.80	0.85
Diphenhydramine	0.48	0.54	Diphenhydramine	0.75	0.79

¹U.S. Department of Health and Human Services (HHS) regions: Region 1 (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont), Region 2 (New Jersey, New York, and New York City), Region 3 (Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, and West Virginia), Region 4 (Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, and Tennessee), Region 5 (Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin), Region 6 (Arkansas, Louisiana, New Mexico, Oklahoma, and Texas), Region 7 (Iowa, Kansas, Missouri, and Nebraska), Region 8 (Colorado, Montana, North Dakota, South Dakota, Utah, and Wyoming), Region 9 (Arizona, California, Hawaii, and Nevada), and Region 10 (Alaska, Idaho, Oregon, and Washington).

NOTES: Drug specificity is calculated by determining the percentage of drug overdose deaths (i.e., deaths with an underlying cause-of-death of X40–X44, X60–X64, X85, or Y10–Y14) that have a multiple cause-of-death of T36–T50.8. The adjustment factor was calculated by dividing the drug specificity in Region 1, the region with the highest drug specificity (i.e., 98.9%), by the drug specificity for the region being examined. For example, for Region 3, the adjustment factor of 1.31 was calculated by dividing 98.9 by 75.4, the drug specificity in Region 3.

SOURCE: NCHS, National Vital Statistics System, Mortality files linked with death certificate literal text.

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