

## International Overdose Awareness Day — August 31, 2016

August 31 is International Overdose Awareness Day, a global event that aims to raise awareness that overdose death is preventable. Goals include providing awareness regarding the risk for overdose, providing information on community services, and preventing and reducing drug-related harm by supporting evidence-based policy and practice (<http://www.overdoseday.com>).

In 2015, the Drug Enforcement Administration and CDC released alerts identifying illicitly manufactured fentanyl as a threat to public health and safety (1,2). Although fentanyl is available as a prescription medication for treating severe pain, including cancer-related pain, the current epidemic of synthetic opioid-involved overdose deaths largely involves illicitly manufactured fentanyl that is mixed with or sold as heroin (1,3).

In contrast to the 2005–2007 fentanyl overdose outbreak, when deaths were confined to several states, the current epidemic is unprecedented in scope and, as described in a report in this issue of *MMWR*, multiple states in several regions of the United States are reporting substantial increases in fatal synthetic opioid-involved overdoses, primarily driven by fentanyl-involved overdose deaths. Further information and data about fentanyl from CDC are available at <http://www.cdc.gov/drugoverdose/opioids/fentanyl.html>.

### References

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2. CDC. CDC Health Advisory: increases in fentanyl drug confiscations and fentanyl-related overdose fatalities. Atlanta, GA: US Department of Health and Human Services, CDC; 2015. <http://emergency.cdc.gov/han/han00384.asp>
3. Drug Enforcement Administration. National heroin threat assessment summary—updated. DEA intelligence report. Washington, DC: US Department of Justice, Drug Enforcement Administration; 2016. [https://www.dea.gov/divisions/hq/2016/hq062716\\_attach.pdf](https://www.dea.gov/divisions/hq/2016/hq062716_attach.pdf)

## Fentanyl Law Enforcement Submissions and Increases in Synthetic Opioid-Involved Overdose Deaths — 27 States, 2013–2014

R. Matthew Gladden, PhD<sup>1</sup>; Pedro Martinez, MPH<sup>1</sup>; Puja Seth, PhD<sup>1</sup>

In March and October 2015, the Drug Enforcement Administration (DEA) and CDC, respectively, issued nationwide alerts identifying illicitly manufactured fentanyl (IMF) as a threat to public health and safety (1,2). IMF is unlawfully produced fentanyl, obtained through

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illicit drug markets, includes fentanyl analogs, and is commonly mixed with or sold as heroin (1,3,4). Starting in 2013, the production and distribution of IMF increased to unprecedented levels, fueled by increases in the global supply, processing, and distribution of fentanyl and fentanyl-precursor chemicals by criminal organizations (3). Fentanyl is a synthetic opioid 50–100 times more potent than morphine (2).<sup>\*</sup> Multiple states have reported increases in fentanyl-involved overdose (poisoning) deaths (fentanyl deaths) (2). This report examined the number of drug products obtained by law enforcement that tested positive for fentanyl (fentanyl submissions) and synthetic opioid-involved deaths other than methadone (synthetic opioid deaths), which include fentanyl deaths and deaths involving other synthetic opioids (e.g., tramadol). Fentanyl deaths are not reported separately in national data. Analyses also were conducted on data from 27 states<sup>†</sup> with consistent death certificate reporting of the drugs involved in overdoses. Nationally, the number of fentanyl submissions and synthetic opioid deaths increased by

426% and 79%, respectively, during 2013–2014; among the 27 analyzed states, fentanyl submission increases were strongly correlated with increases in synthetic opioid deaths. Changes in fentanyl submissions and synthetic opioid deaths were not correlated with changes in fentanyl prescribing rates, and increases in fentanyl submissions and synthetic opioid deaths were primarily concentrated in eight states (high-burden states). Reports from six of the eight high-burden states indicated that fentanyl-involved overdose deaths were primarily driving increases in synthetic opioid deaths. Increases in synthetic opioid deaths among high-burden states disproportionately involved persons aged 15–44 years and males, a pattern consistent with previously documented IMF-involved deaths (5). These findings, combined with the approximate doubling in fentanyl submissions during 2014–2015 (from 5,343 to 13,882) (6), underscore the urgent need for a collaborative public health and law enforcement response.

Data were analyzed from four sources: 1) fentanyl submission data from the DEA National Forensic Laboratory Information System (NFLIS), which systematically collects drug identification results from drug cases submitted for analysis to forensic laboratories<sup>§</sup>; 2) synthetic opioid deaths, calculated using the National Vital Statistics System multiple cause-of-death mortality files<sup>¶</sup>;

<sup>\*</sup>Additional information on approved fentanyl products and their indications is available at <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.SearchAction&SearchTerm=fentanyl&SearchType=BasicSearch>.

<sup>†</sup>Arkansas, California, Colorado, Connecticut, Florida, Illinois, Iowa, Kentucky, Massachusetts, Maine, Maryland, Minnesota, Missouri, Nevada, New Hampshire, New York, North Carolina, Ohio, Oklahoma, Oregon, Tennessee, Texas, Utah, Virginia, Washington, West Virginia, and Wisconsin.

<sup>§</sup>Data were extracted July 1, 2016; additional information on NFLIS is available at <http://www.deadiversion.usdoj.gov/nflis/>.

<sup>¶</sup>[http://www.cdc.gov/nchs/nvss/mortality\\_public\\_use\\_data.htm](http://www.cdc.gov/nchs/nvss/mortality_public_use_data.htm).

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3) national and state fentanyl prescription data that are estimated from IMS Health's National Prescription Audit collecting 87% of retail prescriptions in the United States\*\*; and 4) medical examiner/coroner reports or death certificate data from states with a high burden of synthetic opioid deaths (i.e., a 1-year increase in synthetic opioid deaths exceeding two per 100,000 residents, or a 1-year increase of  $\geq 100$  synthetic opioid deaths during 2013–2014). Synthetic opioid deaths were identified using the following *International Classification of Diseases, 10th Revision* codes: 1) an underlying cause-of-death code of X40–44 (unintentional), X60–64 (suicide), X85 (homicide), or Y10–Y14 (undetermined intent) and 2) a multiple cause-of-death code of T40.4. In 2014, any information on the specific drug or drugs involved in a drug overdose were reported for approximately 80% of drug overdose deaths; this proportion varied over time and by state (7). State analyses were limited to 27 states meeting the following criteria: 1)  $>70\%$  of drug overdose deaths reported at least one specific drug in 2013 and 2014; 2) the change in the percentage of overdose deaths reporting at least one specific drug from 2013 to 2014 was  $<10\%$ <sup>††</sup>; 3)  $\geq 20$  synthetic opioid deaths occurred during 2013 and 2014; and 4) fentanyl submissions were reported in 2013 and 2014.<sup>§§</sup> These 27 states accounted for 75% of synthetic opioid deaths in the United States in 2014. Analyses compared changes in the crude rate of fentanyl submissions, fentanyl prescriptions, and synthetic opioid deaths during 2013–2014 using Pearson correlations. States were classified as high-burden if they experienced a 1-year increase in synthetic opioid deaths exceeding two per 100,000 residents or a 1-year increase of  $\geq 100$  synthetic opioid deaths during 2013–2014. Additional evidence from published state medical examiner/coroner or death certificate reports was reviewed to understand whether increases in synthetic opioid deaths were being primarily driven by fentanyl deaths and not by other synthetic opioids. Demographic characteristics of synthetic opioid deaths for high-burden and low-burden states were described.

During 2013–2014, fentanyl submissions in the United States increased by 426%, from 1,015 in 2013 to 5,343 in 2014, and synthetic opioid deaths increased by 79%, from 3,105 in 2013

to 5,544 in 2014.<sup>¶¶</sup> In contrast, fentanyl prescription rates remained relatively stable (Figure 1). Although changes in fentanyl submissions and synthetic opioid death rates from 2013–2014 among the 27 states were highly correlated ( $r = 0.95$ ) (Figure 2), changes in state-level synthetic opioid deaths were not correlated with changes in fentanyl prescribing (data not shown). During 2013–2014, the synthetic opioid crude death rate in the eight high-burden states increased 174%, from 1.3 to 3.6 per 100,000, and the fentanyl submissions rate increased by 1,000% from 0.5 to 5.5 per 100,000 (Table). Six of the eight high-burden states reported increases in synthetic opioid death rates exceeding 2.0 per 100,000 population, and seven states reported increases in deaths of  $\geq 100$ .<sup>\*\*\*</sup> The eight high-burden states were located in the Northeast (Massachusetts, Maine, and New Hampshire), Midwest (Ohio), and South (Florida, Kentucky, Maryland, and North Carolina). Six of the eight states published data on fentanyl deaths from 2013 and 2014.<sup>†††</sup> Combining results across the state reports, total fentanyl deaths during 2013–2014 increased by 1,008, from 392 (2013) to 1,400 (2014), and the increase in total fentanyl deaths was of nearly the same magnitude as the increase in 966 synthetic opioid deaths in these states (589 [2013], 1,555 [2014]). This finding indicates that increases in fentanyl deaths were driving the increases in synthetic opioid deaths in these six states. Among high-burden states, all demographic groups experienced substantial increases in synthetic opioid death rates. Increases of  $>200\%$  occurred among males (227%); persons aged 15–24 years (347%), 25–34 years

<sup>¶¶</sup> Reported drug submissions to NFLIS decreased from 1.54 million in 2013 to 1.51 million in 2014 suggesting that the increase in fentanyl submissions was not driven by general increases in drug submissions to NFLIS. <https://www.nflis.deadiversion.usdoj.gov/DesktopModules/ReportDownloads/Reports/NFLIS2014AR.pdf>.

<sup>\*\*\*</sup> Six states reported increases of more than two synthetic opioid deaths per 100,000 residents (Kentucky [2.4], Maine [3.0], Maryland [2.2], Massachusetts [5.2], New Hampshire [9.1], and Ohio [3.7]), and seven of the eight states reported increases of  $\geq 100$  in synthetic opioid deaths (Florida [143], Kentucky [103], Maryland [137], Massachusetts [355], New Hampshire [121], North Carolina [100], and Ohio [423]).

<sup>†††</sup> The following reports are from seven of the eight high-burden states: 1) *Florida*: <http://www.fdle.state.fl.us/cms/MEC/Publications-and-Forms/Documents/Drugs-in-Deceased-Persons/2014-Annual-Drug-Report-FINAL.aspx>; 2) *Maine*: <http://pub.lucidpress.com/NDEWSFentanyl/>; 3) *Maryland*: [http://bha.dhmh.maryland.gov/OVERDOSE\\_PREVENTION/Documents/2015.05.19%20-%20Annual%20OD%20Report%202014\\_merged%20file%20final.pdf](http://bha.dhmh.maryland.gov/OVERDOSE_PREVENTION/Documents/2015.05.19%20-%20Annual%20OD%20Report%202014_merged%20file%20final.pdf); 4) *Massachusetts*: <http://www.mass.gov/eohhs/docs/dph/quality/drugcontrol/county-level-pmp/data-brief-overdose-deaths-may-2016.pdf>; 5) *New Hampshire*: <http://nhpr.org/post/nh-medical-examiner-least-10-drug-overdoses-2016-86-cases-pending>, [http://mediad.publicbroadcasting.net/p/nhpr/files/201604/drug\\_data\\_update\\_from\\_nh\\_medical\\_examiner\\_s\\_office\\_4-14-16\\_3\\_.pdf](http://mediad.publicbroadcasting.net/p/nhpr/files/201604/drug_data_update_from_nh_medical_examiner_s_office_4-14-16_3_.pdf); 6) *Ohio*: <http://www.medscape.com/viewarticle/851502>; and 7) *Kentucky*: <http://www.mc.uky.edu/kiprc/programs/kdopp/reports/2015-drug-overdose-deaths.pdf>. Other jurisdictions also reporting sharp increases in fentanyl deaths include 1) *Pennsylvania*: [https://www.dea.gov/divisions/phi/2015/phi111715\\_attach.pdf](https://www.dea.gov/divisions/phi/2015/phi111715_attach.pdf); [https://www.dea.gov/divisions/phi/2016/phi071216\\_attach.pdf](https://www.dea.gov/divisions/phi/2016/phi071216_attach.pdf); 2) *New York City*: <https://a816-health30ssl.nyc.gov/sites/nychan/Lists/AlertUpdateAdvisoryDocuments/Fentanyl-HAN-advisory.pdf>; and 3) *Rhode Island*: <http://www.slideshare.net/OPUNITE/rx16-federal-tues2001gladden2halpin3green>.

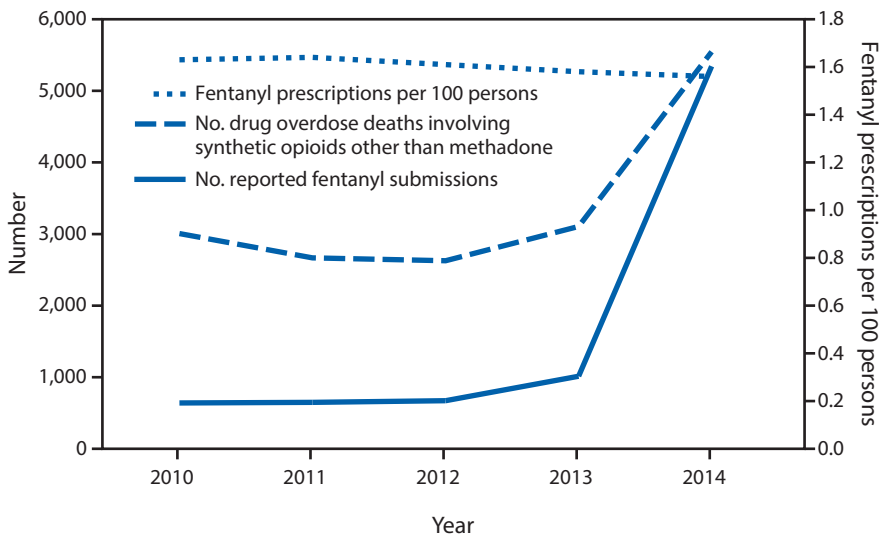
<sup>\*\*</sup> IMS Health's National Prescription Audit is a trademarked product. [http://www.imshealth.com/files/web/IMSH%20Institute/NPA\\_Data\\_Brief-.pdf](http://www.imshealth.com/files/web/IMSH%20Institute/NPA_Data_Brief-.pdf).

<sup>††</sup> The analysis excluded states whose reporting of any specific drug or drugs involved in an overdose changed by  $>10\%$  from 2013 to 2014. These states were excluded because drug specific overdose numbers and rates, including the number and rate synthetic opioid-involved overdose deaths, were expected to change substantially from 2013 to 2014 because of changes in reporting.

<sup>§§</sup> 38 states reported specific drugs on  $\geq 70\%$  of drug overdoses in 2013 and 2014, but only 36 of these states experienced changes in drug reporting of  $<10$  percentage points from 2013 to 2014. Among these 36 states, only 30 reported  $\geq 20$  synthetic opioid-involved overdose deaths in 2013 and 2014, and 27 of these 30 states had fentanyl submissions in both 2013 and 2014.



**FIGURE 1. Trends in number of drug overdose deaths involving synthetic opioids other than methadone,\* number of reported fentanyl submissions,<sup>†</sup> and rate of fentanyl prescriptions<sup>§</sup> — United States, 2010–2014**



\* Synthetic opioid-involved (other than methadone) overdose deaths are deaths with an *International Classification of Diseases, 10th Revision* underlying cause-of-death of X40–44 (unintentional), X60–64 (suicide), X85 (homicide), or Y10–Y14 (undetermined intent) and a multiple cause-of-death of T40.4 (poisoning by narcotics and psychodysleptics [hallucinogens]; other synthetic narcotics).

<sup>†</sup> Drug products obtained by law enforcement that tested positive for fentanyl are referred to as fentanyl submissions. Reports were supplied by the Drug Enforcement Administration's National Forensic Laboratory Information System and downloaded July 1, 2016.

<sup>§</sup> National estimates supplied by IMS National Prescription Audit and include short and long-acting fentanyl prescriptions.

(248%), and 35–44 (230%) years; Hispanics (290%), and persons living in large fringe metro areas (230%).<sup>§§§</sup> The highest rates of synthetic opioid deaths in 2014 were among males (5.1 per 100,000); non-Hispanics whites (4.6 per 100,000); and persons aged 25–34 years (8.3 per 100,000), 35–44 years (7.4 per 100,000), and 45–54 years (5.7 per 100,000) (Table).

### Discussion

In the 27 states meeting analysis criteria, synthetic opioid deaths sharply increased in the eight high-burden states, and complementary data suggest this increase can be attributed to fentanyl. Six of the eight high-burden states reported substantial increases in fentanyl deaths during 2013–2014, based on medical examiner/coroner data or literal text searches of death certificates. The high potency of fentanyl and the possibility of rapid death after fentanyl administration (8), coupled with the extremely sharp 1-year increase in fentanyl

deaths in high-burden states, highlights the need to understand the factors driving this increase.

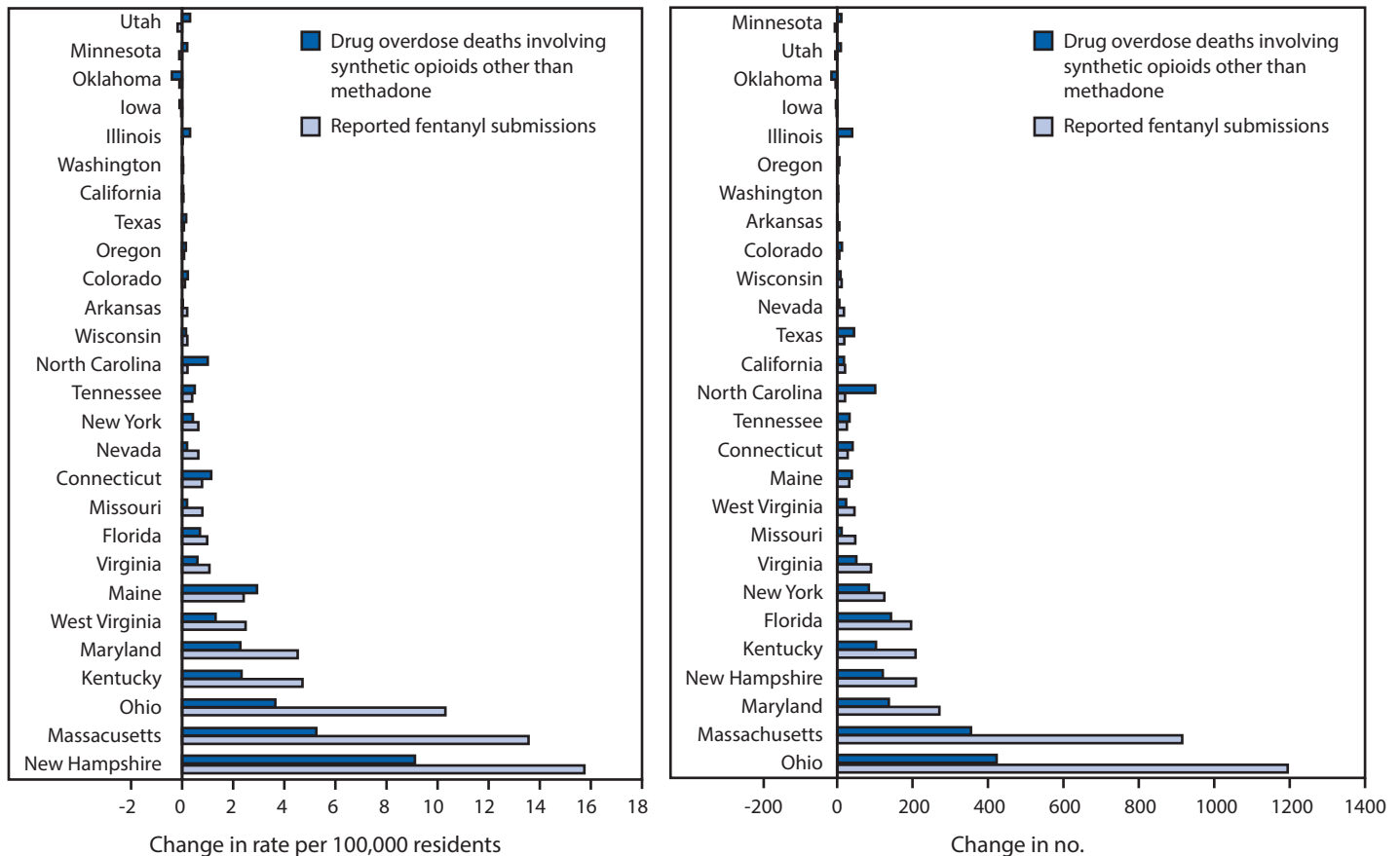
IMF production and distribution began increasing in 2013 and has grown to unprecedented levels in 2016 (3). For example, there were approximately eight times as many fentanyl submissions in 2015 as there were in 2006 during the last multistate outbreak involving IMF (3). DEA has not reported a sharp increase in pharmaceutical fentanyl being diverted from legitimate medical use to illegal uses (4). Given the strong correlation between increases in fentanyl submissions (primarily driven by IMF) (3,4) and increases in synthetic opioid deaths (primarily fentanyl deaths), and uncorrelated stable fentanyl prescription rates, it is hypothesized that IMF is driving the increases in fentanyl deaths. Findings from DEA (3,4), state, and CDC investigations (5) documenting the role of IMF in the observed increases in fentanyl deaths further support this hypothesis. The demographics of synthetic opioid deaths are rapidly changing and are consistent with the changes in demographics of persons using heroin, in particular, increasing use among non-Hispanic white men aged 25–44 years (9).

Historically, the heroin market in the United States has been divided along the Mississippi River, with Mexican black tar and brown powder heroin being sold in the west and white powder heroin being sold in the east. IMF is most commonly mixed with or sold as white powder heroin (4). The concentration of high-burden states east of the Mississippi River is consistent with reports of IMF distribution in white powder heroin markets (3,4).

An urgent, collaborative public health and law enforcement response is needed to address the increasing problem of IMF and fentanyl deaths. Recently released fentanyl submissions data indicate that 15 states experienced >100 fentanyl submissions in 2015. This is up from 11 states in 2014 (6). The national increase of 8,539 in fentanyl submissions from 2014 (5,343) to 2015 (13,882) (6) exceeded the increase of 4,328 from 2013 to 2014. This finding coupled with the strong correlation between fentanyl submissions and fentanyl-involved overdose deaths observed in Ohio and Florida (5) and supported by this report likely indicate the problem of IMF is rapidly expanding. Recent (2016) seizures of large numbers of counterfeit pills containing IMF indicate that states where persons commonly use diverted prescription pills, including opioid pain relievers, might begin to experience increases in fentanyl deaths (3) because many counterfeit pills are

<sup>§§§</sup> Large fringe metro counties are located in metropolitan statistical areas (MSAs) of ≥1 million population that did not qualify as large central metro counties. Large central metro counties are MSAs of ≥1 million population that 1) contain the entire population of largest principal city of the MSA, 2) have their entire population contained in the largest principal city of the MSA, or 3) contain at least 250,000 inhabitants of any principal city of the MSA.

**FIGURE 2. Change in the rate per 100,000 residents and number of overdose deaths involving synthetic opioids other than methadone\* and reported fentanyl submissions<sup>†</sup> — 27 states,<sup>§</sup> 2013–2014**



\* Synthetic opioid-involved (other than methadone) overdose deaths are deaths with an *International Classification of Diseases, 10th Revision* underlying cause-of-death of X40–44 (unintentional), X60–64 (suicide), X85 (homicide), or Y10–Y14 (undetermined intent) and a multiple cause-of-death of T40.4 (poisoning by narcotics and psychodysleptics [hallucinogens]: other synthetic narcotics).

<sup>†</sup> Drug products obtained by law enforcement that tested positive for fentanyl are referred to as fentanyl submissions. Reports were supplied by the Drug Enforcement Administration National Forensic Laboratory Information System and downloaded July 1, 2016.

<sup>§</sup> Change in rate of synthetic opioid-involved overdose deaths from 2013–2014 was significant for Connecticut, Florida, Kentucky, Maine, Maryland, Massachusetts, Ohio, New Hampshire, New York, North Carolina, Texas, and Virginia using gamma or z-tests.

deceptively sold as and hard to distinguish from diverted opioid pain relievers. Finally, the approximate tripling of heroin-involved overdose deaths since 2010 highlights the need for interventions targeting the illicit opioid market.<sup>¶¶</sup>

The findings in this report are subject to at least four limitations. First, national vital statistics data only report synthetic opioid deaths. A review of state-level reports in six of eight high-burden states indicated that the increase in fentanyl deaths was the primary factor driving increases in synthetic opioid deaths during 2013–2014. Because synthetic opioid deaths include deaths involving synthetic opioids besides fentanyl, the absolute number of synthetic opioid deaths occurring in a year such as 2014 should not be considered a proxy for the

number of fentanyl deaths in a year. Second, law enforcement drug submissions might vary over time and geographically because of differences or changes in law enforcement testing practices and drug enforcement activity, which might underestimate or overestimate the number of fentanyl submissions in certain states. Third, findings and implications are restricted to 27 states. Finally, testing for fentanyl deaths might vary across states because toxicologic testing protocols for drug overdoses vary across states and local jurisdictions.

The Secretary of Health and Human Services has launched an initiative to reduce opioid misuse, abuse, and overdose by expanding medication-assisted treatment, increasing the availability and use of naloxone, and promoting safer opioid prescribing (10). Efforts should focus on 1) improving timeliness

<sup>¶¶</sup> <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6450a3.htm>.

TABLE. Number and crude rates per 100,000 persons of synthetic opioid deaths (overdose deaths involving synthetic opioids other than methadone),\* by sex, age group,<sup>†</sup> race and Hispanic origin,<sup>§</sup> reported fentanyl submissions,<sup>¶</sup> and 2013 urbanization\*\* — eight high-burden states<sup>††</sup> and 19 low-burden states,<sup>§§</sup> 2013 and 2014

Decedent characteristic	High-burden states (n = 8)					Low-burden states (n = 19)				
	2013		2014		Percentage increase in rate, 2013–2014	2013		2014		Percentage increase in rate, 2013–2014
	No.	Rate	No.	Rate		No.	Rate	No.	Rate	
All	803	1.32	2,225	3.63	174 <sup>¶¶</sup>	1,559	0.94	1,948	1.16	24 <sup>¶¶</sup>
<b>Sex</b>										
Female	342	1.1	705	2.25	104 <sup>¶¶</sup>	741	0.88	828	0.97	11 <sup>¶¶</sup>
Male	461	1.56	1,520	5.09	227 <sup>¶¶</sup>	818	0.99	1,120	1.35	36 <sup>¶¶</sup>
<b>Age groups (yrs)</b>										
15–24	53	0.66	237	2.92	347 <sup>¶¶</sup>	137	0.59	153	0.65	12
25–34	185	2.38	656	8.28	248 <sup>¶¶</sup>	302	1.29	438	1.84	43 <sup>¶¶</sup>
35–44	170	2.23	560	7.36	230 <sup>¶¶</sup>	316	1.45	415	1.9	31 <sup>¶¶</sup>
45–54	242	2.8	494	5.75	106 <sup>¶¶</sup>	429	1.88	534	2.35	25 <sup>¶¶</sup>
55–64	131	1.66	229	2.85	71 <sup>¶¶</sup>	292	1.45	309	1.51	4
≥65	21	0.22	48	0.48	121 <sup>¶¶</sup>	80	0.36	84	0.4	11
<b>Race/Ethnicity</b>										
White, non-Hispanic	711	1.71	1,925	4.62	170 <sup>¶¶</sup>	1,338	1.35	1,653	1.67	23 <sup>¶¶</sup>
Black, non-Hispanic	61	0.65	172	1.79	178 <sup>¶¶</sup>	82	0.49	136	0.79	64 <sup>¶¶</sup>
Other, non-Hispanic	—***	—***	22	0.94	—***	33	0.25	42	0.31	22
Hispanic	23	0.31	93	1.23	290 <sup>¶¶</sup>	102	0.27	110	0.29	6
<b>2013 urbanization</b>										
Large central metro	156	1.08	429	2.95	171 <sup>¶¶</sup>	483	0.72	577	0.85	18 <sup>¶¶</sup>
Large fringe metro	246	1.3	822	4.31	230 <sup>¶¶</sup>	304	0.84	442	1.21	44 <sup>¶¶</sup>
Medium metro	202	1.32	567	3.67	178 <sup>¶¶</sup>	314	1.06	406	1.36	28 <sup>¶¶</sup>
Small metro	54	1.45	98	2.61	80 <sup>¶¶</sup>	133	1.03	201	1.54	50 <sup>¶¶</sup>
Micropolitan	87	1.61	214	3.95	146 <sup>¶¶</sup>	154	1.33	188	1.62	22
Noncore	58	1.93	95	3.17	64 <sup>¶¶</sup>	171	1.83	134	1.44	-21 <sup>¶¶</sup>
Reported fentanyl submissions	293	0.48	3,340	5.46	1,029 <sup>¶¶</sup>	417	0.25	855	0.51	103 <sup>¶¶</sup>

Source: CDC Wonder Multiple-Cause-of-Death Data at <http://wonder.cdc.gov/mcd.html>.

\* Synthetic opioid-involved (other than methadone) overdose deaths are deaths with an *International Classification of Diseases, 10th Revision* underlying cause-of-death of X40–44 (unintentional), X60–64 (suicide), X85 (homicide), or Y10–Y14 (undetermined intent) and a multiple cause-of-death of T40.4.

<sup>†</sup> Synthetic opioid-involved overdose deaths involving persons aged ≤14 years are not reported because cells have nine or fewer deaths. Also, a small number of synthetic opioid-involved overdose deaths do not report age of the decedent.

<sup>§</sup> Data for Hispanic origin should be interpreted with caution; studies comparing Hispanic origin on death certificates and on census surveys have indicated inconsistent reporting on Hispanic ethnicity. Numbers might not sum to the total because the ethnicity and race of some synthetic opioid-involved overdose deaths are not known.

<sup>¶</sup> Drug products obtained by law enforcement that tested positive for fentanyl are referred to as fentanyl submissions. Reports were supplied by the Drug Enforcement Administration's National Forensic Laboratory Information System and downloaded July 1, 2016.

\*\* Categories of 2013 NCHS Urban-Rural Classification Scheme for Counties ([http://www.cdc.gov/nchs/data/series/sr\\_02/sr02\\_166.pdf](http://www.cdc.gov/nchs/data/series/sr_02/sr02_166.pdf)): *Large central metro*: Counties in metropolitan statistical areas (MSAs) of ≥1 million population that 1) contain the entire population of largest principal city of the MSA, or 2) have their entire population contained in the largest principal city of the MSA, or 3) contain at least 250,000 inhabitants of any principal city of the MSA; *Large fringe metro*: Counties in MSAs of ≥1 million population that did not qualify as large central metro counties; *Medium metro*: Counties in MSAs of populations of 250,000–999,999; *Small metro*: Counties in MSAs of populations less than 250,000; *Micropolitan (nonmetropolitan counties)*: counties in micropolitan statistical areas; *Noncore (nonmetropolitan counties)*: nonmetropolitan counties that did not qualify as micropolitan.

<sup>††</sup> High-burden states (n = 8) include Florida, Kentucky, Maine, Maryland, Massachusetts, New Hampshire, North Carolina, and Ohio.

<sup>§§</sup> Low-burden states (n = 19) include Arkansas, California, Colorado, Connecticut, Illinois, Iowa, Minnesota, Missouri, Nevada, New York, Oklahoma, Oregon, Tennessee, Texas, Utah, Virginia, Washington, West Virginia, and Wisconsin.

<sup>¶¶</sup> Statistically significant at p<0.05 level. Gamma tests were used if cell count was less than 100 in 2013 or 2014, and z-tests were used if cell counts were ≥100 in both 2013 and 2014.

\*\*\* Cells with nine or fewer deaths are not reported and rates based on <20 deaths are not considered reliable and not reported. When rate for a year is suppressed, change in rate is also not reported.

## Summary

### What is already known about this topic?

In 2015, the Drug Enforcement Administration and CDC issued nationwide alerts identifying illicitly manufactured fentanyl (IMF) as a threat. Beginning in 2013, the distribution of IMF increased to unprecedented levels. Individual states have reported increases in fentanyl-involved overdose deaths (fentanyl deaths).

### What is added by this report?

During 2013–2014, the number of drug products obtained by law enforcement that tested positive for fentanyl (fentanyl submissions) increased by 426%, and synthetic opioid-involved overdose deaths (excluding methadone) increased by 79% in the United States. Changes in synthetic opioid-involved overdose deaths among 27 states were highly correlated with fentanyl submissions but not correlated with fentanyl prescribing. Eight high-burden states were identified, and complementary data indicate increases in these states are primarily attributable to fentanyl, supporting the argument that IMF is driving increases in fentanyl deaths.

### What are the implications for public health practice?

An urgent, collaborative public health and law enforcement response is needed, including 1) improving timeliness of opioid surveillance to facilitate faster identification and response to spikes in fentanyl overdoses; 2) expanding testing for fentanyl and fentanyl analogues in high-burden states; 3) expanding evidence-based harm reduction and naloxone access; 4) implementing programs that increase linkage and access to medication-assisted treatment; 5) increasing collaboration between public health and public safety; and 6) planning rapid response in high-burden states and states beginning to experience increases in fentanyl submissions or deaths.

of opioid surveillance to facilitate faster identification and response to spikes in fentanyl overdoses; 2) expanding testing for fentanyl and fentanyl analogs by physicians, treatment programs, and medical examiners/coroners in high-burden states; 3) expanding evidence-based harm reduction and expanding naloxone access, with a focus on persons using heroin; 4) implementing programs that increase linkage and access to medication-assisted treatment, with a focus on persons using heroin; 5) increasing collaboration between public health and public safety; and 6) planning rapid response in high-burden states and states beginning to experience increases in fentanyl submissions or deaths.

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Tamara Haegerich, PhD, Nina Shah, MS, Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, CDC.

<sup>1</sup>Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, CDC.

Corresponding author: R. Matthew Gladden, mgladden@cdc.gov, 770-488-4276.

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