



Community overdose surveillance: Comparing substances collected from the death scene investigation to toxicology results

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ABSTRACT

Background: Recent overdose trends are characterized by increased toxicological detection of stimulants with opioids, yet it is unclear whether these substances are mixed prior to consumption or purposefully used simultaneously.

Methods: Postmortem toxicology data were collected in Marion County, Indiana, from 45 fatal overdose cases involving heroin, fentanyl, methamphetamine, or cocaine. Substances found by death scene investigators at the scene of the fatal overdose (57 samples) were tested using high-pressure liquid chromatography mass-spectrometry (LC-MS) technology. We compared toxicology and LC-MS results to understand whether substances contributing to overdose were found in combination or separately at the scene of the overdose.

Results: Comparing toxicology reports with LC-MS results from substances found at the scene of overdose deaths involving opioids and stimulants reveal that deaths are largely the result of the co-use of opioids and stimulants, rather than use of stimulants combined with opioids.

Conclusions: Collecting and testing physical samples from fatal overdose scenes and comparing these to post-mortem toxicology results is a new way to examine polydrug use patterns. This community overdose surveillance method can be used to improve overdose prevention and response efforts.

1. Introduction

The overdose epidemic remains one of the most pressing public health issues in the United States. There has been a two-fold increase in overdose deaths since 2000 and more than a half million deaths in the past decade (Seth et al., 2018). While many of these deaths have been opioid-related, the specific type of opioid has varied through multiple waves with each resulting in exponential increases in mortality (Ciccarone, 2017; Jalal et al., 2018). This epidemic started with increased availability of prescription opioids, which gave rise to the first wave of overdose deaths in the 1990s (Cicero et al., 2014; Grau et al., 2007). As availability of prescription opioids decreased, there was a second wave of overdose resulted from people transitioning to illicit heroin (Cicero et al., 2014; Rudd et al., 2014; Strickler et al., 2019). Beginning in 2013, the third wave of the overdose epidemic started and was driven by illicitly manufactured fentanyl, a synthetic opioid 50–100 times more potent than morphine (Gladden, 2016; O'Donnell et al., 2017).

The number of overdose deaths involving fentanyl has more than doubled each year since 2012, and since 2017 there has been a sharp increase in overdose deaths associated with fentanyl and illicit stimulants, specifically cocaine and methamphetamines (O'Donnell, 2020). The Centers for Disease Control and Prevention (CDC) reports that the number of overdose deaths associated with cocaine in 2017 represent a two-fold increase since the peak in 2006, while deaths involving psychostimulants with abuse potential (drugs such as methamphetamine) have increased five-fold since 2010, sparking a fourth wave of the overdose epidemic with overdoses involving both opioids and stimulants (Hainer, 2019; Hedegaard et al., 2020).

While overdose associated with illicit stimulants are on the rise, there is no clarity on the role of opioids in these deaths (Jones et al., 2017, 2020; Kariisa, 2019; LaRue et al., 2019). Sources have reported that stimulants are being combined with fentanyl and that people who use illicit drugs are unaware of this adulteration (Amlani et al., 2015; Hayashi et al., 2018; Klar et al., 2016; McCrae et al., 2019; Nolan et al.,

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2019; Tomassoni et al., 2017; United States Drug Enforcement Administration, 2018). However, recent studies suggest that people are seeking both illicit stimulants and illicit opioids (heroin or fentanyl) to engage in “speedballing” or “goofballing,” in search of the unique effect (Al-Tayyib et al., 2017; Meier et al., 2020; Peiper et al., 2019; Rouhani et al., 2019). Addressing this question can help shape overdose prevention and response efforts.

Local jurisdictions have employed tactics to surveil community-level overdose and drug supply trends, allowing for better prevention and response efforts. At an individual level, urine drug screens have often been used to determine the specific type of drug involved in an overdose event (Korneeva et al., 2018; Liu et al., 2018). However, this strategy is only employed with persons who did not overdose or who survived a drug overdose. The National Vital Statistics System has been utilized to track the increased presence of opioids and stimulants in combination in fatal overdoses by geographical location (Hoots et al., 2020; Jones et al., 2017, 2018; Kariisa, 2019); yet the use of death certificates to determine drug-related fatal overdose trends presents the challenge of incomplete information as research has documented undercounting of opioid-involved overdose fatalities on local death certificates (Gupta et al., 2020; Lowder et al., 2018; Ruhm, 2018); indeed, it is important that death certificates be linked to toxicology results to obtain accurate data (Hannah et al., 2017). Combining a variety of surveillance data sources, CDC has linked administrative datasets from participating states to create the State Unintentional Drug Overdose Reporting System (SUDORS). This system utilizes local and national information on opioid overdose deaths, such as information from death scene investigations, toxicology reports, and risk factors associated with fatal overdose events to provide timely updates to local stakeholders (Centers for Disease Control and Prevention, 2019). However, these surveillance methods rely on post-mortem toxicology, which provides information on substances found in a decedent's system and cannot speak to the makeup of the physical substances consumed that contributed to the overdose. While law enforcement provides surveillance insight into local drug supply by conducting tests to identify the presence of combined opioids and stimulants in samples from drug seizures (Park et al., 2020), the vast majority of these interdicted substances are not likely to have corresponded to a fatal overdose event (Hart, 2021).

Given their access to information gleaned at a death scene investigation immediately following discovery of a fatal overdose medical examiners, or death scene investigators, play an important role in community overdose surveillance (Williams et al., 2017). Overdose surveillance involves tracking and recording overdose data at the local level in order to observe trends, patterns, and intervention points, with the overall goal of using this data to implement appropriate prevention strategies. In this paper we report on results from a novel death scene investigation study that surveilled the local drug supply by testing substances found at the scene of fatal overdoses. Analytic testing using high-pressure liquid chromatography mass-spectrometry (LC-MS) was conducted on the chemical composition of all substances and paraphernalia collected from the scene of a suspected drug overdose death by death scene investigators in Marion County, Indiana for one year. We compare the analytic composition of the substances from the overdose scene to post-mortem toxicology results to demonstrate the utility of this novel surveillance methodology in understanding polydrug overdose deaths.

2. Methods

The CDC has provided ongoing funding to the Indiana State Department of Health to collect real-time toxicology data in Marion County. These data have been used to surveil trends in fatal overdose events (Carter et al., 2018; Phalen et al., 2018; Ray et al., 2017, 2019) and document gaps in the death investigation process (Gupta et al., 2020; Lowder et al., 2018). The toxicology results, which include both blood and urine screenings, have been collected on all suspected

accidental drug overdose events in the county since 2010.

In this study, we focused on a subset of overdose cases that occurred during the data collection period (February 1, 2019 to February 1, 2020). The inclusion criteria were deaths for which toxicology reports documented the presence of 6-monoacetylmorphine (metabolite of heroin), fentanyl (and other synthetic analogues such as carfentanyl), methamphetamine, or cocaine (see Supplement 1 for a list of all substances including metabolites for substances previously mentioned tested for in the toxicology panel) and were determined to be accidental overdoses. Toxicology reports were obtained from the Marion County Deputy Coroner's Office. Reporting limits for the toxicology results were determined by the testing agency (NMS Labs), and for each substance listed, is the smallest concentration that could be accurately reported for the displayed analyte (NMS Labs, 2020). Analytes, which were included as contributing causes of death, were determined by the death scene investigator following state and national guidelines for cause of death reporting (Indiana Department of Health, 2020). During the data collection period, there were 380 accidental fatal overdoses that occurred in Marion County. Working with death scene investigators, we collected samples from 56 death scenes, of which 46 were determined to be an accidental overdose death. Of the 46 cases, only a single case's toxicology report did not detect one of the four substances of interest; this case was removed from the study. Our final study size was 45 cases, which represents 11.8 % of all accidental overdoses in Marion County during the study period. Only one decedent was involved in each case—there were no cases with multiple deaths at one scene.

The collection and storage of substances found at a death scene investigation was not previously part of death scene investigation protocol; instead, these substances were disposed of to prevent harm to others in the household of the decedent. Death scene investigators were monetarily incentivized to begin collecting all paraphernalia and substances found at the scene of a fatal overdose for the one-year study period. Personal protective equipment, sample collection and storage supplies, and naloxone kits were provided to ensure safe collection of the substances for later transport to the chemical laboratory. The substances collected by the death scene investigators came from a variety of sources, including spoons, pipes, syringes, cookers, bags, straws, and pill bottles in the form of powder, crystals, or pills. Table 1 displays these sources and indicates what substances were detected in the samples. There was an average of 1.9 (SD = 1.5, Range 1–9) samples collected from each death investigation scene. Each substance was individually bagged and placed into a plastic bin containing all samples from that specific case along with the case number and field deputy report (see Supplement 2 for photos of substances). The bins were then transported to the university laboratory where they were cataloged and photographed, and samples of the substances were prepared for LC-MS analysis. Liquid chromatography mass-spectrometry analysis was performed on all samples. Liquid chromatography with tandem mass-spectrometry (LC-MS-MS) was used to confirm the identities of targeted analytes with multiple reaction monitoring (MRM). The time between sample collection by death scene investigators and LC-MS analysis ranged from two to four weeks given the availability of

Table 1
Sample Type and Substance Detected (N = 57).

Exhibit 1	Fentanyl n (Percent)	Heroin	Cocaine	Meth
Spoon	4 (4.6)	3 (3.4)	1 (1.1)	1 (1.1)
Syringe	3 (3.4)	2 (2.3)	1 (1.1)	0 (0.0)
Pipe	1 (1.1)	0 (0.0)	5 (5.7)	7 (8.0)
Bag/paper/foil	13 (14.9)	7 (8.0)	5 (5.7)	7 (8.0)
Bottle (any)	3 (3.4)	1 (1.1)	1 (1.1)	1 (1.1)
Pill	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.1)
Other*	7 (8.0)	6 (6.9)	0 (0.0)	1 (1.1)

* Includes straws, pen caps, and other miscellaneous containers.

transport and instrumentation. In order to transport and test these substances, researchers obtained certification to handle Schedule I–V substances from the U.S. Drug Enforcement Agency (DEA). Integrity of the samples was maintained by documented chain of custody from the death scene investigators to analysts. Samples were stored for six months after analysis and disposed following the university laboratory's DEA protocol.

We compared the LC–MS analysis from 57 samples collected from 45 fatal overdoses where the postmortem toxicology results indicated presence of an opioid and/or an illicit stimulant. There was at least one sample collected at the death investigation scene from each of these 45 overdose events. In total there were 87 samples of powders, tablets, and drug paraphernalia collected; however, 16 of those samples were leafy materials or paraphernalia (e.g., spoons or cookers) that did not have sufficient drug residues to test and 14 were pharmaceutical tablets and capsules that did not contain any of the four targeted drugs and were excluded from further analysis.

3. Results

3.1. Toxicology and LC–MS analysis

For the four target drugs, toxicology detected fentanyl in almost all (80.0 %; $n = 36$ cases) and methamphetamine in many (31.1 %; $n = 14$ cases) of the cases. Cocaine (28.9 %; $n = 13$ cases) and heroin (26.7 %; $n = 12$) were also detected in many of the cases. Toxicology results also showed that, among the cases studied, nearly half of the fatal overdose cases involved fentanyl in combination with another illicit substance (44.4 %; $n = 20$ cases), and only a fifth had illicit substances without fentanyl (20.0 %; $n = 9$ cases).

As shown in Table 2, over one-third of the case toxicology reports detected only fentanyl (35.6 %; $n = 16$ cases), followed by cocaine only (6.7 %; $n = 3$ cases), methamphetamine only (6.7 %; $n = 3$ cases), and heroin only (2.2 %; 1 case). In fact, based just on post-mortem toxicology results, the illicit stimulants (cocaine and methamphetamine) were more often detected in combination with fentanyl than alone. Fentanyl with methamphetamine (13.3 %; $n = 6$) was twice as common as

methamphetamine alone (6.7 %; $n = 3$ cases). Similarly, fentanyl with cocaine was detected more frequently (11.1 %; $n = 5$ cases) than cocaine alone (6.7 %; $n = 3$ cases). Table 2 also shows that illicit stimulants were more often detected alongside fentanyl than heroin and that only one death involved all four substances.

We linked the LC–MS sample testing to the toxicology results to determine how often we were able to match the drug(s) detected in the toxicology results to the drug(s) found in sample(s) collected from the scene. Liquid chromatography mass-spectrometry information came from the instrumental analysis of the physical samples found at death scenes whereas the toxicology data came from analysis of the decedent's bodily fluids. After LC–MS analysis, fentanyl was detected in slightly more than half (54.4 %; $n = 31$ samples) of the samples, followed by heroin (33.3 %; $n = 19$ samples), cocaine (31.6 %; $n = 18$ samples), and methamphetamine (22.8 %; $n = 13$ samples). We were able to identify the same drug noted in the toxicology report from the sample gathered at the scene in all of the heroin, cocaine, and methamphetamine-involved deaths. However, in the 16 cases where the toxicology report detected only fentanyl, only 12 cases yielded samples with enough material for analysis, and only six cases yielded samples that contained fentanyl or residue from prior fentanyl use. In the other ten cases, fentanyl may have been fully consumed by the decedent, leaving no residue of fentanyl at the scene. Further, of the total number of scene samples where only fentanyl was detected ($n = 12$), six of the samples directly matched decedent toxicology reports. The remaining six samples did not match toxicology reports and may have been the result of the gap in time between when a person used a substance, when they were recovered by the death scene investigator, and when toxicology was run. In all four cases where the toxicology reports indicated both heroin and fentanyl, the LC–MS analysis detected samples that contained this polydrug combination. Other polydrug combinations found in the toxicology reports (fentanyl and cocaine or fentanyl, heroin, and cocaine) did not match compositions of any of the samples found at these death scenes (Table 2).

Table 2
Substances Detected in Post-Mortem Toxicology and LC–MS Results from Samples Collected from the Scene.

Exhibit 2	Scene Samples Tested on LC-MS ($n = 57$)		Post-Mortem Toxicology Results ($n = 45$)		Direct Matches (Toxicology Matched to Scene Sample)		# of Tox Results where Scene Samples Detected Separately	
Any Detection*								
Fentanyl	31	54.4 %	36	80.0 %	—	—	—	—
Heroin	19	33.3 %	12	26.7 %	—	—	—	—
Cocaine	18	31.6 %	13	28.9 %	—	—	—	—
Methamphetamine	13	22.8 %	14	31.1 %	—	—	—	—
Single Substance Detection								
Fentanyl	12	21.1 %	16	35.6 %	6	37.5%	—	—
Heroin	2	3.5 %	1	2.2 %	1	100.0 %	—	—
Cocaine	11	19.3 %	3	6.7 %	3	100.0 %	—	—
Methamphetamine	9	15.8 %	3	6.7 %	3	100.0 %	—	—
Polysubstance Detection								
Four Substances								
Fentanyl + Heroin + Cocaine + Meth	0	0.0%	2	4.4%	—	—	0	0.0%
Three Substances								
Fentanyl + Heroin + Cocaine	1	1.8%	2	4.4%	0	0.0%	1	50.0%
Fentanyl + Heroin + Meth	0	0.0%	1	2.2 %	—	—	0	0.0%
Fentanyl + Cocaine + Meth	0	0.0%	0	0.0%	—	—	—	—
Heroin + Cocaine + Meth	0	0.0%	0	0.0%	—	—	—	—
Two Substances								
Fentanyl + Heroin	16	28.1 %	4	8.9%	4	100.0 %	0	0.0%
Fentanyl + Cocaine	2	3.5 %	5	11.1 %	0	0.0%	1	20.0 %
Fentanyl + Meth	0	0.0%	6	13.3 %	—	—	1	16.7 %
Heroin + Meth	0	0.0%	2	4.4%	—	—	0	0.0%
Heroin + Cocaine	0	0.0%	0	0.0%	—	—	—	—
Cocaine + Meth	4	7.0%	0	0.0%	—	—	—	—

* Substance detection not mutually exclusive. “—” indicates not applicable for substance.

3.2. Combination or Co-use

From our study, toxicology results indicated that in 51 % of the suspected drug overdose deaths, a single substance was detected, and this was predominantly fentanyl (35.6 %; $n = 16$ cases). This result is echoed in the LC-MS results from the samples collected at the death scenes. According to LC-MS analysis, 34 of the 57 samples (59.6 %) contained only a single substance; 21.1 % ($n = 12$) contained only fentanyl, 19.3 % ($n = 11$) contained only cocaine, 15.8 % ($n = 9$) contained only methamphetamine, and 3.5 % ($n = 2$) contained only heroin. For the remainder of deaths, multiple substances were detected by the toxicology screen, usually involving fentanyl as one of the components. Liquid chromatography mass-spectrometry analysis showed that fentanyl and heroin were frequently combined in samples found at overdose scenes (28.1 %; $n = 16$). The situation was just the opposite for the 26 overdose deaths involving illicit stimulants as only four of the samples found at the death scenes tested positive for both cocaine and methamphetamine, while cocaine was found separately in 11 samples and methamphetamine in nine samples.

Only three of the scene samples (5.2 %) contained a mixture of an illicit opioid and a stimulant; two were cocaine with fentanyl and the third contained cocaine, fentanyl, and heroin. One of the cocaine and fentanyl samples was found in a pharmaceutical bottle that contained a rolled cigarette and the other was a small plastic bag of white powder. The sample that included a mixture of heroin, cocaine, and fentanyl was found in the residue on the inside of a straw. It is unclear whether the combination of these samples of drugs occurred during manufacturing or by choice of the person using the drugs. Within the samples studied, there were no instances of fentanyl or heroin combined with methamphetamine in a single substance. Overall, with the exception of fentanyl and heroin, multiple illicit drugs were rarely found combined in a single sample indicating more significant co-use drug behavior rather than use of combined mixtures.

To further explore the polysubstance toxicology results, we analyzed combinations of illicit drugs found in these cases and whether these components were found separately at the scene of the overdose. Among the 22 polysubstance cases identified in toxicology reports, we identified three (13.6 %) in which the separate samples found at the scene matched the same polysubstance combination (see Table 2, rightmost column). Many substances can be detected by sensitive toxicology tests long after they have been ingested, so it is not surprising that substances were sometimes detected in decedents that were not present at the overdose scene (Allan and Roberts, 2009; Hudson, 2020; Pounder and Jones, 1990). This finding reinforces the need to collect more information about the composition of substances that are associated with overdose deaths to assist community health leaders and the implementation of better community overdose surveillance.

4. Discussion

As the overdose epidemic continues to evolve, improved surveillance of the substances linked to overdose remains crucially important. As demonstrated in this study, testing substances from the scene of a fatal drug overdose is a means of surveilling local drug markets. Moreover, comparing these results to post-mortem toxicology results sheds light on polydrug overdose deaths and allows for better overdose prevention planning (Laroche et al., 2019). The key finding from this study is that in Indianapolis, Indiana, from February 2019 through February 2020, stimulants and opioids were not being mixed in the drug supply. This is contrary to claims of illicit stimulants combined with fentanyl. However, fentanyl was frequently found in combination with heroin among the samples examined in this study. This finding is consistent with studies that have shown an increase in the presence of fentanyl in augmenting heroin use (Bode et al., 2017; Carroll et al., 2017; Macmadu et al., 2017; Rhodes et al., 2019; Stein et al., 2019).

5. Limitations

Substances that were collected by death scene investigators do not necessarily represent all of the types of drugs that were used by those who fatally overdosed. There may be instances where substances at the scene were fully consumed by the decedent and thus could not be collected. Also, we are unable to determine if the substances that were collected at the scene were consumed specifically by the decedent. Study protocol directed that all drug paraphernalia and illicit substances be collected from the scene of the death investigation and stored for research. The substances collected may or may not have contributed to the decedent's death. During our collection period we had 16 samples, mostly drug paraphernalia, that did not contain enough physical substance to be tested by the LC-MS. These were not included in our sample set due to the lack of instrumental analysis results. Further, there were 11 cases in which substances were collected at the scene, but the cause of death listed was something other than an accidental overdose and therefore these cases were excluded from the study. The illicit drug market tends to have a great deal of regional variations in sample composition (Hedegaard et al., 2019). It should be noted that work and all samples collected were from Indianapolis, Indiana, a state in the mid-western region of the United States, and these results may differ in other geographical regions (Dombrowski et al., 2016).

6. Conclusion

This study provides a novel overdose surveillance method that includes testing substances from the scene of an overdose and comparing the scene results to the post-mortem toxicology results to understand polydrug use patterns. Based on study findings, and the continued rise in non-fatal overdoses across the United States (Hoots et al., 2020), it is recommended that public health initiatives aimed at reducing overdose risks provide education focused on the risks of stimulant and opioid co-use but also that heroin commonly contains fentanyl. Additionally, the methodology for testing substances at the scene of a fatal overdose described herein may be incorporated in surveillance activities to better identify the local drug supply.

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Contributors

BR and ML designed and oversaw the study procedures. PH and TL had full access to all the data in the study and takes responsibility for the integrity of the analysis and the accuracy of the data. ES and KB assisted with post-mortem toxicology data collection procedures and manuscript development while AR aided TL and ML in chemical analysis procedures. All authors assisted in writing and preparing the manuscript.

Declaration of Competing Interest

The authors have no conflicts of interest to disclose.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.drugalcdep.2021.10.8722>.

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