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Expected and Actual Fentanyl Exposure Among Persons Seeking Opioid Withdrawal Management

Shannon R. Kenney, Ph.D., M.P.H.^{a,b}, Bradley J. Anderson, Ph.D.^a, Micah T. Conti^{a,c}, Genie L. Bailey, M.D.^{b,c}, and Michael D. Stein, M.D.^{a,d}

^aBehavioral Medicine Department, Butler Hospital, Providence, RI, 02906

^bWarren Alpert Medical School of Brown University, Providence, RI, 02912

^cStanley Street Treatment and Resources, Inc., Fall River, Massachusetts 02720

^dBoston University School of Public Health, Boston, MA 02118

Abstract

Objective—Fentanyl-contaminated opioid supplies have led to rising overdose fatalities in recent years. We compared beliefs, behaviors, and risk perceptions related to fentanyl with actual toxicology reports among people who used opioids.

Method—Participants (n = 231) were patients undergoing short-term inpatient opioid withdrawal management in Fall River, Massachusetts. We compared persons testing positive and negative for fentanyl on urine toxicological testing at program entry.

Results—Nearly all (95.7%) participants believed that fentanyl increases risk for overdose/death, and 86.6% of participants tested positive for fentanyl. Positive fentanyl toxicology test results were associated with lower educational attainment, history of injection drug use, and self-reported lifetime use of fentanyl. Of those reporting they had never been exposed to fentanyl (intentionally or unintentionally) (n = 33), two-thirds tested positive for fentanyl; among those believing their tests would be negative (n = 49), 71.4% tested positive for fentanyl. Heroin use was associated with fentanyl exposure; persons who reported past month heroin use (n = 213) were more likely to test positive for fentanyl (91.1%) than persons using non-heroin opioids (n = 18; 33.3%).

Conclusions—Nearly nine in ten participants tested positive for fentanyl, including participants who anticipated their tests would be negative. Leveraging toxicology results in opioid withdrawal settings may be helpful in educating patients about fentanyl exposure and risks.

Keywords

Opioids; Heroin; Fentanyl Exposure; Risk Perceptions; Treatment

Correspondence concerning this article should be addressed to: Shannon R. Kenney, Ph.D., M.P.H., Department of Psychiatry and Human Behavior at Brown University, Butler Hospital, 345 Blackstone Blvd., Providence, RI 02906; Pn: (617) 633-4321. Shannon_Kenney@brown.edu.

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1. Introduction

From 2002 to 2015 there was a 2.8 fold increase in opioid overdose fatalities nationally (National Institute on Drug Abuse, 2017). Although U.S. overdose deaths attributed to prescription opioid pain relievers have remained fairly steady since 2010 (National Institute on Drug Abuse, 2017), heroin-related overdose fatalities tripled from 2010 to 2014 (Rudd, Seth, David, & Scholl, 2016). Since 2013, an increasing proportion of these fatalities are attributed to illicitly manufactured fentanyl, a synthetic mu-opioid receptor agonist 30–50 times more powerful than heroin per mg. (Ciccarone, Ondocsin, & Mars, 2017) that has infiltrated the U.S. heroin supply (Gladden, Martinez, & Seth, 2016; Warner, Trinidad, Bastian, Minino, & Hedegaard, 2016). Fentanyl-contaminated overdose is a particularly significant public health crisis in Massachusetts, where opioid death rates tripled from just 2010 to 2015 and, in the six months of 2016, 74% of available opioid overdose toxicology reports tested positive for fentanyl (Massachusetts Department of Public Health, 2017).

Recent studies demonstrate high prevalence rates of fentanyl in persons who use opioids. Canadian studies report a 14% fentanyl prevalence rate among persons who use illicit drugs (Hayashi et al., 2018) and a 29% prevalence rate among clients seeking harm reduction services (Amlani et al., 2015). In 368 clients undergoing methadone maintenance therapy (MMT) for heroin addiction in Michigan, 38% tested positive for fentanyl at least once during treatment (Arfken, Suchanek, & Greenwald, 2017); these authors anecdotally reported that clients were “surprised and stunned” to learn of their fentanyl-positive results. Fentanyl-exposed persons are more likely to report multiple MMT admissions, leaving treatment sooner, injection drug use (IDU), and using heroin or cocaine (Arfken et al., 2017; Hayashi et al., 2018). Suspected fentanyl exposure is associated with past or current opioid agonist therapy (OAT), history of overdose, and regular IDU, heroin use or cocaine use (Carroll, Marshall, Rich, & Green, 2017). Still, no study to date has examined expected fentanyl exposure and other predictors of positive urine toxicology screens in an opioid dependent population.

Qualitative research supports that people who use heroin acknowledge fentanyl contaminated heroin supply chains (Ciccarone et al., 2017; Somerville et al., 2017), and many consider fentanyl “ubiquitous and unavoidable” (Ciccarone et al., 2017). Macmadu and colleagues (2017) found that 59% of people who reported suspected fentanyl exposure in their heroin were not aware their heroin had been adulterated prior to use (Macmadu, Carroll, Hadland, Green, & Marshall, 2017). In addition to gaining a better understanding about how people’s perceptions of fentanyl risk impact their exposure to fentanyl, there is a need to acknowledge that some users may seek out fentanyl. While some studies show that people who use heroin try to avoid fentanyl (Carroll et al., 2017), other studies find that many people use fentanyl-adulterated heroin intentionally (Ciccarone et al., 2017; Macmadu et al., 2017). In fact, a Massachusetts-based qualitative study found that the fentanyl epidemic did not alter opioid use behaviors (Somerville et al., 2017).

1.1. Study Aims and Hypotheses

In the current study, we advance knowledge about this urgent public health crisis by testing the relationship between beliefs about fentanyl exposure and actual toxicology reports in

people seeking opioid withdrawal management. By assessing participants' self-reported fentanyl use, perceptions about fentanyl-related exposure risk, and other predictors of fentanyl exposure these findings can inform potential directions for clinical practice, education, and intervention.

Although we expected that intentional use of fentanyl and anticipated fentanyl exposure would be associated with greater confirmed positive fentanyl reports, given the increased pervasiveness of fentanyl nationally, we hypothesized that a substantial proportion of respondents anticipating no fentanyl exposure would test positive for fentanyl. Based on national data showing that non-Hispanic white men aged 15–44 are at greatest risk for dying from illicitly manufactured fentanyl (Gladden et al., 2016), we hypothesized that males and Whites would be most likely to test positive for fentanyl. Also grounded in existing research, we expected heroin use, IDU, cocaine use, overdose history, and history of OAT to be associated with fentanyl exposure.

2. Method

2.1. Recruitment

Between April and September 2017, persons seeking inpatient opioid withdrawal management at Stanley Street Treatment and Resources, Inc. (SSTAR) in Fall River, Massachusetts were asked to participate in a survey research study. SSTAR's opioid withdrawal program provides evaluation and withdrawal management using a methadone taper protocol, individual and group counseling, and aftercare case management. Patients admitted stay an average of 4.9 days.

Of patients admitted to SSTAR during the recruitment period for opioid misuse, 251 met the study's eligibility criteria (18 years or older, English-speaking, and able to provide informed consent) as approved by the Butler Hospital Institutional Review Board. Twenty persons refused study participation or were discharged before staff could interview them. The remaining 231 persons completed a non-incentivized, face-to-face interview administered by non-treating research staff over the course of approximately 15 minutes. All participants had urine drug testing for fentanyl and its major metabolite, norfentanyl. Participants were unaware of test results at the time of the interview. Commercial labs test for norfentanyl because fentanyl is metabolized to norfentanyl, which may be detected at concentrations 3–4 times higher than that of fentanyl (Poklis & Backer, 2004).

2.2. Measures

In addition to age, sex, race/ethnicity, years of education, and history of IDU the following variables were assessed.

2.2.1. Heroin use—Respondents were asked how many days in the past 30 days they used heroin.

2.2.2. History of overdose—Respondents were asked if they had ever overdosed. We defined overdose (on any drug) as “you were unarousable (couldn't be woken) with shaking or calling your name because of the drugs you consumed.”

2.2.3. Prior opiate agonist therapy—Respondents responded “yes” or “no” to ever having been prescribed buprenorphine or enrolled in a methadone maintenance program. Each type of OAT was summarized (e.g., “Methadone is a medication-assisted treatment for opioid dependence. Patients typically attend methadone clinics on a daily basis to receive their dose of methadone”).

2.2.4. Ever been given naloxone—Respondents answered “yes” or “no” to ever received or been given naloxone (Narcan)—defined as the “overdose antidote”—because of an overdose.

2.2.5. Fentanyl use—Respondents were asked if they had ever “intentionally, knowingly used fentanyl to get high” and were provided with five answer options. Those answering “no” were coded a never having used fentanyl; those answering “I used fentanyl but it wasn’t intentional (e.g., found out afterwards)” were coded as unintentional fentanyl users; and those responding “Yes, I used it intentionally nasally,” “Yes, I used it intentionally and injected,” or “Yes, I used it intentionally in some other form” were coded as ever intentionally using fentanyl.

2.2.6. Perceived overdose risk of fentanyl—Respondents were asked, “Do you think fentanyl increases risk for overdose?” Answer options included “Yes,” “No,” and “I don’t know.” Missing (n=1) and refusals (n=2) were excluded from analyses.

2.2.7. Anticipated fentanyl exposure—Respondents were asked, “Do you think your tox screen when you arrived at SSTAR had fentanyl in it?” Answer options included “Yes,” “No,” and “I don’t know.” Missing (n=1) and refusals (n=2) were excluded from analyses.

2.2.8. Confirming fentanyl exposure—Enzyme immunoassay testing was performed (Olympus AU640) with confirmatory testing among those initially positive (Triple Quad LCMSMS) at the cutoff for fentanyl set at 2.5 ng/ml and at 5 ng/ml for norfentanyl. Detection time for heroin in urine is 1–3 days and for norfentanyl/fentanyl is 1–2 days following last use.

2.2.9. Additional urine drug testing—Enzyme immunoassay testing was also performed for amphetamines, barbiturates, benzodiazepines, cocaine, and non-heroin opioids (i.e., methadone, morphine, hydromorphone, codeine, hydrocodone, oxycodone).

2.3. Analysis Plan

We present descriptive statistics to summarize the characteristics of the sample. We used t-tests to compare persons testing positive and negative for fentanyl for differences in means, and Pearson χ^2 -tests to compare differences in counts. We used the same procedures to conduct auxiliary analysis exploring the association of other commonly used drugs (benzodiazepines, cocaine, and illicit opiates other than heroin) with fentanyl toxicology results.

3. Results

Participants averaged 34.0 ($\pm$ 9.29) years of age, 73.2% were male, 83.6% were White 2.6% were Black, and 13.0% identified multiple or other racial identities (Table 1). Twenty-seven (11.7%) were Latino/a. Mean educational attainment was 12.0 ($\pm$ 1.7) years. Almost 70% had a lifetime history of OAT (buprenorphine or methadone) and 76.6% had a lifetime history of IDU. Most (92.2%) reported they had used heroin in the past month. On average, participants who reported past month heroin used on 24.4 ($\pm$ 9.8) days, 55.0% had a history of drug overdose and 47.6% had ever been administered naloxone for an overdose.

Of the 18 (7.8%) participants who reported not using heroin in the past month, none tested positive for heroin on the urine drug testing; all reported using other illicit opioids in the past month, and 15 had positive urine toxicology tests for one or more opioids (13 were positive for oxycodone). Among these 18 persons, one tested positive for amphetamines, two for benzodiazepines, and three for cocaine.

A majority (95.7%) of the sample said they believed that fentanyl increases risk for overdose/death. Only 33 (14.5%) believed they had never consumed fentanyl, 35 (15.2%) thought they had unintentionally used fentanyl, and 162 (70.4%) reported intentional fentanyl use. In all, 61.3% said they thought they would test positive for fentanyl on admission to opioid withdrawal management, 21.3% reported they thought they would not test fentanyl positive, and 17.4% said they did not know.

Only 31 (13.4%) participants had urine toxicology tests that were negative for fentanyl (Table 1). Fentanyl toxicology test results were not associated significantly with age, gender, race, or ethnicity. Persons testing fentanyl negative had a significantly ($t = 2.14$, $p = .03$) higher mean level of education than those testing fentanyl positive. Testing positive for fentanyl was not associated significantly with a lifetime history of OAT, but was associated with IDU ($\chi^2 = 4.70$, $p = .03$). Persons who tested positive for fentanyl were significantly more likely ($\chi^2 = 47.63$, $p < .001$) to have used heroin in the past month (97.0% vs 61.3%) than persons who were fentanyl negative. Mean days of heroin use was also significantly higher ($t = -6.62$, $p < .001$) among persons testing fentanyl positive.

Fentanyl toxicology tests were associated significantly with self-reported fentanyl use ($\chi^2 = 27.43$, $p < .001$); persons who were fentanyl negative were more likely (36.7% vs 11.0%) to say they believed they had never used fentanyl, more likely (33.3% vs 12.5%) to say they believed they had unintentionally used fentanyl, and less likely (30.0% vs 76.5%) than persons testing fentanyl positive. Belief about fentanyl status was also associated significantly with actual test results ($\chi^2 = 18.88$, $p < .001$); persons testing fentanyl positive (66.5%) were more likely to say they thought they were positive (66.5% vs 26.7%), less likely to say they thought they were fentanyl negative (17.5% vs 46.7%), and a little less likely to say they didn't know their fentanyl status (16.0% vs 26.7%). While testing positive for fentanyl was associated with heroin use, it should be noted that 6 (33%) of the 18 persons who reported no past month heroin use (confirmed by toxicology tests) tested positive for fentanyl.

Among past month heroin users ($n = 213$), eight (3.8%) tested positive for amphetamines, 4 (1.9%) for barbiturates, 39 (18.3%) for benzodiazepines, 101 (47.4%) for cocaine, and 177 (83.1%) for an illicit opioid other than heroin. As an auxiliary analysis, we examined the association between fentanyl toxicology tests and testing positive for benzodiazepines, cocaine, and other illicit opiates. Persons testing fentanyl positive were not significantly ($p = .45$) more likely to test positive for benzodiazepines or illicit opioids other than heroin, but were considerably (50.5% vs 9.7%; $p < .001$) more likely to test positive for cocaine.

4. Discussion

The current findings point to the omnipresence of fentanyl in the lives of this sample of patients in opioid withdrawal management in Massachusetts. Overall, fentanyl does not appear to discriminate; fentanyl exposure was associated with educational attainment but not with age, gender, race or ethnicity. Surprisingly, many high-risk profile factors (ever overdosed, received naloxone or been in OAT) did not heighten the likelihood for a positive fentanyl urine toxicological test in this sample, although history of IDU and past month heroin use were associated with fentanyl exposure. The vast majority of participants (86.6%) tested positive for fentanyl upon entering withdrawal management, including the majority (71.4%) of those expecting negative toxicology results.

The near universality of fentanyl exposure found in the current sample speaks to the difficulties of avoiding fentanyl exposure in this region, and the high rates of unintentional fentanyl exposure point to the need for harm reduction education. Although some people who use heroin report differentiating pure heroin from fentanyl or fentanyl-adulterated heroin by physiological effects and appearance, taste, and smell (Ciccarone et al., 2017), the Drug Enforcement Administration recently reported that color is not a reliable indicator of the presence of fentanyl (Drug Enforcement Administration, 2016). Expanding technology to improve upon test kits that assess for fentanyl contamination prior to use offers substantial promise (Ciccarone et al., 2017); currently, negative or false negative field results run the risk of providing harmful reassurance that drugs are safe (Gerszak, 2017), thus exacerbating risks. The results showing that nearly half of participants using heroin also had urine drug tests positive for cocaine support recent evidence that fentanyl may be mixed into cocaine supply chains (Ciccarone et al., 2017; Macmadu et al., 2017; O'Donnell, Halpin, Mattson, Goldberger, & Gladden, 2017), presenting additional risk.

A high proportion (70.4%) of this sample reported intentionally using fentanyl. We do not know if these are experimental one-time users or recurrent fentanyl users, nor do we know the reasons why respondents sought fentanyl. However, existing studies and anecdotal reports indicate that fentanyl enables a different drug experience than heroin (Miller, Stogner, Miller, & Blough, 2017). In their qualitative study of persons using heroin in Massachusetts and New Hampshire, Ciccarone and colleagues (2017) found that fentanyl's intensity and potent ability to surpass heroin tolerance or OAT medicine was appealing to some people. Still, qualitative studies may inform the extent to which gaining knowledge about the risks of using fentanyl may impact people's fentanyl use intentions.

We were surprised to find that in the small group of participants who used opioid pills (i.e., those who reported no heroin use in the last month) one-third tested positive for fentanyl. While some of these individuals may have been exposed to fentanyl through contamination of cocaine, fentanyl-contaminated opioid pills and benzodiazepines have recently been detected in U.S. illicit drug supplies (Armenian, Vo, Barr-Walker, & Lynch, 2017). More research is needed to investigate and describe the prevalence of fentanyl contaminated cocaine, benzodiazepines, and other opioid pill supply chains.

Consistent with qualitative studies of people who misuse opioids in Massachusetts (Ciccarone et al., 2017; Somerville et al., 2017), a vast majority (95.8%) of the current sample reported that fentanyl increases risk for overdose. The high prevalence of fentanyl and its heightened risk for overdose confirms the need for widespread public health interventions. Many people who use fentanyl or opioids that may contain fentanyl are implementing strategies to reduce overdose incidence, such as using slowly or in the presence of others, but these strategies alone may be ineffective in reducing risk for overdose (Ciccarone et al., 2017; Somerville et al., 2017). Developing supervised injection centers and training both laypersons and first responders about how fentanyl overdoses may affect naloxone administration (e.g., the need to quickly administer or to use multiple doses) is warranted. Raising awareness about good Samaritan laws that protect those who witness an overdose may encourage witnesses to call for help. Recent studies suggest that most opioid users are not aware of good Samaritan laws (Evans, Hadland, Clark, Green, & Marshall, 2016) even though half of our sample reported having received naloxone for an overdose in the past (although we cannot determine if naloxone was administered by drug confederates or health professionals).

4.1. Limitations

Several limitations of the current study should be noted. First, our findings rely on patient self-reports of illicit drug use behaviors, which may lead to underreporting. Second, the current sample was comprised of persons seeking care a single mid-sized city in Massachusetts (population 88,857) recruited from a single opioid withdrawal center, although patients travel for up to a hundred miles to this center. Collecting data at multiple opioid withdrawal management sites and from people who use opioids in large cities would enhance the generalizability of findings. Third, participants who tested negative may have been exposed to fentanyl at other times and are simply negative at the time point tested. Finally, we do not know if toxicological results impacted patients' engagement in OAT or other forms of opioid addiction treatment that is always recommended at the completion of this withdrawal management program.

4.2. Conclusions

Fentanyl overdose is a widespread public health crisis with a limited empirical understanding. The current study draws attention to the high prevalence of fentanyl in the toxicologies of people seeking opioid withdrawal management in Massachusetts and sheds light on inaccurate expectations about fentanyl exposure. Presenting people who use opioids with toxicology-based evidence that they have recently used fentanyl may provide them with new evidence about their actual risks, allow for a full discussion of fentanyl use and its

consequences, and could potentially prime detoxifying patients for harm reduction skills training and long-term OAT.

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Highlights

- Among persons seeking opioid withdrawal, 86.6% tested positive for fentanyl.
- 91.1% of persons using heroin tested positive for fentanyl.
- 33.3% of persons using non-heroin opioids tested positive for fentanyl.
- Of positive toxicology results, 71.4% believed their tests would be negative.
- Two-thirds of those with positive tests reported never intentionally using fentanyl.

Table 1

Background Characteristics, Substance Use Patterns, and Perceptions About Fentanyl, by Fentanyl Toxicology Test Results.

	Fentanyl Positive			t or χ^2 (p =)
	Sample (n = 231)	No (n = 31)	Yes (n = 200)	
Age of Participant	34.0 ($\pm$ 9.2)	35.8 ($\pm$ 9.3)	33.8 ($\pm$ 9.1)	1.16 (.248)
n (%) Male	169 (73.2%)	23 (74.2%)	146 (73.0%)	0.02 (.889)
Race				
n (%) White	193 (83.6%)	25 (80.7%)	168 (84.0%)	
n (%) Black	6 (2.6%)	0 (0.0%)	6 (3.0%)	1.75 (.417)
n (%) Other	32 (13.0%)	6 (19.4%)	26 (13.0%)	
n (%) Latino/a	27 (11.7%)	4 (12.9%)	23 (11.5%)	0.05 (.821)
Yrs Education	12.0 ($\pm$ 1.7)	12.6 ($\pm$ 2.0)	11.9 ($\pm$ 1.6)	2.14 (.034)
n (%) History of OAT	161 (69.7%)	19 (61.3%)	142 (71.0%)	1.20 (.274)
n (%) Ever Injected	177 (76.6%)	19 (61.3%)	158 (79.0%)	4.70 (.030)
Used Heroin Past Mo.				
n (%) No	18 (7.8%)	12 (38.7%)	6 (3.0%)	47.63 (<.001)
n (%) Yes	213 (92.2%)	19 (61.3%)	194 (97.0%)	
n (%) Ever Overdosed	127 (55.0%)	13 (41.9%)	114 (57.0%)	2.46 (.117)
n (%) Been Given Naloxone	109 (47.6%)	10 (32.2%)	99 (50.0%)	3.38 (.066)
Self-Reported Fentanyl Use				
n (%) Never Used Fentanyl	33 (14.5%)	11 (36.7%)	22 (11.0%)	
n (%) Used (Unintentionally)	35 (15.2%)	10 (33.3%)	25 (12.5%)	27.43 (<.001)
n (%) Used (Intentionally)	162 (70.4%)	9 (30.0%)	153 (76.5%)	
Thinks Fentanyl Positive				
n (%) Yes	141 (61.3%)	8 (26.7%)	133 (66.5%)	
n (%) No	49 (21.3%)	14 (46.7%)	35 (17.5%)	18.88 (<.001)
n (%) Don't Know	40 (17.4%)	8 (26.7%)	32 (16.0%)	