Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

Drug Alcohol Depend. Author manuscript; available in PMC 2020 November 01.

Published in final edited form as:

Drug Alcohol Depend. 2019 November 01; 204: 107515. doi:10.1016/j.drugalcdep.2019.06.017.

Fentanyl exposure and preferences among individuals starting treatment for opioid use disorder

Jan Gryczynski[1], **Helen Nichols**[2], **Robert P. Schwartz**[1], **Shannon Gwin Mitchell**[1], **Paulette Hill**[2], **Kim Wireman**[2]

[1]Friends Research Institute, 1040 Park Avenue, Suite 103, Baltimore, MD 21201, USA

[2]Powell Recovery Center, 14 S. Broadway, Baltimore, MD 21231, USA

Abstract

Background: Fentanyl has become widespread in the illicit opioid supply, and is a major driver of overdose mortality.

Methods: This study used a medical records review at a community opioid use disorder treatment program to examine patient-level correlates of fentanyl exposure as measured by urine testing at admission (N= 1,174). Additionally, an anonymous survey was conducted with 114 patients about their experiences and preferences regarding fentanyl.

Results: Overall, 39% of patients entering treatment tested positive for fentanyl. Prevalence of fentanyl exposure differed based on other drug test results (fentanyl-positive= 81.1% vs. 15.4% among participants positive vs. negative for heroin/opioids, p<.001; 59.0% vs. 38.3% among participants positive vs. negative for methadone, p=.001; 53.8% vs. 24.9% among participants positive vs. negative for cocaine, p<.001), prior addiction treatment (40.6% vs. 32.0% among participants with vs. without prior treatment, p<.05), and mental health (36.7% vs. 43.1% among participants with vs. without co-occurring psychiatric diagnosis, p<.05). Most participants reported knowingly using fentanyl (56.1%) and knowing people who prefer fentanyl as a drug of choice (65.8%). Preference for fentanyl (alone or mixed with heroin) was expressed by 44.7% of

*corresponding author: jgryczynski@friendsresearch.org.

Contributors

JG conceived the study, contributed to the analysis, and led the writing. HN created the dataset from program records, conducted the statistical analysis, and contributed to study conceptualization. KW oversaw the survey data collection and contributed to content on program practices. PH contributed to the sections on treatment protocols. RPS and SGM contributed to study conceptualization and critically revised the manuscript.

Disclosures

JG, RPS, and SGM are employed at the Friends Research Institute. JG is a member of the Board of Directors of Powell Recovery Center (the treatment program that hosted the research), a role for which he receives no compensation. JG is part owner of COG Analytics, LLC (unrelated to the research described in this article), and has received other research support from Indivior through his role at Friends Research Institute (unrelated to the research described in this article). HN is a partner in VTConnect, a telehealth company (unrelated to the research described in this article). HN, PH, and KW are employed by Powell Recovery Center (the treatment program that hosted the research). RPS reports consultation to Verily Life Sciences (unrelated to the research described in this article).

Conflicts of Interest:

The authors report no conflicts of interest. See disclosures statement for disclosures.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

participants. Participants thought fentanyl withdrawal had faster onset (53.5%), greater severity (74.8%), and longer duration (62.0%) than heroin withdrawal.

Conclusions: Recent opioid and cocaine use were strongly associated with fentanyl exposure in this sample. Although fentanyl exposure is often unintentional, there may be a subgroup of individuals come to prefer fentanyl. Future research should examine the relationship between fentanyl use, patient preferences for fentanyl, and treatment outcomes.

Keywords

Fentanyl; opioid use disorder; treatment; buprenorphine; patient preferences

1. Introduction

Opioid overdose deaths are a public health emergency, with death rates rising over 200% since 2000 and still showing no sign of abating (Rudd et al., 2016). Opioid overdoses now cause more deaths than motor vehicle accidents, firearms, and HIV/AIDS did at their historical peaks (Katz, 2017; Scholl et al., 2019). Recent years have seen sustained media attention on the opioid issue, a Surgeon General's Report, new prescribing guidelines from CDC and medical professional organizations, strengthening of Prescription Drug Monitoring Programs in every state, increased government funding to combat the opioid epidemic, and a general tightening of standards and controls on opioid prescriptions. Nevertheless, the most recent data show that opioid overdose mortality continues to rise (CDC, 2018; Katz, 2017; Rudd et al., 2016; Scholl et al., 2019). An epidemic that started with widespread use of prescription opioids has transitioned to one increasingly driven by illicit opioids. Some people who become dependent on prescription opioids and develop opioid use disorder (OUD) turn to illicit opioids due to availability and cost (Cicero et al., 2015; Compton et al., 2016; Tedesco et al., 2017). In recent years there has been a steep increase in deaths related to heroin and illicit synthetic opioids, chiefly fentanyl and its analogues (Dasgupta et al., 2014; Jones, Einstein, & Compton, 2018; Katz, 2017; Scholl et al., 2019).

Fentanyl and its various analogues (e.g., carfentanil, butyrylfentanyl, related synthetics MT-45, etc.) have become common in the illicit opioid supply in many localities. These synthetics are extremely potent, making them highly attractive for trafficking. Misused fentanyl sometimes originates from diverted pharmaceuticals, but is increasingly being synthesized in clandestine laboratories outside of the US (Prekupec et al., 2017; Suzuki and El-Haddad, 2017). The extreme potency of fentanyl and related compounds increases overdose risk. Moreover, the potency leaves little room for error in dose preparation, such that a slight miscalculation by distributors or end-users can easily result in death. In 2016, fentanyl was involved in 20,100 overdose deaths nationwide, compared with 15,400 deaths for heroin and 14,400 for prescription opioids (Katz, 2017; O'Donnell et al., 2017). The latest estimates show that opioid overdose deaths are continuing to rise, with fentanyl remaining the key driver of opioid overdoses (Scholl et al., 2019).

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

1.1. Studies of Fentanyl Exposure and Preferences

Given the rapid emergence of fentanyl as a driver of the overdose epidemic, research in this area is still developing. Nevertheless, several recent studies that have laid important groundwork in examining demand-side responses to fentanyl in local markets, documenting fentanyl exposure, and considering intentional and unintentional exposure.

1.1.1. Qualitative studies documenting fentanyl market penetration and preferences—In a study drawing from 38 ethnographic interviews with people who inject drugs in Massachusetts, Ciccarone and colleagues (2017) developed a typology of new "heroin types" that are available on the street: heroin alone, fentanyl alone, and heroin-fentanyl mix. This study documented that people who inject drugs are seeking to differentiate among these street products and have developed distinct preferences. In another study, 23 participants recruited from needle exchange sites in Baltimore described the emergence of fentanyl in the street-level heroin market (Mars et al., 2017). Ethnographers documented unique responses of attraction and avoidance with respect to fentanyl, as well as strategies to take precautions, such as using "tester shots" with small doses (Mars et al., 2017; see also Mars et al., 2018). A rapid ethnographic study in Vancouver among individuals utilizing safe injection facilities documented that fentanyl overdose is perceived as a distinct phenomenon from other opioid overdoses, especially with respect to potency and onset (Mayer et al., 2018).

1.1.2. Toxicology studies of fentanyl exposure—Several studies with urine testing have documented patterns and correlates of fentanyl exposure in North America. In a recent study from Vancouver, Hayashi and colleagues (2018) administered urine drug screens to 669 people who use drugs, finding that 14.5% tested positive for fentanyl. Predictors of fentanyl exposure included current use of drugs by injection, older age, and testing positive for other drugs including heroin/morphine, buprenorphine, amphetamines, and cocaine. Another recent study in Vancouver documented a rapid increase in fentanyl positive urine tests over time, with a corresponding decrease in other opioid positive tests as fentanyl came to supplant the local opioid supply (Jones et al., 2018). In a study in Fall River, Massachusetts, researchers examined urine toxicology results among entrants to a detoxification program, finding that 86.6% of patients in that sample tested positive for fentanyl. The study found that lower education, injection drug use, heroin use, and lifetime history of known fentanyl use were associated with fentanyl exposure (Kenney et al., 2018). However, these studies did not determine patient preferences for fentanyl.

1.1.3. Studies of fentanyl exposure and intent—In a 2015 study from British Columbia with 242 participants recruited from harm reduction venues, 29% tested positive for fentanyl, although most did not report using it, suggesting potential unintentional exposure (Amlani et al., 2015). A mixed methods study in Rhode Island found that suspected fentanyl exposure was common, but in this sample it was often unintentional (Carroll et al., 2017). Another study in Rhode Island examined prevalence and correlates of suspected fentanyl exposure, finding that 11% of young adult opioid users thought they may have been exposed to fentanyl. Correlates of perceived exposure included heroin use, cocaine use, use to avoid withdrawal, longer histories of opioid use, injection, and prior

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

overdose experience. Notably, 59% of the sample thought fentanyl produced a better high than heroin (Macmadu et al., 2017). In a study using hair testing with 40 individuals in an inpatient detoxification setting, nearly all tested positive for fentanyl or an analogue, while 27.5% and 67.5% reported known and suspected exposure, respectively (Palamar et al., 2019). A survey study using online recruitment examined characteristics and use motives among 122 individuals reporting non-medical fentanyl use. Fentanyl use frequency was correlated with experiencing negative consequences from opioid use. In contrast to some other studies, only 12.3% reported that their use of fentanyl was unintentional (Kilwein et al., 2018). Another recent survey conducted in Baltimore, Boston, and Rhode Island found that, among 256 individuals with suspected fentanyl exposure, a minority (albeit a sizable one of 26%) reported a specific preference for drugs with fentanyl (Sherman et al., 2018).

Thus, the emerging research suggests that responses to fentanyl span the gamut from purposeful avoidance, to reluctant acceptance, to development of specific preferences for fentanyl. In the current study, we sought to examine correlates of fentanyl exposure (determined via urine testing) among admissions to a community OUD treatment program, and to explore patient experiences and preferences regarding fentanyl.

2. Methods

2.1. Study Site

This study was conducted at a non-profit community OUD treatment program in Baltimore, Maryland. Baltimore has been impacted heavily by illicit fentanyl in the heroin supply, and has seen a large number of overdose deaths (Maryland Department of Health, 2018; Mars et al., 2017). The treatment program serves approximately 3,400 unique patients annually, with all treatment funded via public sector insurance. Nearly all patients present with severe OUD and receive buprenorphine as part of their care. The program offers a continuum of addiction treatment, including residential treatment, intensive and standard outpatient, outpatient mental health treatment for dual diagnosis patients, and a community-based crisis housing network. The program conducts routine urine testing for new admissions and regularly during treatment, including fentanyl-specific testing.

2.2. Procedure

2.2.1. Record Review—This study used a review of treatment records of new admissions to the treatment program. Data on patient characteristics (demographics, SUD and mental health treatment history, mental health diagnoses, urine test results at intake) were abstracted from electronic health records for treatment admissions during a 7-month period in 2018 (N= 1,174). Urine testing for fentanyl was conducted at admission using a one-step fentanyl test instant assay dip card (Alltest, inc., cut-off 200 ng/mL). Data were also abstracted for other clinical urine test results at admission, which included tests for other opioids (including tests for heroin, morphine, codeine, hydrocodone, hydromorphone, oxycodone, tramadol, methadone, and buprenorphine), cocaine, and benzodiazepines.

2.2.2. Anonymous Survey—A convenience sample of 114 patients at the treatment program were asked to complete a brief (one-page) anonymous survey in September 2018

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

which focused on fentanyl experiences and preferences. The purpose of the survey was to obtain a rapid, minimally-burdensome snapshot of patient perceptions. The survey asked a series of questions about fentanyl covering topics of perceived exposure, intentional vs. unintentional exposure, fentanyl preferences, perceived preferences among others, availability of fentanyl and unadulterated heroin, and perceived onset, severity, and duration of fentanyl withdrawal as compared to heroin. Data analyses for the exploratory survey were limited to descriptive statistics.

The study was determined to be exempt from IRB review by the Western Institutional Review Board.

2.3. Data Analysis

The prevalence of fentanyl-positive tests upon admission to OUD treatment was examined descriptively by month. The association between patient characteristics and fentanyl exposure prior to treatment entry (i.e., fentanyl positive urine test at intake) were examined using Pearson chi-square tests of independence for categorical variables and independent samples t-tests for continuous variables. A logistic regression model (n= 1,083, due to missing data) was fit to examine independent associations between these patient characteristics and fentanyl exposure. Independent variables included sex, age, race, marital status, prior history of addiction treatment, prior history of mental health treatment, current co-occurring psychiatric diagnosis, and admission urine test results for other opioids (combined) and cocaine. Responses to the anonymous survey were examined using basic descriptive statistics.

3. Results

3.1. Patient Characteristics and Fentanyl Exposure

Participants from the record review were 65.5% male and 59.6% Black/African American, with a mean (SD) age of 40.7 (11.4) years.

The number of monthly admissions to the treatment program ranged from 143 to 182, with a total of 1,174 over the study period. The overall prevalence of fentanyl-positive urine test results at admission during the 7-month study period was 39%, with monthly prevalence ranging from 23% to 52%. Overall, 6% of newly admitted patients tested positive for fentanyl but not for other opioids. Excluding buprenorphine-positive tests, 9% tested positive for fentanyl but not other opioids (buprenorphine-positive tests at intake could have been due to use of diverted buprenorphine, or recently initiating buprenorphine elsewhere such as a hospital Emergency Department or other provider). Overall, 63% of participants tested positive for any opioid (including fentanyl) at admission, although this fell to 48% when buprenorphine-positive tests were excluded. The rate of positive urine tests for any drug considered (all opioids combined, cocaine, or benzodiazepines) was 80% (72% when tests positive only for buprenorphine were excluded).

Table 1 shows patient characteristics and bivariate comparisons by fentanyl urine test results at admission. Participants who were in their first ever substance use disorder treatment episode were less likely to test positive for fentanyl at admission compared with those who

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

had prior treatment experience (percent fentanyl-positive= 32.0% vs. 40.6% for participants who were treatment-naive vs. had prior treatment experience, respectively; p=. 04). Likewise, participants with a mental health diagnosis in the medical record were less likely to have a fentanyl-positive test compared to participants without such diagnosis (percent fentanyl positive= 36.7% vs. 43.1% for participants with vs. without a mental health diagnosis, respectively; p= .03). In examining mental health diagnoses in more detail, these differences were seen for patients diagnosed with bipolar disorder or schizophrenia/ schizoaffective disorder (Table 1).

Participants who tested positive for other opioids (exclusive of methadone or buprenorphine) were significantly more likely to also test positive for fentanyl than participants who did not test positive for other opioids (percent fentanyl-positive= 81.1% vs. 15.4% for participants with a positive vs. negative test for opioids, respectively; p< .001). Although the proportion of participants testing positive for methadone was low (5.2% overall), these participants were more likely to test positive for fentanyl than participants who tested negative for methadone (percent fentanyl-positive= 59.0% vs. 38.3% for participants with a positive vs. negative test for methadone, respectively; p= .001). Participants who tested positive for cocaine at admission were significantly more likely to also test positive for fentanyl compared to participants with a cocaine-negative urine test result (percent fentanyl-positive= 53.8% vs. 24.9% for participants with a positive vs. negative test for cocaine, respectively; p< .001). There were no significant differences in fentanyl exposure on the basis of admission urine test results for buprenorphine (39.7% vs. 38.5%; p= .72) or benzodiazepines (39.7% vs. 37.1%; p= .51).

In a multivariable logistic regression analysis, the only variables significantly associated with fentanyl exposure were urine test results for other drugs. An opioid positive urine test at admission was strongly associated with fentanyl exposure (Adjusted Odds Ratio [AOR]= 18.6, 95% Confidence Interval [CI]= 13.4, 25.9; p< .001). Testing positive for cocaine at admission was associated with over 2 times higher odds of testing positive for fentanyl (AOR= 2.2, 95% CI= 1.6, 3.0; p< .001).

3.2. Fentanyl Preferences

A summary of responses to the survey questions on fentanyl experiences and preferences are shown in Table 2. Most participants reported having knowingly taken fentanyl that was sold on the street (56.1%), and most participants reported knowing people for whom fentanyl was a preferred drug of choice (65.8%). With respect to personal preferences, only 5.3% reported fentanyl alone as their preferred drug of choice, while a full third of the sample reported a preference for “fentanyl and heroin mix”. Including those who chose multiple options, a sizable minority indicated a preference for fentanyl, either alone or mixed with other opioids (44.7%). Survey results indicated perceived easy availability of fentanyl on the street, with nearly all participants reporting that fentanyl was somewhat or very easy to get. Unadulterated heroin, on the other hand, was viewed as less readily available, with only 29.1% reporting that heroin without fentanyl was somewhat or very easy to obtain.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 3 shows participant perspectives on fentanyl withdrawal as compared to heroin. In general, participants viewed fentanyl withdrawal as having faster onset, higher severity, and longer duration relative to heroin withdrawal.

4. Discussion

The proliferation of fentanyl and fentanyl analogues has contributed greatly to overdose mortality, which continues to affect communities across the US. The age of fentanyl has dramatically altered heroin markets and risks, shifting the contours of the opioid epidemic more quickly than public health efforts to address it (Ciccarone, 2017). This study found high rates of fentanyl exposure among new admissions to OUD treatment, and identified patient characteristics that were associated with a fentanyl-positive urine test result at admission. There has been some debate in the field about the degree to which people are using fentanyl intentionally or unintentionally. Although fentanyl is often seen as an undesirable adulterant in the heroin supply, our findings suggest that a small but significant minority of individuals with OUD may have actually developed preferences specifically for fentanyl or fentanyl-containing opioids. These findings echo earlier work from qualitative research, which has shown a wide range of demand-side responses to the influx of fentanyl (Katz, 2017; Compton et al., 2016). The illicit opioid market (excluding diverted pharmaceuticals) has always had a degree of uncertainty and volatility with respect to product purity and purity-adjusted prices. In the age of fentanyl, however, potency of illicit opioids in terms of morphine milligram equivalents has risen dramatically, while prices have dropped (Ciccarone, 2017).

In addition to increased risk of mortality, preference for the highly potent opioid could plausibly place individuals at elevated risk for early treatment dropout and relapse. This could either be due to the pharmacological implications of fentanyl itself (shortened and intense cycles of euphoria and withdrawal), or to individual patient characteristics that may predispose people towards fentanyl preference in the first place and independently predict poor outcome (e.g., sensation-seeking, impulsiveness). Patient preferences for fentanyl likewise hold implications for public health strategies to address OUD and overdose, such as naloxone distribution, given that reversals may require larger doses or multiple administrations of naloxone (Mayer et al., 2018). More research is needed to delineate preferences for or against fentanyl, determine which aspects of fentanyl are particularly appealing to the subset of patients that express a preference for it, and explore the relative salience of factors such as cost, potency, and specific pharmacological properties.

Compared to morphine, fentanyl is characterized by greater potency, faster onset, and shorter analgesic duration, but with similar or even longer elimination half-life (Comer and Cahill, 2018). As might be expected given these properties, many participants perceived that withdrawal from fentanyl had faster onset and greater severity compared to heroin. Importantly, participants also perceived that fentanyl withdrawal was more prolonged. Whether objectively verifiable or not, patient perspectives about withdrawal can play a role in withdrawal distress and early dropout from treatment.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

It is not yet known whether fentanyl exposure or fentanyl preference are related to treatment response, and these are important lines of future investigation (Comer and Cahill, 2018). At least two recent studies have examined the relationship between fentanyl exposure and outcomes in OUD treatment, one with 154 methadone treatment admissions (Stone et al., 2018) and another with 251 patients in office-based buprenorphine treatment (Wakeman et al., in press). Both studies contrasted patient outcomes on the basis of their urine toxicology at intake. The Stone et al. study found that 80% of patients tested positive for fentanyl at intake, and found no significant differences in treatment retention, abstinence, or relapse between patients who initially tested positive for fentanyl only, other opioids only, or both fentanyl and other opioids over 6 months of follow-up. The study by Wakeman and colleagues found no significant differences in outcomes between patients who initially tested positive for fentanyl and those who initially tested positive for heroin, whereas patients who tested positive for fentanyl were less likely to be abstinent at 6 months compared to those who tested negative at intake for both fentanyl and heroin. However, similar to the current study, there was a high rate of patients who tested negative for both heroin and fentanyl at intake. These studies considered exposure irrespective of intention or preference. More research is needed on the role of fentanyl exposure, and patients' intentions/preferences, in OUD treatment outcomes.

4.1. Limitations

This study has several limitations. The record review and corresponding analysis were subject to the usual limitations of this methodology, which include repurposing data for research purposes that were collected in the ordinary course of clinical care. As such, there was missing data on certain variables, although the extent of missing data was negligible. Although all participants were entering treatment for opioid use disorder, a large number tested negative for any opioids (including but not limited to fentanyl) at admission. Negative baseline urine tests even at treatment admission are not uncommon in studies of this type, and may reflect the length of the intake process, timing of the test, type of opioid used, and time since last use. The real-world implications of urine test results at admission are that they may serve as clinically informative data points (e.g., to identify patients who may be at higher risk of overdose). The determination of fentanyl exposure was based on instant test assay strips, which have become available only relatively recently. These test strips have become more widely used clinically, and have also been applied for detecting the presence of fentanyl in drug samples with high accuracy (Sherman et al., 2018). However, they may not detect all fentanyl analogues or other synthetic opioids, and their detection window is short. Thus, the rate of positive fentanyl tests likely represent a lower bound of recent exposure. Although the examination of fentanyl exposure at admission had a robust sample size, the examination of patient preferences and experiences used a convenience sample and a brief anonymous survey. Thus, in this study we were unable to differentiate between intentional and unintentional exposure to fentanyl in the larger sample of patients admitted to treatment, and could not examine how preferences and perspectives may have differed based on patient characteristics.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

5. Conclusions

This study found high prevalence of fentanyl exposure among patients newly admitted to OUD treatment, examined the characteristics of patients recently exposed to fentanyl, and explored patient experiences and preferences surrounding fentanyl. Individuals who tested positive for fentanyl were similar to those who tested negative for it in terms of demographic variables, although unadjusted analyses indicated some differences on the basis of other drug testing profiles at admission, prior addiction treatment history, and mental health characteristics (in adjusted analyses, only other drug test results were significantly associated with fentanyl). The very strong association between fentanyl test results and other opioid test results likely reflects common routes of exposure via illicit opioid products containing a mix of fentanyl and heroin. This association itself is not surprising, although its magnitude is striking. Evidence of recent cocaine use was associated with double the odds of testing positive for fentanyl. In addition to characterizing patterns of fentanyl exposure, this study demonstrated that preference for fentanyl is a real phenomenon in a substantial minority of patients. Moreover, patients perceive fentanyl as having significant and distinct implications for withdrawal onset, severity, and duration. Future research should examine fentanyl preferences in more detail and determine the extent to which fentanyl use and patient preferences for fentanyl impact OUD treatment engagement and outcomes. This study is but an initial step in what should be a broader effort to investigate the dynamics of fentanyl and its implications for OUD treatment.

Acknowledgments

Role of funding source

JG, RPS, and SGM were supported by National Institute on Drug Abuse grants R21DA047580, R01DA037942, and R01DA036604. NIDA had no role in the study design, collection, analysis or interpretation of the data, writing, or the decision to submit the article for publication

References

Amlani A, McKee G, Khamis N, Raghukumar G, Tsang E, Buxton JA, 2015 Why the FUSS (Fentanyl Urine Screen Study)? A cross-sectional survey to characterize an emerging threat to people who use drugs in British Columbia, Canada. Harm. Reduct. J. 12, 54. [PubMed: 26577516]

Carroll JJ, Marshall BDL, Rich JD, Green TC, 2017 Exposure to fentanyl-contaminated heroin and overdose risk among illicit opioid users in Rhode Island: A mixed methods study. Int J Drug Policy 46, 136–145. [PubMed: 28578864]

CDC, 2018 Provisional counts of drug overdoses. Available at: https://www.cdc.gov/nchs/data/health_policy/monthly-drug-overdose-deathestimates.pdf (Accessed on November 12, 2018).

Ciccarone D, 2017 Fentanyl in the US heroin supply: A rapidly changing risk environment. Int J Drug Policy 46, 107–111. [PubMed: 28735776]

Ciccarone D, Ondocsin J, Mars SG, 2017 Heroin uncertainties: Exploring users' perceptions of fentanyl-adulterated and -substituted 'heroin'. Int J Drug Policy, 46.

Cicero TJ, Ellis MS, Harney J, 2015 Shifting Patterns of Prescription Opioid and Heroin Abuse in the United States. N Engl J Med. 373, 1789–1790.

Comer SD, Cahill CM, 2018 Fentanyl: Receptor pharmacology, abuse potential, and implications for treatment. Neurosci Biobehav Rev.

Compton WM, Jones CM, Baldwin GT, 2016 Relationship between Nonmedical Prescription-Opioid Use and Heroin Use. N Engl J Med. 374, 154–163. [PubMed: 26760086]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Dasgupta N, Creppage K, Austin A, Ringwalt C, Sanford C, Proescholdbell SK, 2014 Observed transition from opioid analgesic deaths toward heroin. Drug Alcohol Depend. 145, 238–241. [PubMed: 25456574]

Hayashi K, Milloy MJ, Lysyshyn M, DeBeck K, Nosova E, Wood E, Kerr T, 2018 Substance use patterns associated with recent exposure to fentanyl among people who inject drugs in Vancouver, Canada: A cross-sectional urine toxicology screening study. Drug Alcohol Depend. 183, 1–6. [PubMed: 29220642]

Jones AA, Jang K, Panenka WJ, Barr AM, MacEwan GW, Thornton AE, Honer WG, 2018 Rapid Change in Fentanyl Prevalence in a Community-Based, High-Risk Sample. JAMA Psych. 75, 298–300.

Jones CM, Einstein EB, Compton WM, 2018 Changes in synthestic opioid involvement in drug overdose deaths in the United States, 2010–2016. JAMA, 319(7), 1819–1821. [PubMed: 29715347]

Katz J, 2017 The first count of fentanyl deaths in 2016: Up 540% in three years. New York Times 9 2, 2017. Accessed at: https://www.nytimes.com/interactive/2017/09/02/upshot/fentanyl-drug-overdose-deaths.html

Kenney SR, Anderson BJ, Conti MT, Bailey GL, Stein MD, 2018 Expected and actual fentanyl exposure among persons seeking opioid withdrawal management. J Subst Abuse Treat. 86, 65–69. [PubMed: 29415853]

Kilwein TM, Hunt P, Looby A, 2018 A descriptive examination of nonmedical fentanyl use in the United States: Characteristics of use, motivates, and consequences. J Drug Issues 1–12.

Macmadu A, Carroll JJ, Hadland SE, Green TC, Marshall BD, 2017 Prevalence and correlates of fentanyl-contaminated heroin exposure among young adults who use prescription opioids non-medically. Addict Behav. 68, 35–38. [PubMed: 28088741]

Mars SG, Ondocsin J, Ciccarone D, 2017 Sold as Heroin: Perceptions and Use of an Evolving Drug in Baltimore, MD. J Psychoactive Drugs 1–10. [PubMed: 27918874]

Mars SG, Ondocsin J, & Ciccarone D, 2018 Toots, tastes, and tester shots: User accounts of drug sampling methods for gauging heroin potency. Harm Reduct. J. 15: 26. [PubMed: 29769132]

Maryland Department of Health, 2018 Unintentional drug- and alcohol-related intoxication deaths in Maryland. Available at: https://bha.health.maryland.gov/OVERDOSE_PREVENTION/Documents/Quarterly%20Drug_Alcohol_Intoxication_Report_2017_Q3_20171210%20(2)%20(1)%20(1).pdf . (Accessed on November 12, 2018).

Mayer S, Boyd J, Collins A, Kennedy MC, Fairbairn N, McNeil R, 2018 Characterizing fentanyl-related overdoses and implications for overdose response: Findings from a rapid ethnographic study in Vancouver, Canada. Drug Alcohol Depend. 193, 69–74. [PubMed: 30343236]

O'Donnell JK, Halpin J, Mattson CL, Goldberger BA, Gladden RM, 2017 Deaths Involving Fentanyl, Fentanyl Analogs, and U-47700 — 10 States, July–December 2016. MMWR Morb Mortal Wkly Rep. 1197–1202. [PubMed: 29095804]

Palamar JJ, Salomon A, Bigiarini R, Vincenti M, Acosta P, Tofighi B, 2019 Testing hair for fentanyl exposure: A method to inform harm reudction behavior among individuals who use heroin. Am J Drug Alcohol Abuse, 45(1), 90–96. [PubMed: 30601034]

Prekupec MP, Mansky PA, Baumann MH, 2017 Misuse of Novel Synthetic Opioids: A Deadly New Trend. J Addict Med. 11, 256–265. [PubMed: 28590391]

Rudd RA, Aleshire N, Zibbell JE, Gladden RM, 2016 Increases in Drug and Opioid Overdose Deaths--United States, 2000–2014. MMWR Morb Mortal Wkly Rep. 64, 1378–1382. [PubMed: 26720857]

Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. 2019 Drug and opioid-involved overdose deaths – United States, 2013–2017. MMWR Morb Mortal Wkly Rep. 1419–1427.

Sherman SG, Park JN, Glick J, McKenzie M, Morales K, Christensen T, Green TC. (2018) FORECAST Study Summary Report. Johns Hopkins Bloomberg School of Public Health.

Stone AC, Carroll JJ,. Rich JD, & Green TC, 2018 Methadone maintenance treatment among patients exposed to illicit fentanyl in Rhode Island: Safety, dose, retention, and relapse at 6 months. Drug Alcohol Depend. 192(1), 94–97. [PubMed: 30243145]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Suzuki J, El-Haddad S, 2017 A review: Fentanyl and non-pharmaceutical fentanyls. Drug Alcohol Depend. 171, 107–116. [PubMed: 28068563]

Tedesco D, Asch SM, Curtin C, Hah J, McDonald KM, Fantini MP, HernandezBoussard T, 2017 Opioid Abuse And Poisoning: Trends In Inpatient And Emergency Department Discharges. Health Aff (Millwood) 36, 1748–1753. [PubMed: 28971919]

Wakeman SE, Chang Y, Regan S, Yu L, Flood J, Metlay J, & Rigotti N. (in press). Impact of fentanyl use on buprenorphine treatment retention and opioid abstinence. J Addict Med.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Highlights

- Many patients entering OUD treatment test positive for fentanyl at admission.
- Fentanyl exposure was strongly associated with testing positive for other opioids and cocaine.
- Preference for fentanyl as a drug of choice was expressed by 44.7% of participants.
- Relative to heroin, participants perceived fentanyl withdrawal as having faster onset, greater severity, and longer duration.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 1.

Patient characteristics by fentanyl urine test results at admission (*N*=1,174 unless otherwise noted).

		Fentanyl test results at admission		
	Total sample *N*= 1,174	**Negative *n*= 712**	**Positive *n*= 462**	**p-value**
Age, mean (SD)	40.7 (11.4)	40.7 (11.6)	40.7 (11.2)	.97
	%, column (n)	*%, row (n)*	*%, row (n)*	
Sex				.58
Male	65.5 (769)	60.1 (462)	39.9 (307)	
Female	34.5 (405)	61.7 (250)	38.3 (155)	
Race [1]				.05
Black/African-American	59.6 (689)	63.0 (434)	37.0 (255)	
White/Other	40.4 (468)	57.3 (268)	42.7 (200)	
Marital Status [2]				.17
Currently married	5.5 (63)	52.4 (33)	47.6 (30)	
Not currently married	94.5 (1,088)	61.0 (664)	39.0 (424)	
Prior substance use treatment, lifetime [3]				.04
Yes	86.2 (952)	59.4 (565)	40.6 (387)	
No	13.8 (153)	68.0 (104)	32.0 (49)	
Prior mental health treatment, lifetime				.24
Yes	73.9 (868)	61.6 (535)	38.4 (333)	
No	26.1 (306)	57.8 (177)	42.2 (129)	
Current mental health diagnosis				.03
Yes	58.7 (689)	63.3 (436)	36.7 (253)	
No	41.3 (485)	56.9 (276)	43.1 (209)	
Specific mental health diagnoses				
Major depressive disorder				.92
Yes	40.3 (473)	60.5 (286)	39.5 (187)	
No	59.7 (701)	60.8 (426)	39.2 (275)	
Anxiety disorder				.54
Yes	20.1 (236)	58.9 (139)	41.1 (97)	
No	79.9 (938)	61.1 (573)	38.9 (365)	
Bipolar disorder				.02
Yes	11.7 (137)	70.1 (96)	29.9 (41)	
No	88.3 (1,037)	59.4 (616)	40.6 (421)	
Post-traumatic stress disorder				.28
Yes	7.1 (83)	66.3 (55)	33.7 (28)	
No	92.9 (1,091)	60.2 (657)	39.8 (434)	
Schizophrenia/schizoaffective disorder				.02
Yes	3.6 (42)	78.6 (33)	21.4 (9)	

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

		Fentanyl test results at admission		
	Total sample *N*= 1,174	**Negative *n*= 712**	**Positive *n*= 462**	**p-value**
No	96.4 (1,132)	60.0 (679)	40.0 (453)	
Selected urine test results at admission				
Other opioids[4]				<.001
Negative	63.5 (746)	84.6 (631)	15.4 (115)	
Positive	36.5 (428)	18.9 (81)	81.1 (347)	
Methadone				.001
Negative	94.8 (1,113)	61.7 (687)	38.3 (426)	
Positive	5.2 (61)	41.0 (25)	59.0 (36)	
Cocaine				<.001
Negative	50.0 (587)	75.1 (441)	24.9 (146)	
Positive	50.0 (587)	46.2 (271)	53.8 (316)	

Column percentages are shown for the total sample; Row percentages are shown for the sample stratified by fentanyl test result. *N*=1,174, except:

[1] *n*= 1,157,

[2] 1,151, and

[3] 1,105 due to missing data.

[4] Not including methadone and buprenorphine.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2.

Patients' experiences and preferences regarding fentanyl (n= 114 unless otherwise noted.)

	Responses
Have you ever knowingly taken fentanyl that was sold on the street?	***Yes: 56.1%***
Do you know any people whose drug of choice is fentanyl?	***Yes: 65.8%***
Before you came to treatment, what was your preferred opioid of choice?	Heroin alone (40.4%) Rx opioids (11.4%) Multiple, not including fentanyl (3.5%) Fentanyl alone (5.3%) Fentanyl and heroin mix (33.3%) Multiple, including fentanyl (6.1%) ***Fentanyl (alone or mix): 44.7%***
If someone wanted to get fentanyl on the street, how difficult would it be to get? (n=105)	Very difficult (1.1%) Somewhat difficult (2.9%) Somewhat easy (20.0%) Very easy (76.2%) ***Somewhat/Very easy: 96.2%***
If someone wanted to get heroin without fentanyl on the street, how difficult would it be to get?	Very difficult (39.1%) Somewhat difficult (31.8%) Somewhat easy (15.5%) Very easy (13.6%) ***Somewhat/Very easy: 29.1%***
Before you came to treatment, if you had $10 to spend on opioids, what would you be most likely to buy?	Heroin alone (36.0%) Rx opioids (12.3%) Multiple, not including fentanyl (<1%) Fentanyl alone (17.5%) Fentanyl and heroin mix (30.7%) Multiple, including fentanyl (6.1%) ***Fentanyl (alone or mix): 50.9%***

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 3.

Patient perceptions of fentanyl withdrawal as compared to heroin.

Fentanyl vs. Heroin: How do you think fentanyl withdrawal compares to heroin withdrawal?	
How soon withdrawal starts after last use (n=101)	Starts later than heroin: 16.8%; About the same: 29.7%; ***Starts sooner than heroin: 53.5%***
The severity of withdrawal (n=103)	Less severe than heroin: 3.9%; About the same: 21.4%; ***More severe than heroin: 74.8%***
How long withdrawal lasts (n=100)	Shorter than heroin: 3.0%; About the same: 35.0%; ***Lasts longer than heroin: 62.0%***