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Association between demographic and drug use characteristics on drug use behaviors following fentanyl testing strip use

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Thesis

ASSOCIATION BETWEEN DEMOGRAPHIC AND DRUG USE CHARACTERISTICS ON DRUG USE BEHAVIORS FOLLOWING FENTANYL TESTING STRIP USE

by

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ABSTRACT

Fentanyl and its analogues are highly potent drugs contributing to the continuous rise in opioid-related drug overdose deaths. This is because of rates of fentanyl use are increasing due to its adulteration in the drug supply as well as intentional fentanyl use. To help combat this public health problem, harm reduction techniques are being used. One notable technique, fentanyl testing strips (FTS), can be used to detect the presence of fentanyl and some analogues from a drug sample. Identification of fentanyl through a FTS may promote the implementation of a behavior, such as deciding not to use the drug, or using the drug while implementing an additional harm reducing behavior. Existing literature suggests that FTS use yields drug use behavior change in some users but not all. We hypothesize that there are certain demographic and drug use characteristics that are associated with drug use behaviors in response to FTS testing. This cross-sectional study will allow for the identification of associations between demographic and drug use characteristics and certain drug use behaviors following FTS use. With data from this study, the efficacy of FTS as a harm reduction technique will be measured; and, with this information, harm reduction recommendations and education can be better-tailored and, thus, more effective at preventing opioid-related drug overdose deaths.

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LIST OF ABBREVIATIONS

BU .... Boston University

DEA .... Drug Enforcement Administration

FTS .... Fentanyl testing strips

NIH .... National Institute of Health

PWID .... People who inject drugs

PWUD .... People who use drugs

SCS .... Safe Consumption Site

SSP .... Safe Syringe Program

INTRODUCTION

Background

Deaths from synthetic opioids, which include high potency drugs like fentanyl and its analogues, are on the rise. In 2020, there were more than 56,000 deaths involving synthetic opioids in the United States, more than any other type of opioid.[1] Most (82%) opioid-related deaths in 2020 were attributed to synthetic opioids, a 56% increase in opioid-related death rates from 2019 to 2020.[1] Compared to 2013, the rate of overdose deaths involving synthetic opioids in 2020 was more than 18 times higher.[1] The Drug Enforcement Administration (DEA) states that the presence of illicit fentanyl is a significant contributor to the increasing rates of overdose deaths in the United States and has identified it as a threat to public health and safety.[2]

In response to the opioid crisis, the pharmaceutical industry and federal agencies have been working to develop technologies that prevent overdose and treat opioid addiction.[3] Fentanyl testing strips (FTS), a technology that is able to detect the presence of fentanyl and its analogues in urine, are currently being used as a method of drug-checking, allowing people who use drugs (PWUD) to detect the presence of fentanyl in their drugs before or after use.[4] FTS work by dissolving a small amount of the drug in water, placing the end of the FTS into the solution and letting it absorb for approximately 15 seconds. The appearance of a single pink line indicates the detection of fentanyl or a fentanyl analog, whereas two pink lines indicates that neither fentanyl nor a fentanyl analog were detected.[5]

Despite their utility, FTS are not being used in full capacity. In a study done by Mistler et al. in 2021 that investigated FTS use among 105 individuals on medications for opioid use disorder, only 47% of participants had knowledge of FTS beforehand and only 17% had prior experience using FTS.[6] This lack of knowledge and utilization, coupled with the fact that FTS are considered drug paraphernalia in many states and are, therefore, illegal, limit the accessibility and utility of FTS as a harm reduction technique.[7] However, this study also found that 85% of participants expressed willingness to use FTS, indicating that there is potential for acceptance and utilization of this harm reduction strategy.[6]

As illicit fentanyl continues to contribute to the rising number of opioid-related overdoses in the United States, emphasis on the implementation of effective harm reduction techniques that address fentanyl adulteration are necessary in order to decrease the morbidity and mortality associated with ingestion of fentanyl; therefore, it is important to evaluate the impact that FTS have on drug use behaviors in specific populations, specifically on overdose prevention.

Statement of the Problem

All demographic groups, including age, gender, and race, are experiencing rising numbers of unintentional opioid-related overdoses, despite the existence of harm reduction strategies, such as naloxone administration, safe consumption sites, needle exchange programs, and FTS.[8] This highlights the presence of barriers to accessible, acceptable, and efficacious harm reduction strategies, which contributes to rising morbidity and mortality associated with fentanyl ingestion.

With the increasing adulteration of the nation's drug supply, it is important for PWUD to know if their drugs contain fentanyl, as this can help inform their decision to use or implement harm reducing behaviors. However, there remains limited evidence on the impact that FTS have on drug use behaviors among PWUD, specifically how demographic and drug use characteristics are associated with drug use behaviors in response to FTS results. A study that can identify demographic and drug use characteristics associated with drug use behaviors following FTS results would allow for the identification of populations at risk of overdose and the creation of a better-tailored approach to harm reduction.

Hypothesis

In the setting of a positive FTS result, certain demographic and drug use characteristics are associated with risk reducing behaviors aimed at preventing overdose.

Objectives and specific aims

The goals of this cross-sectional study will be to identify demographic and drug use characteristics that are associated with certain drug use behaviors following FTS testing. Specifically, this study aims to:

1. Determine the association between demographic and drug use characteristics and drug use behaviors following drug following testing with FTS.
2. Assess the relationship between FTS results and PWUD's drug use behavior.

REVIEW OF THE LITERATURE

Overview

According to the Centers for Disease Control and Prevention (CDC), the number of drug overdose deaths has quintupled since 1999 and, specifically, from 2019 to 2020, the number of deaths has increased by 30%.[9] Of the 91,799 drug overdose deaths in 2020, approximately 75% involved an opioid.[9]

Although important to acknowledge the rising number of fatal overdoses, the impact of this opioid epidemic can also be demonstrated through the rising prevalence of non-fatal overdoses. Specifically, lifetime prevalence of a non-fatal overdoses among PWUD ranges from 16.6 to 68% with an average of 45.4%.[10] Moreover, lifetime prevalence of witnessing an overdose among PWUD ranges from 50% to 96% with an average of 73.3%.[10]

The origin of these increases in morbidity and mortality related to opioids traces back to the 1990s. This is when deaths involving prescription opioids began increasing and is considered the first of three waves of opioid-related overdose deaths in the opioid epidemic. The rise in deaths involving prescription opioids is attributed to the false reassurance pharmaceutical companies gave medical professionals that opioids were non-addictive. This led to an increase in opioid prescriptions before the addictive nature of opioids were fully appreciated and served as the catalyst for the widespread misuse of prescription and eventually non-prescription opioids.[11]

The second wave of opioid overdose deaths began in 2010 and was caused by rapid increases in heroin-related overdose deaths.[9] According to a Morbidity and

Mortality Weekly Report (MMWR) published in 2014, the death rate from heroin overdose in 2010 to 2012 doubled, increasing from 1.0 to 2.1 per 100,000.[12] At the same time, the death rate from opioid pain relivers declined from 6.0 to 5.6 per 100,000 and was found to be negatively correlated to the changes in heroin death rates.[12]

The transition from the first to second wave of opioid overdose deaths highlights the science of addiction. As tolerance grew and people who use drugs (PWUD) required greater drug supplies than they could obtain, users transitioned from opioid pills to heroin, which was cheaper and more readily available.[13] This increasing tolerance, which requires an individual to consume larger amounts of a drug to experience a familiar high, is due to changes in the brain's circuitry. When a person uses a drug, the brain compensates by producing fewer neurotransmitters associated with the reward circuit, thereby impeding a person's ability to derive pleasure from naturally rewarding activities. Because a PWUD experiences less joy from activities that were previously pleasurable, they continue to use drugs to experience a normal level of reward, creating a vicious cycle.[14] This is the reason addiction is considered a disorder of the brain—it involves functional changes in brain circuits that are involved in reward, stress and self-control and these changes may persist for a long time, even if the person stops using drugs.[14] Because of this, addiction is a chronic, relapsing disorder characterized by compulsive drug use, despite knowledge of adverse consequences; this contributes to the current issues associated with the present day opioid epidemic.[14]

The third wave of the opioid epidemic is considered from 2013 to present and is marked by an increase in synthetic opioid-related deaths, particularly illicitly manufactured fentanyl.[15] Since its introduction, illicitly manufactured fentanyl has been found in heroin, counterfeit pills and cocaine, and its market continues to evolve.[15] This puts those who ingest the drug, both intentionally and unintentionally, at great risk because fentanyl is a highly potent drug—50 times stronger than heroin and 100 times stronger than morphine—with a rapid onset of action, which can cause central nervous system depression, possibly leading to a fatal overdose.[16] In addition to the physiological harm associated with fentanyl and its potency, it also makes drugs more addictive and have a lower cost of production. Because of these dangers and its saturation of the drug supply, it is important for PWUD to implement harm reduction behaviors to reduce their risk of overdose.

Designed as a set of strategies aimed at reducing the negative consequences that are associated with drug use, harm reduction techniques have been implemented in attempt to combat the morbidity and mortality associated with fentanyl and its analogues. Some current harm reduction techniques include distribution of naloxone, a nasally administered opioid antagonist that reverses the effects of an opioid, as well as safe consumption sites, which encourage PWUD to not use drugs alone by providing them with a safe, secure place to use.

FTS are a harm reduction technique aimed at preventing unintentional fentanyl exposure. FTS are low-cost strips of paper that are able to detect fentanyl in drug samples that are dissolved in water.[5] Compared to two spectroscopy, FTS had the highest sensitivity and specificity and lowest detection limit.[17] As a result, off-label use of FTS can provide PWUD the ability to test their drugs before ingesting, which can inform their drug use behavior.

Despite their ability to inform drug use behaviors, FTS use does not always evoke the implementation of risk reducing behaviors.[18,19,20] This is because there are numerous factors that influence a PWUD's decision to use. In order to maximize the efficacy of FTS as a harm reduction tool, more needs to be known regarding demographic and drug use characteristics and their association with risk reducing behaviors aimed at preventing overdose in the face of FTS results.

In the setting of a positive FTS result, certain demographic and drug use characteristics are associated with risk reducing behaviors aimed at preventing overdose.

Existing Literature:

FTS are being used as a method of drug checking among PWUD; however, their use varies among drug use and demographic characteristics. In regard to drug use characteristics, based off a sample of safe syringe program (SSP) clients in southern Wisconsin, participants that reported injection drug use, heroin as their drug of choice, polysubstance use, and recent methadone use were more likely to report FTS use.[21] This, coupled with the fact that injection drug use, opioid use and polysubstance use have been associated with risk of overdose, supports the fact that FTS use may be higher among those at higher risk of overdosing.[22] This is further supported by data from a study (2018) by Peiper et al. that examined self-reported FTS results among injection drug users who have previously used FTS in Greensboro, NC. Peiper et al. found that a large number of participants that self-reported previous FTS use noted a lifetime overdose (48%), as well as previous use of naloxone (81%).[18] Additionally, certain drug use characteristics were higher among clients who used FTS compared to those who did not, including the average lifetime opioid overdose count (4.7 among FTS users compared to 3.3 among non-FTS users; unadjusted p = 0.020) and the frequency of using drug of choice (unadjusted p = 0.103).[21]

Similar findings were identified in a study (2019) by Sherman et al. that analyzed intention to utilize FTS and logistical preferences among PWUD.[23] Notably, 90% of participants felt that FTS use would help prevent an overdose, and the majority (54%) of those interested indicated utilizing FTS at least daily.[23] Drug use characteristics associated with intent to use FTS included witnessing at least one fatal overdose (aOR: 0.6, 95% CI: 0.5-0.7) and suspected recent fentanyl exposure (aOR: 1.8, 95% CI: 1.1-3.1).[23]

While it is helpful to know which drug use characteristics are associated with FTS use, it is important to acknowledge there are some drug use characteristics with lower rates of FTS use; specifically, rates of testing were lower in those with regular stimulant use, particularly methamphetamines, as well as among participants who regularly use opioid analgesics.[21] Moreover, additional drug use characteristics showed no association with FTS use, including frequency of drug use, other recent treatments (i.e., non-methadone), and years of drug use.[21] Knowing which drug use characteristics are and are not associated with FTS use allows for a better understanding regarding the populations where FTS use is efficacious.

In addition to drug use characteristics, FTS use also varies among different demographics. In regards to race and ethnicity, there are disparities among FTS use.[21,18] In the same sample of SSP clients from southern Wisconsin, the rates of FTS use were lower among African American clients compared to non-Hispanic White or Hispanic clients ($p = 0.009$).[21] A similar disparity was identified in the sample of self-reported FTS injection drug users in Greensboro, NC where the majority of participants were non-Hispanic White (77.6%) compared to non-Hispanic black (12%) and other (10.4%).[18]

Use of FTS varies among other demographic characteristics. For example, FTS use tends to be higher among young people; the Peiper et al. study (2018), which examined self-reported FTS results among PWUD who have reported previously using FTS, found that 70% of participants were aged 20-39 years old.[18] The idea that those who use FTS tend to be younger is further supported by the Tilhou et al. study (2022) where the average age of participants who used FTS was 35.4 years ($SD = 8.1$).[21] Moreover, the use of FTS is higher among those who are unemployed, males, and those with a high school degree or below, although these characteristics were not found to be statistically significant.[21] Regardless, the variation of FTS use by different demographic characteristics impacts their ability to serve as a harm reduction technique among PWUD.

Use of FTS is not only influenced by demographic or drug use characteristics but by situational, logistical and psychosocial factors, as well. For example, being advised by a supplier about potency or a new batch prompted FTS use, as well as having a private or safe place to use the FTS.[21] A further study (2019) by Goldman et al. attributed the desire to use FTS in private due to fear of judgement, stigmatization and legal ramifications associated with FTS use.[19]Additionally, access to transportation, additional distribution sites and mobile delivery services impact FTS use, highlighting how availability of services impacts their use.[21] Additionally, recommendations from SSP (syringe service program) staff were found to impact FTS use more than counselor or doctor recommendations; however, this finding could reflect the limited access to acceptable health care that many PWUD experience.[21] This highlights how many factors play a role in a PWUD's decision to implement harm reduction techniques, particularly FTS.

Existing literature has highlighted some barriers associated with the implementation of FTS. A study by Bardwell et al. (2019), which examined the willingness among PWUD to use drug checking technologies, identified several factors that undermined the willingness of participants to use drug checking technologies.[24] For example, having to give up a drug sample was commonly identified as a barrier among the participants. As noted by one participant, many do not want to give up a sample because "Every bit makes a difference. It could be that one grain that gets you high, right?"[24] Additional barriers identified were having to wait to get results as well as having doubts regarding the accuracy of drug checking technologies.[24] Participants also noted doubts regarding the efficacy of drug checking technologies, particularly in drug markets saturated with fentanyl; this is because this saturation has resulted in an increase in the willingness to use and preference for fentanyl, thereby limiting the effect of drug checking technologies on overdose prevention.

Although there are known barriers to the implementation of FTS, PWUD have identified some benefits. For example, they are thought to be relatively easy to use.[19]According to one participant in the Goldman et al. study (2019), “I mean the packaging was easy. I mean it’s pretty discreet…they weren’t inconvenient, they weren’t hard to use, they weren’t, you know, embarrassing to be seen with or anything.”[26]

In addition to their ease of use, FTS use is associated with an increased perception of safety among many PWUD. Notably, 77% of participants in the Peiper et al. study (2018) indicated that FTS use increased their overdose safety perception.[18] Of note, there are a few factors that impact the perception of overdose safety with FTS among PWUD. For example, those 40 years old or older reported a higher perceived overdose safety when using FTS than those aged 20-29 (aOR = 3.98, 95% CI = 1.18-13.40).[18] Additionally, non-SSP participants had higher perceived safety than existing SSP clients (aOR = 4.06, 95% CI = 1.63-10.13).[18] The increase in perceived overdose safety due to FTS is thought to be due to FTS’ ability to provide information regarding the presence of fentanyl in drug samples, which helps PWUD make an informed decision.[19] One participant in the Goldman et al. study (2019) stated, “those tests opened my eyes, and it has saved my life, and I can gladly say I haven’t taken any more because I was going to take two bags. If I had took those two bags, I think I wasn’t even going to be here right now.”[19] The idea of increased overdose safety perception is further supported by the fact that many PWUD described distributing FTS to those within their networks who they feel are at risk of using a drug with fentanyl.[19] However, it is important to highlight that an increase in perceived overdose safety is different than actual increased overdose safety; the ability of FTS to serve as an efficacious harm reduction tool is limited by their ability to cause drug use behavior change.

The efficacy of FTS as harm reduction techniques is highlighted in the Karamouzian et al. (2018) cross-sectional study that evaluated drug checking intervention on clients at a supervised injection facility.[25] Of participants with a positive pre-consumption drug check, 36.3% reported plan to reduce the dose of their drug, and 11.4% reported plan for disposal of their drug.[25] And although the odds of overdose were higher among participants with a positive drug check compared to those with a negative drug check (OR = 5.97; 95% CI 2.41-14.78), only 4.5% of those who planned to reduce the dose of their drug overdosed.[25] Moreover, intention to reduce dose was associated with both lower odds of overdose (OR = 0.41; 95% CI 0.18-0.89) and naloxone administration (OR = 0.38; 95% CI 0.15-0.96).[25] While intent to implement certain harm reduction behaviors following use of a drug checking technology is associated with lower odds of overdose, it is important to highlight that they do not always evoke behavior change.

Use of FTS elicits behavior change in some, but not all, thereby limiting their efficacy among all PWUD. In Goldman et al.'s study (2019), of the participants that reported a positive FTS, approximately half reported changing the way they used their drug.[19] Specifically, 45.2% used less, 38.7% used with someone else around, 41.9% went slower, 35.5% used a tester shot, 9.7% threw the drug out, 9.7% sold the drug, and 6.5% gave the drug away.[19] Similar findings were identified in Peiper et al.'s study (2018) where 43% reported behavior changes in response to FTS results.[18] Specifically, of those who reported a behavior change, 32% used less of the drug, 17% used a tester shot, 10% snorted instead of injecting, and 9% reported pushing the drug more slowly.[18]

As with Goldman et al. (2019) and Peiper et al. (2018) studies, a pilot study (2022) by Goodman-Meza et al. also identified that use of FTS only yields behavior change in some participants.[18,19,20] Although this preliminary study only examined the injection behavior of 30 women in Mexicali, Mexico at an unsanctioned safe consumption site, it found that half (N=15) of the substances tested positive for fentanyl via FTS; of those whose drugs tested positive with FTS, 8 participants reported some behavior change with 7 (47%) using less of the substance and one not it at all.[20] The remaining participants (n=7; 47%) did not change their behavior in response to the positive FTS.[20] As indicated in the above studies, only half of those with a positive FTS altered their drug use behavior that improved their overdose safety.

Decisions to implement a harm reducing behavior in response to an FTS result are highlighted in a study by Weicker et al. (2020). Many participants believed that FTS had utility, with one participant noting “You know, using [raw] heroin, I was more relaxed when I knew what was in it. Or I’m like ‘Damn, it has heroin and fentanyl.’ So, I should do this much instead of doing that much.”[26] Additionally, participants noted that FTS use allowed them to inform their drug purchases and negotiate with dealers.[26] Moreover, participants noted that FTS use had the ability to promote transparency in the drug market, with one participant describing how he would inform others of positive test results.[26]

While existing literature suggests that FTS use motivated safer behaviors, their use can also result in the implementation of riskier behaviors. At baseline, when comparing differences in overdose risk among individuals that do and do not use FTS for drug check, those who do use FTS were found to perform both safer ($p = 0.001$) and riskier behaviors ($p = 0.018$) than those who do not.[27] Moreover, in cases of suspected fentanyl adulteration, unadjusted models found that FTS use was associated with both safer ($p = 0.033$) and riskier behaviors ($p < 0.001$), although the impact of FTS on safer behaviors lost significance in fully adjusted models ($p = 0.143$).[27] Although the study was cross-sectional and, therefore, cannot identify whether use of FTS is what prompted the implementation of riskier behaviors, the higher rates of both riskier and safer behaviors among those who use FTS raises concerns regarding the ability of drug-checking services to encourage compensatory drug use behaviors.[27] Regardless, the implementation of safer behaviors in conjunction with the riskier behaviors highlights that many make attempts to minimize the risk of harm associated with drug use.[27] When used, FTS can evoke no behavior change, safer behavior or riskier behavior; its ability to change behavior, if at all, is influenced by many factors.

Barriers to the acceptability of FTS influence the ability of FTS to evoke behavior change. Several barriers are identified in a study (2018) by Bardwell et al.. For example, primary drug of choice and drug preferences were found to be of influence[24] When asked who would dispose of their drug in the face of a positive result, one participant noted "No…well I'm only thinking of heroin users. But if I was a jib (e.g., crystal methamphetamine) user and there was a down (i.e., opiates) in it, they would have to throw it away."[24] Moreover, the saturation of the drug supply with fentanyl was noted to impact the efficacy of drug checking technologies on influencing behavior and preventing overdose; specifically, participants noted that the saturation has resulted in an increase in the willingness to use and preference for fentanyl, making behavior change less likely.[24]

A PWUD's desire to use fentanyl has the ability to influence if harm reduction behaviors are implemented. Highlighted in Mars et al. ethnographic study (2017), many participants acknowledged the danger associated with the adulterated drug supply but described being attracted to it, nonetheless.[28] Participants noted enjoying the "rush" and explained that fentanyl can be associated with heighted pleasure, making it worth seeking out.[28] One participant, who has been using since the 1960s, stated that once people experience fentanyl and, more importantly, survive it, they are more likely to want to use it again because of the heightened pleasure.[28] This reality, described as "like Russian roulette", was noted to be accepted by some participants in the 2017 Mars et al. study; because of this acceptance, these participants reported not taking precautions when it came to ingesting.[28] Similar sentiments were echoed in anethnographic study (2017) by Ciccarone et al. where a "powerful rush sensation" was continuously attributed to the benefit of fentanyl and its analogues.[29] Moreover, Peiper et al.'s study (2018) noted that of the 81% of participants who used FTS prior to consuming drugs, 31% reported doing so because they were seeking fentanyl.[18] This preference for fentanyl among some PWUD highlights how the saturation of the drug supply with fentanyl has resulted in an increase in exposure to fentanyl, as well as an increased physical dependence on and greater tolerance to fentanyl among PWUD.[18] And, while this may not directly decrease the rate of FTS use, given some are using FTS to seek out fentanyl, it impacts its efficacy as a harm reduction tool to change behavior.

Overall, the decision to implement a harm reducing behavior is influenced by a variety of factors. While the literature has identified demographic and drug use characteristics associated with FTS use, more needs to be known about the impact that FTS use has on the decision to use. Because of this, a cross-sectional study identifying the demographic and drug use characteristics that influence drug use behaviors following FTS use is needed.

METHODS

Study Design

This will be a cross-sectional study. It will be conducted at OnPoint NYC Overdose Prevention Center (OPC), a safe consumption site (SCS). The study will assess demographic characteristics, injection practices and patterns of substance use associated with drug behaviors following FTS results. This will be performed by having clients at OnPoint NYC Overdose Prevention Center, a SCS, fill out a quantitative survey with information about their demographic information and drug use practices. Afterwards, an employee at OnPoint NYC will test the client's drug with a FTS and will inform the client of the result (i.e., positive or negative). The clients will then complete another survey where they indicate how they plan on using their drug (i.e., identify their drug use behavior) within the SCS. The options for drug use behaviors will be: do not use drug; use drug with additional harm reduction behavior (i.e., using slowly, using tester shot, using less, etc); and use drug. The objective will be to evaluate if there are differences in demographic characteristics, injection practices and patterns of substance use among the drug use behaviors in response to the clients' FTS results.

Study Population and Sampling

Participants are a sample of clients at OnPoint NYC Overdose Prevention Center's safe consumption site. Inclusion criteria include: being at least 18 years old with self-reported recent drug injection (within past 30 days) with plan to use their drug at the SCS. Additionally, the clients must be willing to provide a small sample of their drug for testing with a FTS. Exclusion criteria include those whom employees deem acutely intoxicated or if use of drug poses a risk to the client (i.e., person appears lethargic or somnolent; person is visibly ill).

To calculate sample size, the primary aim is to determine the association of demographic and drug use characteristics among the different drug use behaviors in response to the clients' FTS result. The study will specifically focus on identifying associations between demographic and drug use characteristics and drug use behaviors in the setting of a positive FTS result. Therefore, when analyzing the primary outcome, each demographic or drug use characteristic will be categorized by identified drug use behavior following positive FTS result—did not use drug, used drug with harm reducing behavior, or used drug. One drug use characteristic being studied is experiencing an overdose in the past 12 months. The estimated effect size was determined based on the fact that a multi-stage systematic review and meta-analysis suggested that 15-26.1% of people who inject drugs (PWID) experienced a non-fatal overdose within the 12 months being studied.[30] Therefore, with 2 degrees of freedom, an assumed effect size of 0.25, alpha of 0.05 and beta of 0.8, a minimum sample size of 155 is needed.

Intervention

Study participants will first complete an online, anonymous quantitative survey (Figure 1) about demographic characteristics and drug use behaviors. After completing the survey, study participants will give a small sample of their drug to a staff member who will use it for testing with Rapid Response FTS. The staff member will place 5 mg of the drug sample in a 88 ml cup then mix with 5 ml of tap water; the Rapid Response

FTS will then be placed in the cup for 15 seconds and the results will be read (i.e., two lines indicates negative for fentanyl, one line indicates positive for fentanyl) after 5 minutes, per manufacturer's recommendations.[31] A staff member will then inform the client of the result. After being informed of the FTS result, the clients will fill out an additional online survey where they will indicate their drug use behavior (i.e., will not use drug; will use drug with harm reduction behavior; will use drug).

Figure 1: Example of quantitative survey to be used in this study

Age: ____

Gender:
- [ ] Man
- [ ] Nonbinary
- [ ] Trans
- [ ] Women

Race:
- [ ] American Indian or Alaska Native
- [ ] Asian
- [ ] Black or African American
- [ ] White
- [ ] Other

Are you Hispanic or Latino?
- [ ] Yes
- [ ] No

Education:
- [ ] Less than high school degree
- [ ] High school, GED or equivalent
- [ ] Some college, trade school, or 2 year college
- [ ] 4 year college or beyond

Employment:
- [ ] Employed and not job-seeking
- [ ] Unemployed and not job-seeking
- [ ] Unemployed and job-seeking

Years of drug use: ____

Age at first regular drug use: ____

Current drug of choice:
- [ ] Heroin
- [ ] Fentanyl

[ ] Opioid analgesics
[ ] Cocaine or crack cocaine
[ ] Methamphetamines
[ ] Synthetics
[ ] Prescription anxiety drugs
[ ] Prescription amphetamines
[ ] Other

In the past 3 months, have you been exposed to fentanyl?
[ ] Yes
[ ] No

If answered yes to the above question, were you trying to get drugs with fentanyl?
[ ] Yes
[ ] No

In general, how often do you try to get drugs with fentanyl?
[ ] Every time
[ ] Most of the time
[ ] Sometimes
[ ] Rarely
[ ] Never

Usual route of drug use.
[ ] Inject or shoot into vein
[ ] Inject or shoot into muscle
[ ] Snort it
[ ] Smoke it
[ ] Eat or swallow it
[ ] Insert it rectally
[ ] Other

In the past 30 days, how frequently have you used drug of choice?
[ ] Less than once per day
[ ] 1 time per day
[ ] 2 times per day
[ ] 3 or more times per day

Polysubstance use?
[ ] Yes
[ ] No

Have you experienced an overdose in the past 12 months?
[ ] Yes
[ ] No

In the past 30 days, have you used medications to stop or reduce use?
[ ] Yes
[ ] No

If answered yes to the above question, which type of medication have you used?
[ ] Buprenorphine formulations
[ ] Extended-release naltrexone

[ ] Methadone [ ] Other Indicate which, if any, of the following strategies you implement when using? [ ] Use with others [ ] Personally carry naloxone (Narcan) [ ] Make sure others around you carry naloxone (Narcan) [ ] Use a tester shot [ ] Use in smaller doses [ ] Other [ ] None If indicated yes to any of the above strategies, how often do you implement them when using? [ ] Every time [ ] Most of the time [ ] Sometimes [ ] Rarely

Study Variables and Measurement Tools

The variables this study will evaluate are demographic characteristics, patterns of substance use and injection practices of the study participants in relation to their drug use behavior following FTS testing (Table 1). The primary outcome measure is identifying certain demographic and drug use characteristics associated with risk reducing behaviors aimed at preventing overdose in the face of a positive FTS result. The results will be stratified based on what the study participants self-report as their planned drug use behavior via an online survey.

Table 1: Variables to be measured in this study

Demographic characteristics	• Age • Gender

	• Race • Ethnicity • Education • Employment status
Drug use characteristics	• Years of drug use • Primary drug of choice • Drug use frequency • Polysubstance use • Lifetime overdose count • Harm reduction techniques • Recent exposure to fentanyl • Usual route of injection

Recruitment

Participants will be recruited as they enter OnPoint NYC Overdose Prevention Center by their employees. Clients will be asked to participate upon entering the SCS and prior to injecting their drug. Participants will fill out an informed consent form with an OnPoint NYC Overdose Prevention Center employee.

Data Collection

Immediately following consent, the participant will be given a tablet to fill out the anonymous, online quantitative survey via Redcap about demographic information and drug use characteristics. Following the testing of the drug with FTS and being informed of the result, participants will use the same tablet to fill out another survey to indicate how they plan to use their drug (Figure 2). Of note, the survey regarding drug use behavior will be done prior to injecting the drug and within the SCS.

Figure 2: Example of drug use behavior survey to be used in this study

FTS result:
- [ ] Positive
- [ ] Negative

How do you plan on using your tested drug today?
- [ ] I do not plan on using tested drug
- [ ] I plan on sharing my drug with someone else
- [ ] I plan on using tester dose
- [ ] I plan on using a smaller dose than I normally would
- [ ] I plan on pushing the drug slower than normal
- [ ] I plan on using tested drug

After the client leaves the SCS, the client's drug use behavior based will be interpreted based on what was indicated on the Recap drug use behavior survey and will be added to the dataset. If the client indicates any of the following, they will be recorded as having "used the drug with a harm reduction behavior:"

- "I plan on sharing my drug with someone else"
- I plan on using a tester dose"
- "I plan on using a smaller dose than I normally would"
- "I plan on pushing the drug slower than normal"

If the client indicates “I do not plan on using tested drug”, they will be recorded as having “not used tested drug.” If the client indicates “I plan on using tested drug,” they will be recorded as having “used the tested drug.”

Once the drug use behavior is encoded, an employee will record this in a file that contains the client’s anonymized demographic and drug use characteristic data.

Analysis

Descriptive statistics will summarize the demographic and drug use characteristics for the sample; associations between drug use behavior following FTS result and demographic and drug use characteristics will be determined using chi-square tests.

The primary aim is to determine the association of demographic and drug use characteristics among the different drug use behaviors in response to the clients’ FTS result. Specifically focusing on the relationship between an overdose within the past 12 months with drug use behaviors in the face of a positive FTS result, participants will be dichotomized into two groups: those who have experienced an overdose in the past 12 months and those who have not experienced an overdose in the past 12 months. Then, chi-square will be used to determine the significance of the association between lifetime overdose count and drug use behavior.

The secondary aim is to summarize the demographic and drug use characteristics of the sample. This will be done with descriptive statistics.

Timeline and Resources

This study is expected to be 6 months in duration. The first month will be dedicated to creating the online surveys and having them translated into Spanish, Portuguese and Haitian Creole by a medical interpretation service. Once the surveys have been completed, the study will be submitted for IRB approval; this is expected to take approximately 2 months.

Once approval is obtained, employees at OnPoint NYC Overdose Prevention Center will be trained by members of the research regarding this study. Specifically, they will be trained in how to obtain informed consent, how to use the Rapid Response FTS, and how to interpret and record the data from the drug use behavior survey. This will be expected to take 1 month.

Per OnPoint NYC Overdose Prevention Center, they provided 2,841 individuals with a safe place to use within 12 months with 613 of these participants during the first 2 months.[32] It will be assumed that not all OnPoint NYC Overdose Prevention Center clients will want to participate in this study; so even though data suggests that OnPoint NYC Overdose Prevention Center sees well over the minimal sample size (n = 155) needed for this study in 2 months, we will budget this time to account for those who elect to not participate.

In regard to resources, 10 tablets will be needed, as well as Rapid Response FTS and 88 ml paper cups.

Institutional Review Board

Although participants in this study may be using drugs which in itself poses a risk, this study is strictly observational; therefore, the study itself is not posing more than minimal risk to its subjects. Additionally, this study involves research on individual characteristics or behavior or research employing a survey, thus meeting criteria for a category 7 expedited review based on the Common Rule (10.2.2.4.1.2).

CONCLUSION

Discussion

This study will investigate the demographic and drug use characteristics associated with drug use behaviors following drug testing with FTS. Previous studies have identified demographic and drug use characteristics of those who use FTS, as well quantified drug use behavior in response to positive and negative FTS results. This study adds to the literature by uniquely assessing decisions to use drugs in real-time based on FTS results. Thus, this study adds more robust evidence to the literature about the relationship between FTS use and both subsequent drug use behaviors as well as demographic and drug use characteristics. This has important public health implications, as it will allow providers to identify which groups to emphasize other harm reduction techniques.

This study has several limitations. This observational study cannot estimate the causal effect of FTS results on drug use behaviors, nor of the impact of FTS use on overdose risk. Additionally, the self-reported nature of this study may introduce a social desirability bias. In an attempt to behave in a more “desirable” way, study participants may choose to not use a drug or to implement a harm reduction technique while using when they normally do not, or simply report that they did. As a result, this study may mischaracterize drug use in response to FTS results and, therefore, not accurately estimate the association between drug use behaviors after a positive FTS result with demographic and drug use characteristics. In this study, all participants come from SCS. This may impact the generalizability of the results, such as if clients of SCS are more

Summary

FTS are an important harm reduction technique that can be used to combat persistently rising rates of opioid overdose mortality.

However, FTS use does not automatically warrant drug behavior change in all. While there is existing research analyzing why, as well as which specific demographic and drug use characteristics are associated with FTS use, the association of these characteristics with drug behaviors in response to FTS use remains understudied. This proposed study will help quantify which demographic and drug use characteristics are associated with specific drug use behaviors following FTS use and has the potential to better quantify the efficacy of FTS as a harm reduction technique.

Clinical and Public Health Significance

The proposed study has the potential to inform both clinical practice, as well as public health and policy. Regarding clinical practice, this proposed study may provide insight into the efficacy of FTS, which is dependent on FTS utilization, as well as their ability to influence drug use behavior. Importantly, this proposed study will be helpful in identifying which demographic and drug use characteristics are associated with no behavior change in the face of a positive FTS result. As a result, it will allow providers to better-tailor their recommendations and education when it comes to harm reduction. From a public health perspective, a more individualized approach to harm reduction has the potential to decrease the number of fentanyl-related overdose deaths.

Additionally, there are still a few states where FTS are considered drug paraphernalia; if this study finds that use of FTS is associated with behavior changes that reduce the risk of overdose for certain populations, it may provide additional support for their legalization.

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