



Characterizing fentanyl use in methadone-maintained clients



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ABSTRACT

Aims: Deaths attributed to fentanyl have increased in the United States. However, little is known about fentanyl use among substance abuse treatment clients. To fill this gap, we assessed prevalence of fentanyl exposure, characteristics of clients testing positive for fentanyl, other substances detected concurrently or simultaneously with fentanyl, and clients' perception of how many people are actively seeking to use fentanyl.

Methods: A retrospective chart review was conducted of all clients at one methadone maintenance treatment clinic between January 2015 and May 2016 in Wayne County, Michigan. Urine drug screens (UDS) including fentanyl (and its metabolite norfentanyl) were conducted clinically. To obtain additional data, 113 clients in this clinic subsequently completed an anonymous survey.

Results: Of 368 unique clients with UDS, 38.0% had at least one and 26.1% had ≥ 2 fentanyl-positive UDS results. None had a fentanyl prescription. Clients ever testing positive for fentanyl were significantly ($p < 0.05$) more likely to use cocaine, have multiple treatment admissions to the clinic, and leave treatment sooner. Fentanyl-positive UDS results coincided most commonly with metabolites of cocaine- and heroin-positive UDS results. Of the anonymously surveyed clients, most (67.3%) reported they did not know anyone seeking fentanyl, a proportion significantly higher than for heroin, cocaine, alprazolam, hydrocodone and morphine.

Conclusions: Fentanyl was commonly detected during this period with some clients having multiple fentanyl-positive UDS. Most clients did not know anyone seeking to obtain fentanyl. Regardless, the high exposure underscores that naloxone training and distribution is needed.

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1. Introduction

Fentanyl, a Schedule II medication that is a mu-opioid receptor agonist and about 50–100 times more potent than morphine (DEA, 2016a; EMCDDA, 2015; Volpe et al., 2011), is linked to an increasing number of deaths in the U.S. (Gladden, Martinez, & Seth, 2016), Canada (Canadian Centre on Substance Abuse, 2015), and other countries (Mountney, Giraudon, Denissov, & Griffiths, 2015). In six U.S. states with published data on fentanyl-specific deaths, the number of deaths increased from 392 in 2013 to 1400 in 2014 without a corresponding increase in the quantity of prescription fentanyl medication dispensed (Gladden et al., 2016). The rapid increase in fentanyl-related and other opioid-related deaths in the U.S. prompted the Centers for Disease Control and Prevention (CDC) and Drug Enforcement Administration (DEA) to issue nationwide public health alerts (CDC, 2015; DEA, 2015b).

The increase in fentanyl-related deaths, although concentrated in some states, also corresponds with a 426% increase in the number of fentanyl seizures by law enforcement from 2013 to 2014 (Gladden

et al., 2016). Moreover, the fentanyl appears to be imported from legal manufacturers and mixed with or sold as heroin or cocaine (DEA, 2015b, 2016b). Thus, the fentanyl being distributed does not appear to be illegally made or diverted from patients. There are also scattered reports of fentanyl found in pills sold as hydrocodone/acetaminophen or alprazolam (Arens, van Wijk, Vo, Lynch, Wu, & Smollin, 2016; Armenien, Olson, Anaya, Kurtz, Ruegner, & Gerona, 2016), indicating other paths to fentanyl exposure.

Unfortunately, little is known about illegal fentanyl use and if people actively seek it. To improve understanding and public health, we need data from individuals who were exposed to fentanyl. One small study of people visiting harm reduction sites in British Columbia reported 29% tested positive for fentanyl in urine drug screens (UDS) although only 13% of people indicated they had consumed fentanyl (Amlani, McKee, Khamis, Raghukumar, Tsang, & Buxton, 2015). These findings suggest that people are unknowingly being exposed to fentanyl. However, more studies are needed.

1.1. Michigan and Wayne County data

Michigan has been highlighted as one of 14 states with a significant recent increase in drug-overdose deaths (Rudd, Aleshire, Zibbell, &

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Gladden, 2016). In 2000, the age-adjusted drug overdose rate in Michigan was 8.8 per 100,000; by 2014, the rate was 21.0 per 100,000; and by 2015, it had climbed to 23.9 per 100,000 (CDC Wonder, 2016). The corresponding age-adjusted rates for the U.S. for these same years were 8.9, 14.2 and 15.6 per 100,000. The largest county within Michigan, Wayne County (population 1.76 million, U.S. Census Bureau, 2015), also has experienced an increase in age-adjusted drug overdose rate: 17.5 in 2000, 27.9 in 2014 and 36.5 per 100,000 in 2015.

In addition to the increase in drug overdose deaths, there has been a recent increase in number of drug-related deaths with fentanyl detected in Wayne County (Arfken, 2015; Arfken, 2016). In fiscal year 2013, there were 11 overdose deaths with fentanyl with the numbers in subsequent years climbing to 37 and then to 148. For the six-month period from January to June 2016, the number of overdose deaths with fentanyl was 168.

Another indicator of illegally distributed fentanyl in Wayne County is the number of drug items seized by law enforcement and subsequently identified as fentanyl. During 2014, there were 7 items identified as fentanyl out of 7762 items analyzed (Arfken, 2015). In 2015, the number increased more than 7-fold to 59 items identified as fentanyl out of 7376 (Arfken, 2016). Although a small percentage of the total, the number of items identified as fentanyl translates into its ranking as the 10th most common seized substance in the county. Marijuana, cocaine, and heroin [predominately South American heroin (DEA, 2015a)], accounted for most of the items seized.

1.2. Aims of the study

In this study conducted at one medication-assisted opioid treatment clinic in Wayne County, Michigan, we examined several related questions: (1) Is fentanyl detected in UDS among the clients and if so, is it detected multiple times? (2) What are the characteristics of clients who tested positive for fentanyl compared to those who tested negative? (3) What other substances are detected with fentanyl? (4) Do clients perceive that people are actively seeking to use fentanyl?

2. Methods

2.1. Setting

UDS and client-level data were collected from one urban, university-affiliated methadone maintenance treatment (MMT) clinic serving primarily publicly funded adult clients residing in Wayne County (Levine, Lundahl, Ledgerwood, Lisieski, Rhodes, & Greenwald, 2015). The clinic differs somewhat from others in the community by also having a specialty program for pregnant women and a program for people from the local Veteran's Administration Medical Center. People eligible for treatment must have an opioid use disorder for longer than 1 year (or for pregnant women, at high risk of use) and be 18 years or older.

2.2. Urine drug screening

As part of routine clinical care, clients provide randomly scheduled, visually monitored urine samples weekly or biweekly, based on their progress towards abstinence. In January 2015, UDS testing was moved to an outside vendor (Ameritox; Greensboro, NC). The test panel (Rx Guardian Insight™) evaluates several specific medications. For the present analysis we examined fentanyl (including its metabolite norfentanyl; positive result reflects use within the past 3 days), oxycodone (use within 3 days), benzodiazepines (use within 5–10 days), tetrahydrocannabinol (THC, detection window varies), cocaine (use within 3 days), and the primary metabolites of heroin: 6-monoacetylmorphine [6-MAM] use within 24 h) and morphine (use within 3 days). Morphine results are not specific for heroin as they may also reflect use of prescription morphine obtained legally or illegally. For this analysis, we used a positive test for 6-MAM or morphine as indicating

possible heroin use. Results from the UDS are provided to the clinic in 3 days. The results presented are for January 2015–May 2016.

2.3. Anonymous client survey

After analyzing the UDS findings, we conducted a one-page anonymous survey in September 2016 to obtain MMT clients' perspectives on fentanyl in the community. The survey (available from first author) asked for each of six substances (heroin, cocaine, fentanyl, hydrocodone, morphine and alprazolam) the number of people the client knew who tried to obtain it using a Likert-type scale with labels of 0, 1–3 people, 4–6 people, and 7 or more. The survey also asked clients' perceptions on ease of obtaining it now for each substance using a 5 point Likert-type scale with 1 being "Very Easy" and 5 "Very Hard". The substances selected were commonly found in UDS of people presenting for admission to our clinic (cocaine, morphine) or reported to be used (heroin). We also included hydrocodone and alprazolam as they are medications illegally diverted and seized by law enforcement in Michigan (Arfken, 2016). We hypothesized that clients would be more likely to report no one tried to obtain fentanyl, compared to other drugs. This hypothesis reflected the findings of Amlani et al. (2015) who reported most people testing positive for fentanyl did not know they had used it. Exploratory analyses examined whether fentanyl was harder to obtain now than other drugs.

2.4. Data analysis

Data analysis (using SPSS v.23) included descriptive statistics and tests for departure from uniform distribution (one-sample Kolmogorov-Smirnov test) and for bivariate associations with chi-square, Mann-Whitney and Kruskal-Wallis tests. Principal component analysis for categorical data was performed to identify factors that indicate which substances were used concurrently or simultaneously (i.e., tested positive within the same UDS sample). For the survey, paired *t*-tests, Wilcoxon Signed Ranks tests, and McNemar's tests were used. The study received approval from the Wayne State University Institutional Review Board.

3. Results

3.1. Client-linked UDS

There were 368 unique clients in the sample. On a monthly basis, an average of 147.6 clients had UDS tested (range, 130–167). Of these 368 clients, 216 enrolled during this period. However, 28 of the new clients had been enrolled and discharged from the clinic previously, i.e., they had multiple admissions to the clinic. Overall, the clients were predominantly African American (70.3%) and female (54.6%). All were heroin users (100%) and most non-injection users (63.5%). Some had secondary or tertiary drug of abuse of cocaine (27.0%) or prescription opioids (3.0%). At admission, 38.7% reported chronic pain, 10.9% had prescription for opioid (none for fentanyl or morphine), and 7.9% had prescription for benzodiazepine. No client's health record listed a prescription for fentanyl after admission. In this clinic, Michigan's prescription drug monitoring program is routinely checked for newly prescribed scheduled medications.

Overall, 38.0% of the 368 clients had at least one fentanyl-positive UDS and 26.1% had two or more fentanyl-positive UDS (one client had 17 fentanyl-positive UDS over 37 weeks). Clients testing positive at least once for fentanyl had shorter retention in the clinic ($p < 0.001$) than clients who never tested positive for fentanyl (Table 1). They were also more likely to have multiple admissions to the clinic ($p = 0.012$), and cocaine as a secondary or tertiary drug of abuse ($p = 0.034$). Of those clients admitted during this time period (without prior admission), fentanyl-positive tests were more likely during the

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