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Substance use patterns associated with recent exposure to fentanyl among people who inject drugs in Vancouver, Canada: A cross-sectional urine toxicology screening study

Kanna Hayashi[a,b,*], M.-J. Milloy[a,c], Mark Lysyshyn[d,e], Kora DeBeck[a,f], Ekaterina Nosova[a], Evan Wood[a,c], Thomas Kerr[a,c]

[a] British Columbia Centre on Substance Use, British Columbia Centre for Excellence in HIV/AIDS, St. Paul's Hospital, Vancouver, BC, Canada
[b] Faculty of Health Sciences, Simon Fraser University, Burnaby, BC, Canada
[c] Department of Medicine, University of British Columbia, Vancouver, BC, Canada
[d] Vancouver Coastal Health Authority, Vancouver, BC, Canada
[e] School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada
[f] School of Public Policy, Simon Fraser University, Vancouver, Canada

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ABSTRACT

Introduction: Vancouver, Canada is experiencing an opioid overdose crisis where fentanyl, a potent, synthetic opioid contaminating the illicit drug supply, has been detected in the majority of fatal overdose cases. Despite its growing presence throughout North America, few studies have characterized exposure to fentanyl among people who use illicit drugs (PWUD). We sought to identify the prevalence and correlates of fentanyl exposure among PWUD in Vancouver.

Methods: Data were derived from cohort studies of PWUD in Vancouver. In June—October 2016, we administered multi-panel urine drug screens (UDS) to detect recent exposure to fentanyl and eight other substances. Multivariable logistic regression was used to identify substance use patterns associated with recent fentanyl exposure among participants who injected drugs in the past six months (PWID).

Results: Among 669 PWUD including 250 (37.4%) females and 452 (67.6%) PWID, 97 (14.5%) tested positive for fentanyl. All these individuals also tested positive for other substances, most commonly for morphine/heroin (89.9%), amphetamine/methamphetamine (75.3%) and cocaine (74.2%). A fentanyl detection rate was significantly higher among PWID (19.7%) compared to non-injection drug users (3.9%) ($p < 0.001$). In multivariable analyses, younger age (adjusted odds ratio [AOR]: 0.96) and testing positive for morphine/heroin (AOR: 6.73), buprenorphine (AOR: 4.25), amphetamine/methamphetamine (AOR: 3.26), cocaine (AOR: 2.92) and cannabis (AOR: 0.52) remained independently associated with fentanyl exposure (all $p < 0.05$).

Conclusion: With one in five PWID being exposed to fentanyl, there is an urgent need to design and scale up interventions to reduce overdose risk, including a range of opioid agonist therapies.

1. Introduction

In recent years, many locations in North America have been contending with escalating opioid overdose epidemics (Alberta Health 2017; Gomes et al., 2017; Rudd et al., 2016); British Columbia (BC), Canada is among the hardest hit. Between 2012 and 2016, illicit drug overdose death rates increased more than three-fold, and the rates have continued to rise in 2017 (British Columbia Coroners Service, 2017b). The unprecedented magnitude of the epidemic prompted the local Provincial Health Officer to declare a public health emergency in April 2016 (BC Gov News, 2016). An increasing number of jurisdictions have followed suit, including New Haven, Connecticut (The New York Times, 2016), and the state of Virginia (Virginia Department of Health, 2016).

Available data suggest that illicitly-manufactured fentanyl, a synthetic opioid that is much more potent than heroin, has been involved in a substantial number of overdose deaths in many locations (Canadian Centre on Substance Abuse, 2015; Rudd et al., 2016). In BC, illicit fentanyl was detected in 62% of illicit drug overdose deaths in 2016 (British Columbia Coroners Service, 2017a). In 2016, Health Canada's Drug Analysis Service laboratories analyzed illicit drug samples seized

* Corresponding author at: BC Centre on Substance Use, St. Paul's Hospital Chair in Substance Use Research and Assistant Professor, Faculty of Health Sciences, Simon Fraser University, 608-1081 Burrard Street, Vancouver, BC, V6Z 1Y6, Canada.
E-mail address: bccsu-kh@cfenet.ubc.ca (K. Hayashi).

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by law enforcement agencies and found that fentanyl was combined with many street drugs: particularly heroin (21.6%) but also other drugs such as cocaine (4.8%) and methamphetamine (1.7%) (Miller and Russell, 2016). Therefore, people who regularly use street drugs are at a particularly high risk of overdose, as they may unknowingly ingest fentanyl.

There is an urgent need to characterize exposure to illicit fentanyl among people who use drugs in order to guide public policy and clinical practice and refine targeted overdose prevention interventions. However, to date, only a very small number of studies have examined patterns of exposure to fentanyl among this population. In Rhode Island, U.S., fentanyl-involved overdose deaths have significantly increased from 35% in 2014 to 55.6% during the first nine months of 2016 (Marshall et al., 2017). In this setting, 11% of 199 young adults who misused prescription opioids reported having used known or suspected fentanyl-contaminated heroin in 2015–16, and the use of fentanyl-contaminated heroin was associated with markers of more intense drug use (e.g., injection drug use) (Macmadu et al., 2017). In a slightly more updated, mixed-methods study, 50% of 149 individuals using illicit opioids or misusing prescription opioids self-reported suspected exposure to illicit fentanyl and the suspected exposure to fentanyl was independently associated with heroin use (Carroll et al., 2017). While self-reported strategies to avoid fentanyl exposure included seeking opioid agonist therapy, study participants reported challenges with accessing structured addiction treatment programs (Carroll et al., 2017). A 2015 study administered urine drug screens (UDS) for fentanyl to 242 clients of harm reduction services across BC and found a fentanyl detection rate of 29% (Amlani et al., 2015). However, they did not examine associations between fentanyl exposure and opioid agonist therapy use or test the urine samples for other substances in addition to fentanyl. Building on these previous studies, our study sought to identify the prevalence of exposure to fentanyl and other substances by means of UDS and examine substance use and opioid agonist therapy utilization patterns that may be associated with fentanyl exposure among people who use illicit drugs in Vancouver, BC.

2. Materials and methods

2.1. Study setting, design and participants

Data were derived from three ongoing prospective cohort studies of people who use drugs in Vancouver: the Vancouver Injection Drug Users Study (VIDUS), the AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS), and the At-Risk Youth Study (ARYS). VIDUS started in 1996, while ACCESS and ARYS started in 2005. Detailed descriptions of these cohorts have been previously published elsewhere (Strathdee et al., 1998; Wood et al., 2009; Wood et al., 2006). In brief, VIDUS enrolls HIV-seronegative adults (≥18 years of age) who injected illicit drugs in the month prior to enrollment. ACCESS enrolls HIV-seropositive adults who used an illicit drug other than or in addition to cannabis in the month prior to enrolment. ARYS enrolls street-involved youth aged 14–26 who used an illicit drug other than or in addition to cannabis in the month prior to enrollment. The studies use harmonized data collection and follow-up procedures to allow for combined analyses of the different cohorts. Specifically, the cohorts were administered the identical questionnaires with equal follow-up frequency (i.e., every 6 months).

At baseline and semi-annually thereafter, participants complete an interviewer-administered questionnaire, which elicits a range of information, including demographic data, substance use, and healthcare access. On June 16, 2016, a multi-panel qualitative UDS using BTNX Rapid Response™ Multi-Drug Test Panel (Markham, ON, Canada) was added to the data collection procedures. This rapid, chromatographic immunoassay qualitatively and simultaneously detected nine substances in urine within five minutes. The screened substances (calibrator, cut-off value in ng/mL) included: fentanyl (fentanyl, 100, and norfentanyl, 20); morphine/heroin (morphine, 100); methadone (2-Ethylidine-1, 5-dimethyl-3, 3-diphenylpyrrolidine, 100); buprenorphine (BUP-3-D-Glucoronide, 10); oxycodone (oxycodone, 100); cocaine (benzoylecgonine, 150); amphetamine/methamphetamine (d-amphetamine, 1000); benzodiazepine (oxazepam, 300); and tetrahydrocannabinol, the main psychoactive component of cannabis (11-nor-Δ9-THC-9 COOH, 50) (BTNX, Inc.). According to the product insert, the accuracy of test results was established by testing the same urine samples with gas chromatograph-mass spectrometry specifications and exceeded 95% for all substances listed above (BTNX, Inc.). While detection times for the substances vary depending on many factors, including routes of administration, frequencies of use, and individual metabolism rates, the BTNX fentanyl test panel with the aforementioned cut-off values is commonly believed to detect exposure to fentanyl within a maximum of past three days (Silverstein et al., 1993). All three cohorts have received approvals from the University of British Columbia/Providence Health Care Research Ethics Board.

Eligibility criteria for the present study included: completing both the interviewer-administered follow-up questionnaire and UDS between June 16 and October 26, 2016, and reporting having used any illicit drugs (including non-medical use of prescription drugs) in the past six months. Some participants in the cohorts, particularly those who were enrolled in the cohorts a long time ago, had stopped using illicit drugs altogether during follow-up. Since including such participants in the sample would lead to the underestimation of fentanyl detection rates among the drug-using population, we restricted the sample to those who used illicit drugs at least once in the past six months.

2.2. Measures

The primary outcome was recent exposure to fentanyl, defined as a positive UDS result for fentanyl. In order to describe the sample characteristics, the following variables were considered. Demographic variables included: age (continuous); sex (female *vs.* male); ethnicity/ancestry (White *vs.* non-White); and residence in the Downtown Eastside neighborhood in Vancouver, an area with a large open drug market. Self-reported drug use-related variables included: injection drug use; using stimulants (e.g., powder or crack cocaine, crystal methamphetamine), but not any opioids; and non-fatal overdose. UDS results for the remaining nine substances were also included. Since the descriptive statistics of the sample showed that 91.8% of those testing positive for fentanyl reported injection drug use in the past six months (Table 1), bivariable and multivariable logistic regression analyses were restricted to PWID participants (i.e., those who reported having injected drugs in the past six months), and drug use-related variables were revised for the regression analyses. These variables included self-reported use of each of the following eleven drugs: heroin; fentanyl pills or patches (non-medical use); street methadone (i.e., diverted or illicitly manufactured methadone); street buprenorphine-naloxone (i.e., diverted or illicitly manufactured buprenorphine-naloxone); other prescription opioids (non-medical use); powder cocaine; crack cocaine; crystal methamphetamine; benzodiazepine; and cannabis (both medical and non-medical). The use of opioid agonist therapy (OAT) using either methadone or buprenorphine-naloxone was also included. All variables except for age, sex, ethnicity/ancestry and UDS results referred to the past six months. Unless otherwise stated, all variables were dichotomized as yes *vs.* no.

2.3. Statistical analyses

First, we examined the sample characteristics stratified by UDS results for fentanyl, using the Pearson's Chi-squared test (for binary variables) and Wilcoxon Rank Sum test (for continuous variables). Next, in order to identify a set of substance use patterns associated with a higher odds of recent exposure to fentanyl, we built two multivariable logistic regression models: Model 1 included demographic and UDS