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ORIGINAL PAPER

HIV Risk Among Urban and Suburban People Who Inject Drugs: Elevated Risk Among Fentanyl and Cocaine Injectors in Maryland

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Abstract
Drug overdose remains a leading cause of death in the US, with growing rates attributable to illicit fentanyl use. Recent HIV outbreaks among people who inject drugs (PWID) and service disruptions from COVID-19 have renewed concerns on HIV resurgence. We examined the relationship between fentanyl use and three injection-related HIV risk behaviors among PWID in Baltimore City (BC) and Anne Arundel Country (AAC), Maryland. PWID (N = 283) were recruited to the study through targeted sampling at street-based locations in BC and AAC from July 2018 to March 2020. Receptive syringe sharing (RSS) [adjusted odds ratio (AOR): 2.8, 95% confidence interval (CI): 1.2–6.3] and daily injecting (AOR: 1.9, 95% CI: 1.0–3.6) were associated with injecting fentanyl and cocaine together. Fentanyl availability and COVID-19 bring new HIV prevention challenges, particularly among those who inject fentanyl with cocaine, highlighting the importance to expand and sustain harm reduction, prevention, and treatment services for PWID to reduce HIV and overdose burden.

Keywords HIV/AIDS · Epidemiology · Injection drug use

Introduction

Over the past three decades, people who inject drugs (PWID) have been disproportionately impacted by HIV and drug overdose. Conservatively, it is estimated that 774,434 individuals in the US inject illicit drugs annually, 6% of whom are living with HIV [1]. Racial disparities remain, with greater HIV prevalence observed among Black (9%) and Hispanic/Latino PWID (8%) compared to White PWID (4%) [2]. Drug overdose remains a leading cause of death in the US, accounting for more than 200,000 deaths between 2017 and 2019 [3, 4], with PWID being at exceedingly high risk [5]. Studies conducted in California, Australia, and Estonia have demonstrated associations between self-reported fentanyl use and HIV risk behaviors [6–8].

Trends in drug availability and use have shifted substantially over time. While fentanyl, a potent synthetic opioid, has received attention in recent years for its role in overdose deaths, more than half of synthetic opioid deaths co-involved other substances, including cocaine, methamphetamine, prescription drugs, and alcohol [9]. Cocaine, for example, was the second most common drug involved in overdose deaths in 2018; one fifth of overdose deaths involved cocaine and three quarters of these deaths involved concomitant exposure to opioids, including fentanyl [10].

Substantial progress has been made in reducing HIV transmission among PWID, particularly through the provision of medications for opioid use disorders and syringe services programs (SSP) that reduce risk behaviors like injection drug use and syringe sharing. However, inadequacies in the national response to addressing drug use (e.g., gaps in coverage, overreliance on punitive drug control policies) [11] and the current COVID-19 pandemic [12–14] threaten to reverse these hard-fought gains through major disruptions to service provision. Between 2014 and 2018, new HIV infections among PWID rose nationally by 20% (2000 vs. 2400) [15]. Several HIV outbreaks occurred among PWID,

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including in Indiana, West Virginia, and Massachusetts, in part due to prohibitive policies against SSP as well as rising rates of injection initiation and injection frequency [6–8, 16, 17]. PWID are regularly harassed, arrested, and incarcerated due to the ongoing punitive "War on Drugs," which has only aggravated these public health issues—even before COVID-19—including disrupting medical care for HIV and substance use, and elevating post-release risk of overdose [18–20].

Accordingly, the aim of this study is to improve our understanding of the relationship between fentanyl use and HIV-related risks in Maryland, a state greatly impacted by the fentanyl epidemic. Maryland had the third highest rate of drug overdose mortality in the US in 2018, which was disproportionately concentrated in Baltimore City (BC) and its surrounding suburban counties, including Anne Arundel County (AAC) [3, 21]. These jurisdictions ranked 1st and 3rd, respectively, in Maryland for overdose deaths and differ widely by race and urbanicity (BC is a majority Black city and AAC is a majority White and largely suburban county). The proportion of new HIV diagnoses among PWID in Maryland decreased between 2001 and 2014; however, rates stabilized between 2014 and 2016, and increased slightly from 2016 to 2017 [22]. We examined the relationship between self-reported fentanyl use (with and without cocaine) and three injection-related HIV risk behaviors among PWID in BC and AAC, Maryland. Our hypothesis was that HIV risk behaviors would be more common among those who injected fentanyl with cocaine.

Methods

Data were drawn from the Peer Harm Reduction of Maryland Outreach Tiered Evaluation (PROMOTE) project, an ongoing mixed-methods evaluation of the impact of peer outreach services on overdose risk in BC and AAC. Data for the study were collected in BC and neighboring AAC. In BC, data were collected in two waves, July–October 2018 and April–July 2019, while data in AAC were collected in one wave from November 2019 to March 2020. Participants were recruited using a targeted sampling method, similar to that from a previous study [23], in locations with high drug activity and overdose (non-fatal and fatal); a total of 15 and 7 street-based zones served as study locations in BC and AAC, respectively. The recruitment zones were informed by drug arrest data collected by the police in 2017, which corroborated maps of non-fatal and fatal overdose. Arrest data were mapped in ArcMap 10.4.1 and converted into venue-date-time units using SAS Enterprise Guide software. Interested individuals at these locations were invited to undergo screening at a mobile van parked within the zone.

Eligibility criteria for the PROMOTE study were: (1) being aged 18 or older and (2) reporting illicit opioid use in the past month (e.g., heroin, fentanyl, street prescription opioids). Eligible participants who provided informed consent completed a tablet-based Audio Computer-Assisted Self-Interviewing (ACASI) survey, which included sections on demographic characteristics, current housing and health insurance status, arrest history, drug use, injection risk behaviors, attitudes on fentanyl and overdose risk, overdose history, drug treatment use, HIV testing and pre-exposure prophylaxis (PrEP) history, and SSP access. The current analysis was restricted to individuals who reported injecting in the past 3 months (N = 249 in BC, N = 34 in AAC, N = 283 total). Participants received a $25 prepaid VISA gift card for study completion. This study was approved by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board (IRB#00008666).

Measures

Three main outcomes of interest were selected based on previous work [6, 7]: (1) receptive syringe sharing (RSS) was captured as using syringes/needles known to have been used by someone else in the past 3 months (yes/no); (2) daily injection, captured as how often respondents injected any drug; and (3) the average number of injections on the days injected (captured continuously).

Based on our formative work (i.e., knowledge of the high prevalence of cocaine injection among people who inject heroin or fentanyl), recent fentanyl injection was captured using two separate items: "injected fentanyl by itself" and "injected fentanyl and cocaine together." From these two variables, we constructed a three-tiered variable consisting of injected fentanyl and cocaine together (primary exposure), injection fentanyl without cocaine (secondary exposure), and did not inject fentanyl (reference group).

Covariates of interest from the survey included: age, gender, race/ethnicity (collapsed as Non-Hispanic White vs. Black, Hispanic, or Other), arrest in the past year, current homelessness and health insurance status, HIV testing in the past year, ever hearing of or taking PrEP, and recent SSP access.

Statistical Analysis

First, we compared the two samples (BC vs. AAC) using Fisher's Exact tests on key socio-demographic and health variables in order to assess how the samples differed. The difference in the number of injections was tested using the Mann Whitney nonparametric test for skewed data. Statistical significance was set at $p < 0.05$.

Two separate multivariate logistic regression models were run to examine the associations between recent fentanyl

injection (fentanyl/cocaine; fentanyl/no cocaine; no fentanyl), and (1) RSS (yes/no) and (2) daily injection drug use (yes/no). We also ran a multivariate negative binomial regression, which included the average number of injections per day (count variable) as the outcome. The data from BC and AAC were pooled due to the limited sample size. Each model included confounders that were specified a priori (i.e., county, age, gender, race/ethnicity, and recent SSP access). The three HIV risk behavior outcomes were modeled separately due to the collinear nature of the outcomes. We explored collinearity within each model through Variance Inflation Factors. All data were analyzed using Stata/SE 14.2.

Table 1 Socio-demographic and drug-related characteristics of PWID in Baltimore City (BC) and Anne Arundel County (AAC), 2019–2020

	BC n (%) N = 249	AAC n (%) N = 34	*p* (Fisher's exact test)	Total, n (%) N = 283
Socio-demographic variables				
Younger age (18–29)	27 (11%)	6 (18%)	0.255	33 (12%)
Male	143 (57%)	24 (71%)	0.193	167 (59%)
Race/ethnicity				
Non-Hispanic White	88 (35%)	19 (56%)	**0.024**[e]	107 (38%)
Non-Hispanic Black	142 (57%)	13 (38%)		155 (55%)
Hispanic	6 (2%)	0 (0%)		6 (2%)
Other	13 (5%)	2 (6%)		15 (5%)
Drug variables				
Drugs injected[a]				
Fentanyl and cocaine injection	139 (56%)	18 (53%)	0.849	157 (56%)
Fentanyl injection without cocaine	42 (17%)	5 (15%)		47 (17%)
No fentanyl injection	67 (27%)	11 (32%)		78 (28%)
Injected daily	179 (72%)	19 (56%)	0.072	198 (70%)
Receptive syringe sharing[a]	55 (22%)	12 (35%)	0.13	67 (24%)
No. of injections/day, median (IQR)	4 (2–5)	3 (2–4)	0.152[fs]	3 (2–5)
1–2	67 (30%)	10 (30%)	0.054	82 (30%)
3–4	68 (30%)	16 (48%)		87 (32%)
≥ 5	92 (41%)	7 (21%)		103 (38%)
Structural variables				
Drug-related arrest[b]	42 (17%)	10 (29%)	0.097	52 (18%)
Current homelessness	189 (76%)	30 (88%)	0.128	219 (77%)
Currently has health insurance	184 (78%)	32 (94%)	**0.017**	228 (81%)
HIV variables				
Accessed HIV testing[b, c]	102 (88%)	20 (77%)	0.207	122 (86%)
Currently living with HIV[d]	13 (11%)	0 (0%)	–	13 (9%)
Ever heard of PrEP	146 (59%)	15 (44%)	0.139	161 (57%)
Ever taken PrEP	23 (9%)	1 (3%)	0.33	24 (8%)
Accessed a SSP[a]	186 (75%)	21 (62%)	0.147	207 (73%)

Boldface denotes p-value < 0.05

IQR interquartile range, *PrEP* HIV pre-exposure prophylaxis, *SSP* syringe services program

[a]Self-reported, past 3 months

[b]Past year

[c]n = 142

[d]n = 139, self-reported

[e]Black/Hispanic/Other were collapsed due to small cell sizes

[f]Mann-Whitney non-parametric test

Results

Descriptive Analysis

The BC and AAC samples were similarly distributed in age and gender (Table 1). There were significant differences in race: 56% of AAC participants were White whereas 65% of BC participants were Black, Hispanic, or other races/ethnicities (Fisher's exact test; $p = 0.024$). There were also similarities across locations in the types of drugs injected: 56% of the total sample reported recently injecting fentanyl and cocaine together, 17% reported recently injecting fentanyl by itself, and 28% reported not injecting fentanyl recently. Among those who did not inject fentanyl recently (n = 78), the majority injected heroin (69/78; 88%) or cocaine (31/78; 40%).

A quarter of PWID reported RSS (24%), the majority injected daily (70%), and over one third reported five or more times a day (38%). Eighteen percent had been arrested in the prior year for drugs or drug paraphernalia. Most participants (77%) were homeless at the time of the survey. The prevalence of currently having health insurance differed between the two locations, with PWID from AAC having higher levels of coverage than those in Baltimore (Fisher's exact test; 94% vs. 78%; $p = 0.017$). The overall sample had relatively high uptake of HIV testing (86%, past year) and SSP (73%, past 3 months), but low uptake of PrEP (8%, ever).

Recent RSS

In the presence of confounders (i.e., county of residence, age, gender, race/ethnicity, and SSP access), recent RSS was independently associated with recent fentanyl and cocaine injection [adjusted odds ratio (AOR) = 2.8, 95% confidence interval (CI): 1.2–6.3] (Table 2). The association between RSS and fentanyl injection without cocaine was not significant. Post-estimation testing revealed a significant difference between PWID who injected fentanyl with cocaine, and those who injected fentanyl without cocaine ($p = 0.003$). Non-White PWID were less likely to engage in RSS (AOR = 0.4, 95% CI: 0.2–0.8) and PWID who had recently accessed an SSP were also less likely to engage in RSS (AOR = 0.4, 95% CI: 0.2–0.8).

Daily Injection Drug Use

In the second multivariate logistic regression analysis, daily injection drug use was associated with injecting fentanyl with cocaine (AOR = 1.9, 95% CI = 1.0–3.6) but not that without cocaine (AOR = 1.0, 95% CI = 0.5–2.3). Daily injection drug use was greater among PWID in BC (AOR = 0.4, 95% CI: 0.2–0.9) and those who recently accessed an SSP (AOR = 2.2, 95% CI: 1.2–4.1). The post-estimation test did not detect a significant difference between those who injected fentanyl with cocaine, and fentanyl without cocaine (χ^2: $p = 0.09$).

Table 2 Associations between self-reported fentanyl use and injection risk among HIV-negative PWID in Baltimore City and Anne Arundel County

	Receptive syringe sharing, past 3 months (N = 269)				Daily injection drug use, past 3 months (N = 269)				Average no. of injections per day (N = 260)			
	AOR	95% CI		*p*	AOR	95% CI		*p*	AIRR	95% CI		*p*
Primary outcomes												
No fentanyl injection[a]	1.0 (ref)				1.0 (ref)				1.0 (ref)			
Fentanyl injection without cocaine[a]	0.5	0.1	1.6	0.232	1.0	0.5	2.3	0.950	0.9	0.6	1.2	0.352
Fentanyl and cocaine injection[a]	2.8	1.2	6.3	**0.013**	1.9	1.0	3.6	0.050	1.6	1.2	2.0	**< 0.001**
Confounders												
Anne Arundel County	1.6	0.7	3.7	0.301	0.4	0.2	0.9	**0.031**	0.7	0.5	0.9	**0.014**
Age (continuous)	1.0	0.9	1.0	0.131	1.0	1.0	1.0	0.584	1.0	1.0	1.0	0.207
Male gender	0.8	0.4	1.4	0.413	1.4	0.8	2.5	0.264	0.9	0.8	1.1	0.467
Race/ethnicity												
Non-Hispanic White	1.0 (ref)				1.0 (ref)							
Other	0.4	0.2	0.8	**0.007**	0.6	0.3	1.2	0.162	1.1	0.9	1.4	0.330
Accessed a SSP[a]	0.4	0.2	0.8	**0.012**	2.2	1.2	4.1	**0.008**	1.2	0.9	1.5	0.228

AOR adjusted odds ratio, *CI* confidence interval, *AIRR* adjusted incident rate ratio, *SSP* syringe services program

[a]Past 3 months

Boldface denotes *p*-value < 0.05

Average Number of Injections per Day

In the multivariate negative binomial analysis comparing PWID who injected fentanyl with cocaine to those who did not inject fentanyl, those who injected fentanyl with cocaine had a 1.6 times higher number of injections per day [adjusted incidence rate ratio (AIRR) = 1.6, 95% CI: 1.2–2.0] after adjusting for confounders. The AIRR difference between those who injected fentanyl with and without cocaine was statistically significant in post-estimation testing ($p = 0.0008$). PWID from AAC had 0.7 times less injections per day compared to PWID in BC (AIRR = 0.7, 95% CI: 0.5–0.9).

Discussion

This study is among the first to examine the relationship between fentanyl injection and HIV risk in the US. We found among an urban-suburban sample of fentanyl injectors in Maryland that fentanyl is injected more commonly with cocaine (56%) than without cocaine (17%). Combined fentanyl and cocaine injecting was associated with increased RSS, daily injecting, and number of injections per day. Our findings extend previous domestic and international work on this understudied topic [6–8]. As part of a comprehensive response towards drug use in the US, there is an urgent need to rapidly intervene to close gaps in harm reduction, prevention, and treatment coverage to prevent future HIV and overdose outbreaks.

In this community-based study, we found elevated risk of HIV acquisition among those who co-inject fentanyl with cocaine, after adjusting for county, age, gender, race/ethnicity, and SSP access. The co-use of opioids and stimulants is a well-established behavior among PWID in the US [24–27], and research shows that heroin-cocaine (i.e., speedball) and heroin-methamphetamine (i.e., goofball) injectors are at an exceedingly high risk of overdose and HIV [28, 29]. Heroin and fentanyl markets are interlinked; fentanyl has been marketed as heroin, mixed into heroin supplies, or in some regions (such as Baltimore) has supplanted heroin supplies [30–33]. Given these trends, the rise in combined fentanyl-cocaine injecting among PWID (who historically have injected heroin) and the observed increase in HIV risk behaviors were not unexpected; these patterns may also explain the small rise in HIV diagnoses among Maryland PWID.

In order to reduce harms associated with injection drug use, including both HIV and overdoses among PWID, we need to rapidly implement and expand evidence-based harm reduction services that can simultaneously address HIV and overdose in clinical and community settings. These include SSPs, which, as our data show, can reach PWID at high risk (e.g., daily injectors) and lower the likelihood of sharing syringes with others, as well as naloxone and drug treatment services that can reduce mortality. Notably, Baltimore has had a longstanding SSP run by the local health department, while AAC still does not presently have a SSP. Safe consumption spaces (also known as supervised injection facilities and overdose prevention sites) could also simultaneously address the risks associated with HIV and overdose among PWID; such programs are widely accepted by PWID [11, 34]. There are ongoing efforts to implement safe consumption spaces in high overdose burden jurisdictions, and in some states, they are already successfully operating underground [35]. Although COVID-19 has impacted traditional models of service delivery [12, 14, 36, 37], innovative models are being employed by many harm reduction and clinical communities to meet the challenge, including contactless delivery of sterile syringes and the use of telemedicine. Our work also documented low levels of PrEP awareness (57%) and use (8%) among this population, consistent with national estimates [2]. The co-location of PrEP with substance use services could be a natural avenue for increasing PrEP utilization among PWID [38].

Our findings are subject to limitations. Data collection in AAC was terminated early due to mandatory COVID-19 shutdowns. Injection drug use was also less common in AAC, which reduced our overall sample size. Given this smaller sample size in AAC, it was not possible to conduct a comparative analysis; instead, data were pooled and AAC was entered into the model as a confounder. Another limitation is that self-reported fentanyl use may not be accurate given the uncertainties inherent to illicit drug supplies, particularly in the era of fentanyl [30, 31, 39–41]. In the current legal context, it is also plausible that PWID are underreporting fentanyl use given the climate of fear exacerbated by laws that encourage police crackdowns of those involved in the sale, distribution, or sharing of fentanyl. The findings should be interpreted in light of these limitations.

PWID experience multiple mutually reinforcing vulnerabilities that impact their risk of HIV and overdose. Special attention to the needs of PWID and other vulnerable populations is especially necessary when making programmatic and policy decisions to tackle these challenges. Harm reduction oriented HIV prevention solutions, including SSP and medication-based drug treatment, which have a long history in the US, and innovative solutions such as overdose prevention sites (or supervised injection facilities) and PrEP, are critical components of a holistic approach to protecting one of the most vulnerable and underserved populations in our society.

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