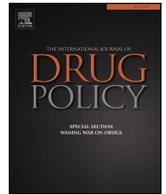




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Research Paper

## Associations between perceived illicit fentanyl use and infectious disease risks among people who inject drugs

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## ABSTRACT

**Background:** Over the last several years, fentanyl has been introduced into the illicit drug supply in the United States. While the impact of fentanyl on overdose fatalities is clear, the increase in fentanyl use may also be affecting drug use practices with implications for infectious disease transmission. We conducted a cross-sectional survey to explore associations of perceived illicit fentanyl use with opioid use frequency, injection frequency and syringe sharing among people who inject drugs in two California cities.

**Methods:** People who inject drugs (PWID) were recruited from community settings in Los Angeles and San Francisco, CA from June 2017 to September 2018. Multivariable logistic regression was used to explore adjusted associations between perceived illicit fentanyl use and high frequency opioid use, high frequency injection and syringe sharing.

**Results:** Among the 395 study participants, the median age of participants was 44 years; 74% of participants were cisgender male; 73% reported to be homeless; 61% lived in San Francisco and 39% in Los Angeles. The prevalence of perceived illicit fentanyl use in the past six months was 50.4% (95% confidence interval (CI): 45.4%–55.3%) among PWID. Findings from our adjusted logistic regression models suggested that people reporting perceived illicit fentanyl use had a greater odds of high frequency opioid use (adjusted odds ratio (aOR) = 2.36; 95% CI: 1.43–3.91;  $p = 0.001$ ), high frequency injection (aOR = 1.84; 95% CI: 1.08–3.13;  $p = 0.03$ ) and receptive syringe sharing (aOR = 2.16; 95% CI: 1.06–4.36;  $p = 0.03$ ), as compared to people using heroin and other street drugs but not fentanyl.

**Conclusion:** People reporting perceived illicit fentanyl use were at increased risk for injection-related infectious disease risks. Actions must be taken to reduce these risks, including improved access to syringe service programs and opioid treatment and consideration of innovative approaches, such as supervised consumption services.

## Introduction

Despite HIV diagnoses among people who inject drugs (PWID) steadily decreasing in the United States since its peak in the 1990s, a 7% increase was observed in 2017 compared to 2016 (Centers for Disease Control & Prevention, 2018a, 2018b). In 2016, a 22% increase from 2015 was observed in reported hepatitis C virus (HCV) among PWID (Centers for Disease Control & Prevention, 2018c). An increase in the number of people who inject drugs have contributed to new cases of HCV (Suryaprasad et al., 2014). In addition, riskier drug use practices accompanying specific opioid formulations have been shown to increase incident HIV and HCV cases. In Scott County, Indiana, high

injection frequency, related to oxycodone (e.g. Opana® extended release) injection, led to an outbreak of HIV in 2014. (Peters et al., 2016) In Montreal, Canada, a recent study observed increases in prescription opioid injection which was associated with higher risk of syringe sharing and incident HCV cases (Bruneau, Roy, Arruda, Zang, & Jutras-Aswad, 2012). These studies demonstrate the need to understand how newly introduced drug formulations into the drug market can influence drug use practices and infectious disease risks.

Over the last five years, fentanyl has been introduced into the illicit drug supply in the United States (Frank & Pollack, 2017). Fentanyl is a highly potent opioid, making its use a high risk for opioid overdose. As a result, fentanyl-involved overdose deaths have been steadily

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increasing, averaging an annual 107% increase from 2013 to 2016 (Hedegaard, Bastian, Trinidad, Spencer, & Warner, 2018). Beginning in 2016, fentanyl became the most common drug detected in drug overdose decedents (Hedegaard et al., 2018). While the impact of fentanyl on overdose fatalities is clear, its increase in use may also be affecting drug use practices with implications for infectious disease transmission. Recent qualitative research from Canada and the United States documented that fentanyl intoxication has a comparatively short duration of effect as compared to heroin (Ciccarone, Ondocsin, & Mars, 2017; Mayer et al., 2018; Somerville et al., 2017). This shorter duration of effect could lead to more frequent use and more injections. Higher injection frequency has been shown to lead to higher likelihood of syringe sharing, which in turn leads to increased number of viral (e.g., HIV and Hepatitis C Virus (HCV)) exposure events (Ciccarone et al., 2017; Mayer et al., 2018; Somerville et al., 2017; Strathdee et al., 1997).

While two studies have investigated the relationship between fentanyl use and infectious disease risks from Australia and Estonia, (Geddes, Iversen, Memedovic, & Maher, 2017; Talu et al., 2010) we are unaware of any quantitative studies along these lines since the emergence of fentanyl into the illicit drug supply in the United States. Understanding the epidemiology of fentanyl use is critical for addressing potentially evolving infectious disease risks. To contribute to this global evidence base, we analyzed data from our cross-sectional survey to explore associations of perceived illicit fentanyl use with frequency of opioid use, frequency of injection and syringe sharing among PWID in two California cities. While the introduction and consequences of fentanyl use were observed much earlier among Northeast and mid-Atlantic states of the United States, California has recently observed an emergence of fentanyl use and significant increases in fentanyl-related overdose fatalities (California Department of Public Health, 2018). In 2017, a record number of overdose deaths involving fentanyl were observed in California – a more than four-fold increase since 2013 (California Department of Public Health, 2018).

## Methods

### Study setting and procedures

From June 2017 to September 2018, we collected survey data from PWID in community settings known to have high levels of injection drug use in San Francisco and Los Angeles, California, as part of a randomized controlled trial of a single session intervention to reduce injection initiation assistance (NCT02774954) (Navarro, 2019 #48). We used targeted sampling methods to recruit PWID (Bluthenthal & Watters, 1995; Kral et al., 2010; Watters & Biernacki, 1989). In brief, outreach workers visited street settings with known drug use – determined by examining secondary data regarding drug arrests and block-by-block observations of drug use within targeted areas by the outreach worker – to recruit study participants based on eligibility criteria. Inclusion criteria for the study were age  $\geq 18$  years, injection drug use in the previous 30 days, and willingness to provide informed consent. If someone met the study criteria and was interested in participating, they were asked to come to an easily accessible field site at specified times to verify eligibility and participate, if eligible, in an informed consent process and a quantitative survey. To prevent duplicate enrollment into the study, we collected biometric information (height, tattoos, etc.) for people who enrolled, and we had one person serve as study coordinator at each site throughout the study. Drug injection was verified by visual inspection for signs of recent venipuncture (i.e., tracks). The survey was conducted face-to-face, with trained interviewers posing items verbally and recording responses in a computer-assisted personal interviewing system (QDS™, Nova Research Company, Silver Spring, MD). Data were collected at the field sites on password-protected computers, and data files were encrypted and transferred daily to the coordinating center at the University of Southern California. All study procedures were reviewed and approved

by a federally accredited Institutional Review Board at University of Southern California. Participants received \$20 remuneration for completing the survey, as well as referrals to medical and social services as appropriate.

### Study measures

Our study outcomes included measures of high frequency opioid use, defined as greater than 90 times in the past 30 days; high frequency injection, defined as greater than 90 injections in the past 30 days; and receptive syringe sharing, defined as “having used syringes or needles that you knew had been used by someone else including a close friend or lover in the past six months.” We used a threshold of greater than 90 injections in the past 30 days for high frequency injection as this represented the highest quartile of the number of injections from studies in these communities in the pre-fentanyl era (Bluthenthal et al., 2018). Opioid use included heroin as a solo product or mixed with other drugs including crack, cocaine or methamphetamine, opiates without a prescription, methadone without a prescription and buprenorphine without a prescription.

Our primary exposure of interest was any perceived illicit fentanyl use in the past six months. After the interviewer read aloud the following statement to the participant “The next questions are about your fentanyl use. I am interested in fentanyl that you have obtained on the streets or illicitly and NOT that was prescribed to you”, we asked the participant the following question, “In the last six months, have you used fentanyl or other drugs that you believe had fentanyl in it?”. This item does not allow us to discern whether fentanyl use was intentional or incidental (as is the case when heroin is contaminated with fentanyl); the distribution of intention and incidental use; the frequency of perceived illicit fentanyl use; or whether fentanyl was manufactured illicitly or diverted from the medical system. In addition, this measure captured perceived illicit fentanyl use and as such, might under-represent actual illicit fentanyl use. Fentanyl appeared in the study region in 2015 as a white powder that was visually distinct from black tar heroin, and once identified, this distinction likely led to an awareness of fentanyl use (Rowe, 2019 #50). However, people also could have unknowingly used fentanyl that was mixed into other drugs and therefore not report its use.

The following variables were treated as potential covariates: age in years; race/ethnicity, defined as Latinx, Black, White, Asian/Pacific Islander, Native American and Mixed Race; gender orientation, defined as cisgender male, cisgender female or transgender; sexual orientation, defined as heterosexual, gay/lesbian or bisexual; income, defined as  $< \$1000$  or  $\geq \$1000$  in the past 30 days; city of residence, defined as San Francisco or Los Angeles; homelessness, defined as whether or not the person considered themselves to be homeless; opioid use, defined as any nonmedical opioid use in the past 30 days; alcohol use, defined as any alcohol use in the past 30 days; recent jail experience, defined as any jail time in the last six months; recent substance use treatment, defined as any alcohol or drug treatment in the past six months and self-reported HIV status, defined as yes or no to whether someone had ever been told by a doctor, nurse or counselor that they were HIV-positive.

### Statistical analysis

Descriptive statistics, including frequencies, median and inter-quartile range, were calculated to describe the distribution of variables in the study population. We calculated the prevalence and accompanying 95% confidence intervals (CI) for perceived illicit fentanyl use in the past 6 months. Multivariable logistic regression was used to assess for differences in perceived illicit fentanyl use in the past six months by participant characteristics. We first built unadjusted, bivariate models between sample characteristics and perceived illicit fentanyl use to generate odds ratios (OR), accompanying 95% CI and *p*-values. All variables having a *p*-value  $< 0.20$  were included in a full

**Table 1**

Sample characteristics of people who inject drugs in Los Angeles and San Francisco in 2017–2018, disaggregated by perceived illicit fentanyl use in the last 6 months ( $N = 395$ ).

	Perceived illicit fentanyl use		Total ( $N = 395$ )
	No (%) ( $n = 196$ )	Yes (%) ( $n = 199$ )	
<b>Gender Orientation</b>			
Cisgender Male	142 (49)	147 (51)	289
Cisgender Female	49 (51)	47 (49)	96
Transgender	3 (75)	1 (25)	4
<b>Race/Ethnicity</b>			
Latinx	56 (66)	29 (34)	85
Black	55 (71)	22 (29)	77
White	64 (37)	111 (63)	175
Asian\Pacific Islander	0 (0)	3 (100)	3
Native Amer	8 (35)	15 (65)	23
Mixed Race	11 (42)	15 (58)	26
<b>Sexual Orientation</b>			
Heterosexual	157 (50)	156 (50)	313
Gay or lesbian	13 (72)	5 (28)	18
Bisexual	23 (41)	33 (59)	56
<b>Age Group</b>			
< 30	14 (25)	43 (75)	57
30–39	37 (37)	64 (63)	101
40–49	61 (53)	53 (46)	114
≥ 50	82 (70)	35 (30)	117
<b>Income</b>			
< \$1000	137 (60)	90 (40)	227
≥ \$1000	57 (35)	107 (65)	164
<b>City of Residence</b>			
San Francisco	88 (36)	157 (64)	245
Los Angeles	108 (72)	42 (28)	150
<b>Currently Homeless</b>			
No	61 (57)	45 (42)	106
Yes	135 (47)	154 (53)	289
<b>Opioid Use, past 30 days</b>			
No	39 (75)	13 (25)	52
Yes	157 (46)	185 (54)	342
<b>Alcohol Use, past 30 days</b>			
No	89 (46)	103 (54)	192
Yes	107 (53)	95 (47)	202
<b>Jail, past 6 months</b>			
No	140 (53)	125 (47)	265
Yes	54 (43)	70 (56)	124
<b>Substance Use Treatment, past 6 months</b>			
No	138 (51)	133 (49)	271
Yes	58 (47)	66 (53)	124

model, and variables were retained in the full adjusted model if the variable, or any category of a variable, had a  $p$ -value < 0.20. The full model provided adjusted odds ratios (aOR), corresponding 95% CI and  $p$ -values of the associations between sample characteristics and perceived illicit fentanyl use.

Similarly, we also used logistic regression models to generate aORs, accompanying 95% CI and  $p$ -values to assess the relationship between perceived illicit fentanyl use and each of our three outcome variables (i.e., three separate logistic regression models). All potential confounding variables were included in a full model, and variables were retained in each final adjusted model if the variable, or any category of a variable, had a  $p$ -value < 0.20. We chose a modest value for variable inclusion so that our approach was more inclusive of potential confounding factors. Statistical significance was set at 0.05. All analyses were conducted in Stata v15.1 (College Station, Texas).

## Results

The analytic sample consisted of 395 study participants who had injected any drugs in the last 30 days (Table 1). The median age of participants was 44 years (Interquartile Range: 34–52), and 74% of participants were cisgender male, 25% cisgender female and 1%

transgender. In addition, 44% were white, 22% Latinx, 20% black, 6% Native American, 6% mixed race and < 1% Asian/Pacific Islander; 80% identified as heterosexual; 73% reported to be homeless; 58% reported to make less than \$1000 per month; 61% lived in San Francisco and 39% in Los Angeles.

The prevalence of perceived illicit fentanyl use in the past six months was 50.4% (95% CI: 45.4%–55.3%). We observed significant differences in the odds of perceived illicit fentanyl use based on sample characteristics (Table 2). Overall, people who were 40–49 years of age (aOR 0.31; 95% CI: 0.14–0.72;  $p = 0.007$ ) and 50–59 years of age (aOR 0.20; 95% CI: 0.09–0.47;  $p < 0.001$ ) had a lower odds of reporting perceived illicit fentanyl use compared to people less than 30 years of age. People reporting a past month income of \$1000 or more reported a higher odds of perceived illicit fentanyl use (aOR 2.09; 95% CI: 1.27–3.41;  $p = 0.003$ ), compared to people reporting less than \$1000 in the last month. In addition, people living in Los Angeles reported a lower odds of perceived illicit fentanyl use (aOR 0.29; 95% CI: 0.18–0.49;  $p < 0.001$ ), compared to people living in San Francisco. Lastly, people who reported opioid use in the past 30 days were more likely to report perceived illicit fentanyl use (aOR 4.11; 95% CI: 1.91–8.82;  $p < 0.001$ ), compared to people who did not have a recent history of opioid use.

Regarding our primary study outcomes, 31% (95% CI: 27–35%) reported high frequency opioid use, 35% (95% CI: 30–39%) reported high frequency injection and 13% (95% CI: 10–17%) reported receptive syringe sharing. Findings from our adjusted logistic regression models suggested that people who reported perceived illicit fentanyl use in the past 6 months had a greater odds of high frequency opioid use (aOR = 2.36; 95% CI: 1.43–3.91;  $p = 0.001$ ), high frequency injection (AOR = 1.84; 95% CI: 1.08–3.13;  $p = 0.03$ ) and receptive syringe sharing (aOR = 2.16; 95% CI: 1.06–4.36;  $p = 0.03$ ), as compared to people using heroin and other street drugs but not fentanyl (Tables 2 and 3).

## Discussion

Against a backdrop of increasing fentanyl use and associated fatalities in the United States, the current study investigated associations between perceived illicit fentanyl use and infectious disease risk behaviors – high frequency injection and receptive syringe sharing – in a community-based study of PWID in San Francisco and Los Angeles. Notably, our findings suggested that participants reporting perceived illicit fentanyl use were more likely to report high frequency opioid use, high frequency injection and receptive syringe sharing compared with people using heroin and other street drugs but not fentanyl.

Our findings are aligned with two recent cross-sectional studies of fentanyl injection. In Estonia, Talu et al. found that people who were primary fentanyl injectors had a higher odds of high injection frequency, sharing needles with someone who had HIV and being HIV-positive, compared to people who were primarily methamphetamine injectors (Talu et al., 2010). Similarly in Australia, Geddes et al. found that people who had recently injected fentanyl were more likely to report higher frequency of injection compared to people injecting other prescription opiates (Geddes et al., 2017).

In addition, our results are consistent with findings from several qualitative studies on fentanyl consumption from North America (Mars, Ondocsin, & Ciccarone, 2018; Mayer et al., 2018; Somerville et al., 2017). Mayer and colleagues, for example, conducted an ethnographic study in which the participants noted that, while stronger, the high from fentanyl-adulterated products did not last as long as a typical heroin high, and consequently, it needed to be taken more frequently than heroin.<sup>8</sup> Our findings are also consistent with fentanyl's pharmacokinetic profile. Fentanyl is a synthetic opioid analgesic targeting the mu receptor and has persistent lipophilicity which results in a rapid onset of action and short duration of effect (Medscape, 2005). When injected, the combination of rapid onset and

**Table 2**  
Characteristics associated with perceived illicit fentanyl use among people who inject drugs in Los Angeles and San Francisco in 2017–2018 (N = 395).

	OR (95% CI)	p-value	aOR (95% CI)	p-value
<b>Gender Identity</b>				
Cisgender Male	–			
Cisgender Female	0.93 (0.58–1.47)	0.746		
Transgender	NC			
<b>Race</b>				
Latinx	–		–	
Black	0.77 (0.40–1.51)	0.448	0.77 (0.36–1.65)	0.505
White	3.35 (1.94–5.77)	<0.001	1.84 (0.96–3.53)	0.068
Asian/Pacific Islander	NC		NC	
Native American	3.62 (1.37–9.53)	0.009	2.27 (0.75–6.86)	0.146
Mixed Race	2.63 (1.07–6.46)	0.035	1.74 (0.63–4.77)	0.284
<b>Sexual Identity</b>				
Heterosexual	–			
Gay or Lesbian	0.39 (0.13–1.11)	0.078		
Bisexual	1.44 (0.81–2.57)	0.212		
<b>Age</b>				
< 30	–		–	
30–39	0.56 (0.27–1.16)	0.121	0.50 (0.21–1.16)	0.108
40–49	0.28 (0.14–0.57)	<0.001	0.31 (0.14–0.72)	0.007
≥ 50	0.14 (0.07–0.29)	<0.001	0.20 (0.09–0.47)	<0.001
<b>Income</b>				
< \$1000	–		–	
≥ \$1000	2.86 (1.88–4.34)	<0.001	2.09 (1.27–3.41)	0.003
<b>City of Residence</b>				
San Francisco	–		–	
Los Angeles	0.22 (0.14–0.34)	<0.001	0.29 (0.18–0.49)	<0.001
<b>Homelessness</b>				
No	–			
Yes	1.55 (0.99–2.42)	0.057		
<b>Opioid Use, past 30 days</b>				
No	–		–	
Yes	3.53 (1.82–6.86)	<0.001	4.11 (1.91–8.82)	<0.001
<b>Alcohol Use, past 30 days</b>				
No	–			
Yes	0.77 (0.52–1.14)	0.190		
<b>Jail, past 6 months</b>				
No	–			
Yes	1.45 (0.94–2.23)	0.089		
<b>Substance Use Treatment, past 6 months</b>				
No	–			
Yes	1.18 (0.77–1.81)	0.444		

**Table 3**  
Perceived illicit fentanyl use and drug use practices among people who inject drugs (N = 395).

Illicit fentanyl use	High frequency opioid use (> 90 times per month)*				High frequency injection (> 90 injections per month)**				Receptive syringe sharing***			
	No n (%)	Yes n (%)	aOR (95% CI)	p-value	No n (%)	Yes n (%)	aOR (95% CI)	p-value	No n (%)	Yes n (%)	aOR (95% CI)	p-value
No	158 (81)	38 (19)	–		149 (76)	47 (24)	–		175 (89)	21 (11)	–	
Yes	114 (58)	84 (42)	2.36 (1.43–3.91)	0.001	107 (54)	92 (46)	1.84 (1.08–3.13)	0.026	168 (85)	30 (15)	2.16 (1.06–4.36)	0.033

aOR = adjusted odds ratio; 95% CI = 95% confidence interval.

\* past 30 days; final covariates included in the model: income, sexual orientation, homelessness, alcohol use and recent substance use treatment.

\*\* Past 30 days; final covariates included in the model: income, race/ethnicity, gender orientation, sexual orientation, recent jail experience, recent substance use treatment, and any opioid use.

\*\*\* past 6 months; final covariates included in the model: city of residence, race/ethnicity, gender orientation and recent jail experience.

short duration translates to an effect best described as a strong “rush” followed by a brief period of euphoria (5–15 min).<sup>8</sup> Furthermore, Firestone and colleagues suggested that practices related to the extraction of fentanyl from diverted pharmaceutical fentanyl products could also be a driver of injection-related risk behaviors (Firestone, Goldman, & Fischer, 2009). More specifically, people reported that fentanyl matrix patches were mostly affordable to groups of people, and the extraction of fentanyl from patches was often collected into one spoon that the entire group would use (Firestone et al., 2009). Though our study does not disentangle the use of different types of fentanyl products, this would be an important area for future

investigation to inform interventions that focus on the supply of fentanyl in the illicit drug supply (Firestone et al., 2009). In addition, fentanyl strips test – another promising approach for helping people discern whether fentanyl is in their drug – should be accessible to PWID (Peiper et al., 2019 #52).

Our findings that perceived illicit fentanyl use was associated with high frequency injection and receptive syringe sharing is particularly concerning for disease prevention efforts because it increases the number of times PWID can be exposed to parenterally-transmitted diseases, such as HIV and HCV infection. In the 1990s when HIV incidence increased and the HIV prevalence doubled among PWID in

Vancouver, Canada, research showed that two main predictors of HIV during this period included sharing syringes and drug injection frequency (Patrick et al., 1997). Correspondingly, in 2015, a large HIV outbreak in Scott County, Indiana was linked to the injection of oxycodone and facilitated by an increase in the number of daily injections and the sharing of syringes (Conrad et al., 2015; Peters et al., 2016). In addition, a number of studies have shown that syringe sharing and injection frequency are predictors of HCV infection (Amon et al., 2008; Paintsil, He, Peters, Lindenbach, & Heimer, 2010; Thorpe et al., 2002).

In light of this evidence, our findings highlight the urgent need for evidence-based interventions that can reduce parenterally-transmitted diseases. Underpinned by a robust body of evidence (Wodak & Cooney, 2006), syringe access programs have served as the backbone of such efforts and should be rapidly scaled-up, especially in regions where people are using fentanyl. In terms of the effectiveness of different delivery models, syringe access programs with less restrictive distribution policies have been shown to have higher levels of syringe coverage, which in turn improves safe injection practices and reduces the risk for and transmission of HIV (Bluthenthal et al., 2007; Bluthenthal, Anderson, Flynn & Kral, 2007; Kerr et al., 2010; Kral, Anderson, Flynn, & Bluthenthal, 2004). Syringe programs can also serve as a platform for providing entry into the HIV and HCV cascade of care (Gardner & Young, 2014; Yehia, Schranz, Umscheid, & Lo Re, 2014), by providing integrated HIV and HCV testing and linkage to care and treatment as needed (Centers for Disease Control & Prevention, 2018d). In addition, improved access to medication-assisted treatments (e.g., methadone and buprenorphine) are indicated and have been demonstrated to reduce infectious disease risk, other comorbidities, and mortality associated with drug injection in multiple studies (Fullerton et al., 2014; Ma et al., 2018; Thomas et al., 2014). A recent systematic review showed that integrated medication assisted treatment and syringe access programs conferred the most protection in preventing HCV (Platt et al., 2018). Finally, our findings emphasize the need to pilot and evaluate innovative approaches, such as supervised consumption spaces, as they have been shown in other countries to reduce syringe sharing (Bravo et al., 2009; Kerr, Tyndall, Li, Montaner, & Wood, 2005). Furthermore, longitudinal observational studies are needed to investigate the unique health risks associated with the introduction of fentanyl into the drug supply.

### Limitations

The current study needs to be understood in the context of several potential limitations. This is an observational epidemiological study and although we included several covariates to address potential confounding, it is possible that unmeasured or mismeasured factors biased our results. In addition, we cannot make causal inference because of the lack of temporality between exposures and outcomes given the cross-sectional nature of our study. For example, people who use opioids more frequently, inject more frequently or share syringes may be more likely to have come across fentanyl in the course of their drug use, compared to someone who uses less frequently, injects less frequently or does not share syringes, respectively. We attempted to ameliorate this bias by defining exposure periods that were longer than outcome periods when possible, but this does not convey the same level of rigor as a longitudinal study. Our exposure also does not capture the frequency of perceived illicit fentanyl use or verify perceived illicit fentanyl use with biospecimen testing. Therefore, this represents a population who perceived that they were using fentanyl. In addition, our measure of perceived illicit fentanyl use combined both injection and non-injection routes of administration. While our measure of perceived illicit fentanyl use was imperfect, we believe that these limitations would make our exposure measure less sensitive to the outcomes under study, making it more difficult to detect associations. Because survey participants self-reported drug injecting behaviors and health

outcomes, memory recall and social desirability may serve as potential biases and limit the impact of the metrics collected. Due to the stigmatization of injection drug use and other drug-related behaviors, social desirability is a common limitation when surveying people who use drugs (Perlis, Des Jarlais, Friedman, Arasteh, & Turner, 2004). Yet, decades of research with PWID has proven that self-report by this population is both reliable and valid for epidemiological purposes (Dowling-Guyer et al., 1994; Needle et al., 1995). Finally, since this study occurred in just two California cities, we are not able to generalize our findings to all PWID in California or elsewhere.

In conclusion, people who reported perceived illicit fentanyl use were at increased risk for infectious disease. Our findings should be considered in light of a strong body of research linking injection frequency and syringe sharing with infectious diseases. Our findings suggest that proactive actions must be taken to head off the potential transmission of infectious diseases. To address these risks, syringe access programs and opioid treatment must be scaled up (Fullerton et al., 2014; Ma et al., 2018; Thomas et al., 2014; Wodak & Cooney, 2006), and innovative approaches, such as supervised consumption services (Marshall, Milloy, Wood, Montaner, & Kerr, 2011), must be considered to avoid increases in infectious disease outbreaks in regions with high levels of fentanyl use. Future longitudinal studies should further investigate ways in which fentanyl is changing drug use, and how these changes are placing PWID at increased risk for injection-related harm.

### Declaration of Competing Interest

We declare that we have no conflicts of interest.

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### Contributors

B.L. was involved in developing, drafting and revising all aspects of the manuscript. B.L. analyzed the data and developed the statistical methods section. R.B. and A.K. assisted in developing the research questions and statistical approach. R.B., J.Z., L.W., K.S. and A.K. drafted sections of the manuscript and revised all sections of the manuscript.

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