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Full length article

Prevalence and correlates of obstructive lung disease among people who inject drugs, San Diego, California

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ABSTRACT

Background: Pulmonary tissue damage leading to obstructive lung disease (OLD) could result from intravenous administration of insoluble particles found in illicit drugs. This study described the prevalence and identified correlates of OLD among people who inject drugs (PWID).

Methods: In 2012–2016, a community-based cohort of PWID who had injected within the past month were enrolled in a study to assess HIV, hepatitis C virus (HCV) and*Mycobacterium tuberculosis* (*Mtb*) infections and their related risk factors. Data were obtained through face-to-face interviews, serological testing and spirometry. Baseline data were used for a cross-sectional analysis of the prevalence and correlates of OLD, defined as FEV1/FVC < 0.7. Univariate and multivariable logistic regression were used to identify factors associated with OLD.

Results: Among 516 participants who had complete spirometry and interview results, the mean age was 43.3 years, 73.6 % were male, 9.5 % were Black, 91.1 % smoked cigarettes and 18.2 % had OLD. Few (9.6 %) PWID with OLD reported a previous diagnosis of COPD although many (44.7 %) reported related symptoms. Black race (AOR = 2.66, 95 %CI: 1.37, 5.17), pack-years smoked (AOR = 1.06/5 years, 95 %CI: 1.01, 1.12), and duration of injection drug use (AOR = 1.13, 95 %CI: 1.01, 1.27) were independently associated with OLD after controlling for age.

Conclusions: The prevalence of OLD was high in this cohort and associated with Black race and cigarette smoking—known risk factors. In addition, OLD prevalence increased with greater duration of injection drug use, suggesting a link between cumulative exposure to injected insoluble particles and OLD. Further examination of these adulterants and lung pathology are needed.

1. Introduction

Obstructive lung disease (OLD) is a group of conditions characterized by episodic or persistent airflow limitation that makes breathing difficult, which may be partially irreversible (Global Initiative for Chronic Obstructive Lung Disease, 2018). These conditions include chronic obstructive pulmonary disease (COPD) and asthma, and are characterized by symptoms of shortness of breath, chest tightness, wheezing, cough, and mucus production. Among United States (U.S.) adults, the number of physician-diagnosed COPD and asthma cases annually is a staggering 14.8 and 25 million, respectively (Office of Disease Prevention and Health Promotion, 2019), and globally the number has reached 251 and 235 million cases, respectively (World Health Organization (WHO), 2017, 2019). COPD is the fourth leading cause of death in the U.S. (Heron, 2018) and remains the third leading cause of death worldwide (World Health Organization (WHO), 2018). Mortality outcomes for individuals with COPD vary by patient phenotype (whether there is overlap with asthma, moderate/severe exacerbations with chronic bronchitis or emphysema, etc.), but is predominantly due to disease progression (Golpe et al., 2018). OLD costs the U.S. healthcare system an estimated $50 billion annually in COPD-related expenditures – $30 billion going to direct healthcare costs, and the rest to indirect costs, such as patients' inability to work or time taken off from work (Guarascio et al., 2013) – and $20.7 billion per year in asthma-related expenditures (Office of Disease Prevention and Health Promotion, 2019).

The leading risk factor for COPD is cigarette smoking (Bhatt et al., 2018), but studies have also reported associations with older age (de Marco et al., 2011), low socioeconomic status (Wheaton et al., 2015), human immunodeficiency virus (HIV) infection (Drummond et al.,

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2012) and history of pulmonary tuberculosis (Byrne et al., 2015). COPD has been found to be associated with injection drug use (Crothers et al., 2006), although this could be confounded by the very high prevalence of smoking among people who inject drugs (PWID) (Clarke et al., 2001). To date, only one study has assessed OLD specifically among PWID (Horyniak et al., 2017). In addition to factors such as age, gender, lower education and history of childhood respiratory illness being associated with COPD among non-smokers (Lamprecht et al., 2011), there is evidence to suggest that the risk of OLD among PWID might not be entirely attributable to smoking (Ward et al., 2000).

One hypothesis is that non-soluble contaminants added to illicit drugs by dealers to increase their volume, or excipients added to oral prescription medications as binders or to help them dissolve faster, may become lodged in the alveoli when they are injected intravenously, causing lung pathology (Gotway et al., 2002). For example, pulmonary fibrosis and granulomas, in addition to emphysema and pulmonary hypertension, have been reported with injection of talc-containing drugs (Griffith et al., 2012; Paré et al., 1989). Other drug excipients like microcrystalline cellulose, crospovidone (an insoluble, hygroscopic powder contained in pills to help them dissolve), and starch have also been reported to lead to pulmonary complications when injected (Fields et al., 2005; Ganesan et al., 2003; Lamb and Roberts, 1972; Nguyen et al., 2014); however, these may be less likely than talc to enter the lungs as they tend to be larger in size (Kringsholm and Christoffersen, 1987). Considering these mechanisms, certain injection drug-related factors (e.g., type of drugs injected, frequency and duration of injection drug use) may increase exposure to adulterants, thereby contributing to the increased risk of OLD among PWID.

The primary objectives of this study were to measure the prevalence of OLD among PWID in San Diego, CA, and to identify PWID-specific correlates of OLD in this population after controlling for known risk factors. It was hypothesized that OLD would be independently associated with factors related to injection drug use. Due to the reported lack of access to healthcare (Chitwood et al., 1999) and/or the over-utilization of emergency department care in this population (Kerr et al., 2004), a secondary analysis evaluated whether there was an association between utilization of healthcare in PWID and OLD.

2. Methods

2.1. Study design

The present study used baseline data from the Study of Tuberculosis, AIDS, and Hepatitis C Risk (STAHR II) cohort for a cross-sectional analysis of the prevalence and correlates of OLD among PWID. STAHR II was a prospective cohort study in which community-recruited PWID who had injected at least once in the prior month (actively injecting) were enrolled in 2012–2014, and followed for two years through semi-annual follow-up visits to determine the prevalence, incidence, and risk factors for *Mycobacterium tuberculosis* (*Mtb*), HIV, and hepatitis C virus (HCV) infections among PWID in San Diego, CA. STAHR II methods were published in detail elsewhere (Robertson et al., 2014).

2.2. Human subjects approval

The STAHR II study protocol was approved by an institutional review board at the University of California San Diego, and all participants provided written informed consent. The current analysis also received a Non-Human Subjects Research Determination from San Diego State University's Human Research Protections Program.

2.3. Study population

Study participants were recruited through targeted sampling, which consisted of street outreach and posting flyers in areas where PWID generally gather (e.g., syringe exchange program sites), print and online advertising (e.g., local newspaper, Craigslist), as well as through participant referrals (Robertson et al., 2014). Eligible participants were at least 18 years old, spoke English or Spanish, had illicitly injected drugs in the past 30 days, were non-institutionalized (i.e., hospitalized, incarcerated or in-patient substance use treatment), and resided in San Diego County without plans to move away in the next 24 months.

2.4. Outcome measure

OLD status (yes/no) was determined at baseline by spirometry using a forced expiratory volume per second/forced vital capacity (FEV1/FVC) ratio without the use of bronchodilators. Spirometry was repeated three times in the same visit and then averaged according to 1994 American Thoracic Society recommendations (Standardization of Spirometry, 1994). OLD was defined as a fixed ratio FEV1/FVC value < 0.70 based on Global initiative for chronic Obstructive Lung Disease (GOLD) cut-offs (Güder et al., 2012).

2.5. Interview measures

Computer-assisted personal interviews were conducted at baseline by trained interviewers in a private setting and lasted an average of $60-90$ min. Interviews collected information about potential correlates and known risk factors for OLD including socio-demographics (i.e., age, gender, race/ethnicity, homelessness), smoking status, lifetime and recent drug use and injection behaviors, symptoms and previous diagnosis of respiratory illness, and healthcare utilization.

Due to the non-linear relationship between age and risk of OLD, age (collected in years) was categorized for this analysis as a binary variable (<40 years and ≥ 40 years) for consistency with other studies as this is the age that COPD symptoms typically begin (National Heart Lung and Blood Institute, COPD, 2020) and COPD prevalence increases (Ntritsos et al., 2018). Eight individuals reported being transsexual/transgender and were grouped by their preferred binary gender (male/female). Since prior studies found only Black race to be associated with OLD compared to other races (Chatila et al., 2006; Drummond et al., 2012), race was dichotomized for this analysis (Black/non-Black). For descriptive purposes, a non-binary race variable (Asian, Black, Hispanic, Other, White) was reported. Self-perceived homelessness was queried, "In the past 6 months, have you ever thought of yourself as homeless?" (yes or no).

To obtain cigarette smoking status, participants were asked about lifetime history of smoking ("Have you ever smoked at least 100 cigarettes in your entire life?" [yes/no]), and current smoking status ("Do you smoke cigarettes now?" [yes/no]). Responses to these questions were used to create a "cigarette smoking status" variable (never smoker, former smoker, current smoker). Pack-years of smoking among former and current smokers was calculated as the number of cigarettes smoked per day times the number of years smoked divided by 20. Participants were also asked if they had ever used marijuana or hash (yes/no).

To examine injection drug use practices, participants were asked to specify the number of years they had been injecting drugs (continuous) and the specific types of drugs (e.g., heroin, cocaine, methamphetamine) they had injected, smoked, or inhaled in their lifetime (yes/no). Types of heroin injected (black tar, white powder, brown powder, other) were assessed among those who reported injecting heroin in the past 6 months.

The main reasons for not seeking medical care in the past 6 months, if applicable, were grouped into 6 categories due to small sample sizes (visit not expected to be helpful, avoidance of bad news; fear of hostility, disrespect, or arrest; too embarrassed, ashamed, tired, sleepy, lazy, depressed, ill, weak, sick, or busy to go; transportation issues; no insurance, too expensive; or other). Questions also queried whether participants had received professional help for drug or alcohol use in

their lifetime (yes/no), and if yes, the type of professional help received (drugs only, alcohol only, both), and the number of times help was received (continuous). Respiratory-related symptoms and previous diagnoses were also assessed.

2.6. Serologic testing

Following the interview, participants received pre-test counselling and serologic testing for HIV (Uni-Gold Recombigen, Trinity Biotech PLC, Bray, Ireland), HCV (OraQuick®, OraSure Technologies, Bethlehem, USA) and *Mtb* (QuantiFERON-TB Gold In-Tube, Qiagen, Hilden, Germany) infection using commercially-available assays (described elsewhere) (Horyniak et al., 2017). Post-test counselling and referrals for care were also provided depending on test results.

2.7. Data analysis

Descriptive statistics were calculated for all variables. For skewed data we report medians and interquartile ranges (IQRs) instead of means. Bivariate associations were assessed between OLD and other covariates using chi-square tests for categorical variables and t-tests or Wilcoxon Rank Sum tests for continuous variables, and simple logistic regression. Covariates with a p-value < 0.10 in bivariate analysis or supported by the literature as potential risk factors for OLD were included in multivariable analyses. Collinearity was assessed using tolerance (< 0.1) and variance inflation (> 10) statistics.

A backwards stepwise regression procedure was used to determine factors independently associated with OLD. Pack-years smoked, age, and race were kept in models examining correlates of OLD to control for known risk factors (Chatila et al., 2006; Global Initiative for Chronic Obstructive Lung Disease, 2018). All other variables were only retained in the final model if they were significant at the alpha = 0.05 level. Statistical analyses were conducted using SAS version 9.4.

3. Results

Of the 573 STAHR II participants, 516 (90.5 %) had complete baseline spirometry and interview data for this analysis. Fifty-five participants had missing spirometry results because of either recent surgery or participant refusal precluded measurement. Most participants were 40 years of age or older (63.6 %), male (73.6 %), and non-Black (90.5 %). Overall, the mean number of years injecting drugs was 20.7 (standard deviation [SD] ± 13.3) and the median number of times injected in the past six months was 200 (IQR 78 − 420). The most common drugs ever injected were heroin (85.6 %), methamphetamine (81.4 %), and cocaine (64.7 %) (lesser used drugs not shown and are available from the authors). The overall prevalence of OLD was 18.2 % (n = 94).

On bivariate analysis (Table 1), we found that having OLD was associated with age greater than 40 (p = 0.030), Black race (p = 0.002), higher smoking intensity (median pack-years: 19.5 vs 12.5, p = 0.002), and longer duration of injection drug use (mean years: 24.9 vs 19.8, p < 0.001). We did not observe statistically significant associations between OLD and other socio-demographics, type of drug injected, frequency of injecting in the past 6 months, behavioral factors and HIV, HCV or *Mtb* infection.

Compared to PWID without OLD (Table 2), a greater proportion of PWID with OLD reported shortness of breath (p = 0.003) or a physician diagnosis of emphysema (p < 0.001) or other lung diseases (p = 0.036). Although 44.7 % of PWID with OLD reported respiratory symptoms, only 10.6 % reported physician-diagnosed emphysema. PWID with OLD were more likely to see a doctor or healthcare provider (p = 0.030) and marginally more likely to report healthcare utilization in the past 6 months in terms of emergency department visits (p = 0.082) and having healthcare coverage/insurance (p = 0.068). The main reason for not seeking medical care when needed differed

Table 1
Participant characteristics by obstructive lung disease (OLD) status among persons who inject drugs, San Diego, CA.

	Overall (n = 516)	OLD (n = 94)	No OLD (n = 422)	p-value*
Age, n (%)				
< 40 years	188 (36.4)	25 (26.6)	163 (38.6)	–
≥40 years	328 (63.6)	69 (73.4)	259 (61.4)	**0.030**
Gender, n (%)				
Male	380 (73.6)	72 (76.6)	308 (73.0)	–
Female	136 (26.3)	22 (23.4)	114 (27.0)	0.473
Race (non-binary), n (%)				
Asian	4 (0.78)	0 (0.0)	4 (0.78)	0.987
Black	49 (9.5)	17 (18.1)	32 (7.6)	**0.004**
Hispanic	156 (30.2)	24 (25.5)	132 (31.3)	0.744
Other	48 (9.3)	10 (10.6)	38 (9.0)	0.477
White	259 (50.2)	43 (45.7)	216 (51.2)	–
Race (binary), n (%)				
Non-Black	467 (90.5)	77 (81.9)	390 (92.4)	–
Black	49 (9.5)	17 (18.1)	32 (7.6)	**0.002**
Homeless in past 6 months, n (%)				
No	197 (38.2)	33 (35.1)	164 (38.9)	–
Yes	319 (61.8)	61 (64.9)	258 (61.1)	0.498
History of smoking, n (%)				
No	45 (8.7)	8 (8.5)	37 (8.8)	–
Yes	470 (91.1)	85 (90.4)	385 (91.2)	0.959
Missing**	1 (0.2)	1 (1.1)	0 (0.0)	
Cigarette smoking status, n (%)				
Never smoked	45 (8.7)	8 (8.5)	37 (8.8)	–
Former smoker	30 (5.8)	5 (5.3)	25 (5.9)	0.901
Current smoker	440 (85.3)	80 (85.1)	360 (85.3)	0.947
Missing**	1 (0.2)	1 (1.1)	0 (0.0)	
Pack-years of cigarette smoking, (n = 513) Median (IQR)	13.5 (5.2 − 29)	19.5 (9 − 37)	12.5 (4.5 − 25)	**0.002**
Ever used marijuana				
No	22 (4.3)	2 (2.1)	20 (4.7)	–
Yes	494 (95.7)	92 (97.9)	402 (95.3)	0.397
Years of injection drug use, Mean (± SD)	20.7 (± 13.3)	24.9 (± 13.8)	19.8 (± 13.1)	< **0.001**
Number of times injected in past 6 months, n = 515 Median (IQR)	200 (78 − 420)	189 (48 − 364)	208 (78 − 420)	0.871
Ever injected heroin, n (%)				
No	74 (14.3)	10 (10.6)	64 (15.2)	–
Yes	442 (85.7)	84 (89.4)	358 (84.8)	0.355[a]
Form of heroin injected in past 6 months, n (%)				
Black tar	327 (63.4)	57 (60.6)	270 (64.0)	–
White powder	5 (1.0)	2 (2.1)	3 (0.7)	0.214
Brown powder	20 (3.9)	5 (5.3)	15 (3.6)	0.395
Other	8 (1.6)	1 (1.1)	7 (1.7)	0.717
N/A**	156 (30.2)	29 (30.9)	127 (30.1)	
Ever smoked heroin, n (%)				
No	190 (36.8)	39 (41.5)	151 (35.8)	–
Yes	326 (63.2)	55 (58.5)	271 (64.2)	0.300
Ever snorted/ inhaled heroin, n (%)				
No	197 (38.2)	34 (36.2)	163 (38.6)	–
Yes	319 (61.8)	60 (63.8)	259 (61.4)	0.658

(*continued on next page*)

Table 1 (*continued*)

	Overall (n = 516)	OLD (n = 94)	No OLD (n = 422)	p-value*
Baseline HIV test result, n (%)				
Nonreactive	466 (90.3)	88 (93.6)	378 (89.6)	–
Reactive	49 (9.5)	6 (6.4)	43 (10.2)	0.252
Missing**	1 (0.2)	0 (0.0)	1 (0.2)	
Baseline HCV test result, n (%)				
Nonreactive	178 (34.5)	149 (35.3)	29 (30.9)	–
Reactive	337 (65.3)	273 (64.7)	64 (68.1)	0.449
Missing**	1 (0.2)	.	1 (1.1)	
Baseline *Mtb* test result, n (%)				
Negative	372 (72.1)	66 (70.2)	306 (72.5)	–
Positive	114 (22.1)	24 (25.5)	90 (21.3)	0.426
Missing**	30 (5.8)	4 (4.3)	26 (6.2)	

Abbreviations: IQR: interquartile range. SD: standard deviation. HCV: hepatitis C virus. HIV: human immunodeficiency virus. Mtb: *mycobacterium tuberculosis*. *P-values were based on Chi-square test, t-test, or simple logistic regression. [a]: ≥25 % of cell sizes < 5, performed Fisher's Exact test.
**Participants that are "missing" or "N/A" were excluded from the analysis. Values are shown for reporting purposes.

between groups, with PWID with OLD more often reporting that the "visit [was] not expected to be helpful, avoidance of bad news" (p = 0.021) and "fear of hostility, disrespect or arrest" (p = 0.065). No other respiratory symptoms or illnesses or healthcare utilization variables were associated with OLD.

In multivariable logistic regression analysis adjusting for age, pack years smoked, and Black race (Table 3), we observed a 13 % increase in the odds of OLD for every 5 years injecting drugs (adjusted odds ratio [AOR] = 1.13, 95 % confidence interval [CI]: 1.01, 1.27). In the final model, OLD was also independently associated with Black race (AOR = 2.66, 95 % CI: 1.37, 5.17) and smoking history, with a 6% increase in the odds of OLD for every 5 pack-years smoked (AOR = 1.06, 95 % CI:1.01, 1.12).

4. Discussion

This study found the prevalence of OLD to be 18.2 % among PWID in San Diego, CA. Black race, pack-years smoked, and duration of injection drug use were independently associated with OLD after adjusting for age. Although PWID with OLD have increased need for healthcare, access to and utilization of health services were not associated with OLD in this study.

The observed prevalence of OLD in this study is similar to that found among current and former PWID in Baltimore, MD (16.3 %) (Drummond et al., 2011). The prevalence among PWID is much higher than the general population where the prevalence of COPD is approximately 3.4 % (World Health Organization (WHO), 2017). This finding highlights the disparity faced by PWID potentially due to behavioral, economic, and environmental factors. Factors that might account for this disparity include a high prevalence of current smokers (Clarke et al., 2001), high rates of HIV (Alcabes and Friedland, 1995; Morris et al., 2011) and *Mtb* infection (Armenta et al., 2017; Byrne et al., 2015), socioeconomic disadvantage (Wheaton et al., 2015), and delayed detection and/or treatment of OLD due to healthcare stigma or limited access (Drummond et al., 2011; Neale et al., 2008). Our findings provide further evidence that OLD disproportionately affects PWID, and a multilevel approach is needed to address the disparity.

Our findings provide novel information about OLD among PWID. Nearly the entire cohort smoked cigarettes, and consistent with the evidence in a smoking population (Jaen Diaz et al., 2003), pack-years smoking was independently associated with OLD status. The fact that smoking was nearly ubiquitous in this cohort was a relative strength of the study in that it allowed for assessment of other correlates of OLD. Black race was found to be independently associated with OLD. Black race has been previously identified as a risk factor for early-onset COPD, defined as age < 55 years (Foreman et al., 2011). The older age category in this study included those considered for early-onset COPD in the prior study, which may explain the high prevalence of OLD among Blacks in this cohort. Higher prevalence of OLD among Blacks may occur because of greater vulnerability to the effects of tobacco smoking (Dransfield et al., 2006). Despite smoking fewer cigarettes per day, Blacks with emphysema showed similar lung impairment to their White counterparts in the National Emphysema Treatment Trial (Chatila et al., 2006). Duration of injection drug use was also independently associated with OLD status. This comports with the hypothesis that exposure to non-soluble particles in illicit drugs or medications meant for oral use might increase the risk for OLD, because injection duration is a proxy for cumulative exposure to excipients.

The specific drug type or administration route (injected, smoked, or inhaled) was not associated with OLD. Without knowing the type or quantity of contaminants and lifetime frequency of exposure, it is difficult to assess whether specific drugs increase the risk of OLD. Assuming all drugs contain some contaminants, it is also the case that lack of specificity between drugs may mask any association. This hypothesis merits further investigation in a larger sample that more precisely measures the quantities and types of contaminants injected over time.

OLD is often not recognized among PWID in healthcare settings (Drummond et al., 2011), despite our finding no association between OLD and healthcare variables in this study. Less than half of this cohort (45.2 %) reported receiving healthcare in the past 6 months and a similar proportion (40.7 %) reported not going to see a doctor or healthcare provider even if they perceived the need to go. While 50 % of PWID in Baltimore had a diagnosis of OLD or emphysema from a physician (Drummond et al., 2011), only 9.6 % and 10.6 %, respectively, had these diagnoses among those with OLD in our cohort; however, 44.7 % reported shortness of breath (dyspnea) suggesting that OLD is underdiagnosed among PWID in San Diego, CA. Dyspnea is one of the most commonly reported symptoms of COPD and is part of its pathophysiology (Anzueto and Miravitlles, 2017). Despite experiencing symptoms indicative of OLD (i.e. dyspnea), few in this cohort sought primary care. PWID with OLD were less likely to seek care because they expected their visit to be unhelpful, they would receive bad news, or they would be mistreated. Prior studies report less access to healthcare among PWID compared to the general population (Chitwood et al., 1999), which could result in underutilization of primary healthcare services. Aside from the obstacles perceived by PWID, healthcare providers also cite that insufficient education on the "unique and demanding nature of PWIDs" (Lang et al., 2013) as an additional obstacle to care.

In addition, PWID may over-utilize emergency department care for injection-related complications (Kerr et al., 2004; Raven et al., 2009). A slight trend of over-utilization was seen in those with OLD; participants only reported on emergency department visits in the past 6 months, which might have attenuated this finding. Specialized treatment programs however were heavily utilized with nearly 80 % having received substance use treatment in their lifetime. Screening for OLD remains important in this underserved population, and better access to healthcare is crucial.

The SARS-CoV-2 virus responsible for a pandemic of novel coronavirus disease (COVID-19) that began in 2019 disproportionately affects older individuals, particularly those with underlying immunosuppressive conditions and lung disease such as COPD (Chinese

Table 2
Respiratory-related symptoms and diagnoses, and health care utilization by obstructive lung disease (OLD) status among persons who inject drugs, San Diego, CA.

	Overall (n = 516)	OLD (n = 94)	No OLD (n = 422)	p-value*
Shortness of breath in last month[a], n (%)				
No	352 (68.2)	52 (55.3)	300 (71.1)	–
Yes	164 (31.8)	42 (44.7)	122 (28.9)	**0.003**
Self-reported physician diagnosis of emphysema[a], n (%)				
No	496 (96.1)	84 (89.4)	412 (97.6)	–
Yes	20 (3.9)	10 (10.6)	10 (2.4)	< **0.001**
Self-reported physician diagnosis of COPD[a], n (%)				
No	477 (92.4)	85 (90.4)	392 (92.9)	–
Yes	39 (7.6)	9 (9.6)	30 (7.1)	0.414
Self-reported physician diagnosis of asthma[a], n (%)				
No	422 (82.2)	76 (80.9)	348 (82.5)	–
Yes	92 (17.8)	18 (19.2)	74 (17.5)	0.712
Self-reported physician diagnosis of other lung disease[a], n (%)				
No	481 (93.2)	83 (88.3)	398 (94.3)	–
Yes	35 (6.8)	11 (11.7)	24 (5.7)	**0.036**
Health coverage/insurance in past 6 months, n (%)				
No	257 (49.8)	39 (41.5)	218 (51.7)	–
Yes	257 (49.8)	55 (58.5)	202 (47.9)	**0.068**
Don't know**	2 (0.4)	0 (0.0)	2 (0.5)	
Received healthcare in the past 6 months, n (%)				
No	283 (54.8)	48 (51.1)	235 (55.7)	–
Yes	233 (45.2)	46 (48.9)	187 (44.3)	0.415
Hospitalized[a] **in past 6 months**, n (%)				
No	424 (82.2)	79 (84.0)	345 (81.8)	–
Yes	92 (17.8)	15 (16.0)	77 (18.3)	0.600
Visited emergency department in past 6 months, n (%)				
No	339 (65.7)	69 (73.4)	270 (64.0)	–
Yes	177 (34.3)	25 (26.6)	152 (36.0)	**0.082**
Visited out-patient clinic in past 6 months, n (%)				
No	370 (71.7)	69 (73.4)	301 (71.3)	–
Yes	146 (28.3)	25 (26.6)	121 (28.7)	0.686
Perceived need to see a doctor or healthcare provider for physical or emotional problems, but did not go in past 6 months, n (%)				
No	305 (59.1)	65 (69.2)	240 (56.9)	–
Yes	210 (40.7)	29 (30.9)	181 (42.9)	**0.030**
Refuse to answer**	1 (0.2)	0 (0.0)	1 (0.2)	
Main reason for not seeking medical care when needed in past 6 months, n (%)				
Visit not expected to be helpful, avoidance of bad news	18 (3.5)	5 (5.3)	13 (3.1)	**0.021**
Fear of hostility, disrespect, or arrest	12 (2.3)	3 (3.2)	9 (2.1)	**0.065**
Too embarrassed, ashamed, tired, sleepy, lazy, depressed, ill, weak, sick, or busy to go	45 (8.7)	6 (6.4)	39 (9.2)	0.247
Transportation issues	12 (2.3)	1 (1.1)	11 (2.6)	0.824
No insurance, too expensive	61 (11.8)	4 (4.3)	57 (13.5)	–
Other	52 (10.1)	7 (7.5)	45 (10.7)	0.226
Not applicable	315 (61.1)	68 (72.3)	247 (58.5)	
Refuse to answer**	1 (0.2)	0 (0.0)	1 (0.2)	
Ever in substance use treatment[b], n (%)				
No	106 (20.5)	14 (14.9)	92 (21.8)	–
Yes	410 (79.5)	80 (85.1)	330 (78.2)	0.134
Type of substance use treatment in lifetime, n (%)				
Drugs only	269 (52.1)	54 (57.5)	215 (51.0)	–
Alcohol only	18 (3.5)	5 (5.3)	13 (3.1)	0.437
Both, drugs and alcohol	123 (23.8)	21 (22.3)	102 (24.2)	0.484
Not applicable	106 (20.5)	14 (14.9)	92 (21.8)	
Number of times in substance use treatment, n = 391 Median (IQR)	3 (2 – 5)	4 (2 – 6)	3 (1 – 5)	0.689

Abbreviations: IQR: interquartile range. SD: standard deviation.
*P-values were based on Chi-square test, t-test, or simple logistic regression.
**Participants that "don't know" or "refuse to answer" were excluded from the analysis. Values are shown for reporting purposes.
[a] Variables are descriptive only and were not considered for multivariable analysis.
[b] Treatment includes rehabilitation center, methadone or other medications, or other programs.

Center for Disease Control and Prevention, 2020). Mortality rates for COVID-19 are reportedly higher for those with chronic respiratory diseases (6.3 % vs 2.3 % overall). Our findings suggest that PWID should be considered an additional high-risk group for developing complications from COVID-19 due to the high prevalence and underdiagnoses of OLD. PWID are also thought to be at higher risk of infection, transmission, and complications from the virus due to the high prevalence of homelessness and incarceration, which make it difficult to maintain social distancing and adequate hygiene precautions. More research is needed to understand the associations between COVID-19 case outcomes and a history of substance abuse as well as the impact caused by the global pandemic (National Institute on Drug Abuse (NIDA), 2020). Clinicians need to be aware of the special challenges in caring for PWID and not postpone rehabilitation efforts (Ornell et al., 2020).

This study had limitations that should be taken into consideration when interpreting the findings. It did not measure the types and quantities of potential contaminants found in the drugs injected by participants. Therefore, duration of injection drug use and frequency of injection in the last 6 months were used as proxies for cumulative

Table 3
Multivariable logistic regression analysis of factors independently associated with obstructive lung disease (OLD) among persons who inject drugs, San Diego, CA (n = 513).

	Adjusted Odds Ratio[a] (95% Confidence Interval)	p-value
Race		
Non-Black	1.00	–
Black	2.66 (1.37, 5.17)	**0.004**
Pack-years smoked (per 5 pack-years)	1.06 (1.01, 1.12)	**0.026**
Years injecting drugs (per 5 years)	1.13 (1.01, 1.27)	**0.030**

[a] Adjusted for age, a known risk factor for COPD (Global Initiative for Chronic Obstructive Lung Disease, 2018), and all other variables in the model.

exposure to these contaminants. Further research is needed to verify whether injecting contaminants caused OLD. Factors such as second-hand smoke, air pollution, occupational dust or fumes, and other lung irritants were not measured, and might contribute to the overall burden of OLD in this population. As this study was cross-sectional, we cannot infer temporality of the associations. Lastly, this study relied on self-report of drug use and healthcare-related factors, potentially leading to misclassification due to recall problems. However, we have no reason to expect that misclassification differed by OLD status; therefore, misclassification would tend to bias our results toward null findings.

5. Conclusions

OLD prevalence was high in this cohort of PWID and consistent with findings from PWID elsewhere (Drummond et al., 2011). We also found a high prevalence of previously undiagnosed and untreated OLD in symptomatic PWID.

While prior research found a relationship between injection drug use and OLD, this study was the first to address whether injection-related factors were associated with OLD in a cohort made up entirely of PWID. This study is also the first to identify an association between duration of injection drug use and OLD, although the mechanisms for this association need further exploration. It is unclear whether an accumulation of exposure to excipients in the drugs or another factor contributed to this relationship. Future research is needed that more precisely measures exposure to injected particles. Smoking also continues to be an important contributor to OLD in PWID. Thus, smoking cessation programs in this population remain extremely pertinent.

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CRediT authorship contribution statement

Hayley J. Koslik: Conceptualization, Methodology, Formal analysis, Writing - original draft. **Jisha Joshua:** Writing - review & editing. **Jazmine Cuevas-Mota:** Investigation, Data curation, Writing - review & editing. **Daniel Goba:** Conceptualization, Writing - review & editing. **Eyal Oren:** Methodology, Writing - review & editing. **John E. Alcaraz:** Methodology, Writing - review & editing. **Richard S. Garfein:** Conceptualization, Methodology, Writing - original draft, Supervision, Funding acquisition.

Declaration of Competing Interest

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