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HIV Infection and Depression Among Opiate Users in a US Epicenter of the Opioid Epidemic

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Abstract
Using a mobile research facility, we enrolled 141 opioid users from a neighborhood of Philadelphia, an urban epicenter of the opioid epidemic. Nearly all (95.6%) met DSM-5 criteria for severe opioid use disorder. The prevalence of HIV infection (8.5%) was more than seven times that found in the general population of the city. Eight of the HIV-positive participants (67.0%) reported receiving antiretroviral treatment but almost all of them had unsuppressed virus (87.5%). The majority of participants (57.4%) reported symptoms consistent with major depressive disorder. Severe economic distress (60.3%) and homelessness were common (57%). Polysubstance use was nearly universal, 72.1% had experienced multiple overdoses and prior medication for opioid use disorder (MOUD) treatment episodes (79.9%), but few currently engaged in addiction care. The prevalence, multiplicity and severity of chronic health and socioeconomic problems highlight consequences of the current opioid epidemic and underscore the urgent need to develop integrated models of treatment.

Keywords Opioid · HIV · Risk behavior · Depression · MOUD

Resumen
Utilizando un Centro de Investigación Móvil, inscribimos a 141 usuarios de opioides del vecindario de Filadelfia, un epicentro urbano de la epidemia de opioides. Casi todos (95,6%) cumplieron con los criterios del DSM-5 para el trastorno del uso severo del consumo de opioides. La prevalencia de la infección de VIH (8,5%) fue más´ de 7 veces superior a las encontrada en la población general de la ciudad. Ocho de los participantes con VIH positivo (67,0%) reportaron haber recibido tratamiento antirretroviral pero casi todos tuvieron virus no suprimido (87,5%). La mayoría de los participantes (57,4%) informaron síntomas compatibles con el Desorden Depresivo Mayor. La angustia severa por lo económico (60,3%) y las

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personas sin hogar fueron comunes (57%). El uso de múltiples sustancias fue casi universal, el 721% había experimentado múltiples sobredosis y previos medicamentos para el tratamiento del trastorno por consumo de opioides (MOUD) (79,9%), pero muy pocos estaban comprometidos con la atención a las adicciones. La prevalencia, la multiplicidad y la seriedad de los problemas de salud crónica y los problemas socioeconómicos destacan las consecuencias de la actual epidemia de opioides y subrayan la urgente necesidad de desarrollar nuevos modelos de tratamiento integrados.

Palabras clave Palabras clave · Opioide · VIH · Comportamiento de riesgo · Depresión · MOUD

Introduction

While the COVID-19 pandemic has necessarily overshadowed all public health concerns globally, the opioid epidemic in the United States continues to be a significant public health crisis (1). It is estimated that 2 million people meet criteria for opioid use disorder in the United States (2). In 2018, 47,600 people died from opioid overdose (3). From 2001 to 2018, the number of opioid-related deaths increased by 345% (1), and currently, more than 130 people die every day from opioid overdose (3). The increased use of prescription opioids, heroin and, more recently, fentanyl (and its analogs) have accounted for the rapidly escalating mortality over the past 15 years (4–8).

Beyond the mortality attributable to overdose, this epidemic has brought with it an increased incidence and prevalence of HIV and HCV infections. HIV outbreaks have occurred in places that had never previously had an HIV problem as well as places where HIV infections among people who inject drugs (PWID) had been considered to be well controlled (9–12). Nationally, increases in new infections with HCV have coincided with increases in injection drug use (12–17). The opioid epidemic has also exacerbated other medical (11, 18–22) and mental health conditions (20, 23–28) and has propelled an expansion of housing instability and homelessness (29, 30).

The City of Philadelphia is an urban epicenter of the opioid epidemic in the United States (31, 32). Eight percent (about 120,000 inhabitants) of the city's population were estimated to have an opioid use disorder. At 49.2 opioid related deaths per 100,000, Philadelphia has the highest age-adjusted rate of fatal overdoses of any of the largest cities in the country. In 2019, 1,150 people died of opioid overdose in Philadelphia (33). Reversing a 25-year downward trend in the City, between 2016 and 2019 there has been a 151% increase in new HIV infections among PWID (34–36). Consequently, Philadelphia represents an important laboratory for testing meaningful interventions to treat opioid use disorder in high-risk populations, however, current data are limited regarding the characteristics of those most affected by the opioid epidemic in Philadelphia.

The current paper reports on data generated by a cross-sectional study supported by the University of Pennsylvania Mental Health AIDS Research Center. The study was designed to inform on the capacity to recruit participants for future HIV prevention research in high-risk PWID using a mobile research facility and to assess the prevalence of HIV infection, viral suppression, risk behaviors and depression among individuals with opioid use disorder. Previous studies showed that depression is associated with risk behavior and poor adherence to antiretroviral treatment in previous studies (37–40). This paper reports on the characteristics (sociodemographic, infectious diseases, substance use, mental health, risk-behaviors) of opioid users who inject drugs in a neighborhood highly impacted by the opioid epidemic. We hypothesize that substance use and risky behavior are associated with both HIV status and mental health after adjusting for sociodemographic characteristics.

Methods

Sample

The study used a convenience sampling strategy to engage individuals who use opioid and have ever injected opioids in the past 30 days. To maximize representation of the target population, inclusion criteria were limited to age over 18 and meeting DSM-5 criteria for opioid use disorder. We targeted the Philadelphia neighborhood most severely impacted by the opioid epidemic (i.e., Kensington). This neighborhood is home to Prevention Point Philadelphia, one of the largest syringe exchange programs in the country and has an estimated population of 12,000 PWID, 80% of whom inject opioids. The neighborhood has a high prevalence of homelessness. Potential participants were recruited via street outreach and word of mouth. Given the rapid response to our presence, no print or social media advertisements were used. Our mobile research unit parked in a highly visible and easily accessible location in close proximity to places of drug sale and use. Individuals interested in participating were encouraged to stop by the mobile unit where they could be pre-screened for an enrollment interview by answering a set of questions designed to include confirmation of opioid use.

Those who reported opioid use were then invited to complete an enrollment interview. Participants received US$20 for their participation in the study visit that was typically completed within 45 min. The University of Pennsylvania Institutional Review Board approved the study prior to the initiation of any research activities in the community.

Measures

After completion of informed consent, a trained research staff provided HIV pre-test counseling and performed a rapid HIV test (Chembio Sure Check® HIV 1/2 Assay). While waiting for the rapid HIV test result, participants completed an interview conducted by the research staff. This interview gathered sociodemographic information, past and current substance use (drug use section of the Addiction Severity Index (41)), a checklist of the DSM-5 opioid use disorder criteria (42), addiction treatment and overdose history, medical and mental health diagnostic and treatment histories. The interview also included the Risk Assessment Battery (RAB) to evaluate injection- and sex-related risk behaviors (43, 44), and the Quick Inventory of Depressive Symptomatology (QIDS) to assess the severity of depressive symptoms (45, 46). If the rapid HIV test was positive or indeterminate, blood was drawn for confirmatory testing and viral load measurement. All participants also provided a urine specimen for rapid assessment of recent substance use. Following the assessment, all participants were encouraged to utilize harm reduction services, referrals were made to local addiction and mental health treatment providers, and all of those who tested positive for HIV and were out of care were linked and confirmed to be connected to HIV care.

Statistical Analyses

Given the design and exploratory aims of the study, the results presented here are primarily descriptive. For the analyses, a QIDS score higher than 13 is considered to indicate severe depressive symptoms and a high probability of a diagnosis of major depressive disorder (45–48). HIV viral load < 50 copies/mL were considered undetectable viral load (i.e., virally suppressed). All variables are reported with percentage or mean and standard deviation.

Significance testing on an exploratory basis was conducted to examine the relation of HIV-status to demographic, substance use, and risk behavior variables using non-parametric tests Kruskall-Wallis or Fisher's exact test comparing HIV-positive and HIV-negative participants.

Because depression has been shown to be associated with risk behavior and poor adherence to antiretroviral treatment in previous studies (37–40), we have examined the variables (demographic, substance use, medical conditions and risk behavior) associated with depression. All

variables that have been found associated in univariate analysis, have been entered in a regression model. The Benjamini–Hochberg technique adjusting the p-values to control the false discovery rate (FDR) for multiple tests has been applied. In the model, likelihood-ratio test has been run to control of type I errors with multiple comparisons. All the analyses were performed using JMP Pro 14® (SAS Institute Inc., Cary, NC, USA).

Results

Sample Demographic Characteristics

The sample consisted of 141 opioid users who have ever injected opioids in the past 30 days, mainly men (70.9%), White (63.8%), about 40 years of age on average (Table 1). Their socioeconomic status was low, three-quarter of them were unemployed (71.6%), reporting very low income (78.0%), receiving public assistance (75.9%), and more than half of them were homeless (57.4%).

Substance-Related Variables

Almost all the participants (n = 135, 95.7%) met DSM 5 criteria for severe (6 + criteria) opioid use disorder, only 4 (2.8%) met criteria for mild (2–3 criteria), and 2 (1.4%) for moderate (3–4 criteria). They were using opioids for 12 years (mean = 12.1, SD = 9.9). The participants reported using mainly heroin (99.3%) and fentanyl (69.5%). They also reported using other opioids (19.1%) and MOUD (buprenorphine and methadone). They were polysubstance users, and reported using tobacco (94.3%), cocaine (68.8%), cannabis (41.8%), benzodiazepines (31.9%) mostly non-prescribed (88.9%), alcohol (28.4%), and amphetamines/ methamphetamines (19.1%), in the past 30 days (Table 1). These self-reports were supported by urine drug screen results. Agreement rates between self-reports and urine drugs screen were high: 0.83 for opioids, 0.88 for methadone, 0.82 for buprenorphine, 0.78 for cannabis, 0.75 for cocaine, 0.85 for amphetamines/ methamphetamines, 0.71 for benzodiazepines.

The majority (n = 111, 79.9%) reported a history of treatment for opioid use disorder, detoxification (n = 107, 76.4%) or MOUD (n = 111, 79.9%). However, slightly more than a third (37.6%) reported current treatment with methadone (14.2%) or buprenorphine/naloxone (20.6%). Among those who reported receiving MOUD, the adherence to treatment was rather low, with participants reporting taking their MOUD only 4 days in the past 30 days on average.

Table 1 Characteristics of the sample (n = 141)

Variables	Descriptive value (n, %, mean, SD)		
Socio-demographic			
Gender—males n (%)	100 (70.9)		
Race—n (%)			
White	90 (63.8)		
African-American / Black	32 (22.7)		
Other	19 (13.5)		
Ethnicity—latin(x) n (%)	26 (18.4)		
Age—mean (SD)	40.5 (10.4)—(range 20–69)		
Marital status—n (%)			
Never married	82 (58.2)		
Married/living w/partner	30 (21.0)		
Divorced/separated	28 (19.8)		
Widowed	6 (4.3)		
Level of education—n (%)			
Some high school	42 (29.8)		
High school diploma	72 (51.1)		
Some college	23 (16.3)		
Work status—unemployed n (%)	101 (71.6)		
Income per year—n (%)			
Under poverty level (< $12,490)	85 (60.3)		
$12,491–$25,000	25 (17.7)		
> $25,000	28 (19.9)		
Running out of money for necessities—yes n (%)	134 (95.0)		
Homeless—yes n (%)	81 (57.4)		
Health Insurance—medicaid n (%)	131 (92.8)		
Receive public assistance—yes n (%)			
Food stamps	107 (75.9)		
Supplemental security income	9 (6.4)		
Substance use			
Urine drug screen (n = 127)—n (%) positive			
Opiates	105 (82.7)		
Methadone	24 (19.0)		
Buprenorphine	31 (24.8)		
Cannabis	36 (28.3)		
Cocaine	81 (63.8)		
Benzodiazepines	29 (23.0)		
Amphetamine	5 (4.0)		
Methamphetamines	15 (11.9)		
Self-report (n = 141)—use past 30 days			
	n (%)	Days—mean (SD)*	Main route—n (%)
Heroin	140 (99.3)	26.7 (7.2)	IV: 136 (97.1)
Any other opiates (morphine, codeine, fentanyl)	106 (75.2)	18.4 (13.5)	IV: 78 (69.0)
Fentanyl only	98 (69.5)		Oral: 25 (22.1)
			Sniff: 10 (8.8)
Methadone	20 (14.2)	4.8 (10.3)	Oral: 82 (95.3)
Buprenorphine	29 (20.6)	3.7 (7.8)	Oral: 82 (90.1)
			IV: 4 (4.4)
Cannabis	59 (41.8)	6.0 (9.6)	Smoke: 112 (91.1)
Cocaine	97 (68.8)	18.8 (10.9)	Smoke: 57 (45.6)
			IV: 46 (36.8)
			Sniff: 22 (17.6)
Benzodiazepines	45 (31.9)	5.1 (8.7)	Oral: 74 (94.9)

Table 1 (continued)

Variables	Descriptive value (n, %, mean, SD)		
Amphet/methamphetamine	27(19.1)	3.0 (6.7)	IV: 28 (49.1) Oral: 18 (31.6)
Hallucinogens	5 (3.5)	1.8 (6.5)	Oral: 33 (76.7) Smoke: 9 (20.9)
Alcohol	40 (28.4)	3.1 (7.4)	Oral: 109 (100)
Tobacco	133 (94.3)	27.8 (7.3)	Smoke: 137 (100)

For *overdose*: means and Standard Deviation (SD) have been calculated among those who have reported overdose. For s*ubstance use*: mean and SD have been calculated among those who have reported using the substance. Main route = route that the subject reported to use the most. Urine drug screen was available for n = 127

About three-quarters (n = 101, 72.1%) experienced overdoses in their life (mean = 5.7, SD = 6.9, range 1–50), a third (n = 42, 33.3%) reported several (mean = 8.8, SD = 3.0, range 1–14) overdoses over the past 6 months.

Infectious Diseases

Twelve participants tested positive for HIV (8.5%). Eight participants reported being aware of their HIV-status and reported receiving antiretroviral therapy (ART).

Blood sample has been collected for viral load measure for eight participants, three participants refused the phlebotomy (one of them reported receiving ART), one participant had poor vein access and blood could not safely be drawn in the mobile unit. Viral load measure was available for eight participants and seven of them (87.5%) exhibited unsuppressed viral load (VL) (VL > 50 copies/mL, range: 133–907,000). Among the 8 HIV-positive participants reporting taking ART, viral load was available for seven of them, and 6 of 7 (85.7%) had unsuppressed viral load.

Eighty-two participants (58.2%) reported being seropositive for Hepatitis C, and a minority of them (2.8%) reported receiving HCV treatment. However, 12.1% of the participants reported being cured for Hepatitis C at the time of the interview.

Other Medical Conditions

Other medical comorbidities were also prevalent in the sample. About two-thirds (65.2%) of the participants reported having a chronic disease (cardiovascular, respiratory, neurological, digestive, metabolic, cancer), and two-thirds (68.5%) reported receiving some treatment for chronic medical conditions.

Risk Behaviors

Table 2 displays drug-related and sex-related risk behaviors. Almost three-quarters of the participants (72.6%) reported at least one injection-related risk behavior including sharing needle (27.0%), rinse water (30.5%), cooker (40.4%), cotton (22.1%), or sharing drugs with others by using one syringe to squirt or load the drugs into the other syringe (40.4%). Three HIV-positive individuals (25%) reported that someone used their needles after them.

Participants also reported sex-related risk behaviors. Among those who were sexually active in the past 6 months (n = 115, 82%), 60 (52%) reported multiple sexual partners and 69% used condoms inconsistently.

There was no difference in reported risk behaviors between HIV-positive and HIV-negative individuals.

Mental Health

The QIDS indicated that more than half of the participants (57.4%) exhibited depressive disorder (QIDS score > 13) (Table 3). In response to individual items, 16.3% reported thinking of suicide or death several times a week, and 11.3% reported thinking of suicide or death several times a day in some detail or have tried to commit suicide (Table 3). Other psychiatric disorders were also commonly reported (Table 3). More than half (56.1%) of the participants had received treatment for a psychiatric disorder in their life, mostly for mood disorder (50.4%) and anxiety disorder (41.1%). However, only a minority (17.0%) reported currently receiving psychiatric treatment.

Factors Associated with HIV Status

The HIV status was not found associated with any demographic, substance use, medical or mental health variables collected in our study, and therefore we did not pursue multivariable models for this outcome.

Factors Associated with Depression

In univariate analysis, participants who had depressive disorder were more often Latin(x) (Pearson Chi^2 = 6.38, Fisher's exact test p = 0.02), reported having at least one chronic disease other than HIV and Hepatitis C (Pearson

Table 2 Drug and sex-related risk-behavior (n = 141)

Risk assessment behaviors			
Injection past month			
Every day—n (%)	112 (79.4)		
Several days every week—n (%)	20 (14.2)		
Few times per month—n (%)	9 (6.4)		
Source of syringes past month			
Needle exchange program—n (%)	128 (90.8)		
On the street—n (%)	34 (24.1)		
Place where users go to inject	4 (2.8)		
	Sample (n = 141)	HIV-negative (n = 129)	HIV-positive (n = 12)
Injection-related risk behavior—past 6 months			
§ At least one injection-related risk behavior—n (%)	102 (72.3)	94 (72.9)	8 (66.7)
Sharing needles—yes n (%)	38 (27.0)	33 (25.6)	5 (41.7)
Use after someone	29 (20.6)	24 (18.6)	5 (41.7)
Someone uses after you	32 (22.7)	29 (22.5)	3 (25.0)
Sharing rinse water	43 (30.5)	38 (29.5)	5 (41.7)
Sharing cooker	57 (40.4)	51 (39.5)	6 (50.0)
Sharing cotton	31 (22.0)	26 (20.2)	5 (41.7)
Sharing drugs/squirt/backload	57 (40.4)	50 (38.8)	7 (58.3)
*RAB Drug-related score (out of 22)	5.2 (4.7) Range: 0–21	5.2 (4.7) Range 0–21	6.6 (5.5) Range 1–17
Sex-related risk behavior—past 6 months			
Sexually active—yes n (%)	115 (81.6)	106 (82.2)	9 (75.0)
Multiple sexual partners	60 (52.2)	55 (42.6)	5 (41.7)
No systematic condom use—n (%)	79 (68.7)	72 (55.8)	7 (58.3)
*RAB Sex-related score (out of 22)	3.9 (2.7) Range: 0–13	3.9 (2.7), Range 0–13	4.0 (3.1), Range 0–11

§*At least one injection-related risk behavior* included either/or sharing needle, rinse water, cooker, cotton, or drugs by using one syringe. *Sharing drugs/ squirt/ backload* means divided or shared drugs with others by using one syringe to squirt or load the drugs into the other syringe (e.g., backloading)

* Score of the drug and sex-related risk behavior sections of the Risk Assessment Battery (RAB) questionnaire

Chi^2 = 8.35, Fisher's exact test p = 0.004), and reported one or more overdoses in the past 6 months (Pearson Chi^2 = 6.55, Fisher's exact test p = 0.01). No associations were found with other socio-demographic, substance use, HIV and Hepatitis C, and risk behavior variables. The variables associated with depression have been entered in a regression model. After Benjamini–Hochberg technique has been applied (chi^2 = 20.0, df = 3, p < 0.0002, lack of fit chi^2 = 3.84, df = 3, p = 0.43), participants with depressive disorder were more likely Latin(x) (OR = 3.3, 95% CI 1.2–9.9), report at least one chronic disease other than HIV and Hepatitis C (OR = 2.9, 95% CI 1.4–6.4), and report one or more overdoses in the past 6 months (OR = 2.3, 95% CI 1.1–5.4).

Discussion

The City of Philadelphia is an epicenter of the opioid epidemic. Consequently, Philadelphia is an important laboratory in which to examine the epidemic's impact on those most affected. Nearly all of the opioid users recruited for this research met DSM-5 criteria for severe opioid use disorder. Polysubstance use was universal. Among these participants with an average age of 40 and 12 years of opioid use, most had experienced multiple overdoses and had a history of prior treatments for addiction. Depressive disorder was common as were reports of suicidal thoughts. History of psychiatric diagnoses and prior treatments for mental health disorders was reported by 56%. While most (93%) had Medicaid coverage, the great majority were not currently engaged in

Table 3 Mental health status and factors associated with depression (n = 141)

Mental health	n (%)
Received treatment for any psychiatric disorders	
Lifetime	78 (56.1)
Past 30 days	24 (17.0)
Received treatment for mood disorder	
Lifetime	71 (50.4)
Past 30 days	20 (14.2)
Received treatment for anxiety disorder	
Lifetime	58 (41.1)
Past 30 days	20 (14.2)
Quick inventory of depressive symptomatology (QIDS)	
Mean (SD)	12.8 (6.1)
No depression (total score: 0–5)—n (%)	20 (14.2)
Mild depression (total score: 6–10)—n (%)	28 (19.9)
Moderate depression (total score: 11–15)—n (%)	40 (28.4)
Severe depression (total score: 16–20)—n (%)	37 (26.2)
Very severe depression (total score: 21 +)—n (%)	16 (11.3)
Depressive disorder (QIDS > 13)—n (%)	81 (57.4)
Item 12: think of suicide or death several times a week—n (%)	23 (16.3)
Item 12: think of suicide or death several times a day or have tried to commit suicide—n (%)	16 (11.3)
Factors associated with depression (QIDS > 13)*	Odds ratio (95% CI)
Ethnicity	
No Latin(x)	1 (Reference)
Latin(x)	3.3 (1.2–9.9)
Chronic disease other than HIV and Hepatitis C	
No chronic disease	1 (Reference)
At least one chronic disease	2.9 (1.4–6.4)
Overdose the past 6 months	
No overdose	1 (Reference)
One or more overdoses	2.3 (1.1–5.4)

*Stepwise regression adjusted on race, ethnicity, chronic disease, overdose past 6 months (chi^2 = 20.0, df = 3, p < 0.0002, lack of fit chi^2 = 3.84, df = 3, p = 0.43). Benjamini–Hochberg to control FDR has been applied. Tests and confidence intervals on odds ratios are likelihood ratio based

care for either substance use or psychiatric problems. The prevalence of HIV infection among these participants was more than 7 times the rate seen in the general population in the city. Importantly, most of the HIV-infected individuals exhibited unsuppressed virus and few were fully engaged in HIV care. Chronic medical conditions and untreated HCV were common. The majority reported severe economic distress and homelessness.

Because we have targeted the neighborhood of Philadelphia most severely affected by the opioid epidemic, our sample consisted of high-risk polysubstance users and cannot be considered representative of all opioid users in Philadelphia. However, the study used a mobile research facility to provide easy access to people who used opioids and was able to recruit all participants in 6 weeks, and has demonstrated the feasibility of this approach to engage both those at high risk of infection as well as those able to transmit HIV to others.

Upon DEA analyses of street drug purchases, fentanyl is likely to be the most widely used substance. In many respects, the opioid epidemic in Kensington has become a fentanyl epidemic. Recent studies show that opioid users who use fentanyl exhibit more severe opioid use disorder, and were more likely to be polysubstance users (6). Within the myriad of severe opioid use disorder, we found that injection related risk behaviors were widely practiced. This high frequency may reflect the more frequent use of fentanyl. Due to the short half-life of fentanyl, injections occur more frequently and require a larger supply of sterile syringes and injection equipment. These risk data are also consistent with findings from a recent study that showed that injection related risk behaviors were more common among heroin and cocaine (speedball) users, a group that was highly represented in our sample (49). Sexual risks were also present. Among those who were sexually active (80%),

condom use was inconsistent and multiple sexual partners common. Collectively, these risk behaviors help to explain the current high rate of increase in HIV infections among PWID in Philadelphia. The prevalence of HIV infection in our sample (8.5%) is significantly higher than that of the general population in the City of Philadelphia (1.2%), and the estimated prevalence in PWID (6901 per 100,000) (35). Furthermore, HIV-positive individuals in our sample were less likely to have been linked to HIV care than overall HIV-positive individuals in Philadelphia (66.7% versus 86.1%, respectively), and the vast majority have been virally unsuppressed, forming a reservoir for potential transmission (34, 35). In order to achieve the goals of the Ending the HIV Epidemic initiative by 2030 (50), there will be a need to improve engagement and retention in HIV care as well as adherence to antiretroviral therapy. Similarly, HCV was also prevalent in our sample and although based on self-report, the prevalence in our sample (58.2%) is close to the 55.5% reported in the literature among PWID (17), and very few have reported being in treatment for their HCV infection. This high rate of HCV among PWID has contributed to an increased incidence of HCV in the U.S. (51), more deaths than HIV (52) and should also be addressed in responding to the opioid epidemic (53).

There is strong evidence that engagement in medication for opioid use disorder (MOUD) decreases the incidence of HIV and HCV infection and improves retention and adherence in HIV and care (54, 55). However, our sample showing a high rate of prior treatment with medications for opioid use disorder (MOUD) is a reminder of the challenge of treating opioid use disorder. Longitudinal studies of methadone and buprenorphine/naloxone suggest that 5-year retention rates are about 50% (56). The data also point to the missed opportunity and the need to support the development of new strategies to help retain individuals in treatment and to facilitate re-engagement in and access for those who leave effective treatment approaches.

Given the severity of opioid use disorder, it is not surprising that symptoms of depression were frequently reported. While depression is well documented as a co-morbid condition among those with opioid use disorder, QIDS scores reported here suggest that 57% of these participants would meet criteria for major depressive disorder. Fifty-six percent reported past treatment for psychiatric disorder, and only a small proportion (17%) reported currently receiving care. Given the chronic nature of psychiatric disorders, the low rate of current treatment is of great concern. Depression and other psychiatric disorders are significant not only as a condition requiring treatment to improve health and quality of life, but their presence significantly complicates the treatment of opioid use disorder. There is a clear need for integrated programs able to address both substance use and mental health (25, 27, 57). Polysubstance use, psychiatric

disorders, low income and homelessness are known to increase the risk of overdose in opioid users (58, 59).

Both polysubstance use (6) and psychiatric disorder, depression in particular, have been shown to be associated with suicidality (26, 60). While the distinction between intentional and unintentional overdose is not easily defined, it is clear that a meaningful proportion of fatal overdoses are in fact suicide (23, 24, 61, 62). Importantly, in this sample, depression was found associated with overdose in the past 6 months. Given the high prevalence of recent thoughts of suicide (27%) and lifetime (72%) and recent (33%) non-fatal overdoses, the risk of intentional overdose in this population is great (63). While these data describe an urgent need for suicide prevention interventions, they also highlight the need for targeted research to better inform those interventions.

Conclusion

The prevalence and severity of opioid use disorder, depression and other psychiatric problems, infectious and chronic diseases, combined with serious socioeconomic challenges experienced by the participants of this study highlight the enormous challenges in developing and implementing effective responses to the opioid epidemic. The common element in this syndemic cluster of conditions is severe opioid use disorder and consequently is the most important target for intervention.

The multiplicity of problems in these participants dramatically increases the vulnerability of this population to other social and health problems including infection with the SARS-CoV-2 virus (64, 65). It is clear that for the segment of the population most affected by the opioid epidemic, effective responses will need new delivery structures and strategies that integrate evidence-based treatments for opioid use disorder, mental health, and primary care. The remote treatment approaches implemented in response to the COVID-19 pandemic by primary and mental health care providers may hold promise in demonstrating ways of reaching those unable to become engaged in traditional models of care. The fact that this study was able to rapidly engage participants using a mobile research facility supports the potential of delivering services to those most in need, in their home neighborhood. It is imperative that we develop effective models of care for this most vulnerable segment of our population, because, as clearly demonstrated by the HIV epidemic, when the health of even a small segment of the population is threatened, the public health is at risk.

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