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Assessment of harm reduction receipt and infectious diseases outcomes in United States Veterans with opioid use disorder and history of injection drug use

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Abstract

Background Injection drug use (IDU) may lead to negative health outcomes and increased healthcare utilization. In US Veterans (USV) with opioid use disorder (OUD), there is sparse information about healthcare utilization, harm reduction prescription, and outcomes associated with IDU, including severe injection-related infections (SIRI). We assessed psychosocial factors, clinical outcomes, and harm reduction receipt in a cohort of USV with OUD, specifically focusing on persons who inject drugs (PWID).

Methods A retrospective cohort study was performed of USV aged ≥ 18 years with a diagnosis of OUD who presented to the Northport Veterans Affairs Medical Center (Long Island, NY) between 2012 and 2022. Demographics, psychosocial factors, history of human immunodeficiency virus (HIV), hepatitis C virus (HCV) infection, and healthcare utilization were compared by IDU status. Prescription of medications for opioid use disorder, naloxone and pre-exposure prophylaxis (PrEP) for HIV were also compared by IDU status. SIRI episodes and associated sequelae were characterized in USV with IDU.

Results A total of 502 USV with OUD were included and 216 (43%) were PWID. Mean age was 52.6 years. PWID were more likely to use multiple stimulants (14.4% PWID vs. 7.3% non-PWID, $p < 0.011$), be hospitalized with an infection (26.4% PWID vs. 12.2% non-PWID, $p < 0.001$) and had more frequent inpatient admissions ($n = 5.5$ PWID vs. $n = 3.51$ non-PWID, $p = 0.003$). Among PWID, 134 (62%) had a history of HCV infection, 9 (4.2%) had HIV, and 35 (16.2%) had at least one SIRI episode. PWID had a higher frequency of current (51.9% PWID vs. 38.5% non-PWID, $p = 0.003$) or previous MOUD use (45.8% PWID vs. 31.1% non-PWID, $p < 0.001$). Overall PrEP receipt in our cohort (0.46% PWID vs. 1.4% non-PWID, $p = 0.4$) was low.

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Conclusions USV with OUD and a history of IDU had a high prevalence of concurrent stimulant use, HCV, SIRI episodes, and were more likely to be hospitalized than USV with OUD and no history of IDU. Harm reduction strategies such as MOUD or PrEP, can help decrease the risk of infectious diseases, yet PrEP was underutilized in our population regardless of IDU status. USV with OUD would benefit from improved integration of OUD treatment, infectious diseases clinical care and harm reduction interventions.

Keywords US Veterans, Opioid use disorder, Persons who inject drugs, Severe injection related infections, Medications for opioid use disorder, Harm reduction

Background

Opioid use disorder (OUD) affects 6.1 million Americans [1]. Among US military Veterans (USV), rates of opioid misuse have significantly increased, leading to a 53% rise in overdose deaths between 2010 and 2019 [2–4] and combined with rises in stimulant use in this population has led to a syndemic [5]. Parenteral opioid use is associated with increased risk for acquisition of severe injection-related infections (SIRI), including acute bacterial skin and skin structure infections, endocarditis and osteoarticular infections, as well as acquisition of HIV, hepatitis B (HBV) and C viruses (HCV) via shared injection equipment (e.g., "shared works") [6, 7].

SIRI are associated with extended hospital stays [8], high readmission rates [9], frequent patient-directed discharges [8], and high post-discharge mortality [10]. Further, the extensive surgical treatments and prolonged parenteral therapy associated with SIRI are linked with increased hospital costs [11]. Harm reduction strategies (e.g., prescribing naloxone for overdose prevention, pre-exposure prophylaxis (PrEP) provision for HIV prevention in persons with a history of injection drug use (IDU), or medications for opioid use disorder (MOUD)) can reduce morbidity and mortality associated with OUD. Currently, there is sparse literature regarding clinical outcomes and harm reduction prescription in USV with OUD and a history of IDU because this population has been difficult to define due to a lack of an International Classification of Diseases (ICD) code for IDU [12].

In this study, we aimed to describe sociodemographic characteristics and infectious diseases-related outcomes in USV with OUD who sought care at the Northport Veterans Affairs Medical Center (NVAMC). We also aimed to identify a cohort of USV with OUD and a history of IDU to evaluate prevalence of HIV, HCV, SIRI-related outcomes, healthcare utilization, and harm reduction receipt. We hypothesized that USV with OUD and a history of IDU would have low receipt of harm reduction interventions, high rates of HCV and HIV infection, frequent SIRI episodes, and higher rates of healthcare utilization than USV with OUD without a history of IDU.

Methods

Study design and population

A retrospective cohort study was performed of USV aged ≥ 18 years with an ICD-9 (codes 304.0x and 305.5x) or ICD-10 (codes F11.10, or F11.20 with concomitant F11.10) diagnosis of OUD that had either an inpatient or outpatient medical encounter at the NVAMC (located on Long Island, NY) between January 1, 2012, and December 31, 2022. This study was approved by the NVAMC institutional board review (IRB) (approval number 1683516-1).

Data collection, variable definitions, and clinical outcomes

For each USV, demographic data, employment, insurance and housing status, incarceration and overdose history, concomitant substance use (e.g., alcohol, cannabis, cocaine, methamphetamine, tobacco) and psychiatric diagnoses, and receipt of MOUD were extracted from the Veterans Health Administration (VHA) Computerized Patient Record System (CPRS). For any missing data within CPRS, the Joint Longitudinal Viewer (JLV) was used to access additional USV information from other VHA locations. Infectious diseases related outcomes, including episodes of SIRI (endocarditis, bacteremia, fungemia, septic arthritis, endophthalmitis, osteomyelitis, bacterial skin and skin structure infections), aspiration pneumonia, hospitalizations, length of inpatient stay, and emergency department (ED) visits were obtained. A positive HIV case was defined as either having a (1) positive screening antibody test with positive confirmatory antibody testing, (2) positive HIV viral load, or (3) documentation of HIV on the electronic health record (EHR) problem list. A positive HCV case was defined as having positive screening antibody test with a concurrent positive HCV viral load, or if HCV was documented in the EHR problem list with a positive RNA viral load. A positive HBV case was defined as surface antigen positive, or core antibody positive with HBV viremia, or HBV viremia. Receipt of MOUD was defined as identification of a current or previous prescription for any of the Food and Drug Administration-approved medications methadone (full opioid agonist), buprenorphine (partial opioid agonist), or extended-release naltrexone (opioid receptor antagonist) within CPRS or JLV. PrEP receipt was defined by prescription of a > 30-day course of tenofovir (either

disoproxil fumarate or alafenamide) and emtricitabine or cabotegravir injection in conjunction with provider documentation in the EHR prior to or during calendar year 2022. A subpopulation of USV with OUD and IDU was identified by manual chart review using a keyword search for corresponding text for IDU (Supplemental Table 1.1 and 1.2). IDU was defined as injection of any opioid or non-opioid substance (licit and illicit). Aspiration pneumonia was defined as any inpatient encounter which encompassed the term "aspiration pneumonia", identified from review of the progress notes.

Statistical analysis

Descriptive statistics were obtained for sociodemographic variables and SIRI-related outcomes. A two-sample T-test was utilized to compare continuous variables between USV with OUD and IDU (Persons who inject drugs, PWID) and USV with OUD who did not inject drugs (non-PWID). Chi-square analysis was utilized to compare differences in psychiatric diagnosis, concomitant substance use, receipt of MOUD, overdose and incarceration histories, HIV, HCV infection, and aspiration pneumonia histories, hospitalization and ED visit frequencies, and inpatient length of stays between PWID and non-PWID. Fisher's exact test was utilized to compare PrEP prescription. Statistical significance was defined as a p-value < 0.05.

Results

Demographic characteristics

There were 502 Veterans with a diagnosis of OUD (Table 1). Mean age was 52.6 years (standard deviation = 14), 469 (93.4%) were male, 33 (6.6%) were female, 396 (78.9%) were White, 28 (5.6%) were Hispanic and 172 (34.4%) were employed. Post-traumatic stress disorder ($n = 275$, 54.8%) and major depression ($n = 266$, 53%) were the two most frequent psychiatric diagnoses, and 71 USV (14.1%) had a history of military sexual trauma of which 18 (3.6%) were female USV. A total of 352 (70.1%) USV had a history of comorbid alcohol use, 357 (71.1%) with tobacco use, 337 (67.1%) with cocaine use, 61 (12.2%) with non-cocaine stimulant use, and 52 (10.4%) with both cocaine and non-cocaine stimulant use (Supplemental Fig. 1). Two hundred sixteen (43%) USV had a history of incarceration, 216 (43%) had a history of homelessness, and 194 (38.7%) had a history of previous drug-overdose, including 120 (23.9%) with an opioid-related overdose.

Among USV with a diagnosis of OUD, 216 (43%) had a history of IDU. PWID were more likely to have a history of homelessness (71.3% PWID vs. 21.7% non-PWID, $p < 0.001$), unemployment (60.2% PWID vs. 43.7% non-PWID, $p < 0.001$), and a history of incarceration (49.1% PWID vs. 38.5% non-PWID, $p = 0.002$). PWID were also more likely to use cocaine (77.8% PWID vs. 59.1%

Table 1 Demographic characteristics of USV with OUD at NVAMC stratified by history of injection drug use

Variable	All Veterans, *N* = 502 *N* (%)	Non PWID *N* = 286 *N* (%)	PWID *N* = 216 *N* (%)	*p* value
Age, mean (SD), years	52.6 (14.0)	52.8 (13.2)	52.5 (14.9)	0.85
Sex				
Male	469 (93.4)	264 (92.3)	205 (94.9)	0.24
Female	33 (6.6)	22 (7.7)	11 (5.1)	
Race				
Caucasian	396 (78.9)	228 (79.7)	168 (77.8)	0.37
Black	94 (18.7)	50 (17.5)	44 (20.3)	
Asian/Pacific Islander	1 (0.20)	1 (0.35)	0 (0)	
Native American	3 (0.60)	1 (0.35)	2 (0.93)	
Other	8 (1.6)	6 (2.1)	2 (0.93)	
Hispanic Ethnicity	28 (5.6)	12 (4.2)	16 (7.4)	0.98
Employment status				
Employed	172 (34.3)	119 (41.6)	53 (24.5)	**< 0.001**
Unemployed	255 (50.8)	125 (43.7)	130 (60.2)	
Retired	51 (10.2)	26 (9.1)	25 (11.6)	
Disabled	24 (4.8)	16 (5.6)	8 (3.7)	
Insurance status	216 (43.0)	106 (37.1)	110 (50.9)	0.34
History of homelessness	216 (43.0)	62 (21.7)	154 (71.3)	**< 0.001**
Concomitant Substance Use				
Alcohol	352 (70.1)	187 (65.4)	165 (76.4)	**0.008**
Cocaine	337 (67.1)	169 (59.1)	168 (77.8)	**< 0.001**
Non-cocaine stimulant	61 (12.2)	25 (8.7)	36 (16.7)	**0.007**
Cocaine and non-cocaine stimulant	52 (10.4)	21 (7.3)	31 (14.4)	**<0.011**
Marijuana	200 (39.8)	111 (38.8)	89 (41.2)	0.59
Tobacco	357 (71.1)	189 (66.1)	168 (77.8)	**0.004**
Previous overdose				
1 overdose	194 (38.7)	78 (27.3)	116 (53.7)	**< 0.001**
>1 overdose	68 (13.6)	22 (7.70)	46 (21.3)	**< 0.001**
Opioid-related OD	120 (23.9)	43 (15.0)	77 (35.7)	**< 0.001**
History of injection substance use	216 (43.0)	---	216 (100)	---
History of Incarceration	216 (43.0)	110 (38.5)	106 (49.1)	**0.002**
Concomitant Psychiatric Diagnosis				
PTSD	275 (54.8)	155 (54.2)	120 (55.6)	0.76
Depression	266 (53.0)	150 (52.5)	116 (53.7)	0.78
Anxiety	47 (9.4)	23 (8.0)	24 (11.1)	0.24
Bipolar	83 (16.5)	43 (15.0)	40 (18.5)	0.30
History of military sexual trauma	71 (14.1)	41 (14.3)	30 (13.9)	0.89

Table 1 (continued)

Variable	All Veterans, *N* = 502 *N* (%)	Non PWID *N* = 286 *N* (%)	PWID *N* = 216 *N* (%)	*p* value
Male	53 (10.6)	29 (10.1)	24 (11.1)	0.73
Female	18 (3.6)	12 (4.2)	6 (2.8)	0.40

NVAMC: Northport Veterans Affairs Medical Center; OD: overdose; OUD: opioid use disorder; PWID: persons who inject drugs; PTSD: post-traumatic stress disorder; SD: standard deviation

non-PWID, $p<0.001$), non-cocaine stimulants (16.7% PWID vs. 8.7% non-PWID, $p=0.007$), concomitant cocaine and non-cocaine stimulants (14.4% PWID vs. 7.3% non-PWID, $p<0.011$), alcohol (76.4% PWID vs. 65.4% non-PWID, $p=0.008$), and tobacco (77.8% PWID vs. 66.1% non-PWID, $p=0.004$). PWID were more likely to have a history of prior overdose (53.7% PWID vs. 27.3% non-PWID, $p<0.001$), including an opioid-related overdose (35.7% PWID vs. 15.0% non-PWID, $p<0.001$).

Harm reduction receipt

Naloxone was prescribed to 357 (71.1%) USV, however there was no difference in naloxone prescription between PWID and non-PWID (72.7% PWID vs. 69.9% non-PWID, $p=0.5$) (Table 2). PWID had a higher frequency of current (51.9% PWID vs. 38.5% non-PWID, $p=0.003$) or previous MOUD use (45.8% PWID vs. 31.1% non-PWID, $p<0.001$). Current prescription of PrEP (0.0% PWID vs. 1.0% non-PWID, $p=0.26$) or previous prescription of PrEP (0.5% PWID vs. 0.3% non-PWID, $p=1.00$) was low and did not differ between the groups.

Infectious diseases outcomes

There were 35 (16.2%) USV with OUD and a history of IDU with at least one episode of SIRI and a total of 56 SIRI episodes (Fig. 1). The most common SIRI was skin and skin-structure infection ($n=32$, 14.8%; 39 episodes), followed by osteomyelitis ($n=6$, 2.8%), and bacteremia ($n=4$, 1.9%) (Table 3). Four USV with OUD and IDU had bacteremia, of which two were methicillin-sensitive *Staphylococcus aureus* (MSSA), one with *Staphylococcus cohnii*, and one with *Serratia marcescens*. Of the four episodes of bacteremia, 2 were in USV with a history of concurrent cocaine use, one episode in a USV with concurrent polystimulant use and one episode in a USV without any stimulant use. One USV with MSSA bacteremia had native tricuspid valve MSSA endocarditis; this USV had concurrent polystimulant use, which was treated with parenteral antibiotics (22 days of ceftriaxone and cefazolin, followed by one 1.5 g dose of dalbavancin); the USV did not undergo any valvular surgeries and made a full clinical recovery.

SIRI episodes in USV with OUD and IDU were further stratified by stimulant use history (Fig. 2). A total of 43 SIRI episodes were present in USV with any history of concurrent stimulant use (e.g., cocaine or non-cocaine), compared with 13 in USV without concurrent stimulant use. Further, in this cohort there were 31 (72%) episodes of skin and skin structure infection (SSTI), 3 (7%) episodes of bacteremia, 2 (5%) episodes of endophthalmitis, 4 (9%) episodes of osteomyelitis, 1 (2%) episode of septic arthritis, 1 (2%) episode of fungemia, and 1 (2%) episode of endocarditis.

USV with OUD and IDU had higher rates of HCV infection (62% PWID vs. 3.5% non-PWID, $p<0.001$) and HIV (4.2% PWID vs. 0.7% non-PWID, $p=0.008$) than USV with OUD and no history of IDU. Among USV with HCV, 80.6% of PWID and 40.0% of non-PWID were treated for HCV and had achieved a sustained virologic response. All USV with OUD and HIV had received treatment and were virally suppressed (e.g., viral load < 200 copies/mL). USV with IDU had higher rates of aspiration pneumonia (4.6% PWID vs. 1.1% non-PWID, $p=0.01$), were more likely to be hospitalized with any infection (26.4% PWID vs. 12.2% non-PWID, $p<0.001$) and had more inpatient admissions ($n=5.5$ PWID vs. $n=3.51$ non-PWID, $p=0.003$). ED visit frequency, inpatient length of stay, and hospitalization outcomes did not differ between the groups.

Discussion

In this study, Veterans with OUD and IDU were more likely to have psychosocial co-morbidities, high prevalence of SIRI, inpatient hospitalization from injection-related infection, and low prescription rates of MOUD and PrEP. In this cohort of USV with OUD, a significant proportion of USV were found to have a history of homelessness, justice system involvement, military sexual trauma, concurrent mental illness, polysubstance use and drug-related overdose. Homelessness and justice-involvement are known to increase challenges with access to healthcare, thus placing them at a greater risk of relapse, overdose, and acquisition of infectious diseases [13–15]. Military sexual trauma was more common in our male USV with OUD. Other studies have noted a significant relationship between OUD and military sexual trauma, which is nearly twice as likely in male compared to female USV [16], and related to trauma related stress (e.g., PTSD) [17] as many USV use substances to cope with emotional trauma making them more susceptible to overdose [18]. Not surprisingly, among USV in this study, PTSD was the most common psychiatric diagnosis, followed by depression, which are important risk factors in developing SUD [19–23] among USV. Understanding the psychosocial risk factors for developing OUD can potentially identify avenues for prevention and comprehensive care in USV with OUD.

Table 2 Naloxone, MOUD, and PrEP uptake among U.S. Veterans with opioid use disorder at NVAMC, stratified by history of injection drug use

Variable	All Veterans, *N* = 502 *N* (%)	Non PWID *N* = 286 *N* (%)	PWID *N* = 216 *N* (%)	*p* value
Prescribed MOUD				
Currently on MOUD	222 (44.2)	110 (38.5)	112 (51.9)	**0.003**
Previously on MOUD	188 (37.5)	89 (31.1)	99 (45.8)	**< 0.001**
Any history of OAT prescription	301 (60.0)	146 (51.0)	155 (71.8)	**< 0.001**
Prescribed Naloxone	357 (71.1)	200 (69.9)	157 (72.7)	0.50
Prescribed PrEP				
Currently prescribed	3 (0.6)	3 (1.0)	0 (0.0)	0.26
Previously prescribed	2 (0.4)	1 (0.3)	1 (0.5)	1.00
Any history of PrEP prescription	5 (1.0)	4 (1.4)	1 (0.46)	0.40

MOUD: medication for opioid use disorder: OAT: opioid agonist therapy; NVAMC: Northport Veterans Affairs Medical Center; PrEP: HIV pre-exposure prophylaxis; PWID: persons who inject drugs

We identified 216 USV with OUD and a history of IDU. To our knowledge, this study is the first to assess harm reduction receipt, infectious diseases epidemiology, and clinical outcomes in USV with OUD and a history of IDU. Previous studies of infectious diseases outcomes in USV with SUD have excluded IDU because this variable has been difficult to define as there is no corresponding ICD code [24, 25]. Studies of infectious diseases outcomes in non-Veterans have relied on clusters of ICD codes that corresponded to likely IDU [26]. One strength of this study is the identification of such a cohort of USV via manual chart review, which allowed for a more thorough understanding of sociodemographic factors, MOUD, naloxone and PrEP receipt, delivery of infectious diseases testing and treatment, healthcare utilization, and infectious diseases clinical outcomes.

When stratified by injection status, USV with OUD and a history of IDU were more likely to have a history of homelessness, justice-involvement, unemployment, polysubstance use, a co-occurring mental-health diagnosis, and history of overdose than USV with OUD and no IDU history. Previous studies have found that PWID have additional psychosocial stressors compared to persons who do not inject drugs, including homelessness, incarceration, and co-occurring mental health disorders that disproportionately increase their risk for overdose, acquisition of infectious diseases, adverse outcomes and mortality [27, 28]. Furthermore, we found that USV with OUD and a history of IDU had significantly higher prevalence of concurrent alcohol, tobacco, and stimulant use than USV with OUD without an IDU history. Among USV, there has been a rise in OUD-related overdoses with increased mortality in those with polysubstance use, particularly alcohol and stimulant use [2, 29]. Moreover, both untreated alcohol and stimulant use have negative implications for HIV anti-retroviral therapy (ART) adherence [30, 31] in people with HIV and thus may potentially increase risk for HIV transmission. Currently NVAMC offers treatment for alcohol and stimulant use disorder with evidence-based therapies (cognitive behavioral therapy, motivational interviewing, and psychotherapy) as well as medications e.g. naltrexone, topiramate, disulfiram. Additionally, as expected in our analysis, PWID had a high prevalence of HCV infection. In a previous study, 50% of PWID were found to have HCV infection [32], aligning with our findings. As such, our data highlights the importance of screening for HCV, and linking direct acting antiviral (DAA) treatment for PWID who test positive to reduce negative sequelae of untreated HCV, and reduce further transmission of HCV infection (treatment as prevention, TasP) [33]. Fortunately, our VA employs routine reflex RNA testing for diagnosing HCV infection, which was implemented across VHA since 2018, and the majority of USV with OUD in our cohort with a history of IDU were previously treated for HCV, highlighting the tremendous efforts made by the VHA to reduce the burden of HCV infection [34]. We also found that there was a lower HIV prevalence in USV with OUD and a history of IDU compared to studies in non-veteran populations [35], however our population of USV with HIV was comparatively small. In the US, 8% of new HIV infections occur in PWID [36] and multiple new HIV outbreaks have occurred among PWID in recent years [37]. Further assessment of HIV prevalence in a national cohort of USV with a history of IDU is needed to better understand the burden of HIV in this population. Finally, USV with OUD and a history of IDU required more frequent inpatient hospitalizations than USV with OUD and no history of IDU. Inpatient hospitalization is itself considered a "risk environment" for PWID, as a previous study noted that these patients often encounter stigma around their substance use from medical staff as well as acute withdrawal symptoms from untreated SUD [38]. Consequently, this may lead to patient directed discharges (PDD), often with incomplete documentation, reduced referrals or medication prescriptions, frequent readmission, and worse outcomes [38]. Thus, improved integration of SUD and infectious diseases care is needed for this population while hospitalized, and with the increased healthcare utilization there may also be opportunities to intervene with social support services (e.g., housing and transportation needs).

SIRI were highly prevalent in our cohort of USV with OUD and a history of IDU, most commonly from SSTI. SSTIs are one of the most frequent infections in IDU and are a common reason for seeking emergency

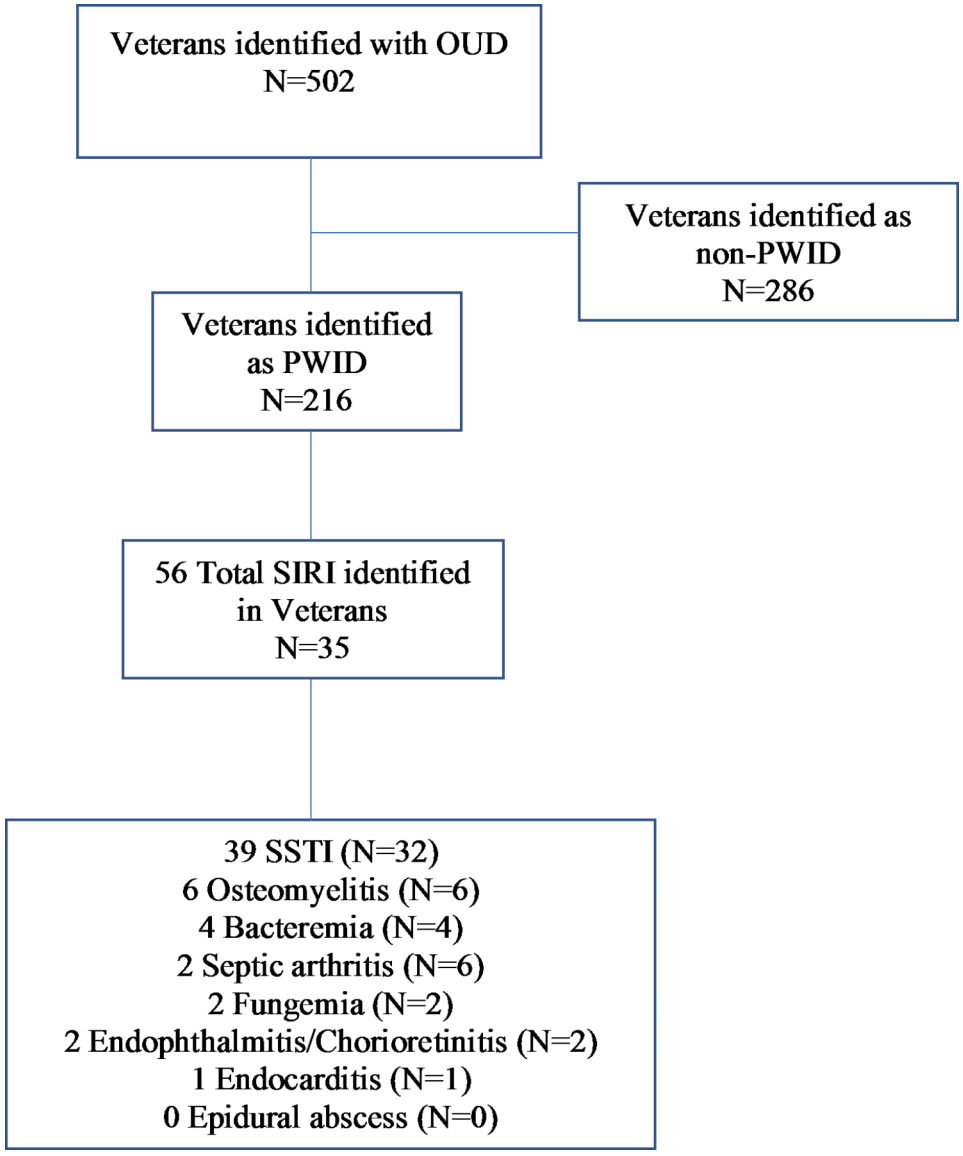

Fig. 1 Flow diagram constructing retrospective control cohort. Diagram demonstrating results of diagnostic code search algorithm to identify severe injection-related infections in the control period at NVAMC between January 1, 2012 and December 31, 2022, *N* = number of Veterans. NVMAC: Northport Veterans Affairs Medical Center; OUD: opioid use disorder; PWID: persons who inject drugs; SIRI: severe injection-related infection; SSTI: skin and skin structure infection

department (ED) and inpatient treatment by PWID [11, 39–41]. Beyond SSTI, in this cohort, episodes of bacteremia, fungemia, endocarditis, osteomyelitis, aspiration pneumonia were also identified. Our data is consistent with previous studies of infectious diseases outcomes in non-veteran PWID, which identified that this cohort is at elevated risk for developing SIRI and in turn requires prolonged parenteral treatment and hospitalization stays [42, 43], leading to increased healthcare expenditures [44]. When examining our cohort more closely, we found that a majority of SIRI episodes were identified in PWID with concurrent stimulant use. This finding is consistent with a previous report that persons with concomitant opioid and stimulant use are more likely to engage in shared works, thus leading to increased risk of developing invasive bacterial infections [26] and, ultimately, poor health outcomes. Models of care that address both opioid and stimulant use are needed in USV with concurrent infectious diseases care.

Hospitalization presents an opportunity for MOUD initiation, with higher initiation rates when offered during inpatient stays [45]. In this cohort, MOUD was prescribed to 44.2% in USV with OUD, and 51.9% in those with a history of IDU. MOUD receipt in non-Veterans is estimated between 22.3 and 27.8% [46, 47], comparatively less than VHA, which is estimated to be 48.9% [48],

Table 3 SIRI and non-SIRI outcomes in USV with OUD who presented to the NVAMC

Variable	All Veterans, *N* = 502 *N* (%)	Non PWID *N* = 286 *N* (%)	PWID *N* = 216 *N* (%)	*p* value
SIRI type				
SSTI	32 (6.4)	---	32 (14.8)	---
Bacteremia	4 (0.80)	---	4 (1.9)	---
Fungemia	2 (0.40)	---	2 (1.0)	---
Endophthalmitis/ Chorioretinitis	2 (0.40)	---	2 (1.0)	---
Septic Arthritis	2 (0.40)	---	2 (1.0)	---
Osteomyelitis	6 (1.2)	---	6 (2.8)	---
Epidural abscess	0 (0.0)	---	0 (0.0)	---
Endocarditis	1 (0.20)	---	1 (0.50)	---
1 SIRI	35 (7.0)	---	35 (16.2)	---
>1 SIRI	13 (2.6)	---	13 (6.0)	---
Total episodes of SIRI	56 (11.2)	---	56 (25.9)	---
Total healthcare encounters with SIRI	51 (10.2)	---	51 (23.6)	---
HIV infection	11 (2.2)	2 (0.70)	9 (4.2)	**0.008**
HBV exposure	50 (10.0)	8 (2.8)	42 (19.4)	**<0.001**
HCV infection	144 (28.7)	10 (3.5)	134 (62.0)	**<0.001**
Any infection, Y/N	273 (54.4)	106 (37.1)	167 (77.3)	**<0.001**
Aspiration pneumonia	13 (2.6)	3 (1.1)	10 (4.6)	**0.01**
HCV treated, Y/N	112 (77.8)	4 (40.0)	108 (80.6)	**0.003**
HIV treated, Y/N	11 (100.0)	2 (100.0)	9 (100.0)	1.00
Hospitalized with any infection, Y/N	92 (18.3)	35 (12.2)	57 (26.4)	**<0.001**
Inpatient hospitalizations past 10 years, mean (range)	4.36 (2,76)	3.51 (0,45)	5.5 (0,76)	**0.003**
ED visits past 10 years, mean (range)	10.49 (0,164)	9.9 (0,164)	11.3 (0,79)	0.29
LOS inpatient admission, infection, mean days (range)	8.36 (1,60)	8.11 (1,60)	8.51 (1,42)	0.85
Outcome inpatient admission, Recovery	92 (100.0)	35 (100.0)	57 (100.0)	1.00

HBV: Hepatitis B virus; HCV: Hepatitis C virus; NVAMC: Northport VA Medical Center; OUD: opioid use disorder; PWID: persons who inject drugs; SIRI: severe injection-related infection. SSTI: skin and skin structure infection; LOS: length of stay; ED: emergency department

highlighting the efforts made within the VHA [2, 49, 50], but there remains potential for improvement. MOUD, including methadone (full opioid agonist), buprenorphine (partial opioid agonist), and extended-release naltrexone (opioid antagonist), are highly effective therapies shown to reduce opioid craving [51–53], reduce injection frequency [54, 55], and improve adherence to HIV antiretroviral therapy (ART) [56–58]. However, both methadone and buprenorphine are associated with reduced overdose risk, illicit opioid use, and death [59–61], HCV integrated care, treatment uptake [62, 63], and improved adherence to HCV DAA therapy [64, 65]. A significant proportion of USV with OUD, including PWID, had a history of overdose, aligning with national trends [66]. In response to this, the VHA has implemented services to facilitate treatment with MOUD in outpatient clinics as a method to co-locate care [67]. However, further areas of improvement within VHA include initiation of MOUD during inpatient hospitalizations or implementation of addiction consultation to improve post-discharge linkage to care, increased MOUD provision, decreased rehospitalizations, and improved outpatient follow-up [68].

In this cohort, 71.1% of USV with OUD were prescribed naloxone, a highly effective opioid antagonist utilized to reverse opioid overdose. Although the VHA's naloxone distribution (OEND) program [69, 70] has increased naloxone access, the national rise in opioid overdose deaths persist [66], and uptake remains low [71, 72] signifying the need for interventions to improve awareness and acceptability of naloxone [73]. In addition to MOUD accessibility and naloxone distribution, VHA provides syringe services and test strips as additional harm reduction measures [74], which is an important aspect of comprehensive harm reduction strategies in conjunction with pharmacotherapy to improve infectious diseases outcomes [75]. However, PrEP prescription was extremely low (<1%) among PWID in our cohort, despite its effectiveness in reducing HIV acquisition and decreasing transmission in PWID [76] as well as improved mental and behavioral health screening [77]. Yet, despite these inclusive benefits, PrEP uptake in both non-Veteran [78, 79] and Veteran populations with a history of IDU is disappointingly low. Integration of PrEP into SUD treatment programs, alongside harm reduction and infectious diseases care, is critical to improving health outcomes for PWID.

This study had several limitations. First, as this was a retrospective study, conducted at a single Suburban VAMC and mainly included a White male population (which mirrors national VA populations [24]), these results may have limited generalizability to other healthcare facilities with different population demographics (e.g., female populations or populations with increased representation of Black or Hispanic USV) or population sizes (e.g., urban, rural). A larger study of a national VHA population is needed to better assess infectious diseases clinical outcomes and harm reduction uptake in USV with OUD and IDU, which could more accurately compare different geographic regions (e.g., Northeast US versus Southeast US), populations (e.g., urban versus rural) and demographics. Furthermore, important temporal relationships could not be established. First, it was

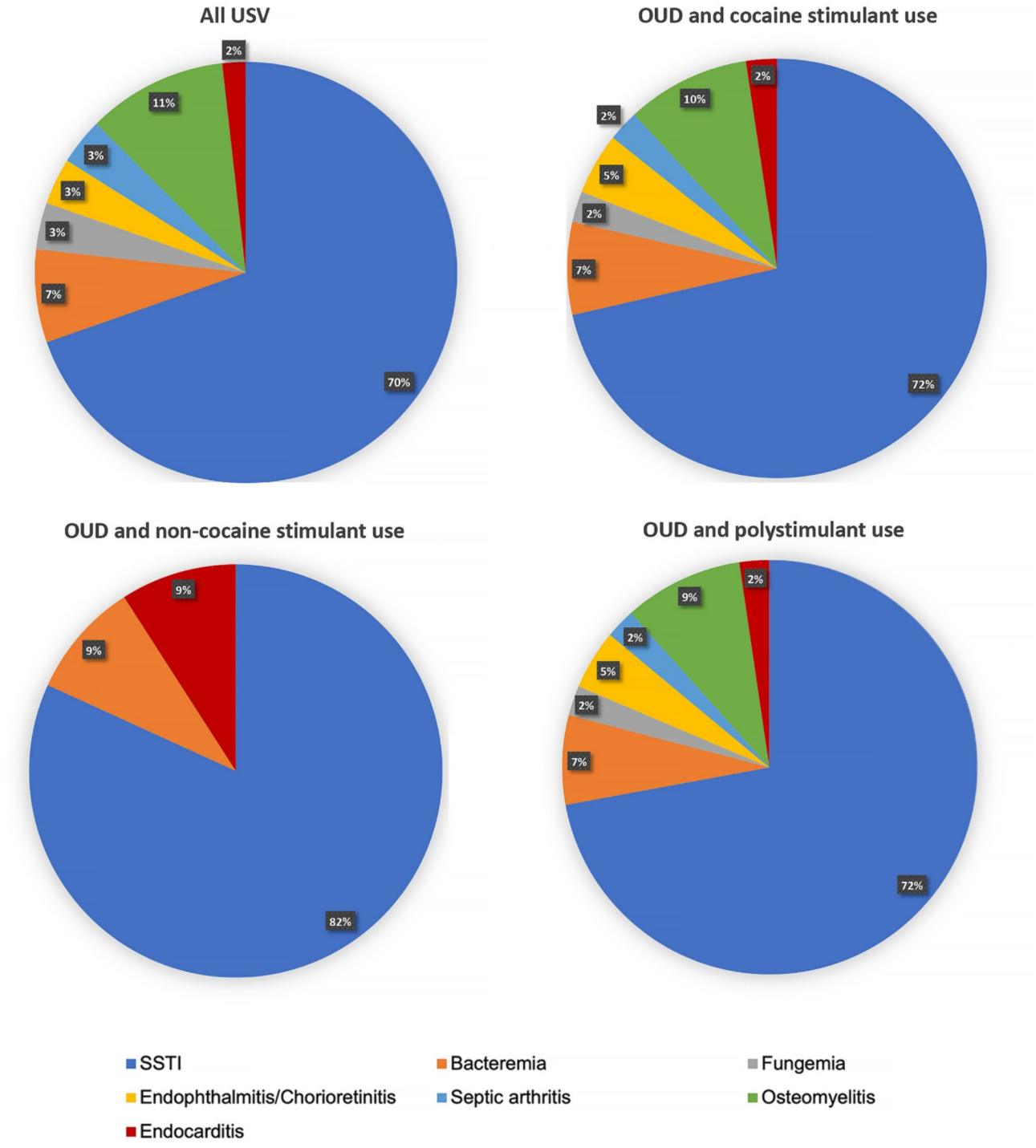

Fig. 2 Proportion of SIRI episodes in all US Veterans with OUD with a history of IDU, stratified by stimulant use history. IDU: injection drug use; SIRI: severe injection-related infection; OUD: opioid use disorder; SSTI: skin and skin structure infection

difficult to assess whether USV with OUD on MOUD exhibited less risky IDU behavior (e.g., reduced injection frequency or sharing injection equipment e.g., shared works). Second, it was difficult to determine whether USV on MOUD had improved PrEP uptake, or improved adherence to HIV or HCV treatment. Third, due to inconsistent documentation, it was difficult to identify which USV were actively injecting substances versus having a remote history of IDU. In addition, the ICD codes that were utilized may not have identified all USV with OUD or IDU as some USV may have been missed due to incorrect coding or had a history of non-opioid injection

use. Lastly, some USV with OUD and IDU may have sought care in the community for SIRI and thus would not have been represented in the study. Furthermore, sexually transmitted infections with OUD were not analyzed in this study but was previously assessed by our research group [80].

Conclusion

IDU increases the risk of acquisition and transmission of infectious diseases in USV with OUD, contributing to SIRI and increased healthcare utilization. Harm reduction strategies, such as provision of MOUD or PrEP, can help mitigate the risk of infectious diseases in persons with OUD. However, because current SUD care occurs separately from infectious diseases care, initiation of MOUD during SIRI related hospitalizations, provision of methadone within the VA, or adding on-site infectious diseases care to MOUD visits can help mitigate some challenges faced by USV to receive efficient and comprehensive care. Ongoing studies to evaluate retention of various MOUD will provide future direction on improving SUD care [81]. While the VHA has made significant efforts to improve MOUD uptake, PrEP is underutilized. Further, OUD (and other substance use disorder) treatment often occurs separately from infectious diseases clinical care. As such, improved integration of substance use care, infectious diseases treatment and screening and harm reduction strategies are needed for USV with OUD, especially PWID, who often have multiple psychosocial challenges. This will allow for more accessible, comprehensive, and patient-centered healthcare, ultimately leading to improved health outcomes in USV with OUD.

Abbreviations

HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
IDU	Injection drug use
MOUD	Medication for opioid use disorder
NVAMC	Northport Veterans Affairs Medical Center
OUD	Opioid use disorder
PrEP	HIV pre-exposure prophylaxis
PTSD	Post-traumatic stress disorder
PWID	Persons who inject drugs
SIRI	Severe injection-related infection
SSTI	Skin and skin structure infection
VHA	Veterans health administration

Supplementary Information

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Supplementary Material 1

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Not applicable.

Author contributions

K.S. drafted and edited the manuscript with critical revisions from A.L.; P.S. collected data, performed data analysis, and edited the manuscript. V.M. collected data and edited the manuscript. A.L. conceptualized and designed the study, performed data analysis, and edited the manuscript. All authors contributed to data interpretation, reviewed and edited the manuscript, and approved the final version.

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Data availability

The datasets generated and/or analyzed during this study are available upon a Freedom of Information Act request as per Veterans Health Administration policy.

Declarations

Ethics approval and consent to participate

This study was approved by the NVAMC institutional board review (approval number 1683516-1).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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