People Who Inject Drugs: Motivations, Initiations, and Socioeconomics

RESEARCH　　　　　　　　　　　　　　　　　　　　　　　　　　　　　**Open Access**

CrossMark

Physical pain is common and associated with nonmedical prescription opioid use among people who inject drugs

Disa Dahlman[1,2*] , Alex H. Kral[3], Lynn Wenger[3], Anders Hakansson[1,2] and Scott P. Novak[4]

Abstract

Background: People who inject drugs (PWID) often have poor health and lack access to health care. The aim of this study was to examine whether PWID engage in self-treatment through nonmedical prescription opioid use (NMPOU). We describe the prevalence and features of self-reported physical pain and its association with NMPOU.

Methods: PWID (*N* = 702) in San Francisco, California (age 18+) were recruited to complete interviewer administered surveys between 2011 and 2013. Multivariate logistic regression analysis was conducted to examine the associations among self-reported pain dimensions (past 24-h average pain, pain interference with functional domains) and NMPOU, controlling for age, sex, psychiatric illness, opioid substitution treatment, homelessness, street heroin use and unmet healthcare needs.

Results: Almost half of the sample reported pain, based on self-reported measures in the 24 h before their interview. The most common pain locations were to their back and lower extremities. Past 24-h NMPOU was common (14.7%) and associated with past 24 h average pain intensity on a 10 point self-rating scale (adjusted odds ratio [AOR] = 2.15, 95% confidence interval [CI] 1.21–3.80), and past 24 h pain interference with general activity (AOR 1.82 [95% CI 1.04–3.21]), walking ability (AOR 2.52 [95% CI 1.37–4.63]), physical ability (AOR 2.01 [95% CI 1.16–3.45]), sleep (AOR 1.98 [95% CI 1.13–3.48]) and enjoyment of life (AOR 1.79 [95% CI 1.02–3.15]).

Conclusion: Both pain and NMPOU are common among PWID, and highly correlated in this study. These findings suggest that greater efforts are needed to direct preventive health and services toward this population.

Keywords: Nonmedical use of prescription drugs, Opioids, Pain reliever, Physical pain, People who inject drugs

Background

The nonmedical use of prescription opioids (NMPOU) has received considerable attention in the United States. Despite attention by the research and public policy communities, it is not surprising that the term "nonmedical use" has developed different definitions and usage within these different stakeholder communities [1]. It has been defined as 'use without a prescription of the individual's own or simply for the experience or feeling the drug caused' [2]. However, it also has been described as misuse to get high, and as self-treatment for perceived physical or

psychiatric problems [3, 4]. Most national surveys, such as the *National Survey on Drug Use and Health* (NSDUH) [5] and *Monitoring the Future* [6], combine both self-treatment and euphoric use into a single category. This definition masks important differences in terms of why individuals engage in NMPOU.

NMPOU has been described as a crisis by US public health authorities [7, 8] because of the dramatic increases in overdoses and substance abuse treatment admissions associated with opioid use [9]. Data from national studies indicate that NMPOU remains highly prevalent, despite recent efforts to control the prescriptions and diversion of medications to others [10, 11]. NSDUH estimates that in 2014, 1.6% of the U.S. population aged 12 years or older had been using prescription analgesics nonmedically in the past month [5]. These data also consistently show that

* Correspondence: disa.dahlman@med.lu.se
[1]Department of Clinical Sciences Lund, Division of Psychiatry, Lund University, Lund, Sweden
[2]Malmo Addiction Centre, Clinical Research Unit, Sodra Forstadsg. 35, plan 4, SE-205 02 Malmo, Sweden
Full list of author information is available at the end of the article

Dahlman *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:29

Page 2 of 11

opioids are the most common prescription drugs used nonmedically.

NMPOU has been linked to numerous adverse health-related consequences, largely due to its depressogenic effects on numerous biological systems, including the central nervous system causing somnolence or even unconsciousness and suppressing respiratory activity, and bowel and lower GI tract (e.g., opioid induced constipation). People who use prescription opioids nonmedically are sometimes also injecting drugs, which is critical from a public health standpoint, because of harms associated with injections such as venous scarring and infectious diseases [12, 13].

It is well documented that people who inject drugs (PWID) often lack stable employment and have inconsistent lines of income [14]. This economic instability means that PWID are often ineligible for government economic subsidies, including employer sponsored health insurance. PWID also experience unstable housing [15, 16] which complicates their ability to achieve a medical home that can provide consistent preventive and acute care. Overall, the highly unstable environment of PWID contributes to poor health and nutrition status, both of which may increase the risk of physical pain related to both chronic and acute conditions [17–20]. There is a longstanding tradition of research on documenting the prevalence of physical pain in general population surveys. Unfortunately, few studies have focused on physical pain in PWID. The limited studies suggest that chronic pain is highly prevalent. In studies by Tsui et al. [21] and Heimer et al. [22], one-third of PWID reported chronic pain. High prevalence of venous insufficiency, causing chronic leg pain, has been shown in PWID [23, 24].

A few large-scale studies have investigated the association among physical pain and NMPOU. Novak et al. [25] showed a positive linear correlation between the level of self-reported pain interference and the likelihood of past year NMPOU in the general North American population. The study further showed that self-reported pain was an independent risk factor for NMPOU, yet its effects were substantially modified by patterns of substance use. A survey of the general population in Sweden showed that more days with poor self-assessed physical health were significantly associated with NMPOU, but not with the nonmedical use of sedatives [26]. Besides these studies, research on NMPOU and its associations with pain is sparse, and studies are conducted mostly in outpatient populations receiving chronic opioid therapy. A meta-analysis by Fishbain et al. [27] showed that a diagnosis of drug abuse, drug dependence or drug addiction was present in 3%-19% of persons with chronic pain. Back pain and multiple pain complaints were factors identifying patients in chronic opioid therapy at high risk for misuse [28]. Other studies of patients with chronic pain

showed no association between pain score and NMPOU [29, 30]. A recent longitudinal study by Martel et al. [31] showed that high level of pain was only weakly associated with opioid craving among patients with chronic pain.

A notable gap in the literature is that few studies have investigated the relationship between different dimensions of pain and NMPOU, particularly among high-risk populations who contend with high levels of pain such as PWID. There have been some studies that have explored rather course measures of self-reported pain. For example, Khosla et al. found a positive association between pain and a single measure of any type of nonmedical prescription drug use (NMPD) in American PWID [32]. The authors found that NMPD among PWID was significantly associated with self-reported bodily pain and pain interference with activity, and also with the hazardous use of alcohol, use of illicit substances, and active injection drug use. Misuse of prescription analgesics was the most common type of NMPD (17% reported opiate use in the past 6 months). However, a limitation of this prior work is that pain was assessed with a single item or that pain interference was concerning global functioning. To our knowledge, no studies have examined the relationship between distinct aspects of pain (e.g., location, duration and severity) and NMPOU.

The current paper provides a more refined examination between pain and NMPOU. A primary aim is to, in a sample consisting solely of PWID, describe the prevalence of recent physical pain, pain duration, pain intensity and pain interference. Then, a second aim is to characterize subgroups at differential impairment and functioning related to pain and investigate the association between NMPOU and pain-related factors.

Methods
Study sample and procedures
The study sample for this cross-sectional study comprised 706 PWID in San Francisco, California, with the data collected between November of 2011 and March of 2013. Potential participants were recruited from community settings using targeted sampling methods [33–35]. Three community field sites, located in neighborhoods near large populations of PWID, were utilized to conduct the interviews. Eligibility criteria included injection drug use in the past 30 days as verified by checking for recent signs of venipuncture, being 18 years of age or older, and the ability to provide informed consent [36]. Four persons were interviewed as part of the study, but whose data were later excluded because they answered on the survey that they had not injected drugs in the past 30 days. The survey was administered by a trained interviewer, and lasted between 45 and 60 min. Study participants received $20 (USD) for completing the interview. All study procedures

Dahlman *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:29

Page 3 of 11

were approved by the Institutional Review Board at RTI International.

Instruments and measures
Outcome variable
The outcome variable was *NMPOU past 24 h*. The definition used the stem from the National Survey on Drug Use and Health, noting that *"The next questions are about drugs that are typically prescribed by physicians. We are interested in your use of these medications without a doctor's prescription and your use of these medications not as directed by your physician."*

NMPOU past 24 h was assessed through the question *"When was the last time you used [prescription analgesic]?"* All persons who replied "within the past 24 h" (multiple choice question) for any of the following prescription analgesics (assessed separately) were recoded as 'NMPOU past 24 h': Vicodin, Oxycontin, Oxycodone, Percocet, Dilaudid, Fentanyl, Tramadol, Morphine, Embeda, Roxicodone, Opana, and other (Specify). We also included those who reported past 24 h nonmedical use of methadone, buprenorphine or Suboxone, i.e. those who replied "within the past 24 h" to any of the multiple choice questions *"When was the last time you used [Methadone/ Buprenorphine or Suboxone] (not prescribed directly to you by a doctor or from a clinic, or the prescription was for you, but you took more than the Dr. prescribed)?"*

Explanatory variables
Explanatory variables were pain intensity, pain location, pain duration, and pain interference. Recent pain prevalence was measured using the yes/no question *"Have you had pain in the past 24 hours? Please include pain that might be masked by your drug or alcohol use."* Pain intensity, and pain interference with general activity, mood, walking ability, physical ability, relationships, sleep and enjoyment of life were assessed using a modified version of the Brief Pain Inventory [37], which uses numeric scales where 0 was 'no pain' or 'does not interfere' and 10 was 'pain as bad as you can imagine' or 'completely interferes.' The Brief Pain Inventory, which has been widely used in studies measuring pain in substance-using populations [38–40], is validated for neuropathic pain [37] and is highly sensitive for pain assessment in patients in opioid substitution therapy [41]. The variables were recoded into three categories: 0 = no pain/interference (i.e. those who rated their pain/interference as 0 + those who didn't have pain at all the past 24 h); 1 = pain/interference score from 1 to median; and 2 = pain/interference score above median. Since clinically relevant cut-off values for levels of pain and pain interference are difficult to estimate in this population, and the pain measurement values were not expected to follow a normal distribution, we dichotomized the values at the median. Median was calculated only for

values 1–10 (0 excluded). The same procedure was conducted for pain duration. Missing data was recoded as 'no pain reported (0)' The rationale is that any person who skipped this item is likely doing so because they misinterpreted the item and felt they had no pain to report. Missing values did not exceed $n = 3$ for any of the variables.

For pain location, the study participants were provided a body chart that outlined 45 separate regions. The instructions of the inventory started with the instructions, *"Please look at the diagram and point to the area of your body that hurts the most."* Several answers were allowed. We recoded the areas checked in the questions above into seven categories according to clinical relevance; head, neck and shoulders, back, upper extremities, lower extremities, abdomen, and genitals. Worst pain location was assessed through the question *"Which of the areas of your body is causing you the most pain?"* Responses according to the body chart were recoded into four mutually exclusive areas: head, neck/shoulders/back, extremities (upper and lower limbs), and abdomen/genitals. Where the response to this question was missing ($n = 103$), recoding into one of the four areas above was conducted if the subject had checked only one painful area for the question "Please look at the diagram and point to the area of your body that hurts the most." Using this procedure, we were able to classify 99 individuals into one of four locations. If the subject had checked several painful areas (i.e. responses that could not be recoded into only one of four mutually exclusive areas), the subject was excluded from statistical analyses ($n = 4$).

Covariates
Based on the literature identifying associations between NMPOU and other substance use [25, 26, 29, 30, 42] and psychiatric disorders [26, 29, 42], we controlled all multivariate analyses for the following variables: Age at interview (left in its original metric) [28, 30]; biological sex at birth (male or female) [26, 30]; homelessness; lifetime psychiatric illness; use of street heroin; recent opioid substitution treatment (OST); and unmet healthcare needs.

Current homelessness was defined as a 'yes' to the question *"Do you consider yourself to be homeless?"*. Lifetime psychiatric disorder was defined as a 'yes' to the question *"As an adult, have you ever been diagnosed with a psychiatric illness (e.g., major depression, bipolar disorder)?"* Use of street heroin in the past 24 h was defined as replying "Within the past 24 h" to the question *"When was the last time you used [drug]?"* for any of the drugs speedball (heroin/cocaine, heroin/crack), goofball (heroin/methamphetamine) or heroin. Note that we did not discriminate routes of administration. OST in the past 30 days was defined as replying 'yes' to any of the

Dahlman et al. Substance Abuse Treatment, Prevention, and Policy (2017) 12:29

Page 4 of 11

questions "*Have you participated in methadone maintenance in the past 30 days?*" or "*In the past 30 days have you participated in buprenorphine (Suboxone) treatment?*".

Unmet healthcare needs in the past 6 months was also included as a covariate. All subjects who replied 'no' to all three questions "*In the past 6 months did you need care for an urgent health problem such as an abscess, strep throat or the flu?*", "*In the past 6 months did you need care for an ongoing health problem (e.g. high blood pressure, diabetes)?*", and "*In the past 6 months did you need dental care?*" were recoded as 'No need for healthcare in the past 6 months'. All subjects who reported need of any healthcare, and replied 'no' to either the question "*In the past 6 months, did you try to get [healthcare]?*" or the question "*In the past 6 months, have you received [healthcare]?*" were recoded as 'Unmet health care need in the past 6 months'. All remaining subjects who were neither recoded as 'No need for healthcare in the past 6 months' nor 'Unmet health care need in the past 6 months' were recoded as 'Met healthcare need in the past 6 months.'

The number of covariates in multivariate analysis was limited to one per 10 cases. Missing data values were recoded as 'no' (0). The number of missing values did not exceed $n = 3$ for any of the variables.

Statistical analysis
We first started by estimating the bivariate associations between each of the 11 pain variables described above and NMPOU. We restricted the reporting window to the past 24 h. All variables were binary or categorical, and for statistical testing significance, we used unadjusted logistic regression analysis for binary outcomes. Multivariate logistic regression analysis was conducted with pain variables associated with NMPOU past 24 h at level $p < 0.05$ in bivariate analysis, adjusted for all pre-defined covariates. A correlation analysis was performed to prevent inclusion of explanatory variables and covariates with correlation 0.7 or more from the same analysis. *P*-values below 0.05 for a two-tailed test were considered statistically significant. All statistical analyses were performed in SPSS version 21.0 [43].

Results
Sample characteristics
Seven hundred and two PWID were included in the study. Twenty-one percent were female (Table 1). Mean age was 45.1 years (range 18–69). The most common street drugs used in the past 24 h were marijuana (36.8%), methamphetamine (27.6%) and heroin (24.6%). Fifteen percent ($n = 103$) reported NMPOU (including methadone and buprenorphine) in the past 24 h.

Pain characteristics
Slightly less than half of the study participants, 47.7% ($n = 335$) reported that they had physical pain in the past 24 h (Table 2). Median pain duration was 36 months (interquartile range [IQR] 6–141 months). The most common pain locations were lower limbs (27.1%) and back (19.7%). Median average pain in the past 24 h was six on a 10-point scale (IQR 5–7). Approximately 40% of the sample reported past 24 h pain interference with the functional domains presented in Table 2.

Associations between pain and NMPOU
In bivariate analysis, scores above median of pain intensity (average pain in past 24 h) and past 24 h level of pain interference with general activity, walking ability, physical ability, sleep and enjoyment of life were significantly and positively associated with NMPOU past 24 h (Table 2). Pain duration, pain location, and pain interference with mood and relationships were not statistically associated with NMPOU. After correlation analysis showing over 0.7 level correlation between all pain-related candidate variables, we conducted separate multivariate analyses assessing the association of each pain variable with NMPOU past 24 h. None of the covariates were excluded due to collinearity.

In multivariate analysis adjusted for age, sex, lifetime psychiatric diagnosis, homelessness, past 30 days OST, past 24 h use of street heroin and unmet healthcare needs in the past 6 months, NMPOU past 24 h was independently and positively associated with all the pain variable associated with NMPOU in bivariate analysis (Table 3).

Discussion
The current study found that both pain and NMPOU were common among PWID, a high-risk population that traditionally lacks access to health care. The findings showing several independent cross-sectional associations between NMPOU and levels of pain and pain interference among PWID are novel and have important clinical implications.

Both recent and long-term pain was common in the study sample, which is similar to the sparse previous research on pain among PWID. Among HIV-positive patients, those who inject drugs have been shown to report more pain than those who do not inject drugs [44, 45]. Also, the prevalence of chronic pain is high among opioid dependent persons in opioid substitution treatment [46]. In one study, 37% reported chronic severe pain [40], and in another 61% reported chronic pain problems [47]. This high pain prevalence is not surprising, considering that homelessness, poverty and several potentially painful conditions such as dental problems [48], abscesses [49–51],

Dahlman *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:29

Page 5 of 11

Table 1 Sample characteristics among people who inject drugs in San Francisco, for total sample (*N* = 702) and subjects reporting past 24 h pain (*n* = 335)

Characteristic	Pain past 24 h n (%)	Total sample n (%)	*P*-value
Mean age (range)	46.6 (19–69)	45.1 (18–69)	<0.001***
Sex			
Female	74 (22.1%)	147 (20.9%)	0.48
Male	261 (77.9%)	555 (79.1%)	
Race			
White	179 (53.4%)	379 (54.0%)	0.91
Black	86 (25.7%)	181 (25.8%)	
Hispanic	20 (6.0%)	46 (6.6%)	
Other	48 (14.3%)	91 (13.0%)	
Missing	*2 (0.6%)*	*5 (0.7%)*	
Homeless	208 (62.1%)	442 (63.0%)	0.65
Graduated from high school/got a GED	250 (74.6%)	509 (72.5%)	0.23
Ever diagnosed with a psychiatric illness*	207 (61.8%)	396 (56.4%)	0.01*
Health care need for an acute, chronic or dental problem in the past 6 months*			
No need	43 (12.8%)	122 (17.4%)	<0.01*
Met healthcare need	94 (28.1%)	204 (29.1%)	
Unmet healthcare need	198 (59.1%)	376 (53.6%)	
NMPOU past 24 h	53 (15.8%)	103 (14.7%)	0.41
NMPOU (except methadone and buprenorphine) past 24 h	50 (14.9%)	89 (12.7%)	0.09
Non-medical use of tranquilizers/sedatives past 24 h	23 (6.9%)	43 (6.1%)	0.44
Non-medical use of prescription stimulants past 24 h	2 (0.6%)	6 (0.9%)	0.48
Non-medical use of Methadone past 24 h	9 (2.7%)	23 (3.3%)	0.40
Non-medical use of buprenorphine/Suboxone past 24 h	0	1 (0.1%)	NA
Non-medical use of Phenergan past 24 h	3 (0.9%)	4 (0.6%)	0.27
Used Speedball (heroin/cocaine or heroin/crack) past 24 h	21 (6.3%)	42 (6.0%)	0.76
Used Goofball (heroin/methamphetamine) past 24 h	24 (7.2%)	40 (5.7%)	0.11
Used Crack or Rock Cocaine past 24 h	66 (19.7%)	139 (19.8%)	0.95
Used Powder Cocaine past 24 h	6 (1.8%)	15 (2.1%)	0.55
Used Methamphetamine past 24 h	92 (27.5%)	194 (27.6%)	0.92
Used Heroin past 24 h	80 (23.9%)	173 (24.6%)	0.65
Used Marijuana for non-medical reasons past 24 h	124 (37.0%)	258 (36.8%)	0.89
Used any type of street heroin past 24 h	93 (27.8%)	194 (27.6%)	0.94

P-value calculated with Pearson's Chi-square test for all variables except age, where Student's T-test was used
*p < 0.05
***p < 0.001

other injection-related injuries [52] and chronic wounds [53] are common among PWID.

The primary contribution of this study was that we examined a diverse range of pain-related characteristics. While there was no statistically significant difference regarding NMPOU between subjects reporting no pain in the past 24 h and average pain median or below on the 10-point modified Brief Pain Inventory scale, subjects reporting average pain intensity above the median had more than doubled odds for NMPOU. Conversely, there

was no association between NMPOU and pain duration. The association between pain intensity and NMPOU was similar to the results from surveys in the general American population study of non-institutionalized persons aged 18 or older showing a positive linear correlation between level of pain and past year NMPOU [25], but counter to previous research, which have not showed an association between pain and NMPOU in non-PWID cohorts consisting of U.S. veterans [29] and patients with chronic pain [30]. Given that we limited

Dahlman *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:29

Page 6 of 11

Table 2 Pain prevalence and association with use of nonmedical prescription opioid use in the past 24 h among people who inject drugs in San Francisco (N = 702). Bivariate logistic regression analysis

Pain characteristics	Median (IQR)	Past 24 h NMPOU n (%)	Total sample n (%)	Unadjusted OR (95% CI)
Pain past 24 h[a]	NA	53 (51.5%)	335 (47.7%)	1.19 (0.78–1.81)
Pain duration in months[c]	36 (6–141)			
No pain (0)		50 (48.5%)	370 (52.7%)	1.00
Duration median or less (1–36)		27 (26.2%)	172 (24.5%)	1.19 (0.72–1.98)
Duration above median (37–776)		26 (25.2%)	160 (22.8%)	1.24 (0.74–2.08)
Pain single worst location (mutually exclusive)	NA			
No pain (0)		50 (49.0%)	367 (52.3%)	1.00
Head (1)		4 (3.9%)	17 (2.4%)	1.95 (0.61–6.22)
Neck/shoulder/back (2)		22 (21.6%)	122 (17.4%)	1.40 (0.81–2.42)
Extremities (3)		18 (17.6%)	158 (22.5%)	0.82 (0.46–1.45)
Abdomen/genitals (4)		8 (7.8%)	34 (4.8%)	1.95 (0.84–4.55)
Missing values (multiple answers)			*4 (0.6%)*	
Pain location (not mutually exclusive)	NA			
Head		10 (9.7%)	31 (4.4%)	NA4
Neck/shoulders		10 (9.7%)	77 (11.0%)	NA4
Back		27 (26.2%)	138 (19.7%)	NA4
Upper limbs		8 (7.8%)	67 (9.5%)	NA4
Lower limbs		28 (27.2%)	190 (27.1%)	NA4
Abdomen/genitals		10 (9.7%)	51 (7.3%)	NA4
Average pain past 24 h[c]	6 (5–7)			
No pain (0)		51 (49.5%)	375 (53.4%)	1.00
Pain median or less (1–6)		24 (23.3%)	201 (28.6%)	0.86 (0.51–1.45)
Pain above median (7–10)		28 (27.2%)	126 (17.9%)	1.82 (1.09–3.03)*
Pain interference with general activity past 24 h[c]	7 (5–9)			
No interference (0)		55 (53.4%)	412 (58.7%)	1.00
Interference median or less (1–7)		21 (20.4%)	165 (23.5%)	0.95 (0.55–1.62)
Interference above median (8–10)		27 (26.2%)	125 (17.8%)	1.79 (1.07–2.99)*
Pain interference with mood past 24 h[b]	7 (5–9)			
No interference (0)		54 (52.4%)	415 (59.1%)	1.00
Interference median or less (1–7)		26 (25.2%)	166 (23.6%)	1.24 (0.75–2.06)
Interference above median (8–10)		23 (22.3%)	121 (17.2%)	1.57 (0.92–2.68)
Pain interference with walking ability past 24 h[b]	8 (5–9)			
No interference (0)		55 (53.4%)	422 (60.1%)	1.00
Interference median or less (1–8)		25 (24.3%)	188 (26.8%)	1.02 (0.62–1.70)
Interference above median (9–10)		23 (22.3%)	92 (13.1%)	2.22 (1.28–3.86)**
Pain interference with physical ability past 24 h[b]	7 (5–9)			
No interference (0)		54 (52.4%)	404 (57.5%)	1.00
Interference median or less (1–7)		19 (18.4%)	161 (22.9%)	0.87 (0.50–1.52)
Interference above median (8–10)		30 (29.1%)	137 (19.5%)	1.82 (1.11–2.98)*
Pain interference with relationships past 24 h[c]	6 (3–8)			
No interference (0)		60 (58.3%)	465 (66.2%)	1.00
Interference median or less (1–6)		21 (20.4%)	122 (17.4%)	1.40 (0.82–2.42)
Interference above median (7–10)		22 (21.4%)	115 (16.4%)	1.60 (0.93–2.74)

Dahlman *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:29

Page 7 of 11

Table 2 Pain prevalence and association with use of nonmedical prescription opioid use in the past 24 h among people who inject drugs in San Francisco (N = 702). Bivariate logistic regression analysis *(Continued)*

Pain interference with sleep past 24 h[b]	7 (5–10)			
No interference (0)		56 (54.4%)	425 (60.5%)	1.00
Interference median or less (1–7)		19 (18.4%)	148 (21.1%)	0.97 (0.56–1.70)
Interference above median (8–10)		28 (27.2%)	129 (18.4%)	1.83 (1.10–3.03)*
Pain interference with enjoyment of life past 24 h[c]	7 (5–9)			
No interference (0)		54 (52.4%)	412 (58.7%)	1.00
Interference median or less (1–7)		23 (22.3%)	163 (23.2%)	1.09 (0.64–1.84)
Interference above median (8–10)		26 (25.2%)	127 (18.1%)	1.71 (1.02–2.86)*

*$p < 0.05$. **$p < 0.005$. P-value calculated with Wald Chi-square test
1. [a]missing value recoded as "no pain". 2. [b]missing values recoded as "no pain". 3. [c]missing values recoded as "no pain"
4. Bivariate analysis was not conducted since pain locations were not mutually exclusive

our measures to pain in the past 24 h, it is not surprising that we observed that pain was associated with NMPOU at the event-level over the previous day. Additional studies, perhaps using event-driven sampling like ecological momentary analysis, would be helpful in understanding the linkages between the onset of pain and NMPOU as a means to self-medicate pain.

We also observed that pain interference above median with general activity, walking ability, physical ability, sleep, and enjoyment of life was independently and positively associated with recent NMPOU.

Back pain and lower extremity pain was common in the study sample of PWID. This finding follows a study by Barry et al. [54] showing that chronic pain among persons seeking OST was most commonly located in back or legs. Lower extremity pain is common among PWID and homeless people, due to dermatological problems [55, 56], foot trauma and venous disorders [23, 24]. These pain locations are not notably different from what could be expected in the general population [57–60]. We did not find any significant association between pain location and NMPOU past 24 h, which is consistent with previous studies [29].

While the cross-sectional design of this study allows no interpretation of causality, our findings imply that PWID who use prescription pain relievers non-medically may be attempting to self-medicate or manage pain problems. Self-medication of pain, with heroin or prescription opioids, has been shown to be prevalent in 98% of PWID with moderate or extreme pain [61] and associated with being denied prescription analgesics. However, Heimer et al. [22] showed that four out of five PWID with chronic pain reported NMPOU before debut of their pain. In addition, up to three-quarters of patients with chronic non-cancer pain have been shown to have a lifetime history of substance use disorder [62]. Co-occurrence of pain and nonmedical substance use appears to be a complex matter, and future, longitudinal studies are necessary to assess causal relationships.

Covariates positively associated with NMPOU were younger age, use of street heroin, and unmet healthcare needs. Interestingly, recent use of street heroin was strongly associated with recent NMPOU in this study, while OST was not. Since all subjects in the study were PWID currently using drugs intravenously, this finding allows no interpretation regarding OST as a potential protective factor for avoiding NMPOU. However, future research assessing OST to diminish NMPOU would be of great clinical relevance. Worth noting is also that over half of the population had unmet healthcare needs in the past 6 months. We recommend future studies assessing unmet healthcare needs specifically as a predictor of NMPOU.

This study has several limitations that should be noted. All results were based on self-reports, and no structured clinical diagnosis or drug testing has been performed. We are unsure how the self-reported nature of the data on pain may bias our results, given that pain cannot be objectively measured. We believe that recall bias is kept to a minimum since the pain-related questions and the prescription and street drug questions were mostly about the past 24 h. The possibility of social desirability bias affecting the study participants' reports of pain and drug use/NMPOU should, however, not be neglected. One additional limitation is that power was low to detect differences in pain as it related to NMPOU. We restricted our time-frame for most of our analyses to the past 24 h. This was done to boost our ability to link the timeframe in which pain could be self-mediated by prescription opioids. Unfortunately, a consequence of this decision was that there were a small number of cases that engaged in NMPOU during that timeframe. If we had expanded the window to the past 30 days, we would have gained statistical power by increasing the number of cases that endorsed NMPOU, but since most of the pain variables in the questionnaire were assessing past 24 h pain, we did not include past 30 days NMPOU data. Since temporality of pain and NMPOU

Table 3 Multivariate logistic regression analysis of nonmedical prescription opioid use among people who inject drugs in San Francisco (N = 702). Outcome variable: NMPOU past 24 h

Characteristic	MODEL 1[a] AOR (95% CI)	MODEL 2[b] AOR (95% CI)	MODEL 3[c] AOR (95% CI)	MODEL 4[d] AOR (95% CI)	MODEL 5[e] AOR (95% CI)	MODEL 6[f] AOR (95% CI)
Average pain past 24 h						
Pain median or less	0.85 (0.49–1.47)	-	-	-	-	-
Pain above median	2.15 (1.21–3.80)*	-	-	-	-	-
Pain interference with general activity past 24 h						
Interference median or less	-	0.96 (0.54–1.70)	-	-	-	-
Interference above median	-	1.82 (1.04–3.21)*	-	-	-	-
Pain interference with walking ability past 24 h						
Interference median or less	-	-	1.05 (0.61–1.80)	-	-	-
Interference above median	-	-	2.52 (1.37–4.63)**	-	-	-
Pain interference with physical ability past 24 h						
Interference median or less	-	-	-	0.87 (0.48–1.57)	-	-
Interference above median	-	-	-	2.01 (1.16–3.45)*	-	-
Pain interference with sleep past 24 h						
Interference median or less	-	-	-	-	0.91 (0.50–1.65)	-
Interference above median	-	-	-	-	1.98 (1.13–3.48)*	-
Pain interference with enjoyment of life past 24 h						
Interference median or less	-	-	-	-	-	1.11 (0.63-1.94)
Interference above median	-	-	-	-	-	1.79 (1.02-3.15)*
Male sex	1.09 (0.64–1.86)	1.14 (0.67–1.93)	1.11 (0.65–1.90)	1.08 (0.63–1.84)	1.12 (0.66–1.90)	1.09 (0.64–1.86)
Age (continuous)	0.96 (0.94–0.98)***	0.96 (0.94–0.98)***	0.96 (0.94–0.98)***	0.96 (0.94–0.98)***	0.96 (0.94–0.98)***	0.96 (0.94–0.98)***
Lifetime psychiatric diagnosis	1.15 (0.72–1.84)	1.17 (0.73–1.87)	1.17 (0.73	1.18 (0.74–1.88)	1.09 (0.68–1.76)	1.18 (0.74–1.88)
Homeless	1.29 (0.78–2.13)	1.25 (0.75–2.06)	1.86)	1.25 (0.76–2.07)	1.24 (0.75–2.05)	1.24 (0.75–2.05)
OST past 30 days	1.64 (1.00–2.69)*	1.61 (0.98–2.63)	1.61 (0.98–2.64)	1.62 (0.99–2.66)	1.63 (0.99–2.67)	1.60 (0.98–2.62)
Street heroin use past 24 h	3.42 (2.17–5.39)***	3.33 (2.12–5.23)***	3.36 (2.14–5.30)***	3.31 (2.10–5.21)***	3.34 (2.12–5.25)***	3.30 (2.10–5.19)***
Healthcare need past 6 months[g]						
Met healthcare need	1.60 (0.69–3.70)	1.60 (0.69–3.70)	1.58 (0.68–3.66)	1.69 (0.73–3.91)	1.63 (0.70–3.78)	1.65 (0.71–3.81)
Unmet healthcare need	2.58 (1.20–5.55)*	2.58 (1.20–5.54)*	2.53 (1.18–5.66)*	2.72 (1.27–5.85)*	2.74 (1.28–5.90)*	2.65 (1.24–5.69)*

*p < 0.05, **p < 0.005, ***p < 0.001. P-value calculated with Wald Chi-square test

All models are adjusted for sex, age, lifetime psychiatric diagnosis, homelessness, opiate substitution treatment, use of street heroin and unmet healthcare needs

[a]Explanatory variable Pain intensity. Reference category is No pain

[b]Explanatory variable Pain interference with general activity. Reference category is No pain interference

[c]Explanatory variable Pain interference with walking. Reference category is No pain interference

[d]Explanatory variable Pain interference with physical ability. Reference category is No pain interference

[e]Explanatory variable Pain interference with sleep. Reference category is No pain interference

[f]Explanatory variable Pain interference with enjoyment of life. Reference category is No pain interference

[g]Healthcare need for an urgent/chronical/dental health problem. Reference category is No healthcare need past 6 months

Dahlman *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:29

Page 9 of 11

could not assess in this cross-sectional study, reverse causality could not be excluded. It would thus be interesting to conduct longitudinal studies to examine whether individuals began NMPOU because of self-management, and then through habituation became tolerant of opioids. Neither physical comorbidity nor current psychiatric illness was possible to control for, which is an important limitation due to the large body of research data showing overlap between psychiatric morbidity and substance use [26, 29, 42].

The clinical implications of the present study are such that medical care is needed to address the high demand medical health needs of the PWID populations. Recently, several insurance companies in the United States have announced reductions in the patient coverage for opioid use as a means to reduce NMPOU [63, 64]. This complicates the situation for PWID, who already are disenfranchised from medical care and pain relief that could ease their pain and suffering, and there is a concern that prescribing restrictions might limit pain medication acquisition among legitimate pain patients. Previous research on pain management among vulnerable populations has identified inadequate analgesic therapy among 85% of patients with AIDS, and especially among AIDS-patients who were female, low-educated or PWID [65]. Voon et al. [66] showed that two-thirds of 462 PWID had ever been denied prescription analgesics, while 92% reported lifetime disability. Additional research is needed to determine whether or not these policies may have adverse impacts on PWID, including further removal from the main-stream medical system, or whether policies like the Affordable Health Care Act or similar reforms can serve to re-introduce those who have traditionally been excluded from the medical system.

Conclusion

In conclusion, both pain and NMPOU were common among PWID, and pain intensity and pain interference were positively associated with NMPOU in this group. These findings implicate a strong need for improved physical healthcare among PWID. There is also a need for future longitudinal studies assessing the temporal nature of the associations between pain indicators and NMPOU, and evaluations of potential consequences of policies that restrict access to prescription opioids for high-risk populations including PWID.

Publisher's Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details
[1]Department of Clinical Sciences Lund, Division of Psychiatry, Lund University, Lund, Sweden. [2]Malmo Addiction Centre, Clinical Research Unit, Sodra Forstadsg. 35, plan 4, SE-205 02 Malmo, Sweden. [3]Behavioral and Urban Health Program, RTI International, San Francisco, USA. [4]Battelle Memorial Institute, Baltimore, MD, USA.

References
1. Boyd CJ, McCabe SE. Coming to terms with the nonmedical use of prescription medications. Subst Abuse Treat Prev Policy. 2008;3:22.
2. Substance Abuse and Mental Health Services Administration (SAMHSA). Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings. NSDUH Series H-41, HHS Publication No. (SMA) 11-4658. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2011. Retrieved 5/10/2016 from http://www.samhsa.gov/data/sites/default/files/NSDUHNationalFindingsResults2010-web/2k10ResultsRev/NSDUHresultsRev2010.pdf. Accessed 28 May 2017.
3. Hernandez SH, Nelson LS. Prescription drug abuse: insight into the epidemic. Clin Pharmacol Ther. 2010;88(3):307–17.
4. Barrett SP, Meisner JR, Stewart SH. What constitutes prescription drug misuse? Problems and pitfalls of current conceptualizations. Curr Drug Abuse Rev. 2008;1(3):255–62.
5. Center for Behavioral Health Statistics and Quality. Behavioral health trends in the United States: Results from the 2014 National Survey on Drug Use and Health (HHS Publication No. SMA 15-4927, NSDUH Series H-50). 2015. Retrieved 5/10/16 from http://www.samhsa.gov/data/. Accessed 28 May 2017.
6. Johnston LD, O'Malley PM, Miech RA, Bachman JG, Schulenberg JE. Monitoring the future national survey results on drug use: 1975-2014: overview, key findings on adolescent drug use. Ann Arbor: Institute for Social Research, The University of Michigan; 2015.
7. Tavernise S. C.D.C. painkiller guidelines aim to reduce addiction risk. New York Times. March 15 2016. Retrieved 10/03/2016 from http://www.nytimes.com/2016/03/16/health/cdc-opioid-guidelines.html.
8. Office of National Drug Control Policy (ONDCP). Epidemic: Responding to America's prescription drug abuse crisis. 2011. Retrieved 09/26/2016 from http://www.obamawhitehouse.gov/sites/default/files/ondcp/issues-content/prescription-drugs/rx_abuse_plan.pdf. Accessed 28 May 2017.

Dahlman *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:29

Page 10 of 11

9. Muhari P, Gfroerer J, Davies C. CBHSQ data review: Associations of nonmedical prescription pain reliever use and initiation of heroin use in the United States. August 2013. Retrieved 10/03/2016 from http://www.samhsa.gov/data/sites/default/files/DR006/DR006/nonmedical-pain-reliever-use-2013.pdf.

10. Reifler LM, Droz D, Bailey JE, Schnoll SH, Fant R, Dart RC, et al. Do prescription monitoring programs impact state trends in opioid abuse/misuse? Pain Med. 2012;13(3):434–42.

11. Fain KM, Alexander GC. Disposing of medicines safely. Am J Public Health. 2014;104(12):e2–3.

12. Wurcel AG, Merchant EA, Clark RP, Stone DR. Emerging and Underrecognized complications of illicit drug use. Clin Infect Dis. 2015;61(12):1840–9.

13. Larney S, Peacock A, Mathers BM, Hickman M, Degenhardt L. A systematic review of injecting-related injury and disease among people who inject drugs. Drug Alcohol Depend. 2017;171:39–49.

14. Heimer R, Barbour R, Palacios WR, Nichols LG, Grau LE. Associations between injection risk and community disadvantage among suburban injection drug users in southwestern Connecticut, USA. AIDS Behav. 2014;18(3):452–63.

15. Lloyd-Smith E, Kerr T, Hogg RS, Li K, Montaner JS, Wood E. Prevalence and correlates of abscesses among a cohort of injection drug users. Harm Reduct J. 2005;2:24.

16. Lloyd-Smith E, Wood E, Zhang R, Tyndall MW, Montaner JS, Kerr T. Risk factors for developing a cutaneous injection-related infection among injection drug users: a cohort study. BMC Public Health. 2008;8:405.

17. Bruggmann P, Grebely J. Prevention, treatment and care of hepatitis C virus infection among people who inject drugs. Int J Drug Policy. 2015;26(Suppl 1):S22–6.

18. Coffin PO, Jin H, Huriaux E, Mirzazadeh A, Raymond HF. Trends in use of health care and HIV prevention services for persons who inject drugs in San Francisco: results from national HIV behavioral surveillance 2005-2012. Drug Alcohol Depend. 2015;146:45–51.

19. Lorvick J, Kral AH, Seal K, Gee L, Edlin BR. Prevalence and duration of hepatitis C among injection drug users in San Francisco, Calif. Am J Public Health. 2001;91(1):46–7.

20. Badiaga S, Raoult D, Brouqui P. Preventing and controlling emerging and reemerging transmissible diseases in the homeless. Emerg Infect Dis. 2008;14(9):1353–9.

21. Tsui JI, Herman DS, Kettavong M, Anderson BJ, Stein MD. Chronic pain and hepatitis C virus infection in opioid dependent injection drug users. J Addict Dis. 2011;30(2):91–7.

22. Heimer R, Zhan W, Grau LE. Prevalence and experience of chronic pain in suburban drug injectors. Drug Alcohol Depend. 2015;151:92–100.

23. Pieper B, Templin T. Lower extremity changes, pain, and function in injection drug users. J Subst Abus Treat. 2003;25(2):91–7.

24. Pieper B, Kirsner RS, Templin TN, Birk TJ. Injection drug use: an understudied cause of venous disease. Arch Dermatol. 2007;143(10):1305–9.

25. Novak SP, Herman-Stahl M, Flannery B, Zimmerman M. Physical pain, common psychiatric and substance use disorders, and the non-medical use of prescription analgesics in the United States. Drug Alcohol Depend. 2009;100(1-2):63–70.

26. Abrahamsson T, Hakansson A. Nonmedical prescription drug use (NMPDU) in the Swedish general population-correlates of analgesic and sedative use. Subst Use Misuse. 2015;50(2):148–55.

27. Fishbain DA, Rosomoff HL, Rosomoff RS. Drug abuse, dependence, and addiction in chronic pain patients. Clin J Pain. 1992;8(2):77–85.

28. Sullivan MD, Edlund MJ, Fan MY, Devries A, Brennan Braden J, Martin BC. Risks for possible and probable opioid misuse among recipients of chronic opioid therapy in commercial and medicaid insurance plans: the TROUP study. Pain. 2010;150(2):332–9.

29. Edlund MJ, Steffick D, Hudson T, Harris KM, Sullivan M. Risk factors for clinically recognized opioid abuse and dependence among veterans using opioids for chronic non-cancer pain. Pain. 2007;129:355–62.

30. Ives TJ, Chelminski PR, Hammett-Stabler CA, Malone RM, Perhac JS, Potisek NM, et al. Predictors of opioid misuse in patients with chronic pain: a prospective cohort study. BMC Health Serv Res. 2006;6:46.

31. Martel MO, Finan PH, McHugh RK, Issa M, Edwards RR, Jamison RN, et al. Day-to-day pain symptoms are only weakly associated with opioid craving among patients with chronic pain prescribed opioid therapy. Drug Alcohol Depend. 2016;162:130–6.

32. Khosla N, Juon HS, Kirk GD, Astemborski J, Mehta SH. Correlates of non-medical prescription drug use among a cohort of injection drug users in Baltimore City. Addict Behav. 2011;36(12):1282–7.

33. Watters JK, Biernacki P. Targeted sampling: options for the study of hidden populations. Soc Probl. 1989;36(4):416–30.

34. Bluthenthal RN, Watters JK. Multimethod research from targeted sampling to HIV risk environments. NIDA Res Monogr. 1995;157:212–30.

35. Kral AH, Malekinejad M, Vaudrey J, Martinez AN, Lorvick J, McFarland W, et al. Comparing respondent-driven sampling and targeted sampling methods of recruiting injection drug users in San Francisco. J Urban Health. 2010;87(5):839–50.

36. Dahlman D, Håkansson A, Kral AH, Wenger L, Ball EL, Novak SP. Behavioral characteristics and injection practices associated with skin and soft tissue infections among people who inject drugs: a community-based observational study. Subst Abus. 2017;38(1):105–12.

37. Zelman DC, Gore M, Dukes E, Tai KS, Brandenburg N. Validation of a modified version of the brief pain inventory for painful diabetic peripheral neuropathy. J Pain Symptom Manag. 2005;29(4):401–10.

38. Breitbart W, Rosenfeld B, Passik S, Kaim M, Funesti-Esch J, Stein K. A comparison of pain report and adequacy of analgesic therapy in ambulatory AIDS patients with and without a history of substance abuse. Pain. 1997;72(1-2):235–43.

39. Passik SD, Kirsh KL, Donaghy KB, Portenoy RK. Pain and aberrant drug-related behaviors in medically ill patients with and without histories of substance abuse. Clin J Pain. 2006;22(2):173–81.

40. Rosenblum A, Joseph H, Fong C, Kipnis S, Cleland C, Portenoy RK. Prevalence and characteristics of chronic pain among chemically dependent patients in methadone maintenance and residential treatment facilities. JAMA. 2003;289(18):2370–8.

41. Dennis BB, Roshanov PS, Bawor M, Paul J, Varenbut M, Daiter J, et al. Usefulness of the brief pain inventory in patients with Opioid addiction receiving methadone maintenance treatment. Pain Physician. 2016;19(1):E181–95.

42. Edlund MJ, Martin BC, Fan MY, Devries A, Braden JB, Sullivan MD. Risks for opioid abuse and dependence among recipients of chronic opioid therapy: results from the TROUP study. Drug Alcohol Depend. 2010;112(1-2):90–8.

43. IBM Corp. Released 2012. IBM SPSS statistics for windows, version 21.0. Armonk: IBM Corp.

44. Del Borgo C, Izzi I, Chiarotti F, Del Forno A, Moscati AM, Cornacchione E, et al. Multidimensional aspects of pain in HIV-infected individuals. AIDS Patient Care STDs. 2001;15(2):95–102.

45. Martin C, Pehrsson P, Österberg A, Sönnerborg A, Hansson P. Pain in ambulatory HIV-infected patients with and without intravenous drug use. Eur J Pain. 1999;3(2):157–64.

46. Voon P, Hayashi K, Milloy MJ, Nguyen P, Wood E, Montaner J, et al. Pain among high-risk patients on methadone maintenance treatment. J Pain. 2015;16(9):887–94.

47. Jamison RN, Kauffman J, Katz NP. Characteristics of methadone maintenance patients with chronic pain. J Pain Symptom Manag. 2000;19(1):53–62.

48. Robbins JL, Wenger L, Lorvick J, Shiboski C, Kral AH. Health and oral health care needs and health care-seeking behavior among homeless injection drug users in San Francisco. J Urban Health. 2010;87(6):920–30.

49. Ivan M, van Beek I, Wand H, Maher L. Surveillance of injecting-related injury and diseases in people who inject drugs attending a targeted primary health care facility in Sydney's kings cross. Aust N Z J Public Health. 2015;39(2):182–7.

50. Phillips KT, Stein MD. Risk practices associated with bacterial infections among injection drug users in Denver, Colorado. Am J Drug Alcohol Abuse. 2010;36(2):92–7.

51. Pollini RA, Gallardo M, Hasan S, Minuto J, Lozada R, Vera A, et al. High prevalence of abscesses and self-treatment among injection drug users in Tijuana, Mexico. Int J Infect Dis. 2010;14(Suppl 3):e117–22.

52. Roose RJ, Hayashi AS, Cunningham CO. Self-management of injection-related wounds among injecting drug users. J Addict Dis. 2009;28(1):74–80.

53. Smith ME, Robinowitz N, Chaulk P, Johnson KE. High rates of abscesses and chronic wounds in community-recruited injection drug users and associated risk factors. J Addict Med. 2015;9(2):87–93.

54. Barry DT, Beitel M, Joshi D, Schottenfeld RS. Pain and substance-related pain-reduction behaviors among opioid dependent individuals seeking methadone maintenance treatment. Am J Addict. 2009;18(2):117–21.

55. Stratigos AJ, Stern R, González E, Johnson RA, O'Connell J, Dover JS. Prevalence of skin disease in a cohort of shelter-based homeless men. J Am Acad Dermatol. 1999;41(2 Pt 1):197–202.

56. Raoult D, Foucault C, Brouqui P. Infections in the homeless. Lancet Infect Dis. 2001;1(2):77–84.

Dahlman *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:29

Page 11 of 11

57. Hoy D, Bain C, Williams G, March L, Brooks P, Blyth F, et al. A systematic review of the global prevalence of low back pain. Arthritis Rheum. 2012;64(6):2028–37.

58. Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. Bull World Health Organ. 2003;81(9):646–56.

59. Manchikanti L, Singh V, Falco FJ, Benyamin RM, Hirsch JA. Epidemiology of low back pain in adults. Neuromodulation. 2014;17(Suppl 2):3–10.

60. Thiem U, Lamsfuß R, Günther S, Schumacher J, Bäker C, Endres HG, et al. Prevalence of self-reported pain, joint complaints and knee or hip complaints in adults aged ≥ 40 years: a cross-sectional survey in Herne, Germany. PLoS One. 2013;8(4):e60753.

61. Voon P, Callon C, Nguyen P, Dobrer S, Montaner J, Wood E, et al. Self-management of pain among people who inject drugs in Vancouver. Pain Manag. 2014;4(1):27–35.

62. Morasco BJ, Gritzner S, Lewis L, Oldham R, Turk DC, Dobscha SK. Systematic review of prevalence, correlates, and treatment outcomes for chronic non-cancer pain in patients with comorbid substance use disorder. Pain. 2011;152(3):488–97.

63. Cigna. Cigna outlines steps to help curb national drug epidemic. May 19 2016. Retrieved 05/25/2016 from http://www.cigna.com/newsroom/news-releases/2016/pdf/cigna-outlines-steps-to-help-curb-national-drug-epidemic.pdf. Accessed 28 May 2017.

64. Coghlan, E. Opioid Prescriptions Drop – Cigna To Reduce Further. Posted on May 21, 2016 in Drug Addiction, Pain Medication. Retreived 3/6/2016 from http://nationalpainreport.com/opioid-prescriptions-drop-cigna-to-reduce-further-8830525.html.

65. Breitbart W, Rosenfeld BD, Passik SD, McDonald MV, Thaler H, Portenoy RK. The undertreatment of pain in ambulatory AIDS patients. Pain. 1996;65(2-3):243–9.

66. Voon P, Callon C, Nguyen P, Dobrer S, Montaner JS, Wood E, et al. Denial of prescription analgesia among people who inject drugs in a Canadian setting. Drug Alcohol Rev. 2015;34(2):221–8.

SHORT REPORT   Open Access

CrossMark

History of medication-assisted treatment and its association with initiating others into injection drug use in San Diego, CA

Maria Luisa Mittal[1], Devesh Vashishtha[1], Shelly Sun[2], Sonia Jain[2], Jazmine Cuevas-Mota[1], Richard Garfein[1], Steffanie A. Strathdee[1] and Dan Werb[1*]

Abstract

Background: Medication-assisted treatment (MAT) remains the gold standard for the treatment of opioid use disorder. MAT also reduces the frequency of injecting among people who inject drugs (PWID). Relatedly, data suggest that PWID play a key role in the initiation of others into drug injecting by exposing injecting practices to injection-naïve drug users. Our primary objective was to test whether a history of MAT enrollment is associated with a reduced odds of PWID providing injection initiation assistance.

Methods: *Preventing Injecting by Modifying Existing Responses* (PRIMER; NIDA DP2-DA040256–01), is a multi-site cohort study assessing the impact of socio-structural factors on the risk that PWID provide injection initiation assistance. Data were drawn from a participating cohort of PWID in San Diego, CA. The primary outcome was reporting ever providing injection initiation assistance; the primary predictor was reporting ever being enrolled in MAT. Logistic regression was used to model associations between MAT enrollment and ever initiating others into injecting while adjusting for potential confounders.

Results: Participants (*n* = 354) were predominantly male (*n* = 249, 70%). Thirty-eight percent (*n* = 135) of participants reported ever initiating others into injection drug use. In multivariate analysis, participants who reported a history of MAT enrollment had significantly decreased odds of ever providing injection initiation assistance (Adjusted Odds Ratio [AOR]: 0.62, 95% Confidence Interval [CI]: 0.39–0.99).

Conclusions: These preliminary findings suggest an association between MAT enrollment and a lower odds that male PWID report providing injection initiation assistance to injection-naïve drug users. Further research is needed to identify the pathways by which MAT enrollment may impact the risk that PWID initiate others into drug injecting.

Keywords: Opioid substitution therapy, HIV prevention, HCV prevention, People who inject drugs, Methadone, Opioid agonist treatment, Injection initiation assistance

Background

Medication-assisted treatment (MAT) remains the gold standard of biomedical care for opioid use disorder, and is effective in reducing the frequency of injecting among people who inject drugs (PWID) [1–4]. This is important given the growing scientific consensus that PWID play a key role in the expansion of injection-related

epidemics by exposing and directly initiating injection-naïve persons into injection drug use (IDU) [5, 6]. With an estimated 12 million PWID worldwide, and an increasing prevalence of opioid-related morbidity and mortality in North America and elsewhere, the prevention of opioid IDU initiation (e.g. heroin) has major public health implications [1, 2, 7, 8]. This is particularly the case as the period immediately following IDU initiation has been shown to be associated with a higher risk of HIV and HCV acquisition [9].

MAT includes opioid agonist treatment (i.e., methadone; also known as opioid substitution therapy), in combination

* Correspondence: dwerb@ucsd.edu
[1]Division of Infectious Diseases and Global Public Health, Department of Medicine, University of California San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0507, USA
Full list of author information is available at the end of the article

Mittal *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:42

Page 2 of 5

with counseling and behavioral therapies to treat opioid use disorder [1–4]. Given that MAT is associated with reductions in the frequency of opioid injecting among PWID as well as street-based injecting in particular, we hypothesize that MAT enrollment may have a secondary preventive impact on the risk that PWID expose and initiate others into injecting [3–10]. This study therefore investigated the potential association between a history of MAT enrollment and reporting injection initiation assistance among PWID.

Methods

Study design
Preventing Injecting by Modifying Existing Responses (PRIMER; NIDA DP2-DA040256–01), is a multi-site study pooling data from cohort studies of PWID in four countries (San Diego, USA; Tijuana, Mexico; Vancouver, Canada; and Paris, Marseille, Bordeaux and Strasbourg, France) to assess the impact of socio-structural factors on the risk that PWID initiate others into injection [5]. For the present analysis, data were drawn from a cohort study of PWID in San Diego, California (*Study of Tuberculosis, AIDS, and Hepatitis C Risk* [STAHR] II; NIDA R01DA031074). To be eligible, participants had to be ≥18 years old, report last IDU ≤ 30 days prior to baseline enrollment.

Participants and measures
Participants completed an interviewer-administered questionnaire assessing sociodemographics, IDU practices, and enrollment in health services including MAT (i.e., methadone) at baseline and at four semiannual follow-up visits. Specific questions related to providing injection initiation assistance were introduced as part of the PRIMER study at the 24-month follow-up wave (i.e., August 2014). Participants provided written informed consent. This study was approved by the University of California San Diego Human Research Protection Program.

Twenty-four month follow-up data were employed in cross-sectional analyses because PRIMER study questions were anchored at this visit. The primary outcome was reporting ever initiating others into IDU, (i.e., reporting having "ever helped someone inject who had never injected before"). The primary predictor of interest was a history of MAT enrollment defined as at least one report of MAT enrollment during any study visit.

Statistical analyses
Fisher's exact test was used to evaluate univariate associations between ever initiating others into IDU and the independent variables. Multivariate logistic regression analysis was performed to determine whether reporting ever initiating others was associated with ever being enrolled in MAT, independent of potential confounders

such as age, gender, and years since first injection. We also studied interactions between gender and MAT enrollment in a separate multivariate model, given previous data suggesting gender differences in injection initiation risk behaviors [6, 11–15]. Statistical analyses were performed in R version 3.1.1 (http://www.r-project.org). The likelihood ratio statistic (LRS) was used to compare nested models; LRS with $p < 0.05$ were used to determine whether a variable should be retained in the model.

Results
Participants ($n = 354$) were predominantly male ($n = 249$, 70%), with a mean age of 47 years (Interquartile Range [IQR]: 38–55), and a median of 24 years of IDU (IQR: 13–35). Thirty-eight percent of participants ($n = 135$) reported ever providing injection initiation assistance, and 39% ($n = 137$) reported ever having been enrolled in MAT. The proportion of MAT enrollment for males was 67.9% ($n = 93$) and 32.1% ($n = 44$) for female and transgender participants. The majority of participants ($n = 304$, 86%) reported having ever injected heroin.

As shown in Table 1, there was a significantly higher proportion of participants ≤30 years old who reported ever providing injection initiation assistance compared with older participants aged 31–50 and ≥51 years (69.0% vs. 37.7% vs. 32.9%, Fisher's exact $p < 0.01$).

As shown in Table 2, each year increase in age was associated with a decreased odds of ever providing injection initiation assistance (Wald χ^2 = 13.27, degrees of freedom [df] = 1, $p < 0.01$), while reporting a higher number of years since first injection was associated with an increased odds initiating others (Wald χ^2 = 5.53, df = 1, $p = 0.02$). PWID reporting a history of MAT enrollment had significantly decreased odds of initiating others into injecting (Wald χ^2 = 4.04, df = 1, $p = 0.04$; see Table 2). Additionally, the inclusion of an interaction term in a separate multivariate model did not significantly impact the association between gender and a history of MAT enrollment (χ^2 = 1.13, df = 1, $p = 0.29$; data not shown).

Discussion
Along with its effectiveness in supporting the management of opioid use disorder [1–4], these preliminary results suggest that MAT enrollment may also be associated with a reduced risk that PWID initiate others into IDU. Specifically, results suggest that among PWID participants, a history of MAT enrollment was associated with a 38% reduction in the odds of having reported initiating others into IDU. This suggests a need to further explore potential pathways by which MAT enrollment may influence the risk that PWID provide injection initiation assistance.

Mittal et al. Substance Abuse Treatment, Prevention, and Policy (2017) 12:42

Page 3 of 5

Table 1 Univariate analysis of factors potentially associated with ever providing injection initiation assistance among persons who inject drugs in San Diego, CA (n = 354)

Variable	Did not ever initiate others into injection (n = 219)	Ever initiated others into injection (n = 135)	P-value[a]
Age			
≤ 30	9 (31.0%)	20 (69.0%)	0.001
31–50	104 (62.3%)	63 (37.7%)	
≥ 51	106 (67.1%)	52 (32.9%)	
Gender, n = 352[b]			
Female	64 (65.3%)	34 (34.7%)	0.460
Transgender	2 (40.0%)	3 (60.0%)	
Male	153 (61.5%)	96 (38.6%)	
Marital Status			
Married	28 (68.3%)	13 (31.7%)	0.398
Other	191 (61.0%)	122 (39.0%)	
Ever been in prison			
No	103 (60.2%)	68 (39.8%)	0.585
Yes	116 (63.4%)	67 (36.6%)	
Years since first injection, n = 353[b]			
≤ 5 years	10 (50.0%)	10 (50.0%)	0.504
6–10 years	30 (61.2%)	19 (38.8%)	
> 10 years	179 (63.0%)	105 (37.0%)	
Ever injected heroin			
No	31 (62.0%)	19 (38.0%)	>0.999
Yes	188 (61.8%)	116 (38.2%)	
Ever injected cocaine			
No	56 (62.9%)	33 (37.1%)	0.900
Yes	163 (61.5%)	102 (38.5%)	
Ever injected meth			
No	29 (76.3%)	9 (23.7%)	0.054
Yes	190 (60.1%)	126 (39.9%)	
Ever enrolled in MAT			
No	128 (59.0%)	89 (41.0%)	0.178
Yes	91 (66.4%)	46 (33.6%)	

[a]Fisher's exact test; [b]Change in sample size due to different number of observations available for each variable; *MAT* Medication-assisted Treatment

Table 2 Multivariate Logistic Regression to assess factors associated with ever providing injection initiation assistance in San Diego, CA

Variable	AOR	95% CI	P-value (df)	Test Statistic[a]
Age	0.94	0.91–0.97	<0.01 (1)	13.27
Years since first injecting	1.04	1.00–1.07	0.02 (1)	5.53
Male gender	1.18	0.72–1.92	0.52 (1)	0.41
Ever enrolled in MAT	0.62	0.39–0.99	0.04 (1)	4.04

[a]Wald test in the multivariate logistic regression model; *AOR* Adjusted Odds Ratio, *95% CI* 95% Confidence Interval, *df* degrees of freedom, *MAT* Medication-assisted Treatment

In line with other studies, we also found that each year increase in age was associated with a decreased risk of providing injection initiation assistance [16, 17]. However, in contrast to these studies we observed an association between a higher number of years since first injection and an increased risk of providing injection initiation assistance.

Multiple studies have reported on gender differences in injection initiation, including data suggesting that men are most often initiated by men comparted to women [12–15, 18]. Additionally, data suggest that some gender-responsive programs may influence the capacity of PWID to engage with supplementary health services offered during MAT enrollment [11, 19–25]. However, the effect of a history of MAT enrollment on providing injection initiation assistance did not differ significantly between male and female participants in our sample. Further quantitative and qualitative studies are needed to more clearly delineate potential differences by gender with respect to injection initiation risk and uptake of MAT.

To our knowledge, this is the first study to investigate the potential impact of MAT enrollment on providing injection initiation assistance. As such, and due to the exploratory nature of this analysis, results should be interpreted cautiously. First, survey items assessing lifetime initiation of others into IDU were limited to the final follow-up of a 24-month observational cohort study, and we were therefore unable to identify the temporal ordering of the dependent and independent variables, and, as such, cannot confirm the direction of the causal association. It may be the case that both enrollment in MAT and avoiding the initiation of others into IDU are both proxy markers of increased capacity by participants to manage their opioid use and we note that this will be the subject of future longitudinal study from our group. Second, providing injection initiation assistance is a highly stigmatized behavior and likely resulted in under-reporting of this behavior [13, 26]. However, there is no reason to believe that differential under-reporting occurred among PWID based on MAT enrollment history; thus, the effect of this bias is likely to be toward a null finding. Despite these limitations, this study provides preliminary evidence particular to opioid users of an association between MAT enrollment and the provision of injection initiation assistance that should be investigated in longitudinal study.

Conclusions

Given the harms associated with recent increases in opioid use across North America [1, 4], this study highlights the need to further investigate the potential impact of MAT as a preventive intervention to reduce not only the incidence of negative injection-related health outcomes experienced by opioid users but also incident cases of IDU initiation.

Mittal *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:42

Page 4 of 5

Authors' contributions
DW, SAS, JCM and RG designed and implemented the survey. MLM, SS, SJ and DW designed the present analysis plan, conducted the statistical analyses, drafted the manuscript, and incorporated suggestions from all co-authors. All authors made significant contributions to the conception of the analyses, interpretation of the data, and drafting of the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate
The study was approved by the research ethics board at the University of California San Diego Human Research Protection Program. All participants provided written informed consent for study participation.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Publisher's Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details
[1]Division of Infectious Diseases and Global Public Health, Department of Medicine, University of California San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0507, USA. [2]Division of Biostatistics and Bioinformatics, Department of Family Medicine and Public Health, University of California San Diego, 9500 Gilman Drive, La Jolla, CA 92093-0622, USA.

REFERENCES
1. Office of the Surgeon General. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. Washington: US Dept of Health and Human Services; 2016. [cited 2016 Nov 16]. Available from: https://addiction.surgeongeneral.gov/surgeon-generals-report.pdf.
2. Substance Abuse and Mental Health Services Administration (SAMHSA). Medication-Assisted Treatment (MAT) [Internet]. SAMHSA; 2016 [cited 2017 Jun 20]. Available from: https://www.samhsa.gov/medication-assisted-treatment
3. Mattick RP, Breen C, Kimber J, Davoli M. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. Cochrane Database Syst Rev. 2009;l8(3):CD002209.
4. Gowing L, Farrell M, Bornemann R, Sullivan L, Ali R. Oral substitution treatment of injecting opioid users for prevention of HIV infection. Cochrane Database Syst Rev. 2011;10(8):CD004145.
5. Werb D, Garfein R, Kerr T, Davidson P, Roux P, Jauffret-Roustide M, Auriacombe M, Small W, Strathdee SA. A socio-structural approach to preventing injection drug use initiation: rationale for the PRIMER study. Harm Reduct J. 2016 Sep 15;13(1):25.
6. Werb D, Buxton J, Shoveller J, Richardson C, Rowell G, Wood E. Interventions to prevent the initiation of injection drug use: a systematic review. Drug Alcohol Depend. 2013;133(2):669–76.
7. United Nations Office on Drugs and Crime. World Drug Report 2016. New York: United Nations publication; 2016. [cited 2016 Nov 16]. Available from: https://www.unodc.org/doc/wdr2016/WORLD_DRUG_REPORT_2016_web.pdf.
8. Degenhardt L, Whiteford HA, Ferrari AJ, Baxter AJ, Charlson FJ, Hall WD, et al. Global burden of disease attributable to illicit drug use and dependence: findings from the Global Burden of Disease Study 2010. Lancet. 2013; 382(9904):1564–74.
9. Garfein RS, Vlahov D, Galai N, Doherty MC, Nelson KE. Viral infections in short-term injection drug users: the prevalence of the hepatitis C, hepatitis B, human immunodeficiency, and human T-lymphotropic viruses. Am J Public Health. 1996;86(5):655–61.
10. Scott N, Caulkins JP, Ritter A, Dietze P. How patterns of injecting drug use evolve in a cohort of people who inject drugs. Trends and Issues in Crime and Criminal Justice. 2015;502:1.
11. Grella CE. From generic to gender-responsive treatment: Changes in social policies, treatment services, and outcomes of women in substance abuse treatment. J Psychoactive Drugs. 2008 Nov 1;40(sup5):327–43.
12. Goldsamt LA, Harocopos A, Kobrak P, Jost JJ, Clatts MC. Circumstances, pedagogy and rationales for injection initiation among new drug injectors. J Community Health. 2010;35(3):258–67.
13. Small W, Fast D, Krusi A, Wood E, Kerr T. Social influences upon injection initiation among street-involved youth in Vancouver, Canada: a qualitative study. Substance Abuse Treatment, Prevention, and Policy. 2009;4(1):1.
14. Bryant J, Bryant J, Treloar C, Bryant J, Treloar C. The gendered context of initiation to injecting drug use: evidence for women as active initiates. Drug and alcohol review. 2007 Jan 1;26(3):287–93.
15. Doherty MC, Garfein RS, Monterroso E, Latkin C, Vlahov D. Gender differences in the initiation of injection drug use among young adults. J Urban Health. 2000;77(3):396–414.
16. Bluthenthal RN, Wenger L, Chu D, Quinn B, Thing J, Kral AH. Factors associated with initiating someone into illicit drug injection. Drug Alcohol Depend. 2014 Nov 1;144:186–92.
17. Bryant J, Treloar C. Initiators: An examination of young injecting drug users who initiate others to injecting. AIDS Behav. 2008 Nov 1;12(6):885–90.
18. Frajzyngier V, Neaigus A, Gyarmathy VA, Miller M, Friedman SR. Gender differences in injection risk behaviors at the first injection episode. Drug Alcohol Depend. 2007;89(2–3):145–52.
19. Greenfield SF, Brooks AJ, Gordon SM, Green CA, Kropp F, McHugh RK, Lincoln M, Hien D, Miele GM. Substance abuse treatment entry, retention, and outcome in women: A review of the literature. Drug Alcohol Depend. 2007 Jan 5;86(1):1–21.
20. Green CA, Polen MR, Dickinson DM, Lynch FL, Bennett MD. Gender differences in predictors of initiation, retention, and completion in an HMO-based substance abuse treatment program. J Subst Abus Treat. 2002 Dec 31;23(4):285–95.
21. Messina N, Grella CE, Cartier J, Torres SA. randomized experimental study of gender-responsive substance abuse treatment for women in prison. J Subst Abus Treat. 2010 Mar 31;38(2):97–107.
22. Jimenez-Treviño L, Saiz PA, García-Portilla MP, Díaz-Mesa EM, Sánchez-Lasheras F, Burón P, et al. A 25-year follow-up of patients admitted to methadone treatment for the first time: mortality and gender differences. Addict Behav. 2011;36(12):1184–90.
23. Marsh JC, Cao D, D'Aunno T. Gender differences in the impact of comprehensive services in substance abuse treatment. J Subst Abus Treat. 2004;27(4):289–300.
24. Haug NA, Sorensen J, Lollo N, Gruber V, Delucchi K, Hall S. Gender differences among HIV-positive methadone maintenance patients enrolled in a medication adherence trial. AIDS Care. 2005;17(8):1022–9.

Mittal *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:42

Page 5 of 5

25. Chatham LR, Hiller ML, Rowan-Szal GA, Joe GW, Simpson DD. Gender differences at admission and follow-up in a sample of methadone maintenance clients. Substance Use & Misuse. 1999;34(8):1137–65.
26. Wenger LD, Lopez AM, Kral AH, Bluthenthal RN. Moral ambivalence and the decision to initiate others into injection drug use: A qualitative study in two California cities. International Journal of Drug Policy. 2016 Nov 30;37:42–51.

RESEARCH　　　　　　　　　　　　　　　　　　　　　　　　　　　　　**Open Access**

CrossMark

Socioeconomic factors associated with cessation of injection drug use among street-involved youth

Derek C. Chang[1,2], Scott E. Hadland[3,4], Ekaterina Nosova[1], Evan Wood[1,5], Thomas Kerr[1,5] and Kora DeBeck[1,6*] ⓘD

Abstract

Background: Although the initiation of injection drug use has been well characterized among at-risk youth, factors that support or impede cessation of injection drug use have received less attention. We sought to identify socioeconomic factors associated with cessation of injection drug use among street-involved youth.

Methods: From September 2005 to May 2015, data were collected from the At-Risk Youth Study (ARYS), a prospective cohort study of street-involved youth in Vancouver, Canada. Multivariate extended Cox regression was utilized to identify socioeconomic factors associated with cessation of injection drug use for six months or longer among youth who were actively injecting.

Results: Among 383 participants, 171 (44.6%) youth reported having ceased injection (crude incidence density 22 per 100 person-years; 95% confidence interval [CI], 19–26) at some point during study follow-up. Youth who had recently dealt drugs (adjusted hazard ration [AHR], 0.50; 95% CI, 0.29–0.87), engaged in prohibited street-based income generation (AHR, 0.41; 95% CI, 0.24–0.69), and engaged in illegal income generating activities (AHR, 0.19; 95% CI, 0.06–0.61) were significantly less likely to report cessation of injection drug use.

Conclusions: Our findings suggest that socioeconomic factors, in particular engagement in prohibited street-based and illegal income generating activities, may pose barriers to ceasing injection drug use among this population. Effort to improve access to stable and secure income, as well as employment opportunities may assist youth in transitioning away from injection drug use.

Trial registration: Our study is not a randomized controlled trial; thus the trial registration is not applicable.

Keywords: Youth, Injection drug, Cessation, Prohibited street-based income generation, Illegal income generation, Drug dealing

Background

Youth who are street-involved, defined as being homeless or using services for homeless youth, experience excess morbidity and mortality relative to the general population of adolescents and young adults [1, 2]. Although injection drug use is recognized as a risky activity by street-involved youth [2], it remains prevalent among this population and is associated with many harms, including infection with human immunodeficiency virus (HIV) and hepatitis C virus (HCV), as well as fatal overdose [1, 3, 4].

Among adult populations of people who inject drugs, numerous factors have been associated with cessation of injection drug use including stable housing, use of supervised injection facilities and engagement with addiction treatment [5, 6]. Among youth populations, multiple studies on drug use trajectories focus on the initiation of injection drug use, and point to the role of unemployment, homelessness, and inability to access addiction treatment as contributing factors to injection initiation [7–9]. Two longitudinal studies drawing on data from 1995 to 2000 and 2000–2008 respectively, found that homelessness, unemployment, and incarceration were associated with a

* Correspondence: uhri-kd@cfenet.ubc.ca
[1]British Columbia Centre on Substance Use, British Columbia Centre for Excellence in HIV/AIDS, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, BC V6Z 1Y6, Canada
[6]Simon Fraser University, School of Public Policy, SFU Harbor Centre, 515 West Hastings Street, Suite 3271, Vancouver, BC V6B 5K3, Canada
Full list of author information is available at the end of the article

Chang *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:50

Page 2 of 7

lower likelihood of ceasing injecting among youth [10, 11]. Collectively, these findings suggest that economic vulnerability plays a role in drug use trajectories and may influence cessation of injection drug use. In an era of high rates of opioid overdose fatalities among young adults and adolescents who use drugs in North America [12, 13], updating the evidence base to better understand factors that influence drug use trajectories, specifically injection cessation, is particularly timely. Therefore, we sought to examine the potential relationship between socioeconomic factors and cessation of injection drug use among street-involved youth in Vancouver, Canada.

Methods

The At-Risk Youth Study (ARYS) is an ongoing prospective cohort study of street-involved youth in Vancouver, Canada. This study has been described in detail previously [14]. In brief, snowball sampling and street-based outreach as well as self-referral were used to recruit participants into the study. Persons between 14 and 26 years of age who had used illicit drugs other than or in addition to cannabis in the past 30 days and provided informed consent were eligible to participate. At baseline and semiannually thereafter, participants complete an interviewer-administered questionnaire. The questionnaire elicits sociodemographic data as well as information regarding participants' substance use and other behavioral and socioeconomic data such as housing, income sources, incarceration, and engagement with health and social services. All participants receive a monetary stipend of $30 (Canadian Dollar) after each interview. The University of British Columbia/Providence Health Care Research Ethics Board approved the study.

All participants who completed a baseline survey and were seen for study follow-up between September 2005 and May 2015 were eligible for the study. The present analysis was restricted to participants who reported active injection (i.e., those who reported any drug injection during the preceding six months, either at their baseline visit or at any follow-up visit) and who returned for at least one additional follow-up visit to assess for cessation of injection drug use. The primary outcome of interest was self-reported cessation of injection drug use during the preceding six months at any follow-up visit. Specifically, participants were asked, "In the last six months, have you used a needle to chip, fix, or muscle even once (yes vs. no)?"

Socioeconomic factors that we hypothesized might be associated with cessation of injection drug use included: homelessness; living with family; eviction from housing; living in the Downtown Eastside neighborhood (Vancouver's drug use epicenter); employment (having a regular, temporary, or self-employed work); loss of income assistance (being cut off or denied income assistance); health care access

(having been to a health care facility); incarceration (being in detention, prison or jail); sex work involvement (exchanging sex for money, gifts, or drugs); drug dealing; engaging in prohibited street-based income generating activities (panhandling, recycling, squeegeeing); and engaging in illegal income generating activities (theft, robbing, fraud, other illegal actives excluding sex work and drug dealing). All socioeconomic factors were time-updated measures based on activities or situations in the preceding six months time period. To protect against reverse causation whereby reported socioeconomic factors were a consequence of injection cessation, measures were taken from the study follow-up visit that preceded the visit at which a participant reported cessation of injection.

The following mental health related factors which we hypothesized might influence socioeconomic status were also considered: self-reported history of mental illness (defined as reporting having ever been diagnosed with a mental illness at study baseline); childhood physical or sexual abuse (defined as affirmative answers at study baseline to the question: "Have you ever been physically/sexually abused?"); and depression at study baseline (based on the Center for Epidemiologic Studies Depression Scale >22). Mental health related measures were not time-updated.

We also considered sociodemographic and drug-use related factors that we hypothesized, based on a review of the prior available literature, might potentially confound the relationship between socioeconomic factors and injection cessation [10, 11]. These factors included: age (per year older); gender (female vs. male); ethnicity (Caucasian vs. non-Caucasian); high school completion; any heroin use; any prescription opioid use; any crystal meth use; any cocaine use and any crack use. As with the time-updated socioeconomic factors, measures for the drug-use variables were also lagged to the prior study visit. This allowed us to account for behaviors during the six months preceding injection cessation to avoid issues related to reverse causation whereby measures were a consequence of injection cessation and not predictors of cessation.

As a first step, we compared sociodemographic characteristics and socioeconomic factors between those who did and did not cease injection drug use at any time during follow-up using Pearson's chi-squared test and Fisher's exact test (for cell counts under 5) for categorical variables and the Wilcoxon test for continuous variables. Participants were right-censored at the time of their first cessation event (i.e., no further person-time at risk was contributed by that participant), but if they reported resuming injection drug use at a later visit, they reentered the cohort of individuals at risk; participants who did not report any cessation were right-censored at the time of their last follow-up visit. We also used an extended Cox proportional hazards regression model with time-updated variables to examine bivariate

Chang *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:50

Page 3 of 7

associations between each of the sociodemographic and socioeconomic factors, and time to cessation of injection drug use. The extended Cox model has been validated [15] and widely used in previous studies [7, 16, 17]. The inclusion of time-updated covariates in an extended Cox model negates the requirement of the proportional hazards assumption [15]. Variables significant at $p < 0.10$ in bivariate analyses were eligible for inclusion in the final multivariate model, which used backward selection to identify the model with the best fit based on minimizing the Akaike Information Criterion (AIC). To help determine if our results were robust, we also ran a fixed multivariate model where all variables of interest were forced into a single model. In addition, multicollinearity was assessed in two ways. First, we assessed for multicollinearity at baseline using "ever ceased using drugs" as an outcome. We then applied variance inflation factors directly to the multivariable Cox model and used "injection drug use cessation" as an outcome. Analyses were performed using R version 3.2.4 (R Foundation for Statistical Computing, Vienna, Austria). All p values were two-sided and tests were considered significant at $p < 0.05$.

Results

Overall, among 383 actively drug-injecting youth who returned for follow-up, the median age was 22 (interquartile range [IQR] 21–24) year, 248 (64.8%) were male and 276 (72.1%) were white. An additional 151 youth reported injection drug use at study enrollment but did not return or were not yet eligible to return for a study visit due to the nature of an open cohort study. The 383 youth who completed a study follow-up visit were similar to the 151 who did not with regard to all study variables at baseline ($p > 0.05$ for all), with the exception that individuals who did not complete a study follow-up visit were more likely to have begun using drugs at a younger age and inject cocaine. Participants contributed 765 person-years of total follow-up with a median of 19 months (IQR, 10–31) of follow-up per participant and a median of 3 (IQR, 2–5) study visits per participant. Based on the follow-up data, 171 (44.6%) youth reported cessation of injection drug use, resulting in a crude incidence density of 22 per 100 person-years (95% confidence interval [CI], 19–26 per 100 person-years).

Table 1 lists sociodemographic characteristics, drug use, mental health, and socioeconomic factors at baseline, stratified by injection cessation at any point during study follow-up. Youth did not differ according to sociodemographic and mental health characteristics at baseline. However, those who ceased injection over study follow-up were significantly more likely to have recently used heroin, prescription opioids, and accessed health care at baseline.

Table 2 displays unadjusted and adjusted hazard ratios for cessation of injection drug use and variables of interest.

Adjusted models demonstrate that youth who had recently dealt drugs (AHR, 0.50; 95% CI, 0.29–0.87), engaged in prohibited street-based income generation (AHR, 0.41; 95% CI, 0.24–0.69), engaged in illegal income generating activities (AHR, 0.19; 95% CI, 0.06–0.61), or used heroin (AHR, 0.55; 95% CI, 0.34–0.87), were significantly less likely to report cessation of injection drug use. The results of the fixed multivariate model were all similar (data not shown) and no multicollinearity was detected based on aforementioned assessment.

Discussion

In this prospective cohort of street-involved youth who inject drugs, 44% of the participants reported having ceased injection drug use at some point during the study period. We found that recent engagement in drug dealing, prohibited street-based, and other illegal income generating activities may pose barriers to injection cessation among youth in our setting.

Our findings build on two previous studies of cessation of injection drug use among street-involved youth conducted by Steensma et al. in Montreal between 1995 and 2000 [10] and Evan et al. in San Francisco between 2000 and 2008 [11]. Similar to our study, both drew on data from a prospective cohort of young people who use illicit drugs. These studies found that homelessness, employment, and history of incarceration were negatively associated with cessation of injection drug use among street-involved youth. Although these specific variables were not found to be associated with injection cessation among our study sample, we did find that other markers of economic vulnerability, namely that generating income through unstable risky income sources correlated negatively with injection drug cessation.

Previous studies have demonstrated that street-involved youth are economically vulnerable and often resort to risky income generating activities including drug dealing (58%) and other prohibited and illegal street-based income sources (82%) [18, 19]. Youth who engaged in risky income generating activities are known to be at increased risk for homelessness, high intensity drug use, encounter with police, and violence [18]. Engaging in drug dealing is also known to be associated with markers of economic and social vulnerability including homelessness, crack cocaine use, and police violence [19].

Our study contributes to the understanding that stable and safe income sources are critical for the health and well-being of street-involved youth [18, 20, 21]. In particular, our findings suggest that stable income support could facilitate cessation of injection drug use in this population. This is consistent with the concept of "recovery capital" [22], which highlights the importance of internal and external resources to achieve and sustain cessation from risky substance use. Similarly, integrating

Chang *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:50

Page 4 of 7

Table 1 Baseline characteristics[a] of street youth who inject drugs stratified by whether they ceased injection at any point during study follow-up: At Risk Youth Study (ARYS), Vancouver, British Columbia, 2005–2015 (n = 383)

	Ceased Injection Drug Use[b]		
	Yes (%) (n = 171)	No (%) (n = 212)	p Value
Sociodemographic characteristics			
Median age, years (IQR)	22 (20–24)	22 (21–24)	0.769
Gender			
Male	103 (60.2)	144 (67.9)	0.118
Female	68 (39.8)	68 (32.1)	
Ethnicity			
Caucasian	126 (73.7)	150 (70.8)	0.573
Non-Caucasian	45 (26.3)	61 (28.8)	
High school education[c]			
Yes	59 (34.5)	62 (29.3)	0.281
No	111 (64.9)	148 (69.8)	
Drug use related factors			
Any heroin use			
Yes	114 (66.7)	175 (82.5)	<0.001
No	57 (33.3)	37 (17.5)	
Any prescription opioid use			
Yes	55 (32.2)	97 (45.8)	0.007
No	116 (67.8)	115 (54.2)	
Any crystal meth use			
Yes	116 (67.8)	162 (76.4)	0.061
No	55 (32.2)	50 (23.6)	
Any cocaine use			
Yes	78 (45.6)	97 (45.8)	0.978
No	93 (54.4)	115 (54.2)	
Any crack use			
Yes	113 (66.1)	131 (61.8)	0.385
No	58 (33.9)	81 (38.2)	
Mental health related factors			
Mental illness history			
Yes	104 (60.8)	138 (65.1)	0.388
No	67 (39.2)	74 (34.9)	
Childhood physical or sexual abuse			
Yes	116 (67.8)	142 (67.0)	0.933
No	45 (26.3)	54 (25.5)	
Depression			
Yes	75 (43.9)	105 (49.5)	0.057
No	53 (31)	46 (21.7)	
Socioeconomic factors			
Homeless			
Yes	121 (70.8)	160 (75.5)	0.305
No	49 (28.7)	51 (24.1)	

Table 1 Baseline characteristics[a] of street youth who inject drugs stratified by whether they ceased injection at any point during study follow-up: At Risk Youth Study (ARYS), Vancouver, British Columbia, 2005–2015 (n = 383) *(Continued)*

	Ceased Injection Drug Use[b]		
	Yes (%) (n = 171)	No (%) (n = 212)	p Value
Living with family			
Yes	20 (11.7)	26 (12.3)	0.865
No	151 (88.3)	186 (87.7)	
Evicted			
Yes	18 (10.5)	25 (11.8)	0.664
No	82 (48.0)	132 (62.3)	
Living in the Downtown Eastside			
Yes	64 (37.4)	82 (38.7)	0.802
No	107 (62.6)	130 (61.3)	
Employed			
Yes	62 (36.3)	93 (43.9)	0.131
No	109 (63.7)	119 (56.1)	
Loss of income assistance			
Yes	13 (7.6)	18 (8.5)	0.899
No	108 (63.2)	157 (74.1)	
Accessed health care			
Yes	133 (77.8)	166 (78.3)	0.045
No	38 (22.2)	46 (21.7)	
Incarcerated			
Yes	35 (20.5)	46 (21.7)	0.792
No	135 (78.9)	166 (78.3)	
Sex work			
Yes	27 (15.8)	31 (14.6)	0.751
No	144 (84.2)	181 (85.4)	
Dealt drugs			
Yes	86 (50.3)	108 (50.9)	0.899
No	85 (49.7)	104 (49.1)	
Prohibited street-based income generating activities[d]			
Yes	54 (31.6)	82 (38.7)	0.149
No	117 (68.4)	130 (61.3)	
Illegal income generating activities[e]			
Yes	40 (23.4)	54 (25.5)	0.638
No	131 (76.6)	158 (74.5)	

[a]Characteristics reported at time of study enrollment
[b]Cells do not uniformly add up to column total due to missing values
[c]Prior completion of or current enrollment in high school
[d]Prohibited street-based income generating activities included panhandling, recycling, and squeegeeing
[e]Illegal income generating activities included theft, robbing, fraud, and other illegal actives excluding sex work and drug dealing

youth into their communities is important for increasing their social capital and prospects for economic security [23]. Nonetheless, lack of meaningful employment and labor market exclusion still exist as barriers to employment for this population [18]. Previous studies have

Chang et al. Substance Abuse Treatment, Prevention, and Policy (2017) 12:50

Page 5 of 7

Table 2 Unadjusted and adjusted hazard ratios (HR) for factors associated with cessation of injection drug use among street youth who inject drugs: At-Risk Youth Study (ARYS), Vancouver, British Columbia, 2005–2015 (n = 383)

	Unadjusted HR (95% CI)	Adjusted HR (95% CI)[a]	p Value[e]
Sociodemographic characteristics			
Age (per year older)	1.00 (0.99–1.01)		
Female Gender	1.01 (0.73–1.40)		
Caucasian Ethnicity	1.09 (0.75–1.60)		
High school education[b]	1.10 (0.79–1.54)		
Drug use related factors			
Any heroin use[c]	0.58 (0.42–0.81)	0.55 (0.34–0.87)	0.010
Any prescription opioid use[c]	0.75 (0.56–1.02)		
Any crystal meth use[c]	0.64 (0.47–0.88)	0.65 (0.42–1.01)	0.054
Any cocaine use[c]	1.16 (0.86–1.56)		
Any crack use[c]	1.08 (0.79–1.47)		
Mental health related factors			
Mental illness history	1.07 (0.76–1.54)		
Childhood physical or sexual abuse[d]	0.82 (0.56–1.18)		
Depression[d]	0.64 (0.43–0.93)	0.64 (0.41–1.01)	0.053
Socioeconomic factors			
Homeless[d]	0.68 (0.51–0.90)	1.25 (0.86–1.83)	0.246
Living with family[d]	1.76 (1.22–2.55)	1.21 (0.73–2.02)	0.459
Evicted[d]	0.44 (0.22–0.89)	0.59 (0.29–1.21)	0.152
Living in the Downtown Eastside[d]	0.58 (0.42–0.82)	0.67 (0.42–1.06)	0.085
Employed[d]	1.49 (1.11–2.01)		
Loss of income assistance[d]	0.54 (0.25–1.16)		
Accessed health care[d]	1.11 (0.81–1.54)		
Incarcerated[d]	0.57 (0.37–0.88)	0.83 (0.46–1.51)	0.546
Sex work[d]	0.40 (0.23–0.72)	0.62 (0.29–1.33)	0.221
Dealt drugs[d]	0.37 (0.25–0.56)	0.50 (0.29–0.87)	0.015
Prohibited street-based income generating activities[d,f]	0.50 (0.34–0.72)	0.41 (0.24–0.69)	0.001
Illegal income generating activities[d,g]	0.25 (0.13–0.50)	0.19 (0.06–0.61)	0.005

[a]Variables significant at p < 0.10 in bivariate models were eligible for possible inclusion in the multivariate model (extended Cox proportional hazards regression model); variables included in the final multivariate model were identified using a backward selection approach to minimize the Akaike Information Criterion (AIC)
[b]Denotes completion of or current enrollment in high school
[c]Includes both non-injection and injection use; drug use behaviors were lagged by one visit in order to assess behaviors during the 6 months when participants who ceased were still injecting
[d]Reported for the 6 months prior to the last follow-up visit at which a participant was still injecting
[e]P-values refer to adjusted HR
[f]Prohibited street-based income generating activities included panhandling, recycling, and squeegeeing
[g]Illegal income generating activities included theft, robbing, fraud, and other illegal actives excluding sex work and drug dealing

pointed to the need for targeted interventions to increase income security among street-involved youth. Proposed interventions include restructuring income assistance, providing low-threshold employment, and reducing barriers to traditional employment by addressing stigma and other harms of criminalization [18, 20, 24, 25]. The potential for these types of interventions to support injection cessation warrants further exploration.

There are several limitations to this study. First, the ARYS cohort is not a random sample. Our snowball sampling methods may have reduced heterogeneity and validity of the findings, although it is noteworthy that the characteristics of the ARYS sample are similar to those from other cohorts of street-involved youth [10, 11]. Another potential limitation of our sample is that participants who were lost to follow-up were more likely to have

Chang *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:50

Page 6 of 7

begun using drugs at an earlier age and more likely to report injecting cocaine. Both these characteristics are associated with higher risk activities [26] and therefore our study may overestimate the true occurrence of injection cessation among street-involved youth. Other potential limitations relate to the reliance on self-report for key measures of interest. Self-report may be affected by socially desirable responding and recall bias. The potential impacts could result to an over or under estimation of our outcome of interest though, overall, we expect the impacts to bias the results towards the null. Lastly, as with all observation studies, despite extensive adjustment for potential confounding, the independent associations that we observed could be influenced by other factors that we are unable to adjust for.

Conclusions

In sum, our study suggests that economic vulnerability characterized by resorting to risky income generation strategies including drug dealing, prohibited street-based and other illegal activities, may pose barriers for street-involved youth to cease injection drug use. These findings underscore the potential for social interventions that provide stable and secured income sources to influence drug use trajectories and reduce drug related harm. Further study in this area is warranted.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions
SH, EW, TK and KD designed the study. DC conducted the literature review and wrote the first draft of the manuscript. DC and KD revised the subsequent drafts of the manuscript with consultations from SH, EW, and TK. KN undertook data management and statistical analyses. All authors read and approved the final manuscript.

Ethics approval and consent to participate
The University of British Columbia/Providence Health Care Research Ethics Board approved the study and consent to participate was obtained from each participant.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Publisher's Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details
[1]British Columbia Centre on Substance Use, British Columbia Centre for Excellence in HIV/AIDS, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, BC V6Z 1Y6, Canada. [2]Department of Family Medicine, University of British Columbia, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, BC V6Z 1Y6, Canada. [3]Grayken Center for Addiction / Department of Pediatrics, Boston Medical Center, One Boston Medical Center Place, Boston, MA 02118, USA. [4]Division of General Pediatrics, Department of Pediatrics, Boston University School of Medicine, 88 East Newton St., Vose Hall, Room 322, Boston, MA 02118, USA. [5]Department of Medicine, University of British Columbia, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, BC V6Z 1Y6, Canada. [6]Simon Fraser University, School of Public Policy, SFU Harbor Centre, 515 West Hastings Street, Suite 3271, Vancouver, BC V6B 5K3, Canada.

References
1. Boivin JF, Roy E, Haley N, Galbaud du Fort G. The health of street youth: a Canadian perspective. Can J Public Health. 2005;96:432–7.
2. Small W, Fast D, Krusi A, Wood E, Kerr T. Social influences upon injection initiation among street-involved youth in Vancouver, Canada: a qualitative study. Subst Abuse Treat Prev Policy. 2009;4:8.
3. Kerr T, Marshall BD, Miller C, Shannon K, Zhang R, Montaner JS, Wood E. Injection drug use among street-involved youth in a Canadian setting. BMC Public Health. 2009;9:171.
4. Roy E, Haley N, Leclerc P, Sochanski B, Boudreau JF, Boivin JF. Mortality in a cohort of street youth in Montreal. JAMA. 2004;292:569–74.
5. Shah NG, Galai N, Celentano DD, Vlahov D, Strathdee SA. Longitudinal predictors of injection cessation and subsequent relapse among a cohort of injection drug users in Baltimore, MD, 1988-2000. Drug Alcohol Depend. 2006;83:147–56.
6. DeBeck K, Kerr T, Bird L, Zhang R, Marsh D, Tyndall M, Montaner J, Wood E. Injection drug use cessation and use of North America's first medically supervised safer injecting facility. Drug Alcohol Depend. 2011;113:172–6.
7. DeBeck K, Kerr T, Nolan S, Dong H, Montaner J, Wood E. Inability to access addiction treatment predicts injection initiation among street-involved youth in a Canadian setting. Subst Abuse Treat Prev Policy. 2016;11:1.
8. Richardson L, DeBeck K, Feng C, Kerr T, Wood E. Employment and risk of injection drug use initiation among street involved youth in Canadian setting. Prev Med. 2014;66:56–9.
9. Feng C, DeBeck K, Kerr T, Mathias S, Montaner J, Wood E. Homelessness independently predicts injection drug use initiation among street-involved youth in a Canadian setting. J Adolesc Health. 2013;52:499–501.
10. Steensma C, Boivin JF, Blais L, Roy E. Cessation of injecting drug use among street-based youth. J Urban Health. 2005;82:622–37.
11. Evans JL, Hahn JA, Lum PJ, Stein ES, Page K. Predictors of injection drug use cessation and relapse in a prospective cohort of young injection drug users in San Francisco, CA (UFO study). Drug Alcohol Depend. 2009;101:152–7.
12. Rudd RA, Seth P, David F, Scholl L. Increases in drug and opioid-involved overdose deaths - United States, 2010-2015. MMWR Morb Mortal Wkly Rep. 2016;65:1445–52.
13. Riley ED, Evans JL, Hahn JA, Briceno A, Davidson PJ, Lum PJ, Page KA. Longitudinal study of multiple drug use and overdose among young people who inject drugs. Am J Public Health. 2016;106:915–7.
14. Wood E, Stoltz JA, Montaner JS, Kerr T. Evaluating methamphetamine use and risks of injection initiation among street youth: the ARYS study. Harm Reduct J. 2006;3:18.
15. Kleinbaum DG, Klein M. Survival analysis: a self-learning text. 3rd ed. New York: Springer-Verlag; 2012.

Chang *et al. Substance Abuse Treatment, Prevention, and Policy* (2017) 12:50

Page 7 of 7

16. Hepburn K, Barker B, Nguyen P, Dong H, Wood E, Kerr T, DeBeck K. Initiation of drug dealing among a prospective cohort of street-involved youth. Am J Drug Alcohol Abuse. 2016;42:507–12.

17. Hoy C, Barker B, Regan J, Dong H, Richardson L, Kerr T, DeBeck K. Elevated risk of incarceration among street-involved youth who initiate drug dealing. Harm Reduct J. 2016;13:32.

18. Cheng T, Kerr T, Small W, Nguyen P, Wood E, DeBeck K. High prevalence of risky income generation among street-involved youth in a Canadian setting. Int J Drug Policy. 2016;28:91–7.

19. Werb D, Kerr T, Li K, Montaner J, Wood E. Risks surrounding drug trade involvement among street-involved youth. Am J Drug Alcohol Abuse. 2008; 34:810–20.

20. DeBeck K, Shannon K, Wood E, Li K, Montaner J, Kerr T. Income generating activities of people who inject drugs. Drug Alcohol Depend. 2007;91:50–6.

21. Pauly BB, Reist D, Belle-Isle L, Schactman C. Housing and harm reduction: what is the role of harm reduction in addressing homelessness? Int J Drug Policy. 2013;24:284–90.

22. Cloud W, Granfield R. Conceptualizing recovery capital: expansion of a theoretical construct. Subst Use Misuse. 2008;43:1971–86.

23. Barman-Adhikari A, Rice E. Social networks as the context for understanding employment services utilization among homeless youth. Eval Program Plann. 2014;45:90–101.

24. Debeck K, Wood E, Qi J, Fu E, McArthur D, Montaner J, Kerr T. Interest in low-threshold employment among people who inject illicit drugs: implications for street disorder. Int J Drug Policy. 2011;22:376–84.

25. Richardson L, Wood E, Li K, Kerr T. Factors associated with employment among a cohort of injection drug users. Drug Alcohol Rev. 2010;29:293–300.

26. Debeck K, Kerr T, Marshall BD, Simo A, Montaner J, Wood E. Risk factors for progression to regular injection drug use among street-involved youth in a Canadian setting. Drug Alcohol Depend. 2013;133:468–72.