Published in final edited form as:
Am J Drug Alcohol Abuse. 2015 January ; 41(1): 100–106. doi:10.3109/00952990.2014.940424.

Prescription Opioid Misuse and Mental Health Among Young Injection Drug Users

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Abstract

Background—Prescription opioid (PO) misuse is a significant concern in the United States.

Objectives—This study describes the prevalence and timing of PO misuse, diagnoses of opiate abuse and dependence, and their associations with psychiatric disorders in a sample of young people who inject drugs (PWID).

Methods—Participants were 570 young (18–25 years) PWID, primarily heroin users, recruited through outreach and respondent-driven sampling. Trained interviewers administered a semi-structured psychiatric interview. Diagnoses of substance use and mental disorders were based on DSM-IV diagnostic criteria.

Results—Estimated rates of lifetime PO abuse and dependence were 19% and 17% respectively. Past year PO misuse was significantly associated with anti-social personality disorder (ASPD, OR = 2.15, 95% CI 1.43–3.24), past year substance-induced major depression (SIMD, OR = 1.81, 95% CI 1.16–2.83), and prior post-traumatic stress disorder (PTSD, OR = 2.45, 95% CI 1.31–4.60). Among male PO users, PTSD was a significant predictor of PO abuse (prior, OR = 7.62, 95% CI 2.16–26.88; past year, OR = 21.67 95% CI 2.46–190.75), and dependence (prior, OR = 4.82, 95% CI 1.48–15.67; past year, OR = 9.65, 95% CI 1.75–53.32).

Conclusion—Among young PWID, PTSD is a significant risk factor for PO misuse for both men and women, and men with PTSD are in addition at increased risk for PO abuse and dependence. These findings have implications for harm reduction and substance abuse prevention efforts.

1. Introduction

The misuse of prescription drugs, particularly opioid pain relievers such as hydrocodone and oxycodone, has increased significantly in the U.S. over the past two decades (1, 2). The public health impact of this trend includes increases in emergency department visits due to misuse or abuse of opioid pain relievers (3), overdose mortality (4–6), and need for substance abuse treatment (7–9). In addition, there has been a good deal of concern that misuse of and consequent dependence on opioid drugs by young people has contributed to

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rising rates of heroin use and injection drug use (10–15), particularly among White suburban residents (16).

Non-medical use of opioid drugs among PWID is common (17, 18). Heroin injectors may use prescription opioids for various reasons, including management of withdrawal symptoms, as a substitute when heroin is not available, or to curb heroin use for other reasons (19). Combining prescription opioid use with heroin to boost its effect, a practice linked to decreased purity or increased tolerance, produces a significant risk for overdose.

Many factors influence substance misuse (20, 21), including mental health problems. Prescription medications in particular may be subject to misuse by self-medication of aversive emotional states (22, 23). Whether mental health problems might differentiate between heroin users who also use prescription opioids and those who do not has not been studied. This association would have implications for both mental health services and addiction treatment and point to differential intervention targets. Providers treating heroin dependence should be aware of the potential psychiatric co-morbidities associated with a history of prescription opioid abuse and dependence in this population. Young people who initiate PO use as a response to a mental health condition and then take up heroin use will have different treatment needs than those who initiate opioid use for other reasons (e.g. sensation-seeking).

Clinical disorders (DSM-IV Axis I)

A number of cross-sectional studies have reported associations between mood and anxiety disorders and PO misuse and disorders (24–31). Using longitudinal data from the National Epidemiological Survey on Alcohol and Related Conditions (NESARC), Martins, et al. (32) found that baseline lifetime PO use was associated with incident major depressive disorder (MDD), bipolar disorder, and generalized anxiety disorder (GAD). In addition, baseline lifetime mood disorders and GAD were associated with incident PO use, while baseline MDD, dysthymia, and panic disorder were associated with incident PO disorder. Schepis and Hakes (33) also found that the risk of incident anxiety disorders was greater among respondents with baseline PO use. The evidence supports multiple pathways between PO misuse, abuse, and dependence and affective disorders, including precipitation of depression and anxiety disorders from PO misuse, self-medication of mental health symptoms by PO misuse, and shared vulnerability for psychiatric and substance use disorders.

Prescription drug misuse (including PO misuse and misuse of other prescription medications) has been linked to exposure to traumatic events and post-traumatic stress disorder (PTSD) (34–36). In contrast to the studies cited above, evidence suggests that PTSD usually precedes substance use disorder onset, and there is little evidence that prior substance use disorder increases the risk of PTSD (37, 38). However, continued substance use may aggravate PTSD symptoms.

Personality disorders (DSM-IV Axis II)

Although specific associations between PO misuse and personality disorders have not been studied, there are reasons to expect such associations, and it would be important to control for these effects when evaluating associations between PO use disorders and clinical (Axis I)

disorders. Anti-social personality disorder (ASPD) is characterized by a long-term pattern of disregard for other people's rights and feelings, and manipulative, exploitative and irresponsible behavior, with evidence of possible conduct disorder beginning in childhood or early adolescence (before age 15). Prescription drug misuse is associated with delinquent behavior among adolescents (34, 39, 40), although perhaps no more so than other illicit drug use (41). One study (42) found that PO use predicted violent behavior (e.g. fighting, assault) above the effect of other illicit drugs. These findings lead us to expect an association between ASPD and PO misuse, but not necessarily abuse or dependence.

Differences in coping and emotion regulation strategies also may help explain different patterns of prescription and illicit drug misuse (43). As borderline personality disorder (BPD) is characterized by deficits in emotion regulation, individuals with BPD may exhibit more problematic patterns of PO misuse, i.e. abuse and dependence (cf. 43).

The current study analyzes data from a study on the mental health of young PWID. We estimate the prevalence of prescription opioid (PO) drug misuse and DSM-IV diagnoses of "other opiate" abuse and dependence, describe the relative timing of heroin and PO misuse, and examine the relationship between PO misuse, abuse, and dependence and major depressive disorders (MDD), post-traumatic stress disorder (PTSD) and other anxiety disorders, borderline personality disorder (BPD), and anti-social personality disorder (ASPD). We also investigate the relative age of onset of PO versus affective disorders as evidence for precipitation or self-medication. Based on the previous research findings described above, we expected to find associations between PO misuse, abuse and dependence, and affective disorders (MDD, PTSD, and other anxiety disorders). We also expected to find ASPD to be associated with PO misuse, and individuals with BPD to exhibit more problematic patterns of PO misuse, i.e. abuse and dependence.

2. Methods

Details of the study procedures have been described previously (44, 45). All study procedures were approved by the Institutional Review Board of the University of Illinois at Chicago. The study was conducted at two field sites of the Community Outreach Intervention Projects in West and Northwest Side neighborhoods in Chicago. These sites provide a variety of services including HIV and hepatitis (HBV, HCV) counseling and testing, substance abuse treatment referrals, and needle exchange. The neighborhood populations are largely Black and Latino, however young White suburban drug users come to these neighborhoods to buy drugs.

2.1. Sample recruitment

Participants were eligible for the study if they had injected drugs at least once in the past 30 days, and were age 18 to 25. Current injection was verified by trained counselors who inspected for injection stigmata, and age was verified with a driver's license or state identification card. Study participants were recruited using outreach and respondent driven sampling (RDS) methods (46, 47). Initial participants were recruited by outreach workers at the two field sites. After completing their interview, these early participants were given up to four coupons to recruit other young PWID, serving as "seeds" for the RDS chains.

Participants received compensation of $15–$20 for each coupon that was brought in by a person eligible to participate in the study. Participants who distributed coupons had to return to the field site to receive compensation, and were paid $10–$15 for the coupon review session, independent of compensation for coupons redeemed. Those who successfully recruited eligible potential participants were given up to four additional coupons at this time. Lost coupons were replaced upon request, and the original coupons voided. Because recruitment chains tended to be short and many recruiters were not productive, outreach workers also continued to recruit participants directly throughout the study. Forty percent of enrolled participants were recruited through outreach.

2.2. Procedures

After screening for eligibility and completing informed consent procedures, participants completed a brief computer-based questionnaire to capture information related to RDS, including the size and composition of their injection drug-using network and the nature of their relationship with their recruiter. Participants then completed an audio computer-assisted self-interview (ACASI) to assess socio-demographic and family background, drug use, injection risk behavior, sexual risk behavior, recent mental health and substance use treatment service use, HIV and hepatitis testing, HIV/hepatitis knowledge, attitudes regarding and subjective norms for HIV risk behavior, and self-efficacy for sex- and injection-related HIV risk reduction behaviors.

Following the ACASI, a trained interviewer administered the Psychiatric Research Interview for Substance and Mental Disorders (PRISM, version 6) (48, 49). On request, or if no interviewer was immediately available, participants were allowed to make an appointment to return for the PRISM interview. Forty participants did not complete a PRISM interview due to scheduling difficulties or failure to return for an appointment. PRISM non-completers were older than PRISM completers (23 vs. 22, t (df 608) = 2.44, p = .015), but did not differ on gender, race/ethnicity, residence, employment, homelessness, or injection frequency. The average time to administer the PRISM was 78 minutes; 92% of interviews were completed within 2 hours. Participant compensation was initially set at $50 and was later increased to $75 due to the demanding nature of the PRISM interview.

2.3. Measures

The PRISM is a semi-structured clinical interview that provides diagnoses based on DSM-IV criteria, and is specifically designed to differentiate between the expected effects of intoxication and withdrawal, and between primary (independent) and substance-induced psychiatric disorders (49–51). For Axis I substance use and psychiatric disorders, diagnoses were made using two time frames: “past year” (criteria were met within the past 12 months) and “prior” (criteria were met prior to the past 12 months). Axis II personality disorders (ASDP, BPD) are diagnosed as lifetime disorders. In the present study, we estimated the prevalence of past year and prior PO misuse (used at least six times in a year), any “problem use” (either the PRISM’s “chronic intoxication” or ever “binge use,” defined as using at least 4 days per week for a month, or as using most of the day for three days straight, respectively), and DSM-IV past year and prior PO abuse and dependence. In the PRISM, misuse is the criteria used as a threshold for further questioning; respondents who do not

meet this minimum threshold are not administered the sections on abuse and dependence for that substance. We examined associations with anti-social personality disorder (ASPD), borderline personality disorder (BPD), and past year and prior post-traumatic stress disorder (PTSD), other anxiety disorders (generalized anxiety disorder, panic disorder, agoraphobia, social phobia, specific phobia), primary major depression (PMD), and substance-induced major depression (SIMD).

2.4. Statistical Analysis

Analyses were conducted in Stata, version 12 (52). RDS analyses were conducted using the user-written -*rds*- program for Stata (53). We computed individualized weights for the outcomes, estimated the population proportions, and computed bootstrap (reps = 500) percentile confidence intervals for the estimated proportions. Weighted and unweighted multivariate regression analyses were conducted on past 12-month PO misuse (used at least six times) and DSM-IV defined past year abuse and dependence with ASPD, BPD, past year and prior PTSD, PMD, and SIMD, and demographic covariates. There was significant co-morbidity between BPD and Axis I disorders (PMD, SIMD, PTSD, other anxiety disorders), between ASPD and PTSD, and between ASPD and BPD. Analyses were performed in a stepwise manner, with demographic variables entered first (step 1), followed by personality disorders (step 2), then prior or past year Axis I disorders (step 3). In this way, we assess the effects of personality disorders controlling for demographic covariates, and we assess the effects of Axis I disorders while controlling for demographic variables and Axis II disorders. Personality disorder variables were entered simultaneously, while Axis I disorders were entered individually. The same analyses were repeated on abuse and dependence on the sub-sample of lifetime PO users (used at least 6 times in past year or in a 12 month period prior to past year). Effects were considered significant with $p < .01$. Interactions with sex were tested and retained if $p < 0.10$.

3. Results

The sample (N = 570) was recruited between June 2008 and August 2010 and included 353 men and 217 women, ages 18 to 25 (Mean 22.2, SD 2.1). Most participants were non-Hispanic White (77%), 14% were Hispanic, and 8% were non-Hispanic Black or other race. The majority resided outside the city of Chicago (72%) and most were unemployed (65%), although 70% reported some income in the past six months from a regular or temporary job. Twenty-six percent reported ever being hospitalized for a medical problem.

Nearly all participants (99%) injected heroin by itself (96%) or with cocaine (13%) in the past six months. Sample rates of PO misuse, problem use, and DSM-IV abuse and dependence, along with population estimates with bootstrap percentile-based confidence intervals are shown in Table 1. There were moderate differences ($p < .05$) by sex on sample prevalence of past year PO abuse (14% of men, 22% of women) and lifetime PO dependence (20% of men, 27% of women). Individuals who used PO were more likely to recruit other individuals who used these drugs (for current year use, homophily = 0.25). They also tended to have larger injecting networks, with an average of 8.5 network

connections vs. 6.6 for non-PO users. Consequently, they had a greater chance of being selected into the sample. RDS estimates correct for this oversampling.

While about half of the study participants (n = 288) reported ever using PO at least six times in a year, the estimated population proportion correcting for recruitment bias was 0.36. One-third of respondents (n = 187) reported problem use of PO. PO abuse was usually but not always accompanied by dependence – 77% of past year and 70% of prior PO abuse cases also were diagnosed with dependence in the same time frame. PO dependence usually entailed abuse, with 84% of past year and 87% of prior PO dependence cases reporting abuse in the same time frame. Among participants who reported any PO problem use, abuse or dependence, 60% (n = 127) reported a younger age of PO misuse than heroin misuse, 20% (n = 43) reported that these occurred at the same age, and 19% (n = 40) reported that misuse of heroin occurred earlier.

The results of the regression analyses are shown in Table 2. The results of weighted analyses were similar to those of unweighted analyses, therefore unweighted analyses are reported. Past year PO misuse (used at least six times in a year) was associated with younger age ($p = .008$), hospitalization for a medical problem ($p < .001$), and ASPD ($p < .001$). While controlling for personality disorders, past year PO misuse was associated with past year SIMD ($p = .009$) and prior PTSD ($p = .005$). Past year PO misuse was not significantly associated with past year or prior other anxiety disorders, or prior depression.

Past year PO abuse was significantly associated with younger age ($p = .003$) and hospitalization ($p < .001$). Interactions between sex and prior PTSD ($p = .017$) and past year PTSD ($p = .034$) indicated significant associations for men on these disorders (past year, $p = .003$; prior, $p<.001$), but not for women. Past year PO dependence was associated with hospitalization ($p < .001$), prior PTSD ($p = .001$), and past year PTSD ($p = .004$). No interactions with sex reached the level of inclusion ($p < .10$).

Although age of initial PO misuse was not collected in the interview, age of initial PO problem use, and onset of abuse or dependence were recorded. Among individuals meeting criteria for PTSD and reporting PO problem use, or abuse or dependence (n = 36), PTSD onset occurred earlier than initial PO problem use or abuse in 61% of cases. The median age of initial PO problem use or abuse was 16 (range 12 – 22), and the median age of PTSD onset was 14.5 (range 3 – 24). Among individuals meeting criteria for SIMD and reporting PO problem use, abuse or dependence (n = 77), PO problem use or abuse occurred earlier than SIMD onset in 64% of cases. The median age of initial PO problem use or abuse was 17 (range 13 – 23), and the median age of SIMD onset was 18 (range 12 – 25).

When analyses were restricted to people who reported PO misuse ever (n = 288), interactions between sex and PTSD on PO abuse again indicated significant effects for men but not for women. Men with prior PTSD had a more than 7-fold greater likelihood (OR = 7.62, 95% CI 2.16 – 26.88, $p = .002$), and those with past year PTSD had a more than 21-fold greater likelihood of PO abuse (OR = 21.67, 95% CI 2.46 – 190.75, $p = .006$). Among PO users, the marginal probability of past year PO abuse among men with past year PTSD was 0.86 compared to 0.26 among those without past year PTSD. In this sub-sample, past

year PO dependence was marginally associated with prior SIMD (OR=2.26, 95% CI 1.17–4.37, p = .016). Interactions between PTSD and sex (p < .10) indicated that among men only, past year PO dependence was associated with prior PTSD (OR = 4.82, 95% CI 1.48 – 15.67, p = .009) and past year PTSD (OR = 9.65, 95% CI 1.75 – 53.32, p = .009).

4. Discussion

About half of this sample of young PWID reported ever using prescription opioids (PO) at least six times in a year, and 32% reported past year PO misuse. However, there was evidence that chain-referral sampling produced inflated rates of PO misuse. RDS-adjusted estimates suggest that about 36% of the population may have ever engaged in PO misuse, and 22% in the past year. A substantial minority (22%, unadjusted) reported PO misuse prior to heroin misuse (30% if we include concurrent initiation). Another study (15) found that in a sample of syringe exchange program (SEP) clients who had used heroin in the previous four months, 39% reported being “hooked on” prescription opioids prior to using heroin. SEP clients may have higher rates of PO misuse than PWID in general. In our sample, people who obtained needles from a SEP in the previous six months were about 42% more likely (p = .041) to report PO misuse prior to the past year (data not shown).

As expected, anti-social personality disorder (ASPD) was associated with PO misuse, but did not contribute to abuse or dependence among users. BPD did not contribute independently of ASPD to a greater likelihood of PO misuse, abuse, or dependence. Contrary to expectations, PO misuse, abuse and dependence were not associated with primary major depression, or with anxiety disorders other than PTSD.

Prior post-traumatic stress disorder (PTSD) predicted past year PO misuse, while both prior and past year PTSD were significantly associated with past year PO abuse and dependence among male PO users only. However, due to the small number of PTSD cases among men (13 past year, 18 prior) the estimates lack precision. PTSD may contribute to PO misuse as a form of (maladaptive) self-medication (22), and/or the association may be due to a shared vulnerability to substance abuse/dependence and PTSD after a traumatic event (35).

In contrast to PTSD, the association between substance-induced major depression (SIMD) and PO misuse was significant for past year but not for prior episodes. Although cross-sectional retrospective data cannot unequivocally determine the sequence of events, the pattern of results suggests that PO misuse contributes to SIMD.

Some limitations of the study have been previously reported, including difficulty in recruiting the sample (44). As a result, the sample may not be representative of the population of young PWID. Nevertheless, comparisons between participants recruited by RDS versus outreach indicated that RDS helped us to reach younger PWID with shorter injection histories and less frequent injection (unpublished data). In spite of the difficulties we encountered, RDS is a useful tool for connecting with those PWID who are less likely to come into contact with outreach workers.

There are also limitations associated with the PRISM interview. Participants often had difficulty recalling past feelings and behaviors. However, previous research suggests that

recall errors are most likely to involve less severe symptoms and behaviors (54, 55). We also note that this was a cross-sectional study and therefore causality cannot be inferred from the findings.

The associations between psychiatric disorders and PO misuse, abuse and dependence may reflect a greater likelihood of polydrug use, abuse and dependence for these individuals rather than a specific predilection for prescription opioids (56–61). Personality disorders, and ASPD in particular, have been associated with polydrug abuse, and PTSD and SIMD may also be associated with misuse of and dependence on multiple substances (62). Alcohol, cannabis and sedatives may serve a similar function as opioids for individuals with PTSD (63, 64), and may induce depression as well (65, 66).

We note that while study participants initiated opioid use during a period of large increases in legally prescribed opioids (1), the majority did not begin their opioid use by misusing these drugs. In those cases where PO misuse preceded heroin misuse, it is important to recognize that many of those individuals might have initiated heroin or other illicit substance use even without exposure to PO.

5. Conclusions

Among young PWID, PTSD is a significant risk factor for PO misuse for both men and women. This is a concern for several reasons. First, among those reporting any PO problem use, abuse or dependence, over half indicated that PO misuse preceded their introduction to heroin. While the study was not designed to examine linkages between PO and heroin use, it is likely that for some young PWID the use of prescription opioids contributed to their decision to try heroin. Second, combining heroin injection and PO use potentially increases the risk for overdose. In addition, young men with PTSD are at increased risk for PO abuse and dependence, suggesting the need for services that address the consequences of traumatic exposure in this population.

Acknowledgements

This research was supported by a grant from the National Institute on Drug Abuse (R01DA020368). The content of this paper is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute on Drug Abuse or the National Institutes of Health. We thank study participants for the time and effort they contributed to this study, and acknowledge the dedication of our staff members who administered RDS, collected data, and otherwise operated field sites in a manner welcoming to potential participants.

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Table 1

Prescription opioid misuse, abuse & dependence: RDS populations estimates with bootstrap percentile based confidence intervals (N = 570)

	Sample prev.	Pop. Est.	95% Conf. Int.	
Misuse, past year	0.32	0.22	0.18	0.28
Misuse, prior	0.47	0.33	0.26	0.40
Misuse, lifetime	0.51	0.36	0.29	0.42
Chronic intoxication, ever [a]	0.28	0.20	0.15	0.25
Binge use, ever [b]	0.28	0.19	0.15	0.25
Any problem use, ever	0.33	0.24	0.18	0.31
PO before heroin problem use	0.20	0.14	0.09	0.19
Abuse, lifetime (no dependence)	0.08	0.04	0.02	0.07
Abuse, lifetime	0.27	0.19	0.14	0.24
Abuse, past year [c]	0.17	0.11	0.08	0.16
Abuse, prior	0.26	0.18	0.14	0.24
Dependence, lifetime [c]	0.22	0.17	0.12	0.22
Dependence, past year	0.16	0.11	0.08	0.15
Dependence, prior	0.21	0.16	0.12	0.21

[a] used at least 4 days per week for a month

[b] used most of the day for three days straight

[c] female > male, $p < .05$

Table 2

Multivariate logistic regression analysis for PO misuse, abuse and dependence (N = 570)

	Past Year Use			Past Year Abuse [a]			Past Year Dependence		
	OR	95% Conf. Interval		OR	95% Conf. Interval		OR	95% Conf. Interval	
Step 1									
Female	1.06	0.73	1.54	1.56	0.99	2.45	1.22	0.74	2.01
Age	**0.89**	**0.81**	**0.97**	**0.85**	**0.76**	**0.95**	0.87	0.78	0.98
Race/Ethnicity (Ref. = NH White)									
Hispanic	1.20	0.69	2.10	1.13	0.56	2.26	0.50	0.19	1.30
NH Black/Other	1.35	0.60	3.02	1.92	0.77	4.80	0.92	0.30	2.85
Ever hospitalized	**2.40**	**1.62**	**3.54**	**2.75**	**1.73**	**4.36**	**2.61**	**1.58**	**4.32**
Step 2									
ASPD	**2.15**	**1.43**	**3.24**	1.86	1.14	3.05	1.94	1.13	3.31
BPD	1.53	0.99	2.38	1.51	0.90	2.53	2.05	1.18	3.55
Step 3									
PTSD, past year	2.00	0.99	4.04	**6.19**	**1.88**	**20.43**	**3.14**	**1.45**	**6.80**
× female				0.20	0.04	0.89			
PTSD, prior	**2.45**	**1.31**	**4.60**	**7.93**	**2.79**	**22.52**	**3.24**	**1.60**	**6.59**
× female				0.20	0.05	0.75			
Other anxiety, past year	1.19	0.63	2.23	0.77	0.35	1.70	1.41	0.65	3.02
Other anxiety, prior	2.52	1.11	5.71	0.81	0.41	1.63	1.20	0.59	2.42
× female	0.30	0.10	0.93						
PMD, past year	0.35	0.12	1.04	0.62	0.19	2.02	0.42	0.09	1.96
PMD, prior	1.44	0.81	2.57	1.76	0.91	3.40	1.23	0.59	2.57
SIMD, past year	**1.81**	**1.16**	**2.83**	1.47	0.86	2.49	1.85	1.05	3.26
SIMD, prior	1.20	0.74	1.94	1.51	0.86	2.64	2.08	1.16	3.75

[a] with or without dependence

Note: Step 2 variables entered together, controlling for Step 1 variables; Step 3 variables entered one at a time, controlling for Step 1 and Step 2 variables

Bold indicates $p < .01$