



Published in final edited form as:

Am J Drug Alcohol Abuse. 2016 November ; 42(6): 689–697. doi:10.1080/00952990.2016.1174706.

Event-level analyses of sex risk and injection risk behaviors among nonmedical prescription opioid users

William A. Zule^{a,*}, Christine Oramasionwu^b, Donna Evon^c, Sayaka Hino^c, Irene A. Doherty^a, Georgiy V. Bobashev^d, and Wendee M. Wechsberg^a

^aSubstance Abuse Treatment Evaluations and Interventions Program, RTI International, Research Triangle Park, NC 27709, United States

^bUNC Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, NC 27599, United States

^cDepartment of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC 27510, United States

^dCenter for Data Science, RTI International, Research Triangle Park, NC 27709, United States

Abstract

Background—Nonmedical prescription opioid use has been linked to hepatitis C virus (HCV) infection among people who inject drugs and with using high dead space syringes that retain more blood and transfer more HIV if shared. Little is known regarding its effects on sex risk behaviors.

Objectives—This paper examines event-level associations between nonmedical prescription opioid use and sharing high dead space syringes (injection risk) and unprotected intercourse (sex risk) behaviors.

Methods—We recruited 1,985 participants from two overlapping risk groups—drug users and men who have sex with men (MSM)—and their sex partners. Participants completed an interview that included event-level sex questions with recent sex partners and injection questions with recent injection partners. We used multivariable generalized estimating equations (GEE) to assess the associations between nonmedical prescription opioid use and unprotected intercourse during sexual encounters and sharing syringes during injection episodes, while adjusting for within-person correlations.

Results—When both partners used nonmedical prescription opioids, its use was independently associated with unprotected intercourse in sexual encounters (OR = 2.24; 95% CI = 1.12, 4.49). The use of nonmedical prescription opioids was also associated with sharing high dead space syringes during injection episodes (OR = 6.57; 95% CI = 1.63, 26.51).

Conclusion—Nonmedical prescription opioid use is associated with an increase in the risk of unprotected sex and sharing high dead space syringes. HIV and HCV prevention interventions for nonmedical prescription opioid users should address sex risk behaviors and encourage the use of acceptable low dead space needles and syringes.

*Corresponding author: William A. Zule, RTI International, 3040 Cornwallis Rd., PO Box 12194, Research Triangle Park, NC, 27709-2194, zule@rti.org.

Keywords

nonmedical prescription opioids; injection drug use; HIV; HCV; high dead space syringes

Introduction

Nonmedical use of prescription opioids has received considerable attention in recent years (1). It has been associated with an increased risk of hepatitis C virus (HCV) infection among people who inject drugs (PWID) (2, 3). It is also an important driver of the increase in deaths due to accidental opioid overdose (4, 5). Nonmedical use of prescription opioids is common in both rural and urban areas (1, 6). Recent changes in prescribing practices (7) now make it more difficult to obtain prescription opioids, but these prescribing practices have yielded the unintended consequence of shifting some nonmedical prescription opioid users to heroin (8).

Despite the growing body of research related to the dangers of nonmedical prescription opioid use, the association between nonmedical prescription opioid use and sex risk behaviors has received little attention. Although an association between nonmedical prescription opioid use and sex risk behaviors has been noted among men who have sex with men (MSM) (9, 10), there are few reports of its effects among heterosexuals. One study identified an association between concurrent heavy alcohol and cocaine use and reporting multiple sexual partners in the last month among nonmedical prescription opioid users entering substance use disorder treatment, 97% of whom reported opposite sex partners (11). In the same study, a history of dependence on a substance other than prescription opioids was associated with unprotected intercourse in the last month. In a qualitative study of 46 nonmedical prescription opioid users in New York City, a number of participants reported engaging in unprotected intercourse while using prescription opioids (12).

The associations between drug use and sexual behavior vary by drug (13) and by characteristics of the sexual encounter (14, 15). Event-level analyses of sexual encounters are required to disentangle the effects of specific drugs (e.g., alcohol, methamphetamine, prescription opioids), characteristics of individuals (e.g., age, race/ethnicity, education level), partner characteristics (e.g., main, casual, transactional), and situational factors (e.g., discordant HIV status, drug use by partner) (16, 17). In this sample, we hypothesized that non-medical prescription opioid use would be associated with unprotected intercourse in event-level analyses.

In contrast with sex risk, about which little is known, evidence suggests that nonmedical prescription opioid use may be associated with increased injection risk. Specifically, nonmedical prescription opioid injection has been identified as an independent risk factor for HCV infection compared with injecting heroin or other drugs in models that adjusted for unsafe injecting practices (18). The specific reasons for this association are not completely clear. However, several reports have noted that nonmedical prescription opioid users often inject volumes of fluid greater than 1-ml (18, 19), which is the maximum volume of most “low dead space” insulin syringes (20, 21). As a consequence, nonmedical prescription opioid users may be more likely to use standard “high dead space” needles and syringes.

Compared with insulin syringes, these syringes retain larger volumes of blood (22) and may transmit higher numbers of HCV viral particles if shared (23). Evidence suggests that exposures involving high dead space needles and syringes carry a greater risk of HIV and HCV transmission than exposures involving low dead space syringes (23–25). The World Health Organization (WHO) recommends low dead syringes as one option for reducing injection-related HCV transmission among PWID (26). To our knowledge, the relationship between nonmedical prescription opioid injection and the use of high dead space syringes has not been assessed in statistical models. Moreover, we are not aware of any published studies that have examined the correlates of high dead space syringe sharing at the level of the injection episode.

We hypothesized that injecting nonmedical prescription opioids would be associated with using and sharing a high dead space syringe. We also hypothesized that using a common syringe to prepare and divide liquefied drug solution would be associated with using and sharing a high dead space syringe. This is because the volume of liquid tends to exceed 1 ml when drugs are prepared for more than one person leading PWID to use larger (high dead space) syringes. Moreover, some PWID prefer to transfer the drug solution directly from one syringe to the other through practices that researchers refer to as “frontloading” and “backloading” (27, 28). Directly transferring liquefied drugs from one syringe to another using a low dead space insulin syringe with a permanently attached needle requires “backloading” (29), which carries a high risk of spilling drugs (27). In contrast, there is little, if any, risk of spilling drugs during “frontloading” (30), which requires a syringe with a detachable needle, which in the US context means a high dead space syringe.

This study analyzed data from 1,985 respondents in a cross-sectional study conducted in two rural and two urban counties in North Carolina. We begin by comparing the demographic, drug use, risk behavior, and other characteristics of participants who reported using nonmedical prescription opioids in the past 30 days with participants who did not report using them. We then examine the associations between nonmedical prescription opioid use and unprotected sex (i.e., vaginal or anal intercourse without using a condom during a sexual encounter) through event-level analyses. Next, we use event-level analyses of injection episodes to examine the association between injecting prescription opioids, the use of a common syringe to prepare and divide drugs (i.e. syringe-mediated drug sharing), and sharing a high dead space syringe.

Methods

Event-level analyses were undertaken to assess associations between nonmedical prescription opioid use and HIV risk behaviors (i.e. unprotected sex and sharing high dead space syringes). Compared with analyses of global associations or of situational associations, analyses of event-level associations provide a more sensitive and rigorous method for assessing relationships between use of a substance and sex risk or injection risk behaviors (31).

The data were collected as part of the North Carolina (NC) site of the Sexual Acquisition and Transmission of HIV Cooperative Agreement Project (SATHCAP), which was funded

by the National Institute on Drug Abuse (32). The methods of the overall SATHCAP and the NC SATHCAP have been described previously (33, 34). All of the SATHCAP sites used respondent driven sampling (RDS) to recruit participants (33, 35).

The purpose of the SATHCAP was to explore the potential for sexual diffusion of HIV from traditional higher risk groups (i.e. men who have sex with men and people who use drugs) to lower risk groups (e.g. women and non-drug users). The SATHCAP used respondent driven sampling (RDS), a coupon-based chain-referral approach (33, 35), to recruit participants. Participants recruited as MSM or people who use drugs were given RDS coupons to recruit other people who met the eligibility criteria as a drug user or as an MSM. In addition, the SATHCAP allowed participants recruited as drug users to recruit their non-drug using sex partners; participants who were recruited as MSM were allowed to recruit their female sex partners. Participants recruited as a sex partner of a drug user or a sex partner of an MSM could also recruit their sex partners, but these partners could not recruit anyone. The SATHCAP used color-coded RDS coupons to help staff distinguish between participants recruited as “core group members” (i.e. drug users and MSM), sex partners, and sex partners of sex partners. The specific eligibility criteria for each category follow:

- Participants in the SATHCAP recruited as drug users had to present a valid “core” coupon and report use of heroin, cocaine (powder or crack), methamphetamine, or injected drug use in the past 6 months;
- Male participants in the SATHCAP recruited as MSM had to report male-to-male anal intercourse in the past year, but they did not have to report using any drugs;
- Participants in the SATHCAP recruited as sex partners (or partners of partners) had to present a valid “sex partner” coupon that they had received from a study participant and report having sex with the person who gave them the coupon. They did not have to report using any drugs.

All study participants were required to be at least 18 years of age and to provide written informed consent.

The sample size at each site, which was agreed upon by all of the SATHCAP sites, was designed to provide a sample large enough to answer the primary site-specific and cross-site research questions. Specifically, a large sample as the one analyzed would provide power over 85% to detect small differences of 0.2 of the outcome’s (i.e. primary research questions) standard deviation. Post-hoc power analyses for the secondary outcomes examined in this manuscript indicated that we had over 90% power to detect associations that were significant at $p < 0.001$ and less than 50% power to detect associations that were non-significant ($p > 0.05$). RDS efficiently recruits participants from study populations engaging in proscribed, stigmatizing, or illegal behaviors who are often difficult to reach (36, 37). Participants completed an audio computer assisted self-interview (ACASI) that included questions on drug use, sex risk behaviors, and injection risk overall and event-level questions. As described in the Measures section, the interview collected information regarding recent sexual encounters with the three most recent sex partners plus up to four special interest sex partners and injection episodes with up to three injection partners. The RTI International Office of Research Protection provided ethical approval for this study.

Measures

The ACASI included sections on socio-demographics (e.g., homelessness, income, gender, education, and marital status). It also included questions on history of incarceration and substance use disorder treatment. Symptoms of depression were measured with the depression subscale of the Brief Symptom Inventory (BSI)-18 (38).

For sexual behavior, the ACASI assessed the number of sex partners in the past six months and the number of occasions of vaginal and anal intercourse during the past 30 days with and without a condom. It also asked detailed questions regarding the most recent sexual encounter with the three most recent sex partners and sex partners of special interest (e.g., a female partner of an MSM, a non-drug using partner of a person who used drugs, the RDS recruiter, and an injecting partner of a person who injects drugs). We asked about the special interest partners because the cooperative agreement was interested in the sexual diffusion of HIV from traditional risk groups (e.g. MSM and people who use drugs) to women, non-drug users, and the general population. Encounter-level questions included the age, race/ethnicity, and gender of the partner; the relationship to the partner; the type(s) (i.e., oral, vaginal, anal) of sex during the encounter; whether a condom was used during vaginal or anal sex; drugs used (if any) by the participant and partner; the specific drugs used during the encounter by each partner; if the encounter involved sex for money or drugs and which partner was buying and which partner was selling; and the perceived HIV status of the partner.

The ACASI assessed lifetime and past 30-day use and injection of methamphetamine, powder cocaine, crack cocaine, heroin by itself, heroin and cocaine in combination (speedball), and nonmedical use of prescription opioids. It also asked about any alcohol use, drinking five or more drinks within two hours (i.e., binge drinking), and marijuana use in the past 30 days.

The ACASI also included questions for PWID about the last injection episode with their three most recent injection partners in the past six months. We restricted the questions to the three most recent injection partners and sex partners (mentioned previously) to reduce recall errors. For each injection episode, the ACASI included questions on the characteristics of the injecting partner, drugs the study participant injected, if he/she engaged in receptive syringe sharing, distributive syringe sharing, or splitting liquefied drug solution, and if the injecting partner was also a sex partner. To assess whether a high dead space syringe was used, a question asked whether the needle could be taken off of the syringe. Low dead space insulin syringes in the US have permanently attached needles; thus, if a study participant reported that the needle could be taken off, we coded this event as using a high dead space syringe.

Comparison of participants who reported using nonmedical prescription opioids with participants who did not report using them

We used the RDS Analysis Tool (RDSAT) (www.respondentdrivensampling.org) to calculate RDS weights, and we ran these comparisons with and without the weights.

We used the Pearson chi-square test to assess the differences in proportions of categorical variables between participants who reported using nonmedical prescription opioids in the

previous 30 days and those who did not report using them. We used a t-test for independent samples to assess differences in means of interval and continuous variables between groups.

Event-level unprotected intercourse analyses

We assessed event-level associations between nonmedical prescription opioid use and unprotected intercourse during heterosexual encounters. We excluded encounters (n=181) in which both partners were male because their HIV risks differ from heterosexual encounters. For these analyses, we used a generalized estimating equations (GEE) approach to perform logistic regression analyses that adjusted for within-person correlation for participants who reported multiple encounters. We assessed demographic characteristics and important event-level covariates (e.g., age and race/ethnicity of each partner, depressive symptoms, sex trading during encounter, and drugs used). For the GEE analyses, we specified an exchangeable correlation structure and logit link function. For the multivariable GEE model, we entered all of the variables that were significant in the univariate analyses at $p < 0.20$. We also retained the ages of both partners in the model regardless of the p-value. Prior to beginning the analyses, we coded each event by who used each drug (i.e., no one, male partner only, female partner only, or both partners) and then ran cross-tabulations on each drug by unprotected intercourse during the event. These analyses showed that the events in which both partners used drugs were the most risky, followed by events in which one partner used. For events where one partner used, the gender of the partner did not make a difference in risk. Accordingly, we analyzed event-level use of each drug as a categorical variable defined as: no use of the drug by either partner (reference category), drug used by one partner, or drug used by both partners.

High dead space syringe analyses

We conducted event-level analyses of injection episodes using a GEE approach. We began by conducting univariate analyses to identify variables that were associated with sharing a high dead space syringe. For the multivariable GEE model, we entered all of the variables that were significant at $p < 0.20$ to determine if they were independently associated with sharing a high dead space syringe. Individual-level independent variables included: age, gender, race/ethnicity, education, and recruitment from a rural area. The event-level variables included the specific drugs that were injected and whether the event involved syringe-mediated drug sharing (i.e., using a syringe to divide liquefied drug solution) (27).

Results

From 2005 through 2008, the NC SATHCAP recruited 1,985 participants from two urban (n=1,414) and two rural counties (n=571). The sample included 393 (20%) participants (urban n=231; rural n=162) who reported nonmedical use of prescription opioids in the previous 30 days.

Differences between nonmedical prescription opioid users and other study participants

The RDS weights did not substantively alter the results; therefore, only the results of the unweighted analyses are reported. The characteristics of the sample by nonmedical prescription opioid use are shown in Table 1. Compared with participants who did not use

nonmedical prescription opioids, those who reported using them were more likely to be young, female, non-Hispanic white, and recruited from a rural area. The groups were similar on other socio-demographic characteristics. Approximately 41% were homeless, 34% had health insurance, 34% legally earned at least \$500/month, and 55% had ever been incarcerated. Compared with participants who did not report recent nonmedical use of prescription opioids nonmedical prescription opioid users were less likely to currently be in substance use disorder treatment. Nonmedical prescription opioid users were more likely than non-users to report binge drinking (64% vs. 48%) and use of methamphetamine (16.3% vs. 2%), as well as to report use of heroin and cocaine in combination (speedball), crack cocaine, powder cocaine, and heroin by itself in the last 30 days. Both unprotected intercourse and injection drug use in the last 30 days were more common among nonmedical prescription opioid users than among non-users. Although the prevalence of HCV was comparable across groups (18%), the prevalence of HIV infection was lower among nonmedical prescription opioid users (4.1%) compared with non-users (9.3%) (Table 1).

Unprotected intercourse

Characteristics of sexual encounters—A total of 1,205 participants reported on 2,006 heterosexual encounters, of which 54% (n=1,077) were unprotected. Thirty-seven percent of encounters involved a study participant who was recruited from a rural county. Both partners were African American in 65% of the encounters and both were non-Hispanic white in 10%. Nonmedical prescription opioids were used by one partner in 3% of the encounters and by both partners in 2%. One partner binge drank in 10% of the encounters, and both partners binge drank in 9%. Methamphetamine was used by one partner in 1% of the encounters and by both partners in < 1%. Crack was used by one partner in 12% of encounters and by both partners in 20%. Powder cocaine was used by one partner in 10% and by both partners in 6% of encounters. One partner used heroin in 3% of encounters and both partners used it in 1%. In 74% of encounters, the participant reported knowing the partner for at least six months. Twenty-nine percent of encounters involved exchanging sex for drugs or money, and according to the perceptions of the participants, 4% of encounters involved HIV discordant partners.

Analyses of unprotected intercourse—In the univariate GEE models, individual-level characteristics associated with reporting unprotected intercourse included being recruited in a rural county, being married or living as married, being homeless, and reporting symptoms of depression (Table 2). At the event level, knowing a partner for at least six months, both partners drinking five or more alcoholic drinks, and both partners using nonmedical prescription opioids increased the odds of unprotected intercourse. Events that involved African Americans, trading sex for drugs or money, or HIV discordant partners were associated with decreased odds of unprotected intercourse (Table 2). In the multivariable analyses, general characteristics associated with increased odds of unprotected intercourse included: being recruited in a rural county, being married or living as married, being homeless, and higher depression scores. Event-level characteristics associated with unprotected intercourse included: knowing the partner for at least six months, both partners drinking five or more alcoholic drinks, and both partners using nonmedical prescription opioids. Events in which one partner or both partners were African American, the partners

were perceived to be HIV discordant, and in which sex trading occurred were associated with lower odds of unprotected intercourse.

Sharing high dead space syringes

Characteristics of injection episodes—A total of 192 study participants reported on 392 injection episodes. The study participant was male in 70% of the injection episodes, non-Hispanic white in 30%, African American in 68%, and recruited in a rural area in 13%. Methamphetamine was injected in 8% of the episodes, heroin and cocaine in combination (speedball) in 28%, powder cocaine in 44%, heroin by itself in 28%, and prescription opioids in 4%. Forty percent of the episodes involved dividing liquefied drug solution, and a high dead space syringe was used in 25% of the episodes.

Analyses of high dead space syringe sharing—In univariate GEE models, being African American was the only individual-level characteristic associated with sharing a high dead space syringe at last injection (Table 3). Event-level characteristics associated with sharing a high dead space syringe at last injection included injecting nonmedical prescription opioids and splitting liquefied drug solution. In the multivariable model, being African American, injecting nonmedical prescription opioids, and splitting liquefied drug solution remained associated with increased odds of sharing a high dead space syringe.

Discussion

To our knowledge, this is the first paper that has examined event-level associations between nonmedical prescription opioid use and unprotected sex and between nonmedical prescription opioid use and sharing a high dead space syringe. In the event-level multivariable model of sexual encounters, nonmedical prescription opioid use by both partners was independently associated with unprotected intercourse. This model adjusted for potential confounders including recruitment location, HIV status, homelessness, previous sex with partner, and alcohol use. This suggests that nonmedical prescription opioid use contributes to unprotected sex in some way. This finding is consistent with findings from a qualitative study that found unprotected sex was common among nonmedical prescription opioid users (12). However, the relationship between alcohol and other drug use and risky sex behaviors is complex (13). In some situations, drugs may impair a person's judgment and lead to him or her forgetting to use a condom (16). It is also plausible that many people use specific drugs with the intention of engaging in specific sexual behaviors (17). Accordingly, event-level associations between use of a specific drug and sex risk are necessary, but not sufficient, to establish a causal association.

Needle and syringe programs were, and remain, illegal in North Carolina. Pharmacies are the primary source of syringes for most PWID (39, 40), and almost all retail pharmacies sell both low dead space insulin syringes and high dead space syringes (20). The finding that nonmedical prescription opioid injection was independently associated with sharing a high dead space syringe is consistent with findings from a previous study. In that study, people who injected prescription opioids were more likely to use high dead space syringes than people who injected heroin but did not inject prescription opioids (18). Since this study was conducted, nonmedical prescription opioid use has increased substantially (41). This

increase has been linked to the growing HCV epidemic among young PWID (2). As noted previously, low dead space 1-ml insulin syringes may not be a viable option for nonmedical prescription opioid injectors who inject volumes of fluid greater than 1-ml (21).

Splitting liquefied drug solution was strongly associated with sharing a high dead space syringe. This is troubling because splitting liquefied drug solutions using a high dead space syringe may transfer many times more blood and virus than directly sharing a low dead space syringe (21). The association between being African American and sharing a high dead space syringe is consistent with findings from a previous study in Texas (42). Although it is not clear why African Americans are more likely to use high dead space syringes, the association is very concerning. The prevalence of HIV and HCV in the US is much higher among African Americans (43, 44), and sharing high dead space syringes could contribute to these disparities.

Limitations

The data for these analyses were collected from 2005 through 2008, and the prevalence and distribution of nonmedical prescription opioid use has likely changed since then. However, there is no evidence that these changes would affect the association between nonmedical prescription opioid use and sex risk or syringe type at the event level. The reliability and validity of self-reported data regarding sexual behaviors and injecting practices are unknown. However, we used ACASI, which has been shown to increase the validity of self-reports of sex risk behaviors (45, 46). As with most studies of people who engage in illicit drug use, the representativeness of the sample is unknown. We used RDS to reduce sampling bias (33, 35). There were only 15 injection episodes in which prescription opioids were injected; therefore, the association between nonmedical prescription opioid injection and sharing of high dead space syringes should be interpreted cautiously. Although the event-level questions regarding sexual encounters and injection episodes were very detailed, we did not include a specific question to assess why a participant did or did not use a condom. Neither did we ask why they injected with a specific type of syringe. Therefore, we cannot explain the underlying reasons for the event-level associations observed.

Conclusions

Future research on nonmedical prescription opioid use should consider its association with sex risk behaviors for HIV and other sexually transmitted infections. Previous studies suggest that nonmedical prescription opioid injection is associated with an increased risk of HCV infection (3). Findings from this study provide additional evidence that nonmedical injection of prescription opioids is associated with sharing a high dead space syringe (18). More research is needed to determine why African Americans are more likely to use high dead space syringes, including identifying structural determinants (e.g., availability of syringes). Additional research is needed to increase our understanding of these risk behaviors. However, evidence-based structural and behavioral interventions to reduce these risky behaviors currently exist and should be broadly implemented.

Acknowledgments

This research was supported by grant no. U01DA017373 from the National Institute on Drug Abuse (NIDA). The interpretations and conclusions do not necessarily represent the position of NIDA or RTI International.

References

1. Keyes KM, Cerda M, Brady JE, Havens JR, Galea S. Understanding the rural-urban differences in nonmedical prescription opioid use and abuse in the United States. *American journal of public health*. 2014; 104(2):e52–59. [PubMed: 24328642]
2. Valdiserri R, Khalsa J, Dan C, Holmberg S, Zibbell J, Holtzman D, Lubran R, Compton W. Confronting the emerging epidemic of HCV infection among young injection drug users. *American journal of public health*. 2014; 104(5):816–821. [PubMed: 24625174]
3. Suryaprasad AG, White JZ, Xu F, Eichler BA, Hamilton J, Patel A, Hamdounia SB, Church DR, Barton K, Fisher C, Macomber K, Stanley M, Guilfoyle SM, Sweet K, Liu S, Iqbal K, Tohme R, Sharapov U, Kupronis BA, Ward JW, Holmberg SD. Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006–2012. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2014; 59(10):1411–1419. [PubMed: 25114031]
4. Albert S, Brason FW 2nd, Sanford CK, Dasgupta N, Graham J, Lovette B. Project Lazarus: community-based overdose prevention in rural North Carolina. *Pain Medicine (Malden, Mass)*. 2011; 12(Suppl 2):S77–85.
5. Okie S. A flood of opioids, a rising tide of deaths. *The New England journal of medicine*. 2010; 363(21):1981–1985. [PubMed: 21083382]
6. Young AM, Havens JR, Leukefeld CG. A comparison of rural and urban nonmedical prescription opioid users' lifetime and recent drug use. *The American journal of drug and alcohol abuse*. 2012; 38(3):220–227. [PubMed: 22211586]
7. Surratt HL, O'Grady C, Kurtz SP, Stivers Y, Cicero TJ, Dart RC, Chen M. Reductions in prescription opioid diversion following recent legislative interventions in Florida. *Pharmacoepidemiology and drug safety*. 2014; 23(3):314–320. [PubMed: 24677496]
8. Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. *JAMA Psychiatry*. 2014; 71(7):821–826. [PubMed: 24871348]
9. Benotsch EG, Martin AM, Koester S, Cejka A, Luckman D. Nonmedical use of prescription drugs and HIV risk behavior in gay and bisexual men. *Sexually transmitted diseases*. 2011; 38(2):105–110. [PubMed: 20838365]
10. Kecojevic A, Silva K, Sell RL, Lankenau SE. Prescription Drug Misuse and Sexual Risk Behaviors Among Young Men Who have Sex with Men (YMSM) in Philadelphia. *AIDS and behavior*. 2015; 19(5):847–856. [PubMed: 25240627]
11. Meade CS, Bevilacqua LA, Moore ED, Griffin ML, Gardin JG, Potter JS, Hatch-Maillette M, Weiss RD. Concurrent substance abuse is associated with sexual risk behavior among adults seeking treatment for prescription opioid dependence. *The American Journal on Addictions*. 2014; 23(1):27–33. [PubMed: 24313238]
12. Mateu-Gelabert P, Guarino H, Jessell L, Teper A. Injection and sexual HIV/HCV risk behaviors associated with nonmedical use of prescription opioids among young adults in New York City. *Journal of substance abuse treatment*. 2015; 48(1):13–20. [PubMed: 25124258]
13. Ross MW, Williams ML. Sexual behavior and illicit drug use. *Annual review of sex research*. 2001; 12:290–310.
14. Scott-Sheldon LA, Carey MP, Venable PA, Senn TE, Coury-Doniger P, Urban MA. Alcohol consumption, drug use, and condom use among STD clinic patients. *Journal of studies on alcohol and drugs*. 2009; 70(5):762–770. [PubMed: 19737501]
15. Zule WA, Costenbader EC, Meyer WJ Jr, Wechsberg WM. Methamphetamine use and risky sexual behaviors during heterosexual encounters. *Sexually transmitted diseases*. 2007; 34(9):689–694. [PubMed: 17471112]

16. Leigh BC. Alcohol and condom use: a meta-analysis of event-level studies. Sexually transmitted diseases. 2002; 29(8):476–482. [PubMed: 12172533]
17. Vosburgh HW, Mansergh G, Sullivan PS, Purcell DW. A review of the literature on event-level substance use and sexual risk behavior among men who have sex with men. AIDS and behavior. 2012; 16(6):1394–1410. [PubMed: 22323004]
18. Zibbell JE, Hart-Malloy R, Barry J, Fan L, Flanagan C. Risk factors for HCV infection among young adults in rural new york who inject prescription opioid analgesics. American journal of public health. 2014; 104(11):2226–2232. [PubMed: 25211717]
19. DHHS. Hepatitis C virus infection in young persons who inject drugs. February 26–27, 2013 Consultation Report. 2013.
20. Oramasionwu CU, Bailey SC, Moore HN, Oramasionwu CO, Russell AL, Zule WA. Dead space in over-the-counter syringes: The implications for HIV and HCV transmission. The International journal on drug policy. 2015
21. Zule WA, Cross HE, Stover J, Pretorius C. Are major reductions in new HIV infections possible with people who inject drugs? The case for low dead-space syringes in highly affected countries. The International journal on drug policy. 2013; 24(1):1–7. [PubMed: 22884539]
22. Zule WA, Ticknor-Stellato KM, Desmond DP, Vogtsberger KN. Evaluation of needle and syringe combinations. Journal of acquired immune deficiency syndromes and human retrovirology : official publication of the International Retrovirology Association. 1997; 14(3):294–295.
23. Paintsil E, He H, Peters C, Lindenbach BD, Heimer R. Survival of hepatitis C virus in syringes: implication for transmission among injection drug users. The Journal of infectious diseases. 2010; 202(7):984–990. [PubMed: 20726768]
24. Vickerman P, Martin NK, Hickman M. Could low dead-space syringes really reduce HIV transmission to low levels? The International journal on drug policy. 2013; 24(1):8–14. [PubMed: 23206493]
25. Zule WA, Bobashev G. High dead-space syringes and the risk of HIV and HCV infection among injecting drug users. Drug and Alcohol Dependence. 2009; 100(3):204–213. [PubMed: 19004579]
26. Walsh N, Verster A, Rodolph M, Akl EA. WHO guidance on the prevention of viral hepatitis B and C among people who inject drugs. International Journal of Drug Policy. 2014; 25(3):363–371. [PubMed: 24561223]
27. Grund JP, Friedman SR, Stern LS, Jose B, Neaigus A, Curtis R, Des Jarlais DC. Syringe-mediated drug sharing among injecting drug users: patterns, social context and implications for transmission of blood-borne pathogens. Social Science & Medicine (1982). 1996; 42(5):691–703. [PubMed: 8685737]
28. Koester S, Glanz J, Baron A. Drug sharing among heroin networks: implications for HIV and hepatitis B and C prevention. AIDS and behavior. 2005; 9(1):27–39. [PubMed: 15812611]
29. Jose B, Friedman SR, Neaigus A, Curtis R, Grund JP, Goldstein MF, Ward TP, Des Jarlais DC. Syringe-mediated drug-sharing (backloading): a new risk factor for HIV among injecting drug users. AIDS (London, England). 1993; 7(12):1653–1660.
30. Grund JP, Kaplan CD, Adriaans NF, Blanken P. Drug sharing and HIV transmission risks: the practice of frontloading in the Dutch injecting drug user population. Journal of Psychoactive Drugs. 1991; 23(1):1–10. [PubMed: 1941362]
31. Weinhardt LS, Carey MP. Does Alcohol Lead to Sexual Risk Behavior? Findings from Event-Level Research Annual review of sex research. 2000; 11:125–157.
32. Compton W, Normand J, Lambert E. Sexual Acquisition and Transmission of HIV Cooperative Agreement Program (SATHCAP), July 2009: introduction. Journal of Urban Health : Bulletin of the New York Academy of Medicine. 2009; 86(Suppl 1):1–4.
33. Iguchi MY, Ober AJ, Berry SH, Fain T, Heckathorn DD, Gorbach PM, Heimer R, Kozlov A, Ouellet LJ, Shoptaw S, Zule WA. Simultaneous recruitment of drug users and men who have sex with men in the United States and Russia using respondent-driven sampling: sampling methods and implications. Journal of Urban Health : Bulletin of the New York Academy of Medicine. 2009; 86(Suppl 1):5–31.

34. Zule WA, Bobashev GV, Wechsberg WM, Costenbader EC, Coomes CM. Behaviorally bisexual men and their risk behaviors with men and women. *Journal of Urban Health : Bulletin of the New York Academy of Medicine*. 2009; 86(Suppl 1):48–62. [PubMed: 19513854]
35. Heckathorn D, Semaan S, Broadhead R, Hughes J. Extensions of Respondent-Driven Sampling: A New Approach to the Study of Injection Drug Users Aged 18–25. *AIDS and behavior*. 2002; 6(1): 55–67.
36. Heckathorn DD. Respondent-driven sampling: a new approach to the study of hidden populations. *Social problems*. 1997:174–199.
37. Salganik MJ, Heckathorn DD. Sampling and estimation in hidden populations using respondent-driven sampling. *Sociological methodology*. 2004; 34(1):193–240.
38. Derogatis, LR. BSI 18, Brief Symptom Inventory 18: Administration, scoring and procedures manual. NCS Pearson, Incorporated; 2001.
39. Costenbader EC, Zule WA, Coomes CC. Racial differences in acquisition of syringes from pharmacies under conditions of legal but restricted sales. *The International journal on drug policy*. 2010; 21(5):425–428. [PubMed: 20097052]
40. Oramasionwu CU, Johnson TL, Zule WA, Carda-Auten J, Golin CE. Using Pharmacies in a Structural Intervention to Distribute Low Dead Space Syringes to Reduce HIV and HCV Transmission in People Who Inject Drugs. *American journal of public health*. 2015; 105(6):1066–1071. [PubMed: 25880955]
41. Kolodny A, Courtwright DT, Hwang CS, Kreiner P, Eadie JL, Clark TW, Alexander GC. The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. *Annual review of public health*. 2015; 36:559–574.
42. Zule WA, Desmond DP, Neff JA. Syringe type and drug injector risk for HIV infection: a case study in Texas. *Social Science & Medicine (1982)*. 2002; 55(7):1103–1113. [PubMed: 12365524]
43. Fleckenstein J. Chronic hepatitis C in African Americans and other minority groups. *Current Gastroenterology Reports*. 2004; 6(1):66–70. [PubMed: 14720456]
44. Moore RD. Epidemiology of HIV infection in the United States: implications for linkage to care. *Clinical Infectious Diseases*. 2011; 52(suppl 2):S208–S213. [PubMed: 21342909]
45. Metzger DS, Koblin B, Turner C, Navaline H, Valenti F, Holte S, Gross M, Sheon A, Miller H, Cooley P, Seage GR 3rd. Randomized controlled trial of audio computer-assisted self-interviewing: utility and acceptability in longitudinal studies. HIVNET Vaccine Preparedness Study Protocol Team *American journal of epidemiology*. 2000; 152(2):99–106. [PubMed: 10909945]
46. Simoes AA, Bastos FI, Moreira RI, Lynch KG, Metzger DS. A randomized trial of audio computer and in-person interview to assess HIV risk among drug and alcohol users in Rio De Janeiro, Brazil. *Journal of substance abuse treatment*. 2006; 30(3):237–243. [PubMed: 16616168]

Table 1

Characteristics of the sample by nonmedical use of prescription opioids in the last 30 days

Socio-demographic characteristics	Nonmedical prescription opioid use last 30 days			p-value
	No (n=1592)	Yes (n=393)	Total	
Mean age (SD)	40.3 (10.3)	36.0 (11.2)	39.5 (10.6)	< 0.001
% > 35 years of age	70.1	52.2	66.6	< 0.001
% male	62.0	54.1	60.5	0.004
% non-Hispanic white	18.7	36.9	22.3	< 0.001
% recruited in a rural area	25.7	41.2	28.8	
% completed high school or GED	66.0	69.2	66.6	0.220
% married or living as married	11.8	13.1	12.1	0.494
% working full or part time	29.3	26.9	28.8	0.344
% made \$500 or more legally last 30 days	33.9	32.6	33.7	0.606
% any type of health insurance	33.9	34.6	34.0	0.779
% currently homeless	41.1	42.5	41.4	0.626
Incarceration and drug treatment				
% ever incarcerated	55.0	55.2	55.0	0.963
% ever in formal drug treatment	50.7	50.4	50.6	0.921
% currently in formal drug treatment	14.0	9.7	13.2	0.022
Alcohol and other drug use				
% drank 5 or more drinks in 2 hours last 30 days	48.3	63.9	51.4	< 0.001
% used methamphetamine last 30 days	2.3	16.3	5.1	< 0.001
% used heroin & cocaine in combination (speedball) last 30 days	4.7	13.0	6.4	0.001
% used crack cocaine last 30 days	45.4	52.4	46.8	0.013
% used powder cocaine last 30 days	27.1	57.3	33.1	< 0.001
% used heroin by itself last 30 days	5.6	15.3	7.5	< 0.001
Sexual behavior				
% > 2 sex partners last 6 months	34.5	39.3	35.5	0.080
% any unprotected intercourse last 30 days	42.0	54.5	44.5	< 0.001
Injecting practices				
% injected last 30 days	10.1	17.4	11.6	< 0.001
% shared syringes last 30 days	3.2	6.1	3.8	0.006
% ever injected	28.3	39.9	30.6	< 0.001
HIV and hepatitis C virus (HCV) test results				
% HCV positive test result	18.6	17.9	18.4	0.770
% HIV positive test result	9.3	4.1	8.2	0.001
Psychological distress				
Mean score BSI-18 depression subscale (SD)	7.9 (5.7)	11.1 (6.7)	8.5 (6.1)	< 0.001

Table 2

Event-level analyses of unprotected vaginal or anal intercourse at last sex (sexual encounters n=2,006)

General characteristics	Odds Ratio (95% CI)	p-value	Adjusted Odds Ratio (95% CI)	p-value
Recruited in rural county	1.78 (1.43, 2.22)	< 0.001	1.57 (1.22, 2)	< 0.001
Completed high school or GED	1.01 (0.81, 1.26)	0.925		
Working full or part time	0.94 (0.75, 1.18)	0.614		
Married or living as married	1.84 (1.33, 2.54)	< 0.001	1.81 (1.29, 2.54)	0.001
Currently homeless	1.22 (0.99, 1.51)	0.061	1.65 (1.28, 2.12)	< 0.001
BSI-18 depression subscale	1.03 (1.01, 1.05)	< 0.001	1.02 (1.00, 1.04)	0.026
Event-level characteristics				
# African Americans in encounter				
both partners	0.44 (0.32, 0.60)	< 0.001	0.62 (0.44, 0.87)	0.006
one partner	0.42 (0.30, 0.59)	< 0.001	0.56 (0.39, 0.80)	0.001
reference category -zero partners	--	--	--	--
Age of male partner	1.00 (0.99, 1.01)	0.653	1.01 (1, 1.02)	0.253
Age of female partner	1.00 (1.00, 1.01)	0.350	1 (0.99, 1.01)	0.758
Perceived HIV discordant	0.55 (0.34, 0.88)	0.012	0.55 (0.33, 0.90)	0.018
Encounter involved sex trading	0.74 (0.60, 0.91)	0.005	0.74 (0.58, 0.95)	0.020
Known partner for 6 months	1.84 (1.50, 2.26)	< 0.001	1.83 (1.45, 2.30)	< 0.001
5 or more alcoholic drinks				
both partners	1.69 (1.23, 2.32)	0.001	1.53 (1.07, 2.18)	0.020
one partner	1.20 (0.89, 1.61)	0.245	1.27 (0.91, 1.77)	0.158
Reference category-- no one used	--	--	--	--
Methamphetamine				
both partners	2.51 (0.36, 17.49)	0.352	1.75 (0.37, 8.28)	0.481
one partner	1.70 (0.82, 3.50)	0.152	1.52 (0.68, 3.40)	0.304
Reference category-- no one used	--	--	--	--
Speedball				
both partners	1.13 (0.52, 2.47)	0.755	1.75 (0.50, 6.13)	0.382
one partner	0.50 (0.30, 0.84)	0.008	0.66 (0.35, 1.24)	0.192
Reference category-- no one used	--	--	--	--
Crack cocaine				
both partners	0.82 (0.65, 1.04)	0.107	0.87 (0.66, 1.15)	0.335
one partner	0.86 (0.66, 1.13)	0.290	0.86 (0.63, 1.18)	0.346
Reference category-- no one used	--	--	--	--
Powder cocaine				
both partners	0.73 (0.50, 1.05)	0.091	0.60 (0.39, 0.92)	0.018
one partner	1.19 (0.89, 1.59)	0.232	1.18 (0.85, 1.65)	0.326
Reference category-- no one used	--	--	--	--
Heroin				
both partners	0.51 (0.23, 1.17)	0.111	0.47 (0.13, 1.69)	0.247
one partner	0.67 (0.42, 1.06)	0.085	0.71 (0.41, 1.25)	0.239

General characteristics	Odds Ratio (95% CI)	p-value	Adjusted Odds Ratio (95% CI)	p-value
Reference category-- no one used	--	--	--	--
Non-medical prescription opioids				
both partners	2.55 (1.36, 4.79)	0.003	2.24 (1.12, 4.49)	0.023
one partner	1.32 (0.85, 2.07)	0.220	1.09 (0.61, 1.93)	0.775
Reference category-- no one used	--	--	--	--

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 3

Event-level analyses of sharing a high dead space syringe at last injection (injection episodes n=392)

General characteristics	OR (95% CI)	p-value	AOR (95% CI)	p-value
Age of study participant	0.99 (0.96, 1.03)	0.743		
African American	2.69 (1.08, 6.69)	0.034	3.12 (1.16, 8.38)	0.024
Non-Hispanic white	0.43 (0.17, 1.07)	0.071		
Male gender (female reference category)	0.72 (0.33, 1.57)	0.413		
Recruited in a rural county	1.49 (0.56, 3.93)	0.423		
# of years since first injection	1.02 (0.98, 1.06)	0.305		
HIV positive	0.92 (0.23, 3.63)	0.904		
Event-level characteristics				
Age of injection partner	1.00 (0.98, 1.01)	0.550		
Ever had sex with partner	1.46 (0.87, 2.46)	0.149	1.72 (0.83, 3.56)	0.145
Injected methamphetamine	2.32 (0.87, 6.2)	0.092	2.75 (0.88, 8.64)	0.083
Injected speedball (heroin & cocaine combination)	1.19 (0.57, 2.49)	0.644		
Injected powder cocaine	1.12 (0.57, 2.17)	0.743		
Injected crack cocaine	2.08 (1.18, 3.69)	0.012	2.44 (1.2, 4.97)	0.014
Injected heroin	1.00 (0.43, 2.31)	0.998		
Injected non-medical prescription opioids	6.25 (1.41, 27.8)	0.016	6.57 (1.63, 26.51)	0.008
Syringe-mediated drug sharing (split liquefied drug solution)	7.77 (3.56, 17)	< 0.001	7.95 (3.32, 19.02)	< 0.001