Published in final edited form as:
Drugs (Abingdon Engl). 2015 ; 22(1): 35–42. doi:10.3109/09687637.2014.970515.

Associations between prescription opioid injection and Hepatitis C virus among young injection drug users

Stephen E. Lankenau[1], **Aleksandar Kecojevic**[2], and **Karol Silva**[3]

[1]Department of Community Health and Prevention, School of Public Health, Drexel University, Philadelphia, PA, USA

[2]Division of Health Promotion and Behavioral Science, Graduate School of Public Health, San Diego State University, San Diego, CA, USA

[3]Department of Psychology, Temple University, Philadelphia, PA, USA

Abstract

Objective—Hepatitis C virus (HCV) incidence has been increasing among young injection drug users (IDUs). This analysis examined whether the emerging practice of prescription opioid (PO) injection is associated with self-reported HCV among young IDUs.

Methods—Young IDUs (n = 162) aged 18–25-years-old who indicated recent misuse of prescription drugs were sampled in New York and Los Angeles during 2009–2011. Participants reported lifetime PO injection history and results from their most recent HCV test as well as demographic characteristics and lifetime drug use. Bivariate analyses examined relationships between covariates and both lifetime PO injection and HCV positivity. Poisson regression examined the associations between lifetime PO injection, HCV positivity, and significant covariates.

Results—A majority reported lifetime PO injection (72.2%) and 30.9% self-reported being HCV positive. Lifetime PO injectors were nearly three times more likely to report being HCV positive than non-PO injectors (adjusted incidence rate ratio (AIRR): 2.69, p<0.05) after controlling for socio-demographic and other drug use variable. Additionally, substituting POs for heroin (AIRR: 2.27, p<0.05), growing up in a lower social class (AIRR: 1.67, p<0.05), age (AIRR: 1.12, p<0.05), age of injection initiation (AIRR: 0.87, p<0.001), and history of being prescribed stimulants (AIRR: 0.64, p<0.05) were independently associated with HCV positivity.

Conclusions—Findings suggest that PO injection should be given further consideration as a contributing factor to rising HCV infection among young adults in the US.

Correspondence: Dr Stephen Lankenau, Drexel University, Philadelphia, PA 19104, USA. sel59@drexel.edu.

Declaration of interest
This research was supported by funding from the National Institute on Drug Use (R01 DA021299). NIDA had no role in the study design, collection, analysis or interpretation of the data, writing the manuscript, or the decision to submit the paper for publication. There are no conflicts of interest to report.

Keywords

Hepatitis C virus; injection drug use; opiates

Introduction

Hepatitis C virus (HCV), which has surpassed HIV as a cause of mortality in the US, was responsible for 15,000 deaths in 2007 (Ly, Xing, Klevens, Jiles, & Ward, 2012). Injection drug use was identified as a primary cause of HCV as early as 1990 (Bell et al., 1990; van den Hoek, van Haastrecht, Goudsmit, de Wolf, & Coutinho, 1990). While HCV incidence has been declining in the U.S. population since 1992, rates have been rising among young adults since 2004 (Klevens, Hu, Jiles, & Holmberg, 2012), and reports indicate increases in HCV among young injection drug use (IDUs)(Centers for Disease Control and Prevention, 2008, 2011; Valdiserri et al., 2014). In the wake of the current prescription opioid (PO) epidemic (Okie, 2010), two studies of older IDUs have reported significant associations between injection of POs and HCV (Bruneau, Roy, Arruda, Zang, & Jutras-Aswad, 2012; Havens et al., 2013). However, no studies have studied the relationship between PO injection and HCV positivity specifically among young urban IDUs.

POs are medications, such as oxycodone, hydrocodone, methadone, and buprenorphine, prescribed by physicians to treat pain or drug dependence (Paulozzi, 2012). PO misuse is a public health concern since it is associated with drug dependence (Kirsh, Peppin, & Coleman, 2012) and overdose (Jones, Mack, & Paulozzi, 2013). In 2011, 22.3% of young adults in the US reported lifetime PO misuse compared to only 1.8% who reported lifetime heroin misuse (Substance Abuse and Mental Health Services Administration, 2011). PO misuse, particularly of oxycodone and methadone, and use of heroin and injection drugs has steadily increased among young adults since 2003 (Substance Abuse and Mental Health Services Administration, 2011). While PO injection has been reported among PO misusers (Black, Trudeau, Cassidy, Budman, & Butler, 2013; Firestone & Fischer, 2008; Surratt, Kurtz, & Cicero, 2011) and drug users in general (Davis & Johnson, 2008), studies on PO misuse and injection practices among young IDUs are limited.

Our prior qualitative research on PO misuse among 50 young IDUs (mean age =21.4) recruited in Los Angeles and New York revealed several descriptive findings on PO injection, heroin use, and injection practices. Most IDUs in the sample reported a history of PO injection (Lankenau et al., 2012a). PO injectors were typically male, white, heterosexual, homeless, while approximately one-third reported being HCV positive. Among PO injectors, less than half initiated injection drug use with a PO and less than one-quarter misused POs on a daily basis. Nearly all had injected heroin in their lifetime and over half reported daily heroin use (Lankenau et al., 2012b). Over half reported sharing syringes or injection paraphernalia when injecting POs (Johnson, Fibbi, Langer, Silva, & Lankenau, 2013), which was reported in the context of experiencing heroin withdrawal. Substituting POs for heroin in the context of heroin withdrawal or lack of access to heroin was also commonly reported (Lankenau et al., 2012a).

Studies capturing a broader age range of IDUs have reported particular behaviours associated with PO injection, and point to an emerging trend of PO injection among younger IDUs. A study of IDUs in Montreal (*n* =60, age range =18–60) reported specific risk behaviours linked to PO injection: sharing of "washes" or PO residuals remaining in a cooker or cotton; multiple injections due to the large amount of water sometimes required to inject a PO; and frequent injections of POs due to low cost POs available in street settings (Roy, Arruda, & Bourgois, 2011). Two quantitative studies have reported significant associations between PO injection and HCV. Bruneau et al.'s (2012) study of IDUs (*n* = 246, mean age = 31.5) reported that HCV incidence was independently associated with recent (past 6 months) PO injection, cocaine injection, incarceration, and more than 30 injections in 1 month. Notably, the authors report that PO injection was more common among younger IDUs compared to older IDUs. Additionally, IDUs who did not inject heroin were more likely to become HCV positive than IDUs who injected both PO and heroin. Haven et al.'s (2013) study of Appalachian IDUs (*n* = 392, median age = 31) found that HCV positivity was independently associated with lifetime PO injection, cocaine injection, incarceration, and post-traumatic stress disorder. Recent (past 6 months) syringe sharing was also independently associated with HCV positivity. Notably, the authors indicate that PO injection was more common among IDUs who were earlier in their injection career, which could point to a trend of PO injection among younger injectors.

Risk factors associated with HCV are well understood, such as sharing syringes (Garfein & Doherty, 1998; Hahn et al., 2002); sharing injection equipment, such as cookers, cottons, and rinse water (Hagan et al., 2010; Thorpe et al., 2002) as well as injection residue (Roy et al., 2012); and injecting heroin or cocaine (Garfein & Doherty, 1998; Miller et al., 2002). However, few studies have examined the relationship between PO injection and HCV positivity since PO injection has become a more commonplace practice among urban IDUs only in recent years. Hence, it is unknown how PO injection, particularly among young IDUs, compares to other known risk factors for HCV.

This quantitative analysis is based on a sample of young adults sampled in Los Angeles and New York who reported both recent injection drug use and misuse of POs. This analysis, which compares IDUs with a history of PO injection with IDUs who have misused POs but not injected them, addresses three research questions: (1) What demographic, social, and behavioural characteristics are associated with lifetime PO injection? (2) What demographic, social, and behavioural characteristics are associated with HCV positivity? (3) Is PO injection associated with HCV positivity, controlling for other covariates?

Methods

The current analysis is part of an exploratory mixed methods study design (Creswell, 2006) that included a formative qualitative phase (*n* = 150) followed by a quantitative phase (*n* = 596). Previous analyses of young IDUs during the qualitative phase focused on initiation into PO misuse (Lankenau et al., 2012b), patterns of PO misuse (Lankenau et al., 2012a), and risky injection behaviours associated with PO injection (Johnson et al., 2013) and provided a foundation for the present quantitative analysis.

Sample and sampling methodology

Participants were recruited and interviewed in Los Angeles and New York between October 2009 and March 2011, which represent contrasting markets for prescription and illicit drugs (Lankenau et al., 2012). Eligible participants were 16–25 years old and had engaged in misuse of a prescription drug, i.e. opioid, tranquilizer, or stimulant, or any combination at least three times in the past 90 d. “Misuse” was defined as taking a prescription drug “when they were not prescribed for you or that you took only for the experience or feeling it caused” (Substance Abuse and Mental Health Services Administration, 2011).

Interviewers employed targeted (Watters & Biernacki, 1989) and chain-referral sampling (Biernacki & Waldorf, 1981) to recruit participants in natural settings, such as parks, streets, and organizations serving at-risk youth, e.g. homeless youth. A brief screening tool was used to determine eligibility, and screened individuals received a $3 gift card. Participants who qualified and were interviewed received a $25 cash incentive.

Across both sites, 4432 individuals were screened, 831 (18.8%) met the enrollment criteria, and 618 (74.4%) were interviewed. Twenty-two participants (3.6%) were excluded after it was determined that they did not meet the inclusion criteria, resulting in 596 completed interviews. Sampling was stratified within each site to enroll three groups of young adults with different risk profiles and access to prescription drugs who reported either: polydrug use within the past 90 d but neither homelessness nor injection drug use (n = 202); homelessness in the past 90 d but not injection drug use (n = 192); or injection drug use in the past 90 d (n = 202). The present analysis is restricted to participants who reported injection drug use in the past 90 d.

Of the 202 IDUs enrolled in the study, one was excluded due to missing data on PO injection risk behaviours. Of the remaining 201 participants, 39 were excluded due to missing data on the outcome of HCV positivity – 10 reported not knowing their HCV status and 29 reported having never been tested for HCV – resulting in a final analytical sample of 162. Excluded participants were significantly less likely than those included in the analytic sample to report lifetime incarceration, drug treatment, cocaine and PO injection (p<0.05).

Data collection

The study instrument was developed using Entryware software (Techneos Systems, Inc., Vancouver, Canada) and loaded onto laptop computers. The instrument was administered during face-to-face interviews with eligible participants by one of two interviewers at each site. Interview data were recorded on laptop computers and digital recorders. The study protocol was approved by institutional review boards at Drexel University, Children’s Hospital Los Angeles, and National Development and Research Institutes, Inc.

Measures

The primary-dependent variable in this analysis is self-reported lifetime HCV positivity. Participants were asked a series of questions about HCV testing practices and testing results that culminated with the question, “What is your Hepatitis C status?” A binary variable was created to capture HCV positivity (Positive =1, Negative = 0). Participants who reported

being HCV positive were then asked, “How old were you when you first tested positive for Hepatitis C?” The main independent variable in this analysis is lifetime PO injection. Additionally, participants were asked, “Have you ever injected any prescription [pain] medications or pills?” A dichotomous variable was created to indicate lifetime history of PO injection (Yes =1, No = 0). Participants who reported ever injecting a PO were then asked, “How old were you the first time you injected a prescription pain medication or pill?”.

Covariates were selected based on previous literature identifying risk factors associated with PO injection and HCV. Socio-demographic variables included age, sex at birth (Female = 1, Male = 0,), race (White = 1, Non-White = 0), and socio-economic status (SES) while growing up (Poor/Working Class = 1, Middle/Upper Class = 0). We also investigated if site (LA = 1, NY = 0) and lifetime homelessness (Yes = 1, No = 0), were associated with PO injection or HCV positivity. Participants were asked if they had ever been in drug treatment, ever incarcerated, or ever received care in a psychiatric hospital. (Yes = 1, No = 0, for each of these variables). To assess lifetime prescribed use of medications, study participants were asked, “Were you ever prescribed [opioids, tranquilizers, stimulants] by a doctor for any past injury or health condition?” (Yes = 1, No = 0).

Participants were asked specific questions regarding alternative methods of PO administration, including lifetime history of sniffing (Yes = 1, No = 0), and smoking (Yes =1, No = 0) and injecting (Yes = 1, No = 0). We also asked whether a PO had ever been used as a substitute for heroin (Yes = 1, No =0). A number of questions were asked regarding history of injection drug use, including lifetime heroin and cocaine (Yes = 1; No =0), and drug used at injection initiation (“What was the first drug you ever injected?”). We also inquired about age of initiation into various drug behaviours, such as PO misuse, injection of any drug, PO injection, and heroin injection.

Data analysis

All bivariate and multivariable analyses were conducted using Poisson regression with robust error variance (Zou, 2004). Given the relatively high prevalence of outcomes of interest (>10%), we chose Poisson regression since the odds ratios produced through logistic regression would not provide an accurate estimate of the risk ratios (Barros & Hirakata, 2003; Horyniak et al., 2013; Zhang & Yu, 1998). In the first step, bivariate associations were calculated for lifetime PO injection and HCV positivity with all covariates of interest. Second, we used multivariable regression to adjust for confounding factors and to calculate the best effect estimate of the relationship between lifetime PO injection and HCV status. Secondary variables were included in analysis if they had a statistically significant ($p<0.05$), or marginally significant ($p<0.1$) relationship with both lifetime PO injection and HCV status in bivariate associations (Mickey & Greenland, 1989). Lifetime PO injection and all significant secondary variables were included in an initial model, and a backward selection approach was employed. Reduced models were constructed, each by removing one secondary explanatory variable that corresponded to the smallest change in coefficient for the primary explanatory variable, between the full model and the reduced model. This process was repeated until the smallest change in coefficient exceeded 10% and resulted in the final, most parsimonious model, which retained only covariates significantly

confounding the relationship of interest. To prevent over-fitting the model, collinearity between predictor variables was assessed using a correlation matrix procedure. Variables were considered collinear if the value of the correlation coefficient was greater than 0.6 (Tabachnick & Fidell, 2006). None of the variables demonstrated this degree of collinearity. Adjusted incidence rate ratios (IRR) were obtained for the final model by exponentiation of the Poisson regression coefficient. All analyses were conducted using the Predictive Analytics Software (PASW, formerly SPSS), version 20.0.

Results

A majority of young IDUs reported lifetime PO injection (72.2%) while a minority self-reported being HCV positive (30.9%). Among participants who were both PO injectors and reported having tested positive for HCV (Table 1), initiation of PO injection occurred at a significantly earlier age (17.7) than first testing positive for HCV (19.2). Among this group, only 15% (n = 7) reported first opioid injection occurring after testing positive for HCV.

Bivariate analyses comparing lifetime PO injectors to non-PO injectors revealed several statistically significant relationships (Table 2). PO injectors were more likely to be white (Incidence Rate Ratio [IRR] = 1.39, 95% confidence intervals [CI]: 1.10, 1.77), report a lifetime history of incarceration (IRR = 1.86, 95% CI: 1.15, 3.02), drug treatment (IRR = 1.53, 95% CI: 1.16, 2.01), and psychiatric hospitalization (IRR = 1.24, 95% CI: 1.01, 1.50), and have been prescribed tranquilizers (IRR = 1.31, 95% CI: 1.05, 1.62). PO injectors were more likely to report various drug using behaviours such as sniffing POs (IRR = 1.43, 95% CI: 1.01, 2.03), substituting POs for heroin (IRR = 1.53, 95% CI: 1.18, 1.99), lifetime heroin injection (IRR = 2.04, 95% CI: 1.17, 3.56), and lifetime cocaine injection (IRR = 1.55, 95% CI: 1.17, 2.03). Finally, those who reported PO injection behaviour were more likely to report HCV positive status (IRR = 1.45, 95% CI: 1.23, 1.71). A few trends (significant at p<0.1) were also observed: PO injectors were more likely to experience lifetime homelessness (IRR =2.23, 95% CI: 0.88, 5.66), to have a history of prescribed stimulants (IRR = 1.21, 95% CI: 1.00, 1.48), and to report smoking POs (IRR =1.20, 95% CI: 0.99, 1.44).

Bivariate analyses comparing HCV positive and negative IDUs revealed several statistically significant relationships not found in Table 2 (Table 3). HCV positive IDUs were more likely to report lifetime PO injection (IRR = 4.42, 95% CI: 1.69, 11.61), use PO as substitute for heroin (IRR = 3.87, 95% CI: 1.76, 8.55), inject PO for a greater number of years (IRR = 1.10, 95% CI: 1.03, 1.17), report lifetime cocaine injection (IRR = 3.40, 95% CI: 1.55, 7.48), and report an earlier age of initiation for the first injection of any drug (IRR = 0.89, 95% CI: 0.83, 0.98). A few trends (significant at p<0.1) were also observed: HCV positive IDUs were less likely to have been recruited in LA (IRR = 0.62, 95% CI: 0.39, 1.01), to be older (IRR = 1.11, 95% CI: 1.00, 1.22), and to have grown up poor/working class (IRR = 1.52, 95% CI: 0.94, 2.44).

Table 4 displays the final multivariable model with HCV positivity as the outcome of interest. Controlling for other significant covariates, participants who reported a history of PO injection had a HCV positivity rate 2.69 times greater than those without history of PO

injection (AIRR: 2.69, 95% CI: 1.07, 6.78). Participants who substituted POs for heroin had a rate of HCV positivity 2.28 times higher than those who did not (AIRR: 2.27, 95% CI: 1.02, 5.10). For participants who grew up in poor/working class families, there was an average 67% increase in HCV positivity compared to those who grew up middle/upper class (AIRR: 1.67, 95% CI: 1.09, 2.57). For each additional year of age, we observed a 12% increase in being HCV positive (AIRR: 1.12, 95% CI: 1.02, 1.23), while each 1 year increase in age of injection initiation was associated with an average 13% reduction in HCV positivity (AIRR: 0.87, 95% CI: 0.80, 0.94). Finally, a 36% reduction in HCV positivity was associated with having a history of prescribed stimulants (AIRR: 0.64, 95% CI: 0.42, 0.97).

Discussion

Our results indicate that lifetime PO injection was independently associated with self-reported HCV positivity among a sample of young IDUs with a history of PO misuse. Overall, PO injectors were nearly three times more likely to report being HCV than non-PO injectors after controlling for socio-demographic and other lifetime drug use variables. Additionally, self-report data on age of first opioid injection and age of HCV positivity indicate that IDUs began injecting POs an average of 1.5 years prior to testing positive for HCV. Taken together, these results suggest that PO injection may be a risk factor for HCV positivity among IDUs with a history of PO misuse. These findings, based upon samples of young IDUs recruited in New York and Los Angeles, corroborate results from studies of older IDUs in Montreal (Bruneau et al., 2012) and Appalachia (Havens et al., 2013) that identify PO injection as a potential risk factor for HCV. Collectively, these results from diverse settings – urban and rural, U.S. and Canada – suggest that PO injection has become an alternative or complement to other types of injection drug use (Valdiserri et al., 2014).

A history of cocaine and heroin injection was associated with PO injection in the bivariate analysis. These findings indicate that polydrug injection (Lankenau & Clatts, 2005; Lankenau et al., 2010), heroin in particular, was common among PO injectors in this sample. However, neither cocaine nor heroin injection was associated with HCV positivity in the final multivariable model. The fact that these two drug injection variables were not significant, but have been found to be associated with HCV among young IDUs in other studies (Garfein & Doherty, 1998; Miller et al., 2002), provides additional evidence of the potential importance of PO injection as an independent risk factor of HCV positivity among young IDUs.

A potentially important new finding is the practice of substituting POs for heroin as an independent risk factor for HCV. Our previous qualitative research indicated that young IDUs substituted POs for heroin during heroin withdrawal or when heroin was unavailable (Lankenau et al., 2012a). These findings situate PO misuse and HCV risk in the context of active heroin use, which differs from previous studies that placed PO injection and HCV in the context of POs (rather than heroin) as the primary type of opioid available to IDUs (Bruneau et al., 2012; Havens et al., 2013). Hence, our results suggest that PO injection is associated with HCV in both heroin rich locations, such as New York and Los Angeles (NIDA 2011), in addition to heroin scarce locations, such as Montreal (Fischer, Patra, Cruz, Gittins, & Rehm, 2008) or Appalachia (U.S. Department of Justice, 2008).

Similar to other studies, young IDUs in this sample were typically white (Hagan et al., 2010; Hahn et al., 2002; Roy et al., 2012), male (Hagan et al., 2010; Hahn et al., 2002; Roy et al., 2012), heterosexual (Hagan et al., 2010), and homeless (Roy et al., 2012). PO injectors in particular were significantly more likely to be white (Havens et al., 2013) and homeless (Johnson et al., 2013), suggesting that the practice of PO injection may be penetrating the same groups most likely to inject heroin (Fischer et al., 2008). None of these demographic characteristics, however, were associated with HCV positivity in the final multivariable model. Notably, growing up poor/working class, which was marginally significant in the bivariate models, was significantly associated with HCV positivity in the final model. Disparities associated with growing up in a poor/working class environment, such as unequal access to education, income, and healthcare (Krieger, Williams, & Moss, 1997), have been linked to HCV positivity among drug users in some studies (Alter et al., 1982) but have not been previously reported to be associated with HCV among young IDUs. No differences were found by site in the bivariate model focused on PO injection or in final multivariable model centered on HCV, which indicates that young IDUs in New York and Los Angeles were more similar than different regarding PO injection and HCV positivity.

Age was associated with HCV positivity in this sample: being an older IDU and initiating injection drug use at a younger age were both independently associated with a greater likelihood of being HCV positive. In essence, the likelihood of becoming HCV positive increased: if one began injecting at a younger age and with more years as an injector. Both of these findings, which mirror other research examining HCV prevalence among IDUs in relation to age and duration of injection (Clatts, Colon-Lopez, Giang le, & Goldsamt, 2010; Garfein, Vlahov, Galai, Doherty, & Nelson, 1996; Hagan et al., 2007), reinforce the importance of prevention programmes that delay the onset of injection initiation and risk-reduction resources for persons who have initiated injection drug use.

IDUs who had ever been prescribed stimulants, such as Ritalin or Adderall, were found to be at a lower risk for HCV in the multivariable model. However, in the bivariate analysis of PO injection, PO injectors were found to have an increased likelihood of ever being prescribed stimulants. To our knowledge, there have been no studies examining the relationship between conditions for which stimulants are prescribed for, such as attention deficit hyperactivity disorder (ADHD), and injection drug use. Hence, future studies could include questions about ADHD and prescription stimulants to understand how these psychological and prescription histories relate to injection drug use and risk for HCV.

Given the associations between PO injection and HCV found in this study, an important question for future studies should focus on whether PO injectors engage in particular kinds of injection practices or whether PO injection is a marker for some other kind of risk behaviour. While not reported in this analysis, our prior qualitative research found that sharing injection paraphernalia was common in the context of PO injection (Johnson et al., 2013). Havens et al. (2013) found that only receptive needle sharing – not cookers or other injection paraphernalia (Roy et al., 2011) – was independently associated with HCV positivity among PO injectors. Future research – both quantitative and qualitative studies – should pay closer attention to practices used to inject POs since it is not clear how common it is to share PO residuals in cookers (Roy et al., 2011) or whether there are additional risk

behaviours associated with injecting POs beyond those commonly associated with injecting other drugs.

These results offer some implications for treatment and prevention. A high proportion of PO injectors in this sample had been in drug treatment, a majority obtained syringes from needle exchange, and a majority reported a recent HCV test. Hence, PO injectors in this study had been utilizing treatment and prevention services. Consequently, these various points of contact between young IDUs and services offer opportunities for providers to suggest particular risk reduction strategies in the context of PO injection and misuse, such as treatment for substance use, HCV testing and treatment, and ongoing education about the risks associated with sharing injection paraphernalia. At a minimum, treatment and prevention specialist should be made aware of PO injection among young IDUs, which may be an emerging practice in both New York and Los Angeles.

Limitations

There are limitations to this study. First, since the study did not conduct HCV serologic testing, all data on HCV are self-report, including history of testing and HCV status. Self-report data for HCV status may be subject to social desirability and recall biases, but studies on HCV self-report data among IDUs indicate that large proportions know their true HCV serologic status – particularly IDUs who self-report being HCV positive (Day et al., 2008; Hagan et al., 2006; O'Keefe, Aitken, Higgs, & Dietz, 2013). In the present study, IDUs who did not know their status or had never been tested were excluded from the analysis. Excluded participants were less likely to be PO injectors, which suggest that PO injection could be associated with some kind of health seeking behaviour, e.g. access or interest in HCV testing. A second limitation is the relatively small sample size of 162, which reduced the power to detect meaningful statistical differences in the bivariate and multivariable analyses. Related, only 46 HCV positive PO injectors and 4 HCV positive non-PO injectors were available for analysis, which may have resulted in less precise IRRs. Third, lifetime injection risk behaviours, such as sharing syringes or other injection paraphernalia, were not included in the analysis (only 90d injection risk behaviours were queried during the interview). However, as described above, specific questions that capture particular kinds of injection risk behaviours may be necessary to fully understand the types of injection practices specific to PO injection. Finally, since results are based upon cross-sectional data, causal relationships between variables, such as PO injection and HCV positivity, cannot be determined.

Conclusion

PO injection, which was common in this sample of young IDUs with a history of PO misuse, was independently associated with HCV positivity. PO injection was more typical among participants who were younger, white, homeless, and had injected heroin. Findings suggest that PO injection should be given further consideration as a contributing factor to rising HCV infection among young adults in the US.

Acknowledgments

The authors acknowledge Ceaser Arauz-Cuadra, Meghan Treese, and Alex Harocopos for participant recruitment and interviews. We also would like to acknowledge the young adults who participated in this study.

References

Alter MJ, Gerety RJ, Smallwood L, Sampliner RE, Tabor E, Deinhardt F, Matanoski GM. Sporadic non-A, non-B hepatitis: Frequency and epidemiology in an urban U.S. population. The Journal of Infectious Diseases. 1982; 145:886–893. [PubMed: 6806403]

Barros AJ, Hirakata VN. Alternatives for logistic regression in cross-sectional studies: An empirical comparisson of models that directly estimate the prevalence ratio. BMC Medical Research Methodology. 2003; 3:21. [PubMed: 14567763]

Bell J, Batey RG, Farrell GC, Crewe EB, Cunningham AL, Byth K. Hepatitis C virus in intravenous drug users. The Medical Journal of Australia. 1990; 153:274–276. [PubMed: 2118227]

Biernacki P, Waldorf D. Snowball sampling: Problems, techniques and chain-referral sampling. Sociological Methods and Research. 1981; 10:141–163.

Black RA, Trudeau KJ, Cassidy TA, Budman SH, Butler SF. Associations between public health indicators and injecting prescription opioids by prescription opioid abusers in substance abuse treatment. Journal of Opioid Management. 2013; 9:5–17. [PubMed: 23709299]

Bruneau J, Roy É, Arruda N, Zang G, Jutras-Aswad D. The rising prevalence of prescription opioid injection and its association with hepatitis C incidence among street-drug users. Addiction. 2012; 107:1318–1327. [PubMed: 22248184]

Centers for Disease Control and Prevention. Use of enhanced surveillance for hepatitis C virus infection to detect a cluster among young injection-drug users–New York, November 2004-April 2007. Morbidity And Mortality Weekly Report. 2008; 57:517–521. [PubMed: 18480744]

Centers for Disease Control and Prevention. Hepatitis C virus infection among adolescents and young adults — Massachusetts, 2002–2009. Morbidity And Mortality Weekly Report. 2011; 60:537–541. [PubMed: 21544042]

Clatts M, Colon-Lopez V, Giang le M, Goldsamt L. Prevalence and incidence of HCV infection among Vietnam heroin users with recent onset of injection. Journal of Urban Health. 2010; 87:278–291. [PubMed: 20041309]

Creswell, JP. Mixed methods design. Thousand Oaks, CA: Sage; 2006.

Davis WR, Johnson BD. Prescription opioid use, misuse, and diversion among street drug users in New York City. Drug and Alcohol Dependence. 2008; 92:267–276. [PubMed: 17913395]

Day C, White B, Thein H, Doab A, Dore G, Bates A, Maher L. Experience of hepatitis C testing among injecting drug users in Sydney, Australia. AIDS Care. 2008; 20:116–123. [PubMed: 18278622]

Firestone M, Fischer B. A qualitative exploration of prescription opioid injection among street-based drug users in Toronto: Behaviours, preferences and drug availability. Harm Reduction Journal. 2008; 5:30. [PubMed: 18928556]

Fischer B, Patra J, Cruz MF, Gittins J, Rehm J. Comparing heroin users and prescription opioid users in a Canadian multi-site population of illicit opioid users. Drug and Alcohol Review. 2008; 27:625–632. [PubMed: 19378446]

Garfein R, Doherty M. Prevalence and incidence of hepatitis C virus infection among young adult injection drug users. JAIDS. 1998; 18:11–19.

Garfein R, Vlahov D, Galai N, Doherty M, Nelson K. Viral infections in short-term injection drug users: The prevalence of the hepatitis C, hepatitis B, human immunodeficiency, and human T-lymphotropic viruses. American Journal of Public Health. 1996; 86:655–661. [PubMed: 8629715]

Hagan H, Campbell J, Thiede H, Strathdee S, Ouellet L, Kapadia F, Garfein RS. Self-reported hepatitis C virus antibody status and risk behavior in young injectors. Public Health Reports. 2006; 121:710–719. [PubMed: 17278406]

Hagan H, Des Jarlais D, Stern R, Lelutiu-Weinberger C, Scheinmann R, Strauss S, Flom PL. HCV synthesis project: Preliminary analyses of HCV prevalence in relation to age and duration of injection. International Journal of Drug Policy. 2007; 18:341–351. [PubMed: 17854721]

Hagan H, Pouget ER, Williams IT, Garfein RS, Strathdee SA, Hudson SM, Ouellet LJ. Attribution of hepatitis C virus seroconversion risk in young injection drug users in 5 US cities. Journal of Infectious Diseaes. 2010; 201:378–385.

Hahn JA, Page-Shafer K, Lum PJ, Bourgois P, Stein E, Evans JL, Moss AR. Hepatitis C virus seroconversion among young injection drug users: Relationships and risks. Journal of Infectious Diseases. 2002; 186:1558–1564. [PubMed: 12447730]

Havens JR, Lofwall MR, Frost SDW, Oser CB, Leukefeld CG, Crosby RA. Individual and network factors associated with prevalent hepatitis C infection among rural Appalachian injection drug users. American Journal of Public Health. 2013; 103:e44–e52. [PubMed: 23153148]

Horyniak D, Dietze P, Degenhardt L, Higgs P, McIlwraith F, Alati R, Burns L. The relationship between age and risky injecting behaviours among a sample of Australian people who inject drugs. Drug Alcohol Dependence. 2013; 132:541–546. [PubMed: 23664499]

Johnson K, Fibbi M, Langer D, Silva K, Lankenau S. Prescription drug misuse and risk behaviors among young adult IDUs. Journal of Psychoactive Drugs. 2013; 45:112–121. [PubMed: 23908999]

Jones CM, Mack KA, Paulozzi LJ. Pharmaceutical overdose deaths, United States, 2010. JAMA. 2013; 309:657–659. [PubMed: 23423407]

Kirsh K, Peppin J, Coleman J. Characterization of prescription opioid abuse in the United States: Focus on route of administration. Journal of Pain & Palliative Care Pharmacotherapy. 2012; 26:348–361. [PubMed: 23675595]

Klevens RM, Hu DJ, Jiles R, Holmberg SD. Evolving epidemiology of hepatitis C virus in the United States. Clinical Infectious Diseases. 2012; 55:S3–S9. [PubMed: 22715211]

Krieger N, Williams DR, Moss NE. Measuring social class in US public health research: Concepts, methodologies, and guidelines. Annual Review of Public Health. 1997; 18:341–378.

Lankenau S, Clatts M. Patterns of polydrug use among ketamine injectors in New York City. Substance Use & Misuse. 2005; 40:1381–1397. [PubMed: 16048823]

Lankenau S, Schrager S, Silva K, Kecojevic A, Jackson Bloom J, Wong C, Iverson E. Prescription and illicit drug use among high-risk young adults in Los Angeles and New York. Journal of Public Health Research. 2012; 1:1–9. [PubMed: 25170438]

Lankenau S, Teti M, Silva K, Jackson Bloom J, Harocopos A, Treese M. Patterns of prescription drug misuse among young injection drug users. Journal of Urban Health. 2012a; 89:1004–1016. [PubMed: 22684424]

Lankenau S, Teti M, Silva K, Jackson Bloom J, Harocopos A, Treese M. Initiation into prescription opioid misuse amongst young injection drug users. International Journal on Drug Policy. 2012b; 23:37–44. [PubMed: 21689917]

Lankenau S, Wagner K, Jackson Bloom J, Sanders B, Hathazi D, Shin C. The first injection event: Differences among heroin, methamphetamine, cocaine, and ketamine initiates. Journal of Drug Issues. 2010; 40:241–262. [PubMed: 21423792]

Ly KN, Xing J, Klevens RM, Jiles RB, Ward JW. The increasing burden of mortality from viral hepatitis in the United States between 1999 and 2007. Annals of Internal Medicine. 2012; 156:271–278. [PubMed: 22351712]

Mickey J, Greenland S. A study of the impact of confounder-selection criteria on effect estimation. American Journal of Epidemiology. 1989; 129:125–137. [PubMed: 2910056]

Miller CL, Johnston C, Spittal PM, Li K, Laliberté N, Montaner JSG, Schechter MT. Opportunities for prevention: Hepatitis C prevalence and incidence in a cohort of young injection drug users. Hepatology. 2002; 36:737–742. [PubMed: 12198668]

O'Keefe D, Aitken C, Higgs P, Dietz P. Concordance between self-reported and actual hepatitis C virus infection status in a cohort of people who inject drugs. Drug and Alcohol Review. 2013; 32:208–210. [PubMed: 22943595]

Okie S. A flood of opioids, a rising tide of deaths. New England Journal of Medicine. 2010; 363:1981–1985. [PubMed: 21083382]

Paulozzi L. Prescription drug overdose: A review. Journal of Safety Research. 2012; 43:283–289. [PubMed: 23127678]

Roy E, Arruda N, Bourgois P. The growing popularity of prescription opioid injection in downtown Montréal: New challenges for harm reduction. Substance Use & Misuse. 2011; 46:1142–1150. [PubMed: 21370963]

Roy E, Arruda N, Leclerc P, Haley N, Bruneau J, Boivin JF. Injection of drug residue as a potential risk factor for HCV acquisition among Montréal young injection drug users. Drug and Alcohol Dependence. 2012; 126:246–250. [PubMed: 22699096]

Substance Abuse and Mental Health Services Administration. NSDUH Series H-41, HHS Publication No. (SMA) 11-4658. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2011. Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings.

Surratt H, Kurtz SP, Cicero TJ. Alternate routes of administration and risk for HIV among prescription opioid abusers. Journal of Addictive Diseases. 2011; 30:334–341. [PubMed: 22026525]

Tabachnick, BG.; Fidell, LS. Using multivariate statistics. 5. Needham Heights, MA: Allyn and Bacon; 2006.

Thorpe LE, Ouellet LJ, Hershow R, Bailey SL, Williams IT, Williamson J, Garfein RS. Risk of hepatitis C virus infection among young adult injection drug users who share injection equipment. American Journal of Epidemiology. 2002; 155:645–653. [PubMed: 11914192]

U.S. Deparment of Justice. Appalachia: High intensity drug trafficking area. National Intelligence Drug Center; 2008.

Valdiserri R, Khalsa J, Dan C, Holmberg S, Zibbell J, Holtzman D, Compton W. Confronting the emerging epidemic of HCV infection among young injection drug users. American Journal of Public Health. 2014; 104:816–821. [PubMed: 24625174]

van den Hoek JAH, van Haastrecht HJA, Goudsmit J, de Wolf F, Coutinho RA. Prevalence, incidence, and risk factors of hepatitis C virus infection among drug users in Amsterdam. Journal of Infectious Diseases. 1990; 162:823–826. [PubMed: 2119400]

Watters JK, Biernacki P. Targeted sampling: Options for the study of hidden populations. Social Problems. 1989; 36:416–430.

Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. JAMA. 1998; 280:1690–1691. [PubMed: 9832001]

Zou G. A modified poisson regression approach to prospective studies with binary data. American Journal of Epidemiology. 2004; 159:702–706. [PubMed: 15033648]

Table 1

Pairwise comparison on age of initiation into injection drug use of any drug and PO and self-reported age of testing positive for self-reported Hepatitis C virus (HCV).

Variable 1 (mean age, SD)	Variable 2 (mean age, SD)	*t*-test
Injected any drug[a] (16.4, 2.2)	HCV + (19.1, 2.5)	$t(49) = -8.69^{***}$
Injected PO[b] (17.7, 2.8)	HCV + (19.2, 2.5)	$t(45) = -3.37^{***}$

[a] IDU and tested positive for HCV ($n = 50$).

[b] PO injectors and tested positive for HCV ($n = 46$).

*** $p<0.001$.

Table 2

Bivariate associations between lifetime prescription opioid (PO) injection and socio-demographic and behavioural characteristics among 162 young IDUs.

Variable	Total *n* = 162 % (*n*)	PO injectors *n* = 117 % (*n*)	Non-PO injectors *n* = 45 % (*n*)	Unadjusted IRR
Socio-demographic characteristics				
Site (LA)	47.5 (77)	45.3 (53)	53.3 (24)	0.91 (0.75–1.11)
Age, mean (SD)	21.4 (2.2)	21.4 (2.2)	21.3 (2.3)	1.00 (0.96–1.05)
Sex at birth (Female) (*n* = 161)	36.0 (58)	35.3 (41)	37.8 (17)	0.97 (0.79–1.19)
Race (White) (*n* = 161)	63.4 (102)	70.7 (82)	44.4 (20)	1.39 (1.10–1.77)**
Sexual identity (Heterosexual)	65.4 (106)	66.7 (78)	62.2 (28)	0.95 (0.77–1.17)
Poor/working class growing up (*n* = 161)	49.7 (80)	51.3 (60)	45.5 (20)	1.07 (0.88–1.29)
Completed high school	63.0 (102)	62.4 (73)	64.4 (29)	0.97 (0.80–1.19)
Lifetime homelessness	94.4 (153)	97.4 (114)	86.7 (39)	2.23 (0.88–5.66)†
History of institutionalization				
Incarceration	85.2 (138)	91.5 (107)	68.9 (31)	1.86 (1.15–3.02)*
Drug treatment	68.5 (111)	76.9 (90)	46.7 (21)	1.53 (1.16–2.01)**
Psychiatric hospital	49.4 (80)	54.7 (64)	35.6 (16)	1.24 (1.01–1.50)*
Lifetime prescribed use				
Opioids	82.7 (134)	86.3 (101)	73.3 (33)	1.32 (0.94–1.84)
Tranquilizers	58.6 (95)	65.0 (76)	42.2 (19)	1.31 (1.05–1.62)*
Stimulants	52.5 (85)	57.3 (67)	40.0 (18)	1.21 (1.00–1.48)†
Lifetime drug using behaviours				
Sniffed PO	81.5 (132)	86.3 (101)	68.9 (31)	1.43 (1.01–2.03)*
Smoked PO	24.7 (40)	28.2 (33)	15.6 (7)	1.20 (0.99–1.44)†
PO as substitute for heroin	65.4 (106)	74.4 (87)	42.2 (19)	1.53 (1.18–1.99)***
Injected Heroin (*n* = 161)	87.0 (140)	93.2 (109)	70.5 (31)	2.04 (1.17–3.56)*
Cocaine (*n* = 161)	68.3 (110)	76.9 (90)	45.5 (20)	1.55 (1.17–2.03)**
1st injection – heroin (*n* = 155)	57.4 (89)	58.8 (67)	53.7 (22)	1.06 (0.87–1.28)
1st injection – PO (*n* = 117)	–	19.7 (23)	–	–
Age of 1st misuse of PO	14.6 (2.49)	14.5 (2.4)	14.9 (2.8)	0.98 (0.94–1.02)
Age of 1st injection of any drug (*n* = 156)	17.6 (6.3)	17.5 (7.1)	18.0 (3.4)	1.00 (0.98–1.01)
Age of 1st PO injection (*n* = 117)	–	18.0 (2.6)	–	–
HCV testing (self-report)				
HCV+	30.9 (50)	39.3 (46)	8.9 (4)	1.45 (1.23–1.71)***
Age of HCV + diagnosis	19.1 (2.5)	19.2 (2.5)	18.3 (2.5)	1.01 (0.98–1.05)

*** $p<0.001$,

** $p<0.01$,

* $p<0.05$,

$^{\dagger}p<0.10$.

Table 3

Bivariate associations between self-reported Hepatitis C virus (HCV) positivity and socio-demographic and behavioural characteristics among 162 young IDUs.

Variable	Total *n* = 162 % (*n*)	HCV positive *n* = 50 % (*n*)	HCV negative *n* = 112 % (*n*)	Unadjusted IRR
Socio-demographic characteristics				
Site (LA)	47.5 (77)	36.0 (18)	52.7 (59)	0.62 (0.39–1.01)†
Age, mean (SD)	21.35 (2.2)	21.8 (2.1)	21.1 (2.3)	1.11 (1.00–1.22)†
Sex at birth (Female) (*n* = 161)	36.0 (58)	38.8 (19)	34.8 (39)	1.12 (0.69–1.81)
Race (White) (*n* = 161)	63.4 (102)	74.0 (37)	58.6 (65)	1.65 (0.95–2.84)
Sexual identity (Heterosexual)	65.4 (106)	74.0 (37)	61.6 (69)	0.67 (0.39–1.15)
Poor/working class growing up (*n* = 161)	49.7 (80)	60.0 (30)	45.0 (50)	1.52 (0.94–2.44)†
Completed high school	63.0 (102)	56.0 (28)	66.1 (74)	0.75 (0.47–1.19)
Lifetime homelessness	94.4 (153)	96.0 (48)	93.8 (105)	1.41 (0.41–4.92)
History of institutionalization				
Incarceration	85.2 (138)	92.0 (46)	82.1 (92)	2.00 (0.79–5.05)
Drug treatment	68.5 (111)	76.0 (38)	65.2 (73)	1.45 (0.83–2.55)
Psychiatric hospital	49.4 (80)	52.0 (26)	48.2 (54)	1.11 (0.70–1.76)
Lifetime prescribed use				
Opioids	82.7 (134)	84.0 (42)	82.1 (92)	1.10 (0.58–2.08)
Tranquilizers	58.6 (95)	66.0 (33)	55.4 (62)	1.37 (0.83–2.25)
Stimulants	52.5 (85)	46.0 (23)	55.4 (62)	0.77 (0.49–1.23)
Lifetime drug using behaviours				
Sniffed PO	81.5 (132)	78.0 (39)	83.0 (93)	0.81 (0.47–1.38)
Smoked PO	24.7 (40)	18.0 (9)	27.7 (31)	0.67 (0.36–1.26)
Injected PO	72.2 (117)	92.0 (46)	63.4 (71)	4.42 (1.69–11.61)**
PO as substitute for heroin	65.4 (106)	88.0 (44)	55.4 (62)	3.87 (1.76–8.55)***
Injected Heroin (*n* = 161)	87.0 (140)	94.0 (47)	83.8 (93)	2.35 (0.80–6.90)
Cocaine (*n* = 161)	68.3 (110)	88.0 (44)	59.5 (66)	3.40 (1.55–7.48)**
1st injection – heroin (*n* = 155)	57.4 (89)	63.3 (31)	54.7 (58)	1.28 (0.78–2.08)
1st injection – PO	14.8 (24)	18.0 (9)	13.4 (15)	1.26 (0.71–2.25)
Age of 1st misuse of PO	14.6 (2.49)	14.4 (2.2)	14.7 (2.6)	0.96 (0.88–1.05)
Age of 1st injection of any drug (*n* = 156)	17.6 (6.3)	16.4 (2.2)	18.2 (7.4)	0.89 (0.83–0.96)**
Age of 1st PO injection (*n* = 117)	18.0 (2.59)	17.7 (2.8)	18.2 (2.5)	0.96 (0.88–1.05)
Duration of PO injection in years (*n* = 117)	3.4 (2.7)	4.1 (2.6)	2.9 (2.8)	1.10 (1.03–1.17)**
HCV testing (self-report)				
Age of HCV+ diagnosis	–	19.1 (2.5)	–	–

*** $p<0.001$,

** $p<0.01$,

† $p<0.10$.

Table 4

Covariate-adjusted associations between self-reported Hepatitis C virus (HCV) positivity and lifetime prescription opioid injection among 162 young IDUs[a].

Variable	Adjusted incidence rate ratio (IRR) (95% CI)
Injected PO	2.69 (1.07–6.78)*
PO substituted for heroin	2.28 (1.02–5.10)*
Poor/working class growing up	1.67 (1.09–2.57)*
Age	1.12 (1.02–1.23)*
Age of 1st injection of any drug	0.87 (0.80–0.94)***
Lifetime prescribed stimulants	0.64 (0.42–0.97)*

[a] All variables significant at $p<0.1$ found in Tables 2 and 3 were included in the initial model with the exception of "Duration of PO injection in years".

Including this variable would have reduced the analytical sample size to 117.

*** $p<0.001$,

* $p<0.05$.