Title

Sex differences in the multilevel determinants of injection risk behaviours among people who inject drugs in Tijuana, Mexico

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Abstract

Introduction and Aims: HIV and HCV transmission among people who inject drugs (PWID) is fueled by personal and environmental factors which vary by sex. We studied PWID in Mexico to identify sex differences in multilevel determinants of injection risk.

Design and Methods: From 2011-2013, 734 PWID (female: 277, male: 457) were enrolled into an observational cohort study in Tijuana. Participants completed interviews on injection and sexual risks. Utilizing baseline data, we conducted multiple generalized linear models stratified by sex to identify factors associated with injection risk scores (e.g., frequency of injection risk behaviors).

Results: For both sexes, difficult access to sterile syringes was associated with elevated injection risk (*b*=1.24, 95% confidence interval [CI]=1.16-1.33), using syringes from a safe source (e.g., needle exchange programs) was associated with lower injection risk (*b*=0.87, 95% CI=0.82-0.94), and for every one-unit increase in safe injection self-efficacy we observed a 20% decrease in injection risk (*b*=0.80, 95% CI=0.76-0.84). Females had a higher safe injection self-efficacy score compared to males (median=2.83 Interquartile range [IQR]=2.2-3 vs. median=2.83 [IQR=2-3], p=0.01). Among females, incarceration (*b*=1.22, 95% CI=1.09-1.36), and police confiscation of syringes in the past six months (*b*=1.16, 95% CI=1.01-1.33), were associated with elevated injection risk. Among males, sex work

(*b*=1.16, 95% CI=1.04-1.30), and polysubstance use in the past six months (*b*=1.22, 95% CI=1.13-1.31), were associated with elevated injection risk.

Discussion and Conclusions: Interventions to reduce HIV and HCV transmission among PWID in Tijuana should be sex-specific and consider multilevel determinants of injection risk to create safer drug use environments.

Keywords: people who inject drugs, injection risk behaviors, sex differences, HIV and HCV transmission, safe injection self-efficacy, and Mexico.

Introduction

Tijuana has one of the highest rates of illicit drug use consumption, and one of the largest populations of people who inject drugs (PWID) in Mexico (1–3). The prevalence of HIV among PWID in Tijuana is approximately 17.5 times higher than that among the general population in Mexico (3.5% verses 0.2%) (4). Further, 96% of PWID in Tijuana are living with hepatitis C (HCV) antibodies (anti-HCV) (5), which is nearly twice as high as the estimated prevalence of PWID living with anti-HCV worldwide (52.3%)(6). The spread of HIV and HCV among PWID is driven by the dynamic interaction between personal and environmental factors (7,8).

HIV and HCV risk among PWID in Tijuana is exacerbated by various environmental influences. Limited access to needle exchange programs (NEPs) reduces access to sterile syringes thereby increasing syringe sharing practices (9). Police confiscation of syringes also increases HIV and HCV risk by reducing access to injection equipment (10). Further, PWID's participation in sex work is associated with sexual and injection risk behaviors which are

driven by adverse sociostructural conditions (e.g., sexual violence and economic vulnerability) (11). Additionally, the high rates of methamphetamine and heroin injection in this region which are fueled by Tijuana's placement along a prominent drug trafficking route (1), are also associated with HIV and HCV infection via increased injection risk behaviors (12).

Worldwide HIV prevalence (13) and HCV incidence (14,15), tend to be significantly higher among female PWID compared to males. These disparities are driven by personal and environmental risk factors that vary by sex such as; stigma among female substance users (16), sexual violence (17), economic vulnerability (18), and participation in sex work (19). As such, drug use environments for male and female PWID are differentially shaped by multiple levels of HIV and HCV risk (16,19). However, despite these known sex disparities there is still a surprising lack of data disaggregated by sex among PWID globally, limiting our ability to uncover sex-related trends in the determinants of injection risk (16,20). More research is needed to examine sex differences in the correlates of injection risk in order to inform intervention efforts for male and female PWID, especially in low-and middle-income countries like Mexico.

To address this gap in research, we applied the social ecological model (SEM) and studied male and female PWID in Tijuana to identify sex differences in the personal and environmental factors associated with injection risk. We hypothesized that HIV and HCV risk factors (e.g., sex work,

incarceration, police confiscation, homelessness, and difficult to access sterile syringes) would differ by sex, such that females would experience greater barriers to practicing injection risk reduction compared to males. As such, this research will add to the body of literature on sex differences in the multilevel determinants of injection risk among PWID in Mexico, and may help inform the development of comprehensive sex-specific prevention packages for PWID in this region.

Methods

Theoretical Framework. SEM is a widely accepted theoretical framework that considers how individuals and environments interact (8,23,24). SEM recognizes the following five levels of influence on human behavior; intrapersonal, interpersonal, institutional, community and policy. Given the increasing recognition of various levels of HIV and HCV risk and the need to create multilevel prevention strategies, we used this framework to guide our research (Figure 1).

Baseline data were drawn from *'Proyecto El Cuete'* an ongoing prospective cohort study of PWID in Tijuana, Mexico. A detailed description of the study protocol has been published elsewhere (21). All study procedures were approved by Institutional Review Boards at the University of California, San Diego, and the University of Xochicalco in Tijuana. All participants provided written informed consent at baseline.

Recruitment, screening and enrollment. A total of 734 individuals were enrolled between 2011 and 2013. Participants were recruited using targeted sampling techniques (i.e., street-based outreach). Eligible participants were required to: 1) be at least 18 years old, 2) self-report injection drug use in the past month, 3) have visual evidence of injection drug use (e.g. track marks), 4) be able to speak English or Spanish, 5) be able to provide written informed consent, 6) have no plans to leave Tijuana for 24 months, 7) and report no current participation in an intervention study. All participants received $5.00 US dollars (USD) for completing the screening process.

Baseline survey. Participants completed a baseline assessment that lasted approximately 90 minutes, and was administered by trained bilingual and bicultural interviewers with extensive experience working with PWID in Mexico. To enhance the reliability and validity of self-reported sensitive behaviors (e.g., HIV risk behaviors), data were collected using computer-assisted participant interview software (22) and conducted in a private setting. Participants were compensated $20.00 USD at baseline.

Measures

Outcome. The primary outcome of interest was an “injection risk score”, which was modeled closely after a composite variable created for the Drug User’s Intervention Trial (26), and has demonstrated strong predictive validity in prior research (27,28). This score was calculated from an index of five likert-scaled variables assessing the frequency of injection risk behaviors

in the past six months. Response options include: never, sometimes, about half of the time, often, and always. These items were averaged to create an average injection risk score ranging from 1-5. Item five was reverse coded to ensure that higher values correspond to higher risk. This measure demonstrated good internal consistency (Cronbach's alpha=0.72). The items in this measure include: (1) *"Of the times you injected in the last six months, how often did you use a syringe that you knew or suspected that it had been used before by someone else?"* (2) *"Of the times you injected in the last six months, how often did you divide up drugs with somebody else by using a syringe?"* (3) *"Of the times you injected in the last six months, how often did you use a cooker, cotton, or water with someone or after someone else used it?"* (4) *"Of the times you injected in the last six months, how often did you buy drugs that came already prepared in a syringe?"* and (5) *"Of the times you injected in the last six months, how often did you inject with a new, sterile syringe?"*

Intrapersonal level factors. Informed by the SEM (25), variables that represent beliefs, behaviors, or individual characteristics were placed at the intrapersonal level. Age in years, self-reported sex (female sex/male sex), number of years of education completed starting at first grade, marital status (married/common law marriage verses single/divorced/separated or widowed), monthly average income of at least 3,500 Mexican pesos (yes/no), number of years lived in Tijuana, and the ability to speak English. Participants were also asked to report their age at first injection, which was

used to calculate the total number of years of injection drug use by subtracting each participant's current age from the age they reported first injecting. Data were also collected on substances injected at least twice a day or more in the past six months including: methamphetamine, and methamphetamine and heroin together.

We considered 'safe injection self-efficacy' using a six-item index that has been tested and validated among PWID in the United States (US) (29). Likert-scaled responses for this index include: absolutely sure I cannot, pretty sure I cannot, pretty sure I can, and absolutely sure I can. These items were averaged to create an average safe injection self-efficacy score ranging from 1-4, with higher scores representing higher levels of self-efficacy. This measure demonstrated strong internal consistency (Cronbach's alpha=0.94). The items in this measure include: (1) *"I can avoid injecting with a needle someone else has used, even if I am injecting with people I know well."* (2) *"I can avoid injecting with a needle someone else used even if I am dope sick or in withdrawal."* (3) *"I can avoid using cookers, cottons, or rinse water that someone else used, even if I am injecting with people I know well."* (4) *"I can avoid using my injecting partner's needle, even if we have shared needles before."* (5) *"I can avoid using my injecting partner's cooker, cotton, or rinse water, even if we've shared them before."* (6) *"I can avoid injecting with a needle someone else used, even if I have had sex without condoms with that person."*

Interpersonal level factors. Informed by the SEM (25), variables that represent relationships or power dynamics were placed at the interpersonal level. Sex work in the past six months (yes/no), was defined as receiving something one needed (e.g., money, drugs, food etc.) in exchange for sex in the past six months. Forced sex (yes/no) was defined as ever having been forced into having sex by someone using physical or emotional pressure.

Institutional level factors. Informed by SEM (25), variables which represent formal or informal regulations or implementation gaps were placed at the institutional level. Incarceration in the past six months, police confiscation of syringes without arrest in the past six months (yes/no), and reporting ever being beaten by law enforcement.

Community level factors. Informed by the SEM (25), variables which represent populations experiencing limited access to sources of community power were placed at the community level. Homelessness (e.g., sleeping in abandoned buildings and/or on the street) in the past six months (yes/no).

Policy level factors. Informed by the SEM (25), variables which represent or serve as proxies for public health policies were placed at the policy level. Used syringes from a ‘safe source’ (e.g., pharmacies, needle exchange programs (NEPs), hospitals or clinics) (yes/no), and finding it difficult to access sterile syringes in the past six months (yes/no).

Statistical analyses

Utilizing baseline data, we compared females and males with respect to factors in the SEM, using chi-square tests for dichotomous variables and depending on distributional assumptions T-tests or Wilcoxon Ranksum Tests for continuous variables (Table 1). Then, simple generalized linear regression models with a lognormal distribution stratified by sex were used to identify factors associated with injection risk by sex. Each exposure in bivariate analyses (Table 2) with a p-value ≤0.05 was explored further in adjusted analyses.

Multiple generalized linear regression models with a lognormal distribution stratified by sex were performed to estimate the association of statistically significant exposures from bivariate models with injection risk scores by sex, while controlling for identified confounders (Table 3). We controlled for the following factors that have been identified as correlates of injection risk among PWID in Tijuana (13): age, education, income, and length of residence in Tijuana. In order to avoid committing a “table two fallacy” (30,31), all primary exposures were estimated in separate models, and secondary effects were not interpreted. A “table two fallacy” is where one adjusts for primary effect measures and mistakenly reports and interprets these coefficients as total effects instead of controlled direct effects (30). All beta coefficients were exponentiated to facilitate interpretation. Analyses were conducted using STATA 14.2.

Results

Of 734 PWID, 277 (37.7%) were female and 457 (62.3%) were male. The average age was 37.4 (Standard deviation [SD]=8.9), and the median age at first injection was 14 (Interquartile range [IQR]=12.0-16.0). Over a third (39.4%) of the sample reported being able to speak English. One fifth of males (21.8%) reported ever having sex with another male (MSM).

Intrapersonal level differences by sex. Baseline comparisons of female and male PWID suggested that the two groups differed with respect to some intrapersonal level factors. Females were significantly younger compared to males (35.1 [SD=8.9], vs. 38.8 [SD=8.7], p<0.001), and initiated injection drug use at a significantly older age compared to males (median 15 [IQR=13.0-17.0] vs. 14 [IQR=12.0-16.0]). Males reported living in Tijuana for significantly longer durations compared to females (median=14.4 [IQR=8.0-21.0]) vs. median=10 [IQR=4.7-17.5], p<0.001). A higher proportion of females reported earning ≥ $3,500 Mexican pesos on average each month compared to males (32.6% vs. 24.5%, p=0.02). A significantly higher proportion of females reported being married compared to males (57.0% vs. 38.3%, p<0.001). Males reported a higher median number of years injecting drugs compared to females (18 [IQR=12.0-24.0] vs. 12 [IQR=5.0-20.0], p<0.001). Finally, females reported a higher median score for safe injection self-efficacy compared to males (2.8 [IQR=2.2-3.0] vs. 2.8 [2.0-3.0], p=0.01) (Table 1).

Interpersonal level differences by sex. A significantly greater proportion of females compared to males, reported engaging in sex work in

the past six months (65.7% vs. 10.7%, p<0.001), and reported ever being forced into having sex (35.9% vs. 3.9%, p<0.001) (Table 1).

Institutional level differences by sex. A greater proportion of males reported incarceration in the past six months compared to females (43.3% vs. 30.2%, p<0.001), and a significantly greater proportion of males reported ever being beaten by the police compared to females (64.8% vs. 22.5%, p<0.001) (Table 1).

Community level differences by sex. Females were significantly more likely to report being homeless in the past six months compared to males (33.2% vs. 23.4%, p<0.01) (Table 1).

Policy level differences by sex. A significantly greater proportion of males reported using syringes from a 'safe source' compared to females (51.9% vs. 34.7%, p<0.001) (Table 1).

In adjusted analyses, among both sexes finding it difficult to access sterile syringes was associated with a 24% increase in average injection risk scores (*b*=1.24, 95% CI=1.16-1.33). Using syringes from a 'safe source' was associated with a 13% decrease in average injection risk scores (*b*=0.87, 95% CI=0.82-0.94). Similarly, for every one-unit increase in safe injection self-efficacy we observed a 20% decrease in average injection risk scores (*b*=0.80, 95% CI=0.76-0.84).

Among females, incarceration and police confiscation of syringes in the past six months were associated with a 22% (*b*=1.22, 95% CI=1.09-1.36), and a 16% increase in average injection risk scores (*b*=1.16, 95% CI=1.01-

1.33), respectively. Among males, sex work and injecting methamphetamine and heroin together ≥ twice a day in the past six months were associated with a 16% (b=1.16, 95% CI=1.04-1.30), and a 22% increase in average injection risk scores (b=1.22, 95% CI=1.13-1.31), respectively.

Discussion

Our study examining sex differences in the determinants of injection risk among male and female PWID in Mexico identified several important findings. Among both sexes, safe injection self-efficacy and using syringes from a safe source were associated with lower injection risk. Also, finding it difficult to access sterile syringes was associated with elevated injection risk. Further, we uncovered several risk factors that were independently associated with injection risk and varied by sex. Sex work and polysubstance use were associated with elevated injection risk among males only. Recent incarceration and police confiscation of syringes were associated with elevated injection risk among females only. These findings may help inform the development of sex-specific interventions that seek to address the multilevel determinants of injection risk among PWID in Mexico.

The strong association between safe injection self-efficacy and lower injection risk has important implications for behavioral interventions that seek to reduce HIV and HCV transmission among PWID. According to former research, a sexual and injection risk reduction intervention increased safe injection self-efficacy which in turn decreased receptive needle sharing among female sex worker-PWID in the Mexico-US border region (32). This

suggests that safe injection self-efficacy can be enhanced through behavioral interventions. Based on our findings, we recommend that interventions aiming to reduce the spread of HIV and HCV among PWID utilize strategies to enhance safe injection self-efficacy. Our study adds to the body of literature on safe injection self-efficacy (26,32–34), by showing how it is associated with risk reduction for both male and female PWID in Tijuana. This is promising as it suggests that safe injection self-efficacy may act as a buffer against injection risk behaviors for both sexes. As such, this study fills an important gap in research regarding the correlates of safer injection practices among PWID in Mexico.

We also found that using syringes from a safe source was associated with lower injection risk, and finding it difficult to access sterile syringes was associated with elevated injection risk. These findings underscore the importance of harm reduction programs in reducing injection risk by providing free access to sterile injection equipment, offering risk reduction counseling and providing referrals to health and social services (35–37). Unfortunately, in February of 2013 the Global Fund for HIV, Tuberculosis and Malaria withdrew support for NEPs in Mexico due to their rising gross domestic product (38). Consequently there are only two sanctioned NEPs in Tijuana serving an estimated 6,000-10,000 PWID (39). Based on our findings we recommend: reinstating funding for NEPs, in order to increase access to sterile injection equipment and facilitate connections to key health and social services for PWID in Tijuana (35).

Interestingly, we found that sex work was associated with an increase in injection risk among males only. One potential explanation for this finding is that the majority of males in our sample who reported sex work were also MSM (data not shown; 83.7%), and HIV and HCV prevention service coverage among MSM in Tijuana remains low (40,41). Further, sex work among males in Tijuana may be less organized compared to sex work among females, which may contribute to greater risk overall. Similarly, other studies among PWID in Canada and the US found independent associations between needle sharing and homosexual and bisexual sex, which may have been explained by sex work that was underreported (42,43). Our finding underscores the need to increase access to harm reduction services for this subpopulation of PWID in order to reduce the excess risk associated with injection drug use.

This study also found that polysubstance use (i.e., methamphetamine and heroin co-injection) was associated with elevated injection risk among males only. Former research among PWID in Estonia and Russia found that opiate and stimulant co-injection was associated with injection and sexual risk behaviors, but no differences by sex were reported (Tavitian-Exley et al., 2018). Similarly, research among PWID in Tijuana found that polydrug use was independently associated with HIV risk, but no differences by sex were found (12,44). Findings from our study add to this body of literature (12,44,45) by demonstrating sex differences in the relationship between polysubstance use and injection risk. Future interventions in Tijuana should: scale-up access to medication-assisted treatments for opioid use disorder

(46), develop pharmacotherapies for stimulant use disorder (47), and consider delivering medication treatments in conjunction with proven behavioral therapies (48).

In our study, recent incarceration was associated with elevated injection risk for females only. In Latin America, the number of women incarcerated nearly doubled between 2006 and 2011 when recruitment for this study began, and the vast majority (60-80%) of these women were incarcerated for non-violent drug-related crimes (49). Incarceration has been shown to increase HIV and HCV risk among PWID in several settings (50,51), but these studies reported no evidence that the impact of incarceration on injection risk was greater among females compared to males. Findings from this study expand upon former research (50,51) by demonstrating that the impact of incarceration on injection risk is differentially associated with sex among PWID in Mexico.

The association between police confiscation of syringes and elevated injection risk among female PWID maps onto former research conducted among PWID in Mexico, which documented that such punitive policing practices increase syringe sharing (10,52–56). In Mexico, syringe purchase and possession without a prescription is legal, therefore this finding also highlights a significant implementation gap (54,55). Our results support this previous work, suggesting that policing practices in Tijuana continue to exacerbate injection risk especially among female PWID. Interventions should aim to: enhance law enforcement’s knowledge of harm reduction,

reduce stigma among female PWID, and ensure that policing practices are consistent with current drug policy and international guidelines (57).

Although this study provides important insight into the factors that differentially shape injection risk for male and female PWID in Mexico, our study has limitations. We used non-probability sampling methods which limits the generalizability of our findings to PWID in other settings. We used cross-sectional data, which limits our ability to draw causal inferences and assess temporal associations. Future research should examine whether the factors associated with injection risk predict behavior change in longitudinal analyses. Baseline data were collected between 2011 and 2013 and may not represent current trends among PWID in Tijuana, which further limits the generalizability of our findings. Although the outcome measure for this study was modeled closely after a measure used in a large intervention trial designed to reduce sexual and injection risk among PWID (26), it has not been psychometrically validated. However, it is important to note that this measure has demonstrated strong predictive validity (27,28), and internal consistency. Responses on injection risk from female PWID may be subject to differential misclassification bias, which can arise from heightened stigma among women who use drugs. Finally, our measure of safe injection self-efficacy may not accurately capture the experiences of female PWID who rely on male partners for drug injection.

In summary, this study shows how personal and environmental factors contribute to injection risk and differ markedly by sex among PWID in

Mexico. In doing so, this study highlights several key factors which shape injection risk among male and female PWID. As such, findings from this study may help inform the development of comprehensive sex-specific interventions that address several levels of HIV and HCV risk.

Contributors: JPJ, EVP, BSW and SS conceived of the study design. JPJ analyzed the data. JPJ, led the manuscript with feedback from EVP, SS and BSW. PGZ and GR oversaw data collection and in Mexico. All authors reviewed and approved of the final version of this manuscript.

Conflicts of interest: None.

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Table 1. Intrapersonal, interpersonal, institutional, community and policy level factors among females and males who inject drugs in Tijuana, Mexico (N=734)

	Females (n=277) n (%)	**Males (n=457) n (%)**	***P***	**Total (N=734) N (%)**
Intrapersonal level factors				
Average age (standard deviation=SD)	35.1 (8.9)	38.8 (8.7)	<0.001	37.4 (8.9)
Median age at first injection (Interquartile range [IQR])	15 (13-17)	14 (12-16)	<0.001	14 (12-16)
Married[1]	158 (57.0)	175 (38.3)	<0.001	333 (45.4)
Median number of years of education since first grade (IQR)	8 (6-11)	8 (6-9)	0.06	8 (6-10)
English speaking	116 (41.9)	173 (37.9)	0.28	289 (39.4)
Earned at least 3,500 Mexican pesos on average monthly[2]	90 (32.6)	111 (24.5)	0.02	201 (27.5)
Median number of years lived in Tijuana (IQR)	10 (4.7-17.5)	14.4 (8-21)	<0.001	12 (6-20)
Males reporting ever having sex with another male (MSM)	--	160 (35.24)	--	160 (21.8)
Median number of years injecting drugs (IQR)[3]	12 (5-20)	18 (12-24)	<0.001	16 (9-22)
Methamphetamine and heroin co-injection ≥ twice a day+	86 (31.1)	171 (37.4)	0.08	257 (35.0)
Methamphetamine injection ≥ twice a day+	38 (13.7)	58 (12.7)	0.70	96 (13.1)
Median safe injection self-efficacy score (Range: 1-	2.83 (2.2-3)	2.83 (2-3)	0.01	2.83 (2-3)

4) (IQR)[4]				
Median injection risk score (Range: 1-5) (IQR)[5]	2.2 (1.6-3)	2.2 (1.6-2.8)	0.10	2.2 (1.6-2.8)
Injection risk indicators				
Syringe sharing ≥ half of the time+	103 (37.2)	145 (31.7)	0.13	248 (33.8)
Syringe mediated drug sharing[6] ≥ half of the time+	95 (34.4)	172 (37.7)	0.37	267 (36.5)
Injection equipment sharing ≥ half of the time+	137 (49.6)	218 (47.8)	0.63	355 (48.5)
Bought drugs already prepared in a syringe ≥ half of the time+	16 (5.8)	26 (5.7)	0.94	42 (5.8)
Used a sterile syringe for each injection ≥ half of the time+	140 (50.9)	227 (49.8)	0.77	367 (50.2)
Interpersonal level factors				
Sex work+[7]	176 (65.7)	49 (10.7)	<0.001	225 (31.0)
MSM who reported sex work[8]	---	41.0 (9.0)	---	41.0 (9.0)
Ever forced into having sex[9]	99 (35.9)	18 (3.9)	<0.001	117 (16.0)
Institutional level factors				
Incarceration+	83 (30.2)	198 (43.3)	<0.001	281 (38.4)
Syringe confiscation by police+	37 (13.4)	46 (10.1)	0.17	83 (11.3)
Ever beaten by the police	62 (22.5)	296 (64.8)	<0.001	358 (48.8)
Community level factors				
Homeless[10]+	92 (33.2)	107 (23.4)	<0.1	199 (27.1)
Policy level factors				
Used syringes from a safe source[11]+	96 (34.7)	237 (51.9)	<0.001	333 (45.4)
Found it hard to access new or sterile syringes+	49 (17.7)	87 (19.1)	0.63	136 (18.6)

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