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Article *in* Journal of Urban Health · August 2017

DOI: 10.1007/s11524-017-0188-4

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Non-injection Drug Use and Injection Initiation Assistance among People Who Inject Drugs in Tijuana, Mexico

Amen Ben Hamida · Claudia Rafful · Sonia Jain · Shelly Sun · Patricia Gonzalez-Zuniga · Gudelia Rangel · Steffanie A. Strathdee · Dan Werb

Abstract Although most people who inject drugs (PWID) report receiving assistance during injection initiation events, little research has focused on risk factors among PWID for providing injection initiation assistance. We therefore sought to determine the influence of non-injection drug use among PWID on their risk to initiate others. We used generalized estimating equation (GEE) models on longitudinal data among a prospective cohort of PWID in Tijuana, Mexico (*Proyecto El Cuete IV*), while controlling for potential confounders. At baseline, 534 participants provided data on injection initiation assistance. Overall, 14% reported ever initiating others, with 4% reporting this behavior recently (i.e., in the past 6 months). In a multivariable GEE model, recent non-injection drug use was independently associated with providing injection initiation assistance (adjusted odds ratio [AOR] = 2.42, 95% confidence interval [CI] = 1.39–4.20). Further, in subanalyses examining specific drug types, recent non-injection use of cocaine (AOR = 9.31, 95% CI = 3.98–21.78), heroin (AOR = 4.00, 95% CI = 1.88–8.54), and methamphetamine (AOR = 2.03, 95% CI = 1.16–3.55) were all significantly associated with reporting providing injection initiation assistance. Our findings may have important implications for the development of interventional approaches to reduce injection initiation and related harms. Further research is needed to validate findings and inform future approaches to preventing entry into drug injecting.

Keywords Injection initiation · Injection drug use · People who inject drugs · Non-injection drug use · Tijuana · Border health · Prevention

A. Ben Hamida · C. Rafful · P. Gonzalez-Zuniga · S. A. Strathdee · D. Werb
Division of Global Public Health, University of California San Diego, San Diego, CA, USA

A. Ben Hamida · C. Rafful
Graduate School of Public Health, San Diego State University, San Diego, CA, USA

S. Jain · S. Sun
Department of Family Medicine and Public Health, Biostatistics Research Center, University of California San Diego, San Diego, CA, USA

G. Rangel
Secretariat of Health, Mexico City, Mexico

G. Rangel
Mexico-United States Border Health Commission, El Paso, TX, USA

D. Werb
Centre for Urban Health Solutions, St. Michael's Hospital, Toronto, ON M5B 1W8, Canada

D. Werb (✉)
University of California School of Medicine, 9500 Gilman Drive, La Jolla, CA 92093-0507, USA
e-mail: dwerb@ucsd.edu

Introduction

Twelve million people are estimated to inject drugs worldwide [1]. People who inject drugs (PWID) are more susceptible to human immunodeficiency virus (HIV)

Published online: 16 August 2017

transmission compared with other adults [2], leading to an estimated 1.6 million HIV-seropositive PWID worldwide [1]. Hepatitis C virus (HCV) is also a significant cause of morbidity among PWID, with an estimated 6 million PWID worldwide believed to be HCV-seropositive [1], which represents a leading cause of death among this population, particularly among those co-infected with HIV [3–6]. Furthermore, PWID are exposed to a higher risk of cutaneous infections [7], infective endocarditis [8], and fatal drug overdose [9]. Given these many harms, experts have increasingly focused on preventing the initiation of injection drug use itself as a way to reduce the risk of a variety of negative health and social outcomes [10–12]. Data suggest that street-involved youth may progress quickly to regular injection drug use after the first experimentation with injecting [13], and that the risk of acquiring HIV, HCV, and other blood-borne pathogens is very high within the first few months and years after injection initiation [14–18]. As such, preventing entry into injection drug use is increasingly seen as a public health priority [10–12, 19].

Tijuana, Baja California, is a Mexican city situated on the western Mexico-USA border, on a major migration and drug trafficking route [20] stretching from the coca-producing Andean region in South America to Canada. Tijuana's location along this route has made it particularly vulnerable to a range of drug-related problems. In 2003, for instance, it was estimated that about 6000 PWID injected in semi-public settings such as "shooting galleries" in the city [21] although the total PWID population is likely closer to 10,000 [22]. Studies conducted in Tijuana have estimated HIV prevalence at 4% [22] as well as an HIV incidence rate of 2.18 per 100 person-years among PWID [23].

To date, research on injection initiation has largely focused on the characteristics and circumstances of first injection events largely from the perspective of the individual being initiated [24]. Importantly, having peers, friends, or intimate partners who inject drugs has been repeatedly shown to be a risk factor for injection initiation [14, 25–31]. However, fewer studies have investigated the specific characteristics of persons who already inject drugs and who provide initiation assistance to others, despite the fact that the majority of sampled PWID report receiving assistance with their first injection [26, 32]. While more research is needed, individual characteristics identified as possible risk factors for initiating other people into injection include being unemployed [32, 33], having described how to inject to non-injectors [34], having ever spoken positively about injecting to a non-injector [32], having been in prison or detention [35], and having obtained needles and syringes from informal sources such as friends and dealers [35]. However, existing studies have also been limited by small sample sizes [32] and cross-sectional designs [26, 32–35].

Non-injection drug use generally precedes injection initiation, with some drugs, such as heroin [14, 31], cocaine [14, 31], methamphetamine [36], and certain opioids [37, 38] shown to be associated with this transition among injection-naïve drug users. However, there remain knowledge gaps regarding the impact that the use of non-injection drugs by PWID may have on their risk of initiating others into injecting, particularly in settings characterized by large high-risk drug-using populations. Indeed, to our knowledge, only one cross-sectional study has investigated this topic, finding that recent non-injection powder cocaine use among PWID in California was associated with providing injection initiation assistance [34]. We therefore sought to investigate the impact of non-injection drug use on the risk of providing injection initiation assistance among a prospective cohort of PWID in Tijuana, Mexico. We hypothesized that non-injection drug use among PWID is associated with higher rates of injection initiation.

Methods

Preventing Injecting by Modifying Existing Responses (PRIMER) is an on-going international multisite prospective study seeking to assess the impact of a range of socio structural factors on the risk that PWID initiate others into drug injecting. The methods used in the PRIMER study have been previously described [39]. In brief, PRIMER includes quantitative data from existing cohort studies of PWID to assess risks associated with their provision of injection initiation assistance. Because we sought to determine the potential impact of non-injection drug use among PWID in a high-risk, under-resourced setting, the present analysis was restricted to data from participants in the *Proyecto El Cuete IV* (ECIV) cohort in Tijuana, Mexico.

Study Sample and Recruitment

ECIV participants are community-recruited, with eligibility restricted to individuals who are over 18 years old, report recent injection drug use (i.e., in the last 6 months), and speak either Spanish or English. Written

consent is obtained from each participant prior to enrolment. All participants receive financial compensation for their time commitment.

Data Collection and Variable Definition

The PRIMER baseline was defined as the visit at which questions specific to the provision of injection initiation assistance were first introduced into the ECIV questionnaire. For most participants ($n = 475$), baseline interviews coincided with follow-up 7 (September 2014). However, some participants missed visit 7 and thus, the PRIMER questions were first introduced to them at follow-up 8 or later (29 at follow-up 8; 20 at follow-up 9; 5 at follow-up 10; and 3 at follow-up 11). At baseline and at 6-month follow-up intervals, participants completed interviewer-administered questionnaires on their involvement in providing injection initiation assistance, including specific experiences initiating others into injecting, motivations for doing so, the relationships between initiators and initiates, and participants' perceived risk of initiating others into injecting in the future. For the purpose of this study, ECIV follow-up 7 was translated to PRIMER visit 1. Longitudinal data from September 2014 (PRIMER visit 1) to August 2016 (PRIMER visit 5) were included in the analysis. The main outcome measure was defined as reporting the provision of injection initiation assistance in the past 6 months. The main independent variable of interest was defined as any recent (i.e., past 6 months) non-injection drug use. Further, non-injection and injection drug use in the past 6 months was stratified by drug type (i.e., heroin, cocaine, methamphetamine, and other opioids). Other independent variables considered in the analyses included age, gender, housing situation, and injection frequency.

Analysis

Cross-sectional analyses were performed at the PRIMER baseline. Univariate cross-tabulations along with Fisher's exact test were used to assess the association between baseline demographics and drug use characteristics, and the provision of recent injection initiation assistance.

To incorporate longitudinal data, we used generalized estimating equation (GEE) methods, which allow for the determination of independent associations between variables across follow-ups, while adjusting for within-subject correlation among participants who provide data at multiple time points [40]. Participants providing data for at least one visit were included in the models. The dependent variable was defined as recent (i.e., past 6 month) provision of injection initiation at each visit (yes vs. no). The main independent variable of interest was recent non-injection drug use (yes vs. no) at each visit. We employed an a priori approach whereby variables assessing participants' socio-demographic (i.e., age, gender, and housing situation [stable vs. other]) and injection frequency (i.e., daily vs. less than daily vs. none) were included in the final multivariable model. First, we examined the independent impact of recent non-injection use of any drug on injection initiation assistance. We then carried out subanalyses wherein we developed multivariable GEE models to investigate the impact of recent non-injection use of specific types of drugs (i.e., heroin, cocaine, and methamphetamine) on the provision of injection initiation assistance.

All statistical analyses were performed using R statistical software (version 3.3.2).

Results

Baseline Data

Overall, study participants ($n = 534$) were predominantly male (62%, 329) and ranged in age from 21 to 67 years old (median = 40, interquartile range [IQR] = 35–47). At baseline, 14% ($n = 76$) of participants reported ever providing injection initiation assistance, while 4% ($n = 23$) participants reported initiating others in the past 6 months. The median number of initiates per initiator in the past 6 months was 2 (IQR = 1–3).

The majority of the participants (83%, 442) reported having recently injected at least one drug. The largest proportion of participants reported injecting heroin in the past 6 months (81%, 433), followed by methamphetamine (53%, 283) and cocaine (1%, 6), while no participant reported having recently injected opioids. The median number of years injecting was 20 (IQR = 13–26) and the majority of participants reported injecting daily (76%, 404).

Approximately one third of participants (33%, 178) reported having used at least one drug by non-injection recently. Methamphetamine was the most commonly used non-injection drug among participants in the past 6 months (32%, 169), followed by heroin (4%, 20) and cocaine (1%, 6). Methamphetamine was mostly

uniquely smoked (95%, 161), while heroin was mostly uniquely snorted (55%, 11), and half of non-injection cocaine users reported uniquely snorting it (50%, 3). Only one participant reported using opioids via non-injection in the last 6 months (by swallowing).

In univariate cross-tabulations, being man ($p = 0.046$) and having reported non-injection use of cocaine ($p = 0.024$) or opioids ($p = 0.043$) in the 6 months prior to baseline were associated with providing injection initiation assistance (Table 1).

Longitudinal Data

Across the study period (i.e., visit 1 to visit 5), providing injection initiation assistance in the last 6 months ranged from 1.64% in visit 3 ($n = 7$) to 4.84% in visit 1 ($n = 23$). In bivariate analysis, non-injection use of any drug was significantly associated with injection initiation for both visit 3 and visit 5 ($p = 0.009$) (Table 2).

In the GEE multivariable model, recent non-injection use of any drug was independently associated with providing injection initiation assistance (adjusted odds ratio [AOR] = 2.42; 95% confidence interval [CI] = 1.39–4.20). In subanalyses exploring the impact of specific types of non-injection drug use in separate GEE models, recent non-injection use of cocaine (AOR = 9.31, 95% CI = 3.98–21.78), heroin (AOR = 4.00, 95% CI = 1.88–8.54), and methamphetamine (AOR = 2.03, 95% CI = 1.16–3.55) were all significantly associated with providing injection initiation assistance (Table 3).

Table 1 Baseline characteristics stratified by injection initiation assistance in the past 6 months among a cohort of people who inject drugs in Tijuana, Mexico, 2014–2016 ($n = 532$)

Characteristic	Injection initiation assistance		*p* value
	No $n = 509$	Yes $n = 23$	
Age			
(Median, IQR)	40.5 (34.7–47.0)	39.2 (37.4–44.3)	0.931
Sex			
Women	201 (98.1%)	4 (2.0%)	*0.046*
Men	308 (94.2%)	19 (5.8%)	
Housing situation			
Stable housing	316 (95.8%)	14 (4.2%)	>0.999
Other	193 (95.5%)	9 (4.5%)	
Non-injection heroin			
No	490 (95.7%)	22 (4.3%)	0.594
Yes	19 (95.0%)	1 (5.0%)	
Non-injection cocaine			
No	505 (96.0%)	21 (4.0%)	*0.024*
Yes	4 (66.8%)	2 (33.3%)	
Non-injection crystal methamphetamine			
No	350 (96.2%)	14 (3.9%)	0.492
Yes	159 (94.6%)	9 (5.4%)	
Non-injection any drug			
No	342 (96.3%)	13 (3.7%)	0.365
Yes	167 (94.4%)	10 (5.7%)	
Injection drug use frequency			
None	89 (96.7%)	3 (3.3%)	0.927
Less than daily	36 (97.3%)	1 (2.7%)	
Daily	384 (95.3%)	19 (4.7%)	

Note: *IQR* interquartile range, $p < 0.05$ are italicized

Discussion

Within a prospective cohort of PWID in Tijuana, 14% of participants reported having ever provided injection initiation assistance, and 4% reported initiating others in the 6 months prior to the PRIMER baseline. In multi-

Table 2 Univariate associations between non-injection drug use and injection initiation assistance in the past 6 months among a prospective cohort of people who inject drugs in Tijuana, Mexico, 2014–2016 ($n = 1987$ participant visits)

Any non-injection drug use	Injection initiation		*p* value
	No	Yes	
Visit 1 ($n = 475$)			
No	301 (95.9%)	13 (4.1%)	0.368
Yes	151 (93.8%)	10 (6.2%)	
Visit 2 ($n = 463$)			
No	312 (97.5%)	8 (2.5%)	>0.999
Yes	140 (97.9%)	3 (2.1%)	
Visit 3 ($n = 428$)			
No	275 (99.6%)	1 (0.4%)	*0.009*
Yes	146 (96.1%)	6 (4.0%)	
Visit 4 ($n = 371$)			
No	233 (97.9%)	5 (2.1%)	0.127
Yes	126 (94.7%)	7 (5.3%)	
Visit 5 ($n = 250$)			
No	170 (97.7%)	4 (2.3%)	*0.009*
Yes	68 (89.5%)	8 (10.5%)	

Note: $p < 0.05$ are italicized

Table 3 Adjusted odds ratios for non-injection of different drugs related to the provision of injection initiation assistance among people who inject drugs, in Tijuana, Mexico, 2014–2016 (n = 1987 participant visits)

	GEE model 1 (any non-injection drug use)		GEE model 2 (non-injection cocaine use)		GEE model 3 (non-injection heroin use)		GEE model 4 (non-injection methamphetamine use)	
	AOR	95% CI	AOR	95% CI	AOR	95% CI	AOR	95% CI
Any non-injection drug use[a]	2.42	*[1.39–4.20]*						
Non-injection cocaine use[a]			9.31	*[3.98–21.78]*				
Non-injection heroin use[a]					4.00	*[1.88–8.54]*		
Non-injection methamphetamine use[a]							2.03	*[1.16–3.55]*
Age	0.97	*[0.94–1.00]*	0.97	[0.95–1.00]	0.97	*[0.94–1.00]*	0.97	*[0.94–1.00]*
Male gender	2.5	*[1.27–4.93]*	2.13	*[1.09–4.16]*	2.22	*[1.14–4.35]*	2.40	*[1.22–4.69]*
Stable housing[a]	0.75	[0.46–1.23]	0.71	[0.44–1.16]	0.71	[0.44–1.15]	0.74	[0.45–1.21]
Injecting frequency: less than daily[a]	0.71	[0.12–4.04]	0.88	[0.17–4.64]	0.84	[0.17–4.08]	0.73	[0.13–4.14]
Injecting frequency: daily[a]	1.80	[0.74–4.38]	1.95	[0.79–4.81]	1.99	[0.82–4.86]	1.81	[0.74–4.41]

$p < 0.05$ are italicized

GEE generalized estimating equation, *AOR* adjusted odds ratio, *CI* confidence interval

[a] In the past 6 months

variable analysis, multiple forms of non-injection drug use were associated with recently providing injection initiation assistance. These findings have implications for future research as well as efforts to prevent the entry of individuals into injection drug use.

Reporting recent non-injection use of cocaine or heroin was associated with a tenfold and fourfold increase, respectively, in the odds of reporting recent injection initiation assistance (though low frequencies of non-injection cocaine use in the sample contributed to wide confidence intervals), while non-injection use of methamphetamine was associated with a doubling of the odds. To our knowledge, the impact of non-injection drug use among potential initiators has not yet been extensively studied (the present study building on only one previous cross-sectional study by Bluthenthal and colleagues [34]). These findings provide further confirmation of the central role that non-injection drug use among PWID appears to play in increasing the risk that others will be initiated into drug injecting.

We posit that use of non-injection drugs by PWID may reflect their greater participation in social networks that include injection-naïve drug users. The interaction between PWID and non-injectors in drug-using settings may weaken social norms protective against injecting and may also provide injection-naïve drug users with access to sources of injection education and initiation assistance through increased exposure to injecting practices. This suggests that efforts to prevent epidemics of drug-related harms (i.e., blood-borne disease transmission and overdose) may require approaches that seek to reduce the risk of injection initiation assistance posed by PWID, particularly those that engage in both injection and non-injection forms of drug use. In this regard, interventions such as medically supervised consumption facilities (i.e., for either non-injection [inhalation] or injection drug use) have been shown to reduce a range of drug-related harms [41–45]; our findings suggest that they may also reduce the risk that PWID expose injecting behaviors to others, and thereby disrupt population mixing between PWID and those at risk of initiating drug injecting. As such, future research should seek to clarify to what extent such facilities may support broader goals of preventing entry into injection drug use. Further, given the well-established role of PWID in initiating others into drug injecting [26, 32], our findings suggest that the development of interventions to prevent injection initiation should focus specifically on the subset of PWID who report both injection and non-injection drug use, as they likely act as a bridge population facilitating entry into drug injecting, and that programming such interventions for PWID who use cocaine by non-injection should be explored. Further research delineating the risk profile of such individuals will be required to optimize intervention development in this area.

Finally, we note that studies investigating injection initiation assistance in other settings have reported that PWID samples report initiating others in proportions ranging from 17 to 69% [26, 32–35]. While these differences may be attributed to variations in inclusion criteria, study designs, sampling techniques, and study settings, it is worth noting that the proportion of ECIV participants reporting lifetime history of initiating others is lower than Bryant's study (17%), which was limited to young and new injectors [35]. This suggests that ECIV study participants may initiate others at uniquely low levels. More research, including studies employing qualitative or mixed-methods designs, may be useful to investigate the context for these differences and their potential applicability to injection prevention goals.

Our study results should be viewed in light of some potential limitations typical of observational research among drug-using populations. First, study recruitment relied on non-randomized methods, and we therefore caution against generalization of findings to the broader population of PWID in Tijuana. Second, the survey questionnaire relied on self-reporting and, consequently, in addition to the possibility for recall bias, the social norms and stigma related to injection drug use in general and injection initiation in particular likely resulted in under-reporting on these topics [46, 47]. However, we know of no reason why this phenomenon may have differentially impacted participants who did and did not report non-injection drug use. Third, this is an ongoing prospective community-recruited study. As such, some participants may not have reached their last visit when we started analyzing the data. Fourth, this study focused on the specific effects of the use of individual drugs by non-injection. We note that a study conducted recently by Meacham and colleagues in the same setting suggested that poly-drug and poly-route users may represent specific subgroups with an increased risk of engaging in HIV risk behaviors [48]. This may underline the need for future research studies to assess whether these subgroups are at greater risk of providing injection initiation assistance.

Lastly, it is worth noting that the majority of existing longitudinal studies on injection initiation have been conducted in high-income settings (i.e., the Netherlands, Canada, and the USA) [36, 49, 50], characterized by relatively stable PWID populations that face fewer daily risks related to drug law enforcement compared with Tijuana [51–54]. For instance, during the spring of 2015, the municipal government in Tijuana undertook a forced evacuation of the river canal encampment known as "*El Bordo*," where many homeless PWID and other vulnerable populations such as recent deportees resided [55]. The evacuation was conducted by police raids and many of the canal residents, which included some ECIV participants, were placed in mandatory rehabilitation centers, prison, or have not been located.

In conclusion, this study reports on an independent association between non-injection drug use and the provision of injection initiation assistance observed among PWID in Tijuana, Mexico, an under-resourced setting characterized by a large and dynamic population of PWID. These findings have important implications for the development of interventional approaches to reduce injection initiation and related harms.

Acknowledgements Dan Werb is supported by a grant to the PRIMER study from the National Institute on Drug Abuse (NIDA DP2-DA040256-01) and by the Canadian Institutes of Health Research via a New Investigator Award. El Cuete IV is also supported by NIDA via a MERIT Award (R37 DA019829). C. Rafful was supported by a UC-MEXUS/CONACyT scholarship grant number 209407/313533, the UC MEXUS Dissertation grant number DI 15-42, and R25 DA026401.

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