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## THE IMPACT OF RECENT HOMELESSNESS ON THE PROVISION OF INJECTION DRUG USE INITIATION ASSISTANCE AMONG PERSONS WHO INJECT DRUGS IN TIJUANA, MEXICO AND VANCOUVER, CANADA

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### Abstract

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Each author contributed to the production of this article and approved this final version for submission. Charles Marks contributed to manuscript production (original writing), project conceptualization, analytic design, and data analysis. Zachary Bouck contributed to manuscript production (editing) and analytic design. Sonia Jain contributed to data curation and analytic design. Xiaoying Sun contributed to data curation and analytic design. Steffanie A. Strathdee contributed to data collection and manuscript production (editing). Peter Vickerman contributed to manuscript production (editing). Kora DeBeck contributed to data collection and manuscript production (editing). M-J Milloy contributed to data collection and manuscript production (editing). Kanna Hayashi contributed to data collection and manuscript production (editing). Dan Werb contributed to project conceptualization, funding acquisition, analytic design, data collection, project supervision, and manuscript production (editing).

#### Declaration of Competing Interest

The authors report no declarations of interest.

**Appendix A.** Supplementary data

**Objective**—To assess the relationship between experiencing homelessness and assisting injection drug use (IDU) initiation among people who inject drugs (PWID) in Tijuana, Mexico and Vancouver, Canada.

**Methods**—We used self-reported questionnaire data collected semi-annually on PWID from Tijuana (n = 703) and Vancouver (n = 1551) between 2014 and 2017. Within each setting, the effect of recent (i.e., past six months) homelessness on recent provision of injection initiation assistance (i.e., helping anybody inject for the first time in the past six months) was estimated using inverse-probability-of-treatment (IPT)-weighted estimation of a marginal structural model.

**Results**—Across follow-up, the prevalence of recent homelessness at a given visit ranged from 11.6%–16.5% among Tijuana-based participants and 9.4%–18.9% among Vancouver-based participants; the prevalence of recent provision of injection initiation at a given follow-up visit was lower, ranging from 3.3%–5.4% in Tijuana and 2.5%–4.1% in Vancouver. Based on the IPT-weighted estimates, recent homelessness was associated with 66% greater odds among Tijuana-based PWID (Adjusted Odds Ratio [AOR] = 1.66; 95% CI: 1.01–2.73) and 47% greater odds among Vancouver-based PWID (AOR = 1.47, 95% CI: 1.02–2.13) of providing injection initiation assistance over the same six-month period.

**Conclusion**—We found that recently experiencing homelessness was associated with an increased likelihood of PWID reporting IDU initiation assistance over time in both Tijuana and Vancouver. Addressing homelessness may decrease the initiation of IDU via multiple pathways.

## Keywords

Injection drug use; People who inject drugs; Homelessness; Housing instability

## 1. INTRODUCTION

People who inject drugs (PWID) are disproportionately impacted by harms associated with injecting, including overdose and infection with HIV and hepatitis C virus (Degenhardt et al., 2017; Gicquelais et al., 2019). Relatedly, people who experience homelessness (defined differently across studies and contexts, but generally understood as the chronic or episodic condition of not having a residence to meet basic living needs such as sleeping) are at increased risk of initiating injection drug use (IDU) (Feng et al., 2013; Roy et al., 2003). Between 40%–61% of PWID in North America are estimated to have experienced homelessness in the prior year (Degenhardt et al., 2017). PWID who experience homelessness are subject to additional structural and environmental barriers—such as poverty and exposure to violence—that amplify the IDU-related harms they face (Latkin et al., 2013; Wenger et al., 2016). Further, among PWID, experiencing homelessness is associated with an additional elevated risk of acquiring HIV and hepatitis C (Arum et al., 2021). While preventing injection-naïve individuals from transitioning into IDU has long been a public health goal (Vlahov et al., 2004), better characterizing the role of homelessness in transitions into IDU could directly inform strategies to respond to some of the upstream drivers of IDU-related morbidity and mortality.

Recent research has highlighted the key role of experienced PWID in assisting injection-naïve individuals initiating IDU (Bluthenthal et al., 2015; Werb et al., 2016). Across study

samples, between 75%–95% of PWID reported that their IDU initiation was assisted by established PWID (Gicquelais et al., 2020). While research has demonstrated that experiencing an episode of homelessness in the past six months (referred to hereafter as ‘recent homelessness’) increases the risk that injection-naïve individuals initiate IDU (Feng et al., 2013; Roy et al., 2003), there is a lack of research concerning the relationship between recent homelessness and the provision of IDU initiation assistance among PWID. In fact, prior studies of IDU initiation assistance have operationalized recent homelessness or housing status as a covariate to be controlled for in subsequent analyses, rather than as a critical factor in and of itself (Gicquelais et al., 2020; Marks et al., 2019). In the present study, we therefore assessed the association between recent homelessness and providing IDU initiation assistance among PWID from two cities in North America (Tijuana, Mexico and Vancouver, Canada).

## 2. METHODS

### 2.1. Study design, setting, and data sources

Preventing Injecting by Modifying Existing Responses (PRIMER) is a multi-cohort, multi-country, mixed-methods study with a primary aim of identifying socio-structural factors that influence the likelihood that PWID help injection-naïve individuals inject for the first time (Werb et al., 2016). For this study, data were drawn from four PRIMER-affiliated longitudinal cohort studies in Tijuana, Mexico and Vancouver, Canada. In Tijuana, PRIMER was conducted within the Proyecto El Cuete (ECIV) cohort study (Robertson et al., 2014). For ECIV, at baseline, all participants were at least 18 years old, had reported IDU in the prior month, spoke at least Spanish or English, were residing in Tijuana with no plans to relocate, and were not participating in any other intervention studies (Werb et al., 2016). In Vancouver, data were collected within three ongoing cohort studies: the At-Risk Youth Study (ARYS); the AIDS Care Cohort to Evaluate exposure to Survival Services (ACCESS) study; and the Vancouver Injection Drug Users Study (VIDUS). For ARYS, recruited participants were between the ages of 14 and 26, reported illicit drug use (other than or in addition to cannabis) in the past month, and reported recently being homeless or accessing services intended for homeless youth at baseline (Cheng et al., 2018). For ACCESS, recruited participants were at least 18 years old, HIV seropositive, and reported illicit drug use (other than or in addition to cannabis) at baseline (Prangnell et al., 2017). For VIDUS, recruited participants were at least 18 years old, HIV seronegative, and reported IDU on at least one occasion in the past month at enrolment. At recruitment and semi-annually thereafter, all participants of these PRIMER-affiliated cohort studies completed interviewer-administered questionnaires that capture participant-reported information on socio-demographic characteristics and drug use behaviors.

Starting in late 2014, corresponding cohort questionnaires were amended under PRIMER to add survey items concerning participants’ experiences with providing injection initiation assistance to others. The first interview completed by a participant involving the PRIMER items on injection initiation assistance is referred to as that participant’s PRIMER baseline interview (Werb et al., 2016). The present study includes data collected on ECIV and ARYS/ACCESS/VIDUS participants from 2014 to 2017. The PRIMER study was approved by the

Institutional Review Board of the University of California San Diego (IRB 150866). No protocol or prespecified analysis plan was registered for this study.

It is also important to highlight that the dynamics of homelessness and IDU are different across these two sites. While there are challenges in estimating the number of people who experience homelessness, estimates indicate that, at minimum, several thousand individuals experience homelessness each year in both Tijuana and Vancouver (British Columbia Non-Profit Housing Association, 2020; Guerrero, 2018). In Vancouver, homelessness and IDU are concentrated and highly visible in the Downtown Eastside neighborhood (Fast et al., 2010). This centralization reduces barriers to recruiting and providing resources to PWID. Whereas, in Tijuana, homelessness is more dispersed and encampments that do arise are frequently subject to law enforcement interaction (Gaines et al., 2015; Melo et al., 2018; Pinedo et al., 2015). As such, our study reflects on the relationship between homelessness and IDU initiation assistance provision across two heterogeneous settings, expanding the potential generalizability of our findings.

## 2.2. Participants

Our study was restricted to members of the ECIV and ARYS/ACCESS/VIDUS cohorts who: 1) completed a PRIMER baseline interview (hereafter, referred to as ‘baseline’) within the study window; 2) reported a history of IDU at baseline; and 3) completed at least one follow-up visit six months after baseline. Eligible participants contributed a minimum of 1 and a maximum of 5 follow-up visits. If a participant had missing baseline data for any time-varying measure (including exposure, outcome, and covariates; see Measures), then baseline was redefined to be that participant’s first subsequent visit with complete data. All subsequent PRIMER follow-up visits within the study period with complete data for a participant were included. If a participant had missing data for a follow-up visit, then that follow-up visit and all subsequent follow-up visits for that participant were excluded from the analysis.

## 2.3. Measures

The outcome of interest was recent provision of IDU initiation assistance (yes/no). To operationalize this measure, participants were asked if they had helped an injection-naïve individual inject for the first time in the past six months. This question is intended to capture participants’ recent experiences with direct assistance (i.e., respondent physically injected the initiate) and/or indirect assistance (e.g., respondent helped initiate inject by explaining, describing, or demonstrating how to inject) (Werb et al., 2016). The exposure of interest was recent homelessness (yes/no), defined via self-report as experiencing an episode of homelessness in the past six months. Due to differences in the cohort questionnaires by setting, the self-reported exposure was measured differently for participants from Tijuana and Vancouver. In Tijuana, participants were given a set of locations (in the form of a checklist) and asked to mark all the places they have lived or slept in the past six months. Participants that reported having lived or slept in their workplace, in a vehicle, in an abandoned building, in a shelter, on the streets, or in a shooting gallery in the past six months were deemed to have recently experienced homelessness. In Vancouver, participants were asked a single yes/no question: “Have you been homeless in the last six months?”

with those responding “yes” deemed to have recently experienced homelessness. Both the exposure and outcome were repeatedly assessed at each visit over follow-up.

We identified a set of covariates a priori that might confound the relationship between our exposure (recent homelessness) and outcome (recent provision of injection initiation assistance) of interest based on prior literature. The set consists of both baseline-fixed (or time-invariant) and time-varying covariates. Baseline-fixed covariates included: age (in years; treated as continuous), gender (cis-male/not cis-male), and cohort (for Vancouver only; i.e., ARYS, ACCESS, or VIDUS). Time-varying covariates included: whether participants reported being stopped by law enforcement in the past six months (yes/no) (Melo et al., 2018); whether participants reported being incarcerated in the past six months (yes/no) (Bryant and Treloar, 2008); whether participants reported IDU in the past six months (yes/no) (Marks et al., 2019); and for Vancouver participants only, neighborhood of residence (Downtown Eastside or Downtown South/other) (Chami et al., 2013).

Excluding the baseline-fixed covariates, values of all other variables (i.e., exposure, outcome, and time-varying covariates) were allowed to vary (or update) over time to reduce misclassification bias. Prior to any analyses, time-varying covariate values at a given follow-up visit  $t$  were recoded to their corresponding value at visit  $t-1$  occurring six months earlier. This lagging was done to ensure that covariate measurement always preceded both exposure and outcome measurement at the same visit.

#### 2.4. Statistical analysis

Due both to differences in underlying study design and how the exposure was defined between the Tijuana and Vancouver cohorts (all three [ARYS/ACCESS/VIDUS] pooled together), all analyses described herein were undertaken separately by setting. Given our interest in estimating the effect of recent homelessness (a time-varying exposure) on recent provision of injection initiation assistance (a repeated measures outcome), it is important to note that traditional regression-based approaches to control for measured confounding (e.g., covariate adjustment or stratification) may yield a biased effect estimate when the set of covariates includes time-varying variables that are caused by prior exposure and also influence (i.e., confound) subsequent exposure and outcome values (Hernán et al., 2002; Robins et al., 2000). This consideration is relevant to our study, as we have measured several time-varying covariates that may satisfy these criteria; for example, recent IDU may be both a consequence of prior homelessness and a confounder of subsequent homelessness and providing injection initiation assistance). Alternatively, an unbiased estimate of the effect of interest can be obtained from an inverse-probability-of-treatment-weighted marginal structural model, which accounts for baseline-fixed and time-varying confounding via weights (Cole and Hernán, 2008; Hernán et al., 2002; Robins et al., 2000). Estimation of this marginal structural model requires two steps: first, we calculate stabilized inverse-probability-of-treatment weights (IPTW) for each person-visit occurring after baseline to account for confounding; and, second, we fit a generalized estimating equations (GEE) logistic regression model to the weighted sample to estimate the parameters of a marginal structural model.

IPTWs are calculated in order to evenly distribute potential confounders across the different treatment groups (in this case, those who had recently experienced homelessness and those who had not) – the application of the weights to the study sample generates an artificially balanced pseudo-sample in which recent homelessness status is independent of all measured confounders (Cole and Hernán, 2008). The IPTW approach is particularly appropriate given that it can effectively account for confounding caused by time-varying measures in longitudinal analyses (Cole and Hernán, 2008; Hernán et al., 2002). See the Supplemental Materials for full details on the calculation of IPTWs.

Next, we fit a GEE logistic model to the inverse-probability-of-treatment-weighted sample with our repeated measures outcome (recent provision of IDU initiation assistance) regressed on terms for exposure (recent homelessness), time (i.e., follow-up visit [t in {1,2,3,4,5}]; treated as continuous), and all baseline-fixed covariates (Cole and Hernán, 2008). A first-order autoregressive working correlation matrix was specified to account for repeated measures within participants – meaning that the model assumed that a participant’s outcome response at follow-up visit t was correlated with their outcome response at visit t-1 (Hernán et al., 2002). Assuming the absence of model misspecification, unmeasured confounding, and informative censoring, the inverse-probability-of-treatment-weighted GEE coefficient estimates estimate the corresponding causal parameters of a marginal structural model (Cole and Hernán, 2008; Hernán et al., 2002; Robins et al., 2000). In other words, under these assumptions, the exponentiated exposure coefficient estimate from our weighted model – which is an adjusted odds ratio (AOR) – may be interpreted as the relative effect of recent homelessness on a participant’s odds of providing injection initiation assistance over the same six-month period (Cole and Hernán, 2008; Hernán et al., 2002; Robins et al., 2000). Corresponding 95% confidence intervals (CI) were calculated for effect estimates using robust sandwich-type standard errors with clustering by participant.

**2.4.1. Sensitivity analyses**—We performed two sensitivity analyses to assess the influence of measured confounding on our estimates of the association between recently experiencing homelessness and recently providing IDU initiation assistance: first, to assess the influence of measured time-varying confounding, we ran the GEE logistic model as described above without the IPTWs; second, to assess the influence of measured time-varying and baseline-fixed confounding, we ran the GEE logistic model as described above without the IPTWs and without adjusting for baseline-fixed covariates.

## 2.5. Code implementation

All analyses were performed in R (version 3.6.1), with the `ipwtm` function in the `ipw` package used to calculate weights (van der Wal and Geskus, 2021) and the `geeglm` function in the `geepack` library used to perform both weighted and unweighted GEE analyses (see Supplemental Materials for R Code) (Halekoh et al., 2021).

## 2.6. Results evaluation framework

In line with statistical expert recommendation (Amrhein et al., 2019), we evaluate and present results applying the Post-significance Communications Structure (POCS), which does not rely upon bright-line significance testing (Cummins and Marks, 2020). Instead of

evaluating results through a null hypothesis significance testing framework where estimates are either significant or not, we present point estimates, CI, and p-values together and consider their meaning in relation to our over-arching question of scientific interest.

### 3. RESULTS

#### 3.1. Baseline characteristics

We identified 703 eligible participants in Tijuana (2619 follow-up visits) and 1551 eligible participants in Vancouver (5617 follow-up visits). At baseline, 12.5% of participants in Tijuana ( $n = 88$ , Table 1) and 23.3% of participants in Vancouver ( $n = 362$ ) reported experiencing homelessness in the past six months. Individuals in Vancouver who reported recent homelessness at baseline were younger (median = 32 years, Interquartile Range [IQR]: 25–44) on average than those who had not (median = 49 years, IQR: 39–55). In both Tijuana and Vancouver, individuals who reported recent homelessness at baseline reported higher prevalence of being stopped by police in the past six months. In Vancouver, 21.0% of those who recently experienced homelessness at baseline reported recent incarceration versus just 3.0% of those who did not report recent homelessness. In Tijuana, past six-month IDU was more prevalent among those reporting recent homelessness at baseline (63.6%) than those who did not (61.0%). The same was true in Vancouver, where 80.9% of recently homelessness participants reported IDU in the past six months compared to 58.9% of participants who did not report recent homelessness. A higher proportion of those reporting recent homelessness at baseline also reported recently providing IDU initiation assistance in both Tijuana (10.2% vs. 4.7%) and Vancouver (7.2% vs. 3.9%).

#### 3.2. Prevalence of recent homelessness and recent provision of injection initiation assistance over follow-up

The median number of follow-up visits was 5 (IQR: 2–5, Table 2) in Tijuana and 4 in Vancouver (IQR: 3–5). At a given follow-up visit, between 11.6% and 16.5% of participants in Tijuana and between 9.4% and 18.9% of participants in Vancouver reported experiencing homelessness in the past six months. Between 3.3% and 5.4% of participants in Tijuana and 2.5% and 4.1% of participants in Vancouver reported recently assisting an IDU initiation at each follow-up visit. In Tijuana and Vancouver, respectively, 79 and 150 participants reported assisting at least one IDU initiation across the study period, with 19 (24%) and 28 (19%) of these participants reporting recent injection initiation assistance provision at multiple follow-up visits. In Tijuana, at a given follow-up visit, between 12.5% and 30.4% of participants who reported recently assisting a first-time injection also reported recent homelessness during the same six-month period. In Vancouver, through the first 4 follow-up visits between 18.4% and 36.5% of participants reporting recently assisting IDU initiation also reported recent homelessness, though this fell to 5.6% at the 5th follow-up. Among Vancouver participants there was an apparent downward trend in the proportion of participants reporting recent homelessness across follow-up visits.

#### 3.3. Results of regression analyses

The distribution of stabilized IPTWs was narrow at each follow-up visit in both settings, ranging from 0.65 to 1.40 in Tijuana and from 0.38 to 2.75 in Vancouver, respectively.



Fig. 1 plots the distribution of log-transformed stabilized weights across follow-up visits for Tijuana and Vancouver. Given that, for each site-specific IPTW distribution, the mean untransformed weight over follow-up is approximately 1 (i.e., mean log-transformed weight approximately 0), the interquartile ranges are relatively balanced, and the minimum and maximum weight values are not too extreme, we were satisfied with the estimated weights and did not alter them further (e.g., trimming or truncating) prior to analysis.

Based on our inverse-probability-of-treatment-weighted estimates – which are conditional on participants' baseline age, gender, and their origin cohort (Vancouver only) – we found that recent homelessness was associated with increased odds of having recently assisted an IDU initiation event among PWID in Tijuana and Vancouver (see Table 3). In Tijuana (based on 2619 person-visits made by 703 participants), recent homelessness was associated with 66% greater odds (Adjusted Odds Ratio [AOR] = 1.66, 95% CI: 1.01–2.73) of having provided IDU initiation assistance over the same six-month period. In Vancouver (based on 5617 person-visits made by 1551 participants), recent homelessness was associated with 47% greater odds (AOR = 1.47, 95% CI: 1.02–2.13) of having provided IDU initiation assistance over the same six-month period. Results of our sensitivity analyses indicate that, in both Tijuana and Vancouver, the weighting and adjustment procedures applied in this study attenuated the observed effect of recent homelessness on recently assisting IDU initiation.

#### 4. DISCUSSION

This is the first quantitative study to assess the longitudinal relationship between recent homelessness and assisting others in initiating IDU, while accounting for potential time-varying confounders through inverse-probability-of-treatment weights. Based on 2619 visits made by 703 PWID in Tijuana over three years, we found that recent homelessness was associated with 66% greater odds (AOR = 1.66; 95% CI: 1.01–2.73) of having provided IDU initiation assistance over the same six-month period. Based on 5617 visits made by 1551 PWID in Vancouver, we found that recent homelessness was associated with 47% greater odds (AOR = 1.47; 95% CI: 1.02–2.13) of having provided IDU initiation assistance over the same six-month period. Given the concentrated intersection of homelessness and IDU in North America, this study adds insight into the potential influence of housing on IDU initiation. Prior literature has indicated that experiencing homelessness may, for injection-naïve individuals, increase the risk of initiating IDU (Feng et al., 2013; Roy et al., 2011) or, for former PWID, increase the risk of reinstating IDU (Goldman-Hasbun et al., 2019; Linton et al., 2013) – taken together with our results, these findings indicate that interventions aimed broadly at addressing homelessness, such as Housing First models (Baxter et al., 2019; Padgett et al., 2006), have the potential to reduce IDU and related harms via multiple pathways.

Our findings in Vancouver are consistent with previous research exploring the dynamics of housing and IDU in the region. The Downtown Eastside of Vancouver, in particular, is an area with a high concentration of both homelessness and public IDU (Fast et al., 2010). Chami et al. (2013) found that, among a cohort of street-involved youth, that those living in the Downtown Eastside were more than twice as likely to initiate IDU compared to

those living elsewhere. Further, findings from DeBeck et al. (2009) indicate that, throughout Vancouver, those experiencing homelessness are almost seven times as likely to report IDU in public spaces than those not experiencing homelessness. This high visibility and the high density of PWID in the Downtown Eastside may provide injection-naïve individuals ready access to those with knowledge about IDU practices and thereby make PWID who inject in public more likely to be recipients of injection initiation assistance requests. Given the high concentration of homelessness and public injection in the Downtown Eastside (DeBeck et al., 2009), these findings add an additional dimension to our understanding of this drug-using context, particularly with respect to how the endemic homelessness experienced by many of its drug-using residents may be contributing to an expansion of IDU practices across injection-naïve individuals vulnerable to drug use transitions.

The context of IDU and homelessness in Tijuana, though, is substantially different than that of Vancouver. In particular, the over-policing of PWID experiencing homelessness (Gaines et al., 2015; Pinedo et al., 2015) may play a more determinative role in shaping IDU trajectories compared to housing status. It is noteworthy that a previous pooled analysis undertaken by our group, which included data from the same cohorts as the present study, found that a higher frequency of police interactions was associated with a higher odds of assisting IDU initiation (Melo et al., 2018). What this study also found, though, was that in Tijuana 71% of police interactions were arrests and detainments, whereas in Vancouver only 24% were arrests and detainments with 63% described as “neutral interactions” (Melo et al., 2018) – indicating a more severe impact of policing on PWID in Tijuana than in Vancouver. It is likely that policing also plays a differential role for PWID experiencing homelessness in each of these settings. The over-reliance on policing in Tijuana is highlighted by the Tijuana Mejora program in which, from December 2014 to March 2015, law enforcement detained approximately 1000 people, most of whom were PWID, living along the Tijuana River Channel and forced many of them into unregulated, involuntary drug treatment programs (which has been linked to a subsequent HIV outbreak and expansion in related risk behaviors) (Rafful et al., 2019). This indicates a potential mediating pathway, in which both IDU and homelessness in Tijuana increase exposure to policing, and that this exposure to policing then results in an array of harms. It is important that future research into the phenomenon of IDU initiation assistance be designed to capture and evaluate the validity of such mediating pathways in order to better characterize the role that experiencing homelessness may play in providing IDU initiation assistance across heterogeneous geographic settings.

#### 4.1. Limitations

The provision of injection initiation assistance is a highly stigmatized behavior among PWID and, as stated in prior PRIMER studies, our outcome measure is likely prone to underreporting, which may have contributed in part to the low observed frequency of injection initiation assistance in our study (Guisse et al., 2017). Non-probability sampling methods were used in both Tijuana and Vancouver to recruit participants, meaning our findings may not be generalizable to other populations and settings. While this study leveraged the longitudinal nature of the data, we modelled contemporaneous measures of recent homelessness and recent IDU injection initiation, i.e., both reflect behaviors over the

same six-month period. Correspondingly, it is possible that the observed association may be driven, in part, by the outcome causing the exposure (rather than the exposure leading to the outcome as inferred). Despite reverse causality as an alternative explanation for our main findings, we elected to lag the covariate measures for a given visit (versus lagging both covariates and exposure) to ensure that potential confounder values always preceded both exposure and outcome measures; if we had lagged both exposure and covariate values instead—to alleviate concerns of reverse causality—it is possible that some covariates, now contemporaneously measured with the exposure, might be acting as mediators versus as confounders, resulting in an effect estimate closer to the null. We observed a decline in the proportion of participants reporting recent homelessness across follow-up visit for Vancouver, which may indicate that participants experiencing homelessness were more likely to be lost to follow-up over time than those not experiencing homelessness. We note as well that research indicating more severe law enforcement exposure among people experiencing homelessness in Tijuana may have resulted in challenges in recruiting and following-up with participants experiencing homelessness due to higher rates of incarceration (Morales et al., 2020; Rafful et al., 2019). Given that our homelessness exposure was operationalized differently in each setting, it is not immediately clear if the findings across settings are readily comparable. Finally, while estimates indicate that 40%–61% of PWID in North America experience homelessness each year, the proportion of participants in our study who reported an experience of homelessness in the past six months (a shorter timeframe) was substantially lower. This is likely due to the challenges of recruiting and retaining individuals experiencing more severe homelessness. If severity of homelessness is inversely related to selection into our study (and/or the final analytic sample) and also directly related to risk of providing injection initiation assistance, then our findings likely underestimate the relationship between severe homelessness and assisting in IDU initiation events among PWID.

## 5. CONCLUSION

While accounting for potential time-varying confounding through inverse-probability-of-treatment weights, we found that PWID in both Vancouver and Tijuana who recently experienced homelessness had increased odds of assisting IDU initiation over the same six-month period. This suggests that efforts to reduce the rate of IDU initiation incidence and the expansion of these practices across vulnerable populations should address the housing needs of PWID who may be most likely to provide IDU initiation assistance to injection-naïve individuals.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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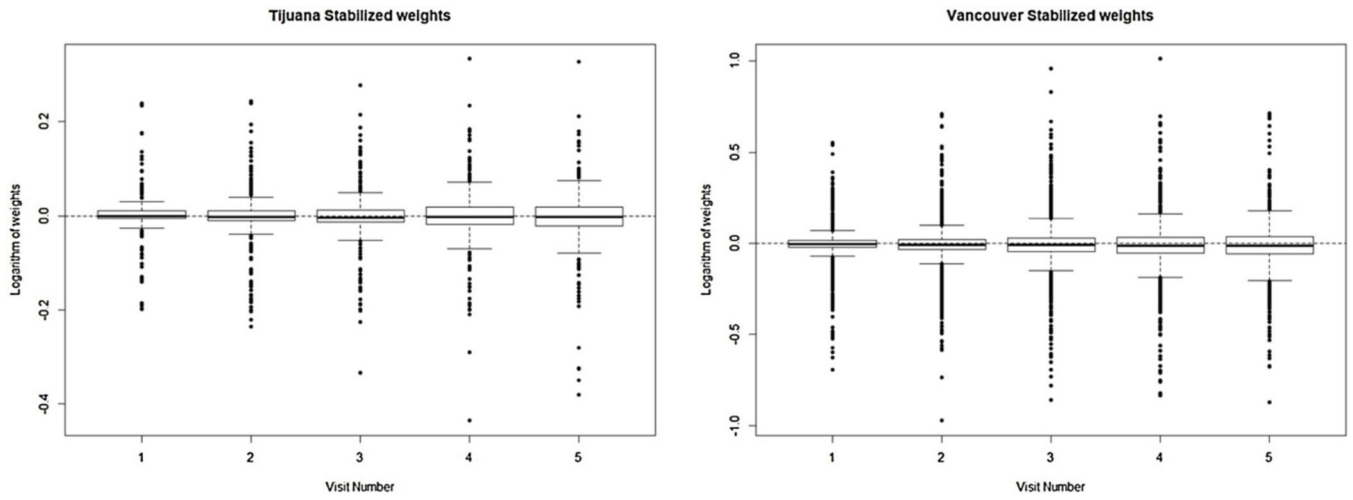
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### Highlights

- Study involving people who inject drugs in Tijuana, Mexico and Vancouver, Canada.
- Examined effect of experiencing homelessness on assisting injection initiation.
- Used inverse-probability-of-treatment-weighted marginal structural modeling approach.
- Found experiencing homelessness increases odds of assisting injection initiation.
- Results consistent across the two North American settings.



**Fig. 1.** Box plots displaying the distribution of log-transformed stabilized weights across follow-up visits for persons with a history of injection drug use in Tijuana, Mexico and Vancouver, Canada, stratified by setting – PRIMER study, 2014–2017.



Baseline characteristics of participating persons who inject drugs from Tijuana, Mexico and Vancouver, Canada, stratified by setting and recent homelessness – PRIMER study, 2014–2017.

**Table 1.**

Characteristic	Tijuana (N = 703)		Vancouver (N = 1551)	
	Yes (n = 88)	No (n = 615)	Yes (n = 362)	No (n = 1189)
Age (years), median (Q1 – Q3)	39.6 (33.6–45.5)	40.0 (34.3–47.2)	32.0 (25.0–44.0)	49.0 (39.0–55.0)
Gender – Cis-male, n (%)	58 (65.9%)	362 (58.9%)	229 (63.3%)	735 (61.8%)
Neighborhood – DTES/DTS, n (%)	--	--	255 (70.4%)	794 (66.8%)
Recent law enforcement interaction – Yes, n (%)	48 (54.5%)	274 (44.6%)	215 (59.4%)	344 (28.9%)
Recent incarceration – Yes, n (%)	19 (21.6%)	166 (27.0%)	76 (21.0%)	36 (3.0%)
Recent injection drug use – Yes <sup>a</sup> , n (%)	56 (63.6%)	375 (61.0%)	293 (80.9%)	700 (58.9%)
Recent provision of injection initiation assistance – Yes, n (%)	9 (10.2%)	29 (4.7%)	26 (7.2%)	46 (3.9%)

Notes: 'Recent' refers to past six months. Q1 = first quartile, Q3 = third quartile, DTES/DTS = Vancouver Downtown Eastside and Downtown South.

<sup>a</sup> All participants have a history of injection drug use at baseline, but some may have not injected in the past six months.

**Table 2.**

Prevalence of recent homelessness and recent provision of injection initiation assistance among persons who inject drugs from Tijuana, Mexico and Vancouver, Canada, stratified by setting and follow-up visit – PRIMER study, 2014–2017.

Follow-up visit	Tijuana				Vancouver			
	N	Recent homelessness, n (%)	Recent provision of injection initiation assistance, n (%)	Recent homelessness among those with recent provision of injection initiation, n (%)*	N	Recent homelessness, n (%)	Recent provision of injection initiation assistance, n (%)	Recent homelessness among those with recent provision of injection initiation, n (%)*
1	703	92 (13.1%)	24 (3.4%)	3 (12.5%)	1551	294 (18.9%)	63 (4.1%)	23 (36.5%)
2	631	85 (13.5%)	21 (3.3%)	5 (23.8%)	1342	206 (15.4%)	34 (2.5%)	11 (32.4%)
3	499	58 (11.6%)	20 (4.0%)	4 (20.0%)	1156	151 (13.1%)	33 (2.9%)	7 (21.2%)
4	425	58 (13.6%)	23 (5.4%)	7 (30.4%)	941	109 (11.5%)	38 (4.0%)	7 (18.4%)
5	361	60 (16.5%)	15 (4.2%)	4 (26.7%)	627	59 (9.4%)	18 (2.9%)	1 (5.6%)

\* Denominator of proportion is the total number of participants who recently provided injection initiation assistance. 'Recent' refers to past six months.

**Table 3.**

Results of generalized estimating equations (GEE) logistic regression analyses assessing the association between recent homelessness and recent provision of injection initiation assistance over time based on persons who inject drugs from Tijuana, Mexico (n = 2609 person-visits; 703 participants) and Vancouver, Canada (n = 5617 person-visits; 1551 participants), stratified by setting – PRIMER study, 2014–2017.

Model specification	Tijuana		Vancouver	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Primary analysis (IPT-weighted)				
Adjusted * GEE <sup>a</sup>	1.66 (1.01–2.73)	.046	1.47 (1.02–2.13)	.037
Sensitivity analyses (unweighted)				
Unadjusted GEE	1.75 (1.07–2.88)	.026	2.07 (1.43–3.00)	<.001
Adjusted * GEE	1.64 (1.00–2.69)	.049	1.51 (1.06–2.17)	.024

Notes: OR = odds ratio; CI = confidence interval; IPT = inverse-probability-of-treatment. All models adjusted for time (i.e., follow-up visit) as a covariate and accounted for repeated measures on participants via GEE with working first-order autoregressive correlation structure.

\* Model adjusted for the following covariates (in addition to follow-up visit): age, gender, and (in Vancouver only) cohort.

<sup>a</sup> IPT-weighted GEE model estimates are unbiased estimates of marginal structural model parameters in the absence of unmeasured confounding, informative censoring, and model misspecification (for weights and outcome).