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Publication Date

2023-06-15

DOI

10.1111/dar.13687

Received: 9 February 2022 | Revised: 17 March 2023 | Accepted: 5 May 2023

DOI: 10.1111/dar.13687

ORIGINAL PAPER

Drug and Alcohol REVIEW APSAD WILEY

Latent polydrug use patterns and the provision of injection initiation assistance among people who inject drugs in three North American settings

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Funding information
Institute of Population and Public Health, Grant/Award Number: 175276; National Institute on Drug Abuse, Grant/Award Number: DP2- DA040256-01; National Institutes of Health, Grant/Award Number: U01DA038886; New Frontiers in Research Fund, Grant/Award Number: NFRFR-R-2022-00077

Abstract

Introduction: We sought to identify latent profiles of polysubstance use patterns among people who inject drugs in three distinct North American settings, and then determine whether profile membership was associated with providing injection initiation assistance to injection-naïve persons.

Methods: Cross-sectional data from three linked cohorts in Vancouver, Canada; Tijuana, Mexico; and San Diego, USA were used to conduct separate latent profile analyses based on recent (i.e., past 6 months) injection and non-injection drug use frequency. We then assessed the association between polysubstance use patterns and recent injection initiation assistance provision using logistic regression analyses.

Results: A 6-class model for Vancouver participants, a 4-class model for Tijuana participants and a 4-class model for San Diego participants were selected based on statistical indices of fit and interpretability. In all settings, at least one profile included high-frequency polysubstance use of crystal methamphetamine and heroin. In Vancouver, several profiles were associated with a greater likelihood of providing recent injection initiation assistance compared to the referent profile (low-frequency use of all drugs) in unadjusted and adjusted analyses, however, the inclusion of latent profile membership in the multivariable model did not significantly improve model fit.

Discussion and Conclusions: We identified commonalities and differences in polysubstance use patterns among people who inject drugs in three settings disproportionately impacted by injection drug use. Our results also suggest that other factors may be of greater priority when tailoring interventions to reduce the incidence of injection initiation. These findings can aid in efforts to identify and support specific higher-risk subpopulations of people who inject drugs.

KEYWORDS
injection drug use, injection initiation, latent profile analysis, non-injection drug use, polysubstance use

1 | INTRODUCTION

People who inject drugs are at high risk of a range of harms, including overdose and infectious disease acquisition (e.g., HIV and hepatitis C virus) [1–3]. People who inject drugs are also at a heightened risk of developing skin and soft tissue infections, venous health problems and infective endocarditis [4–7]. Due to the multitude of harms associated with injection drug use (IDU) and its high prevalence worldwide (an estimated 11.3 million people inject drugs internationally [8]) experts have called for greater efforts to prevent injection-related harms upstream; that is, by preventing the initiation of IDU among those at highest risk [9, 10].

While numerous pathways towards IDU have been documented, it is estimated that the vast majority (74–100%) involve an established person who injects drugs providing assistance to the injection-naïve individual during initiation events [9–15]. Experts have therefore suggested that interventions to prevent injection initiation should address the factors that make people who inject drugs more likely to participate in these events [9, 16]. To that end, recent evidence suggests that certain drug use behaviours are associated with a greater likelihood that people who inject drugs will provide injection assistance to injection-naïve individuals [17–19]. For example, high-intensity IDU (i.e., high frequency of use, such as daily injecting) has been linked to initiation assistance provision, at least in part due to the financial need to support one's own substance use [15, 20, 21]. In addition, previous research has demonstrated an inverse (and potentially protective) association between opioid agonist treatment enrolment and risk of initiation assistance provision among people who inject drugs [17, 22, 23]; this relationship may be explained in part by opioid agonist treatment's effectiveness in managing opioid dependence and thereby reducing IDU frequency. It is also possible that, due to the social nature of IDU, reductions in injection frequency may reduce the likelihood that people who inject drugs encounter injection-naïve peers in drug-using venues [24].

Both high-frequency IDU and polysubstance IDU have been shown to be associated with injection initiation assistance in multiple cross-sectional investigations [17, 19, 25]. However, no studies have yet determined how complex patterns of polysubstance use—including the frequency, mode of consumption and drug type—may influence the likelihood that people who inject drugs provide injection initiation assistance. Identifying both global patterns and local distinctions in polysubstance use profiles is crucial to designing and adapting harm reduction interventions to the dynamic needs of people who use drugs. This study therefore sought to: (i) identify latent profiles of drug use among people who inject drugs in three settings disproportionately impacted by IDU: Vancouver, Canada; Tijuana, Mexico; and San Diego, USA; (ii) compare drug use patterns across these three settings; and (iii) determine whether profile membership was associated with providing injection initiation assistance to injection-naïve persons in each setting.

2 | METHODS

2.1 | Study design

Preventing Injecting by Modifying Existing Responses (PRIMER) is an international cohort consortium investigating socio-structural factors that influence the likelihood that people who inject drugs provide IDU initiation assistance [10]. PRIMER comprises observational data from four cohorts of people who use drugs (primarily people who inject drugs) in six different cities in North America and France, and is the largest study of injection initiation to date. A full account of the PRIMER methodology has been described previously [10]. In the present analysis, we included data from North American cohorts of people who use drugs participating in PRIMER: the Proyecto El Cuete IV (ECIV) cohort in Tijuana, Mexico; the Study to Assess Hepatitis C Risk (STAHR II) cohort in San Diego, California; and three linked cohorts in Vancouver: the Vancouver Injection Drug Users Study (VIDUS), the At-Risk Youth Study (ARYS) and the AIDS Care Cohort to evaluate Exposure to Survival Services (ACCESS).

2.2 | Data collection and measures

The current analysis was restricted to individuals who reported IDU in the 6 months prior to the PRIMER baseline. The PRIMER baseline was defined as the first visit at which participants in each cohort responded to identical survey items soliciting responses on experiences with injection initiation assistance; PRIMER baseline interviews began in August 2014. Participants completed questionnaires

administered by an interviewer, during which time quantitative data were collected, including information about the individual's experience assisting others with injection initiation, either directly (i.e., injecting someone who has never injected before) or indirectly (i.e., explaining or demonstrating how to inject). The primary outcome measure was reporting assisting any injection initiation events in the past 6 months versus none, which was assessed via participants' responses (yes/no) to the question: 'In the last 6 months, have you helped anybody inject who had never injected before?' The wording for this question was identical across all three cohorts.

The survey also collected recent (i.e., past 6 months) frequency of both IDU and non-IDU (NIDU). In Vancouver, the type of drugs included heroin, crystal methamphetamine, cocaine and illicit prescription opioids. Frequency of drug use was rated in 5 levels (0 = none; 1 = less than once a month; 2 = 1–3 times a month; 3 = once a week; 4 = more than once a week; 5 = daily). In Tijuana and San Diego, the type of drugs included heroin, crystal methamphetamine, cocaine, combined heroin/meth and combined heroin/cocaine. Frequency was rated in 7 levels (0 = none; 1 = once a month; 2 = 2–3 days a month; 3 = once a week; 4 = 2–3 days a week; 5 = 4–6 days a week; 6 = once a day; 7 = more than once a day). The number of subjects who reported prescription opioid use was low in both Tijuana and San Diego. Drug use frequencies will hereafter be reported as 'low', 'medium', or 'high', as defined in Table A1, Appendix.

2.3 | Statistical analysis

We employed latent profile analysis (LPA) to assess the complex relationship between drug type and drug-related behaviours, given that, as a latent variable mixture modelling approach, LPA is well-equipped to capture the complexities associated with polysubstance use that may be imperceptible when analysing individual factors alone [26]. Furthermore, LPA is similar to latent class analysis (LCA) in that they both use mixture modelling to identify hidden groups based on observed data, although importantly, LPA identifies different groups based on group-specific means, while LCA identifies groups defined by the item's category-specific endorsement probability [27]. Although we considered both approaches, we opted for LPA over LCA given that we employed 5- and 7-level ordered categorical variables, which cannot be effectively leveraged by LCA as a result of its limitation in effectively accounting for ordinal data [28, 29].

Profiles were generated using the following characteristics: (i) type(s) of drugs used; (ii) frequency of use; and (iii) route(s) of administration (i.e., IDU vs. NIDU) [30–33]. Past 6-month IDU and NIDU frequency ratings of heroin, crystal methamphetamine, cocaine and prescription opioid use were used as indicators for LPA using Gaussian mixture modelling. We assessed models with 2–7 profiles for the Vancouver cohort and 2–6 profiles for the Tijuana and San Diego cohorts. Model selection was primarily based on the interpretability of results, as well as congruence with statistical indices of model fit, including log-likelihood, Akaike Information Criterion, Bayesian Information Criterion, sample size-adjusted Bayesian Information Criterion and entropy.

Upon determining the optimal number of profiles for each site, we studied the association of profile membership with demographic and other risk factors, as well as its association with the outcome of providing injection initiation assistance. We defined the referent profile for each cohort as the profile with the lowest overall frequency of drug use. Logistic regression analyses were conducted separately for each cohort given the distinctiveness of local drug use scenes, heterogeneity in study design, and differences in policy and legal contexts. Covariates included in the analyses were selected based on a priori identification of an association with increasing injection frequency and/or injection initiation assistance provision, as described in the literature. The extent of influence of these contextual factors differ across each setting and was selected accordingly [34]. In the Vancouver model, this included age, gender, housing status, public injecting, duration of injecting career and recent law enforcement interaction [17, 19, 33–37]. The Tijuana model included age, gender, housing status, duration of injection career and recent law enforcement interaction [17, 19, 33–37]. The San Diego model included age, gender and housing status as covariates interaction [33, 34, 36, 37]. The Wald chi-square test was used to assess the overall impact of LPA classes on the fit of each multivariable model. *P*-values for pairwise comparisons of latent profiles were adjusted using Tukey's method. All statistical analyses were performed using R statistical software (version 3.6.1) [38].

3 | RESULTS

A total of 2140 participants were included in the analysis: 1228 (57.4%) from Vancouver (VIDUS/ARYS/ACCESS), 663 (31.0%) from Tijuana (ECIV) and 249 (11.6%) from San Diego (STAHR II) (Table 1). At all three sites, participants were predominantly male (61.6% in Vancouver; 60.8% in Tijuana; 71.7% in San Diego), with a median age of 41 (interquartile range 29–51 years) in Vancouver, 40 (interquartile range 34–47) in Tijuana and 49 (interquartile range 38–55) in San Diego. A majority of participants

TABLE 1 Participant characteristics by cohort.

Characteristic	Vancouver ($n = 1228$)	Tijuana ($n = 663$)	San Diego ($n = 249$)
Age (median, [Q1,Q3])	41 [29,51]	40 [34, 47]	49 [38, 55]
Gender			
Female/transgender	471 (38.4%)	260 (39.2%)	70 (28.1%)
Male	754 (61.6%)	403 (60.8%)	177 (71.7%)
Housing status			
Unstable	404 (32.9%)	258 (38.9%)	115 (46.2%)
Stable	823 (67.1%)	405 (61.1%)	134 (53.8%)
Years since first injection			
>10	809 (65.9%)	530 (80.2%)	204 (82.3%)
6–10	159 (12.9%)	94 (14.2%)	28 (11.3%)
≤5	260 (21.2%)	37 (5.6%)	16 (6.5%)
Recent* law enforcement interaction			
Yes	556 (45.4%)	332 (50.1%)	130 (52.2%)
No	670 (54.6%)	331 (49.9%)	119 (47.8%)
Recent* public injecting			
Yes	601 (49.1%)	–	120 (48.2%)
No	623 (50.9%)	–	129 (51.8%)
Recent* injection initiation assistance			
Yes	85 (7.0%)	38 (5.7%)	17 (6.9%)
No	1133 (93.0%)	625 (94.3%)	231 (93.1%)

*Recent is defined as within the past 6 months.

also reported they had been injecting longer than 10 years across all three sites: 65.9% ($n = 809$) in Vancouver, 80.2% ($n = 530$) in Tijuana and 82.3% ($n = 204$) in San Diego.

3.1 | Identification and description of Vancouver LPA model

The 6-class model maintained the best balance between statistical fit and interpretability (Table A2, Appendix). In the 6-class model for Vancouver data (Figure S1), Class 1 ($n = 163$, 13.3%) was characterised by high-frequency crystal methamphetamine IDU and low-moderate NIDU. Class 2 ($n = 129$, 10.4%) was characterised by moderate-high-frequency heroin IDU, high-frequency heroin NIDU and moderate-high-frequency crystal methamphetamine IDU and NIDU. Class 3 ($n = 298$, 24.3%) was characterised by low-frequency use of all drugs and was selected as the reference class. Class 4 ($n = 204$, 17%) was characterised by high-frequency heroin IDU and crystal methamphetamine IDU, and low-moderate-frequency prescription opioid IDU and crystal methamphetamine NIDU. Class 5 ($n = 280$, 22.8%) was characterised by high-frequency heroin IDU. Class 6 ($n = 154$, 12.5%) was characterised by high-frequency cocaine IDU and low-moderate heroin IDU (Table 2).

3.2 | Identification and description of Tijuana LPA model

A 4-class model for Tijuana data was selected (Table A2; Figure S2). Class 1 ($n = 209$, 31.5%) was characterised by high-frequency heroin and crystal methamphetamine co-injection. Class 2 ($n = 130$, 19.6%) was characterised by high-frequency heroin IDU, high-frequency heroin and crystal methamphetamine co-injection and low-moderate crystal methamphetamine NIDU. Class 3 ($n = 80$, 12%) was characterised by high-frequency heroin IDU, high-frequency heroin-crystal methamphetamine co-injection, high-frequency crystal methamphetamine IDU and low-moderate-frequency crystal methamphetamine NIDU. Class 4 ($n = 244$, 36.8%) was characterised by high-frequency heroin IDU and low-moderate crystal methamphetamine NIDU (Table 2), and was selected as the reference class due to having overall lower intensity drug use relative to other classes.

TABLE 2 Summary of latent profiles and bivariate associations with recent (i.e., past 6 months) injection initiation assistance.

				Injection initiation assistance			
Profile	**Drug**	**Route**	**Frequency***	**Yes**	**No**	**Total**	***p*-value****
Vancouver (VIDUS/ACCESS/ARYS)				$n = 85$ (7.0%)	$n = 1133$ (93.0%)	$n = 1218$ (100%)	
1	Crystal methamphetamine	Injection	High	16 (9.9%)	146 (90.1%)	162 (100%)	<0.001
		Non-injection	Low-moderate				
2	Heroin	Injection	Moderate-high	16 (12.5%)	112 (87.5%)	128 (100%)	
		Non-injection	High				
	Crystal methamphetamine	Injection	Moderate-high				
		Non-injection	Moderate-high				
3	All drugs	Injection	Low	6 (2.0%)	289 (98.0%)	295 (100%)	
		Non-injection	Low				
4	Heroin	Injection	High	23 (11.4%)	178 (88.6%)	201 (100%)	
	Crystal methamphetamine	Injection	High				
		Non-injection	Low-moderate				
	Prescription opioids	Injection	Low-moderate				
5	Heroin	Injection	High	16 (5.7%)	263 (94.3%)	279 (100%)	
6	Heroin	Injection	Low-moderate	8 (5.2%)	145 (94.8%)	153 (100%)	
	Cocaine	Injection	High				
Tijuana (ECIV)				$n = 38$ (5.7%)	$n = 625$ (94.3%)	$n = 663$ (100%)	
1	Crystal methamphetamine + heroin co-injection	Injection	High	12 (5.7%)	197 (94.3%)	209 (100%)	0.083
2	Heroin	Injection	High	10 (7.7%)	120 (92.3%)	130 (100%)	
	Crystal methamphetamine + heroin combined	Injection	High				
	Crystal methamphetamine	Non-injection	Low-moderate				
3	Heroin	Injection	High	8 (10.0%)	72 (90.0%)	80 (100%)	
	Crystal methamphetamine + heroin combined	Injection	High				
	Crystal methamphetamine	Injection	High				
		Non-injection	Low-moderate				
4	Heroin	Injection	High	8 (3.3%)	236 (96.7%)	244 (100%)	
	Crystal methamphetamine	Non-injection	Low-moderate				
San Diego (STAHR II)				$n = 17$ (6.9%)	$n = 231$ (93.2%)	$n = 248$ (100%)	
1	Crystal methamphetamine + heroin combined	Injection	High	1 (8.3%)	11 (91.7%)	12 (100%)	0.410
	Heroin	Injection	High				
	Crystal methamphetamine	Injection	Moderate				
		Non-injection	Moderate				
2	Crystal methamphetamine	Injection	Low	4 (4.7%)	81 (95.3%)	85 (100%)	
		Non-injection	Moderate				
3	Heroin	Injection	High	5 (5.8%)	82 (94.3%)	87 (100%)	

(Continues)

TABLE 2 (Continued)

Profile	Drug	Route	Frequency*	Injection initiation assistance			
				Yes	No	Total	*p*-value**
4	Crystal methamphetamine	Injection	High	7 (10.9%)	57 (89.1%)	64 (100%)	
		Non-injection	High				

Note: Profiles refer to site-specific samples and are not comparable across sites. Ten participants in the Vancouver cohort and one participant in the San Diego cohort had missing information for the outcome variable; these incomplete cases accounted for <1% of their respective samples.
Abbreviations: ACCESS, AIDS Care Cohort to evaluate Exposure to Survival Services; ARYS, At-Risk Youth Study; ECIV, Proyecto El Cuete IV; IDU, injection drug use; NIDU, non-injection drug use; STAHR II, Study to Assess Hepatitis C Risk; VIDUS, Vancouver Injection Drug Users Study.
*High-frequency refers to more than once a week or daily IDU/NIDU in Vancouver, and 2–3 days/week to more than once a day in Tijuana and San Diego; moderate-frequency refers to 1–3 times/month to daily in Vancouver, and 2–3 days/month to once a week in Tijuana and San Diego; low-frequency refers to either less than once a month IDU/NIDU or none in Vancouver, and either once a month or none in Tijuana and San Diego.
**p-values derived from Fisher's exact test.

3.3 | Identification and description of San Diego LPA model

A 4-class model for San Diego data was selected (Table A2; Figure S3). Class 1 ($n = 12$, 5%) was characterised by high-frequency heroin IDU, high-frequency heroin and crystal methamphetamine co-injection and moderate crystal methamphetamine IDU and NIDU. Class 2 ($n = 85$, 34%) was characterised by low and moderate-frequency crystal methamphetamine IDU and NIDU, respectively, and was selected as the reference class due to having overall lower intensity drug use relative to other classes. Class 3 ($n = 87$, 35%) was characterised by high-frequency heroin IDU. Class 4 ($n = 65$, 26%) was characterised by high-frequency crystal methamphetamine IDU and NIDU (Table 2).

3.4 | Association of profile membership with provision of recent injection initiation assistance

In bivariate analysis of the Vancouver data, several profiles were associated with a greater likelihood of providing recent injection initiation assistance (Table 3). Specifically, compared to Class 3 (referent), Class 1 (odds ratio [OR] = 5.28, 95% confidence interval [CI] 2.02, 13.77, $p = 0.009$); Class 2 (OR = 6.88, 95% CI 2.63, 18.03, $p = 0.001$); and Class 4 (OR = 6.21, 95% CI 2.49, 15.63, $p = 0.001$) were all significantly associated with the outcome. After adjustment, this association was maintained in Class 1 (adjusted OR = 3.11, 95% CI 1.16, 8.33) and Class 4 (adjusted OR = 3.02, 95% CI 1.15, 7.93) (Table 4), however, results of the Wald Chi-square test indicated that, overall, the inclusion of LPA classes in the multivariable model did not significantly improve model fit.

In bivariate and multivariate analyses in San Diego and Tijuana (Tables 3–6), no statistically significant differences in the odds of injection initiation assistance provision were detected between classes.

4 | DISCUSSION

In a multi-site analysis undertaken in three countries in North America, we identified distinct polysubstance use patterns in each setting, and then the association of these with the provision of injection initiation assistance. To our knowledge, this is the first study to characterise latent profiles of polysubstance use across settings in all three North American countries.

Across all three sites, we consistently detected classes of people who inject drugs engaged in high-frequency polysubstance crystal methamphetamine and opioid use. Crystal methamphetamine use is prevalent in a number of North American cities [39–43], where it has been shown to be predictive of subsequent injection initiation [39–44] and identified as a common drug of first injection among street-involved youth [39, 41, 45]. Moreover, among people who inject drugs in Tijuana, crystal methamphetamine NIDU has been shown to double the odds of providing injection initiation assistance [24]. It has been hypothesised that people who inject drugs who engage in NIDU may do so among injection-naïve individuals in their social network [24].

The results presented herein are consistent with this initial finding and suggest that further efforts to elucidate the role of complex drug-using patterns involving crystal methamphetamine in the process of injection initiation should be undertaken. Specifically, further research should seek to longitudinally investigate the role of polysubstance use involving crystal methamphetamine IDU and NIDU to determine its contribution to injection initiation assistance provision over time. Characterising global and local patterns of polysubstance use across regions disproportionately impacted by injection drug use is critical in

TABLE 3 Recent (i.e., past 6 months) injection initiation assistance provision by latent profile membership in the Vancouver 6-class model; the Tijuana 4-class model; and the San Diego 4-class model.

Latent profile	OR [95% CI]	*p*-value
Vancouver (VIDUS/ ACCESS/ARYS)		
Class 3 (referent)	–	–
Class 1	5.28 [2.02, 13.77]	0.009
Class 2	6.88 [2.62, 18.03]	0.001
Class 4	6.21 [2.49, 15.63]	0.001
Class 5	2.94 [1.12, 7.69]	0.232
Class 6	2.63 [0.90, 7.69]	0.480
Tijuana (ECIV)		
Class 4 (referent)	–	–
Class 1	0.56 [0.22, 1.39]	0.591
Class 2	0.41 [0.16, 1.06]	0.252
Class 3	0.31 [0.11, 0.84]	0.100
San Diego (STAHR II)		
Class 2 (referent)	–	–
Class 1	0.54 [0.06–5.32]	0.953
Class 3	0.81 [0.21–3.12]	0.990
Class 4	0.40 [0.11–1.44]	0.499

Note: Profiles refer to site-specific samples and are not comparable across sites. Ten participants in the Vancouver cohort ($n = 1228$) and one participant in the San Diego cohort ($n = 249$) had missing information for the outcome variable; these incomplete cases accounted for <1% of their respective samples.

Abbreviations: ACCESS, AIDS Care Cohort to evaluate Exposure to Survival Services; ARYS, At-Risk Youth Study; CI, confidence interval; ECIV, Proyecto El Cuete IV; OR, odds ratio; STAHR II, Study to Assess Hepatitis C Risk; VIDUS, Vancouver Injection Drug Users Study.

implementing and optimising harm reduction interventions (e.g., supervised injection/consumption facilities, needle-syringe exchanges, methadone clinics) for specific settings. In particular, resources should be allocated based on the polysubstance use profiles most prevalent in the region. This could include differences in investments in syringe distribution and safer inhalation kits based on the relative proportion of IDU versus NIDU classes, or tailored harm reduction services for opioid versus stimulant users. This could also include implementation factors for supervised consumption services—including age restrictions, client volume, accommodation of inhalation and injection and linkages with relevant services such as opioid agonist treatment, housing or culturally-relevant programming.

Overall LPA membership was not significantly associated with initiation assistance provision in multivariable analysis, although we detected significant pairwise differences between certain LPA classes. We nevertheless found that, in general, profile membership was more strongly associated with injection initiation assistance provision in Vancouver than in Tijuana or San Diego. This suggests that, at minimum, we had insufficient statistical power to confidently detect the direction of effect in each setting and, at most, people who inject drugs who engage in crystal methamphetamine and heroin IDU and NIDU may have an increased odds of assisting others into injection initiation. In any event, we can reasonably conclude that these results imply that factors other than polysubstance use patterns are more strongly determinative of providing assistance in these settings than drug use alone. One such factor may involve the variable extent of social network formation between these settings. For example, in Vancouver, a well-established community of people who inject drugs is largely located in one geographic area (the Downtown Eastside neighbourhood) [46]. In contrast, Tijuana is characterised by high cross-border migration [47, 48] and deportation in particular [49], along with high intraurban mobility and police intervention [50], which is disruptive to the formation and maintenance of social networks and may therefore impede the ability of people who inject drugs to develop and maintain lasting social networks, within which injection initiation assistance could occur [51, 52].

It has been previously shown that in Vancouver, younger people who inject drugs are at higher risk of engaging in frequent injection drug use compared to older individuals [30] and that those who begin injecting drugs at an earlier age are more likely to provide injection initiation assistance compared to older individuals who have been injecting for the same number of years [35]. Indeed, those who reported recently providing injection initiation assistance in the Vancouver cohort had a median age of 29 and were more likely to have been injecting for less than 10 years, while those who did not report recent injection initiation assistance had a median age of 42. Taken together, it is plausible that the combined factors of younger age and lesser time injecting may be partially driving the association between certain profiles and injection initiation assistance within the Vancouver cohort.

Injection initiation has been defined as a social phenomenon, with the initiation of injection-naïve individuals often facilitated within drug-using social networks [53–55]. In San Diego and Tijuana, it has been shown that injection initiation events are strongly influenced by gendered power dynamics within intimate partnerships. Women engaging in IDU in these settings are often initiated by male sexual partners, while men are typically initiated by other men with whom they are not intimately involved [56, 57]. With respect to reducing or delaying injection initiation events, our findings imply that local

TABLE 4 Multivariable logistic regression analysis of factors associated with providing recent (i.e., past 6 months) injection initiation assistance among people who inject drugs in Vancouver, Canada.

Independent variable	AOR [95% CI]	Wald chi-square	*p*-value
Age	0.94 [0.90, 0.97]	13.69	<0.001
Male gender	1.39 [0.85, 2.29]	1.72	0.190
Unstable housing	0.58 [0.34, 0.98]	4.09	0.043
Years since first injection		1.79	0.408
6–10 years versus ≤5 years	1.54 [0.81, 2.92]		
>10 years versus ≤5 years	1.38 [0.65, 2.92]		
Public injecting	1.71 [0.95, 3.08]	3.14	0.076
Law enforcement interaction	1.63 [0.98, 2.72]	3.52	0.061
Latent profile membership (referent = Class 3)		6.62	0.251
Class 1	3.11 [1.16, 8.33]		
Class 2	2.60 [0.94, 7.22]		
Class 4	3.02 [1.15, 7.93]		
Class 5	2.06 [0.78, 5.49]		
Class 6	2.92 [0.95, 8.96]		

Note: $n = 1228$.
Abbreviations: AOR, adjusted odds ratio; CI, confidence interval.

TABLE 5 Multivariable logistic regression analysis of factors associated with providing recent (i.e., past 6 months) injection initiation assistance among people who inject drugs in Tijuana, Mexico.

Independent variable	AOR [95% CI]	Wald chi-square	*p*-value
Age	0.96 [0.92, 1.01]	3.05	0.081
Male gender	1.45 [0.66, 3.18]	0.84	0.360
Unstable housing	1.25 [0.63, 2.46]	0.40	0.526
Years since first injection		1.59	0.452
6–10 years versus >10 years	0.50 [0.16, 1.63]		
≤5 years versus >10 years	0.56 [0.12, 2.68]		
Law enforcement interaction	1.97 [0.95, 4.07]	3.31	0.069
Latent profile membership (referent = Class 4)		3.73	0.292
Class 1	1.36 [0.53, 3.50]		
Class 2	1.91 [0.71, 5.10]		
Class 3	2.58 [0.91, 7.37]		

Note: $n = 663$.
Abbreviations: AOR, adjusted odds ratio; CI, confidence interval.

socio-structural factors may be more relevant to influencing injection initiation assistance patterns than drug use patterns. Specifically, drug-related social network formation, facilitated by methadone maintenance therapy and treatment access, housing, law enforcement and criminalisation, and drug use venues may exert more top-down influence on the likelihood that people who inject drugs will provide initiation assistance, compared to drug use patterns alone [10, 58]. This suggests that intervening to alter factors that contribute to socio-structural vulnerability (i.e., vulnerability experienced by people who inject drugs due to marginalisation within social hierarchies [59]) is likely to be more effective in reducing the provision of IDU initiation assistance compared to efforts that prioritise altering drug use patterns. As such, these should be prioritised as targets for intervention efforts to prevent injection initiation events.

TABLE 6 Multivariable logistic regression analysis of factors associated with providing recent (i.e., past 6 months) injection initiation assistance among people who inject drugs in San Diego, USA.

Independent variable	AOR [95% CI]	Wald chi-square	*p*-value
Age	0.99 [0.95, 1.037]	0.12	0.731
Male gender	1.28 [0.39, 4.21]	0.16	0.687
Unstable housing	0.35 [0.12, 1.03]	3.65	0.056
Latent profile membership (referent = Class 2)			
Class 1	1.77 [0.17, 18.23]	1.81	0.612
Class 3	1.25 [0.32, 4.93]		
Class 4	2.26 [0.62, 8.20]		

Note: $n = 249$.
Abbreviations: AOR, adjusted odds ratio; CI, confidence interval.

This study has limitations typical of multi-site observational studies of people who inject drugs. First, latent profiles were constructed using baseline survey responses, therefore, we cannot determine causality between the independent variables of interest (i.e., LPA classes) and the outcome. Second, because IDU initiation assistance is highly stigmatised [20, 60, 61], this behaviour was likely underreported in the study, and thereby may have contributed to an overall lower effect size. However, we know of no reason why participants in different LPA classes would differentially report on their provision of IDU initiation assistance. Third, as has been shown, the results described in this study are highly context-dependent, therefore the data could not be pooled without increasing risk of misclassification bias and limiting the interpretability of the results. Relatedly, while we sought to align measures as much as possible across settings, this may have resulted in some misclassification. Fourth, although the outcome for this study, injection initiation assistance, is dependent on both the individual providing assistance as well the individual receiving assistance, this study only considered the polysubstance use patterns of the provider. The PRIMER study was established to generate knowledge about people who provide injection initiation assistance given that consideration of this population was largely absent in the scientific literature [10], however, we note that this also limits the ability to interpret the study results fully. Finally, because each observational cohort used convenience sampling for participant recruitment, we cannot assume generalisability with the broader population of people who inject drugs in each setting. These findings do, however, shed light on the complex drug use patterns that shape behaviours (including the provision of injection initiation assistance) among highly marginalised groups of people who inject drugs in each study setting, and at the very least illuminate the risks that these vulnerable populations experience.

5 | CONCLUSION

Across three distinct settings disproportionately impacted by substance-related harms, we identified LPA classes of people who inject drugs defined by distinct IDU and NIDU polysubstance use patterns. In particular, in all three settings, classes involving high-frequency crystal methamphetamine IDU and NIDU as well as opioid IDU were identified. Our findings suggest that LPA classes were more highly associated with injection initiation provision in Vancouver compared to Tijuana or San Diego, although the inclusion of latent profile membership in the adjusted model did not improve model fit. The results of this study suggest that factors other than latent polysubstance use patterns may be of greater priority when evaluating interventions to mitigate injection initiation. Taken together, these findings can aid in efforts to identify and support specific higher-risk subpopulations of people who inject drugs at risk of providing IDU initiation assistance.

AUTHOR CONTRIBUTIONS

Each author certifies that their contribution to this work meets the standards of the International Committee of Medical Journal Editors.

ACKNOWLEDGEMENTS

We would like to thank the study participants for their time and willingness to participate in this work. We also acknowledge those who have lost their lives—both in the ongoing opioid overdose crisis and long before—due to policies of drug criminalisation.

FUNDING INFORMATION

The VIDUS and ARYS studies are supported by the US National Institutes of Health (NIH) (U01DA038886). Kanna Hayashi holds the St. Paul's Hospital Chair in Substance Use Research and is supported by the National Institutes of Health (U01DA038886), a Michael Smith

Foundation for Health Research Scholar Award, and the St. Paul's Foundation. PRIMER is supported by a US National Institute on Drug Abuse Avenir Award (DP2- DA040256-01) and a project grant from the Canadian Institutes of Health Research. Additional project funding was provided by the New Frontiers in Research Fund (NFRFR-R-2022-00077). Dan Werb is supported by the Canadian Institutes of Health Research via a New Investigator Award, the Ontario Ministry of Research, Innovation and Science via an Early Researcher Award, and the St. Michael's Hospital Foundation.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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APPENDIX A

TABLE A1 Drug use frequency definitions by cohort.

Frequency rating		Frequency definition
Vancouver (VIDUS/ACCESS/ARYS)		
0	None	Low
1	Less than once a month	
2	1–3 times a month	Moderate
3	Once a week	
4	More than once a week	High
5	Daily	
Tijuana and San Diego (ECIV; STAHR II)		
0	None	Low
1	Once a month	
2	2–3 days a month	Moderate
3	Once a week	
4	2–3 days a week	High
5	4–6 days a week	
6	Once a day	
7	More than once a day	

Abbreviations: ACCESS, AIDS Care Cohort to evaluate Exposure to Survival Services; ARYS, At-Risk Youth Study; ECIV, Proyecto El Cuete IV; STAHR II, Study to Assess Hepatitis C Risk; VIDUS, Vancouver Injection Drug Users Study.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Rammohan I, Jain S, Sun S, Marks C, Milloy M-J, Hayashi K, et al. Latent polydrug use patterns and the provision of injection initiation assistance among people who inject drugs in three North American settings. Drug Alcohol Rev. 2023. https://doi.org/10.1111/dar.13687

TABLE A2 Goodness of fit statistics for latent profile models of recent (i.e., past 6 months) injection and non-injection drug use frequency ratings.

Model	Log-likelihood	AIC	BIC	SABIC	Entropy
Vancouver (VIDUS/ACCESS/ARYS)					
2-class model	−16753.794	33557.588	33685.417	33606.006	0.989
3-class model	−15832.775	31733.550	31907.396	31799.398	0.990
4-class model	−15489.451	31064.901	31284.766	31148.180	0.977
5-class model	−15605.405	31314.810	31580.693	31415.519	0.951
6-class model	**−15421.347**	**30965.695**	**31276.596**	**31082.834**	**0.926**
7-class model	−15175.346	30490.693	30848.613	30626.263	0.924
Tijuana (ECIV)					
2-class model	−7290.529	14631.058	14743.478	14664.102	0.999
3-class model	−7118.261	14304.523	14457.413	14349.462	0.971
4-class model	**−6847.598**	**13781.196**	**13974.557**	**13838.030**	**0.980**
5-class model	−6823.716	13751.433	13985.265	13820.163	0.934
6-class model	−6811.961	13745.922	14020.225	13826.548	0.947
San Diego (STAHR II)					
2-class model	−3234.528	6519.057	6606.993	6527.741	0.998
3-class model	−3113.629	6295.257	6414.851	6307.069	0.952
4-class model	**−3004.501**	**6095.003**	**6246.253**	**6109.941**	**0.950**
5-class model	−3000.110	6104.319	6287.127	6122.284	0.900
6-class model	−2961.144	6044.288	6258.853	6065.480	0.911

Note: Bolded items indicate selected models based on statistical indices as well as contextual interpretability. For Vancouver, past 6-month IDU and NIDU frequency ratings (0–5) of heroin, crystal methamphetamine, cocaine, and prescription opioid use were used as indicators for LPA. For San Diego and Tijuana, past 6-months IDU frequency ratings (0–7) of heroin, cocaine, crystal methamphetamine, crystal methamphetamine/heroin co-injection, heroin/cocaine co-injection and past 6-month NIDU frequency ratings of heroin, cocaine, and crystal methamphetamine were used as indicators for LPA. Report of prescription opioid use was low in San Diego and Tijuana and so it was ignored in the LPA.

Abbreviations: ACCESS, AIDS Care Cohort to evaluate Exposure to Survival Services; AIC, Akaike Information Criterion; ARYS, At-Risk Youth Study; BIC, Bayesian Information Criterion; ECIV, Proyecto El Cuete IV; IDU injection drug use; LPA, latent profile analysis; NIDU, non-injection drug use; SABIC, Sample-Size Adjusted Bayesian Information Criterion; STAHR II, Study to Assess Hepatitis C Risk; VIDUS, Vancouver Injection Drug Users Study.