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Drugs, Discipline and Death: Causes and Predictors of Mortality among People who Inject Drugs in Tijuana, 2011–2018

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Abstract

Background: People who inject drugs (PWID) experience multiple risk factors for mortality; yet, we know little about causes of death among PWID in Tijuana, Mexico, an area with high levels of injecting and changes in policy/law enforcement responses to substance use. This study examines rates, causes, and predictors of mortality among Tijuana PWID.

Methods: Data come from a community-based cohort of PWID aged ≥18 who injected drugs in the past month. Mortality was confirmed by death certificate over 78 months during 2011–2018. Predictors of mortality were identified using time-updated Cox regression, controlling for age.

Results: Among 734 participants, there were 130 deaths (54 confirmed, 76 unconfirmed), with an incidence rate of 17.74 deaths per 1000 person-years for confirmed deaths (95% Confidence Interval (CI)=13.01, 22.48) and 39.52 for unconfirmed deaths (CI=32.72, 46.31). Confirmed deaths resulted from homicide/trauma (26%), overdose (26%), septic shock (18%) and HIV-related causes (9%). In multivariable analysis of confirmed deaths, baseline HIV seropositivity (adjusted Hazard Ratio [aHR]=6.77, CI=1.98, 23.17), incident HIV infection (aHR=3.19, CI=1.02, 9.96), and number of times being beaten by police in the past 6 months at baseline (aHR=1.08 per time, CI=1.04, 1.12) were predictive of death; whereas, injection cessation for 6+ months during time at risk (aHR=0.25, CI=0.33, 0.79) was protective.

Conclusion: In addition to overdose and HIV prevention efforts, attention to structural conditions that potentiate mortality is needed, including improved access to medication-assisted treatment to support injection cessation and a shift from police as a source of harm to harm reduction.

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Keywords

injection drug use; mortality; law enforcement; drug policy; injection cessation; HIV; drug treatment; violence; overdose; Mexico

INTRODUCTION

It is well established that people who inject drugs (PWID) are at increased risk of mortality; however, more research is needed on the causes and predictors of death in low and middle income country contexts, like Mexico, and in border communities, like Tijuana. There are an estimated 10,000 PWID living in Tijuana, a city with substantial markets for drugs and sex work that is one of the busiest land border crossings in the world (Strathdee, Magis-Rodriguez, Mays, Jimenez, & Patterson, 2012). HIV prevalence among PWID in this context is high, 4% among PWID, with higher prevalence among key sub-populations, like female PWID who trade sex (12%) (Strathdee et al., 2012; Strathdee, Philbin, et al., 2008), but HIV is only one factor that may underlie increased risk for mortality. This border community is characterized by high levels of homelessness and public injecting (Kori, Roth, Lozada, Vera, & Brouwer, 2014), injection-related risk behaviours (Strathdee, Lozada, et al., 2008), and limited opportunities for access to quality affordable drug treatment (Instituto de Psiquiatria del Estado de Baja California, 2014; Werb et al., 2015).

Globally, crude all-cause mortality rates among PWID vary substantially, with rates per 1000 person-years of 9 among young injectors in San Francisco (Evans et al., 2012), 32 among PWID in Vancouver (Hayashi et al., 2016), 33 among new-onset PWID in Baltimore (Vlahov et al., 2004), 38 among PWID in Thailand (Quan et al., 2010), and up to 63 deaths per 1000 person-years in Vietnam (Quan et al., 2011). Across studies, HIV is one of the primary causes of mortality among PWID (Cao et al., 2013; Colon et al., 2006; Hayashi et al., 2016; Mathers & Degenhardt, 2014; Miller, Kerr, Strathdee, Li, & Wood, 2007; Quan et al., 2011; Quan et al., 2007; Sheehan et al., 2015; Spittal et al., 2006; Tyndall et al., 2001). Other major causes of mortality include overdose (Colon et al., 2006; Darke, Mills, Ross, & Teesson, 2011; Evans et al., 2012; Hser, Kagihara, Huang, Evans, & Messina, 2012; Miller et al., 2007; Parashar, Collins, Montaner, Hogg, & Milloy, 2016; Quan et al., 2011; Tyndall et al., 2001), suicide (Evans et al., 2012; Miller et al., 2007; Quan et al., 2011), violence or homicide (Miller et al., 2007; Quan et al., 2011), accidents (Evans et al., 2012; Quan et al., 2011), but also health conditions like cardiovascular disease, pulmonary conditions, sepsis and alcohol or drug related illnesses (e.g. cirrhosis) (Colon et al., 2006; Evans et al., 2012; Hser et al., 2012; Parashar et al., 2016).

A number of factors that increase the risk of death among PWID have been identified in other studies. Across contexts, the risk of death tends to be greater among men than women (Cao et al., 2013; Colon et al., 2006; Mathers & Degenhardt, 2014; Stoové, Dietze, Aitken, & Jolley, 2008) and among older individuals (Colon et al., 2006; Hser et al., 2012; Sheehan et al., 2015; Tyndall et al., 2001; Van Haastrecht et al., 1996). Injection-related behaviours can also impact mortality, especially a longer duration of drug injection (Quan et al., 2007; Stoové et al., 2008), the use of a shared cooker (J. M. Davis, Suleta, Corsi, & Booth, 2017)

and history of opioid overdose (Darke et al., 2011). In some studies, daily use of benzodiazepines or injection of cocaine was also associated with an increased risk of death (Tyndall et al., 2001; Van Haastrecht et al., 1996). Importantly, in a systematic review of mortality among PWID globally, the risk of death was more than three times greater during periods out of medication assisted treatment (MAT) for opioid dependence than for periods on MAT (Mathers & Degenhardt, 2014) and increased duration of MAT has been associated with a lower risk of death (Cao et al., 2013; Huang et al., 2011).

Aspects of the sociostructural environment are also associated with elevated levels of mortality among PWID. For instance, in Canada, unstable housing was an important factor related with time to death (Spittal et al., 2006; Zivanovic et al., 2015), as was involvement in sex work (Miller et al., 2007; Spittal et al., 2006). Population level analysis of changes in AIDS-related mortality among PWID in 96 larger US cities over time also highlights how social and policy factors, including drug-related arrest rates and income inequality were associated with lower relative declines in mortality rates (Friedman et al., 2013). Further, research in Australia demonstrated that extensive experience of incarceration was associated with increased risk of PWID mortality (Stoové et al., 2008). Periods of detention and incarceration are associated with highly-elevated risk of overdose mortality (Beletsky et al., 2015; Fiscella, Wakeman, & Beletsky, 2018; Rafful et al., 2018; Saloner et al., in press). Police encounters are understood to act as a barrier to substance use treatment (Werb et al., 2016) and overdose response help-seeking (Latimore & Bergstein, 2017), as well as predicting HIV risk behaviour and seroconversion (Beletsky et al., 2013). Police violence, including killings by police incidental to drug law enforcement, is a noted public health issue that is under-studied in cohort studies of PWID.

In Mexico, recent changes in legislation also impact the lives of PWID. New drug policies, which passed in 2009, both decriminalized the possession of small quantities of illegal substances and mandated the expansion of addiction treatment with the expectation that law enforcement officials would divert individuals to treatment (Beletsky et al., 2016). Given that Tijuana is an area with high levels of drug injecting and with dynamic changes in policy/law enforcement responses to substance use that may impact mortality, this study examines rates, causes, and predictors of mortality among Tijuana PWID.

MATERIALS AND METHODS

Study Population

Proyecto El Cuete is a prospective community-based cohort of PWID in Tijuana, Mexico, which includes individuals aged 18 or older who resided in Tijuana, spoke Spanish or English, and reported injecting drugs in past 30 days. Injection drug use was confirmed by a visual assessment of needle track marks to ensure the inclusion of active injectors. The most recent phase of *El Cuete* began recruiting a convenience sample of participants in 2011 through self-referral, word of mouth, and street outreach across Tijuana, including shooting galleries and clinics (Robertson et al., 2014). At baseline and semiannually thereafter, participants completed an interviewer-administered questionnaire that elicited a range of data, including sociodemographic characteristics, injection and non-injection drug use, and interactions with law enforcement, for example. In addition, study participants received a

rapid HIV test at each visit. Positive HIV tests were sent for confirmatory testing at the San Diego Public Health Labs and, if needed, referrals for free healthcare through local health clinics operated by Mexico's universal health care system were provided for HIV treatment or care. All participants had private interviews and were offered both pre- and post-test counselling with trained staff. Participants were given a USD $20 stipend at each study visit for their time and transportation. This study was approved by the Ethics Board at the University of California San Diego and Xochicalco University in Tijuana. All participants provided written informed consent.

Measures

The present analysis included PWID recruited between April 2011 and June 2013, covering a 78 month period (visits 1 through 14) that ended January 15, 2018. The primary outcome was all-cause mortality rates among study participants, which was determined by death certificate from the Servicio Médico Forense del Estado de Baja California (SEMEFO) and through ongoing follow up with contacts provided by participants. Confirmed deaths include those ascertained by death certificate and unconfirmed deaths include those reported by family or friends for which we were unable to obtain a death certificate.

In order to confirm deaths and ascertain cause of death via death certificate among participants in this study, study staff made multiple attempts to reach relatives or friends of the decedent through contact information provided by participants (i.e. phone numbers and addresses), but also through street outreach. However, even when were able to contact family members or friends of the decedent, there were a number of reasons why we were unable to view death certificates, limiting our ability to ascertain official cause of death and thus relegating an individual to the 'unconfirmed' category. For instance, some participants never obtain official identification or legal documentation (e.g. migrants, deportees, homeless, people who used different name, and marginalized groups like PWID with high mobility). Fear or the shame related to disclosure of their relationship with a person who uses drugs or someone involved in a violent death, as well as the trauma related to the death itself, also served as a deterrent to family members obtaining the certificate. Long bureaucratic processes were also a barrier, including stricter rules to obtain reports in cases of violent deaths with ongoing investigations and frequent changes in rules around access of records at the City Morgue.

Causes of mortality for confirmed deaths were determined through review of death certificates and coroner's notes by an *El Cuete* staff member who is a Mexican physician. The underlying cause of death (i.e. the specific disease or injury) reported on each death record was coded using WHO classifications. Of note, deaths related to overdose are often underreported due to the stigma associated with substance use and we encountered cases that were labelled 'undetermined' by the coroner because they had little information about the case and an autopsy was not conducted (e.g., when homeless persons are found dead on a street).

We examined a range of potential predictors of mortality, which may contribute to the disease or injury that caused the death, including sociodemographic characteristics (e.g. number of years of education; ever deported from the US; homelessness in past 6 months;

traded sex for money, goods, shelter or drugs in past 6 months), drug use practices (e.g. duration of injection; daily injection of heroin or methamphetamine; receptive syringe sharing in past 6 months; divided drugs with some else using a syringe in past 6 months; used a cooker, cotton or water with someone or after someone in past 6 months; number of times overdosed (lifetime); enrolled in a methadone program in past 6 months), law enforcement interactions (e.g. arrested in past 6 months; number to times syringes confiscated by police in past 6 months; number of times harassed by police in past 6 months; number of times beaten by police in past 6 months), and health status (e.g. tested positive for HIV at baseline). The aforementioned variables were measured at baseline, but we also examined the time-updated effect of HIV incidence during the period at risk and injection cessation for a period of 6 months or more during time at risk (injection cessation was not measured at baseline). We were not powered to assess other time-updated predictors (see Limitations). Potential confounders examined include sex (male vs. female) and age (per year older).

Statistical Analyses

Participants who did (confirmed cases only) and did not die during the course of the study were described with respect to baseline characteristics by using frequencies and percentages for binary variables and means and standard deviations for continuous variables. Incidence density rates of mortality per 1000 person-years were calculated by taking the ratio between the number of cases and the number of person-years at risk accumulated over the follow-up period and multiplying it by 1000. The corresponding 95% confidence intervals (CI) were calculated using a Poisson distribution for the total sample and separately by HIV status at baseline since HIV is one of the primary causes of mortality among PWID across studies globally. Depending on whether a variable was time-invariant or time-updated, either a univariate Cox proportional hazards or a time-dependent regression model was used to examine the associations between each explanatory variable and time to all-cause mortality. To assess the proportional hazards assumptions, for continuous variables we examined plots of Schoenfeld residuals against the time variable, and for categorical variables we examined plots of log-minus-log of the survival function against the time variable. Additionally, to ensure that the proportional hazards assumption was met, interactions terms between predictors and time were included and tested in the models by using likelihood ratio tests. Martingale residuals plots were used to verify the linear relationship between each continuous explanatory variable and the log hazard of death.

A multivariable model was constructed using extended Cox regression to allow for inclusion of time-updated covariates. The model building strategy consisted of a “purposeful selection of variables” approach (Hosmer, Lemeshow, & May, 2011) guided by subject matter significance, relationships among potential explanatory variables (e.g. correlations, confounding, and interactions) and statistical significance. All variables associated with time to all-cause mortality, in univariate analyses at $p =< 0.10$, were considered as candidates for inclusion in the multivariable model, while controlling for age. Only variables that yielded a 5% significance level in the multivariable model were retained. Furthermore, the final multivariable model was checked for multicollinearity, which was ruled out by proper values of the variance inflation factors and of the largest condition index. All interactions between

explanatory variables were assessed and ruled out. Statistical analyses were performed using SAS software version 9.4 (SAS, Cary, NC). All *p*-values were two-sided.

RESULTS

At baseline, among 658 participants (excluding 76 unconfirmed deaths), 245 participants (37.2%) were female, the mean age was 37.3 (Standard Deviation [SD]=8.9), and the mean years of education was 7.8 (SD=3.2). Over one-fifth (22.4%) of the sample reported that they moved to Tijuana because they were deported from the US and recent homelessness was reported by more than a quarter of the sample (27.2%). Almost one-third (30.6%) of participants traded sex for money goods, shelter or drugs in the previous 6 months. In terms of substance use, at baseline, 88.6% of the study sample injected heroin at least daily, 15.2% injected methamphetamine at least daily, and 70.4% reported receptive syringe sharing in the past six months. During the period at risk, a quarter of the sample indicated that they stopped injecting for 6 or more months. On average, respondents reported 1.7 overdoses in their lifetime and 27.4% had ever been enrolled in a methadone program. Over half of the sample (52.2%) reported arrest in the previous 6 months, and in addition, 11.6% reported that police recently confiscated syringes (without arrest), 52.7% reported recent police harassment, and 45.6% had were beaten by a law enforcement officer in the past 6 months (not shown in Table). At baseline, 3% of participants tested positive for HIV, but over the period at risk, HIV incidence infection was 4.8%. Descriptive statistics are shown in Table 1.

A total of 734 eligible individuals were recruited between April 2011 and June 2013 and were followed up to 78 months (Median = 66.8 months; Interquartile range [IQR]: 34.7–74.3 months). As shown in Table 2, among 734 participants, there were 130 deaths (54 confirmed, 76 unconfirmed), with an incidence density of mortality of 17.74 deaths per 1000 person-years (95% Confidence Interval [CI]=13.01, 22.48) for confirmed deaths and 39.52 for all (confirmed and unconfirmed) deaths (CI=32.72, 46.31). Confirmed deaths resulted primarily from homicide/trauma (26%), overdose (26%), septic shock (18%), HIV-related causes (9%), organ failure from chronic substance use (9%), Hepatitis C (7%), and tuberculosis (5%).

Results from univariate and multivariable cox regressions assessing associations between mortality and participant characteristics are presented in Table 3. In univariate analyses, factors predictive of mortality among the study population (at the $p =< 0.10$ level) were ever enrolled in a methadone program (HR=1.65; CI=0.96, 2.84), number of times syringes confiscated by police in past 6 months (HR=1.01, CI=1.00, 1.02 per time), number of times beaten by a police officer in the past 6 months (HR=1.08; CI=1.03, 1.13 per time), HIV infection at baseline (HR=2.94; CI=1.02, 8.53), and incident HIV infection during period at risk (HR=3.06; CI=1.00, 9.37). Moving to Tijuana because of deportation from the US (HR=0.36; CI=0.14, 0.90) and injection cessation during period at risk (HR=0.34; CI=0.16, 0.75) were protective factors of mortality.

In multivariable analysis using extended Cox regression, factors independently associated with mortality were baseline HIV infection (aHR=6.77; CI=1.98, 23.17), incident HIV infection (aHR=3.19; CI: 1.02, 9.96), and number time being beaten by a police officer

(aHR=1.08 per time; CI=1.04, 1.12). Injection cessation for at least 6 months during period at risk remained protective (aHR=0.25; CI=0.33, 0.79),

DISCUSSION

The mortality rate observed among this population of PWID in Tijuana was high and stemmed, in part, from HIV, as in other studies (Mathers et al., 2013), but more frequently from factors associated with the structural context. Earlier estimates of mortality among PWID in Tijuana are not available, but mortality rates of 17.74 and 39.52 per 1000 per-years for confirmed and unconfirmed deaths, respectively, are high and comparable to rates in other global contexts (Hayashi et al., 2016; Mathers & Degenhardt, 2014; Quan et al., 2010).

In this analysis, a number of structural factors underlie the high rates of mortality among PWID. Particularly concerning was the proportion of preventable deaths due to overdose, homicide, and trauma. Overdose was the cause of a quarter of all deaths in this analysis. Although past experience of overdose was not independently associated with mortality, previous studies in Tijuana demonstrate that involuntary drug treatment, recent tranquilizer use, using hit doctors, more injections per day and younger age were associated with report of a non-fatal overdose (Rafful et al., 2018). Homicide or trauma also accounted for about a quarter of all deaths, indicating that PWID in this community are at risk of exposure to high levels of violence. Other studies have demonstrated that PWID experience substantially higher rates of physical and sexual violence, which is a key driver of morbidity and mortality (Degenhardt & Hall, 2012), but which also results in physical injury, posttraumatic stress disorder, suicidal ideation, depression, anxiety, overdose, unsafe injection practices, and impedes access to harm reduction (Braitstein et al., 2003; Fischbach & Herbert, 1997; McNeil, Shannon, Shaver, Kerr, & Small, 2014; Taylor & Jason, 2002).

These results point to the need to think critically about how best to support the health and lives of PWID, while simultaneously recognizing the structural constraints they face. In Tijuana, preventing overdose, homicide and violence against PWID means creating safer environments, including supervised consumption facilities, and making sure that PWID have access to naloxone and MAT (Beletsky et al., 2018). It also means addressing the marginalization of PWID. For instance, programs providing alternative income generation strategies could reduce exposure to violence and save lives by decreasing the economic need for participation in the drug trade. Other studies have shown that the costs of maintaining substance use can lead individuals to rely on illegal sources of income, like drug sales and sex work, both of which introduce numerous threats to health and increase interactions with law enforcement (DeBeck et al., 2007; Sherman & Latkin, 2002). At the same time, active PWID face difficulty finding legitimate employment due to limited skills, education and unstable housing (Sherman, German, Cheng, Marks, & Bailey-Kloche, 2006). Low threshold employment and skills building interventions that offer an alternative means of garnering income could reduce exposure to violence, criminal activity and mortality (DeBeck et al., 2007). In conjunction with improved access to no-cost MAT, which would reduce reliance on substances, such programs could prove effective in preventing PWID deaths. Simultaneous attention to these structural constraints, along with health promotion and violence prevention within communities, may therefore help to mitigate deaths.

Importantly, violence exposure extended to interactions with law enforcement, and being beaten by police was a significant predictor of mortality in this study. Deceased PWID reported being beaten by police twice as many times at baseline and risk of death increased by 1.08 times for each additional time beaten. Experiences of police violence may increase mortality in a few ways, both directly through injuries sustained during beatings, but also by increasing substance use to deal with pain and by increasing drug-related risks (i.e. needle sharing, transitioning to higher risk forms of substance use like injection rather than snorting). Police violence may also induce fear that displaces people to remote locations or leads to riskier injection behaviors, including rushed injections, which increase risk of vascular accidents or overdose (Kerr, Small, & Wood, 2005). In Ukraine, police beatings were independently associated with higher HIV incidence, which was attributed to its relationship with needle sharing (Strathdee et al., 2010), suggesting that police violence can increase risk for other diseases that can increase mortality. Individuals targeted by police may also be more vulnerable in terms of homelessness, severity of substance use, or engagement in sex work, factors independently associated with increased risk for mortality in other contexts (Miller et al., 2007; Spittal et al., 2006; Zivanovic et al., 2015). For instance, injuries could prevent individuals from working, creating or exacerbating economic and housing instability or increasing reliance on sex work or work in the drug trade. More research is needed to better understand these relationships in this and other contexts.

Police practices can also drive mortality by preventing PWID from accessing a range of necessary health and harm reduction services, including HIV prevention and care and needle exchanges (Beletsky, Grau, White, Bowman, & Heimer, 2011; Beletsky et al., 2014; Bluthenthal, Heinzerling, Martinez, & Kral, 2005; Cooper, Moore, Gruskin, & Krieger, 2005; C. S. Davis, Burris, Kraut-Becher, Lynch, & Metzger, 2005). Arrest or physical assault by police also deters PWID from accessing substance use treatment (Strathdee et al., 2010), which is necessary for reducing mortality (Bluthenthal, Kral, Lorvick, & Watters, 1997; Wood et al., 2003). In Tijuana, despite drug law reforms designed to shift to a public health model, research suggests that police encounters for PWID are common, including arrest, detainments, harassment and violence (Beletsky et al., 2013) and that drug reform has had limited impact on HIV among PWID in Tijuana (Borquez et al., 2018). Indeed, in this analysis, over half of the sample had been arrested in the past 6 months. These findings suggest that interactions with law enforcement, which could serve as an opportunity to connect PWID with supportive services, may instead be a source and facilitator of health harms. Trainings and other structural interventions focused on the integration of law enforcement and public health continue to be needed to reduce mortality among PWID in this context (Borquez et al., in press). Additionally, new models of drug policy, which embrace policing reform and true, rather than partial, decriminalization of substance use might also serve to prevent deaths.

Similar to other studies, HIV infection was an important factor contributing to high rates of mortality among PWID in Tijuana. Although HIV-related factors were the cause of 9% of the deaths we were able to evaluate, baseline HIV seropositivity was significantly higher (7.4%) among deceased participants than among survivors (2.6%). The PWID mortality rate was nearly three-fold higher among HIV-positive PWID and both baseline and incidence HIV infection were associated with a higher risk of mortality. A 2012 meta-analysis showed

that people who use drugs have a 74% greater risk of overdose if they have HIV than those who are not HIV-positive, resulting from biological, behavioral and structural factors, which suggests a need for increased overdose prevention efforts among HIV-positive individuals (Green, McGowan, Yokell, Pouget, & Rich, 2012). People with HIV also have higher levels of health and social harms, like comorbidities, socioeconomic disadvantage, inadequate contact with the health system, and may also have greater exposure to violence and stigma (Mathers & Degenhardt, 2014).

Elevated mortality among HIV-positive individuals may also reflect pre-AIDS mortality, which is high in PWID populations and related to viral/bacterial infection, but which can be mitigated by use of antiretroviral treatment (ART) (Wang et al., 2004). In Mexico, health care is universal, including ART; however, access to care is limited, especially for marginalized and stigmatized populations, like PWID (Goldenberg, Strathdee, Perez-Rosales, & Sued, 2012; Herrera, Campero, Caballero, & Kendall, 2008; Infante et al., 2006). In a pooled analysis of epidemiological data from six studies in Tijuana, PWID were the least likely to have been previously tested or to have initiated HIV care compared to other key populations (Smith et al., 2016). Ensuring that PWID have sufficient access to HIV prevention and treatment services is essential to reducing mortality in this population, but the loss of Global Fund resources that supported HIV testing and free sterile syringes poses challenges to outreach and the necessary scale-up of services. Although efforts are being made to improve ART distribution in Tijuana, more work is needed to promote the well being of PWID and to prevent deaths associated with HIV.

In this study, we also found that injection cessation for a period of 6 or more months at any point during the study period was protective. That even short periods of injection cessation were associated with a substantially lower risk of mortality indicates a need for improved access to MAT to reduce injecting among PWID in Tijuana. At the time of this analysis, there were three private methadone maintenance clinics operating in Tijuana, all which charged a fee (Werb et al., 2015), which can make treatment unattainable for PWID who are often economically marginalized. Although the Mexican federal government has placed a high priority on expanding MAT, especially in Tijuana (Moreno, Licea, & Rodriguez-Ajenjo, 2010), the findings presented here indicate that injection cessation in an important factor in preventing death, and thus have salient implications for programming in Mexico. Successful scale-up of MAT must address the diverse challenges faced by PWID and the social and structural barriers that impede access to care.

This study is not without limitations. Mortality rates may be underestimated because of deaths not captured through either formal or informal reporting. For the majority of the deaths among study participants, we were unable to obtain death certificates. Participants without death certificates were more likely to have been deported from the US, 26.3% vs. 9.4% (p=0.02). Deportees may have lacked legal documents, which prevented identification of death certificates. Additionally, the causes of death, especially for deaths related to overdose, may not be accurate as they are subject to the reporting of the medical examiner who may be less likely to report deaths from stigmatized causes. Analyses largely relied on baseline predictor data, which for some variables may change over time, so these results should be interpreted with caution. The nature of data collection, which occurred over 14

visits, resulted in missing data during follow-up (due to either complete loss to follow-up or missing a visit during ongoing data collection). This, coupled with the relatively small number of confirmed deaths did not allow for proper assessment of time-varying predictors. Specifically, we lacked statistical power to detect significance for most time-varying covariates, even if such significance existed. However, the effect size for incident HIV infection and injection cessation during the period at risk, respectively, was large enough to yield statistically significant results. Additionally, the relatively small sample of confirmed deaths resulted in large confidence intervals for some variables. Finally, the unique context of Tijuana may limit the generalizability of our findings to other settings.

CONCLUSIONS

In this study, mortality among PWID resulted primarily from preventable causes and was driven by structural factors that increase vulnerability. The results suggest that there is a need for improved overdose prevention, access to MAT, as well as the integration of HIV treatment and substance use services to adequately meet the needs of PWID in Tijuana and to reduce mortality. In addition, there is a need for explicit attention to all forms of violence, since homicide and trauma were major causes of death, including legal and policy reform to ensure that the law on the books is reflected on the streets, especially in terms of how law enforcement officers interact with PWID. Law enforcement officials are uniquely situated to contribute to harm reduction, but too often are a source of harm. The high rates of mortality among PWID should serve as a call to action for public health agencies to prioritize the lives of this population by preventing their deaths.

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Table 1.

Sample characteristics at baseline for confirmed incident cases vs. not incident cases

Variable	Confirmed Incident Case (n=54)	Not Incident Case (n=604)	Total (N=658)
Mean age (SD)	39.3 (9.7)	37.2 (8.8)	37.3 (8.9)
Female	20 (37.0%)	225 (37.3%)	245 (37.2%)
Mean years of education (SD)	7.9 (3.5)	7.8 (3.2)	7.8 (3.2)
Moved to Tijuana because was deported from the U.S.	5 (9.4%)	142 (23.5%)	147 (22.4%)
Experienced homelessness, past 6 months	11 (20.4%)	168 (27.8%)	179 (27.2%)
Traded sex for money, goods, shelter or drugs, past 6 months	12 (23.1%)	187 (31.2%)	199 (30.6%)
Mean years of injection (SD)	17.4 (10.3)	16.4 (9.4)	16.5 (9.5)
Daily heroin injection, past 6 months	50 (92.6%)	533 (88.2%)	583 (88.6%)
Daily methamphetamine injection, past 6 months	9 (16.7%)	91 (15.1%)	100 (15.2%)
Receptive syringe sharing, past 6 months	37 (68.5%)	426 (70.5%)	463 (70.4%)
Divided drugs with someone else by using a syringe (back loading), past 6 months	36 (66.7%)	356 (59.1%)	392 (59.8%)
Used a cooker, cotton, or water with someone or after someone else used it, past 6 months	35 (64.8%)	394 (65.4%)	429 (65.4%)
Mean number of times overdosed during lifetime (SD)	2.1 (3.2)	1.7 (2.5)	1.7 (2.5)
*Stopped injection for at least 6 months, reported ever during the time at risk	7 (13.0%)	157 (26.0%)	164 (24.9%)
Ever enrolled in a methadone program	21 (38.9%)	159 (26.3%)	180 (27.4%)
Arrested by police, past 6 months	25 (46.3%)	318 (52.7%)	343 (52.2%)
Mean number of times had syringes confiscated by police (without being arrested), past 6 months (SD)	3.9 (27.2)	1.1 (9.7)	1.37 (12.13)
Mean number of times harassed by police, past 6 months (SD)	14.5 (68.7)	8.4 (32.0)	8.89 (6.36)
Mean number of times beaten by police, past 6 months (SD)	0.8 (4.1)	0.4 (1.1)	0.39 (1.55)
Tested positive for HIV at baseline	4 (7.4%)	16 (2.6%)	20 (3.0%)
*Incident HIV infection during time at risk	3 (6.0%)	28 (4.7%)	31 (4.8%)

*Time-updated variable

Table 2:

Incidence density rates of mortality for total sample and by HIV serostatus for confirmed and unconfirmed deaths over 78 Months

	Confirmed Deaths (N=658)		Confirmed and Unconfirmed Deaths (N=734)	
	Number of Cases	**Incidence Density per 1000 person-years (95% Confidence Interval)**	**Number of Cases**	**Incidence Density per 1000 person-years (95% Confidence Interval)**
HIV-negative	50	16.89 (12.21, 21.57)	120	37.54 (30.82, 44.26)
HIV-positive	4	48.14 (0.96, 95.33)	10	107.14 (40.73, 173.54)
Total Sample	54	17.74 (13.01, 22.48)	130	39.52 (32.72, 46.31)

Table 3:

Univariate and multivariable models examining factors associated with confirmed deaths among PWID during 2011–2018 using Cox regression

Variable	Univariate Models			Multivariable Model		
	Hazard Ratio	95% CI	*p*-value	Hazard Ratio	95% CI	*p*-value
Age (in years)	1.03	0.99, 1.06	0.13	1.03	1.00, 1.07	0.058
Female	0.98	0.56, 1.70	0.94			
Number of years of education	1.02	0.93, 1.11	0.75			
Moved to Tijuana because was deported from the U.S.	0.36	0.14, 0.90	0.03			
Experienced homelessness, past 6 months	0.69	0.36, 1.33	0.27			
Traded sex for money, goods, shelter or drugs, past 6 months	0.63	0.33, 1.20	0.16			
Duration (years) of injection	1.01	0.98, 1.04	0.57			
Daily heroin injection, past 6 months	1.49	0.54, 4.14	0.44			
Daily methamphetamine injection, past 6 months	1.15	0.57, 2.34	0.70			
Divided drugs with someone else by using a syringe (back loading), past 6 months	1.37	0.78, 2.40	0.28			
Used a cooker, cotton, or water with someone or after someone else used it, past 6 months	0.98	0.56, 1.72	0.95			
Receptive needle sharing, past 6 months	0.95	0.54, 1.67	0.85			
*Stopped injection for at least 6 months, reported ever during the time at risk	0.34	0.16, 0.75	0.01	0.25	0.33, 0.79	0.002
Number of times overdosed during lifetime	1.06	0.96, 1.16	0.25			
Ever enrolled in a methadone program	1.65	0.96, 2.84	0.07			
Arrested by police, past 6 months	0.79	0.46, 1.35	0.39			
Number of times had syringes confiscated by police (without being arrested), past 6 months	1.01	1.00, 1.02	0.05			
Number of times harassed by police, past 6 months	1.003	1.00, 1.01	0.19			
Number of times beaten by police, past 6 months	1.08	1.03, 1.13	0.003	1.08	1.04, 1.12	<0.0001
Tested positive for HIV at baseline	2.94	1.02, 8.53	0.05	6.77	1.98, 23.17	0.002
*Incident HIV infection during time at risk	3.06	1.00, 9.37	0.05	3.19	1.02, 9.96	0.046

*Time-updated variable