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UNIVERSITY OF CALIFORNIA SAN DIEGO

Access to and utilization of harm reduction practices and services among people who use drugs
in San Diego, California and Tijuana, Mexico

A Dissertation submitted in partial satisfaction of the requirements
for the degree Doctor of Philosophy

in

Interdisciplinary Research on Substance Use

by

Katie Bailey

Committee in charge:

University of California San Diego

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Professor Peter J. Davidson
Professor Thomas L. Patterson

San Diego State University

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Professor Jaime Arredondo Sánchez Lira

2024

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Chair

University of California San Diego

San Diego State University

2024

DEDICATION

This dissertation is dedicated to people who use drugs. In particular, I dedicate this dissertation to the study participants in San Diego, California and Tijuana, Baja California, Mexico who provided data and expert insights that allowed me to develop this dissertation. I aimed to accurately represent their experiences and contribute research that promotes their health and wellbeing.

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LIST OF ABBREVIATIONS

AdjOR	Adjusted Odds Ratio
AIC	Akaike Information Criteria
BIC	Bayesian Information Criteria
CI	Confidence interval
FTIR	Fourier-transform infrared
FTS	Fentanyl test strips
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
IQR	Interquartile range
LCA	Latent class analysis
MOUD	Medications for opioid use disorder
OEND	Overdose education and naloxone distribution
OLR	Ordinal logistic regression
OR	Odds ratio
OUD	Opioid use disorder
PWID	People who inject drugs
PWUD	People who use drugs
SISE	Safe injection self-efficacy
SSP	Syringe services program
SUD	Substance use disorder

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ABSTRACT OF THE DISSERTATION

Access to and utilization of harm reduction practices and services among people who use drugs
in San Diego, California and Tijuana, Mexico

by

Katie Bailey

Doctor of Philosophy in Interdisciplinary Research on Substance Use

University of California San Diego, 2024

San Diego State University, 2024

Professor Steffanie Strathdee, Chair

Background: Overdose and infectious disease are major causes of morbidity and mortality among people who use drugs (PWUD). Harm reduction is a public health approach to reducing the negative consequences of criminalized substance use. This dissertation explored

access to and utilization of harm reduction practices and services among PWUD in Tijuana, Baja California, Mexico and San Diego, California, United States (U.S.).

Methods: This dissertation utilized survey data from the *La Frontera* binational cohort study. Chapter 1 compared overdose prevention strategies utilized by PWUD in Tijuana (n=343) and San Diego (n=143) between May 2022–March 2023. Latent class analysis (LCA) identified underlying groups of PWUD based on their probabilities of utilizing these strategies. Chapter 2 compared Tijuana (n=345) and San Diego (n=129) participant scores on a safe injection self-efficacy (SISE) scale between October 2020–September 2021 and assessed correlates of SISE score levels using ordinal logistic regression. Chapter 3 assessed naloxone accessibility among PWUD in San Diego between December 2021–December 2022 using qualitative interviews (N=20) and survey data (N=194).

Results: Chapter 1 revealed that participants’ primary overdose prevention strategies were *trying to avoid fentanyl* among Tijuana residents (84%) and *trying to stop/reduce injecting* among San Diego residents (52%). LCA revealed four latent classes among Tijuana participants characterized by unique overdose prevention strategies. Chapter 2 demonstrated that Tijuana residents had lower mean SISE scores than San Diego residents (1.93 vs. 3.46 out of 4). Among Tijuana participants, White race and previous San Diego residence were positively associated with greater SISE scores, whereas HCV and HIV seropositivity, homelessness, fentanyl use, polysubstance co-injection, and greater injection frequency were negatively associated. Chapter 3 showed that among PWUD in San Diego, 24% reported never having accessible naloxone, 52% sometimes did, and 24% always did. Qualitative findings revealed PWUD generally felt naloxone was easy to obtain in San Diego due to community distribution from harm reduction providers and satellite distribution among peers, but experienced some barriers. In quantitative

analyses, greater naloxone accessibility was positively associated with female sex, witnessing an overdose, and knowing where to get free naloxone, while monthly income $\leq$ USD\$500 was negatively associated.

Conclusions: These findings highlight multi-level opportunities to improve access to harm reduction services in Tijuana and San Diego, including drug checking, naloxone distribution and overdose response education, and medications for opioid use disorder (MOUD). Additionally, PWID in Tijuana could benefit from syringe service program (SSPs) expansion and safe injection self-efficacy education.

INTRODUCTION

Addiction and harms related to illicit substance use are major public health issues in North America, particularly in the U.S.,¹ where more than 340,000 people have fatally overdosed in the past ten years, reaching an annual record of 109,357 deaths in 2022.² Importantly, the annual fatal overdose count decreased in the U.S. in 2023 for the first time since 2018 as harm reduction policies and programs have become more widespread.³ Drug overdose has been the leading cause of accidental deaths in the U.S. since 2013,^{4,5} with a majority of fatal overdoses associated with opioids.⁶ However, death rates due to drug overdose spiked drastically beginning in 2013 with the widespread introduction of illicitly manufactured fentanyls (fentanyl) in the unregulated drug supply.⁷ In addition to being a public health tragedy, the opioid crisis in the U.S. represents trillions of dollars of economic burden annually due to health care and criminal-legal systems costs and loss of life.^{8,9} Although historically Mexico has reported low levels of opioid use and overdose,¹⁰ there has been an increase in fatal overdose in recent years.¹¹ Between 2014 – 2021 there was a 79% increase in the rate of fatal overdose among people aged 15 to 64 years in Mexico.¹¹ Further, recent research among people who use drugs (PWUD) in Mexican cities near the Mexico–U.S. border indicate elevated rates of opioid use, a growing presence of fentanyl, and increased overdose risk.^{12–16}

Relative to the general population, PWUD also face elevated morbidity and mortality associated with communicable and non-communicable disease, infections, mental illness, and injury.^{17,18} People who inject drugs (PWID) have an increased risk of overdose and exposure to bloodborne disease such as HCV and HIV relative to PWUD who do not use drugs intravenously.^{19–21} Reliable estimates indicated approximately 1.46% of the adult population in

the U.S. injected drugs in 2018²² and around 1.3% of the population aged 12 – 65 in Mexico reported injecting illegal drugs in 2017, with greater prevalence in Mexican-U.S. border states.¹⁰

Harm reduction is a public health model of addressing the potential harms associated with substance use. As a philosophy, harm reduction emphasizes pragmatism, individual autonomy and nonjudgment, recognition of structural and social influences on drug use, and a focus on potential harms rather than the cessation of drug use.^{23,24} Harm reduction programs and policies, therefore, are practical efforts to help PWUD avoid negative consequences that can occur when using drugs. There is considerable evidence for the efficacy and effectiveness of some harm reduction programs and practices, including medications for opioid use disorder (MOUD), overdose education and naloxone distribution (OEND) programs, and syringe service programs (SSPs). Efficacy refers to the performance of interventions under controlled circumstances (such as a randomized controlled trial), while effectiveness refers to the success of an intervention in real-world settings. There are also promising preliminary findings for drug checking services and safe consumption facilities. Additionally, research on harm reduction programs suggests considerable acceptability among stakeholders and PWUD.^{25–37}

MOUD with demonstrated effectiveness for persons with opioid use disorder (OUD) include methadone and buprenorphine.^{25–38} Methadone is a full opioid agonist (i.e., binds to and activates mu opioid receptors) and buprenorphine is a partial agonist. In adequate doses,^{39,40} these treatments alleviate opioid withdrawal symptoms, reduce illicit opioid use relative to placebos, attract and retain more patients relative to abstinence-based approaches, reduce the risk of premature death, and contribute to improved health and quality of life.^{38,41–45} As OUD is considered a chronic condition, MOUD treatment is not considered a “cure,” but rather a

supportive tool in the long-term management of OUD.⁴⁶ As such, duration of treatment is a key predictor of treatment outcomes.⁴⁷

Naloxone is a medication for opioid overdose reversal. OEND programs provide education on overdose prevention, recognition, and response, and distribute naloxone to the community. Research demonstrates that OENDs improve overdose knowledge and participant attitudes toward naloxone and are effective in reducing opioid-related mortality.⁴⁸ SSPs provide a variety of harm reduction services, but were initially conceived to distribute sterile injection equipment to reduce receptive syringe sharing. SSPs have demonstrated effectiveness in preventing bloodborne disease transmission.^{49–52} Additionally, SSPs connect PWUD to drug treatment and other health services.^{53,54}

Drug checking services allow PWUD to check their drugs for unwanted contaminants prior to using them. The most common drug checking tool utilized in the U.S. are fentanyl test strips (FTS), which are the most sensitive tool for detecting the presence of fentanyl in a drug sample.⁵⁵ Other drug checking tools include colorimetric tests that determine the presence or absence of a given substance in a drug sample and advanced spectrometry devices that can detect various substances and provide quantitative information in a single test.⁵⁶ Drug checking interventions have demonstrated a positive influence on overdose prevention behaviors, such as discarding fentanyl-containing drugs, and perceived self-efficacy to reduce drug use risks.⁵⁷ Safe consumption facilities provide PWUD a hygienic place to use their drugs under the supervision of qualified staff who can respond to overdose if needed. Research demonstrates safe consumption facilities are associated with reduced overdose risk^{58,59} and decreased hospitalization and emergency department visits.⁶⁰

The purpose of this dissertation was to assess accessibility and utilization of different harm reduction strategies and services among PWUD in the Tijuana/San Diego border region to identify potential needs, service gaps, disparities, and opportunities for harm reduction expansion. This dissertation was guided by three specific aims: (1) identify patterns in utilization of overdose prevention strategies among PWUD in Tijuana and San Diego, (2) determine factors associated with safe injection self-efficacy among PWID in Tijuana and San Diego, and (3) assess naloxone accessibility among PWUD in San Diego.

Setting and Context

San Diego County is home to approximately 3.3 million people,⁶¹ situated along the busiest international land border crossing in the U.S., with Tijuana just to the south. Tijuana has a population of approximately 2.2 million⁶² and is the most populous city of Baja California, the state with the highest prevalence of illicit drug use in the country according to the most recent national survey from 2016–2017.¹⁰ The San Diego/Tijuana border region is considered a high intensity drug trafficking area by the U.S. Drug Enforcement Administration⁶³ where fentanyl has become ubiquitous.^{15,64}

The age-adjusted fatal overdose rate in California increased by 26% between 2020 and 2022 (21.6 to 27.1 per 100,000), and preliminary data indicate similar trends for 2023.⁶⁵ San Diego County exceeds the state's trends, with a 51% increase in the rate of fatal overdose between 2020 and 2022 (15.1 to 22.8 per 100,000).⁶⁵ There were 990 overdose deaths in San Diego County in 2022, two-thirds of which were fentanyl-involved.⁶⁵ Although exact numbers are unknown, there were an estimated 35,000 PWID in San Diego County in 2007.⁶⁶ Of 485 people newly diagnosed with HIV in San Diego County in 2021, about 10% of cases were related to injection drug use.⁶⁷ A report from 2019 estimated 31.5% of HCV infections in San

Diego are among PWID.⁶⁶ In a study of 567 PWID in San Diego between 2012–2014, researchers found an HIV prevalence of 9% and HCV prevalence of 66%.⁶⁸ A 2019 street intercept survey among 235 PWID in San Diego found that 14% of participants reported HIV seropositive status and 38% HCV seropositive status,⁶⁶ although confirmatory tests were not conducted.

There is a growing overdose rate in Mexico, particularly in the Northwestern region.¹¹ Tijuana had a fatal overdose rate of 1.75 per 100,000 from 2020–2021, an 84% increase from the period between 2008–2010.¹¹ Recent studies among PWID in Tijuana report that around half or more of participants have experienced a nonfatal overdose.^{16,69,70} In a study of mortality among 734 PWUD in Tijuana between 2011–2018, 26% of 130 deaths were due to overdose and 18% due to HIV-related causes.⁷¹ A 2010 report estimated there were roughly 12,000 PWID in Tijuana with an estimated HIV prevalence of 4.2%.^{72,73} A recent study among PWID in Tijuana between 2020–2021 found an HIV prevalence of 16%, with greater prevalence among cisgender women relative to men (2.36 vs. 0.82) and among transgender/non-binary relative to cisgender persons (21.77 vs 1.23).⁷⁴ Estimates from 2017–2018 indicate an HCV prevalence of up to 89% among PWID recruited from drug consumption sites in three Mexican cities on the U.S.-Mexico border, including Tijuana.⁷⁰

Importantly, San Diego and Tijuana have overlapping PWUD populations, with studies indicating between 15% – 66% of PWID in San Diego cross the border to use drugs in Mexico^{16,68,75,76} in part due to perceptions of easier access to better quality drugs.^{76,77} Indeed, possession of small amounts of drugs for personal use was decriminalized in Mexico in 2009, which may contribute to the decisions of San Diego PWUD to travel to Tijuana to obtain and/or use drugs.⁷⁸ As such, it is important to study PWUD populations and harm reduction in both

cities, as there are public health implications of cross-border drug use, including differential risks of overdose due to variations in drug supply,^{16,64} differences in harm reduction services availability,¹³ and the potential for cross-border infectious disease spread through sharing of drug injection paraphernalia.⁷⁴

Background and contributions of this dissertation

Aim 1. In Chapter 1, I assessed PWUD utilization of various overdose prevention strategies and employed latent class analysis (LCA) to identify subgroups of participants according to their probabilities of utilization these strategies. Public health harm reduction interventions often promote individual-level strategies to prevent fatal overdose, such as carrying naloxone, avoiding using drugs alone, or using drug checking methods, such as fentanyl test strips (FTS), to detect and avoid fentanyl. However, the extent to which PWUD engage in such behaviors outside of a healthcare or harm reduction services context is not well understood. Understanding utilization of overdose prevention strategies can provide information on what may be missing in terms of harm reduction services and education, what structural barriers may prevent use of these strategies, and which strategies are practical for PWUD given the constraints of their daily lives.

Prior research examining overdose prevention strategies has largely focused on a limited number of behaviors following an intervention and drawn from participant samples recruited from healthcare or harm reduction settings, which may not represent broader populations of PWUD.^{79–86} Aim 1 built upon prior research by examining utilization of ten overdose prevention strategies among PWUD recruited through street outreach in Tijuana and San Diego, comparing strategies utilized by city of residence, determining underlying groups of PWUD based on their probabilities of using each strategy, and comparing descriptive individual- and structural-level

characteristics of latent groups to inform potential tailored strategies to increase uptake of overdose prevention strategies.

Aim 2. In Chapter 2, I compared safe injection self-efficacy (SISE) among PWID in Tijuana and San Diego and determined factors associated with SISE scores. I utilized a scale measure of SISE developed for the multi-site Drug Users Intervention Trial (DUI).⁸⁷ This SISE measure is based on the general self-efficacy scale (GSE-6), which has demonstrated reliability and validity.⁸⁸ SISE is an important indicator of injection risk behaviors that can lead to bloodborne disease transmission among PWID.^{87,89–93} Therefore, assessing correlates of SISE can provide information for individual- or structural-level interventions to decrease injection risk. This study built upon two prior studies that utilized an SISE measure in research with PWID in Tijuana. One study from 2013 determined there was a negative association between SISE and injection risk scores among a cohort of PWID (i.e., higher self-efficacy is related to lower injection risk).⁹⁴ Another study of an intervention for female sex workers who inject drugs that aimed to reduce injection risk through improving safe injection self-efficacy determined that police interactions moderated the intervention effect by reducing self-efficacy.⁹⁰ The analysis in Chapter 2 was the first to consider SISE as a dependent variable and identified additional factors that may influence SISE among PWID in the region.

Aim 3. In Chapter 3, I used mixed methods to assess perceptions of naloxone accessibility among PWUD residing in San Diego. Naloxone was approved for opioid overdose reversal by the FDA for limited prescription use in 1971.⁹⁵ Community OEND programs have been providing the antidote and training for its use in community settings since 1996, with programs expanding rapidly since 2010 owing to multiple state standing orders that allowed for community organizations to distribute naloxone to persons at risk of opioid overdose.^{96,97}

Although naloxone became more widely available in San Diego following California's standing order, recent San Diego County reports indicated a need to expand overdose prevention efforts, including naloxone distribution.^{66,98} However, no prior reports assessed differences in naloxone accessibility or determined factors associated with greater personal naloxone accessibility among PWUD in the county. Chapter 3 built upon prior County assessments by examining variations in personal naloxone accessibility and highlighting potential explanations for differential accessibility among PWUD with quantitative and qualitative data. This analysis also included a novel outcome variable for determining naloxone accessibility that considered how often participants reported that they had the medication easily accessible rather than whether they were currently carrying it. Naloxone carriage has been a common performance indicator of naloxone expansion efforts that may inaccurately estimate naloxone access.⁹⁹ Chapter 3 serves to inform efforts to improve naloxone accessibility among PWUD in San Diego County.

Conceptual frameworks

This dissertation was informed by the Risk Environment Framework.^{100,101} Rhodes recognized an emphasis in harm reduction programs on individual behavior change, while neglecting to account for the context in which individual behaviors take place.¹⁰⁰ An overemphasis on individual cognition and behavior ignores the social, institutional, political, policy, economic, and legal systems that influence drug use and related harms as well as the effectiveness of harm reduction programs. The Risk Environment Framework promotes focus on how different types of environmental factors (social, economic, policy, and physical) interact at different levels (micro and macro) throughout time to influence risk for PWUD.¹⁰⁰ It is important to assess risk environments, as this focus shifts the responsibility of harm prevention from PWUD to actors that influence the socio-political landscape.¹⁰⁰

The Risk Environment Framework does not delineate causal pathways but allows for the selection and interpretation of variables that can account for environmental context. In this dissertation, the Risk Environment framework informed variable selection and interpretation of findings to account for the environment that serves as the context for drug use and harm reduction behaviors. Figure 1 provides a visualization of the risk environment context for the dissertation aims, including variables assessed in analyses and their possible level of influence on dependent variables. While several of the variables were used in all three aims, only those that have theoretical associations with the outcome of interest were included in each analysis.

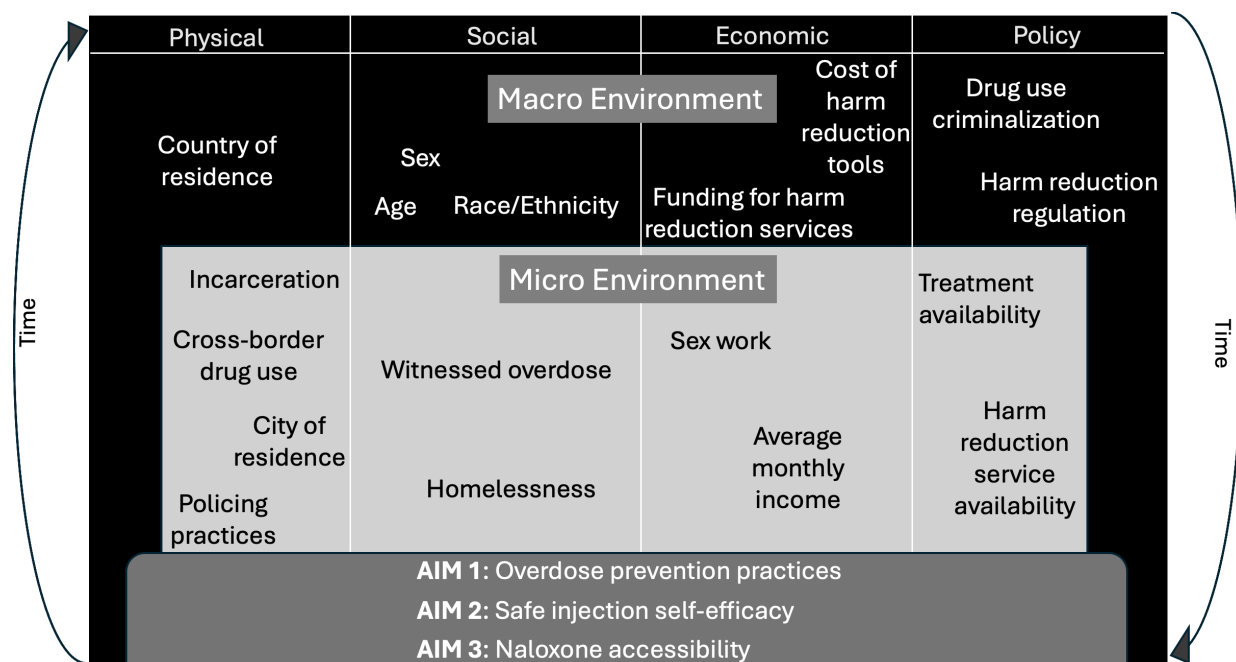


Figure 1. The Risk Environment Framework applied to select and interpret variables used in dissertation aims

Social Cognitive Theory was incorporated in Chapter 2 examining SISE. Self-efficacy is a construct with origins in Social Cognitive Theory and refers to a person's belief in their capacity to complete a given behavior, which in turn is hypothesized to be associated with actual behavior.^{102,103} Social Cognitive Theory posits that self-efficacy is an internal, cognitive process

and that cognitive, environmental, and behavioral processes interact to influence outcomes, a concept referred to as reciprocal interactions.¹⁰⁴ Social Cognitive Theory was applied in Aim 2 to select variables representing other cognitive, environmental, and behavioral processes and health factors, including hepatitis C virus (HCV) and human immunodeficiency virus (HIV), and assess their relationships with SISE (Figure 2). In this model, environmental factors represent the risk environment.

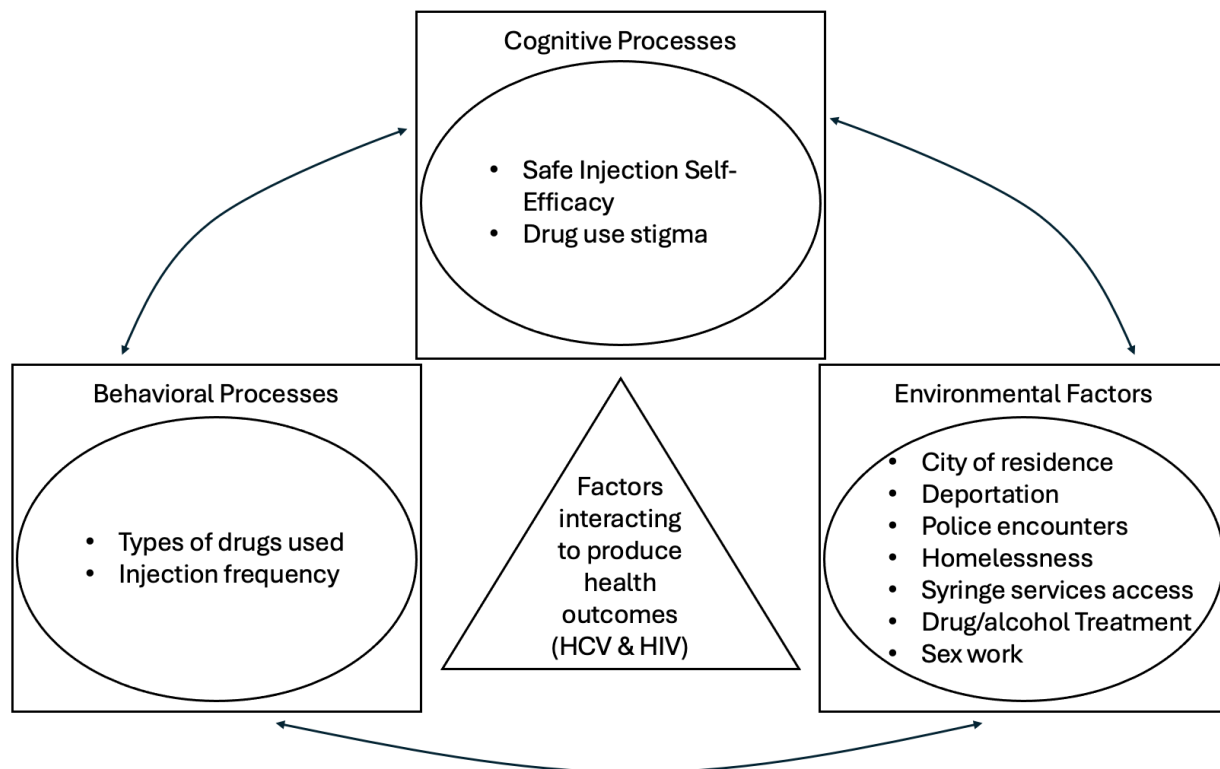


Figure 2. Application of Social Cognitive Theory to assess associations between safe injection self-efficacy and other cognitive, behavioral, environmental, and health factors

Data Sources

Overview. This dissertation utilizes data collected for a longitudinal cohort study of PWUD in San Diego and Tijuana called *La Frontera* (Principal Investigator Dr. Steffanie Strathdee) that was designed to collect information about infectious disease, overdose, drug use,

and drug market trends in a binational context.¹⁰⁵ Participants were originally recruited in San Diego and Tijuana between October 2020 – September 2021 (Cohort 1) and additional participants were recruited in February 2022 – June 2022 in San Diego only to accommodate a COVID-19 vaccination sub-study called Link-UP (Cohort 2). Follow-up survey data was collected by *La Frontera* field staff from study participants every six months. Each dissertation chapter involved secondary data analysis from the *La Frontera* study, with additional qualitative data collection by this dissertation’s author from *La Frontera* participants for Chapter 3. For Chapters 1 and 2, the Cohort 1 follow-up dataset that was most recent and had the greatest number of respondents for the outcome of interest was selected. For Chapter 3, I utilized data from surveys and interviews conducted with participants of both cohorts prior to San Diego County’s naloxone expansion initiatives that began near the end of 2022. Each aim examined cross-sectional data. Table 1 demonstrates the survey data utilized for each aim. Study procedures, including the collection of qualitative data, were approved by the Xochicalco University and UCSD Institutional Review Boards (project number 191390).

Table 1. La Frontera study datasets utilized by dissertation chapter

	Cohort 1				Cohort 2
	Baseline	Follow-up 1	Follow-up 2	Follow-up 3	Baseline
	10/2020–9/2021	5/2021–5/2022	12/2021–12/2022	3/2022–3/2023	2/2022–6/2022
Chapter 1					
Chapter 2					
Chapter 3					

Participants and recruitment. Inclusion criteria for the *La Frontera* study were residing in San Diego or Tijuana, being 18 years or older, speaking English and/or Spanish, and past-month injection drug use as evidenced by injection stigmata. One aim of the *La Frontera* study was to assess cross-border disease transmission. As such, San Diego-resident participants were

purposively recruited to ensure that approximately half had engaged in cross-border drug use, defined as having used drugs in Mexico in the previous two years, which was determined through a preliminary screening question.

La Frontera participants were recruited for baseline surveys between October 2020 – September 2021 through street-outreach by two full-time, bilingual teams of trained interviewers in San Diego and Tijuana. Recruitment efforts were focused on structurally marginalized PWID, many of whom were located in areas where homelessness was common. The survey teams recruited participants in a variety of locations, including streets, parks, shelters, motels, river embankment, canyons, encampments, and parking lots. Participants in Tijuana were also recruited in the downtown red-light district. Those found eligible were invited to participate and provided with written informed consent. Field staff had physical offices as well as mobile vans where they could meet with participants.

During initial recruitment, 612 participants were enrolled in the *La Frontera* study, of whom 202 indicated their primary past six-month residence was Tijuana and 410 San Diego, with 206 San Diego participants reporting cross-border drug use (Cohort 1). Additional *La Frontera* participants who were recruited in San Diego by the same methods previously described between February – June 2022 (Cohort 2) for a sub-study of COVID-19 testing and vaccination (*LinkUP*).¹⁰⁶ Data from Cohort 1 was utilized in Chapters 1 and 2, and Chapter 3 incorporated data from Cohorts 1 and 2. While survey instruments were similar for both cohorts, they did not include all of the same questions, which precluded the use of Cohort 2 data in Chapters 1 and 2.

Not all participants initially recruited were included in each chapter. Some participants were lost to follow-up, the implications of which are described in each chapter. Additionally,

some participants reported no longer injecting drugs in follow-up surveys. As self-efficacy related to safer injection practices was the focus of Chapter 2, those who indicated they stopped injecting drugs more than six months before survey completion were excluded from that analysis but were included in Chapters 1 and 3. The focus of Chapter 3 was naloxone accessibility in San Diego only and therefore excluded *La Frontera* participants residing in Tijuana.

Twenty *La Frontera* participants were recruited in August 2022 for qualitative interviews utilized in Chapter 3 and represented both cohorts. Inclusion criteria for interviews was being a *La Frontera* participant and residing in San Diego, with purposive efforts to recruit a variety of participants based on sex, race/ethnicity, age, and location. Interviews included a separate informed consent.

Data collection. *La Frontera* survey data was collected using computer-assisted, interviewer-administered surveys using Questionnaire Development Systems software developed in Maryland by NOVA Research.¹⁰⁷ Surveys included skip-logic where possible to reduce respondent burden. Surveys were conducted in English or Spanish. Participants received USD\$20 for each semi-annual survey completed, and USD\$5 for updating their contact information at quarterly intervals.

Qualitative interviews for Aim 3 were semi-structured with a focus on perceptions of naloxone accessibility. All interviews were conducted in English as per participant preference. Interviews lasted approximately twenty minutes to one hour each and participants received USD\$20. All interviews were audio recorded and transcribed using a professional transcription service (dailytranscription.com). Transcriptions were assessed for accuracy and edited as necessary.

Formative work: Drug checking awareness, utilization and interest

This dissertation's author initiated research to assess access to and utilization of harm reduction services among *La Frontera* participants prior to finalizing dissertation aims. A manuscript examining drug checking awareness, utilization, and interest among *La Frontera* participants residing San Diego was developed by the author of this dissertation and published in 2023.¹⁰⁸ Because of its relevance to the overarching theme of this dissertation, a summary is included below.

We examined San Diego-residing *La Frontera* participant experiences with drug checking services (e.g., FTS, colorimetric tests, or other) according to surveys completed between February – July 2022 among participants from Cohorts 1 and 2 who indicated primary residence in San Diego at baseline (N=426).¹⁰⁸ We found only 34% of participants had ever heard of drug checking tools or services, and only 19% had ever used them, most of whom had used FTS, but infrequently. In a multivariable model we also found disparities in lifetime utilization of FTS, with non-White participants and participants experiencing homelessness having a reduced likelihood of ever using drug checking tools or services. However, an interaction term indicated that for non-White participants, SSP engagement significantly increased their likelihood of having used drug checking services relative to non-White participants who were not SSP clients. Finally, we found that less than half (44%) of participants were interested in receiving free FTS, perhaps because many used fentanyl purposefully. When asked if they had any concerns with using FTS, some participants indicated they believed FTS results were unreliable. Among a subset of participants who were asked about interest in advanced spectrometry drug checking (N=196), most (84%) said they would be interested in this service. The implications of this study were: (1) drug checking was uncommon among

participant PWUD in San Diego, (2) there were racial/ethnic disparities in drug checking utilization, (3) structural factors (e.g., homelessness and SSP engagement) influenced drug checking likelihood, (4) there is a need to expand FTS access and education, and (5) that FTS may not fully meet the drug checking needs of San Diego PWUD. Chapters 1–3 of this dissertation examined additional aspects of accessibility and utilization of harm reduction strategies and services among *La Frontera* participants.

Chapter 1 Individual-level overdose prevention strategies utilized by people who use drugs in San Diego, California and Tijuana, Baja California, Mexico

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Abstract

Background: Identifying subgroups of individuals utilizing different overdose prevention strategies is important for targeted intervention development amidst a toxic drug supply in North America. Few studies have assessed utilization of overdose prevention strategies among people who use drugs (PWUD) outside of harm reduction or healthcare settings, and none have examined these in the San Diego-Tijuana border region.

Methods: Survey data was collected between May 2022 – March 2023 among PWUD in San Diego, California and Tijuana, Mexico. We compared utilization of ten overdose prevention strategies among PWUD based on city of residence. Latent class analysis (LCA) was used to identify groups of PWUD based on probabilities of utilizing various strategies.

Results: Participants (N=470) were primary non-White (88%), male (74%), Tijuana residents (72%). The most commonly used drugs were methamphetamine (68%), heroin (60%), and fentanyl (33%). Overdose prevention strategies varied drastically based on city of residence. San Diego participants primarily tried to stop/reduce injecting (52%) and Tijuana participants primarily tried to avoid fentanyl (84%). Tester shots, seeking treatment, drug checking, and

slower injection were strategies endorsed by <5%. LCA was inconclusive for the San Diego subsample but revealed four classes in the Tijuana subsample. Classes were characterized by 1) trying to use the same drug supplier, 2) stopping/reducing injecting, 3) avoiding fentanyl only, and 4) avoiding using alone.

Conclusions: Several key overdose prevention strategies were underutilized, partially explainable by limited availability of harm reduction services. Interventions targeted at subgroups of PWUD based on identifiable characteristics could increase uptake of overdose prevention strategies.

Introduction

Individual-level harm reduction strategies (HRS) are practices people who use drugs (PWUD) employ to protect themselves from potential harms of using drugs, including bloodborne disease transmission or overdose. In an era characterized by an increasingly toxic unregulated drug supply,¹⁰⁹ individual-level overdose prevention HRS are important in the absence of effective community- and policy-level interventions to address major public health crises associated with criminalized drug use.¹¹⁰

Researchers have assessed overdose prevention HRS (sometimes called risk or harm reduction behaviors) among PWUD with a variety of measures. Quantitative studies have examined actual or intended utilization of HRS among PWUD such as employing tester shots to gauge drug potency, carrying naloxone or ensuring others have the overdose reversal medication nearby, using in small doses, avoiding using alone, communicating about overdose, or smoking rather than injecting drugs.^{84,85,111–113} Related intervention evaluation studies from North American settings have focused on uptake of specific harm reduction programs or practices, such as drug checking with fentanyl test strips (FTS), or adopting safer behaviors following a positive

FTS result, such as discarding the drug.^{81,82,114,115} Qualitative inquiry has offered additional insights into overdose prevention HRS from PWUD, such as avoiding drug use in a locked room,¹¹⁶ being mindful of personal tolerance,¹¹⁷ building reliable relationships with drug suppliers,¹¹⁸ and seeking medications for opioid use disorder (MOUD).¹¹⁹

Most of these studies draw from samples of PWUD in specific healthcare or harm reduction services contexts, such as SSPs or emergency departments,^{79,81–85,111,120} limiting generalizability of findings to PWUD who may not seek or have access to such services.

The present study builds on this literature by assessing utilization of ten overdose prevention HRS among PWUD recruited through street outreach in a location where these measures have not been broadly examined: San Diego, California and Tijuana, Mexico. First, we compared overdose prevention HRS utilization between PWUD in the two cities. Our second objective was to determine whether there were underlying groups of PWUD in both cities based on patterns in their utilization of overdose prevention HRS using latent class analysis (LCA). Finally, we compared latent groups based on demographic, structural, substance use, and overdose measures to identify observable differences between latent groups. These methods can be useful for informing targeted interventions aimed at addressing the specific needs and preferences of otherwise unobserved subgroups.

Materials and Methods

Study setting

San Diego and Tijuana share the busiest land border crossing in the U.S., a region that is considered a high intensity drug trafficking area⁶³ where fentanyl has become ubiquitous.^{15,64} San Diego County has a population of around 3.3 million people¹²¹ and Tijuana approximately 2.2 million.⁶² San Diego experienced a 33% increase in fatal overdoses between 2020 and 2022,⁶⁵ with 965 overdose deaths in 2022, two-thirds of which were fentanyl-involved.⁶⁵ While

surveillance data is limited in Tijuana, studies among people who inject drugs (PWID) report that around half or more experienced a nonfatal overdose.^{16,69,70} Recent studies also document an increasing prevalence of fentanyl and fentanyl-contaminated drugs in Tijuana.^{15,16,64} San Diego and Tijuana have overlapping PWUD populations, with studies indicating between 15% – 66% of PWID in San Diego cross the border to use drugs in Mexico,^{16,68,75,76} in part due to perceptions of easier access to better quality drugs.^{76,77}

Participants and recruitment

Participants were recruited between October 2020 – September 2021 for the La Frontera longitudinal cohort study of PWID in the San Diego-Tijuana border region as detailed elsewhere.^{16,105} Bilingual research staff identified potential participants through street outreach based on inclusion criteria (18 years or older, spoke English or Spanish, lived in San Diego or Tijuana, and engaged in past-month injection drug use) in locations known to be inhabited or frequented by PWUD. San Diego-based participants were oversampled to include 50% who reported cross-border drug use, defined as having gone to Mexico to use drugs within the prior two-year period. Field staff invited those eligible to participate in the study and sought informed consent. Follow-up surveys are conducted with participants every six months until study completion in 2025. The present study utilized cross-sectional data from the third follow-up survey, which took place between May 2022 – March 2023, and was the most recently completed follow-up survey.

Survey measures and data collection

The survey instrument was available in both English in Spanish and was administered by field staff using laptops. Participants received \$20 for each survey. The Human Research

Protections Program and Biosafety Committee at the University of California San Diego and the institutional review board at Xochicalco University approved study protocols.

Overdose prevention strategies

We drew from the literature to develop overdose prevention survey questions, with input from field staff and community partners. Field staff asked participants if they did any of the following practices in the last six months to avoid an overdose: carried naloxone, didn't use drugs alone, stopped or cut down on injecting drugs, went to drug treatment, injected drugs more slowly, did a tester shot, tried to use the same supplier, tried not to use fentanyl, used testing strips or other drug checking service, or some other strategy. Participants responded either "yes" or "no" for each overdose prevention HRS. When participants indicated they used some other strategy, staff recorded this in an open-ended field. Open-ended responses that fit into predefined overdose prevention HRS categories were reclassified as such. For example, one participant responded with "I stopped injecting," so we indicated an affirmative response to the "stopped or cut down on injecting drugs" predefined question. We identified several open-ended "other" responses whereby participants referred to using a strategy related to controlling the dose of the drugs they ingest. Due to this being a moderately common "other" response, we created an additional overdose prevention HRS category called "tried to control dose." Additional "other" responses that were not included in analysis are provided in Supplementary Table 1.

Demographics and structural factors

Participants provided sociodemographic data including age, sex, race, and ethnicity as well as information on structural factors including homelessness, number of hours spent on the street daily, police encounters, and SSP engagement in the prior six months.¹⁰⁸ We also created a variable indicating whether a participant specified their primary city of residence was San Diego

at baseline, but by the May 2022 – March 2023 follow-up reported primary past six-month residence in Tijuana.

Substance use

Binary substance use variables indicated whether participants knowingly consumed each drug type by any means in the previous six months. A polysubstance co-injection variable indicated whether a participant simultaneously injected a combination of opioids with stimulants in the prior six months. Participants reported past six-month overdose which we dichotomized, as well as lifetime overdose, included as both dichotomous and count measures.

Statistical analysis

Participant characteristics

We summarized San Diego and Tijuana participants' demographic, structural, substance use, overdose, and overdose prevention HRS measures using descriptive statistics including frequencies and percentages for binary variables and means and standard deviations (SD) or medians and interquartile ranges (IQR) for continuous variables. Analyses were conducted using base R¹²² and RStudio.¹²³

Latent class analysis

We used the R glca package¹²⁴ to discern groups of PWUD based on patterns in their responses to overdose prevention HRS questions, conducting separate LCAs for Tijuana and San Diego residents. In LCA models we only included overdose prevention HRS that were reported by at least 5% of each subsample.

We compared 2-, 3-, 4-, 5- and 6-class models and determined the best model based on fit statistics. Akaike information criterion (AIC) and Bayesian information criterion (BIC) balance goodness of fit with model complexity, with lower values indicating stronger models. Entropy is

a measure between 0 – 1 with higher values indicating greater certainty in classification of individuals to latent groups. A likelihood ratio test (LRT) G^2 statistic and bootstrap p-value indicate absolute model fit, with a p-value $<.05$ signifying poor fit. A LRT deviance statistic and bootstrap p-value indicate relative fit between two competing models, where a p-value $<.05$ signifies a more complex model is a better fit compared to a simpler model with fewer classes.¹²⁵ The number of bootstrap samples generated for LRTs was set to 50 and the number of iterations to estimate the model using different starting probability values was set to 500. To avoid problems of generalizability that arise when classes are so small that meaningful inferences cannot be made, or classes are so large that distinct patterns are not interpretable, we established *a priori* that latent classes should represent no fewer than 5% and no greater than 50% of sample participants.

Class comparisons

After determining the best model, we assigned study participants to the latent class for which they had the greatest posterior probability of membership. While this simple method does not explicitly address the uncertainty inherent in class assignment, it effectively minimizes the likelihood of incorrect assignments when contrasted with alternative methodologies.¹²⁶ Next, we compared classes based on demographic, structural, substance use, and overdose measures using T-tests or Kruskal-Wallis tests for continuous variables and Chi-square or Fisher's exact tests for categorical variables. Measures for which preliminary statistical tests indicated a significant difference across latent classes were assessed using a post-hoc Tukey's test to determine which classes influenced significance. For class comparisons, we only included categorical variables that represented at least 5% of the subsample.

Results

Study sample

The May 2022 – March 2023 follow-up survey was completed by 486 participants representing 79% of those recruited at baseline (N=612). Missing participants (n=126) were lost to death (n=48, 38%) or otherwise could not be located. Those lost to follow-up were more likely to have been white and unhoused with primary residence in San Diego at baseline (Supplementary Table 2). An additional 16 participants were removed from analysis because they reported no illicit drug use in the prior six months, yielding a total sample size of 470.

Most participants identified as non-White race/ethnicity (88%, n=412) and were majority male (74%, n=348) with an average age of 45 years (SD = 10.2) (Table 2). Most (81%, n=381) were unhoused, spending an average of 15 hours per day in the street. Fourteen percent (n=75) reported stop/arrest by police in the prior six months and 21% (n=100) were SSP clients. About one-third (32%, n=150) reported primary residence in San Diego at baseline and primary residence in Tijuana at follow-up.

Methamphetamine was the most commonly consumed drug (68%, n=323), followed by heroin (60%), fentanyl (33%), and china white (22%). China white is a fine powder heroin that Tijuana PWUD report has increasing potency in recent years, likely due to being mixed with fentanyl^{15,64}. Polysubstance co-injection was reported by 39% (n=183) and the median number of average daily injections was 2.5 (IQR = 2.4). Four percent (n=18) reported an overdose in the preceding six months. Over half (55%, n=260) reported having ever overdosed with a median of one prior overdose.

Comparison of San Diego and Tijuana sample characteristics

Relative to San Diego residents, more Tijuana residents indicated

Hispanic/Latinx/Mexican ethnicity (93% versus 50%), while San Diego residents were slightly more diverse in terms of other races. A greater proportion of Tijuana residents were men (76% vs. 70%). Participants in both cities had similar mean ages and a majority experiencing homelessness (81%). A greater proportion of San Diego residents reported stop/arrest by police and SSP engagement relative to Tijuana residents (42% vs. 6% and 53% vs. 9% respectively). Heroin was the substance most prominently used in Tijuana (71%), while methamphetamine was the most common in San Diego (79%). Fentanyl use was more prevalent in San Diego than Tijuana (67% vs. 20%), while china white was almost exclusively used by Tijuana residents (30% vs. 1%). Polysubstance co-injection was more common among Tijuana residents (49% vs. 14%) and the median number of average daily injections was greater in Tijuana (2.5 versus 0.1). A greater proportion of San Diego residents reported past six-month and lifetime overdose compared to Tijuana residents (12% vs. 1% and 65% vs. 52%).

Utilization of overdose prevention strategies

The most common overdose prevention HRS was avoiding fentanyl (65%), followed by avoiding using alone (31%), stopping/reducing injecting (19%), using the same supplier (13%), and carrying naloxone (10%) (Figure 1). Treatment, drug checking, dose control, and injecting more slowly were each endorsed by less 3%. Three percent reported no overdose prevention HRS.

Comparisons in utilization of overdose prevention strategies by city of residence

There were distinctions in overdose prevention HRS utilization based on city of primary residence. A larger proportion of Tijuana residents reported trying to avoid fentanyl (84% vs. 15%), avoid using alone (37% vs. 16%), and use the same supplier (15% vs. 8%). Relative to Tijuana residents, a larger proportion of San Diego residents reported trying to stop/reduce

injecting (52% vs. 6%) and carrying naloxone (30% vs. 2%). Tester shots, drug checking, dose control, and injecting more slowly were strategies endorsed by 4 – 8% of San Diego residents, but 0% of Tijuana residents. Entering drug treatment as an overdose prevention HRS was not common in either subsample.

Latent class analysis

Model fit statistics

Based on the predetermined standard for inclusion, overdose prevention HRS included in the LCA among San Diego residents were: avoid fentanyl, avoid using alone, stop/reduce injecting, use the same supplier, carry naloxone, tester shot, drug checking, dose control, and no practices. Those included in the LCA among Tijuana residents were: avoid fentanyl, avoid using alone, stop/reduce injecting, and use the same supplier. Fit statistics for the Tijuana and San Diego models are provided in Table 3. The San Diego LCA was inconclusive: while the 4-class model bootstrap p-values for the LRT of absolute model fit indicated adequate fit, bootstrap p-values for the test of relative model fit indicated that none of the models were a better fit than the k-1 model before it. We further explored the 4-class solution for the San Diego subsample, and it did not meet our predetermined standards for model stability where class prevalence should be >5% and <50% of the sample (Table 4). Indeed, a sample size of 130 may not be large enough to uncover true class distinctions.¹²⁷ Therefore, we did not further analyze the San Diego subsample. For the Tijuana sample, we selected a four-class solution based on model fit statistics.

Determination of class membership for Tijuana residents

All four classes had a >50% conditional probability of trying to avoid fentanyl (61% – 100%) (Table 4). Class 1, representing 17% of the sample was uniquely characterized by the

overdose prevention HRS of using the same supplier (64% conditional probability). Class 2 represented 6% of the sample and was uniquely characterized by stopping/reducing injecting (86% conditional probability). Class 3 was 49% of the sample and was characterized by a 100% conditional probability of avoiding fentanyl and very low probabilities of endorsing other strategies. Class 4, 29% of the sample, was uniquely characterized by avoiding using alone (96% conditional probability).

Class comparisons among Tijuana sample

There were no significant differences by class on any demographic characteristics (Table 5). A larger proportion of those who used the same supplier (Class 1) and avoided using alone (Class 4) were unhoused and spent more hours per day in the street. Those who used the same supplier (Class 1) relative to those who avoided fentanyl only (Class 3) had a larger proportion of participants who were stopped/arrested by police. Relative to participants who used the same supplier (Class 1) and avoided using alone (Class 4), those who avoided fentanyl only (Class 3) were significantly less likely to be SSP clients. Compared to those who used the same supplier (Class 1) and avoided using alone (Class 4), a larger proportion of those who avoided fentanyl only (Class 3) switched primary residence from San Diego to Tijuana between baseline and follow-up.

There were significant differences in substance use measures between classes. Those who stopped/reduced injecting (Class 2) had lower median average daily injections, fewer participants who avoided using alone (Class 4) reported heroin use, fewer participants who avoided fentanyl only (Class 3) reported fentanyl use, and a smaller proportion of those who stopped/reduced injecting (Class 2) and avoided fentanyl only (Class 3) reported china white use and polysubstance co-injection. There were no significant differences between groups on measures of

overdose. Finally, participants who avoided fentanyl only (Class 3) reported utilizing a lower average number of overdose prevention HRS (approximately 1 vs. 2 for Classes 1, 2, and 4).

Discussion

We compared overdose prevention HRS among PWUD in two bordering cities, classified PWUD based on their probabilities for utilizing these strategies, and contrasted descriptive characteristics between classes. We identified important differences in overdose prevention HRS utilized based on PWUD city of residence; San Diego residents primarily tried to cut down on injecting and Tijuana residents overwhelmingly tried to avoid fentanyl. Finally, we identified four latent classes of Tijuana residents based on their reported overdose prevention HRS and found key differences between groups.

PWUDs' agency to employ overdose prevention HRS is constrained by availability of harm reduction services. San Diego has SSPs and community organizations that offer a variety of harm reduction services, including drug checking tools and naloxone distribution. However, some organizations initiated services around the same time as the present study and the COVID-19 pandemic limited service availability. Only half of San Diego residents in the present study reported getting syringes from an SSP in the previous six months, despite 78% reporting injection drug use. This finding, as well as a low prevalence of drug checking and naloxone carrying strategies, may indicate some participants were not consistently accessing harm reduction services. This parallels findings from other California cities where SSPs were available, but naloxone possession among PWID was low, even before the pandemic.¹²⁸ Importantly, the County initiated a naloxone expansion program in 2022 that included placement of harm reduction vending machines in key locations, all of which dispense naloxone and some FTS.¹²⁹ However, it is possible that PWUD did not employ some overdose prevention strategies

due a lack of perceived overdose risk or a feeling of futility in their capacity to prevent overdose.^{130,131} Substance use disorder (SUD) treatment, including MOUD, is available in San Diego, although with limitations, such as cost and stigma.¹³² These and other well-documented gaps in SUD treatment^{133,134} may be related to the low likelihood of reporting treatment as an overdose prevention HRS among San Diego participants. Also notable, over half of San Diego participants reported stopping/reducing injecting which aligns with documented changes in switching from injecting to smoking drugs among PWUD in North America.^{135,136} Recent research suggests that smoking versus injecting drugs may be associated with perceived and actual reduced overdose risk.^{137,138} However, overdose deaths associated with smoking drugs have increased in recent years.¹³⁹

In contrast to San Diego, at the time of this study Tijuana had only one community harm reduction service provider, a non-governmental organization (NGO) that began providing services in 2007. Providers have faced political and financial challenges in meeting local demand for harm reduction services in Tijuana. For example, in 2019 Mexico's president rescinded federal government funding from NGOs, including community-based harm reduction providers.¹⁴⁰ Naloxone remains difficult to access in the country due to its classification as a prescription medication,^{13,141} community drug checking services are unsanctioned, and there is a shortage of MOUD exacerbated by the federal government's prolonged closure of Mexico's only methadone manufacturing plant in 2023.¹⁴² Access to services may also be hindered by the threat of violence from organized crime.¹⁴³ These realities are evident in our findings of low rates of SSP engagement as well as few indications of naloxone carrying, drug checking, and drug treatment as overdose prevention HRS among Tijuana participants.

There were discernible patterns in overdose prevention HRS utilized among Tijuana

participants. For example, those who avoided using alone had the highest prevalence of homelessness and SSP engagement. Given their primary strategy to avoid using alone, a social network-based overdose prevention intervention for unhoused persons could be offered through the local harm reduction NGO as a low-barrier strategy. Notably, use of china white was commonly reported, even among those whose primary strategy was to avoid fentanyl. Expansion of drug checking can help PWUD identify drugs that do not contain fentanyl.

There were no associations between latent classes and measures of non-fatal overdose. Only 1% of Tijuana participants reported overdose in the prior six months, which may be due in part to the overdose prevention HRS they employ. Notably, only 1% of Tijuana participants indicated they utilized no overdose prevention HRS. It is also important to note the influence of structural factors on overdose risk. For example, we previously found that police encounters were significantly associated with past six-month overdose among this cohort at baseline.¹⁶ However, in the present study, relative to San Diego-residents, Tijuana residents reported much lower rates of law enforcement encounters, perhaps due to Mexico's partial decriminalization of drug possession and subsequent police training program to reinforce this change in the law.^{144–146}

Limitations

Although our survey allowed for open-ended responses, our study may have benefitted from explicit inclusion of additional overdose prevention HRS to better capture the variety of strategies PWUD might use. Further, the wording of our question may have precluded measuring the full extent of HRS utilized by PWUD. For example, asking participants if they used HRS *to avoid overdose* may have prevented those who used such strategies for some other purpose from responding affirmatively. Finally, we did not measure the duration or frequency with which participants employed each overdose prevention HRS, which would likely influence overdose

risk. Changes to survey questions could potentially enhance the classification of individuals using LCA methods to more clearly identify opportunities for intervention.

Participants were not randomly selected and likely represent especially marginalized PWUD in the region. San Diego participants at baseline were also oversampled for cross-border drug use and, as such, our study sample may be more likely than the general PWUD population to frequent both San Diego and Tijuana. All data was self-reported and may be subject to social desirability or recall biases. Our findings are also subject to survivorship bias.

Conclusions

We found key differences in overdose prevention HRS utilization among PWUD in San Diego and Tijuana and identified latent classes of Tijuana participants based on patterns in their use of overdose prevention HRS. Assessing individual-level HRS can support the development of targeted interventions to increase uptake of overdose prevention practices.

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Tables and Figures

Table 2. Participant characteristics stratified by past six-month city of residence in a cohort of people who use drugs in San Diego, California and Tijuana, Baja California, Mexico (N = 470), May 2022 – March 2023

	Overall	San Diego residents	Tijuana residents
N (%)	470	130 (28)	340 (72)
Demographics			
Race/Ethnicity			
Non-White Race/Ethnicity (n(%))	412 (88)	84 (65)	328 (97)
American Indian ^a (n(%))	7 (2)	5 (4)	2 (1)
Black ^a (n(%))	18 (4)	13 (10)	5 (2)
Asian ^a (n(%))	0 (0)	0 (1)	0 (0)
Pacific Islander ^a (n(%))	2 (0)	2 (2)	0 (0)
White ^a (n(%))	75 (16)	60 (46)	15 (4)
Other ^a (n(%))	372 (79)	55 (42)	320 (93)
Hispanic/Latinx/Mexican ethnicity ^a (n(%))	389 (80)	72 (50)	317 (93)
Sex assigned at birth (Male) (n(%))	348 (74)	91 (70)	257 (76)
Age (Mean (SD))	45.0 (10.2)	44.7 (11.8)	45.1 (9.6)
Structural Factors^b			
Unhoused (n(%))	381 (81)	105 (81)	276 (81)
Average hours spent per day in the street (mean (SD))	15.0 (6.0)	18.3 (8.2)	13.8 (4.2)
Stopped/Arrested by police (n(%))	75 (16)	54 (42)	21 (6)
SSP Client (n(%))	100 (21)	69 (53)	31 (9)
Cross-border residence^b			
San Diego resident at baseline, Tijuana resident at follow-up 4 (n(%))	150 (32)	–	150 (44)
Substance Use^b			
Rx opioids (n(%))	4 (1)	4 (3)	0 (0)
Heroin (n(%))	281 (60)	41 (32)	240 (71)
Fentanyl (n(%))	155 (33)	87 (67)	68 (20)
China white (n(%))	104 (22)	1 (1)	103 (30)
Cocaine (n(%))	17 (4)	13 (10)	4 (1)
Methamphetamine (n(%))	323 (68)	102 (79)	221 (65)
Ecstasy (n(%))	0 (0)	0 (0)	0 (0)
Benzodiazepines/Tranquilizers (n(%))	27 (6)	2 (2)	25 (7)
Barbiturates (n(%))	4 (1)	4 (3)	0 (0)
Hallucinogens (n(%))	11 (2)	8 (6)	3 (1)
Inhalants (n(%))	1 (0)	1 (1)	0 (0)
Polysubstance co-injection (n(%))	183 (39)	18 (14)	165 (49)
Average injections per day (median (IQR))	2.5 (2.4)	0.1 (1.0)	2.5 (3.0)
Stopped injecting 6 or more months ago (n(%))	29 (6)	28 (22)	1 (0)
Overdose			
Past 6-month overdose ^b (n(%))	18 (4)	16 (12)	2 (1)
Lifetime overdose (n(%))	260 (55)	85 (65)	175 (52)
Lifetime overdose count (median (IQR))	1 (3)	2 (5)	1 (3)
Notes: ^a Indicated race categories are not mutually exclusive.			
^b Indicated variables refer to the prior six months.			

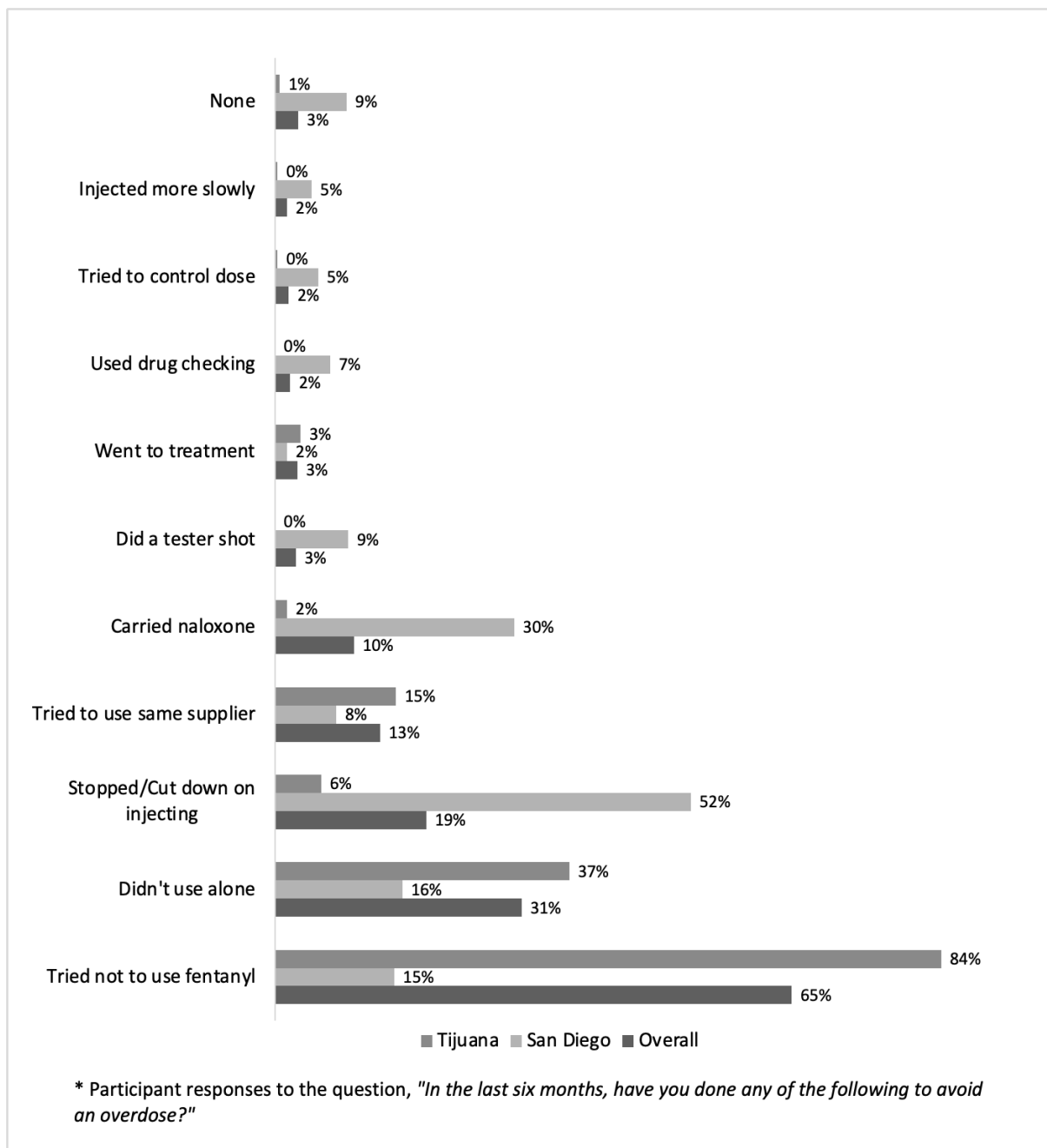


Figure 3. Overdose prevention strategies utilized among a cohort of people who use drugs in San Diego, California and Tijuana, Baja California, Mexico (N = 470), May 2022 – March 2023*

Table 3. Fit statistics of latent class models based on overdose prevention strategies utilized by people who use drugs in San Diego, California and Tijuana, Baja California, Mexico (N = 470), May 2022 – March 2023

	Log likelihood	AIC	BIC	Entropy	G ²	Absolute value bootstrap p-value	Deviance	Relative model bootstrap p-value
San Diego (n = 130)								
2-class	-459.44	960.88	1021.10	1.00	129.02	0.04	–	–
3-class	-447.62	959.24	1051.00	1.00	105.38	0.04	23.64	0.00
4-class	-438.33	962.66	1085.96	0.81	86.80	0.12	18.58	0.02
5-class	-432.74	973.48	1128.33	0.92	75.62	0.08	11.18	0.04
6-class	-427.53	985.07	1171.46	0.88	65.21	0.08	10.41	0.08
Tijuana (n = 340)								
2-class	-575.07	1168.14	1202.60	0.48	24.58	0.00	–	–
3-class	-568.01	1164.01	1217.62	0.85	8.46	0.06	14.13	0.00
4-class	-565.51	1169.01	1241.76	0.71	3.45	0.38	5.00	0.00
5-class	-564.10	1176.20	1268.10	0.78	0.65	0.52	2.81	0.22
6-class	-564.10	1186.20	1297.24	0.68	0.65	0.34	0.00	0.82

Table 4. Latent class conditional probabilities for overdose prevention strategies utilized by people who use drugs in San Diego, California and Tijuana, Baja California, Mexico (N = 470), May 2022 – March 2023

	n (%)	San Diego (n = 130)				Tijuana (n = 340)			
		Class 1	Class 2	Class 3	Class 4	Class 1	Class 2	Class 3	Class 4
		11 (8)	26 (20)	6 (5)	87 (67)	57 (17)	19 (6)	167 (49)	97 (29)
No strategies		100%	0%	0%	0%	–	–	–	–
Injected more slowly		0%	16%	11%	0%	–	–	–	–
Tried to control dose		0%	0%	0%	9%	–	–	–	–
Used drug checking		0%	15%	0%	5%	–	–	–	–
Did a tester shot		0%	27%	23%	2%	–	–	–	–
Carried naloxone		0%	21%	86%	35%	–	–	–	–
Tried not to use fentanyl		0%	59%	0%	1%	67%	75%	100%	61%
Didn't use alone		0%	4%	93%	14%	45%	20%	13%	96%
Stopped or cut down on injecting		0%	27%	62%	68%	0%	86%	0%	0%
Tried to use the same supplier		0%	10%	51%	3%	64%	5%	0%	0%
<i>Notes:</i> All overdose prevention strategies included in the latent class analysis (LCA) were 5% prevalent in the prior 6-months among the whole sample. Those that were used with less than 5% prevalence in the prior 6 months did not meet the inclusion criteria for the LCA.									

Table 5. Comparisons by latent class: Overdose prevention strategies utilized by people who use drugs in Tijuana, Baja California, Mexico (N=340), May 2022 – March 2023

	Class 1 Used Same Supplier	Class 2 Stopped/Cut Down on Injecting	Class 3 Avoided Fentanyl Only	Class 4 Avoided Using Alone	p	Overall
N (%)	57 (17)	19 (6)	167 (49)	97 (29)	–	340
Demographics						
Race/Ethnicity ^a						
Non-White Race/Ethnicity (n(%))	56 (98)	19 (100)	159 (95)	94 (97)	0.561	328 (97)
Hispanic/Latinx/Mexican Ethnicity (n(%))	53 (93)	19 (100)	153 (92)	89 (92)	0.619	314 (92)
Sex assigned at birth (male) (n(%))	49 (86)	13 (68)	124 (74)	71 (73)	0.229	257 (76)
Age (mean (SD))	46.4 (9.1)	48.6 (8.7)	44.5 (9.5)	44.5 (10.1)	0.199	45.1 (9.6)
Structural Factors^b						
Unhoused (n(%))	51 (90)	11 (58)	124 (74)	90 (93)	<0.001	276 (81)
Average hours per day in the street (mean (SD))	15.8 (5.4)	12.1 (1.2)	13.0 (3.4)	14.4 (4.4)	<0.001	13.8 (4.2)
Stopped/Arrested by police (n(%))	8 (14)	0 (0)	5 (3)	8 (8)	0.012	21 (6)
SSP client (n(%))	9 (16)	0 (0)	5 (3)	17 (18)	<0.001	31 (9)
Cross-border residence^b						
San Diego resident at baseline, Tijuana resident at follow-up 4 (n(%))	17 (30)	8 (42)	92 (55)	33 (34)	<0.001	150 (44)
Substance Use^b						
Average injections per day (median (IQR))	2.5 (1.5)	0.3 (1.3)	2.5 (1.5)	2.5 (1.5)	<0.001	2.5 (3.0)
Heroin (n(%))	37 (65)	14 (74)	132 (79)	57 (59)	0.004	240 (71)
Fentanyl (n(%))	20 (35)	3 (16)	13 (8)	32 (33)	<0.001	68 (20)
China white (n(%))	21 (37)	1 (5)	37 (22)	44 (45)	<0.001	103 (30)
Methamphetamines (n(%))	40 (70)	13 (68)	100 (60)	68 (70)	0.302	221 (65)
Tranquilizers/Benzos (n(%))	3 (5)	0 (0)	10 (6)	12 (12)	0.106	25 (7)
Polysubstance co-injection (n(%))	40 (70)	4 (21)	58 (35)	63 (65)	<0.001	165 (49)
Overdose						
Past 6-month overdose ^b (n(%))	1 (2)	0 (0)	0 (0)	1 (1)	0.432	2 (1)
Lifetime overdose (n(%))	31 (54)	11 (58)	84 (50)	49 (51)	0.888	175 (52)
Lifetime overdose count (median (IQR))	1.0 (3.0)	1.0 (3.0)	0.5 (3.0)	1.0 (3.0)	0.431	1.0 (3.0)
Overdose Prevention Strategies^b						
Tried not to use fentanyl (n(%))	34 (59)	15 (79)	167 (100)	69 (71)	<0.001	285 (84)
Didn't use alone (n(%))	23 (40)	4 (21)	0 (0)	97 (100)	<0.001	124 (37)
Stopped or cut down on injecting (n(%))	0 (0)	19 (100)	0 (0)	0 (0)	<0.001	19 (6)
Tried to use the same supplier (n(%))	51 (90)	1 (5)	0 (0)	0 (0)	<0.001	52 (15)
Count of OD prevention strategies utilized (mean (SD))	2.0 (0.8)	2.3 (0.8)	1.0 (0.2)	1.7 (0.5)	<0.001	1.5 (0.7)
Notes: ^a Race/ethnicity categories are not mutually exclusive.						
^b Indicated variables refer to the prior six months.						

Supplementary Table 1. Open-ended "other" responses to survey question soliciting past six-month overdose prevention strategies utilized in a cohort of people who use drugs in San Diego and Tijuana, May 2022 – March 2023^a

1	Reduce the amount of drug(s) used
2	Only smokes fentanyl
3	The heroin is not that strong anymore
4	Just know what to do
5	Flush system with lemon or Benadryl
6	Tries to sleep
7	Knows CPR
8	Built up tolerance
9	Using fentanyl with meth
10	Take a smaller hit and more time between hits
11	Stay close to a Narcan location
Notes: ^a Responses in Spanish were translated to English	

Supplementary Table 2. Study retention by baseline characteristics^a

	Not lost to follow-up	Lost to follow-up	p-value	Overall
n	470	126		596
Residence city (Tijuana) (n(%))	190 (40.4)	11 (8.7)	<0.001	201 (34)
Non-White Race/Ethnicity (n(%))	412 (88)	84 (66.7)	<0.001	496 (83)
Sex assigned at birth (male) (n(%))	348 (74)	98 (78)	0.430	446 (75)
Age (mean (SD))	43.5 (10.3)	41.7 (12.5)	0.093	43.1 (10.8)
Unhoused (n(%))	278 (59.1)	95 (75.4)	0.001	373 (62.6)
Stopped/arrested by police ^b (n(%))	155 (33.0)	32 (25.4)	0.128	187 (31.4)
SSP engagement ^b (n(%))	163 (34.7)	55 (43.7)	0.080	218 (36.6)
Polysubstance co-injection ^b (n(%))	282 (60.0)	59 (46.8)	0.011	341 (57.2)
Heroin ^b (n(%))	375 (79.8)	101 (80.2)	1.00	476 (79.9)
Cocaine ^b (n(%))	46 (9.8)	28 (22.2)	<0.001	74 (12.4)
Methamphetamine ^b (n(%))	340 (72.3)	106 (84.1)	0.010	446 (74.8)
China white ^b (n(%))	93 (19.8)	18 (14.3)	0.201	111 (18.6)
Fentanyl ^b (n(%))	145 (30.9)	54 (42.9)	0.015	199 (33.4)
Benzodiazepines/Tranquilizers ^b (n(%))	137 (29.1)	18 (14.3)	0.001	155 (26.0)
Average daily injections ^b (median(IQR))	2.5 (3.3)	2.5 (3.0)	0.280	2.5 (3.3)
Prior overdose (n(%))	236 (50.2)	74 (58.7)	0.110	310 (52.0)
Count of past overdoses (median(IQR))	1.0 (3.0)	1.0 (3.0)	0.133	1.0 (3.0)
Notes: ^a Table does not include 16 participants removed from analysis due to no longer using drugs in the May 2022 – March 2023 follow-up survey.				
^b Indicated variables refer to the prior six months.				

Chapter 2 Safe Injection Self-Efficacy is associated with HCV and HIV seropositivity among people who inject drugs in the San Diego-Tijuana border region

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Abstract

Background: Safe injection self-efficacy (SISE) is negatively associated with injection risk behaviors among people who inject drugs (PWID) but has not been examined in differing risk environments. We compared responses to a validated SISE scale between PWID in San Diego, California and Tijuana, Mexico, and examine correlates of SISE among PWID in Tijuana.

Methods: PWID were recruited via street outreach for a longitudinal cohort study from October 2020 – September 2021. We compared SISE scale items by city. Due to low variability in SISE scores among San Diego residents, we restricted analysis of factors associated with SISE to Tijuana residents and identified correlates of SISE scores (low, medium, high) using ordinal logistic regression.

Results: Of 474 participants, most were male (74%), Latinx (78%) and Tijuana residents (73%). Mean age was 44. Mean SISE scores among San Diego residents were high (3.46 of 4 maximum) relative to Tijuana residents (mean: 1.93). Among Tijuana residents, White race and

having previously resided in San Diego were associated with higher SISE scores. HCV and HIV seropositivity, homelessness, fentanyl use, polysubstance co-injection, and greater injection frequency were associated with lower SISE scores.

Conclusions: We found profound inequalities between Tijuana and San Diego SISE, likely attributable to differential risk environments. Associations with fentanyl and polysubstance co-injection, injection frequency, and both HIV and HCV seropositivity suggest that SISE contribute to bloodborne infection transmission risks in Tijuana. SISE reflects an actionable intervention target to reduce injection risk behaviors, but structural interventions are required to intervene upon the risk environment.

Introduction

People who inject drugs (PWID) are at elevated risk of exposure to blood-borne infections such as Hepatitis C (HCV) and human immunodeficiency virus (HIV), in part due to injection practices such as receptive syringe sharing.¹⁴⁷ An important factor hypothesized to influence disease transmission risk for PWID is self-efficacy to engage in safer injection practices. Self-efficacy is a construct with origins in Bandura's Social Cognitive Theory (SCT) and refers to a person's belief in their capacity to complete a given behavior.¹⁰⁴

SCT posits that self-efficacy is one of several internal, cognitive processes that influence behaviors. Cognitive processes are mental functions involving how individuals perceive and interpret information. Moreover, SCT recognizes that behavior is shaped by the dynamic interplay between cognitive processes, behavioral factors, and environmental influences, a concept referred to as reciprocal interactions.¹⁰⁴ Behavioral processes encompass the observable actions undertaken by individuals. Environmental factors are those external to the individual, including physical and social surroundings. In the context of injection drug use (IDU),

behavioral factors include the types of drugs PWID use and frequency of use. Environmental factors comprise the risk environment in which drug use occurs, influencing the potential for negative health outcomes related to drug use, such as overdose and sharing of injection equipment that can increase transmission of bloodborne viruses, such as HIV and hepatitis B and C.¹⁹

The general self-efficacy scale (GSE-6) has been shown to be a valid and reliable instrument to measure self-efficacy.⁸⁸ Self-efficacy is associated with behavior in a variety of contexts,¹⁴⁸ including safer drug injection practices.^{91,92,94,149,150} The safe injection self-efficacy (SISE) scale was developed in the multi-site Drug Users Intervention Trial (DUIT)⁸⁷ and has been applied among various groups, including PWID in the United States (U.S.) and Mexico.^{94,149,151} This research has shown that greater SISE is an indicator of lower IDU risk behaviors. However, studies have not examined SISE in differing risk environments.

We assessed participant responses to items in the SISE scale among a cohort of PWID recruited through street outreach in San Diego, California, U.S. and Tijuana, Baja California, Mexico, comparing residents of the two cities. We further assessed associations with SISE scores, which may help identify PWID who could benefit from risk reduction interventions.

Setting

The San Diego-Tijuana border is the busiest land border crossing in the U.S. and is considered a high intensity drug trafficking area by the U.S. Drug Enforcement Administration.⁶³ The populations of San Diego County and Tijuana are approximately 3.3 million¹²¹ and 2.2 million⁶² respectively. Although exact numbers are unknown, there are at least 35,000 PWID in San Diego County.⁶⁶ There were 485 people newly diagnosed with HIV in San Diego in 2021, with about 10% of cases attributed to IDU.⁶⁷ HCV prevalence in San Diego is 2.1% and an

estimated one-third of infections are among PWID.¹⁵² There are an estimated 8,000 – 10,000 PWID in Tijuana,¹⁵³ with an HCV prevalence of up to 90%⁷⁰ and an HIV prevalence of up to 16% among this population.¹⁵⁴

There is overlap in the PWID communities of San Diego and Tijuana, with research suggesting that 15% to 66% of PWID in San Diego cross the border into Mexico to engage in drug use.^{68,76} PWID motivations to cross the border from San Diego to Tijuana include perceived accessibility to higher quality and less expensive drugs.⁷⁶

Methods

Theoretical Framework and Hypotheses

Given San Diego and Tijuana have very different risk environments, particularly regarding harm reduction service availability, we expected SISE to be higher among San Diego residents. To explore the SCT reciprocal interactions concept, we also assessed associations between cognitive, behavioral, environmental, and health-related factors and low, medium, and high SISE scores (Figure 2).

We explored several hypotheses. Since stigma is associated with injection risk behaviors,^{155,156} we hypothesized that internalized and anticipated substance use stigma, which are internal cognitive processes related to possessing a socially devalued characteristic,¹⁵⁷ would be inversely associated with SISE. Research suggests that fentanyl use¹⁵⁸ (a behavioral process) is associated with more frequent injection among PWID.¹⁵⁹ We therefore hypothesized that fentanyl use would be inversely associated with SISE, as PWID who inject more frequently might feel less self-efficacy to consistently use sterile injection equipment. Additionally, we hypothesized that accessing syringe service programs (SSPs) (an environmental factor) would be

associated with greater SISE due to the social and instrumental support (i.e., provision of sterile injection equipment) that SSPs provide.

Participants and Recruitment

Data were drawn from a prospective cohort study among PWID in the San Diego-Tijuana border region (La Frontera) that was designed to assess drug markets, cross-border mobility and their relationship to incidence of HIV, HCV and overdose, as described elsewhere.¹⁰⁵

Participants were recruited between October 2020 – September 2021 by trained bilingual research field staff. There was one outreach team per city with three to five members who conducted recruitment together during daylight hours on weekdays. Recruitment occurred via street outreach with a mobile van. Field staff focused recruitment on areas of concentrated drug use in both cities as described elsewhere.¹⁰⁸ Staff approached individuals in these areas to describe the study purpose, discuss potential risks (e.g., possibility of being identified as a participant of a study examining drug use) and benefits (e.g., access to free health tests such as HIV and HCV and healthcare referrals), and answer any questions. Participants were informed that their involvement was voluntary, and they could withdraw at any time without negative consequences. Inclusion criteria were being 18 years or older, speaking English or Spanish, living in either San Diego or Tijuana, and past-month IDU which, when needed, was verified by staff inspection of injection marks with participant consent. Since one goal of La Frontera was to examine cross-border mobility, participants who were San Diego residents were purposively oversampled so that 50% engaged in cross-border drug use within the preceding two years based on self-report.

Data Collection

Surveys were developed in English, translated to Spanish, back-translated to English, and reviewed by bilingual research staff to ensure accuracy. Field staff acquired written informed consent and conducted computer-assisted interviewer-administered surveys with participants at baseline and biannually thereafter using QDS software.¹⁰⁷ Surveys were completed individually either in the outreach van or in a public space where conversations could not be heard. Participants were assigned a unique study identification number which was used for recording data. No identifying information was stored with the data which was managed by research staff on password protected computers in encrypted files.

The present study used cross-sectional data from the second follow-up survey which took place between December 2021 – December 2022 because it was the most recently completed follow-up survey in which all participants who injected drugs answered questions pertaining to SISE. Participants were compensated USD\$20 for each completed survey. Study protocols were approved by institutional review boards at the University of California San Diego (UCSD) and Xochicalco University.

Measures

Safe Injection Self-Efficacy

The SISE scale measure included six questions asking participants about confidence in their ability to avoid injecting with a needle someone else used or sharing other injection equipment in a variety of scenarios. For example, “I can avoid injecting with a needle someone else used, even if I am injecting with people I know well.” Response options were a Likert scale from 1–4 (1 = absolutely sure I cannot, 2 = pretty sure I can, 3 = pretty sure I cannot, 4 = absolutely sure I can) and scores were averaged for a mean composite score between 1 and 4,

where 1 reflects low self-efficacy. The SISE scale has been demonstrated good internal consistency among PWID in the U.S. and Mexico (Cronbach's alphas = .84 – .94)^{94,149,151}.

For our multivariable model, we categorized Tijuana participants into three ordinal groups based on their relative SISE mean scores (low, medium, and high). Based on the range of participant scores, low scores were $x = 1$ (the lowest possible score), medium scores were $1 < x \leq 2$, and high scores were $x > 2$ (Table 6).

Socio-demographics

Participants provided demographic information related to race/ethnicity, sex assigned at birth, gender identity, and age. Race categories were not mutually exclusive. Those who reported a race other than White or reported Latinx, Hispanic, or Mexican ethnicity were classified as non-White, including those who indicated mixed-race where White was one of two or more races denoted. Participants' average monthly income was recorded in pre-set categories. We created a binary variable indicating average monthly income below the federal income level in Mexico (below \$3,000 pesos per month) and the U.S (below USD\$1,000 per month).

Health measures

Measures of HCV and HIV serostatus were based on serological tests approved for use in the U.S. or Mexico. San Diego participants were tested using Medmira® Miriad combined HIV/HCV immunoassay rapid tests.¹⁶⁰ Positive results were confirmed with a second test using Orasure® HIV and HCV¹⁶¹. Tijuana participants were tested with Accurak® HIV and HCV. Positive results were confirmed with Intec® for HIV¹⁶² and Quality® for HCV. Confirmatory testing was conducted at UCSD's Center for AIDS Research (CFAR) laboratory. Participants were tested for both HCV and HIV infection at baseline and those with a previously negative result were re-tested in follow-up assessments. Pre- and post-test counseling was provided

following national guidelines in the U.S. and Mexico. Participants with positive test results were referred for follow-up healthcare.

Substance Use Stigma

We included two subscales of the Substance Use Stigma Mechanisms Scale (SU-SMS) that assess experiences of internalized and anticipated drug use stigma,¹⁵⁷ and were shown to be valid and reliable among PWUD samples (Cronbach's alphas = .83 – .94). The internalized stigma and anticipated stigma subscales each include six questions with Likert-scale response options from 1–5 (strongly disagree to strongly agree). Responses to each subscale were used to compute a total mean score. Mean stigma scores can be interpreted as 1 = very low stigma, 2 = low to moderate stigma, 3 = moderate stigma, 4 = moderate to high stigma, 5 = very high stigma.¹⁵⁷

Environmental Factors

A measure of cross-border residence indicated whether participants who indicated their primary city of residence was San Diego at baseline reported their past six-month primary residence as Tijuana in the December 2021 – 2022 follow-up survey. Tijuana residents indicated at baseline if they had ever been deported from the U.S. We measured law enforcement encounters by asking participants if they had been stopped or arrested by police in the past six months. Homelessness was based on participant reports of sleeping always or most often in a shelter or places not meant for habitation, such as the street or in a vehicle. Relatedly, we included a variable indicating how many hours per day participants spent on the street on average. SSP engagement was a binary indication of whether participants obtained syringes from an SSP in the prior six months. We did not capture engagement with an SSP for services other than syringe distribution. Participants also reported if they had enrolled in a drug or alcohol

rehabilitation program in the preceding six months. Finally, we asked whether participants had earned money from sex work in the past six months.

Drug Use

We created binary drug use variables indicating whether participants knowingly used each type of substance in the prior six months by any method, regardless of frequency. Of note, we include the drug called “china white” in our analysis, which is a street formulation of fine powder heroin often containing fentanyl.¹⁵ A polysubstance co-injection variable indicated whether participants reported co-injecting an opioid mixed with a stimulant. Finally, participants estimated an average number of times per day they injected any kind of drug in the prior six months.

Statistical Analysis

All analyses were conducted using base R¹²² and RStudio.¹²³ First, we compared participant demographic characteristics, HIV and HCV serostatus, drug use stigma scores, environmental factors, drug use, and SISE measures based on their primary city of residence in the prior six months (San Diego vs. Tijuana) using t-tests for continuous variables and Chi-square tests or Fisher’s exact tests for categorical variables.

The outcome of interest was SISE mean scores. Due to skewness in SISE mean scores that precluded using parametric methods that assume normal distribution, we created an ordered categorical measure of SISE. We divided SISE mean scores into three ordinal groups based on the range of participant scores (i.e., low, medium, and high). Presenting SISE scores in categorical form allowed for more straightforward interpretations of the relationships between independent variables and SISE. Additionally, this strategy helped stabilize model predictions by reducing the impact of nonlinearities and outliers in the SISE mean scores.

We used the POLR R package¹⁶³ to conduct ordinal logistic regression (OLR) analyses. First, we assessed univariable associations between the independent variables and the outcome. We included variables that were significant at the $p \leq 0.1$ threshold in univariable models in a multivariable, manual forward selection regression modeling process. We chose this threshold because it allowed for a more comprehensive exploration of potential predictors without prematurely excluding variables that could be marginally significant or have meaningful effects when considered collectively in the multivariable context. We added variables to the multivariable model one-by-one prioritizing theoretical relevance followed by lowest p-values and largest effect sizes in univariable models. Only variables that independently maintained significance at the $p \leq 0.05$ threshold were included in the final model. We evaluated the final model for multicollinearity by examining correlation matrices and variance inflation factors, tested for interactions between covariates and assessed the proportionality of odds assumption using the Brant test.¹⁶⁴ Additionally, we checked for independence of observations and assessed linear relationships between continuous predictors and the log odds of the outcome.

Results

Study Sample

The parent study baseline sample consisted of 612 PWID.¹⁶ Eighty-two percent ($n=500$) of baseline participants completed the December 2021 – 2022 follow-up survey utilized in the present analysis. Missing participants ($n=112$) were lost due to death (45%, $n=50$) or otherwise could not be located for follow-up. Over half of deaths (52%, $n=25$) were confirmed via obituary or local government records and others were reported by next of kin. We removed an additional 26 participants from analysis who indicated they had not injected drugs in the prior six months, for a total analytic sample of 474. Those who were lost to follow-up were more likely to reside in

San Diego at baseline and more likely to be White, non-Hispanic (see [Supplementary Table 3](#)). Those lost to follow-up were also more likely at baseline to have been experiencing homelessness; have been SSP clients; have been enrolled in drug/alcohol rehabilitation; and have used fentanyl, methamphetamine, or cocaine in the prior six months.

Safe Injection Self-Efficacy

Overall, the mean SISE score was 2.35 out of 4 (standard deviation [SD]=1.08) and the median score was 2 (interquartile range [IQR]=2). The Cronbach's alpha for the SISE scale among this sample was 0.99.

Sample Descriptive Statistics

Among the analytic sample (N=474), 27% (n=129) indicated San Diego was their primary residence in the preceding six months while 73% (n=345) primarily resided in Tijuana ([Table 7](#)). This included 154 (33%) participants whose primary residence switched from San Diego to Tijuana during the study period.

Participants were mostly non-White (83%) and reported Latinx/Hispanic/Mexican ethnicity (78%). Most were assigned male at birth (74%). Participants were an average age of 44 years (SD=10.25), half (50%) had an average monthly income below the respective country's federal poverty line, and 57% had less than a high school education. Nearly half (48%) tested HCV-seropositive and 11% tested HIV-seropositive.

Participants reported low to moderate levels of internalized drug use stigma, with an average score of 1.93 out of 5 (SD=0.96), and slightly more moderate levels of anticipated drug use stigma, with an average score of 2.77 (SD=1.10). Cronbach's alphas for internalized and anticipated stigma subscales were 0.9 and 0.88 respectively.

At baseline, 11% reported having been deported from the U.S to Mexico. Twenty-two percent reported being stopped/arrested in the prior six months. Most (81%) were unhoused in the prior six months, spending an average of 16 hours (SD=6.5) per day on the street. Nearly 30% reported receiving syringes from an SSP in the prior six months, 8% reported being enrolled drug or alcohol rehabilitation program, and 5% had earned money from sex work.

The drugs most commonly used were methamphetamine (62%), followed by heroin (54%), and fentanyl (51%). Just over half reported co-injection. Participants reported a median of 2.5 (IQR = 3.7) injections per day.

Comparison of San Diego and Tijuana Samples

Comparison of Safe Injection Self-Efficacy

The mean and median SISE scores for San Diego residents (N=129) were significantly higher than those of Tijuana residents (N=345) (3.46 vs. 1.93 and 4.0 vs. 2.0, $p<0.001$) (Table 7). For all six scale items, a greater proportion of San Diego participants indicated they were “absolutely sure” or “pretty sure” they could avoid sharing injection equipment in each proposed scenario (Figure 5). Due to low variability in the outcome among San Diego residents, we restricted the OLR analysis to Tijuana residents only.

The SISE mean score distribution among Tijuana residents was right-skewed (i.e., lower SISE scores, see Figure 6). As described, we categorized Tijuana participants into three ordinal groups based on their relative SISE mean scores with 41% (n=142) in the “low” category, 26% in the “medium” category, and 33% in the “high” category (Table 6).

Comparison of Descriptive Statistics

Relative to San Diego residents, a higher proportion of Tijuana residents were non-White (90% vs. 61%, $p<0.001$), with most reporting Latinx/Hispanic/Mexican ethnicity (89%). Tijuana

residents were less likely to have an average monthly income below the federal poverty line (39% vs. 80%, $p<0.001$) but more likely to have less than a high school education (63% vs. 39%, $p<0.001$). Compared to Tijuana residents, San Diego residents were more likely to test HCV-seropositive (69% vs. 42%, $p<0.001$), but less likely to test HIV-seropositive (4% vs. 13%, $p=0.012$).

While residents of both cities reported low to moderate levels of internalized drug use stigma, mean scores were significantly lower among Tijuana residents compared to San Diego residents (1.87 vs. 2.12, $p=0.02$), but there was no significant difference in anticipated stigma scores between residents of the two cities.

Compared to Tijuana, a significantly larger proportion of San Diego residents reported past six-month law enforcement encounters (34% versus 18%). Although the difference between cities in terms of homelessness was not statistically significant, San Diego residents indicated they spent a greater number of hours in the street per day relative to Tijuana residents (mean: 18 vs. 15 hours). Compared to Tijuana, past six-month SSP engagement was much more common in San Diego (64% vs. 17%) as was drug/alcohol rehab (23% vs. 3%).

Relative to Tijuana residents, fentanyl and methamphetamine use were more common in San Diego (60% vs. 48% and 80% vs. 56%, respectively). Tijuana residents more commonly reported use of china white and benzodiazepines or tranquilizers (20% vs. 5% and 22% vs. 8%, respectively). Compared to San Diego residents, Tijuana residents much more commonly reported polysubstance co-injection (65% vs. 26%) and reported a higher number of average daily injections (2.5 vs. 0.3).

Univariable Associations with Safe Injection Self-Efficacy among Tijuana participants

Due to low variability in SISE scores among San Diego participants, we explored associated factors among the Tijuana resident sample only (n=345). The Cronbach's alpha for the SISE scale among Tijuana residents was 0.99 and a Mokken scale analysis yielded Loevinger's H coefficients that demonstrated good fit for the scale overall (H=0.994; Standard Error [SE]=0.003) and for individual items (Hs $\geq$.990; SEs <0.006), indicating strong unidimensionality, consistent response patterns, and high precision.¹⁶⁵ In univariable analyses, factors positively associated with SISE scores at the $p \leq 0.1$ threshold were female sex, switching primary residence from San Diego to Tijuana during the study period, engaging in sex work, and heroin use ([Table 8](#)). Factors negatively associated with SISE were non-White race/ethnicity, less than high school education, average monthly income below the federal poverty line, HIV and HCV seropositivity, anticipated drug use stigma, ever having been deported, having been stopped/arrested by police, homelessness, more hours spent in the street, SSP engagement, fentanyl use, china white use, benzodiazepine/tranquilizer use, polysubstance co-injection, and reporting a higher number of daily injections during the last six months.

Multivariable Associations with Safe Injection Self-Efficacy among Tijuana participants

In the final multivariable model, those who switched residence from San Diego to Tijuana during the study period had over four times greater odds of being in a higher SISE level (i.e., 'medium' or 'high' vs. 'low', and 'high' vs. 'low' or 'medium') relative to those who consistently reported Tijuana as their primary residence during the study (Adjusted Odds Ratio [AdjOR]: 4.65; 95% Confidence Interval [CI]: 2.88–7.59) ([Table 3](#)). Non-White race/ethnicity was associated with 62% reduced odds of being in a higher SISE level (AdjOR: 0.38; 95% CI: 0.15–0.90). HCV-seropositivity was linked to 62% decreased odds (AdjOR: 0.38; 95% CI: 0.24–

0.62), and HIV-seropositivity corresponded to 80% lower odds (AdjOR: 0.20; 95% CI: 0.09–0.45). Participants experiencing homelessness had 49% reduced odds of being in a higher SISE level (AdjOR: 0.51; 95% CI: 0.26–0.99). Three drug use factors were negatively associated with SISE levels. Fentanyl use and polysubstance co-injection were respectively associated with 57% and 66% lower odds of being in a higher SISE level (AdjOR: 0.43; 95% CI: 0.26–0.71). Finally, each additional daily injection was related to 25% lower odds of being in a higher SISE level (AdjOR: 0.75; 95% CI: 0.60–0.93).

Discussion

In this binational study of SISE among PWID, we found that participants with primary residence in San Diego at the December 2021 – 2022 follow-up had relatively high SISE scores compared to those residing in Tijuana. Further, Tijuana residents had lower SISE median scores than reported in an earlier study among PWID in Tijuana.⁹⁴ Among Tijuana residents, we found a positive association between SISE and prior San Diego residence, and negative associations with non-White race/ethnicity, HIV and HCV seropositivity, homelessness, fentanyl use, polysubstance co-injection, and greater injection frequency. Contrary to our hypothesis, SSP engagement was not significantly associated with higher SISE scores, and the direction of the association was in the opposite direction than anticipated. This relationship may be explained by research suggesting that SSP participants may engage in more high-risk drug use relative to those who are not engaged with SSPs.¹⁶⁶

Although SISE is an individual-level psychological construct, it may interact with and be influenced by environmental factors as described by SCT. There were key differences in access to harm reduction services between San Diego and Tijuana that likely explain some of the relative differences in SISE scores between participants in these cities. Amidst the escalating

severity of the addiction and overdose crises in the U.S., there has been growing political and government support for harm reduction initiatives at the national, state, and local levels,^{167–169} notwithstanding historical resistance that continues to stymie progress.^{170,171} In recent years this has translated to an increase in harm reduction service provision in San Diego, including several new SSP providers. The increased availability of SSPs and syringe distribution likely promoted SISE among PWID in San Diego.

Conversely, harm reduction services are more limited in Tijuana and there is currently only one SSP in the city. Despite supportive harm reduction policies introduced in Mexico near the turn of the millennium, including partial decriminalization of drug possession for personal use¹⁷², scholars have identified a current lack of political will to comprehensively confront addiction and overdose issues prevalent in Mexico-U.S. border cities.¹³ Rescinded global¹⁵³ and federal government funding to civil society organizations¹⁴⁰ had a negative impact on SSP engagement and was associated with increased receptive syringe sharing among PWID in Tijuana.¹⁵³ Additionally, there are significant barriers to syringe access via pharmacies in Tijuana.¹⁷³ The threat of violence related to organized crime may also impede access to SSP services among PWID in Tijuana.¹⁴³ These key differences in harm reduction service provision and access between San Diego and Tijuana are thought to be key drivers in the differential risk environments of the two cities.¹⁹ Our findings that White race and prior residence in San Diego were positively associated with SISE among Tijuana resident-participants are likely reflections of these distinct differences. Accordingly, those who had access to harm reduction services in San Diego, despite primarily residing in Tijuana, perceived greater self-efficacy to employ safe injection practices. A lack of harm reduction availability and related barriers to access in Tijuana

likely contributed to lower perceptions of personal SISE among those who do not have access to San Diego-based services.

Our finding that HCV and HIV serostatus was negatively associated with SISE has important ramifications for public health. Prior research has shown that behavioral interventions that enhance SISE can reduce the risk of acquiring blood-borne infections among female sex workers who engage in IDU in Mexican border cities.¹⁴⁹ Motivational interviewing¹⁷⁴ and risk education interventions¹⁷⁵ have also been shown to reduce injection risk behaviors. While lower SISE has been found to indicate future injection risk behaviors, it is also possible that an individual's sense of SISE is deflated following a positive HCV or HIV test. As such, a positive HCV or HIV test may be an important time to implement interventions to bolster SISE. Efforts to scale up individual-level interventions to improve SISE among PWID in Tijuana are warranted. However, such efforts may be undermined by ongoing structural barriers in Tijuana that require intervention at a policy level. Indeed, proposed legislation in the U.S. and Mexico to further criminalize fentanyl use would likely intensify health risks for PWID.¹⁷⁶

Our findings suggest the need to increase access to rapid point-of-care HCV and HIV testing among PWID in Tijuana.^{177,178} HCV testing, diagnosis, and counseling alone can reduce injection risk behaviors among PWID, ultimately reducing further disease transmission.¹⁷⁹ Importantly, HCV can be treated and cured, although barriers to treatment among PWID persist.¹⁸⁰ More frequent testing among PWID is key for reaching HCV and HIV elimination targets set by the World Health Organization, to which Mexico has committed.¹⁸¹ Recent research among PWID in the San Diego-Tijuana border region suggests the high potential for HIV self-testing,¹⁸² particularly for those who do not regularly access health services. HCV self-testing may also be a feasible way to increase uptake among PWID,¹⁸³ although these testing

platforms are not yet approved in either country. Harm reduction services that prioritize destigmatizing practices are important intervention points for facilitating HCV and HIV testing and treatment connections in this population.¹⁸⁰ HIV prevention medications including pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) are also vital prevention measures, although identifying strategies to increase awareness and uptake among PWID is needed.^{184,185}

Illicitly manufactured fentanyl has a shorter half-life relative to heroin and other opioids,¹⁸⁶ and is associated with increased injection frequency among PWID to avert withdrawal symptoms and maintain a prolonged effect.¹⁸⁷ As such, it is logical that this behavioral factor and other indicators of heightened injection frequency, such as polysubstance co-injection, were negatively associated with SISE. Importantly, recent research by members of our team found fentanyl use to be an independent predictor of HCV seroconversion.¹⁸⁸ Our study suggests SISE could be a mediator of this relationship through its potential impact on injection risk behaviors, which warrants further study. Improved access to a sufficient supply of sterile syringes is needed for PWID who inject frequently. Additionally, increasing access to medications for opioid use disorder (MOUD) treatment with nuanced dosing approaches tailored to persons with fentanyl addiction can reduce injection frequency.¹⁸⁹ However, there is currently a shortage of affordable MOUD services in Tijuana,¹⁹⁰ intensified by the closing of the only methadone manufacturer in Mexico in 2023.¹⁴² Finally, the expansion of safe smoking supplies may also reduce injection frequency and subsequently enhance SISE if PWID smoke instead of inject drugs.¹³⁷

In our study, homelessness was associated with lower levels of SISE, which is an environmental factor consistently found to be associated with riskier drug use behaviors among

people who use drugs (PWUD).^{191,192} Homelessness is related to other environmental factors that may influence cognitive processes like self-efficacy. For example, people experiencing homelessness have limited capacity to carry sterile injection equipment and access harm reduction services in light of regular displacement, police harassment, violence, and incarceration.^{193–195} Involuntary displacement of PWUD experiencing homelessness is a common practice that exacerbates health problems.¹⁹⁴ Interventions to expand access to low-barrier, stable housing may help reduce injection risk behaviors¹⁹⁶ and improve many other health outcomes for this population.¹⁹⁷

Future longitudinal research should explore potential causal and temporal relationships between SISE and housing instability, drug use practices, and HIV and HCV seroconversion to inform intervention development and timing. Further, SISE could be considered as a short-term outcome to measure the impact of future interventions attempting to reduce injection risk behaviors, including structural interventions such as increased syringe distribution, or individual-level behavioral interventions with PWID.

Limitations

Participants recruited for the present study were not randomly sampled and represent a particularly marginalized community of PWID in the San Diego-Tijuana border region; therefore, our findings may not generalize to other cities or rural populations. Additionally, participants residing in San Diego at baseline were oversampled to ensure representation of cross-border drug use. As such, findings may not represent the broader population of PWID in the region. Recruitment and data collection occurred during the COVID-19 pandemic, which may have resulted in the exclusion of PWID who were hospitalized or died due to related health complications and may have influenced cognitive, behavioral, and environmental factors

assessed in the present analysis. Notably, a recent study by members of our team found that COVID-19 restrictions did not influence the rate of surveys conducted per month in the restrictive versus unrestricted periods and that border closure did not reduce cross-border HIV transmission.⁷⁴

Some measures used in analysis might underestimate risk factor estimates. The deportation measure only reflected those who indicated at baseline that they had been deported; it is unknown if any participants who switched residence from San Diego to Tijuana during the study period were deported. Additionally, our drug use measures were based on self-report, yet participants may have unintentionally or unknowingly used some substances (e.g., fentanyl). Our SSP measure may underestimate SSP engagement for services other than syringe distribution and does not account for satellite distribution. The SISE categories used in the present study were created based on the distribution of SISE scores in the Tijuana sample. These categories should not be directly compared to SISE score categories in other studies.

Our study findings are subject to survivorship and attrition bias. PWID lost to follow-up had indications of both higher and lower risk based on several structural and drug-use factors. For example, those lost to follow-up were more likely to reside in San Diego at baseline (i.e., lower risk). Additionally, those lost to follow-up were likely to have used fentanyl and be unhoused at baseline (i.e., higher risk), and our final multivariable model may have underestimated the associations between homelessness, fentanyl use, and SISE levels. Finally, our study utilized cross-sectional data, precluding causal and temporal inferences between independent variables and SISE.

Conclusions

Our study suggests that SISE can vary significantly by drug use risk environment. Further, our findings highlight the potential for SISE interventions to impact HCV and HIV transmission risk among PWID, particularly for those who inject more frequently.

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Tables and figures

Table 6. Categories of Safe Injection Self-Efficacy mean scores among people who inject drugs in Tijuana, Baja California, Mexico, December 2021 – December 2022 (N=345)

Category level	SISE score range	Mean SISE Score	Size (n)
High	$x > 2$	3.05	114
Medium	$1 < x \leq 2$	2.00	89
Low	$x = 1$	1.00	142

Table 7. Participant characteristics stratified by prior 6-month city of primary residence in a cohort of people who inject drugs in San Diego, California and Tijuana, Baja California, Mexico, December 2021 – December 2022

	San Diego residents	Tijuana residents	P-value	Overall
n	129	345		474
Demographics				
Race / Ethnicity (n(%)) ^a				
Non-White Race/Ethnicity (n(%))	79 (61.2)	312 (90.4)	<0.001	391 (82.5)
Native American (n(%))	5 (3.9)	0 (0.0)	0.002	5 (1.1)
Black (n (%))	11 (8.5)	4 (1.2)	<0.001	15 (3.2)
Asian (n(%))	1 (0.8)	1 (0.3)	1	2 (0.4)
Pacific Islander (n(%))	2 (1.6)	0 (0.0)	0.128	2 (0.4)
White (n(%))	70 (54.3)	25 (7.2)	<0.001	95 (20.0)
Other (n(%))	47 (36.4)	188 (54.5)	0.001	235 (49.6)
Latinx/Hispanic/Mexican ethnicity (n(%))	62 (48.1)	307 (89.0)	<0.001	369 (77.8)
Sex assigned at birth (female) (n(%))	38 (29.5)	87 (25.2)	0.415	125 (26.4)
Non-binary/trans/other identity (n(%))	1 (0.8)	7 (2.0)	0.587	8 (1.7)
Age (mean (SD))	43.57 (11.76)	44.18 (9.61)	0.565	44.01 (10.25)
Safe Injection Self Efficacy (1–4)				
Mean score (mean(SD))	3.46 (0.65)	1.93 (0.90)	<0.001	2.35 (1.08)
Median score (median(IQR))	4.0 (1.0)	2.0 (2.0)	<0.001	2.0 (2.0)
Health				
HCV Seropositive (n(%))	73 (68.9)	143 (41.6)	<0.001	216 (48.0)
HIV Seropositive (n(%))	4 (3.8)	45 (13.1)	0.012	49 (10.9)
Substance Use Stigma				
Internalized (mean(SD))	2.12 (1.12)	1.87 (0.89)	0.019	1.93 (0.96)
Anticipated (mean SD))	2.65 (1.26)	2.81 (1.04)	0.205	2.77 (1.10)
Environmental Factors				
San Diego → Tijuana residence (n(%))	–	154 (44.6)	–	154 (32.5)
Deported (reported at baseline) (n(%))	–	51 (14.8)	–	51 (10.8)
Stopped/arrested by police ^b (n(%))	44 (34.1)	63 (18.3)	<0.001	107 (22.6)
Unhoused ^b (n (%))	100 (77.5)	285 (82.6)	0.258	385 (81.2)
Avg. hrs./day spent in street ^b (mean(SD))	18.0 (8.3)	14.7 (5.5)	<0.001	15.6 (6.5)
SSP engagement ^b (n (%))	82 (63.6)	57 (16.5)	<0.001	139 (29.3)
Drug or alcohol rehabilitation ^b (n(%))	30 (23.3)	10 (2.9)	<0.001	40 (8.4)
Sex work ^b (n(%))	3 (2.3)	19 (5.5)	0.222	22 (4.6)
Drug Use^b				
Fentanyl (n(%))	77 (59.7)	165 (47.8)	0.028	242 (51.1)
China white (n(%))	7 (5.4)	70 (20.3)	<0.001	77 (16.2)
Heroin (n(%))	65 (50.4)	192 (55.7)	0.357	257 (54.2)
Rx Opioids (n(%))	3 (2.8)	2 (0.5)	0.161	5 (1.1)
Methamphetamine (n(%))	102 (79.1)	194 (56.2)	<0.001	296 (62.4)
Cocaine (n(%))	25 (10.5)	6 (2.6)	0.001	31 (6.5)
Benzodiazepines/Tranquilizers (n(%))	10 (7.8)	76 (22.0)	0.001	86 (18.1)
Polysubstance injection (n(%))	34 (26.4)	225 (65.2)	<0.001	259 (54.6)
Average daily injections (median (IQR))	0.3 (2.5)	2.5 (1.5)	<0.001	2.5 (3.7)
Notes: ^a Race variables are not mutually exclusive, except for Non-White Race/Ethnicity.				
^b Indicated variables refer to the prior six months.				

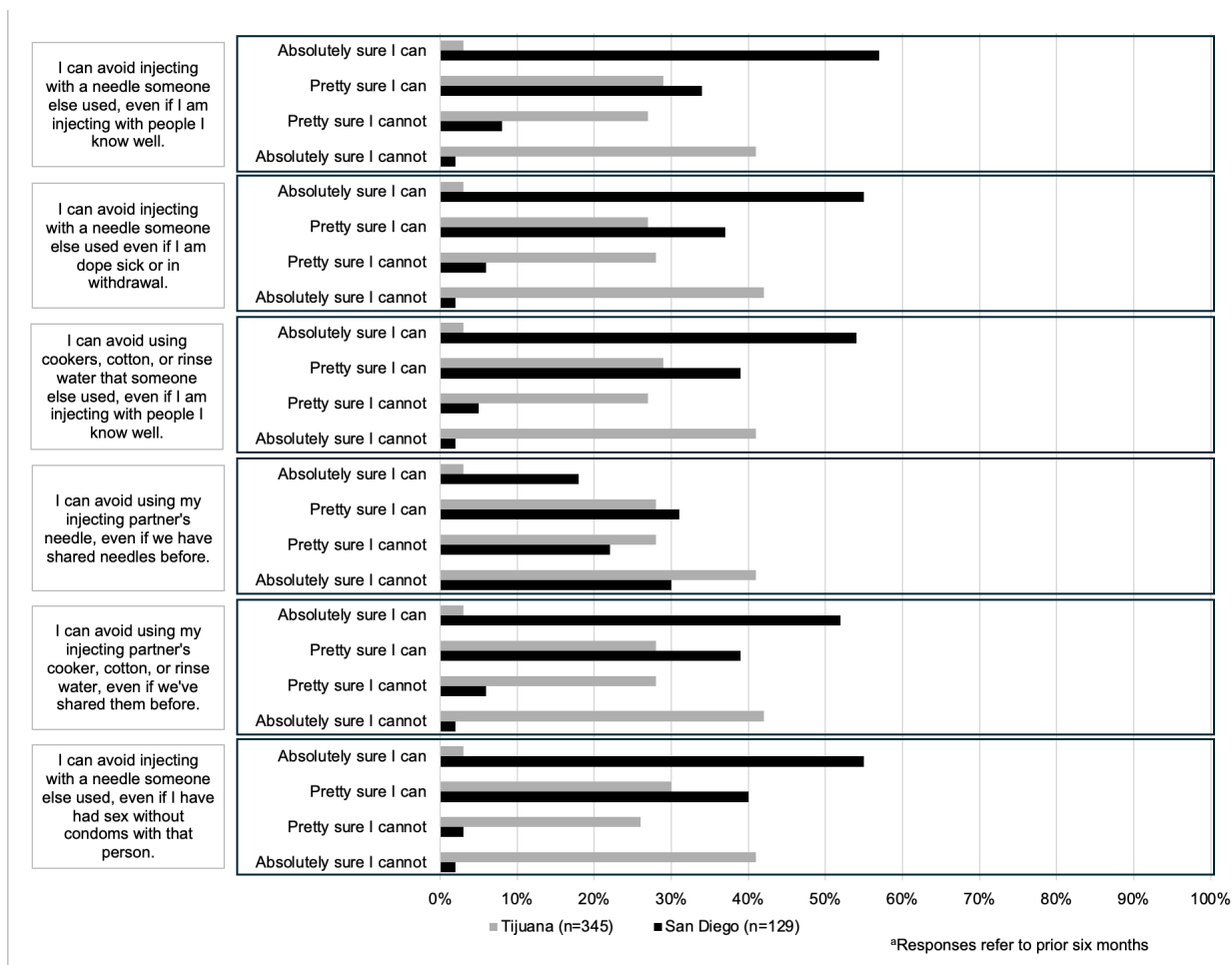


Figure 4. Participant responses to Safe Injection Self-Efficacy questions among a cohort of people who inject drugs in San Diego, California and Tijuana, Baja California, Mexico, December 2021 – December 2022^a

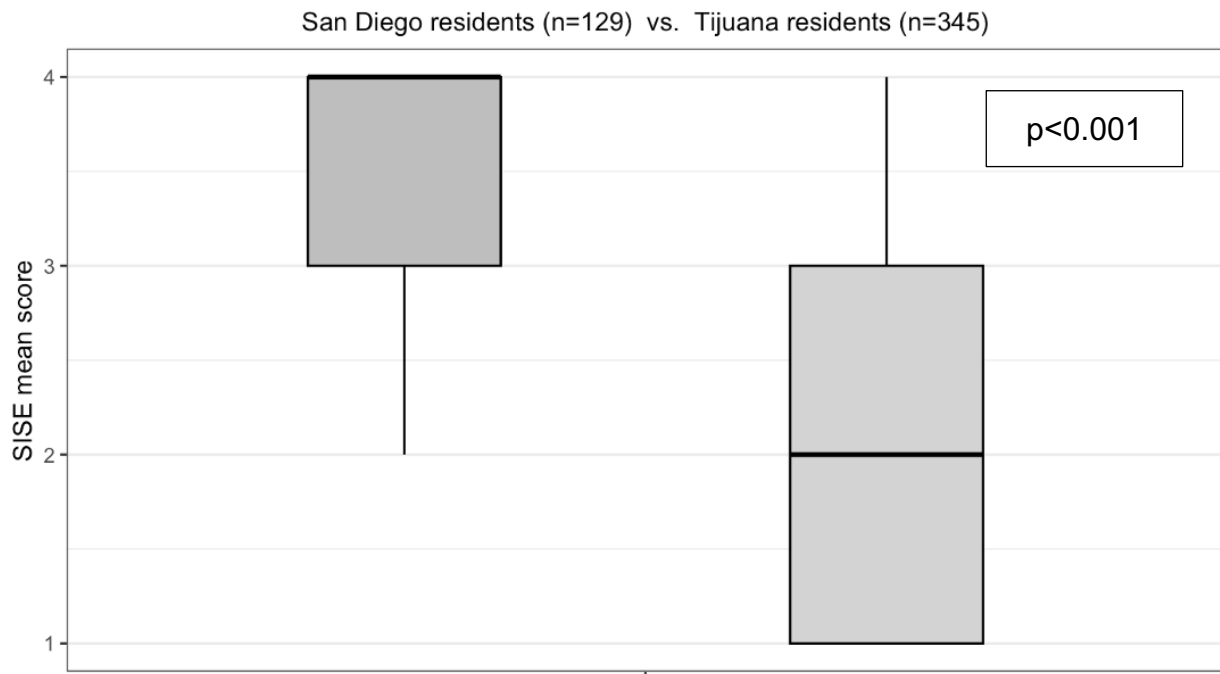


Figure 5. Safe injection self-efficacy (SISE) mean scores by city of residence

Table 8. Factors associated with safe injection self-efficacy score (low, medium, high) using univariable and multivariable ordinal logistic regression among people who inject drugs in Tijuana, Baja California, Mexico, December 2021– December 2022 (N=345)

	OR	95% CI	p-value	AdjOR	95% CI	p-value
Demographics						
Sex (Female)	1.71	1.09, 2.69	0.022			
Non-binary/trans/other identity	3.05	0.76, 15.0	0.115			
Age (per year increase)	1.01	0.99, 1.04	0.251			
Non-White race/ethnicity	0.27	0.12, 0.55	<0.001			
Health						
HCV Positive	0.25	0.16, 0.38	<0.001	0.38	0.24, 0.62	<0.001
HIV Positive	0.18	0.08, 0.35	<0.001	0.20	0.09, 0.45	<0.001
Substance Use Stigma						
Internalized	0.87	0.69, 1.09	0.234			
Anticipated	0.79	0.65, 0.96	0.015			
Environmental Factors						
San Diego → Tijuana residence	4.94	3.25, 7.57	<0.001	4.65	2.88, 7.59	<0.001
Deportation (reported at baseline)	0.40	0.22, 0.70	0.001			
Stopped/arrested by police ^a	0.40	0.23, 0.67	<0.001			
Homelessness ^a	0.22	0.12, 0.38	<0.001			
Avg. hrs/day spent in street ^a (per-hour increase)	0.84	0.80, 0.87	<0.001			
SSP engagement ^a	0.31	0.18, 0.55	<0.001			
Drug or alcohol rehab ^a	0.63	0.18, 1.98	0.427			
Sex work ^a	2.25	0.94, 5.65	0.070			
Drug Use^a						
Fentanyl	0.25	0.17, 0.38	<0.001	0.43	0.26, 0.71	0.001
China white	0.39	0.23, 0.65	<0.001			
Heroin	3.17	2.11, 4.80	<0.001			
Methamphetamine	0.83	0.56, 1.23	0.355			
Benzodiazepines/tranquilizers	0.66	0.41, 1.07	0.093			
Polysubstance co-injection	0.11	0.07, 0.18	<0.001			
Average daily injections (per-injection increase)	0.54	0.46, 0.64	<0.001			
<i>Notes:</i> ^a Indicated variables refer to the prior six months.				0.34	0.19, 0.63	0.001
				0.75	0.60, 0.93	0.010

Notes: ^aIndicated variables refer to the prior six months.

Supplementary Table 3. Study retention by baseline characteristics^a

	Not lost to follow-up	Lost to follow-up	p-value	Overall
n	474	112		586
Residence city (Tijuana) (n(%))	191 (40.3)	9 (8.0)	<0.001	200 (34.1)
Non-White Race/Ethnicity (n(%))	391 (82.5)	75 (67.0)	<0.001	466 (79.5)
Hispanic Ethnicity (n(%))	369 (77.8)	54 (48.2)	<0.001	430 (72.2)
Sex assigned at birth (female) (n(%))	125 (26.4)	28 (25.0)	0.859	153 (26.1)
Non-binary/trans/other identity (n(%))	6 (1.3)	0 (0.0)	0.500	6 (1.0)
Age (mean(SD))	43.1 (10.3)	43.0 (12.6)	0.939	43.1 (10.7)
HCV Seropositive (n(%))	170 (35.9)	51 (45.5)	0.073	221 (37.7)
HIV Seropositive (n(%))	42 (8.9)	3 (2.7)	0.044	45 (7.7)
Ever deported	51 (10.8)	3 (2.7)	0.013	54 (9.2)
Stopped/arrested by police ^b (n(%))	161 (34.0)	25 (22.3)	0.023	186 (31.7)
Unhoused ^b	280 (59.1)	85 (75.9)	0.001	365 (62.3)
SSP engagement ^b (n(%))	151 (31.9)	58 (51.8)	<0.001	209 (35.7)
Drug or alcohol rehabilitation ^b (n(%))	12 (2.5)	10 (8.9)	0.003	22 (3.8)
Sex work ^b (n(%))	48 (10.1)	3 (2.7)	0.020	51 (8.7)
Fentanyl ^b (n(%))	146 (30.8)	46 (41.1)	0.049	192 (32.8)
China white ^b (n(%))	92 (19.4)	18 (16.1)	0.497	110 (18.8)
Heroin ^b (n(%))	375 (79.1)	88 (78.6)	1.000	463 (79.0)
Rx Opioids ^b (n(%))	40 (8.4)	9 (8.0)	1.000	49 (8.4)
Methamphetamine ^b (n(%))	343 (72.4)	96 (85.7)	0.005	439 (74.9)
Cocaine ^b (n(%))	47 (9.9)	24 (21.4)	0.001	71 (12.1)
Benzodiazepines/Tranquilizers ^b (n(%))	141 (29.7)	11 (9.8)	<0.001	152 (25.9)
Polysubstance co-injection ^b (n(%))	282 (59.5)	54 (48.2)	0.039	336 (57.3)
Average daily injections ^b (median (IQR))	2.5 (3.3)	2.5 (3.7)	0.221	2.5 (3.3)
Notes: ^a This table does not include participants who were removed from analysis because they no longer injected drugs at the December 2021 – December 2022 follow-up.				
^b Indicated variables refer to the prior six months.				

Chapter 3 A mixed methods study to inform fatal overdose prevention in San Diego, California: perspectives from people who use drugs, December 2021 – December 2022

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Abstract

Background: In the United States, community overdose education and naloxone distribution (OEND) programs have demonstrated efficacy in reducing opioid-related mortality. OEND programs have expanded across San Diego County, California, but differential naloxone accessibility among people who use drugs (PWUD) has not been assessed. We examined factors that shape personal naloxone accessibility in San Diego.

Methods: We employed a convergent parallel mixed methods design using surveys (n=194) and qualitative interviews (n=20). Ordinal logistic regression examined factors associated with personal naloxone accessibility, defined as the frequency with which participants could access naloxone within five minutes (categorized as *never*, *sometimes*, or *always*). Qualitative interviews explored participant perceptions of naloxone accessibility generally, personal experiences (including barriers) acquiring and maintaining naloxone, and engaging in overdose response.

Results: In quantitative and qualitative samples, participants were majority male (72% and 70% respectively), non-White race/ethnicity (55% and 75%), with an average age around 42

years. In the quantitative sample, 24% never had personally accessible naloxone, 52% sometimes did, and 24% always did. Factors independently associated with greater personal naloxone accessibility were female sex (Adjusted Odds Ratio [AdjOR]: 2.51, 95% Confidence Interval [CI]: 1.31–4.85), monthly income <\$500 (AdjOR: 0.42, 95%CI:0.19, 0.90), witnessing an overdose (AdjOR: 3.51, 95%CI:1.67–7.55), and knowing where to get free naloxone (AdjOR: 3.44, 95%CI: 1.79–6.75). Qualitative data suggested that naloxone was generally easy to acquire in San Diego from community harm reduction outreach and mutual aid among peers. Individual attitudes toward overdose risk, naloxone, and community responsibility contributed varied personal naloxone accessibility. Access barriers included distance to harm reduction providers and frequent relocation/displacement for those experiencing homelessness.

Conclusions: OEND programs in San Diego may benefit from increased mobile naloxone distribution and overdose response education. OENDs should consider proactive recruitment of women and those with a sense of community responsibility for satellite naloxone distribution.

Introduction

The overdose epidemic in the United States has resulted in over one million deaths since 1999¹⁹⁸, fueled by an increasingly toxic, unregulated drug supply¹⁹⁹. Most drug overdoses are attributable to opioids, particularly illicitly manufactured fentanyl and its analogues²⁰⁰.

In the United States (US), community overdose education and naloxone distribution (OEND) programs have demonstrated efficacy in reducing opioid-related mortality^{48,201}. It is particularly important for OENDs to reach people who use drugs (PWUD) as they are often the nearest bystanders to overdose events²⁰² and are generally willing and able to intervene^{203–205}. While OENDs have expanded rapidly since the early 2010s, program reach varies widely^{48,206}. Considerable racial/ethnic and geographic disparities in naloxone access have been documented

^{128,207–212}, likely due to organizational, financial, political, regulatory, and logistical barriers ^{213,214}. Studies have found greater naloxone access was related to homelessness ^{215,216}, drug use behaviors (e.g., injecting heroin) ²¹⁷, and prior overdose experiences ²¹⁶. Research has also identified individual-level barriers to naloxone uptake among PWUD, including stigma toward substance use, indifference toward overdose, fear of law enforcement repercussions, and fear of misusing naloxone or precipitating side effects such as severe withdrawal symptoms ^{218,219}.

Community organizations in California received authorization to distribute naloxone in 2017 ²²⁰ and could utilize state and federal funding for OEND programs by 2018 ²²¹. Although naloxone became more available in San Diego County following this approval, recent assessments among harm reduction service providers and PWUD indicated a need for continued OEND expansion ^{66,98}. Indeed, there was a 33% increase in drug overdose fatalities in San Diego County between 2020 – 2022 ⁶⁵. In 2022, the County initiated efforts to “saturate the community with naloxone,” ¹²⁹ yet specific plans to identify and address variations in naloxone accessibility among PWUD were not specified. To inform ongoing efforts to improve overdose prevention across San Diego, we undertook a mixed methods study to determine factors that shaped differences in naloxone accessibility among PWUD. In both qualitative and quantitative inquiry, we drew from guidance set forth by McDonald et al. ⁹⁹, who encouraged using measures of naloxone accessibility that account for its location relative to its owner and the owner’s capacity to access it when needed rather than solely assessing current carriage or possession of the medication.

Methods

Mixed methods integration

This study utilized a convergent parallel mixed methods design.²²² Quantitative and

qualitative data were collected concurrently and findings from both datasets were integrated in the results and considered with equal weight in interpretations (QUAN+QUAL). The goal of mixing data was complementarity, allowing both methods to provide insights into understanding factors associated with differential personal naloxone accessibility in San Diego ([Figure 6](#)). Survey data enabled the examination of associations between personal naloxone accessibility and factors representing demographic, structural, drug use, overdose, and naloxone experiences. Qualitative interviews provided context around participant experiences accessing naloxone and partially informed the selection of pre-existing survey measures to test associations with our quantitative naloxone accessibility measure.

Study design and participants

This mixed methods study drew from *La Frontera*, a longitudinal, observational cohort study of cross-border mobility, drug supply trends, bloodborne disease transmission and overdose among PWUD in the San Diego, California and Tijuana, Baja California, Mexico border region (National Institute on Drug Abuse [NIDA] R01DA049644).¹⁰⁵ Bilingual field staff recruited 612 participants (“Cohort 1”) between October 2020–October 2021 via mobile street outreach. Inclusion criteria were being ≥ 18 years old, speaking English or Spanish, residing in San Diego or Tijuana, and past-month injection drug use. San Diego resident participants (n=410) were purposively recruited such that around half (n=206) had engaged in cross-border drug use in the preceding two years, indicating they had gone to Mexico to use drugs. Eligible persons were invited to participate and provided written informed consent. The institutional review boards (IRBs) of the University of California, San Diego (UCSD) and Xochicalco University approved study protocols.

Additional *La Frontera* participants (“Cohort 2”, n=108) were recruited between

February–June 2022 using similar methods for a supplemental study of COVID-19 testing and vaccination (*LinkUP*)¹⁰⁶ that required additional San Diego-based participants. The UCSD IRB approved the re-opening of recruitment and study procedures specific to Cohort 2. The focus of the present study was naloxone accessibility in San Diego and, as such, we included only participants who reported past six-month residence in San Diego.

A subset (n=20) of participants from Cohorts 1 and 2 were recruited for qualitative interviews. In August 2022, author 1 (KB) accompanied the outreach team to recruit participants, employing purposive sampling based on age, sex, race/ethnicity, and location to attain a diversity of experiences.

Data collection

Quantitative data were collected by field staff via computer-assisted surveys conducted in English or Spanish. Participants completed a baseline survey and follow-up surveys every six months, receiving USD\$20 for each. As we aimed to assess naloxone accessibility prior to the County’s 2022–2023 naloxone expansion efforts, this study utilized data from the second follow-up survey from Cohort 1 (December 2021–December 2022) and the baseline survey from Cohort 2 (February–June 2022).

Qualitative interviews were semi-structured, with an emphasis on perceptions of naloxone accessibility in San Diego and related personal experiences accessing the medication. Interviews lasted between 20 minutes and one hour. Participants were asked their preferred language and all preferred to complete interviews in English. Participants received USD\$20 compensation.

Measures

Quantitative. Our dependent measure of “personal naloxone accessibility” asked

participants, “In the past six months, how often have you had naloxone on you where you could get it within five minutes?” to which they could respond always, mostly, sometimes, or never.

After examining the distribution of the data, we collapsed “mostly” into “sometimes” resulting in a three-category ordinal variable indicating “never,” “sometimes,” and “always.”

Based on prior research, we selected a priori independent variables to explore potential associations with naloxone accessibility, including demographic, structural, drug use, overdose, and naloxone experiences. Further, drawing from qualitative findings, we included additional pre-existing independent variables representing areas of residence in San Diego County, drug or alcohol treatment, smoking opioids, stopping injecting, and responding to overdose with alternative methods as described below.

Study participants reported demographic information including age, sex, race, and ethnicity. We reported descriptive statistics of all racial categories, but additionally created a binary variable indicating whether participants were White or non-White race/ethnicity.

Structural factors included past six-month residence within San Diego County, cross-border drug use, having been stopped or arrested by police, having been in jail or prison, homelessness, income, syringe services program (SSP) engagement, and drug/alcohol treatment. We created a binary measure indicating whether participants resided in Downtown San Diego zip codes or elsewhere in the County. Homelessness was determined based on participant reports of sleeping “always or most often” in a “shelter, workplace, hotel/motel, vehicle, abandoned building, or on the street” in the prior six months. We created a binary variable indicating an average monthly income (from any source) of less than USD\$500. Drug/alcohol treatment included receiving rehabilitation, medication, or other program to help reduce or stop alcohol or drug use in the preceding six months.

Drug use variables indicated the substances participants knowingly used by any method in the prior six months. We also created a binary variable indicating whether a participant had smoked opioids as participant interviews suggested this may be associated with perceptions of decreased overdose risk. Participants also reported whether they had injected a combination of opioids with stimulants (polysubstance co-injection), the average number of times they injected drugs daily, or when they stopped injecting drugs. Participants reported past six-month and lifetime overdose experiences and whether they witnessed an overdose in the prior six months (and, if so, whether they administered naloxone or responded with alternative methods including administering rescue breathing, rubbing the person's chest, pouring cold water or ice on the person, or hitting or slapping the person). Finally, participants indicated if they were currently carrying naloxone and if they knew where they could get free naloxone on the day of survey completion.

Qualitative. Key domains of open-ended interview questions were perceptions of general naloxone access in San Diego, perceived importance of naloxone carriage and ensuring personal naloxone accessibility, and experiences acquiring naloxone responding to overdose. Additional probes were included to ascertain structural and individual-level barriers to acquiring and maintaining naloxone access.

Data analysis

Quantitative. Cohort 1 included 153 participants who reported living in San Diego in the preceding six months. Seventeen people from Cohort 1 and 50 from Cohort 2 were removed from this analysis due to nonresponse on key survey questions. Although surveys for both cohorts were very similar, when a participant from Cohort 1 expressed unfamiliarity with naloxone, field research staff clarified that it was the medication used to reverse opioid

overdoses and proceeded to ask further naloxone-related questions. In contrast, the Cohort 2 survey included skip-logic that precluded participants who indicated they had never heard of naloxone before (n = 50) from further answering questions about naloxone. The final sample size was 194, with 136 (70%) from Cohort 1 and 58 (30%) from Cohort 2. We compared those included and excluded from analysis and found excluded participants were older and less likely to use fentanyl and methamphetamine (Supplementary Table 4).

In quantitative analyses, we first we compared study participants based on their reported naloxone accessibility (i.e., *never*, *sometimes*, *always*) using analysis of variance (ANOVA) for continuous variables and Chi-square or Fisher's exact tests for categorical variables. When these analyses indicated a significant difference between groups, we conducted post-hoc pairwise comparisons to determine which groups were significantly different from one another.

Next, we assessed univariable associations with naloxone accessibility using ordinal logistic regression where "*never*" was the reference category. Factors associated with the dependent variable in univariable models at an alpha level of 0.1 were considered in a multivariable ordinal logistic regression modeling process. We used a manual forward selection process including variables one at a time, prioritizing theoretical relevance and the largest effect sizes from univariable models. The final model included only variables that had significant associations with the dependent variable at an alpha level of 0.05. We checked the final model for multicollinearity using variance inflation factors, tested for interactions between independent variables, and assessed the proportionality of odds assumption with the Brant test.¹⁶⁴ All analyses were conducted using base R¹²² and RStudio,¹²³ and regression analyses were conducted using the POLR R package.¹⁶³

Qualitative. Interviews were digitally recorded, professionally transcribed, and assessed

for accuracy. We used an inductive analysis approach to identify naloxone accessibility themes from the data.²²³ First, two researchers (KB and AS) used inductive open coding to develop memos from their initial read of all 20 interview transcripts to establish potential codebook codes and definitions. Next, KB, AS, and WHE used the preliminary codebook to independently code an initial set of five interviews and convened to discuss the process, find consensus, and agree upon a coding scheme. Coders then independently coded an additional five transcripts each according to the agreed upon strategy, taking notes of additional emerging themes. Final themes were refined through consensus discussions between team members and presented to four *La Frontera* study participants for member checking and co-authors for feedback.

Results

Sample characteristics

Quantitative. Participants had an average age of 42 years (standard deviation [SD] = 11.3) and were mostly male (n = 139, 72%) ([Table 9](#)). About half identified as non-White (n = 106, 55%), and 39% Hispanic/Latinx/Mexican ethnicity. Thirty percent (n = 57) resided Downtown San Diego and few reported cross-border drug use (n = 17, 9%). Nearly 40% were stopped or arrested by police and 12% spent time in jail or prison in the preceding six months. Most were unhoused (n = 143, 74%) and 18% had an average monthly income less than \$500. Over half (n = 118, 61%) reported SSP engagement while less than one in five (n=35, 18%) had enrolled in drug/alcohol treatment in the preceding six months.

Methamphetamine was the most commonly used drug in the preceding six months (n = 162, 84%), followed by fentanyl (n = 118, 61%) and heroin (n = 87, 45%). Nearly 30% reported polysubstance co-injection and over half (n = 105, 54%) smoked opioids in the preceding six months. Participants injected drugs an average of 1.1 times per day (SD = 1.4) and 15 (8%) had

stopped injecting. Sixteen percent experienced a non-fatal overdose in the preceding six months ($n = 31$) and 62% had ever overdosed in their lifetimes ($n = 121$). A majority witnessed someone else overdose in the preceding six months ($n = 120$, 62%). Nearly half ($n = 90$, 46%) administered naloxone to someone else and 21 (11%) responded to an overdose using alternative methods in the preceding six months. About a third ($n = 69$, 36%) were carrying naloxone at the time of the interview and nearly 70% ($n = 134$) knew where they could get free naloxone. About a quarter (24%) always had naloxone, 52% sometimes had accessible naloxone, and 24% never did.

Qualitative. Similar to the overall quantitative cohort, most qualitative interview participants were male (70%) and had an average age of 41 ($SD = 7.7$) ([Table 10](#)). Around half were White (55%), 65% reported Hispanic/Latinx/Mexican ethnicity, and about half resided in Downtown San Diego. One difference from the quantitative sample was the larger proportion of qualitative participants who identified as Hispanic/Latino/Mexican ethnicity. Fentanyl was the most commonly used drug among interview participants (80%), followed by methamphetamine (70%), heroin (25%), and benzodiazepines or other tranquilizers (10%). Five (25%) experienced one or more overdoses in the preceding six months and over half ($n=11$, 55%) had ever overdosed in their lifetimes.

Integrated findings

Naloxone versus Narcan

An important finding relevant for assessing naloxone accessibility was that participants often did not recognize naloxone by its generic name but were familiar with and most likely to refer to it as “Narcan[®],” the brand name of what was then the only FDA-approved nasal spray formulation. On several occasions when the interviewer framed questions using the term

“naloxone,” participants expressed confusion:

Interviewer: Do you think it would be useful if they gave you naloxone too?

Participant: What’s naloxone?

Interviewer: Naloxone, for when someone overdoses...

Participant: Like Narcan? (Male, 44)

Naloxone availability in San Diego

Of 194 survey participants, 47 (24%) indicated they *never* had accessible naloxone, 101 (52%) *sometimes* had accessible naloxone, and 46 (24%) *always* did (Table 9). Interview participants overwhelmingly viewed naloxone as very easy to acquire in San Diego. Several expressed that nearly anyone who wanted naloxone in San Diego would not have trouble acquiring it, implying that having accessible naloxone was related to individual desires to obtain and keep it readily available rather than structural or other barriers to access:

Somebody who uses drugs and wants Narcan, it’s easy to get... That stuff is thrown at us sometimes. I mean, I just don’t see it as something that’s hard to get. (Male, 31)

Some participants noted that naloxone has become more easily accessible relative to the recent past, indicative of California’s 2017 law allowing community organizations to distribute naloxone:²²⁰

At first [naloxone] wasn’t [easy to access in San Diego], but now it’s like everywhere. If you ask for it, most likely they’ll give it to you, because they’re trying to reduce the rate of people falling out [overdosing] so quickly, especially with the fentanyl outbreak. (Male, 32)

However, some participants reported that naloxone was particularly easy to acquire in Downtown and more difficult to obtain in other parts of San Diego County. Participants recruited in Chula Vista, a city south of the City of San Diego, described how, relative to Downtown, there were fewer programs distributing naloxone:

People in the downtown have more [naloxone]...out here [in Chula Vista] it's a little harder because there's not that many programs. (Male, 42)

When asked whether additional mobile outreach for naloxone distribution would be helpful, one participant living in an encampment in Chula Vista compared the relative SSP availability in the County, describing a need specific to Chula Vista:

They have a needle exchange over there in Hillcrest [a neighborhood in San Diego City] and they have one in Downtown. They don't have nothing for the down south area. So, this is actually a good point for [mobile naloxone distribution]. (Male, 32)

The County's website devoted to naloxone access provides three ways to acquire free naloxone in Chula Vista:¹²⁹ (1) request by phone or email delivery from a local SSP, (2) visit the County Health and Human Services Agency regional office, or (3) visit a substance use treatment center where a naloxone dispensing machine was placed in 2022. However, participants in Chula Vista, who were all unhoused, described that the process of traveling to access naloxone was an obstacle, further emphasizing the value of mobile distribution:

Transportation's probably why [PWUD] don't want to go through the whole process [of acquiring naloxone]. Because, like, oh I got to take the bus. I got to wait in line and, you know, stuff like that. (Male, 56)

Additionally, regarding a capacity to request naloxone delivery, another participant in Chula Vista described not having a phone or “resources to [make a] call” as a barrier to naloxone access in the area (Female, 31).

Another participant who was recruited while he was visiting the downtown area described the relative availability of naloxone there versus the Pacific Beach neighborhood where he lived. Pacific Beach is located along the coast within San Diego City but requires

approximately one-hour to travel to downtown via public transportation.

[Naloxone] is not available like it is downtown... I have a place in Pacific Beach and you can't get Narcan at Pacific Beach. I mean, it's not like it is down here [downtown]. (Male, 36)

The County's naloxone website does not list any free naloxone access points near the Pacific Beach area, although mobile harm reduction providers may periodically visit the neighborhood.

Homelessness is a concern across San Diego County, but is concentrated in the City of San Diego²²⁴ and is highly visible in certain downtown areas. Homelessness may make drug use more visible and, as such, many social services for this population, including harm reduction services, have become concentrated in the downtown area. Studies of naloxone accessibility in other urban areas found homelessness was positively associated with naloxone access, attributed to the high visibility of people experiencing homelessness that makes them more likely to come into contact with social services.^{212,215}

Our binary quantitative measure of geographic location (residing near downtown San Diego vs. elsewhere in the county) was not independently associated with reported naloxone accessibility in the final multivariable model, nor was homelessness. However, as interview participants described, some PWUD were determined to acquire and ensure personal accessibility of naloxone regardless of geographic location or other potential barriers to acquiring naloxone. Those participants would have likely endorsed sometimes or always having naloxone accessibility in surveys.

Carrying naloxone versus having it easily accessible

Among the quantitative sample, 36% (n = 69) were carrying naloxone at the time of survey completion, and those who reported “always” having accessible naloxone were

significantly more likely to report carrying it relative to those who sometimes or never had accessible naloxone (74% vs 33% and 4% respectively, $p < 0.001$) (Table 1). Interview participants reported a range of personal naloxone access behaviors, from always carrying it to actively avoiding it. Most, however, reported either always carrying naloxone or having it nearby. For some, consistently carrying naloxone was routine behavior:

I carry it with me everywhere I go, you know, usually I'll have my backpack so for me it's not really an issue... (Female, 31)

Other participants reported that they do not typically carry naloxone, but that they keep it in an easily accessible location. As one participant described, although she never carries naloxone, she and her peers created a system to ensure it is always visible and easily accessible:

We have it up on the walls and shit, you know. In a bag, so it'll be easy to find if somebody's screaming, 'Narcan!'" (Female, 51)

Some participants shared that they keep naloxone in the place where they are most likely to use drugs, rather than consistently carrying it, to ensure it is accessible if needed for personal use. This highlights the importance of having a consistent place to stay and leave personal belongings:

I don't usually have it on me because usually I do my drugs there [near my tent], so I make sure everything stays there. It's not like I'm gonna be out on the street [using drugs]. Most of the time I'll just leave it there at my spot. (Male, 32)

Mutual aid among PWUD

Participant perceptions of easily accessible naloxone in San Diego were also related to satellite distribution and mutual aid among peers. Some participants reported keeping naloxone around in case others needed it or actively seeking naloxone to distribute to others:

I like to have [naloxone doses] close on hand just in case anybody needs them, I could always run [to get it]. Or anytime I know someone who's doing black [tar heroin] or fentanyl, I give it to them like, 'Here, just to be sure.' And I give them that same 30-second lesson that I was given. (Male, 32)

Usually, I'm the one [who] keeps Narcan with me all the time. I get it like once every two months, but I get a bunch every time I get it. And I always keep some, just make sure that it stays with me, but I usually end up giving it to other people. (Male, 41)

Some participants described their desire to keep naloxone on hand was related to a personal overdose experience of themselves or a peer. One participant shared that he overdosed two days before the interview after spending two months in jail where he underwent unmedicated detoxification. He shared that he kept naloxone on him, “*especially now... my tolerance has gone down a lot recently, so I always have it on me now*” (White male, 36). Notably, however, he did not receive naloxone upon release from jail. Another participant explained she always kept naloxone with her, “*because you never know... my friend, they left him [overdosed] in the park. And so, if I can try to help prevent that from happening, I'm gonna do it... I can't have that on my conscience*” (Female, 31).

Our quantitative analyses revealed that, relative to those who never had accessible naloxone, those who always or sometimes had accessible naloxone were significantly more likely to have overdosed themselves (17% and 21% vs. 4%), witnessed an overdose (80% and 70% vs. 26%), and administered naloxone (63% and 38% vs. 11%) in the previous six months ($p < 0.036$) (Table 9). Furthermore, in our multivariable model, having witnessed an overdose in the prior six months was associated with greater levels of naloxone accessibility (Adjusted Odds Ratio [AdjOR]: 3.51, 95% Confidence Interval [CI]: 1.67–7.55) (Table 11).

Several participants reported they could rely on their partners, close friends, or other peers to have accessible naloxone, easing the burden of having to consistently carry it:

It's always available to where, you know, if you walk up and down the street and if you know a couple of people...of course they'll get you a Narcan. (Male, 36)

Additionally, some participants noted that particular people were known for their role as reliable naloxone distributors, which has been underscored as a key component of community naloxone distribution efforts that contributes to reductions in fatal overdose²²⁵. As one participant described a peer:

The girl with the black shorts on, I always go to her. If I haven't gotten any [naloxone] and I need it, or I have it in my bag and I need more... I'll go to that girl and she's got the huge supply of anything that we need. She's kind of like a mother hen out here. (Female, 55)

While we interviewed both men and women who reported carrying naloxone out of concern for themselves and others, quantitative analyses revealed a strong association between female sex and greater naloxone accessibility (AdjOR: 2.51, 95% CI: 1.31–4.85 in the multivariable model). Women may be more concerned with personal naloxone accessibility due to elevated perceptions of overdose risk for themselves and others relative to men.²²⁶ Prior research has identified community responsibility as a motivator for women's intentions to acquire, provide education, and distribute naloxone.²²⁷ The exemplary quote above demonstrated this sense of community responsibility.

Sources of naloxone

In addition to reports of receiving naloxone via satellite distribution from peers, most participants indicated they acquired naloxone from an SSP or other street-outreach providers. Several participants described proactively seeking naloxone from a local SSP as part of their regular “routine,” as one woman said, “*I go [to the SSP] and get [naloxone] once a week, I have*

a routine.” (Female, 55)

Routinely visiting SSPs for naloxone and other supplies was echoed in other interviews, highlighting the importance of a reliable SSP outreach schedule for this population. Knowing where to get naloxone for free was significantly associated with greater levels of reported accessibility in the final multivariable model (AdjOR: 3.44, 95% CI: 1.79–6.75).

Other participants said they typically acquired naloxone passively thanks to regular street-outreach distribution, which is provided by multiple community organizations in San Diego County:

People from organizations come walking around with Narcan... They keep us full supplied right here. (Male, 40)

Finally, some participants also shared that they received naloxone in healthcare settings, including hospitals or clinics providing medications for opioid use disorder (MOUD), which was previously identified as a predictor of naloxone access among PWID:²¹²

I was just in the hospital recently getting Subutex [buprenorphine] ... And they'll give you Narcan just in case... like they'll ask if you want it just because they know most likely we're gonna go back out and use. (Female, 31)

Although SSPs and treatment settings were identified as important sources of naloxone, neither was significantly associated with naloxone accessibility in quantitative analyses.

Barriers to naloxone accessibility

Housing instability

Some participants described difficulties related to housing instability as barriers to keeping naloxone on hand. Participants who reported frequent relocation explained they struggled to keep track of their belongings, particularly while staying in the street:

It's just been hard to really carry anything on me lately. Like, when I was staying in my vehicle, I had Narcan in there and everything else like that because it was my place to stay and just mine, and I knew it wasn't going to get messed with... But being out here [unsheltered] and getting all my stuff stolen all the time, it's hard to have [naloxone] on me. (Male, 28)

As described by this participant, persons experiencing homelessness are subject to disproportionate rates of robbery and theft.²²⁸ Policing practices also contributed to lack of control over personal belongings and recurrent displacement for some participants experiencing homelessness. One participant staying downtown was upset that his belongings had been taken by police in preparation for a street sweep prior to the interview and described the frustrating process of being placed on a waitlist for a shelter bed, yet being regularly displaced or arrested while staying in the street:

You get on a list [for a shelter bed] and while we are waiting for the bed, we're still homeless. And we get pushed around all over the place while waiting for the bed...Now we're getting even arrested for being homeless and waiting for a bed. (Male, 41)

Goldshear and colleagues²²⁹ recently detailed the negative consequences of street sweeps for PWUD experiencing homelessness, including the frequent loss of important personal items and medications, such as naloxone. Additional research has estimated negative health outcomes related to frequent relocation and involuntary displacement of PWUD experiencing homelessness, including higher odds of overdose.^{194,195}

Personal attitudes toward overdose response and risk

While most participants felt naloxone was generally available, some reported personal attitudes that kept them from ensuring naloxone accessibility. For example, some participants who did not typically keep naloxone on them expressed a preference for using lay remedies for

preventing or responding to an overdose:

I've learned to, you know, put water on people. Put ice down people. Give them mouth-to-mouth... make sure, you know, keep the guy up... I've learned a lot of things without the Narcan... You can snap people [inject them] with salt water, too... Or crystal [methamphetamine], crystal wakes you up, too. Coke [cocaine] wakes you up. They're uppers, you know, so you do that and you throw people in the shower or... throw cold water on them. And, you know, slap them around a little bit... just keep them up so they can stay alive, you know. (Male, 56)

Such strategies are not uncommon among laypersons for preventing or treating an opioid overdose,^{204,230–232} and were the only available strategies for most people prior to OEND programs. Among survey participants, 11% (n = 21) reported responding to an overdose with alternative methods similar to those described above in the prior six months. While rescue breathing is a recommended overdose response strategy,²³³ others, such as injecting methamphetamine, could potentially increase fatal overdose risk.²³⁴ Preclinical research suggests injection of salt does not prevent mortality caused by high doses of opioids, but may increase the efficacy of naloxone if used in tandem.²³⁵ Stimulation with cold water, hitting, or slapping may help wake a person up if they have passed out, but do not reverse an opioid overdose. Despite this participant's extensive experiences with lay remedies to address opioid overdose, he was receptive to using naloxone in such situations, had it been available:

Interviewer: If you had naloxone in those situations, do you think you would use it?

Interviewee: Yes... now that I know more about it, yeah. (Male, 56)

Some participants shared experiences related to the side effects of naloxone administration for themselves or others, which may result in aversions to its use. While some

reported using up to four doses of naloxone to revive a person, others were particularly concerned with the side effects related to excessive dosing of the medication that one participant described as “*almost life threatening*” (Male, 31). As another participant described, “*Actually, I think they put too much [naloxone in me] because I got sick real quick*” (Male, 56). Similar sentiments regarding the potentially extreme side effects of excessive naloxone administration have been documented among PWUD elsewhere.²¹⁹

One participant did not feel a need to consistently keep naloxone on him because he perceived a low risk of overdose for himself and his peers, which he attributed to a behavioral change from injecting to smoking opioids:

I felt like the need for me to have [naloxone] on me has become less important... I think it has something to do with the fact that heroin used to affect us as a whole more because we would shoot it rather than smoke it. So, because everybody was shooting, there were more overdoses. And now, everyone's just smoking fentanyl. And there seems to be less overdoses. (Male, 31)

This participant's description of switching from injecting to smoking drugs reflects a broader trend in North America,^{236,237} which some research has suggested may be associated with reduced overdose risk.¹³⁷ In our quantitative sample, over half (54%, n = 105) reported spiking opioids, although this was not significantly associated with personal naloxone accessibility.

Finally, one participant shared that his decision not to keep naloxone on hand was related to a desire to avoid the emotional toll of responding to overdose:

Hopefully you won't judge me too harshly, but I haven't really been carrying [naloxone]... I just don't wanna be involved... if they're doing too much and they overdose then it's like, I don't really care... I just feel like I've lost too many friends and it's a lot to deal with. It really is a lot

to deal with. It's like, very emotionally fucking draining. (White male, 36)

Wagner and colleagues reported similar feelings of emotional strain among PWUD who had witnessed and responded to multiple overdoses in Los Angeles, California.²³⁸

Discussion

In our study among PWUD conducted prior to San Diego County's naloxone expansion program, combined qualitative and quantitative findings provided explanations for variations in personal naloxone accessibility, elucidating the role of individual attitudes toward acquiring naloxone and keeping it on hand as well as the role of familiarity with naloxone access sites.

Participants generally felt naloxone was easy to acquire in San Diego, which appeared to be related to regular street-outreach distribution efforts from local health and harm reduction programs and perceptions that peers would have the medication available if necessary. This underscores the importance of OEND programs that have increased general naloxone accessibility, even if individual PWUD do not always carry the medication.

We found that women were significantly more likely to report greater levels of personal naloxone accessibility. This result may be related to qualitative findings describing a sense of mutual aid that contributes to naloxone accessibility in San Diego combined with gendered socialization of women that results in more prosocial behavior relative to men.²³⁹ Previous literature assessing the effect of safer injection practice interventions on PWID injection networks found that a greater presence of women in a network was related to a more robust intervention effect.^{240,241} This may indicate network effects whereby women with more connections to other women have greater agency to adopt harm reduction strategies due to lower exposure to gendered and unequal power dynamics. Future research should further explore the role of gendered socialization, power dynamics, and peer network composition in the uptake of

harm reduction strategies like ensuring personal naloxone accessibility.

Participant interviews highlighted perceptions that naloxone was considerably more available in some parts of the County (particularly downtown) relative to others, although this finding was not confirmed with available quantitative data. Some PWUD in areas where naloxone distribution is less common may proactively seek naloxone and ensure it is accessible, despite the extra effort required. San Diego OEND programs should consider PWUD input regarding the relative geographic availability of naloxone and consider increased mobile distribution efforts outside of the downtown area. As our study was unable to determine relative accessibility by geographic location, spatial mapping techniques overlaying naloxone access points and area-specific overdose rates may help illuminate gaps in accessibility.²⁴²

Having witnessed an overdose in the prior six months was strongly associated with greater levels of naloxone accessibility. As described in interviews, witnessing an overdose may influence PWUD to ensure personal naloxone accessibility.²⁴³ Alternatively, places where overdose occurs more frequently may be areas where harm reduction service provision is more common, such as downtown San Diego. Finally, some PWUD who distribute naloxone may frequent community spaces where overdose is more frequent in case a reversal is called for. Peer naloxone administrators may be motivated by a sense of community responsibility²²⁷ and empowerment in their capacity to prevent fatal overdose, particularly in light of the powerlessness they may feel in other aspects of life.²⁴⁴ Responding to overdose can cause emotional strain and those who perform this critical social role should be recognized and supported.²³⁸

Despite the increase in free naloxone distribution in San Diego in recent years, having an average monthly income of less than \$500 was negatively associated with naloxone accessibility.

While income was not a focus of qualitative interviews, participant accounts of poverty and housing instability, including difficulty maintaining naloxone and other belongings, may partially explain this association. In areas where free naloxone distribution was less common, PWUD with little or no income may have perceived naloxone to be less accessible due to the barriers associated with purchasing it in a pharmacy, including availability, lack of prescription, lack of insurance, and cost.^{245,246} The Federal Drug Administration only recently approved over-the-counter Narcan[®] nasal spray naloxone in 2023,²⁴⁷ which costs around \$50 for two doses,²⁴⁸ a price that is unaffordable for many PWUD in our study.

Qualitative inquiry elucidated additional potential barriers to naloxone accessibility related to personal attitudes toward overdose risk and response, such as a perception that smoking rather than injecting reduces overdose risk and the need for naloxone. Distribution of safe smoking supplies has become more common across the U.S., including San Diego County, to reduce bloodborne disease transmission and overdose risk.²⁴⁹ However, a recent national study found increases in fatal overdoses associated with smoking drugs,¹³⁹ highlighting the importance of ensuring that those who smoke drugs are aware of the potential risk and provided naloxone. Some participants shared a preference for lay remedies to respond to overdose, such as injecting stimulants. Moreover, others referenced instances in which themselves or others experienced negative side effects following naloxone administration. Community overdose response education that includes evidence-based options to prevent fatal overdose, such as oxygen administration²⁵⁰ and rescue breathing,²⁵¹ may be appealing for this subgroup of PWUD. In the process of member checking, one participant confirmed that he previously received rescue breathing training from a local SSP, although others had not. Further, education regarding appropriate naloxone dosing strategies are important for reducing the potentially severe side

effects associated with excessive naloxone use.^{252,253} Indeed, one participant mentioned he received a “30-second training” which suggests insufficient attention to appropriate dosing and revival techniques. Further research should assess the prevalence of these attitudes among PWUD to determine the extent to which such educational efforts are needed.

Limitations

We identified an important consideration for measuring naloxone access related to terminology. Several interview participants expressed unfamiliarity with the term “naloxone” and most commonly referred to it as “Narcan®.” Use of the word naloxone in surveys and interviews may have confused some participants. Although the qualitative interview guide was adjusted once this pattern was detected, skip-logic for Cohort 2 resulted in premature exclusion of 50 participants who were not familiar with the generic term but may have recognized the medication by its brand name, which has implications for assessing naloxone accessibility, but also for community education and outreach. First, offering naloxone to PWUD using its generic name may dampen uptake. Further, as additional formulations of overdose reversal medications from alternative companies become more prevalent,²⁵⁴ it will be important for PWUD to differentiate between them.

In addition to the 50 persons excluded from Cohort 2, 17 from Cohort 1 were excluded due to nonresponse. Excluded participants were slightly older and significantly less likely to report past six-month fentanyl and methamphetamine use. Based on these characteristics, it is possible that those excluded may have had lower personal naloxone accessibility, although they were otherwise similar to included participants.

Although Spanish-only speakers were not purposefully excluded from qualitative interviews, none were conducted in Spanish. However, over half of interview participants were of Hispanic/Latinx/Mexican ethnicity. Survey and interview data are subject to recall and social

desirability bias. *La Frontera* participants were purposively sampled to meet parent study objectives and may not broadly represent PWUD in San Diego. Finally, our study used cross-sectional data, limiting causal and temporal inferences in the relationships between independent variables and naloxone accessibility.

Conclusions

Although there were variations in reported accessibility, PWUD generally perceived that naloxone was easy to acquire in San Diego, which is likely attributable to successful OEND efforts and mutual aid among peers. Although we did not identify geographic differences in naloxone accessibility in quantitative analyses, qualitative insights indicated there may be location-related disparities in naloxone distribution. Importantly, women reported greater naloxone accessibility relative to men. Qualitative interviews revealed individual preferences and attitudes that may explain variations in naloxone accessibility not accounted for in quantitative analyses.

As of 2024, San Diego County's naloxone expansion efforts include distribution partnerships with 85 community organizations and the placement of 16 naloxone-dispensing harm reduction vending machines in various locations, including community organizations, methadone clinics, tribal reservations, and jails.²⁵⁵ It will be important to ensure PWUD awareness of these additional efforts and determine if perceptions of naloxone accessibility change in areas of the county where it was not previously widely available.

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Tables and figures

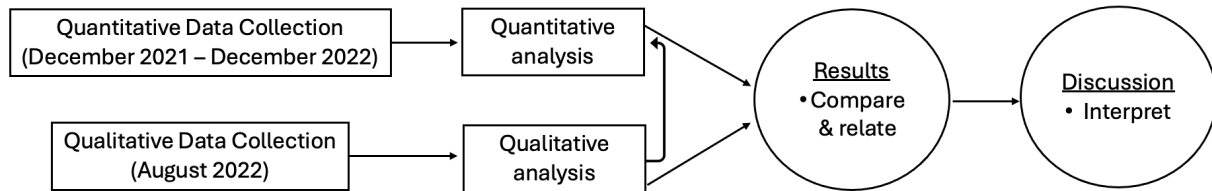


Figure 6. Convergent parallel mixed methods study design of naloxone accessibility among people who use drugs in San Diego, California

Table 9. Participant descriptive characteristics by personal naloxone accessibility category^a among people who use drugs in San Diego, California, December 2021 – December 2022 (N=194)

	Never	Sometimes	Always	p-value	Overall
n (%)	47 (24)	101 (52)	46 (24)	0.085	194
Cohort 1 (n(%))	39 (83)	67 (66)	30 (65)		136 (70)
Cohort 2 (n(%))	8 (17)	34 (34)	16 (35)		58 (30)
Demographics					
Age (mean(SD))	39.6 (9.3)	43.3 (12.4)	41.9 (10.4)	0.181	42.1 (11.3)
Sex (assigned female at birth) (n(%))	10 (21)	25 (25)	20 (44)	0.030	55 (28)
Sex (assigned male at birth) (n(%))	37 (79)	76 (75)	26 (57)		139 (72)
Race					
Indigenous ^b (n(%))	0 (0)	4 (4)	4 (9)	0.108	8 (4)
Black ^b (n(%))	5 (11)	11 (11)	6 (13)	0.916	22 (11)
Asian ^b (n(%))	1 (2)	0 (0)	1 (2)	0.334	2 (1)
Pacific Islander ^b (n(%))	0 (0)	0 (0)	1 (2)	0.198	1 (1)
White ^b (n(%))	25 (53)	63 (62)	29 (63)	0.517	117 (60)
Other race ^b (n(%))	16 (34)	28 (28)	15 (33)	0.690	59 (30)
Hispanic/Latinx/Mexican ethnicity (n(%))	21 (45)	34 (34)	21 (46)	0.260	76 (39)
Non-White race/ethnicity (n(%))	27 (57)	50 (50)	29 (63)	0.282	106 (55)
Structural factors ^c					
Resides near downtown San Diego (n(%))	19 (40)	27 (27)	11 (24)	0.152	57 (30)
Cross-border drug use (n(%))	3 (6)	7 (7)	7 (15)	0.207	17 (9)
Stopped/Arrested by police (n(%))	12 (26)	41 (41)	23 (50)	0.049	76 (39)
Jail/prison (n(%))	4 (9)	11 (11)	8 (17)	0.379	23 (12)
Homelessness (n(%))	36 (77)	75 (74)	32 (70)	0.731	143 (74)
Income less than \$500/mo (n(%))	11 (23)	20 (20)	4 (9)	0.146	35 (18)
SSP client (n(%))	26 (55)	62 (61)	30 (65)	0.611	118 (61)
Received drug or alcohol treatment ^c (n(%))	9 (19)	15 (15)	11 (24)	0.405	35 (18)
Drug use ^c					
Heroin (n(%))	19 (40)	45 (45)	23 (50)	0.648	87 (45)
Methamphetamine (n(%))	35 (75)	84 (83)	43 (94)	0.047	162 (84)
Fentanyl (n(%))	27 (57)	61 (60)	30 (65)	0.739	118 (61)
Rx opioids (n(%))	1 (2)	6 (6)	4 (9)	0.386	11 (6)
Benzodiazepines/Tranquilizer (n(%))	3 (6)	11 (11)	1 (2)	0.172	15 (8)
China White (n(%))	3 (6)	10 (10)	1 (2)	0.237	14 (7)
Smoked any opioid (n(%))	23 (49)	52 (52)	30 (65)	0.215	105 (54)
Polysubstance Co-injection (n(%))	9 (19)	30 (30)	12 (26)	0.398	51 (26)
Average number injections/day (mean (SD))	0.7 (1.2)	1.3 (1.4)	1.2 (1.6)	0.101	1.1 (1.4)
Stopped injecting (n(%))	3 (6)	6 (6)	6 (13)	0.302	15 (8)
Overdose experiences					
Past 6mo overdose ^c (n(%))	2 (4)	21 (21)	8 (17)	0.036	31 (16)
Lifetime overdose (n(%))	22 (47)	70 (69)	29 (63)	0.031	121 (62)
Witnessed overdose ^c (n(%))	12 (26)	71 (70)	37 (80)	<0.001	120 (62)
Overdose response & naloxone experiences					
Administered naloxone ^c (n(%))	5 (11)	38 (38)	29 (63)	<0.001	72 (37)
Overdose response alternative methods ^c (n(%))	1 (2)	17 (17)	3 (7)	0.015	21 (11)
Currently carrying naloxone (n(%))	2 (4)	33 (33)	34 (74)	<0.001	69 (36)
Knows where to get free naloxone today (n(%))	18 (38)	78 (77)	38 (83)	<0.001	134 (69)
Notes: ^a Participant responses to the question "In the last six months, how often have you had naloxone on you where you could get it within five minutes?"					
^b Indicated race variables are not mutually exclusive.					
^c Indicated variables refer to the preceding six months.					

Table 10. Sample characteristics of qualitative interview participants, August 2022 (N=20)

Sex (female) (n(%))	6 (30)
Age (mean(SD))	41 (7.7)
Race (n(%))	
Black	1 (5)
Indigenous	1 (5)
White	11 (55)
Other	6 (30)
Hispanic/Latinx/Mexican ethnicity	13 (65)
Resides near downtown San Diego (n(%))	11 (55)
Cohort 2 (n(%))	3 (15)
Drug preferences (n(%))	
Fentanyl	16 (80)
Methamphetamine	14 (70)
Heroin	5 (25)
Benzodiazepines/Tranquilizer	2 (10)
Past 6-month overdose (n(%))	5 (25)
Lifetime overdose (n(%))	11 (55)

Table 11. Ordinal logistic regression univariable and multivariable associations with personal naloxone accessibility (never, sometimes, always) among people who use drugs in San Diego, California, December 2021–2022 (N=194)

	OR	95% CI	p-value	AdjOR	95% CI	p-value
Demographics						
Sex (Female)	2.10	1.15, 3.90	0.016	2.51	1.31, 4.85	0.006
Age	1.01	0.99, 1.03	0.343			
Non-White Race/Ethnicity	1.15	0.68, 1.98	0.599			
Structural Factors^b						
Resides near downtown San Diego	0.58	0.32, 1.06	0.076			
Cross-border drug use	2.15	0.81, 5.76	0.123			
Stopped/Arrested by police	1.98	1.14, 3.48	0.015			
Jail/prison	1.77	0.77, 4.11	0.182			
Unhoused	0.79	0.43, 1.45	0.441			
Income less than \$500/mo	0.53	0.26, 1.05	0.070	0.42	0.19, 0.90	0.027
SSP client	1.32	0.76, 2.29	0.327			
Received drug or alcohol treatment	1.24	0.61, 2.54	0.549			
Drug Use^b						
Heroin	1.29	0.75, 2.22	0.353			
Methamphetamine	2.46	1.20, 5.12	0.014			
Fentanyl	1.24	0.72, 2.15	0.444			
Rx opioids	2.19	0.70, 6.99	0.176			
Benzodiazepines/Tranquilizer	0.71	0.28, 1.84	0.485			
China White	0.70	0.26, 1.85	0.467			
Polysubstance co-injection	1.26	0.69, 2.31	0.447			
Smoked any opioid	1.54	0.90, 2.65	0.117			
Average number injections/day	1.17	0.96, 1.42	0.111			
Stopped injecting	1.92	0.68, 5.47	0.217			
Overdose experiences						
Past 6mo overdose	1.83	0.91, 3.72	0.093			
Lifetime overdose	1.61	0.92, 2.84	0.096			
Witnessed overdose	5.67	3.07, 10.8	<0.001	3.51	1.67, 7.55	0.001
Overdose response & naloxone experiences						
Administered naloxone ^b	4.95	2.71, 9.29	<0.001			
Responded to an overdose with alternative methods ^b	1.31	0.59, 2.92	0.510			
Knows where to get free naloxone today	4.58	2.45, 8.76	<0.001	3.44	1.79, 6.75	<0.001
Notes: ^a Participant responses to the question "In the last six months, how often have you had naloxone on you where you could get it within five minutes?"						
^b Indicated variables refer to the preceding six months.						

Supplementary Table 4. Participants included vs. excluded from analysis due to nonresponse^a

	Included	Excluded	p-value	Overall
n	194	67		261
Non-White Race/Ethnicity (n(%))	106 (55)	34 (51)	0.683	140 (54)
Sex assigned at birth (female) (n(%))	55 (28)	25 (37)	0.223	80 (31)
Age (mean(SD))	42.1 (11.3)	46.3 (11.7)	0.009	43.2 (11.5)
Unhoused ^a	143 (74)	57 (85)	0.084	200 (77)
SSP engagement ^a (n(%))	118 (61)	46 (69)	0.319	164 (63)
Fentanyl ^a (n(%))	118 (61)	30 (45)	0.032	148 (57)
Heroin ^a (n(%))	87 (45)	35 (52)	0.366	122 (47)
Methamphetamines ^a (n(%))	162 (84)	47 (70)	0.029	209 (80)
Benzodiazepines/Tranquilizers ^a (n(%))	15 (8)	6 (9)	0.955	21 (8)
No longer injecting (n(%))	15 (8)	9 (13)	0.251	24 (9)
Average daily injections ^a (median (IQR))	1.1 (1.4)	1.3 (1.3)	0.281	1.2 (1.4)
Lifetime overdose (n(%))	121 (62)	34 (51)	0.127	155 (59)
Notes: ^a Indicated variables refer to the prior six months				

DISCUSSION

Overview

This research addressed gaps in understanding the extent to which PWUD in the Tijuana/San Diego border region have access to and utilize a variety of harm reduction practices and services. The findings herein identified several structural and individual-level opportunities to increase uptake of harm reduction practices and services among PWUD in Tijuana and San Diego. Further, because participants in this study were recruited through street outreach rather than from harm reduction or healthcare settings as is common in this field, the findings provide information regarding a community-based sample of PWUD, some of whom were connected to key services while others were not. Each chapter also uniquely contributed key findings to the harm reduction literature as described below.

Chapter 1 identified underutilization of several overdose prevention strategies among participants, including drug checking, carrying naloxone, doing tester shots, seeking treatment, and not using drugs alone. Among PWUD residing in Tijuana, the primary strategy to prevent overdose was to avoid fentanyl, as reported by 83% of participants. Use of drug checking tools to identify fentanyl or other contaminants were used by none and only 2% of Tijuana participants reported carrying naloxone to avoid fatal overdose, as these harm reduction tools are scarce in Mexico. The next most prominent overdose prevention strategy among Tijuana participants was trying not to use alone, endorsed by 36%. In contrast, the primary strategy to prevent overdose among participants in San Diego was to stop or cut down on injecting, which may reflect recently documented trends of switching from injecting to smoking drugs among PWUD in North America.^{135,256} Only 30% of San Diego-based participants reported carrying naloxone and only 6% had used drug checking tools as overdose prevention strategies. Substance abuse

treatment, including MOUD, was endorsed by just 4% of Tijuana participants and 2% of San Diego participants.

Chapter 1 also employed LCA to identify subgroups of PWUD in Tijuana based on their probabilities of utilizing each overdose prevention strategy, revealing four unique groups with distinct overdose prevention strategies: (1) those who try to use the same drug supplier, (2) those who try to cut down on injecting, (3) those whose only strategy is to try to avoid fentanyl, and (4) those who try to avoid using alone. Notably, trying to avoid fentanyl was a strategy with high probability of use in each group. This analysis also revealed micro-environmental and individual-level factors that differed between latent groups. Figure 8 provides a final summary of these factors and their location within an adapted Risk Environment framework. Factors in blue are key elements of the risk environment incorporated to interpret findings. For example, a lack of government support for harm reduction services in Mexico is related to our finding that naloxone carriage and drug checking strategies were utilized by less than 2% of Tijuana participants. At the micro-social level, the latent group of participants who were trying to cut down on injecting as a primary overdose prevention strategy may be related to the recently documented trends in smoking rather than injecting drugs.

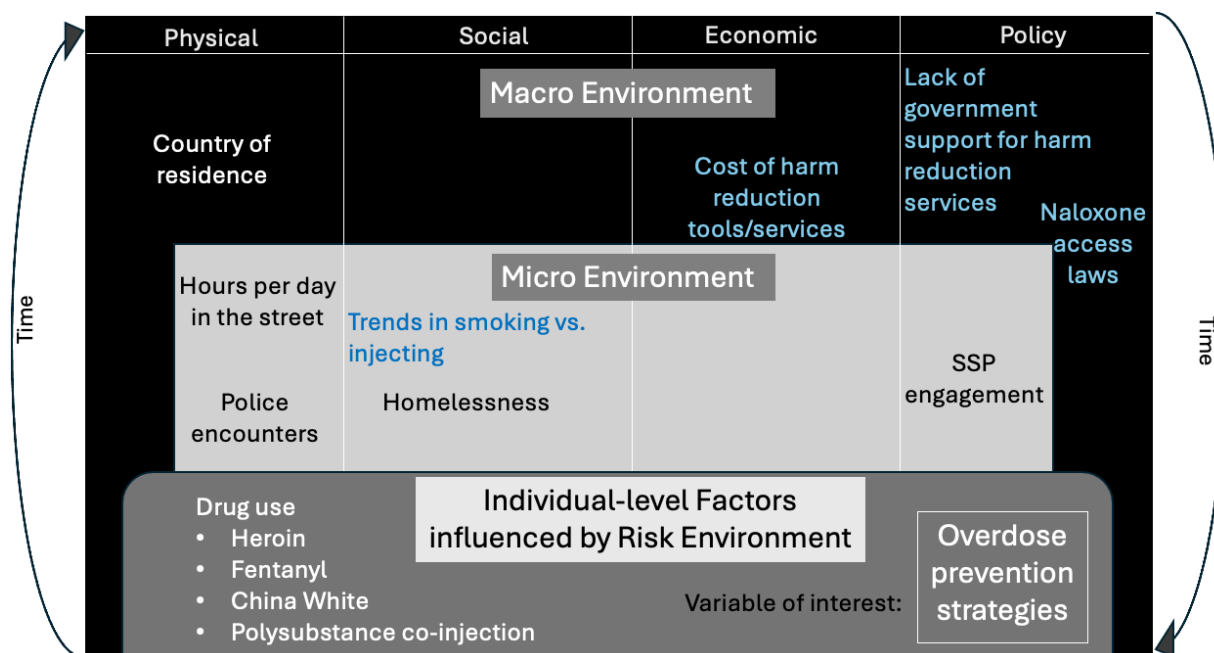


Figure 7. Aim 1: Summary of factors influencing utilization of overdose prevention strategies among people who use drugs in Tijuana, Mexico in an adapted Risk Environment framework

Chapter 2 applied Social Cognitive Theory to examine potential associations between SISE and cognitive, behavioral, environmental, and health factors. First, this study revealed that PWUD in San Diego had much higher SISE scores relative to those living in Tijuana, likely attributable to the availability of SSPs in San Diego that widely distribute free sterile syringes, injection equipment, and safer injection education to PWUD. Chapter 2 also revealed key factors associated with SISE levels among PWUD in Tijuana. Figure 8 provides a summary of these factors and their place within the Social Cognitive Theory framework. First, we found that White persons and those who had previously resided in San Diego (environmental factors) had greater SISE scores, likely due to their connections with San Diego-based harm reduction services. Homelessness was also negatively associated with greater SISE, perhaps reflective of the unique difficulties of poverty and housing instability that influence a person's capacity to consistently acquire sterile injection equipment. Polysubstance co-injection, a greater number of average

daily injections, and fentanyl use (behavioral factors) were independently associated with lower SISE scores, reflecting greater difficulty consistently utilizing sterile injection equipment. Finally, HCV and HIV seropositivity (health factors) were independently associated with lower SISE scores. This may indicate an opportunity for interventions that aim to increase SISE to reduce HCV and HIV risk. Figure 9 summarizes these associations in an adapted Risk Environment Framework and environmental factors in blue were incorporated in the interpretation of findings.

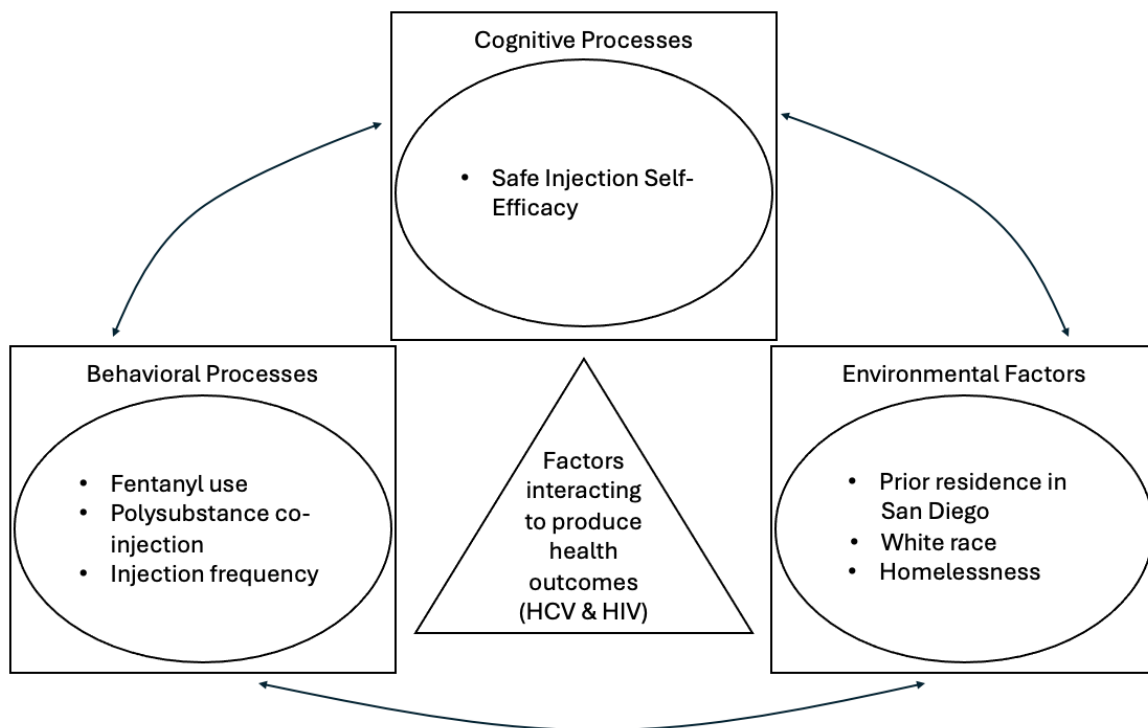


Figure 8. Aim 2: Summary of factors associated with Safe Injection Self-Efficacy scores among people who use drugs in Tijuana, Mexico in an adapted Social Cognitive Theory framework

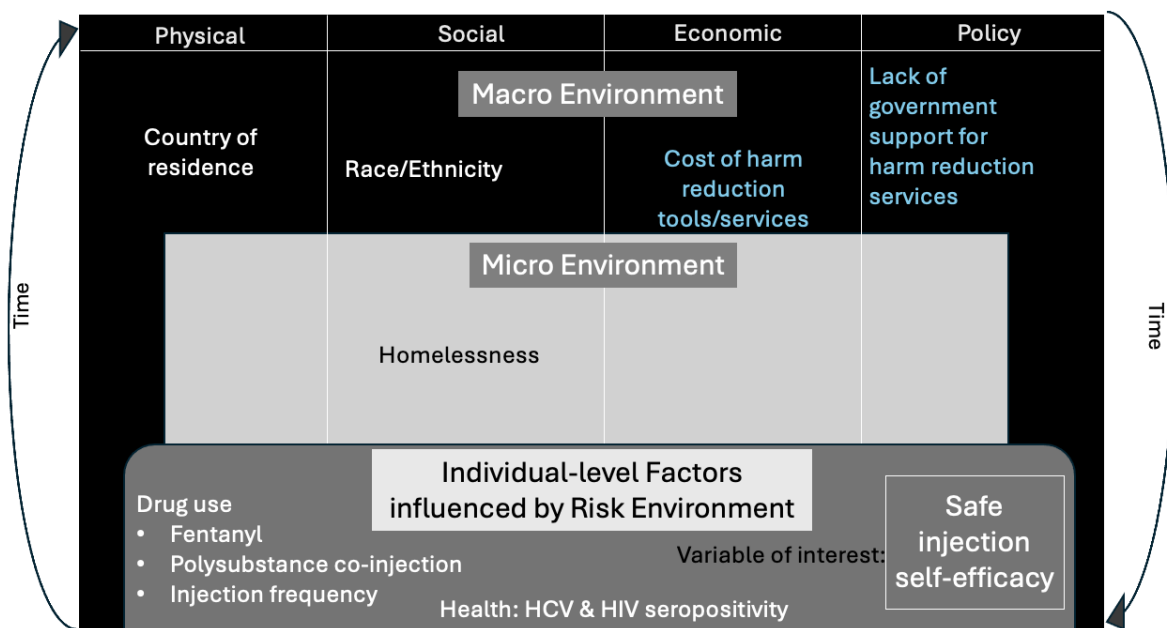


Figure 9. Aim 2: Summary of factors associated with Safe Injection Self-Efficacy scores among people who use drugs in Tijuana, Mexico in an adapted Risk Environment framework

Using a mixed methods design, Chapter 3 focused on naloxone accessibility among PWUD in San Diego prior to the County’s efforts to further expand community naloxone distribution at the end of 2022. We found there was variability in personal naloxone accessibility, measured as the frequency with which an individual had naloxone on them where they could get it within five minutes within the last six months. An analysis of factors associated with increased naloxone accessibility coupled with qualitative interviews among PWUD revealed several explanations for varied accessibility. We found that women were significantly more likely to report greater naloxone accessibility. Further, satellite distribution and mutual aid among peers were identified in qualitative data as key aspects of the general perception among PWUD that naloxone is easily accessible in San Diego. It is plausible that women are relatively more willing to take on the role of carrying, distributing, and administering naloxone and may have an elevated overdose risk perception for themselves and others. Those who had witnessed an overdose in the prior six months were also more likely to report greater naloxone accessibility.

We also found that witnessing an overdose was associated with increased personal naloxone accessibility. Witnessing an overdose may elevate overdose risk perceptions and influence a person's motivation to prevent death among peers, as highlighted in qualitative interviews. Other insights from qualitative interviews revealed additional potential barriers to naloxone accessibility, including location relative to naloxone distribution programs, housing instability and frequent relocation, negative perceptions of naloxone side effects, and emotional drain due to witnessing multiple overdoses. Importantly, interview participants reported regularly acquiring naloxone either proactively or passively from SSPs or other community organizations, highlighting the crucial role that OEND expansion has played thus far in contributing to naloxone accessibility in San Diego. However, despite OEND programs that have provided access to free naloxone in San Diego, income $\leq$ UDS\$500 was negatively associated with naloxone accessibility and may indicate that some people are not connected with these programs. Knowing where to get free naloxone was associated with greater naloxone accessibility, underscoring the importance of being connected with harm reduction service providers. Figure 10 summarizes these findings within an adapted Risk Environment framework with factors that provide context from qualitative inquiry provided in orange and environmental factors utilized for interpreting findings in blue.

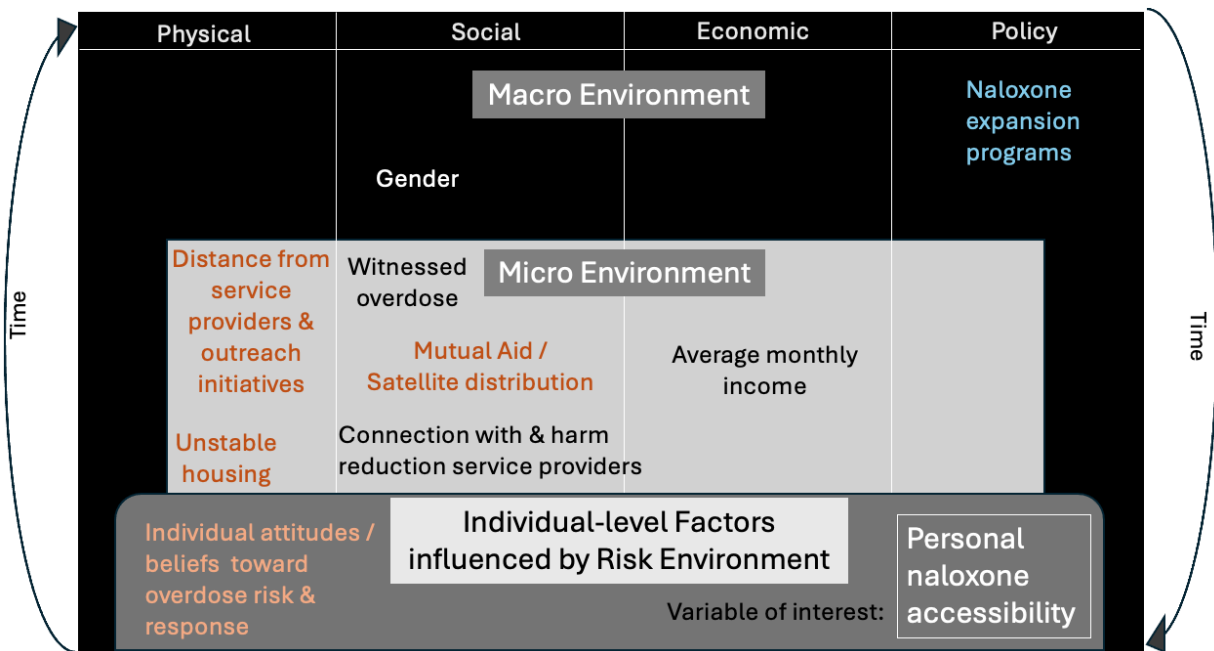


Figure 10. Aim 3: Summary of factors associated with personal naloxone accessibility among people who use drugs in San Diego, California in an adapted Risk Environment framework

Implications

This dissertation research has several implications for the health and wellbeing of PWUD. Chapter 1 findings highlight opportunities for the expansion and uptake of harm reduction services in Tijuana and San Diego, including drug checking, naloxone provision, and MOUD. Although most Tijuana participants reported their primary overdose prevention strategy was avoiding fentanyl, tools to test drugs for fentanyl are not widely available in Mexico. Provided an increased presence of fentanyl in the region's drug supply,^{15,64} policies to support widespread access to FTS and other drug checking services, such as portable spectrometry devices used in point-of-care locations, would benefit this population.

There are a variety of drug checking tools, each of which has pros and cons associated with cost, sensitivity and specificity, portability, speed, and ease of use.^{56,257} FTS and other immunoassay test strips indicate the presence or absence of a specific substance in a drug sample

and are highly sensitive relative to other tools.⁵⁵ Test strips provide fast results and are the least expensive and simplest drug checking tool to use, necessitating only a brief training for new users.^{26,33,258} However, FTS may produce false positive results in samples with high stimulant concentrations.²⁵⁹ A few studies have successfully employed FTS to identify fentanyl in drug samples in Tijuana and Mexicali,^{15,64,115} but the availability of these tools is sporadic.

There are several advanced spectrometry drug checking devices with key differences in complexity of use, portability, and cost.²⁵⁷ These devices can test for multiple substances simultaneously and provide estimates of quantity,²⁶⁰ but are less sensitive relative to immunoassay test strips and, as such, may not recognize some substances in low concentrations. Advanced spectrometry devices are more costly than immunoassay test strips and require a technician to interpret results.²⁵⁷ However, relative to other advanced methods, FTIR devices are lower in cost, easier to use, and have been successfully employed for drug checking in several North American community harm reduction programs,^{32,257} including in electronic music festivals in Mexico City.²⁶¹ Importantly, several other advanced spectrometry devices have been used in point-of-care services and communities should carefully assess PWUD needs and available resources to determine the best drug checking methods to pursue. Ideally, given each drug checking technology has strengths and limitations, communities would employ multi-instrument approaches, as demonstrated by the Vancouver Island drug Checking Project in Victoria, Canada.²⁵⁷

Community drug checking services should be expanded in Mexico, particularly in cities like Tijuana where overdose rates are relatively high.¹¹ In Tijuana, it is important to provide mobile services where possible, as many PWUD are unhoused and living in precarious locations with limited mobility.^{64,193} Fear of criminalization and policing is a common barrier to drug

checking services²⁶² and policing practices in Tijuana have contributed to riskier behaviors and negative outcomes for PWUD.^{16,263–266} As such, expansion of drug checking services should be accompanied by supportive policies and protections for service providers and persons who utilize drug checking tools.

In Chapter 1, few Tijuana participants reported carrying naloxone. Availability of naloxone is limited in Mexico, as it is classified as a psychotropic substance requiring prescription, is cost-prohibitive, is not widely available in pharmacies, and there is no centralized government support for community-based organizations to distribute the medication.^{13,14} As such, harm reduction providers in Tijuana maintain a limited supply of naloxone donated by other countries and risk legal sanctions when transporting the medicine to Mexico.¹⁴¹ Recent efforts from Mexican senators to pass laws to declassify and create a budget for community acquisition and distribution of naloxone failed following President Andrés Manuel Lopez Obrador’s suggestion in April 2023 that naloxone “prolongs the agony” of addiction rather than curing it.²⁶⁷ Government representatives in Mexico should acknowledge the developing opioid overdose epidemic¹¹ and readdress efforts to declassify naloxone so it is accessible without a prescription. Additionally, it will be important to allocate public funding and create programs to widely distribute naloxone to laypersons and public health and safety officials.¹² Existing harm reduction service providers should be consulted in leading these efforts, as many are experienced in naloxone application and have close connections with persons at risk of overdose.¹⁴

Many Tijuana participants reported trying to avoid using alone as an overdose prevention strategy, and the LCA in Chapter 1 highlighted a subgroup of participants for whom this was their primary strategy. This emphasizes the importance of layperson naloxone administration and spaces where PWUD can use drugs with overdose response support. Safe consumption facilities

operate with legal ambiguity in Mexico, but an unsanctioned site in Mexicali for female PWUD has shown success in preventing fatal overdose.^{14,115} Prior research occurring between 2016 – 2018 among 771 police officers and 220 persons with lived experience of substance use in Tijuana indicated high levels of personal support and positive attitudes for safe consumption facilities in the city among both groups.³⁷ In 2022, the first unsanctioned safe consumption facility was opened by Tijuana’s primary harm reduction service provider. However, these harm reduction services operate under fear of political reprisal as the Mexicali location was previously closed by local government officials.²⁶⁸ Safe consumption facilities should be supported in Mexico and legal protections should be developed to preserve their operation.

Generally, harm reduction service providers in Mexico who strive to address the country’s inadequate public health response to opioid use and overdose lack political support and funding, face social and political stigma, and experience public and legal insecurity.²⁶⁹ The President’s minimization of problems of addiction and overdose in the country²⁷⁰ and stigmatizing characterization of civil society organizations²⁶⁹ signal limited federal support for the expansion of harm reduction services in the country. Indeed, federal funding for all civil society organizations in Mexico was withdrawn in 2019, leading to a financial crisis among harm reduction organizations.²⁷¹ Additionally, the current administration promotes substance use as an issue of morality rather than public health, an approach that contributes to social stigma toward PWUD and programs that serve them.^{13,269} Public campaigns to promote evidence-based education and harm reduction strategies are important for counteracting prominent stigmatizing messages. Policies to increase access to overdose prevention tools and services are crucial for interrupting the increasing rate of fatal overdoses in Mexico’s northern region.¹¹ Existing civil

society organizations are poised to provide harm reduction services, but are in need of government support and funding.²⁶⁹

In Chapter 1, we found that few Tijuana participants reported accessing substance abuse treatment as a way to manage overdose risk, consistent with previous findings of low MOUD engagement among PWID in Tijuana.²⁷² Access to evidence-based MOUD treatment in Mexico is very limited. Methadone is the only medication permitted for OUD in Mexico, yet there has been a short supply for several years throughout the country, in part due to bureaucratic restrictions and a lack of prioritization.²⁷³ Further, a 2021 government report indicated there were just two public and nine private methadone clinics in the country.²⁷⁴ In recent years, several private clinics in the Northern region abruptly closed with no contingency plans for their opioid-dependent patients.²⁷⁵ Importantly, persons who experience a disruption in their MOUD treatment are at heightened risk of overdose upon returning to illicit opioid use.²⁷⁵ Despite an increase in overdose rates¹¹ and fentanyl use²⁷⁶ during this time, between 2016 – 2022, the number of patients receiving methadone maintenance treatment in Mexico decreased by 42%.²⁷⁷ Further exacerbating this treatment shortage, the country's primary producer of methadone was shut down in 2022 following inspections citing irregularities in the production of certain medications.¹⁴² This led several clinics in Tijuana to close their methadone treatment services and resulted in fatal overdose among former patients,²⁷⁷ and by May 2024, only one methadone clinic had re-opened.

Expanding and ensuring access to consistent MOUD services is particularly important in Mexico's northern region, where opioid misuse and fatal overdose is most prevalent.¹¹ Authorities should prioritize the production of methadone and continuity of methadone maintenance programs. Buprenorphine is currently only available in Mexico as a prescription

pain management,²⁷⁸ but its use should be expanded for MOUD purposes. Additionally, Suboxone, a coformulation of buprenorphine with naloxone, should be made available¹² and clinics should provide a variety of medication options, as research documents varied patient preferences.^{279,280} Importantly, methadone and buprenorphine have been listed as essential medicines by the World Health Organization since 2005.²⁸¹ Current barriers to methadone maintenance treatment in Tijuana include prohibitive costs¹⁹⁰ and police harassment.²⁷² Mexico should ensure MOUD treatment is covered under the country's universal health care system¹³ and interventions to shift policing practices are warranted.²⁸²

It is important to note that, despite a lack of support for harm reduction services, only 1% of Tijuana participants examined in Chapter 1 reported a prior six month overdose, similar to nonfatal overdose reported among Tijuana participants in the *La Frontera* baseline survey,¹⁶ and much lower relative to the past six-month overdose prevalence among San Diego participants. Qualitative research should further explore Tijuana participants' strategies to avoid fentanyl and otherwise prevent overdose amidst an increase in fatal overdose rates in the region.¹¹ However, it is possible that some Tijuana participants lost to follow-up died from overdose and that a lower proportion of nonfatal overdoses are reported among participants in Tijuana due to a lack of naloxone availability to reverse overdoses. As cause of death data becomes available, future research should assess the extent to which Tijuana participants were lost to fatal overdose.

As described in Chapter 1, San Diego participants most commonly endorsed stopping or cutting down on injecting as an overdose prevention strategy. Recent research among *La Frontera* participants also found an increase in smoking drugs and a decrease in injecting drugs over time.²³⁶ PWUD in San Diego may benefit from increased distribution of safe smoking supplies and related overdose prevention education.²⁴⁹ Few San Diego participants reported use

of drug checking tools and only 30% reported carrying naloxone, reasons for which were expanded upon in Chapter 3 and may include perceptions of low overdose risk, preferences for alternative overdose response methods, or perceptions that the medication is generally accessible when needed regardless of personal carriage. These findings highlight opportunities to increase drug checking services and naloxone uptake. In a recent study led by this dissertation author, we found that FTS were the most commonly used drug checking tools in San Diego, although more than half of PWUD surveyed expressed disinterest in receiving additional free test strips¹⁰⁸. This may be due to a preference for fentanyl use among many, which has also been documented elsewhere in the country,^{283,284} or perceptions that fentanyl is unavoidable due to its infiltration in the illicit drug supply.²⁸⁵ In this study, most San Diego PWUD surveyed expressed interest in utilizing advanced drug checking technologies to detect the presence of multiple substances in a small drug sample and inform drug use behaviors, although none had used such services.¹⁰⁸ Advanced drug checking technologies in community harm reduction programs can benefit San Diego PWUD by identifying the presence of fentanyl and many other cutting agents or potential contaminants, as well as providing information about the concentration of each substance in a small drug sample.²⁸⁶ Such community drug checking programs can also serve as a public health surveillance tool, providing information on test results to convey risk alerts to the community.²⁸⁷ One San Diego SSP began providing FTIR drug checking services in 2022,²⁸⁸ but there is still a need to expand these services and implement related public health surveillance systems locally and regionally.²⁸⁹

Finally, low reported engagement in substance abuse treatment among San Diego PWUD may reflect an opportunity to expand low-threshold MOUD through mobile outreach,²⁹⁰ particularly since 61% of San Diego participants reported fentanyl use and 77% were

experiencing homelessness. Another promising low-barrier MOUD initiation strategy was recently implemented at the San Diego public library,²⁹¹ which has seen an increase in patrons experiencing housing instability, opioid overdoses, and related issues.²⁹² Consistent availability, medication delivery, and the possibility of take-home doses are important considerations for MOUD treatment retention and decreased overdose risk.^{293–295} Prior research has identified that a lack of MOUD knowledge among PWUD in Southern California as well as stigma toward this treatment modality may be barriers to uptake.^{132,296} Additionally, MOUD may be cost-prohibitive for persons who are not covered by insurance, and several MOUD clinics in the region only accept private insurance.²⁹⁷

Chapter 2 presented a negative association between SISE and HCV/HIV seropositivity among PWUD in Tijuana. The lack of support for harm reduction programs in Mexico described previously has contributed to a dearth of sterile syringes and injection equipment that is required for averting bloodborne infections among PWID.²⁹⁸ Additionally, previous international support for syringe distribution was withdrawn in 2013 and resulted in a significant reduction in the number of syringes distributed per PWID in Tijuana.²⁹⁹ A 2019 report indicated that 5.6 syringes were distributed per PWID in Mexico,³⁰⁰ far below the United Nations target of 200 per person,³⁰¹ which does not account for individual differences in injection frequency.³⁰²

A deficiency in sterile injection equipment availability is one environmental factor that influences the cognitive process of SISE. Importantly, SISE was previously found to be a key indicator of injection risk behaviors among PWID in Tijuana⁹⁴ and an intervention aimed at increasing SISE among female PWID engaged in sex work in Ciudad Juarez, Mexico successfully reduced injection risk.³⁰³ Together, these findings underscore the potential for SISE interventions to reduce HCV and HIV risk among PWID in Tijuana. Importantly, drug use

factors that indicated greater injection frequency, including fentanyl use, were associated with lower SISE, indicating that those who use fentanyl are an important intervention target. Homelessness among Tijuana participants was also related to lower SISE, pointing to one of several recently documented negative health outcomes for unhoused PWID in the region.^{193,304} Importantly, recent studies among PWID in Tijuana found those experiencing unsheltered homelessness had more frequent contact with contaminated water.^{304,305} This, coupled with limited syringe access and low SISE, can exacerbate other health conditions, such as skin and soft tissue infections.³⁰⁵ This study also highlights an opportunity to expand low-barrier HCV and HIV testing, counseling, and medication for PWID, which has shown to reduce injection risk behaviors.¹⁷⁹

Chapter 3 indicated that naloxone distribution efforts in San Diego have been important for reaching PWUD at risk of overdose. SSPs and other community outreach organizations, as well as satellite distribution amongst peers, were identified as important sources of naloxone. While most study participants knew where to access naloxone, about a third did not, suggesting some PWUD may not have been connected with OEND programs. Our findings indicate that women may be key satellite naloxone distributors and could be meaningfully incorporated into OEND efforts. Some PWUD expressed relative difficulty in acquiring naloxone in some areas of San Diego County outside of the downtown area which should be considered for increased mobile outreach.

Another barrier to naloxone accessibility was unstable housing and frequent relocation which, for some who were experiencing homelessness, was related to policing practices and street sweeps. Loss of medications such as naloxone is just one of several negative impacts of involuntary relocation for this population. Naloxone distribution could be timed with regular

street sweep activities. However, cost of living and homelessness are major policy and public health problems in southern California and Housing First models that thoughtfully incorporate harm reduction principles are key.^{306,307} In 2024, California voters narrowly approved highly contested Proposition 1 that will reform the state's response to homelessness, mental health, and SUD, prioritizing the development of mental health and substance use treatment centers and new housing initiatives.³⁰⁸ It will be important to align public housing and public health efforts and study the effects of new initiatives on homelessness and health outcomes. Importantly, Proposition 1 opponents caution against efforts to advance compulsory treatment, which could result in human rights abuses and potentially cause harm.^{309,310}

Attitudes related to overdose risk and response highlighted a potential need for additional overdose education to accompany naloxone distribution, including appropriate responses, such as rescue breathing and oxygen administration, and clarifying naloxone dosing needs. Future research should further assess PWUD knowledge and attitudes toward overdose response and naloxone administration to inform possible educational interventions. Finally, community education on the various formulations of naloxone will be important for PWUD to differentiate between naloxone products with different brand names.

Limitations

Data utilized in this dissertation were drawn from participants recruited through comprehensive street outreach efforts focused on structurally marginalized PWID, which is an important recruitment strategy for connecting with persons who may not be engaged with services. However, due to the criminalized nature of drug use, probability sampling of this population is not possible, and findings represent the experiences of particularly marginalized PWUD in terms of health risks, unstable housing, and low income. Further, San Diego

participants may be more likely than the general population of PWUD to engage in cross-border drug use due to purposive sampling strategies to meet the objectives of the *La Frontera* study. Importantly, data were collected during the COVID-19 pandemic which negatively impacted the availability of health and harm services and exacerbated health conditions for many.³¹¹

Findings from this dissertation may not be generalizable to other geographic regions with different drug markets, cultures of drug use, community and policy responses to issues of drug use, and languages. Drug availability differs by geographic region and harm reduction needs depend on the types of drugs used and methods of ingestion. For example, as an opioid overdose reversal medication, naloxone is crucial where opioids are present in the drug market. Further, the relative need for harm reduction supplies, such as sterile syringes, smoking supplies or other tools, differs based on PWUD preferred methods of ingestion, which can be influenced by cultural factors. Additionally, community and policy responses to issues of substance use, such as harm reduction services acceptability and availability, criminalization, treatment availability and quality, and other factors are shaped by the attitudes and beliefs of the dominant culture. These aspects of the risk environment are critical to consider when assessing access to and utilization of harm reduction strategies and services among PWUD. Finally, the participants of the *La Frontera* were PWUD who spoke English or Spanish, and findings of this dissertation may not be generalizable to people who speak other languages or come from different cultural backgrounds. Consequently, caution should be exercised when applying these results to other settings without considering the local geographic, cultural, policy, and language dynamics.

Importantly, some participants in the analyses herein were lost to follow up or otherwise excluded from analysis due to non-response to key variables ($n = 67\text{--}126$), representing survivorship, attrition, and nonresponse bias. This dissertation included secondary analyses for

each chapter comparing those included versus excluded to demonstrate how this may have affected results. Generally, we found that those excluded from analysis had indications of both higher and lower risk based on structural and drug use factors, suggesting that their exclusion likely did not drastically impact study results. However, as of May 2024, there is a 5.5% mortality rate among *La Frontera* study participants,¹ exclusion of whom may have resulted in an underestimation of risks. For example, in Chapter 1, we found no association between overdose prevention practices and *nonfatal* overdose. However, this chapter did not include information on overdose prevention strategies that may or may not have been utilized by persons who might have been lost to follow-up due to fatal overdose. In Chapter 2, because persons who might have died due to HIV or HCV related complications or overdose may have been excluded, our SISE scores may have been overestimated. In Chapter 3, naloxone accessibility may have been overestimated due to exclusion of participants who may have died of overdose. As death data becomes available, future studies should determine factors associated with all-cause mortality as well as fatal overdose specifically.

Importantly, in Chapter 3, some participants who were not familiar with the generic term “naloxone” but who may have been familiar with the brand name of the medication, were excluded from analysis due to survey skip-logic. This may have resulted in inaccurate estimation of naloxone accessibility among PWUD in San Diego. This skip-logic was reprogrammed for future iterations of the survey. Survey data is also subject to response bias, including social desirability, agreement, and recall bias, which may result in over- or underestimation of key phenomena. However, the *La Frontera* research team mitigates the potential for these biases

¹ Personal communication with La Frontera principal investigator, Dr. Steffanie Strathdee

through careful construction and continuous reassessment of survey measures with input from field research staff.

In analyses for Chapters 1 and 2, it was important to separately analyze participants residing in Tijuana and San Diego, as their drug use risk environments differ in important ways, particularly with regard to the availability of harm reduction services. However, small sample sizes of participants based in San Diego resulted in inconclusive LCA results (Chapter 1) and OLR results (Chapter 2). Future research should include the additional *La Frontera* participants recruited for the *LinkUp* study (i.e., Cohort 2) where survey variable alignment allows. Chapter 3 focused on naloxone accessibility among San Diego participants only. However, it is important to examine naloxone accessibility in Tijuana, particularly in light of the previously described structural constraints in Mexico.²⁶⁹

All analyses utilized cross-sectional data which precludes inferences of causality and temporality. Future studies should utilize longitudinal *La Frontera* data to establish causality where possible. For example, it will be important to understand whether the associations between SISE and HCV/HIV seropositivity found in Chapter 2 are causal (i.e., whether SISE is a predictor of HCV/HIV seroconversion or vice versa). Mixed methods research including interviews with PWUD living with HCV and HIV could also help to disentangle these relationships. Additionally, it will be important to utilize longitudinal data to assess whether naloxone accessibility increased over time with expanded naloxone distribution efforts initiated in San Diego County in 2022. Importantly, drug markets¹⁹⁹ as well as policies, practices, and public opinion³¹² affecting harm reduction service provision can change over time. For example, some southern California communities are experiencing a backlash against harm reduction services.³¹³ In Mexico where previous administrations were supportive of harm reduction

measures, the current administration has demonstrated otherwise.³¹⁴ It will be essential to conduct ongoing research on the evolving risk environments in Tijuana and San Diego to determine the impact of these developments on access to and utilization of harm reduction practices and services among PWUD.

Finally, some measures included in analyses may underestimate key exposures. For example, our measure of SSP engagement in each chapter was based on whether participants received syringes from an SSP in the prior six months and may have underestimated use of SSPs if they were accessed for other services. Future research should examine access to SSPs for syringe acquisition as well as other services among PWUD in Tijuana and San Diego. Drug use measures used in each chapter represented participant self-reports of the drugs they knowingly ingested. However, given the opaque nature of the unregulated drug supply and limited availability of drug checking services, participants may have unintentionally used other substances, resulting in an underestimation of drug exposure. For example, prior research found that many PWUD in Tijuana were unknowingly exposed to fentanyl.¹⁵ This limitation could be partially overcome in the future by including drug checking during study visits.

In Chapter 1, overdose prevention strategies were assessed using a list of pre-determined strategies drawn from the literature and, although “*other*” responses were included, they may have underassessed key strategies utilized by PWUD. Qualitative inquiry could help to elucidate other overdose prevention strategies utilized, such as those expressed by interview participants in Chapter 3 who described use of lay remedies for overdose prevention, such as methamphetamine or salt injection. Additionally, because we asked about use of strategies *to avoid overdose*, we may have underestimated the use of harm reduction strategies for reasons other than for overdose prevention. For example, some participants may have carried naloxone to support others, rather

than to prevent their own fatal overdose. Further, we measured utilization of overdose prevention strategies, but not frequency of their use, which is important for estimating overdose risk. Future research should determine how often PWUD incorporate overdose prevention strategies in their daily drug use routines.

In Chapter 2, we likely underestimated deportation among Tijuana participants, as this measure was only assessed at baseline and not in follow-up surveys. As such, this precluded a true estimation of the relationship between deportation and SISE. As a result, future survey iterations should include additional questions related to deportation, and this measure should be reexamined as deportation was previously identified as a key determinant of health outcomes among PWUD in the region.^{193,315–317} Finally, our quantitative measure of naloxone accessibility in Chapter 3 assessed PWUD perceptions of personal naloxone accessibility, which may not reflect the relative difficulty with which participants acquire naloxone based on structural factors, such as location of service providers or barriers to transportation. Future research should map naloxone access points related to community need and assess time taken to travel to obtain specific services.³¹⁸

Conclusions

This dissertation provides important insights into structural and individual-level factors that shape access to and utilization of various harm reduction practices and services for PWUD in Tijuana and San Diego. We found that overdose prevention strategies vary between PWUD in Tijuana and San Diego and that several strategies that have been shown to be effective are underutilized in both cities. We found that PWUD in San Diego have much higher SISE scores relative to those in Tijuana and identified important associations between SISE and HCV, HIV, fentanyl use, injection frequency, and homelessness. Finally, we identified factors associated

with individual naloxone accessibility among PWUD in San Diego, including sex, income, witnessing an overdose, and awareness of harm reduction services, and examined PWUD perceptions of naloxone accessibility.

This work highlights opportunities for policy change to enhance access to harm reduction tools and services in Tijuana, including naloxone, drug checking, MOUD, and sterile injection equipment. Mexican authorities should acknowledge the growing substance use and overdose rates in the country's northern states, embrace evidence-based harm reduction services, and provide support and funding for harm reduction service providers on the frontlines of the country's overdose response. Additionally, there is a need for legislation to reclassify naloxone for non-prescription use and develop a system for widespread distribution of the medication, provide legal protections and funding support for community drug checking, allow for buprenorphine to be used for OUD and expand and ensure the continuity of MOUD treatment, and increase syringe availability and distribution.

There is an opportunity to coordinate the provision of multiple harm reduction interventions to achieve Mexico's HIV and HCV elimination targets. A recent modelling analysis found that a 40% increase in MOUD in Tijuana could avert 22% of fatal overdoses over a ten year period, and would have a synergistic effect on overdose and HIV outcomes if coupled with increased antiretroviral therapy.³¹⁹ Another modeling analysis determined that combined expansion of MOUD, syringe provision, and antiviral treatments would also have a synergistic effect in reaching HCV elimination goals among PWID in Tijuana.³²⁰ Such modeling analyses are important for understanding the overlapping effects of health and harm reduction interventions on public health outcomes, and demonstrate that efforts to reach HIV and HCV

targets should incorporate a multitude of coordinated services for PWID. Including cost estimates in modeling analyses may provide key evidence needed for policy changes.

This work also identified opportunities to promote drug checking, distribution of safe smoking supplies, and low-threshold MOUD in San Diego. Advanced drug checking services should be offered more widely in San Diego and local government should work with harm reduction providers and researchers to develop surveillance systems to inform public health responses to hazards identified in the unregulated drug supply. If drug checking becomes more widely available in Tijuana, programs could be coordinated between the two cities to develop a regional alert system. It will be important to assess the potential impact of community drug checking with advanced technologies on PWUD behavior change and overdose incidence.

In light of a trend of switching from injecting to smoking drugs supported by this dissertation's findings, the provision of safe smoking supplies among San Diego PWUD is important for preventing salivary-transmitted infections.²⁴⁹ Preliminary research suggests that smoking rather than injecting may be protective against overdose, although this relationship is not certain. Future research should assess the association between this behavior shift and overdose among PWUD and develop related harm reduction recommendations.³²¹

There is a need to develop low-threshold MOUD treatment modalities in San Diego with consideration of PWUD experiencing structural challenges, including homelessness, little or no income, and lack of insurance, as well as co-occurring health issues.³²² This dissertation also highlighted opportunities to increase naloxone accessibility among San Diego PWUD, particularly through mobile outreach with overdose response education. However, we also found that past OEND efforts have led to PWUD perceptions that naloxone was relatively easy to

acquire in San Diego. Future research should assess the extent to which the County's additional naloxone expansion efforts have reached PWUD in need.

This dissertation also emphasizes the relationships between individual behaviors, cognitive processes, and personal attitudes in shaping health risks, indicating opportunities for individual-level intervention. Chapter 1 considered how individual overdose prevention strategies, particularly avoiding fentanyl, may be effective in preventing overdose for PWUD in Tijuana. Additional research should seek to further understand the role of individual protective behaviors and develop behavioral interventions to increase uptake of overdose prevention strategies in this under resourced setting. Chapter 2 found that low SISE scores and fentanyl use may play a role in HCV and HIV risk. It will be important to further explore these associations and develop interventions to improve SISE for PWID who use fentanyl in Tijuana. Chapter 3 identified several attitudes that may shape personal naloxone accessibility, including a sense of community responsibility and perceptions of overdose risk and naloxone side effects. Additional research is needed to understand potential gaps in knowledge and attitudes toward overdose risk and naloxone administration that may contribute to naloxone aversion.

Finally, it is worth noting that drug user organizing and activism can contribute to the health and wellbeing of PWUD by changing the drug use risk environment and empowering marginalized individuals. As an example, the Vancouver Area Network of Drug Users (VANDU) is a group of former and active PWUD that over the past 20 years has worked to improve conditions for PWUD in Vancouver by developing peer support services,³²³ giving a voice to marginalized communities in public and political settings,³²⁴ and shaping important harm reduction research.³²⁵ There are opportunities for this type of organizing in both Tijuana and San Diego. Research and public health efforts to address addiction, overdose, and related

issues can benefit from the deliberate inclusion of drug user organizations who are best positioned to communicate PWUD needs.

Collectively, the findings in this dissertation provide a snapshot of harm reduction access and utilization among PWUD in Tijuana and San Diego. This dissertation identified multiple avenues for future research and could contribute to the development of multi-level interventions that aim to increase the availability and uptake of harm reduction practices and services in the US-Mexico border region.

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