UNIVERSITY OF CALIFORNIA, SAN DIEGO
SAN DIEGO STATE UNIVERSITY

Research on the epidemiology of prefilled syringe use among persons who inject drugs in San Diego, CA

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

in

Public Health (Epidemiology)

by

Richard Frank Armenta

Committee in Charge:

University of California, San Diego

Professor Richard S. Garfein, Chair
Professor Maria Rosario Araneta

San Diego State University

Professor Stephanie K Brodine
Professor Hector Lemus
Professor Ramona Perez

2015

The Dissertation of Richard Frank Armenta is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

_____

_____

_____

_____

_____
Chair

University of California, San Diego

San Diego State University

2015

DEDICATION

To my wonderful and supportive husband Matt,
my family and friends who have stuck by my side through this crazy adventure,
and my mentors who have helped me develop into the researcher I am

EPIGRAPH

If you can’t explain it simply, you don’t understand it well enough

Albert Einstein

TABLE OF CONTENTS

LIST OF ACRONYMS

AIDS	Acquired Immune Deficiency Disorder
BBV	Bloodborne Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
MSM	Men Who Have Sex With Men
PFSU	Prefilled Syringe Use
PWID	Persons Who Inject Drugs
SAS	Statistical Analysis Software
STI	Sexually Transmitted Infection
US	United States of America
VIF	Variance Inflation Factor

LIST OF FIGURES

LIST OF TABLES

ACKNOWLEDGEMENTS

This dissertation research was supported by a NIDA T32, a NIDA Diversity supplement, and a UC President's Diversity Dissertation Year Fellowship. I would first like to thank the participants for their time and valuable contributions to this research. I would like to acknowledge Dr. Richard Garfein, the chair of my committee, for his support, guidance, and wisdom. He provided words of encouragement and helped me find the strength to make it through this journey. He has been an inspirational mentor, teacher, and supporter and I am grateful for his guidance. I would also like to thank Dr. Stephanie Brodine for the guidance, mentorship, and especially, the opportunities she provided me throughout this process. I would not be where I am today were it not for the wisdom of Dr. Brodine. I would like to thank Dr. Ramona Perez for always believing in me. She was a strong supporter from the time I entered the masters program. She has helped me look at research and mentoring in a different way, and for that I am thankful. I would like to thank Dr. Happy Araneta for her guidance, mentorship, and kind heart. She always provides thoughtful feedback and advice that serves me well in all parts of my life. I thank Dr. Lemus for his support, mentorship, and expertise in biostatistics. He gave me a new appreciation for data and statistics and for that, I am thankful. I am grateful for the staff at the STAHR study, especially Jazmine Cuevas-Mota, for their support and the work they put into this research.

I would also like to thank my cohort, Amanda Rondinelli-Ratigan, Carmel Witte, Jennifer Radin, and Corinne McDaniels-Davidson, all of whom have

become lifelong friends. They were my backbone throughout this process and provided me inspiration and direction to help me make it to this point. I want to thank Kelly Collins for her support, guidance, and most of all friendship through this process. I am thankful for my best friend, Erin Warrell, for her support, friendship, shared love of spicy food, and her work editing my work so I could become a better writer. I also want to thank my family and friends for sticking with me through all of this education. Even though there were times no one was sure why I kept pursuing more college degrees, everyone supported me and stuck by my side.

Lastly, I would like to thank my husband, Matt Wood, who is my best friend and my biggest supporter. He has provided me undying love, a shoulder to cry on, an ear to vent to, and time to complete all of my work and respond to e-mails at all hours of the night.

Chapter 2, in full, has been submitted to the Journal of Urban Health for publication of material. Co-Authors include Garfein, Richard; Munoz, Fatima; Roth, Alexis; Wagner, Karla; Cuevas-Mota, Jazmine; Strathdee, Steffanie; Brodine, Stephanie. The dissertation author is the primary author of this material.

Chapter 3, in full, is being prepared for submission to Substance Abuse and Misuse for publication of material. Co-Authors include Garfein, Richard; Roth, Alexis; Wagner, Karla; Cuevas-Mota, Jazmine; Strathdee, Steffanie; Perez, Ramona. The dissertation author is the primary author of this material.

Chapter 4, in full, is currently being prepared for submission for publication of material. Co-Authors include Garfein, Richard; Cuevas-Mota, Jazmine;

Strathdee, Steffanie; Ojeda, Victoria; Araneta, Happy; Lemus, Hector. The dissertation author is the primary author of this material.

VITA

EDUCATION

Doctor of Philosophy in Public Health (Epidemiology) (2015)
University of California, San Diego, Division of Family Medicine and Public Health/ San Diego State University, Graduate School of Public Health

Master of Public Health in Epidemiology (2011)
San Diego State University, Graduate School of Public Health

Master of Arts in Latin American Studies (2011)
San Diego State University, Center for Latin American Studies

Bachelor of Science Degree in Biology (2008)
Bachelor of Arts Degree in Psychology (2008)
University of California, San Diego

PROFESSIONAL POSITIONS

UC Presidents Diversity Dissertation Fellow
University of California, San Diego
September 2014-present

Division of Global Public Health, Department of Medicine, University of California, San Diego
August 2012-August 2014
Graduate Student Researcher IV

Division of Global Public Health, Department of Medicine, University of California, San Diego
August 2011-August 2012
NIDA T32 Trainee/ Research Assistant IV

Predictive Science Inc.
August 2011-August 2012
Data Analyst

California Department of Public Health, Early Warning Infectious Disease Surveillance Program
February 2011-December 2011
Project Assistant

California Department of Public Health-Office of Binational Border Health
August 2010-August 2011
Project Assistant

San Diego County Public Health Office, Immunization Branch
January 2009-May 2009
Student Intern

FELLOWSHIPS

2014	University of California President's Dissertation Year Diversity Fellowship ($22,000)
2014	Hispanic Centers of Excellence Fellowship ($1,300)
2012	Diversity Supplement, National Institute on Drug Abuse ($56,000)
2012	Hispanic Centers of Excellence Fellowship ($1,000)
2011-2012	T32 Pre-Doctoral Fellowship Training Grant, National Institute on Drug Abuse ($22,000)

COURSES TAUGHT AND ASSISTED

Fall 2014	**Guest Lecturer,** SDSU, PH 626: International Health, Survey Design and Data Management
Fall 2014	**Small Group Facilitator, UC San Diego School of Medicine,** Epidemiology, Biostatistics, and Medical Informatics for Medical Students
Fall 2013	**Guest Lecturer**, SDSU, Statistical Analysis Using SAS (Linear Regression)
Fall 2013	**Guest Lecturer**, SDSU, Statistical Analysis Using SPSS (Descriptive Statistics)
Sum. 2014	**Instructor,** UCSD COGS 14B: Introduction to Statistical Analysis
Spring 2014	**Teaching Assistant,** UCSD FPMU 101A-Epidemiology and Biostatistics
Winter 2014	**Teaching Assistant,** UCSD FPMU 101A-Epidemiology and Biostatistics
Fall 2013	**Teaching Assistant and Small Group Facilitator, UC San Diego School of Medicine,** Epidemiology, Biostatistics, and Medical Informatics for Medical Students
Fall 2013	**Teaching Assistant,** UCSD, FPMU 50-Public Health and Primary Care

Fall 2013 **Guest Lecturer**, SDSU, Statistical Analysis Using SAS (Data manipulation and descriptive data)

Fall 2013 **Guest Lecturer**, SDSU, Statistical Analysis Using SAS (t-tests, ANOVA, and linear regression)

Fall 2013 **Guest Lecturer**, SDSU, Statistical Analysis Using SAS (Logistic regression)

Spring 2013 **Co-Instructor,** SDSU, Statistical Analysis Using SAS

Fall 2012 **Teaching Assistant and Small Group Facilitator, UC San Diego School of Medicine,** Epidemiology, Biostatistics, and Medical Informatics for Medical Students

RESEARCH PUBLICATIONS

PEER-REVIEWED PUBLICATIONS

1. **Armenta RF,** Abramovitz D, Lozada R, Strathdee SA. Correlates of Perceived Risk of HIV among Injection Drug Users in Tijuana, Baja California, Mexico. In press. *Salud Publica*. April 2015.
2. **Armenta RF,** Araneta H, Kritz-Silverstein D, Wooten W, Barrett-Connor E. Effects of breastfeeding among parous post-menopausal women from three ethnic groups. In press. *Obesity.* 2014.
3. Roth AM, **Armenta RF,** Wagner KD, Roesch S, Bluthenthal R, Cuevas-Mota J, Garfein R. Patterns of drug use, risky behavior, and health status among persons who inject drugs in San Diego, California. In Press. Substance Use and Misuse. 2014
4. Collier MG, Bhaurla SK, Cuevas-Mota J, **Armenta RF**, Teshale RH, Garfein RS. Awareness of hepatitis C virus infection among persons who inject drugs. In Press. *American Journal of Public Health*, 2014
5. Wagner KD, **Armenta RF**, Roth AM**,** Maxwell JC, Cuevas-Mota J, Garfein RS. Use of synthetic cathinones and cannabimimetics among injection drug users in San Diego, California. *Drug and Alc Dep.* 2014; http://dx.doi.org/10.1016/j.drugalcdep.2014.05.007
6. Riley P, Ben-Nun M, **Armenta RF,** Linker J, Eick A, Sanchez J, George D, Bacon D, Riley S. Multiple estimates of the transmissibility for the 2009 influenza pandemic based on influenza-like-illness data from small US military populations. PLoS Comput Biol 9(5), 2013.

PUBLICATIONS CURRENTLY UNDER REVIEW

1. Bhaurla S, Collier M, **Armenta RF,** Cuevas-Mota J, Moran M, Teshale EH, Lindsay S, Garfein RS. Correlates of Prior Hepatitis C Antibody Testing

among Persons Who Inject Drugs, San Diego, CA. Submitted to American Journal of Public Health, July 2014.
2. **Armenta RF,** Laniado-Laborin R, Rodwell T, Cuevas-Mota J, Zonana A, Cerecer-Callu, P, Burgos J.L., Garfein RS. Care-Seeking Delay among Newly Diagnosed Tuberculosis Patients in Tijuana, Baja California, Mexico. Submitted to International Journal of TB and Lung Disease, August 2014.
3. Roth AM, **Armenta RF,** Wagner KD, Strathdee SA, Cuevas-Mota J, Garfein RS. Factors associated with injecting "cold cooked" heroin among a cohort of persons who inject drugs in San Diego, CA. Submitted to Substance Use and Misuse, September 2014.

PUBLICATIONS IN PROGRESS

1. **Armenta RF,** Collins KC, Cuevas-Mota J, Strathdee SA, Garfein RS. Prevalence and Correlates of LTBI among PWID in San Diego, CA. Will submit to *Journal of Infectious Disease*, November 2014.
2. Garfein RS, **Armenta RF,** Collins K. Prevalence and Correlates of HIV and HCV among PWID in San Diego, CA. Will submit to *Substance Abuse and Misuse*, December 2014.
3. Garfein RS, **Armenta RF,** Liu L, Strathdee SA. Drug tourism to Mexico among injection drug users from the United States. Will submit to *Drug and Alcohol Dependence*, December 2014.

RESEARCH PRESENTATIONS

1. Roth AM, **Armenta RF,** Wagner KD, Roesch SC, Bluthenthal RN, Garfein RS. Patterns of drug use, risky behavior, and health status among persons who inject drugs in San Diego, California. Oral Presentation at: 139th Annual Meeting of the American Public Health Association; November 2014; New Orleans, LA.
2. Muñoz FA, **Armenta RF,** Cuevas-Mota J, Wagner K, Garfein RS. Drug Treatment Services Utilization and Correlates among Persons Who Inject drugs (PWID) Living in a U.S. City Bordering Mexico. Poster presented at the NIDA Diversity Supplement Workshop, Bethesda, MD, on April 10-11, 2014
3. Muñoz FA, **Armenta RF,** Cuevas-Mota J, Wagner K, Garfein RS. Utilization of safe sources of sterile syringes among persons who inject drugs (PWID) in San Diego, CA. Submitted to Eighteen Annual United States Conference on AIDS (USCA) San Diego, CA, October 2-5, 2014
4. Garfein RS, **Armenta RF,** Wagner, KD, Cuevas-Mota, J, Munoz, FA, Strathdee, S. Drug tourism to Mexico among injection drug users from the United States. Poster presentation at the College of Problems on Drug Dependence, San Diego, CA. June, 2013
5. Wagner KD, Cuevas-Mota J, **Richard RF**, Strathdee SA, Garfein RS. Use of synthetic drugs among people who inject drugs in San Diego, CA. Oral Presentation at CPDD, on June 18, 2013.
6. **Armenta RF,** Araneta H, Kritz-Silverstein, D, Wooten, W, Barrett-Connor, E. Effects of breastfeeding among parous post-menopausal women from three

ethnic groups. Oral Presentation at Epidemiology Research Exchange, San Diego, California, May 2013.
7. Ferran K, **Armenta RF,** Marikos S, Iniguez-Stevens E. Animal Health Providers Network Database and Directory. Poster Presentation, BIDS Annual Conference. El Paso, Texas, June 2011.
8. **Armenta RF**, Abramovitz D, Lozada R, Lindsay S, Perez R, Lemus H, Strathdee S. Correlates of Perceived Risk of HIV among Injection Drug Users in Tijuana, Baja California, Mexico. Oral Presentation at Epidemiology Research Exchange, San Diego, California, April 2011.
9. Aldridge N, **Armenta RF**, Cuevas J, Burgos J, Garfein RS. Provider Knowledge, Attitudes, and Practices Regarding Drug Resistant Tuberculosis Care in Tijuana, Baja California, Mexico. Poster presentation at UCSD Division of Global Public Health, January 2011.
10. **Armenta RF**, Sotomayor S. Rocky Mountain Spotted Fever in San Quentin, Baja California, Mexico. Oral presentation at Student Research Symposium, San Diego State University, March 2010.

OTHER REPORTS AND PUBLICATIONS

1. Welton M, **Armenta RF,** Martinez A., LaFuente C., Fernandez A. Southern California Promotores (Community health workers) Needs Assessment, San Diego and Imperial Counties, 2010-2011. California Office of Binational border Health. 2011. http://www.cdph.ca.gov/programs/cobbh/Documents/Promotores%20Needs%20Assessment22712.pdf
2. Welton M, **Armenta RF,** Dumbauld J, Fernandez A. 2010 Health status in the California border region. California Office of Binational Border Health. http://www.cdph.ca.gov/programs/cobbh/Documents/COBBH%20%20Health%20Status%20in%20CA%20Border%20(02-27-12).pdf
3. **Armenta RF,** Welton M, Fernandez A. Overweight and obesity rates and trends in California border counties. Health Brief by the California Office of Binational border Health. Posted July, 2011. http://www.cdph.ca.gov/programs/cobbh/Documents/Obesity%201-page%20Brief%20SPNandENG%202011%20-%20Final.pdf
4. **Armenta RF,** Welton M, Fernandez A. Diabetes in California border communities. Health Brief by the California Office of Binational border Health. Posted July, 2011. http://www.cdph.ca.gov/programs/cobbh/Documents/Diabetes%201-page%20Brief%20SPNandENG%202011%20-Final.pdf

PROFESSIONAL ORGANIZATIONS

2012-Present	Society for Advancement of Hispanic/Chicanos and Native Americans in Science (SACNAS)
2011-Present	Delta Omega Sigma Chapter, Honorary Society of Public Health
2010-Present	American Public Health Association

AWARDS

Outstanding TA Award-UC San Diego Bachelors of Science in Public Health Program, 2013-2014 school year

SACNAS Travel Scholarship, 2014

Student Research Award- San Diego Epidemiology Research Exchange, 2013

ABSTRACT OF THE DISSERTATION

Research on the epidemiology of prefilled syringe use among persons who inject drugs in San Diego, CA

by

Richard Frank Armenta

Doctor of Philosophy in Public Health (Epidemiology)

University of California, San Diego, 2015

San Diego State University, 2015

Professor Richard S. Garfein, Chair

Background: Persons who inject drugs (PWID) are at increased risk of HIV and HCV infection through the use of blood contaminated syringes and paraphernalia. Obtaining illicit drugs in prefilled syringes might appeal to some PWID for convenience or necessity, yet this practice could lead to infections and drug overdose since syringe hygiene and drug concentrations cannot be known.

Objectives: This dissertation research sought to characterize prefilled syringe use, estimate their prevalence and incidence, and identify factors associated with their use. It also sought to elucidate practices and motivations behind prefilled syringe use among PWID in San Diego, California.

Methods: This dissertation is comprised of three studies assessing different aspects of prefilled syringe use among PWID enrolled in a longitudinal cohort study. Study one was a cross-sectional logistic regression analysis of baseline data from 574 PWID to determine the prevalence and correlates of ever using prefilled syringes. Study two was a qualitative study of 25 PWID, 10 of whom reported using prefilled syringes to describe contextual factors that influence their use. Study three included data from three study visits and used GEE to determine factors associated with prefilled syringe use in the last 6 months.

Results: For Study one, participants were predominately white (50.9%) males (73.9%) with a mean age of 43.4 years (range 18-80); 33.3% reported ever using prefilled syringes. PFSU was independently associated with ever having a rushed injection due to police presence, ever being in prison, injecting most often in public versus private places, ever overdosing on opioids, and injecting drugs in

Mexico. A number of themes emerged during the interviews conducted for study two, including: 1) unknown contents; 2) trust; 3) pressure to inject quickly; and 4) disease transmission risk. Study three found participants who reported PFSU in the last 6 months were more likely to report an overdose, sharing other injection paraphernalia, being homeless, and to report using the syringe exchange program, all in the last 6 months.

Conclusion: HIV, HCV, and overdose interventions should focus on factors that influence risky behaviors and be targeted towards individuals who face the greatest barriers to safe injection such as limited access to clean syringes and homelessness.

CHAPTER 1: INTRODUCTION

OVERVIEW

Persons who inject drugs (PWID) constitute one of the largest risk groups for Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV) infection. The risk of HIV and HCV transmission through receptive syringe sharing has been well documented,[1-5] and to a lesser extent, transmission may also occur through sharing other injection paraphernalia.[6-10] However, researchers and prevention specialists must stay alert to the possibility that new risk behaviors may emerge that require assessment and intervention to better describe risk factors of these diseases. Studies to date have also shed little light on longitudinal correlates of high risk behaviors and how they change over time.[11] It is important to understand barriers to safe injection over time because different contextual factors (e.g. environment, individual factors, social norms) may change and influence disease transmission.[12-15]

In the absence of a cure for HIV infection, and limited access to HCV treatment among PWID, interventions are needed to prevent the spread of disease in those highest at risk for infection. Research on the development of HIV prevention programs has focused on behavioral changes to reduce risky behaviors that are driving the epidemic. Among PWID those behaviors include sharing of syringes and other injection paraphernalia (i.e., cookers, cotton, water), and risky sexual behaviors such as unprotected sex and sex exchange, especially while under the influence. Research also calls for the development of

structural interventions that focus on factors that are exogenous to the individual that may influence their health such as policing practices, policies surrounding drug possession, access to clean syringes and injection paraphernalia, education, and social norms, among others. However, to create effective intervention programs, research is needed to understand the types of risky behaviors that are driving the epidemics. This includes vigilant surveillance about changing and emerging behaviors.

The use of prefilled syringes has been described as an emerging threat to HIV/HCV control among PWID in some cities,[12, 16-20] but is unknown how prevalent this practice is in San Diego, California. Prefilled syringes for this study are described as the distribution and use of illicit substances in syringes that have already been filled with drug solution for distribution and personal use, meaning, the drugs were prepared and put in a syringe prior to their use. Prefilled syringes pose a risk for disease transmission and overdose because their contents are unknown and the source of the syringes and preparation methods are unknown. Studies have shown that HIV and HCV can survive for up to 7 days[7, 21-27] and 11 days,[26, 28-30] respectively, in syringes or injection paraphernalia (including prefilled syringes) given the right conditions. Studies have also found that HIV can survive in drug solutions and that using pre-mixed drugs to fill syringes may pose an increased risk for infection.[31, 32] Given this information, there is potential that prefilled syringes can impact HIV and HCV transmission.

Reports from PWID in San Diego, which shares a border with Tijuana, Baja California, Mexico, not only indicates that PWID use prefilled syringes and purchased them in San Diego, but also that some venues in Tijuana sell drugs in prefilled syringes.[33] While research in Europe indicates the use of prefilled syringes may be influenced by individual (e.g. years injecting) and environmental (e.g. rushed injection due to police presence) factors,[34] there is a dearth of information about the contextual and individual factors contributing to the use of prefilled syringe use in the San Diego, CA and the US. Among PWID enrolled in the parents study, STAHR II, a longitudinal study of drug use, 33.5% of participants had ever used prefilled syringes; however, little is known about correlates of use of prefilled syringes and how their use might be associated with HIV and HCV risk.

This dissertation research elucidates the epidemiology of prefilled syringe use (i.e. injecting illicit drugs that were acquired in syringes that were filled prior to their distribution and use) by determining the prevalence and correlates of this practice and obtaining a better understanding of its influence on HIV, HCV, and overdose risk among persons who inject drugs (PWID) in San Diego, CA. Despite the wide availability of information about risk factors for HIV and HCV, and the numerous observational and intervention studies conducted to understand and curb the spread of disease, there is little information about novel drug distribution and injection practice information among PWID in San Diego, CA.

BACKGROUND

In 2009 there were an estimated 149-271 million persons who used illicit drugs worldwide, 11-22 million of whom injected drugs.[5, 35-37] There are four major classes of illicit drugs that include: Amphetamine-type stimulants (e.g. Synthetic sympathomimetic amines), Cannabis (e.g., marijuana, hashish), Cocaine (alkaloid derived from coca plant), and Opioids (Opium poppy, e.g., heroin, morphine). Globally, cannabis use is the highest with an estimated 2.8-4.5% of persons 15-64 years reporting their use [125-203 million people total]. In 2012, there was an estimated 23.9 million persons who reported illicit substance use in the US. Over 6.6 million (2.6% of the population) persons reported ever injecting drugs in the US. In 2011, there were an estimated 774,434 (range: 494,605-1,054, 263) PWID in the US.[38] In San Diego County, there are an estimated 21,000-28,000 PWID.[39]

One time use and/or occasional illicit substance use is not associated with measurable increases in morbidity or mortality; however, health risks increase as both the frequency and quantity as illicit substance use increases. Drug dependence or addiction is defined by the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) as being indicated by three or more of the following criteria in the last 12 months: Tolerance, withdrawal symptoms, continued use despite harm, loss of control, attempt to cut down, salience, and reduced involvement. Substance abuse is defined by the DSM-IV criteria as a maladaptive pattern of substance use that results in significant negative physical, social, interpersonal, or legal consequences. Substance abuse is distinct from

substance dependence in that the criterion does not require increased tolerance, the presence of withdrawal symptoms or the loss of control. In addition, addiction includes both physical dependence and cognitive loss of control.

Findings from a systematic review of available data documented injection drug use in 151 countries with prevalence data available in 61 countries. Greater than 40% of persons who inject drugs globally live in Russia, China, and the United States (US).[1, 37] There are various sequelae associated with drug use practices that include four broad types of adverse health outcomes: Adverse effects of chronic use include both blood-borne bacterial and viral infection (e.g. HIV, Hepatitis C, TB), and chronic diseases (e.g. cardiovascular disease and cirrhosis); Acute toxic effects (e.g., overdose); acute effects of intoxication (e.g., accidental injury, violence); and development of dependence.[37] Among PWID, many studies have indicated associations between injection and sexually related behaviors and adverse health outcomes, especially unintentional overdose and bloodborne virus infection (HIV and Hepatitis C). Many studies have found both individual (e.g., gender, race/ethnicity, age, homelessness) and environmental factors (e.g., local drug markets, syringe access, policing practices) influence drug use practices.[2, 40]

HIV/AIDS Epidemic

Human Immunodeficiency Virus (HIV) is an enveloped RNA retrovirus, classified as a lentivirus, which contains 9 genes and 15 proteins. HIV causes acquired immunodeficiency syndrome (AIDS). AIDS is defined when CD4 T-Cell

counts drop below 200/mm3. An HIV infection can go undetected for up to ten years before clinical symptoms occur, but the progression from HIV to AIDS is determined by many factors, including genetics. HIV is transmitted via three primary routes: sexual contact, contact with blood or vertical mother to child transmission. In developed nations, men who have sex with men and use injection drugs constitute the largest risk groups for infection. Worldwide, heterosexual transmission is the most significnat means of HIV transmission.

Global Overview

An estimated 35.0 [33.1-37.2] million people are living with Human Immunodeficiency Virus (HIV) worldwide with another 2.1 [1.9-2.4] million new infections in 2013[41]. Approximately 0.8% percent of the adult population is living with HIV and there were 1.5 [1.4-1.7] million AIDS-related deaths worldwide in 2013.[42, 43] Over 19 million of the 35 million HIV infected individuals are unaware of their infection.[43, 44] The majority of persons living with HIV/AIDS worldwide are living in low and middle-income countries. Sub-Saharan Africa alone accounts for 24.7 million of the HIV infections worldwide. The majority of HIV infections globally are transmitted through heterosexual sex, though men who have sex with men, injection drug users, and sex workers remain high risk populations.[44]

United States

In the United States more than 1.2 million people are infected with HIV; approximately 1 in 7 (14%) of whom are unaware of their infection.[45] The CDC estimates there are approximately 50,000 new HIV infections per year, with MSM

continuing to have the highest rates of infection.[46] The HIV epidemic is both geographically concentrated and focused in specific at-risk populations such as PWID and men who have sex with men (MSM). The prevalence of HIV is highest among the socially marginalized and disenfranchised population and remains low in the general population.[47] PWID accounted for 8% of new HIV infection and 15% of those living with HIV. Among women, 16% of new HIV infections were attributable to injection drug use, while 84% were attributable to heterosexual contact. Among men, MSM also accounts for 63% of all new HIV infections.[45]

San Diego

In San Diego County there were a total of 1819 individuals diagnosed with HIV between 2007 and 2009, an overall rate of 59.4 cases per 100,000 population.[48, 49] The primary mode of HIV transmission is MSM (75.6% of case), IDU (6.0%) and MSM/IDU (4.2%).[49] PWID also comprise 19.1% of cumulative AIDS cases in San Diego County.[50] The prevalence of HIV has been previously reported at 4% among PWID in San Diego County.[51]

Hepatitis C Virus (HCV)

Hepatitis C Virus (HCV), an RNA virus, is an infectious pathogen that causes liver inflammation and Hepatitis C in humans.[52, 53] It begins as an acute infection that often goes unnoticed due to its asymptomatic nature. In about 75-85% of cases, HCV remains in the body and becomes a chronic infection with a majority of infected individuals unaware of their disease status; the remaining 15-25% spontaneously clear the virus.[1, 54] Chronic HCV infection can lead to hepatic

fibrosis, cirrhosis, and complications of liver failure or hepatocellular carcinoma. HCV infection is also associated with an increase in extra-hepatic diseases such as circulatory disease, neuropsychiatric disorders, and renal disease. Evidence shows that treatment attenuates HCV related morbidity and all-cause mortality. Progression to advanced liver disease is slow and generally takes 10-20 years of asymptomatic infection.[55] HCV is primarily transmitted through contact with blood from a person who is infected with HCV and less commonly through sexual contact and sharing personal items such as toothbrushes. There is treatment available that can cure HCV and new advancements in medicine have developed treatment that have fewer side effects and shorter durations.[56-58]

Global Overview

Globally, an estimated 130-150 million persons have chronic Hepatitis C, which results in an estimated 350-500 thousand deaths yearly.[59, 60] In total, thirty-one countries accounted for 80% of HCV infections with Central and East Asia and North Africa accounting for the majority of infections.[59] In developed nations a majority of HCV transmission occurs among PWID and is related to the use of non-sterile syringes and injection paraphernalia used to inject drugs. [61] It is estimated that the global prevalence of HCV among PWID is >67% (more than 10 million infected PWID). Many PWID are infected young, and access to testing and treatment is low. HCV incidence remains high in many settings with annual estimated incidence ranging between 5-45% among PWID.[62]

United States

HCV infection is the most common chronic bloodborne infection in the US with more than 3.2 [2.7-3.9] million persons chronically infected. Every year there are an approximated 17,000 incident cases of HCV in the US, most of which occur in people who inject drugs (PWID).[52] HCV incidence also significantly increased among young PWID in the US between 2006-2012[63]. In the US, approximately 12,000 persons die annually as a result of HCV related liver disease. The prevalence of HCV infection ranges between 14-89% among PWID nationally.

San Diego County

In San Diego County there were 2,522 new cases of Hepatitis C, which marks a decline from the 4,368 cases that were reported in 2008; however, the County reports that most cases go undetected or unreported, and cases are expected to rise.[64] Previous studies indicated an HCV prevalence of 36% among PWID who were tested at an sexually transmitted infection (STI) Clinic, and 26.9% among 18-40 year PWID who participated in a cross-sectional study, STAHR I.[51] In our current research with PWID, STAHR II, the prevalence of HCV is 67% among PWID aged 18-80.

HIV/HCV and injection drug use

Persons who inject drugs (PWID) are at increased risk for hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infection. [1-5] [6-10, 65] Between 1.3%-1.9% of the U.S. population are infected with HCV,[66] with a much higher

prevalence among PWID. While considerable research has been conducted to understand HIV and HCV risk factors among PWID, ethnographic evidence suggests that injection practices are continuously evolving, and that novel risk practices may emerge and have new implications for health outcomes.[32, 67] When crack injection was first reported many researchers did not believe that PWID were using crack via this novel route of administration.[68] It was not until ethnographic observation and mixed methods research was conducted that the risk of injecting crack was recognized. Not only does the injection of crack pose a risk for excess HIV and HCV transmission, it also introduced the potential for fungal infections as PWID were using lemon juice to dissolve the drug for injection. This example highlights the importance of examining novel and changing behaviors that have been observed qualitatively.[33]

HIV/HCV and prefilled syringe use

The use of prefilled syringes may pose a threat for HIV and HCV infection, since it is more likely in these cases that the origin of the syringe is unknown and potential for cross-contamination is greater.[20, 69] Rhodes reports that a common drug container is often used to fill syringes and if the container becomes contaminated, then all subsequent syringes filled may become contaminated.[20] The impact of syringe exchange programs on reducing HIV and HCV prevalence may also be reduced if the drug solution itself is contaminated with HIV or HCV.[9] Laboratory data suggest that HIV and HCV can remain infectious in drug solution and in contaminated syringes for between 7 and 11 days, respectively,[26, 28-30]

suggesting that this practice may pose a significant health risk. With the use of prefilled syringes the survivability of HIV and HCV depends on the acidity of the solution and the time between preparation and distribution of drugs.[25] While the use of prefilled syringes has been reported in Russia and Eastern Europe,[14] and has been cited as a reason for the rapid spread of HIV in Eastern Europe,[70] there is a dearth of information in the literature about their use in the United States. The use of prefilled syringes in the US may differ by the type of drug distributed and availability, among other things. Rhodes et al. found that drug users are skeptical of prefilled syringes citing concerns that the drugs might be diluted and potential HIV contamination.[12] Despite these concerns, there are still reports of their use.

The sharing of syringes, injection paraphernalia, and prefilled syringes go hand in hand and constitute risk behaviors for HIV transmission. Research on the distribution of drugs found that drugs distributed in liquid form, such as in prefilled syringes constitutes higher risk drug distribution, potentially due to the link between liquid drugs and sharing syringes and injection paraphernalia.[71] Though few studies have found a direct link between prefilled syringe use and BBV infection,[13, 18] because most PWID participate in many high risk behaviors the association between prefilled syringes and HIV may be overshadowed by other risk behaviors such as sharing injection paraphernalia and syringes.[31] This is especially important because PWID who use prefilled syringes are more likely to engage in receptive syringe sharing and sharing of injection paraphernalia.

Others have found that when prefilled syringes are used the contents are often shared via syringe mediated sharing (frontloading/backloading).[31]
Research in Russia and the Ukraine on prefilled syringe found that prefilled syringe use in the last 30 days was reported by between 6% and 55% of PWID.[17, 72-74] In a study by Taran et al. they found that few PWID reported receptive syringe sharing and that more PWID reported prefilled syringe use and using drugs from a common drug container.[75] Although they found that PWID who share injection paraphernalia, but not those who use prefilled syringes, were at higher risk for HIV infection, they noted that prefilled syringes may become contaminated through backloading/frontloading and increase risk for transmission.[75] Further, some PWID may be reporting prefilled syringe use as sharing syringe or injection paraphernalia because they also engage in many risk behaviors.

In the US, the use of prefilled syringes has been documented among PWID who inject ketamine (a dissociative hallucinogen commonly used as an anesthetic in veterinary practice but also used illicitly).[76] The use of prefilled syringes may be associated with properties of the drug (e.g., liquid or powdered form) and recent initiates' unfamiliarity with injection practices. Younger and less experienced drug users have also reported the use of prefilled syringes.[12, 16, 17, 34] PWID engage in many high risk behaviors that increase their likelihood of BBV infection making it difficult to pinpoint one behavior that leads to increased transmission. It is important to remain diligent in monitoring trends in high risk

behaviors to determine how they influence disease transmission. In other setting researchers have uncovered novel and potentially risky injection behaviors.[77, 78]

Novel trends among persons who inject drugs

Despite our understanding of the various injection related risk factors for HIV and HCV, there is a need to continually monitor emerging trends. Ethnographic research has uncovered important factors that increase disease transmission. Michael Clatts concluded that: Transmission associated with the ways that illegal drugs such as heroin are prepared, distributed, and self-administered have been shown to have emerged as adaptive responses to opportunities and constraints in the local physical and social environments.[77]

Studying novel and emerging trends is important because atypical injection practices and drug distribution methods might affect the spread of disease. The importance of using both quantitative and qualitative research has been demonstrated in the literature by uncovering emerging trends that have greatly affected the rates of HIV and HCV transmission.[67, 79, 80] While there have been significant strides in the prevention of HCV and HIV, constant vigilance for emerging risk behaviors is needed to help curb the epidemics and to better understand risk factors for disease.

Several injection practices have been identified that may be more region/culture or drug specific, and may confer risk for bloodborne pathogens through cross contamination, even in the presence of expanded syringe access. Exposure to bloodborne pathogens occurs at various steps of the drug

preparation and injection process. “Indirect Sharing,” or sharing that does involve directly sharing syringes, behaviors, such as the sharing of injection paraphernalia (e.g., cookers, cotton, rinse water) and the dividing of drugs while prepping, have been previously described.[81] These processes often involve sharing the contents of the syringes rather than the syringe itself. Backloading, or removing the plunger from the receiving syringe and squirting drugs from another syringe into its barrel, and frontloading, or removing the needle from one syringe and using the needle from another syringe to squirt the drug solution drugs into the hub, can increase disease transmission because the receiving syringe, even if sterile, can become contaminated if the donor syringe is not sterile.[82-85]

Another novel behavior described by Clatts et al. is an injection practice known as “Cay ma” translated as “injection sac,” a process where a hypodermic needle is repeatedly inserted into the skin creating a hardened sac area and forming fibrocytes and fibroblasts. Once this site is formed users insert their needle through the sac into the vein. This process decreases the amount of bleeding and increases the chances the substance will be injected into the vein.[64] This practice appears to have emerged as a result of policies, such as policing practices, that heighten the need for rapid and higher risk injection practices in Vietnam[77].

McCurdy et al. have also described the practice of ‘flashblood’, a process by which blood is drawn back into a syringe immediately after injection and passed on to an injection partner to use.[78] The idea is that the blood will contain enough heroin for the user to avoid withdrawal symptoms. This practice emerged

as a result of the increased cost of heroin and heightened policing activities. Flashblood has been reported in East Africa in places such as Tanzania and Zanzibar.[78, 86-88]

Further, research on the initiation of ketamine injection introduced new risks for bloodborne pathogen infection. Ketamine is a club drug that emerged during the 1980s, but was originally developed legally as an anesthetic surgical use. Ketamine can be purchased in liquid or powder form, both of which can be injected. In liquid form, ketamine is sold in pharmaceutical vials that are pierced by hypodermic needles to fill syringes. Indirect sharing through the use of multi-dose vials can increase HIV and HCV risk if the solution becomes contaminated by a non-sterile syringe.

RISK ENVIRONMENT

A majority of research on HIV related risk behaviors focuses on individual behaviors, but fails to recognize or measure the structural environment in which those behaviors emerge, coined as the HIV 'Risk Environment' by Tim Rhodes.[69] A recent ecological study grounded in power based theory, which posits that an individuals' power is based on their ability to meet their own survival needs, found between nations, structural differences could explain differences in HIV prevalence throughout the world[89]. The authors measured five predictors in countries throughout the world, which included: knowledge, material resources, wholeness, legitimacy, and sexuality. The indices measure the amount of power individuals' have and the authors posit that "the more readily available these

social-structural sources of power are, the less we would expect people to engage in HIV-risk behavior."[89] The authors found that the five predictors accounted for 43% of the variance in HIV infection and that homicide rates and women's social rights were associated with HIV infection. Further, nations that had lower homicide rates and more protection for women have lower HIV prevalence. The findings underscore the need to focus on social-structural factors that influence risk behaviors.[89]

The HIV risk environment is comprised of all things that are outside of the locus of control of the individual but that may influence individual behaviors. This mainly focuses on how physical, economic, social, and political factors exogenous to the individual interact to increase risk of HIV transmission. These factors interact at both the micro and macro-environmental level to influence risk behaviors among PWID. Macroenvironmental factors include larger environmental influences that indirectly influence behaviors such as drug trafficking patterns (physical), gender inequalities (social), criminal justice expenditure (economic), and policies and laws for harm-reduction programs (political). Microenvironmental factors include influences that more directly influence injection behaviors such as homelessness or injection location (physical), relationship dynamics and sexual orientation (social), cost of injection equipment and protective measures (economic), and availability of harm reduction programs such as syringe exchange programs and drug treatment (political).[2]

The HIV risk environment is a product of the interplay between the continual interaction of endogenous and exogenous factors that have synergistic effects to create HIV risk.[2] Research that focuses on the HIV risk environment has found that micro and macro environmental factors and the interplay between them, greatly influence HIV risk behaviors. These factors include trade and population movement, neighborhood disadvantage and transition, injection locations, criminal justice systems, social norms and networks, social capitol, social suffering and socio-political economy, law enforcement and policing, and armed conflict and complex emergencies.

Policing and HIV risk

A growing body of evidence demonstrates that laws that affect drug and injection paraphernalia access and use, and policing practices influence HIV risk among PWID. Macroenvironmental factors, such as drug and paraphernalia possession laws, and microenvironmental factors, such as policing practices, directly influence PWID behaviors by affecting how they access drugs and reduce their ability to practice harm reduction strategies.[90] For example, police confiscation of syringes and injection equipment from PWID particularly limits their ability to practice harm reduction because it reduces their access to sterile syringes and injection equipment.[91]

Studies have found that fear of getting caught with injection equipment forces PWID to rush injection so they inject in public places, use shooting galleries, and participate in other high risk behaviors such as sharing syringes or

injection paraphernalia.[90] In Russia, laws also influence harm reduction by limiting the availability of syringe exchange programs, drug possession, and opioid agonist therapy.[92] Other studies in the US and Mexico have found that policing practices are also associated with syringe sharing[93, 94] and increased mortality from overdoses.[95, 96] Among other high-risk populations, such as female sex workers (FSW), policing practices also influence their ability to practice harm reduction. FSWs report confiscation of condoms[97] and syringes[91] and that police use condoms as a proof of sex work.[97, 98]

In Odessa, Ukraine, HIV positive PWID were also more likely to report negative interactions with the police such as confiscation of prefilled syringes, rushed injection due to fear of police, avoiding arrest by paying police, and being threatened by police.[92] Most importantly, another study found that those who were most likely to have negative experiences with the police also faced other microenvironmetal factors such as homelessness and macroenvironmetal factors such as perceived changes in the drug market.[99, 100] Further, those who accessed the syringe exchange program were more likely to report policing related harms, suggesting that police may target those who use the syringe exchange.[90, 99, 101, 102] This practice could indirectly influence HIV and HCV transmission by limiting PWID access to sterile injection equipment.

STUDY SETTING

The proposed research will be conducted in San Diego, CA, located in the California/ Baja California border region. The San Diego/Tijuana border region

has the busiest land border crossing in the world with a reported 43.7 million northbound crossings in 2008, including more than 42,000 Tijuana residents crossing daily into San Diego for work.[103] Because of its location, San Diego offers a unique setting to study drug abuse and because of the high rate of border crossing between Tijuana and San Diego, there is potential for trends and disease to spread across the border. The parent study, STAHR II, is assessing the impact of cross border drug use and the 2009 change in Mexican law that decriminalized possession of small amount of drugs for personal use. The prevalence of HIV infection among PWID is similar in Tijuana and San Diego (approximately 5%-10% in both cities), but the prevalence of HCV is much higher is Tijuana (96% compared to 27%), suggesting the potential for cross-border epidemic spread.[51, 104] There have been reports of the use of prefilled syringes in Tijuana and their availability at popular bars and clubs.[76] This research offers timely data about how drug use trends and availability of drugs may be different on both sides of the border, and how those differing trends may aid in the spread of disease by determining where participants are purchasing and using prefilled syringes (San Diego vs. Tijuana). Given the need to understand factors associated with HIV and HCV transmission and that they are still a significant problem in PWID, our findings in this dissertation will have significant implications for public health by highlighting potentially important risk factors and may be useful in developing intervention programs to prevent the spread of HIV and HCV.

CONCEPTUAL FRAMEWORK

The proposed research is based on a conceptual model of the contextual determinants of risk behaviors among injection drug users proposed by Galea, et

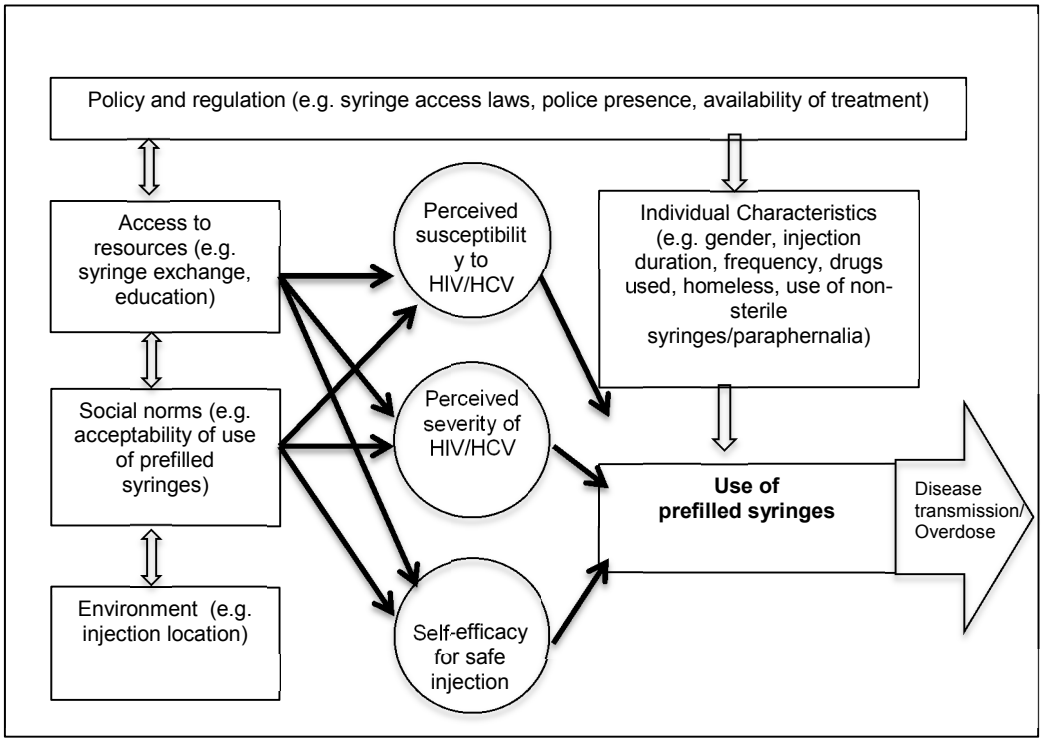

Figure 1.1: Conceptual Framework

al. (2003)[105] and on the Rhodes Risk Environment Framework.[69] Based on these models there are several determinants of drug use behaviors and HIV/HCV risk that are influenced by the interplay between policy, regulation, social and environmental factors, contextual factors and individual level factors that may influence the use of prefilled syringes. Policy and regulation such as the availability of syringes, policing practices and available drug treatment services may influence the environment (e.g. injection locations, housing status), social norms (e.g. acceptability of the use of prefilled syringes, injection partners), and

access to resources (e.g. availability of syringes and injection paraphernalia, education, health care). These factors all influence both individual characteristics and risk behaviors and may lead to the transmission of HIV and HCV. This conceptual framework will be used to describe the relationships between contextual and individual factors that influence risk behaviors and the use of prefilled syringes and how the use incidence and predictors of the use of prefilled syringes change over time. Constructs from the health belief model (HBM) will be used to determine how perceived susceptibility to HIV and HCV infection, severity of the diseases and self-efficacy to practice safe injection practices influence the use of prefilled syringes. Research has shown that if PWID don't perceive disease risk, or feel that they have the power to engage in safe practices, then they are not likely to take measures to prevent disease transmission.[106-109] These models were also be used to help guide the qualitative interviews to develop a better understanding of the use of prefilled syringes.

REFERENCES

1. Nelson, P.K., et al., *Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews.* Lancet, 2011. **378**(9791): p. 571-83.

2. Strathdee, S.A., et al., *HIV and risk environment for injecting drug users: the past, present, and future.* Lancet, 2010. **376**(9737): p. 268-84.

3. Strathdee, S.A., et al., *Individual, social, and environmental influences associated with HIV infection among injection drug users in Tijuana, Mexico.* Jaids-Journal of Acquired Immune Deficiency Syndromes, 2008. **47**(3): p. 369-376.

4. Hammett, T.M., et al., *Correlates of HIV status among injection drug users in a border region of southern China and northern Vietnam.* J Acquir Immune Defic Syndr, 2005. **38**(2): p. 228-35.

5. Mathers, B.M., et al., *Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review.* Lancet, 2008. **372**(9651): p. 1733-45.

6. Needle, R.H., et al., *HIV risk behaviors associated with the injection process: multiperson use of drug injection equipment and paraphernalia in injection drug user networks.* Subst Use Misuse, 1998. **33**(12): p. 2403-23.

7. Page, J.B., et al., *Detection of HIV-1 in injection paraphernalia: risk in an era of heightened awareness.* AIDS Patient Care STDS, 2006. **20**(8): p. 576-85.

8. Thiede, H., et al., *Prevalence and correlates of indirect sharing practices among young adult injection drug users in five U.S. cities.* Drug Alcohol Depend, 2007. **91 Suppl 1**: p. S39-47.

9. Wodak, A. and A. Cooney, *Do needle syringe programs reduce HIV infection among injecting drug users: a comprehensive review of the international evidence.* Subst Use Misuse, 2006. **41**(6-7): p. 777-813.

10. Yang, C., K. Tobin, and C. Latkin, *Perceived serosorting of injection paraphernalia sharing networks among injection drug users in Baltimore, MD.* AIDS Behav, 2011. **15**(1): p. 16-21.

11. Green, T.C., et al., *Prevalence and predictors of transitions to and away from syringe exchange use over time in 3 US cities with varied syringe dispensing policies.* Drug Alcohol Depend, 2010. **111**(1-2): p. 74-81.

12. Rhodes, T., et al., *Situational factors influencing drug injecting, risk reduction and syringe exchange in Togliatti City, Russian Federation: a qualitative study of micro risk environment.* Soc Sci Med, 2003. **57**(1): p. 39-54.

13. Rhodes, T. and M. Simic, *Transition and the HIV risk environment.* BMJ, 2005. **331**(7510): p. 220-3.

14. Rhodes, T., et al., *The social structural production of HIV risk among injecting drug users.* Soc Sci Med, 2005. **61**(5): p. 1026-44.

15. Rhodes, T. and C. Treloar, *The social production of hepatitis C risk among injecting drug users: a qualitative synthesis.* Addiction, 2008. **103**(10): p. 1593-603.

16. Booth, R.E., et al., *Drug injectors and dealers in Odessa, Ukraine.* J Psychoactive Drugs, 2003. **35**(4): p. 419-26.

17. Booth, R.E., et al., *Predictors of self-reported HIV infection among drug injectors in Ukraine.* J Acquir Immune Defic Syndr, 2004. **35**(1): p. 82-8.

18. Rhodes, T., et al., *HIV infection associated with drug injecting in the newly independent states, eastern Europe: the social and economic context of epidemics.* Addiction, 1999. **94**(9): p. 1323-36.

19. Rhodes, T., et al., *Explosive spread and high prevalence of HIV infection among injecting drug users in Togliatti City, Russia.* AIDS, 2002. **16**(13): p. F25-31.

20. Rhodes, T., et al., *Prevalence of HIV, hepatitis C and syphilis among injecting drug users in Russia: a multi-city study.* Addiction, 2006. **101**(2): p. 252-66.

21. Abdala, N., et al., *Survival of human immunodeficiency virus type 1 after rinsing injection syringes with different cleaning solutions.* Subst Use Misuse, 2004. **39**(4): p. 581-600.

22. Abdala, N., et al., *Can HIV-1-contaminated syringes be disinfected? Implications for transmission among injection drug users.* J Acquir Immune Defic Syndr, 2001. **28**(5): p. 487-94.

23. Abdala, N., et al., *Survival of HIV-1 in syringes: effects of temperature during storage.* Subst Use Misuse, 2000. **35**(10): p. 1369-83.

24. Heimer, R. and N. Abdala, *Viability of HIV-1 in syringes: implications for interventions among injection drug users.* AIDS Read, 2000. **10**(7): p. 410-7.

25. Heimer, R., et al., *The effect of acids on the survival of HIV during drug injection.* J Acquir Immune Defic Syndr, 2007. **45**(2): p. 144-50.

26. Zule, W.A. and G. Bobashev, *High dead-space syringes and the risk of HIV and HCV infection among injecting drug users.* Drug Alcohol Depend, 2009. **100**(3): p. 204-13.

27. Zule, W.A., D.P. Desmond, and J.A. Neff, *Syringe type and drug injector risk for HIV infection: a case study in Texas.* Soc Sci Med, 2002. **55**(7): p. 1103-13.

28. Doerrbecker, J., et al., *Transmission of hepatitis C virus among people who inject drugs: viral stability and association with drug preparation equipment.* J Infect Dis, 2013. **207**(2): p. 281-7.

29. Doerrbecker, J., et al., *Inactivation and survival of hepatitis C virus on inanimate surfaces.* J Infect Dis, 2011. **204**(12): p. 1830-8.

30. Paintsil, E., et al., *Survival of hepatitis C virus in syringes: implication for transmission among injection drug users.* J Infect Dis, 2010. **202**(7): p. 984-90.

31. Gyarmathy, V.A., et al., *Liquid drugs and high dead space syringes may keep HIV and HCV prevalence high - a comparison of Hungary and Lithuania.* Eur Addict Res, 2010. **16**(4): p. 220-8.

32. Platt, L., et al., *Measuring risk of HIV and HCV among injecting drug users in the Russian Federation.* Eur J Public Health, 2009. **19**(4): p. 428-33.

33. Wagner, K.D., et al., *The social and environmental context of cross-border drug use in Mexico: findings from a mixed methods study of young injection drug users living in San Diego, CA.* J Ethn Subst Abuse, 2012. **11**(4): p. 362-78.

34. Burrows, D., et al., *Responding to HIV infection associated with drug injecting in Eastern Europe.* Drug Alcohol Rev, 1998. **17**(4): p. 453-63.

35. Degenhardt, L. and W. Hall, *Extent of illicit drug use and dependence, and their contribution to the global burden of disease.* The Lancet, 2012. **379**(9810): p. 55-70.

36. Degenhardt, L., et al., *What data are available on the extent of illicit drug use and dependence globally? Results of four systematic reviews.* Drug Alcohol Depend, 2011. **117**(2-3): p. 85-101.

37. United Nations Office on Drugs and Crime, *World Drug Report 2014*. 2014: http://www.unodc.org/documents/wdr2014/World_Drug_Report_2014_web.pdf.

38. Lansky, A., et al., *Estimating the number of persons who inject drugs in the united states by meta-analysis to calculate national rates of HIV and hepatitis C virus infections.* PLoS One, 2014. **9**(5): p. e97596.

39. City of San Diego. *Clean Syringe Exchange Pilot Program*. [cited 2015 March 6]; Available from:

http://www.sandiego.gov/communityservices/programs/cleansyringe/index.shtml - facts.

40. Strathdee, S.A., L. Beletsky, and T. Kerr, *HIV, drugs and the legal environment.* Int J Drug Policy, 2015. **26 Suppl 1**: p. S27-32.

41. World Health Organization. *HIV/AIDS Data and Statistics*. 2015; Available from: http://www.who.int/hiv/data/en/.

42. Mathers, B.M., et al., *Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review.* The Lancet, 2008. **372**(9651): p. 1733-1745.

43. World Health Organization, *Global Update on the Health Sector response to HIV, 2014*, in *HIV Reporting*. 2014: http://apps.who.int/iris/bitstream/10665/128494/1/9789241507585_eng.pdf?ua=1.

44. Joint United Nations Programme on HIV/AIDS (UNAIDS), *Global AIDS response progress reporting 2015*. 2015: http://www.unaids.org/sites/default/files/media_asset/JC2702_GARPR2015guidelines_en.pdf.

45. Centers for Disease Control and Prevention, *Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas—2012*. 2014: http://www.cdc.gov/hiv/pdf/surveillance_Report_vol_19_no_3.pdf.

46. Centers for Disease Control and Prevention, *Estimated HIV incidence in the United States, 2007–2010*, in *HIV Surveillance Supplemental Report*. 2012.

47. El-Sadr, W.M., K.H. Mayer, and S.L. Hodder, *AIDS in America--forgotten but not gone.* N Engl J Med, 2010. **362**(11): p. 967-70.

48. County of San Diego Health and Human Services Agency, *HIV in San Diego County, 2007-2011*. 2013: http://www.sandiegocounty.gov/content/dam/sdc/hhsa/programs/phs/documents/HAEU_HIV_SDC_2007_2011.pdf.

49. County of San Diego Health and Human Services Agency, *HIV/AIDS Epidemiology Report*. 2012: http://www.sandiegocounty.gov/content/dam/sdc/hhsa/programs/phs/documents/HAEU_BiAnnual_Report_2012_final.pdf.

50. County of San Diego Health and Human Services Agency, *AIDS in Injecting Drug Users, San Diego County, 2013*. 2013: http://www.sandiegocounty.gov/content/dam/sdc/hhsa/programs/phs/Epidemiology/IDU2013_Final.pdf.

51. Garfein, R.S., et al., *HCV infection prevalence lower than expected among 18-40-year-old injection drug users in San Diego, CA.* J Urban Health, 2013. **90**(3): p. 516-28.

52. Centers for Disease Control and Prevention. *Hepatitis C Information for the Public*. February 10, 2014 [cited 2014 February 25]; Available from: http://www.cdc.gov/hepatitis/c/cFAQ.htm - statistics.

53. in *Hepatitis C Viruses: Genomes and Molecular Biology*, S.L. Tan, Editor. 2006: Norfolk (UK).

54. *<WHO | Hepatitis C.pdf>.*

55. Suzuki, T., et al., *Hepatitis C viral life cycle.* Adv Drug Deliv Rev, 2007. **59**(12): p. 1200-12.

56. North, C.S., et al., *Hepatitis C treatment and SVR: the gap between clinical trials and real-world treatment aspirations.* Gen Hosp Psychiatry, 2013. **35**(2): p. 122-8.

57. Grebely, J. and G.J. Dore, *Can hepatitis C virus infection be eradicated in people who inject drugs?* Antiviral Res, 2014. **104C**: p. 62-72.

58. Gilead. *U.S. Food and Drug Administration Approves Gilead's Sovaldi™ (Sofosbuvir) for the Treatment of Chronic Hepatitis C*. 2013 [cited 2014 February 25]; Available from: http://www.gilead.com/news/press-releases/2013/12/us-food-and-drug-administration-approves-gileads-sovaldi-sofosbuvir-for-the-treatment-of-chronic-hepatitis-c.

59. Gower, E., et al., *Global epidemiology and genotype distribution of the hepatitis C virus infection.* J Hepatol, 2014. **61**(1 Suppl): p. S45-57.

60. Mohd Hanafiah, K., et al., *Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence.* Hepatology, 2013. **57**(4): p. 1333-42.

61. Edlin, B.R.C., Michael R. , *Injection Drug Users: The Overlooked Core of the Hepatitis C Epidemic.* Clin Infect Dis, 2006. **42**(5): p. 673-676.

62. Hagan, H., E.R. Pouget, and D.C. Des Jarlais, *A systematic review and meta-analysis of interventions to prevent hepatitis C virus infection in people who inject drugs.* J Infect Dis, 2011. **204**(1): p. 74-83.

63. Suryaprasad, A.G., et al., *Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006-2012.* Clin Infect Dis, 2014. **59**(10): p. 1411-9.

64. *County of San Diego Monthly STD Report*, County of San Diego Health and Human Services Agency, Editor. 2013: http://www.sandiegocounty.gov/content/dam/sdc/hhsa/programs/phs/documents/STDMonthlyReport_Issue_53.pdf.

65. Des Jarlais, D.C., S.R. Friedman, and R.L. Stoneburner, *HIV infection and intravenous drug use: critical issues in transmission dynamics, infection outcomes, and prevention.* Rev Infect Dis, 1988. **10**(1): p. 151-8.

66. CDC Division of Viral Hepatitis - Statistics and Surveillance. *Disease Burden from Viral Hepatitis A, B, and C in the United States 2007*. Available from: http://www.cdc.gov/hepatitis/HCV/StatisticsHCV.htm.

67. Clatts, M.C., et al., *An ethno-epidemiological model for the study of trends in illicit drug use: reflections on the 'emergence' of crack injection.* International Journal of Drug Policy, 2002. **13**(4): p. 285 - 295.

68. Lankenau, S.E., et al., *Crack Cocaine Injection Practices and HIV Risk: Findings From New York and Bridgeport.* J Drug Issues, 2004. **34**(2): p. 319-332.

69. Rhodes, T., *The 'risk environment': a framework for understanding and reducing drug-related harm.* International Journal of Drug Policy, 2002. **13**(2): p. 85 - 94.

70. Dehne, K.L., *The emerging AIDS crisis in Russia: review of enabling factors and prevention needs.* Int J STD AIDS, 2001. **12**(4): p. 277-8.

71. Hartnoll, R., A. Gyarmathy, and T. Zabransky, *Variations in problem drug use patterns and their implications for harm reduction.* MONOGRAPHS, 2010: p. 405.

72. Adelekan, M.L. and R.A. Lawal, *Drug use and HIV infection in Nigeria: a review of recent findings.* African Journal of Drug & Alcohol Studies, 2006. **5**(2): p. 119-129.

73. Lau, J.T.F., et al., *Changes in the prevalence of HIV-related behaviors and perceptions among 1832 injecting drug users in Sichuan, China.* Sexually transmitted diseases, 2008. **35**(4): p. 325-335.

74. Rhodes, T., et al., *Injecting equipment sharing among injecting drug users in Togliatti City, Russian Federation: maximizing the protective effects of syringe distribution.* JAIDS Journal of Acquired Immune Deficiency Syndromes, 2004. **35**(3): p. 293-300.

75. Taran, Y.S., et al., *Correlates of HIV risk among injecting drug users in sixteen Ukrainian cities.* AIDS Behav, 2011. **15**(1): p. 65-74.

76. Wagner, K.D., et al., *Control over drug acquisition, preparation and injection: Implications for HIV and HCV risk among young female injection drug users.* ISRN Addict, 2013. **2013**.

77. Clatts, M.C., et al., *Novel heroin injection practices: implications for transmission of HIV and other bloodborne pathogens.* Am J Prev Med, 2007. **32**(6 Suppl): p. S226-33.

78. McCurdy, S.A., et al., *A theme issue by, for, and about Africa: new injecting practice increases HIV risk among drug users in Tanzania.* BMJ, 2005. **331**(7519): p. 778.

79. Agar, M., *Recasting the "ethno" in "epidemiology".* Med Anthropol, 1996. **16**(4): p. 391-403.

80. Samuels, J.F., et al., *Measurement of HIV risk behaviors among intravenous drug users.* Br J Addict, 1992. **87**(3): p. 417-28.

81. Koester, S.K. and L. Hoffer, *" Indirect Sharing": Additional HIV Risks Associated with Drug Injection.* AIDS and Public Policy Journal, 1994. **9**: p. 100-100.

82. Grund, J.P., et al., *The limitations of the concept of needle sharing: the practice of frontloading.* AIDS, 1990. **4**(8): p. 819-21.

83. Grund, J.P., et al., *Drug sharing and HIV transmission risks: the practice of frontloading in the Dutch injecting drug user population.* J Psychoactive Drugs, 1991. **23**(1): p. 1-10.

84. Jose, B., et al., *Syringe-mediated drug-sharing (backloading): a new risk factor for HIV among injecting drug users.* AIDS, 1993. **7**(12): p. 1653-60.

85. Grund, J.P.C. and C.D. Kaplan, *HIV-transmissie in het dagelijks ritueel van intraveneuze druggebruikers.* Nederlands Tijdschr. Geneesk, 1989. **133**: p. 899.

86. McCurdy, S.A., et al., *Flashblood: blood sharing among female injecting drug users in Tanzania.* Addiction, 2010. **105**(6): p. 1062-70.

87. McCurdy, S., et al., *Harm reduction in Tanzania: an urgent need for multisectoral intervention.* Int J Drug Policy, 2007. **18**(3): p. 155-9.

88. Dahoma, M.J.U., et al., *HIV and substance abuse: the dual epidemics challenging Zanzibar.* African Journal of Drug and Alcohol Studies, 2006. **5**(2): p. 129-38.

89. Tan, J.Y., et al., *Social-structural indices and between-nation differences in HIV prevalence.* Int J STD AIDS, 2015. **26**(1): p. 48-54.

90. Beletsky, L., et al., *Syringe access, syringe sharing, and police encounters among people who inject drugs in New York City: a community-level perspective.* Int J Drug Policy, 2014. **25**(1): p. 105-11.

91. Beletsky, L., et al., *Syringe confiscation as an HIV risk factor: the public health implications of arbitrary policing in Tijuana and Ciudad Juarez, Mexico.* J Urban Health, 2013. **90**(2): p. 284-98.

92. Booth, R.E., et al., *Law enforcement practices associated with HIV infection among injection drug users in Odessa, Ukraine.* AIDS Behav, 2013. **17**(8): p. 2604-14.

93. Pollini, R.A., et al., *Syringe possession arrests are associated with receptive syringe sharing in two Mexico-US border cities.* Addiction, 2008. **103**(1): p. 101-8.

94. Wagner, K.D., R. Simon-Freeman, and R.N. Bluthenthal, *The association between law enforcement encounters and syringe sharing among IDUs on skid row: a mixed methods analysis.* AIDS Behav, 2013. **17**(8): p. 2637-43.

95. Bohnert, A.S., et al., *Policing and risk of overdose mortality in urban neighborhoods.* Drug Alcohol Depend, 2011. **113**(1): p. 62-8.

96. Lunze, K., et al., *Punitive policing and associated substance use risks among HIV-positive people in Russia who inject drugs.* J Int AIDS Soc, 2014. **17**: p. 19043.

97. Pauw, I. and L. Brener, *'You are just whores—you can't be raped': barriers to safer sex practices among women street sex workers in Cape Town.* Culture, health & sexuality, 2003. **5**(6): p. 465-481.

98. Shannon, K., et al., *Survival sex work involvement as a primary risk factor for hepatitis C virus acquisition in drug-using youths in a canadian setting.* Arch Pediatr Adolesc Med, 2010. **164**(1): p. 61-5.

99. Volkmann, T., et al., *Factors associated with drug-related harms related to policing in Tijuana, Mexico.* Harm Reduct J, 2011. **8**(1): p. 7.

100. Werb, D., et al., *Effects of police confiscation of illicit drugs and syringes among injection drug users in Vancouver.* Int J Drug Policy, 2008. **19**(4): p. 332-8.

101. Davis, C.S., et al., *Effects of an intensive street-level police intervention on syringe exchange program use in Philadelphia, PA.* Am J Public Health, 2005. **95**(2): p. 233-6.

102. Cooper, H.L., et al., *Drug-related arrest rates and spatial access to syringe exchange programs in New York City health districts: combined effects on the risk of injection-related infections among injectors.* Health Place, 2012. **18**(2): p. 218-28.

103. SANDAG. *San Diego Region - Baja California Ports of Entry Border Crossing Statistics. 2009*. 2009 [cited 2013 December 10].

104. Iñiguez-Stevens, E., et al., *[Estimating the 2006 prevalence of HIV by gender and risk groups in Tijuana, Mexico].* Gac Med Mex, 2009. **145**(3): p. 189-95.

105. Galea, S., J. Ahern, and D. Vlahov, *Contextual determinants of drug use risk behavior: a theoretic framework.* J Urban Health, 2003. **80**(4 Suppl 3): p. iii50-8.

106. Wagner, K.D., et al., *The perceived consequences of safer injection: An exploration of qualitative findings and gender differences.* Psychology Health & Medicine, 2010. **15**(5): p. 560-573.

107. Adedimeji, A.A., F.O. Omololu, and O. Odutolu, *HIV risk perception and constraints to protective behaviour among young slum dwellers in Ibadan, Nigeria.* Journal of Health Population and Nutrition, 2007. **25**(2): p. 146-157.

108. Akwara, P.A., N.J. Madise, and A. Hinde, *Perception of risk of HIV/AIDS and sexual behaviour in Kenya.* Journal of Biosocial Science, 2003. **35**(3): p. 385-411.

109. Rhodes, T., et al., *The social structural production of HIV risk among injecting drug users.* Social Science & Medicine, 2005. **61**(5): p. 1026-1044.

CHAPTER 2: PREVALENCE AND CORRELATES OF THE USE OF PREFILLED SYRINGES AMONG PERSONS WHO INJECT DRUGS IN SAN DIEGO, CA

Richard F. Armenta [a,b]
Alexis M. Roth [c]
Karla D. Wagner[d]
Steffanie A. Strathdee[a]
Stephanie K Brodine[b]
Jazmine Cuevas-Mota[a]
Fatima Munoz[a]
Richard S. Garfein[a]

[a]Division of Global Public Health, School of Medicine University of California San Diego, USA

[b]Division of Epidemiology, Graduate School of Public Health, San Diego State University, USA

[c]Department of Community Health & Prevention, School of Public Health, Drexel University, USA

[d]School of Community Health Sciences, University of Nevada, Reno, USA

ABSTRACT: Persons who inject drugs (PWID) are at increased risk for blood-borne virus (BBV) infections and overdose resulting from high-risk injecting practices. Studies of prefilled syringe use ([PFSU] using a syringe that already contained drug solution when it was obtained by the user), an injection practice previously described in Eastern Europe, suggest that it increases susceptibility to BBV. However, little is known about this practice in the United States. Data were obtained from an ongoing cohort study of PWID to determine the prevalence and assess correlates of PFSU in San Diego, CA. Baseline interviews assessed socio-demographics and drug use behaviors. Logistic regression was used to identify factors independently associated with ever using a prefilled syringe (yes/no). Participants (n=576) were predominately males (73.9%) and white (50.9%) with a mean age of 43.4 years (range 18-80); 33.3% reported ever using prefilled syringes, although only 4.9% reported use in the past 6 months. In multivariable analyses, PFSU was independently associated with ever having a rushed injection due to police presence (AOR=2.38, 95% CI: 1.56, 3.61), ever being in prison (AOR=1.45, 95% CI: 1.15, 2.49), injecting most often in public versus private places in the past 6 months (AOR=1.65, 95% CI: 1.1, 2.47), having ever overdosed on opioids (AOR=1.45, 95% CI: 0.99, 2.13), and injecting drugs in Mexico (AOR=1.63, 95% CI: 1.12, 2.39). Results indicate that a history of PFSU is common and associated with environmental factors that may increase risk for overdose and other adverse health outcomes. Studies are needed to better understand PFSU in order to develop interventions to prevent adverse outcomes associated with their use.

INTRODUCTION

Persons who inject drugs (PWID) are at increased risk for infection with blood borne viruses (BBV) including hepatitis C virus (HCV) and human immunodeficiency virus (HIV).[1-5] Though the prevalence of HCV is low among the general population, it is much higher in PWID with approximately one-third of young (18-30 years old) and 50-90% of older PWID estimated to be infected in the United States (US).[6, 7] Clatts (2007) suggests "transmission associated with the ways that illegal drugs such as heroin are prepared, distributed, and self-administered have emerged as adaptive responses to opportunities and constraints in the local physical and social environments."[8] Thus, it is important for substance use researchers to be mindful of emerging trends in drug using practices.

Studying novel and emerging trends is important because atypical injection practices and drug distribution methods might affect the spread of disease. One such practice is prefilled syringe use (PFSU), which is defined as using a syringe that already contained drug solution when it was obtained by the user. PFSU may have influenced HIV transmission among PWIDs in some Eastern European countries (e.g., Russia and Ukraine); however, drug preparation methods and time between preparation and distribution of prefilled syringes influences their infectivity and potential for the spread of disease.[9-12] There is a dearth of information about this practice from the US.

The most common drugs obtained in prefilled syringes differ by location. For instance, in Togliatti, Russia, drug users reported that "vint"—a mixture of

methamphetamine and pseudoephedrine—is available in prefilled syringes, but heroin is not.[13] It is posited that distribution and use of prefilled syringes may be associated with properties of the drug (i.e., liquid or powdered form), the need for rapid drug transactions, and individual factors of discreet drug users.[14, 15] In Eastern Europe, younger and less experienced drug users are more likely to report PFSU.[13, 16-18] In the US, the use of prefilled syringes has been documented among PWID who inject ketamine (a dissociative hallucinogen commonly used in as an anesthetic in veterinary practice but also used illicitly).[19]

The interplay between the physical, economic, social, and political environment affects the distribution and use of drugs. Globally, HIV transmission has been linked to environmental factors that influence risk behaviors.[20] Rhodes describes the risk environment as the social norms and physical spaces that interact to impact health behaviors and health outcomes.[20] In regards to PFSU, micro-environmental factors such as policing practices and availability of syringes and injection equipment influence their use.[21, 22] Evidence suggests that while increased police presence may lessen the visibility of drug use in public spaces, there can be negative public health consequences due to environmental changes as a result of increased monitoring of drug use.[23] One example of this is the increased use of shooting galleries, often cited as riskier injection sites where more syringe and paraphernalia sharing happens, as a result of police arrests for syringe possession.[24] Thus, with heightened monitoring of drug practices there is an increase in syringe sharing, rushed injection, and potentially PFSU, which may be an easy way to thwart arrest because drug transactions and injection of

drugs can be quicker if the drugs are already prepared. Consequently, the utilization of safe sources of syringes may also decrease and participation in higher risk injection practices, such as sharing injection equipment, unsafe injection, and improper disposal of injection equipment, may increase.[23]

There are two predominant concerns associated with PFSU. First, the concentration and composition of the solution in the syringes is unknown to the user – potentially resulting in unintended overdose. Second, the source and sterility of the syringes and injection paraphernalia is unknown to the user—this could lead to BBV transmission. In many settings, a common drug container is used to fill syringes and if that container becomes contaminated then all subsequent syringes filled may become contaminated.[17, 25, 26] While PFSU may result in increased risk of BBV infection, PWID engage in many high risk behaviors such as using non-sterile syringes and a common drug container that are additive to risk associated with PFSU.[11, 17, 27]

Despite our understanding of the various injection-related risk factors for HIV, HCV, and overdose there is a need to continually monitor trends, especially in locations that cross international borders, bridging two drug markets. Located on the US-Mexico border, San Diego, CA is adjacent to the busiest land border crossing in the world (San Ysidro/ Tijuana, Baja California, Mexico) and along major production and trafficking routes for drugs entering the US from Mexico. [28] Previous studies reported that 20% of PWID in San Diego travel to Mexico to purchase, use or inject drugs—a practice that could increase potential of disease transmission as the rates of HCV are much higher in Tijuana.[29] Using drugs in

different social and structural environments may introduce novel drug use practices that could then be disseminated amongst PWID's social networks. In 2011, a qualitative study among PWID from San Diego who reported injecting drugs in Tijuana referred to the finding that some PWID purchased prefilled syringes in Mexico; however, no additional information about the frequency or rationale behind this practice was collected.[30] The purpose of the present analysis is to determine the prevalence and correlates of PFSU and associated factors in a sample of PWID recruited in San Diego, CA.

METHODS

Between June 2012 and January 2014 PWID were recruited into the Study of Tuberculosis, AIDS, and Hepatitis C Risk (STAHR II)—an ongoing longitudinal cohort study, in San Diego, CA—to assess sociodemographic, behavioral, and contextual factors associated with HIV, HCV and *Mycobacterium tuberculosis* (*Mtb*) infection.[31] This study has been described in detail elsewhere.[32] Eligibility criteria included 1) being ≥18 years of age; 2) having injected illicit drugs in the past 30 days; 3) reporting no plans to move from San Diego County within the next 2 years; 3) agreeing to a blood draw and serologic testing for HIV, HCV and TB; 4) ability to speak English or Spanish; and 5) the ability to provide written, informed consent.

Participants were recruited using targeted outreach methods including advertising and street outreach in areas of known high drug use prevalence and word-of-mouth. The study took place in a storefront office and on a mobile unit

that parked in locations throughout San Diego County to increase representativeness of the sample. A bilingual (Spanish-English) outreach worker provided potential participants with information about the study and helped them to make appointments for the interviews. The institutional review board at the University of California, San Diego approved the study and all participants provided written informed consent.

Data Collection

Face-to-face interviews were conducted using Computer Assisted Personal Interviewing (CAPI), a process in which trained interviewers read questions from a computer to participants in English or Spanish and enter their responses on a laptop computer. The questionnaire included sociodemographics and behavioral factors associated with PFSU. Serologic testing was conducted to determine the prevalence of infection with HIV and HCV. Participants who tested positive for HIV or HCV were provided counseling and referrals for follow up medical care and treatment. Participants were offered $25 USD at baseline for time and travel to complete the interview and serologic testing.

Measures

Sociodemographics: age, sex, race/ethnicity, relationship status (single versus in a relationship), highest level of education (> high school versus ≤high school), income (<$10,000 versus ≥$10,000 USD annually), and housing status (homeless versus not). Substance use and injection practices: number of years injecting, number of injecting partners in the US, frequency of heroin use in the past 6 months (daily versus less frequently), frequency of crack/cocaine injection

in the past 6 months (weekly versus less frequently), most frequent syringe source in the past 6 months (safe [i.e., syringe exchange program, doctor/clinic/hospital, veterinary clinic/pet store, market] versus unsafe [i.e., spouse, family member, or sex partner, friend, drug dealer, "Hit doctor," shooting gallery, on the street, some other place]), primary injection location in the past 6 months (private [i.e., my/someone else's home, car] versus public location [i.e., shooting gallery, construction site, alleyway, bar/club, on the street, vacant lot, park, freeway overpass/bridge/canyon, public restroom], frequency of syringe sharing in the past 6 months (any vs. none), frequency of sharing injection paraphernalia (cookers, cotton, rinse water) in the past 6 months(any vs. none), and rushed injection due to police presence in the past 6 months(ever/never). Health care utilization: hospitalizations and emergency room (ER) visits in the past 6 months and opioid overdose, ever. Health outcomes: HIV and HCV seropositivity were detected using HIV Unigold Recombigen rapid antibody test (Trinity Biotech PLC, Bray, Ireland) and OraQuick HCV rapid antibody test (Orasure Technologies Inc., Bethlehem, PA).

Outcome: We assessed the use of prefilled syringes as a binary variable: "*Have you ever used drugs that were purchased in prefilled syringes, meaning syringes that already had drugs in them before you purchased them?"* (yes/no). In addition to lifetime PFSU, we also assessed any PFSU in the past 6 months. Lifetime PFSU was used as the outcome in subsequent analyses because only 27 (4.9%) of participants reported PFSU in the past 6 month; thus, we lacked sufficient power to use PFSU in the past 6 month as our outcome.

Statistical Methods

For this analysis, we used data from the STAHR II baseline visit. Descriptive statistics were calculated. Chi-squared and t-test statistics were used to describe the sample and compare PWID who reported lifetime PFSU to those who did not. Bivariate logistic regression was used to determine factors associated with PFSU. Factors with a p-value<0.20 were considered for inclusion in the final multivariable logistic regression model. Forward stepwise procedures were used to produce the final model, which only contained variables with a p-value <0.05. Confounding was assessed by comparing crude and adjusted odds ratios and assessing meaningful changes, using a 10% change as a reference point, in associations after adjusting for new variables. Variables that were found to be confounders were maintained in the final model. [33] Collinearity was tested in the final model using condition indices and variance inflation factors.[34] All analyses were completed using SAS 9.3.

RESULTS

A total of 576 participants enrolled in the study responded to the PFSU questions and were eligible for this analysis. Half of the participants were white (50.9%), nearly three-quarters (73.9%) were male, and the mean age was 43.4 years (range 18-80). Sixty-one percent reported being homeless, most were single (88.7%), and one-third (32.1%) reported a yearly income greater than $10,000. Mean age of first injection was 22.6 years and mean duration of injecting was 20.8 years (table 1).

Of the 576 participants who responded to the PFSU questions, 193 (33.5%) reported ever using prefilled syringes and 27(4.7%) reported PFSU in the past 6 months. As reported in Table 1, in bivariate analysis, participants who reported lifetime PFSU at baseline were more likely to report a high school education or less compared to greater than high school (40.2% vs. 27.5%), to be currently homeless (67.4% vs. 58.0%) and to be younger at first injection (mean age: 21.5 vs. 23.1 years). Participants who reported lifetime PFSU were more likely to report ever rushing injection due to police presence (39.5% vs. 19.9%) and to agree that police presence had ever affected where they purchase (47.9% vs. 36.1%) and use drugs (48.3% vs. 33.3%). Participants who reported lifetime PFSU were also more likely to have ever been in prison (60.5% vs. 46.7%), to report injecting drugs most often in public compared to private places in the past six months (38.8% vs. 24.7%), shared syringes more often in the past six months (74.9% vs. 50.9%), shared other injection paraphernalia more often (89.2% vs. 63.3%) and were more likely to report injecting drugs in Mexico in their lifetime (46.2% vs. 31.5%).

In regards to health care utilization and status, in bivariate analysis participants who reported lifetime PFSU were more likely to report hospital (23.4% vs. 13.9%) or ER (44.8% vs. 28.6%) visits in the past six months, to have ever had an abscess (73.4% vs. 66.6%), to have ever overdosed on opioids (52.8% vs. 35.9%), and to have tested anti-HCV positive (71.4% vs. 63.2%).

In multivariable analysis (table 2), reporting lifetime PFSU was associated with having ever rushed an injection due to police presence (AOR=2.38, 95% CI:

1.56, 3.61), ever being in prison (AOR=1.45, 95% CI: 1.15, 2.49), ever overdosing on opioids (AOR=1.45, 95% CI: 0.99, 2.13), ever injecting drugs in Mexico (AOR=1.63, 95% CI: 1.11, 2.39), and injecting most often in public versus private places in the past six months (AOR=1.65, 95% CI: 1.11, 2.47).

Among those who reported lifetime PFSU, 27 (13%) reported PFSU in the past 6 months. The majority (92.6%) reported purchasing prefilled syringes in the past 6 months in the US, while only one participant purchased them in Mexico and one participant reported purchasing them in both the US and Mexico. Most participants reported purchasing prefilled syringes from their injection partners or friends (88.4%) or drug dealers (42.3%), while other places such as shooting galleries, bars/clubs, the casino, and in jail were also reported infrequently (data not shown).

DISCUSSION

In this study of the prevalence and correlates of PFSU among PWID in San Diego, CA, we uncovered several factors suggesting that those who have engaged in this practice are more vulnerable and take higher risks as a result of both micro and macroenvironmental factors. Specifically, we found that lifetime PFSU was independently associated with ever having rushed injection due to police presence, having been in prison, injecting most often in public versus private locations, ever overdosing, and ever injecting drugs in Mexico.

Our finding that PFSU is associated with both rushed injection due to police presence and injecting in mostly public spaces is consistent with other

research that suggests that environmental factors may lead to risky injection behaviors.[2] While the purchase of syringes at pharmacies and use of the SEP is legal in San Diego, micro-level enforcement of laws, such as syringe access and possession laws, shape drug injection practices by discouraging the possession of syringes and injection paraphernalia, which may necessitate sharing or PFSU. The SEP in San Diego is also limited to two days per week and does not provide an adequate number of syringes to sustain most PWIDs safe injection between SEP visits.[35] PWID also often report getting stopped for possession regardless of the law.[36] As such, PFSU could have emerged as a mechanism to get a "quick" high when no other options, namely safer places to inject drugs or time to prepare their own solution were available, or due to fear of enforcement of paraphernalia laws.[20, 37, 38] Those with a prison record have even greater reason to fear police and thus, may be more likely to use prefilled syringes to avoid being apprehended by the police with syringes or other injection paraphernalia.

Our finding that PWID who have ever used prefilled syringes are more likely to report ever injecting drugs in Mexico highlights the importance of cross-border surveillance of trends. Previous studies indicate that 27% of PWID in San Diego report traveling to Mexico to inject drugs and an even higher number report traveling for other reasons.[29] Macroenvironmental factors such as the spill over from drug trafficking and population mixing, and microenvironmental factors such as arrest for possession of injection paraphernalia in Mexico may lead to the altering of behaviors among PWID from San Diego, though we could not assess the temporality of these behaviors. Others have found that sharing of

syringes and other injection paraphernalia is also influenced by the availability of syringes and other equipment and social norms, which may be different in Mexico than in the US.[13, 39-41] Thus, PWID who travel to Mexico may be influenced by a number of factors that could increase their risk BBV infection.

PFSU was associated with lifetime overdose. Studies with PWID indicate that overdose is associated sharing of injection equipment, polydrug use, homelessness, injecting on the streets, requiring help injecting and lifetime history of incarceration.[42-44] Risk factors for PFSU and overdose are similar such as rushed injection and having been in prison; therefore, it is important to take notice of the environmental conditions that impact PWIDs ability to inject safely. Overdose may also be a result of the unknown contents of prefilled syringes. Given the high prevalence of overdose, PWID should also receive overdose response training that includes the administration of naloxone, an opioid antagonist, to prevent adverse overdose outcomes.[45] While naloxone is becoming more available in the US, the same is not true in other settings such as Mexico where PWID could benefit from its availability.

Physical microenvironmental factors (e.g., drug injection locations) and social microenvironmental factors (e.g, local policing practices, injection locations, and social norms) that may influence PFSU and increase overdose risk may also increase likelihood of disease transmission.[46, 47] While we did not find an association between PFSU and HIV or HCV infection, PFSU could increase the likelihood of BBV infection if the syringe is not sterile or the drugs are drawn from a common container that becomes infected.[12] Further, others report that

prefilled syringes are often shared.[27] Thus, it is important that education messages address PFSU as well as related high risk behaviors for HIV infection. Further, studies have found that HCV and HIV transmission are often a result of the setting in which drugs are injected, highlighting the importance of developing structural interventions to address policing practices and the availability of sterile syringes.[10, 48, 49]

The results of this study must be interpreted in light of certain limitations. Cross-sectional data were utilized and the outcome was measured as any lifetime use. Thus, we were unable to assess temporal associations between PFSU and the independent variables, which were measured using both lifetime and proximal timeframes. Future studies that assess PFSU over time and incident disease status are needed to better understand the risks associated with PFSU and to determine whether there are any changes in the prevalence of this behavior over time. Our reliance on self-report data may introduce bias into our study. However, we would expect underreporting of risky behaviors, which would bias our results towards the null. It is also possible that PFSU may include both syringes that were purchased already filled and those that were prepared and filled by an injection partner with whom they were injected. Though these are separate behaviors, they are similar in that the person injecting has less control over preparation methods.

High risk behaviors among PWID constantly evolve in response to changes in environmental, social, and structural factors that impact the ways in which drugs are distributed and used. While research has described how

different drug preparation (e.g., sharing cookers, cotton, water, and using common drug containers) and distribution methods (e.g., backloading/frontloading, prefilled syringes) influence BBV transmission individually, further research is needed to understand how a previously unrecognized behavior, PFSU, influences HIV and HCV transmission in our setting, if at all. Our findings suggest that PFSU is shaped by environmental factors that produce risk among PWID. Namely, vulnerability to policing practice, unavailability of safe injection sites, and restricted access to syringes might create environments that prevent PWID from practicing harm reduction strategies. While individual factors such as knowledge of risk behaviors are often identified in intervention programs, they fail to recognize circumstances over which PWID have little control.[50] Qualitative and longitudinal studies that contextualize the use of prefilled syringes are needed to understand why PWID choose to prefilled syringes and to better understand situations in which they are used.

Acknowledgements: Chapter 2, in full, has been submitted to the Journal of Urban Health for publication of material. Co-Authors include Garfein, Richard; Munoz, Fatima; Roth, Alexis; Wagner, Karla; Cuevas-Mota, Jazmine; Strathdee, Steffanie; Brodine, Stephanie. The dissertation author is the primary author of this material.

REFERENCES

1. Nelson, P.K., et al., *Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews.* Lancet, 2011. **378**(9791): p. 571-83.

2. Strathdee, S.A., et al., *HIV and risk environment for injecting drug users: the past, present, and future.* Lancet, 2010. **376**(9737): p. 268-84.

3. Strathdee, S.A., et al., *Individual, social, and environmental influences associated with HIV infection among injection drug users in Tijuana, Mexico.* Jaids-Journal of Acquired Immune Deficiency Syndromes, 2008. **47**(3): p. 369-376.

4. Hammett, T.M., et al., *Correlates of HIV status among injection drug users in a border region of southern China and northern Vietnam.* J Acquir Immune Defic Syndr, 2005. **38**(2): p. 228-35.

5. Mathers, B.M., et al., *Global epidemiology of injecting drug use and HIV among people who inject drugs: a systematic review.* Lancet, 2008. **372**(9651): p. 1733-45.

6. Thomas, D.L., et al., *Correlates of hepatitis C virus infections among injection drug users.* Medicine (Baltimore), 1995. **74**(4): p. 212-20.

7. Garfein, R.S., et al., *A peer-education intervention to reduce injection risk behaviors for HIV and hepatitis C virus infection in young injection drug users.* AIDS, 2007. **21**(14): p. 1923-32.

8. Clatts, M.C., et al., *Novel heroin injection practices: implications for transmission of HIV and other bloodborne pathogens.* Am J Prev Med, 2007. **32**(6 Suppl): p. S226-33.

9. Dehne, K.L., *The emerging AIDS crisis in Russia: review of enabling factors and prevention needs.* Int J STD AIDS, 2001. **12**(4): p. 277-8.

10. Rhodes, T., et al., *The social structural production of HIV risk among injecting drug users.* Soc Sci Med, 2005. **61**(5): p. 1026-44.

11. Heimer, R., et al., *The effect of acids on the survival of HIV during drug injection.* J Acquir Immune Defic Syndr, 2007. **45**(2): p. 144-50.

12. Bobkov, A.F., et al., *Human immunodeficiency virus type 1 in illicit-drug solutions used intravenously retains infectivity.* J Clin Microbiol, 2005. **43**(4): p. 1937-9.

13. Rhodes, T., et al., *Situational factors influencing drug injecting, risk reduction and syringe exchange in Togliatti City, Russian Federation: a qualitative study of micro risk environment.* Soc Sci Med, 2003. **57**(1): p. 39-54.

14. Rhodes, T., et al., *HIV infection associated with drug injecting in the newly independent states, eastern Europe: the social and economic context of epidemics.* Addiction, 1999. **94**(9): p. 1323-36.

15. Taran, Y.S., et al., *Correlates of HIV risk among injecting drug users in sixteen Ukrainian cities.* AIDS Behav, 2011. **15**(1): p. 65-74.

16. Booth, R.E., et al., *Drug injectors and dealers in Odessa, Ukraine.* J Psychoactive Drugs, 2003. **35**(4): p. 419-26.

17. Booth, R.E., et al., *Predictors of self-reported HIV infection among drug injectors in Ukraine.* J Acquir Immune Defic Syndr, 2004. **35**(1): p. 82-8.

18. Burrows, D., et al., *Responding to HIV infection associated with drug injecting in Eastern Europe.* Drug Alcohol Rev, 1998. **17**(4): p. 453-63.

19. Wagner, K.D., et al., *Control over drug acquisition, preparation and injection: Implications for HIV and HCV risk among young female injection drug users.* ISRN Addict, 2013. **2013**.

20. Rhodes, T., *The 'risk environment': a framework for understanding and reducing drug-related harm.* International Journal of Drug Policy, 2002. **13**(2): p. 85 - 94.

21. Rhodes, T., et al., *Explosive spread and high prevalence of HIV infection among injecting drug users in Togliatti City, Russia.* AIDS, 2002. **16**(13): p. F25-31.

22. McCurdy, S., et al., *Harm reduction in Tanzania: an urgent need for multisectoral intervention.* Int J Drug Policy, 2007. **18**(3): p. 155-9.

23. Cooper, H., et al., *The impact of a police drug crackdown on drug injectors' ability to practice harm reduction: a qualitative study.* Soc Sci Med, 2005. **61**(3): p. 673-84.

24. Philbin, M., et al., *Shooting gallery attendance among IDUs in Tijuana and Ciudad Juarez, Mexico: Correlates, prevention opportunities, and the role of the environment.* Aids and Behavior, 2008. **12**(4): p. 552-560.

25. Rhodes, T., et al., *Prevalence of HIV, hepatitis C and syphilis among injecting drug users in Russia: a multi-city study.* Addiction, 2006. **101**(2): p. 252-66.

26. Koester, S., R. Booth, and W. Wiebel, *The risk of HIV transmission from sharing water, drug mixing containers and cotton filters among intravenous drug users.* Int J Drug Policy, 1990. **1**(6): p. 28-30.

27. Gyarmathy, V.A., et al., *Liquid drugs and high dead space syringes may keep HIV and HCV prevalence high - a comparison of Hungary and Lithuania.* Eur Addict Res, 2010. **16**(4): p. 220-8.

28. Brouwer, K.C., et al., *Trends in Production, Trafficking, and Consumption of Methamphetamine and Cocaine in Mexico.* Substance Use & Misuse, 2006. **41**(5): p. 707-727.

29. Volkmann, T., et al., *Border crossing to inject drugs in Mexico among injection drug users in San Diego, California.* J Immigr Minor Health, 2012. **14**(2): p. 281-6.

30. Wagner, K.D., et al., *Cross-border drug injection relationships among injection drug users in Tijuana, Mexico.* Drug Alcohol Depend, 2011. **113**(2-3): p. 236-41.

31. Robertson, A.M., et al., *Evaluating the impact of Mexico's drug policy reforms on people who inject drugs in Tijuana, B.C., Mexico, and San Diego, CA, United States: a binational mixed methods research agenda.* Harm Reduct J, 2014. **11**: p. 4.

32. Robertson, A.M., et al., *Evaluating the impact of Mexico's drug policy reforms on people who inject drugs in Tijuana, B.C., Mexico, and San Diego, CA, United States: a binational mixed methods research agenda.* Harm Reduct J, 2014. **11**: p. 4.

33. *Other Factors Accounted for? Confounding and Interaction*, in *A Pocket Guide to Epidemiology*. 2007, Springer New York. p. 161-178.

34. Dormann, C.F., et al., *Collinearity: a review of methods to deal with it and a simulation study evaluating their performance.* Ecography, 2013. **36**(1): p. 27-46.

35. City of San Diego. *Clean Syringe Exchange Pilot Program*. Community Services [cited 2015 February 10]; Available from: http://www.sandiego.gov/communityservices/programs/cleansyringe/index.shtml.

36. Gaines, T.L., et al., *Examining the Spatial Distribution of Law Enforcement Encounters among People Who Inject Drugs after Implementation of Mexico's Drug Policy Reform.* Journal of Urban Health, 2014: p. 1-14.

37. Koester, S.K. and L. Hoffer, *" Indirect Sharing": Additional HIV Risks Associated with Drug Injection.* AIDS and Public Policy Journal, 1994. **9**: p. 100-100.

38. Grund, J.P.C., et al., *Drug use contexts and HIV‐consequences: the effect of drug policy on patterns of everyday drug use in Rotterdam and the Bronx.* British journal of addiction, 1992. **87**(3): p. 381-392.

39. Latkin, C., et al., *The relationship between drug use stigma and HIV injection risk behaviors among injection drug users in Chennai, India.* Drug Alcohol Depend, 2010. **110**(3): p. 221-7.

40. Neblett, R.C., et al., *Social network characteristics and HIV sexual risk behavior among urban African American women.* Journal of Urban Health, 2011. **88**(1): p. 54-65.

41. Davey-Rothwell, M.A. and C.A. Latkin, *HIV-related communication and perceived norms: an analysis of the connection among injection drug users.* AIDS Education & Prevention, 2007. **19**(4): p. 298-309.

42. Ochoa, S.C. and J. Sampalis, *Risk perception and vulnerability to STIs and HIV/AIDS among immigrant Latin-American women in Canada.* Cult Health Sex, 2014. **16**(4): p. 412-25.

43. Ochoa, K.C., et al., *Overdosing among young injection drug users in San Francisco.* Addict Behav, 2001. **26**(3): p. 453-60.

44. Ochoa, K.C., et al., *Heroin overdose among young injection drug users in San Francisco.* Drug Alcohol Depend, 2005. **80**(3): p. 297-302.

45. Wagner, K.D., et al., *Evaluation of an overdose prevention and response training programme for injection drug users in the Skid Row area of Los Angeles, CA.* Int J Drug Policy, 2010. **21**(3): p. 186-93.

46. Bluthenthal, R., et al., *Collateral damage in the war on drugs: HIV risk behaviors among injection drug users.* International Journal of Drug Policy. **10**(1): p. 25-38.

47. Beletsky, L., et al., *Syringe confiscation as an HIV risk factor: the public health implications of arbitrary policing in Tijuana and Ciudad Juarez, Mexico.* J Urban Health, 2013. **90**(2): p. 284-98.

48. Rhodes, T. and M. Simic, *Transition and the HIV risk environment.* BMJ, 2005. **331**(7510): p. 220-3.

49. Volkmann, T., et al., *Factors associated with drug-related harms related to policing in Tijuana, Mexico.* Harm Reduct J, 2011. **8**(1): p. 7.

50. Syme, S.L., *Social determinants of health: the community as an empowered partner.* Prev Chronic Dis, 2004. **1**(1): p. A02.

Table 2.1: Sociodemographic and behavioral factors associated with lifetime prefilled syringe use among persons who inject drugs in San Diego, CA (n=574)

	Total	Ever Used PFS	Never Used PFS	OR	95% CI	P-value
Demographics		193(33.5%)	383(66.5%)			
Mean age, years (mean, sd)	43.4 (11.7%)	43.4(11.8%)	43.3(11.7%)	1.00	0.99, 1.02	0.92
Male gender	420(73.9%)	147(77.0%)	273(72.4%)	0.83	0.57, 1.20	0.32
Race/Ethnicity						0.12
White	293(50.9%)	101(52.3%)	192(50.1%)	-	-	
Hispanic	178(30.9%)	67(34.7%)	111(29.0%)	1.15	0.78, 1.69	
Black	51(8.9%)	12(6.2%)	39(10.2%)	0.59	0.29, 1.17	
Other	54(9.4%)	13 6.7%)	41(10.7%)	0.60	0.31, 1.18	
Yearly Income (≥$10,000 vs. <10,000)	184(32.1%)	62(32.3%)	122(31.9%)	0.98	0.69, 1.43	0.93
Single vs. Married	511(88.7%)	172(89.1%)	339(88.5%)	1.06	0.61, 1.84	0.83
Education level (<=High School vs. >High School)	207(35.9%)	53(27.5%)	154(40.2%)	1.78	1.22, 2.59	<0.01
Homeless (yes vs. no)	352(61.1%)	130(67.4%)	222(58.0%)	1.50	1.04, 2.15	0.03
Mean years injecting (mean, sd)	20.8(13.5)	21.9(13.4)	20.3(13.5)	1.00	1.00, 1.02	0.17
Mean age first injection, years (mean, sd)	22.6(8.2)	21.5(7.3)	23.1(8.6)	0.98	0.95, 1.00	0.06
Substance abuse related factors						
Injected crack weekly, last 6 months (yes vs. no; n=552)	19(3.4%)	10(5.3%)	9(2.4%)	2.23	1.01, 6.07	0.05
Injected heroin weekly, last 6 months (yes vs. no)	310(56.2%)	114(60.3%)	196(54.0%)	1.30	0.91, 1.85	0.16
Injected heroin more than daily, last 6 months (yes vs. no)	170(30.8%)	73(38.6%)	97(26.7%)	1.73	1.19, 2.51	<0.01
Used two or more drugs per week, last 6 months (yes vs. no)	317(55.0%)	118(61.1%)	198(52.0%)	1.61	1.13, 2.29	0.04
Ever rushed injection due to police presence (yes vs. no)	151(26.4%)	75(39.5%)	76(19.9%)	2.63	1.79, 3.86	<0.001
Police presence affected where buy drugs (yes vs. no)	229(40.3%)	91 (47.9%)	138(36.1%)	1.61	1.13, 2.29	<0.01
Police presence affected where use drugs (yes vs. no)	219(38.3%)	92 (48.4%)	127 (33.3%)	1.86	1.31, 2.66	<0.001
Ever been in jail (yes vs. no)	516(90.7%)	176(92.6%)	340(89.7%)	1.44	0.76, 2.73	0.26
Ever been in prison (yes vs. no)	292(51.3%)	115(60.5%)	177(46.7%)	1.75	1.23, 2.49	0.002
Number of people know who inject (mean, sd)	28.0(37.1)	31.3(37.7)	26.4(36.7)	1.003	1.00, 1.01	0.14
Number of people know who inject who are friends (mean, sd)	5.2(10.6)	6.7(12.4)	4.5(9.6)	1.02	1.00, 1.04	0.03
Obtained syringes most often from safe vs. unsafe source, last 6 months	354(62.7%)	108(57.1%)	246(65.4%)	1.42	0.99, 2.03	0.05
Injected most often in public vs. private place, last 6 months	166(29.4%)	73(38.8%)	93(24.7%)	1.93	1.33, 2.81	0.001
Used syringe exchange, last 6 months (yes vs. no)	238(41.3%)	81(42.0%)	157(41.0%)	1.04	0.73, 1.48	0.82
Shared syringes, last 6 months (yes vs. no)	289(59.3%)	128(74.9%)	161(50.9%)	2.88	1.92, 4.35	<0.001
Shared any injection paraphernalia, last 6 months (yes vs. no)	394(72.0%)	165(89.2%)	229(63.3%)	4.83	2.90, 8.04	<0.001
Ever bought drugs in Mexico (yes vs. no)	267(47.7%)	106(56.7%)	161(43.2%)	1.72	1.21, 2.46	<0.01
Ever used drugs in Mexico (yes vs. no)	215(38.5%)	83(44.4%)	132(35.5%)	1.45	1.01, 2.08	0.04
Ever injected drugs in Mexico (yes vs. no)	203(36.4%)	86(46.2%)	117(31.5%)	1.87	1.31, 2.69	<0.001
Health Care Utilization and Health Status						

Table 2.1 Cont: Sociodemographic and behavioral factors associated with lifetime prefilled syringe use among persons who inject drugs in San Diego, CA (n=574)

	Total	Ever Used PFS	Never Used PFS	OR	95% CI	P-value
Any ER visit, last 6 months (yes vs. no)	195(34.0%)	86(44.8%)	109(28.6%)	2.03	1.41, 2.90	<0.001
Any hospital visit, last 6 months (yes vs. no)	98(17.1%)	45(23.4%)	53(13.9%)	1.90	1.22, 2.95	<0.01
Ever had an abscess (yes vs. no)	394(68.9%)	141(73.4%)	253(66.6%)	1.39	0.94, 2.04	0.10
Ever overdosed on opioids (yes vs. no)	239(41.6%)	102(.52.8%)	137(35.9%)	2.00	1.41, 2.85	<0.001
HIV positive (seroconfirmed; n=553)	52 (9.4%)	18(9.7%)	34(9.2%)	1.06	0.58, 1.93	0.85
HCV positive (seroconfirmed; n=552)	364(65.9%)	132(71.4%)	232(63.2%)	1.45	0.99, 2.13	0.05
Likelihood of getting infected with HIV (more vs. same or less likely; n=529)	146(27.6%)	57(32.4%)	89(25.2%)	1.42	0.96, 2.11	0.08
Ever smoked cigarettes (yes vs. no; n=522)	488(93.5%)	163(92.1%)	325(94.2%)	0.72	0.35, 1.45	0.36

Table 2.2: Multivariable analysis of factors associated with lifetime prefilled syringe use among persons who inject drugs in San Diego, CA (n=543)

Variable	Adjusted Odds Ratio	95% Confidence Interval	*P-Value*
Ever Rushed injection due to police presence (Yes vs. No)	2.38	1.56, 3.61	<0.001
Ever been in prison (Yes vs. No)	1.45	1.15, 2.49	<0.01
Injected most often in public vs. private place, last 6 months	1.65	1.11, 2.47	0.02
Ever overdosed on opioids (Yes vs. No)	1.45	0.99, 2.13	0.05
Ever Injected drugs in Mexico (Yes vs. No)	1.63	1.11, 2.39	<0.01

CHAPTER 3: "GET WELL NOW, GET HIGH NOW… DEAL WITH DISEASE LATER": USE OF PREFILLED SYRINGES TO INJECT DRUGS IN SAN DIEGO, CALIFORNIA

Richard F. Armenta[a,b]
Richard S. Garfein[a]
Alexis M. Roth[c]
Ramona Perez[b]
Robby Malebranche[a]
Jazmine Cuevas-Mota[a]
Steffanie A. Strathdee[a]
Karla D. Wagner[d]

[a]Division of Global Public Health, School of Medicine University of California San Diego, USA

[b]Division of Epidemiology, Graduate School of Public Health, San Diego State University, USA

[c]Department of Community Health & Prevention, School of Public Health, Drexel University, USA

[d]School of Community Health Sciences, University of Nevada, Reno, USA

ABSTRACT: Vulnerability to bloodborne infections among persons who inject drugs (PWID) is shaped by the Risk Environment, and how micro and macro-environmental factors such as policing practices, social norms, and laws regarding syringe access and drug possession influence risk behaviors. We conducted guided in-depth interviews with 25 PWID, 10 of whom were recruited because they reported prefilled syringe use (PFSU). Interviews with participants who reported PFSU were conducted to understand contextual factors associated with their use in San Diego, California. Interviews with participants not recruited based on their PFSU (n=15) asked questions about the availability and perception of PFSU and associated health risks. Mean age of participants who reported PFSU was 44.4 (range 19-58) and the majority of participants were male (80%). Participants described situations in which their regular drug preparation methods were not possible and there was a need to inject quickly. PFSU was influenced by fear of arrest for possession of drugs and injection equipment, and injecting in certain environments. Participants reported knowing PFSU can increase disease transmission, overdose risk, and even death from a 'hot shot' (a hit that is meant to kill the injector). Results suggest that PFSU is driven by structural factors that prevent harm reduction strategies. Interventions that address structural level barriers to protective behaviors among PWID are needed to prevent adverse health outcomes.

INTRODUCTION

Behaviors that are linked to HIV and HCV infection, such as receptive syringe sharing (RSS) and injection paraphernalia sharing (e.g., cookers, cotton, and rinse water), are common among persons who inject drugs (PWID).[1-5] Factors that influence RSS and paraphernalia sharing among PWID include homelessness, risk perception, injecting in a shooting gallery or other public space,[6] and the legal environment.[7] Exposure to bloodborne pathogens can occur at various steps of the drug preparation and injection process. “Indirect sharing,” or sharing that does not involve directly sharing syringes, includes the sharing of injection paraphernalia (e.g., cookers, cotton, rinse water) and the dividing of drug solution using a syringe (i.e., frontloading/backloading or syringe-mediated drug sharing).[8, 9] These processes often involve sharing the contents of the syringes rather than the syringe itself.

One of the most well-studied risk reduction interventions is to expand access to syringes, which has helped to reduce RSS and resulting HIV prevalence among IDUs.[10-16] However, even expanded syringe access has not fully eliminated RSS and injection paraphernalia sharing.[17, 18] The most recent National HIV Behavioral Surveillance program found that 30% of PWID reported RSS despite the availability of syringe exchange programs,[18] which could mean that not all PWID have access to syringe exchange programs or that there is insufficient coverage of syringe exchange programs. There are also other factors that influence risk behaviors. Environmental factors influence risk behaviors and may be social, economic, physical, and/or related to policy.[19] The micro-risk

environment involves personal decisions and community norms that play out in the setting where injection drug use occurs, whereas the macro-risk environment includes structural factors such as laws, drug-related policing practices, economic conditions, and cultural beliefs.[20] These factors impact the ability of PWID to engage in healthful drug use practices such as accessing sterile syringes, or may lead them to practice riskier behaviors. One such behavior of interest is prefilled syringe use (PFSU). PFSU is defined as injecting drugs with a syringe that was already filled prior to the user obtaining the syringe.

Several studies have documented PFSU.[21-23] In a study of young female ketamine injectors, women reported injecting the drug using syringes that had been prepared by others.[22] In another study of young PWID in San Diego participants reported purchasing prefilled syringes in cafes in Tijuana, Baja California, Mexico.[24] PFSU has been associated with an injector being younger and less experienced, with rushed injection, injecting most often in public places, sharing other injection paraphernalia, and accessing the syringe exchange program,[19, 21] however, few studies have been conducted to determine factors associated with their use. A study by Heimer et al. indicated that PFSU influence on disease transmission is largely dependent on drug preparation methods and time between preparation and administration of drugs. For instance, in highly acidic solutions, HIV survivability is low, especially during longer periods of time.[25] Distribution of drugs in liquid form is considered greater risk for HIV infection due to the number of ways a syringe and drug solution can become contaminated during the preparation process.[26] Further, our previous research

also found an association between overdose and PFSU, leading to further concern about the use of prefilled syringes. The association between overdose and PFSU may be due to the unknown nature contents of the syringe (quality and concentration) and environment in which the drugs are injected.

The purpose of this study was to supplement existing knowledge derived from quantitative research with more qualitative data that could begin to elucidate the social and environmental context of PFSU, rationales for their use, and attitudes about prefilled syringes using a theoretical framework derived from Rhodes's Risk Environment Framework.[19] Public health literature points to the need to understand how the social and political environment influence risky behaviors and HIV transmission.[27]

METHODS

San Diego County, adjacent to Tijuana, Baja California, Mexico, is home to the busiest land border crossing in the world with more than 52,000 North bound crossings in 2012.[28] The region sits on a major drug trafficking route[29] and bridges two drug using populations. San Diego has an estimated 25,000-28,000 PWID and a syringe exchange program that operates two days a week for two hours each day.[30] Participants for this study come from the Study of Tuberculosis, AIDS, and Hepatitis C Risk (STAHR II) among PWID in San Diego County. STAHR-II participants (n=576) were enrolled between June 2012 and January 2014 based on the following criteria: ≥18 years old; reported injection drug use in the past 30 days, confirmed by the presence of track marks; no plans

to move from San Diego County within the next 2 years; agree to a blood draw and serologic testing for HIV, HCV, and TB; ability to speak English or Spanish; and the ability to provide written informed consent. Participants of STAHR-II were recruited using targeted outreach methods, as described elsewhere.[31] Participants who were determined to be eligible and provided informed consent were enrolled in the longitudinal study, which included quantitative interviews and serologic testing every six months for 24 months. Participants were compensated $30 USD for their time and travel. The institutional review boards at San Diego State University and the University of California, San Diego approved this study.

As part of the larger STAHR II, qualitative interviews were conducted for a subset of participants that elicited information about injection practices and travel to Mexico to use or inject drugs. Participants were selected to participate in these interviews if they reported traveling to Mexico ever, or in the 6 months prior to their baseline quantitative interview. Additional participants who did not report traveling to Mexico were also selected to complete qualitative interviews. To gather more information about PFSU during these interviews participants were asked to answer questions about prefilled syringes. Of the participants who completed these qualitative interviews fifteen were asked questions about PFSU. The questions were designed to understand why and how prefilled syringes are used and to understand perceptions of PFSU. While these participants were not selected based on their PFSU, one participant reported PFSU in the past 6 months and two participants reported ever using prefilled syringes. These interviews elicited important information about perceptions of PFSU by those who

had never used them and provided insight as to why and how they are used by those, as described by the participants who reported PFSU.

To better understand PFSU an additional ten participants were recruited from STAHR II based on their PFSU. We used criterion sampling to purposively sample PWID from STAHR II to participate in these qualitative interviews about the social/environmental context and rationale for PFSU.[32, 33] To determine eligibility for participation, we used a single question that asked participants whether they engaged in PFSU in the 6 months prior to their most recent study visit. The question was asked as follows: In the last 6 months, have you injected drugs with a prefilled syringe? (By prefilled syringe, I mean a syringe that was already filled with drugs when you got it.) Participants who reported PFSU at any study visit (n=10 of the 62 participants who reported PFSU) were selected. All participants who completed qualitative interviews were compensated $30 USD for their time and travel.

Data Collection

In interviews with participants who were recruited based on their reporting traveling to Mexico to use and inject drugs (n=15), questions mainly focused on their motivations for using and injecting drugs in Mexico. However, the interview guide included questions about the availability of prefilled syringes, perceptions of prefilled syringes, and for those who reported using prefilled syringes, questions about why they used them and the context that led to PFSU.

Participants who were recruited specifically based on their PFSU (n=10) were also asked questions to understand the availability of prefilled syringes and

perceptions of prefilled syringes. The interview guide consisted of a series of open-ended questions where participants were asked to describe and reflect upon their experiences using and purchasing prefilled syringes.[34] These interviews were designed to explore the social and environmental context and rationale for PFSU. Interviewers wrote detailed notes that summarized the main interview topics and documented the physical and mental condition of the participant.

All interviews lasted between 30 minutes and 1 hour and were audio recorded. Audio recordings were transcribed verbatim and crosschecked by another team member for quality control.[35] The institutional review boards at the University of California, San Diego and San Diego State University approved this study. All participants provided written informed consent.

Analysis

MAXQDA 10 (VERBI, Marburg, Germany) was used to manage coding and analysis. Analysis and codebook development involved two team members (RFA and RM) independently reading through transcripts and generating a list of codes. Codes were arranged in a hierarchical structure during the initial round of coding to organize information by broad topics, and analysts broke down sub-codes on PFSU to better understand contextual factors associated with PFSU. Codes were both deductively developed based on topics in the interview guide and inductively developed based on themes that emerged during the interviews.[34, 36, 37] Codes were organized into a codebook and applied to all transcripts. When discrepancies in coding occurred, differences were resolved by

discussion between the study team until consensus was achieved. In the final phase of analysis, codes were applied to blocks of text and representative quotes were selected to illustrate the findings.

RESULTS

In total, 576 participants were enrolled in STAHR II and to date 376 participants have completed at least one follow up visit, providing a total of 951 interviews during which PFSU could be reported. Across all visits a total of 62 (9.6%) participants reported PFSU in the last 6 months. Participants who were selected to participate in this study based on their PFSU were predominately male (80%) with a mean age of 40 (range 19-58). The majority of participants were white (50%) or Hispanic (30%). Almost half (40%) of participants reported using the syringe exchange in the 6 months prior to their interview. Additional sociodemographic information of participants who reported PFSU are shown in table 1; these data approximate the sample in the larger STAHR-II study.

Themes that emerged from our interviews highlight environmental factors that not only influence PFSU but can also lead to increased risk for disease transmission and overdose. Participants discussed the availability of prefilled syringes and the situations in which they were used. These situations often emerged as a result of physical and political microenvironmental factors, such as injection location, the availability of syringes and other injection equipment, and homelessness, and political macroenvironmental factors such as policies governing the possession of drugs of injection equipment. Participants described

how these factors influence not only their PFSU, but also other risk behaviors and their perceptions about disease transmission risk.

Prefilled Syringe Availability— A majority of participants reported that while prefilled syringes were sold and available in our setting, their use is not common among most PWID but emerges in certain injection environments. Several participants reported that they purchased prefilled syringes because they were the only thing available.

> Not as a matter of routine, no, that they [will] sell like prefilled syringes to go. I've never heard of that. I mean I've bought them before just because that was the only thing the guy had you know. The guy's like "Well I got this." I'm like "Give it to me." You know. But that was just like a fluke. It wasn't like how it was packaged, it was just that way. I mean that one time I did it that was just all the guy had. He's like "Well I got this you know. I don't have anything." I'm like, "You have nothing?" He's like, "Well I got this. There's about a dime in there." So I said ok. [Male, age 49]

Participants also reported that there are specific areas within San Diego where prefilled syringes are available and sold more often. These areas were often described as places where PWID participated in other high risk behaviors such as sharing syringes and injecting frequently. Though many participants reported that they know where those areas are located they also reported that they tend to avoid those areas. However, a few participants reported purchasing prefilled syringes as a matter of routine, especially in certain situations such as being at work or in public spaces.

What are the situational, social, and environmental factors that influence

PFSU?

The convenience of prefilled syringes and the need for a quick high emerged as main themes. Participants described a variety of situations in which they use prefilled syringes. Most clients contextualized their use in two situations: 1) They did not have time to prepare their drugs themselves, 2) They were having withdrawal symptoms and prefilled syringes were the only things available. Risky injection events, including prefilled syringe use, were almost always described in the context of avoiding withdrawal symptoms. Drug injection locations influence how participants are able to access and use drugs. This often came up when participants talked about being at work or in other locations where injection was difficult or where taking too long would cause suspicion. The environments in which participants reported injecting were described as altering their behaviors because of some external pressure or circumstance causing them to inject quickly and often without regard to the consequences of that injection event in relation to disease transmission of overdose risk.

Pressure to inject quickly

Due to Police Presence—PFSU was discussed in terms of police presence and risk of getting stopped for possession of drugs or injection paraphernalia. One participant described it as a way to not get your hands dirty and not get caught in the possession of drugs or injection equipment. Participants also talked about the convenience of being able to go to a location, purchase drugs in prefilled syringes to use in that location, and leave without having to deal with anything

else. This was reported as a positive factor because it was convenient and protected them from police interactions.

> For you know, to don't [not have to] carry that stuff. To don't [not] have it with you, in your possession…to prevent… you don't get your hands dirty. Yeah, you know, you don't have to worry about, you know, carrying… you know, a needle or… the dope. [Male, age 38]

Due to employment—Participants also described competing obligations such as work as influencing their drug use practices. A male participant described the first time he used prefilled syringes as being convenient because his connect was able to bring the drugs directly to his work so he didn't have to leave for a long period of time to prepare the drugs for injection.

> The first time because I was at work. I couldn't leave. And they brought it to me as [a] courtesy. I mean they're like, here. Here's a couple filled for you. [Male, age 48]

Another participant described a situation where she would leave work, go to a house to get high using a prefilled syringe and then be able to go back to work without any issues. She also described not having to worry about getting stopped to and from going to inject because she did not have possession of drugs or injection equipment.

> Well when I go to purchase the prefilled syringe. When I'm there I go, you know, go to his house and I can sit down and do it right there. And then, get up within a couple of minutes and then leave. And now I don't have to worry about getting in trouble on the way there or on the way back. Unless they're going to get me for under the influence and if that's the case then I'm got. But I mean that worked really good as far as work went. I could go there, give him, you know, hand him 20 bucks, get a good shot, and go back to work. [Female, age 36]

Due to other structural factors/injection location—Other structural factors and injection locations also influenced prefilled syringe use. Participants described situations where they felt rushed to inject and therefore, purchasing and using a prefilled syringe was most convenient. A majority of participants talked about using drugs in public bathrooms and needing to get in and out as quickly as possible so people were not suspicious or knocking on the door trying to get in. These public injection locations influence risk behaviors by rushing the injection process so prefilled syringes are a convenient way to avoid spending too much time and looking suspicious. This could also decrease the chance a person would get caught by the police while injecting.

> Usually in a bathroom. If you're in a bathroom, like at Starbucks, Ralphs, wherever and you're using you want to do it as quick as you can. It sucks when you've got people knocking on the door, and you're trying to find a vein. [Male, age 36]

Being in the midst of addiction/chaotic lifestyle— For most participants, PFSU occurred in the context of active addiction and a chaotic lifestyle. Overall, prefilled syringes were thought of as a risky behavior. Participants discussed how their behaviors were a result of environmental factors or situations they had little or no control over. Many of these situations resulted from trying to avoid withdrawal symptoms but also from being in a public environment such as a bathroom or even at work, as discussed previously. Physical microenvironmental factors such as drug injection locations affect users ability to practice safe behaviors. One participant who used prefilled syringes talked about his use in terms of being a heroin addict. Prefilled syringes were discussed as being just

another risky behavior but one that was less important than the other problems he was already facing.

> I, I mean a lot of risky behavior comes with living on the street and being a heroin addict, a lot of risky behavior. You get to the point where [you'll do just about anything to get high]… I mean I've had it to where, I was in a [restaurant] by the border, the dope spills on the floor and I suck it back up with a syringe. I've been in a [restaurant] where I forgot to bring water with me, but wanted a fix so bad I drew water from the toilet; I flushed it and drew. I've done a lot of risky behavior. Comes with that life style. Where you just don't care. You're already homeless. You're already addicted. You're already sick with life. You're already, wishing for you to cross the street and have a car just take you out. It's pretty… it's pretty crazy. [Male, Age 33]

What are participants' rationales for and attitudes towards this behavior?

Unknown contents of the syringe— Several participants reported they have never purchased prefilled syringes but that they know they are sold in San Diego. Among those who reported they have never purchased prefilled syringes, it was discussed as being riskier and something they would never do because they don't know what the actual contents of the syringes are.

> Not from my experiences, but yeah there is an area there, that they would sell that. …we don't take anything that's already in the syringe because we don't know what's in it, it's already dangerous that we do this stuff. Well to me I tell him that I don't want it ya know like, I would want it in the bag. Safer. But yeah, there is an area there, there's like a bridge actually. Everybody's sharing, and everybody's sharing syringes, and selling it in the syringes and selling the stuff, too. [Female, age 34]

> Yeah. I never will shoot anything that I don't see drawn up cuz [because] it might just, might not be what you think it is. Could be a hot shot. It could be just water. It could be nothing. It could be a tootsie roll. If it looks like the color of what you're used to and it might not be what it is. You don't know what the heck they drew up.

> I would never in my life buy something that ain't [I did not] draw up. [Male, age 54]

Could get ripped off—related to the unknown contents of the syringe and trust, getting ripped off was another theme that several participants discussed. Several participants talked about only trusting their friends when it comes to something like prefilled syringes. One participant who purchased prefilled syringes talked about the fact that he wouldn't buy them because he doesn't trust others and because he didn't want to get ripped off, however, he had purchased them a few times because they were the only thing available.

> Yeah it is happening here. It is. I mean I just don't buy it 'cause [because] you never know how much sits in there you know they could mix it with something. You know you never know so it could be a rip off so that's why I never buy it that way. You know I get my money's worth. Unless I'm buying it from a friend that I trust then I, I would. [Male, age 23]

Could get a hot shot—Participants reported that one of the fears of using prefilled syringes is receiving a "Hot Shot", which they define as the last shot you will ever get because it is meant to kill you. According to participants a hot shot could be a number of things including a stronger than normal dose or a syringe filled with poison or another deadly substance.

> That's gonna [going to] be your last shot if you get one of those [hot shot]. I don't know exactly what they make them with, but I know they're not nice and they're on purpose… I could never figure out why anybody would do- want to do that [kill someone]. [Male, age 48]

Participants who reported they never used prefilled syringes talked about the danger of "hot shots" as a reason they would never use prefilled syringes.

Hot shots were discussed in relation to trust and respect. As discussed previously trust played a major role in a participants willingness to use prefilled syringes and engage in other risky behaviors. Respect was also discussed in the context of participants' drug dealers and drug circle. A few participants talked about having mutual respect and if that did not happen then a user could receive a hot shot. Putting trust in another person to prepare your drugs can be a risky endeavor.

> I wouldn't put that much trust into somebody, so I don't know. I've never bought one, I'm sure you could. I mean, I've done some silly things, like draw water out of a toilet, but made sure I flushed it a couple of time to, to mix up my drugs. It's that a sad choice for somebody. But ya [you] know, when I was growing up, people had etiquette and if you were not respectful to your drug dealer or your drug circle, a lot of people died. One of the ways is a "hot shot" and [it is] called [that] when they put poison in your syringe and you shoot it up and you die. And so, and that's always been a haunt in my-my closet, so I don't let anybody mix up my dosage. [Male, age 43]

Trust—A recurring theme among PWID who did not report prefilled syringe use was trust. Most participants reported they don't trust what others would put in the syringe, fear "hot shots", as described in the quote above, and getting ripped off. Trust was also discussed in terms of control over their own situation. PWID want to have control over their own preparation process because they do not trust others but when they are dope sick, their behaviors change because there is an immediate need to deal with withdrawal.

How do participants think this influences their HIV risk?

Disease transmission risk—In terms of disease transmission risk for HIV and Hepatitis C, several participants reported a fear of using prefilled syringes

because of the risk of disease transmission. Several participants reported there are PWID who are upset they got infected with HIV therefore they try to spread their infection to others. Participants described disease transmission risk in terms of the inevitability of getting infected, in response to competing risks/priorities, and in terms of good/bad luck or wishful thinking.

> Yes. My biggest worry is now with hepatitis because you know you can get several types of forms of hepatitis by sharing needles. But my biggest [worry] is using a needle, [after someone who] has AIDS and [HIV] is still active into the needle, you know, that's my biggest worry. [Male, age 58]

Several participants also discussed how those who are infected are sometimes angry they are infected and try to infect others. This is particularly worrisome with prefilled syringes because the person who prepares the syringe could knowingly contaminate the syringe and the drug solution in an attempt to infect others. The user may not be aware of disease status of the person who prepared the syringes, which could significantly increase their chance of getting infected. One participant even said that others have told him they intentionally tried to infect him after he had already injected.

> There [are] people out here that have HIV. And they're angry about it you know. I've seen it, and I know people that have it and [they] are angry and have given it to other people. There [are] people that have told me, they've given the [me] HIV or poison[ed] me through needles. [Male, age 36]

There was a common theme of the wishful/hopeful thinking about disease transmission. Given medical advancements in treatment for hepatitis C and other diseases, PWID reported they were hopeful there would be a cure before they

could die from infection making them care less about their risk behaviors. This was coupled with participants talking about the inevitability of infection; that HIV/HCV infection is part of being a drug user.

> [I] think about it as, get well now, get high now… deal with disease later. Hopeful thinking. Yeah, there'll be a cure by the time it [kills you], you know. Carefree attitude, you know, wishful thinking, hopeful thinking, or just not caring at all. Some people are [very] meticulous, you know. No it has to be [clean] even if they're sick. They'll go through, they're snort it or smoke it or do whatever they have to do. Some people, like I was, sadly to say, was [were] just care free. I mean, not to the HIV, to the Hep [Hepatitis] C because I already Hep [Hepatitis] C. [Male, age 33]

Participants also describe disease transmission in terms of competing risks, especially when discussing preventing withdrawal symptoms as more important than preventing disease transmission. PWID may weigh their participation in high risk behaviors not only based on their perception of the risks associated with that behavior, but also on the consequences of not engaging in that behavior, such as experiencing withdrawal symptoms. The same is true when related to the theme of trust. If a person refuses a prefilled syringe from a dealer or a friend there could be other consequences such as loss of trust, or loss of a drug dealer, that could impact them in other ways.

DISCUSSION

Our findings illustrate that PFSU among our participants emerges as a result of both micro (e.g., drug injection location, homelessness, local policing practices, and sterile injection equipment availability) and macro (e.g., drug trafficking routes, gendered risk) environmental influences. Recent PFSU was

not common and there is some stigma surrounding their use. Among participants who did not report PFSU, they reported not using them because they could increase risk of overdose, disease transmission, and because of the unknown contents of the syringes. Among those who reported PFSU, risks associated with their use were recognized, but situational factors such as the need for a quick high and to avoid withdrawal drove their use.

The convenience of PFSU, especially as it results to policing and the need for a quick high, emerged as a main them. Previous research has described environmental situations where PWID cannot engage in recommended behaviors due to factors such as the need for rapid injection because of fear of arrest.[38, 39] Policing and fear of arrest emerged as a major theme in our interviews and PFSU was discussed in terms of participants' being able to protect themselves from law enforcement. This was described in many situations, such as avoiding getting stopped for possession of drugs and/or injection equipment, and also in avoiding being suspicious from being in the bathroom or another public location too long. Policing practices also influences SEP use and studies indicate that PWID who use prefilled syringes are more likely to have negative interactions with police, including having their syringes confiscated.[38, 40, 41] Macroenvironmental factors such as laws about drug and injection equipment possession can alter how PWID obtain and use drugs because they do not want to get caught using. This may be particularly important for users who have a past police record.

User/dealer relationships were brought up in the context of trust and social norms. Participants reported their dealer often required they first inject with the dealer before they can purchase drugs. This process often involves the use prefilled syringes the dealer has prepared. In other situations dealers would give users prefilled syringes for a quick high and/or to test the quality during drug transactions. Research on user/dealer relationship, especially in the context of the “social supply” of drugs, highlights how drug distribution is linked with friendship and trust and can be recognized as a cultural norm to develop friendships before distribution.[42] The friendship and trust aspects of dealing serve as a form of risk management of dealers because their friends are less likely to report them to the police and it also ensures higher quality and quantities of drugs for users.[43-45] In the context of prefilled syringes, distribution of prefilled syringes may represent a sign of trust, but also one of control over the supply by the dealer.

In terms of disease transmission risk, most participants discussed disease transmission in terms of drug use and PFSU. Among those who did not report PFSU, risk of infection was a common theme because participants reported they did not know where the syringes or drug solution come from. Many also described PFSU as a death warrant because the syringe could be filled with solution that is meant to kill, what participants describe as a “hot shot”. In many setting HCV infection has become normative and is thought of as inevitable by many drug users. PWID report that they have a limited ability to control disease

transmission and thus think of infection as a matter of bad luck. PWID also often take a fatalistic view and about the risk from other situations, such as getting hit by a car, as one participant in our interviews described. Others have described this fatalistic type of risk neutralization as risk comparison.[46, 47] Similar notions among our participants were talked about when comparing the risk of dying from Hepatitis C to the risk of dying from overdose. PWID in other studies have described their health in terms of "good or back luck" [47] and rationalize disease transmission in terms of being an accident. [47]

Participants also describe disease transmission in terms of competing risks, especially when discussing preventing withdrawal symptoms as more important than preventing disease transmission. PWID may weigh their participation in high risk behaviors not only based on their perception of the risks associated with that behavior, but also on the consequences of not engaging in that behavior, such as experiencing withdrawal symptoms. The same is true when related to the theme of trust. If a person refuses a prefilled syringe from a dealer or a friend there could be other consequences such as loss of trust, or loss of a drug dealer, that could impact them in other ways.

Limitations

Our small sample size of PWID who reported PFSU may limit our generalizability, however, smaller sample sizes are generally sufficient when studying emerging behaviors.[48] PWID are hard to reach, especially those who are homeless and who engage in the riskiest behaviors. STAHR II did not

specifically recruit participants based on PFSU. While efforts were made to recruit a diverse sample of participants who reported PFSU, however our results may not be generalizable to all PWID who report PFSU. Studies of sensitive and stigmatized behaviors are subject to socially desirable responses that may result in underreporting of results. We made every effort possible to reduce socially desirable responding by ensuring participants of their confidentiality, phrasing questions in non-judgmental ways, and developed a rapport with participants to ensure their comfort. We also informed participants they didn't have to discuss anything they did not feel comfortable discussing. During the interviews, several participants were hesitant to report and discuss some of their riskiest behaviors, including PFSU and at times did not provide details to contextualize PFSU.

Conclusions

Our findings suggest that PFSU is a result of the situational context in which PWID inject drugs and are directly influenced by their risk environment. PFSU is shaped by both microenvironmental factors such as local policing practices, availability of syringes and location of the syringe exchange program, and perhaps, power dynamics, and macroenvironmental factors such as laws which affect the frequency of the syringe exchange program, drug and injection equipment possession laws, and social norms. Individual knowledge influences risk behaviors, however, focusing on individual level behaviors only address part of the larger problem that are social, political, physical, and economic factors that influence disease transmission.[27] Recommendations include providing education

about the harms associated with PFSU while addressing the larger physical and social factors that influence risk taking. This includes expanding the syringe exchange program to other areas of San Diego County and changing policy that results in the confiscation of syringes and other injection equipment. Trust of injection partners and dealers should also be addressed to understand how trust of the source of syringes and drugs could be used to develop intervention programs to prevent risk injection practices. Additional research is needed to understand how PFSU changes over time, and to recruit frequent users of prefilled syringes to better understand this behavior.

Acknowledgements: Chapter 3, in full, is being prepared for submission to Substance Abuse and Misuse for publication of material. Co-Authors include Garfein, Richard; Roth, Alexis; Wagner, Karla; Cuevas-Mota, Jazmine; Strathdee, Steffanie; Perez, Ramona. The dissertation author is the primary author of this material.

REFERENCES

1. Bailey, S.L., et al., *Perceived risk, peer influences, and injection partner type predict receptive syringe sharing among young adult injection drug users in five U.S. cities.* Drug Alcohol Depend, 2007. **91 Suppl 1**: p. S18-29.

2. Hagan, H., et al., *Attribution of hepatitis C virus seroconversion risk in young injection drug users in 5 US cities.* J Infect Dis, 2010. **201**(3): p. 378-85.

3. Thorpe, L.E., et al., *Risk of hepatitis C virus infection among young adult injection drug users who share injection equipment.* Am J Epidemiol, 2002. **155**(7): p. 645-53.

4. Palmateer, N., et al., *Risk of transmission associated with sharing drug injecting paraphernalia: analysis of recent hepatitis C virus (HCV) infection using cross-sectional survey data.* Journal of Viral Hepatitis, 2014. **21**(1): p. 25-32.

5. McCoy, C.B., et al., *Parenteral transmission of HIV among injection drug users: assessing the frequency of multiperson use of needles, syringes, cookers, cotton, and water.* J Acquir Immune Defic Syndr Hum Retrovirol, 1998. **18 Suppl 1**: p. S25-9.

6. Magis-Rodriguez, C., et al., *HIV prevalence and correlates of receptive needle sharing among injection drug users in the Mexican-US border city of Tijuana.* Journal of Psychoactive Drugs, 2005. **37**: p. 333-339.

7. Wagner, K.D., R. Simon-Freeman, and R.N. Bluthenthal, *The association between law enforcement encounters and syringe sharing among IDUs on skid row: a mixed methods analysis.* AIDS Behav, 2013. **17**(8): p. 2637-43.

8. Koester, S.K. and L. Hoffer, *" Indirect Sharing": Additional HIV Risks Associated with Drug Injection.* AIDS and Public Policy Journal, 1994. **9**: p. 100-100.

9. Needle, R.H., et al., *HIV risk behaviors associated with the injection process: multiperson use of drug injection equipment and paraphernalia in injection drug user networks.* Subst Use Misuse, 1998. **33**(12): p. 2403-23.

10. Abdul-Quader, A.S., et al., *Effectiveness of structural-level needle/syringe programs to reduce HCV and HIV infection among people who inject drugs: a systematic review.* AIDS Behav, 2013. **17**(9): p. 2878-92.

11. Bramson, H., et al., *State laws, syringe exchange, and HIV among persons who inject drugs in the United States: History and effectiveness.* Journal of public health policy, 2015.

12. Des Jarlais, D.C., et al., *High coverage needle/syringe programs for people who inject drugs in low and middle income countries: a systematic review.* BMC public health, 2013. **13**(1): p. 53.

13. Bluthenthal, R.N., et al., *Higher syringe coverage is associated with lower odds of HIV risk and does not increase unsafe syringe disposal among syringe exchange program clients.* Drug and Alcohol Dependence, 2007. **89**(2): p. 214-222.

14. Strathdee, S.A. and D. Vlahov, *The effectiveness of needle exchange programs: a review of the science and policy.* AIDScience, 2001. **1**(16): p. 13.

15. Hagan, H., E.R. Pouget, and D.C. Des Jarlais, *A systematic review and meta-analysis of interventions to prevent hepatitis C virus infection in people who inject drugs.* J Infect Dis, 2011. **204**(1): p. 74-83.

16. Cooper, H.L.F., et al., *Spatial access to syringe exchange programs and pharmacies selling over-the-counter syringes predicts drug injectors' use of sterile syringes.* American journal of public health, 2011. **101**(6): p. 1118.

17. Des Jarlais, D.C., et al., *Residual injection risk behavior, HIV infection, and the evaluation of syringe exchange programs.* AIDS Education & Prevention, 2007. **19**(2): p. 111-123.

18. Spiller, M.W., et al., *HIV Infection and HIV-Associated Behaviors Among Persons Who Inject Drugs-20 Cities, United States, 2012.* MMWR. Morbidity and mortality weekly report, 2015. **64**(10): p. 270-275.

19. Rhodes, T., *The 'risk environment': a framework for understanding and reducing drug-related harm.* International Journal of Drug Policy, 2002. **13**(2): p. 85 - 94.

20. Rhodes, T. and M. Simic, *Transition and the HIV risk environment.* BMJ, 2005. **331**(7510): p. 220-3.

21. Booth, R.E., et al., *Drug injectors and dealers in Odessa, Ukraine.* J Psychoactive Drugs, 2003. **35**(4): p. 419-26.

22. Wagner, K.D., et al., *Control over drug acquisition, preparation and injection: Implications for HIV and HCV risk among young female injection drug users.* ISRN Addict, 2013. **2013**.

23. Rhodes, T., et al., *Explosive spread and high prevalence of HIV infection among injecting drug users in Togliatti City, Russia.* AIDS, 2002. **16**(13): p. F25-31.

24. Wagner, K.D., et al., *The social and environmental context of cross-border drug use in Mexico: findings from a mixed methods study of young injection drug users living in San Diego, CA.* J Ethn Subst Abuse, 2012. **11**(4): p. 362-78.

25. Heimer, R., et al., *The effect of acids on the survival of HIV during drug injection.* J Acquir Immune Defic Syndr, 2007. **45**(2): p. 144-50.

26. Koester, S., J. Glanz, and A. Barón, *Drug sharing among heroin networks: implications for HIV and hepatitis B and C prevention.* AIDS Behav, 2005. **9**(1): p. 27-39.

27. Syme, S.L., *Social determinants of health: the community as an empowered partner.* Prev Chronic Dis, 2004. **1**(1): p. A02.

28. SANDAG. *2012 San Diego-Baja California Border Crossings and Trade Statistics*. San Diego Association of Governments (SANDAG)-Committee on Binational Regional Opportunities 2013 [cited 2014 January 18, 2014].

29. Brouwer, K.C., et al., *Trends in Production, Trafficking, and Consumption of Methamphetamine and Cocaine in Mexico.* Substance Use & Misuse, 2006. **41**(5): p. 707-727.

30. City of San Diego. *Clean Syringe Exchange Pilot Program*. Community Services [cited 2015 February 10]; Available from: http://www.sandiego.gov/communityservices/programs/cleansyringe/index.shtml.

31. Robertson, A.M., et al., *Evaluating the impact of Mexico's drug policy reforms on people who inject drugs in Tijuana, B.C., Mexico, and San Diego, CA, United States: a binational mixed methods research agenda.* Harm Reduct J, 2014. **11**: p. 4.

32. Michael Quinn, P., *Qualitative Research & Evaluation Methods*. 2002: SAGE Publications.

33. Strauss, A. and J.M. Corbin, *Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory*. 1998: SAGE Publications.

34. Glaser, B.G., *Theoretical sensitivity: advances in the methodology of grounded theory*. Advances in the methodology of grounded theory. 1978: Sociology Press.

35. Carey, J.W. and D. Gelaude, *Systematic methods for collecting and analyzing multidisciplinary team-based qualitative data.* Handbook for team-based qualitative research, 2008: p. 227-274.

36. Crabtree, B.F. and W.L. Miller, *A template approach to text analysis: Developing and using codebooks, in doing qualitative research*, ed. W.L.M. B.F. Crabtree. 1992, Newbury Park, CA: Sage.

37. Matthew, B.M. and A.M. Huberman, *Qualitative Data Analysis: An Expanded Sourcebook*. 1994: SAGE Publications.

38. Beletsky, L., et al., *Syringe access, syringe sharing, and police encounters among people who inject drugs in New York City: a community-level perspective.* Int J Drug Policy, 2014. **25**(1): p. 105-11.

39. Beletsky, L., et al., *Syringe confiscation as an HIV risk factor: the public health implications of arbitrary policing in Tijuana and Ciudad Juarez, Mexico.* J Urban Health, 2013. **90**(2): p. 284-98.

40. Davis, C.S., et al., *Effects of an intensive street-level police intervention on syringe exchange program use in Philadelphia, PA.* Am J Public Health, 2005. **95**(2): p. 233-6.

41. Cooper, H.L., et al., *Drug-related arrest rates and spatial access to syringe exchange programs in New York City health districts: combined effects on the risk of injection-related infections among injectors.* Health Place, 2012. **18**(2): p. 218-28.

42. Taylor, M. and G.R. Potter, *From" Social Supply" to" Real Dealing": Drift, Friendship, and Trust in Drug Dealing Careers.* Journal of Drug Issues, 2013: p. 0022042612474974.

43. Coomber, R. and P. Turnbull, *Arenas of drug transactions: adolescent cannabis transactions in England—social supply.* Journal of Drug Issues, 2007. **37**(4): p. 845-865.

44. Akhtar, S. and N. South, *Hidden From Heroin's History: Heroin Use and Dealing within an English Asian Community-A Case Study.* Crime Prevention Studies, 2000. **11**: p. 153-178.

45. South, N., *Managing work, hedonism and'the borderline'between the legal and illegal markets: Two case studies of recreational heavy drug users.* Addiction Research & Theory, 2004. **12**(6): p. 525-538.

46. Peretti-Watel, P., *Neutralization theory and the denial of risk: some evidence from cannabis use among French adolescents.* Br J Sociol, 2003. **54**(1): p. 21-42.

47. Miller, P.G., *Scapegoating, self-confidence and risk comparison: The functionality of risk neutralisation and lay epidemiology by injecting drug users.* International Journal of Drug Policy. **16**(4): p. 246-253.

48. Patton, M.Q., *Qualitative evaluation and research methods*. 1990: SAGE Publications, inc.

Table 3.1: Sociodemographic characteristics of participants who reported prefilled syringe use (n=10)

Variable	Frequency n (%)
Gender	
Male	8(80%)
Female	2(20%)
Race/Ethnicity	
White	5 (50%)
Hispanic	3 (30%)
Black	1 (10%)
Other	1 (10%)
Age, years (mean, range)	40 (19-58)
Income (>10,000 yearly)	3 (30%)
Homeless (last 6 months)	9 (90%)
Education (≥ HS)	7 (70%)
Used syringe exchange program, last 6 months	4 (40%)
Years injecting (mean, sd)	18.5 (10.76)
Injected drugs in Mexico, last 6 months	2 (20%)

CHAPTER 4: PREDICTORS OF PREFILLED SYRINGE USE AMONG PERSONS WHO INJECT DRUGS IN SAN DIEGO, CA

Richard F. Armenta [1,2]
Hector Lemus[2]
Steffanie A. Strathdee[1]
Maria Rosario Araneta[3]
Victoria D. Ojeda[3]
Jazmine Cuevas-Mota[1]
Richard S. Garfein[1]

[1]University of California San Diego, School of Medicine, Division of Global Public Health, USA

[2]San Diego State University, Graduate School of Public Health, Division of Epidemiology, USA

[3]Division of Epidemiology, Department of Family and Preventive Medicine, University of California, San Diego, La Jolla, CA

ABSTRACT

Background: Behaviors that increase HIV and hepatitis C virus (HCV) infection and overdose risk are common among persons who inject drugs (PWID) and often result from environmental factors that impact harm reduction practices. One such behavior is prefilled syringe use (PFSU). The objective of this study was to determine predictors of PFSU in the last 6 months.

Methods: Beginning in June 2011, a community-based sample of PWID were enrolled into a longitudinal cohort in San Diego, CA. We analyzed data from three semi-annual follow-up visits (n=376) for participants who had at least one follow-up visit using generalized estimating equations.

Results: Among participants who completed a 6-month visit (n=293) 75% were male and mean age was 45.6 years (range: 19-76). Overall, 62 participants (9.5%) reported PFSU at any visit. In multivariable analysis adjusted for PFSU at baseline and time, opioid overdose (adjusted odds ratio [AOR]=3.17 95% confidence interval [CI]=1.70-5.93), sharing cookers, cotton, rinse water(AOR=4.86, 95% CI: 2.18, 10.82), being homeless (AOR=2.42, 95% CI: 1.33-4.42), and syringe exchange program (SEP) use (AOR=1.85, 95% CI: 0.99-3.44), all measured in the last 6 months, were associated with PFSU in the past 6 months.

Conclusions: PWID may use prefilled syringes as a consequence of their circumstances, such as being homeless, and out of necessity or because they cannot get enough sterile syringes. While SEPs are effective at reducing disease transmission, their expansion is warranted to provide more syringes and

larger coverage areas. Circumstances that lead to PFSU may also increase overdose risk. Interventions are needed that address the environmental influences that lead to high risk behaviors.

INTRODUCTION

In the United States, persons who inject drugs (PWID) are the highest risk group for infection with hepatitis C virus (HCV)[1] and constitute one of the main risk groups for human immunodeficiency virus (HIV) infection.[2] While there has been a considerable decline in new HIV infections in the US[3], PWID still account for approximately 8% of new HIV infections[3]. Furthermore, 15% of those living with HIV[4] and approximately 43.1% of PWID are infected with HCV.[5] Studies show that behaviors linked to HIV and HCV infection, such as the sharing of syringes and injection paraphernalia (cookers, cotton, and rinse water), are common among PWID.[6-9] There are a number of factors that influence syringe and paraphernalia sharing among PWID such as homelessness, risk perception, injecting in a shooting gallery or other public space,[10] and the legal environment.[11] Among older PWID, receptive syringe sharing is associated with limited access to clean syringes, not using a syringe exchange program (SEP), injecting stimulants (methamphetamine and cocaine), and injecting with people with whom they have close social relationships such as family, spouses, or close friends.[6, 12-14]

While the health risks and factors associated with adverse outcomes among PWID are well documented, high-risk behaviors are still prevalent. However, there is less information available about how the practice of injecting drugs changes over time. Younger PWID are more likely to report unsafe injection practices [15] and thus, are at heightened risk of blood borne virus (BBV) infection. Studies found that HCV infection was acquired first and typically within

the first year of initiation of injection, while HIV infections occurred later, mainly due to the lower transmission efficiency of HIV.[16, 17] Research also suggests that PWID who initiate injecting at a younger age are more likely to develop high-risk injection behaviors such as syringe and paraphernalia sharing, high frequency injection, and injection in shooting galleries or other risky locations.[18]

Our previous research found that 32% of PWID in San Diego report ever using prefilled syringes, however, recent use was lower (4.6% reported using the past 6 months). This is concerning because we do not know how the drugs are prepared, or whether the syringes and injection paraphernalia used to prepare prefilled syringes are sterile. Risk for disease transmission may increase if non-sterile syringes are used, or if the drug solution or injection paraphernalia becomes contaminated. Overdose risk increases if the potency of the drug solution is greater than normal or unknown. Quantitative analyses showed that structural and environmental factors, such as access to syringes, homelessness, policing practice, and fear of arrest, influence prefilled syringe use. Qualitative interviews with PWID who reported prefilled syringe use uncovered that convenience, the need for a quick high, and fear of getting caught by police are driving factors for their use.[19] In other settings PFSU has been associated with younger age, more recent injection, and injecting homemade drugs.[20]

San Diego County, CA is a unique environment in that it shares the busiest land border crossing in the world with Tijuana, Baja California, Mexico and sits on a major drug trafficking route, which contributes to a high prevalence of drug abuse.[21] Approximately 20% of a sample San Diego based PWID

reported buying, using, and injecting drugs in Mexico[22]—behaviors potentially increasing the risk of HCV infection. The prevalence of HCV is 95% among PWID in Tijuana[23] compared to 27% among young PWID[24] and 38% among PWID tested at an Sexually Transmitted Infection (STI) clinic in San Diego.[25] This also may lead to behavior change as trends and behaviors may be shared in drug using environments, such as the use of prefilled syringe, or use of syringes that have already been filled with drug solution. PWID in Tijuana have reported prefilled syringe use and that prefilled syringes can be purchase in certain locales such as bars and clubs.[26]

The “risk environment” framework provides a conceptual model to guide our analysis, which includes the following aims: 1) quantify and characterize PWID who report PFSU in the past 6 months in a longitudinal study, and 2) identify factors associated with PFSU in the past 6 months. The analysis was based on the “risk environment”, which posits that micro and macro-environmental factors exogenous to the individual impact behaviors. Microenvironmental factors such as drug injection locations, income, and access to syringes, combined with macroenvironmental factors such as drug possession laws and policing practices, interact to produce HIV risk and other drug related harms.[27] Our hypotheses were based on our previous work that showed ever using prefilled syringes was associated with rushed injection due to police presence, lifetime overdose, injecting in public places, and injecting in Mexico.[19] Thus, we hypothesized that prior history of negative police interaction among PWID would promote high risk injection practices such as sharing syringes and

injection paraphernalia and PFSU. The results of this analysis will help researchers better understand how injection practices change over time, and how the structural HIV-related vulnerabilities influence risky behaviors.

METHODS

Study Population: Data for this study came from the Study of Tuberculosis, AIDS and Hepatitis C Risk (STAHR-II)—a longitudinal cohort study among PWID in San Diego County. As previously described,[28] participants were recruited between June 2012 and January 2014. Eligible participants were: 1) at least 18 years of age; 2) reported injecting drugs within the past month (i.e., staff confirmed observation of track marks or other physical evidence of injecting); 3) spoke English or Spanish; 4) planned to reside in San Diego County over the next 24 months; 5) were not participating in an intervention study related to their drug use or disease status; 6) agreed to venipuncture for serologic testing; and 7) provided written informed consent. Participants who were eligible to participate completed a total of 4 visits spaced 6 months apart. At enrollment the study protocols were explained to participants and informed consent was obtained prior to data collection. Participants completed a behavioral assessment and serologic testing for HIV and HCV at baseline and were scheduled to complete four semiannual follow-up assessment visits (five visits total). At follow-up visits, participants completed behavioral assessments to assess changes in behaviors during the 6 months prior to the interview and underwent serologic testing for HIV and HCV to measure incident infections if their previous test result was negative.

Eligible participants were compensated for time and travel at each visit.[28] The institutional review board at UC San Diego approved this study.

Participants were recruited through convenience sampling using targeted outreach methods, which included street outreach, advertising in areas known for high drug use, and word of mouth. Interviews were conducted at a storefront office and on a mobile van that parked in high drug-use neighborhoods throughout San Diego County. During baseline visits, all enrolled participants were asked to provide contact information that included name, address, phone number, and contact information for up to three additional individuals who could be contacted to remind participants about their appointments. Information about locations the participant frequented and defining marks such as tattoos and scars were also recorded to assist with retention efforts. All participants were given an appointment reminder card at each visit that listed all of their upcoming appointments and were sent post-card reminders about their appointments two weeks prior to their appointment. All participants were also called the day before to remind them of their upcoming appointment. In addition, all participants were sent birthday and holiday cards from the study to show our appreciation for their participation to remind them about the study. To increase retention, the outreach team also visited the local syringe exchange program (SEP) weekly and conducted outreach using a mobile RV unit set up to complete interviews and serologic testing. The mobile RV unit was taken to locations where it was known drug users frequent. At the time of this analysis the baseline, 6 month, and 12 month study visits were completed and participants were still being followed and

completing 18 and 24-month visits. The cut-off for follow-up for this analysis was January 31, 2015.

Data Collection and Laboratory Methods: Interviews were administered using computer–assisted personal interviewing (CAPI) software and were completed by trained interviewers who read the questions aloud and entered participant responses on a laptop computer. HIV testing was conducted using the HIV Unigold Recombigen rapid antibody test (Trinity Biotech PLC, Bray, Ireland). Those testing HIV seropositive were administered a second rapid antibody test using the OraQuick HIV rapid antibody test (Orasure Technologies Inc.) and blood samples were sent to San Diego County Health Department laboratory for confirmatory testing using Western blot assay. Confirmatory test results were available three weeks after testing. HCV testing was conducted using the OraQuick HCV rapid antibody test (Orasure Technologies Inc., Bethlehem, PA). Participants received pre- and post-test counseling. and test results were provided three weeks following their appointment. All participants testing negative for HIV and HCV were tested at subsequent follow-up visits, whereas those testing positive were not retested for that infection at subsequent visits. In addition, those testing positive were referred to a healthcare provider for clinical care, and all participants were offered referrals to drug treatment and local social services (e.g., housing, metal health services, food distribution centers).

Measures: The outcome of interest was PFSU in the previous 6 months as measured at the 6, 12, and 18-month visits. Other measures for this study come from the 6, 12, and 18-month interviews with baseline measures used as

covariates in the analysis. Baseline measures include age, gender, race/ethnicity, homelessness (self-perceived in the last 6 months), and PFSU in the past 6 months. Self-reported injection-related risk behaviors were assessed at each follow-up visit including receptive syringe sharing (yes vs. no) and cooker/cotton/rinse water sharing (yes vs. no). Other substance use variables assessed include duration of injecting, number of injecting partners, frequency of injecting heroin, methamphetamine, or crack/cocaine (weekly vs. less than weekly). Microenvironmental factors included education (≥high school vs. <high school), syringe source used most often, coded as safe (syringe exchange program, doctor/clinic/hospital, veterinary clinic/pet store, market) versus unsafe (spouse, family member, or sex partner, friend, drug dealer, "Hit doctor", or a person who helps you inject, shooting gallery, on the street, some other place), injection location most often coded as public (shooting gallery, construction site, alleyway, bar/club, on the street, vacant lot, park, freeway overpass/bridge, canyon, public restroom) versus private (my/someone else's home, car, hotel room), use of the syringe exchange program in the last 6 months, and whether they injected drugs in Mexico in the last 6 months because injecting in Mexico may influence PFSU due to PWIDs unfamiliarity with where to obtain drugs or injection equipment. Macroenvironmental factors included rushed injection due to police presence in the last 6 months (yes vs. no) and whether police presence affected where PWID buy or use drugs in the last 6 months (yes vs. no). Sexual risk behavior variable include engaging in sexual activities for money or other goods in the last 6 months. Health care utilization was assessed as any

hospitalization or emergency room (ER) visits in the past 6 months to measure access to care and its relation to overdose and PFSU. Finally, self-report overdose in the last 6 months (yes/no) and self-report abscesses in the last 6 months (yes vs. no) were assessed, and HIV and HCV prevalence and incidence were included from serologic testing. Participants who tested HIV or HCV positive at baseline were considered prevalent cases. Those testing positive at any follow-up visit were considered incident for that visit and prevalent thereafter.

Statistical Analysis: To examine predictors of PFSU in the past 6 months we first conducted univariate analyses and provide descriptive statistics of our baseline and follow-up samples. As a preliminary analysis, we compared the sociodemographic and behavioral characteristics and PFSU in the past 6 months at the 6-month follow-up visit and conducted a naïve analysis not taking repeated measures into account to describe the frequencies and distribution of our sample. To account for missing data in the sharing injection paraphernalia variable responses from the baseline visit were carried forward because data was not available for a subset of participants (n=133). A Lost to follow up analysis was conducted to determine if loss to follow-up resulted in participants represented in follow-up visits to be significantly different from those in the baseline sample. Pearson's chi-square and Wilcoxon rank sum tests were used to assess associations with categorical and continuous covariates, respectively. We further examined bivariate associations between sociodemographic and substance use characteristics with PFSU in the past 6 months. Since this analysis included repeated measures at three time points, we used generalized

estimating equations (GEE) with a logit link for binary outcomes and designed for analysis of correlated data. The median number of follow-up visits was 2 and median time between follow up visits was 6.1 months. We used data from the 6, 12, and 18 month follow-up visits in this analysis. Baseline data on PFSU was used as a covariate in the analysis to control for PFSU differences at baseline. Time was calculated as time since last visit, which ranged from 4 months to 18 months (mean of 6 months). The best variance-covariance matrix was fit based on parameters in the data by comparing the quasi-likelihood information criterion (QIC).[29] Our models use the exchangeable variance-covariance matrix. Variables that were significant at the p=0.20 level in bivariate analyses were considered for inclusion in multivariable logistic GEE analysis. Forward stepwise model building was conducted and confounding was assessed by determining changes in the odds ratio of greater than 10%. Variables with a p-value<0.05 were maintained in the final model. Meaningful interactions were assessed and none were found to be statistically significant. All analyses were conducted using SAS software version 9.3 (SAS, Cary, NC).

RESULTS

Sample characteristics

Among those who completed the 6 month follow-up visit, 75% were male with a mean age of 45.6 years (SD 11.3; range 19-70). Over half (60.0%) reported homelessness in the past 6 month and 94% reported earning less than $10,000 annually. Participants reported injecting heroin and methamphetamine in

the last 6 months (54% and 62%, respectively), but crack/cocaine injection was only reported by 6% of participants. High-risk behaviors such as sharing syringes and other injection paraphernalia were reported by 32% and 67% of participants, respectively. Eight percent of participants overdosed on opioids in the last 6 months. Additional participant characteristics are presented in Table 1.

Among the 576 participants enrolled in the study, 6 were lost to follow-up due to incarceration, 9 died during follow-up, and 17 moved out of San Diego County, leaving 544 (94.4%) able to return for follow-up. In total, 293 (51%) completed the 6-month visit and 49% completed the second follow-up visit; 65% (n=376) have completed at least one follow-up visit to date.

Given the large loss to follow-up, we compared baseline characteristics between participants who did and did not return for the 6 month follow-up visit (Table 1). The groups were similar except that PWID who were lost to follow-up were slightly younger (mean age 41.1 vs. 44.5 years), less likely to be HIV positive (5% vs. 12%), less likely to use the syringe exchange program (36% vs. 44%), reported greater need for drug treatment (80% vs. 71%), were more likely to have injected heroin in the past 6 months (80% vs. 62%) and less likely to have injected meth in the past 6 months (58% vs. 69%; data not shown). There were no differences in injection related risk behaviors (i.e. sharing syringes, cooker, cotton, rinse water) between the groups. In general, those lost to follow-up appeared to be less stable, higher intensity users.

Prefilled syringe use

A total of 42(14.4%), 29(10.9%), and 21(9.6%) participants reported PFSU in the past 6 months at the 6, 12, and 18 month follow up visits, respectively. Additionally, 26 (4.5%) participants reported purchasing prefilled syringes at baseline. Participants who reported PFSU in the past 6 months at their 6 month visit were slightly younger [mean age: 43.05(sd=10.73) vs. 46.08(sd=11.32)]. Those who reported PFSU in the past 6 months were also slightly younger at first injection (mean 21.71 vs. 23.56 years, p-value=0.07), reported receiving something in exchange for sex (21% vs. 6%, p-value<0.01), obtained their syringes most often from unsafe vs. safe locations most often (31% vs. 23%, p-value<0.03), injected most often in public vs. private places (39% vs. 22%, p-value<0.01), and were more likely to use the syringe exchange program (79% vs. 54%, p-value<0.01). Participants who reported PFSU in the past 6 months were more likely to report rushed injection due to police presence (36% vs. 12%, p-value<0.001) and that police presence affected where they buy/use drugs (50% vs. 32%, p-value=0.06), and were more like to report an overdose in the past 6 months (17% vs. 7%, p-value=0.02). Additional results are shown in table 2.

Longitudinal correlates of prefilled syringe use

Table 3 presents unadjusted longitudinal analyses using GEE to determine associations using with PFSU in the last 6 months. Bivariate analyses indicate that PWID who reported PFSU in the last 6 months were more likely to report being homeless, being stopped by the police in the last 6 months, and injecting with more people in the last 6 months. Participants who reported PFSU in the past 6 months were also more likely to use the SEP in the last 6 months, to

report sharing syringes, or other injection paraphernalia, in the last 6 months, to report rushed injection due to police presence in the last 6 months, and to report an overdose in the last 6 months.

In multivariable analysis adjusting for time to interview and PFSU at baseline, PWID who reported PFSU were more likely to report having overdosed on opioid drugs in the past 6 months (adjusted odds ratio [AOR]=3.17, 95% CI: 1.70-5.93), having shared other injection paraphernalia in the past 6 months (AOR=4.86, 95% CI: 2.18, 10.82), being homeless (self-perceived in the last 6 months) (AOR=2.42, 95% CI: 1.33-4.42), and were marginally more likely to report using the SEP in the past 6 months (AOR=1.85, 95% CI: 0.99-3.44; table 4).

DISCUSSION

In this community-based study of PWID in San Diego, we found that PFSU was not uncommon (13.2%) and was associated with homelessness; sharing cookers, cotton or rinse water; using the syringe exchange program; and opioid overdose in the past 6 months. Homelessness, injection paraphernalia sharing and SEP use suggest that PFSU may be practices out of necessity due to limited access to new injection equipment. Overdose might be a consequence of PFSU because the user cannot be certain of the preparation methods and contents of the syringe obtained.

Our finding that PFSU is associated with overdose in the past 6 months is particularly concerning as accidental overdose is the leading cause of death in

the United States.[30] Risk factors for overdose include injecting drugs, drug use frequency, drug purity, presence of adulterants in drug solutions, sexual abuse history, and loss of tolerance after periods of abstinence.[31-35] PFSU may increase overdose risk because many factors surrounding their use such as the purity and concentration of the drug solution in the syringe or how the solution was prepared (i.e., what the drugs are mixed/cut with) are unknown. Drug users may also obtain powdered drugs of unknown purity, however, prefilled syringes may increase overdose risk because PWID if they are used because the user is in a situation where injection needs to be rushed. Rapid administration of drugs increases blood concentration of the drug and increases overdose risk.[36] Risk of fatal overdose is also increased because PWID often do not report overdoses or call the police when an overdose occurs due to fear of arrest.[37]

Homelessness has been cited as a risk factor for injection initiation and mediates the relation between adverse events, such as being incarcerated or experiencing childhood abuse, and drug abuse.[38-41] Research suggests there is a temporal relation between injection related risk behaviors and homelessness. [38-42] Homeless PWID are more likely to report rushed injection, failure to cook and filter drugs, and unsafe disposal of syringes and other injection paraphernalia. [38-41] Further, homeless PWID are more likely to share injection paraphernalia due to insufficient income to obtain clean syringes and injection paraphernalia.[43] Paraphernalia sharing has also been reported as a result of confiscation of equipment by police.[44] PFSU among homeless PWID may be a result of police

presence and the need to inject but the inability to access clean syringes and injection paraphernalia.

In multivariable analysis, PFSU was associated with sharing other injection paraphernalia (i.e., cookers, cotton, rinse water). PWID who use PFSUs engage in other risky behaviors.. Parenteral exposure to HCV is one of the greatest risk factors for transmission among PWID.[8, 45] Though we did not find that PFSU was associated with HCV transmission in our sample, our population mean age is older (mean=45.6, SD=11.3) with a longer injection history (mean=21 years) and research shows that many PWID, especially those who engage in the riskiest behaviors, are at greatest risk for infection shortly after initiation into injection drug use.[46] Further, the fact that PWID who reported PFSU were more likely to share injection paraphernalia and to report using the SEP indicates they have greater need for services to protect themselves from BBV infection. The stronger association between sharing injection paraphernalia and PFSU than with sharing syringes and PFSU may indicate that PWID may not assume the syringes have been previously used, thus, education about the risks associated with PFSU is needed. In qualitative interviews PWID more often discussed the unknown nature of the drugs and preparation methods rather than the unknown nature of the syringe itself.

In San Diego, syringe access via the syringe exchange is limited to just two days a week for two hours each day in two locations.[47] While the locations are central, access may be difficult to access for remote users. The quantity of syringes distributed to each user is also limited to 20 per exchange; thus, those

who access the SEP may still have limited quantities of clean syringes, especially if they are frequent users. Our finding the PFSU was associated with using the SEP in the last 6 months may be a proxy for higher risk users. It is possible that those who access the SEP have greater need for syringes because they have limited access to them elsewhere. Though it is legal to purchase syringes in pharmacies in California[48], PWID report not all pharmacies are willing to sell to them. A systematic review of the literature found that while SEPs are an effective harm reduction strategy[49], their effectiveness is minimized among PWID who don't get all of their syringes from the SEP. PWID who report exclusively obtaining syringes from SEPs are significantly less likely to report syringe sharing,[13] however, not having access to sterile needles is often cited as a main factor driving injecting with a used syringe.[13, 50] Research also suggests that police activity interferes with PWID ability to access SEPs and that PWID who report SEP use are more likely to report arrest from injection paraphernalia possession.[11, 51, 52]

Though no criminal justice related variables remained significant in our final model, our bivariate analysis showed PFSU is associated with rushed injection due to police presence and that participants who report PFSU are more likely to report that police presence affects where they buy/use drugs. PWID who report PFSU were also more likely to report having been stopped by the police in the past 6 months. Previous research has described environmental situations where PWID cannot engage in recommended behaviors due to factors such as the need for rapid injection because of fear of arrest.[53, 54] Further, policing

practices influences SEP use and studies indicate that PWID who use SEPs are more likely to have negative interactions with police, including having their syringes confiscated.[51, 53, 55]

Results of this study should be interpreted with certain limitations in mind. First, PFSU was not the primary focus of the parent study; thus, important information about the context of PFSU is lacking. Though generalizability might be limited, the findings are still important in that they are the first to describe this behavior in our setting. Since PFSU is a recently recognized behavior, the specificity of our interview questions on this topic might have been suboptimal. For example, while the question about using prefilled syringes specifically excluded those that were prepared by injecting partners, and interviewers were trained to emphasize this point, some participants might have answered “yes” to this question even if they were present when the syringe was being prepared. Likewise, some participants might have answered “no” if they knew the dealer who sold drugs in prefilled syringes. Thus, there may be misclassification of the dependent variable which would like bias our findings towards the null hypothesis. Our data also suffered from lost to follow up of participants, however, sensitivity analyses showed there were few differences between those retained in the study and those lost to follow up. Motivating factors for PFSU were not ascertained in this study; therefore, more information is needed to better understand why PWID use prefilled syringes. Although our data are longitudinal our results cannot be used to infer causality and more information is needed to understand how PFSU might influence disease transmission among PWID. We

were unable to ascertain whether PFSU is a risk factor for HIV and HCV infection due to low numbers of incident cases of infection in our sample. Our data is self-reported; therefore, our results may suffer from socially desirable responses, reporting bias, and measurement error, which could all lead to weaker associations. Interviewers developed a rapport with participants to ensure accurate reporting of results. Further, in our 6 month data about half of participants were missing data on sharing injection paraphernalia due to skip pattern errors, therefore we carried their baseline observation forward to account for missing data. While the last observation carried forward can produce biased results,[56] behaviors among PWID are fairly consistent across time[57] and expect this to bias our results towards the null hypothesis.

Conclusion

Findings from this study suggest that PWID who use prefilled syringes might have structural and individual level factors that promote PFSU. Factors such as homelessness cause PWID to rely on others for their injection equipment due to a lack of a secure place to keep them and lack of resources. Additionally, unstable housing may lead to rushed injections because homeless PWID are concerned about being arrested while injecting in public. While the potential for HIV and HCV infection could be increased from using prefilled syringes that have been used before, we could not confirm this association in our study; however, the risk of opioid overdose was increased among those who used prefilled syringes suggesting that either the drug dosage is harder to gauge when the drug is obtained already in solution, or PFSU is associated with rushed injections

causing some PWID to inject more than they can tolerate. Interventions are also needed to address inequality within certain subgroups of PWID, especially those who access SEPs and who are homeless. Additional research is needed to look at incident PFSU in larger samples of PWIDs and should address associations with incident HIV, HCV, and overdose.

Acknowledgements: Chapter 4, in full, is currently being prepared for submission for publication of material. Co-Authors include Garfein, Richard; Cuevas-Mota, Jazmine; Strathdee, Steffanie; Ojeda, Victoria; Araneta, Happy; Lemus, Hector. The dissertation author is the primary author of this material.

REFERENCES

1. Suryaprasad, A.G., et al., *Emerging epidemic of hepatitis C virus infections among young nonurban persons who inject drugs in the United States, 2006-2012.* Clin Infect Dis, 2014. **59**(10): p. 1411-9.

2. Centers for Disease Control and Prevention, *HIV Surveillance Report, 2011*. 2011: http://www.cdc.gov/hiv/pdf/statistics_2011_HIV_Surveillance_Report_vol_23.pdf.

3. Centers for Disease Control and Prevention, *Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas—2012*. 2014: http://www.cdc.gov/hiv/pdf/surveillance_Report_vol_19_no_3.pdf.

4. Centers for Disease Control and Prevention, *Estimated HIV incidence in the United States, 2007–2010*, in *HIV Surveillance Supplemental Report*. 2012.

5. Lansky, A., et al., *Estimating the number of persons who inject drugs in the united states by meta-analysis to calculate national rates of HIV and hepatitis C virus infections.* PLoS One, 2014. **9**(5): p. e97596.

6. Bailey, S.L., et al., *Perceived risk, peer influences, and injection partner type predict receptive syringe sharing among young adult injection drug users in five U.S. cities.* Drug Alcohol Depend, 2007. **91 Suppl 1**: p. S18-29.

7. Hagan, H., et al., *Attribution of hepatitis C virus seroconversion risk in young injection drug users in 5 US cities.* J Infect Dis, 2010. **201**(3): p. 378-85.

8. Thorpe, L.E., et al., *Risk of hepatitis C virus infection among young adult injection drug users who share injection equipment.* Am J Epidemiol, 2002. **155**(7): p. 645-53.

9. Palmateer, N., et al., *Risk of transmission associated with sharing drug injecting paraphernalia: analysis of recent hepatitis C virus (HCV) infection*

using cross-sectional survey data. Journal of Viral Hepatitis, 2014. **21**(1): p. 25-32.

10. Magis-Rodriguez, C., et al., *HIV prevalence and correlates of receptive needle sharing among injection drug users in the Mexican-US border city of Tijuana.* Journal of Psychoactive Drugs, 2005. **37**: p. 333-339.

11. Wagner, K.D., R. Simon-Freeman, and R.N. Bluthenthal, *The association between law enforcement encounters and syringe sharing among IDUs on skid row: a mixed methods analysis.* AIDS Behav, 2013. **17**(8): p. 2637-43.

12. Rhodes, T., M. Davis, and A. Judd, *Hepatitis C and its risk management among drug injectors in London: renewing harm reduction in the context of uncertainty.* Addiction, 2004. **99**(5): p. 621-33.

13. Wood, E., et al., *Factors associated with persistent high-risk syringe sharing in the presence of an established needle exchange programme.* AIDS, 2002. **16**(6): p. 941-3.

14. Ksobiech, K., *A meta-analysis of needle sharing, lending, and borrowing behaviors of needle exchange program attenders.* AIDS Educ Prev, 2003. **15**(3): p. 257-68.

15. Novelli, L.A., et al., *Circumstances surrounding the first injection experience and their association with future syringe sharing behaviors in young urban injection drug users.* Drug Alcohol Depend, 2005. **77**(3): p. 303-9.

16. Garfein, R.S., et al., *Viral infections in short-term injection drug users: the prevalence of the hepatitis C, hepatitis B, human immunodeficiency, and human T-lymphotropic viruses.* Am J Public Health, 1996. **86**(5): p. 655-61.

17. Doherty, M.C., et al., *Correlates of HIV infection among young adult short-term injection drug users.* AIDS, 2000. **14**(6): p. 717-26.

18. Hahn, J.A., et al., *Hepatitis C virus seroconversion among young injection drug users: relationships and risks.* J Infect Dis, 2002. **186**(11): p. 1558-64.

19. Richard F. Armenta, A.M.R., Karla D. Wagner, Steffanie A. Strathdee, Stephanie K. Brodine, Jazmine Cuevas-Mota, Fatima Munoz, Richard S. Garfein, *Prevalence and Correlates of the Use of Prefilled Syringes Among People Who Inject Drugs in San Diego, CA.* Journal of Urban Health, 2015.

20. Booth, R.E., et al., *Drug injectors and dealers in Odessa, Ukraine.* J Psychoactive Drugs, 2003. **35**(4): p. 419-26.

21. SANDAG. *2012 San Diego-Baja California Border Crossings and Trade Statistics*. San Diego Association of Governments (SANDAG)-Committee on Binational Regional Opportunities 2013 [cited 2014 January 18, 2014].

22. Volkmann, T., et al., *Border crossing to inject drugs in Mexico among injection drug users in San Diego, California.* J Immigr Minor Health, 2012. **14**(2): p. 281-6.

23. White, E.F., et al., *Prevalence of hepatitis C virus and HIV infection among injection drug users in two Mexican cities bordering the U.S.* Salud Publica Mex, 2007. **49**(3): p. 165-72.

24. Garfein, R.S., et al., *HCV infection prevalence lower than expected among 18-40-year-old injection drug users in San Diego, CA.* J Urban Health, 2013. **90**(3): p. 516-28.

25. Gunn, R.A., et al., *Screening for chronic hepatitis B and C virus infections in an urban sexually transmitted disease clinic: rationale for integrating services.* Sex Transm Dis, 2001. **28**(3): p. 166-70.

26. Wagner, K.D., et al., *The social and environmental context of cross-border drug use in Mexico: findings from a mixed methods study of young injection drug users living in San Diego, CA.* J Ethn Subst Abuse, 2012. **11**(4): p. 362-78.

27. Rhodes, T., *The 'risk environment': a framework for understanding and reducing drug-related harm.* International Journal of Drug Policy, 2002. **13**(2): p. 85 - 94.

28. Robertson, A.M., et al., *Evaluating the impact of Mexico's drug policy reforms on people who inject drugs in Tijuana, B.C., Mexico, and San Diego, CA, United States: a binational mixed methods research agenda.* Harm Reduct J, 2014. **11**: p. 4.

29. Pan, W., *Akaike's information criterion in generalized estimating equations.* Biometrics, 2001. **57**(1): p. 120-5.

30. Centers for Disease Control and Prevention, *Web-based Injury Statistics Query and Reporting System (WISQARS)* 2014.

31. Britton, P.C., J.D. Wines, Jr., and K.R. Conner, *Non-fatal overdose in the 12 months following treatment for substance use disorders.* Drug Alcohol Depend, 2010. **107**(1): p. 51-5.

32. Brugal, M.T., et al., *Factors associated with non-fatal heroin overdose: assessing the effect of frequency and route of heroin administration.* Addiction, 2002. **97**(3): p. 319-27.

33. Coffin, P.O., et al., *Opiates, cocaine and alcohol combinations in accidental drug overdose deaths in New York City, 1990-98.* Addiction, 2003. **98**(6): p. 739-47.

34. Darke, S. and W. Hall, *Heroin overdose: research and evidence-based intervention.* J Urban Health, 2003. **80**(2): p. 189-200.

35. Silva, K., et al., *Factors associated with history of non-fatal overdose among young nonmedical users of prescription drugs.* Drug Alcohol Depend, 2013. **128**(1-2): p. 104-10.

36. Davidson, P., *Circumstances of Death: As Assessment of the Viability of Using Non-toxicological Coronial Data to Investigate Opiate Overdose Risk Factors*. 1999: National Centre for Research into the Prevention of Drug Abuse.

37. Davidson, P.J., et al., *Fatal heroin-related overdose in San Francisco, 1997-2000: a case for targeted intervention.* J Urban Health, 2003. **80**(2): p. 261-73.

38. Krishnan, A., et al., *Post-release substance abuse outcomes among HIV-infected jail detainees: results from a multisite study.* AIDS Behav, 2013. **17 Suppl 2**: p. S171-80.

39. Briggs, D., et al., *Injecting drug use and unstable housing: Scope for structural interventions in harm reduction.* Drugs: Education, Prevention, and Policy, 2009. **16**(5): p. 436-450.

40. Aidala, A., et al., *Housing status and HIV risk behaviors: implications for prevention and policy.* AIDS Behav, 2005. **9**(3): p. 251-65.

41. Small, W., et al., *Impacts of intensified police activity on injection drug users: Evidence from an ethnographic investigation.* International Journal of Drug Policy, 2006. **17**(2): p. 85-95.

42. Linton, S.L., et al., *The longitudinal association between homelessness, injection drug use, and injection-related risk behavior among persons with a history of injection drug use in Baltimore, MD.* Drug Alcohol Depend, 2013. **132**(3): p. 457-65.

43. Bourgois, P., *The moral economies of homeless heroin addicts: confronting ethnography, HIV risk, and everyday violence in San Francisco shooting encampments.* Subst Use Misuse, 1998. **33**(11): p. 2323-51.

44. Werb, D., et al., *Effects of police confiscation of illicit drugs and syringes among injection drug users in Vancouver.* Int J Drug Policy, 2008. **19**(4): p. 332-8.

45. Mathei, C., et al., *Evidence for a substantial role of sharing of injecting paraphernalia other than syringes/needles to the spread of hepatitis C among injecting drug users.* J Viral Hepat, 2006. **13**(8): p. 560-70.

46. Garfein, R.S., et al., *Prevalence and incidence of hepatitis C virus infection among young adult injection drug users.* J Acquir Immune Defic Syndr Hum Retrovirol, 1998. **18 Suppl 1**: p. S11-9.

47. City of San Diego. *Clean Syringe Exchange Pilot Program*. Community Services [cited 2015 February 10]; Available from: http://www.sandiego.gov/communityservices/programs/cleansyringe/index.shtml.

48. California Department of Public Health-Office of AIDS. *Access to Sterile Syringes*. 2015 [cited 2015 March 15]; Available from: http://www.cdph.ca.gov/programs/aids/Pages/OASyringeAccess.aspx.

49. Abdul-Quader, A.S., et al., *Effectiveness of structural-level needle/syringe programs to reduce HCV and HIV infection among people who inject drugs: a systematic review.* AIDS Behav, 2013. **17**(9): p. 2878-92.

50. Strathdee, S.A., et al., *Needle exchange is not enough: Lessons from the Vancouver injecting drug use study.* Aids, 1997. **11**(8): p. F59-F65.

51. Davis, C.S., et al., *Effects of an intensive street-level police intervention on syringe exchange program use in Philadelphia, PA.* Am J Public Health, 2005. **95**(2): p. 233-6.

52. Miller, C.L., et al., *Injecting drug users' experiences of policing practices in two Mexican-US border cities: Public health perspectives.* International Journal of Drug Policy, 2008. **19**(4): p. 324-331.

53. Beletsky, L., et al., *Syringe access, syringe sharing, and police encounters among people who inject drugs in New York City: a community-level perspective.* Int J Drug Policy, 2014. **25**(1): p. 105-11.

54. Beletsky, L., et al., *Syringe confiscation as an HIV risk factor: the public health implications of arbitrary policing in Tijuana and Ciudad Juarez, Mexico.* J Urban Health, 2013. **90**(2): p. 284-98.

55. Cooper, H.L., et al., *Drug-related arrest rates and spatial access to syringe exchange programs in New York City health districts: combined effects on*

the risk of injection-related infections among injectors. Health Place, 2012. **18**(2): p. 218-28.

56. Streiner, D.L., *Missing data and the trouble with LOCF.* Evid Based Ment Health, 2008. **11**(1): p. 3-5.

57. Anthony, J.C. and K.R. Petronis, *Early-onset drug use and risk of later drug problems.* Drug Alcohol Depend, 1995. **40**(1): p. 9-15.

Table 4.1: Lost to follow up analysis comparing participants who have completed at least one follow up visit to those who have not completed any follow up visits at baseline

Variable	Total n=574	≥1 Follow up n=376	Lost to follow up n=198	p-value
Demographics				
Mean age, years (mean, sd)	43.34(11.7)	44.51(11.29)	41.11(12.18)	0.001
Male gender				0.79
Male	418(72.9%)	272(72.5%)	146(73.7%)	
Female	149(26.0%)	98(26.1%)	51(25.8%)	
Transgender male-to-female	5(0.9%)	4(1.1%)	1(0.5%)	
Transgender female-to-male	1(0.2%)	1(0.3%)	0(0.0%)	
Race/Ethnicity				0.29
White, non-Hispanic	292(50.9%)	196(52.1%)	96(48.5%)	
Hispanic	178(31.0%)	107(28.5%)	71(35.9%)	
Black, non-Hispanic	50(8.7%)	36(9.6%)	14(7.1%)	
Other	54(9.4%)	37(9.8%)	17(8.6%)	
Monthly Income (>10,000 vs. <=10,000)	182(31.8%)	112(29.9%)	70(35.5%)	0.17
Single vs. Married	509(89%)	329(88%)	180(91%)	0.22
Education level (>=HS vs. <HS)	378 (66%)	247(65%)	131 (66%)	0.83
Homeless (yes vs. no)	351(61%)	227(60%)	124(63%)	0.60
Traveled to MX, last 6 months	161(28.3%)	112(29.8%)	49(25.5%)	0.29
Used/Injected drugs in MX, last 6 months	102(18.0%)	72(19.1%)	30(15.6%)	0.30
Drug Use				
Mean years injecting (mean, sd)	20.80(13.44)	21.50 (13.23)	19.48 (13.78)	0.07
Mean age first injection, years (mean, sd)	22.53(8.22)	23.01 (8.66)	21.63 (7.24)	0.16
Injected heroin, last 6 months	374(68.0%)	226(62.1%)	148(79.6%)	<0.001
Injected crack, last 6 months	86(15.5%)	53(14.5%)	33(17.3%)	0.39
Injected meth, last 6 months	359(64.9%)	250(68.7%)	109(57.7%)	0.01
Used two or more drugs simultaneously, last 6 months	166(28.9%)	101(26.9%)	65(32.8%)	0.13
Used syringe exchange program, last 6 months (yes vs. no)	236(41.1%)	165(43.9%)	71(35.9%)	0.06
Shared syringes, last 6 months (yes vs. no)	289(59.2%)	189(59.6%)	100(58.5%)	0.81
Shared any injection paraphernalia, last 6 months (yes vs. no)	394(68.2%)	251(66.2%)	143(71.9%)	0.26
Health care utilization and health status				
Any ER visit, last 6 months	195(34.2%)	138(36.7%)	57(29.2%)	0.07
Any hospital visit, last 6 months	98(17.2%)	70(18.6%)	28(14.4%)	0.20
Had an abscess, last 6 months	131(27.0%)	82(26.0%)	49(28.7%)	0.53

Table 4.1 Cont: Lost to follow up analysis comparing participants who have completed at least one follow up visit to those who have not completed any follow up visits at baseline

Variable	Total n=574	≥1 Follow up n=376	Lost to follow up n=198	p-value
Overdosed, last 6 months	45(7.9%)	29(7.7%)	16(8.1%)	0.86
HIV results (positive vs. negative; n=553)	52(9.4%)	43(11.8%)	9(4.8%)	<0.01
HCV results (positive vs. negative; n=552)	365(66.1%)	241(66.4%)	124(65.6%)	0.85
TB results (positive vs. negative; n=502)	120(23.9%)	80(23.6%)	40(24.5%)	0.82
Need for drug treatment (Any need vs. no need)	421(74.1%)	265(71.2%)	156(79.6%)	0.03

Table 4.2: Characteristics of participants by self-reported prefilled syringe use at the 6-month follow-up visit (n=291)

	Total	Yes	No	p-value
Socio-demographics				
Mean age, years (mean, sd)	45.64 (11.27)	43.05(10.73)	46.08(11.32)	0.09
Male gender	218(75%)	32(76%)	186(75%)	0.76
Race/Ethnicity				0.36
White	146(50%)	20(48%)	126(51%)	
Hispanic	84(29%)	16(38%)	68(27%)	
Black	32(11%)	2(5%)	30(12%)	
Other	28(10%)	4(10%)	24(10%)	
Annual income (>10,000 vs <=10,000)	18(6%)	4(10%)	14(6%)	0.34
Single vs. married	169(60%)	25(64%)	144(59%)	0.57
Education level (>HS vs. <=HS)	104(36%)	17(40%)	87(35%)	0.79
Homeless (yes vs. no)	174(60%)	34(81%)	140(56%)	<0.01
Country of birth	272(94%)	38(90%)	234(94%)	0.56
Substance use				
Mean years injecting (mean, sd)	21.9 (13.2)	21.7 (12.5)	21.9 (13.3)	0.93
Mean age first injection, years (mean, sd)	23.1 (8.6)	20.5 (6.9)	23.6 (8.7)	0.07
Received something in exchange for sex	23(8%)	9(21%)	14(6%)	<0.001
Obtained syringes most often from safe vs. unsafe source, last 6 months				0.03
Safe source	185(64%)	29(69%)	156(63%)	
Unsafe source	70(24%)	13(31%)	57(23%)	
Unknown	36(12%)	0(0%)	36(14%)	
Injected most often in public vs. private place, last 6 months				<0.01
Private place	182(63%)	25(61%)	157(63%)	
Public place	72(25%)	16(39%)	56(22%)	
Unknown	36(12%)	0(0%)	36(14%)	
Used syringe exchange program, last 6 months	168(58%)	33(79%)	135(54%)	<0.01
Shared syringes, last 6 months				0.31
Yes	92(32%)	17(40%)	75(30%)	
No	78(27%)	8(19%)	70(28%)	
Unknown	121(42%)	17(40%)	104(42%)	
Shared any injection paraphernalia, last 6 months				<0.01
No	81(28%)	4(10%)	77(31%)	
Yes	194(67%)	37(88%)	157(63%)	

Table 4.2 Cont: Characteristics of participants by self-reported prefilled syringe use at the 6-month follow-up visit (n=291)

	Total	Yes	No	p-value
Unknown	16(5%)	1(2%)	15(6%)	
Rushed injection police presence, last 6 months				<0.01
No	194(67%)	22(52%)	172(69%)	
Yes	45(15%)	15(36%)	30(12%)	
Unknown	52(18%)	5(12%)	47(19%)	
Police presence affected where buy/use drugs, last 6 months				0.06
No	130(45%)	16(38%)	114(46%)	
Yes	101(35%)	21(50%)	80(32%)	
Unknown	60(21%)	5(12%)	55(22%)	
Injected drugs in Mexico, last 6 months	25(9%)	5(12%)	20(8%)	0.41
Injected heroin, last 6 months	157(54%)	29(69%)	128(51%)	0.03
Injected crack, last 6 months	24(8%)	6(14%)	18(7%)	0.12
Injected meth, last 6 months	180(62%)	32(76%)	148(59%)	0.04
Health care utilization and health status				
Any hospital/ER visit, last 6 months	136(47%)	20(48%)	116(47%)	0.90
Had an abscess, last 6 months	98(34%)	19(45%)	79(32%)	0.09
Overdosed, last 6 months	23(8%)	7(17%)	16(7%)	0.02
HIV results				0.74
Non reactive	204(70%)	32(76%)	172(69%)	
Incident	1(0%)	0(0%)	1(0%)	
Prevalent	33(11%)	3(7%)	30(12%)	
Unknown/negative at baseline	53(18%)	7(17%)	46(18%)	
HCV results				0.11
Non reactive	86(30%)	8(19%)	78(32%)	
Incident	12(4%)	0(0%)	12(5%)	
Prevalent	181(63%)	33(79%)	148(60%)	
Unknown/negative at baseline	10(3%)	1(2%)	9(4%)	

Table 4.3: Unadjusted factors associated with prefilled syringe use in the past 6 months using GEE among persons who inject drugs in San Diego, CA (n=376)

	Odds Ratio	95% Confidence Interval	p-value
Sociodemographic factors			
Age, 5 year increase (mean, SD)	0.93	0.84, 1.04	0.21
Gender	Ref	Ref	Ref
Male			
Female	1.30	0.74, 2.31	0.83
Transgender	1.89	0.20, 17.13	0.30
Race/Ethnicity			
White	Ref	Ref	Ref
Hispanic	1.14	0.65, 1.98	0.64
Black	0.58	0.16, 2.15	0.42
Other	1.14	0.49, 2.69	0.76
Annual Income, < $10,000 (vs. > $10,001 USD)	0.81	0.44, 1.51	0.51
Relationship status, single (vs. partnered)	1.05	0.67, 1.63	0.84
Educational attainment			
≤High School	Ref	Ref	Ref
>High School	0.76	0.45, 1.28	0.30
Housing status, homeless (vs. housed)	2.46	1.40, 4.32	0.001
Stopped by police, last 6 months	1.95	1.20, 3.16	<0.01
Traveled to Mexico, last 6 months	1.16	0.65, 2.08	0.61
Injected drugs in Mexico, past 6 months	1.00	0.45, 2.20	0.99
Substance abuse-related factors			
Prefilled syringe use at baseline (yes vs. no)	5.80	2.14, 15.74	<0.001
Number of years injecting (mean, SD)	1.00	0.98, 1.02	0.74
Number of persons injected with in last 6 months (mean, SD)	1.02	1.01, 1.03	0.01
Obtained most syringes from unsafe sources, last 6 months * (vs. safe sources)	1.04	0.62, 1.74	0.51
Injected most often in public place, last 6 months (vs. private places)	1.07	0.67, 1.71	0.53
Used syringe exchange (vs. no), last 6 months	2.17	1.27, 3.72	<0.01
Shared syringes, last 6 months			
Any vs. none	2.52	1.41, 4.51	<0.01
Unknown vs. none	1.89	0.97, 3.68	0.06
Shared other injection equipment, last 6 months			
Any vs. none	7.95	3.41, 18.55	<0.01
Unknown vs. none	4.09	1.35, 12.38	0.01
Rushed injection due to police, last 6 months			
Yes vs. no	3.24	1.89, 5.54	<0.01
Unknown vs. no	1.17	0.49, 2.78	0.71
Injected heroin, last 6 months	2.64	1.59, 4.39	<0.01
Injected Meth, lasts 6 months	2.83	1.65, 4.86	<0.01
Injected Crack/cocaine, last 6 months	1.42	0.63, 3.24	0.40
Health care utilization and health outcomes			
Any hospital/ER visit, last 6 months	1.29	0.82, 2.05	0.27
Had an abscess, last 6 months	2.06	1.29, 3.28	<0.01
Overdosed, last 6 months	4.81	2.55, 9.06	<0.01

*safe sources (syringe exchange program, doctor/ clinic/ hospital/, veterinary clinic/pet store, market); unsafe sources (spouse, family member, or sex partner, friend, drug dealer, "Hit doctor," shooting gallery, on the street, some other place)

**private location (my/someone else's home, car); public location (shooting gallery, construction site, alleyway, bar/club, on the street, vacant lot, park, freeway overpass/bridge/canyon, public restroom)

Table 4.4: Multivariable logistic GEE analysis of factors associated with prefilled syringe use in the last 6 months among persons who inject drugs in San Diego, CA (n=376)

Variable	Adjusted Odds Ratio	95% Confidence Interval	p-value
Opioid overdose in the past 6 months (yes vs. no)	3.17	1.70,5.93	<0.01
Shared other injection paraphernalia (cookers, cotton, rinse water), in the past 6 months			
Yes vs. no	4.86	2.18,10.82	<0.001
Unknown vs. no	2.48	0.77,8.00	0.13
Housing status in the last 6 months (homeless vs. housed)	2.42	1.33,4.42	<0.01
Used syringe exchange program (yes vs. no)	1.85	0.99,3.44	0.05

*Final model additionally adjusted for time and PFSU in the last 6 months at baseline

CHAPTER 5: DISCUSSION AND CONCLUSIONS

OVERVIEW

This dissertation research was undertaken to better understand prefilled syringe use among PWIDs in San Diego, California. The following aims were addressed by this research: **Aim 1.** To identify socio-demographic and behavioral factors associated with the use of prefilled syringes among PWID in San Diego, CA. **Aim 2.** To explore individual, motivational, situational, social and environmental factors that contribute to the use of prefilled syringes through qualitative interviews with PWID in San Diego, CA. **Aim 3.** To describe the correlates of prefilled syringes use over time among people who inject drugs in San Diego, CA. Qualitative and quantitative methods were used to integrate individual, environmental, policy and regulation, and contextual factors to better understand novel injection-related HIV and HCV risk among PWID. This research shed light on the importance environmental factors that impact the ways in which drugs are distributed and used. Results of this research can be use to develop monitoring programs and to tailor data collection for injection related risk behaviors among PWID.

PREFILLED SYRINGE USE IN SAN DIEGO, CALIFORNIA

Results from the study on the prevalence and correlates of PFSU among PWID in San Diego, CA uncovered several factors suggesting that those who engage in this practice are more vulnerable and take greater risks as a result of both micro- and macroenvironmental factors. Specifically, we found that lifetime PFSU was independently associated with ever having rushed injection due to police presence, having been in prison, reporting injecting most often in public versus private locations, having ever overdosed, and having ever injected drugs in Mexico. Longitudinally, after adjusting for time and baseline PFSU, we found that PFSU was associated with homelessness, sharing other injection paraphernalia, using the syringe exchange program, and overdosing in the past 6 months. Our qualitative analysis identified the following key themes that influence prefilled syringe use: 1) unknown contents, 2) trust, 3) fear of/need to avoid withdrawal, and 4) disease transmission risk. These findings illustrate that prefilled syringe use among our participants emerges as a result of both micro (e.g., drug injection location, homelessness, local policing practices, and sterile injection equipment availability) and macro (e.g., drug trafficking routes, gendered risk) environmental influences.

Needle exchange programs reduce the risk of HIV and HCV transmission, especially among participants who exclusively obtain their injection equipment from the needle exchange. In fact, several of our participants discussed the necessity of not only the expansion of the hours of the needle exchange program, but also the availability of more syringes per user and greater diversity

in the types of syringes provided. One participant said that the group he injects with stopped using the needle exchange when they discontinued carrying certain types of syringes. Without the needle exchange, the group resorted to sharing syringes due to limited quantities.

Our findings that PFSU is longitudinally associated with overdose in the past 6 months and cross-sectionally associated with ever overdosing are particularly concerning as accidental overdose is the leading cause of injury death in the United States.[1] Risk factors for overdose include injecting drugs, drug use frequency, the purity of drugs being injected, presence of adulterants in drug solutions, sexual abuse history, and loss of tolerance after periods of abstinence.[2-6] PFSU may increase overdose risk due to factors such as the purity and concentration of the drug solution in the syringe or how the solution was prepared (i.e., what it is mixed or cut with) are unknown. Further, in qualitative analyses, PWID reported skepticism of PFSU because of the unknown content and risk of overdose and “hot shots”, or a syringe filled with a solution that is meant to be lethal.

PFSU emerges as a result of the situational context in which PWID inject drugs, and their use is directly influenced PWIDs risk environment. PFSU is shaped by both microenvironmental factors such as local policing practices, and availability of syringes, and by macroenvironmental factors such as laws affect the availability of the needle exchange, drug and injection equipment possession laws, and social norms. Individual knowledge influences risk behaviors; however, focusing on individual level behaviors only addresses one piece in a constellation

of factors influencing disease transmission.[7] Recommendations include providing education about the harms associated with PFSU while addressing the larger physical and social factors that influence risk taking. This includes expanding the syringe exchange program to other areas of San Diego County and changing policies that results in the confiscation of syringes and other injection equipment. Additional research is also needed to understand how prefilled syringe use changes over time, and to recruit frequent users of prefilled syringes to better understand this behavior.

These findings also support the need to provide greater services (i.e., needle exchange program and housing assistance) for the most vulnerable PWID including those who are homeless and have the least access to services. Findings indicate that PWID who use prefilled syringes might be a specific type of drug user who are more likely to participate in risky behaviors as a consequence of their situation. These individuals may have a greater need for assistance, and thus rely on free services such as the needle exchange or on borrowing equipment from other people as a consequence of their circumstances. Interventions are needed to address inequality within certain subgroups of PWID, especially those who access the needle exchange and who are homeless.

LIMITATIONS

Generalizability

The data used for this study were collected as part of the Study of HIV, Hepatitis C, and Tuberculosis Risk among PWID in San Diego, California.

STAHR II is the first longitudinal study among PWID in San Diego and highlights some of the important risk behaviors that influence disease transmission among PWID. Because the study was conducted among PWID, results are only generalizable to similar populations of PWID. Further, STAHR II recruited PWID who reported injecting at least one time in the past thirty days and who had no plans to move out of the county within the next two years, therefore our results only represent recent injectors with plans to stay in San Diego. Participants' were not recruited specifically based on their prefilled syringe use; therefore our results may not represent all PWID who use PFSU in San Diego County. Data used to assess associations with lifetime prefilled syringe use in chapter two were limited because more detailed data about prefilled syringe use was not collected. While chapter three elicited in-depth information about PFSU from participants who reported recent use, this information is limited to those who met the enrollment criteria for the parent study. PFSU was not common in our sample, however, the data represent a wide range of participants who report using prefilled syringes.

Statistical power

The findings reported in chapters two and four use all data available from the parent study for the analyses. While we would have liked to assess the association of prefilled syringe use and HIV and HCV transmission longitudinally, incident cases of infection were low, therefore we did not have the power to assess these associations.

RECOMMENDATIONS AND FUTURE RESEARCH NEEDS

This research expands on current knowledge of high risk behaviors among PWID; however, more evidence is needed to determine whether prefilled syringe use increases disease transmission and overdose risk. The studies above lay the groundwork for understanding PFSU in San Diego and can adapted in other settings. Future studies among a larger sample of prefilled syringe users and among those who exclusively use prefilled syringes are needed to better understand risk factors associated with their use. Further research is also needed to examine how drugs distributed in prefilled syringes are prepared, and why drug dealers distribute drugs in prefilled syringes and whether dealers take measures to ensure the sterility of syringes and drug preparation equipment. Further, information regarding the source of syringes used for prefilled syringes is needed to better describe the risk environment surrounding PFSU.

The findings also support the need to develop risk behavior interventions that address structural barriers to safer injection practices. Interventions should first focus on the structural barriers to safer injection, such as education of police and other law enforcement individuals about high-risk behaviors of PWID. This education should include information about high-risk behaviors, how behaviors are influenced by policing practices, and best practices for responding to overdose calls. Education programs about how best to reduce the risk of disease when injecting drugs are also needed for PWID. This should include not only information about the risks associated with certain behaviors, but also

information about access to sterile injection equipment and services for PWID, including drug treatment.

Interventions will require changes in the legal landscape surrounding drug use to improve the relationship between the legal system and individual users who participate in high-risk behaviors. Policies surrounding drug use, drug possession, and syringe, and injection equipment possession limit PWID ability to engage in harm reduction practices that education programs advocate.

Interventions to prevent HIV and HCV among PWID should focus on: 1) reducing high risk behaviors including sharing injection paraphernalia; 2) increasing HIV and HCV screening; 3) expanding needle exchange programs; 4) expanding substance use treatment; 5) address structural barriers to prevention efforts.[8] Intervention programs should integrate services to improve their efficacy. A systematic review and meta-analysis of interventions to prevent HCV among PWID by Hagan et al. found that interventions that combined substance-use treatment and support for safe injection were most effective at preventing HCV transmission and that interventions using multiple strategies reduced the risk of seroconversion by up to 75%.[9] Research has also pointed to the integration of HIV prevention services in one location to include a “one-stop” venue that includes syringe exchange, substance use treatment include opioid substitution, counseling and testing, education, and linkage to care, including antiretroviral treatment for those who are HIV positive.[10]

CONCLUSIONS

High-risk behaviors among PWID constantly evolve in response to changes in environmental and social factors that impact the ways in which drugs are distributed and used. Our findings suggest that PFSU is shaped by structural and environmental factors that produce risk among PWID. Namely, vulnerability to policing practice and the unavailability of safe injection sites might create environments that prevent PWID from practicing harm reduction strategies. While individual factors such as knowledge of risk behaviors are often identified in intervention programs, they fail to recognize circumstance that PWID have little control over.[7]

This dissertation research expands on the current knowledge of current high-risk behaviors for HIV and HCV infection and overdose risk among PWID in San Diego, California. Given the significant global impact of HIV and HCV among PWID, understanding high-risk behaviors and factors that influence them is important to continue to fight the spread of disease. In particular, research needs to focus on the structural barriers to harm reduction including how the legal environment influences access to clean syringes and participation in high-risk behaviors. Policing activities emerged as significant in several of our analyses and PWID reported altering their own behaviors in response to the law and the desire to avoid repercussions. However, many PWID were also aware of their heightened risk for disease transmission, especially when engaging in high-risk behaviors such as PFSU. PWID report the inevitability of HIV and HCV infection but often report their disease status is out of their control. More salient outcomes,

such as withdrawal symptoms, are often more important than disease prevention. Therefore, efforts are needed to improve PWID self-efficacy to practice harm reduction and prevent disease transmission.

REFERENCES

1. Centers for Disease Control and Prevention, *Web-based Injury Statistics Query and Reporting System (WISQARS)* 2014.

2. Britton, P.C., J.D. Wines, Jr., and K.R. Conner, *Non-fatal overdose in the 12 months following treatment for substance use disorders.* Drug Alcohol Depend, 2010. **107**(1): p. 51-5.

3. Brugal, M.T., et al., *Factors associated with non-fatal heroin overdose: assessing the effect of frequency and route of heroin administration.* Addiction, 2002. **97**(3): p. 319-27.

4. Coffin, P.O., et al., *Opiates, cocaine and alcohol combinations in accidental drug overdose deaths in New York City, 1990-98.* Addiction, 2003. **98**(6): p. 739-47.

5. Darke, S. and W. Hall, *Heroin overdose: research and evidence-based intervention.* J Urban Health, 2003. **80**(2): p. 189-200.

6. Silva, K., et al., *Factors associated with history of non-fatal overdose among young nonmedical users of prescription drugs.* Drug Alcohol Depend, 2013. **128**(1-2): p. 104-10.

7. Syme, S.L., *Social determinants of health: the community as an empowered partner.* Prev Chronic Dis, 2004. **1**(1): p. A02.

8. Page, K., et al., *Injection drug use and hepatitis C virus infection in young adult injectors: using evidence to inform comprehensive prevention.* Clinical infectious diseases, 2013. **57**(suppl 2): p. S32-S38.

9. Hagan, H., E.R. Pouget, and D.C. Des Jarlais, *A systematic review and meta-analysis of interventions to prevent hepatitis C virus infection in people who inject drugs.* J Infect Dis, 2011. **204**(1): p. 74-83.

10. Strathdee, S.A., et al., *Towards combination HIV prevention for injection drug users: addressing addictophobia, apathy and inattention.* Curr Opin HIV AIDS, 2012. **7**(4): p. 320-5.

APPENDIX

SUPPLEMENTARY TABLE

Table S.1: Characteristics of participants enrolled in STAHR II, a longitudinal study of persons who inject drugs in San Diego, CA

	Baseline n=574		Follow-up 6 months n=291		12 months n=267		18 months n=220		p-value[‡]
Characteristic	No.	%	No.	%	No.	%	No.	%	
Demographics									
Age (mean, sd)	43.3	11.7	45.6	11.3	46.1	11.1	46.9	10.5	<0.01
Race/Ethnicity									0.66
White, non-Hispanic	292	50.9%	146	50%	134	51%	113	51%	
Hispanic	178	31.0%	84	29%	80	30%	61	28%	
Black, non-Hispanic	50	8.7%	32	11%	25	9%	24	11%	
Other	54	9.4%	28	10%	26	10%	22	10%	
Gender									0.87
Male	418	72.9%	217	75%	194	73%	163	74%	
Female	149	26.0%	69	24%	69	26%	54	25%	
Transgender male-to-female	5	0.88%	4	1%	3	1%	2	1%	
Transgender female-to-male	1	0.17%	1	0%	1	1%	0	0%	
Homeless, past 6 months	351	61.2%	174	60%	148	55%	126	57%	0.14
Annual income (>10,000 vs <=10,000)	182	31.8%	18	6%	27	10%	16	7%	<0.01
Education level (High school or more)	378	65.6%	195	67%	179	67.5%	141	64.1%	0.79
Traveled to Mexico, past 6 months	161	28.4%	52	18%	47	18%	33	15%	<0.01
Injected in Mexico, past 6 months	87	15.3%	25	9%	29	11%	19	9%	<0.01
Drug Use									
Duration of drug injecting, years (mean, sd)	20.8	13.4	21.9	13.2	21.8	12.9	22.2	12.8	0.51
Use syringe exchange program, past 6 months	236	41.1%	168	58%	149	56%	116	55%	<0.01
Prefilled syringe use, past 6 months	26	4.7%	42	14.4%	29	10.9%	21	9.6%	0.08
Sharing syringes, past 6 months	289	59.2%	92	32%	135	51%	123	56%	<0.01
Sharing cookers/cotton/water, past 6 months	394	68.4%	194	67%	143	54%	137	62%	<0.01
Injected heroin, past 6 months	310	56.4%	157	54%	126	47%	101	46%	0.07
Injected meth, past 6 months	222	40.1%	180	62%	141	53%	108	49%	0.01
Injected crack/cocaine, past 6 months	19	3.4%	24	8%	15	6%	9	4%	0.05
Health Status									
Overdosed on opioids, last 6 months	45	7.9%	23	8.0%	19	7.2%	15	7%	0.63
HIV Test Result*									
Negative	501	90.6%	207	70%	162	61%	115	52%	<0.01
Incident HIV	-	-	1	0%	0	0%	0	0%	
Prevalent HIV	52	9.4%	33	11%	31	12%	21	10%	
Previously negative/unknown[+]	-	-	53	18%	74	28%	84	38%	
HCV Test Result*									<0.01
Negative	187	33.9%	86	30%	74	28%	45	20%	
Incident HCV	-	-	12	4%	4	2%	0	0%	
Prevalent HCV	365	66.1%	181	63%	170	65%	156	71%	
Previously negative/unknown[+]	-	-	10	3%	12	5%	19	9%	

*n=553 for baseline, incidence not calculated during baseline
[‡]p-value indicates differences between visits; Mantel Hanzel Chi-square was used for categorical variables and ANOVA for continuous variables
[+]Previously negative/unknown refers to participants who do not have test results from that visit so the value is missing. If they had test result that was negative they are included in this category but their current status is not known.

QUALITATIVE INTERVIEW GUIDE

Thanks for agreeing to talk with me today. The first thing I'd like to do is to just confirm with you that you know that the recorder is on and that you gave your consent for the interview to be recorded. Are you OK with that? [ask participant for verbal response] Remember, you can refuse to answer any question at any time or decide you no longer want to participate in the study and that is just fine.

OK, thank you.

Do you have any questions before we begin? [respond to questions before proceeding.]

For the recording, I just want to say that this is Participant number [STUDY ID]. It is [date] at [time]. To begin with, I'm going to ask you to tell me about some of your experiences with injection drug use. We are specifically interested in peoples' experiences and opinions using and injecting drugs, especially prefilled syringes. So during this interview, I'd like you to tell me about times that you've used or purchased drugs in prefilled syringes. There are no right or wrong answers to these questions, I'm just interested in hearing your stories.

1. For about how many years have you been injecting drugs? Do you remember the first time you injected? Can you tell me the story of the first time you injected? (PROBE: who were you with, what, where, WHY)

2. We are interested in learning more about the practice of injecting drugs and preparing drugs to inject.
    a. Can you tell me more about the process you go through when injecting drugs?
    b. Where do you purchase drugs? Where do you get you injection equipment (e.g. syringe, cooker, cotton, works)?
    c. How do you prepare your drugs?
    d. Are there certain situations when you prepare your drugs differently.
    e. Who do you normally inject drugs with? Who prepares the drugs for you?

3. You said in your previous interview that you have used syringes that were already filled with drug solution. For the sake of this interview I'm going to call that a prefilled syringe. Can you tell me a little bit about the first time you did that?
    a. How common is it that you inject that way?

b. What are the conditions under which you would use a syringe that was already filled with drug solution? That is, are there certain times, or situations in which you tend to do that?"

4. Do you remember the first time you purchased (or were given) a prefilled syringe? Can you tell me a story about that? (PROBE: who, what, where, WHY). How was that day different than other days before when you had not used a prefilled syringe?

a. Who did you get it from?
b. Do you remember how you felt about injecting with a prefilled syringe (PROBE: emotions, scared because they didn't know what was in it, did they trust the person who have it to them, did you think the syringe had ever been used before, etc)?
c. Who prepared the drug solution? Did you see it?
d. What kind of drug(s) were in the syringe? Who injected you? Who else used the syringe?

5. I'd like to know a bit more about your experiences with prefilled syringes since that time?

a. Roughly, how many times in your lifetime have you used them?
b. About how many other people do you know who use prefilled syringes? How common do you think their use is?
c. What are some of the reasons why you (or anybody else) might use a prefilled syringe?
    i. Do you think it's preferable to use a prefilled syringe?
    ii. Are there any advantages to using prefilled syringes? Disadvantages?
    iii. Why or why not?
d. Where have you purchased prefilled syringes?

6. Now, I'd like you to describe for me what a typical injection event looks like. Begin with how you got your drug and equipment; who you were with and where; who prepares your hit for injection; the order of injection; whether or not everyone has their own syringe; what drug you injected; etc.

a. How is the situation different when you use a prefilled syringe?

7. Now, I'd like to know a little bit about the LAST time you injected with a prefilled syringe. Can you tell me about what happened that time?

a. How long ago was this?
b. Where did you get the prefilled syringe from? (Did you buy it or was it given to you? If given, by who)
c. Where were you?

d. You stated you preferred to mix your own drugs, but you recently injected with a prefilled syringe (insert approximate date), what was going on? Why do you think you used a prefilled syringe instead of preparing the drugs yourself?
e. Did you trust the source of your drugs? (PROBE: why or why not?)
f. Did you trust the source of your syringe? (PROBE: why or why not?)
g. What were your concerns about what could happen from injecting with the prefilled syringe?
h. Do you do anything different where you're using a prefilled syringe (e.g. cleaning the injection site, backloading drugs into their own syringe.)
i. Is this behavior more or less typical for certain types of drugs?
j. Is this behavior more or less typical in certain contexts (e.g., in MX vs. at home?).

8. Under what circumstances do you think you would use a prefilled syringe again?

9. Have you ever obtained or used a prefilled syringe in Mexico? Tell me about that occasion?

10. Have you ever gone to Mexico specifically to purchase or use prefilled syringes? Can you tell me about the LAST time that you traveled to Mexico and used prefilled syringes drugs there?
a. When was this?
b. Where did you go?
c. How do you get around?
d. Why did you go there?
e. What type of drugs did you buy/use?
f. Who did you use with?
g. Why did you use a prefilled syringe instead of prepping drugs on your own?

11. Is the experience you just told me about fairly representative of your experience buying or using prefilled syringes in Mexico? If no, how was it different?
a. Is there any other time that you've bought or used prefilled syringes in Mexico that comes to mind, maybe one that is different or exceptional in some way? Or, how does this experience differ from prefilled syringe use in the US?

12. If you buy/use prefilled syringes in both Mexico and San Diego, which do you prefer? Why?

13. Do you ever talk with other people about using prefilled syringes? What do they think about using prefilled syringes? How does that influence your thoughts about using them?

14. Do syringe access laws influence you decision to buy/use prefilled syringes?