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Early Substance Use Experiences and Trajectories Leading to Injection Drug Use among Male and Female Current Injection Drug Users in the Mexico-US Border Region

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

in

Doctor of Philosophy in Public Health (Global Health)

by

Meghan Diane Morris

Committee in Charge:

University of California, San Diego

Professor Steffanie A. Strathdee, Chair

Professor Richard S. Garfein

San Diego State University

Professor Elva M. Arredondo

Professor John D. Clapp

Professor Hector Lemus

2011

The Dissertation of Meghan Diane Morris is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

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Chair

University of California, San Diego

San Diego State University

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DEDICATION

To my mother, who always encouraged me to spread my wings and fly.

To Stevan, my co-pilot for this adventure called life.

TABLE OF CONTENTS

LIST OF FIGURES

Chapter V

Chapter VII

LIST OF TABLES

Chapter I

Chapter III

Chapter IV

Chapter V

Chapter VII

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border region. The dissertation author was the primary investigator and author of this paper.

CURRICULUM VITA

EDUCATIONAL TRAINING

2011	Ph.D., Global Health University of California, San Diego San Diego State University
2007	MPH, Concentration Epidemiology San Diego State University
2003	B.S. Biochemistry & Cellular Biology, Minor Cultural Anthropology University of California, San Diego

RESEARCH EXPERIENCE

2007-2011	Graduate Research Assistant University of California, San Diego Division of Global Pubic Health
2006- 2008	Project Coordinator, Assessment of Health Conditions of Recently Resettled Refugees University of California, San Diego Division of Cross Cultural Medicine and International Health
2006-2007	Research Associate/Health Counselor San Diego Center for Health Intervention
2004-2005	Project Coordinator Naval Health Research Center, San Diego
2003-2004	Project Intern LifeAIDS International, San Diego
2001	Research Assistant Novartis Pharmaceuticals, San Diego

TEACHING EXPERIENCE

Spring 2010	San Diego State University HHS 350, Applied International Health & Human Services Appointment: Instructor of Record
Winter 2009	University California, San Diego

	MED 287, Emerging and Re-Emerging Infectious Diseases Appointment: Graduate teaching assistant
Fall 2008	University California, San Diego MED 160, Introduction to Epidemiology and Biostatistics Appointment: Graduate teaching assistant
Spring 2007	San Diego State University PH670, VIIDAI, International Epidemiology & Field Practice Appointment: Graduate teaching assistant

PUBLICATIONS

Morris MD, Case P, Robertson AM, Lozada R, Vera A, Medina-Mora M, Strathdee SA. Prevalence and correlates of 'agua celeste' use among female sex workers who inject drugs in Ciudad Juarez, Mexico. Drug Alcohol Depend. March 2011.

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Morris MD, Liang B. Human Papilloma Virus Vaccine: Addressing Policy Issues to Fulfill Social Potential. The Journal of Biolaw and Business. December 2006.

PUBLICATIONS IN PREPARATION

Morris MD, Lemus H, Wagner K, Martinez G, Remedios L, Gudelia Rangel Gomez, M, Strathdee SA. Examining the path to concurrent sex work and injection drug use behaviors: predictors of initiation of sex work and injection drug use among females in Northern Mexico. Addiction. *In Preperation*

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Stockman JK, **Morris MD**, Martinez G, Lozada R, Patterson TL, Ulibarri MD, Vera AL, Strathdee SA. Prevalence and Correlates of Female Condom Use and Interest among Female Sex Workers Who Inject Drugs in Two Mexico-U.S. Border Cities. AIDS & Behavior. *In preparation*

Adbi RA, Abdi FA, **Morris MD**, Rodwell TC, Moser KS, Paulino P, Brouwer KC. Reproductive needs of recently resettled refuges in San Diego County. Patient Education and Counseling. *In Preparation.*

PRESENTATIONS AT SCHOLARLY MEETINGS

Stockman JK, Martinez G, Lozada R, Patterson TL, Ulibarri MD, Vera AL, **Morris MD**, Strathdee SA. Prevalence and Correlates of Female Condom Use and Interest among Female Sex Workers Who Inject Drugs in Two Mexico-U.S. Border Cities. UC Global Health Day. Irvine, CA November 2010

Morris, MD, Pollini, RA, Lozada, RM, Gallardo M, Brouwer, KC, Vera A, Strathdee, SA. "Injection First": A Unique Group of Injection Drug Users in Tijuana, Mexico. SDSU Student Research Symposium. San Diego, CA March 2010.

Rondinelli AJ, **Morris MD**, Rodwell TC, Popper ST, Brouwer KC. Under- and Oer-Nutrition among Refugees in San Diego County, California. 134th Annual American Public Health Association Conference. San Diego, CA October, 2008.

SCHOLARSHIPS & RESEARCH SUPPORT

- Diversity Supplement. NIDA Grant DA023877-02S1; Parent Grant R01 DA023877 with Dr. Steffanie Strathdee; $85,964 for 2009 to 2011.
- NIDA Women & Sex/Gender Junior Investigator Travel Award; $750 to attend 2011 CPDD meeting in Hollywood, Fl

- Travel Award Recipient for College on Problems of Drug Dependence (CPDD) conference 2010. $750 for June 2010.
- NIDA Pre-Doctoral Training Fellowship in Substance Abuse, HIV, and Related Infections. Grant # T32DA023356-02 with Dr. Steffanie Strathdee; $50,000 for 2007 to 2009.
- BIXBY Scholarship in population research recipient. $6,000 for 2005 to 2007.
- San Diego State University Graduate Studies International Travel Grant. $1,500 2007.

HONORS

- Edward Bouchet Honor Society, 2010-present.
- 1st place-President's Award for Scholarly Research, SDSU Student Research Symposium, 2010
- Award for Oral Presentation, Reliability of Recruit Assessment Program data. Operational Research Competition, 44th Navy Occupational Health and Preventive Medicine Workshop, February 2005

VOLUNTEER ACTIVITIES & ACADEMIC WORKING GROUPS

- Reviewer for *American Journal on Addictions*, 2011 to present (1 article to date)
- Reviewer for *Drug and Alcohol Dependence*, 2010 to present (2 articles to date)
- Student Representative for Education Steering Committee, UC School of Global Health, 2008
- Graduate Student Representative, SDSU-UCSD Global Health, 2007-2009
- Panel Member and Guest Lecturer, McNair Program, UCSD 2008, 2009
- HIV research field-study in Kingston, Jamaica: Summer of 2007
- Internship, Border Infectious Disease Surveillance Project
- San Diego County of Health and Human Services, Division of Border Health. Summer 2006.
- Volunteer Research Assistant, Hispanic Health Awareness and Practices Survey
  San Diego County of Health and Human Services, CDC Quarantine and Border Health Services, Summer 2006.
- Volunteer Research Assistant, Chula Vista Community Clinic.
  The California Endowment: Healthy Eating & Active Communities. Fall 2005.
- Mentor, Expanding Your Horizon, 2006, 2007
- Volunteer for UCSD, OWENS clinic (2004-2005)

- Volunteer, Orphanage in Quito, Ecuador, Summer, 2000

MENTORED STUDENTS

- Ridwa Abdi UCSD undergraduate student, 2009 to present
- Farah Abdi UCSD undergraduate student, 2009 to present
- Liliana Quezada undergraduate UABAC/UCSD student, 2009-2011
- Priya Bhat, UCSD post-baccalaureate student, 2010-present

PROFESSIONAL ASSOCIATIONS

2008-2010	Society for Epidemiologic Research
2006-2010	American Public Health Association (APHA) student member
2005-2010	Association for Women in Science (AWIS) member, San Diego Chapter

ABSTRACT OF THE DISSERTATION

Early Substance Use Experiences and Trajectories Leading to Injection Drug Use among Male and Female Current Injection Drug Users in the Mexico-US Border Region

by

Meghan Diane Morris

Doctor of Philosophy in Public Health (Global Health)

University of California, San Diego, 2011

San Diego State University, 2011

Professor Steffanie A. Strathdee, Chair

Background: The research proposed herein investigates factors associated with substance use trajectories leading to injection drug use (injection) and the circumstances surrounding injection within two different populations of injection drug users (IDUs). This study aims to identify factors associated with: (1) initiation of substance use through injection, (2) lifetime and current agua celeste use (an inhalant unique to Northern Mexico), and (3) time to initiation of sex work, and initiation of injection.

Methods: Three manuscripts form the basis of this dissertation using existing data from two datasets. Manuscript 1 uses data from IDU from the Proyecto El Cuete phase III dataset, and Manuscript 2 and 3 use data from female sex workers who inject drugs (FSW-IDU) in the Mujer Mas Segura dataset.

Results: Manuscript 1 identified a sub-group of IDUs who initiated illicit drug use by injecting the drug (‘injection first’). ‘Injection first’ IDUs were more

likely to first inject heroin and inject alone, but were not significantly riskier in their current drug use or sexual behaviors compared to IDUs who used illicit drugs prior to injection. Manuscript 2 found that only FSW-IDUs in Ciudad Juarez reported agua celeste use and prevalence overall (53%) and within the past 6 months (47%) was high. Manuscript 3 identified that early abuse and illicit drug use was associated an accelerated time to initiation of both sex work and injection. Low education and a perceived need to enter sex work to support family were associated with a shorter time to sex work initiation, and geographical migration was found to decelerate time to injection initiation. Having an intimate partner suggest sex work and injecting to deal with feelings of depression accelerated time to both sex work and injection initiation when they occurred at the same age.

Conclusions: The unique populations of IDUs studied and novel research questions make the findings within this dissertation valuable to the larger field of research on substance use careers. These findings build on previous literature showing that inhalant use is an important risk factor for subsequent injection and may help identify possible avenues for intervention that can delay or prevent onset of initiation of injection drug use and/or sex work.

CHAPTER I.

INTRODUCTION

Many people experiment with drug use and stop after a period of recreational use; whereas a subset become regular or dependent users. Dependent users can experience a multitude of problems related to their drug use including fatal and non-fatal overdose, social stigmatization, mental health problems and exposure to infectious diseases. Duration of use, mode of administration (snorting, smoking, injecting, etc.), drug type, and drug purity are just some of the factors that can increase the incidence of these associated health problems, factors outside the individual also contribute to how and when drugs are used. The social and health costs associated with drug abuse in the United States alone have been estimated to be $180 billion annually.[1]

Given the social and economic impact of substance abuse and the individual harms associated with substance abuse, considerable research on the initiation of drug use has been carried out. Much of this research has been focused on the context of initiation within adolescent populations of casual drug users who do not progress toward more serious abuse and dependence. Further, the studies that have focused on populations of serous drug users are primarily within developed countries, and few are conducted among women. Studies examining patterns of substance use onset within regular drug using populations suggest that drug users progress through various different

patterns of drug use.[2-5] Many point to marijuana or alcohol as the first drug used prior to transition to more serious drugs such as cocaine, heroin, or methamphetamine,[2,6,7] but other studies have also shown that many initiated use of other illicit drugs prior to either alcohol or marijuana.[6,8,9] Drug use careers are determined by more than prior drug use; contextual factors proximal to the individual influence drug use and abuse.

Mexico has experienced an increase in drug use due to its role in trafficking and production of illicit drugs. Mexico-US border towns, such as Tijuana and Ciudad Juarez, are areas of increased consumption of illicit drugs in the country.[10] Few studies have examined substance use initiation, particularly injection drug use initiation, among populations in the Mexico-US border region. The research proposed herein investigates the factors associated with substance use trajectories leading to injection drug use and the circumstances surrounding injection drug use initiation within two different populations of injection drug users. It takes into account social and environmental influences at multiple levels on individual's substance use behavior at various stages of their drug use career. The goal of this research is to identify risk factors and critical periods for implementation of interventions to delay the onset of drug use or the progression toward problem use.

A. Specific Aims

This study proposes to examine early substance use experiences and factors associated with initiation of injection drug use through the following aims:

1. Identify background characteristics of individuals who 'inject first' and examine how current drug using and sexual behaviors differ across the 'injection first' and those who initiated illicit drug use through snorting, sniffing, or ingesting the drug.

2. Determine the prevalence and correlates of lifetime and current *agua celeste* use, an inhalant unique to northern Mexico, among female sex workers who inject drugs.

3. Examine physical and social micro-level factors associated with time to sex work initiation and time to injection drug use initiation among a group of current female sex workers who inject drugs.

In this dissertation, the candidate will provide a literature review and background information on the epidemiology of drug use and gender differences in drug use careers leading to injection drug use initiation internationally with specific focus on the Mexico-US border region. The three published manuscripts, each of which addresses a specific aim of the dissertation, will then be presented. The dissertation will conclude with a discussion of the major findings of the research, the strengths and limitations

of the studies, discussion on the public health implications to these findings, and suggestions for future research directions.

B. Background & Significance

Global epidemiology of drug abuse

Worldwide, in 2007, it was estimated that between 18 and 38 million people between the ages of 15 and 64 were regular or heavy illicit drug users;[11] with the majority living in developing countries. Culture, drug trafficking routes, and socio-demographic factors influence which types of drugs predominate in specific regions in the world. The most commonly injected drugs are heroin and other opiates, cocaine, and amphetamines. The prevalence of each varies according to location and population group. Heroin is the most common drug injected in most of Western Europe, and Asia.[11] Across Latin America, with the exception of Mexico, cocaine is the most prevalent drug injected.[11] In Mexico, heroin followed by cocaine have been the most prevalent drugs injected, with methamphetamine injection being reported in the Mexico-U.S. border region.[11,12] Within the U.S. and Canada, drug use patterns differ widely. Heroin is the most common drug injected in the U.S. In Canada, both heroin and cocaine are widely used among injection drug using populations.[11]

Health effects of injection drug use

Although injection drug users (IDUs) represent a small proportion of all illicit drug users, they suffer a disproportionate share of drug related morbidity and mortality. In any form, the use of illicit drugs can have adverse health

effects; however, much of the harm from illicit drug use can be attributed to the way in which the drugs are administered. Compared to other routes of administration, such as swallowing, sniffing, or smoking, injection drug use carries an elevated risk of overdose[13] and blood borne viral infections like HIV,[14] hepatitis C virus,[15] and hepatitis B virus;[16] and bacterial infections like endocarditis.[17,18] Much of the harm related to injection drug use often results from a combination of limited needle availability, poor hygiene, and unsafe injection practices. Skin, tissue, and vein damage can result from injecting with dull needles or repetitive injection at the same site resulting in abscesses, ulceration, and circulatory damage.[17,19]

Injection drug use is an established HIV transmission route through sharing of contaminated needles.[20] As of 2010, there were 33.3 million people infected with HIV worldwide; 96% are in middle and low income countries;[21] with ten percent of the HIV/AIDS cases worldwide attributed to injection drug use. Globally, in 2007 an estimated 15.9 million individuals (range: 11.0 to 22.1 million) injected drugs, of whom approximately 3 million were living with HIV.[22] Currently, the countries with the highest number of drug injectors are China, the U.S., and Russia.[22] However, in countries such as Mexico, Kenya, and Indonesia, an increase in injection drug use has been reported within specific regions.[23-25] Furthermore, female IDUs have a higher HIV incidence than male IDUs in many industrialized countries.[26] Importantly, IDUs can act as a bridging population spreading HIV infection from high

prevalence populations to low prevalence populations through drug users who engage in unprotected sex.[27,28]

Drug use careers leading to injection drug use

Due to the considerable burden of adverse health outcomes associated with injection drug use, the transition from non-injection to injection drug use has been an important topic of public health research. For persons who initiate injection drug use, the majority of the peer-reviewed literature indicates that a period of non-injection illicit drug use precedes the first injection drug use experience.[29,30] However, early initiation of illicit drug use increases the risk of subsequent drug abuse and drug dependence. Studies focused on identifying pathways to early substance use initiation and progression toward injection drug use initiation are essential to the design of effective prevention measures.

Injecting, smoking, and sniffing are the usual routes of administration of most illicit drugs. Different routes of administration can affect the rate and efficiency of delivery, with injecting being the most efficient mode.[31] Drug use patterns and popular routes of administration have been found to vary by sociodemographic factors such as class,[32] age,[33] and gender,[34,35] and by social factors like culture.[36,37] While each mode of drug delivery exposes individuals to drug related harms, injection drug use has been shown to put individuals at the highest risk for blood borne infections such as HIV.[38,39] Initiating injection drug use earlier in one's substance use career therefore

increases their exposure to infection. A study of Puerto Rican IDU suggests that early initiation of injection drug use also produces an increased spectrum of psychosocial and psychological problems, contributing to future drug abuse and creating another barrier for successful treatment.[40] Aim 1 identifies a unique subgroup of substance users who initiated illicit drug use by injecting and assesses current drug use and sexual behaviors associated with this accelerated pathway of injection drug use.

Studies of the sequence of drug initiation among adolescents have shown that tobacco and alcohol are typically the first drugs used, followed by marijuana, and then other illicit drugs.[41] Additionally, findings suggest that early inhalant use may be an important predictor of transitioning to heroin and injection drug use later in life.[42-45]

There are four main types of inhalants: volatile solvents, gases, aerosols and nitrites. Inhalants may alter moods and create a euphoric state that can be accompanied by lightheadedness and hallucinations [46]. Nitrites, sometimes known as “poppers,” may enhance sexual pleasure. Sometimes referred to as “sniffing”, “huffing”, or “bagging”, the primary objective of inhaling volatile substances is to deliver the highest concentration of the substance to the lungs and subsequently the brain [47]. The intoxication typically lasts only a few moments, requiring inhalant users to engage in repeated use in order to prolong the effects. Serious health effects may occur with successive inhalations, including loss of consciousness, seizures, nervous

system damage, and even death [48,49]. Cognitive damage is a particularly serious health effect, especially common in individuals who huff the solvents [50].

The relative inexpensiveness, ease of availability, and rapidly achieved intoxicating effects of inhalants make them particularly attractive to adolescents. A U.S. national survey in 2006 estimated that 9.3% of adolescents 12 years and older had used inhalants in their lifetime;[51] rates in other cities were slightly lower.[52,53] Antisocial behavior, tramatic-exposure, suicide, psychiatric symptoms and substance-related problems have all been shown to associated with inhalant abuse.[54-56] A cross-sectional sample of adolescents from Missouri, U.S. found among life-time inhalant users levels of depression, prior suicide attempt, and lifetime exposure to abuse and trauma were associated with inhalant abuse and dependence.[54]

Literature surrounding early substance use among adolescents suggest that inhalants may play an important early role in individuals' drug use trajectories leading to later use of heroin and/or injection drug use.[7,43,44,57] In a prospective study of 600 African American youth from Chicago, Johnson et al. reported that those who used inhalants prior to age 16 were 9 times more likely to subsequently use heroin later in life.[58] Data from the 1990 U.S. National Household Survey on Drug Abuse demonstrated that after adjusting for sex, age, race, socioeconomic status, and use of marijuana, inhalant users were more than 5 times more likely than non-users to transition to injection

drug use.[43] Few studies have looked at inhalant abuse within adult samples.[59,60] Wu et al (2007) examined adult inhalant users in the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) and found that among adults who reported a history of inhalant use, 70% met the criteria for one or more lifetime personality, mood, or anxiety disorder.[59]

The majority of epidemiological studies group all inhalants together when estimating use, or include inhalants in a wider group of illegal drugs thus biasing prevalence estimates. Aim 2 proposes to investigate factors associated with use of a specific inhaled solvent known on the street as *agua celeste*. *Agua Celeste,* or "heavenly water," is a sky blue colored solvent that is inhaled from soaked cloths or ingested to produce an intoxicating effect.[61] Within Mexico's illicit drug market, the substance has been mainly targeted to children and teens along the Mexico-U.S. border. *Agua celeste* is typically a homemade combination of a variety of everyday solvents and most often contains leather thinner and/or ephedrine. Because *agua celeste* most often contains either benzene, formaldehyde, or methyl ethyl ketone, it produces an effect similar to nitrates or "poppers," and may cause long term health damage.[62] Data from the 2008 Mexico national household survey found that 0.2% of inhalant users used *Agua Celeste* and were mainly from the state of Chihuahua.[63]

Theoretical perspectives contributing to illicit drug use pathways

The gateway drug theory posits that the use of certain drugs precedes the use of other drug types, but progression is not inevitable. Rather than predicting a pattern of drug use, the gateway theory suggests that the sequence of drug use includes an element of sequence between classes of drugs, and a risk relationship between drug classes.[64] For example, this theory hypothesizes that use of marijuana increases the risk of using more serious drugs such as cocaine or heroin. However, the gateway theory is based on U.S. studies conducted on high school and neighborhood samples, which rarely represent habitual or dependent drug users. Although much work has been done to identify the possible stages a drug user may move through, the gateway theory does not identify risk or protective factors underlying progression from one drug to another.

As an alternative to the gateway drug theory which postulates that the use of gateway drugs, such as marijuana, cause youths to have an increased risk of progressing to other, more serious drugs,[6,64,65] the dissertation herein is guided by an adapted framework from Rhodes and colleagues. Since its initial development, the risk environment framework has been defined as the "space-whether social or physical—in which a variety of factors interact to increase the chances of drug-related harm on an individual."[66] Several studies have acknowledged that a focus on the risk environment, rather than just the pattern

of drug use, encourages the researcher to think about the how to implement realistic interventions at the physical, social, economic, and policy levels.[67,68]

The risk environment heuristic originated from the social determinants of health theory. Two main dimensions comprise the risk environment; type of environment (physical, social, economic, and policy), and level of environmental influence (micro and macro). While the framework was developed to study HIV associated harms within populations of IDUs, it has been extended to homeless, populations of sex workers, and clients of sex workers.[69-71] The proposed study has adapted the Rhodes framework to identify and understand the physical, social, economic, and policy forces influencing initiation of injection drug use. Table 1, adapted from Rhodes et al. (2002), serves as a summary of influences that come together to create the risk environment surrounding initiation of injection drug use. Physical, social, economic, and environmental forces influence the individual at both the micro and macro level to either protect or enable initiation of injection drug use. Micro and macro factors are in constant interplay and often overlap.

The countries and cities most successful in averting or reversing the HIV epidemic have adopted behavioral-level interventions coupled with structural level policy changes that alter the risk environment.[72] The dissertation outlined herein utilizes an adapted framework from the Rhodes risk environment to guide the examination of early substance use behaviors and factors at the physical, social, economic, and policy factors at the micro-

and macro- levels associated with injection drug use initiation. The findings from this project will increase the understanding of the risk environment surrounding initiation, and hopefully motivate future studies to look outside of individual-level factors when studying illicit drug use careers.

Table 1.1. Summary of risk factors influencing drug use careers and initiation of injection drug use adapted from the Risk Environment heuristic*

	Micro-environment	Macro-environment
Physical Risk Factors	Neighborhood characteristics	Drug trafficking and distribution routes
	Homelessness	Geographic mobility/migration
	Incarceration	Neighborhood and population mixing
	Exposure to violence, trauma	
	Access to education	
Social Risk Factors	Social and peer group norms	Social capital
	Family drug use/Parental influences	Stigmatization and marginalization of drug users
	Relationship/network dynamics	Weak civil society and community advocacy
	Romantic/sexual partner relationships	Police per capita
	Culture surrounding drug use	Exposure to social instability/war/conflict/disasters
	Education	Ethnic/Racial inequalities
	Ease of drug access	Gender inequalities/gendered risk
Economic Risk Factors	Socioeconomic status/cost of living	Economic stability
	Cost of drugs	Growth of informal economies
	Purity of drugs	Uncertain economic transition
	Lack of income generation and employment	Changes in drug prices/availability due to drug trade changes
	Sex work participation	Sex trafficking
Policy Risk Factors	Availability/drug legality	Policy and laws governing drug use and availability
	Coverage of drug abuse treatment	Policy and laws governing drug abuse treatment
	Program-level policies governing distribution of injection equipment	Public health policy governing sex work -- and enforcement status
	Programs policies surrounding housing, service utilization, and other social welfare	Laws governing possession of drugs and drug paraphernalia – and enforcement status
	Policy surrounding sex work	Laws governing protection of human and health rights
		Immigration policies and laws

*adapted from Rhodes et al., 1999; and Strathdee et al. 2010.

The "first hit": circumstances surrounding initiation of injection drug use

As previously discussed, the majority of research surrounding substance use careers, particularly injection drug use initiation, has focused on identifying factors at the individual level and been conducted in developed countries.[29,32,73-75] The few studies examining initiation to injection drug use within developing countries provide general descriptions of circumstances surrounding the initial injection experience rather than examine specific behavioral/physical, social, and environmental predictors associated with initiation.[76-78]

Micro-level factors within the risk environment surrounding injection drug use initiation. Even though the majority of micro-level factors were initially seen as individual-level influences, they also fit within various spheres of the risk environment framework as described in the section above. Micro-physical level factors include neighborhood characteristics such as homelessness or number of hours working on the street per day, which can increase one's exposure to substance use. It is important to acknowledge that while individual factors at any sphere may influence the risk for initiation of injection drug use, these factors collide to simultaneously or progressively influence risk for substance use. History of physical or sexual abuse is an example of such a factor. Abuse can be acknowledged as a micro level physical factor. For example, if a woman experienced abuse as a child by a

family member, she may then run away from her home to escape the abuse (micro-physical factor) and move to Tijuana in search of a better life where she then crosses the border (micro-physical) into the United States and is then immediately deported (macro-policy) back to Tijuana where she knows no one (micro-social). Sometime after that first experience of abuse, she begins injecting drugs; the abuse plays a role but is unlikely the isolated factor that predicts initiation. This points again to the strength of examining the complete risk environment surrounding initiation and acknowledges that risk environments vary across different geographically and across different cultures.

Social level factors at the micro-level associated with progression to injection drug use include a pattern of social instability, peer and family injection drug use, and a history of non-injection drug use.[79,80] Problematic parental drug and alcohol use has also been found to be related to drug use in children.[81,82] Social networks have also been reported as a strong social predictor of transitioning into injection drug use,[83] specifically having a sex partner who injects.[75] Previous studies examining circumstances surrounding the first injection experience have reported individuals are likely to be younger with an unstable social environment including homelessness, family drug use, incarceration, or unemployment.[30,32,77] Additional studies emphasize the role of social circumstances and networks in aiding the adoption of injection practices, they describe that the majority of drug users are introduced to

injection by a family member, friend, or peer who is an injection drug user.[32,84,85] Under Aim 1, an examination of the influence of family illicit drug use and injection drug use on injection initiation is carried out.

There are few economic and policy micro-level factors that previous studies have identified. Examples of economic micro-level factors include individual income earned, and number of dependents financially responsible for. Policy micro-level factors associated with injection initiation may include lack of access to socially supported housing or lack of access to syringe exchange programs.

Macro-level factors within the risk environment surrounding injection drug use initiation. Less research has been focused on macro-level factors of injection drug use initiation. Within the HIV risk environment research, macro-level factors such as migration, sexual violence, social capital, and economic conditions have been found to be associated with increased risk for HIV.[86-88] An example of a macro-level factor within both the physical and economic sphere of influence includes change in the drug market which has been noted in several North American studies can affect the availability of drugs as well as the purity.[89,90] A multi-site study in south Florida identifying associates of transition from sniffing to injecting found that changes in drug purity influenced how people were administering the drug; a drop in drug purity occurring concurrently with an increase in drug price which can result in a transition into injecting.[91] A longitudinal study among 1416 school students in Baltimore

found that students in disadvantaged neighborhoods were at greater odds for exposure to cocaine and heroin.[92]

Policies and laws concerning harm reduction programs are another example of macro-level factors found to be associated with risky HIV behaviors such as sharing syringe equipment, and attending shooting galleries,[93,94] but can also influence how and when individuals initiate injection drug use. These same macro-policy level factors may also increase one's likelihood to initiate injection drug use. For example, strict laws regarding drug possession results in a high number of drug users being incarcerated. A cross-sectional study of incarcerated IDUs in Ireland found that 20% reported first injecting drugs in prison.[95] Aim 3 will examine macro-level influences such as geographic migration as part of the risk environment contributing to beginning sex work and injection drug use initiation. A wider-lens will hopefully encourage future studies to consider the role of influences outside of the individual sphere of influence on drug use careers.

Substance using behaviors among women

Worldwide, females comprise approximately one-third of the total IDU population, but some studies suggest that they are at greater risk for morbidity and mortality compared to male IDUs. Specifically, studies have found that female IDUs are more likely to participate in receptive sharing of syringes and injection equipment than male IDUs.[96-98] A community based survey of female IDUs in China indicated that 37% reported having shared syringe equipment at

least once in the past three months.[99] Furthermore, female IDUs are more likely to have sex partners who are also IDUs thus further compounding their risk[100] by injecting drugs with these drug using sexual partners[101] and having unprotected sex with them.[102] Within a group of female IDUs in Bangladesh, Azim et al. (2006) found that close to one third of all female IDUs reported unprotected sex with their injection partners.[103]

Regarding initiation to injection drug use, women appear to be influenced by their sexual partners.[96] In a cross-sectional study with 334 recently initiated injecting drug users in New South Wales and Queensland, Australia, Bryant et al. (2007) found that after adjusting for socio-demographic characteristics, and drug use history women had shorter illicit drug use careers prior to injection drug use and were more likely to have their romantic sexual partner facilitate the initiation (adjusted OR 4.64, 95%CI: 1.21 - 17.73).[104] Women's power dynamics in intimate partner relationships will be a focus in Aim 3.

Interplay between sex trade and substance use among women. The overlap between sex work and substance use among women has been documented in populations world-wide.[71,105-107] The prevalence of injection drug use among female sex worker (FSW) populations has been reported to range from 32% to 81%.[108-112] Independently, injection drug use and sex work can place individuals at risk for exposure to blood borne infections and sexually transmitted infections (STI), but engagement in both behaviors

elevates the risk substantially. Little research has been done on female sex workers who also engage injection drug use (FSW-IDU). The findings from this dissertation will help conceptualize the environment surrounding early substance use and trajectories leading to engagement in concurrent sex work and injection behaviors among women. Specifically, the findings from Aim 2 will provide the first prevalence estimate of an inhalant unique to the Northern Mexico border region and provide a description of inhalant use by FSW-IDU. Inhalant use has been linked to early sex work intiation.[113] Aim 3 will build on this finding, and explore the role of early inhalant use on initiation pathways leading to concurrent sex work and injection drug use.

There is scarcity of research on the temporality of sex work initiation compared to injection initiation. A few studies have acknowledged the relationship between prior and current engagement in sex work and injection drug use;[39,114,115] fewer have reported prior injection drug use associated with beginning sex work.[116,117] Studies have found that female IDUs are more likely to sell sex for drugs, money, or goods then male IDUs.[97,102,118] A cross-sectional study of FSWs in Montreal, Canada found that previous injection drug use was associated with a 2.7-fold increased odds in the risk of initiating prostitution.[117] However, these findings come from studies of HIV risk behaviors rather than analyses of factors associated with initiation of sex work and injection drug use. Aim 3 attempts to untangle the relationship between sex work and injection drug use by examining the risk environments

surrounding first sex work, and sex work initiation. By identifying differences in the risk environments across these two initiation pathways, prevention methods can be targeted to the unique needs of these groups; thus increasing their potential for change.

C. Significance

Although studies examining initiation of substance use have been conducted for decades, this is still an area of increasing concern and many questions about substance use careers leading to injection drug use remain unanswered. Despite the amount of research of initiation of injection drug use, none have examined factors associated with initiation of injection drug use as the first mode of illicit drug use. Few studies among female injection drug users examine lifetime inhalant use and behaviors associated with current inhalant use. There is little research on the potential associations between contextual factors and pathways of initiation among populations of FSW-IDU. In fact, there does not appear to be pervious research examining the context of injection initiation within populations of FSW-IDU. Further, the few studies examining the onset of injection drug use within female samples focus their examination on associated HIV-risks rather than physical and social factors influencing injection initiation. Given the harms associated with injecting, examining pathways leading to initiation of injection drug use, the risk environments surrounding various pathways, and the temporal relationship between specific physical, social, economic, and policy level factors is important in identifying targets of effective prevention and intervention programs.

This dissertation focuses on these identified gaps in the literature and the three papers aim to contribute to the literature by identifying and

examining the relationships between contextual factors and early onset substance use. Further, an exploration of the role early substance use, physical, and social level factors have on how and when injection drug use is initiated will be carried out.

D. Chapter I References

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CHAPTER II.

METHODS

This study uses existing data from two datasets to identify factors associated with initiation of substance use through injection, lifetime and current inhalant use, and time to initiation of sex work, and initiation of injection drug use. Three manuscripts form the basis of this dissertation and examine the sociodemographic characteristics, contextual factors, and motivations for initiating use and current use behaviors. The first manuscript uses data from the Proyecto *El Cuete* phase III dataset, which is a study based in Tijuana, Mexico. The second and third manuscript use data from FSW-IDUs in the *Mujer Mas Segura* dataset, which is a study based in Tijuana and Ciudad Juarez. Two additional analyses examined the associations between background sociodemographic factors and injecting as the first route of administration for illicit drug use among current FSW-IDU (Appendix 1), and physical and social level factors associated with time to transition to concurrent sex work and injection drug use behaviors among current FSW-IDU (Appendix 2). The following sections outline methods used for the three manuscripts.

A. Study Setting

The Mexico-U.S. border region

There are an estimated 0.7–1.3 million IDUs in Latin America.[1] After Colombia, Mexico is the second most important source of heroin entering the U.S., accounting for 30% of all heroin sold in the U.S. and 98% of heroin sold west of the Mississippi river.[2] In addition, 90% of all methamphetamine entering the U.S. is produced in Mexico, and 70% of all cocaine entering the U.S. passes through Mexico en route from South America.[2] The 2,000-mile border the U.S. shares with Mexico encompasses four U.S. states and six Mexican states, including Baja California (adjacent to California) and Chihuahua (adjacent to Texas). Of the 11.8 million people who live in the U.S.-Mexico border region, 5.5 million live in Mexico, 50% of whom live in Tijuana or Ciudad Juarez.[3] Border cities in Mexico are economically depressed, and commercial sex work is quasi-legal. Border towns are often home to people who have migrated from other parts of Mexico, Central and South America in search for occupational opportunities, or were traveling to the U.S. Within a study examining associations between migration and sexually transmitted infections found that 79% of all FSWs in Tijuana migrated from another state in Mexico.[4] In a comparison of IDUs in Tijuana and Ciudad Juarez, Ramos et al. (2009) found that although the two populations were similar in terms of many sociodemographic characteristics, they differed in many contextual factors including family drug use, migration, and drug use patterns.[5] All

analyses under aims 2 and 3 herein, will stratify by study site to examine potential differences in the two samples of FSW-IDUs.

The influence of physical, social, economic, and policy level factors on drug use behaviors varies according to culture and geography. Border regions are particularly interesting environments to examine these influences, since there are often extreme contrast in policies, culture, and available resources between neighboring countries.

Tijuana. Tijuana is located in the Mexican state of Baja California and adjacent to San Diego, CA. According to the 2005 census, the Tijuana metropolitan area was the sixth-largest in Mexico, with a population of 1,483,992, and one of the fastest growing cities in Mexico.[6] The San Ysidro border crossing separates San Diego and Tijuana, which is the busiest land border crossing in the world and leads all Mexico-U.S. border crossings in drug seizures. Both Tijuana and San Diego are located on a major North American drug-trafficking corridor. As such, it serves as a major distribution center for drugs entering the United States, such as marijuana, methamphetamine, heroin, and cocaine coming from Mexico and other Latin American countries.[7] "Spillover" from drug shipments along this route can result in increased availability of drugs in local communities; drugs that are unable to be ferried into the U.S. are sold cheaply in on the Mexican side of the border. The result is a growing injection drug use problem in northwestern Mexico. The highest consumption of illegal drugs in Mexico is in the

northwestern state of Baja California, whose largest city is Tijuana. The proportion of the general population in Tijuana aged 12–65 years who reported having ever used an illegal drug was 15%, almost three times the national average. Tijuana has one of the fastest growing IDU populations in Mexico.[8] In 2008, it was estimated that approximately 6,000 IDUs were estimated to attend shooting galleries in Tijuana.[9] However, the actual number of IDUs in Tijuana is may be as high as 10,000.[10]

In Tijuana, a government regulation system operates whereby sex work permits are provided to FSWs aged 18 years or older who then may work in the *Zona Roja* district where sex work is tolerated. To receive these permits, women are required to undergo HIV and STI tests on a regular basis. However, approximately half of women who work as prostitutes do so without a permit in the *zona roja*, and sex work often occurs outside the *Zona Roja*. It is estimated that approximately 6000 FSWs reside in Tijuana. In 2008 it was estimated that 14% of FSWs injected drugs. [11]

Ciudad Juarez. Ciudad Juarez has an estimated population of 1.5 million people[6] and is adjacent to El Paso, Texas. El Paso and Ciudad Juarez comprise one of the largest bi-national metropolitan areas in the world with a combined population of 2.4 million people. It is the port of entry from the U.S. city of El Paso, Texas. [12] In 2000, 36% of Ciudad Juarez's inhabitants were born outside the state of Chihuahua.[12] In 2006, there were 36 million northbound border crossings between Ciudad Juarez and El Paso.[12] Like

Tijuana, the main industry in Ciudad Juarez is maquiladora assembly plants. In Ciudad Juarez, it was estimated that there are 3000-3500 heavy heroin users and an estimated 6000 IDUs in 2008.[9]

Unlike Tijuana, a permit is not required for sex workers and sex work is tolerated in two informal *Zona Rojas* in Ciudad Juarez. As is the case in Tijuana, FSWs in Ciudad Juarez work out of cantinas, bars, hotels, nightclubs, and on street corners. While estimates vary, a study from 2008 estimates that approximately 4000 women engage in regular sex work in Ciudad Juarez; of whom 22% also engage in injection drug use.[13]

B. Research Design

1. METHODS FOR AIM 1: Proyecto El Cuete

Study Overview

The Proyecto *El Cuete* phase III project was funded by National Institutes of Health (NIH) and The National Institute of Drug Abuse (NIDA) (grant number: R01DA019829; Principal investigator: Steffanie A. Strathdee, PhD) between 2006 and 2010. The overall goal of this study was to characterize the epidemiology of HIV and tuberculosis among injecting drug users (IDUs) in Tijuana, Mexico. Specific overall aims of the Proyecto El Cuete study were: 1) to determine HIV, HCV and syphilis prevalence and estimate HIV incidence based on the detuned assay among IDUs in Tijuana; 2) To determine the extent to which potentially modifiable individual, social and environmental factors influence the prevalence and incidence of HIV and HCV and risk behaviors for blood borne infections. The Institutional Review Board of the University of California, San Diego and the Ethics Board of the Tijuana General Hospital approved protocols. Aim 1 of this dissertation is based on the baseline data from this study.

Sampling and Measures

Between 2006 and 2007, 1,056 current IDUs residing in Tijuana, Mexico were recruited into a longitudinal study using respondent driven sampling (RDS) to achieve a heterogeneous sample.[14] RDS is a sampling

technique that enables the calculation of less biased estimates of HIV prevalence and risk behaviors.[15] A group of “seeds” selected for heterogeneity with respect to age, gender, and geographical location were given uniquely coded coupons to recruit members of their social networks into the study. Recruitment waves continued as subjects returning with coupons were trained to recruit their peers using the same process. Eligibility criteria included being ≥18 years of age; having injected illicit drugs within the past month; ability to speak Spanish or English; ability to provide informed consent; and having no plans to move out of the city in the next 18 months. Participants were not excluded with specific psychiatric conditions. However, participants who could not complete the informed consent process were excluded, and participants who were under the influence of drugs were rescheduled for the next day.

Local outreach workers conducted interviews at either a fixed location in the community or at various neighborhood locations through use of a mobile clinic. Questions were translated into Spanish and back-translated into English by a bilingual team of researchers and reviewed for cultural appropriateness. For aim 1 under this dissertation, only baseline data were used. The baseline interviewer-administered survey elicited information on sociodemographic, behavioral and contextual characteristics. Drug use questions included an in-depth history of lifetime and recent illicit drug use, including age of first use by all routes of administration (i.e., smoking, snorting, or injection) and specific

questions regarding the circumstances surrounding the first injection experience.

Laboratory tests

The “Determine”® rapid HIV antibody test was used to detect the presence of HIV antibodies (Abbott Pharmaceuticals, Boston, MA). Reactive samples were confirmed using an HIV-1 enzyme immunoassay and immunofluorescence assay. Syphilis serology was conducting using the rapid plasma reagin (RPR) test (Macro-Vue, Becton Dickenson, Cockeysville, MD, USA); RPR-positive samples were confirmed using the Treponema pallidum particle agglutination assay (TPPA) (Fujirebio, Wilmington, DE, USA). Syphilis titers ≥1:8 were considered to be consistent with active infection, whereas the remainder of positive specimens was considered to reflect lifetime, rather than current, infection. Specimen testing was conducted at the San Diego County Health Department. Participants testing positive for HIV or other sexually transmitted infections (STIs) were referred to the Tijuana municipal health clinic for free care.

Variables

Mode of illicit drug use initiation*:* The dependent variable for aim 1 was injecting drugs before or at the same age as any other illicit drug use, referred to as ‘injection first’. This variable was created using answers to a series of items. The first was age of first injection drug use (at what age did you first

inject drugs?). This age was compared to the youngest age of first non-injection use for marijuana, methamphetamine, cocaine, crack, and heroin (at what age did you first smoke or snort the [insert drug type]?).

Socio-Demographic Characteristics: Data on age (How old are you?), marital status, education level (what is the highest level of education completed?), living situation (where do you currently live? and Who do you currently live with?), and number of years injecting drugs were collected.

Background characteristics*:* Family illicit drug use (have any member of your family ever used illicit drugs? and What family members used illicit drugs (mark all that apply)?) were both used to create two binary explanatory variables to examine the association with (1) any family illicit drug use and (2) a parent/sibling vs. aunt, cousin, grandparent's illicit drug use with 'injecting first'. Questions pertaining to the first injection context included: drug first injected (e.g. methamphetamine, heroin, cocaine, speedball, other drug, etc.), and the person with at time of first injection (e.g. alone, friend, family member, sexual partner, etc.). Additionally, using the age of first vaginal sex act (at what age did you first have intercourse?), a binary variable indicating sexual debut was before or at the same age as first injection drug use was created. Similarly, using age of first sex trade (at what age did you first exchange sex for money, drugs, goods, or shelter?) was used to create the nominal variable indicating the temporal relationship between first sex trade and first injection drug use (eg. before or at same age, after, or never traded sex).

Recent risk behavior variables: Current drug use behaviors included number of times inject drugs per day (in the past month, on average how many times per day did you inject drugs?), most common drug injected (in the past month, what drug do you inject most often?), location where inject most often (where do you inject most often?), and receptive (In the past 6 months, how often did you give, rent or lend a syringe to someone else that you had already used?), and distributive (In the past 6 months, how often have you shared or divided drugs by using a syringe to load drugs into another syringe?) sharing.

Frequency and mode of lifetime and recent (past month) use of the following non-injection drugs: marijuana, alcohol, methamphetamine, cocaine, crack, and heroin were assessed with the following measures: have you ever used [drug type]?; How old were you the first time you used [drug type]?; During the past month, how often did you used the [drug type] (never, <1 time a month, 2-3 days/month, once a week, 2-3 days/week, 4-6 days/week, everyday)? What ways did you used [drug type] (ingested, injected, smoked/sniffed, other)?

Syringe access was evaluated using the following: In the past 6 months, when you used a syringe for injecting (shooting) drugs, from where did you get the syringe (pharmacist, spouse/family member/friend, drug dealer, 'hit doctor' shooting gallery, needle exchange program, on the street, doctor/clinic/store, veterinary clinic, market, other)?

Sexual Behaviors*:* Frequency of condom use with regular (spouse, boyfriend, steady partner) and casual partners, and lifetime and recent (past 6-months) engagement in sex trade for money, goods, food, or shelter was asked.

Access to services: Lifetime access of drug treatment items included: have you received treatment for a drug related problem?; and how many times in your life have you been treated for a drug problem?; Have you ever been enrolled in any of the following programs (detoxification with medication, detoxification without medication, methadone, drug free residential treatment center, drug free outpatient center, inpatient (hospital) drug treatment center, other). Participation in syringe exchange programs items included: Are you aware of any needle or syringe exchange programs in your area?; have you used a local needle/syringe exchange program in the past 6-months?.

2. METHODS FOR AIMS 2 AND 3: *Mujer Mas Segura*

Study Overview

A second dataset is used for analysis of both aim 2 and aim 3 under the dissertation study. The *Mujer Mas Segura* project was funded by the NIH and NIDA (Grant number R01 DA023877; Principal Investigator: Steffanie Strathdee, PhD) and is an intervention study with the goal to simultaneously reduce high risk sexual and injection behaviors among FSW-IDUs in Tijuana and Ciudad Juarez. An earlier study conducted among FSWs in these cities from 2004 to 2006 (*Mujer Segura*) found that among whom HIV prevalence has recently increased from 2% to 14%; 46% had at least one active STI. Aims 2 and 3 were based on baseline data from the *Mujer Mas Segura* study.

Sampling & Measures

Between November 2008 and July 2010, FSW-IDUs from Tijuana (N=307) and Ciudad Juarez (N=316) were recruited using convenience sampling into a behavioral intervention study designed to reduce both high risk injection and sexual behaviors. Eligibility criteria included being ≥18 years of age; having had unprotected vaginal or anal sex with a male client at least once during the previous month; having shared syringes or injection paraphernalia (i.e. cookers, cotton, rinse water) at least once within the past month; ability to speak Spanish or English; ability to provide informed consent; and having no plans to move out of the city in the next 12-months. Trained,

bilingual interviewers collected baseline data from all eligible subjects independent of their HIV status. Women were reimbursed $15 USD for their participation in the baseline interview. The Institutional Review Board of the University of California, San Diego and the Ethics Boards of the Tijuana General Hospital and Universidad Autonoma de Ciudad Juarez approved all study protocols.

At baseline, participants underwent an interview-administered survey eliciting information on sociodemographics, sexual risk behaviors, injection risk behaviors, and experiences representing contextual factors surrounding sex work initiation, illicit drug use careers, and the context of first injection drug use. Additionally, questions pertaining to sexual, illicit drug use, and injection drug use behaviors during the previous 6-month and over their lifetime were asked. Sociodemographic questions included age, marital status, city of birth, migration history, sexual and physical abuse history, income and living arrangements. Questions on history of sexual behavior included age at initiation into sex work, reasons for entering sex work, and protected and unprotected sex acts with regular and casual clients and intimate partners.

Laboratory Tests

The “Determine”® rapid HIV antibody test was administered to determine the presence of HIV antibodies (Abbott Pharmaceuticals, Boston, MA). All reactive samples were tested using an HIV-1 enzyme immunoassay and immunofluorescence assay at the County of San Diego, Public Health

Laboratory. Those testing HIV-positive were referred to the local municipal health clinics in Tijuana or Ciudad Juarez for monitoring and care.

Syphilis serology used the rapid plasma reagin (RPR) test (Determine™ Syphilis TP). RPR-positive samples were subjected to confirmatory testing using the Treponema pallidum particle agglutination assay (TPPA) (Fujirebio, Wilmington, DE, USA) at the County of San Diego, Public Health Laboratory.

Initially, Gonorrhea and Chlamydia were detected using a rapid test kit (BioStar® OIA® GC and CHLAMYDIA) and positive samples were confirmed on urine specimens using APTIMA COMBO 2® Assay (Genprobe, San Diego, CA). However, upon release of recommendations from the U.S. Centers for Disease Control and Prevention that questioned the sensitivity of the Biostar rapid GC test, this test was discontinued on March 24, 2009. After this date, all participants provided urine for GC screening using a transcription-mediated assay (Genprobe, San Diego, CA). Samples were batched periodically and shipped to the San Diego County Health Department for confirmatory testing. Women with reactive STI tests were provided with free on-site treatment in accordance with U.S. and Mexican guidelines.

Variables

Lifetime and recent *agua celeste* use (paper 2): Two dependent variables guided the analysis for paper 2. Lifetime *agua celeste* use (have

you ever used *agua celeste*?) and among those who had reported lifetime use a question about frequency of use in the previous 6 months was also asked (never, once a month or less, 2-3 days a month, once a week, 2-3 times a week, everyday).

Sex work and injection drug use initiation (paper 3): Three outcomes of interest guided the analysis for paper 3 using the following questions: age of first sex trade (how old were you the first time you traded sex for money, drugs, goods, or shelter?), and age of first injection drug use (how old were you the first time you injected drugs?). Answers were used to construct the three outcomes of interest: time to first (a) sex work, (b) injection drug use, and (c) initiation of both sex work and injection drug use when initiation occurred at the same age.

Socio-demographic Characteristics: Data on age (How old are you?), marital status, education level (what is the highest level of education completed?), living situation (where do you currently live? and Who do you currently live with?), and number of years injecting drugs, number of years in sex work, city of birth (in what city were you born?), financial income (how much did you earn in the past month?), number of children, and study site (Tijuana vs. Ciudad Juarez) were collected.

Substance use: Frequency and mode of administration of cocaine, heroin, methamphetamine, speedball (heroin and cocaine) use was assessed with the following questions: Have you ever used drug type (yes, no)?; How

old were you when you first used [drug type]?; During the past month, how often did you use the drug (never, <1 a month, 2-3 days/month, once a wk, 2-3 days/wk, 4-6 days/wk, everyday)?; What ways did you use this drug(s) (ingested, injected, smoked/sniffed, other)? They were also asked if in the last month, they used alcohol and drugs before or during sex with a client and how many of their sex partners had ever injected drugs. Participants were also asked if they ever shared needles or injection equipment with another person, including a regular sex partner.

History of family drug use (have any of your family members ever used illicit drugs? and which of your family members used hard drugs such as heroin, cocaine, methamphetamine, or crack?) and history of family injection drug use (have any of your family members ever injected drugs? and Which family members injected illegal drugs?) was also asked.

The participants were asked if in the last month, they used alcohol before or during sex with a client and how often they used an illegal drug before or during sex with a client. They were also asked how many of their sex partners had ever injected drugs (None, A Few, Some, Most All Don't Know).

Context of sex work initiation (paper 3 only): Participants were asked about reasons for first trading sex: what is the main reason you traded sex the first time (money to pay for bills, money to pay for child's needs, money to buy drugs, pressure from friends pressure from family, pressure from boyfriend/spouse, forced into sex work, high from drugs, other)?; who

suggested it: whose idea was it to trade sex (mine, boyfriend, employer's, sister's, parent's, drug dealer's, husband's, friend's, relative's, another sex worker's, stranger, other)?; what promised: Were you promised anything in exchange for sexual relations, even if you did not receive it later? and What was it you were promised? (housing, drugs, food, employment, transportation, money, jewelry, clothes, nothing, other).

Context of first injection drug use (paper 3 only): Location of first injection drug use: where were you the first time you injected? (at own home, some else's home, shooting gallery, construction site, alleyway, bar, street, vacant lot, park, hotel/rented room, jail, other); What drug was first injected? (heroin, cocaine, crack, heroin and cocaine, methamphetamine, methamphetamine and heroin, methamphetamine and heroin, tranquilizers, barbiturates, other); reasons for first injecting: What were all the reasons you first injected? (pain due to withdrawal, encouraged by friends or family or spouse, depressed, stressed out and needed a way to deal, deal with work/work better, someone injected me against my will, cost of drugs too high, wasn't getting high from other methods, other); person with: who did you inject with the first time? (alone, friend, spouse/partner, family member, sexual partner (non-spouse), acquaintance, stranger, sex worker, client, other).

Physical and sexual abuse*:* Age of first physical abuse (caused or threatened by physical harm such as slapping, punching, kicking, hitting

assaulting with a knife or other weapons, etc.) and age of first sexual abuse (rape, forced sexual advances or non-consensual sexual acts).

Substance use with clients*:* Participants were asked if in the past month, they used alcohol before or during sex with a client and how often they used any illicit drug before or during sex with a client, and how often they used an injection drug before or during sex with a client.

Recent condom use*:* Frequency of condom use during vaginal and anal sex with regular and casual clients and with regular partners was asked of all participants.

C. Statistical Methods

For all three manuscripts, descriptive statistical analyses examined variables using means or medians for continuous measures, and frequencies and percentages for categorical variables. Differences across groups were examined using chi-squared tests for categorical variables, t-texts or Wilcoxon rank sum tests for continuous variables depending on whether the data was normally distributed. All analyses were carried out using SAS 9.2.

Logistic Regression

Manuscript 1 and 2 both utilized logistic regression to assess the bivariate and multivariate associations of factors with the dependent variables (‘injection first’, ‘lifetime agua celeste’ and ‘current agua celeste’).

All variables attaining a significance of ≤ 10% through bivariate analysis were considered for inclusion in multivariate analysis. Forward stepwise regression steps were performed manually to produce the most parsimonious model. Based on likelihood ratio tests comparing full to reduced models, only factors attaining significance at ≤ 5% were retained in the final multivariate models. Multicollinearity was assessed using the Variance Inflation Factor (VIF) measures that estimate the impact of collinearity among the variables in a regression model.

Accelerated Failure Time Model

Manuscript 3 utilized a parametric survival model called an accelerated failure time (AFT) model to assess the bivariate and multivariate associations of factors with the outcome variable (time to first sex work, time to first injection drug use, and time to initiation of both sex work and injection at the same age). AFT models allow the shape of the hazard function to be estimated. By being able to specify the survival distribution, AFT models produce more efficient estimates with smaller standard errors than semi-parametric survival models (e.g. Cox Proportional Hazard Models).[16] Further, AFT models can easily generate predicted event times for any specified set of covariate values.[16] Lastly, AFT models can accommodate tied outcome data much more efficiently than Cox Proportional Hazard Models can, thus further contributing to efficient estimates of the effects.[16,17] AFT models accommodate left, right, and interval censoring for individuals. However, in all analysis under aim 3, all participants have data on time to event, and therefore no cases were censored.

Fit diagnostics were assessed for each of the three outcomes by comparing Akaike's information criterion (AIC) values across models with identical covariates. AIC values were compared for the following specified distributions of time: Weibull, exponential, gamma, log-logisitic, and log-normal. These alternative distributions were explored because they have different implications for hazard functions that may, in turn, lead to different interpretations of the effects.[16] Prior to all bivariate and multivariate analysis,

fit diagnostics were carried out for the three outcomes of interest. A description of these fit statistics for each outcome can be found in Appendix 3.

Under AFT models beta-estimates were exponentiated to create a time (rate) ratio, and thus allow for an interpretation on the time scale. For accelerated failure time models, the effect of a covariate is expressed as either accelerating (shortening time to event; rate ratios >1) or decelerating (lengthening time to event; rate ratios <1). For example, women have a shorter time to event of 5.7% compared to men. Or for continuous covariates, each additional year of age increases the time to even by 1.9%.

D. Purpose of the Dissertation Study

The overall purpose of the collective studies for this dissertation is to expand the understanding of substance use trajectories leading to injection drug use initiation. This was accomplished by conducting three publishable studies including: (i) a study that identified factors associated with initiating illicit drug use through injection; (ii) a study that estimates the prevalence and correlates of lifetime and recent use of an inhalant drug used primarily in the Northern Mexico border region; and (iii) a study that identifies factors associated with a shorter time to sex work initiation and shorter time to injection drug use initiation among current FSW-IDU in the Mexico-US border region.

E. Research Objectives and Associated Hypotheses

The overall objective of this dissertation is to develop a better understanding of gender specific factors associated with substance use trajectories leading to injection drug use, specific primary research objectives were devised and addressed in three independent manuscripts.

Paper 1: 'Injection First': A Unique Group of Injection Drug Users in Tijuana, Mexico

Objective 1a. Identify background characteristics of individuals who injected as their first illicit drug use experience.

Hypothesis 1a. 'Injection first' individuals would be more likely to report a family member involved in illicit drug use.

Objective 1b. Examine how current drug using and sexual behaviors differed across 'injection first' individuals and those who initiated illicit drug use through snorting, smoking, or ingesting the drug.

Hypothesis 1b. Those who injected as their first illicit drug use experience would be more likely to report riskier current drug use behaviors.

Paper 2: Prevalence and Correlates of 'Agua Celeste' Use among Female Sex Workers who Inject Drugs in Ciudad Juarez, Mexico

Objective 2a. Identify prevalence of lifetime and recent use of *agua celeste* within a study of FSW-IDU in two northern Mexican cities.

Objective 2b. identify factors associated with lifetime and current use of *agua celeste* in the sample.

Paper 3: The context of first sex work and injection drug use. Factors associated with a shorter time to initiation among current FSWs who inject drugs in the Mexico-US border region.

Objective 3a. Identify factors associated with shorter time to initiation of sex work among women who initiated sex work before injection drug use.

Objective 3b. Identify factors associated with a shorter time to initiation of injection drug use among women who initiated injection drug use before sex work.

Objective 3c. Identify factors associated with a shorter time to both injection drug use and sex work initiation among women who first engaged in both behaviors at the same age.

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CHAPTER III.

MANUSCRIPT 1

'Injection First': A Unique Group of Injection Drug Users in Tijuana, Mexico

A. Abstract

Using baseline data from a study of injection drug users (IDU) in Tijuana, Mexico (N=1052), we identified social and behavioral factors associated with injecting at the same age or earlier than other administration routes of illicit drug use (e.g. 'injection first') and examined whether this IDU subgroup had riskier drug using and sexual behaviors than other IDUs. Twelve-percent 'injected first'. Characteristics independently associated with a higher odds of 'injection first' included being younger at first injection, injecting heroin as their first drug, being alone at the first injection episode, and having a sexual debut at the same age or earlier as when they initiated drug use; family members' illicit drug use was associated with lower odds of injecting first. When adjusting for age at first injection and number of years injecting, 'injection first' IDUs had *lower* odds of ever overdosing, and ever trading sex. On the other hand, they were less likely to have ever been enrolled in drug treatment, and more commonly obtained their syringes from potentially unsafe sources. In conclusion, a sizable proportion of IDUs in Tijuana injected as their first drug using experience, although evidence that this was a riskier subgroup of IDUs was inconclusive.

B. Introduction

Most literature indicates that a period of non-injection illicit drug use precedes the first injection drug use experience. [1,2] Factors that influence injection initiation are diverse, but are usually related to the desire to achieve a stronger or more efficient high, or to curiosity about injection as a mode of administration.[2-4] A study of young IDUs in Melbourne, Australia, found that reasons for injecting included a desire to experience an immediate high, curiosity about the effect of the injected drug, and belief that it is cheaper or less wasteful than other administration routes.[2,3] Similar findings have been reported among IDUs in Baltimore, MD.[4]

The few studies examining initiation to injection drug use provide general descriptions of initial drugs injected and circumstances surrounding the initial experience.[5-7] Within a sample of IDUs from Rio de Janeiro, Brazil, most injected the first time in a public place with a drug that they bought themselves (e.g., cocaine), and the majority were injected by either a friend or relative.[6] Similarly, in a study of young IDUs in Baltimore, MD, the majority reported injecting the first time in a social setting. However, 22.6% reported self-injecting and 12.7% were alone during their first injection experience.[8] Previous studies of circumstances surrounding the first injection experience report that individuals are likely to be in their adolescence at first injection episode with an unstable social environment including homelessness, family drug use, incarceration, or unemployment.[2,3,6]

Social influences, such as peer networks have also been reported as strong predictors of transitioning into injection drug use,[9] specifically having a sex partner who injects drugs.[4] Studies suggest family members, friends, or peers most often introduce others to injection drugs.[3,10,11] Family substance abuse may shape adolescent substance use through both inattentive parenting,[12] and by providing an environment where drugs are readily available and drug using behaviors are modeled.[13] However, little research has examined how family illicit drug use may influence initiation into injection.

The aims of the present study were two-fold. First, we aimed to identify background characteristics of individuals who injected as their first illicit drug use experience. Specifically, we hypothesized that 'injection first' individuals would be more likely to report a family member involved in illicit drug use. Second, given these individuals' accelerated transition into injection drug use, we also examined how their current drug using and sexual behaviors differed compared to individuals who initiated illicit drug use through snorting, smoking, or ingesting. We hypothesized that those who injected at their first drug use experience would be more likely to report riskier current drug use behaviors.

C. Methods

Study Setting

San Diego, California, and Tijuana, Mexico are located on a major drug-trafficking corridor that brings drugs like methamphetamine, heroin and marijuana to the United States. The San Ysidro border crossing, which separates the two cities, is the busiest land border crossing in the world.[14] A "spillover" effect from northbound drug shipments has resulted in drugs being sold cheaply and plentifully in Tijuana,[15] resulting in a growing injection drug using problem. In 2003, it was estimated that approximately 6,000 IDUs attend shooting galleries in Tijuana;[16] however, the total number of IDUs may be as high as 10,000.[16]

Study Population

From 2006 to 2007, IDUs residing in Tijuana, Mexico, were recruited into a longitudinal study examining behavioral and contextual factors associated with HIV, syphilis, and tuberculosis infection, as previously described.[17] IDUs were recruited using respondent-driven sampling (RDS).[17] A group of "seeds" selected for heterogeneity with respect to age, gender, and geographical location were given uniquely coded coupons to recruit members of their social networks into the study. Recruitment waves continued as subjects returning with coupons were trained to recruit their peers using the same process. Eligibility criteria included being ≥18 years of age; having

injected illicit drugs within the past month; ability to speak Spanish or English; ability to provide informed consent; and having no plans to move out of the city in the next 18 months. We did not exclude participants who had specific psychiatric conditions. However, participants who could not complete the informed consent process were excluded, and participants who were under the influence of drugs were rescheduled for the next day. The Institutional Review Board of the University of California, San Diego and the Ethics Board of the Tijuana General Hospital approved protocols.

Data Collection

Local outreach workers conducted interviews at either a fixed location in the community or at various neighborhood locations through use of a mobile clinic. The interviewer-administered survey elicited information on sociodemographic, behavioral and contextual characteristics. Drug use questions included an in-depth history of lifetime and recent illicit drug use, including age of first use by all routes of administration (i.e., smoking, snorting, or injection) and specific questions regarding the circumstances surrounding the first injection experience.

Data Analysis

The primary dependent variable for all analyses was injecting drugs before any other illicit drug use, referred to as ‘injection first’. This binary variable was created by identifying participants who reported injecting any

substance at either a younger or the same age as they reported using any illicit drug through a non-injection route. Drug types considered included: marijuana, methamphetamine, cocaine, crack and heroin; as these were the most common drugs used within the sample. For example, if a participant reported first injecting a drug at age 16 and reported first using either marijuana, cocaine, methamphetamine, or heroin (through snorting or smoking) earlier than age 16, then they were categorized into the non-'injection first' category.

The explanatory variable to address our first research question came from the following measure: "Have any members of your family ever used illicit drugs?" Answers from a follow up multiple response item asking which family member used illicit drugs were collapsed into two items that reflected either first generation (e.g. parent or sibling) or second generation (e.g. cousin, grandparent) relatives, thus capturing the different degrees of influence. Additional background characteristics included place of birth, number of years currently living in Tijuana, age of first sexual debut, drug first injected, and who they were with during this first injection episode.

To address our second aim, the following five domains were considered in examining differences in sexual and drug use risk behaviors within the past 6 months: (1) frequency of injection drug use; (2) type of location where drugs were most often injected; (3) syringe sharing behaviors: receptive and distributive syringe sharing; (4) syringe sources; (5) condom use with regular

and casual sexual partners; and (6) trading sex for money, drugs, goods, or shelter (i.e., survival sex). Lifetime drug related variables that pertained to periods following the first drug use experience (i.e., overdose, experience with drug treatment, and survival sex trade) were also considered in these analyses.

Analyses were based on 1,052 subjects out of 1,056 enrolled (four participants lacked data on age at first injection). Characteristics of 'injection first' IDUs were compared to non-'injection first' individuals using Pearson Chi-square tests for categorical variables and t-tests for all normally distributed continuous variables. Univariate and multivariate logistic regression were performed to identify factors independently associated with reporting 'injection first'. Guided by the two study aims, we developed two multivariate logistic regression models. The first multivariate model explored characteristics or behaviors prior to or surrounding the injection initiation experience, thus creating a model describing predictors of "injecting first". The second multivariate model focused on examining sexual and drug using behaviors in order to characterize risk behaviors of 'injection first' IDUs. Models were developed using a manual procedure where all variables of interest that attained a significance level of <10% were considered in multivariate analyses in order of most to least significant. The likelihood ratio statistic was used to compare nested models, retaining variables that were significant at the 5% level. Lack of multicollinearity between covariates in the final models was

confirmed by appropriate values of the largest condition index and of the variation inflation factors. RDS-adjusted models were also run to explore potential effects of the RDS recruitment method on our estimates, as described previously [17,18]. No significant differences between the RDS adjusted and unadjusted models were identified; therefore, unadjusted values are presented. A sub-analysis excluding age-ties for those who reported initiating injection and non-injection at the same age was also performed.

D. Results

Characteristics

Of 1,052 IDUs, 124 (12%) reported 'injection first', with 26 of these (20%) reporting the same age for marijuana and injection drug use initiation, and 19 (15%) reporting the same age for non-injection use of either methamphetamine, cocaine/crack, or heroin as injection initiation. Overall, the median age was 36 (interquartile range [IQR], 31-42) and just over one-quarter (28.5%) were born in Tijuana. Over half had a monthly income of less than 3,500 pesos (approximately 335 USD). No differences in income, age, or birthplace were found across the two groups. 'Injection first' IDUs were significantly more likely to be born in the state of Baja California rather than another Mexican state or another country (41.1% vs. 31.8%, p=0.04), and had lived in Tijuana a lower number of years (median: 11 years [IQR: 5-27], vs. 15 years [IQR: 5-30], p=0.91). HIV prevalence, TB prevalence, and lifetime prevalence of syphilis infection as confirmed by TPPA was 4.5%, 67% and 16% respectively, and did not differ significantly between those who injected first and those who first used drugs through other modes of administration (HIV: 6.5% vs. 4.1%, p=0.23; TB: 70% vs. 66%, p=0.33; syphilis: 19% vs. 15%, p=0.32).

Antecedents of Injection Initiation

'Injection first' IDUs were more likely to initiate injection drug use at a younger age than other IDUs (Table 1). A significantly lower proportion of 'injection first' IDUs had a family member who had ever used illicit drugs, with the large proportion of those (21%) reporting this being a parent or sibling. Heroin was the most common drug first injected for 'injection first' IDUs, followed by cocaine, and methamphetamine. Although not significant, a lower proportion of 'injection first' IDUs had ever been told by a health care provider they had depression or anxiety.

Within the context of their first injection drug use experience, compared to other IDUs, the majority of 'injection first' respondents injected heroin (87% vs. 79%) in the company of a friend(s), with a considerable proportion (16%) being alone during this experience (Table 1). Overall, the majority of participants (n=895) reported their first sexual experience being at a younger age than initiating injection drug use. However, a higher proportion of 'injection first' than non-'injection first' IDUs reported their sexual debut being earlier or at the same age as their first injection drug use experience. Only one 'injection first' respondent (1%) reported trading sex for money, drugs, goods, or shelter before initiating injection drug use, compared to 113 (13%) non-'injection first' respondents.

Background Factors Independently Associated with 'Injection First'

A total of five background factors were independently associated with 'injection first' (Table 1): being younger at the first injection drug use experience (Adjusted OR [AOR]= 0.89, 95% CI, 0.85-0.93); having a family member who ever used illicit drugs (AOR=0.56, 95%CI, 0.35-0.88); reporting heroin as the first drug injected (AOR= 1.90, 95% CI, 1.08-3.37); being alone at the first injection drug use experience (AOR= 2.02, 95%CI, 1.15-3.57); and reporting a sexual debut earlier or at the same age as initiating injection drug use (AOR=2.61, 95%CI 1.60-4.27). Excluding age ties did not change the direction or the significance of these associations, nor lead to any new associations.

Risk Behaviors following the first injection experience

Very few differences were found across the two groups regarding drugs used, sexual behaviors within the previous 6 months, or other variables that reflected the period since initiation of injection. Both groups reported the drug most frequently injected to be heroin alone, or in combination with methamphetamine (Table 2). However, when compared to the non-'injection first' group of IDUs, the 'injection first' IDUs were less likely to report smoking or snorting heroin, methamphetamine, or cocaine either in the previous 6-months or during their lifetime. Both lifetime use and recent use of marijuana was significantly lower in the 'injection first' group, as well as lifetime use of

alcohol (data not shown). However, 'injection first' IDUs were more likely to inject drugs at least once per day compared to other IDUs.

The drug use context across these two groups did differ in some respects. Not surprisingly, 'injection first' IDUs had been injecting for a greater number of years (table 2). 'Injection first' IDUs were more likely to inject most often in their homes, and less likely to inject at shooting galleries or on the street. 'Injection first' IDUs were also significantly less likely to report distributive or receptive syringe sharing. When asked about where they most often purchased syringes, 'injection first' IDUs were more likely to report purchasing syringes from a *tiendita* [market]. They were also more likely to be aware of the local needle exchange program (NEP). Among those who were aware of the Tijuana NEPs, a greater, proportion of 'injection first' IDUs reported ever obtaining syringes at NEPs compared to other respondents, but this difference was not statistically significant (82% vs. 67%, p=0.13). A lower proportion of 'injection first' IDU had ever accessed drug treatment. The proportion of drug related overdose was lower both within the previous 6-months and during their drug use career. Regarding health care access in the previous 6-months, while only marginally significant, 'injection first' IDUs were more likely to report accessing health care services, and less likely to report needing to access medical care but not seeking it.

Of the total 1,052 participants, only 280 (27%) reported having intercourse in the previous 6 months. Among these sexually active IDUs,

'injection first' IDUs were more likely to report always using a condom with casual sexual partners, but were less likely to report condom use with regular sex partners, and were less likely to have traded sex in exchange for money, drugs, or housing.

Risk Behaviors Independently Associated with 'Injection First'

When adjusting for age of first injection drug use and number of years injecting drugs, five factors were independently associated with 'injecting first' (table 2). Injection first IDUs were more likely to inject drugs at home in the past 6 months (AOR: 1.47, 95%CI: 1.37-2.07) and were less likely to have ever experienced a drug-related overdose (AOR: 0.53, 95% CI: 0.38-0.75) or to have ever traded sex for money, drugs, goods, or shelter (AOR:0.50, 95%CI: 0.32-0.80). On the other hand, they were more likely to report *tienditas* as their primary syringe source (AOR: 1.52, 95%CI: 1.03-2.25) and were less likely to have ever accessed any form of drug treatment (AOR: 0.62, 95%CI: 0.44-0.88). Excluding age ties did not change the direction or the significance of these associations.

E. Discussion

To our knowledge, this is the first examination of a subgroup of IDUs who initiated injection drug use earlier or at the same age as other routes of drug administration. In our study of IDUs from Tijuana, Mexico, approximately 12% reported having 'injected first', with the majority of these individuals initiating with heroin. Our prevalence estimate is significantly larger than the aforementioned Brazilian study of mainly cocaine users which found that <1% of IDUs initiated injection prior to other modes of drug use.[6] Younger age at first injection, having a sexual debut prior to initiating injection, first injecting heroin, and injecting alone were all independently associated with injecting as the first drug use experience. In contrast to our hypothesis, having a family member who used illicit drugs was inversely associated with 'injecting first'.

Surprisingly, although this subgroup of IDUs entered into illicit drug use in an atypical manner, they were not significantly riskier in terms of their recent drug use or sexual behaviors. Instead, after controlling for differences in age of first injection drug use and number of years injecting drugs, 'injection first' IDUs were more likely to inject at home, and less likely to have ever experienced a drug related overdose, or to have participated in survival sex in their lifetime. However, they were less likely to have ever been enrolled in drug treatment, and more commonly obtained their syringes from potentially unsafe sources (i.e., *tienditas*).

Literature surrounding injection initiation shows that first injection episodes typically involve friends, or drug using peers who provide expertise or assistance with injecting.[19-21] Interestingly, when compared to non-'injection first' IDU, the subgroup of IDUs who injected first were more likely to inject alone. While other studies examining the context of injection initiation report a small minority of subjects inject alone upon their first injection experience,[2,7,8] unlike our sample, the majority of individuals in these studies did inject drugs prior to a period of non-injection drug use. Our findings may imply that these IDU were knowledgeable enough about the mechanics of injecting that they were able to administer the drug themselves. We speculate that the subgroup of IDUs who 'injected first' were most likely exposed to drug use through their communities, peer networks or sexual partners, but our study lacked additional information on the context of first injection to explore this more closely. While few participants reported ever being diagnosed with depression or anxiety, it remains possible that injecting alone at the first episode is a proxy for depression or social isolation. Qualitative or mixed-methods studies are needed to provide more information on the social context of injecting first.

We also found that IDUs who injected first were more likely to inject in their home. IDUs who shoot up in their home, instead of public locations such as shooting galleries or the street, typically lack the same circumstance to share used syringes. In a study of IDUs in the South Bronx, New York, those who injected most frequently in their home were less likely to share drugs and

syringes.[22] Initiating alone and self-injecting may reflect a desire for a level of autonomy or control over the injection experience or personal agency which may translate into a pattern of safer drug use behaviors.

In contrast to our original hypothesis, those with a drug using family member were at lower odds of initiating illicit drug use through injecting. There is some literature to support that second hand experiences with family drug abuse may motivate some young people to avoid or delay injection drug use.[23-25] In a recent multi-city study in the United States, Broz et al. found a tendency for young African-American drug users to delay or avoid injecting drugs, with no such trend in young whites, which they speculated may be related to observing the consequences of drug dependency in their communities.[24] Using data from the U.S. Household Survey on Drug Abuse, Armstrong reported a similar trend with Blacks born in birth cohorts after 1955.[23] Even though our study participants with a drug using family member were less likely to 'inject first', they did eventually transition into injecting drugs. Future prospective studies of young non-IDUs are needed to examine how the role of family drug use and drug dependence affects drug use trajectories, since our study lacked a non-IDU comparison group.

Although 'injection first' IDUs were generally no more risky in terms of their drug use practices than other IDUs, we found some evidence to suggest that they were more severely drug dependent. 'Injection first' IDUs were more likely to inject at least once per day, have injected for a longer duration, and

have a lower odds of ever accessing drug treatment. Apart from these indicators, there was only one risk behavior that posed a potential risk of acquiring blood borne infections among IDUs who injected first. Specifically, 'injection first' IDUs were more likely to purchase syringes most often from *tienditas* (markets), and did not obtain syringes more often from the local NEP, even though they were more aware of this program than other IDUs. Anecdotal accounts from study participants and outreach staff describe *tienditas* as a widely used alternative to pharmacies for syringe purchase that sell syringes at a slightly higher price than pharmacies (approximately 12-15 pesos compared to 5-10 pesos). IDUs may experience less stigma and prejudice from *tienditas* than from pharmacy workers, and may be less subject to police harassment. While *tienditas* are preferable to dangerous syringe sources such as shooting galleries, they are not regulated like pharmacies and could be selling reused or tampered syringes thus not representing a safe syringe source.

We also found that 'injection first' IDUs were at lower odds of experiencing a drug related overdose in their lifetime. Even though these IDUs have injected drugs for a longer duration of time, their less risky and potentially more stable drug use patterns may have contributed to a lower risk of overdose. Lower levels of lifetime incarceration and homelessness also may have contributed to fewer disruptions in their drug use and thus fewer overdose experiences. Given the extended period of heroin use among the

entire study population, it was not surprising to find low levels of sexual behaviors in both groups of IDUs, as chronic opiate use has been shown to decrease libido and impair sexual performance.[26-28]

Since IDUs who 'injected first' tended to practice safer sexual and drug using behaviors, they may represent a group of potential opinion leaders[29] who could be trained to deliver safer injection messages to their peers through outreach. Community popular opinion leaders have been used successfully to disseminate HIV prevention messages to accelerate behavior change.[30] A similar model successfully implemented in Mexico, *Pasa La Voz,* applied RDS sampling to the traditional *promotores* (peer outreach) model to increase HIV testing and related services; such an approach could potentially be applied to the 'injection first' subgroup.[31]

Some limitations to our study must be taken into account in the interpretation of results. First, like most epidemiologic studies on drug abuse, ours relied on self-reported data and thus is subject to recall bias. Because the study instrument was not specifically designed to examine factors related to injecting first, the outcome variable relies on the reported age of several drug use measures. However, our subgroup analysis showed no differences in multivariate models when age-ties were removed. Additionally, our study was limited to the measures available for assessing family exposure to illicit drugs. Future studies that examine family size, family structure, and drug use dynamics within the family in relation to injection initiation experiences are

required. Finally, the ‘injection first’ group may be subject to some degree of survival bias if the riskiest of this subgroup died before they could be recruited into this study, and thus generalizability of these data are limited. While the findings reported here are descriptive in nature, they provide a foundation and highlight the need for future prospective studies to examine the broad range of drug use trajectories prior to and following injection initiation.

To our knowledge, this is the first study to characterize individuals who initiate illicit drug use through injection, and one of the few studies to examine injection initiation in a resource-limited setting. However, this accelerated pathway into injection drug use may occur more often than previously recognized. Our data provide little support that this IDU subgroup engaged in behaviors that placed them at higher risk of acquiring blood-borne infections. Instead this unique subgroup of IDUs may represent a more stable, less risky group who could act as potential leaders in their community to change social norms and motivate behavior change.

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Table 3.1: Background characteristics of IDUs who initiated injection drug use before or at the same time as other routes of drug administration

	'Injection First' n=124 N (%)	Non-'Injection First' n=928 N (%)	Univariate Odds Ratio (95% CI)	Adjusted* Odds Ratio (95% CI)
Median age at first injection drug use** (per year)	16.0 (14-20)	20.0 (17-26)	0.87 (0.84-0.91)	0.89 (0.85-0.93)
Primary school education or higher	64 (52)	558 (60)	0.70 (0.49-1.03)	--
Ever been told by healthcare provider had depression or anxiety	4 (3)	58 (6)	0.50 (0.18-1.41)	--
Any family member ever used illicit drugs	30 (24)	308 (33)	0.64 (0.42-0.99)	0.56 (0.35-0.88)
Parent or siblings used illicit drugs	25 (21)	217 (24)	0.84 (0.53-1.34)	--
Cousin, aunt/uncle, or grandparent used illicit drugs	4 (3)	43 (5)	0.70 (0.45-1.97)	--
Drug first injected:				
Heroin	108 (87)	729 (79)	1.84 (1.07-3.19)	1.90 (1.08-3.37)
Cocaine	7 (6)	104 (11)	0.47 (0.22-1.04)	--
Methamphetamine	4 (3)	25 (3)	1.20 (0.41-3.52)	--
Person with first time injected:				
Alone	20 (16)	98 (11)	1.63 (0.96-2.74)	2.02 (1.15-3.57)
Friend	71 (75)	573 (62)	0.83 (0.56-1.21)	--
Family member	10 (8)	54 (6)	1.62 (0.46-5.71)	--
Sexual partner	4 (3)	22 (2)	1.42 (0.70-2.86)	--
Acquaintance/stranger	13 (10)	76 (8)	1.31 (0.71-2.44)	--
Sexual debut before or at same age as first injection drug use	45 (36)	112 (12)	4.15 (2.74-6.23)	2.61 (1.60-4.27)
Age first traded sex for money, drugs, goods, or shelter:				
Before or at same age as first injection drug use	1 (1)	113 (13)	0.06 (0.01-0.42)	--
After first injection drug use	16 (13)	111 (11)	0.94 (0.54-1.66)	--
Never traded sex	107 (86)	700 (76)	--	--

*Adjusted for all other variables in the model (N=1015), **Median, Intra-quartile range reported (IQR) reported

Table 3.2: Past and current risk behaviors of IDUs who initiated injection drug use before or at the same time as other routes of drug administration

	'Injection First' n=124 N (%)	Non-'injection first' n=928 N (%)	Univariate Odds Ratio (95% CI)	Adjusted* Odds Ratio (95% CI)
Sociodemographics				
Heterosexual	122 (98)	898 (97)	1.90 (0.45-8.08)	--
Married	67 (54)	483 (52)	1.08 (0.74-1.58)	--
Tested HIV-positive at time of study	8 (7)	38 (4)	1.61 (0.73-3.54)	--
Slept in a car, abandoned building, shelter or street in past month	24 (19)	178 (19)	1.01 (0.63-1.63)	--
Ever been incarcerated	108 (87)	852 (92)	0.60 (0.34-1.07)	--
Principal source of income was legal job	40 (32)	222 (24)	1.50 (1.01-2.27)	--
Accessed health care services**	46 (38)	263 (29)	1.46 (0.98-2.16)	--
Needed medical care but did not access it	5 (4)	87 (9)	0.41 (0.16-1.03)	--
Median age of first injection drug use (IQR)***	16 (14-20)	20 (17-26)	0.87 (0.84-0.91)	0.87 (0.84-0.91)
Median number of years injecting drugs (IQR)***	18 (11-25)	14 (9-21)	1.05 (1.03-1.07)	1.02 (1.0-1.04)
Drug Use Behaviors				
Inject at least once daily**	109 (88)	739 (80)	1.80 (0.99-3.29)	--
Drug most frequently injected:**				
Heroin	64 (52)	533 (58)	0.78 (0.54-1.16)	--
Heroin+Cocaine (combination)	2 (2)	9 (1)	1.68 (0.36-7.86)	--
Heroin+Methamphetamine (combination)	54 (44)	362 (39)	1.21 (0.83-1.77)	--
Most often inject at:**				
Home	79 (64)	510 (55)	1.44 (0.98-2.12)	1.47 (1.37-2.07)
Street, alley, or vacant lot	8 (6)	77 (8)	0.76 (0.36-1.62)	--
Shooting gallery	24 (19)	214 (23)	0.80 (0.50-1.28)	--
Receptive syringe sharing**	63 (51)	556 (60)	0.69 (0.48-1.01)	--
Distributive syringe sharing**	63 (51)	585 (63)	0.61 (0.42-0.88)	--
Lifetime use of marijuana	69 (56)	893 (93)	0.09 (0.06-0.14)	--

Table 3.2 continued. Past and current risk behaviors of IDUs who initiated injection drug use before or at the same time as other routes of drug administration

	'Injection First' n=124 N (%)	Non-'injection first' n=928 N (%)	Univariate Odds Ratio (95% CI)	Adjusted* Odds Ratio (95% CI)
Recent use of marijuana **	28 (23)	361 (39)	0.43 (0.28-0.68)	--
Lifetime use of alcohol	61 (49)	770 (83)	0.20 (0.13-0.29)	--
Ever experienced drug related overdose	44 (36)	426 (45)	0.65 (0.44-0.95)	0.53 (0.38-0.75)
Had an Abscess**	28 (27)	305 (33)	0.67 (0.43-1.04)	--
Purchased syringe most often from a 'safe source'†	116 (94)	873(94)	0.91 (0.42-1.97)	--
Purchased syringe most often from a *tiendita* or market	45 (36)	253 (27)	1.52 (1.03-2.25)	1.53 (1.08-2.17)
Aware of needle exchange programs	33 (27)	218 (23)	1.18 (0.77-1.81)	--
Used a needle exchange program**	27 (82)	150 (67)	2.04 (0.81-5.17)	--
Ever accessed drug treatment	45 (39)	444 (49)	0.61 (0.42-0.91)	0.62 (0.44-0.88)
Sexual Behaviors				
Always used condom with regular sex partner** Δ	1 (6)	18 (12)	0.51 (0.06-4.13)	--
Always used condom with casual sex partner** ‡	8 (45)	69 (42)	1.10 (0.41-2.93)	--
Ever traded sex for money, drugs, goods, or shelter	17 (14)	224 (24)	0.50 (0.29-0.85)	0.50 (0.32-0.80)
Traded sex for money, drugs, goods, or shelter**	9 (7)	107 (12)	0.60 (0.29-1.2)	--

*Adjusted for all other variables in the model (N=1020).
**Previous 6 months
*** Median, Intra-quartile range reported (IQR) reported
† Pharmacist, needle exchange program, doctor/clinic/hospital, veterinary clinic, or market
Δ 162 participants reported a regular sex partner
‡ 182 participants reported

CHAPTER IV.

MANUSCRIPT 2

Prevalence and Correlates of 'Agua Celeste' Use among Female Sex Workers who Inject Drugs in Ciudad Juarez, Mexico

A. Abstract

Background**:** *Agua celeste*, or "heavenly water," is the street name for a sky-blue colored solvent reportedly inhaled or ingested to produce an intoxicating effect. Study aims were to (1) describe prevalence of *AC* use, and (2) identify correlates of lifetime and recent use of *AC* use among female sex workers who also inject drugs (FSW-IDUs) in northern Mexico.

Methods**:** Between 2008 and 2010, baseline data from FSW-IDUs ≥ 18 years old living in Tijuana or Ciudad Juarez participating in a longitudinal behavioral intervention were analyzed using logistic regression.

Results**:** Among 623 FSW-IDUs (307 from Tijuana and 316 from Ciudad Juarez), 166 (26%) reported ever using *AC,* all of whom lived in CJ. Among the CJ sample, lifetime prevalence of *AC* use was 53%, median age of first use was 16 years (IQR: 14-23), and 10% reported it as their first abused substance. Ever using *AC* was independently associated with ever being physically abused and younger age, and was marginally associated with

initiating injection drug use and regular sex work at age eighteen or younger. Among those ever using *AC*, 70/166 (42.2%) reported using it within the last 6 months, which was independently associated with using drugs with clients before or during sex, being on the street more than 8 hours per day, and younger age.

Discussion**:** We observed considerable geographic variation in the use of *AC* in northern Mexico. Future studies exploring factors influencing use, its precise formulation(s), and its potential health effects are needed to guide prevention and treatment.

B. Introduction

The relative inexpensiveness, ease of availability, and rapidly achieved intoxicating effects of inhalants make them particularly attractive to adolescents. There are four main types of inhalants: volatile solvents, gases, aerosols and nitrites. Inhalants may alter moods and create a euphoric state that can be accompanied by lightheadedness and hallucinations [1]. Nitrites, sometimes known as “poppers,” may enhance sexual pleasure. Sometimes referred to as “sniffing”, “huffing”, or “bagging”, the primary objective of inhaling volatile substances is to deliver the highest concentration of the substance to the lungs and subsequently the brain [2]. “Sniffing” typically means the solvent is inhaled from an open container, whereas “huffing” refers to covering the nose and mouth with a solvent-soaked cloth while inhaling. “Bagging” involves placing a solvent soaked bag over one’s mouth while inhaling. “Huffing” and “bagging” are especially harmful because solvents are often ingested during the inhalation process [3]. Independent of the mode of delivery, the intoxication typically lasts only a few moments, requiring inhalant users to engage in repeated use in order to prolong the effects. Serious health effects may occur with successive inhalations, including loss of consciousness, seizures, nervous system damage, and even death [4,5]. Cognitive damage is a particularly serious health effect, especially common in individuals who huff the solvents [6].

According to data from Mexico's 1998 National Survey on Addictions, inhalants were the third most prevalent drug used in Mexico after marijuana and cocaine [7]. In 1998, household surveys conducted in urban areas throughout Mexico among populations 12 to 65 years of age provided a cumulative prevalence of lifetime inhalant use of 0.80%, with prevalence at 1.07% in Tijuana and 0.30% in Ciudad Juarez, suggesting some degree of regional variation [7,8]. By 2005, the prevalence of inhalant use had increased to 2.83% in Tijuana and to 0.78% in Ciudad Juarez [9].

Due to their accessibility, the most commonly abused inhalants in Mexico include paint thinner, glues, and aerosol sprays [10,11]. A national high school survey conducted in 1998 in Mexico City found that among female adolescents, inhalants were the most common drug used after marijuana [10]. The most recent school surveys in Mexico show inhalants are the most common substance of abuse among male and female students between 7th and 9th grade [12]. Inhalant use is more common within this age group than marijuana use, with 7.4% of males and 6.7% of females reporting inhalant use compared to 5.6% and 2.7% respectively for marijuana [12].

In the context of an ongoing study of female sex workers who inject drugs (FSW-IDUs) in Tijuana and Ciudad Juarez, our study team became aware that some participants were using an inhalant referred to as *agua celeste*, or "heavenly water." A literature search revealed that *agua celeste* was reported as part of the Mexican pharmacoepia as early as 1885, when it

was described as a mixture of copper sulfate and ammonia which creates a sky-blue color [13]. Within Mexico's illicit drug market, early anecdotal reports suggest that *agua celeste* has mainly been used among children and adolescents along the Mexico-U.S. border [14], in a similar way that toluene was introduced four decades ago [15].

Although reports of *agua celeste* are lacking in the peer-reviewed literature, one account of *agua celeste* use within the Mexico-US border region dates back more than a decade [16]. A mixed-methods study among not-in-treatment drug users in San Antonio and El Paso, Texas reported *agua celeste* as a mixture of tannery processing products including benzene, formaldehyde, and methyl ethyl ketone, with a small jar selling for $2 to $3 USD [16]. More recently in a Mexican article, *agua celeste* was referred to as a mixture of solvents and ephedrine, a precursor used to manufacture methamphetamine that was recently banned in Mexico. This combination is then reportedly ingested and inhaled from soaked cloths [14]. An article from the Washington Post described *agua celeste* as a "cheap industrial solvent" [17]. Although the exact formulation of *agua celeste* may have changed over time and may differ depending on which solvents are regionally available, repeated exposure to these agents can lead to short and long term health damage [18].

Mexico's 2008 National Household Survey reported that the national lifetime prevalence of *agua celeste* use was 0.83%, with all cases detected in the central state of Aguascalientes and northeastern state of Chihuahua [11]. In

Mexico City, 0.2% of high school students reported use of *agua celeste* [12], and an ongoing study of drug users in treatment who report use of *agua celeste* refer to its effects as similar to the euphoric effects of toluene but stronger [19]. Use of a similar compound has been reported in other regions; 30% of 8th grade students in Leon, Guanajuato, (central Mexico) that were asked to list the different substances abused in their environment named "*agua de celaste*" [20].

The aims of the present study were two-fold. First, we determined prevalence of lifetime and recent use of *agua celeste* within an ongoing study of FSW-IDUs in two northern Mexican cities. Second, we identified factors associated with lifetime and current use of *agua celeste* in this sample. Based on our findings, we suggest areas for future research that have implications for prevention and treatment.

C. Methods

Study Setting

This study was conducted in Tijuana and Ciudad Juarez, Mexico, two cities along the Mexico-U.S. border with large populations of female sex workers. Tijuana is adjacent to San Diego, California and is the largest Mexican-U.S. border city. Tijuana and San Diego form the world's largest and busiest land border crossing [21]. Ciudad Juarez is adjacent to El Paso, Texas and is the largest city in the Mexican state of Chihuahua. In 2000, 36% of Ciudad Juarez inhabitants were born outside of Chihuahua [21]. In 2008, approximately 18% of FSWs from Tijuana and Ciudad Juarez reported ever injecting drugs, with a higher proportion of FSWs in Tijuana reporting recent injection drug use (15.8%, vs. 8.7%, p=0.001) [22].

2.2 Study Population and Sample

Between November 2008 and July 2010, FSW-IDUs from Tijuana (N=307) and Ciudad Juarez (N=316) were recruited using convenience sampling into a behavioral intervention study designed to reduce both high risk injection and sexual behaviors. Eligibility criteria included being ≥18 years of age; having had unprotected vaginal or anal sex with a male client at least once during the previous month; having shared syringes or injection paraphernalia (i.e. cookers, cotton, rinse water) at least once within the past month; ability to speak Spanish or English; ability to provide informed consent;

and having no plans to move out of the city in the next 12-months. Trained, bilingual interviewers collected baseline data from all eligible subjects independent of their HIV status. Women were reimbursed $15 USD for their participation in the baseline interview. The Institutional Review Board of the University of California, San Diego and the Ethics Boards of the Tijuana General Hospital and Universidad Autonoma de Ciudad Juarez approved all study protocols.

Measures

We restricted this analysis to baseline data from this longitudinal intervention study. Participants underwent an interview-administered survey eliciting information on sociodemographics, sexual risk behaviors, injection risk behaviors, and experiences representing their physical, social, and economic environments in their lifetime and over the last six months. Sociodemographic questions included age, marital status, city of birth, migration history, sexual and physical abuse history, income and living arrangements. Questions on history of sexual behavior included age at initiation into sex work, reasons for entering sex work, and protected and unprotected sex acts with regular and casual clients and intimate partners.

Questions on history of drug use behaviors included age of first use and/or injection of specific drugs alone and in combination, sharing of injection

equipment and drug use with clients. Two dependent variables guided the analysis. First, a single “yes/no” item asking participants if they had ever used *agua celeste* defined lifetime *agua celeste* use. Second, a follow-up question about the frequency of *agua celeste* use in the past 6 months was asked of all participants who reported ”ever” using *agua celeste*. This multiple response item (never, once a month or less, 2-3 days a month, once a week, etc.) was then collapsed into a dichotomous outcome of “recent use” versus “no recent use.”

Laboratory Tests

The “Determine”® rapid HIV antibody test was administered to determine the presence of HIV antibodies (Abbott Pharmaceuticals, Boston, MA). All reactive samples were tested using an HIV-1 enzyme immunoassay and immunofluorescence assay at the County of San Diego, Public Health Laboratory. Those testing HIV-positive were referred to the local municipal health clinics in Tijuana or Ciudad Juarez for monitoring and care.

Syphilis serology used the rapid plasma reagin (RPR) test (Determine™ Syphilis TP). RPR-positive samples were subjected to confirmatory testing using the *Treponema pallidum* particle agglutination assay (TPPA) (Fujirebio, Wilmington, DE, USA) at the County of San Diego, Public Health Laboratory.

Initially, Gonorrhea and Chlamydia were detected using a rapid test kit (BioStar® OIA® GC and CHLAMYDIA) and positive samples were confirmed on urine specimens using APTIMA COMBO 2® Assay (Genprobe, San Diego, CA). However, upon release of recommendations from the U.S. Centers for Disease Control and Prevention that questioned the sensitivity of the Biostar rapid GC test, this test was discontinued on March 24, 2009. After this date, all participants provided urine for GC screening using a transcription-mediated assay (Genprobe, San Diego, CA). Samples were batched periodically and shipped to the San Diego County Health Department for confirmatory testing. Women with reactive STI tests were provided with free on-site treatment in accordance with U.S. and Mexican guidelines.

Statistical Analysis

Prevalence of lifetime and recent *agua celeste* use was calculated for respondents in Tijuana and Ciudad Juarez. Given that all use of *agua celeste* was reported in Ciudad Juarez, remaining analyses were restricted to respondents from this city. First, FSW-IDUs who reported lifetime use of *agua celeste* were compared to FSW-IDUs who reported never using *agua celeste*. Second, among those who reported ever using *agua celeste*, FSW-IDUs who reported any use within the past six months were compared to FSW-IDUs who reported not using *agua celeste* in the past six months. Wilcoxon rank sum

tests and Chi-Square tests were used to examine distributional differences between groups for continuous and binary variables.

Next, separate univariate and multivariate logistic regression analyses identified factors associated with lifetime and recent *agua celeste* use. For both analyses, all variables attaining a significance level of $p \leq 0.10$ in univariate models were considered for inclusion in multivariate models. These variables were entered into multivariate logistic regression models in a manual forward stepwise fashion. The likelihood ratio statistic was used to compare nested models, retaining variables that were significant at an alpha level of 0.05. Since this was a descriptive study, all two-way interactions were assessed. Lack of multi-collinearity between the predictor variables in the final model was confirmed by appropriate values of the largest condition index and variance inflation factors.

D. Results

Overall Sample Characteristics

Among the 307 participants in Tijuana, median age was 33 years (intra-quartile range [IQR]: 28-41) and 59% had at least a primary school education. Heroin was the drug most commonly injected in the past month (59%), followed by a combination of heroin and methamphetamine ("speedball," 34%). Prevalence of lifetime *agua celeste* use in Tijuana was 0%.

Of the 316 participants in Ciudad Juarez, the median age was 33 years (IQR: 27-39), and 35% had at least a primary school education. Heroin was the drug injected most often over the previous month (82%), followed by speedball (15%). In Ciudad Juarez, over half of women (53%) reported ever using *agua celeste*, and the median age of first *agua celeste* use was 16 years (IQR: 14-23 years). The median duration of *agua celeste* use was 12 years (IQR: 5-18) (Table 1).

Results reported hereafter are restricted to the Ciudad Juarez sample. Among those who ever used *agua celeste*, (N=166), 10% reported using it earlier than their first use of marijuana, methamphetamine, heroin, or cocaine. Among these 166 women, 45% used *agua celeste* prior to initiating injection drug use and 40% reported using *agua celeste* prior to initiating regular sex work (data not shown). Additionally, 83% had experienced physical or sexual abuse prior to *agua celeste* use. Among those ever using *agua celeste*, 42%

reported using it within the last six months, of whom 24% reported using at least once daily, 30% used it at least one day per week, and 46% at least once per month.

Correlates of Lifetime Use of Agua Celeste

Compared to FSW-IDUs who had never used *agua celeste,* those who had ever done so were younger (31 years vs. 35 years, $p<0.001$), less likely to have ever traveled to the U.S. (42% vs. 54%, $p=0.04$), and marginally more likely to have ever been arrested (85% vs. 77%, $p=0.06$) (Table 1). Those who had ever used *agua celeste* were significantly younger when they began injecting drugs (18 years vs. 22 years, $p<0.0001$) and when they began regularly participating in the sex trade (18 years vs. 20 years, $p<0.0001$). *Agua celeste* users were also more likely to have ever been physically abused (72% vs. 54%, $p=0.002$) and marginally more likely to have ever been raped (66% vs. 56%, $p=0.08$). There were no differences between groups with respect to HIV prevalence, active syphilis infection, Chlamydia, or gonorrhea infection, nor were there differences relating to birthplace, sexual orientation, educational level, marital status, or the duration of time injecting drugs or trading sex regularly.

3.3 Factors Independently Associated with Lifetime Use of Agua Celeste

Two factors were independently associated with ever using *agua celeste* (Table 2), which included being younger (adjusted odds ratios [AOR]: 0.97 per 1-year increase (95% confidence interval [95% CI]: 0.94-0.99) and ever being physically abused (AOR: 2.03; 95% CI: 1.25-3.31). Two additional factors were marginally associated with lifetime use: initiating drug injection at age 18 years or younger (AOR: 1.73 per year; 95% CI: 0.99-3.03) and beginning regular sex work at age 18 or younger (AOR: 1.55 per year; 95% CI: 0.97-2.72).

Correlates of Recent Use of Agua Celeste

Among those who had ever used *agua celeste* (N=166), 70 (42.2%) reported using it in the past six months. Recent *agua celeste* users were marginally younger than those who had not used it in the past 6 months (Table 3). FSW-IDUs who recently used *agua celeste* were significantly more likely to have used non-injection heroin in the past month compared to non-current users (30% vs. 9%, $p<0.001$). Compared to non-current users, FSW-IDUs who recently used *agua celeste* reported spending more hours on the street per day (median: 12 vs. 8.5 hours, $p=0.01$), and were more likely to live and work at the same location (34% vs. 19%, $p=0.02$).

A significantly greater proportion of FSW-IDUs who recently used *agua celeste* reported often or always using drugs with their clients (73% vs. 56%,

p=0.03). Although women tended to report using heroin (82%) or cocaine/crack (10%) with clients, of the four women reporting that they used other drugs with clients, three reported using *agua celeste* with clients in the past month. There were no differences found in terms of type of recent sexual behaviors, income, ease of acquiring drugs, homelessness, condom use, recent sexual abuse, or relationship status.

Factors Independently Associated with Recent Use of Agua Celeste

Recent use of *agua celeste* was independently associated with often or always using drugs with their clients before or during sex (AOR: 2.08; 95% CI: 1.04-4.15) and being on the street for more than 8 hours per day (AOR: 2.70; 95% CI: 1.36-5.33). Being younger was also independently associated with recent *agua celeste* use, with those 18-25 years old having a three-fold higher odds of using *agua celeste* (AOR: 3.00; 95% CI: 1.02-8.86), compared to those 40 years and older (Table 4).

E. DISCUSSION

To our knowledge, this is the first study to describe correlates of *agua celeste* use. Overall, *agua celeste* was widely used among FSW-IDUs in Ciudad Juarez but was not used at all among FSW-IDUs in Tijuana. In Ciudad Juarez, over half of FSW-IDUs had used *agua celeste* in their lifetime, which was associated with ever being physically abused and marginally associated with initiating injection drug use and sex work at a young age. Among those who ever used *agua celeste*, nearly half had used it in the past six months. Recent *agua celeste* users were more likely to report using drugs with sex work clients before or during sex and to spend more time on the street per day, suggesting a higher risk profile.

Our prevalence estimates contrast the estimates of general inhalant use in Mexico, which show higher overall inhalant use in Tijuana compared to Ciudad Juarez [7,8]. However, our findings are consistent with the results from the National Household Survey that detected *agua celeste* use only in two states, one being Chihuahua [9]. Although our data support the notion that there is substantial current geographic variation in *agua celeste* use, given the high levels of population mobility in the Mexico-U.S. border region [23], its use could spread to other cities on either side of the US-Mexico border.

Lifetime *agua celeste* use was marginally associated with beginning to engage in sex work at a younger age, which is consistent with other studies of inhalant use in Mexico [24,25]. In a previous study of adult FSWs in Tijuana and

Ciudad Juarez by members of our team, Loza et al. showed that after adjusting for age, FSWs who initiated sex work prior to 18 years were nearly three time more likely to have used inhalants prior to initiating sex work [25]. In our study, 40% of *agua celeste* users in our study began using *agua celeste prior* to initiating sex work.

We found that women who had ever used *agua celeste* were younger than those who had never used the drug, and that 10% of ever users reported using *agua celeste* as their first drug of use. These findings are similar to literature suggesting that inhalants may play an important early role in individuals' drug use trajectories leading to later use of heroin and/or injection drug use. For example, in a prospective study of 600 African American youth from Chicago, Johnson et al. reported that those who used inhalants prior to age 16 were 9 times more likely to subsequently use heroin later in life [26]. Data from the 1990 U.S. National Household Survey on Drug Abuse demonstrated that after adjusting for sex, age, race, socioeconomic status and use of marijuana, inhalant users were more than 5 times more likely than non-users to transition to injection drug use [27].

FSW-IDUs who had a history of sexual or physical abuse were significantly more likely to report ever using *agua celeste*. While the direction of this relationship cannot be discerned from this study, the majority of women who reported ever using *agua celeste* did so after their first report of physical or sexual abuse. In ethnographic studies of drug-involved adults in New York

City, Fendrich et al. found that heavy inhalant use was associated with physical abuse during childhood [28]. In a cross-sectional study of public high school students in South Carolina, Zullig et al. found lifetime inhalant use to be strongly associated with life dissatisfaction, especially among students with a history of abuse [29]. In Mexico, children working or living on the streets, those with unstable family environments and who have been abused are most often the ones who use inhalants [30,31]. These findings suggest that women in our study may have turned to *agua celeste* as a way to cope with the emotional and psychological effects of physical and sexual abuse or other negative events experienced in childhood or adolescence.

Recent *agua celeste* use was three times more prevalent among women between 18 and 25 years old compared to older women. Using U.S. National Surveys on Drug Use and Health data from 2002 and 2003, Wu et al. also found that the pattern of inhalant use in the previous year was inversely related to participant age [32] which is also the case in Mexico [11,12].

While our cross-sectional study precludes inferences about predictors of recent *agua celeste* use, the finding that recent users spent more time on the street per day suggests that these women may comprise a more marginalized or socioeconomically disadvantaged group of drug users. Anecdotal accounts by study staff suggest *agua celeste* may be an alternative when their drug of choice (e.g., heroin) is not available to help them cope with

withdrawal symptoms. Future qualitative studies to explore motivations for current *agua celeste* use are necessary to better understand this relationship.

Finally, women who recently used *agua celeste* had greater odds of using drugs with clients before or during sex compared to non-current users. Since our study instrument did not specifically inquire about use of *agua celeste* use with clients, we are likely under-estimating the prevalence of its use in the context of sexual transactions. Our findings do suggest, however, that recent *agua celeste* users are more likely to be 'high' during their sexual transactions. This could compromise their ability to negotiate condom use or have control over other circumstances in the context of sexual transactions, possibly increasing the potential for exposure to HIV/STIs or violence.

Limitations of our analysis include a cross sectional analysis that limits our ability to draw causal inferences or clearly establish temporality. Self-reported data may also be subject to recall and social desirability bias. We lacked detail on some critical measures pertaining to *agua celeste* use (e.g. reasons for use, social context of use, etc.), which reduced our ability to examine factors that motivated initial and continued use. Since the study sample was recruited into a behavioral intervention study designed to reduce injection and sexual risk behaviors among FSW-IDUs, we may have over-estimated the prevalence of *agua celeste* use in this highly marginalized population. However, since our study excluded women below age 18, we may

have under-estimated the prevalence of recent *agua celeste* use, since it is reportedly common among youth [14].

While this descriptive study offers information about *agua celeste* users in Ciudad Juarez, we lacked information about the composition of the drug, routes of administration, and immediate short and long term health effects. Anecdotal information on *agua celeste* suggests that the drug can be made from a variety of volatile organic substances. The toxic substances that comprise *agua celeste* and the repetitive exposure to the substance could place users at high risk of both acute and long term health effects including damage to the central nervous system, respiratory arrest, cancer, and even death [33-35]. Ethnographic and epidemiological studies are needed to better understand the contents of the drug and the motivations and social context surrounding initial, recent, and continued use of the drug. These studies will help inform potential avenues for prevention and treatment.

Our findings build on previous literature showing that inhalant use is an important risk factor for subsequent injection drug use. The majority of epidemiologic studies group all inhalants together when estimating prevalence of use, or include inhalants in a wider group of illegal drugs, thus biasing prevalence estimates and preventing a more nuanced understanding of the role of specific inhalants in individuals' drug use trajectories. To our knowledge, this is the first community-based study to estimate *agua celeste* use and describe correlates of its use. Although findings cannot be

generalized to other populations, the widespread use of *agua celeste* among FSW-IDUs in Ciudad Juarez is concerning. In a population already experiencing elevated risk for STIs, HIV and other blood borne pathogens and high exposure to violence, the use of *agua celeste* may pose yet an additional danger.

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Table 4.1: Characteristics of Ever Using *Agua Celeste* Among Female Sex Workers Who Inject Drugs in Ciudad Juarez, Mexico (N=316).

	Ever used *Agua Celeste* N=166 N (%)	Never used *Agua Celeste* N=150 N (%)	p-value	Univariate Odds Ratio (95% confidence interval)
Sociodemographic characteristics				
Median age at time of interview (IQR)	31 (25-36)	35 (30-41)	**0.0002**	0.95 (0.93-0.97)
Ever married	82 (49)	78 (52)	0.6440	0.90 (0.62-1.31)
Has at least one child	153 (92)	142 (94)	0.3733	0.663 (0.31-1.42)
Median number of children (IQR)	3 (2-4)	3 (2-4)	0.2207	0.92 (0.82-1.03)
Mexican region of birth				
Northern States[a]	36 (23)	30 (21)	0.7270	0.69 (0.37-1.33)
Baja California	0	1(<1)	--[b]	--
Chihuahua	113 (71)	104 (73)	0.6853	1.31 (0.75-2.29)
Central States	6 (4)	6 (4)	0.8512	1.35 (0.34-5.33)
Southern States	4 (3)	1 (<1)	0.4839	1.38 (0.26-7.31)
Ever traveled to U.S.	70 (42)	81 (54)	**0.0355**	0.62 (0.43-0.90)
Sexual orientation (heterosexual)	142 (86)	135 (90)	0.2289	0.66 (0.37-1.2)
Completed more than primary school	53 (32)	59 (39)	0.1693	0.72 (0.49-1.07)
Ever been arrested	141 (85)	115 (77)	**0.0610**	1.71 (1.07-2.77)
HIV prevalence	33 (5)	30 (5)	0.8099	0.88 (0.32-2.42)
Active syphilis[c]	20 (13)	14 (10)	0.4210	1.34 (0.65-2.78)
Chlamydia	28 (17)	17 (12)	0.2001	1.53 (0.79-2.92)
Gonorrhea	5 (3)	3 (2)	0.6249	1.43 (0.34-6.11)
Past Drug Use Behaviors				
Median age began injecting drugs (IQR)	18 (16-23)	22 (17-30)	**<0.0001**	0.94 (0.92-0.96)
Median years injecting drugs (IQR)	10 (4-17)	10 (3-16)	0.5348	1.01 (0.99-1.03)
Began injecting drugs at 18 years or before	88(53)	48 (32)	**0.0002**	2.40 (1.63-3.52)
Ever used heroin (non-injection)	85 (51)	53 (35)	**0.0045**	1.92 (1.31-2.81)
Ever used methamphetamine (non-injection)	36 (22)	11 (7)	**0.0003**	3.50 (1.92-6.40)
Ever used cocaine (non-injection)	122 (73)	96 (64)	**0.0685**	1.56 (1.04-2.33)
Ever used marijuana	166 (88)	109 (73)	**0.0006**	2.75 (1.67-4.50)

Table 4.1 continued: Characteristics of Ever Using *Agua Celeste* Among Female Sex Workers Who Inject Drugs in Ciudad Juarez, Mexico (N=316)

	Ever used *Agua Celeste* N=166 N (%)	Never used *Agua Celeste* N=150 N (%)	p-value	Univariate Odds Ratio (95% confidence interval)
Ever been in drug treatment	108 (65)	81 (54)	**0.0452**	1.59 (1.09-2.31)
Past Sexual Behaviors				
Median age first sold sex for money, goods, food, housing (IQR)	17 (15-20)	20 (17-28)	**<0.0001**	0.90 (0.87-0.93)
Median age began selling sex regularly (IQR)	18 (15-20)	20 (17-29)	**<0.0001**	0.90 (0.88-0.93)
Median number of years trading sex regularly (IQR)	12 (6-19)	12 (6-17)	0.5022	1.01 (0.99-1.03)
Began selling sex regularly at 18 years old or before	98 (59)	55 (36)	**<0.0001**	2.49 (1.70-3.64)
History of Abuse				
Ever been raped	109 (66)	84 (56)	**0.0785**	1.50 (1.03-2.20)
Median age first time raped (IQR)	15 (11-20)	16 (11.5-23)	0.1874	0.09 (0.95-1.01)
Ever been physically abused	119 (72)	82 (54)	**0.0017**	2.1 (1.42-3.11)
Median age first time physically abused (IQR)	18 (16-25)	19 (16-26)	0.4415	0.98 (0.96-1.02)
Physical or sexual abuse preceded first agua celeste use[d]	137 (83)	--	--	--

Median (interquartile range [IQR]) reported for continuous variables
Bold indicates p-values <0.10
[a] Northern states excluding Baja and Chihuahua
[b] p-value not estimated due to zero cell counts
[c] active syphilis defined as ≥1:8 titer at baseline
[d] Among those who reported ever using *agua celeste*, age of first physical or sexual assault/abuse act was younger than first reported use of *agua celeste*

Table 4.2: Factors Independently Associated with Ever Using *Agua Celeste* Among Female Sex Workers Who Inject Drugs in Ciudad Juarez, Mexico (N=316)

Characteristic	AOR[a]	95%CI
Began injecting drugs at 18 years or younger	1.73	0.99-3.03
Began regular sex work at 18 years old or younger	1.55	0.99-2.72
Ever been physically abused	2.03	1.25-3.31
Age at time of interview (per 1-year increase)	0.97	0.94-0.99

[a] Adjusted for all other variable in the model (alpha=0.05)

Table 4.3: Characteristics of Recent[a] *Agua Celeste* Use Among Female Sex Workers Who Inject Drugs in Ciudad Juarez, Mexico (N=166)

	Recent *Agua Celeste* use (N=70)	No recent *Agua Celeste* use (N=96)	p-value	Univariate Odds Ratio (95% confidence interval)
Sociodemographic characteristics				
Median age at time of interview (IQR)	30.5 (23-35)	31 (26-38)	**0.0633**	0.96 (0.93-0.99)
Type of sex worker				
Street worker	61 (87)	94 (98)	**0.0147**	--
Professional brothel worker	3 (4)	1 (1)	--[*]	--
Other[b]	6 (1)	1 (<1)	--[*]	--
Income in past month is greater than 3500 pesos	42 (60)	55 (57)	0.7266	1.12 (0.66-1.89)
Median number of hours on street per day (IQR)	12 (8-15)	8.5 (7-12)	**0.0101**	1.09 (1.03-1.16)
On street more than 8 hours per day	51 (73)	48 (50)	**0.0030**	2.68 (1.54-4.68)
Homeless[c] in past month	4 (6)	5 (5)	0.8870	1.10 (0.36-3.43)
Live and work at same location[d]	24 (34)	18 (19)	**0.0230**	2.61 (1.24-4.11)
Spouse or steady partner	27 (39)	41 (43)	0.5925	0.84 (0.50-1.43)
Recent drug use behaviors				
Injected more than one time per day in past month	65 (93)	83 (86)	0.1904	2.04 (0.69-6.0)
Injection drug use in past month:				
Heroin	54 (77)	82 (85)	0.2238	--
Cocaine	0 (0)	3 (<1)	--*	--
Speedball	14 (20)	11 (11)	0.1846	--
Non-injection drug use in past month:				
Marijuana	29 (42)	32 (33)	0.2854	1.42 (0.83-2.42)
Inhalants[e]	15 (37)	0 (0)	--[*]	--
Non-injection cocaine	34 (51)	44 (46)	0.5783	1.19 (0.71-2.02)
Non-injection	4 (6)	0 (0)	--[*]	--

Table 4.3 continued: Characteristics of Recent[a] *Agua Celeste* Use Among Female Sex Workers Who Inject Drugs in Ciudad Juarez, Mexico (N=166)

	Recent *Agua Celeste* use (N=70)	No recent *Agua Celeste* use (N=96)	p-value	Univariate Odds Ratio (95% confidence interval)
methamphetamine				
Non-injection heroin	21 (30)	9 (9)	**0.0006**	4.14 (2.02-8.50)
Somewhat or very difficult to get drugs in past month	39 (56)	55 (57)	0.8395	0.94 (0.56-1.58)
Someone else has bought drugs for them in past month	19 (27)	21 (22)	0.4332	1.33 (0.73-2.43)
Substance use with client before or during sex in past month:				
Alcohol use	48 (69)	61 (64)	0.5003	1.25 (0.72-2.17)
Drug use	51 (73)	54 (56)	**0.0284**	2.09 (1.20-3.64)
Injection drug use	15 (21)	18 (19)	0.6694	1.18 (0.62-2.25)
Recent Sexual behaviors				
Always used condoms with clients in past month	5 (7)	3 (3)	0.7838	0.81 (0.19-3.57)
Forced to have sex against will by client in past month	11 (16)	13 (14)	0.0831	1.19 (0.57-2.47)

Median (interquartile range [IQR]) reported for continuous variables

Bold indicates p-values <0.10

[*] p-value not estimated due to zero cell counts

[a] Past six-months

[b] dance hostess, barmaid, taxi girl, professional brothel worker, call girl, companion

[c] Slept most often in abandoned building, shelter, street, or shooting gallery in past month

[d] Lives and works in the same location (e.g., some women live in the back of the bar where they work)

[e] due to missing values N=77

Table 4.4: Factors Independently Associated with Recent[a] *Agua Celeste* Use Among Female Sex Workers Who Inject Drugs in Ciudad Juarez, Mexico (N=166)

Characteristic	AOR[b]	95% CI
Use drugs often or always with client before or during sex	2.08	1.04-4.15
On street for more than an average of 8 hours a day	2.70	1.36-5.33
Age at time of interview		
18 to 25 years	3.00	1.02-8.86
26-39 years	2.03	0.75-5.51
40 years and older	1	--

[a] Past six-months

[b] Adjusted for all other variable in the model (alpha=0.05)

CHAPTER V.

MANUSCRIPT 3

The context of sex work and injection drug use initiation: Factors associated with time to initiation among current female sex workers who inject drugs in the Mexico-US border region.

A. Abstract

Aims: To identify factors associated with initiation of (1) sex work, (2) injection drug use, and (3) sex work and injection drug use when both behaviors were initiated at the same age among female sex workers who currently inject drugs (FSW-IDU) in two northern Mexico cities.

Design: Parametric survival analysis of baseline interview data for time to sex work initiation, time to injection drug use initiation, and time to sex work and injection drug use initiation among women who initiated both at the same age.

Setting: Tijuana and Ciudad Juarez, two Mexican cities on the US border situated on major drug trafficking routes and where prostitution is quasi-legal.

Participants: 575 FSW-IDUs aged ≥18 years.

Measurements: Interview-administered survey data on context of initiation of sex work and injection drug use.

Findings: Nearly half initiated sex work prior to beginning to inject, a third initiated injection first, and a quarter initiated both sex work and injection drug use at the same age. Any early non-injection stimulant use accelerated time to initiation of sex work, time to initiation of injection drug use, and time to initiation of both events when they began at the same age; conversely early inhalant use delayed time to injection initiation. Low education and living in Ciudad Juarez shortened the time to sex work initiation. Being from a southern Mexican state greatly delayed the time to first injection drug use. Factors associated with initiating both sex work and injection drug use at the same age included having an intimate partner encourage them to begin sex work, and first injecting drugs to help deal with depression. Early physical abuse shortened the time to sex work initiation and the time to injection initiation, and substantially shortened the time to initiation for women who initiated both sex work and injection at the same age.

Conclusions: Contextual factors differ for women who initiate sex work before injection drug use and women who initiate injection drug use before engaging in sex work; and particularly for women who initiate both sex work and injection drug use at the same age. These findings may help identify possible avenues for intervention that can delay or prevent onset of initiation of injection drug use and/or sex work.

B. Introduction

Globally, considerable overlap between sex work and injection drug use behaviors has been documented [1-5], with the prevalence of injection drug use among female sex worker (FSW) populations ranging from 32% to 81% [2, 4-7]. Independently, injection drug use and sex work can place individuals at risk for exposure to blood borne infections and sexually transmitted infections (STI), but engagement in both behaviors elevates the risk substantially. Little research on early sex work and injection drug use initiation has been done on FSWs who also engage in injection drug use (FSW-IDUs).

There is a paucity of research on the temporal relationship between sex work initiation and injection initiation. For women who engage in both sex work and injection drug use, they followed one of three initiation trajectories. Some may begin participating in sex work and then later begin injecting. Others may have a trajectory that moves from injection drug use and subsequently, sex work. Finally, some women may initiate injection drug use and sex work at the same time or within a very short period of time. Influence from intimate partners, prior drug use, and history of abuse are a few factors found to be associated with prior sex work and current injection drug use [1, 8, 9]. While injection drug users (IDUs) resort to sex work as an income generating activity and to support their drug habit, and sex work has been linked to drug scenes [3, 10]. These studies suggest that the pathway leading to concurrent sex

work and injection drug use may differ depending on whether individuals first initiated sex work or first begin injection drug use.

An examination of predictors of initiation into sex work and injection drug use needs to take into account predictors beyond the level of the individual, and consider the risk environment. Drawing from the social determinants of health theory [11], the “risk environment” includes influences that are exogenous to the individual that are socially produced through an interplay of micro- and macro-level factors [12]. Two main dimensions comprise the risk environment; type (physical, social, economic, and policy) and level of environmental influence (e.g., micro and macro). This framework has been applied to populations of IDUs, FSWs, and clients of sex workers to understand HIV risk [13-16]. For example, peer networks can be seen as micro-social level factors that influence injection drug use behaviors. Peer networks, and the availability of drugs within them (a micro-physical factor), are in turn influenced by drug trafficking routes (a macro-physical level factor). This concept of an individual’s environment interacting at multiple spheres to influence behavior can be extended to behaviors such as initiation of sex work and injection drug use.

Tijuana, Baja California and Ciudad Juarez, Chihuahua are the largest Mexico-US border cities. Both cities experience a unique HIV risk environment due to their position along major drug trafficking routes for heroin, methamphetamine, and cocaine; the number of IDUs has been estimated at

10,000 and 6,500 respectively [17]. In both cities, prostitution is quasi-legal and FSWs work out of cantinas, bars, hotels, nightclubs, and street corners. Qualitative research suggests that many entered sex work for financial reasons; many needing money to pay for their children's needs or to protect themselves from homelessness [18]. While estimates vary, there are approximately 6000 FSW in Tijuana, and 4000 in Ciudad Juarez [19]. In 2008, the proportion of FSW-IDUs in Tijuana and Ciudad Juarez, Mexico was 14% and 22%, respectively. Compared to non-injection drug using FSW, FSW-IDUs were found to have particularly high prevalence of HIV (12.3% vs. 5.1%), syphilis (22.7% vs. 13.1%), gonorrhea (15.2% vs. 5.2%), and Chlamydia (21.2% vs. 11.9%) [20].

The present study was guided by findings from previous studies of sex work and injection drug use initiation and an adapted framework of the HIV risk environment model [11, 21, 22]. Herein, we sought to examine how physical and social factors at the micro and macro levels influence time to initiation of sex work and injection drug use across the three different initiation trajectories defined above. Overall this study aimed to identify factors associated with (1) time to initiation of sex work among women who initiated sex work earlier than beginning injection drug use; (2) time to first injection drug use among women who initiated injection drug use prior to beginning sex work; and (3) time to both injection drug use and sex work initiation among women who first engaged in both behaviors at the same age. We

hypothesized that early lifetime illicit drug use would play a role at both the micro-physical level (e.g. timing and type of first illicit drug used), micro-social (e.g. peer drug use dynamics and intimate partner drug use) and macro-physical level (e.g. geographical migration) within all three initiation trajectories. Specifically, we postulated the following: (1) pressure from drug using peers would be associated with a shorter time to injection drug use initiation; (2) first trading sex to pay for drugs would be associated with a shorter time to sex work initiation; and (3) family illicit drug use would be associated with a shorter time to initiating both sex work and injection drug use at the same age. Given the intertwined nature of the relationship between sex work and injection drug use, identifying characteristics and factors exogenous to the individual associated with pathways to concurrent sex work and injection drug use may help to direct prevention efforts to delay or prevent initiation of injection drug use and sex work.

C. Methods

Between November 2008 and July 2010, a total of 622 FSW-IDU were recruited using convenience sampling from Tijuana (N=314) and Ciudad Juarez (N=312) into a behavioral intervention study aimed at decreasing both risky injection and sexual behaviors, as previously described [23, 24]. Briefly, eligibility requirements included: being at least 18 years of age, having had unprotected vaginal or anal sex with a male client at least once during the previous month; having shared syringes or injection paraphernalia (i.e. cookers, cotton, rinse water) at least once within the past month; ability to speak Spanish or English; ability to provide informed consent; and having no plans to move out of the city in the next 12-months. In both cities, recruitment involved both venue based and street outreach approaches using staff and outreach workers who were all trained on study procedures prior to the beginning the study. Women were reimbursed $15 USD for their participation in the baseline interview. The Institutional Review Board of the University of California, San Diego and the Ethics Boards of the Tijuana General Hospital and Universidad Autonoma de Ciudad Juarez approved all study protocols.

Data collection

We restricted this post-hoc analysis to baseline data. At baseline, trained, female, bilingual interviewers administered a detailed structured questionnaire lasting approximately 60 minutes. During piloting, questionnaires were translated into Spanish and back-translated into English.

Measures included four domains: (i) baseline sociodemographic characteristics, (ii) context of first sex work, (iii) context of first injection drug use, and (iv) contextual factors preceding both sex work and injection drug use initiation.

Outcomes of interest: time to initiation

Participants were asked, “how old were you the first time you traded sex for money, drugs, goods, foods, or housing” and “how old were you when you first injected drugs?” At the time of the study, all participants engaged in concurrent sex work and injection behaviors. Therefore, three temporal sequences of sex work and injection drug use initiation (referred to hereafter as “initiation trajectories”) were possible: (i) initiated sex trade prior to injection drug use initiation; (ii) initiated injection drug use prior to sex trade initiation; and (iii) initiated injection drug use and sex work within the same year of age. Three overall outcomes relating to these three groups were then constructed: time from birth to (1) first sex trade, (2) first injection drug use, and (3) first sex trade and first injection drug use when these events happened at the same age.

Baseline socio-demographic characteristics

Sociodemographic variables included age, language proficiency (English, and Spanish), years of education completed, marital status, and study location.

Context of first sex work initiation

Guided by an adapted risk environment heuristic [11], we examined specific micro- and macro-level factors specific to the context of sex work initiation, injection drug use initiation, prior illicit drug use, and early abuse experiences.

Micro-physical level factors surrounding sex work initiation included reasons for first trading sex, and what was promised at the time of first sex trade. Reasons for first trading sex included: money to pay bills, money for drugs, money for children's needs, varying types of external pressure (e.g. pressure from spouse), and was forced into sex work against their will. Participants were asked if they were promised anything in exchange for sex (yes/no) and if so, what they were promised (e.g. money, drugs, housing, jewelry, employment). Micro-social level factor included person who first suggested or motivated first sex trade. Response options for "whose idea was it to trade sex" included "mine", boyfriend, boss, family member (e.g. parent), husband, and stranger.

Context of first injection drug use

Factors at the micro-physical environment included physical location (e.g. own home, shooting gallery, park, jail/prison, etc.), and the type of drug first injected. Micro-social environmental factors included whom was present at time of injection (e.g. alone, friend(s), sexual partner, sex worker, clients,

etc.), and the reason for first injection. Response options for reasons for first injecting drugs included drug-related reasons (e.g. deal with withdrawal, curious about high, cost of drugs too high, etc.), social influence (e.g. encouraged by friends, family, or spouse), and emotional reasons (e.g. depressed, to deal with stress, or to deal with work better).

Contextual factors preceding both sex work and injection drug use

Contextual factors at the micro-physical environment included illicit drug use preceding both sex work and injection drug use initiation, family drug involvement, geographic mobility, and physical abuse history. Macro-physical environmental factors included geographic migration history. Contextual factors at the micro-social environment included history of family drug use, and family involvement in sex work.

Questions on history of drug use included age of first use and non-injection use of specific illicit drugs alone and in combination including cocaine, crack, methamphetamine, heroin, general inhalants, agua celeste (a solvent prevalent in Northern Mexico), speedball (heroin combined with cocaine), barbiturates, and tranquilizers. These items were then categorized into dichotomous variables indicating substance use prior to first sex work/injection.

Participants were asked if they ever experienced physical abuse (i.e., hit or assaulted), and if they had ever experienced forced or coerced non-

consensual sex/rape. Additionally, the age of first physical assault and first rape was ascertained. Based on the temporal relationship with age of first sex work and age of first injection, responses were then categorized into the following dichotomous variables: first physical abuse occurred earlier than first sex work/injection, and first rape occurred before first sex work/injection.

To assess micro-social level influences within the risk environment, information regarding lifetime family substance use, and involvement of family members in injection drug use or sex work across the three groups were assessed. Further, information about who within the family (e.g. parent, sibling, cousin, or uncle/aunt) used illicit drugs was then used to create a variable measuring parent or sibling involvement in these behaviors.

To assess the influence of more macro-level factors information on geographical location of birthplace, migration (e.g. number of cities lived in) and number of years lived in current city were assessed across the groups. Geographical location of birthplace was collapsed into a six regions: (1) northern Mexican state not including the study states of Baja California and Chihuahua, (2) central Mexican states, (3) southern Mexican states, (4) Chihuahua, (5) Baja California, and (6) United States.

Statistical Analyses

The sample included in the present study (N=575) was compared to the overall population (N=622) by simple Chi-square tests for categorical variables

and t-tests or non-parametric tests for continuous variables. No significant differences were found across the two groups.

Three separate time to event analyses were performed on the sample: (1) among those who initiated sex work first, time to sex work initiation; (2) among those who initiated injection drug use first, time to injection drug use initiation; and (3) among those who first traded sex and first injected drugs at the same age, time to initiation of concurrent behaviors.

Factors affecting time to initiation were evaluated using parametric survival models with a specified distribution for the overall model (accelerated failure time model) [25]. A parametric survival model allows for more efficient estimates and smaller standard errors than semi-parametric models by being able to specify the underlying distribution of the hazard function. Further, parametric models are not subject to the same limitations as semi-parametric survival models are for tied event times. For accelerated failure time models, the effect of a covariate is expressed as either accelerating (shortening time to event; rate ratios >1) or decelerating (lengthening time to event; rate ratios <1). Further, covariate effects are shown as time (rate) ratios rather than hazard ratios, thus allowing for an interpretation on the time scale.

Multivariate models were developed using a manual procedure where all variables attaining marginal significance of ≤ 10% in univariate analyses were considered in multivariate analysis in order of most to least significant and assessed for possible modifying effects. Differences across study sites

were assessed for all models. All variables attaining significance at ≤ 5% were retained in the final multivariate models.

D. Results

Of the total sample of 622 FSW-IDU, 557 had complete data on measures surrounding both first sex work and injection drug use initiation and thus, eligible for this analysis. Among 557 FSW-IDU, the median age was 33 years (interquartile range [IQR]: 28-40), and the median years of education completed was 5 (IQR: 2-6 years) (table 1). The median duration of time in sex work was 19 years (IQR: 15-24), with the majority of participants currently working as street workers (88%); small proportions worked as bar waitresses (4%) or escorts (1%). The median duration of injection drug use was 20 years (IQR: 17-25), with heroin as the most common drug injected in the past month. Fewer proportions reported injecting heroin in combination with methamphetamine (18%), or heroin in combination with cocaine (7%). By study design, equal proportions were from Tijuana (n=279) and Ciudad Juarez, Mexico (n=278).

Overall 557 women, 46% (n=258) initiated sex work first, 29% (n=163) initiated injection drug use first, and 24% (n=136) initiated both at the same age. HIV prevalence was 5%; 4% among those who initiated sex work first, 6% among those who initiated injection drug use first, and 8% among those who began both at the same age (p=0.13). Figure 1 shows the Kaplan-Meier curves for the unadjusted time to first initiation event for each group.

Context of first sex work. The majority of women who initiated sex work first did so to obtain money to pay for drugs (65%), or to pay for child's needs

(31%), decided “on their own” (59%) or was encouraged by a friend/acquaintance (28%) to first trade sex, and were promised either money (57%) or drugs (12%) (table 1). Similarly, the largest proportions of women who initiated sex work and injection drug use at the same age first traded sex for money to pay for drugs (64%), or to pay for child’s needs (35%), decided “on their own” (64%), and were promised either money (64%) or drugs (15%).

Context of first injection drug use. The majority of women who first injected drugs before engaging in sex work did so at someone else’s home (29%) or at a shooting gallery (29%), first injected heroin (78%), or a combination of heroin and cocaine (12%), first injected with a friend (87%), and injected because they were curious about the high (59%), felt peer pressure (27%) or wanted to deal with depression or anxiety (23%) (table 1). For women who initiated both sex work and injection at the same age, the majority first injected at someone else’s house (36%) or in a hotel or rented room (26%), first injected heroin (77%) or a combination of heroin and cocaine (10%), with a friend (83%), and because they were curious about the high (56%), to help deal with depression or anxiety (32%), or because of external pressure from peers (28%).

Bivariate associations

Time to sex work initiation. Factors found to be associated with shorter time to first sex work included younger age (time ratio [TR]=0.96 per 5-years), fewer years of education completed (TR=0.97 per year), and first trading sex

for money to pay for drugs (TR=1.10) (table 2). In contrast, time to initiating sex work was longer for women who first traded sex for money to pay for their child's needs (TR=0.91 per 5 years). Median time to first sex work was longer for women who used any non-injection drug before initiating sex work, compared to women who did not use any non-injection illicit drugs, by 16% (TR=1.16), and 26% longer for women who used a non-injection stimulant (TR=1.26). Being born in a southern Mexican state, compared to elsewhere in Mexico or the United States, lengthened the time to first sex work by 28% (TR=0.72). Time to sex work initiation was 9% longer for women who had a parent or sibling who used an illicit drug compared to those who did not (TR=0.91).

Experiencing physical abuse (TR=1.09) or rape (TR=1.11) shortened the time to initiating sex work. Among the women who experienced physical abuse (65%), median age of first abuse was 15 (IQR: 10-17) and either a husband or regular partner (43%), stranger (17%), or male relative (10%) were the perpetrators (data not shown). For women who experienced rape prior to initiating sex work (77%), the median age when first rape occurred was 11 (IQR: 7-14 years); and the perpetrator was either a male relative (35%), a stranger (28%), or a spouse or partner (12%).

Time to injection drug use initiation. For women who initiated injection earlier than sex work, factors surrounding the context of first injection drug use were not found to significantly influence time to first injection drug use initiation

(table 2). Considering prior non-injection drug use, use of any non-injection illicit drug shortened the time by 9% compared to no use (TR=1.09), and 56% for those who used heroin as their first non-injection drug (TR=1.56). Being born in a southern state of Mexico (compared to any other state or the United States) significantly lengthened the time to first injection drug use (TR=0.62).

Time to initiation when both sex work and injection drug use began at the same age. Among women who first injected drugs and traded sex at the same age, a shorter time to initiation was associated with being younger (TR=0.92 per 5-years) (table 2). Trading sex for money to purchase drugs compared to all other reasons lengthened the time by 10%; whereas the time was shortened by 12% if the main reason for first sex work was to obtain money to pay for their child's needs (TR=1.12). Time to initiating sex work was also shortened if women were encouraged to first trade sex by a boyfriend, sexual partner, or spouse compared to those who decided on their own and those who were encouraged by a friend/acquaintance, family member, or fellow sex worker (TR=1.32).

Initiating illicit drug use with methamphetamine (TR=1.26, pvalue=0.069), and first injecting to deal with depression or anxiety (TR=1.09, p=0.08) were marginally associated with a shorter time to initiation of both behaviors at the same age, but first injecting due to external pressure from friends or family was marginally associated with a longer time to initiation of both behaviors (TR=0.90, p=0.05). Use of any non-injection drug prior to either

sex work or beginning injecting was not significantly associated with initiating both sex work and injection drug use at the same age, but using a stimulant drug compared to heroin, inhalants, or agua celeste, as the first non-injection drug significantly shortened the time to initiation of both behaviors by 17% (TR=1.17). Physical abuse was associated with a 16% shorter time to initiation of injection compared to women who did not experience abuse prior to initiation (TR=1.16). Among those who experienced physical abuse, the median age of first abuse was 17 (IQR: 12-19), with a spouse or regular partner (69%), male relative (38%), or stranger (13%) responsible for inflicting the abuse.

Factors independently associated with time to initiation

Time to first sex work. Factors independently associated with a shorter time to initiating sex work (table 3) included younger age (adjusted (adj) TR=0.97 per 5-years), less years of education completed (adj TR=0.97 per year), using a stimulant as the first non-injection drug ever used prior to first sex work (adj TR=1.26), first selling sex to obtain money to pay for their child's needs (adj TR=1.08), experiencing physical abuse (adj TR=1.08), and currently living in Ciudad Juarez (adj TR=1.09). Conversely, having a parent or sibling who used illicit drugs was associated with longer time to initiating sex work (adj TR=0.90).

Stratifying by study location uncovered that women in Tijuana who first traded sex to obtain money to pay for their child's needs experienced a

significantly shorter time to sex work initiation (adj TR=1.18). Whereas early physical abuse (adj TR=1.09) shortened the time, and having a parent or sibling who used illicit drugs lengthened the time (adj TR=0.86) to sex work initiation among women from Ciudad Juarez.

Time to first injection drug use. Factors independently associated with a shorter time to first injection drug use (table 4) included younger age (adj TR=0.94 per 5-years), having previously used any non-injection drug (adj TR=1.16), and experiencing physical abuse prior to first injection (adj TR=1.08). Inhalant use as the first illicit drug used and being born in a southern state in Mexico were both independently predictive of a longer time to first injection drug use (adj TR=0.85 and 0.70 respectively).

Time to first sex work and first injection drug use at the same age. Factors independently associated with a shorter time to initiating sex work and injection drug use at the same age (table 5) included being younger (adj TR=0.92 per 5-years), first trading sex because a regular partner, boyfriend or spouse encouraged it (adj TR=1.29), using a stimulant as their first illicit drug (adj TR=1.18), first injecting drugs to help deal with depression, anxiety, or stress (adj TR=1.08), and experiencing prior physical abuse (adj TR=1.13).

E. Discussion

The purpose of this study was to examine the context of sex work and injection drug use initiation and provide information on the influence of micro and macro level factors on the time to initiation of sex work and injection among a sample of current FSW-IDUs in the northern Mexico border region. We found that nearly half initiated sex work prior to beginning to inject, nearly one third initiated injection drug use before beginning sex work, and one quarter initiated both sex work and injection drug use at the same age. Although the cross-sectional nature of this study precludes inference of causality, the findings highlight differences associated with early behaviors of sex work and injection drug use that can guide targeted prevention efforts. Such prevention programs could delay or evade initiation of sex work and injection drug use and influence later transition to concurrent sex work and injection drug use behaviors.

As anticipated, early illicit drug use contributed to an accelerated time to initiation across all three groups. Using either methamphetamine or cocaine/crack as the first illicit non-injection drug was independently associated with an accelerated rate of initiating sex work, and initiating both sex work and injection at the same age. Our findings contribute to the literature which shows that for women, early crack use and methamphetamine use were associated with entering survival sex for women [26] and early

cocaine and crystal methamphetamine use increases risk for later injection drug use [27], and for initiating injection drug use at a younger age [28, 29].

In contrast, for women who initiated injection drug use first, inhalant use was associated with a slower progression to first injection. Due to their accessibility, inhalants are commonly used by adolescents in Mexico. A study of male and female students between 7th and 9th grade reports inhalant use to be the most common drug used for students with 7% of female students reporting inhalant use compared to 3% reporting marijuana use [30]. Inhalant use has also been associated with subsequent injection drug use [31, 32]. Although our findings suggest that early illicit drug use shortens time to subsequent sex work and injection drug use initiation, there may be a window of opportunity to alter this trajectory.

For women who initiated sex work prior to injecting, markers of vulnerability appeared to influence time to sex work, such as low levels of education, early exposure to physical abuse, and the perceived need to engage in sex work to obtain money for their child's needs. Previous studies in the Mexico-US border region report that high proportions of sex workers have children and often these women act as the primary provider for their families [18, 33]. Similarly, a mixed methods study of current sex workers in Nagaland, India reported 45% of women beginning sex work did so to obtain money to support themselves or their family [34]. Our findings further support the need for family planning programs and avenues for women to access free

or reduced cost contraception. Micro-finance programs have been shown to provide economic opportunities for women [35, 36] that may serve as viable alternatives to the sex trade. Preventing young girls from dropping out of school reduces their risk for future participation in sex work [37-41], and drug use [8, 42]; even a small increase in educational attainment can have a large impact on opportunities available to young women [43-46].

We found that being born in a southern Mexican state greatly delayed time to first injection drug use among those who initiated injection before beginning sex work. Geographical mobility has been found to initially reduce the risk of HIV among female IDU [47] and protective against any STI acquisition among FSW who relocated to Tijuana [48]; however, this protection appears to diminish for every year women live in Tijuana [47]. Migration and mobility have been shown to influence drug use behaviors in Tijuana, and Ciudad Juarez at the macro level by influencing the availability of drugs, and at the micro level by changing peer-networks [14, 17, 49]. Within our study, the majority of women who moved from a Southern state migrated because their family relocated there or to seek economic opportunities. Often planned moves happen in a context of stability, which may explain the delayed initiation of injection drug use.

Micro-social and micro-physical level factors pertaining to intimate partner relationships were associated with a shorter time to initiation of both sex work and injection drug use at the same age. Female injectors have

greater overlap in their sexual and injecting networks than male injectors [50, 51]. Having an intimate partner encourage them to begin sex work was associated with initiating both sex work and injection drug use at the same age. Childhood physical and sexual abuse puts females at higher risk for later illicit drug use and vulnerability for initiating sex work [40, 52-54]. Similarly, we found early physical abuse was found to shorten the time to initiation across all groups. Prior physical abuse substantially shortened the time to initiation for women who initiated both sex work and injection at the same age; the majority of whom experienced this abuse from a boyfriend or spouse. Numerous studies have shown the traumatic effect of abuse has been associated with intense and long term depression in women [55-57]. This may provide context for our finding that women who first injected drugs to help deal with feelings of depression experienced a shorter time to initiation of both sex work and injection drug use at the same age. Depression in women becomes more complex when substance abuse is involved [58], which further supports the need for support programs that help women cope with the trauma associated with incest and intimate partner violence. By giving women the power to take control of their environment and remove themselves from damaging relationships increases their opportunity for long term change in their social capital.

Several limitations must be taken into account in the interpretation of these results. Of primary importance is that this is a post-hoc analysis using

baseline data from a longitudinal study of current FSW-IDU. Because of this we lacked information on early childhood and adolescent measures for peer-networks, homelessness, and family characteristics. Although one strength of survival models is the ability to handle time-dependent covariates, our study did not provide any such measures. Second, misclassification may have influenced all three subgroups and thus may bias our estimates toward the null. It is unlikely that misclassification severely biased our results since we did observe different correlates across the three groups examined. Future longitudinal studies following girls and women through different trajectories of sex work initiation and stages of illicit drug use would greatly enrich the understanding of the exogenous factors influencing the initiation and temporality of both behaviors. Future studies are warranted that further examine the relationship between physical, social, economic, and policy levels influences at the micro and macro levels.

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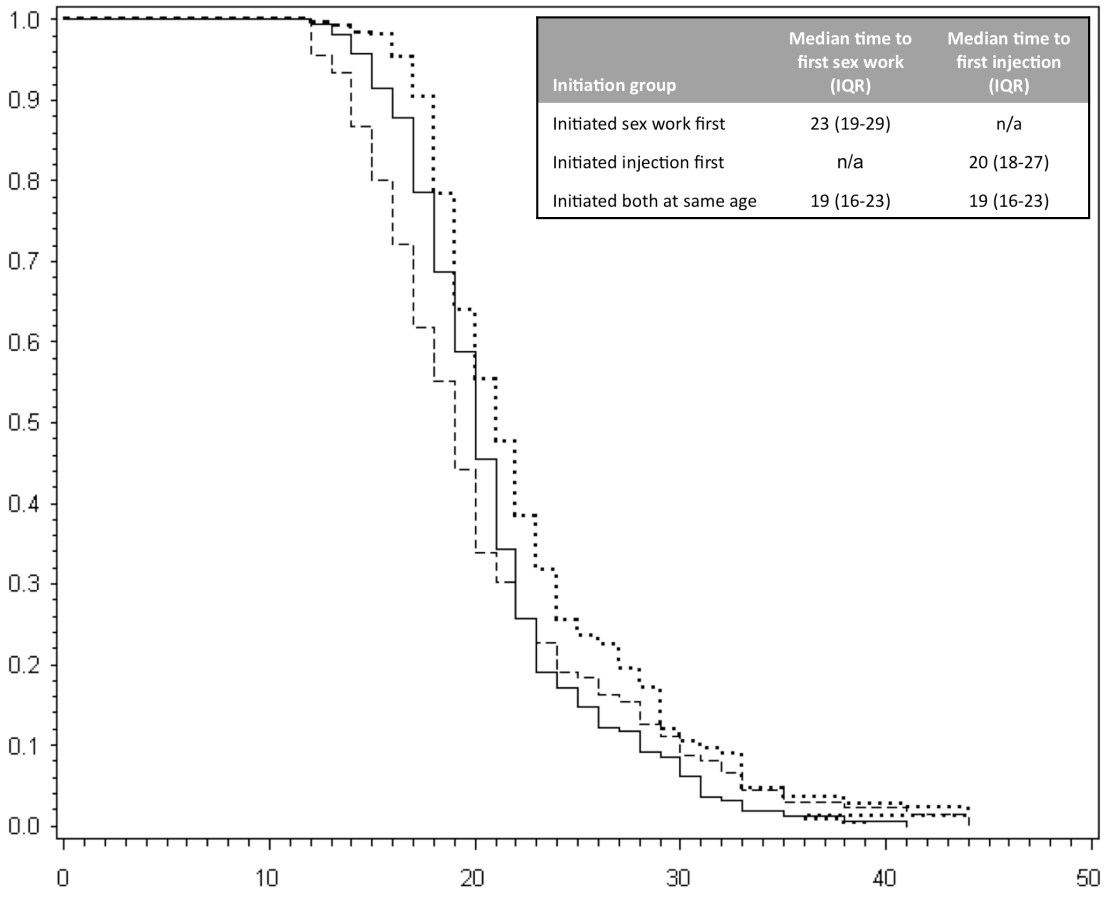

Initiation group	Median time to first sex work (IQR)	Median time to first injection (IQR)
Initiated sex work first	23 (19-29)	n/a
Initiated injection first	n/a	20 (18-27)
Initiated both at same age	19 (16-23)	19 (16-23)

Figure 1: Kaplan-Meier of observed time from birth to event of interest across three initiation groups.

Table 5.1: Summary of demographic characteristics for baseline sociodemographics, circumstances surrounding sex work initiation, and injection drug use initiation among 557 current FSW-IDU overall and stratified by initiation trajectories.

Characteristic	Overall sample (N=557)	Temporal sequence of initiation events: Initiated sex work first (N=258)	Initiated injection drug use first (N=163)	Initiated both events at the same age (N=136)
Baseline sociodemographics				
Median age in years (IQR)	33 (28-40)	33 (27-41)	35 (29-41)	31 (26-37)
Speaks English	157 (28)	66 (25)	64 (39)	27 (20)
Mean highest year of school completed (IQR)	5 (2-6)	5 (2-6)	7 (5-9)	6 (5-9)
Married/common law	217 (39)	99 (38)	60 (37)	58 (42)
Born outside of study city	336 (59)	160 (62)	104 (63)	72 (53)
City of residence				
Tijuana	279 (50.1)	127 (50)	90 (11)	62 (46)
Ciudad Juarez	278 (49.9)	131 (51)	73 (44)	74 (55)
HIV positive[†]	30 (5)	9 (4)	10 (6)	11 (8)
Context of sex work initiation				
Main Reason first traded sex				
Money for drugs	357 (64.2)	167 (65)		86 (64)
Money for child's needs	179 (31.2)	81 (31)		48 (35)
Who's idea for you to first trade sex?				
Own	341 (61)	151 (59)		86 (64)
Boyfriend/husband	22 (3)	9 (3)		5 (4)
Friends/acquaintance	158 (28)	77 (30)		37 (27)
Promised anything in exchange for sex the first time, even if you didn't get it?	412 (74)	191 (74)		110 (81)

Table 5.1 continued: Summary of demographic characteristics for baseline sociodemographics, circumstances surrounding sex work initiation, and injection drug use initiation among 557 current FSW-IDU overall and stratified by initiation trajectories.

Characteristic	Overall sample (N=557)	Temporal sequence of initiation events: Initiated sex work first (N=258)	Initiated injection drug use first (N=163)	Initiated both events at the same age (N=136)
Among those promised something, What did you obtain in exchange for sex the first time?				
Drugs	80 (14)	32 (12)		21 (15)
Money	316 (57)	147 (57)		87 (64)
Context of injection drug use initiation				
Physical location when first injected				
At your home/parent's home	84 (15)		30 (19)	20 (15)
At someone else's home	166 (30)		48 (29)	48 (36)
Shooting gallery	78 (14)		24 (29)	14 (10)
Hotel/Rented Room	153 (27)		31 (19)	36 (26)
Jail or prison	11 (2)		5 (3)	1 (<1)
Drug first injected				
Heroin	429 (78)		125 (78)	106 (77)
Cocaine or crack	33 (6)		8 (5)	8 (6)
Speedball (cocaine and heroin)	47 (9)		18 (12)	13 (10)
Meth	29 (5)		6 (1)	5 (1)
All reasons first injected				
External pressure from friends, family, partner	141 (25)		44 (27)	37 (28)
Depressed or stressed out	154 (28)		37 (23)	44 (32)
I was curious about the high	326 (59)		96 (59)	76 (56)
Who did you inject with the first time?				
Friend	476 (86)		141 (87)	112 (83)
Spouse/partner	71 (13)		18 (11)	20 (14)

† HIV results based on confirmation using Western Blot and HIV-1 enzyme immunoassay.

Table 5.2. Unadjusted models for factors associated with time to initiation for women who initiated sex work prior to injecting, women who initiated injection drug use prior to sex work, and women who initiated both sex work and injection drug use at the same age.

	Time to first sex work* (N=258)		Time to first injection drug use ** (N=163)		Time to initiation of sex work and injection drug use at same age*** (N=136)	
Characteristic		p-value		p-value		p-value
Baseline sociodemographics						
Age (per 5-years)	**0.96**	0.0006	**0.95**	<0.0001	**0.92**	<0.0001
Study location (TJ vs. CJ)	0.99	0.84	0.99	0.86	1.04	0.37
Number of education years completed (per year)	**0.97**	<0.0001	1.00	0.35	0.99	0.25
Speaks English	0.99	0.95	0.97	0.53	1.00	0.95
Context of sex work initiation						
Main Reason first traded sex						
Money for drugs	**1.10**	0.0049			**0.90**	0.034
Money for child's needs	**0.91**	0.011			**1.12**	0.023
Who's idea for you to first trade sex?						
Own	1.04	0.27			0.97	0.56
Boyfriend/husband	0.96	0.25			**1.32**	0.032
Friends/acquaintance	0.91	0.28			0.99	0.73
Promised anything in exchange for sex the first time, even if you didn't get it?	0.99	0.98			1.01	0.86
Among those promised something, What did you obtain in exchange for sex the first time?						
Drugs	0.99	0.96			0.96	0.57
Money	1.03	0.41			1.01	0.83
Context of injection drug use initiation						

Table 5.2. continued: Unadjusted models for factors associated with time to initiation for women who initiated sex work prior to injecting, women who initiated injection drug use prior to sex work, and women who initiated both sex work and injection drug use at the same age.

	Time to first sex work* (N=258)	Time to first injection drug use ** (N=163)		Time to initiation of sex work and injection drug use at same age*** (N=136)	
Characteristic	p-value		p-value		p-value
Physical location when first injected drugs:					
Own house or parent's house		1.01	0.80	1.03	0.69
Someone else's house		1.06	0.21	0.94	0.19
Shooting gallery		1.09	0.13	0.89	0.17
Hotel/rented room		0.95	0.36	1.09	0.17
Jail or prison		0.89	0.31	1.48	0.17
Drug first injected:					
Heroin		1.04	0.34	1.02	0.70
Cocaine or crack		0.95	0.61	*0.85*	0.13
Speedball (cocaine and heroin)		0.90	0.11	0.90	0.23
Methamphetamine		0.98	0.81	*1.26*	0.069
Primary reason first injected:					
External pressure from friends, family, or partner		1.03	0.48	*0.90*	0.054
To deal with stress or feelings of depression		1.08	0.12	*1.09*	0.083
Curiosity about the drug or the effect		0.99	0.74	0.95	0.26
Person with:					
Friend		0.92	0.19	1.07	0.31
Spouse/partner		0.85	0.38	0.95	0.43
Contextual Factors preceding sex work and injection drug use initiation					
Illicit drug use					

Table 5.2. continued: Unadjusted models for factors associated with time to initiation for women who initiated sex work prior to injecting, women who initiated injection drug use prior to sex work, and women who initiated both sex work and injection drug use at the same age.

	Time to first sex work* (N=258)		Time to first injection drug use ** (N=163)		Time to initiation of sex work and injection drug use at same age*** (N=136)	
Characteristic		p-value		p-value		p-value
Used any non-injection illicit drug before initiating either sex work or injection drug use†	**1.16**	<0.0001	**1.09**	0.04	0.98	0.72
Heroin (non-injection)	0.97	0.85	**1.56**	0.01	0.96	0.91
Cocaine, crack, or methamphetamine (non-injection stimulant)	**1.26**	<0.0001	1.09	0.25	**1.17**	0.013
Inhalant	0.99	0.96	0.93	0.25	0.87	0.17
Agua Celeste	1.06	0.41	1.08	0.50	0.81	0.16
Migration						
Born outside of study city	1.02	0.68	0.99	0.92	1.05	0.29
Region of birth city:						
Northern Mexican state (not Baja or Chihuahua)	1.03	0.38	1.04	0.51	*1.11*	0.096
Chihuahua, Mexico	0.98	0.75	1.02	0.65	0.96	0.45
Baja, Mexico	1.01	0.74	1.02	0.71	0.97	0.62
Central Mexican state	1.05	0.31	1.03	0.69	1.05	0.53
Southern Mexican State	**0.72**	0.009	**0.62**	0.008	1.02	0.87
United States	0.91	0.16	0.92	0.21	*0.82*	0.087
Number of cities lived (per city)††	1.01	0.28	1.00	0.77	1.33	0.61
History of Abuse						

Table 5.2. continued: Unadjusted models for factors associated with time to initiation for women who initiated sex work prior to injecting, women who initiated injection drug use prior to sex work, and women who initiated both sex work and injection drug use at the same age.

	Time to first sex work* (N=258)		Time to first injection drug use ** (N=163)		Time to initiation of sex work and injection drug use at same age*** (N=136)	
Characteristic		p-value		p-value		p-value
Experienced physical abuse before initiating either sex work or injection drug use	**1.09**	0.01	1.07	0.11	**1.16**	0.0042
Experienced rape before initiating either sex work or injection drug use	**1.11**	0.007	1.05	0.28	1.04	0.56
History of Family drug use and sex work involvement						
Any family member used illicit drugs††	*0.95*	0.13	0.99	0.80	0.98	0.73
Parent or sibling used illicit drugs††	**0.91**	0.005	0.98	0.58	0.99	0.83
Any family member used injection drugs††	0.98	0.56	1.01	0.88	1.05	0.48
Parent or sibling used injection drugs††	0.94	0.11	1.00	0.94	1.02	0.69
Any family member participated in sex trade††	0.94	0.14	1.05	0.37	0.98	0.73

* Time >1 indicates shorter time to sex work initiation per year and hence “higher risk”. Survival model assuming a gamma distribution

** Time>1 indicates shorter time to injection drug use initiation per year and hence “higher risk”. Survival model assuming a log-normal distribution

*** Time>1 indicates a shorter time to initiation and hence “higher risk”. This group initiated both sex work and injection drug use at the same age. Survival model assuming a log-normal distribution.

† excluding marijuana.

††Lifetime

Bold indicate significant at alpha <0.05; *italic* indicate significant at alpha<0.10.

All variables significant at alpha ≤0.10 were considered in the multivariate model

Table 5.3: Independent factors associated with time to sex work initiation among women who initiated sex work before injection drug use (N=258).

		Stratified by study site	
		Tijuana N=127	Ciudad Juarez N=131
Baseline Contextual Factor	Adjusted time to first sex work* (95% CI)	Adjusted time to first sex work (95%CI)	Adjusted time to first sex work (95% CI)
Age (per 5-years)	**0.97 (0.95, 0.98)**	**0.96 (0.94, 0.98)**	**0.97 (0.94, 0.98)**
Education completed (per year)	**0.97 (0.96, 0.98)**	**0.99 (0.97, 1.00**	**0.97 (0.95, 0.98)**
Stimulant was first non-injection drug used prior to first sex work †	**1.26 (1.15, 1.37)**	**1.28 (1.15, 1.42)**	**1.29 (1.12, 1.50)**
Reason for first sex trade was for money to pay for child's needs††	**1.08 (1.02, 1.14)**	**1.18 (1.08, 1.30)**	1.01 (0.93, 1.08)
Parent or sibling used illicit drugs	**0.90 (0.86, 0.96)**	0.98 (0.90, 1.06)	**0.86 (0.80, 0.93)**
Experienced physical abuse prior to first sex work	**1.08 (1.02, 1.15)**	1.06 (0.98, 1.17)	**1.09 (1.01, 1.17)**
Living in Ciudad Juarez at time of interview†††	**1.09 (1.02, 1.16)**	**--**	**--**

*Time >1 indicates shorter time to first sex work and hence "higher risk"

Survival model with a specified gamma distribution.

† Methamphetamine, Cocaine, or Crack.

††Compared to sex for drugs, housing, external pressure, or because high on drugs.

††† compared to Tijuana.

In addition to the above measures, the following measures were significant at ≤ 0.10 level in univariate models and were assessed for inclusion in the multivariate model using a manual forward stepwise procedure: first traded sex for money to buy drugs, used any non-injection drug prior to first sex work, experienced rape before first sex work, family sex work involvement and born in a southern state in Mexico.

Table 5.4: Independent factors associated with time to first injection drug use among women who initiated injection drug use before sex work (N=163)

Baseline Contextual Factor	Adjusted time to injection drug use initiation* (95% CI)
Age (per 5-years)	**0.94 (0.92, 0.97)**
Used any non-injection illicit drug before injection initiation†	**1.16 (1.07, 1.25)**
Inhalant was first non-injection drug used	**0.85 (0.76, 0.95)**
Experienced physical abuse prior to injecting drugs	**1.08 (1.00, 1.17)**
Born in a southern state in Mexico††	**0.70 (0.51, 0.97)**

*Time >1 indicates a shorter time to injection drug use initiation and thus “higher risk”.

Survival model with a specified log-normal distribution

† Excludes marijuana

†† Representation from the following southern states include: Chiapas, Campeche, Guerrero, Oaxaco, Puebla, Quintana Roo, Tabasco, Veracruz, Yucatán.

In addition to the above measures, the following measures were significant at ≤ 0.10 level in univariate models and were assessed for inclusion in the multivariate model using a manual forward stepwise procedure: first injected drugs in a shooting gallery, injected drugs to deal with depression or anxiety, and interview location.

Table 5.5: Independent factors associated with time to initiating sex work and injection drug use at the same age (N=136).

Baseline Contextual Factor	Adjusted time to initiation of both injection and sex work at same age* (95% CI)
Age (per 5-years)	**0.92 (0.90, 0.99)**
Sexual partner or spouse's idea to first trade sex†	**1.30 (1.05, 1.57)**
Stimulant was first non-injection drug used prior to injecting	**1.18 (1.06, 1.31)**
Reason first injected was to deal with anxiety/stress or feelings of depression††	**1.08 (1.00, 1.12)**
Experienced physical abuse prior to injecting drugs or first sex work	**1.12 (1.04, 1.22)**

*Time >1 indicates shorter time to initiation of both injection and sex work and hence "higher risk"

Survival model with a specified log-normal distribution.

† Compared to own idea, friends/acquaintance, family member, or sex worker's idea.

†† compared to because of peer pressure, pressure from family, pressure from boyfriend/spouse, to deal with withdrawal symptoms or for more efficient high, curious about high/drug, or injected against will.

In addition to the above measures, the following measures were significant at ≤ 0.10 level in univariate models and were assessed for inclusion in the multivariate model using a manual forward stepwise procedure: reason for selling sex was for money to pay for child's needs; reason for selling sex for money to pay for drugs, born in Northern state in Mexico (not Baja or Chihuahua), born in the United States, and study site.

CHAPTER VI.

DISCUSSION

The overall aim of these studies was to expand the understanding of substance use trajectories leading to injection drug use initiation among male and female current injectors. These findings can inform researchers and could improve identification of target populations to optimize the design and content of prevention and intervention programs. Factors exogenous to the individual play a critical role in determining if and when injection drug use begins, the motivations for initiation, and the context of initiation itself (e.g. drug used, person with, physical location, etc).[1-3] This dissertation aimed to examine characteristics and factors at the physical, social, economic, and policy levels that comprise the risk environment contributing to injection initiation. Additionally, this study assessed current drug related risk behaviors associated with individuals who 'initiated first' (Aim 1), currently use *agua celeste (Aim 2)*, and across the three different initiation trajectories leading to concurrent sex work and drug use behaviors (Aim 3). The following chapter includes a summary of findings, study limitations and overall strengths, and recommendations for future research.

A. Summary of Studies and Major Findings

Manuscript 1 identified a unique sub-group of injection drug users (IDUs) who initiated injection drug use earlier or at the same age as other

routes of drug administration (i.e. 'injection first'). In this study, 12% of IDUs reported having 'injected first', with the majority of these individuals initiating with heroin. Our prevalence estimate is significantly larger than the only other study that identified a population of individuals who initiated illicit drug use through this pathway. A Brazilian study of mainly cocaine users found that <1% of IDUs initiated injection prior to other modes of drug use.[4] Younger age at first injection drug use, having a sexual debut prior to initiating injection, first injecting heroin, and injecting alone were all independently associated with injecting as the first drug use experience. Although this subgroup entered into illicit drug use in an atypical manner, they were not significantly riskier in terms of their recent drug use or sexual behaviors, as hypothesized. Instead, after controlling for differences in age of first injection drug use and number of years injecting, 'injection first' IDUs were more likely to inject at home, and less likely to have ever experienced a drug related overdose. On the other hand, they were also less likely to have been enrolled in drug treatment, and more commonly obtained their syringes from potentially unsafe sources (i.e. tienditas [market places]). We did not find that 'injection first' IDUs had higher odds of having a family who used illicit drugs, as hypothesized.

Manuscript 2 described the prevalence of *agua celeste* use and identifies correlates of lifetime and recent use of *agua celeste* among FSW-IDU in northern Mexico. This paper was the first to identify correlates of *agua celeste* use in a community-based sample. Overall, *agua celeste* was widely

used in Ciudad Juarez, but not at all in Tijuana. In Ciudad Juarez, over half of FSW-IDUs had used *agua celeste* in their lifetime, and among those who reported lifetime use nearly half had used *agua celeste* in the past six months. Lifetime *agua celeste* use was associated with beginning to engage in sex work or injection drug use at an earlier age, and women who used it were more likely to have a history of abuse. Women who recently used *agua celeste* were more likely to report using drugs with sex work clients before or during sex and to spend more time on the street per day, suggesting higher risk profiles. These findings build on previous literature showing that inhalant use is an important risk factor for subsequent injection drug use.

Manuscript 3 examined physical and social factors within individuals' risk environment that may influence time to initiation of sex work and injection drug use. Among a sample of FSW-IDU in two northern Mexican cities, we found that nearly half initiated sex work prior to beginning injection drug use, a third initiated injection before beginning sex work, and one quarter initiated both sex work and injection drug use at the same age. Across all three groups, early illicit drug use contributed to an accelerated time to initiation. Prior stimulant use was associated with a shorter time to sex work initiation and a shorter time to initiation of both behaviors, but inhalant use as the first illicit drug lengthened the time to first injection drug use. For women who initiated sex work first, markers of vulnerability at the micro- level appear to influence time to sex work, such as low level of education, and the perceived need to

engage in sex work to obtain money to pay for their child's needs (micro economic level).

Geographical migration and mobility have been shown to influence drug use behaviors at both the micro and macro levels.[5,6] We found that being born in a southern Mexican state greatly delayed the time to injection drug use initiation. Factors associated with initiating both sex work and injection drug use at the same age included social micro- influences such as having a boyfriend or spouse who encouraged them to begin sex work, and first injecting drugs to help deal with depression of feelings of anxiety accelerated time to initiation. For all three groups, early physical abuse (physical micro-factor) greatly shortened the time to initiation, substantially for the group who initiated both sex work and injection drug use at the same age. These findings may help identify possible avenues for intervention that can delay or prevent onset of initiation of injection drug use and/or sex work.

B. Study Limitations

Misclassification of the outcomes

'Injection first': Participants were not asked directly if they initiated illicit drug use by injecting, the outcome for aim 1. Instead, participants' responses to a series of questions were used to categorize the dichotomous outcome variable. For example, participants were asked: "at what age did you first inject drugs." We also determined the youngest age of first non-injection illicit drug use from a series of questions asking "at what age did you first [snort or smoke] [drug type]?" Participants may not have accurately recalled the age of first injection drug use and/or the ages for each of the responses for non-injection drug used, therefore the variable may be prone to misclassification. Subgroup analysis did not show differences in multivariate models when age-ties were removed. Assuming that participants reported their actual age and had no reason to inflate or deflate the age of first injection drug use, estimates would be expected to bias toward the null. Hence the significant associations found with 'injection first' may actually be stronger.

Time to initiation event: A similar misclassification of the outcome is also possible in manuscript 3. Women were not asked directly if they initiated injection drug use before sex work, sex work before injection, or both behaviors at the same age, the outcome for Aim 3. Instead, responses from two measures were used to construct the outcome of interest as well as categorize women into specific initiation trajectory groups. Women were

asked (1) “at what age did you first inject drugs?” and (2) “when did you first trade sex for money, drugs, good, or shelter?” If misclassification of the outcomes did occur, it occurred at the time of study collection, and likely did not differ across groups. Therefore, outcomes are subject to non-differential misclassification with the usual effect of the associations tends to be diluted, and shifted toward the null. Even though sex work is quasi-legal in both Tijuana and Ciudad Juarez, underage sex work is an especially sensitive topic. Some women may have reported an older age of first sex work than actually occurred and could result in differential misclassification. Results would tend to inflate effect sizes for the group who initiated injection drug use first, and possibly for the group who initiated both sex work and injection drug use at the same age. On the other hand, this would tend to bias effect sizes toward the null for the group of women who initiated sex work first.

Bias

Recall bias: Recall bias can be caused by differences in accuracy or completeness of recall of past events or experiences, and can influence both outcomes and covariate measures. Recall bias may exist in the reporting of lifetime or recent (past 6 months) of *agua celeste* use (manuscript 2) or lifetime and current drug use (covariates used across all manuscripts). Literature has shown that correct recall of drug use behaviors did not differ for a recall period of 1 month compared to 6 months.[7] However, if participants across both groups (recent *agua celeste use* vs. no recent *agua celeste* use)

incorrectly reported their use of *agua celeste* in the previous 6 months, the bias would tend to dilute associations toward the null.

Socially desirable responding: Socially desirability responding may introduce potential reporting bias across all three manuscripts. The social undesirability of drug use often leads to drug users being stigmatized for their behaviors. This could result in under reporting of their current or past drug use. In both studies, we used trained interviewers, many of whom were ex-FSW or ex-IDUs able to gain rapport with participants. By engaging study staff with these characteristics, the likelihood of truthful responding increased thus decreasing the potential for socially desirable responding.

An alternative to face-to-face interviews is Audio Computer Assisted Self Interviewing (ACASI) through which a computer based interview tool administers the survey. This has become a popular mode of administering surveys on sex, drugs, and other sensitive behaviors since it encourages participants to provide answers privately and thus encourages more valid responses.[8,9]. Unfortunately, it was not possible to use ACASI to collect data for this dissertation, but the tool could be used in future projects to help further reduce social desirability bias.

Survival bias: Even though all three manuscripts utilized data from prospective studies, participants were not recruited to capture participants at different stages within their substance use careers. Instead, in both *Proyecto El Cuete phase III* and *Mujer Mas Segura,* recruitment targeted current IDUs.

The overall study populations examined in manuscript 1 and manuscript 3 are therefore subject to survival bias. Survival bias occurs when a study only considers individuals who survived and inadvertently overlooks those who died. This bias can lead to results that only extend to a subset of the sample. Manuscript 1 used data from participants recruited after they began injecting, therefore introducing an artificial survival advantage within both 'injection first' and 'non-injection first' groups. Typical mortality for IDU populations is 1% per year, although it appeared higher (at 2% per year) within the *Proyecto El Cuete phase III* sample.[10] This non-differential bias does not change the direction of the effects, but may have biased them toward the null. Furthermore, because the population assessed only represented individuals who survived drug use long enough to be included in the study, results may not be generalizable to other groups of drug users.

Generalizability: Eligibility criteria for both *Proyecto El Cuete* phase III (manuscript 1) and *Mujer Mas Segura* (manuscripts 2 and 3) were designed to recruit high risk individuals in order to enable the assessment of HIV risk and to allow the testing of a behavioral intervention within *Mujer Mas Segura*. All participants in both populations were current IDUs; therefore results of manuscripts 1 and 3 are not generalizable to the other drug using populations in Mexico, or to injection drug using populations in other settings.

C. Study Strengths

Each of the three studies provides new information on areas of early substance use and the pathway to injection drug use. By using data from two rich datasets of under-studied but high risk individuals and asking novel research questions, the dissertation contributes findings to guide interventions and inform future research studies.

Manuscript 1 draws attention to a unique sample of IDUs who initiated illicit drug use through injection drug use; a route of administration that places individuals at substantial risk for both exposure to blood borne infections like Hepatitis C virus, but also extreme vulnerability and marginalization. Further, the large overall sample size, and the large proportion of 'injection first' identified allowed adequate power to identify correlates. These findings will help guide future studies of substance use trajectories by encouraging investigators to examine the importance of both the type of drug first used and the route of administration on risk behaviors and future drug use careers. In the next section, suggestions on avenues for future studies and prevention efforts are provided.

The majority of studies examining prevalence and correlates of inhalant use among adults do so by grouping all inhalants together, or include inhalants as part of a larger class of illegal drugs, thus contributing to misclassification. Manuscript 2 was the first community-based study to identify correlates of use of *agua celeste*, an inhalant that is prevalent in northern

Mexico. Although findings from this high risk sample of women cannot be generalized to other populations, the widespread use of *agua celeste* in Ciudad Juarez is concerning and provides support for future mixed-method studies to identify the motivations for current use and determine the formulations used to create *agua celeste*.

The majority of research pertaining to illicit drug use initiation, particularly injection drug use initiation, has been conducted among males. Manuscript 3 provides valuable findings from a sample of FSW-IDUs, and utilizes a conceptual model adapted from the Rhodes' HIV risk environment conceptual framework. Manuscript 3 identified key factors within the physical and social environment that influence the time to initiation of both injection drug use and sex work within the broader trajectory of initiation of sex work and injection behaviors. In addition, this study helped elucidate some important characteristics (e.g., family drug use, and intimate partner dynamics) that may be potential targets for intervention efforts aimed at preventing initiation of concurrent sex work and injection drug use by preventing the onset of injection drugs and first sex work.

D. Implications for Prevention and Intervention Development

Preventing Entry into Sex Work

Results from manuscript 3 may help guide prevention efforts to target physical and social level factors within the developmental stage to avert entry into sex work and injection drug use initiation occur. Across all three groups, being younger was associated with a shorter time to initiation of injection, sex work or concurrent initiation of both behaviors. For women who initiated sex work first, having completed fewer years of education was also found to accelerate time to initiation of sex work. The literature suggests that preventing young girls from dropping out from school reduces their risk for future participation in sex work,[11-15] and engaging in drug use behaviors.[16,17] Efforts to retain girls in school would increase their level of education and access to other economic opportunities later in life. Among young women, more education is associated with increased self-esteem, increased self-advocacy, and reduces power imbalances in relationships.[18-20] Research has indicated that girls who have completed a secondary education have a lower risk of HIV infection and practice safer sex compared to girls with only a primary level education.[21] Education has been suggested as a 'social vaccine' to prevent the spread of HIV and change social norms surrounding attitudes toward women.[20] Programs to encourage girls to stay in school, and to provide incentives for families to keep girls in school could protect against future vulnerability. Research has indicated that even a small increase in

educational attainment can have a large impact on opportunities available to young women.[22]

In manuscript 3, women who initiated sex work before injection drug use experienced a shorter time to sex work initiation if they first traded sex for the perceived need to obtain money to pay for their child's needs. Childcare programs for women and economic opportunities for women with children would allow women the flexibility to provide for their families. Further, 93% of women in the study who reported having children draws attention to the need for family planning programs and avenues for women to access free or reduced cost contraception. Micro-finance programs have been shown to provide economic opportunities for women and greatly improve the lives of women, their families, and the larger community.[23,24] Increasing economic opportunities among girls and women may also improve gender dynamics and protect women from pressures from partners or clients to start using drugs. Connell et al. (1987) suggested that gender based power inequities in society (macro level) and within intimate relationships (micro level) may contribute to a reduction in women's control over their decisions regarding specific behaviors.[25] For example, Mexican culture places emphasize on machismo that refers to the assumption that masculinity is superior to femininity, which condones male-perpetrated violence against women and suggests a sense of power to dominate. Machismo limits women's ability to advocate for herself in the relationship, and results in a subordinate role for the woman. Future

qualitative studies seeking participant narratives about relationship dynamics and their influence on substance use behaviors are necessary to further understand the mediating gender inequality factors amendable to change.

Preventing Early Illicit Drug Use and Entry into Injection Drug Use

More education was associated with a lower lifetime odds of *agua celeste* use in manuscript 2. Retaining girls in school may also prove beneficial for reducing inhalant use. [26,27]. A national high school survey conducted in 1998 in Mexico City found that among female adolescents, inhalants were the most common drug used after marijuana [26]. The most recent school surveys in Mexico show inhalants are the most common substance of abuse among male and female students between 7th and 9th grade [28]. Inhalant use is more common within this age group than marijuana use, with 7.4% of males and 6.7% of females reporting inhalant use compared to 5.6% and 2.7% respectively for marijuana [28]. School-based programs aimed at educating students about the dangers of inhalant use and identifying students at risk of inhalant use could help prevent or delay its onset. Further, such programs could then refer inhalant users to youth-centered treatment centers that may alter the trajectory of other types of drug use.

Manuscript 2 also found that among women who ever used *agua celeste* first used this drug at an earlier age, and that 10% of ever users reported using *agua celeste* as their first drug of use. These findings are similar to literature suggesting that inhalants may play an important role in

individuals' early drug use trajectories leading to later use of heroin and/or injection drug use. Acting on early inhalant use within school-age populations could help reduce the likelihood of women entering into sex work and engaging in future substance use behaviors.[14,29-31]

Across all three dissertation studies, early life experiences of victimization through exposure to physical and sexual abuse had a significant impact on their future substance use behaviors. While few participants in manuscript 1 reported ever being diagnosed with depression or anxiety, it remains possible that injecting alone at the first episode is a proxy for depression or social isolation. In manuscript 2, FSW-IDUs who had a history of sexual or physical abuse were significantly more likely to report ever using *agua celeste*. These findings suggest that women in our study may have turned to *agua celeste* as a way to cope with the emotional and psychological effects of physical and sexual abuse or other negative events experienced as a child or adolescent. Women across all three initiation groups in manuscript 3 who were physically abused early in their lifetime experienced an accelerated trajectory to initiation of sex work and injection drug use. Programs to provide counseling or support services for women who have been abused or who are in abusive relationships are important for providing coping mechanisms and prevent women from turning to substance use.

Reducing Risk Behaviors among IDUs

In manuscript 1, although 'injection first' IDUs were generally no more risky in terms of their drug use practices than other IDUs, we found some evidence to suggest that they were more severely drug dependent. On the other hand, we also found that 'injection first' IDUs were at lower odds of experiencing a drug related overdose in their lifetime. Even though these IDUs have injected drugs for a longer duration of time, their less risky and potentially more stable drug use patterns may have contributed to a lower risk of overdose. Lower levels of lifetime incarceration and homelessness may have also contributed to fewer disruptions in their lifestyle and thus fewer overdose experiences. The 'injection first' group was not found to be riskier in terms of current drug use and sexual behaviors. Instead, this unique subgroup of IDUs may represent a more stable, less risky group who could act as potential leaders in their community to change social norms and motivate behavior change.

Since IDUs who 'injected first' tended to practice safer sexual and drug using behaviors, they may represent a group of potential opinion leaders[32] who could be trained to deliver safer injection messages to their peers through outreach. Community popular opinion leaders have been used to disseminate HIV prevention messages to accelerate behavior change in various countries. Results on community popular opinion leaders as conduits for disseminating intervention messages appear mixed. A 5-country group randomized trial

conducted from 2002 to 2007 found that both intervention and comparison conditions showed declines of 30% in risk behavior prevalence and had comparable diseases incidence across countries.[33] The intensive nature of the prevention services provided to both the control and intervention groups may have contributed to the ineffectiveness found in the community popular opinion leader intervention. Interventions using community popular opinion leaders rely on formal social network assessments to guide the development of the intervention and recruit leaders. It has been suggested that the community popular opinion leader approach has value in leading behavior change in populations, and an effective network-based intervention approach.[34] A similar model successfully implemented in Mexico, *Pasa La Voz,* applied RDS sampling to the traditional *promotores* (peer outreach) model to increase HIV testing and related services; such an approach could potentially be applied to the 'injection first' subgroup.[35]

The majority of literature on inhalant use is within adolescent populations, but manuscript 2 identified a large proportion of adult women who use agua celeste. Future qualitative studies to explore motivations for current *agua celeste* use among FSWs are necessary to better understand this relationship. Our findings do suggest, however, that recent *agua celeste* users are more likely to be 'high' during their sexual transactions. This could compromise their ability to negotiate condom use or have control over other circumstances in the context of sexual transactions possibly increasing the

potential for exposure to HIV/STIs or violence. Understanding the context of use with sexual partners and sex work clients can help tailor intervention programs to aid sex workers to protect themselves from exposure to HIV/STIs or violence. Additionally, findings from manuscript 2 suggested that FSW-IDUs who recently used *agua celeste* were more likely to use an illicit drug during or before trading sex with clients.

In manuscript 3, micro-social and micro-physical level factors pertaining to intimate partner relationships were associated with a shorter time to initiation of both sex work and injection drug use at the same age. Having an intimate partner who encouraged them to begin sex work was associated with initiating both sex work and injection drug use at the same age. Prior physical abuse substantially shortened the time to initiation for women who initiated both sex work and injection at the same age, the majority of whom experienced this abuse from a boyfriend or spouse. Depression in women becomes more complex when substance abuse is involved,[36] which further supports the need for programs that help women cope with the aftermath of incest and intimate partner violence and provide women with the skills to remove themselves from abusive relationships. Female injectors have greater overlap in their sexual and injecting networks than male injectors [37,38]. Increasing a woman's social capital can both directly and indirection reduce drug related harms such as overdose, receptive syringe sharing, and HIV infection.[22,39,40]

E. Recommendations and Future Directions

Although the dissertation findings contribute to the existing literature on early substance use trajectories and injection drug use initiation, future studies are warranted to further characterize contextual factors interacting with different risk environments influencing drug use trajectories. Future prospective studies to examine a broad range of trajectories leading to injection initiation and following individuals once they initiated injection drug use would provide detailed information on individual characteristics and micro and macro level forces at the physical, social, economic, and policy levels creating different types of risk environments across pathways of drug use. More importantly, it would provide a comparison group of individuals at each stage (first illicit drug use, different patterns of drugs used, and age of first injection drug use) since not all individuals would progress in the same manner or initiate injection drug use.

Identifying correlates of early initiation of injection drug use may help to identify critical points of intervention and prevention among IDUs in these two border cities, and potentially other settings. Based on the results of the first manuscript, when compared to non-'injection first' IDU, the subgroup of IDUs who injected first were more likely to inject alone. Literature surrounding injection initiation shows that first injection episodes typically involve friends, or drug using peers who provide expertise or assistance with injecting.[41-43] Our findings may imply that these IDU were knowledgeable enough about the

mechanics of injecting that they were able to administer the drug themselves and that this subgroup of IDUs who 'injected first' were most likely exposed to drug use through their communities, peer networks or sexual partners. However, our study lacked additional information on the context of first injection to explore this more closely. Qualitative or mixed-methods studies would help provide important information on the social context of injecting first so that this route of entry to injection drug use can be averted. Including an examination on macro-physical level factors (e.g. access to syringes) and macro-social level factors (e.g. social and peer attitudes surrounding injection drug use) provide participant's perspectives on how their environment influenced their ability to 'inject first'. The availability, quality, and price of drugs can also contribute to decisions about beginning to inject drugs.[44] Extending future mixed-method studies to the examination of macro-level factors such as retail drug market prices could contribute to design of structural interventions.

A good deal of literature has focused on the role of peers on substance use initiation. In both manuscript 1 and manuscript 3, we attempted to assess the role of family illicit drug use on the onset of injection drug use. The lack of refined measures to assess drug use dynamics within the family made it difficult to identify associations within these two studies. Future studies that examine family size, family structure, and drug use dynamics within the family in relation to injection initiation experiences would provide a more complete

picture of family illicit drug use. Having a more complete picture of family drug use and their influence on adolescent substance use initiation could inform interventions. For example, parents who are abusing drugs often is the cause of poor family relationships and can create situations with excessively high family conflict, low parent-child attachment, and limited positive experiences for children. Programs that provide alternate opportunities for children to develop positive relationships with adults outside of their family could have a protective effect on future drug use. Findings in manuscript 1 suggest that this accelerated pathway into injection drug use (injection first) may occur more often than previously recognized. Future prospective studies of young non-IDUs are needed to examine how the role of family drug use and drug dependence affects drug use trajectories unique to women, since our study lacked a non-IDU comparison group.

Even though both *Proyecto El Cuete phase III* and *Mujer Mas Segura* were longitudinal studies, they were not designed to assess drug use careers. A prospective study that recruited adolescents or younger adults at various stages of their drug use career would allow investigators to follow these individuals as they move across different trajectories. This could provide for general trends of drug use patterns to be assessed. Complementing a longitudinal study with a qualitative study to assess the context of first illicit drug use periodically across drug users careers would provide a deeper understanding of the relationship between individuals environment and drug

use trajectories. Furthermore, in a prospective study design time dependent measures could be collected on important covariates at the micro level such as income avenues available for women, and drug availability, and at the micro-level such as family drug use dynamics, housing, peer networks, and individual measures like feelings of stress/anxiety and self-esteem. Time-dependent covariates would further enrich the understanding of drug use trajectories leading to injection drug use by taking the evolving nature of behaviors (e.g., periods of drug use, abuse, and dependence) and environmental forces (e.g., periods of incarceration, or drug availability). This information would provide a narrowed focus for personalized intervention strategies. A multi-level study assessing individual drug careers and drug policy changes at the state level could provide a platform to begin to assess the interplay between micro- and macro-level environmental spheres that influence drug use careers.

While manuscript 2 offers important information about *agua celeste* users in Ciudad Juarez, because of its post hoc design it lacked information about the composition of the drug, routes of administration, and immediate short and long term health effects. The study also lacked information on reasons why use was limited to Ciudad Juarez. Ethnographic and epidemiological studies are needed to better understand the contents of the drug and the motivations and social context surrounding initial, recent, and continued use of the drug. These future studies are critical for defining the

pathway for prevention necessary to develop individual and policy level interventions. Although our data suggest substantial current geographic variation in *agua celeste* use, given the high levels of population mobility in the Mexico-U.S. border region, *agua celeste* use could spread to other cities on either side of the US-Mexico border. Projects currently being conducted in the Mexico-US border region need to include items about *agua celeste* use in order to assess changing trends surrounding use in both Ciudad Juarez and Tijuana. Given the proximity to the US and the significant cross-border mobility, it is worthwhile to also examine *agua celeste* use among populations in the US.

Although a major strength of this study is the large datasets of injection drug users, because these were not comparable samples, gender differences could not be assessed.[45] Developing gender specific interventions and services that take into account the unique needs of women are essential for helping to curb these trends. Future studies that explore gender differences in contextual and biological factors related to onset of illicit drug use and progression toward dependence would help inform the development of interventions and treatment programs for women as well as men.

F. Conclusions

The unique populations of IDUs studied and novel research questions make the findings within this dissertation valuable to the larger field of research on substance use careers. To our knowledge, this is the first study to characterize individuals who initiate illicit drug use through injection, and one of the few studies to examine injection initiation in a resource-limited setting. It is also the first to use a community based sample to estimate *agua celeste* use and describe correlates of its use. In a population already experiencing elevated risk for STIs, HIV and other blood borne pathogens and high exposure to violence, use of *agua celeste* may pose yet an additional danger. Indentifying drug use trajectories leading to injection drug use and examining the relationship between injection drug use and sex work among women is critical for untangling the reinforcing behaviors of sex work and injection drug use among FSW-IDU. This dissertation study began to examine such relationships and the influences at multiple levels (physical, social, economic, and policy) that integrate to create the risk environment contributing to initiation of injection drug use and sex work. Future research is still warranted to better understand macro-level factors within the risk environment that influence drug use careers and injection initiation.

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CHAPTER VI

APPENDIX 1.

A. Study Purpose: This study compared differences in background characteristics and current behaviors across women who initiated illicit drug use by injection ('injection first') to women who used any illicit drugs before beginning to inject within a sample of current female sex workers who inject drugs (FSW-IDU).

B. Methods: Baseline data from the *Mujer Mas Segura* study collected from November 2008 and July 2010 from Tijuana and Ciudad Juarez, Mexico. 622 participants were recruited using convenience sampling. Data from 525 FSW-IDU using logistic regression to assess differences in background characteristics and current behaviors for women who 'injected first' compared to women smoked, snorted, or ingested marijuana, cocaine, methamphetamine, or heroin before injecting drugs.

C. Results: The study sample had a median age of 33 years (Interquartile range [IQR]: 27-40) about half (47%) had at least a primary school education, few (9%) reported being homeless in the past month, and 43% reported a monthly income of 3500 pesos per month (~300 USD). Women who 'injected first' were likely to be slightly older when they initiated injection drug use (median 16 vs. 15 years, $p<0.0001$) and slightly older when they first began trading sex (median: 15 vs. 14 years, $p<0.0001$). No differences were found

across the two groups for characteristics of first injection drug use context, family drug use, childhood abuse, or reasons for beginning to inject drugs. Women who 'injected first' were 10 times more likely to begin sex work after injecting (OR=10.5, 95% CI: 4.25, 26.13) and 5 times more likely to initiated both sex work and injection drug use at the same age (OR=5.07, 95% CI: 1.90, 13.54), compared to beginning sex work earlier than initiating injection drug use. Women who 'injected first' reported living in the study site for longer, injecting most often at home (OR=3.01, 95% CI: 1.31, 6.92), and being less likely to have unprotected sex with regular clients (OR=0.049, 95%CI: 0.27, 0.91) in the past month. No differences were found in drug type, drug treatment, or current injection drug use.

D. Conclusion: Even though the 'injection first' subgroup of FSW-IDU entered into illicit drug use in an atypical manner, they did not significantly differ in regards to factors surrounding the first injection drug use context or background factors such as history of abuse and family drug use. Contrary to expectation, we did not find the 'injection first' group to differ regarding their current drug using behaviors. Findings suggest that FSW-IDU who 'inject first' are at heightened risk of also beginning sex work at the same age or shortly after.

Table A1.1: Background factors associated with injection drug use before or at the same time as other routes of drug administration

	Overall n=528 N (%)	'Injection First' n=49 N (%)	Non-'Injection First' n=476 N (%)	p-value	Odds Ratio (95% CI)
Age	33 (27-40)	34 (29-39)	33 (27-40)	0.908	1.00 (0.97, 1.03)
Age when sex work was initiated	14 (12-16)	15 (13-17)	14 (12-16)	<0.0001	**1.15 (1.10, 1.21)**
Age when injection drug use was initiated	15 (13-17)	16 (15-19)	15 (13-17)	<0.0001	**1.13 (1.07, 1.20)**
Study site Tijuana (vs. Ciudad Juarez)	242 (46%)	21 (43%)	221 (46%)	0.63	1.16 (0.64, 2.10)
Primary school education or higher	248 (47%)	26 (53%)	222 (47%)	0.39	1.30 (0.72, 2.33)
Any family member ever used illicit drugs	299 (64%)	30 (71%)	269 (63%)	0.29	1.46 (0.73, 2.93)
Parent or siblings used illicit drugs	251 (48%)	27 (55%)	224 (47%)	0.28	1.38 (0.77, 2.49)
Family member used injection drugs*	165 (58%)	18 (62%)	147 (57%)	0.66	1.25 (0.54, 2.63)
Parent or sibling used injection drugs	132 (25%)	14 (29%)	118 (24%)	0.56	1.21 (0.63, 2.33)
Drug first injected:					
Heroin	358 (68%)	35 (71%)	323 (67%)	0.60	1.18 (0.61, 2.26)
Cocaine	28 (5%)	1 (2%)	27 (6%)	0.28	0.35 (0.05, 2.67)
Methamphetamine	24 (5%)	1 (2)	23 (5%)	0.37	0.41 (0.05, 3.10)
Person with first time injected:					
Alone	3 (1%)	2 (3%)	1 (<1%)	--	--

Table A1.1 continued: Background factors associated with injection drug use before or at the same time as other routes of drug administration

	Overall n=528 N (%)	'Injection First' n=49 N (%)	Non-'Injection First' n=476 N (%)	p-value	Odds Ratio (95% CI)
Friend	400 (85%)	36 (86%)	364 (85%)	0.63	0.85 (0.43, 1.66)
Family member	3 (<1%)	1 (1%)	2 (<1%)	--	--
Sexual partner	62 (13%)	2 (3%)	60 (14%)	0.078	0.29 (0.07, 1.25)
Location first injected drugs					
At your home/parent's home	71 (14%)	5 (10%)	66 (14%)	0.47	0.71 (0.27, 1.85)
At someone else's home	139 (26%)	10 (20%)	129 (27%)	0.31	0.69 (0.33, 1.42)
Shooting gallery	63 (12%)	7 (14%)	56 (12%)	0.61	1.25 (0.54, 2.92)
Hotel/Rented Room	137 (26%)	7 (14%)	130 (27%)	0.053	0.44 (0.19, 1.01)
Jail or prison	7 (1%)	1 (2%)	6 (1%)	0.65	1.65 (0.19, 13.89)
Reason first initiated injection drug use					
External pressure from friends, family, partner	121 (23%)	12 (24%)	109 (23%)	0.80	1.09 (0.55, 2.17)
Depressed or stressed out	131 (25%)	8 (16%)	123 (26%)	0.14	0.56 (0.26, 1.23)
I was curious about the high	281 (53%)	29 (59%)	252 (52%)	0.40	1.29 (0.71, 2.34)
Age first traded sex for money, drugs, goods, or shelter:				<0.0001	
Before first injection drug use	254 (48%)	6 (12%)	248 (52%)	--	Ref
After first injection drug use	143 (27%)	29 (59%)	114 (24%)	--	**10.5 (4.25, 26.13)**
At same age as first injection drug use	128 (24%)	14 (28%)	114 (24%)	--	**5.07 (1.90, 13.54)**
Experienced abuse in childhood **	139 (28%)	14 (29%)	125 (27%)	0.70	1.14 (0.59, 2.19)
Experienced sexual abuse or rape in childhood **	184 (35%)	14 (29%)	170 (36%)	0.33	0.73 (0.38, 1.39)

*among those who reported any family illicit drug use (N=283).

** childhood defined as younger than 18 years of age.

Table A1.2: Current risk behaviors associated with injection drug use before or at the same time as other routes of drug administration

	Overall N=525	'Injection First' n=49 N (%)	Non-'injection first' n=476 N (%)	p-value	Odds Ratio (95% CI)
Sociodemographics					
Heterosexual	454 (86%)	44 (89%)	410 (86%)	0.47	1.41 (0.54, 3.70)
Married	261 (49%)	28 (57%)	233 (49%)	0.27	1.39 (0.77, 2.52)
Tested HIV-positive at time of study	25 (5%)	4 (8%)	21 (4%)	0.24	1.92 (0.63, 5.84)
Slept in a car, abandoned building, shelter or street in past month	47 (9%)	3 (6%)	44 (9%)	0.49	0.64 (0.19, 2.14)
Ever been in jail, prison, or detention	408 (78%)	40(82%)	368 (77%)	0.49	1.30 (0.61, 2.77)
Income in past year was more than 3500 pesos per month	261 (43%)	21 (43%)	240 (50%)	0.31	0.74 (0.41, 1.34)
Number of years lived in study site	23 (11-33)	28 (21-35)	22 (11-32)	<0.0001	**1.03 (1.01, 1.05)**
Number of years injecting drugs (per year)	11 (4-17)	18 (14-23)	10 (4-17)	<0.0001	**1.10 (1.06, 1.14)**
Drug Use Behaviors					
Inject at least once daily**	492 (94%)	48 (98%)	444 (93%)	0.19	3.45 (0.46, 25.88)
Drug most frequently injected:**					
Heroin	374 (72%)	32 (67%)	342 (73%)	0.38	0.75 (0.40, 1.42)
Heroin+Cocaine (combination)	39 (8%)	7 (15%)	32 (7%)	0.051	2.34 (0.97, 5.63)
Heroin+Methamphetamine (combination)	9 (2%)	0 (0%)	9 (2%)		
Most often inject at:**					
Home	54 (10%)	12 (24%)	42 (8%)	0.0072	**3.01 (1.31, 6.92)**
Street, alley, or vacant lot	64 (12%)	5 (10%)	64 (13%)	0.15	0.48 (0.18, 1.33)
Shooting gallery	12 (2%)	0 (0%)	12 (3%)	0.16	0.48 (0.18, 1.33)

Table A1.2: Current risk behaviors associated with injection drug use before or at the same time as other routes of drug administration

	Overall N=525	'Injection First' n=49 N (%)	Non-'injection first' n=476 N (%)	p-value	Odds Ratio (95% CI)
Hotel or rented room	58 (11%)	6 (12%)	52 (11%)		
Receptive syringe sharing**	501 (95%)	47 (96%)	484 (96%)	0.91	1.09 (0.25, 4.78)
Distributive syringe sharing**	488 (93%)	45 (92%)	443 (93%)	0.71	0.81 (0.28, 2.40)
Purchased syringe most often from a 'safe source'†					
Ever accessed drug treatment	281 (53%)	25 (51%)	256 (54%)	0.71	0.89 (0.49, 1.61)
Ever had a gynecological exam	109 (24%)	12 (24%)	97 (21%)	0.52	1.25 (0.63, 2.49)
Sexual Behaviors					
Unprotected sex acts with regular client in past month	384 (73%)	29 (59%)	355 (76%)	0.021	**0.049 (0.27, 0.91)**
Unprotected sex acts with non-regular client in past month	399 (76%)	33 (67%)	366 (78%)	0.14	0.62 (0.32, 1.17)
Always used condom with non-casual client	183 (35%)	21 (42%)	162 (34%)	0.22	1.45 (0.80, 2.64)

*Adjusted for all other variables in the model; alpha=0.10.
**Previous 6 months
† Pharmacist, needle exchange program, doctor/clinic/hospital, veterinary clinic, or market
∆ 162 participants reported a regular sex partner
‡ 182 participants reported a casual sex partner

APPENDIX 2.

A. Study Purpose: The purpose of this study was to identify characteristics associated with time to concurrent sex work and injection drug use initiation among (1) women who initiated sex work prior to injection drug use, and (2) women who initiated injection drug use prior to sex work.

B. Methods: Data from a longitudinal study aimed at reducing both risky sexual and injection drug use behaviors collected from November 2008 to July 2010 in Tijuana, and Ciudad Juarez, Mexico. We restricted this post-hoc analysis to baseline data. Outcomes of interest were created based on two questionnaire items: (1) “how old were you the first time you traded sex for money, drugs, goods, foods, or housing?” and (2) “How old were you when you first injected drugs?” Two outcomes were then created: (1) among women who initiated sex work at a younger age than injection drug use, time from sex work initiation to concurrent sex work and injection drug use; and (2) among women who initiated injection drug use at a younger age than sex work, time from injection drug use initiation to concurrent sex work and injection drug use.

Two separate time to event analyses were performed. Factors affecting time to concurrent sex work and injection drug use across the two samples were evaluated using parametric survival models with a specified distribution (accelerated failure time model) [26]. The effect of a covariate is expressed as either accelerating (shortening the time to event; rate ratios >1) or decelerating

(lengthening time to event, rate ratios <1). Multivariate models were developed using a manual procedure where all variables attaining a marginal significance of ≤ 10% in univariate analyses were considered in multivariate models in order of most to least significant. All variables attaining significance at ≤ 5% were retained in the final multivariate models.

C. Results: Among women who initiated sex work earlier than injection drug use, three factors were found to be independently associated with transitioning to concurrent sex work and injection drug use. A younger age was independently associated with a 25% longer time to concurrent sex work and injection drug use (time ratio [TR]: 0.85, 95% confidence interval [95% CI]: 0.80, 0.89 per five years). Fewer years of education was associated with a 3% shorter time to concurrent sex work and injection drug use (TR: 1.03, 95% CI: 1.02, 1.04 per year) and a 26% shorter time to concurrent sex work and injection drug use was associated with initiating injection drug use in a hotel or rented room (TR: 1.26, 95% CI: 1.03, 1.54).

Among women who initiated injection drug use earlier than sex work, three factors were found to be independently associated with transitioning to concurrent sex work and injection drug use. A younger age was independently associated with a 12% longer time to concurrent sex work and injection drug use (TR: 0.88, 95% CI: 0.81, 0.94 per 5 years), and first trading sex for money to pay for drugs was associated with a 25% longer time to concurrent sex work and injection drug use (TR: 0.75, 95% CI: 0.60, 0.95).

Migration was found to be independently associated with a shorter time to concurrent sex work; Living in two cities shortened the time by 26% (TR: 1.26, 95% CI: 095, 1.69), living in three cities by 53% (TR: 1.53, 95% CI: 1.08, 2.15), and living in four or more cities shortened the time by 74% (TR: 1.74, 95% CI: 1.20, 2.50) compared to living in the study site since birth.

D. Conclusion: These findings suggest that the pathway leading to concurrent sex work and injection drug use differ in terms of key contextual factors for women who initiated sex work prior to injection drug use and women who initiated injection drug use prior to sex work. For women who initiated sex work first low education and initiated injection drug use were found to be associated with a shorter time to concurrent sex work and injection. First injecting in a hotel room suggests initiation may take place in the context of sex work. Future qualitative studies exploring the environment women are exposed to shortly after initiating sex work and the motivators (e.g., feelings regarding beginning sex work and their connection for initiating injection drug use) and social influences (e.g., drug availability from fellow sex workers, pressure from clients to inject drugs) are warranted to better understand the mechanisms underlying the relationship between sex work and initiating injection drug use.

For women who initiated injection drug use before sex work, an inverse relationship with number of cities lived in was associated with time to concurrent sex work and injection drug use. These findings preclude

information about where along the migration trajectory injection drug use and later concurrent sex work and injection drug use began. Nevertheless, it appears that a destabilizing effect may be in place for women who live in more cities across their life thus making them more vulnerable for both injection drug use and sex work at a younger age. Studies taking life narratives for current female sex workers who inject drugs may elucidate the role migration has on early illicit drug use behaviors and later sex work initiation.

Table A2.1: Multivariate associations based on a gamma survival model for time to concurrent injection drug use and sex work among women who initiated sex work first (N=258).

Baseline Contextual Factor	Time from sex work initiation to injection drug use initiation (95% CI)
Age (per 5-year increase)	**0.85 (0.80, 0.89)**
Education completed (per year)	**1.03 (1.02, 1.04)**
In a hotel or rented room when first injected drugs†	**1.26 (1.03, 1.54)**

* Time >1 indicates shorter time to concurrent injection drug use and sex work per year and hence “higher risk”
† Compared to own house, partner/boyfriend’s house, shooting gallery, street or vacant lot, or prison/jail.

In addition to the above measures, the following measures were significant at <0.10 level in univariate models and were assessed for inclusion in the multivariate model using a manual forward stepwise procedure: number of cities lived, first injected at hotel, first injected with a partner/boyfriend, interview location, physical abuse, and rape.

Table A2.2: Multivariate associations based on a gamma survival model for time to concurrent sex work and injection drug use among women who initiated injection drug use first (N=163).

Baseline Contextual Factor		Time from injection drug use initiation to sex work initiation (95% CI)
Age (per 5-year increase)		0.88 (0.81, 0.94)
First traded sex for money to pay for drugs†		0.75 (0.60, 0.95)
Migration history:		
	Lived in study city entire life	Ref
	Lived in two cities	1.26 (0.95, 1.69)
	Lived in three cities	1.53 (1.08, 2.15)
	Lived in four or more cities	1.74 (1.20, 2.50)

* Time >1 indicates shorter time to concurrent sex work and injection behaviors per year and hence “higher risk”
† Compared to money to pay for child’s needs, housing, bills, or due to external pressure, or high on drugs
In addition to the above measures, the following measures were significant at <0.10 level in univariate models and were assessed for inclusion in the multivariate model using a manual forward stepwise procedure: promised drugs first time traded sex, number of years lived in study site, physically abused, rape, family sex work.

APPENDIX 3.

One of the strengths of an accelerated failure time model (AFT model) is the ability to specific the underlying distribution of time (outcome) which produces more efficient estimates (with smaller standard errors) than with semi-parametric models (e.g., Cox Proportional Model). Five general distributions for ε are assessed under the PROC LIFEREG procedure in SAS: extreme value (2 parameter), extreme value (1 parameter), gamma, normal, and log-logistic. For each of these distributions there is a corresponding distribution for time (T).

Table A3.1: Examples of outcome distributions for parametric survival models

Distribution of ε	Distribution of T
Extreme value (2 parameter)	Weibull
Extreme value (1 parameter)	Exponential
Log-gamma	Gamma
Logistic	Log-logistic
Normal	Log-normal

Different distributions have a different affect on the hazard functions that may different interpretations of the effects. The exponential model is the simplest model, where ε has a standard extreme-value distribution and scale parameter (σ) is held constant. This distribution is slightly skewed to the left. The weibull model is a slightly modified version of the exponential distribution. Under a specified weibull distribution it is assumed that ε has a standard extreme-value distribution, but the scale parameter (σ) is allowed to vary.

When $\sigma>1$ the hazard decreases with time, and when $0<\sigma<0.5$ the hazard is increasing at an increasing rate. The log-normal model is not a proportional hazard model, its hazard function is expressed as a regression model in which the dependent variable is the logarithm of the hazard. The log-logistic model allows for an inverted U-shaped hazard, and assumes that ε has a logistic distribution. The distribution under a log-logistic model is symmetric with similar shape to the normal distribution. The generalized gamma model has one more parameter than any of the other models which means the hazard function can take on a wide variety of shapes.

Fit statistics are assessed for the five distributions for each of the outcomes under Aim 3 and Appendix 2. The Akaike's information criterion (AIC) value, which is a modification of the -2 log-likelihood that penalizes models for the number of covariates specified (κ), is used to compare model fit under the five specified distributions of T.

AIC= 12logL + 2κ

The smaller the AIC value the better the model fit. An assessment for the 5 outcome distributions of time are included below, along with the raw distribution of T.

Table A3.2: Model fit diagnosis for time to sex work initiation, among women who initiated sex work before injection drug use (n=258)

Distribution	AIC value
Weibull	149.650
Exponential	540.934
Log-Normal	79.103
Gamma	69.696

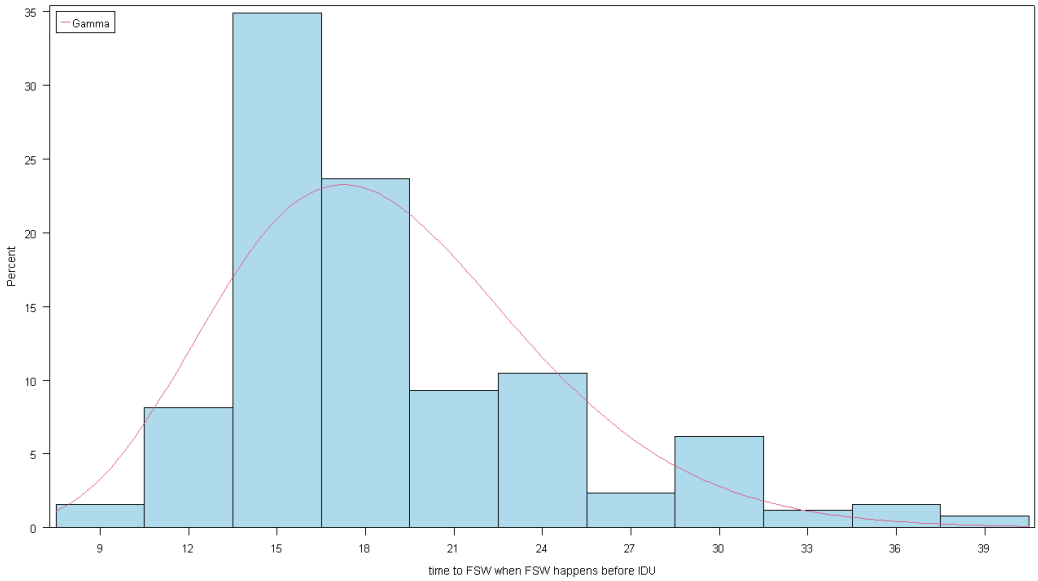

Figure: A3.1 Distribution of time to initiation of sex work.

Table A3.3: Model fit diagnosis for time to injection drug use initiation, among women who initiated injection drug use before sex work (n=163)

Distribution	AIC value
Weibull	68.583
Exponential	341.078
Log-Normal	26.360
Gamma	27.093

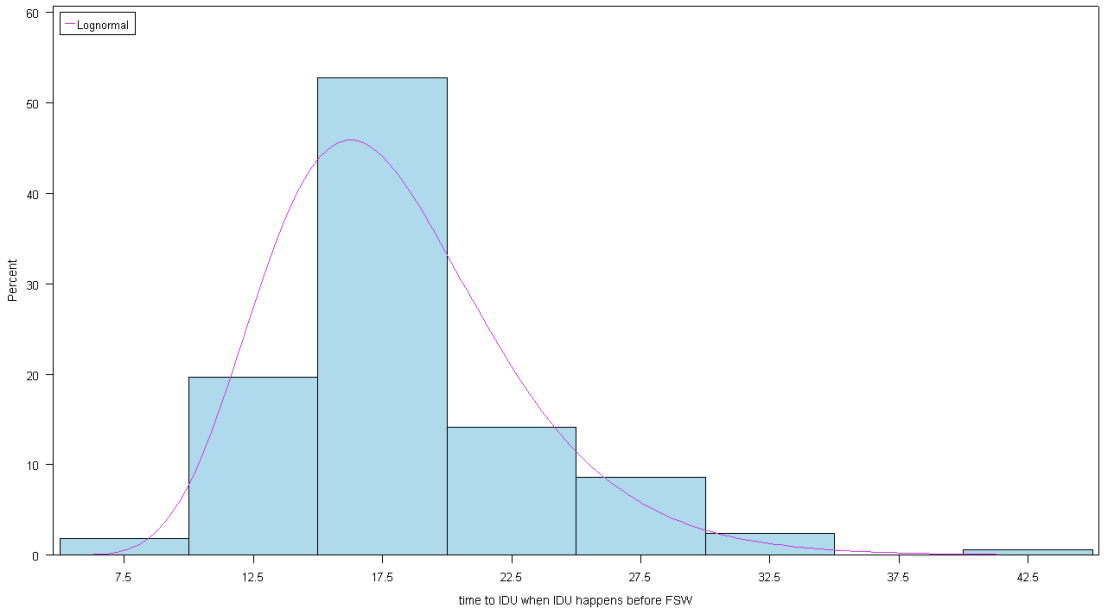

Figure A3.2: Distribution of time to initiation of injection drug use.

Table A3.4: Model fit diagnosis for time initiation among women who initiated both sex work and injection drug use at the same age (n=136).

Distribution	AIC value
Weibull	94.602
Exponential	287.757
Log-Normal	50.867
Gamma	41.402

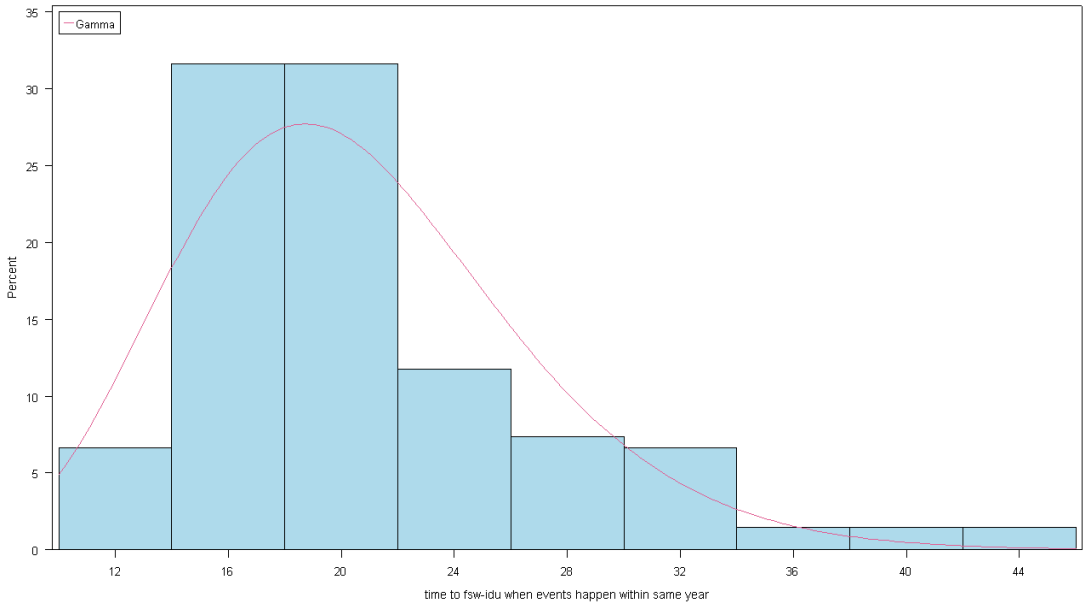

Figure A3.3: Distribution of time to initiation when both sex work and injection drug use are initiated at the same age.

Table A3.5: Model fit diagnosis for time to concurrent sex work and injection drug use among women who initaited sex work first (n=163)

Distribution	AIC value
Weibull	687.365
Exponential	704.048
Log-Normal	669.616
Gamma	670.626

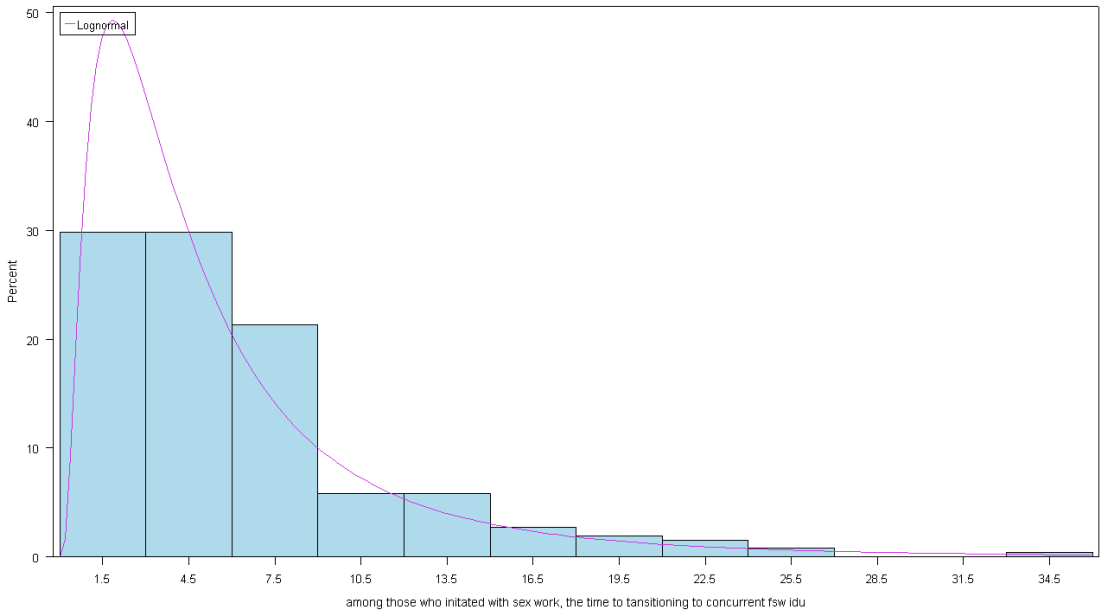

Figure A3.4: Distribution of time to concurrent sex work and injection drug use, among women who initiated sex work first.

Table A3.6: Model fit diagnosis for time to concurrent sex work and injection drug use among women who initaited injection drug use first (n=163)

Distribution	AIC value
Weibull	445.503
Exponential	451.351
Log-Normal	417.433
Gamma	414.774

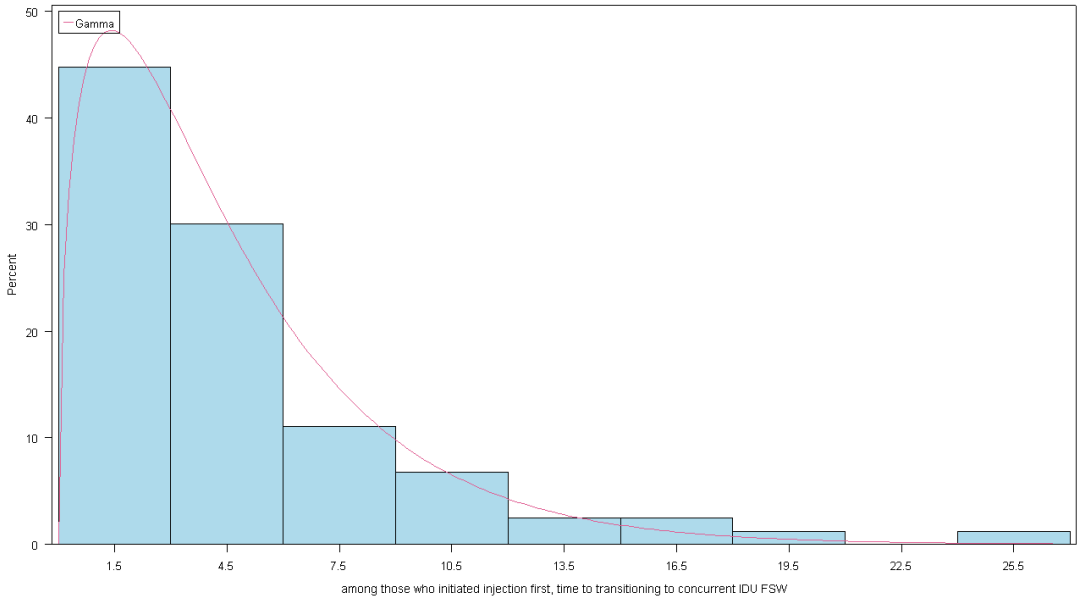

Figure A3.5: Distribution of time to concurrent sex work and injection drug use, among women who initiated injection drug use first.

APPENDIX 4.

A. Study objective*:* The aim of this study was to assess the differences in context of sex work and injection drug use initiation across three groups of female sex workers who inject drugs in Tijuana and Ciudad Juarez, Mexico.

B. Methods*:* Baseline data from a longitudinal study aimed at decreasing both risky sexual and injection drug use behaviors among women was used for the analyses. Multinomial logistic regression was used to assess differences in context of first sex work and injection initiation for women who initiated sex work earlier than injection drug use, and women who initiated injection drug use before beginning sex work, compared to women who initiated both sex work and injection drug use at the same age.

Multinomial logistic regression compares multiple groups through a combination of binary logistic regressions. Multinomial logistic regression is used when an outcome has more than two groups and is not ordered. Here participants were assigned to one of three groups: (1) initiated sex work at a younger age than beginning to inject drugs, (2) initiated injection drug use at a younger age than beginning sex work, and (3) initiating both sex work and injection drug use at the same age. For all analyses the reference group is women who initiated both sex work and injection drug use at the same age. Similar to binary logistic regression, multinomial logistic regression provides effects in terms of odds ratios; probability of belonging to a specific outcome

group compared to the probability of belonging to the referent group. For analyses purposes here the odds for multinomial logistic regression are:

$$\frac{\text{Probability (initiating sex work before injection drug use)}}{\text{Probability (initiated both sex work and injection at same age)}}$$

and

$$\frac{\text{Probability (initiating injection drug use before sex work}}{\text{Probability (initiating both sex work and injection at same age}}$$

Any of the three groups could be used as the reference group, but it was decided to use the initiation at same age group for all analyses shown below. Multinomial logistic regression does not make any assumptions of normality, linearity, and homogeneity of variance for the independent variables.

C. Results:

Characteristics of women who initiated sex work earlier than injection drug use

Women who initiated sex work before injection drug use were found to be older at time of the study interview (OR=1.14, 95% Confidence interval [95% CI]: 1.32, 1.89) and to initiate sex work at a younger age (OR=0.77, 95% CI: 0.64, 0.92 per 5 years), compared to women who initiated both sex work and injection drug use at the same age. No other contextual factors surrounding either sex work or injection drug use initiation differed significantly across the two groups. While only marginally significant, women who initiated sex work before injection drug use were less likely to methamphetamine (snorting or

smoking) before initiating either sex work or injection drug use (OR=0.69, 95% CI:0.45, 1.05). No other drug use behaviors differed across the two groups. Marginal associations were found across the two groups for migration characteristics, with women who initiated sex work before injection drug use being more likely to be born outside of the study city (OR=1.48, 95% CI: 0.98, 2.26), and to have lived in more cities (OR=1.13, 95% CI: 0.0.98, 1.31), compared to women who initiated both sex work and injection at the same age. No differences were detected for history of family drug use or sex work involvement or early abuse.

Characteristics of women who initiated injection drug use earlier than sex work

Women who initiated injection drug use before beginning sex work were older at the time of interview (OR=1.28, 95% CI: 1.10, 1.47 per 5 years) and were more likely to speak English (OR=2.42, 95% CI: 1.43, 4.10) compared to women who initiated both sex work and injection drug use at the same age. Women who initiated injection earlier were also more likely to initiate injection drug use at an older age (OR=1.25, 95% CI:1.05, 1.48 per 5 years), and less likely to have been promised anything at the time of first sex trade (OR=0.51, 95% CI: 0.29, 0.86), when compared to women who initiated both sex work and injection at the same age. Differences across the two groups for contextual factors surrounding injection drug use initiation were only found to be marginally significant, these included: first injecting to deal with depression or feelings of anxiety or stress (OR=0.61, 95% CI: 0.37, 1.03). Women who

initiated injection drug use before beginning sex work were less likely to have used any illicit drug prior to initiation (OR=0.62, 95% CI: 0.288, 0.98), and less likely to have snorted or smoked methamphetamine prior to injection drug use (OR=0.327, 95% CI:0.11, 0.95), but more likely to have used an inhalant prior to injecting (OR=2.37, 95% CI: 1.02, 5.53), compared to women who initiated both sex work and injection drug use at the same age. Women who initiated injection were more likely to have been born outside of the study site (OR=1.49, 95% CI:0.94, 2.37), and to have moved to the study site due to deportation (OR=2.89, 95% CI: 1.26, 6.66). No significant differences were detected for family drug use and sex work involvement, or early lifetime abuse.

D. Conclusions

The purpose of this study was to compare contextual factors surrounding sex work and injection drug use initiation across three groups of current female sex workers who initiated drugs. It appears that women who initiated sex work earlier than injection drug use, and women who initiated injection drug use before sex work did not differ very much from women who initiated both sex work and injection drug use at the same age in regards to the context of sex work and injection initiation. Instead differences were found for early experiences of illicit drug use. Women who initiated injection drug use before sex work were less likely to have used any non-injection illicit drug before injection drug use, and were less likely to have used methamphetamine than women who initiated both sex work and injection drug use at the same age. In

contrast, early inhalant use was associated with initiated injection drug use before sex work. Similar to previous studies within the Northern US-Mexico border region, deportation appears to influence women to initiated injection drug use. Future mixed method studies examining the context of deportation within females and the effect on future illicit drug use, particularly injection drug use, is warranted. While differences in initiation circumstance across the three groups were not detected, differences likely do exist. Understanding differences in underlying motivations for first sex work and injection drug use, sociodemographic characteristics, and environmental influences across these three groups could provide targets for both prevention programs and direction for intervention programs aimed at changing their current drug use and sexual behaviors.

Table A4.1: Univariate associations for contextual factors associated with women who initiated sex work earlier than injection drug use (N=258), and women who initiated injection drug use earlier than sex work (N=163), compared to women who initiate both sex work and injection drug use at the same age (N=136).

	Initial initiation event was sex work			**Initial initiation event was injection drug use**		
Baseline Characteristic	**OR**	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
Sociodemographic factors						
Age (per 5-years)	**1.145**	1.006, 1.304	0.0409	**1.278**	1.110, 1.472	0.0007
Study location (CJ vs. TJ)	0.864	0.570, 1.311	0.4923	*0.680*	0.430, 1.074	0.0979
Speaks English	1.36	0.820, 2.257	0.2341	**2.415**	1.425, 4.092	0.0011
Married vs. single, widowed, divorced	0.837	0.549, 1.278	0.4101	0.783	0.492, 1.248	0.3041
Time to engaging in concurrent sex work and injection drug use behaviors (per 5-years)	**1.585**	1.329, 1.891	<0.0001	**1.306**	1.081, 1.579	0.0058
Contextual factors surrounding sex work and injection drug use initiation						
Sex Work Initiation						
Age first traded sex (per 5-years)	**0.774**	0.647, 0.924	0.0049	**1.247**	1.051, 1.481	0.0116
Reason initiated sex work: needed money to pay for drugs	1.067	0.693, 1.644	0.7685	1.025	0.639, 1.645	0.9185
Reason initiated sex work: needed money for child's needs	0.824	0.531, 1.279	0.3880	0.835	0.15, 1.353	0.4638
Own idea to trade sex first time	0.820	0.535, 1.258	0.3644	1.025	0.639, 1.644	0.9190
Friend/acquaintance idea to trade sex first time	0.947	0.311, 2.883	0.9236	1.352	0.432, 4.234	0.6043
Boyfriend/husband's idea to trade sex first time	1.139	0.717, 1.808	0.5819	0.990	0.593, 1.651	0.9681
Promised anything in exchange for sex the first time	0.674	0.405, 1.122	0.1294	**0.505**	0.294, 0.866	0.0130
Promised drugs the first time traded sex†	0.853	0.464, 1.567	0.6083	1.362	0.716, 2.593	0.3464
Promised money the first time traded sex†	0.814	0.401, 1.652	0.5688	0.929	0.415, 2.078	0.8569
Injection drug use initiation						
Age first injected drugs (per 5-year)	**1.537**	1.296, 1.822	<0.0001	**0.619**	0.490, 0.782	<0.0001
Physical location when first injected drugs:						

Table A4.1 continued: Univariate associations for contextual factors associated with women who initiated sex work earlier than injection drug use (N=258), and women who initiated injection drug use earlier than sex work (N=163), compared to women who initiate both sex work and injection drug use at the same age (N=136).

	Initial initiation event was sex work			**Initial initiation event was injection drug use**		
Baseline Characteristic	**OR**	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
Own house or parent's house	0.880	0.487, 1.598	0.6751	1.308	0.705, 2.427	0.3942
Someone else's house	0.683	0.437, 1.066	0.0934	0.765	0.470, 1.245	0.2814
Shooting gallery	1.598	0.836, 3.054	0.1559	1.504	0.745, 3.036	0.2549
Hotel/rented room	1.566	0.681, 3.601	0.2912	0.718	0.254, 2.033	0.5327
Jail or prison	2.667	0.309, 23.05	0.3727	4.270	0.493, 39.99	0.1875
Drug first injected:						
Heroin	0.934	0.568, 1.536	0.7879	0.931	0.540, 1.604	0.7967
Cocaine or crack	1.129	0.474, 2.686	0.7845	0.826	0.302, 2.262	0.7097
Speedball (cocaine and heroin)	0.625	0.292, 1.342	0.2281	1.174	0.553, 2.493	0.6758
Methamphetamine	1.965	0.713, 5.414	0.1914	1.001	0.299, 3.55	0.9984
Primary reason first injected:						
External pressure from friends, family, or partner	0.811	0.504, 1.304	0.3873	0.989	0.593, 1.651	0.9672
To deal with stress or feelings of depression	0.825	0.526, 1.294	0.4023	*0.614*	0.368, 1.026	0.0625
Curiosity about the drug or the effect	1.169	0.768, 1.779	0.4662	1.131	0.714, 1.793	0.5997
Person with:						
Friend	0.872	0.474, 1.605	0.6592	0.764	0.384, 1.523	0.4449
Spouse/partner	0.525	0.033, 8.464	0.6499	1.677	0.150, 18.696	0.6743
Contextual Factors preceding sex work and injection drug use initiation						
Illicit drug use						
Used any non-injection illicit drug before initiating either sex work or injection drug use	*0.690*	0.452, 1.053	0.0852	**0.615**	0.388, 0.977	0.0392
Crack or cocaine (non-injection)††	0.603	0.263, 1.384	0.2347	0.509	0.263, 0.192	0.1759
Heroin (non-injection) ††	1.055	0.095, 11.740	0.9654	1.677	0.150, 18.703	0.6742
Meth (non-injection)††	0.868	0.411, 1.834	0.7114	**0.327**	0.112, 0.953	0.0405

Table A4.1 continued: Univariate associations for contextual factors associated with women who initiated sex work earlier than injection drug use (N=258), and women who initiated injection drug use earlier than sex work (N=163), compared to women who initiate both sex work and injection drug use at the same age (N=136).

	Initial initiation event was sex work			Initial initiation event was injection drug use		
Baseline Characteristic	**OR**	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
Inhalant††	1.870	0.825, 4.238	0.1336	**2.366**	1.013, 5.528	0.0467
Migration						
Born outside of study city	*1.495*	0.982, 2.275	0.0607	*1.491*	0.940, 2.367	0.0898
Region of birth city:						
Northern Mexican state (not Baja or Chihuahua)	1.479	0.862, 2.538	0.1551	1.036	0.560, 1.916	0.9107
Chihuahua, Mexico	0.768	0.502, 1.175	0.2241	0.725	0.454, 1.160	0.1802
Baja, Mexico	0.931	0.559, 1.552	0.7848	1.540	0.906, 2.619	0.1108
Central Mexican state	1.331	0.670, 2.645	0.4142	0.864	0.385, 1.940	0.7244
Southern Mexican State	0.341	0.095, 1.234	0.1004	0.269	0.053, 1.356	0.1116
United States	1.435	0.547, 3.749	0.4641	2.195	0.827, 5.823	0.1142
Number of cities lived (per city)**	*1.134*	0.983, 1.308	0.0844	*1.159*	0.998, 1.345	0.0524
Reason moved to city was due to deportation from US	1.126	0.474, 2.687	0.7845	**2.899**	1.262, 6.658	0.0121
History of Abuse						
Experienced physical abuse before initiating either sex work or injection drug use	0.792	0.507, 1.238	0.3061	1.132	0.685, 1.870	0.6291
Experienced rape before initiating either sex work or injection drug use	*0.*874	0.527, 1.452	0.6041	0.853	0.491, 1.481	0.5718
History of Family drug use and sex work involvement						
Parent or sibling used illicit drugs**	0.956	0.631, 1.448	0.8322	1.290	0.817, 2.038	0.2751
Parent or sibling used injection drugs**	1.163	0.717, 1.886	0.5399	*1.655*	0.992, 2.763	0.0539
Any family member participated in sex trade**	0.875	0.526, 1.454	0.6058	0.809	0.456, 1.427	0.4643

*reference group for dependent variable is women who initiate both sex work and injection drug use within the same age (n=163)

** Lifetime

† Among those who were promised something in return for sex

†† Among those who used any non-injection drug before initiating either sex work or injection drug use (n=412).

Bold indicate significant at alpha<0.05; *italic* indicate significant at alpha<0.15.
All variables significant at alpha<0.010 were considered in the multivariate model