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Assessing the impact of cumulative incarceration, public health oriented drug law reform, and a police education program, on the hepatitis C virus epidemic among people who inject drugs in Tijuana, Mexico.

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for the degree Doctor of Philosophy

in

Public Health (Global Health)

by

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The Dissertation of Carlos D. Rivera Saldana is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

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DEDICATION

To my wife and parents for always believing in me.

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LIST OF ABBREVIATIONS

aOR	adjusted Odds Ratio
AR1	Autoregressive
BBI	Blood Borne Infections
BC	Baja California
CI	Confidence Interval
CC	Compensated Cirrhosis
DC	Decompensated Cirrhosis
DAA	Direct Acting Antivirals
DALY	Disability Adjusted Life Years
ESLD	End Stage Liver Disease
GEE	Generalized Estimating Equations
HCC	Hepatocellular Carcinoma
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
IQR	Interquartile Range
LMIC	Low– and Middle–Income Countries
MAR	Missing at Random
MI	Multiple Imputation/Multiply imputed
NSP	Needle/Syringe Exchange Programs
OAT	Opioid Agonist Therapy
OR	Odds Ratio

PAF	Population Attributable Fraction
PEP	Police Education Program
PRCC	Partial Rank Correlation Coefficients
PWID	People Who Inject Drugs
RR	Relative Risk
SVR	Sustained Viral Response
UI	Uncertainty Interval
WHO	World Health Organization

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Chapter 3, entitled “Modelling the contribution of incarceration and public health oriented drug law reform to HCV transmission and elimination among PWID in Tijuana, Mexico,” is, in full, currently being prepared for submission for publication of the material. Co-authors include Beletsky Leo, Borquez Annick, Kiene Susan M, Marquez, Lara K, Strathdee Steffanie A, Zúñiga Maria Luisa, Cepeda Javier, Martin Natasha K. The dissertation author, Rivera Saldana Carlos D, was the primary researcher and author of this material.

Chapter 4, entitled “Estimating the impact of a police education program on hepatitis C virus (HCV) transmission and disease burden among PWID in Tijuana, Mexico: A dynamic modeling analysis,” is, in full, currently being prepared for submission for publication of the material. Co-authors include Abramovitz Daniela, Beletsky Leo,

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ABSTRACT OF THE DISSERTATION

Assessing the impact of cumulative incarceration, public health oriented drug law reform, and a police education program, on the hepatitis C virus epidemic among people who inject drugs in Tijuana, Mexico

by

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Doctor in Philosophy in Public Health (Global Health)

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Background: Incarceration is associated with increased risk of hepatitis C virus (HCV) among people who inject drugs (PWID). If properly implemented, public health oriented drug law reforms can reduce adverse health outcomes among PWID. This dissertation investigates (1) the cumulative effect of repeated incarceration on injecting risks among PWID in Tijuana; (2) the potential impact of implementing Mexico's drug law reform on the HCV epidemic among PWID in Tijuana; and (3) the impact of a police education program on the burden of HCV among PWID in Tijuana.

Methods: Chapter 2 examines the longitudinal association between cumulative incarceration with receptive syringe sharing using cohort data among PWID in Tijuana. Chapter 3 presents a mathematical model of incarceration and HCV transmission among PWID to estimate the 10-year population attributable fraction of incarceration to HCV incidence among PWID, and the impact of implementing drug law reform on HCV incidence among PWID in Tijuana. Chapter 4 estimates the impact of a real-life police education program on HCV disease burden among PWID in Tijuana, using epidemic modeling.

Results: Chapter 2 showed every additional incarceration episode increased the odds of syringe sharing by 17% (95% confidence interval [CI] 1.05-1.29). The increased odds of receptive syringe sharing persisted up to 1.5 years post-incarceration. Chapter 3 projected that incarceration is associated with 5.4% (95% uncertainty interval [UI] 0.6-11.9%) of new HCV infections among PWID in Tijuana between 2022–2032. Also, fully implemented drug law reforms (decriminalization and OAT diversion) could reduce HCV incidence rate by 10.6% (UI: 3.1-19.2%) across 10 years. Chapter 4 showed that, over the 2-year implementation, Escudo reduced HCV incidence from 21.1 per 100 person years (/100py) (UI 17–27/100py) in 2016 to 20.7/100py (UI:16-26/100py) in 2018, averting 13 (UI: 3-26) infections from 2016-2018. Using a 50-year time horizon, a 2-year reduction in incarceration from Escudo could avert a total of 120 (UI: 19-260) cases of cirrhosis.

Conclusions: These findings broaden the knowledge of the deleterious effects of incarceration on the health of PWID and inform evidence-based policymaking and interventions at the intersection of drug law reform, policing, and injection drug use.

Chapter 1. Introduction

Overview

Across global settings, robust evidence base exists on the deleterious effects of policing and incarceration on health of people who inject drugs (PWID) (1-3). If properly implemented, public health oriented drug-law reforms can help reduce adverse health outcomes among PWID (1). However, obstacles such as lack of access to basic health and harm reduction services among PWID (4, 5) or shortfalls at street level implementation (6, 7), can thwart reform's expected impacts.

To inform evidence-based policymaking surrounding criminalization and drug use, further research is needed to acquire a deeper understanding of (1) the elevated risk of infection associated to incarceration; (2) how public health oriented drug law reforms can impact drug-related harms among PWID; and (3) the effectiveness of police education programs in reducing drug-related harms among PWID. This dissertation aims to shed light on these issues from the perspective of the HCV epidemic among PWID living in Tijuana– a Mexican city situated across the border from San Diego County in the United Sates. Specifically, in this thesis, I investigate (1) the cumulative impact of repeated incarceration on injecting risks among PWID in Tijuana; (2) the potential impact of proper implementation of Mexico's public health oriented drug law reform (decriminalization and diversion to opioid agonist therapy [OAT]) on the HCV epidemic among current PWID in Tijuana; and (3) the impact of a real-life intervention, a police education program, on the burden of HCV among current and former PWID in Tijuana.

This dissertation includes the introduction (Chapter 1), three original research manuscripts (Chapters 2, 3 and 4), and an overall discussion (Chapter 5). The three original research manuscripts address the three primary aims. Chapter 2 entitled "Impact of cumulative incarceration and the post-release period on syringe-sharing among people who inject drugs in Tijuana, Mexico: a longitudinal analysis," investigates the association between cumulative incarceration and injecting risks, i.e., receptive syringe sharing, over time. This longitudinal analysis incorporates measures for repeated incarceration and different post-release periods. To estimate the elevated risks associated to repeated incarceration and the post-release risk, we used data from an ongoing community-based cohort study of PWID in Tijuana, Mexico, El Cuete-IV (R37 DA019829, PI: Strathdee) (8). Chapter 3 entitled "Modelling the contribution of incarceration and public health oriented drug law reform to HCV transmission and elimination among PWID in Tijuana, Mexico," uses mathematical modeling to examine the contribution of incarceration to the HCV epidemic among PWID. Also, it explores the impact of a fully implemented drug law reform on HCV transmission. Finally, Chapter 4 entitled "Estimating the impact of a police education program on hepatitis C virus (HCV) transmission and disease burden among PWID in Tijuana, Mexico: A dynamic modeling analysis," extends the mathematical model in Chapter 3 to assess the impact of a real-life intervention, a police education program, Proyecto Escudo (R01DA039073, PIs: Strathdee, Beletsky), on the burden of HCV among PWID in Tijuana, Mexico.

Background

The burden of hepatitis C virus (HCV) infection is still increasing (9). Estimates suggest that more than 70 million individuals worldwide have chronic HCV infection, with nearly 400,000 HCV-related deaths happening each year (10). Between 10-20% of chronically infected individuals will develop liver disease including decompensated cirrhosis, hepatocellular carcinoma, and death (11, 12). Injection drug use is an important risk factor for the transmission of blood-borne viruses, attributable to sharing syringes and injecting equipment (13). Consequently, people who inject drugs (PWID) are a key risk group for hepatitis C virus (HCV), with global estimates indicating 67% (~10 million) of PWID having a history of HCV infection (13).

Police encounters, incarceration, and PWID health

Among PWID, criminalization of drug use and enforcement of punitive drug policies have been associated with injecting risks and adverse health outcomes including HIV and HCV (3, 5, 6, 14-16). For example, safe injecting practices, such as carrying clean syringes, may be compromised due to concerns about syringe confiscation and arrest (17-20). A study among PWID in Tijuana, Mexico, found that PWID who had been arrested for carrying clean syringes had a two-fold increased odds of sharing syringes (odds ratios [OR] 2.05, CI 1.26-3.35), even when syringe possession is not a crime in Mexico (21). Other police interactions can fuel risk; a study among PWID in Thailand found that being arrested and beaten by police resulted in increased risk of sharing syringes (relative risks [RR] 1.44, 95% confidence interval [CI] 1.15-1.80) (22).

Furthermore, compared to non-injection drug users, PWID face higher rates of incarceration and reincarceration (2, 23, 24) that can result in increased health risks (25).

Even when PWID inject less often inside prisons than in community settings, increased frequency of syringe sharing occurs inside prisons (25, 26) and has been identified as a mechanism elevating HIV/HCV infection risks (2). For example, a global meta-analysis showed a strong association between recent incarceration and increased risk of acquiring HIV ((RR 1.81, CI 1.40-2.34)) and HCV (RR 1.62, 95% CI 1.28-2.05) among PWID (16). Previous incarceration was also associated with increased HIV and HCV risks (16). While the link between recent incarceration and syringe sharing has been studied (25, 27, 28), less is known about how the longer-term effect of repeated incarceration may impact receptive syringe sharing.

Consistent with global evidence, in Mexico, studies among PWID in Tijuana suggest a high proportion, around 80%, with a history of incarceration (29) and about a third having shared syringes inside prison (30). Moreover, a different study found that recent incarceration (released in past 6 months) was associated with a 1.30 (95% confidence interval [CI]: 1.15-1.46) increased odds of receptive syringe sharing (31). Nonetheless, the cumulative effect of incarceration over time, was not assessed. Chapter 2 in this dissertation examines this association.

Injecting drug use and PWID health in Tijuana, Mexico

The city of Tijuana, Baja California, Mexico— the site of our research– is one of the busiest land crossings in the world and the largest border hub between Mexico and the United Sates. Compared to the rest of the country, prevalence of drug use is higher in Tijuana. This can be attributed to its location along a major drug trafficking route to the United Sates, resulting in “spillover” from trafficked heroin, cocaine, and

methamphetamine (32). In 2016, the state of Baja California (BC), where Tijuana is located, had a prevalence of illegal drug use of 7.6% among adults (nationwide 4.6%) and the highest prevalence of amphetamine use in the country of 5% (nationwide 1.5%) (33). Around 10,000 PWID in Tijuana face homelessness and lack of access to health and harm reduction services, placing them at increased risk of blood borne infections (BBI) (34, 35). Some previous studies suggest most PWID (~90%) have been infected with HCV in 2018 (36, 37), and HIV prevalence is 4% in 2008 (38, 39).

Public health oriented drug law reform and police education programs in Mexico

In 2009, Mexico enacted drug and health law reforms ('Narcomenudeo' reforms) deregulating possession of small amounts of cocaine, heroin, methamphetamine, and marijuana for personal consumption and required drug treatment upon reoffending instead of incarceration (40, 41). Despite this, PWID reported experiencing little changes in policing practices (2009 and 2014) (7). Moreover, a study using mathematical modelling found little impact of Narcomenudeo reforms on HIV transmission but suggested that a properly implemented reform could prevent 20% of new HIV infections between 2018 and 2030 (31). This work sheds light on the dynamics connecting incarceration, decriminalization, and the HIV epidemic among PWID in Tijuana. However, the impact on HCV has not been studied. Chapter 3 in this dissertation undertakes a similar approach to investigate potential impacts of the Narcomenudeo reform on the HCV epidemic among PWID in Tijuana.

Some of the shortfalls of the Narcomenudeo reform can be backtracked to police lack of knowledge of the reform's legal content (6, 42). Nonetheless, using the police

contact to operationalize diversion to drug treatment was a core element of the Narcomenudeo reform (6). Therefore, to improve reform implementation, a police education program (PEP) ("Escudo" ("Project Shield") was launched. Escudo focused on occupational safety (mostly through needle stick injury) together with legal and harm reduction content (6, 7, 43). One of Escudo's goals is to reduce police encounters as a source of arrests and incarceration related to syringe or injection paraphernalia possession (15). Chapter 4 in this dissertation examines the impact of the Escudo intervention on the HCV epidemic among PWID in Tijuana.

Mexico HCV elimination goals

In 2016, the World Health Organization (WHO) set goals to eliminate HCV as a public health threat, consisting of an 80% reduction in HCV incidence and a 65% reduction in HCV-related mortality by 2030 (44). Following the WHO, Mexico became one of the first Latin-American country to launch an HCV elimination strategy in 2019 (45, 46). In a first stage, the strategy would concentrate efforts on patients from three priority segments: HIV positive individuals, PWID, and incarcerated individuals (45). However, at the time this dissertation was being written, treatment distribution or progress towards achieving elimination targets remains unknown. In Chapter 3, we offer estimates of how drug law reform may facilitate achieving HCV elimination. Chapter 4, while not directly addressing the elimination question, sheds light on how interventions such as Escudo could contribute to enhancing the ability of Mexico in achieving HCV elimination targets.

Theoretical Framework

The risk environment framework conceptualizes individual risk creation and prevention as part of a more complex environmental system. In this sense, behaviors that increase or reduce risks are defined and influenced by different social, cultural, economic, policy, and political environments (47, 48). Risk environment is defined as the "space, whether social or physical, in which a variety of factors exogenous to the individual interact to increase the chances of HIV transmission" (47). These factors interact at the micro-level or interpersonal relations (e.g. negotiations about the use of injecting equipment between PWID), meso-level or group norms and institutional responses (e.g. when local policing disrupts syringe exchange use), and macro-level or structural factors including laws and polices (e.g. large scale social, organizational, or policy systems), shaping the risk environments where individual decisions and behaviors occur (48). Based on Rhodes, Singer (48), this study will think of incarceration, not as a discrete event, but as a transitional context, or continuum, that involves stages and several risk elements within each stage; an environment with the capacity to influence individuals' risk decision-making and behaviors. Incarceration involves a complex interplay of individual, social, and environmental factors along a continuum (before, during, and after) that results in increased risks of infectious diseases, including HCV (3).

Based on this framework, this dissertation aims to explore factors at different levels affecting HCV risks among PWID in Tijuana. In **Aim I** we will explore how, at the meso-level, drug use criminalization and punitive policing in the form of incarceration, can impact injecting risks among PWID (micro-level). In **Aim II**, we will model public health oriented drug policy reform scenarios (macro-level). These policies work through

interconnections with the meso- and the micro-levels, altering the risk environment within which PWID decisions impact their health. In **Aim III**, we examine the impact of the implementation of a police education program that seeks to reduce police encounters as a structural driver of blood borne infections among PWID in Tijuana. This program promotes changes in policing behaviors at the meso-level, to counteract criminalization and punitive policing among PWID.

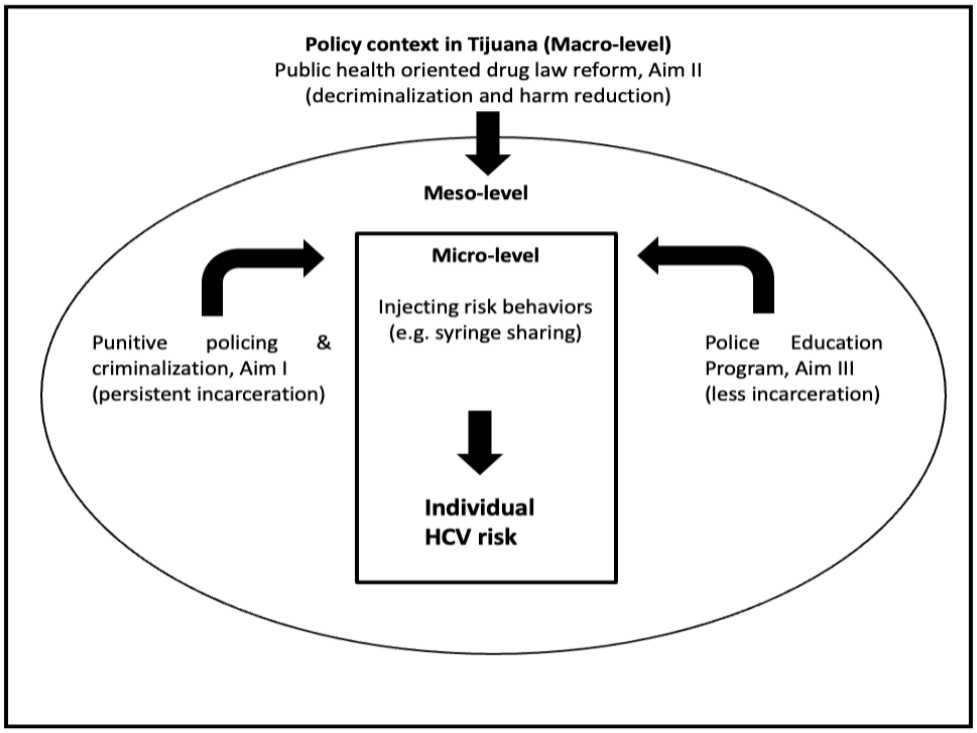


Figure 1. 1. HCV risk environment for PWID in Tijuana

Each analytical chapter in this dissertation stands on its own but are also complementary to one another. Chapter 2, using statistical tools, examines the association between cumulative incarceration and receptive syringe sharing. Chapter 3 incorporates this association to inform a dynamic mathematical model of incarceration,

HCV transmission and disease progression among current PWID. Chapter 4 extends the model in Chapter 3, to assess the impact of a real-life intervention on HCV incidence and liver disease progression among both current and former PWID.

Chapter 2. Impact of cumulative incarceration and the post-release period on syringe sharing among people who inject drugs in Tijuana, Mexico: A longitudinal analysis

Abstract

Aims: Syringe sharing, which can occur during incarceration and post-release, has been linked with increased risk of blood borne infections. We aim to investigate the cumulative effect of repeated incarceration and the post-release period, on receptive syringe sharing.

Methods: Ongoing community-based cohort, in Tijuana, Mexico, recruited through targeted sampling between 2011-2012 with six-month follow-ups. Sample of 185 participants (median age 35 years; 67% female) with no history of incarceration at study entry, followed to 2017. Cumulative incarceration and post-release period were constructed from incarceration events reported in the past 6 months for each study visit. Receptive syringe sharing in the past 6 months was assessed as a binary variable. We used logistic regression with generalized estimating equations to examine the association between cumulative incarceration events and the post-release period, with receptive syringe sharing over time. Missing data were handled through multiple imputation.

Findings: At baseline, 65% of participants engaged in receptive syringe sharing in the prior 6 months. At follow-up, 150 (81%) participants experienced a total of 358 incarceration events (median 2; IQR 1-3). We found the risk of receptive syringe sharing to increase with the number of repeated incarcerations. Compared with never incarcerated, those with one incarceration had 1.28 (95% CI 0.97-1.68) higher adjusted odds of syringe sharing, 2 to 3 incarcerations 1.42 (95% CI 1.02-1.99), and more than

three incarcerations 2.10 (95% CI 1.15-3.85). Participants released within past 6 months had 1.53 (95% CI 1.14-2.05) higher odds of sharing syringes compared to those never incarcerated. This post-release risk continued up to 1.5 years post-incarceration (aOR 1.41 95% CI 1.04-1.91) but then waned.

Conclusions: The effects of incarceration on injecting risk are cumulative and persist in the post-release period. Greater efforts should be directed towards reducing incarceration among PWID to reduce injecting risks.

Introduction

Growing evidence suggests that punitive drug policies have failed to reduce drug use, crime, and adverse health outcomes (1). Globally, people who inject drugs (PWID) face disproportionately higher rates of incarceration and higher prevalence of associated infections such as HIV, hepatitis C virus (HCV), and tuberculosis than persons who do not inject drugs (2, 23). Among PWID, having a drug related sentence and resuming injection drug use after release from prison have been associated with a twofold higher risk of reincarceration (24). A recent meta-analysis found a strong association between recent incarceration and increased risk of acquiring HIV (twofold increase) and HCV (1.5 increase) among PWID. Past incarceration was also associated with increased HIV and HCV risks (16). However, understanding the mechanisms driving the elevated risk of infection associated with incarceration, warrants further study. While the link between recent incarceration and syringe sharing has been previously established (25, 27, 28), to our knowledge, no studies have examined whether there is an association between the cumulative effect of repeated incarceration and receptive syringe sharing. As opposed to

distributive syringe sharing, receptive syringe sharing is of more relevance as it is a proxy for direct exposure to study blood-borne infections.

While blood borne infections are prevalent among PWID (2), for those not infected, the risk may increase during incarceration and upon release (3, 49). Inside prisons, continued injection drug use, lack of harm reduction services, and increased frequency of syringe sharing have been associated with incident HIV/HCV infection (2, 26, 50, 51). During the post-release period, which is characterized by lack of treatment and harm reduction, and disruption of social networks, transitioning back to the community has been associated with increased risk of relapse, fatal overdose, and injection risk behaviors (3, 52-56).

The border city of Tijuana, Baja California, Mexico, is situated along a major drug trafficking route to the United Sates. Characterized by homelessness, public injecting, and lack of access to health services, an estimated 10,000 PWID are at increased risk of blood borne infections (BBI) (34, 35). In 2009, the Mexican government passed a public health-oriented drug reform, decriminalizing small possession of illicit drugs for personal use and adopting a harm reduction strategy through diverting individuals to treatment instead of incarceration (57). Despite this, approximately 75% of PWID in Tijuana have a history of incarceration (29) and about a third had shared syringes inside prison (30). A study among PWID in Tijuana, found that recent incarceration (released in past 6 months) has been associated with increased odds of receptive syringe sharing at baseline (31). However, as the number of previous incarcerations was unaccounted, it is unknown if there was a cumulative effect of repeated incarcerations.

This study aims to fill this gap by investigating the longitudinal association between cumulative incarceration events and receptive syringe sharing among a sample of PWID in Tijuana, with no history of incarceration. Given the risk of receptive syringe sharing post-incarceration, we also assessed the post-release period on the odds of receptive syringe sharing.

Methods

Study Sample

We used data from an ongoing community-based cohort study of PWID in Tijuana, Mexico (El Cuete-IV) (32). Between 2011 and 2012 baseline data were collected with follow-up surveys every 6 months. Targeted sampling consisting of street outreach in 10 neighborhoods across Tijuana was used to recruit participants who were 18 years of age or older, had injected drugs in the past month, and were currently living in Tijuana. At baseline and semiannually thereafter, trained interviewers using computer-assisted personal interviews administered questionnaires collected data on socio-demographics, drug use behaviors, drug treatment experiences, justice involvement, migration history, and drug related harms and health outcomes (32). For the present analysis we included PWID recruited between April 2011 and June 2012 and followed for approximately 54 months (visits 1 through 10). We included only those participants who reported never being incarcerated at baseline to exclude participants who may already have been at increased risk of reincarceration and/or syringe sharing associated with previous incarceration (Supplemental Table A1 shows characteristics of participants included compared to those excluded from this analysis). This study was approved by the Ethics

Board at the University of California San Diego and Xochicalco University in Tijuana. All participants provided written informed consent.

Measures

Outcome: The outcome of this study was self-reported receptive syringe sharing in the past 6 months, which was defined as the frequency of using a syringe that had been, or suspected to have been, used by others (with categories ranging from 1-5; “never” to “always”). We dichotomized to “never” versus “ever,” because we considered that injecting with a used syringe (regardless if it is always or a few times) already puts individuals at significantly increased risk of acquiring blood borne infections compared to always using clean syringes.

Exposure: Our study had two main exposures, cumulative incarceration events and post-release period.

We defined cumulative incarceration as the number of incarceration events reported by participants over the follow-up period. To construct this variable, we first defined recent incarceration (past 6 months) as any jail or detention event reported in the previous 6 months in any of the study visits after baseline. In Mexico, detention implies remaining in custody between 48 to 144 hours until formally charged or released (usually within 72 hours). Individuals are jailed if convicted of a crime for periods longer than 3 months (58). Under specific circumstances, detention can be extended for weeks and individuals jailed for shorter periods. Access to medical services and harm reduction in

jails is limited (59). From the first follow-up (visit 2) to visit 10, we ascertained an incarceration event by inquiring “During the last 6 months, have you spent time in jail?” After visit 6, a separate question was introduced for detention: “In the last 6 months, how many times have you been in a detention center?” Therefore, after visit 6, both variables, “been in detention” and “spent time in jail,” could potentially be reported in the same visit. If participants answered yes to either measure, we considered it to be an incarceration event, which was dichotomized to “never” versus “ever.” Then, we used recent incarceration to construct the cumulative incarceration variable by aggregating the number of recent incarceration events reported by each participant over the study follow-up period. This variable was analyzed both continuously and categorically, by dividing it into four groups (never incarcerated, one incarceration, 2 to 3 incarcerations, and more than 3).

We defined the post-release period variable as the time elapsed (i.e., number of visits) after a participant had reported being incarcerated. This variable was grouped into five categories: never incarcerated, released within the past six months, released in the past 6 months to 1.5 years, released in the past 1.5 to 2.5 years, and released more than 2.5 years ago (Supplemental Figure S6).

Covariates: We selected covariates for this study based on factors associated with syringe sharing among previously incarcerated PWID, mainly from studies in Tijuana (21, 30, 34, 60, 61). Sociodemographic characteristics included variables assessed at baseline such as age, gender, time spent daily on the street, years of education, and receiving income from a formal source. Drug use characteristics included time-varying

covariates such as using heroin, methamphetamine, cocaine (including crack), injecting heroin and injected methamphetamine, all reported within the past 6 months. We also constructed a polysubstance use variable from the most prevalent drugs reported in El Cuete cohort at baseline (heroin, methamphetamine, crack/ cocaine, and tranquilizers) considering all routes of administration (62). Individuals consuming more than one drug in the previous 6 months, were counted in the polysubstance group. Injection drug use characteristics included time-varying variables such as getting syringes from a shooting gallery or a syringe exchange program in the past 6 months, and also included age at first injection. We considered injection frequency variables as important covariates in this context; however, these were not included because frequency was inconsistently reported across study visits. We also controlled for: 1) Environmental factors, e.g., living whole life in Tijuana and sex work, both assessed at baseline; 2) access to drug treatment, e.g., getting professional help for alcohol and drug use, time-varying, and; 3) encounters with law enforcement, e.g., being stopped and arrested, time-varying.

Data analysis

We summarized baseline data using frequency and proportions or median and interquartile range (IQR). Participants' characteristics for those who reported receptive syringe sharing at baseline were compared to those who did not, using the Wilcoxon rank sum test for continuous variables and Chi-square test, or Fisher's exact, for categorical variables.

In order to investigate the longitudinal association between cumulative incarceration and receptive syringe sharing, we used logistic regression with generalized estimating equations (GEE). We specified an exchangeable correlation structure to account for the correlated nature of the repeated measurements among study participants. We assessed the unadjusted association between receptive syringe sharing and each of our *a priori* selected factors. We then fitted a multivariable adjusted model, where we first included all of our *a priori* selected factors and retained a final set after backward elimination using a cut-off p-value of 0.20 (63). This process was repeated for each outcome variable. Cumulative incarceration events were assessed continuously and categorically. Additionally, we tested for a dose-response relationship between cumulative incarceration categories and receptive syringe sharing using the Cochran-Armitage trend test. This test examines if there is a monotonic trend between an ordered categorical exposure and a dichotomous outcome (64).

We developed a separate multivariable GEE model to assess the post-release period.

Treatment of missing data

We assessed the proportion and patterns of missing data across study visits. We initially performed analyses on those with complete data. To account for the potential selection bias derived from this approach, participants with missing observations were incorporated to the analysis using multiple imputation by chained equations (MICE package, R) (65). This method can handle missing data assuming data are missing at

random, i.e., missingness can be accounted for by observed covariates (66). We imputed all covariates measured at each visit after baseline using our full set of covariates as predictors. We imputed 15 data sets that were used to conduct our analyses. The estimates obtained from each imputed dataset were pooled based on Rubin's criteria (65). A detailed account of this process is provided in the supplement.

Results

From the 734 participants in El Cuete-IV study, this analysis included 185 who met the criteria of never being incarcerated at baseline.

Missing data over follow-up

Across study visits, we identified both monotonic (permanent loss to follow-up) and intermittent (missing a visit but subsequently participating again) missing data patterns (supplemental Figures A1-A2). After baseline, starting at the first follow-up (visit 2) the proportion of missing observations (both monotonic and intermittent) was 21% which increased to 42% by visit 10. Monotonic missing data accounted for 3.5% of the total missing data at visit 2 and progressed to 4.9% in visit 10.

Baseline characteristics

Baseline characteristics are presented in Table 2.1. Participants were predominantly female (67%). Median age was 35 years (interquartile range [IQR] 29-42).

Participants had injected drugs for a median of 13 years (IQR 5-20) and heroin injection was the main drug and administration route of choice (96%). At baseline, 65% participants reported engaging in receptive syringe sharing in the past 6 months, 81% reported ever having received professional help for drugs or alcohol use, and 21% reported getting syringes from a syringe exchange program in the past 6 months. Less than half of participants (38%) reported having been stopped and arrested in the 6 months prior to the baseline interview.

Incarceration events over follow-up

Among the complete cases, 113 (61%) participants experienced a total of 245 incarceration events over the follow-up period (9 visits after baseline). After multiple imputation, 150 (81%) participants experienced a total of 358 incarceration events over the same follow-up period (median 2; IQR 2-3; min 0, max 8, per person).

Overall, 85 (75%) participants reported remaining in custody between one and three days (median=2, IQR: 1-3, min=1, max=180), with only 9% reporting over 1 month in custody. Also, 75% of participants experienced up to three short-term incarcerations with 9 (5%) reaching 6-8 in a 5-year period.

Univariable analysis

From multiply imputed (MI) data, compared to those who were never incarcerated, participants who experienced 2 to 3 incarcerations had higher odds of reporting receptive

syringe sharing over the past 6 months (odds ratio [OR] 1.45, 95% confidence interval [CI] 1.05–2.00) and those with more than 3 incarcerations had an almost twofold increase in the odds of engaging in receptive syringe sharing (OR 1.98, 95% CI 1.11-3.52) (Table 2.2). Injecting methamphetamine (OR 1.63, 95% CI 1.14-2.33), using cocaine (including crack cocaine) (OR 2.15, 95% CI 1.30-3.55), getting syringes from a shooting gallery (OR 2.02, 95% CI 1.29-3.17), and being arrested (OR 1.51, 95% CI 1.38-1.65) were positively associated with receptive syringe sharing. Polysubstance use was negatively associated with receptive syringe sharing (OR 0.70, 95% CI 0.56-0.87).

Cumulative incarceration and receptive syringe sharing

In multivariable analyses from imputed data, we found that compared to those never incarcerated, the odds of receptive syringe sharing increased for participants reporting one incarceration (adjusted odds ratio [aOR] 1.28, 95% CI 0.97-1.68), 2 to 3 incarcerations (aOR 1.42, 95%CI 1.02-1.99), and those with three or more incarcerations had double the odds of engaging in receptive syringe sharing over follow-up (aOR 2.10, 95% CI 1.15-3.85) (Table 2.3). The Cochran-Armitage test showed evidence of a trend between increasing number of incarceration events and receptive syringe sharing (p=0.003). When cumulative incarceration was treated as a continuous variable, each additional incarceration event increased the odds of syringe sharing by 18% (aOR 1.17, 95% CI 1.05-1.29).

Injecting methamphetamine (aOR 1.58, 95% CI 1.06-2.36), using cocaine (aOR 2.06, 95% CI 1.19-3.58), and receiving syringes from shooting gallery (aOR 1.88, 95% CI

1.17-3.04) were independently associated with receptive syringe sharing. Polysubstance use resulted in a decreased risk of receptive syringe sharing (aOR 0.70, 95% CI 0.55-0.89).

Post-release period and receptive syringe sharing

Compared to participants never incarcerated during follow-up, those released within the past 6 months had 1.53 (95% CI 1.14-2.05) higher odds of sharing syringes and those released in the previous 6 months to 1.5 years had 1.41 (95% CI 1.04-1.91) higher odds of sharing syringes (Table 2.4). There was limited evidence of increased syringe sharing for those reporting being released in the previous 1.5 to 2.5 years (aOR 1.15, 95% CI 0.74-1.78), as well as for those reporting release 2.5 years ago or longer (aOR 1.21, 95% CI 0.67-2.19).

We report results for incarceration as a dichotomous variable (Table A7) and from complete case analyses in the supplement (Tables A3 to A7).

Discussion

In this longitudinal study of PWID in Tijuana, Mexico, we included participants with no history of incarceration at study entry, to examine the association between cumulative incarceration events and the post-release period, with receptive syringe sharing over time. We found that individuals with more cumulative incarceration experiences had increased odds of receptive syringe sharing compared to individuals who had never been incarcerated, with every additional incarceration episode increasing the odds of syringe

sharing by 17% (aOR 1.17, 95% CI 1.05-1.29). Furthermore, the post-release period was associated with increased odds of receptive syringe sharing, which persisted up to 1.5 years post-incarceration but then waned. These findings suggest that the effects of incarceration on injecting risk are cumulative and persist in the post-release period.

These results contribute to identifying a risk profile of PWID in Tijuana who, in the context of *de facto* criminalization, are more likely to engage in injecting risks. Indeed, we previously identified some of the disruptive effects of criminalization on PWID in Tijuana (21, 57, 67-69). For example, being arrested for carrying unused/sterile syringes, even when syringe purchase and possession is legal in Mexico, was independently associated with a twofold higher odds of receptive syringe sharing (21). However, we still knew little about the long-term effects of punitive policing in this setting.

Our findings expand upon the above as increased exposure to punitive policing, in the form of repeated incarceration, likely due to possession of drugs or drug paraphernalia related infractions (67), inhibits PWID from safe injecting practices (17). Similarly, the post-release period has been characterized by high injecting risks, which might disrupt engagement in safe injecting practices due to the lasting effects of punitive policing such as fear of carrying clean syringes or injecting hurriedly in the street, both previously associated with syringe sharing (18, 19).

Understanding the iatrogenic effect of incarceration in the PWID cohort has a number of policy implications. First, it highlights the imperative to reduce the number of encounters with the criminal legal system, even among those with a history of such encounters. Effective implementation of deflection and diversion programs can help operationalize this. When encounters do occur, public health prevention dictates that the

harm from these encounters must be anticipated and addressed. This includes improving harm reduction programming inside detention settings (70). In Tijuana, this includes syringe service programs and opioid agonist treatment (OAT) (71). Such a policy shift becomes particularly relevant among PWID communities in Tijuana and other border cities in Mexico, where injection drug use is more common than in the rest of the country (33).

Previously, Mexico adopted a public health-oriented drug policy reform (2009-2012) that favored treatment and harm reduction instead of incarceration but failed to materialize (41, 42, 57, 67). Relying on incarceration has likely worsened health outcomes among PWID. This article underscores the impact of detention experience on BBI risk, but that is only one area of health harms emanating from carceral systems to PWID, their partners, and broader community. Effective implementation of these policies and shift towards evidence-based drug treatment during incarceration and after incarceration (e.g., OAT), would decrease the risk of BBI (72, 73). This is especially urgent during the COVID-19 pandemic, when detention settings are an important driver of infection spread.

About polysubstance use's protective effect on receptive syringe sharing. We think this effect is driven by the inclusion of different routes of drug administration in this variable which may not directly impact injecting risks. For example, approximately 41% of participants reported smoking methamphetamine compared to 28% injecting. Also, around 20% of participants ingested tranquilizers (no alternative route was reported). These, in contrast with participants in the non-polysubstance group mostly constituted by individuals injecting heroin (95%).

Limitations

Our study is not without limitations. The El Cuete survey was not specifically developed to explore pre-, during-, and post-incarceration behaviors and risks. As we did not collect data on the specific dates of incarceration and release, our precision on behavior change is limited. Another limitation may stem from the heterogeneity in incarceration exposures. While most of our participants (75%) were in custody for only 1-3 days, a minority remained in custody for more than a month and up to 6 months. The impact of time spent in custody, not assessed in our analysis due to lack of precise data, may be critical in terms of the changes in risk behaviors around the incarceration continuum and warrants further exploration.

We also recognize the high proportion of missing data as a limitation. We believe that our assumption of missing at random (MAR) is plausible as it was assessed through observable variables included in our imputation model (66, 74-76). Complete case analyses under MAR could be biased (i.e., missing observations are related to patients' characteristics), and the multiple imputation combined with the GEE have been shown to be suitable for addressing this selection bias (66).

Additional limitations may include the following. As is common in research with PWID, data collected through self-report may be subject to imprecision due to recall and social desirability (77). Generalizing our results to other contexts should be taken with caution. For example, border cities like Tijuana have drug use patterns that differ from other cities in Mexico. Also, our subsample consisted of a higher proportion of female (67%) than male (33%) participants, which is not commonly observed among PWID populations. This was due to most men (72%) reporting previous incarceration at baseline

who were excluded from the study, while only 28% of women had been previously incarcerated (Supplemental Table A7). However, we also consider this a strength as women have been underrepresented in studies among PWID (78). We did not examine HIV incidence because it is low and could not detect a difference between exposure groups in our already narrowed subsample. We did not conduct HCV testing however previous evidence indicates that most PWID in Tijuana have already been exposed (36). All-cause mortality has already been assessed in West, Abramovitz (35). This analysis was not pre-registered, results should be considered exploratory.

Overall, recent incarceration was associated with increased risk of receptive syringe sharing. The association was stronger for individuals reporting repeated incarceration events and persisted in the post-release period. Our results underpin the need to reduce incarceration and strengthen the link to harm reduction services in the community. This linkage is particularly germane to Tijuana and similar settings, where incarceration and reincarceration for low-level offenders is high and access to health services is poor.

Acknowledgements

Chapter 2, entitled “Impact of cumulative incarceration and the post-release period on syringe-sharing among people who inject drugs in Tijuana, Mexico: a longitudinal analysis” is, in full, a reprint of the material as it appears in the Journal Addiction 2021. Rivera Saldana CD, Beletsky L, Borquez A, Kiene SM, Strathdee SA, Zúñiga ML, Martin NK, Cepeda J. “Impact of cumulative incarceration and the post-release period on

syringe-sharing among people who inject drugs in Tijuana, Mexico: a longitudinal analysis.” Addiction. 2021 Oct;116(10):2724-2733. doi: 10.1111/add.15445. Epub 2021 Mar 3. PMID: 33620749; PMCID: PMC8380753. The dissertation author, Rivera Saldana Carlos D, was the primary investigator and author of this paper.

Tables

Table 2. 1. Baseline characteristics of people who inject drugs enrolled in El Cuete-IV cohort in Tijuana, Mexico, who reported never being incarcerated, stratified by receptive syringe sharing in the past 6 months

Variables (1)(2)(3)(4)	*Overall*	*Receptive Syringe Sharing*		
		No	*Yes*	*p-value*
n	**185**	**64**	**121**	
Age (median [IQR])(5)	35.0 [29.0, 42.0]	37.0 [30.75, 43.0]	35.0 [29.0, 42.0]	0.242
Gender (%)				
Male	62 (33.5)	22 (34.4)	40 (33.1)	0.987
Female	123 (66.5)	42 (65.6)	81 (66.9)	
Hours spent on Street (median [IQR])	10.0 [6.0, 13.0]	8.50 [4.75, 12.00]	11.0 [8.0, 15.0]	**0.013**
Years of Education (median [IQR])	9.0 [6.0, 11.0]	9.0 [6.0, 10.3]	9.0 [7.0, 11.0]	0.075
Income from Formal Source (%)				
No	161 (87.0)	56 (87.5)	105 (86.8)	>0.99
Yes	24 (13.0)	8 (12.5)	16 (13.2)	
Time Injecting (median [IQR])	13.0 [5.0, 20.0]	16.0 [9.0, 20.3]	12.0 [4.0, 20.0]	0.067
Whole Life in Tijuana (%)				
No	118 (63.8)	34 (53.1)	84 (69.4)	**0.042**
Yes	67 (36.2)	30 (46.9)	37 (30.6)	
Used Heroin (%)				
No	8 (4.4)	2 (3.2)	6 (5.1)	0.716
Yes	173 (95.6)	61 (96.8)	112 (94.9)	
Used Methamphetamine (%)				
No	91 (49.2)	34 (53.1)	57 (47.1)	0.533
Yes	94 (50.8)	30 (46.9)	64 (52.9)	
Used Cocaine/Crack (%)				
No	161 (87.0)	57 (89.1)	104 (86.0)	0.712
Yes	24 (13.0)	7 (10.9)	17 (14.0)	
Injected Heroin (%)				
No	8 (4.4)	2 (3.2)	6 (5.1)	0.716
Yes	173 (95.6)	61 (96.8)	112 (94.9)	
Injected Methamphetamine (%)				
No	135 (73.0)	49 (76.6)	86 (71.1)	0.532

Table 2.1. Baseline characteristics of people who inject drugs enrolled n El Cuete-IV cohort in Tijuana, Mexico who reported never being incarcerated m stratified by receptive syringe sharing in the past 6 months, Continued

Variables (1)(2)(3)(4)	*Overall*	*Receptive Syringe Sharing*		*p-value*
		No	*Yes*	
Yes	50 (27.0)	15 (23.4)	35 (28.9)	
Polysubstance use				
No	69 (38.3)	29 (45.3)	40 (34.5)	0.204
Yes	111 (61.7)	35 (54.7)	76 (65.5)	
Got syringes from shooting gallery (%)				
No	169 (91.4)	62 (96.9)	107 (88.4)	0.058
Yes	16 (8.6)	2 (3.1)	14 (11.6)	
Got syringes from exchange program (%)				
No	164 (88.6)	57 (89.1)	107 (88.4)	>0.99
Yes	21 (11.4)	7 (10.9)	14 (11.6)	
Professional Help for Drugs/Alcohol (%)				
No	104 (56.2)	38 (59.4)	66 (54.5)	0.635
Yes	81 (43.8)	26 (40.6)	55 (45.5)	
Stopped and Arrested (%)				
No	114 (61.6)	42 (65.6)	72 (59.5)	0.512
Yes	71 (38.4)	22 (34.4)	49 (40.5)	
Income from Sex Work				
No	124 (67)	43 (67.2)	81 (66.9)	>0.99
Yes	61 (33)	21 (32.8)	40 (33.1)	

(1) All variables are reported for the past 6 months except for age, gender, years of education, and sex work (past year).
(2) Median [IQR] reported for continuous variables and proportions otherwise.
(3) A small percentage of missing values was reported for years of education (2.2%) and for Heroin Use and Heroin Injecting (6.5%).
(4) Chi-square test with continuity correction for categorical variables (except for used heroin, heroin injection, and got syringes from shooting gallery, which display cell counts <5 observations, in which case the Fisher's exact test was used) and Wilcoxon rank sum (Mann-Whitney U) test for continuous variables.
(5) Full range for age [min, max]: overall [18, 60], receptive syringe sharing (yes) [18, 59], receptive sharing syringes (no) [19, 60].

Table 2. 2. Cumulative incarceration and other factors associated with receptive syringe sharing. Univariable GEE for multiply imputed data.

Variable (1)	Unadjusted odds ratio (OR)	95% CI (2)	
Cumulative incarceration (ref: no)			
One	1.23	0.95	1.61
2 to 3	**1.45**	**1.05**	**2.00**
>3	**1.98**	**1.11**	**3.52**
Age	0.99	0.97	1.00
Time injecting (3)	0.99	0.98	1.01
Gender (ref: male)	0.95	0.74	1.20
Always living in Tijuana (ref: no)	1.29	1.00	1.65
Hours spent on Street	1.02	1.00	1.04
Heroin injecting (ref: no)	1.17	0.92	1.49
Methamphetamine injecting (ref: no)	**1.63**	**1.14**	**2.33**
Cocaine Use (ref: no)	**2.15**	**1.30**	**3.55**
Polysubstance use (ref: no)	**0.70**	**0.56**	**0.87**
Getting professional help for alcohol and drug use (ref: no)	0.82	0.60	1.12
Syringe Exchange (ref: no)	1.28	0.96	1.69
Getting syringes from shooting gallery (ref: no)	**2.02**	**1.29**	**3.17**
Arrested	**1.51**	**1.38**	**1.65**
Income from Sex Work	0.83	0.67	1.07

(1) Multiple imputation using chained equations generating 15 imputed data sets. Imputed sets come from longitudinal data including 9 follow-ups after baseline (10 visits).
(2) Covariates in bold if significant at 5% in the univariable regression.
(3) Time injecting was not included in multivariable analyses due to high correlation with age.

Table 2. 3. Cumulative incarceration and other factors associated with receptive syringe sharing. Multivariable adjusted GEE for multiply imputed data.

Variable (1) (2)	Adjusted odds ratio (aOR)	95% CI (3)	
Cumulative Incarceration (ref: none) (4)			
One	1.28	0.97	1.68
2 to 3	**1.42**	**1.02**	**1.99**
>3	**2.10**	**1.15**	**3.85**
Age	0.98	0.97	1.00
Heroin injecting (ref: no)	1.27	0.97	1.66
Meth injecting (ref: no)	**1.58**	**1.06**	**2.36**
Cocaine use (ref: no)	**2.06**	**1.19**	**3.58**
Polysubstance use (ref: no)	**0.70**	**0.55**	**0.89**
Getting syringes from shooting gallery (ref: no)	**1.88**	**1.17**	**3.04**

(1) Multiple imputation using chained equations generating 15 imputed data sets. Imputed sets come from longitudinal data including baseline and 9 follow-ups.
(2) Covariates reported are the final set retained after backward elimination using a cut-off p-value of 0.20.
(3) Covariates in bold if significant at 5% in the multivariable regression.
(4) We also assessed cumulative incarceration as continuous variable, instead of categorical, same set of covariates were retained (aOR 1.17, 95% CI 1.05-1.29).

Table 2. 4**.** Post-Release Period and other factors associated with receptive syringe sharing. Multivariable adjusted GEE for multiply imputed data.

Variable (1) (2)	Adjusted odds ratio (aOR)	95% CI (3)	
Post-Release Categories (ref: none)			
Recent (p6m)	**1.53**	**1.14**	**2.05**
Past (6m-1.5yrs	**1.41**	**1.04**	**1.91**
Past (1.5yrs-2.5yrs)	1.15	0.74	1.78
Past (> 2.5)	1.21	0.67	2.19
Age	0.98	0.97	1.00
Heroin injecting (ref: no)	1.23	0.95	1.61
Meth injecting (ref: no)	**1.52**	**1.03**	**2.25**
Cocaine use (ref: no)	**1.99**	**1.15**	**3.48**
Polysubstance use (ref: no)	**0.70**	**0.55**	**0.88**
Getting syringes from shooting gallery (ref: no)	**1.90**	**1.18**	**3.01**

(1) Multiple imputation using chained equations generating 15 imputed data sets. Imputed sets come from longitudinal data including baseline and 9 follow-ups.
(2) Covariates reported are the final set retained after backward elimination using a cut-off p-value of 0.20.
(3) Covariates in bold if significant at 5% in the multivariable regression.

Chapter 3. Modelling the contribution of incarceration and public health oriented drug law reform to HCV transmission and elimination among PWID in Tijuana, Mexico

Abstract

Background: Incarceration is associated with increased risk of hepatitis C virus (HCV) and HIV acquisition among people who inject drugs (PWID). Mexico's previous attempt in implementing a public health-oriented drug law reform (partially decriminalizing possession of drugs and diversion to drug treatment) resulted in minimal impact on incarceration among PWID. However, implementation of reforms alongside Mexico's HCV elimination program has the potential to dramatically reshape the HCV epidemic among PWID in the next decade. We use data from a longitudinal cohort of PWID in Tijuana, Mexico, to inform epidemic modeling to assess the contribution of incarceration and fully implemented drug reform on HCV transmission and elimination among PWID.

Methods: We developed a dynamic, deterministic model of incarceration, HCV transmission and disease progression among PWID. The model was calibrated to data from Tijuana, Mexico, with 90% HCV seroprevalence among an estimated 10,000 PWID. Compared to those never incarcerated, previously incarcerated PWID had a 1.10-1.42 relative risk of syringe sharing, depending on recency and cumulative number of incarcerations. Using our calibrated model, we estimated the 10-year population attributable fraction (PAF) of incarceration on HCV incidence among PWID. We additionally simulated the potential impact of the following scenarios: 1) decriminalization (80% reduction in incarceration and reincarceration rates from 2022); 2) fully implemented drug law reform from 2022 (decriminalization and diversion to opiate agonist therapy

[OAT]); 3) integrating drug law reform with HCV treatment (direct-acting antivirals [DAA]), scale-up to 500 DAA/year from 2022. We also assessed the number DAA needed to reach the 80% incidence reduction elimination target by 2030 under these scenarios.

Findings: Our model projected that incarceration is associated with 5.4% (95% uncertainty interval [UI]: 0.6-11.9%) of new HCV infections among PWID in Tijuana between 2022–2032. Fully implemented drug law reforms (decriminalization and OAT diversion) could reduce HCV incidence rate by 10.6% (UI: 3.1-19.2%) across 10 years (corresponding to 304 [95%UI: 82-576] infections). Fully implemented drug law reform could reduce the number of DAA required to achieve Mexico's HCV incidence elimination goal by 14.3% (UI: 5.3-17.1%).

Conclusions: Among PWID in Tijuana, Mexico, incarceration continues to drive HCV transmission but full implementation of public health-oriented drug law reform with decriminalization and diversion to OAT could play an important role in reducing HCV incidence. This approach, if delivered alongside scale-up of DAA, could improve the feasibility of reaching the HCV incidence elimination target by 2030.

Introduction

Approximately, 71 million adults worldwide live with hepatitis C virus (HCV) infection (44), around 80% of these among people living in low- and middle-income countries (LMICS) (5). If left untreated, HCV infection can progress to chronic liver disease, hepatocellular carcinoma, and death (11). People who inject drugs (PWID) are a key risk group for HCV transmission with global estimates pointing to 67% (~10 million)

having a history of HCV infection (13). Moreover, estimates suggest that removing the increased risk for HCV transmission among PWID would prevent 43% of overall incident HCV infections between 2018 and 2030 (79).

For PWID, the incarceration continuum (detention, incarceration, and post-release) represents a period of elevated injecting risks characterized by disruption of harm reduction services, increased risks of syringe sharing, disruption of social networks, among others (2, 3, 26, 53, 80). Results from a global meta-analysis show a strong association between recent incarceration and increased risk of acquiring HIV ((relative risk [RR] 1.81, 95% confidence interval [CI] 1.40-2.34)) and HCV (RR 1.62, 95% CI 1.28-2.05) among PWID (16). Increased frequency of syringe sharing along the incarceration continuum has been identified as a mechanism elevating HIV/HCV infection risks (2, 26). One epidemic modeling study estimated that the risks associated with incarceration and post-release contribute to 28% of HCV transmission among PWID in Scotland from 2015–2030 (81).

In Tijuana, Mexico— the site of our analysis and a border city situated along a major trafficking route to the United Sates— our previous longitudinal analysis found that individuals with repeated incarceration experiences had increased odds of receptive syringe sharing compared to individuals who had never been incarcerated, with every additional incarceration episode increasing the odds of syringe sharing by 17% (aOR 1.17, 95% CI 1.05-1.29). Furthermore, the elevated risk observed among recently released PWID persisted after the first 6 months of release (82). In Tijuana, among PWID, close to 80% have a history of incarceration (30), 90% had a history of HCV infection in 2018 (36, 37), and HIV prevalence is 4% in 2008 (38, 39). A previous modeling study

estimated that incarceration could contribute to 7% (95%CI: 3-14%) of new HIV infections among PWID in Tijuana from 2012 to 2030 (31), but its impact on HCV transmission among PWID in Tijuana is unknown.

Public health oriented drug-law reform including decriminalization may facilitate achieving HCV elimination by reducing the risk associated with incarceration and facilitating access to evidence-based drug treatment. In 2009, Mexico enacted a series of drug and health law reforms ('Narcomenudeo' reforms) including decriminalization of small amounts of selected drugs for personal consumption and diversion to drug treatment upon reoffending (henceforth fully implemented public health oriented drug reform) (40). Among PWID in Tijuana, a study modeling the impact of the Narcomenudeo reforms on HIV transmission found little impact— mainly due to short-falls at street level implementation including lack of knowledge of the reforms (42, 67)— but that proper implementation of drug policy reform could prevent 20% of new HIV infections between 2018 and 2030 (31). However, the impact of incarceration and implementation of drug law reform on the HCV epidemic among PWID in Mexico has not been evaluated.

In 2016, the World Health Organization (WHO) set goals to eliminate HCV as a public health threat, consisting of an 80% reduction in HCV incidence and a 65% reduction in HCV-related mortality by 2030 (44). Consistent with the WHO's HCV elimination targets, Mexico became one of the first Latin-American country to launch an HCV elimination strategy in 2019 (45, 46). However, since Mexico's strategy included modest HCV treatment provision (13,500 direct-acting antiviral treatments (DAA) among an estimated 500,000 infected (46)), it is unclear whether this is sufficient to achieve elimination targets.

In this study, we use epidemic modeling to assess the contribution of incarceration through injecting risks to HCV transmission among PWID in Tijuana. We also assess the impact of fully implemented public health oriented drug law reform on HCV incidence and elimination. This work will inform policymaking surrounding criminalization of drug use and how fully implemented public health oriented drug law reform could support HCV elimination in Mexico.

Methods

Model description

We developed a deterministic, compartmental model of incarceration, HCV transmission and disease progression among current PWID, and additionally track disease progression among former PWID who have permanently cessated from injecting (Figure 3.1; model equations in Supplement). The model structure was stratified by HCV infection and disease stage (susceptible, pre-cirrhosis, compensated cirrhosis, decompensated cirrhosis, and hepatocellular carcinoma), incarceration history (never incarcerated, previously incarcerated but not as a PWID, 1 incarceration as a PWID, 2 incarcerations as a PWID, 3 incarcerations as a PWID, and more than 3 incarcerations as a PWID), incarceration recency (recent incarceration [past 6 months] or non-recent incarceration [longer than 6 months]), opiate agonist therapy [OAT] status (on/off), and current injection status (PWID, former PWID).

Incarceration dynamics: New PWID enter the model as uninfected, a proportion with a history of incarceration prior to becoming a PWID. PWID become incarcerated and

re-incarcerated at constant rates based on local cohort data (31). We simulate elevated risks associated with new incarcerations as a PWID (no elevated risk among those with a history of incarceration prior to becoming a PWID). The model tracks both number of incarceration as a PWID as well as recency of incarceration (Figure 3.2), with elevated risks of syringe sharing associated with these factors based on our cohort data analysis (82).

HCV natural history: The model is dynamic, such that infection occurs at a per-capita rate proportional to the HCV prevalence among PWID in Tijuana, incarceration stage, and OAT status. Those who do not spontaneously clear their acute infection (~75%) progress to chronic infection, which if untreated can progress through the different HCV disease stages: pre-cirrhosis, compensated cirrhosis (CC), decompensated cirrhosis (DC), hepatocellular carcinoma (HCC), and death. We assume disease progression is unidirectional (i.e., there is no backward movement from a later state to an earlier one) (83).

HCV treatment: PWID can be treated for HCV in the form of direct-acting antivirals (DAA) at a fixed number per year. If there are fewer numbers of chronic infections than treatments, then the total number of infected PWID would be treated. After treatment, a proportion achieves sustained viral response (SVR) while the remainder fail treatment and remain chronically infected. Individuals who are successfully treated remain in their disease stage but progress to the previously infected compartment where they are at risk of re-infection. For those with SVR, individuals in the pre-cirrhosis stage experience no further disease progression, whereas those in later disease stages continue to progress at decreased rates compared to untreated individuals (84). At baseline, we assumed no

HCV treatment among PWID based on cohort data and the only recent availability of DAA in Mexico (85).

Opiate agonist therapy [OAT]: PWID can enter OAT, where we assume a RR 0.50 (95% CI 0.40-0.63) in reduction in the risk of HCV acquisition based on a global systematic review (72). As the coverage of OAT is very low in Tijuana (<5%, (32)), we assume no coverage at baseline. However, we explore scenarios of diversion to OAT (instead of incarceration) in our decriminalization scenarios.

Model parameters

Parameters for the full model are shown in Table 3.1. The model was parametrized to Tijuana, Mexico, with an estimated 10,000 current PWID (34). We calculated a 67% chronic HCV prevalence based on a 90% HCV seroprevalence among community PWID in Tijuana in Fleiz-Bautista (36) and a 26% spontaneous clearance rate in Micallef, Kaldor (86). Demographic, incarceration, mortality, and injecting behavior parameters were obtained from El Cuete IV study, a longitudinal cohort of PWID in Tijuana (8, 31, 35). HCV disease progression rates were obtained from published literature (12, 87-89) (see Table 3.1 and Supplemental Table B1).

Our model assumed that previously incarcerated individuals have an elevated risk of syringe sharing, specific to their incarceration history (frequency and recency). Using El Cuete data, among participants with no history of incarceration at baseline, we assessed the association between incarceration and receptive syringe sharing over time (10 visits follow-up time including baseline, approximately 4.5 years). From a log-binomial regression with generalized estimating equations, we obtained relative risks of receptive

syringe sharing for the different combinations of number and recency of incarceration categories: never incarcerated (reference category); 1-2 incarcerations as PWID and recently incarcerated (past 6 months [p6m]) (RR 1.24, 95% CI 1.05-1.47); 1-2 incarcerations as PWID and non-recently incarcerated (more than 6 months [>6m]) (RR 1.10, 95% CI 0.95-1.27); 3 or more incarcerations and recently incarcerated (p6M) (RR 1.42, 95% CI 1.15-1.74); 3 or more incarcerations and non-recently incarcerated (>6m) (RR 1.27, 95% CI 0.93-1.72). We incorporated these relative risks as parameters in our model to represent the increased risk in HCV transmission along the incarceration and post-release stages (Table 3.1; details about relative risk calculation in supplement).

Model calibration

To introduce uncertainty in the model's input parameters, we randomly sampled values from each of the parameters' uncertainty distribution to obtain 1,000 parameter sets (Table 3.1). For each parameter set, the model was calibrated to HCV chronic prevalence among PWID in 2018, assuming HCV is at steady-state based on studies showing a stable historic chronic prevalence among PWID in Tijuana (36, 37). Model calibration was achieved by minimizing the least squares fit to the prevalence data using a global optimization solver (*lsqnonlin* with *multistart* in MATLAB version R2021a), generating 1,000 model fits to the prevalence data.

Model analyses and scenarios

10-year population attributable fraction (PAF) of incarceration estimation: We estimated the PAF of incarceration to the cumulative HCV incidence over a 10-year interval from 2022 to 2032 by simulating the following scenarios:

- Baseline: *status quo* levels of incarceration and re-incarceration, no DAA or OAT.
- No elevated risks associated with incarceration: RR for all incarceration stages set to 1 from 2022.

We calculate the 10-year PAF of incarceration by: PAF = 100* ((Cumulative # of new HCV infections 2022-2032 for baseline– cumulative # new HCV infections for the no elevated risks scenario) / Cumulative # of new HCV infections 2022-2032 for baseline). We additionally simulate a scenario with no elevated risks associated with non-recent incarceration (RR associated with non-recent incarceration = 1) and calculated the associated PAF of non-recent incarceration as above.

10-year impact of decriminalization reforms on HCV incidence (2022-2032): We assessed the impact of different decriminalization scenarios on HCV incidence:

- Decriminalization: 80% reduction in incarceration and re-incarceration rates from 2022–2032 (based on the proportion of injection drug use-related detentions among PWID in Tijuana (31)).
- Fully implemented drug law reform, including decriminalization and diversion to OAT from 2022–2032: 80% reduction in incarceration and reincarceration rates; Individuals who are not incarcerated/reincarcerated are diverted to OAT, as originally intended in the Narcomenudeo reform.

- Integrated drug law reform and DAA scale-up from 2022–2032: Fully implemented drug law reform (as above) and DAA treatment of 500 PWID/year through 2032 based on estimates for national DAA allocation to Tijuana if allocated proportionally to HCV cases (355-600) from Marquez, Cepeda (85).

Combination intervention to reach HCV elimination goals by 2030: We also determined the levels of DAA required to achieve the HCV elimination goal of 80% reduction in HCV incidence from 2015-2030, considering the following combinations: only DAA, DAA and decriminalization, DAA and fully implemented drug law reform (decriminalization + OAT diversion) from 2022–2032.

Sensitivity analyses

We calculated partial rank correlation coefficients (PRCC) to assess the sensitivity of the PAF of incarceration to parameters' uncertainty (90, 91). The PRCC capture the independent effects between each input parameter and the outcome variable while keeping all other parameters constant (92).

Results

Status quo model projections

Among the estimated 10,000 current PWID in Tijuana, our calibrated model estimated that 6,700 (95% Uncertainty Interval (UI): 6,690-6,740) were chronically

infected with HCV in 2022. HCV incidence was estimated at 21 per 100 person years (100py) (UI: 17-27 per 100py) resulting in 700 (UI: 550-900) new infections among current PWID in 2022. Moreover, 188 (95% UI: 120-280) PWID advanced to end stage liver disease (ESLD) with 34 (UI: 19-51) HCV-related deaths, in that same year.

According to model estimates, by the year 2022, approximately 55% of current PWID had experienced incarceration (among these 9% were recently incarcerated). Of those who had experienced incarceration, 1,830 (UI: 1,280-2,310) current PWID were incarcerated one time, 1,155 (UI: 670-1,339) were incarcerated two times, and 2,570 (UI: 320-4,710) were incarcerated 3+ times.

10-year PAF of incarceration to HCV transmission among PWID in Tijuana (2022 to 2032)

The model projected that between 2022-2032, removing the elevated risk of incarceration would prevent 5.4% (UI: 0.6-11.9%) of new HCV infections (in other words, the 10-year PAF of incarceration to HCV incidence is 5%), equivalent to 404 (UI: 47-912) newly infected PWID across this period. The majority of these infections are due to the persistently elevated risk more than 6 months after release; removing elevated risks associated with non-recent incarceration would prevent 4.3% (UI: 0.08-10.6%) of new HCV infections, equivalent to 325 (UI: 6-791) newly infected PWID (see Figure 3.3).

10-year impact of decriminalization reforms on HCV incidence (2022-2032)

The model projected that if decriminalization were partially implemented in 2022 (and associated with an 80% reduction in incarceration among PWID), over the next 10 years, the HCV incidence rate would be reduced by a relative 5.2% (UI: 1-10.7%; see Figure 3.4). If drug law reform were fully implemented (80% reduction in incarceration and diversion to OAT), the HCV incidence rate would be reduced by 10.6% (UI: 3.1-19.2%), from 21 per 100py (UI: 17-27 per 100py) to 19 per 100py (UI: 14-25 per 100py) by 2032. Fully implemented drug law reform plus scale-up of DAA to 500 treatments/year could reduce HCV incidence rate by 41.8% (UI: 33.2-49.7%) over the 10 year period.

Achieving an 80% incidence reduction among PWID in Tijuana by 2030

Modeling indicated that if DAA is not scaled-up, drug law reform would not be enough to meet the HCV elimination targets (Figure 3.5), but could play an important role in increasing the feasibility of HCV elimination. To achieve Mexico's 80% HCV incidence reduction goal by 2030 (equivalent to reducing incidence from 21 per 100py to 4 per 100py over 2015-2030) among PWID in Tijuana, the annual treatment rates for different intervention combinations during the first year of implementation are shown in Figure 3.6. Under a DAA only strategy, 1,400 (UI: 950-2,050) DAA per year, equivalent to reducing 20% of chronic infections in the first year, would be required to achieve the HCV incidence reduction goal by 2030. If in addition to DAA, decriminalization was implemented, the mean annual rate of DAA needed to achieve the HCV incidence target would diminish to 1,350 (UI: 850-1,850) individuals. Furthermore, DAA implemented in combination with fully implemented drug reform would reduce the annual DAA needed to achieve the HCV

incidence target (to 1,200 [UI: 900-1,700]) PWID, saving 200 DAA treatments per year compared to the DAA only scenario (a 14.3% reduction in the number of DAA).

Sensitivity analysis

Sensitivity analysis revealed that the most influential parameters contributing to prediction imprecision of the incarceration PAF, were the reincarceration rate (correlation coefficient (r)=0.86, p-value (p)<0.001), the longer-term elevated risks from non-recent incarceration (more than 6 months) for those people who had been incarcerated 1-2 times (r=0.80, p<0.001) and the proportion of PWID incarcerated 3-4 times (r=0.84, p<0.001). See Figure 3.7 (PRCC and significance levels provided in supplement).

Discussion

We investigated the contribution of incarceration to the HCV epidemic among PWID in Tijuana, and the impact of public health-oriented drug law reform on HCV elimination strategies. Our projections suggest that incarceration is associated with 5% of new HCV infections among PWID in Tijuana over the next decade. Full implementation of the public health-oriented drug law reforms in Mexico (including decriminalization and diversion to OAT) could reduce HCV incidence by 11% between 2022-2032, and also reduce the number of DAA required to achieve Mexico's HCV elimination goals by 2030 saving 200 DAA treatments per year compared to the DAA only scenario (a 14.3% reduction in the number of DAA).

Comparison with existing studies

Our results are consistent with findings from an earlier study among PWID in Tijuana focusing on the impact of drug policy reform on HIV transmission, which found that an 80% reduction in incarceration would result in 9% reduction of new HIV infections between 2018-2030, similar to our 5% reduction in new HCV infections from 2022-2032. Examples from other regions with harsh criminalization practices among PWID, include a study in Ukraine suggesting 28-55% of new HIV infections over a 15 year period, to be attributable to heightened HIV transmission risk among current or previously incarcerated PWID (93).

Our estimates of incarceration PAF is lower than a modeling study in Scotland which found that incarceration and the post-release period contributed to 28% of new HCV infections over 2015-2030 (81). Although the Scotland study did not incorporate residual risk among non-recent incarcerated PWID, both their elevated risk among recent incarcerated PWID and reincarceration rate were higher than ours which could have led to a higher PAF.

Our estimates of the annual treatments required to achieve the HCV incidence elimination goal (approx. 1,400 the first year from 2022) is higher than our previous publication, which estimated 770/year from 2019 (85), which was partly due to the shorter time period to achieve elimination (8 years vs 11).

Implications

From a public health implementation perspective, we find that incarceration remains an important contributor to the HCV epidemic among PWID in Tijuana, underscoring the importance of a public health-oriented approach to drug policy reform. Further, if fully implemented, a public health-oriented drug policy approach could enhance the ability for Mexico to achieve its HCV elimination target of reducing incidence by 80% by 2030.

Although access to DAA among PWID has been historically very low, the present administration in Mexico has embarked in a national hepatitis C elimination program, through which DAA would be prioritized to vulnerable groups including incarcerated individuals, sex workers, and PWID (45, 46). So far, it seems the program has mainly focused on expanding HCV testing capabilities and training across the country (94). However, it is still unclear how treatments have been administered across different population groups or its geographical distribution. Nonetheless, the HCV elimination program remains one of the administration's flagships and substantial scale-up remains possible.

For a combination of interventions to synergistically create the most benefits, diversion to OAT is also necessary. Currently, OAT is prohibitively expensive for PWID and not widely available (95). This scale-up is long overdue. Our estimates, together with those of previously cited modeling studies, offer renewed prospects to rethink a public health-oriented drug reform. Even with the WHO deadline fast approaching, substantial gains can be achieved from implementing drug policy reform by 2030 and beyond.

Strengths and limitations

A particular strength of our study is the use of longitudinal cohort data among PWID in Tijuana to inform estimates of the elevated risk of syringe sharing (and therefore HCV transmission) among those with a history of incarceration, stratified by number and recency of incarceration. To our knowledge this is the first modeling study in a middle-income setting to assess the impact of repeated and recent/non-recent incarceration on HCV transmission among PWID. It is also the first to assess the impact of properly implemented public health-oriented drug law reform on HCV elimination.

Our study is not exempt from limitations. First, although our estimates of the association between incarceration history (recency and number of incarcerations) and recent syringe sharing were derived from a longitudinal study of PWID in Tijuana, we could not explicitly establish a causal relationship. Second, there is uncertainty in model parameters. For example, there is uncertainty in our estimates for duration of injection. This parameter is notoriously difficult to estimate (85), as the survey question of number of years injecting does not equal number of years until permanent cessation. This estimate is both right and left censored, i.e., people have not given up injecting yet and the survey likely never captures those who inject for a very brief time and then give up, so the direction of bias is unclear. Nonetheless, we used a wide uncertainty interval in this estimate to represent the substantial uncertainty in the data. Third, we do not incorporate the impact of the recent COVID-19 pandemic on future epidemic trajectory. It is plausible that the pandemic could have affected HCV transmission through a number of routes – a disruption to access to harm reduction (96, 97) or general health services (98), as has been reported for other settings, could have increased HCV transmission. Conversely, it is possible that a reduction in injection network size due to border closures

or stay at home orders could have reduced HCV transmission risk. Given hospital reconversions in Mexico (99) to address the COVID-19 pandemic, it is highly likely that COVID-19 diverted human and material resources from competing health priorities, particularly HCV. The impact of COVID-19 on the HCV elimination strategy in Mexico remains unaccounted for, but data from the United States indicates that sustained reductions in DAA initiations were observed through the end of 2020, and perhaps beyond (100). Further research on the impact of COVID-19 on the risk environment and health among PWID in Mexico and elsewhere is warranted.

Conclusion

Among PWID in Tijuana, Mexico, incarceration continues to drive HCV transmission and full implementation of public health oriented drug law reform with decriminalization and diversion to OAT could play an important role in reducing HCV incidence. This approach, if delivered alongside scale-up of DAA, could additionally improve the feasibility of reaching Tijuana's HCV incidence elimination target by 2030.

Acknowledgements

Chapter 3, entitled Modelling the contribution of incarceration and public health oriented drug law reform to HCV transmission and elimination among PWID in Tijuana, Mexico, in full, is currently being prepared for submission for publication of the material. Co-authors inlcude Beletsky Leo, Borquez Annick, Kiene Susan M, Marquez, Lara K, Strathdee Steffanie A, Zúñiga Maria Luisa, Cepeda Javier, Martin Natasha K,. The

dissertation author, Rivera Saldana Carlos D, was the primary researcher and author of this material.

Tables and Figures

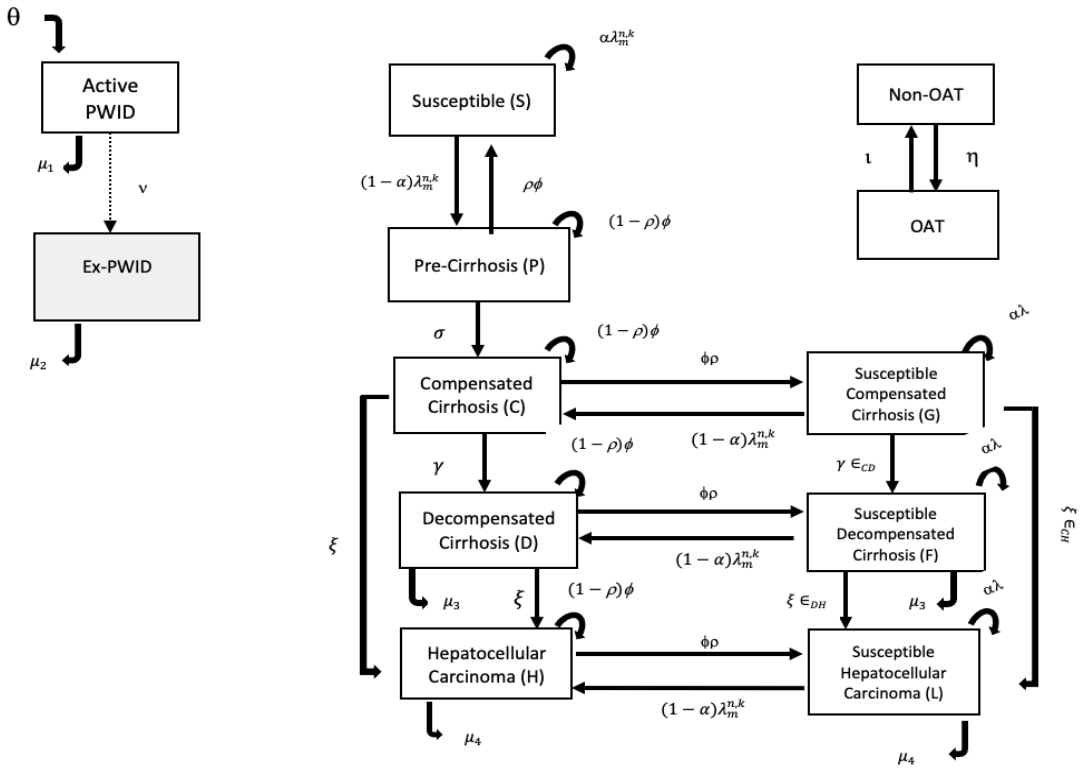
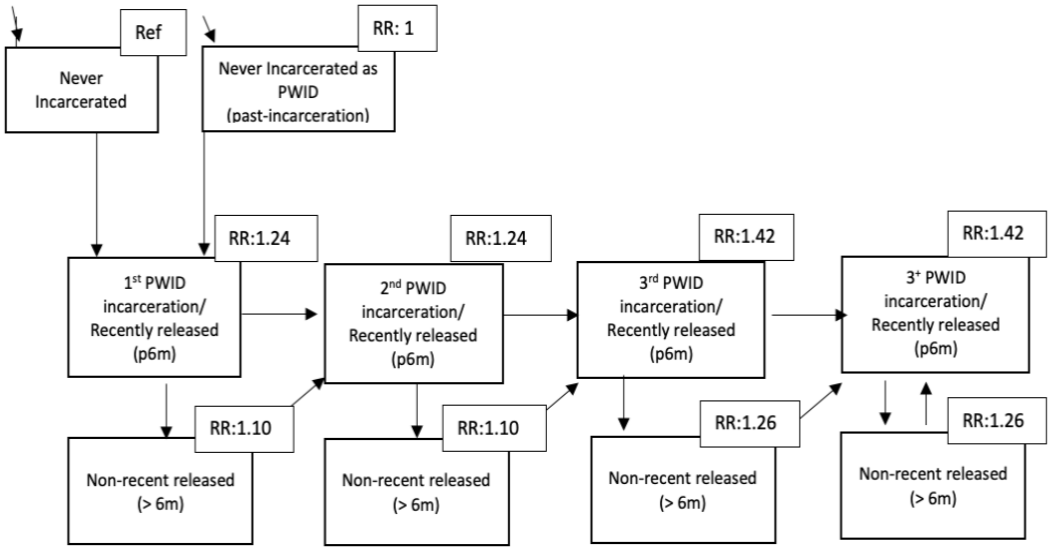


Figure 3.1. HCV model schematic



*Squares denote mean elevated relative risks of HCV transmission. 95% CI for relative risks presented in Table 1.

Figure 3.2. Incarceration submodel schematic*

Table 3. 1. Parameters used in full model and their sampling distributions				
Parameter (unit) (1) (2)	**Symbol**	**Sampled parameter's mean and 95% confidence interval**	**Sampling distribution**	**Source and comments**
Rate of new PWID initiations (per year)	θ	Fit to 10,000 PWID		
Proportion of individuals with a history of incarceration before entering the model	*propHist*	.8		(31)
Average duration of injecting until permanent cessation (years)	I	17.45 (11.4-23.7)	Uniform (min=11, max=24)	(31)
Rate at which PWID stop injecting (per year)	ν	0.0573 (0.0881-0.0423)	Calculated as 1/Average duration of injecting until permanent cessation	
Mortality rate among PWID (per year)	$\mu 1$	0.0394 (0.0270-0.0530)	Poisson (0.040)	West, Abramovitz (35)

Table 3.1. Parameters used in the full model and their sampling distributions, Continued				
Parameter (unit) (1) (2)	**Symbol**	**Sampled parameter's mean and 95% confidence interval**	**Sampling distribution**	**Source and comments**
Relative risk reduction of mortality among PWID who cease injecting	M	0.2492 (0.1803-0.3550)	Lognormal (aHR 0.25, 95% CI=0.33-0.79)	Based on reduced risk of mortality among PWID who had cessated in West, Abramovitz (35)
Mortality rate for former PWID (per year)	$\mu 2$			Calculated as $\mu 2=\mu 1*(1-M)=0.03$
Rate at which never incarcerated PWID become primarily incarcerated (per year)	τ_1	0.0261 (0.0017-0.0506)	Uniform (min=0.0007, max=0.052)	Borquez, Beletsky (31)
Reincarceration rate (per year)	ω	0.2291 (0.0538-0.4080)	Uniform (min=0.047, max=0.42)	Borquez, Beletsky (31)
Rate PWID transition from recently released (p6m) to non-recent released (>6m)	δ	2		From duration of time PWID spent in recent incarceration compartment (6 months) 12 m/6m=2
Number of PWID recruited to treatment (per year)	ϕ			0 at baseline, varied from 2022 to meet WHO goals by 2030

Table 3.1. Parameters used in the full model and their sampling distributions, Continued				
Parameter (unit) (1) (2)	**Symbol**	**Sampled parameter's mean and 95% confidence interval**	**Sampling distribution**	**Source and comments**
Proportion of treated PWID who achieve SVR	ρ	0.9421 (0.8875-0.9771)	Beta (alpha=97, beta=6)	Grebely, Dalgard (101)
OAT recruitment rate (per year)	η			Varied for different decriminalization scenarios
Rate PWID leave OAT (per year)	ι	1.5005 (1.4823-1.5186)	Uniform (min=1, max=2)	Cornish, Macleod (102)
Reduced risk of HCV transmission on OAT compared to off OAT	Π	0.5020 (0.4039-0.6417)	Normal (mean=-0.69, SD=0.12) [1]	Calculated from RR 0.50 (95% CI 0.40-0.63) in (72)
HCV Seroprevalence	o			90% (36).
Proportion of PWID who clear infection	α	0.2609 (0.2272-0.2934)	Beta (alpha=176, Beta=499)	Micallef, Kaldor (86)
Chronic prevalence	P	0.6652 (0.6359-0.6956)		0.67 from $P=o*(1-\alpha)$
Disease transition rate from pre-cirrhosis to compensated cirrhosis (CC) (per year)	σ	0.0270 (0.0254-0.0287)	Normal (mean=0.027, SD=0.0008)	Calculated from METVIR scores (F0 to F4) reported in Thein, Yi (12).

Table 3.1. Parameters used in the full model and their sampling distributions, Continued				
Parameter (unit) (1) (2)	**Symbol**	**Sampled parameter's mean and 95% confidence interval**	**Sampling distribution**	**Source and comments**
Transition probability from CC to DC (per year)	γ	0.0385 (0.0213-0.0598)	Beta (alpha=14.6168,beta=360.1732)	Beta distribution parameters from Martin, Vickerman (103) based on Fattovich, Giustina (87)
Disease transition probability from CC/DC to HCC (per year)	ξ	0.0142 (0.0015-0.0405)	Beta (alpha=1.9326, beta=136.1074)	Beta distribution parameters from Martin, Vickerman (103) based on Fattovich, Giustina (87)
Reduced relative risk from CC to DC (γ) due to SVR	$\in_{CD}$	0.0696 (0.0256-0.1741)	Lognormal (mean=-2.66, SD=0.48)[1]	van der Meer, Veldt (88)
Reduced relative risk from CC to HCC (γ) due to SVR	$\in_{CH}$	0.2293 (0.1544-0.3368)	Lognormal (mean=-1.47, SD=0.20) [1]	Morgan, Baack (104).

Table 3.1. Parameters used in the full model and their sampling distributions, Continued				
Parameter (unit) (1) (2)	**Symbol**	**Sampled parameter's mean and 95% confidence interval**	**Sampling distribution**	**Source and comments**
Reduced relative risk from DC to HCC (ξ) due to SVR	$\in_{DH}$	1		This transition is assumed same with and without SVR
Disease transition probability per year from DC to death[2]	μ_3	0.1328 (0.0992-0.0.1715)	Beta (alpha=51, beta=333)	Fattovich, Giustina (87)
Disease transition probability per year from HCC to death (per year)	μ_4	0.4292 (0.3734-0.4868)	Beta (alpha=117.1033, beta=155.23)	Beta distribution parameters from Martin, Vickerman (103) based on Fattovich, Giustina (87)
Factors altering force of infection by incarceration state:		Relative risks for incarceration states were estimated using longitudinal data from El Cuete study (see supplement)		
1-2 incarceration events + released within p6m	Γ	1.2433 (1.0483-1.4785)	Lognormal (mean=0.2151, SD=0.0858)[1]	Calculated from RR 1.24 (95% CI 1.05-1.47)

Table 3.1. Parameters used in the full model and their sampling distributions, Continued				
Parameter (unit) (1) (2)	**Symbol**	**Sampled parameter's mean and 95% confidence interval**	**Sampling distribution**	**Source and comments**
1-2 incarceration events + released >6m ago	Θ	1.1005 (0.9489-1.2948)	Lognormal (mean=0.0953, SD=0.0741) [1]	Calculated from RR 1.10 (95% CI 0.95-1.27)
>3 incarceration events + released within p6m	K	1.4185 (1.1393-1.7471)	Lognormal (mean=0.3507, SD=0.1056) [1]	Calculated from RR 1.42 (95% CI 1.15-1.74)
>3 incarceration events + released >6m ago	H	1.2592 (0.9331-1.7191)	Lognormal (mean=0.2390, SD=0.1569) [1]	Calculated from RR 1.27 (95% CI 0.93-1.72)

1. Lognormal distribution transformed to normal distribution for sampling, then back to log scale.
2. Disease transition probabilities converted to instantaneous rates for the model.

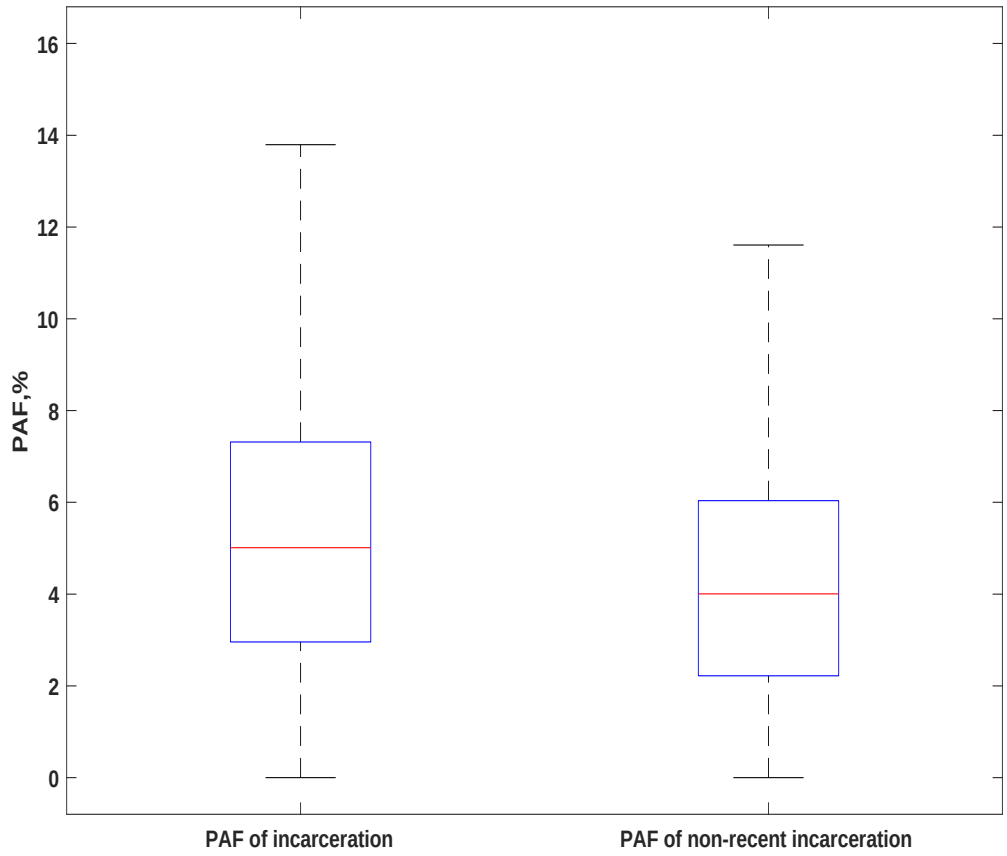


Figure 3.3. Population attributable fraction (PAF) of incarceration to HCV incidence 2022-2032

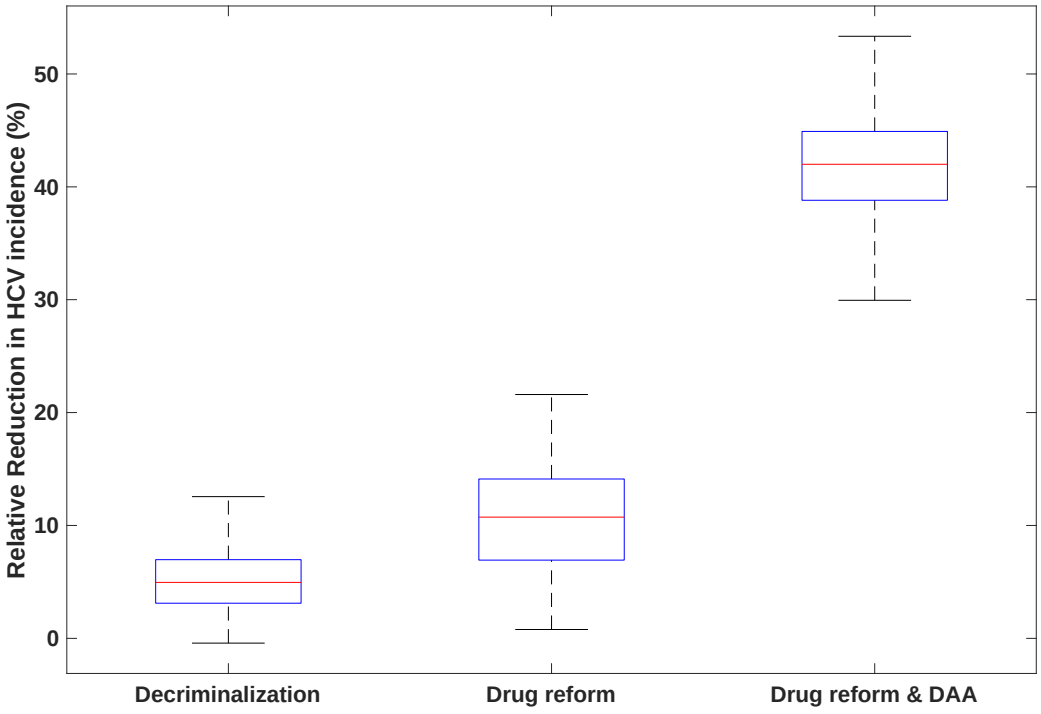


Figure 3.4. Relative reduction in HCV incidence rate among PWID in Tijuana, Mexico for different intervention scenarios compared to baseline 2022-2032

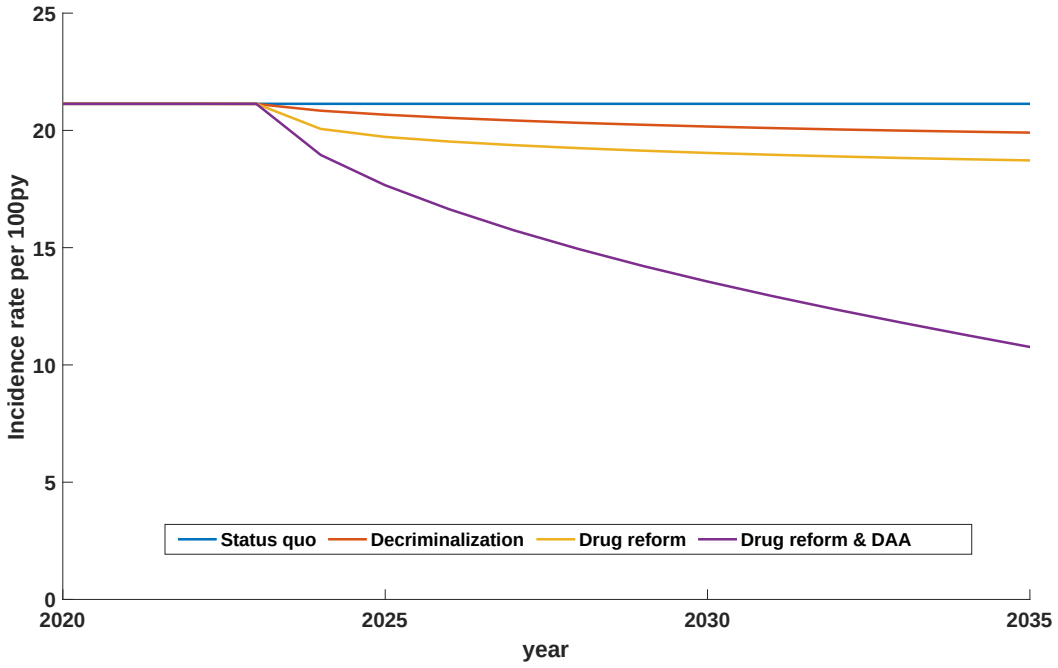


Figure 3.5. Mean HCV incidence projection for PWID in Tijuana, Mexico by intervention combination

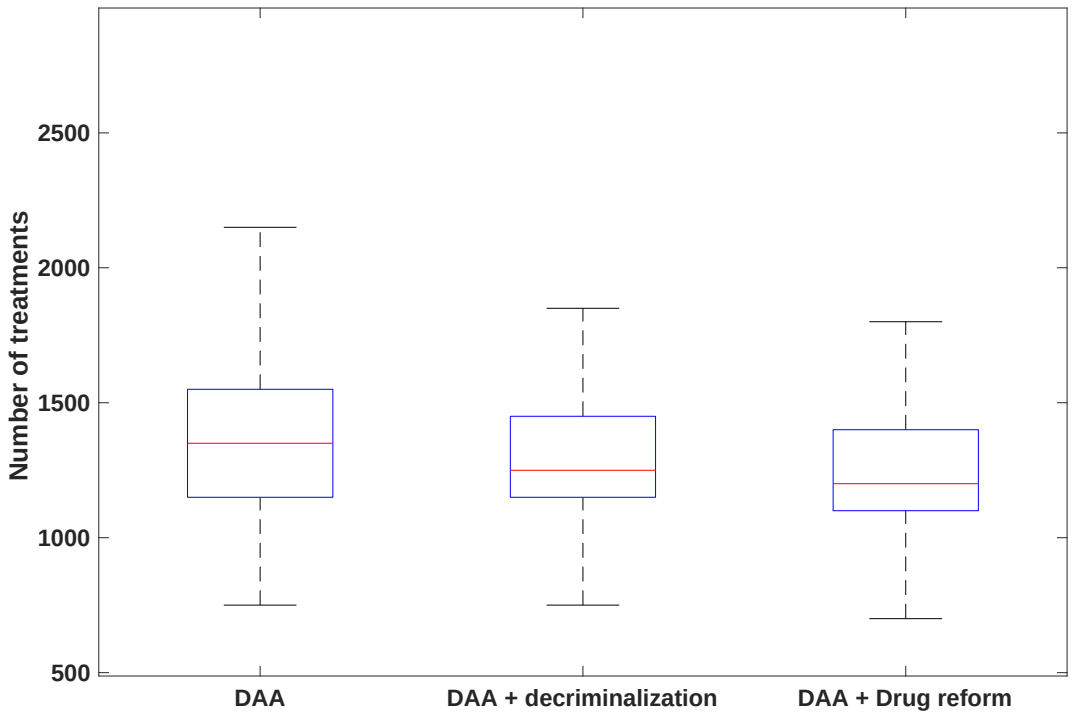


Figure 3.6. First year HCV treatment numbers needed to meet WHO HCV incidence reduction (80%) target by 2030 among PWID in Tijuana, Mexico

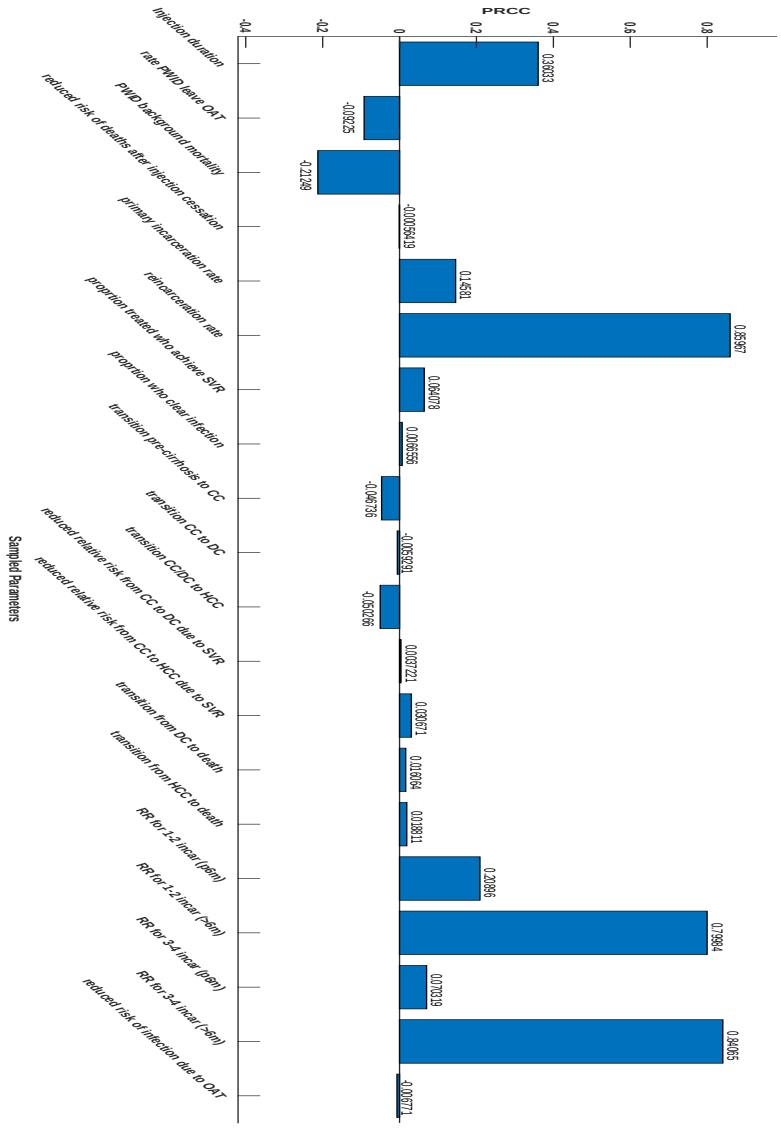


Figure 3.7. Sensitivity of the PAF to model parameters

Chapter 4. Estimating the impact of a police education program on hepatitis C virus (HCV) transmission and disease burden among PWID in Tijuana, Mexico: A dynamic modeling analysis

Abstract

Background: Criminalization of drug use and some policing practices are key structural drivers of hepatitis C virus (HCV) and HIV transmission, and overdose among people who inject drugs (PWID). In 2009, Mexico enacted a series of drug and health law reforms ('Narcomenudeo' reforms) including decriminalization of small amounts of selected drugs and diversion to drug treatment. Lack of knowledge of the reforms among police thwarted expected impacts. To close this gap, "Proyecto Escudo," a police education program (PEP) delivering training on occupational safety together with drug policy changes and harm reduction content was implemented between 2015-2016 with officer follow up until 2018. We used data from a parallel longitudinal cohort of PWID in Tijuana, Mexico, to inform epidemic modeling and assess the long-term impact of Proyecto Escudo on HCV transmission and burden among PWID in Tijuana.

Methods: We developed a dynamic deterministic model of HCV transmission and incarceration among PWID and tracked liver disease progression among current and former PWID. The model was calibrated to data from Tijuana, Mexico, with 90% HCV seroprevalence among ~10,000 PWID. Compared to those never incarcerated, previously incarcerated PWID had a 1.1-1.42 elevated risk of syringe sharing, depending on recency and cumulative number of incarcerations. Comparing the period before implementation of Proyecto Escudo to the period after, PWID experienced a 68% reduction in the risk of incarceration. We used these metrics to inform our calibrated

model and estimate the potential impact of the observed (2-year reduction in incarceration) and an extended (10-year reduction in incarceration) police education program over a fifty year follow up (2016-2066) on HCV outcomes (incidence, cirrhosis, HCV-related deaths, and disability adjusted life-years [DALYS] averted).

Findings: We estimate that over the 2-year observed follow-up, Proyecto Escudo reduced HCV incidence from 21.1 per 100 person years (/100py) (95% Uncertainty Interval [UI]: 17–27/100py) in 2016 to 20.7/100py (UI:16-26/100py) in 2018, averting 13 (UI: 3-26) infections from 2016-2018. Using a 50-year time horizon, a 2-year reduction in incarceration from Proyecto Escudo could avert a total of 22 (UI: 3-45) new infections (0.06% [UI: 0.01-0.13%] averted) and 120 (UI: 19-260) cases of cirrhosis (0.05% [UI: 0.01-0.1%] averted), and 4 (UI: 1-9) deaths (0.05% [0.01-0.1%] averted) compared to no intervention. If continued for 10 years, Escudo could reduce HCV incidence to 20.1/100py (16-26/100py) by 2026 and avert a total of 122 (20-255) new infections (0.4% [0.06-0.7%] averted) and 640 (100-1,350) cases of cirrhosis (0.3% [0.05-0.6%] averted), and 22 (4-50) deaths (0.5% [0.1-1.1%] averted) compared to no intervention over a 50-year time horizon. This equates to a reduction of 9 (UI: 1-19) and 45 (UI: 7-100) DALYs for the 2- and 10-year programs, respectively, a relative reduction of 0.05% (UI: 0.01-0.1%) and 0.3% (UI: 0.05-0.6%) compared to no police education program.

Conclusions: Implementation of public health-oriented police education programs can play an important role in reducing HCV transmission among PWID. Additional benefits would likely be observed in terms of prevention of HIV and overdose. Cost-effectiveness evaluations of police education programs incorporating these multiple benefits are warranted.

Introduction

Globally, the burden of hepatitis C virus (HCV) infection continues to rise (9). HCV is the most common infection among people who inject drugs (PWID), with global estimates indicating 67% (~10 million) of PWID have a history of HCV infection (13).

Criminalization together with restrictive drug laws and their enforcement have been identified as key structural drivers of health harms such as HCV and HIV transmission, and overdose among PWID (3, 5, 6, 14-16). For example, syringe confiscation and worry about arrest may disrupt engagement in safe injecting practices through fear of carrying clean syringes or rushed injection on the street (17-20). Whereas the incarceration continuum (detention, incarceration, and post-release) represents a period of elevated injecting risks characterized by disruption of harm reduction services, increased risks of syringe sharing, disruption of social networks, among others (2, 3, 26, 53, 80). A recent global systematic review and meta-analysis found that PWID with a history of incarceration have an elevated risk of HIV and HCV acquisition compared to those with no history of incarceration (16). Although this risk was highest for those recently incarcerated (released within past 12 months), the risk persists among those with past incarceration (released longer than 12 months) (16). Our earlier work with PWID in Tijuana found that both recent incarceration and number of incarcerations were associated with increased risk in receptive syringe sharing (82). Other policing practices such as syringe confiscation by the police, are associated with receptive syringe sharing among PWID (17). As such, policing practices are important structural drivers of HIV and HCV acquisition and transmission risk. Indeed, our previous modeling study found that

incarceration will contribute to 5.4% (uncertainty interval [UI]: 0.6-11.9%) of new HCV infections among PWID by 2032 (unpublished) and 7% (95% confidence interval [CI]: 3-14%) of new HIV infections among PWID in Tijuana by 2030 (31). Conversely, police encounters with PWID can serve as an opportunity for deflection away from the justice system and referral to harm reduction services (6).

Tijuana, Mexico is a border city situated along a major trafficking route to the United States. Approximately 80% of PWID in this region have a history of drug-related arrests and incarceration (30), 90% have a history of HCV infection in 2018 (36, 37), and HIV prevalence was 4% in 2008 (38, 39).

In 2009, Mexico enacted a series of drug and health law reforms ('Narcomenudeo' reforms) including decriminalization of small amounts of selected drugs for personal consumption and diversion to drug treatment for repeat low-level offenders (40). Previous modeling found that changing the drug laws would have minimal impact on averting HIV, likely due to poor implementation from police (31) and studies with PWID in Tijuana supported this prediction; PWID reported experiencing no changes in policing practices (2009 and 2014) (42, 67). To improve implementation of the Narcomendeo reforms, U.S.-based investigators collaborated with the Tijuana Police Department leadership to deliver a police education program (PEP), "Proyecto Escudo,"("Project Shield," henceforth Escudo) which focused on occupational safety, increasing officer knowledge of changes in federal drug policy, and harm reduction content (6, 7, 43). Goals of Escudo included a reduction of police occupational hazards when coming into contact with PWID (mostly through needle stick injury) and concomitantly, reducing police encounters as a driver of blood borne infections (BBI) among PWID (e.g. arrests and incarceration for syringe or

injection paraphernalia possession) (15). Earlier work found a promising impact of Escudo in improvements in officer knowledge about policing practices that pose occupational safety and attitudes toward addiction and PWID (7, 105). However, the impact of the police education program on the HCV epidemic among PWID in Tijuana remains unexplored.

In this study, we used estimates of the reduction in incarceration among PWID in Tijuana after the implementation of Escudo derived from a community cohort of PWID to inform epidemic modeling to predict the long-term impact of the Escudo program on HCV incidence, disease burden, and mortality. This work will inform policymaking involving criminalization of drug use and how police educational programs may contribute towards HCV elimination among PWID in Mexico.

Methods

Model description

We extended our previously developed deterministic compartmental model of incarceration and HCV transmission to track disease progression among both current PWID and former PWID who have permanently cessated from injecting (Figures 1 & 2; model equations in Methodological Supplement). The model was stratified by HCV infection and disease stage (susceptible, pre-cirrhosis, compensated cirrhosis, decompensated cirrhosis, and hepatocellular carcinoma), incarceration history (never incarcerated, previously incarcerated but not as a PWID, 1 incarceration as a PWID, 2

incarcerations as a PWID, 3 incarcerations as a PWID, and more than 3 incarcerations as a PWID), incarceration recency (recent incarceration [past 6 months] or non-recent incarceration [longer than 6 months]), and current injection status (PWID, former PWID).

HCV natural history: The model is dynamic, such that infection occurs at a PWID per-capita rate proportional to the HCV prevalence among PWID in Tijuana, and incarceration stage. Those who do not spontaneously clear their acute infection (~75%) progress to chronic infection, which if untreated can progress through the different HCV disease stages: pre-cirrhosis, compensated cirrhosis (CC), decompensated cirrhosis (DC), hepatocellular carcinoma (HCC), and death. Disease progression is unidirectional (i.e., there is no backward movement from a later state to an earlier one) (83). Progression through HCV disease stages continues for infected PWID who have permanently cessated from injecting.

Incarceration dynamics: New PWID enter the model as uninfected, with a proportion having a history of incarceration prior to injection initiation. PWID become incarcerated and re-incarcerated at constant rates based on local cohort data (31). We simulate elevated risks associated with new incarcerations as a PWID (no elevated risk among those with a history of incarceration prior to becoming a PWID). The model tracks both number of incarceration as a PWID as well as recency of incarceration (Figure 3), with elevated risks of syringe sharing associated with these factors based on our cohort data analysis, described below (82). Once PWID report permanently cessate injecting drugs, they are assumed to no longer be at risk for incarceration.

Model parameters

Parameters for the full model are shown in Table 1. The model was parametrized to Tijuana, Mexico, with an estimated 10,000 current PWID (34). We calculated a 67% chronic HCV prevalence based on a 90% HCV seroprevalence among community PWID in Tijuana in Fleiz-Bautista (36) and a 26% spontaneous clearance rate (Micallef, Kaldor (86). Incarceration, background mortality, and injecting behavior parameters were obtained from El Cuete IV study, a prospective, observational study among PWID in Tijuana, Mexico (8, 31, 35). HCV disease progression rates were obtained from published literature (12, 87-89) (see Table 1 and Supplemental Table C1).

Statistical analyses

Risk of receptive syringe sharing after repeated incarceration: Our model assumed that previously incarcerated individuals had an elevated risk of syringe sharing (1.1-1.42, see Table 1), specific to their incarceration history (frequency and recency). Using El Cuete data, among participants with no history of incarceration at baseline, we assessed the association between incarceration and receptive syringe sharing over time (10 follow-up visits including baseline, approximately 4.5 years). We used a log-binomial model with generalized estimating equations and an exchangeable correlation structure to account for within-subject correlations, to obtain relative risks of receptive syringe sharing for the different combinations of number and recency of incarceration categories. We defined these categories as never incarcerated (reference category); 1-2 incarcerations as PWID and recently incarcerated (past 6 months [p6m]) (RR 1.24, 95% CI 1.05-1.47); 1-2 incarcerations as PWID and non-recently incarcerated (more than 6 months [>6m]) (RR

1.10, 95% CI 0.95-1.27); 3 or more incarcerations as PWID and recently incarcerated (p6M) (RR 1.42, 95% CI 1.15-1.74); 3 or more incarcerations and non-recently incarcerated (>6m) (RR 1.27, 95% CI 0.93-1.72). We incorporated these relative risks as parameters in our model to increase HCV transmission along the incarceration and post-release stages (Table 1).

Impact of Escudo on incarceration among PWID: We quantified the change in the risk of recent (past 6 month) incarceration among PWID in Tijuana before and after the Escudo police education program, using data from El Cuete study. To obtain this risk we used a marginal log-binomial regression with generalized estimating equations assuming an autoregressive (AR1) correlation structure to account for correlated observations across time, with a robust sandwich estimator as the covariance estimator for fixed effects. We compared the period that spans from the beginning of El Cuete study to the beginning of the training component of the Escudo program (2011-2015) with the 2-year follow-up period after the implementation of the Escudo training component (2016-2018). We estimated a 68% lower risk of incarceration during Escudo follow-up period compared to the period before implementation of Escudo (adjusted relative risk [aRR]: 3.1 [95% CI 2.5-3.8; Table 1]).

Additional details about El Cuete study and each statistical analysis can be found in the methodological supplement.

Model calibration

To introduce uncertainty in the input model parameters, we randomly sampled 1,000 parameter sets from each of the parameter's uncertainty distribution (Table 1). For each parameter set, the model was calibrated to HCV chronic prevalence among PWID in 2018, assuming HCV is at steady-state based on studies showing a stable prevalence among PWID in Tijuana (36, 37). Model calibration was achieved by minimizing the least squares fit to the prevalence data using a global optimization solver (*lsqnonlin* with *multistart* in MATLAB version R2021a), generating 1000 model fits to the prevalence data.

Model analyses and scenarios

The scenarios assessed included:

- **Baseline**: *status quo* levels of incarceration and re-incarceration, i.e., no Escudo program.
- **2-year Escudo implementation**: 68% reduction in incarceration and re-incarceration rates from 2016 to 2018. We chose 2 years because this was the amount of time we could triangulate the PWID data (in reductions in incarcerations) with the police data (in reductions of arrests for heroin).
- **10-year Escudo implementation**: 68% reduction in incarceration and re-incarceration rates from 2016 to 2026.

We simulated impact of the above scenarios across 2 years, 10 years, and 50 years (2016-2066), to assess the long-term impact on HCV transmission, morbidity, and mortality, given the long natural history of HCV disease progression.

Model outcomes

We explore impact of the intervention on HCV incidence (rate and new infections), HCV-related cirrhosis, HCV-related deaths, and a composite measure of disease burden (measured in disability-adjusted life years [DALYs]). DALYs provide a composite measure of disease burden capturing the years of healthy life lost due to a particular disease (106). We calculated DALYs for each HCV sequalae as the yearly number of HCV cases obtained from our model multiplied by the disability weight associated to each disease stage (106). Hence, the DALYs for HCV is the sum of all the years lost to disability associated to all health states along the disease progression model (107). Disutility weights are reported in Table 1.

Sensitivity analyses

We calculated partial rank correlation coefficients (PRCC) to assess the sensitivity of the DALYs averted with the police education program to parameters' uncertainty (90, 91). The PRCC capture the independent effects between each input parameter and the outcome variable while keeping all other parameters constant (92).

Results

Status quo model projections

The calibrated model estimated 10,000 current PWID and 16,270 former PWID (95% uncertainty Interval [UI]: 9,910-26,160) in Tijuana in 2016. According to model

estimates, in 2016, around 55% of current PWID had experienced incarceration as a PWID (among these, 9% were recently incarcerated).

At the time of Escudo implementation in 2016, we estimated a HCV incidence rate of 21 per 100 person years (/100py) (95% Uncertainty Interval [UI]: 17-27/100py) among PWID (Supplemental Figure C1). For this same year, among the approximately 26,000 current and former PWID, model projections estimated 16,000 (UI: 12,600-21,500) chronic infections with 4,520 (UI: 2,770-7,170) cases of cirrhosis, 130 (UI: 15-330) cases of liver cancer, and 161 (UI: 100-250) HCV-related deaths.

Impact of a two-year implementation of the Escudo program on HCV incidence and disease burden

We estimate that the 2-year implementation of Escudo (2016-2018) reduced HCV incidence from 21.1/100py (UI: 17-27/100py) in 2016 to 20.7/100py (UI:16-26/100py) in 2018 (Figures 3 & 4), averting 13 (UI: 3-26) infections between 2016 and 2018 (Figures 5). Using a 50-year time horizon (2016-2066) to capture long-term benefits of Escudo on morbidity and mortality, a 2-year reduction in incarceration from Escudo could avert a total of 22 (UI: 3-45) new HCV infections (0.06% [UI: 0.01-0.13%]), 120 (UI: 19-260) cases of cirrhosis (0.05% [UI: 0.01-0.1%]), and 4 (UI: 1-9) deaths (0.05% [UI: 0.01-0.1%] averted; Figure 6) compared to baseline. This equates to 9 (UI: 1-19) DALYs averted for the 2-year program, a relative reduction of 0.05% (UI: 0.01-0.1%) compared to no intervention (Figure 7).

Impact of a ten-year implementation of the Escudo program on HCV incidence and disease burden

We estimate that if Escudo was implemented and impact sustained for 10 years (2016-2026, perhaps with repeat trainings) this could reduce HCV incidence from 21.1/100py (UI: 17-27/100py) in 2016 to 20.1/100py (UI: 16-26/100py) in 2026 (Figures 3 & 4), averting 121 (UI: 26-262) infections between 2016 and 2026 (Figures 5). Using a 50-year time horizon (2016-2066), a 10-year reduction in incarceration from Escudo could avert a total of 122 (UI: 20-255) new infections (0.4% [UI: 0.06-0.7%] averted) and 640 (UI: 100-1,350) cases of cirrhosis (0.3% [UI: 0.05-0.6%] averted), and 22 (UI: 4-50) deaths (0.5% [UI: 0.1-1.1%] averted; Figure 6) compared to baseline. This equates to 45 (UI: 7-100) DALYs averted for the 10-year program, a relative reduction of 0.3% (UI: 0.05-0.6%) compared to no Escudo (Figure 7).

Sensitivity analysis

Sensitivity analysis revealed that the most influential parameters contributing to uncertainty in the DALYs averted with the police education program, were average injection duration (rho (r)=-0.38, p-value (p)<0.001), the reincarceration rate (r=0.78, p<0.001), elevated risk of 1-2 non-recent incarcerations (r=0.46, p<0.001), elevated risk of 3-4 non-recent incarcerations (r=0.86, p<0.001), and the disutility weight for CC (r=0.40, p<0.001). See Figure 8 (PRCC and significance levels for all parameters provided in supplement).

Discussion

We investigated the impact of a police education program (PEP), through its observed reduction in the risk of incarceration among PWID, on the incidence and burden of HCV among PWID in Tijuana. We estimate that the 2-year reductions in incarceration observed during Proyecto Escudo could avert 22 (UI: 3-45) new infections, 120 (UI: 19-260) cases of cirrhosis, and 4 (UI: 1-9) deaths over 50 years among PWID in Tijuana, Mexico. To our knowledge, this is the first modeling analysis evaluating a structural intervention aimed at reducing structural risk from police.

Implications

Incarceration is strongly associated with behaviors that could increase the risk of HCV transmission among PWID in Tijuana, underscoring the importance of public health-oriented approaches to policing and drug enforcement. Our previous modeling analysis among PWID in Tijuana suggested that a fully implemented Narcomenudeo drug law reform (decriminalization and opiate agonist therapy [OAT] diversion) could avert 11% (95%UI: 3-19%) of incident HCV infections across 10 years. However, previous studies on the impact of the Narcomenuedo reform in Tijuana found that gaps in translating formal laws to policing practice may have thwarted expected impacts (7). In this regard, PEP initiatives that bundle occupational safety information with knowledge about drug law and harm reduction have shown promising results in modifying officers' occupational risks and attitudes towards PWID health (6). In this context, our study is important as it shows how a PEP program's benefits can spillover to reducing HCV among PWID.

Mexico was one of the first countries in Latin America to launch an HCV elimination program, with the goal of reducing HCV incidence by 80% and HCV-related mortality by 65% by 2030 compared to the 2015 benchmark (45, 46). Our study indicates that structural interventions such as police education programs should be part of a comprehensive strategy of targeting both population- and individual-level reductions in transmission risk, that can be paired with scale-up of HCV treatment and harm reduction programs (e.g., OAT and needle/syringe exchange programs [NSP]) to achieve HCV elimination goals. While the present administration in Mexico has embarked in a national HCV elimination program prioritizing HCV treatment (i.e. direct acting antivirals [DAA]) to vulnerable groups including incarcerated individuals, sex workers, and PWID (45, 46), at the time this manuscript was being written, it's still unclear how treatments have been administered geographically and across different population groups. Moreover, for PWID in Tijuana access to harm reduction such as OAT is prohibitively expensive and not widely available (95) and NSP provision limited (108). Given these limitations, our research is important as it provides new evidence supporting the role of interventions that address structural drivers of the HCV epidemic among PWID that can complement medication– and harm reduction–based approaches. Further, extending the implementation of PEP such as Escudo could enhance the ability for Mexico to achieve substantial reductions in the HCV epidemic among PWID, which can contribute towards the WHO elimination goals.

Strengths and limitations

A particular strength of our study is the use of real-world evidence from an implemented education program in Mexico. Also, we used longitudinal cohort data among PWID in Tijuana to inform estimates of the impact of the police education program on policing exposures and risk among PWID, which we use to determine resulting impact on HCV transmission. Nevertheless, our study is not exempt from limitations. First, even though our estimates of the reductions in incarceration were derived from a longitudinal study, we could not explicitly establish a causal relationship between the PEP intervention and these exposures. However, data among police officers who participated in El Escudo indicate that less than half of participants surveyed after the implementation of Escudo reported arresting someone for heroin possession (43%) and that officers who had favorable views on laws that treat addiction as a public health issue had lower odds of arresting PWID (adjusted Odds Ratio=0.78; 95% CI: 0.59-1.03) (6). Thus, while it is plausible from this data triangulation that the intervention led to reductions in incarceration among PWID, we cannot be certain that there were not other contributing factors. Second, even if the intervention did result in reduced incarceration among PWID, the duration of the intervention effect is unclear. As such, we simulate a 2-year sustained impact (because this was the amount of time we could triangulate data with the police self-report) but it is possible the impact could be maintained longer and therefore our estimates are conservative. We additionally simulated the impact of a 10-year program which would likely require re-training, which may have different impact than those observed with the first training program. It is possible that the effectiveness of these re-trainings could remain similar, could decrease, or even increase. This could depend on many factors such as how the training is reinforced and assimilated by increasing

numbers of police officers, how individual-level barriers (e.g. educational background (7)) could limit the impact over time, and continued institutional leadership support. Third, there is uncertainty in model parameters which we observed to influence the uncertainty in results, such as estimates for duration of injection. This parameter is difficult to estimate (85), as the survey question of number of years injecting obtained from the survey does not equal number of years until cessation. This estimate is both right and left censored, i.e., people have not given up injecting yet and the survey likely never captured those who inject for a very brief time and then stop injecting, so the direction of bias is unclear. Nonetheless, we used a wide uncertainty interval in this estimate to represent the substantial uncertainty in the data. Fourth, we do not incorporate the impact of the recent COVID-19 pandemic on future epidemic trajectory. It is plausible that the pandemic could have affected HCV transmission through a number of routes – a disruption to access to harm reduction (96, 97) or general health services (98), as has been reported for other settings, could have increased HCV transmission. Conversely, since injection networks include individuals from both sides of the US-Mexico border, it is possible that a reduction in injection network size due to border closures or stay at home orders could have reduced HCV transmission risk. Given hospital reconversions in Mexico (99) to address the COVID-19 pandemic, it is highly likely that COVID-19 diverted human and material resources from competing health priorities, particularly for HCV. Furthermore, the impact of COVID-19 on policing practices towards PWID remains unknown. Further research on the impact of COVID-19 on the risk environment and health among PWID in Mexico and elsewhere is warranted.

Conclusion

Among PWID in Tijuana, Mexico, incarceration remains an important contributor to HCV transmission and disease burden. Implementation of Escudo, a police education program, can complement treatment and harm reduction scale up, to reduce the burden of HCV among PWID in Tijuana. Also, this approach can underpin the implementation of a public health-oriented drug law reform, through reducing knowledge gaps in occupational health and awareness of the health implications of harsh policing among PWID. Cost-effectiveness evaluations and duration of the impact of Escudo, incorporating potential benefits on both HIV and HCV transmission among PWID, are warranted.

Acknowledgements

Chapter 4, entitled Estimating the impact of a police education program on hepatitis C virus (HCV) transmission and disease burden among PWID in Tijuana, Mexico: A dynamic modeling analysis, in full, is currently being prepared for submission for publication of the material. Co-authors include Abramovitz Daniela, Beletsky Leo, Borquez Annick, Kiene Susan M, Marquez, Lara K, Strathdee Steffanie A, Zúñiga Maria Luisa, Cepeda Javier, Martin Natasha K,. The dissertation author, Rivera Saldana Carlos D, was the primary researcher and author of this material.

Tables and Figures

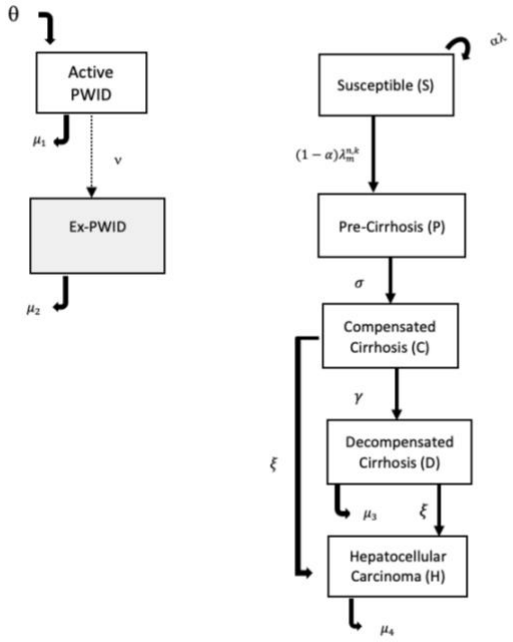
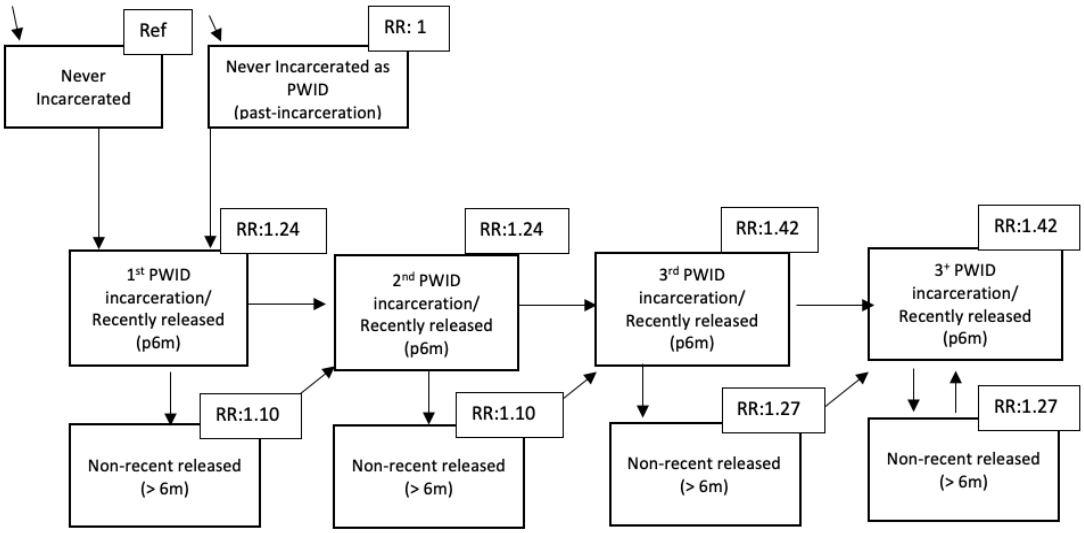


Figure 4.1. Hepatitis C Virus model schematic



*Squares denote mean elevated relative risks of HCV transmission

Figure 4.2. Incarceration submodel schematic*

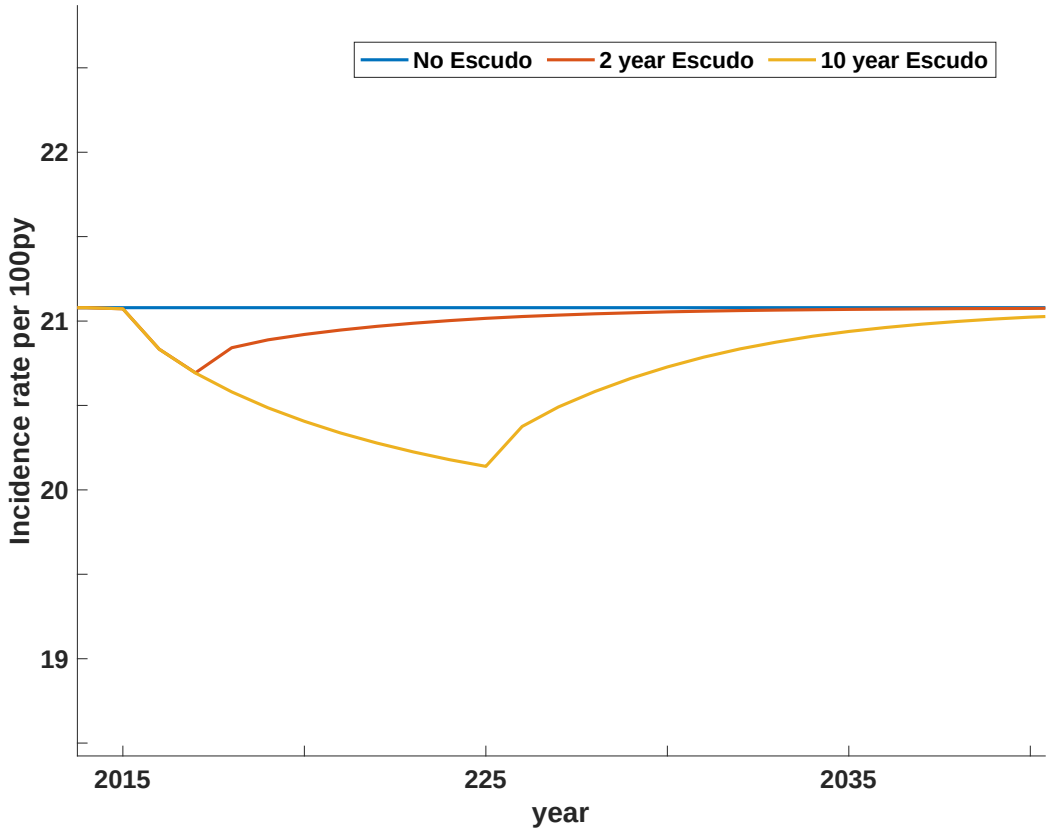


Figure 4.3. Fifty-year trajectory for mean HCV incidence rate among PWID in Tijuana, Mexico for different Escudo implementation scenarios

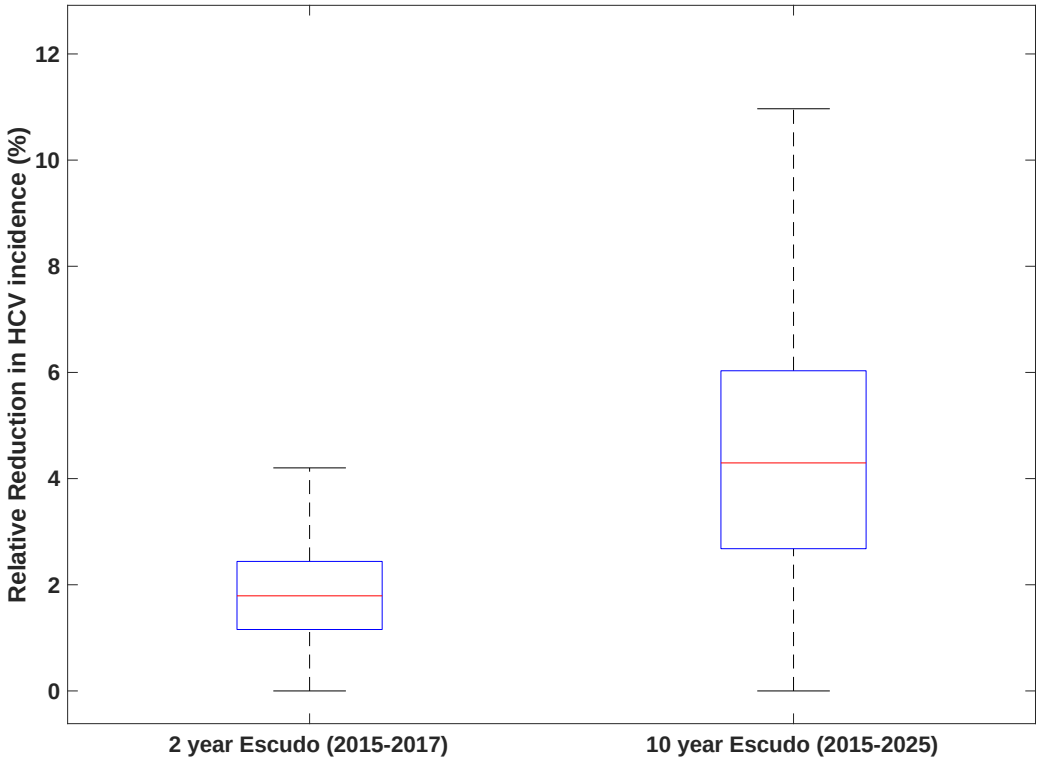


Figure 4.4. Relative reduction in HCV incidence rate among PWID in Tijuana, Mexico for the 2- and 10-year Escudo implementation periods

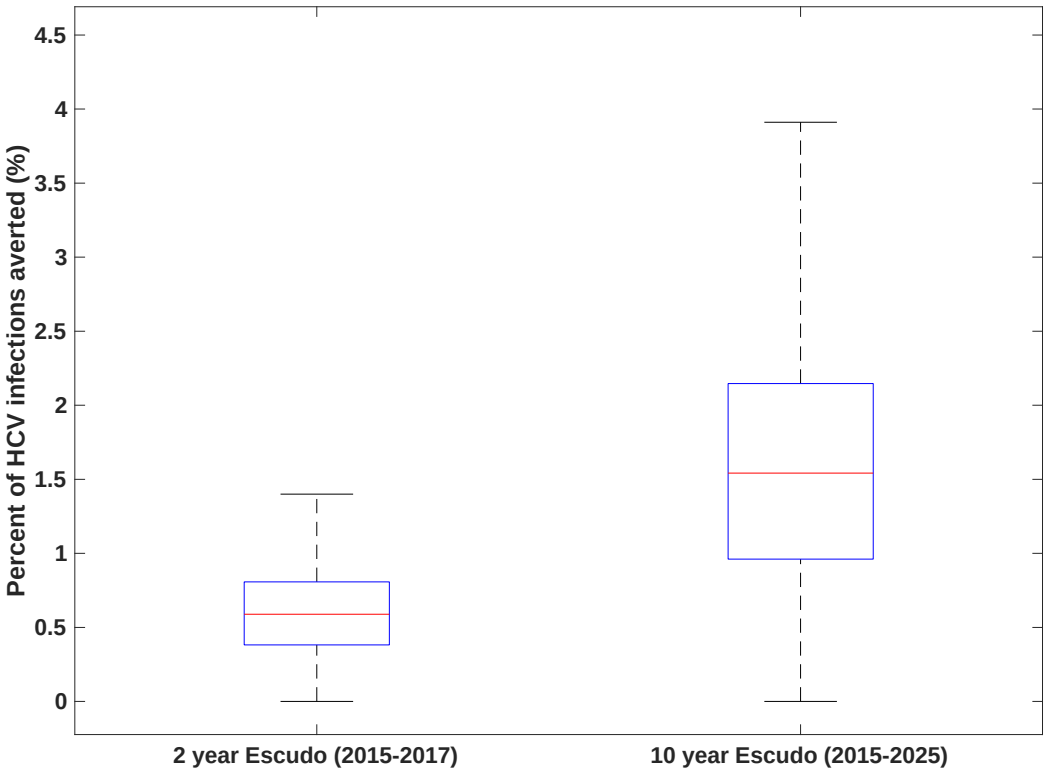


Figure 4.5. Relative reduction in new HCV infections averted among PWID in Tijuana, Mexico for the 2- and 10-year Escudo implementation periods

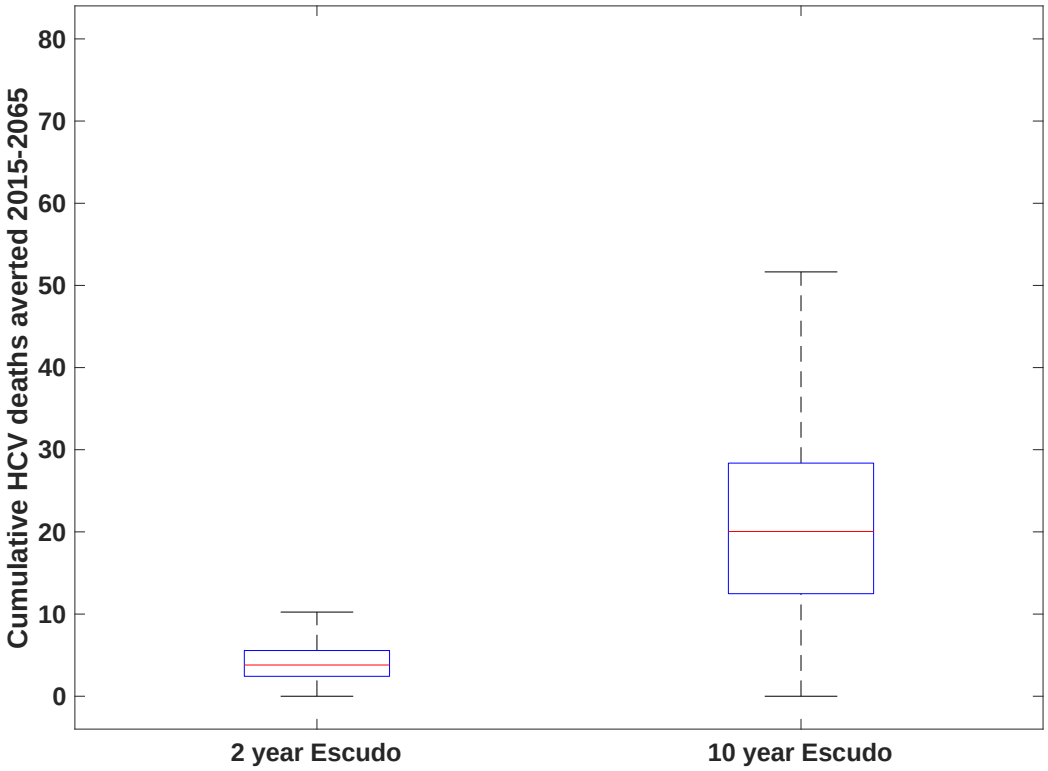


Figure 4.6**.** Fifty-year impact in cumulative HCV deaths averted among current and former PWID for each Escudo implementation period

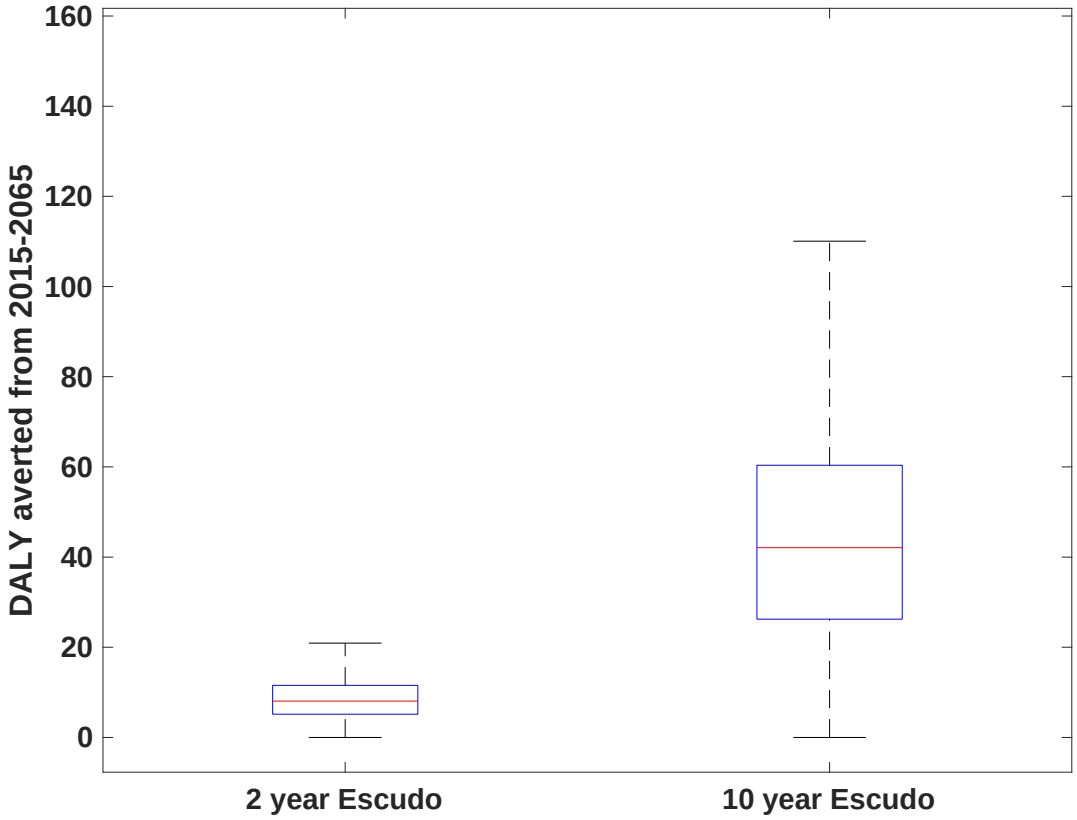


Figure 4.7. Fifty-year impact in HCV disease burden measured in DALYs among current and former PWID for each Escudo implementation period

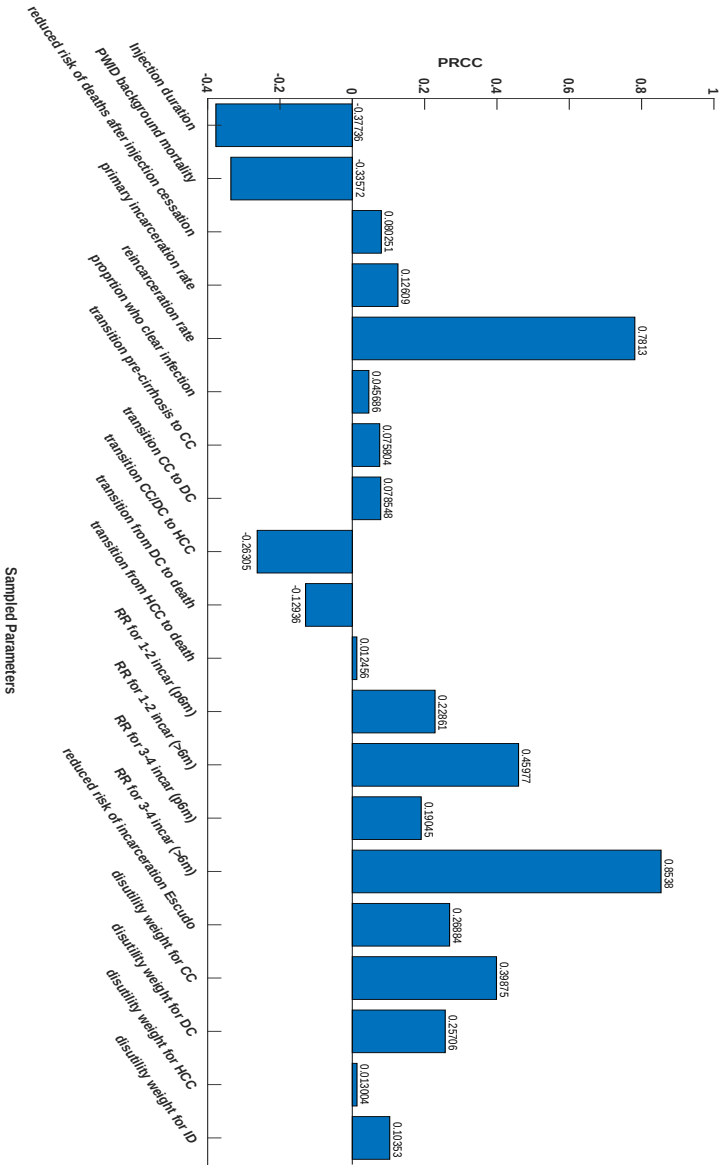


Figure 4. 8. Sensitivity of the DALY to model parameters

CC: compensated cirrhosis; DC: decompensated cirrhosis; HCC: hepatocellular carcinoma; RR: relative risk

Table 4. 1. Parameters used in full model and their sampling distributions				
Parameter (unit) (1) (2)	**Symbol**	**Sampled parameter's mean and 95% confidence interval**	**Sampling distribution**	**Source and comments**
Rate of new PWID initiations (per year)	θ	Fit to 10,000 PWID		
Proportion of individuals with a history of incarceration before entering the model	*propHist*	0.8		(31)
Average duration of injecting until permanent cessation (years)	I	17.45 (11.4-23.7)	Uniform (min=11, max=24)	(31)
Rate at which PWID stop injecting (per year)	ν	0.0573 (0.0881-0.0423)	Calculated as 1/Average duration of injecting until permanent cessation	
Mortality rate among PWID (per year)	$\mu 1$	0.0394 (0.0270-0.0530)	Poisson (0.040)	West, Abramovitz (35)
Relative risk reduction of mortality among PWID who cease injecting	M	0.2492 (0.1803-0.3550)	Lognormal (aHR 0.25, 95% CI=0.33-0.79)	Based on reduced risk of mortality among PWID who had cessated in West, Abramovitz (35)

Table 4.1. Parameters used in the full model and their sampling distributions, Continued				
Parameter (unit) (1) (2)	**Symbol**	**Sampled parameter's mean and 95% confidence interval**	**Sampling distribution**	**Source and comments**
Mortality rate for former PWID (per year)	$\mu 2$			Calculated as $\mu 2=\mu 1*(1-M)=0.03$
Rate at which never incarcerated PWID become primarily incarcerated (per year)	τ_1	0.0261 (0.0017-0.0506)	Uniform (min=0.0007, max=0.052)	Borquez, Beletsky (31)
Reincarceration rate (per year)	ω	0.2291 (0.0538-0.4080)	Uniform (min=0.047, max=0.42)	Borquez, Beletsky (31)
Rate PWID transition from recently released (p6m) to non-recent released (>6m)	δ	2		Defined by the duration of time in PWID spend in the recent incarceration compartment (6 months) 12 m/6m=2.
HCV Seroprevalence	o			90% (36).
Proportion of PWID who clear infection	α	0.2609 (0.2272-0.2934)	Beta (alpha=176, Beta=499)	Micallef, Kaldor (86)
Chronic prevalence	P	0.6652 (0.6359-0.6956)		0.67 from $P=o*(1-\alpha)$

Table 4.1. Parameters used in the full model and their sampling distributions, Continued

Parameter (unit) (1) (2)	**Symbol**	**Sampled parameter's mean and 95% confidence interval**	**Sampling distribution**	**Source and comments**
Disease transition rate from pre-cirrhosis to compensated cirrhosis (CC) (per year)	σ	0.0270 (0.0254-0.0287)	Normal (mean=0.027, SD=0.0008)	Calculated from METVIR scores (F0 to F4) reported in Thein, Yi (12).
Transition probability from CC to DC (per year)	γ	0.0385 (0.0213-0.0598)	Beta (alpha=14.6168,beta=360.1732)	Beta distribution parameters from Martin, Vickerman (103) based on Fattovich, Giustina (87)
Disease transition probability from CC/DC to HCC (per year)	ξ	0.0142 (0.0015-0.0405)	Beta (alpha=1.9326, beta=136.1074)	Beta distribution parameters from Martin, Vickerman (103) based on Fattovich, Giustina (87)
Disease transition probability per year from DC to death[2]	μ_3	0.1328 (0.0992-0.0.1715)	Beta (alpha=51, beta=333)	Fattovich, Giustina (87)

Table 4.1. Parameters used in the full model and their sampling distributions, Continued				
Parameter (unit) (1) (2)	**Symbol**	**Sampled parameter's mean and 95% confidence interval**	**Sampling distribution**	**Source and comments**
Disease transition probability per year from HCC to death (per year)	μ_4	0.4292 (0.3734-0.4868)	Beta (alpha=117.1033, beta=155.23)	Beta distribution parameters from Martin, Vickerman (103) based on Fattovich, Giustina (87)
Factors altering force of infection by incarceration state (relative risks):		Relative risks for incarceration states were estimated using longitudinal data from El Cuete study (see supplement)		
1-2 incarceration events + released within p6m	Γ	1.2433 (1.0483-1.4785)	Lognormal (mean=0.2151, SD=0.0858)[1]	Calculated from RR 1.24 (95% CI 1.05-1.47)
1-2 incarceration events + released >6m ago	Θ	1.1005 (0.9489-1.2948)	Lognormal (mean=0.0953, SD=0.0741) [1]	Calculated from RR 1.10 (95% CI 0.95-1.27)
>3 incarceration events + released within p6m	K	1.4185 (1.1393-1.7471)	Lognormal (mean=0.3507, SD=0.1056) [1]	Calculated from RR 1.42 (95% CI 1.15-1.74)
>3 incarceration events + released >6m ago	H	1.2592 (0.9331-1.7191)	Lognormal (mean=0.2390, SD=0.1569) [1]	Calculated from RR 1.27 (95% CI 0.93-1.72)

Table 4.1. Parameters used in the full model and their sampling distributions, Continued				
Parameter (unit) (1) (2)	**Symbol**	**Sampled parameter's mean and 95% confidence interval**	**Sampling distribution**	**Source and comments**
Incarceration risk reduction from Escudo	E	3.1281 (2.5471-3.8196)	Lognormal (mean=1.1378, SD=0.1054)	Calculated from RR 3.12 (95% CI 2.54-3.84)
Disutility weights for HCV disease stages				
Disutility weight for HCV-related death		0		
Disutility weight for compensated cirrhosis		0.0518 (0.0334-0.0778)	Lognormal (mean=-2.9759, SD=0.2139) [1]	(109)
Disutility weight for decompensated cirrhosis		0.1822 (0.1258-0.2610)	Lognormal (mean=-1.7260, SD=0.1809) [1]	(109)
Disutility weight for hepatocellular carcinoma		0.5799 (0.4229-0.7877)	Lognormal (mean=-0.5639, SD=0.1595) [1]	(109)
Disutility weight for active injected drug use		0.7051 (0.5414-0.8908)	Lognormal (mean=-0.3610, SD=0.1282) [1]	(109)

1. Lognormal distribution transformed to normal distribution for sampling, then back to log scale
2. Disease transition probabilities converted to instantaneous rates for the model.

Chapter 5. Discussion

In this last chapter, we first summarize findings from each of the three analytical chapters (2, 3, and 4). We then talk about how results in each analytical chapter advance the literature and their respective implications for drug policy. Later, we offer a summary of the most relevant limitations of the analyses performed. Then, we suggest some ideas about the direction future research could take. Finally, we close the chapter with some concluding remarks.

Summary of key findings

In Chapter 2, we identified a group of PWID in Tijuana, Mexico, with more cumulative incarceration experiences who had increased odds of receptive syringe sharing compared to individuals who had never been incarcerated. Every additional incarceration episode increased the odds of syringe sharing by 17% (aOR 1.17, 95% CI 1.05-1.29). Furthermore, the post-release period was associated with increased odds of receptive syringe sharing, which persisted up to 1.5 years post-incarceration but then waned. These findings suggest that the effects of incarceration on injecting risk are cumulative and persist in the post-release period.

Examining the contribution of incarceration to the HCV epidemic among PWID in Tijuana, model estimates from Chapter 3 suggest that incarceration is associated with 5% of new HCV infections among PWID in Tijuana between 2022-2032. Moreover, projections showed that full implementation of the public health-oriented drug law reforms

in Mexico (including decriminalization and diversion to OAT) could reduce HCV incidence by 11% between 2022-2032, and also reduce the number of DAA required to achieve Mexico's HCV elimination goals.

In Chapter 4, investigating the impact of a police education program on the incidence and burden of HCV among PWID in Tijuana, projections over a 50-year follow-up period suggested that a 10-year implementation of the program in Tijuana could result in a 4.7% (UI: 3.7-5.9%) reduction in the HCV incidence rate. This amounts to approximately 122 (UI: 20-255) new infections averted compared to baseline. Moreover, 45 (UI: 7-100) DALYs could be averted which is equivalent to a 0.3% (UI: 0.05-0.6%) reduction in the burden of HCV disease compared to baseline.

Contribution to research and policy implications

While the link between incarceration and syringe sharing had been previously established (25, 27, 28), this dissertation adds to the literature identifying a risk profile of PWID in Tijuana experiencing repeated incarceration, who are more likely to engage in injecting risks (Chapter 2). This new understanding underlines the need to reduce encounters with the criminal legal system. If encounters occur, a public health approach should incorporate the implementation of diversion programs. In Tijuana, this includes syringe service programs and OAT (71).

Previous modeling had investigated the contribution of incarceration– and the impact of a public health oriented drug law reform– on the HIV epidemic among PWID in Tijuana. However, a similar task had not been undertaken to address the HCV epidemic among PWID in Tijuana. Projections in Chapter 3 shed new light on the potential public

health benefits of comprehensively implementing drug law reform. Our work is important as it shows how significant reduction in HCV incidence can be achieved over a 10 year period when pairing decriminalization together with harm reduction. These result is of particular relevance for settings like Tijuana with increasing prevalence of drug use and health harms among PWID compared to the rest of the country (33, 110), while health and harm reduction services remain inaccessible for PWID (39, 95).

Chapter 4, to our knowledge, presents the first modeling analysis evaluating a structural intervention aimed at reducing structural risk from police. In this regard, police education programs that bundle occupational safety information with knowledge about drug law and harm reduction have shown promising results in modifying officers' occupational risks and attitudes towards PWID health (6). Findings in Chapter 4 are important as they show how a PEP program's benefits can spillover to reducing HCV among PWID. Further, extending the implementation of PEP such as Escudo could enhance the ability for Mexico to achieve substantial reductions in the HCV epidemic among PWID.

While each of the three analytical chapters have an independent contribution to research and policy, they are also complementary to one another. In Chapter 1 we introduced the risk environment framework (48) to conceptualize our work from a perspective where individuals and environments define the creation and prevention of drug harms (111). This framework considers environmental factors at three levels, i.e., individual interactions (micro), institutional responses (meso), and laws and polices (macro). Understanding the risk environment helps to recognize the limits and opportunities of polices and interventions (47). In this sense, results from this dissertation

are important as they emphasize the interconnections among the different risk environment levels, showing how, e.g., drug policy and a policing intervention situated at different levels can shape injecting risks and health outcomes for PWID in Tijuana. For instance, results in Chapter 2 show how the risk of syringe sharing (micro-level) increases for individuals facing persistent criminalization (meso-level) over time. In Chapter 3, projections from modelling the impact of drug policy reform scenarios (macro-level) show how the macro environment interconnects with the meso-level (incarceration/reincarceration), potentially modifying injecting risks (micro-level) and adverse health outcomes among PWID. Results in Chapter 4 show how the implementation of a police education program (meso-level), initially aimed at facilitating implementation of drug policy reform (macro-level), can also produce positive impacts on the health of PWID. This impact occurs through counteracting the deleterious effects of punitive policing, also at the meso-level, through reductions in incarceration and eventually modifying risky injecting decisions (micro-level). In sum, our work shows how risk prevention can be achieved through policy and intervention complementarities working at different levels. Alternatively, risk creation can persist in the absence of properly implemented polices and interventions.

Limitations

Data for the statistical analyses came from a prospective, observational study among PWID (El Cuete). A limitation common to this type of study arises from the self-reported nature of data collected from PWID which may be subject to imprecision due to recall and social desirability (77). Also, generalizing our results to other contexts should

be taken with caution. For example, border cities like Tijuana have drug use patterns that differ from other cities in Mexico.

Importantly, even when estimates for the association between incarceration history and recent syringe sharing were derived from a longitudinal analysis, we could not unambiguously establish a causal relationship. This is true for our estimates in Chapter 2 and for those used to incorporate elevated risks of HCV transmission derived from incarceration to models in Chapters 3 and 4. Similarly, in Chapter 4, for our estimates of the reduction in incarceration derived from implementing the PEP, we could not explicitly establish a causal relationship between the PEP intervention and recent incarceration.

Also, we do not incorporate the impact of the recent COVID-19 pandemic on our statistical associations. It could be the case that incarceration and injecting risk patterns changed during or after the pandemic. This also applies to our modeling analyses, as we do not incorporate covid pandemic on our estimates of future epidemic trajectory. The pandemic could have affected HCV transmission through a number of routes including the previously discussed changes in incarceration/injecting risk patterns, or changes in access to harm reduction (96, 97) and general health services (98), as reported for other settings, which could have increased HCV transmission.

Another limitation for Chapters 3 and 4 may stem from neglecting other potential impacts on health outcomes associated with incarceration including HIV, tuberculosis, and overdose, underestimating the true impact of incarceration on the health of PWID. This is also true for our main exposure, incarceration. Previous work has found other measures of deleterious interactions between law enforcement and PWID (e.g. confiscation of drug paraphernalia, beating, arrests, incarceration and reincarceration)

(21, 22, 67). Using only one single exposure could be underestimating the impact of punitive policing on PWID's health risks.

Likewise, another limitation particular to Chapter 4, stems from assessing only one potential impact from implementing the PEP intervention. Escudo can impact other aspects of the interaction between PWID and law enforcement that we fail to measure and can have implications on health outcomes for PWID. Examples include changes in the intensity of police encounters or harassment which could have additional health benefits. Further, the impact of escudo could be larger if PWID increase their exposure to OAT and other harm reduction/health services referrals, changing model estimates which could be currently underestimating Escudo's impact.

Future Directions

Statistical estimates for the relationships between incarceration and syringe sharing, or Escudo and recent incarceration, do not explicitly establish a causal relationship. Causal inference methods can be used when randomized trials, the gold standard for establishing causality, are not available due to ethical considerations or limited time and resources (112). Randomization makes exposure groups comparable across all characteristics in such a way that differences in the outcome of interest can be attributed solely to the exposure of interest. If the appropriate randomized trial does not exist, we may need to use observational population data to make causal inferences (113). Specific causal inference methods exist to analyze repeated measures derived from longitudinal data (112). Future work could carefully assess the suitability of applying the causal framework to the statistical questions raised in this dissertation. Particularly

interesting would be applying this methodology to a treatment, such as a police education program (Escudo), on an outcome with health implications for PWID, such as incarceration.

Also, our work focuses exclusively on one exposure, i.e., incarceration, as a measure of criminalization and punitive policing. This single exposure could be underestimating the impact of punitive policing on PWID's health risks. Extensive literature has reported on different other measures of deleterious interactions between law enforcement and PWID, and their implications on health and risk behaviors (21, 22, 67). Nonetheless, work examining how a number of these exposures could jointly impact health risks among a population of PWID is lacking. Future work could look into incorporating some relevant measures operationalizing harsh policing (e.g. confiscation of drug paraphernalia, harassment, arrests, incarceration and reincarceration, etc.) into one composite measure and assess how it impacts health risks among PWID. Estimates from such measures can be further used to inform mathematical models. For example, in Borquez, Beletsky (31) syringe confiscation is assessed in addition to incarceration, but other measures were not considered, nor an aggregate measure generated. Incorporating additional measures in the same analysis is important if we want to comprehensively assess the policing environment on health risks of PWID, as well as obtaining more robust estimates of the impact of drug law reform and police education interventions.

Similarly, in Chapter 4 we assess the impact of Escudo based on its effect on recent incarceration. However, there are other measures that could be used separately or aggregately to measure Escudo's impact. Future work could incorporate other

measures for potential impacts of police education programs on a wider range of outcomes. For example, changes in other forms of punitive policing including beating, arrests, and syringe confiscations, or changes in harm reduction and treatment uptake.

Future research should engage in exploring the economic impact of implementing a police education program like Escudo on the HCV epidemic among PWID in Tijuana. Estimates in Chapter 4 have already paved the way for economic analysis of Escudo by representing HCV burden with an objective, summary measure (DALY) that can be translated to costs and used to assess the cost-effectiveness of implementing Escudo. Additionally, incorporating potential benefits on both HIV and HCV transmission among PWID, are warranted. Additional data to carefully assess the cost structure of the Escudo program and, for example, estimating the duration of its impact, are key for strengthening this analysis.

Finally, extensions of these analyses could examine the impact of incarceration, drug law reform or police education on other health outcomes common among PWID with a history of incarceration such as HIV, tuberculosis, and overdose (2, 93). These outcomes could be examined jointly through the use of DALYs or similar objective, composite measures, that can make the burden of these health outcomes comparable and, thus, amenable for aggregation.

Conclusion

In this dissertation we sought to broaden knowledge of the deleterious effects of policing and incarceration on the health of people who inject drugs (PWID), and how drug law reforms and police education can improve health outcomes among PWID. For

achieving our goals, we had the unique opportunity of using data from El Cuete study, a longitudinal study among PWID in Tijuana. This data provided insights on the repeated dynamics of drug use, injecting behaviors, encounters with law enforcement, and health outcomes among PWID. Data was collected over a decade, before, during, and after the police education program (Escudo), within an evolving landscape of the enforcement of drug policy in Mexico. We performed statistical analyses and obtained estimates to inform mathematical models using El Cuete data.

From Chapter 2 we learned that the effect of incarceration on syringe sharing is cumulative and persists post-release. In Chapter 3, through modeling techniques, we found that incarceration continues to drive HCV transmission among PWID in Tijuana, and full implementation of public health oriented drug law reform with decriminalization and diversion to OAT can play an important role in reducing HCV incidence. In Chapter 4, we found that implementation of Escudo, a police education program, can reduce the burden of HCV among PWID in Tijuana, and potentially buttress proper implementation of a public health oriented drug law reform.

Overall, these findings underpin the need of replacing police encounters as a structural driver of injecting risks and blood borne infections with evidence based drug policy and interventions that can effectively, positively change health outcomes for PWID. Undertaking this approach is imperative in settings like Tijuana, characterized by increasing drug use, persistent incarceration, and poor access to health and harm reduction services. Findings from this dissertation contribute to the promotion of a public health oriented policy approach and targeting of compassionate prevention interventions at the intersection of drug policy, law enforcement, and injection drug use.

Appendix A. Supplementary materials to Chapter 2

I. Additional detail on the multiple imputation by chained equations method used to address missing data

We observed both monotonic (loss to follow-up) and intermittent (missing one or more visits during ongoing data collection) missing data patterns (Figure A1 & Figure A2). After baseline, starting at the first follow-up (visit 2) the proportion of missing observations was 21% which gradually increased to 42% at visit 10. Monotonic missing data accounted for 3.5% of the total missing data at visit 2 and progressed to 4.9% in visit 10. We compared the characteristics of individuals who completed all follow-up visits in our study (until visit 10) with those who were last seen before visit 10 (Table A1). We initially performed analyses on those with complete data. To account for the potential selection bias derived from this approach, participants with missing observations were incorporated to the analysis using multiple imputation by chained equations (MICE), using the MICE package in R (65). We assumed data were missing at random (MAR) (66). We imputed each covariate measured at each visit after baseline specifying a *logistic regression* model for binary variables (time-varying covariates were only binary) and using the full set of covariates as predictors (except for sex work, assessed at baseline, which was incorporated later to the analysis). For each covariate, we excluded the variable itself as a predictor. While included as predictors for the time-varying covariates, baseline variables were not imputed due to having a negligible amount of missing observations

(only one variable had 2.1% of missing observations at baseline and another had 6%). The imputation model for each variable included sociodemographic characteristics assessed at baseline such as age, gender, time spent daily on the street, years of education, and receiving income from a formal source. Time-varying drug use characteristics included using heroin, using methamphetamine, injecting heroin, injecting methamphetamine, and using cocaine (including crack), getting syringes from a shooting gallery, getting syringes from a syringe exchange program, and age at first injection (at baseline). Additional variables included living whole life in Tijuana (at baseline), getting professional help for alcohol and drug use (assessed repeatedly), being stopped and arrested (assessed repeatedly). Additional variables were considered for the model (e.g. arrested for syringe possession), however discarded due to being added to the survey at a later date or having very small or null cell counts early in the follow-up and getting worse as visits progressed (see West, Abramovitz (35) for similar considerations while conducting longitudinal analyses on the same data set). After an initial imputation test run, heroin injection at baseline (used as a predictor) was removed due to the default mice program diagnostics indicating multicollinearity for this variable. After removing this variable, in subsequent runs, no other variable had this indication. We imputed 15 data sets that were used to conduct our analyses. The estimates obtained from each imputed dataset were pooled based on Rubin's criteria (114).

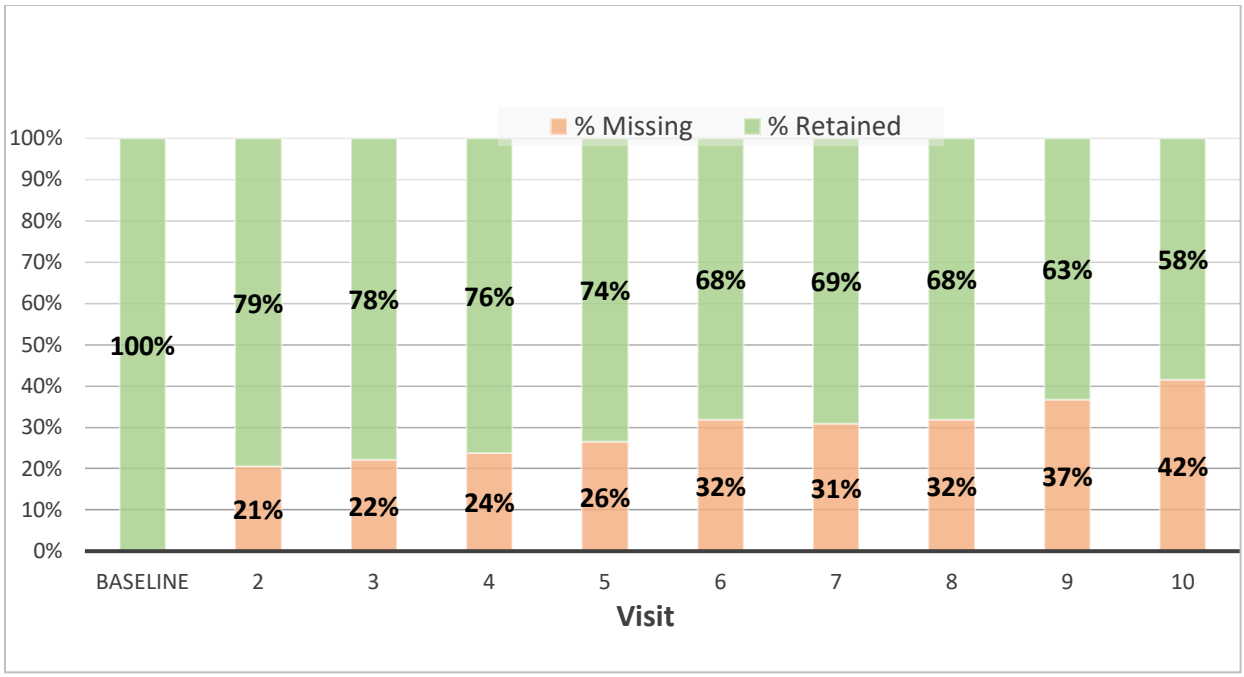


Figure A.1. Percent of missing observations at each visit from baseline to visit 10 in our sample of PWID (n=185) from El Cuete cohort

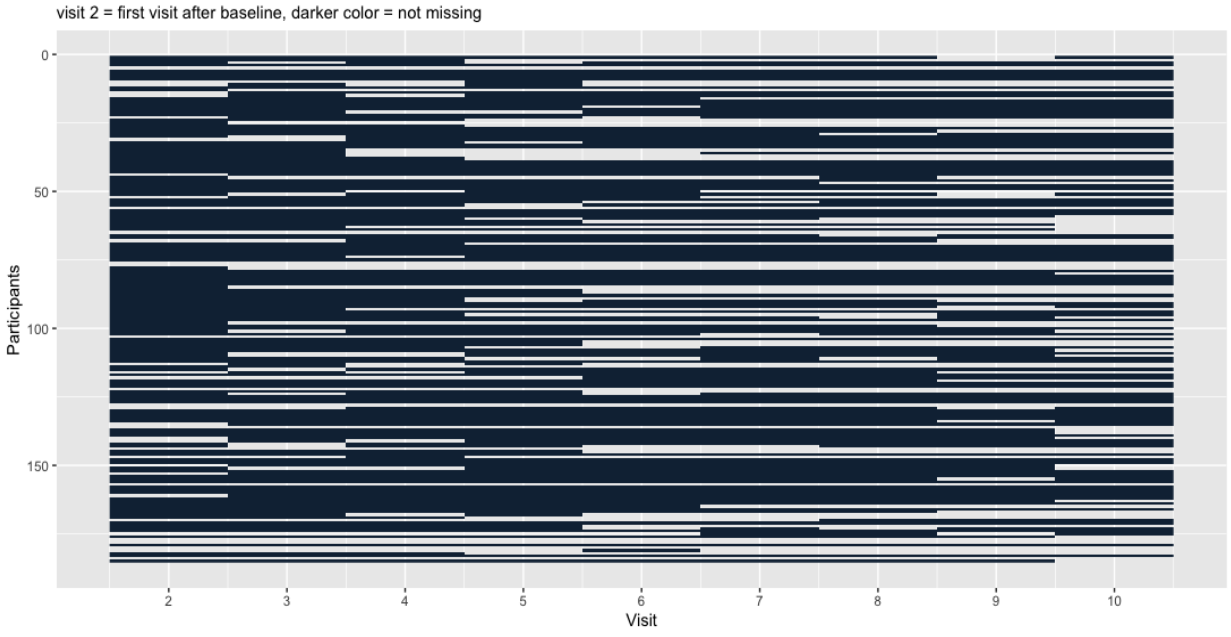


Figure A.2. Missing Data Pattern: missing observations by study visit

Table A.1. Selected baseline characteristics for individuals never incarcerated at study entry (included in the study) and those with a history of incarceration (excluded from study)

variables	*Incarcerated at study entry*		*p-value (1)*
	Never	*Ever*	
n	**185**	**547**	
Age (median [IQR])	35 [29, 42]	38 [31, 44]	0.005
Gender (%)			
Male	62 (33.5)	395 (72.2)	**<0.001**
Female	123 (66.5)	152 (27.8)	
Hours spent on Street (median [IQR])	10.0 [6, 13]	12.00 [10, 20]	**<0.001**
Years of Education (median [IQR])	9.0 [6, 11]	8.0 [6, 9]	**<0.001**
Income from Formal Source (%)			
No	161 (87.0)	474 (86.7)	0.997
Yes	24 (13.0)	73 (13.3)	
Years Injecting (median [IQR])	13 [5, 20]	16 [10, 23]	**0.001**
Injected Heroin (%)			
No	8 (4.4)	18 (3.3)	0.654
Yes	173 (95.6)	522 (96.7)	
Injected Methamphetamine (%)			
No	135 (73.0)	392 (71.7)	0.804
Yes	50 (27.0)	155 (28.3)	
Got syringes from shooting gallery (%)			
No	169 (91.4)	507 (92.7)	0.666
Yes	16 (8.6)	40 (7.3)	
Receptive Syringe Sharing (%)			
No	64 (34.6)	145 (26.5)	0.044
Yes	121 (65.4)	402 (73.5)	
Sex Work (%)			
No	124 (67.0)	469 (85.7)	**<0.001**
Yes	61 (33.0)	78 (14.3)	
Stopped and Arrested (%)			
No	114 (61.6)	57 (10.4)	**<0.001**
Yes	71 (38.4)	490 (89.6)	

(1) Chi-square test with continuity correction for categorical variables and Wilcoxon rank sum (Mann-Whitney U) test for continuous variables.

Table A.2. Selected characteristics of participants at last visit seen					
			Last Visit Seen		
	level	*Overall (1)*	*V10*	*<V10*	*p-test (2)*
n		**154**	**108**	**77**	
Age (median[IQR])		35 [29,42]	35 [29,42]	36 [28,43]	0.87
Gender (%)	*male*	62 (33.5)	36 (33.3)	26 (33.8)	>0.9
	female	123 (66.5)	72 (66.7)	51 (66.2)	
Hours spent on street (median [IQR])		10 [6,13]	10 [6,14]	10 [8,13]	0.382
Years of education (median [IQR])		9 [6,11]	8 [6,10.75]	9 [7,12]	0.06
Income from a formal source (%)	*No*	161 (87)	95 (88)	66 (85.7)	0.82
	Yes	24 (13)	13 (12)	11 (14.3)	
Age at first injection (median [IQR])		19[17,26]	19 [17, 26]	20 [17,25]	0.95
Living in Tijuana entire life (%)	*No*	118 (63.8)	67 (62.2)	51 (66.2)	0.66
	Yes	67 (36.2)	41 (38)	26 (33.6)	
Incarcerated (%)	*No*	124 (80.5)	87 (80.6)	37 (80.4)	>0.9
	Yes	30 (19.5)	21 (19.4)	9 (19.6)	
Receptive Syringe Sharing (%)	*No*	88 (57.9)	61 (57.5)	27 (58.7)	>0.9
	Yes	64 (42.1)	45 (42.5)	19 (41.3)	
Heroin Use (%)	*No*	27 (17.5)	22 (20.4)	5 (10.9)	0.23
	Yes	127 (82.5)	86 (79.6)	41 (89.1)	

Table A.2. Selected characteristics of participants at last visit seen, Continued					
			Last Visit Seen		
	level	*Overall (1)*	*V10*	*V10*	*p-test(2)*
Methamphetamine Use (%)	*No*	54 (35.1)	36 (33.3)	18 (39.1)	0.613
	Yes	100 (64.9)	72 (66.7)	28 (60.9)	
Cocaine Use (%)	*No*	145 (94.2)	103 (95.4)	42 (91.3)	0.453
	Yes	9 (5.8)	5 (4.6)	4 (8.7)	
Injected Heroin (%)	*No*	67 (43.5)	54 (50.0)	13 (28.3)	**0.021**
	Yes	87 (56.5)	54 (50.0)	33 (71.7)	
Injected Methamphetamine (%)	*No*	113 (73.4)	100 (92.6)	13 (28.3)	**<0.001**
	Yes	41 (26.6)	8 (7.4)	33 (71.7)	
Getting syringes from shooting gallery (%)	*No*	148 (96.7)	104 (97.2)	44 (95.7)	0.637
	Yes	5 (3.3)	3 (2.8)	2 (4.3)	
Getting syringes from exchange program (%)	*Never*	116 (75.8)	82 (76.6)	34 (73.9)	0.877
	Ever	37 (24.2)	25 (23.4)	12 (26.1)	
Getting professional help for drug/EtOH(%)	*No*	131 (85.1)	92 (85.2)	39 (84.8)	>0.99
	Yes	23 (14.9)	16 (14.8)	7 (15.2)	
Stopped and arrested (%)	*No*	126 (81.8)	95 (88.0)	31 (67.4)	**0.005**
	Yes	28 (18.2)	13 (12.0)	15 (32.6)	

(1) Total for overall (154) and for last visit seen (108 + 77=185) do not match. Overall reflects participants seen at visit 10, while those stratified at last visit seen also include participants screened at baseline (185).
(2) Chi-square test with continuity correction for categorical variables (except for cocaine use and getting syringes from shooting gallery, which display cell counts with less than 5 observations, in this case the Fisher's exact test was employed) and Wilcoxon rank sum (Mann-Whitney U) test for continuous variables.

II. Multiple imputation diagnostics

Following van Buuren (114), we assessed the MICE output by comparing the observed and imputed data. We first checked that all imputed values were plausible (i.e., no extraneous values), by tabulating each variable and also by visually checking xy-plots for observed and imputed data. The xy-plots show the range of values of the original variable (blue) and the values that the imputed variables acquired (red) after imputation. Thus, one can visually assess if the imputed values are plausible. Examples for selected variables (syringe sharing, recent incarceration, injecting methamphetamine, and getting syringes from a shooting gallery) are shown. For the xy-plot see, Figure A3. No extraneous values were identified. Also, while kernel density plots are mostly used for continuous variables, we used this plot to compare the distribution of observed (blue curve) with the distribution of imputed values (red curve) for each variable (see examples in Figure A4 for syringe sharing and Figure A4.2 for incarceration). Even though a kernel density plot shows a continuous curve, our binary variables can only take the values of zero or one (probability density can acquire values larger than one). The plot depicts the values imputed and gives a sense of their relative proportion for the values observed and the value imputed across all 15 imputations.

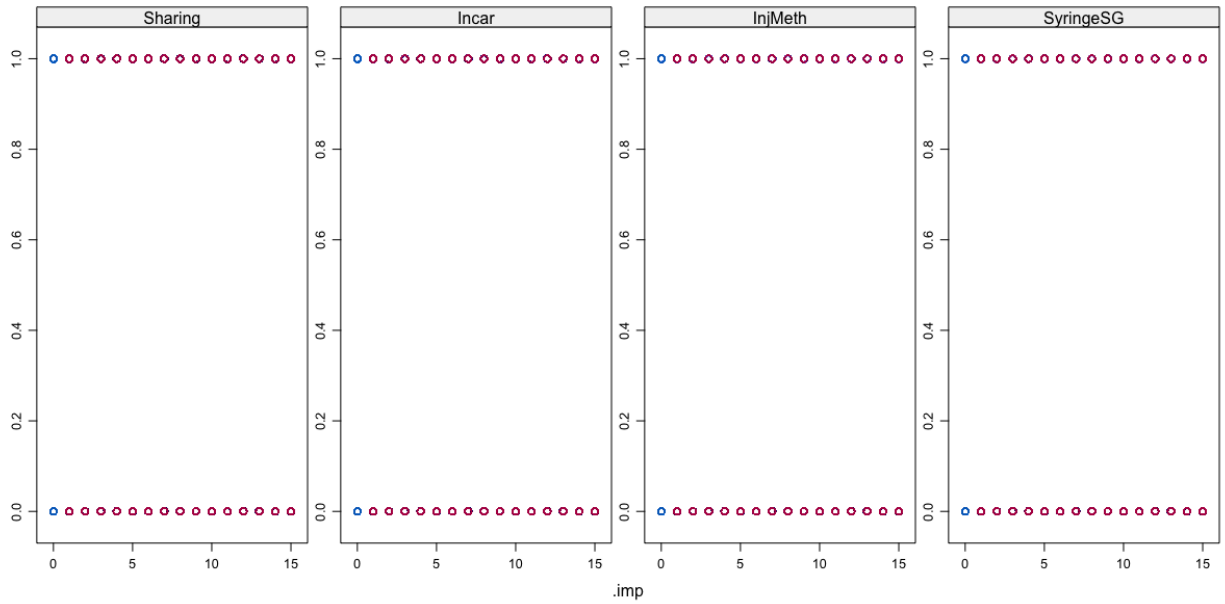


Figure A3. XY-Plot for observed (blue) and imputed (red) data

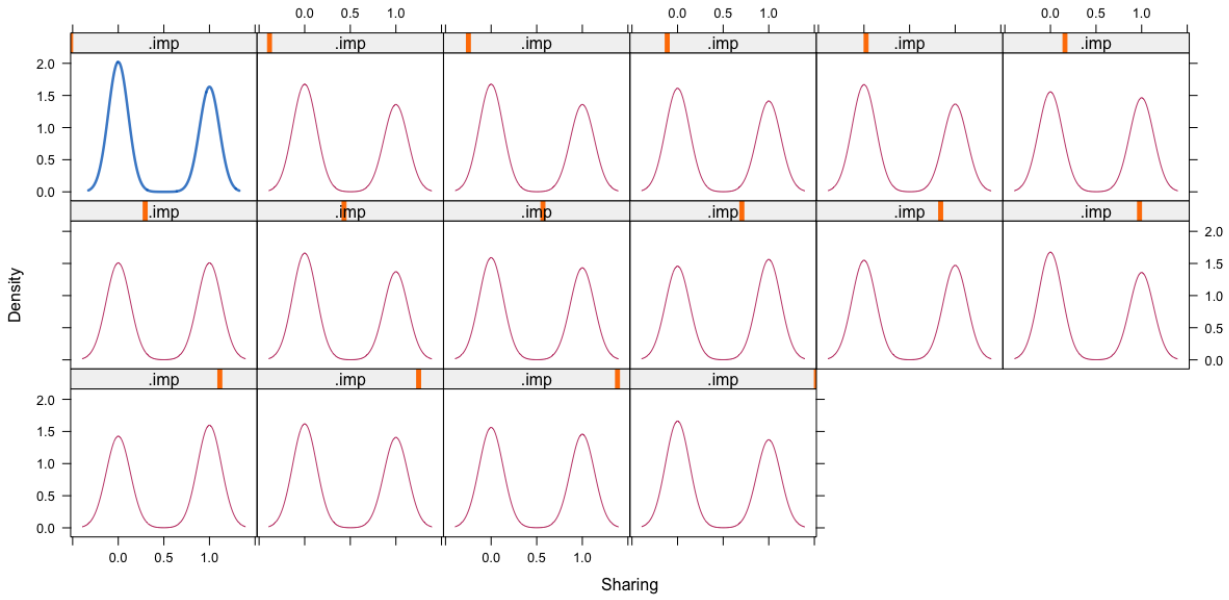


Figure S4. Kernel density plot for Syringe Sharing (observed=blue, imputed=red)

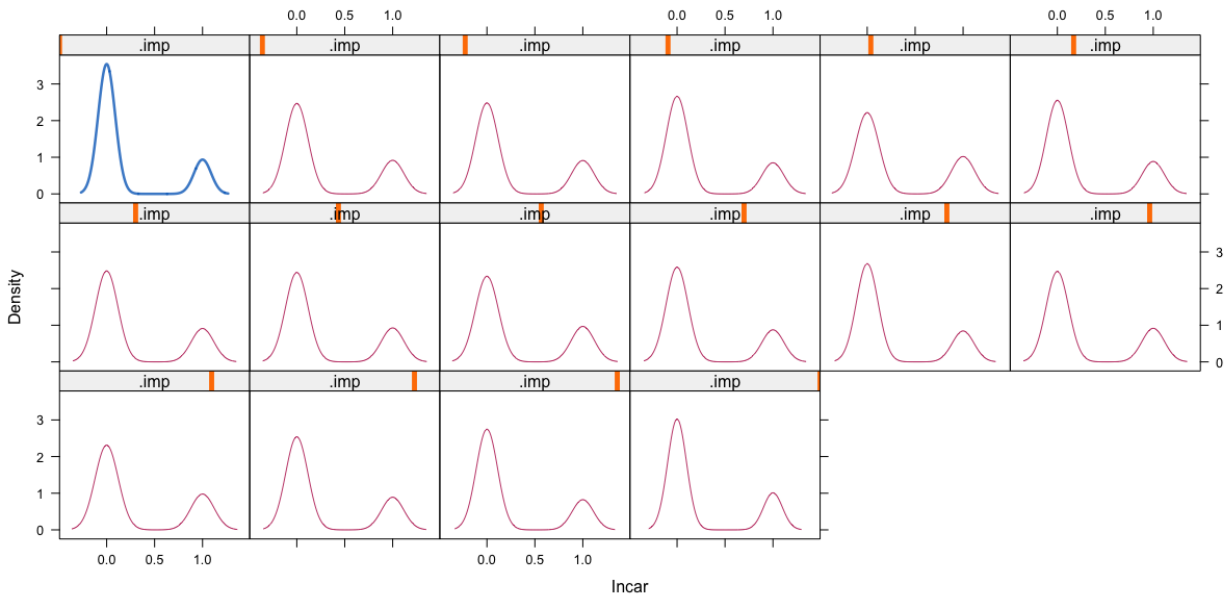


Figure A4.2. Kernel density plot for incarceration (observed=blue, imputed=red)

Convergence assessment

As suggested in van Buuren and Groothuis-Oudshoorn (65), we also plotted a mice class object to assess model convergence. The plot shows the mean and the standard deviation of an imputed variable plotted against each iteration. Lack of convergence is represented by straight lines, lines not crossing, or strong trends (e.g. exponential growth curves). For our variables, convergence was confirmed as shown in figures A5A and A5B.

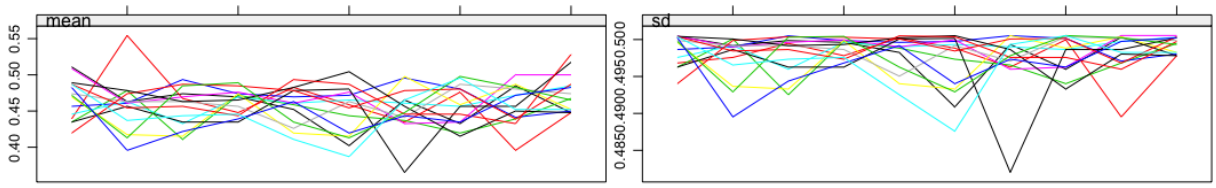


Figure A.5.a. Syringe Sharing mean and standard deviation plotted against iteration

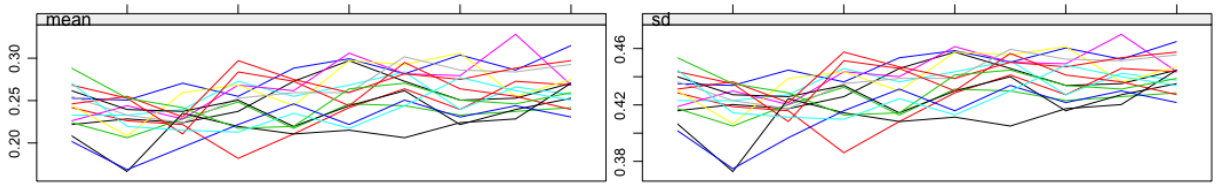


Figure A.5.b. Incarceration mean and standard deviation plotted against iteration

Post-release period variable

We defined the post-release period variable as the time elapsed (i.e., number of visits) after a participant had reported being incarcerated. This variable was grouped into five categories: never incarcerated, released within the past 6 months, released in the past 6 months to 1.5 years, released in the past 1.5 to 2.5 years, and released more than 2.5 years ago.

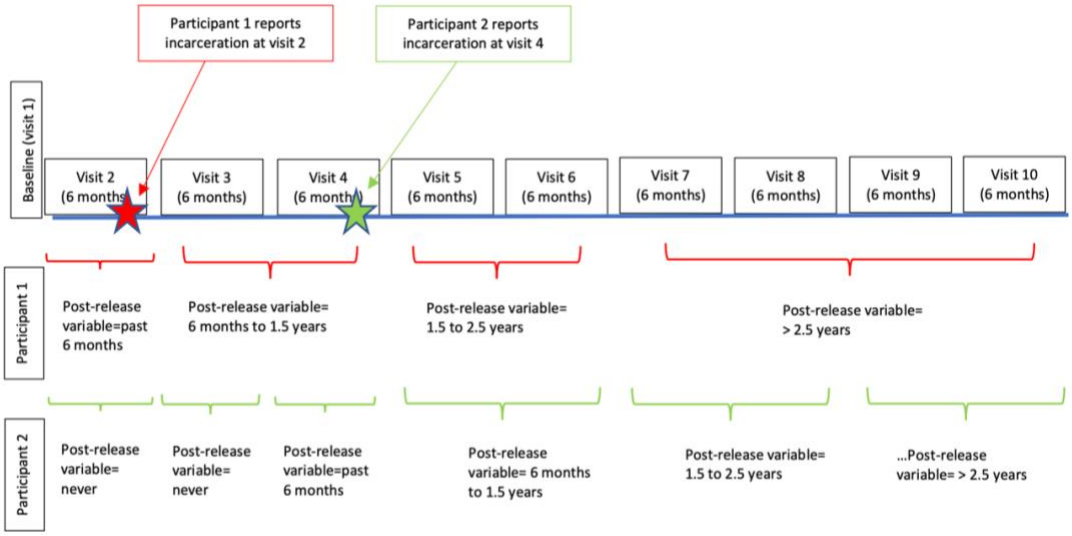


Figure A.6. Schematic explaining post-release period variable

III. Results from multiply imputed data sets (presented in main text) and complete case analysis.

Table A.3. Cumulative incarceration and other factors associated with syringe sharing.
Univariable GEE for multiply imputed data with chained equations and complete case analysis. (1)

Variable	Univariable MICE			Univariable Complete Case		
	OR	95% CI (2)		OR	95% CI (2)	
Cumulative incarceration (ref: no)						
One	1.23	0.95	1.61	1.33	0.98	1.80
2 to 3	**1.45**	**1.05**	**2.00**	**1.48**	**1.03**	**2.11**
>3	**1.98**	**1.11**	**3.52**	1.80	0.94	3.46
Age	0.99	0.97	1.00	**0.98**	**0.97**	**0.99**
Gender (ref: male)	0.95	0.74	1.2	0.96	0.75	1.23
Always living in Tijuana (ref: no)	1.29	1.00	1.65	**1.42**	**1.12**	**1.80**
Hours spent on Street	1.02	0.99	1.04	1.02	1.00	1.03
Heroin Injecting (ref: no)	1.17	0.92	1.50	1.19	0.94	1.51
Methamphetamine Injecting (ref: no)	**1.63**	**1.14**	**2.33**	**1.67**	**1.19**	**2.35**
Cocaine Use (ref: no)	**2.15**	**1.30**	**3.55**	**2.10**	**1.22**	**3.62**
Polysubstance use (ref: no)	**0.70**	**0.56**	**0.87**	**0.62**	**0.49**	**0.79**

Table A.3. Cumulative incarceration and other factors associated with syringe sharing.
Univariable GEE for multiply imputed data with chained equations and complete case analysis, Continued (1)

Variable	Univariable MICE			Univariable Complete Case		
	OR	95% CI (2)		OR	95% CI (2)	
Getting professional help for alcohol and drug use (ref: no)	0.82	0.60	1.12	0.87	0.63	1.20
Getting syringes from syringe exchange (ref: no)	1.28	0.96	1.69	1.17	0.89	1.52
Getting syringes from shooting gallery (ref: no)	**2.02**	**1.29**	**3.17**	**2.13**	**1.37**	**3.31**
Arrested	**1.51**	**1.38**	**1.65**	**1.70**	**1.31**	**2.21**
Sex Work	0.83	0.67	1.07	0.86	0.67	1.09

(1) Multiple imputation using chained equations generating 15 imputed data sets. Imputed sets and complete case analysis performed from longitudinal data including baseline and 9 follow-ups (10 visits).
(2) Covariates in bold if significant at 5%.

Table A.4. Cumulative incarceration and other factors associated with syringe sharing. Multivariable adjusted GEE for multiply imputed data and complete case analysis. (1)

Variable (2)	Multivariable MICE			Multivariable Complete Case		
	aOR	95% CI (3)		aOR	95% CI (3)	
Cumulative Incarceration (ref: none)						
One	1.28	0.97	1.68	1.28	0.93	1.76
2 to 3	**1.42**	**1.02**	**1.99**	1.29	0.88	1.88
>3	**2.10**	**1.15**	**3.85**	1.69	0.85	3.37
Age	0.98	0.97	1.00			
Always living in Tijuana (ref: no)				1.30	0.97	1.73
Hours spent on street				1.02	0.99	1.04
Heroin injecting (ref: no)	1.27	0.97	1.66			
Methamphetamine Injecting (ref: no)	**1.58**	**1.06**	**2.36**	**1.52**	**1.02**	**2.28**
Cocaine Use (ref: no)	**2.06**	**1.19**	**3.58**	**2.26**	**1.21**	**4.24**
Polysubstance use (ref: no)	**0.70**	**0.55**	**0.89**	**0.70**	**0.52**	**0.93**
Getting syringes from shooting gallery (ref: no)	**1.88**	**1.17**	**3.04**	**2.10**	**1.24**	**3.56**

(1) Multiple imputation using chained equations generating 15 imputed data sets. Imputed sets come from longitudinal data including baseline and 9 follow-ups.
(2) Covariates reported are the final set retained after backward elimination using a cut-off p-value of 0.20.
(3) Covariates in bold if significant at 5% in the multivariable regression.

Table A.5. Post-Release Exposure and other Factors Associated with Syringe Sharing. Multivariable adjusted GEE for multiply imputed data and complete case analysis. (1)

Variable (2)	Multivariable MICE aOR	95% CI (3)		Multivariable complete case aOR	95% CI (3)	
Post release categories (ref: none)						
Recent (p6m)	**1.53**	**1.14**	**2.05**	**1.40**	**1.01**	**1.94**
Previous (6m-1.5yrs)	**1.41**	**1.04**	**1.91**	1.43	0.95	2.18
Past (1.5yrs-2.5yrs)	1.15	0.74	1.78	1.29	0.89	1.89
Past (> 2.5)	1.21	0.67	2.19	1.28	0.56	2.93
Age	0.98	0.97	1.00	0.99	0.98	1.00
Always living in Tijuana (ref: no)				1.29	0.98	1.70
Heroin injecting (ref: no)	1.23	0.95	1.61			
Methamphetamine Injecting (ref: no)	**1.52**	**1.03**	**2.25**	1.43	0.98	2.10
Cocaine Use (ref: no)	**1.99**	**1.15**	**3.48**	**2.49**	**1.34**	**4.65**
Polysubstance use (ref: no)	**0.70**	**0.55**	**0.88**	**0.63**	**0.48**	**0.83**
Getting professional help for alcohol and drugs (ref: no)						
Getting syringes from shooting gallery (ref: no)	**1.90**	**1.18**	**3.01**	**1.86**	**1.16**	**2.97**

(1) Multiple imputation using chained equations generating 15 imputed data sets. Imputed sets come from longitudinal data including baseline and 9 follow-ups.
(2) Covariates reported are the final set retained after backward elimination using a cut-off p-value of 0.20.
(3) Covariates in bold if significant at 5% in the multivariable regression.

Table A.6. Cumulative incarceration (continuous) and other factors associated with syringe sharing. Multivariable adjusted GEE for multiply imputed data and complete case analysis. (1)

Variable (2)	Multivariable MICE			Multivariable complete case		
	aOR	95% CI (3)		aOR	95% CI (3)	
Cumulative Incarceration (continuous)	**1.17**	**1.05**	**1.29**	1.12	1.00	1.26
Age	0.99	0.97	1.00			
Always living in Tijuana (ref: no)				1.30	0.97	1.74
Gender (ref: male)						
Hours spent on street				1.02	0.99	1.04
Heroin injecting (ref: no)	1.27	0.97	1.66	1.04	0.79	1.39
Methamphetamine Injecting (ref: no)	**1.59**	**1.06**	**2.36**	**1.53**	**1.03**	**2.29**
Cocaine Use (ref: no)	**2.07**	**1.20**	**3.58**	**2.29**	**1.22**	**4.29**
Polysubstance use (ref: no)	**0.70**	**0.56**	**0.89**	**0.69**	**0.51**	**0.92**
Getting professional help for alcohol and drug use (ref: no)						
Getting syringes from syringe exchange (ref: no)						
Getting syringes from shooting gallery (ref: no)	**1.88**	**1.17**	**3.04**	**2.11**	**1.24**	**3.60**

(1) Multiple imputation using chained equations generating 15 imputed data sets. Imputed sets come from longitudinal data including baseline and 9 follow-ups.
(2) Covariates reported are the final set retained after backward elimination using a cut-off p-value of 0.20.
(3) Covariates in bold if significant at 5% in the multivariable regression.

Table A.7. Incarceration (dichotomous) and other factors associated with syringe sharing.
Multivariable adjusted GEE for multiply imputed data and complete case analysis. (1)

Variable (2)	Multivariable MICE			Multivariable Complete Case		
	aOR	95% CI (3)		aOR	95% CI (3)	
Incarceration (ref: no)(4)	**1.34**	**1.02**	**1.75**	1.29	0.96	1.73
Age	0.99	0.97	1.00	**0.98**	**0.97**	**0.99**
Always living in Tijuana (ref: no)	1.20	0.91	1.57	1.24	0.97	1.60
Heroin Injecting (ref: no)	1.21	0.93	1.57	1.17	0.91	1.51
Methamphetamine Injecting (ref: no)	**1.49**	**1.01**	**2.20**	**1.51**	**1.04**	**2.18**
Cocaine Use (ref: no)	**2.04**	**1.16**	**3.57**	**2.05**	**1.16**	**3.63**
Polysubstance use (ref: no)	**0.70**	**0.55**	**0.89**	**0.62**	**0.48**	**0.80**
Getting professional help for alcohol and drug use (ref: no)	0.79	0.56	1.11			
Getting syringes from shooting gallery (ref: no)	**1.92**	**1.19**	**3.06**	**1.87**	**1.19**	**2.95**

(1) Multiple imputation using chained equations generating 15 imputed data sets. Imputed sets come from longitudinal data including baseline and 9 follow-ups.
(2) Covariates reported are the final set retained after backward elimination using a cut-off p-value of 0.20.
(3) Covariates in bold if significant at 5% in the multivariable regression.
(4) This is a dichotomous version of the incarceration variable (yes/no), reported as reference.

Table A.8. Incarceration exposure definitions			
Variable	**Definition**	**Type**	**Categories**
Recent incarceration	Incarceration event reported in the past 6 months.	Dichotomous	Yes, No
Cumulative incarceration	Total number of recent incarcerations accrued by each participant over the follow-up period.	Categorical (Also tested as continuous)	None, One, Two to three, More than three
Post-release period	Time elapsed after a recent incarceration event	Categorical	Past 6 months, 6 months to 1.5 years, 1.5 years to 2.5 years, More than 2.5 years

Appendix B. Supplementary materials to Chapter 3

Index

1) Mathematical model

We developed a deterministic compartmental model of HCV transmission among current and former PWID (permanently ceased injecting), accounting for injecting risk, i.e., syringe sharing. The model structure is based on HCV disease progression stages (Susceptible-Pre Cirrhosis-Compensated Cirrhosis-Decompensated Cirrhosis-Hepatocellular Carcinoma). The full model is obtained by stratifying the PWID population by incarceration status, number of incarcerations, harm reduction status, and current injection status. PWID population size was assumed to be constant overtime.

New PWID enter the model at a constant rate (θ) as uninfected, never incarcerated as a PWID -however we allowed for a proportion to have a history of incarceration before starting injection use (*propHist)*- and not engaged in any treatment or intervention. Upon incarceration, PWID become recently incarcerated (p6m) at a rate τ. They spend an average of 6 months in the recently incarcerated compartment before transitioning to the

non-recent incarcerated (>p6m) stage at a rate δ, where they will stay unless reincarcerated. Reincarceration can occur from any of the released stages at rates ω.

All PWID are initially susceptible (S). A proportion (α) spontaneously clears the infection with the remaining (1-α) becoming chronically HCV infected at a per-capita rate (force of infection) $\lambda_m^{n,k}$, specific to the incarceration and intervention state. PWID at any stage can permanently cease injecting (i.e. transition to former PWID) at a rate ν. PWID and ex-PWID are treated at a fixed number ϕ per year. If fewer than ϕ per year individuals are chronically infected, then ϕ would equal the number of PWID infected at each stage. After treatment, a proportion ρ achieves sustained viral response (SVR), while the remainder, 1-ρ, fail treatment and remain chronically infected. Furthermore, on top of treatment, active PWID can enter OAT at a rate η_m, determined for specific decriminalization-intervention scenarios, equal to the number of PWID not incarcerated or re-incarcerated, and exit this state at a per-capita rate ι_m. PWID and ex-PWID exit all compartments due to related all-cause mortality, μ1 and μ2, respectively.

As previously noted, the structure of the model incorporates progression through four chronic disease states: pre-cirrhosis, compensated cirrhosis (CC), decompensated cirrhosis (DC), and hepatocellular carcinoma (HCC). We assume disease progression is unidirectional (i.e. there is no backward movement from a later state to an earlier one) (83). Individuals in the pre-cirrhosis state transition to CC at a rate σ. They can then progress to DC at a rate γ, and to HCC at a rate ξ. Achieving SVR has been associated with slower disease progression from CC to both DC and HCC, resulting in lower risks ϵ_{DC} and ϵ_{HCC}, respectively (83). Moreover, we assume individuals who have already progressed to cirrhotic stages and achieve SVR through successful treatment, will no

longer be infected but will remain in their present disease stage (84). Individuals who get to DC and HCC, die at rates μ3 and μ4, respectively. Additional compartments represent former PWID moving through the HCV disease stages described above.

Model equations

Variables and indices that characterize the full set of model equations

$S_m^{n,k}$ (t) = *Susceptible*

$P_m^{n,k}$ *(t) = Pre-cirrhotic (infected)*

$G_m^{n,k}$ (t) = *Compensated cirrhosis (susceptible)*

$C_m^{n,k}$ *(t) = Compensated cirrhosis (infected)*

$F_m^{n,k}$ (t) = *Decompensated cirrhosis (susceptible)*

$D_m^{n,k}$ *(t) = Decompensated cirrhosis (infected)*

$L_m^{n,k}$ (t) = *Hepatocellular carcinoma (susceptible)*

$H_m^{n,k}$ *(t) = Hepatocellular carcinoma (infected)*

Where,

Index	Strata	Values*	Meaning
n	Number of incarcerations	1,2,3,4,5,6	1=never incarcerated 2=never incarcerated as PWID, but previous incarceration before starting injecting 3=one incarceration as a PWID; 4=two incarcerations as a PWID; 5=three incarcerations as a PWID; 6=more than three incarcerations as a PWID
k	Post-release state	1,2,3	1=Never 2=Recently released (p6m) 3=Previously released (>6m)
m	OAT	1,2	Off=1, On=2
*Index values do not start at cero due to MATLAB requiring positive integers for indexing.			

Values for some parameters in our model are dependent on one or more of the indexes above (n,k,m). The rate at which new PWID enter the model, θ, acquires the value of θ when m=1 (OAT off), and is equal to zero when m=2, simulating how new PWID are not engaged with OAT at time of entry. Along the incarceration continuum, PWID are recently incarcerated (p6m) at a rate τ. When k=1, τ<0; when k=2, τ>0, τ=0 in any other case. They spend an average of 6 months out of prison before transitioning to the non-recent incarcerated stage (>p6m) at a rate δ, where they will stay unless reincarcerated. When k=2, δ<0; k=3, δ>0; δ=0, in any other case. Reincarceration can occur from any of the released stages at rates ω. When k=1, ω_1>0; when n=3,4,or 5 and k=2 or 3, ω_k>0; when n=6 and k=2, ω_k<0; when n=6 and k=3, ω_k>0. Furthermore, active PWID can be diverted to OAT at a per-capita rate η_m (equal to the rate incarceration and reincarceration

are reduced by) and exit this state at a per-capita rate ι_m. When m=1 (OAT=off), then η>0 and ι>0; when m=2 (OAT=on), then η<0 and ι<0.

Conditions for indexed parameters		
Individuals entering the model	Theta (θ)	When m=1, $\theta_m = \theta$; when m=2, $\theta_m = 0$
Primary incarceration	Tau (τ)	when k=1 or k=2,τ_k>0; in any other case τ_k =0
Reincarceration rates	Omega (ω)	When k=1, ω_1>0; When n=3,4,or 5 and k=2 or 3, ω_k>0; when n=6 and k=2, ω_k<0; when n=6 and k=3, ω_k>0
Transition from recent to non-recent incarceration	Delta (δ)	when k=2, δ<0; k=3, δ>0; δ=0, in any other case
Entering and leaving OAT	Eta (η) and iota (ι)	when m=1, η>0 and ι>0; when m=2 η<0 and ι<0

In the equations below, the total number of infected individuals (i.e. eligible for treatment) is defined as:

$$totInfected\ (totInf) = sum\ (P_m^{n,k} + C_m^{n,k} + D_m^{n,k} + H_m^{n,k})$$

Full model equations, expanded by number of incarcerations, are as follows:

For PWID **never incarcerated (n=1)**:

$$\frac{dS_m^{1,1}}{dt} = \theta_m * (1 - propHist) - \left((1-\alpha)\lambda_m^{1,1} + \mu_1 + \nu\right) S_m^{1,1} + \rho\phi(P_m^{1,1}/totTreat) - \eta_m S_1^{1,1} + \iota_m S_2^{1,1} - \tau_1 S_m^{1,1}$$

$$\frac{dP_m^{1,1}}{dt} = (1-\alpha)\lambda_m^{1,1} S_m^{1,1} - \rho\phi(P_m^{1,1}/totTreat) - (\sigma + \mu_1 + \nu) P_m^{1,1} - \eta_m P_1^{1,1} + \iota_m P_2^{1,1} - \tau_1 P_m^{1,1}$$

$$\frac{dG_m^{1,1}}{dt} = \rho\phi(C_m^{1,1}/totTreat) - ((1-\alpha)\lambda_m^{1,1} + \gamma \in_{CD} + \xi \in_{CH} + \mu_1 + \nu) G_m^{1,1} - \eta_m G_1^{1,1} + \iota_m G_2^{1,1} - \tau_1 G_m^{1,1}$$

$$\frac{dC_m^{1,1}}{dt} = \sigma P_m^{1,1} + (1-\alpha)\lambda_m^{1,1} G_m^{1,1} - \rho\phi(C_m^{1,1}/totTreat) - (\gamma + \xi + \mu_1 + \nu) C_m^{1,1} - \eta_m C_1^{1,1} + \imath_m C_2^{1,1} - \tau_1 C_m^{1,1}$$

$$\frac{dF_m^{1,1}}{dt} = \gamma \in_{CD} G_m^{1,1} + \rho\phi(D_m^{1,1}/totTreat) - ((1-\alpha)\lambda_m^{1,1} + \xi \in_{DH} + \mu_1 + \mu_3 + \nu) F_m^{1,1} - \eta_m F_1^{1,1} + \imath_m F_2^{1,1} - \tau_1 F_m^{1,1}$$

$$\frac{dD_m^{1,1}}{dt} = \gamma C_m^{1,1} + (1-\alpha)\lambda_m^{1,1} F_m^{1,1} - \rho\phi(D_m^{1,1}/totTreat) - (\xi + \mu_1 + \mu_3 + \nu) D_m^{1,1} - \eta_m D_1^{1,1} + \imath_m D_2^{1,1} - \tau_1 D_m^{1,1}$$

$$\frac{dL_m^{1,1}}{dt} = \rho\phi(H_m^{1,1}/totTreat) + \xi \in_{DH} F_m^{1,1} + \xi \in_{CH} G_m^{1,1} - ((1-\alpha)\lambda_m^{1,1} + \mu_1 + \mu_4 + \nu) L_m^{1,1} - \eta_m L_1^{1,1} + \imath_m L_2^{1,1} - \tau_1 L_m^{1,1}$$

$$\frac{dH_m^{1,1}}{dt} = \xi(C_m^{1,1} + D_m^{1,1}) + (1-\alpha)\lambda_m^{1,1} L_m^{1,1} - \rho\phi(H_m^{1,1}/totTreat) - (\mu_1 + \mu_4 + \nu) H_m^{1,1} - \eta_m H_1^{1,1} + \imath_m H_2^{1,1} - \tau_1 H_m^{1,1}$$

For PWID **never incarcerated as PWID but previously incarcerated (n=2)**:

$$\frac{dS_m^{2,1}}{dt} = \theta_m * propHist - \left((1-\alpha)\lambda_m^{2,1} + \mu_1 + \nu\right) S_m^{2,1} + \rho\phi(P_m^{2,1}/totTreat) - \eta_m S_1^{2,1} + \imath_m S_2^{2,1} - \omega_1 S_m^{2,1}$$

$$\frac{dP_m^{2,1}}{dt} = (1-\alpha)\lambda_m^{2,1} S_m^{2,1} - \rho\phi(P_m^{2,1}/totTreat) - (\sigma + \mu_1 + \nu) P_m^{2,1} - \eta_m P_1^{2,1} + \imath_m P_2^{2,1} - \omega_1 P_m^{2,1}$$

$$\frac{dG_m^{2,1}}{dt} = \rho\phi(C_m^{2,1}/totTreat) - ((1-\alpha)\lambda_m^{2,1} + \gamma \in_{CD} + \xi \in_{CH} + \mu_1 + \nu) G_m^{2,1} - \eta_m G_1^{2,1} + \imath_m G_2^{2,1} - \omega_1 G_m^{2,1}$$

$$\frac{dC_m^{2,1}}{dt} = \sigma P_m^{2,1} + (1-\alpha)\lambda_m^{2,1} G_m^{2,1} - \rho\phi(C_m^{2,1}/totTreat) - (\gamma + \xi + \mu_1 + \nu) C_m^{2,1} - \eta_m C_1^{2,1} + \imath_m C_2^{2,1} - \omega_1 C_m^{2,1}$$

$$\frac{dF_m^{2,1}}{dt} = \gamma \in_{CD} G_m^{2,1} + \rho\phi(D_m^{2,1}/totTreat) - ((1-\alpha)\lambda_m^{2,1} + \xi \in_{DH} + \mu_1 + \mu_3 + \nu) F_m^{2,1} - \eta_m F_1^{2,1} + \imath_m F_2^{2,1} - \omega_1 F_m^{2,1}$$

$$\frac{dD_m^{2,1}}{dt} = \gamma C_m^{2,1} + (1-\alpha)\lambda_m^{2,1} F_m^{2,1} - \rho\phi(D_m^{2,1}/totTreat) - (\xi + \mu_1 + \mu_3 + \nu) D_m^{2,1} - \eta_m D_1^{2,1} + \imath_m D_2^{2,1} - \omega_1 D_m^{2,1}$$

$$\frac{dL_m^{2,1}}{dt} = \rho\phi(H_m^{2,1}/totTreat) + \xi \in_{DH} F_m^{2,1} + \xi \in_{CH} G_m^{2,1} - ((1-\alpha)\lambda_m^{2,1} + \mu_1 + \mu_4 + \nu)L_m^{2,1} - \eta_m L_1^{2,1} + \imath_m L_2^{2,1} - \omega_1 L_m^{2,1}$$

$$\frac{dH_m^{2,1}}{dt} = \xi(C_m^{2,1} + D_m^{2,1}) + (1-\alpha)\lambda_m^{2,1} L_m^{2,1} - \rho\phi(H_m^{2,1}/totTreat) - (\mu_1 + \mu_4 + \nu)H_m^{2,1} - \eta_m H_1^{2,1} + \imath_m H_2^{2,1} - \omega_1 H_m^{2,1}$$

PWID **one incarceration (n=3, k>1)**:

$$\frac{dS_m^{3,k}}{dt} = -\left((1-\alpha)\lambda_m^{3,k} + \mu_1 + \nu\right)S_m^{3,k} + \rho\phi(P_m^{3,k}/totTreat) - \eta_m S_1^{3,k} + \imath_m S_2^{3,k} + \tau_k S_m^{1,1} + \omega_1 S_m^{2,1} - \delta^k S_m^{3,2} - \omega_k RRreincar_2 S_m^{3,k}$$

$$\frac{dP_m^{3,k}}{dt} = (1-\alpha)\lambda_m^{3,k} S_m^{3,k} - \rho\phi(P_m^{3,k}/totTreat) - (\sigma + \mu_1 + \nu)P_m^{3,k} - \eta_m P_1^{3,k} + \imath_m P_2^{3,k} + \tau_k P_m^{1,1} + \omega_1 P_m^{2,1} - \delta^k P_m^{3,2} - \omega_k RRreincar_2 P_m^{3,k}$$

$$\frac{dG_m^{3,k}}{dt} = \rho\phi(C_m^{3,k}/totTreat) - ((1-\alpha)\lambda_m^{3,k} + \gamma \in_{CD} + \xi \in_{CH} + \mu_1 + \nu)G_m^{3,k} - \eta_m G_1^{3,k} + \imath_m G_2^{3,k} + \tau_k G_m^{1,1} + \omega_1 G_m^{2,1} - \delta^k G_m^{3,2} - \omega_k RRreincar_2 G_m^{3,k}$$

$$\frac{dC_m^{3,k}}{dt} = \sigma P_m^{3,k} + (1-\alpha)\lambda_m^{3,k} G_m^{3,k} - \rho\phi(C_m^{3,k}/totTreat) - (\gamma + \xi + \mu_1 + \nu)C_m^{3,k} - \eta_m C_1^{3,k} + \imath_m C_2^{3,k} + \tau_k C_m^{1,1} + \omega_1 C_m^{2,1} - \delta^k C_m^{3,2} - \omega_k RRreincar_2 C_m^{3,k}$$

$$\frac{dF_m^{3,k}}{dt} = \gamma \in_{CD} G_m^{3,k} + -\rho\phi(D_m^{3,k}/totTreat) - ((1-\alpha)\lambda_m^{3,k} + \xi \in_{DH} + \mu_1 + \mu_3 + \nu)F_m^{3,k} - \eta_m F_1^{3,k} + \imath_m F_2^{3,k} + \tau_k F_m^{1,1} + \omega_1 F_m^{2,1} - \delta^k F_m^{3,2} - \omega_k RRreincar_2 F_m^{3,k}$$

$$\frac{dD_m^{3,k}}{dt} = \gamma C_m^{3,k} + (1-\alpha)\lambda_m^{3,k} F_m^{3,k} - \rho\phi(D_m^{3,k}/totTreat) - (\xi + \mu_1 + \mu_3 + \nu)D_m^{3,k} - \eta_m D_1^{3,k} + \imath_m D_2^{3,k} + \tau_k D_m^{1,1} + \omega_1 D_m^{2,1} - \delta^k D_m^{3,2} - \omega_k RRreincar_2 D_m^{3,k}$$

$$\frac{dL_m^{3,k}}{dt} = \rho\phi(H_m^{3,k}/totTreat) + \xi \in_{DH} F_m^{3,k} + \xi \in_{CH} G_m^{3,k} - ((1-\alpha)\lambda_m^{3,k} + \mu_1 + \mu_4 + \nu)L_m^{3,k} - \eta_m L_1^{3,k} + \imath_m L_2^{3,k} + \tau_k L_m^{1,1} + \omega_1 D_m^{2,1} - \delta^k L_m^{3,2} - \omega_k RRreincar_2 L_m^{3,k}$$

$$\frac{dH_m^{3,k}}{dt} = \xi(C_m^{3,k} + D_m^{3,k}) + (1-\alpha)\lambda_m^{3,k} L_m^{3,k} - \rho\phi(H_m^{3,k}/totTreat) - (\mu_1 + \mu_4 + \nu)H_m^{3,k} - \eta_m H_1^{3,k} + \imath_m H_2^{3,k} + \tau_k H_m^{1,1} + \omega_1 H_m^{2,1} - \delta^k H_m^{3,2} - \omega_k RRreincar_2 H_m^{3,k}$$

PWID **two incarcerations (n=4, k>1)**:

$$\frac{dS_m^{4,k}}{dt} = -\left((1-\alpha)\lambda_m^{4,k} + \mu_1 + \nu\right) S_m^{4,k} + \rho\phi(P_m^{4,k}/totTreat) - \eta_m S_1^{4,k} + \imath_m S_2^{4,k} + \omega_k RRreincar_2 S_m^{3,k} - \delta^k S_m^{4,2} - \omega_k RRreincar_2 S_m^{4,k}$$

$$\frac{dP_m^{4,k}}{dt} = (1-\alpha)\lambda_m^{4,k} S_m^{4,k} - \rho\phi(P_m^{4,k}/totTreat) - (\sigma + \mu_1 + \nu) P_m^{4,k} - \eta_m P_1^{4,k} + \imath_m P_2^{4,k} + \omega_k RRreincar_2 P_m^{3,k} - \delta^k P_m^{4,2} - \omega_k RRreincar_2 P_m^{4,k}$$

$$\frac{dG_m^{4,k}}{dt} = \rho\phi(C_m^{4,k}/totTreat) - ((1-\alpha)\lambda_m^{4,k} + \gamma \in_{CD} + \xi \in_{CH} + \mu_1 + \nu) G_m^{4,k} - \eta_m G_1^{4,k} + \imath_m G_2^{4,k} + \omega_k RRreincar_2 G_m^{3,k} - \delta^k G_m^{4,2} - \omega_k RRreincar_2 G_m^{4,k}$$

$$\frac{dC_m^{4,k}}{dt} = \sigma P_m^{4,k} + (1-\alpha)\lambda_m^{4,k} G_m^{4,k} - \rho\phi(C_m^{4,k}/totTreat) - (\gamma + \xi + \mu_1 + \nu) C_m^{4,k} - \eta_m C_1^{4,k} + \imath_m C_2^{4,k} + \omega_k RRreincar_2 C_m^{3,k} - \delta^k C_m^{4,2} - \omega_k RRreincar_2 C_m^{4,k}$$

$$\frac{dF_m^{4,k}}{dt} = \gamma \in_{CD} G_m^{4,k} + -\rho\phi(D_m^{4,k}/totTreat) - ((1-\alpha)\lambda_m^{4,k} + \xi \in_{DH} + \mu_1 + \mu_3 + \nu) F_m^{4,k} - \eta_m F_1^{4,k} + \imath_m F_2^{4,k} + \omega_k RRreincar_2 F_m^{3,k} - \delta^k F_m^{4,2} - \omega_k RRreincar_2 F_m^{4,k}$$

$$\frac{dD_m^{4,k}}{dt} = \gamma C_m^{4,k} + (1-\alpha)\lambda_m^{4,k} F_m^{4,k} - \rho\phi(D_m^{4,k}/totTreat) - (\xi + \mu_1 + \mu_3 + \nu) D_m^{4,k} - \eta_m D_1^{4,k} + \imath_m D_2^{4,k} + \omega_k RRreincar_2 D_m^{3,k} - \delta^k D_m^{4,2} - \omega_k RRreincar_2 D_m^{4,k}$$

$$\frac{dL_m^{4,k}}{dt} = \rho\phi(H_m^{4,k}/totTreat) + \xi \in_{DH} F_m^{4,k} + \xi \in_{CH} G_m^{4,k} - ((1-\alpha)\lambda_m^{4,k} + \mu_1 + \mu_4 + \nu) L_m^{4,k} - \eta_m L_1^{4,k} + \imath_m L_2^{4,k} + \omega_k RRreincar_2 L_m^{3,k} - \delta^k L_m^{4,2} - \omega_k RRreincar_2 L_m^{4,k}$$

$$\frac{dH_m^{4,k}}{dt} = \xi(C_m^{4,k} + D_m^{4,k}) + (1-\alpha)\lambda_m^{4,k} L_m^{4,k} - \rho\phi(H_m^{4,k}/totTreat) - (\mu_1 + \mu_4 + \nu) H_m^{4,k} - \eta_m H_1^{4,k} + \imath_m H_2^{4,k} + \omega_k RRreincar_2 H_m^{3,k} - \delta^k H_m^{4,2} - \omega_k RRreincar_2 H_m^{4,k}$$

PWID **three incarcerations (n=5, k>1)**,

$$\frac{dS_m^{5,k}}{dt} = -\left((1-\alpha)\lambda_m^{5,k} + \mu_1 + \nu\right) S_m^{5,k} + \rho\phi(P_m^{5,k}/totTreat) - \eta_m S_1^{5,k} + \imath_m S_2^{5,k} + \omega_k RRreincar_2 S_m^{4,k} - \delta^k S_m^{5,2} - \omega_k RRreincar_2 S_m^{5,k}$$

$$\frac{dP_m^{5,k}}{dt} = (1-\alpha)\lambda_m^{5,k} S_m^{5,k} - \rho\phi(P_m^{5,k}/totTreat) - (\sigma + \mu_1 + \nu) P_m^{5,k} - \eta_m P_1^{5,k} + \imath_m P_2^{5,k} + \omega_k RRreincar_2 P_m^{4,k} - \delta^k P_m^{5,2} - \omega_k RRreincar_2 P_m^{5,k}$$

$$\frac{dG_m^{5,k}}{dt} = \rho\phi(C_m^{5,k}/totTreat) - ((1-\alpha)\lambda_m^{5,k} + \gamma \in_{CD} + \xi \in_{CH} + \mu_1 + \nu) G_m^{5,k} - \eta_m G_1^{5,k} + \imath_m G_2^{5,k} + \omega_k RRreincar_2 G_m^{4,k} - \delta^k G_m^{5,2} - \omega_k RRreincar_2 G_m^{5,k}$$

$$\frac{dC_m^{5,k}}{dt} = \sigma P_m^{5,k} + (1-\alpha)\lambda_m^{5,k} G_m^{5,k} - \rho\phi(C_m^{5,k}/totTreat) - (\gamma + \xi + \mu_1 + \nu) C_m^{5,k} - \eta_m C_1^{5,k} + \imath_m C_2^{5,k} + \omega_k RRreincar_2 C_m^{4,k} - \delta^k C_m^{5,2} - \omega_k RRreincar_2 C_m^{5,k}$$

$$\frac{dF_m^{5,k}}{dt} = \gamma \in_{CD} G_m^{5,k} + -\rho\phi(D_m^{5,k}/totTreat) - ((1-\alpha)\lambda_m^{5,k} + \xi \in_{DH} + \mu_1 + \mu_3 + \nu) F_m^{5,k} - \eta_m F_1^{5,k} + \imath_m F_2^{5,k} + \omega_k RRreincar_2 F_m^{4,k} - \delta^k F_m^{5,2} - \omega_k RRreincar_2 F_m^{5,k}$$

$$\frac{dD_m^{5,k}}{dt} = \gamma C_m^{5,k} + (1-\alpha)\lambda_m^{5,k} F_m^{5,k} - \rho\phi(D_m^{5,k}/totTreat) - (\xi + \mu_1 + \mu_3 + \nu) D_m^{5,k} - \eta_m D_1^{5,k} + \imath_m D_2^{5,k} + \omega_k RRreincar_2 D_m^{4,k} - \delta^k D_m^{5,2} - \omega_k RRreincar_2 D_m^{5,k}$$

$$\frac{dL_m^{5,k}}{dt} = \rho\phi(H_m^{5,k}/totTreat) + \xi \in_{DH} F_m^{5,k} + \xi \in_{CH} G_m^{5,k} - ((1-\alpha)\lambda_m^{5,k} + \mu_1 + \mu_4 + \nu) L_m^{5,k} - \eta_m L_1^{5,k} + \imath_m L_2^{5,k} + \omega_k RRreincar_2 L_m^{4,k} - \delta^k L_m^{5,2} - \omega_k RRreincar_2 L_m^{5,k}$$

$$\frac{dH_m^{5,k}}{dt} = \xi(C_m^{5,k} + D_m^{5,k}) + (1-\alpha)\lambda_m^{5,k} L_m^{5,k} - \rho\phi(H_m^{5,k}/totTreat) - (\mu_1 + \mu_4 + \nu) H_m^{5,k} - \eta_m H_1^{5,k} + \imath_m H_2^{5,k} + \omega_k RRreincar_2 H_m^{4,k} - \delta^k H_m^{5,2} - \omega_k RRreincar_2 H_m^{5,k}$$

PWID **four or more incarcerations (n=6, k>1)**,

$$\frac{dS_m^{6,k}}{dt} = -\left((1-\alpha)\lambda_m^{6,k} + \mu_1 + \nu\right) S_m^{6,k} + \rho\phi(P_m^{6,k}/totTreat) - \eta_m S_1^{6,k} + \imath_m S_2^{6,k} + \omega_k RRreincar_2 S_m^{5,k} - \delta^k S_m^{6,2} - \omega_k RRreincar_2 S_m^{6,3} - \omega_k RRreincar_2 S_m^{6,4}$$

$$\frac{dP_m^{6,k}}{dt} = (1-\alpha)\lambda_m^{6,k} S_m^{6,k} - \rho\phi(P_m^{6,k}/totTreat) - (\sigma + \mu_1 + \nu) P_m^{6,k} - \eta_m P_1^{6,k} + \imath_m P_2^{6,k} + \omega_k RRreincar_m P_m^{5,k} - \delta^k P_m^{6,2} - \omega_k RRreincar_2 P_m^{6,3} - \omega_k RRreincar_2 P_m^{6,4}$$

$$\frac{dG_m^{6,k}}{dt} = \rho\phi(C_m^{6,k}/totTreat) - ((1-\alpha)\lambda_m^{6,k} + \gamma \in_{CD} + \xi \in_{CH} + \mu_1 + \nu) G_m^{6,k} - \eta_m G_1^{6,k} + \imath_m G_2^{6,k} + \omega_k RRreincar_2 G_m^{5,k} - \delta^k G_m^{6,2} - \omega_k RRreincar_2 G_m^{6,3} - \omega_k RRreincar_2 G_m^{6,4}$$

$$\frac{dC_m^{6,k}}{dt} = \sigma P_m^{6,k} + (1-\alpha)\lambda_m^{6,k} G_m^{6,k} - \rho\phi(C_m^{6,k}/totTreat) - (\gamma + \xi + \mu_1 + \nu) C_m^{6,k} - \eta_m C_1^{6,k} + \imath_m C_2^{6,k} + \omega_k RRreincar_m C_m^{5,k} - \delta^k C_m^{6,2} - \omega_k RRreincar_2 C_m^{6,3} - \omega_k RRreincar_2 C_m^{6,4}$$

$$\frac{dF_m^{6,k}}{dt} = \gamma \in_{CD} G_m^{6,k} + -\rho\phi(D_m^{6,k}/totTreat) - ((1-\alpha)\lambda_m^{6,k} + \xi \in_{DH} + \mu_1 + \mu_3 + \nu) F_m^{6,k} - \eta_m F_1^{6,k} + \imath_m F_2^{6,k} + \omega_k RRreincar_m F_m^{5,k} - \delta^k F_m^{6,2} - \omega_k RRreincar_2 F_m^{6,3} - \omega_k RRreincar_2 F_m^{6,4}$$

$$\frac{\mathrm{dD_m^{6,k}}}{\mathrm{dt}} = \gamma \mathrm{C_m^{6,k}} + (1-\alpha)\lambda_{\mathrm{m}}^{6,\mathrm{k}} \mathrm{F_m^{6,k}} - \rho\phi(D_m^{6,k}/totTreat) - (\xi + \mu_1 + \mu_3 + \nu)\mathrm{D_m^{6,k}} - \eta_{\mathrm{m}} \mathrm{D_1^{6,k}} + \imath_{\mathrm{m}} \mathrm{D_2^{6,k}} + \omega_k RRreincar_m \mathrm{D_m^{5,k}} - \delta^{\mathrm{k}} \mathrm{D_m^{6,2}} - \omega_k RRreincar_2 \mathrm{D_m^{6,3}} - \omega_k RRreincar_2 \mathrm{D_m^{6,4}}$$

$$\frac{\mathrm{dL_m^{6,k}}}{\mathrm{dt}} = \rho\phi(H_m^{6,k}/totTreat) + \xi \in_{\mathrm{DH}} \mathrm{F_m^{6,k}} + \xi \in_{\mathrm{CH}} \mathrm{G_m^{6,k}} - ((1-\alpha)\lambda_{\mathrm{m}}^{6,\mathrm{k}} + \mu_1 + \mu_4 + \nu)\mathrm{L_m^{6,k}} - \eta_{\mathrm{m}} \mathrm{L_1^{6,k}} + \imath_{\mathrm{m}} \mathrm{L_2^{6,k}} + \omega_k RRreincar_m \mathrm{L_m^{6,k}} - \delta^{\mathrm{k}} \mathrm{L_m^{6,2}} - \omega_k RRreincar_2 \mathrm{L_m^{6,3}} - \omega_k RRreincar_2 \mathrm{L_m^{6,4}}$$

$$\frac{\mathrm{dH_m^{6,k}}}{\mathrm{dt}} = \xi(\mathrm{C_m^{6,k}} + \mathrm{D_m^{6,k}}) + (1-\alpha)\lambda_{\mathrm{m}}^{6,\mathrm{k}} \mathrm{L_m^{6,k}} - \rho\phi(H_m^{6,k}/totTreat) - (\mu_1 + \mu_4 + \nu)\mathrm{H_m^{6,k}} - \eta_{\mathrm{m}} \mathrm{H_1^{6,k}} + \imath_{\mathrm{m}} \mathrm{H_2^{6,k}} + \omega_k RRreincar_m \mathrm{H_m^{5,k}} - \delta^{\mathrm{k}} \mathrm{H_m^{6,2}} - \omega_k RRreincar_2 \mathrm{H_m^{6,3}} - \omega_k RRreincar_2 \mathrm{H_m^{6,4}}$$

Force of Infection

Among PWID, baseline force of infection, $\lambda_m^{n,k}$, is determined by an HCV transmission rate, β, and the proportion of infected PWID. Incarcerated individuals have an elevated risk of acquiring infection associated to parenteral transmission, i.e., receptive syringe sharing, specific to their incarceration status. This increased risk is obtained by multiplying the relative risk of receptive syringe sharing associated to each incarceration category, $RR_{n,k}$, by the transmission coefficient (see Supplemental section 2 below for details on the estimation of the relative risks). The force of infection may be further altered by a factor Π corresponding to the reduction in infection risk from OAT state.

For $\lambda_m^{n,k}$:

$\lambda_1^{1,1}$=

$$\beta\frac{(\Omega_1^{1,1}+\Omega_1^{2,1}+\Gamma\Omega_1^{3,2}+\Gamma\Omega_1^{4,2}+K\Omega_1^{5,2}+K\Omega_1^{6,2}+\Theta\Omega_1^{3,3}+\Theta\Omega_1^{4,3}+\ H\Omega_1^{5,3}+H\Omega_1^{6,3}+\Pi(\Omega_2^{1,1}+\Omega_2^{2,1}+\Gamma\Omega_2^{3,2}+\Gamma\Omega_2^{4,2}+K\Omega_2^{5,2}+K\Omega_2^{6,2}+\Theta\Omega_2^{3,3}+\Theta\Omega_2^{4,3}+\ H\Omega_2^{5,3}+H\Omega_2^{6,3}))}{(N_1^{1,1}+N_1^{2,1}+\Gamma N_1^{3,2}+\Gamma N_1^{4,2}+KN_1^{5,2}+KN_1^{6,2}+\Theta N_1^{3,3}+\Theta N_1^{4,3}+\ HN_1^{5,3}+\Theta HN_1^{6,3}+\Pi(N_2^{1,1}+N_1^{2,1}+\Gamma N_2^{3,2}+\Gamma N_2^{4,2}+KN_2^{5,2}+KN_2^{6,2}+\Theta N_2^{3,3}+\Theta N_2^{4,3}+\ HN_2^{5,3}+HN_2^{6,3}))}$$

For m=1 (off OAT):

$\lambda_1^{1,1} = \lambda_1^{1,1}$

$\lambda_1^{2,1} = \lambda_1^{1,1}$

$\lambda_1^{3,2} = \Gamma\lambda_1^{1,1}$

$\lambda_1^{4,2} = \Gamma\lambda_1^{1,1}$

$\lambda_1^{5,2} = \mathrm{K}\lambda_1^{1,1}$

$\lambda_1^{6,2} = \mathrm{K}\lambda_1^{1,1}$

$\lambda_1^{3,3} = \Theta\lambda_1^{1,1}$

$\lambda_1^{4,3} = \Theta\lambda_1^{1,1}$

$\lambda_1^{5,3} = \mathrm{H}\lambda_1^{1,1}$

$\lambda_1^{6,3} = \mathrm{H}\lambda_1^{1,1}$

For m=2 (on OAT):

$\lambda_2^{1,1} = \Pi\lambda_1^{1,1}$

$\lambda_2^{2,1} = \Pi\lambda_1^{1,1}$

$\lambda_2^{3,2} = \Pi\Gamma\lambda_1^{1,1}$

$\lambda_2^{4,2} = \Pi\Gamma\mathrm{B}\lambda_1^{1,1}$

$\lambda_2^{5,2} = \Pi\mathrm{K}\lambda_1^{1,1}$

$\lambda_2^{6,2} = \Pi\mathrm{K}\lambda_1^{1,1}$

$\lambda_2^{3,3} = \Pi\Theta\lambda_1^{1,1}$

$\lambda_2^{4,3} = \Pi\Theta\lambda_1^{1,1}$

$\lambda_2^{5,3} = \Pi\mathrm{H}\lambda_1^{1,1}$

$\lambda_2^{6,3} = \Pi\mathrm{H}\lambda_1^{1,1}$

Where:

$\Omega_m^{n,k} = P_m^{n,k} + C_m^{n,k} + D_m^{n,k} + H_m^{n,k}$ (infected)

$\mathrm{S}_m^{n,k} = S_m^{n,k} + G_m^{n,k} + F_m^{n,k} + L_m^{n,k}$ (susceptible)

$N_m^{n,k} = \Omega_m^{n,k} + \mathrm{S}_m^{n,k}$ (total)

2) METVIR transitions table

Table B.1. METAVIR fibrosis stages (annual transitions)			
Parameter	*Point Estimates*	*Ranges/CIs*	*Reference, Source & Comments*
METAVIR F0-F1	0.117	(0.104-0.130)	(12)
METAVIR F1-F2	0.085	(0.075-0.096)	(12)
METAVIR F2-F3	0.120	(0.109-0.133)	(12)
F3 to compensated cirrhosis (CC) [2]	0.116	(0.104-0.129)	(12)
F0-F4 referrer to fibrosis stages. F0-F2 can be associated to mild, F3 to moderate, and F4 to cirrhosis according to the Laennec scoring system (115).			

3) Incarceration categories' relative risks estimation

To estimate the elevated risks associated to repeated incarceration and the post-release risk, we used data from an ongoing community-based cohort study of PWID in Tijuana, Mexico (El Cuete-IV) (8). Between 2011 and 2012 baseline data were collected with follow-up surveys every 6 months. Targeted sampling consisting of street outreach in 10 neighborhoods across Tijuana was used to recruit participants who were 18 years of age or older, had injected drugs in the past month, and were currently living in Tijuana. Trained interviewers collected data on socio-demographics, drug use behaviors, drug treatment experiences, justice involvement, migration history, and drug related harms and health outcomes (32). For the present analysis we included PWID recruited between April 2011 and June 2012 and followed for approximately 54 months (visits 1 through 10). We included only those participants who reported never being incarcerated at baseline to exclude participants who may already have been at increased risk of reincarceration and/or syringe sharing associated with previous incarceration. This study was approved

by the Ethics Board at the University of California San Diego and Xochicalco University in Tijuana. All participants provided written informed consent.

The outcome of this study was self-reported receptive syringe sharing in the past 6 months, a dichotomous variable with categories “never” and “ever.” The exposure variable was constructed from combining cumulative number and recency of incarcerations into five categories. We first defined cumulative incarcerations as the number of incarceration events reported by participants over the follow-up period. Then, we defined recency of incarceration as the time elapsed post-release (i.e., number of visits) after a participant had reported being incarcerated. From these variables, specifically for this study, we created five mutually exclusive categories categories: never incarcerated, 1-2 incarcerations and recently incarcerated (past 6 months [p6m]), 1-2 incarcerations and non-recently incarcerated (more than 6 moths [>6m]), 3-4 incarcerations and recently incarcerated (p6m), and 3-4 incarcerations and non-recently incarcerated (>6m).

To estimate the longitudinal association between our incarceration/post-release categories, we used log-binomial regression with generalized estimating equations (GEE). We specified an exchangeable correlation structure to account for the correlated nature of the repeated measurements among study participants. We chose a log-binomial specification to assure obtaining relative risks instead of odds ratios. However, the log-binomial regression reported a failed convergence when using a multivariable adjusted model, a common issue with this type of regression (116), so we ran an unadjusted model. Participants with missing observations were incorporated to the analysis using multiple imputation by chained equations (MICE package in R, van Buuren and Groothuis-

Oudshoorn (117)). The model outputs are shown in Table B2 below. For further details on El Cuete study, the subsample of PWID, the longitudinal setup, handling of missing data and multiple imputation, construction of the outcome variable, and construction of the cumulative incarceration and post-release variables see Rivera Saldana, Beletsky (82). The categories defined for the exposure variable described were designed exclusively for the present study.

Table B.2. Impact of the Cumulative Incarceration-Recent Release variable on Receptive Syringe sharing (unadjusted log-binomial)

Category description:	**Category**	**RR**	95% CI **Lower**	**Upper**	**p=value**
never incarcerated	0	na	na	na	na
1-2 incarcerations & recently incarcerated	1	1.24	1.05	1.47	0.01
1-2 incarcerations & non-recently incarcerated	2	1.10	0.95	1.27	0.22
>3 incarcerations & recently incarcerated	3	1.42	1.15	1.74	0.001
>3 incarcerations & non-recently incarcerated	4	1.27	0.93	1.72	0.13

4) Sensitivity analysis

Table B.3.
Partial rank correlation coefficients (PRCC)
The results are significant at the 0.05 level (*), the 0.01 level (**) or the 0.001 level (***).

#	Parameter	PRCC	
1	Injection duration (I)	-0.346	***
2	Rate at which PWID leave OAT (iota)	-0.04	
3	PWID background mortality (mu1)	0.203	***
4	Reduced risk of death for former PWID (M)	-0.01	
5	Primary incarceration rate (tau)	0.074	*
6	Reincarceration rate (omega)	0.747	***
6	Proportion treated achieving SVR (rho)	0.007	
7	Proportion who spontaneously clear infection (alpha)	0.128	***
8	Annual transition from pre-cirrhosis to CC (sigma)	0.014	
9	Annual transition from CC to DC (gamma)	0.058	
10	Annual transition from CC/DC to HCC (xi)	-0.04	
11	Reduced relative risk from CC to DC due to SVR (ecd)	0.016	
12	Reduced relative risk from CC to HCC due to SVR(ech)	0.036	
13	Annual transition from DC to death (mu3)	-0.01	
14	Annual transition from HCC to death (mu4)	0.092	**
15	Elevated risk for PWID incarcerated 1-2 times (p6m) (G1)	0.226	***
16	Elevated risk for PWID incarcerated 1-2 times (>6m) (Th1)	0.618	***
17	Elevated risk for PWID incarcerated 3-4 times (p6m) (K1)	0.029	
18	Elevated risk for PWID incarcerated 3-4 times (>6m) (H1)	0.719	***
19	Reduced risk of infection due to OAT (P)	0.001	

Appendix C. Supplementary materials to Chapter 4

Index

1) Mathematical model

We developed a deterministic compartmental model of HCV transmission among current and former PWID (permanently ceased injecting), accounting for injecting risk, i.e., syringe sharing. The model structure is based on HCV disease progression stages (susceptible-re cirrhosis-compensated cirrhosis-decompensated cirrhosis-hepatocellular carcinoma). The full model is obtained by stratifying the PWID population by incarceration status, number of incarcerations, and current injection status. PWID population size was assumed to be constant over time.

New PWID enter the model at a constant rate (θ) as uninfected, never incarcerated as a PWID -however we allowed for a proportion to have a history of incarceration before starting injection use (*propHist)*. Upon incarceration, PWID become recently incarcerated (p6m) at a rate τ. They spend an average of 6 months in the recently incarcerated

compartment before transitioning to the non-recent incarcerated (>p6m) stage at a rate δ, where they will stay unless reincarcerated. Reincarceration can occur from any of the released stages at rates ω.

All PWID are initially susceptible (S). A proportion (α) spontaneously clears the infection with the remaining (1-α) becoming chronically HCV infected at a per-capita rate (force of infection) $\lambda^{n,k}$, specific to the incarceration and intervention state. PWID at any stage can permanently cease injecting (i.e., transition to former PWID) at a rate ν. PWID and ex-PWID exit all compartments due to related all-cause mortality, μ1 and μ2, respectively.

As previously noted, the structure of the model incorporates progression through four chronic disease states: pre-cirrhosis, compensated cirrhosis (CC), decompensated cirrhosis (DC), and hepatocellular carcinoma (HCC). Disease progression is unidirectional (i.e., there is no backward movement from a later state to an earlier one) (83). Individuals in the pre-cirrhosis state transition to CC at a rate σ. They can then progress to DC at a rate γ, and to HCC at a rate ξ. Individuals who get to DC and HCC, die at rates μ3 and μ4, respectively. Additional compartments represent former PWID moving through the HCV disease stages described above.

Model equations

Variables and indices that characterize the full set of model equations

$S^{n,k}$(t) = Susceptible

$P^{n,k}$ *(t) = Pre-cirrhotic (infected)*

$C^{n,k}$ *(t) = Compensated cirrhosis (infected)*

$D^{n,k}$ *(t) = Decompensated cirrhosis (infected)*

$H^{n,k}$ *(t) = Hepatocellular carcinoma (infected)*

Where,

Index	**Strata**	**Values***	**Meaning**
n	Number of incarcerations	1,2,3,4,5,6	1=never incarcerated 2=never incarcerations as PWID, but previous incarceration before starting injecting 3=one incarceration as a PWID; 4=two incarcerations as a PWID; 5=three incarcerations as a PWID; 6=more than three incarcerations as a PWID
k	Post-release state	1,2,3	1=Never 2=Recently released (p6m) 3=Previously released (>6m)
*Index values do not start at cero due to MATLAB requiring positive integers for indexing.			

Values for some parameters in our model are dependent on one or more of the indexes above (n or k). Along the incarceration continuum, PWID are recently incarcerated (p6m) at a rate τ. When k=1, τ<0; when k=2, τ>0, τ=0 in any other case. They spend an average of 6 months out of prison before transitioning to the non-recent incarcerated stage (>p6m) stage at a rate δ, where they will stay unless reincarcerated. When k=2, δ<0; k=3, δ>0; δ=0, in any other case. Reincarceration can occur from any of the released stages at rates ω. When k=1, ω_1>0; when n=3,4,or 5 and k=2 or 3, ω_k>0; when n=6 and k=2, ω_k<0; when n=6 and k=3, ω_k>0.

Conditions for indexed parameters		
Primary incarceration	Tau (τ)	when k=1 or k=2,τ_k>0; in any other case τ_k =0
Reincarceration rates	Omega (ω)	When k=1, ω_1>0; When n=3,4,or 5 and k=2 or 3, ω_k>0; when n=6 and k=2, ω_k<0; when n=6 and k=3, ω_k>0
Transition from recent to non-recent incarceration	Delta (δ)	when k=2, δ<0; k=3, δ>0; δ=0, in any other case

Full model equations, expanded by number of incarcerations, are as follows:

For PWID **never incarcerated (n=1)**:

$$\frac{dS^{1,1}}{\mathrm{dt}} = \theta * (1 - propHist) - \big((1-\alpha)\lambda^{1,1} + \mu_1 + \nu\big)S^{1,1} - \tau S^{1,1}$$

$$\frac{dP^{1,1}}{\mathrm{dt}} = (1-\alpha)\lambda^{1,1}S^{1,1} - (\sigma + \mu_1 + \nu)P^{1,1} - \tau P^{1,1}$$

$$\frac{dC^{1,1}}{\mathrm{dt}} = \sigma P^{1,1} - (\gamma + \xi + \mu_1 + \nu)C^{1,1} - \tau C^{1,1}$$

$$\frac{dD^{1,1}}{\mathrm{dt}} = \gamma C^{1,1} - (\xi + \mu_1 + \mu_3 + \nu)D^{1,1} - \tau D^{1,1}$$

$$\frac{dH^{1,1}}{\mathrm{dt}} = \xi(C^{1,1} + D^{1,1}) - (\mu_1 + \mu_4 + \nu)H^{1,1} - \tau H^{1,1}$$

For PWID **never incarcerated as PWID but previously incarcerated (n=2)**:

$$\frac{dS^{2,1}}{\mathrm{dt}} = \theta * propHist - \big((1-\alpha)\lambda^{2,1} + \mu_1 + \nu\big)S^{2,1} - \omega S^{2,1}$$

$$\frac{dP^{2,1}}{\mathrm{dt}} = (1-\alpha)\lambda^{2,1}S^{2,1} - (\sigma + \mu_1 + \nu)P^{2,1} - \omega P^{2,1}$$

$$\frac{dC^{2,1}}{\mathrm{dt}} = \sigma P^{2,1} - (\gamma + \xi + \mu_1 + \nu)C^{2,1} - \omega C^{2,1}$$

$$\frac{dD^{2,1}}{\mathrm{dt}} = \gamma C^{2,1} - (\xi + \mu_1 + \mu_3 + \nu)D^{2,1} - \omega D^{2,1}$$

$$\frac{dH^{2,1}}{\mathrm{dt}} = \xi(C^{2,1} + D^{2,1}) - (\mu_1 + \mu_4 + \nu)H^{2,1} - \omega H^{2,1}$$

PWID with **one incarceration (n=3, k>1)**:

$$\frac{dS^{3,k}}{\mathrm{dt}} = -\left((1-\alpha)\lambda_{\mathrm{m}}^{3,\mathrm{k}} + \mu_1 + \nu\right)S^{3,k} + \tau S^{1,1} + \omega S^{2,1} - \delta^{\mathrm{k}} S^{3,2} - \omega_k S^{3,k}$$

$$\frac{dP^{3,k}}{\mathrm{dt}} = (1-\alpha)\lambda^{3,k} S^{3,k} - (\sigma + \mu_1 + \nu)P^{3,k} + \tau P^{1,1} + \omega P^{2,1} - \delta^{\mathrm{k}} P^{3,2} - \omega_k P^{3,k}$$

$$\frac{dC^{3,k}}{\mathrm{dt}} = \sigma P^{3,1} - (\gamma + \xi + \mu_1 + \nu)C^{3,k} + \tau C^{1,1} + \omega C^{2,1} - \delta^{\mathrm{k}} C^{3,2} - \omega_k C^{3,k}$$

$$\frac{dD^{3,k}}{\mathrm{dt}} = \gamma C^{3,k} - (\xi + \mu_1 + \mu_3 + \nu)D^{3,k} + \tau D^{1,1} + \omega D^{2,1} - \delta^{\mathrm{k}} D^{3,2} - \omega_k D^{3,k}$$

$$\frac{dH^{3,k}}{\mathrm{dt}} = \xi(C^{3,k} + D^{3,k}) - (\mu_1 + \mu_4 + \nu)H^{3,k} + \tau H^{1,1} + \omega H^{2,1} - \delta^{\mathrm{k}} H^{3,2} - \omega_k H^{3,k}$$

PWID with **two incarcerations (n=4, k>1)**:

$$\frac{dS^{4,k}}{\mathrm{dt}} = -\left((1-\alpha)\lambda_{\mathrm{m}}^{4,\mathrm{k}} + \mu_1 + \nu\right)S^{4,k} + \omega_k S^{3,k} - \delta^{\mathrm{k}} S^{4,2} - \omega_k S^{4,k}$$

$$\frac{dP^{4,k}}{\mathrm{dt}} = (1-\alpha)\lambda^{4,k} S^{4,k} - (\sigma + \mu_1 + \nu)P^{4,k} + \omega_k P^{3,k} - \delta^{\mathrm{k}} P^{4,2} - \omega_k P^{4,k}$$

$$\frac{dC^{4,k}}{\mathrm{dt}} = \sigma P^{4,1} - (\gamma + \xi + \mu_1 + \nu)C^{4,k} + \omega_k C^{3,k} - \delta^{\mathrm{k}} C^{4,2} - \omega_k C^{4,k}$$

$$\frac{dD^{4,k}}{\mathrm{dt}} = \gamma C^{4,k} - (\xi + \mu_1 + \mu_3 + \nu)D^{4,k} + \omega_k D^{3,k} - \delta^{\mathrm{k}} D^{4,2} - \omega_k D^{4,k}$$

$$\frac{dH^{4,k}}{\mathrm{dt}} = \xi(C^{4,k} + D^{4,k}) - (\mu_1 + \mu_4 + \nu)H^{4,k} + \omega_k H^{3,k} - \delta^{\mathrm{k}} H^{4,2} - \omega_k H^{4,k}$$

PWID with **three incarcerations (n=5, k>1)**,

$$\frac{dS^{5,k}}{\mathrm{dt}} = -\left((1-\alpha)\lambda_{\mathrm{m}}^{5,\mathrm{k}} + \mu_1 + \nu\right)S^{5,k} + \omega_k S^{4,k} - \delta^{\mathrm{k}} S^{5,2} - \omega_k S^{5,k}$$

$$\frac{dP^{5,k}}{\mathrm{dt}} = (1-\alpha)\lambda^{5,k} S^{5,k} - (\sigma + \mu_1 + \nu)P^{5,k} + \omega_k P^{4,k} - \delta^{\mathrm{k}} P^{5,2} - \omega_k P^{5,k}$$

$$\frac{dC^{5,k}}{\mathrm{dt}} = \sigma P^{5,1} - (\gamma + \xi + \mu_1 + \nu)C^{5,k} + \omega_k C^{4,k} - \delta^{\mathrm{k}} C^{5,2} - \omega_k C^{5,k}$$

$$\frac{dD^{5,k}}{\mathrm{dt}} = \gamma C^{5,k} - (\xi + \mu_1 + \mu_3 + \nu)D^{5,k} + \omega_k D^{4,k} - \delta^{\mathrm{k}} D^{5,2} - \omega_k D^{5,k}$$

$$\frac{dH^{5,k}}{\mathrm{dt}} = \xi(C^{5,k} + D^{5,k}) - (\mu_1 + \mu_4 + \nu)H^{5,k} + \omega_k H^{4,k} - \delta^{\mathrm{k}} H^{5,2} - \omega_k H^{5,k}$$

PWID with **more than three incarcerations (n=6, k>1)**,

$$\frac{dS^{6,k}}{\mathrm{dt}} = -\left((1-\alpha)\lambda_{\mathrm{m}}^{6,\mathrm{k}} + \mu_1 + \nu\right) S^{6,k} + \omega_k S^{5,k} - \delta^{\mathrm{k}} S^{6,2} - \omega_k S^{6,3} - \omega_k S^{6,4}$$

$$\frac{dP^{6,k}}{\mathrm{dt}} = (1-\alpha)\lambda^{6,k} S^{6,k} - (\sigma + \mu_1 + \nu)P^{6,k} + \omega_k P^{5,k} - \delta^{\mathrm{k}} P^{6,2} - \omega_k P^{6,3} - \omega_k P^{6,4}$$

$$\frac{dC^{6,k}}{\mathrm{dt}} = \sigma P^{6,1} - (\gamma + \xi + \mu_1 + \nu)C^{6,k} + \omega_k C^{5,k} - \delta^{\mathrm{k}} C^{6,2} - \omega_k C^{6,3} - \omega_k C^{6,4}$$

$$\frac{dD^{6,k}}{\mathrm{dt}} = \gamma C^{6,k} - (\xi + \mu_1 + \mu_3 + \nu)D^{6,k} + \omega_k D^{5,k} - \delta^{\mathrm{k}} D^{6,2} - \omega_k D^{6,3} - \omega_k D^{6,4}$$

$$\frac{dH^{6,k}}{\mathrm{dt}} = \xi(C^{6,k} + D^{6,k}) - (\mu_1 + \mu_4 + \nu)H^{6,k} + \omega_k H^{5,k} - \delta^{\mathrm{k}} H^{6,2} - \omega_k H^{6,3} - \omega_k H^{6,4}$$

For Former-PWID:

$$\frac{\mathrm{dSF}}{\mathrm{dt}} = \nu \sum_{n=1}^{n=5} \sum_{k=1}^{k=4} S^{n,k} - \mu_2 \mathrm{SF}$$

$$\frac{\mathrm{dPF}}{\mathrm{dt}} = \nu \sum_{n=1}^{n=5} \sum_{k=1}^{k=4} P^{n,k} - (\sigma + \mu_2)\mathrm{PF}$$

$$\frac{\mathrm{dCF}}{\mathrm{dt}} = \nu \sum_{n=1}^{n=5} \sum_{k=1}^{k=4} C^{n,k} + \sigma \mathrm{PF} - (\gamma + \xi + \mu_2)\mathrm{CF}$$

$$\frac{\mathrm{dDF}}{\mathrm{dt}} = \nu \sum_{n=1}^{n=5} \sum_{k=1}^{k=4} D^{n,k} + \gamma \mathrm{CF} - (\xi + \mu_2 + \mu_3)\mathrm{DF}$$

$$\frac{\mathrm{dHF}}{\mathrm{dt}} = \nu \sum_{n=1}^{n=5} \sum_{k=1}^{k=4} H^{n,k} + \xi(\mathrm{CF} + \mathrm{DF}) - (\mu_2 + \mu_4)\mathrm{HF}$$

Force of Infection

Among PWID, baseline force of infection, $\lambda^{n,k}$, is determined by an HCV transmission rate, β, and the proportion of infected PWID. Incarcerated individuals have an elevated risk of acquiring infection associated to parenteral transmission, i.e.,

receptive syringe sharing, specific to their incarceration status. This increased risk is obtained by multiplying the relative risk of receptive syringe sharing associated to each incarceration category, $RR_{n,k}$, by the transmission coefficient (see Supplemental section 2 below for details on the estimation of the relative risks).

For $\lambda^{n,k}$:

$$\lambda^{1,1}=\beta\frac{\Omega^{1,1}+\Omega^{2,1}+\Gamma\Omega^{3,2}+\Gamma\Omega^{4,2}+\mathrm{K}\Omega^{5,2}+\mathrm{K}\Omega^{6,2}+\Theta\Omega^{3,3}+\Theta\Omega^{4,3}+\mathrm{H}\Omega^{5,3}+\mathrm{H}\Omega^{6,3}}{N^{1,1}+N^{2,1}+\Gamma N^{3,2}+\Gamma N^{4,2}+\mathrm{K}N^{5,2}+\mathrm{K}N^{6,2}+\Theta N^{3,3}+\Theta N^{4,3}+\mathrm{H}N^{5,3}+\mathrm{H}N^{6,3}}$$

$$\lambda^{1,1} = \lambda^{1,1}$$

$$\lambda^{2,1} = \lambda^{1,1}$$

$$\lambda^{3,2} = \Gamma\lambda^{1,1}$$

$$\lambda^{4,2} = \Gamma\lambda^{1,1}$$

$$\lambda^{5,2} = \mathrm{K}\lambda^{1,1}$$

$$\lambda^{6,2} = \mathrm{K}\lambda^{1,1}$$

$$\lambda^{3,3} = \Theta\lambda^{1,1}$$

$$\lambda^{4,3} = \Theta\lambda^{1,1}$$

$$\lambda^{5,3} = \mathrm{H}\lambda^{1,1}$$

$$\lambda^{6,3} = \mathrm{H}\lambda^{1,1}$$

Where:

$\Omega^{n,k} = P^{n,k} + \mathrm{C}^{n,k} + \mathrm{D}^{n,k} + \mathrm{H}^{n,k}$ (infected)

$S^{n,k} = S^{n,k}$(susceptible)

$N^{n,k} = \Omega^{n,k} + S^{n,k}$ (total)

2) METVIR transitions table

Table C.1. METAVIR fibrosis stages (annual transitions)			
Parameter	*Point Estimates*	*Ranges/CIs*	*Reference, Source & Comments*
METAVIR F0-F1	0.117	(0.104-0.130)	(12)
METAVIR F1-F2	0.085	(0.075-0.096)	(12)
METAVIR F2-F3	0.120	(0.109-0.133)	(12)
F3 to compensated cirrhosis (CC) [2]	0.116	(0.104-0.129)	(12)
F0-F4 referrer to fibrosis stages. F0-F2 can be associated to mild, F3 to moderate, and F4 to cirrhosis according to the Laennec scoring system (115).			

3) Relative Risks estimation from El Cuete-IV Study

For estimating the incarceration related relative risks that informed our model, we used data from an ongoing community-based cohort study of PWID in Tijuana, Mexico (El Cuete-IV) (8). Between 2011 and 2012 baseline data were collected with follow-up surveys every 6 months. Targeted sampling consisting of street outreach in 10 neighborhoods across Tijuana was used to recruit participants who were 18 years of age or older, had injected drugs in the past month, and were currently living in Tijuana. Trained interviewers collected data on socio-demographics, drug use behaviors, drug treatment experiences, justice involvement, migration history, and drug related harms and health outcomes (32). This study was approved by the Ethics Board at the University of California San Diego and Xochicalco University in Tijuana. All participants provided written informed consent.

a. Incarceration categories

For estimating the elevated risks associated to repeated incarceration and the post-release risk, we included PWID recruited between April 2011 and June 2012 and followed for approximately 54 months (visits 1 through 10). We included only those participants who reported never being incarcerated at baseline to exclude participants who may already have been at increased risk of reincarceration and/or syringe sharing associated with previous incarceration.

The outcome of this study was self-reported receptive syringe sharing in the past 6 months, a dichotomous variable with categories “never” and “ever.” The exposure variable was constructed from combining cumulative number and recency of incarcerations into five categories. We first defined cumulative incarcerations as the number of incarceration events reported by participants over the follow-up period. Then, we defined recency of incarceration as the time elapsed post-release (i.e., number of visits) after a participant had reported being incarcerated. From these variables, specifically for this study, we created five mutually exclusive categories: never incarcerated, 1-2 incarcerations and recently incarcerated (past 6 months [p6m]), 1-2 incarcerations and non-recently incarcerated (more than 6 moths [>6m]), 3-4 incarcerations and recently incarcerated (p6m), and 3-4 incarcerations and non-recently incarcerated (>6m).

To estimate the longitudinal association between our incarceration/post-release categories, we used log-binomial regression with generalized estimating equations (GEE). We specified an exchangeable correlation structure to account for the correlated nature of the repeated measurements among study participants. We chose a log-binomial specification to assure obtaining relative risks instead of odds ratios. However, the log-

binomial regression reported a failed convergence when using a multivariable adjusted model, a common issue with this type of regression (116), so we ran an unadjusted model. Participants with missing observations were incorporated to the analysis using multiple imputation by chained equations (MICE package in R, van Buuren and Groothuis-Oudshoorn (117)). The model outputs are shown in Table C2 below. For further details on El Cuete study, the subsample of PWID, the longitudinal setup, handling of missing data and multiple imputation, construction of the outcome variable, and construction of the cumulative incarceration and post-release variables see Rivera Saldana, Beletsky (82). The categories defined for the exposure variable described were designed exclusively for the present study.

Table C.2. Impact of the Cumulative Incarceration-Recent Release variable on Receptive Syringe sharing (unadjusted log-binomial)

			95% CI		
Category description:	**Category**	**RR**	**Lower**	**Upper**	**p=value**
never incarcerated	0	na	na	na	na
1-2 incarcerations & recently incarcerated	1	1.24	1.05	1.47	0.01
1-2 incarcerations & non-recently incarcerated	2	1.10	0.95	1.27	0.22
>3 incarcerations & recently incarcerated	3	1.42	1.15	1.74	0.001
>3 incarcerations & non-recently incarcerated	4	1.27	0.93	1.72	0.13

b. Impact of Escudo on risk of recent incarceration

To assess the impact of Escudo's time period effect on the risk of recent incarceration (past 6 months) among PWID in Tijuana, we included all PWID recruited to El Cuete between April 2011 and June 2012 and followed for approximately 78 months

(visits 1 through 14). To obtain this risk we used a mixed-effects log-binomial regression with generalized estimating equations assuming an autoregressive (AR1) correlation structure to account for correlated observations across time, with a robust sandwich estimator as the covariance estimator for fixed effects. Comparing the period that spans from the beginning of El Cuete study to the beginning of the Escudo program (2011-2015) with the period after the implementation of Escudo (2016-2017), we estimated the time period relative risk of being recently incarcerated (past 6 months [p6m]) as RR 3.12 (95% CI 2.54-3.84). We then used the inverse of this estimate to include in our model as the reduction in the risk of recent incarceration among PWID derived from the implementation of Escudo (68% [95% CI 61-74%]).

4) Disutility weights for DALY calculations

We obtained the disutility weights associated to HCV-disease sequalae, i.e., decompensated cirrhosis and hepatocellular carcinoma, from the global burden of disease study (109). Disutility weights for compensated cirrhosis were not available so we instead used those for moderate acute episode of infectious disease (109). We also considered disability weights associated to active PWID status using the disability weights reported for moderate to severe heroin and other opioid dependence (109). Additionally, we considered a disutility reduction for PWID on OAT (obtained from Nosyk, Marsh (118)).

5) Sensitivity analysis

Table C.3.
Partial rank correlation coefficients (PRCC)
The results are significant at the 0.05 level (*), the 0.01 level (**) or the 0.001 level (***)

#	Parameter	PRCC	
1	Injection duration (l)	-0.38	***
2	PWID background mortality (mu1)	-0.34	***
3	Reduced risk of death after injection cessation (M)	0.08	**
4	Primary incarceration rate (tau)	0.13	***
5	Reincarceration rate (omega)	0.78	***
6	Proportion who spontaneously clear infection (alpha)	0.05	
7	Annual transition from pre-cirrhosis to CC (sigma)	0.08	*
8	Annual transition from CC to DC (gamma)	0.08	**
9	Annual transition from CC/DC to HCC (xi)	-0.27	***
10	Annual transition from DC to death (mu3)	-0.13	***
11	Annual transition from HCC to death (mu4)	0.01	
12	Elevated risk for PWID incarcerated 1-2 times (p6m) (G1)	0.23	***
13	Elevated risk for PWID incarcerated 1-2 times (>6m) (Th1)	0.46	***
14	Elevated risk for PWID incarcerated 3-4 times (p6m) (K1)	0.19	***
15	Elevated risk for PWID incarcerated 3-4 times (>6m) (H1)	0.86	***
16	Reduced risk of incarceration Escudo	0.27	***
17	Disutility weight from compensate cirrhosis	0.40	***
18	Disutility weight from decompensated cirrhosis	0.26	***
19	Disutility weight from hepatocellular carcinoma	0.01	
20	Disutility weight from active injection drug use	0.1	**

6) Additional plots

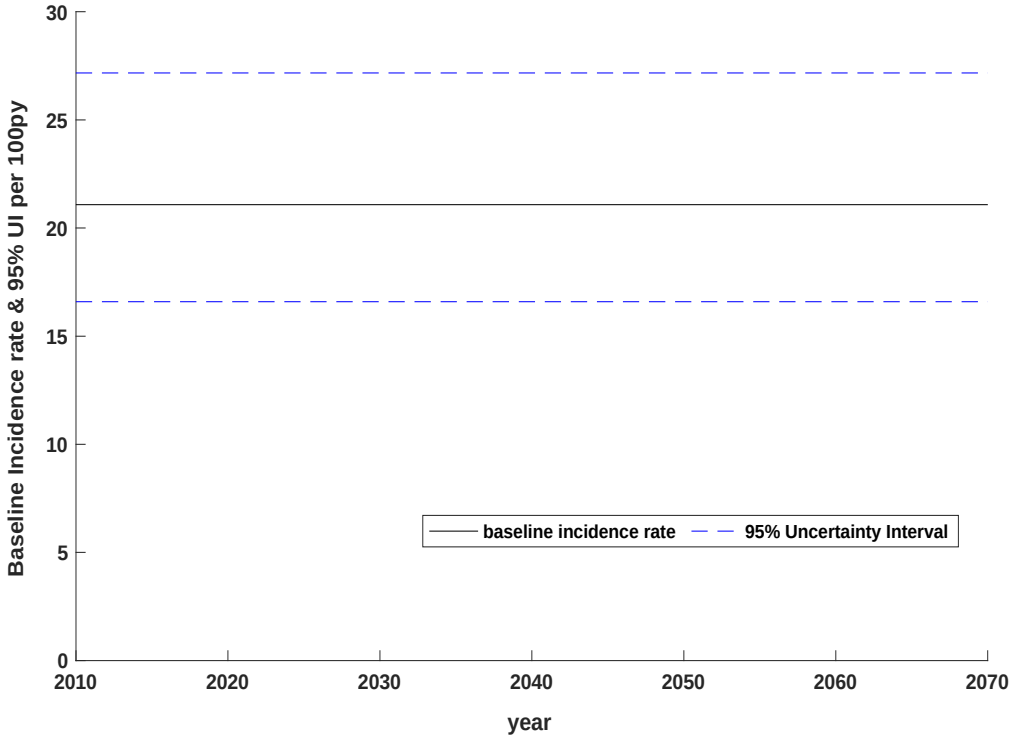


Figure C.1. Baseline (no Escudo) incidence rate projection and 95% uncertainty interval per 100 person-years. UI: uncertainty interval; py: person-years

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