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RESEARCH REPORT

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Estimating the impact of a police education program on hepatitis C virus transmission and disease burden among people who inject drugs in Tijuana, Mexico: A dynamic modeling analysis

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Abstract

Background and aims: Criminalization of drug use and punitive policing are key structural drivers of hepatitis C virus (HCV) risk among people who inject drugs (PWID). A police education program (Proyecto Escudo) delivering training on occupational safety together with drug law content was implemented between 2015 and 2016 in Tijuana, Mexico, to underpin drug law reform implementation. We used data from a longitudinal cohort of PWID in Tijuana to inform epidemic modeling and assess the long-term impact of Escudo on HCV transmission and burden among PWID in Tijuana.

Methods: We developed a dynamic, compartmental 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. We used segmented regression analysis to estimate impact of Escudo on recent incarceration among an observational cohort of PWID. By simulating the observed incarceration trends, we estimated the potential impact of the implemented (2-year reduction in incarceration) and an extended (10-year reduction in incarceration) police education program over a 50-year follow-up (2016–2066) on HCV outcomes (incidence, cirrhosis, HCV-related deaths and disability adjusted life-years averted) compared with no intervention.

Results: Over the 2-year follow-up, Proyecto Escudo reduced HCV incidence among PWID from 21.5 per 100 person years (/100py) (95% uncertainty interval [UI] = 15.3–29.7/100py) in 2016 to 21.1/100py (UI = 15.0–29.1/100py) in 2018. If continued for 10 years, Escudo could reduce HCV incidence to 20.0/100py (14.0–27.8/100py) by 2026 and avert 186 (32–389) new infections, 76 (UI = 12–160) cases of cirrhosis and 32 (5–73) deaths per 10 000 PWID compared with no intervention over a 50-year time horizon.

Natasha K. Martin and Javier Cepeda contributed equally.

Conclusions: In Tijuana, Mexico, implementation of a police education program delivering training on occupational safety and drug law content appears to have reduced hepatitis C virus incidence among people who inject drugs.

KEYWORDS
Epidemic modelling, HCV, incarceration, police education, PWID, Tijuana

INTRODUCTION

Globally, the burden of hepatitis C virus (HCV) infection continues to rise [1]. 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 [2].

Punitive drug laws and their enforcement have been identified as key structural drivers of HCV and HIV transmission among PWID [3–8]. For example, fear of arrest because of syringe possession may disrupt safe injecting practices [9–12]. Additionally, the justice involvement continuum (detention, incarceration and post-release) represents a period of elevated injecting risks characterized by disruption of harm reduction services and increased risks of syringe sharing [8, 13–16]. A global 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 [7]. 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) [7].

Tijuana, Mexico, is a border city situated along a major trafficking route to the United States (US). Approximately 80% of PWID in this region have a history of drug-related arrests and incarceration [17], 90% HCV seroprevalence in 2018 [18, 19] and HIV prevalence was 4% in 2008 [20, 21]. Among PWID in Tijuana both recent incarceration and number of incarcerations were associated with increased risk of receptive syringe sharing [22]. Moreover, previous modeling among PWID in Tijuana found that incarceration will contribute to 5.4% (95% CI = 0.6%–11.9%) of new HCV infections between 2022 and 2032 [23] and 7% (95% CI = 3%–14%) of new HIV infections between 2018 and 2030 [24]. Conversely, police encounters with PWID can serve as an opportunity to deflect away from the justice system and link to harm reduction services [5].

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 [25]. Previous modeling found that the drug laws had minimal impact on averting HIV, likely because of poor implementation from police [24]. To improve implementation of the Narcomendeo reforms, US-based investigators collaborated with the Tijuana Police Department to deliver a police education program (PEP), "Proyecto Escudo" ("Project Shield"), which aimed at reducing police occupational needlestick injury and concomitantly, reducing police encounters as a driver of blood borne infections (BBI) among PWID [5, 6, 26, 27]. Earlier work found a promising impact of Escudo in improvements in officer knowledge and attitudes toward addiction and PWID [26, 28] including reductions in self-reported arrests of individuals for drug-related crimes [5, 29]. However, the potential spill over impact of the PEP 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 impact of the Escudo program on HCV incidence, disease burden and mortality. This work will inform policymaking involving criminalization of drug use and how PEPs may contribute toward HCV elimination among PWID in Mexico.

METHODS

Model description

We developed a 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 and 2; model equations in Supporting information). 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 susceptible PWID become infected at a 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. no backward movement from a later state to an earlier one) [30]. Progression through HCV disease stages continues for infected PWID who have permanently cessated from injecting.

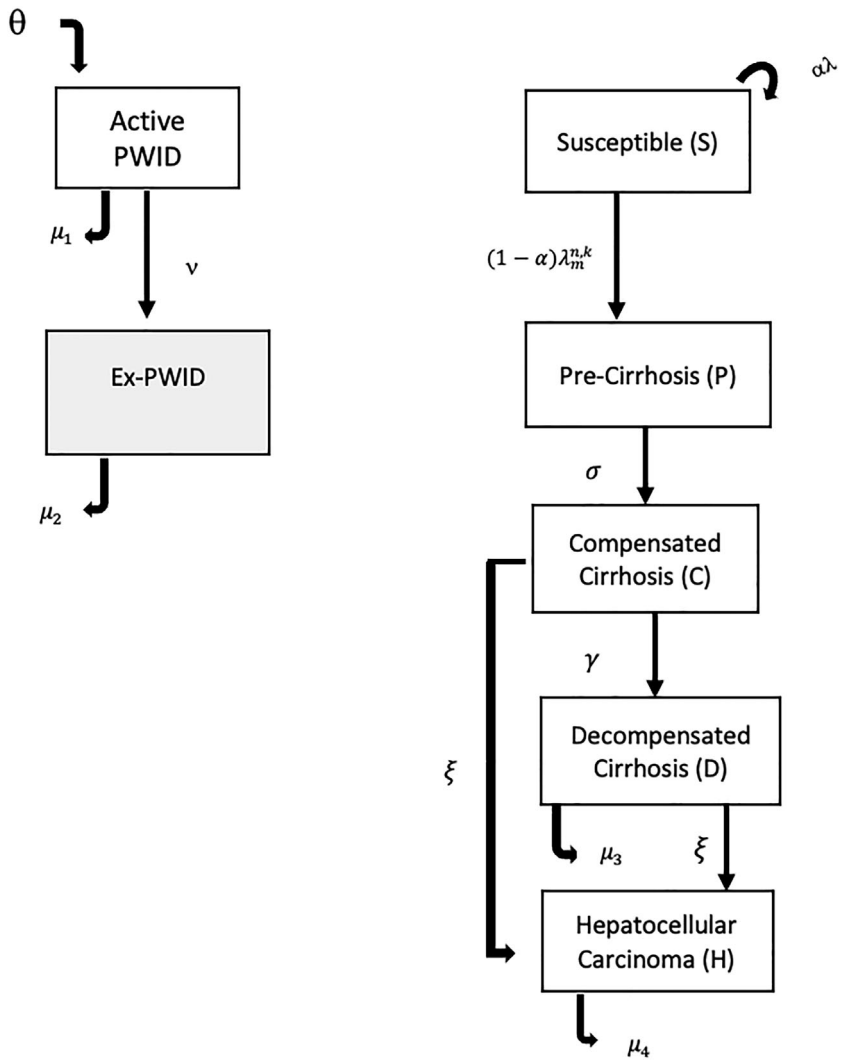

FIGURE 1 Hepatitis C virus transmission and disease progression model schematic among people who inject drugs (PWID) and ex-PWID. Boxes represent disease stages and arrows represent transitions.

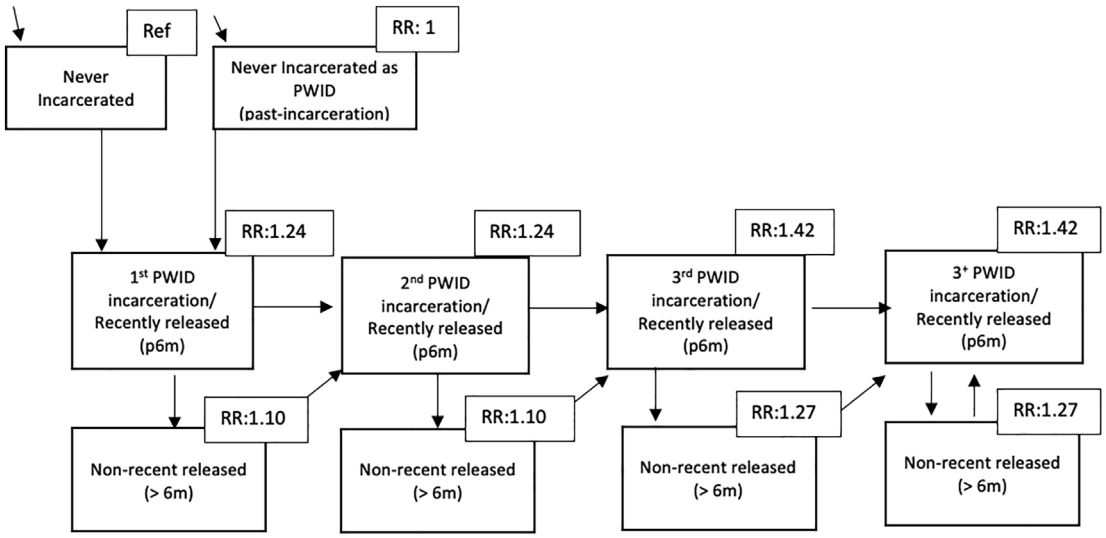

FIGURE 2 Incarceration submodel schematic among people who inject drugs (PWID) and relative risks (RR) of hepatitis C virus (HCV) transmission for each stage compared to a referent group of never incarcerated.

Incarceration dynamics

New PWID enter the model as uninfected, with a proportion having a history of incarceration before injection initiation. PWID become incarcerated/re-incarcerated at constant rates based on local cohort data [24]. We simulate elevated risks associated with new incarcerations as a PWID (no elevated risk among those with a history of incarceration before becoming a PWID). The model tracks both number of incarcerations as a PWID as well as recency of incarceration (Figure 2), with elevated risks of syringe sharing associated with these factors [22].

Model parameters

Parameters for the full model are shown in Table 1. The model was parameterized to Tijuana, Mexico, to a simulated cohort of 10 000 current PWID. Current PWID population size estimates are unknown, with a 2005 study estimating 10 000 PWID [31]. We, therefore, present all results as per 10 000 PWID. We calculated a 67% chronic HCV prevalence based on a 90% HCV seroprevalence among PWID in Tijuana in 2018 obtained from Fleiz-Bautista et al. [18] and a 26% spontaneous clearance rate obtained from Micallef et al. [33] Incarceration, background mortality and injecting behavior parameters were obtained from the El Cuete IV study, a prospective, observational study among PWID in Tijuana, Mexico (approved by ethics boards at University of California San Diego and Xochicalco University in Tijuana, study details in Supporting information) [24, 32, 39]. HCV disease progression rates were obtained from published literature [34, 36, 40, 41] (see Table 1 and Table S1).

Statistical analyses

Risk of receptive syringe sharing after repeated incarceration

Our model assumed that previously incarcerated individuals had an elevated risk of syringe sharing (Table 1), specific to their incarceration history (frequency and recency). Among participants with no history of incarceration at baseline, we assessed the association between incarceration and receptive syringe sharing over time (~4.5 years of follow-up). 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 as a PWID (reference category); 1 to 2 incarcerations as PWID and recently incarcerated (past 6 months [p6m]) (RR = 1.24, 95% CI = 1.05–1.47); 1 to 2 incarcerations as PWID and non-recently incarcerated (more than 6 months [>6 m]) (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 (>6 m) (RR = 1.27, 95% CI = 0.93–1.72). See Table S2 in Supporting information. We incorporated these relative risks as parameters in our model as multipliers on the HCV transmission risk along the incarceration and post-release stages (Table 1).

Impact of Escudo on incarceration among PWID

As detailed in a companion publication Cepeda et al. (under review), we assessed the impact of Escudo on incarceration among PWID in El Cuete using segmented regression analysis to model the linear trends in the log-risk of incarceration over the pre-Escudo (March 2012–March 2015) and post-Escudo (June 2016–March 2019) periods, using 3-month periods. As officers were trained from March 2015 to May 2016, we excluded these periods. The primary outcome was PWID-reported incarceration (jail or prison) in the past 6 months. To generate a mean log-risk for each period, we conducted log-binomial regression with an autoregressive correlation structure to model incarceration adjusting for the following covariates: calendar period, gender, receptive syringe sharing in the past 6 months and an indicator for the change in the ruling party of the local government that occurred in November 2016, which could have influenced street-level policing practices. We, then, fit a segmented regression with a first order autoregressive term to adjust for autocorrelation. We found a significant reduction in the incarceration risk trend of the entire post-Escudo period compared to pre-Escudo period (Table S4). In this simulation model, the observed decreasing trend was best captured through implementing an exponential decay function multiplied by the risk of incarceration and reincarceration post-Escudo. Using the results from the segmented regression analysis, we determined the exponential decay rate that matched the segmented regression analysis results at 2 years, which was used for simulating the Escudo intervention effect (see Figure 3 for model fit, and Supporting information for additional detail).

Model calibration

To introduce uncertainty in the input model parameters, we assigned distributions (empirical or theoretically derived) appropriate for each parameter and randomly sampled 5000 parameter sets (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 [18, 19]. 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 5000 model fits. Calibrated model fit to observed HCV chronic prevalence data shown in Figure S1 and to observed proportion of recently incarcerated individuals from a cohort of PWID in Tijuana between 2011 and 2017 [22] in Figure S2.

Model analyses and scenarios

We simulate the following scenarios:

TABLE 1 Parameters used in the model their sampling distributions.

Parameter (unit)	Symbol	Sampled parameter, mean and 95% CI	Sampling distribution	Source and comments
Rate of new PWID initiations (per year)	θ	Calculated to ensure 10 000 PWID		Scaled to a constant PWID population size of 10 000 as estimated in Magis-Rodriguez et al. [31]
Proportion of individuals with a history of incarceration before entering the model	*propHist*	0.8		[24]
Average duration of injecting until permanent cessation (years)	I	17.43 (11.3–23.6)	Uniform (min = 11, max = 24)	[24]
Rate at which PWID stop injecting (per year)	ν	0.0574 (0.0885–0.0424)		Calculated as 1/average duration of injecting until permanent cessation
Mortality rate among PWID (per year)	μ1	0.0394 (0.0280–0.0520)	Poisson (0.040)	Sampled from Poisson distribution of expected number of deaths per 1000 person years in West et al. [32], then divided by 1000 to calculate mortality rate
Relative risk reduction of mortality among PWID who cease injecting	M	0.2486 (0.1780–0.3457)	Lognormal (aHR = 0.25, 95% CI = 0.33–0.79)	Based on reduced risk of mortality among PWID who had cessated in West et al. [32]
Mortality rate for former PWID (per year)	μ2	0.0296 (0.023–0.034)		Calculated as μ2 = μ1*(1-M)
Rate at which never incarcerated PWID become primarily incarcerated (per year)	τ	0.0265 (0.0020–0.0508)	Uniform (min = 0.0007, max = 0.052)	Weighted average for 85% males and 15% females of fitted values reported in Borquez et al. [24]
Reincarceration rate (per year)	ω	0.2340 (0.0580–0.4108)	Uniform (min = 0.047, max = 0.42)	Weighted average for 85% males and 15% females of fitted values reported in Borquez et al. [24]
Rate PWID transition from recently released (p6m) to non-recent released (>6 m)	δ	2		Defined by the duration of time in the recent incarceration compartment (6 months) 12 m/6 m = 2
HCV seroprevalence	o	0.908 (0.857–0.949)	Beta (alpha = 141.74, beta = 14.48)	Sampled from a Beta distribution generated from data in Fleiz-Bautista et al. [18]
Proportion of PWID who clear infection	α	0.2608 (0.2289–0.2946)	Beta (alpha = 176, beta = 499)	Micallef et al. [33]
Chronic prevalence	P	0.671 (0.624–0.715)		P = o*(1-α)
Disease transition rate from pre-cirrhosis to CC (per year)	σ	0.0270 (0.0254–0.0286)	Normal (mean = 0.027, SD = 0.0008)	Calculated from Metavir scores (F0 to F4) reported in Thein et al. [34] (see Table S1)
Transition probability from CC to DC (per year)	γ	0.0390 (0.0218–0.0608)	Beta (alpha = 14.6168, beta = 360.1732)	Beta distribution parameters from Martin et al. [35] based on Fattovich et al. [36]
Disease transition probability from CC/DC to HCC (per year)	ξ	0.0139 (0.0017–0.0399)	Beta (alpha = 1.9326, beta = 136.1074)	Beta distribution parameters from Martin et al.[35] based on Fattovich et al. [36]
Disease transition probability from DC to death (per year)[b]	μ_3	0.1325 (0.1003–0.1686)	Beta (alpha = 51, beta = 333)	Fattovich et al. [36]
Disease transition probability from HCC to death (per year)	μ_4	0.4292 (0.3710–0.4883)	Beta (alpha = 117.1033, beta = 155.23)	Beta distribution parameters from Martin et al. [35] based on Fattovich et al. [36]
Elevated risk of syringe sharing for PWID reporting 1–2 incarceration events and released within p6m vs never incarcerated		1.2405 (1.0531–1.4649)	Lognormal (mean = 0.2151, SD = 0.0858)[a]	Calculated from El Cuete IV

(Continues)

TABLE 1 (Continued)

Parameter (unit)	Symbol	Sampled parameter, mean and 95% CI	Sampling distribution	Source and comments
Elevated risk of syringe sharing for PWID reporting 1–2 incarceration events and non-recently released vs never incarcerated		1.1005 (0.9540–1.2713)	Lognormal (mean = 0.0953, SD = 0.0741)[a]	Calculated from from El Cuete IV
Elevated risk of syringe sharing for PWID reporting >3 incarceration events and recently released vs never incarcerated		1.4229 (1.1565–1.7505)	Lognormal (mean = 0.3507, SD = 0.1056)[a]	Calculated from from El Cuete IV
Elevated risk of syringe sharing for PWID reporting >3 incarceration events and non-recently released vs never incarcerated		1.2675 (0.9292–1.7386)	Lognormal (mean = 0.2390, SD = 0.1569)[a]	Calculated from from El Cuete IV
Decay constant for Escudo's effect	*decaycte*	1.4961 (0.7862–2.3987)	gamma (shape = 12.45, scale = 0.1204)	Used as the constant term in an exponential decay function to simulate Escudo's effect over time based on segmented regression (see Supporting information)
Disability weight for death		1.0		[37]
Disability weight for CC		0.051		No estimate for CC used moderate infectious disease acute episode [38]
Disability weight for DC		0.178		[38]
Disability weight for HCC		0.569		[38]

Abbreviations: aHR, adjusted hazard ratio; CC, compensated cirrhosis; DC, decompensated cirrhosis; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; max, maximum; min, minimum; PWID, people who inject drugs.

[a]Lognormal distribution transformed to normal distribution for sampling, then back to log scale.

[b]Disease transition probabilities converted to instantaneous rates for the model.

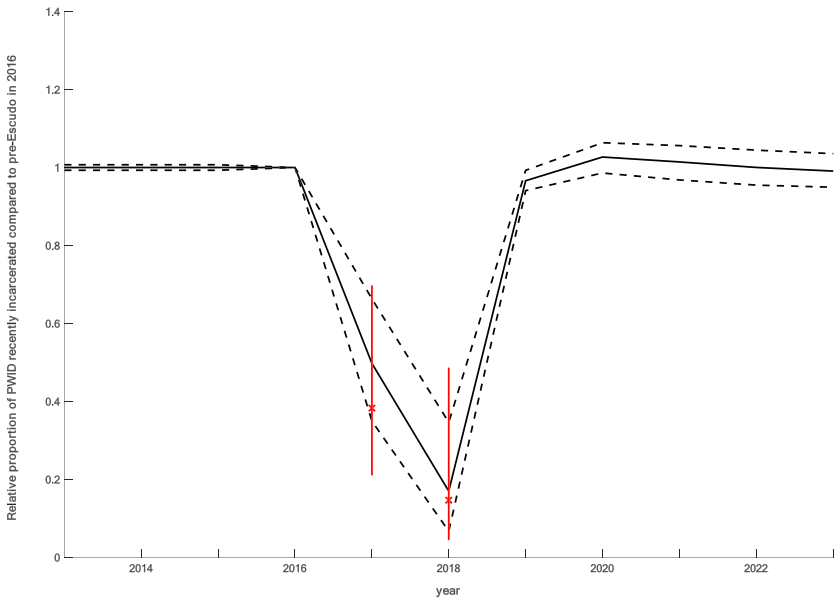

FIGURE 3 Model fit to segmented regression analysis trend in relative proportion of people who inject drugs (PWID) recently incarcerated in the 2 years after Escudo compared to pre-Escudo in 2016. Solid line presents the mean projections with dashed lines representing the 95% CI projections. Red crosses represent the predicted trends after 1 and 2 years of Escudo implementation from the segmented regression analysis, with vertical lines representing the 95% CI of the data.

- No Escudo (counterfactual): extending historical rates of incarceration and reincarceration from 2016 onward
- Baseline Escudo (2 years observed): reductions in rates of incarceration and reincarceration from 2016 to 2018 as obtained from the segmented regression analysis trends (implemented via an exponential decay) and then back to pre-Escudo rates after 2018
- 10 year Escudo: hypothetically extending Escudo's intervention effect through reductions in rates of incarceration and reincarceration from 2016 to 2026 (assuming continual decay obtained via

segmented regression trends) and then back to pre-Escudo rates after 2026.

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]) per 10 000 PWID. We simulated impact of the above scenarios across 2, 10 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.

Sensitivity analyses

We calculated partial rank correlation coefficients (PRCC) to assess the sensitivity of the outcome (DALYs averted in our 10 year Escudo scenario compared to no Escudo) to parameters uncertainty [42, 43]. PRCC captures the independent effects between each input parameter and an outcome variable while keeping all other parameters constant [44]. We additionally conducted a sensitivity analysis of the impact of Escudo implementation scenarios over a 20-year time horizon.

This analysis was not pre-registered, and results should be considered exploratory.

RESULTS

Status quo model projections

At the time of Escudo implementation in 2016, we estimated a stable HCV incidence rate of 21.5 per 100 person years (/100py) (95% uncertainty interval [UI] = 15.3–29.7/100py) among PWID in Tijuana (Figure S3).

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 21.5/100py (UI = 15.3–29.7/100py) in 2016 to 21.1/100py (UI = 15.0–29.1/100py) in 2018 (Figures 4 and 5). This results in averting 12 (UI = 3–25) new infections per 10 000 PWID between 2016 and 2018 (Figure S4). 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 potentially avert a total of 24 (UI = 4–50) new infections per 10 000 PWID (0.07% [UI = 0.01%–0.14%] averted), 9 (UI = 1–20) cases of cirrhosis per 10 000 PWID (0.06% [UI = 0.01%–0.13%] averted), and 4 (UI = 1–10) deaths per 10 000 PWID (0.05% [UI = 0.01–0.11%] averted) (Figure 6) compared to no Escudo. This equates to 111 (UI = 16–258) DALYs averted per 10 000 PWID for the 2-year program, a relative reduction of 0.01% (UI = 0.001–0.02%) compared to no intervention (Figure S5).

Impact of a 10-year implementation of the Escudo program on HCV incidence and disease burden

We estimate that if the effect of Escudo extends to 10-years (2016–2026, through sustained impact or retraining) this could reduce HCV incidence from 21.5/100py (UI = 15.3–29.7/100py) in 2016 to 20.0/100py (UI = 14.0–27.8/100py) in 2026 (Figures 4 and 5). This equates to averting 180 (UI = 34–375) new infections per 10 000 PWID between 2016 and 2026 (Figure S4). Using a 50-year time horizon (2016–2066), a 10-year reduction in incarceration from Escudo

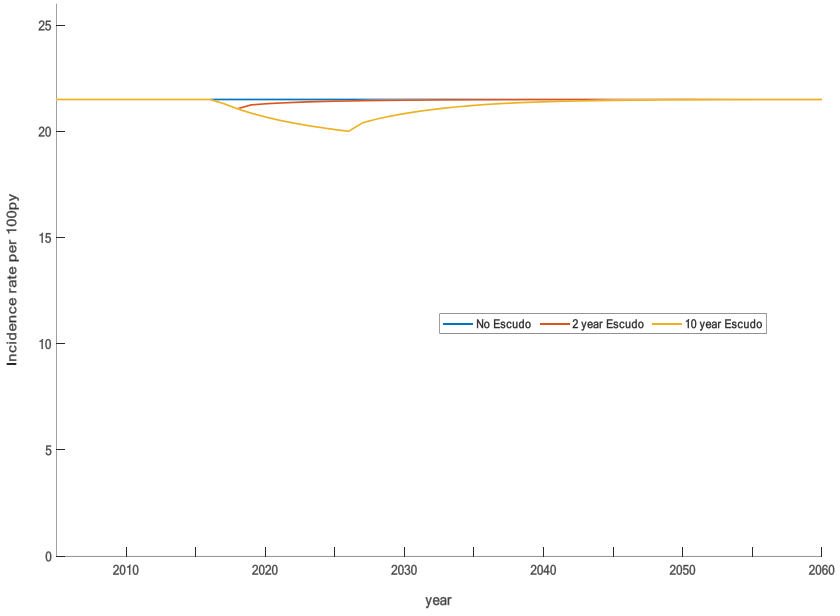

FIGURE 4 Fifty-year trajectory for mean hepatitis C virus (HCV) incidence rate among people who inject drugs (PWID) in Tijuana, Mexico for different Escudo implementation scenarios from 2010 to 2060.

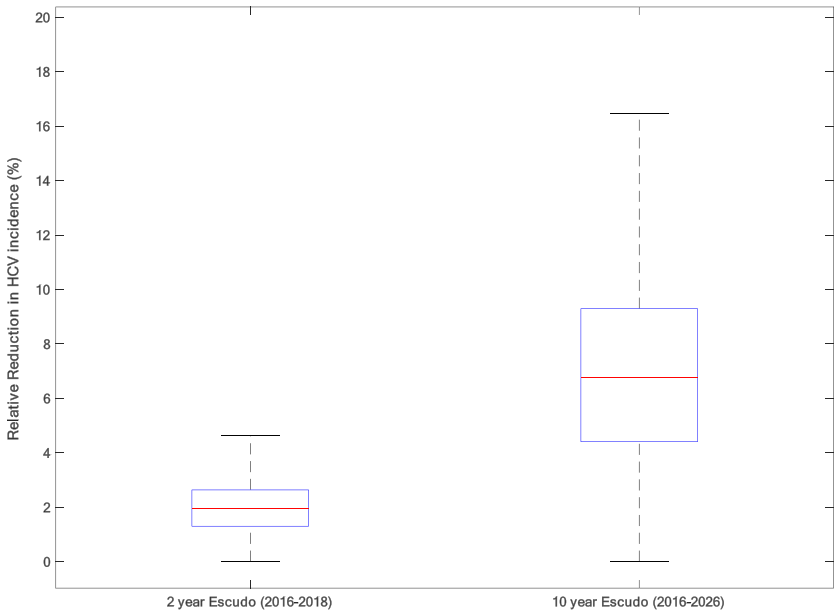

FIGURE 5 Relative reduction in hepatitis C virus (HCV) incidence rate among people who inject drugs (PWID) in Tijuana, Mexico simulating a 2- and 10-year Escudo intervention effect. Lines represent the median estimate, boxes 25%–75% centiles and whiskers 2.5%–97.5% centile projections.

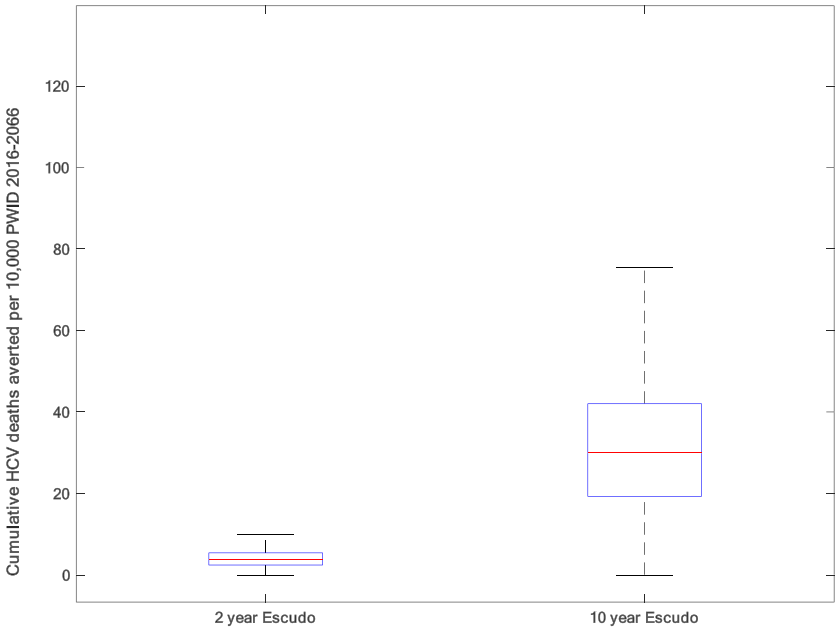

FIGURE 6 Fifty-year impact in cumulative hepatitis C virus (HCV) deaths averted among current and former people who inject drugs (PWID) for each Escudo implementation period, per 10 000 PWID.

could potentially avert a total of 186 (UI = 32–389) new infections per 10 000 PWID (0.5% [UI = 0.09%–1.1%] averted) and 76 (UI = 12–160) cases of cirrhosis per 10 000 PWID (0.5% [UI = 0.08%–1.0%] averted), and 32 (UI = 5–73) deaths per 10 000 PWID (0.4% [UI = 0.07%–0.9%] averted) (Figure 6) compared to no Escudo. This equates to 764 (UI = 130–1720) DALYs averted per 10 000 PWID for the 10-year program, a relative reduction of 0.05% (UI = 0.01%–0.11%) compared to no Escudo (Figure S5).

Sensitivity analysis

Sensitivity analysis revealed the most influential parameters contributing to uncertainty in the DALYs averted were years of injection duration (rho (r) = −0.34, *P*-value (*P*) < 0.001), the reincarceration rate (r = 0.83, *P* < 0.001), elevated risk of 1–2 non-recent incarcerations (r = 0.62, *P* < 0.001), elevated risk of 3 to 4 non-recent incarcerations (r = 0.82, *P* < 0.001). See Figure S6 and Table S3, PRCC and significance levels for all parameters provided in Supporting information. Using a 20 year time horizon, 90% fewer DALYs were averted compared to a 50 year time horizon (Figure S7).

DISCUSSION

We investigated the impact of a PEP, through its estimated 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 associated to Proyecto Escudo could avert 24 (UI = 4–50) new infections, 9 (UI = 1–20) cases of cirrhosis and 4 (UI = 1–10) deaths per 10 000 PWID over 50 years in Tijuana, Mexico. To our knowledge, this is the first modeling analysis evaluating a structural intervention aimed at reducing operational risk from police.

Implications

Incarceration is 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 [23]. However, previous studies on the impact of the Narcomenudeo reform in Tijuana found that gaps in translating formal laws to policing practice may have thwarted expected impacts [26]. 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 toward the health of PWID [5].

Our study indicates that interventions such as PEP should be part of a comprehensive strategy 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 targets. Although the present administration in Mexico has embarked in a national HCV elimination program prioritizing HCV treatment (i.e. direct acting antivirals) to key populations including people with HIV, incarcerated individuals and PWID [45, 46], PWID treatment programs are nascent with significant barriers to health care access observed in this population historically. Moreover, for PWID in Tijuana access to harm reduction, such as OAT [47] and NSP [48], is limited. Given these restrictions, 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 can contribute to enhancing the ability for Mexico to achieve their HCV 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. In this regard, we did not rely on outcomes reported by police, but rather had a chance to estimate impact in a parallel cohort of PWID in Tijuana. Nevertheless, our study is not exempt from limitations. First, although our estimates of intervention effect were derived from a longitudinal study using causal inference methods, we could not definitively confirm a causal relationship between the PEP intervention and incarceration. However, data among police officers who participated in Escudo indicate that knowledge improvement was associated with decreases in drug-related and syringe possession arrests over time [29], supporting plausibility that the intervention was associated with changes in incarceration among PWID. Additionally, even if Escudo reduced incarceration, the duration of the intervention effect is unclear. As such, we simulated a 2-year impact, but it is possible impact could be maintained longer and therefore, our estimates are conservative. Although we additionally simulated 10-year impact that would likely require retraining, is unclear whether retraining could sustain impact.

Second, although based on observational cohort data, we were unable to validate neither our model predictions of impact, nor our estimation of HCV risk by incarceration status. The recent HCV serosurvey among PWID in Tijuana [18] did not ask about incarceration, but if collected in the future could confirm whether there are observed trends in HCV incidence or prevalence stratified by history of incarceration.

Third, there is uncertainty in parameters such as HCV chronic prevalence and duration of injection [49]. We sampled these using wide uncertainty intervals to propagate uncertainty into the projections, but estimates, in particular for chronic HCV, would strengthen future analyses.

Fourth, our model examined benefits related to prevention of post-incarceration risks because of a lack of data on within-prison risks in Tijuana. A recent modeling and data analysis in five countries in Eastern Europe and Central Asia found one country had evidence of increased HIV transmission risk in prison compared to the community, whereas others had decreased risk [50]. Although the frequency of injecting may be low in prison because of restricted access to drugs, syringe sharing is often high [8, 51]. Therefore, it is difficult to assess how the inclusion of this would affect our study's results and characterization of HCV risk in prison compared to the community in Tijuana would allow for further refinement.

Fifth, we assume no HCV treatment among PWID in this study based on our unpublished data among PWID in Tijuana indicating no reports of treatment as of 2019. Mexico's HCV elimination response has focused first on testing and treatment among people with HIV [52]. Only a small fraction of PWID have HIV in Tijuana (4%), and there are high barriers to health care access, with <10% of PWID on Antiretroviral Th (ART) [21]. Further, the coronavirus disease 2019 (COVID-19) pandemic has likely further hampered the delivery of HCV treatment broadly and specifically to PWID [53].

Sixth, 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 [54, 55] or general health services [56], as has been reported for other settings, could have increased HCV transmission.

Finally, there may be additional benefits of PEPs not captured in our analysis. For example, police officers in Tijuana reported modest increases in referrals of PWID to harm reduction [5]. However, important structural barriers to accessing treatment and services, such as

high cost and long distances to the nearest OAT clinic, would need to be addressed to fully exploit Escudo's impact.

CONCLUSION

Among PWID in Tijuana, Mexico, incarceration remains an important contributor to HCV transmission and disease burden. Implementation of Escudo, a PEP, can underpin a public health-oriented drug law reform, through increasing awareness of the health implications of harsh policing among PWID. Our study is important as it shows how Escudo's impact can spill over to reducing HCV among PWID. Cost-effectiveness evaluations, incorporating potential benefits on both HIV and HCV transmission among PWID, are warranted.

AUTHOR CONTRIBUTIONS

Carlos Demian Rivera Saldana: Conceptualization; formal analysis; writing—original draft. **Daniela Abramovitz:** Formal analysis; writing—review and editing. **Leo Beletsky:** Investigation; writing—review and editing. **Annick Borquez:** Writing—review and editing. **Susan M Kiene:** Writing—review and editing. **Lara K. Marquez:** Writing—review and editing. **Thomas Patton:** Writing—review and editing. **Steffanie A Strathdee:** Investigation; writing—review and editing. **Maria Luisa Zuniga:** Writing—review and editing. **Natasha K. Martin:** Conceptualization; formal analysis; supervision; writing—original draft. **Javier Cepeda:** Conceptualization; formal analysis; supervision; writing—original draft.

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DECLARATION OF INTERESTS

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DATA AVAILABILITY STATEMENT

Data sharing not applicable - no new data generated.

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