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Supplementary appendix

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Technical Appendix

Evaluating the impact of public health oriented drug law reform on HIV incidence among people who inject drugs in Tijuana, Mexico: an epidemic modelling analysis.

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The Technical Appendix is divided into 6 main sections. Section 1 provides a table with drugs and thresholds covered under the Mexican drug law reform.
Section 2 provides supporting information on the statistical analyses carried out using data from the El Cuete IV cohort study among people who inject drugs (PWID) in Tijuana to inform the epidemic model parameterization.
Section 3 provides detailed information on the epidemic model including 1) the model structure, 2) representation of HIV transmission, 3) model equations, 4) calibration to prison demography data, 5) calibration to HIV epidemiology data, 6) detail on the HIV/syphilis co-infection epidemic model used to estimate the contribution of sexual transmission to HIV incidence among PWID, 7) description of the epidemic modelling analyses implemented to estimate the impact of the Narcomenudeo reform, 8) sensitivity analysis.
Section 4 provides extracts from qualitative interviews among PWID their experience of compulsory abstinence programs (CAP).
Section 5 provides extracts from qualitative interviews among police officers in Tijuana that contextualize the Narcomenudeo reform implementation (and lack of thereof).
Section 6 provides methodological considerations for a multi-sectoral economic evaluation of drug law reform and a description of data available in Tijuana.

1. Mexican drug law reform drug possession thresholds

Drug	Narcomenudeo possession threshold
Opium	2g
Heroin	50mg
Marijuana	5g
Cocaine	500mg
LSD	0.015mg
MDMA	40mg (powder, granulate, crystal)
	200mg (one unit tablet or caplet)
MDA	40mg (powder, granulate, crystal)
	200mg (one unit tablet or caplet)
Methamphetamine	40mg (powder, granulate, crystal)
	200mg (one unit tablet or caplet)

Table S1. Drugs and thresholds covered under the Narcomenudeo reform.[1] LSD: Lysergic acid diethylamide; MDMA: 3,4-methylenedioxy-methamphetamine; MDA: 3,4-Methylenedioxyamphetamine

2. Statistical analyses informing the mathematical model

To inform the mathematical modeling analysis, we used data from the ongoing El Cuete IV study among 734 PWID in Tijuana, an observational longitudinal cohort which collects data bi-annually on drug-using and sexual behaviors as well as experiences of incarceration, police harassment and access to HIV and harm reduction services since 2011.
Recruitment was carried out using convenience sampling and eligibility criteria were: having injected drugs in the past month, being over 18 years old, speaking Spanish or English, planning to stay in Tijuana for the next two years, being able to provide informed consent to answer a structured questionnaire and to be tested for HIV every 6 months.
The study was approved by the Human Subjects Protections Program of the University of California, San Diego and of the Colegio de la Frontera Norte, Tijuana.

We investigated two exposure variables expected to be affected by the implementation of the Narcomenudeo reform and associated changes in policing: exposure to incarceration and syringe confiscation by the police. Syringe possession is legal in Mexico, and therefore syringe confiscation by the police is a form of harassment. However, police officers are allowed to confiscate syringes during arrests for personal safety, so we restricted the definition to exposure to "syringe confiscation when stopped but not arrested by the police".

2.1. Time trends in recent exposure to syringe confiscation and incarceration

We investigated time trends in the proportion of PWID exposed to either factor in the past 6 months from 2011 to Jan 2016. We stratified the data by 6 month time periods and tested for significant changes in time using mixed effects logistic regression (with subject as a random effect and time period as a fixed effect). The proportion of PWID exposed to recent syringe confiscation by period is shown in **Table S1**. Detail on the odds ratios comparing each period with the previous period is shown in **Figure S1**. A significant decline in exposure to recent syringe confiscation is observed between periods 3 (3/2012-9/2012) and 4 (9/2012-3/2013) ($p<0.01$) and between periods 4(9/2012-3/2013) and 5 (3/2013-9/2013) ($p=0.0036$), with reductions in exposure to syringe confiscation between periods. The decline in exposure continued to reach 0% in period 10 (10/2015-1/2016). No measure of lifetime exposure to syringe confiscation was available from El Cuete IV.

The definition of incarceration changed during the study to differentiate between being held at a detention center (for up to 36 hours), jail or prison (for longer periods) at period 6. We therefore examined trends in recent (past 6 months) exposure to incarceration in any of these facilities through time, as well as incarceration in prison alone (from period 6 onwards) shown in **Tables S2** and S**3**, respectively. Although there are fluctuations between periods, no trend was observed over time (**Figures S2** and S**3**).

	Men	**Women**	**Total**	**p***
Period 1 (03/29/11 to 09/27/11)	n= 302	n= 127	n= 429	NA
	10·6%	10·2%	10·5%	
Period 2 (09/28/11 to 03/28/12	n= 320	n= 211	n= 531	0·111
	7·2%	8·1%	7·5%	
Period 3 (03/29/12 to 19/27/12)	n= 388	n= 221	n= 609	0·271
	7·0%	13·6%	9·4%	
Period 4 (09/28/12 to 03/28/13)	n= 287	n= 197	n= 484	<.0001
	1·4%	5·6%	3·1%	
Period 5 (04/01/13 to 09/27/13)	n= 301	n= 226	n= 527	0·036
	1·0%	1·3%	1·1%	
Period 6 (09/30/13 to 03/28/14)	n= 309	n= 221	n= 530	0·522
	1·0%	0·5%	0·8%	
Period 7 (03/31/14 to 09/29/14)	n= 308	n= 222	n= 530	0·738
	1·0%	0·9%	0·9%	
Period 8 (09/30/14 to 03/31/15)	n= 295	n= 198	n= 493	0·311
	0·3%	0·5%	0·4%	
Period 9 (04/01/15 to 09/30/15)	n= 275	n= 203	n= 478	0·632
	0·4%	1·0%	0·6%	
Period 10 (10/01/15 to 01/18/16)	n= 151	n= 113	n= 264	NA
	0%	0%	0%	

Table S2. Proportion of PWID exposed to recent syringe confiscation by the police through time and *p value of the mixed effects logistic regression testing for the significance of difference with previous period. n is the number of PWID surveyed at each time period.

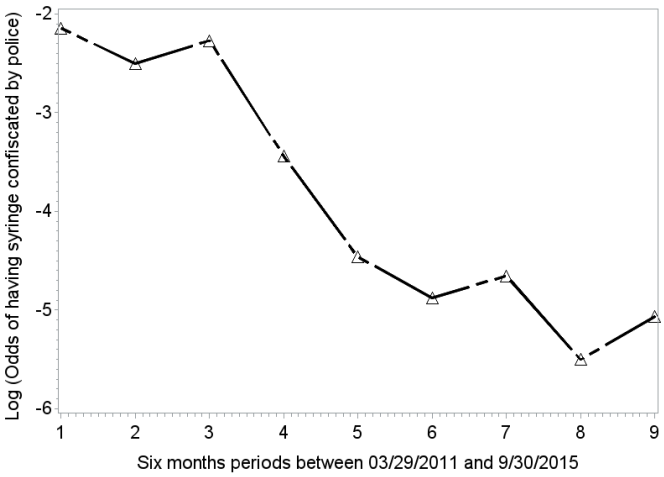

Figure S1. Mixed effect logistic regression for the proportion of PWID in El Cuete IV exposed to recent (previous 6 months) syringe confiscation by the police at each time period compared to the previous period.

	Men	Women	Total	p*
Period 1 (03/29/11 to 09/27/11)	n= 302	n= 127	n= 429	NA
	31·1%	31·5%	31·2%	
Period 2 (09/28/11 to 03/28/12	n= 319	n= 211	n= 530	0·819
	41·1%	18·0%	31·9%	
Period 3 (03/29/12 to 19/27/12)	n= 388	n= 221	n= 609	0·031
	28·9%	22·6%	26·6%	
Period 4 (09/28/12 to 03/28/13)	n= 287	n= 196	n= 483	<·0001
	52·6%	27·6%	42·4%	
Period 5 (04/01/13 to 09/27/13)	n= 299	n= 225	n= 524	<·0001
	37·5%	19·1%	29·6%	
Period 6 (09/30/13 to 03/28/14)	n= 309	n= 221	n= 530	0·088
	29·4%	18·6%	24·9%	
Period 7 (03/31/14 to 09/29/14)	n= 308	(n= 222)	n= 530	0·014
	40·6%	18·5%	31·3%	
Period 8 (09/30/14 to 03/31/15)	n= 295	n= 198	n= 493	0·013
	44·1%	29·3%	38·1%	
Period 9 (04/01/15 to 09/30/15)	n= 275	n= 203	n= 478	0·001
	33·8%	21·2%	28·5%	
Period 10 (10/01/15 to 01/18/16)	n= 151	n= 113	n= 264	0·250
	31·8%	15·9%	25·0%	

Table S3. Proportion of PWID recently incarcerated (previous 6 months) including in detention centers, jails or prisons through time and *p value of the mixed effects logistic regression testing for the significance of difference with previous period

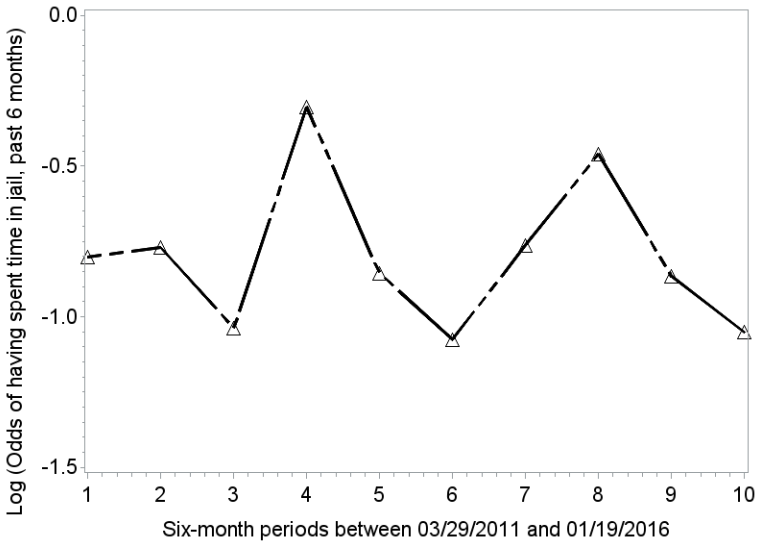

Figure S2. Mixed effect logistic regression for the proportion of PWID in El Cuete IV recently incarcerated in detention centers, jails and prisons at each time period compared to the previous period.

	Men	Women	Total	p*
Period 6 (09/30/13 to 03/28/14)	n= 168	n= 83	n= 251	NA
	9·5%	0·0%	6·4%	
Period 7 (03/31/14 to 09/29/14)	n= 290	n= 172	n= 462	0·950
	8·6%	2·9%	6·5%	
Period 8 (09/30/14 to 03/31/15)	n= 280	n= 186	n= 466	0·187
	5·7%	2·7%	4·5%	
Period 9 (04/01/15 to 09/30/15)	n= 259	n= 194	n= 453	0·947
	6·2%	2·1%	4·4%	
Period 10 (10/01/15 to 01/18/16)	n= 143	n= 107	n= 250	0·122
	9·1%	4·7%	7·2%	

Table S4. Proportion of PWID recently incarcerated in prison through time and *p value of the mixed effects logistic regression testing for the significance of difference with previous period

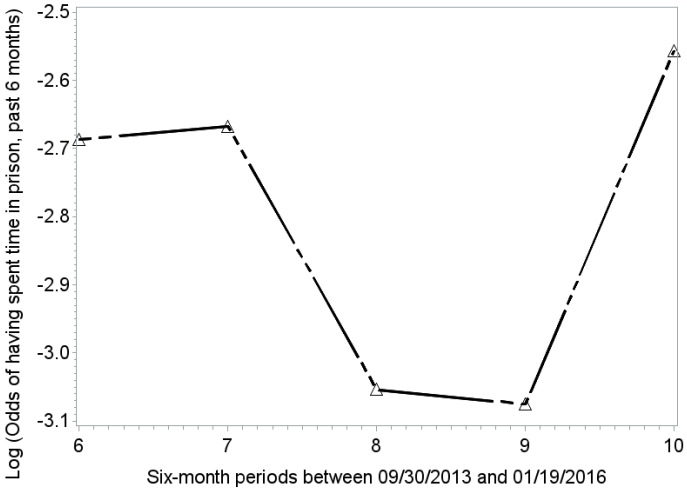

Figure S3. Mixed effect logistic regression for the proportion of PWID in El Cuete IV recently incarcerated in prison at each time period compared to the previous period.

2.2 Associations between exposure to incarceration, syringe confiscation, or compulsory abstinence based programmes (CAP) and HIV risk behaviors

Analyses in other settings have found associations between history of incarceration, and in particular recent incarceration, and increased HIV and HCV prevalence among PWID.[7,8] Among participants to El Cuete III in 2006, incarceration was significantly associated with receptive needle sharing while in prison among those who continued injecting.[9]

Therefore, for this analysis we explored associations between exposure to incarceration by the police in the past 6 months and reported receptive syringe sharing among PWID in Tijuana in 2011. We carried out log-binomial regression analyses using baseline data to estimate the relative risk of receptive syringe sharing in the past 6 months among those exposed to recent incarceration (defined as being released <6 months ago) or non-recent incarceration (released >6 months ago)) versus never incarcerated, controlling for the duration of injection. Significant and borderline significant associations used for the modeling are as follows: in the first 6 months post release, PWID in Tijuana were 1·30 (95% CI: 1·15-1·46, p-value<0·0001) times more likely to share syringes, compared to those never or not recently incarcerated. Changes in risk while in prison were not investigated because data on HIV risk behavior in prison was not available at baseline for El Cuete IV.

Similarly, police harassment has been found to increase HIV risk behaviours in other settings,[10,11] and exposure to recent syringe confiscation by police was associated with elevated HIV prevalence among FSW-IDU in Tijuana.[13]

We carried out log-binomial regression analyses using baseline El Cuete IV data in 2011 to estimate the relative risk of receptive syringe sharing in the past 6 months among exposed to recent syringe confiscation by the police in the past 6 months versus not exposed, controlling for duration of injection. Syringe confiscation in the past 6 months was found to increase the risk of syringe sharing by 1·16 (95%CI: 1·03-1·29, p-value=0.01) compared to not exposed. No association was found between exposure to recent syringe confiscation and incarceration, and no interaction was found on their effect on receptive syringe sharing, therefore we assumed that these mechanisms operate independently.

Studies in East and Southeast Asia, where compulsory drug treatment centres are widespread, have shown that CAP treatment can negatively affect HIV risk and morbidity among PWID through the lack of prevention and treatment services in these centres and through dissuading PWID who have been released from these centres from seeking healthcare for fear of being institutionalised again.[14-16] Given the Narcomenudeo reform mandates drug treatment at the third apprehension and that government investments in Tijuana have so far been allocated to non-evidence based treatment centres (while OAT centres are few and unaffordable for most PWID), it is likely that more PWID will be exposed to CAP if the reform was enforced. We calculated the relative risk of receptive syringe sharing in the past 6 months among ever exposed to CAP versus never exposed. We did not stratify by recent exposure as the number exposed

to CAP at baseline was small (77 participants) and further stratification would have compromised the identification of changes in drug using behaviors due to insufficient power. PWID ever exposed to CAP were 1·14 (95%CI: 1·00-1·30, p-value=0·04) times more likely to engage in receptive syringe sharing compared to those never exposed to CAP.

3. Mathematical modelling

3.1 Model structure

We developed a deterministic compartmental mathematical model of HIV transmission among PWID accounting for parenteral and sexual transmission. The PWID population is disaggregated by sex, by incarceration status, by exposure to syringe confiscation by the police and by HIV status. A model schematic is provided in **Figure S4**.

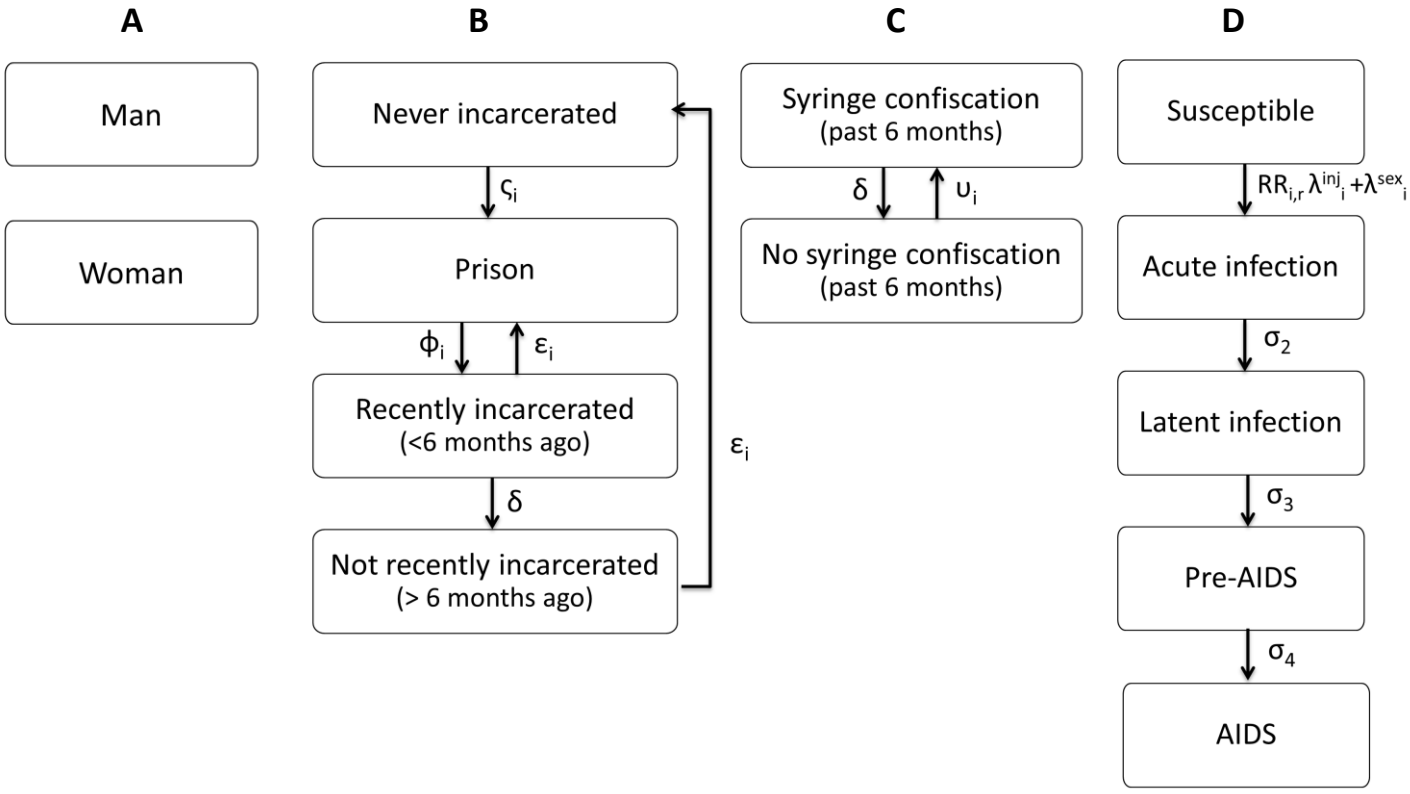

Figure S4. Model diagram showing the disaggregation of the PWID population by A) sex, B) incarceration, C) syringe confiscation and D) HIV status and the flows and corresponding rates between states within each model dimension. *In prison, no syringe confiscation by the police occurs as there is no interaction with the police

Incarceration was disaggregated into four stages: never incarcerated, currently incarcerated, recently released (<6 months ago) and not recently incarcerated (>6 months ago). PWID with a history of incarceration previous to starting injecting entered the "not-recently incarcerated" compartment. Exposure to syringe confiscation was disaggregated into recently exposed (<6 months) and not recently exposed, with PWID entering as non-recently exposed and transitioning between these states. No syringe confiscation was assumed to occur while PWID were currently incarcerated given there is no contact with police in prison.

HIV infection was disaggregated into the following stages: susceptible, acute, latent, pre-AIDS and AIDS. ART was not incorporated in the model given the very low coverage among PWID in Tijuana (<1% of HIV positive participants of El Cuete IV at baseline). An elevated risk of transmission is associated with the acute and pre-AIDS stages due to higher viraemia.[17,18] The PWID population size was assumed to be constant through time given a lack of data to indicate otherwise. The population is replenished by susceptible individuals according to a constant distribution by sex and incarceration history.

3.2 HIV transmission

The model incorporates transmission among PWID through injecting and sexual routes. Parenteral transmission was represented as a function of the number of syringe sharing events per year, the probability of transmission through syringe sharing, the HIV prevalence and HIV stage among men and women injecting partners, assuming random mixing between men and women who inject drugs. Additionally, we include an elevated risk of HIV infection among PWID exposed to recent syringe confiscation and those with a history of recent incarceration to represent the associations with receptive syringe sharing identified through the data analysis. We interpret these data in the model by applying a relative risk to the force of infection among those exposed reflecting an increased frequency of receptive sharing events.

Sexual transmission between PWID was represented as a function of the number of sexual partners per year, sex acts per partner, frequency of condom use, HIV transmission probability by sex act and HIV prevalence among sexual partners for the different types of partners (i.e. stable, casual and commercial). Based on El Cuete IV data indicating that a small fraction of PWID have sexual partners who also are PWID, we also applied an external prevalence corresponding to that of the general population of Tijuana. Prevalence among non-PWID sexual partners was assumed to linearly increase until 2005 and to remain stable thereafter. We assume that all PWID enter as sexually active, given the median age of 20 upon initiation of injecting. We assume incarcerated PWID only share injecting equipment with incarcerated PWID of the same sex, as prisons are segregated by sex in Tijuana. While in prison, we assume that their sexual risk remains the same as among not incarcerated.

3.3 Model equations

The state variables are given by $X_{i,r,s,h}(t)$. *t* is the time elapsed in the simulation; i is the sex (1=men, 2=women), r is the incarceration stage (1=never incarcerated, 2=currently incarcerated, 3=recently incarcerated (<6 months ago), 4=Not recently incarcerated (>6 months ago)), *s* is the syringe confiscation exposure status (1=exposed, 2=not exposed), h is the HIV infection-status (1= susceptible, 2= acute infection, 3= latent infection, 4= pre-AIDS, 5=AIDS). N corresponds to the total population. The equations determining both the infection process and the movement through incarceration and syringe confiscation stages are presented below:

Never incarcerated

$$\frac{dX_{i,1,s,1}(t)}{dt} = k_i(1-g_{i,r})w_{i,s}\left[lN + \sum_i t_i N_i + \sum_{i,r,s,5} s_5 X_{i,r,s,5}\right] - RR_{i,s}^{SC} I_i^{inj} X_{i,1,s,1} - I_i^{sex} X_{i,1,s,1}$$
$$- u_{i,s} X_{i,1,2,1} + d_s X_{i,1,1,1} - (V_i + t_i + l) X_{i,1,s,1}$$

$$\frac{dX_{i,1,s,2}(t)}{dt} = RR_{i,s}^{SC} I_i^{inj} X_{i,1,s,1} + I_i^{sex} X_{i,1,s,1} - u_{i,s} X_{i,1,2,2} + d_s X_{i,1,1,2} - (s_2 + V_i + t_i + l) X_{i,1,s,2}$$

$$\frac{dX_{i,1,s,3}(t)}{dt} = s_2 X_{i,1,s,2} - u_{i,s} X_{i,1,2,3} + d_s X_{i,1,1,3} - (s_3 + V_i + t_i + l) X_{i,1,s,3}$$

$$\frac{dX_{i,1,s,4}(t)}{dt} = s_3 X_{i,1,s,3} - u_{i,s} X_{i,1,2,4} + d_s X_{i,1,1,4} - (s_4 + V_i + t_i + l) X_{i,1,s,4}$$

$$\frac{dX_{i,1,s,5}(t)}{dt} = s_4 X_{i,1,s,4} - u_{i,s} X_{i,1,2,5} + d_s X_{i,1,1,5} - (s_5 + V_i + t_i + l) X_{i,1,s,5}$$

Currently incarcerated

$$\frac{dX_{i,2,s,1}(t)}{dt} = -\lambda_i^{inj,prison} X_{i,2,s,1} - \lambda_i^{sex,prison} X_{i,2,s,1} + \nu_i X_{i,1,s,1} + \varepsilon_i X_{i,3,s,1} + \varepsilon_i X_{i,4,s,1} - (\gamma_i + \tau_i + l) X_{i,2,s,1}$$

$$\frac{dX_{i,2,s,2}(t)}{dt} = \lambda_i^{inj,prison} X_{i,2,s,1} + \lambda_i^{sex,prison} X_{i,2,s,1} + \nu_i X_{i,1,s,2} + \varepsilon_i X_{i,3,s,2} + \varepsilon_i X_{i,4,s,2} - (\sigma_2 + \gamma_i + \tau_i + l) X_{i,2,s,2}$$

$$\frac{dX_{i,2,s,3}(t)}{dt} = \sigma_2 X_{i,2,s,2} + \nu_i X_{i,1,s,3} + \varepsilon_i X_{i,3,s,3} + \varepsilon_i X_{i,4,s,3} - (\sigma_3 + \gamma_i + \tau_i + l) X_{i,2,s,3}$$

$$\frac{dX_{i,2,s,4}(t)}{dt} = \sigma_3 X_{i,2,s,3} + \nu_i X_{i,1,s,4} + \varepsilon_i X_{i,3,s,4} + \varepsilon_i X_{i,4,s,4} - (\sigma_4 + \gamma_i + \tau_i + l) X_{i,2,s,4}$$

$$\frac{dX_{i,2,s,5}(t)}{dt} = \sigma_4 X_{i,2,s,4} + \nu_i X_{i,1,s,5} + \varepsilon_i X_{i,3,s,5} + \varepsilon_i X_{i,4,s,5} - (\sigma_5 + \gamma_i + \tau_i + l) X_{i,2,s,5}$$

Recently incarcerated (<6 months ago)

$$\frac{dX_{i,3,s,1}(t)}{dt} = -RR_{i,s}^{SC} RR_i^{RInc} \lambda_i^{inj} X_{i,3,s,1} - \lambda_i^{sex} X_{i,3,s,1} + \gamma_i X_{i,2,s,1} - u_{i,s} X_{i,3,2,1} + \delta_s X_{i,3,1,1} - (\delta_i + \varepsilon_i + \tau_i + l) X_{i,3,s,1}$$

$$\frac{dX_{i,3,s,2}(t)}{dt} = RR_{i,s}^{SC} RR_i^{RInc} \lambda_i^{inj} X_{i,3,s,1} + \lambda_i^{sex} X_{i,3,s,1} + \gamma_i X_{i,2,s,2} - u_{i,s} X_{i,3,2,2} + \delta_s X_{i,3,1,2} - (\sigma_2 + \delta_i + \varepsilon_i + \tau_i + l) X_{i,3,s,2}$$

$$\frac{dX_{i,3,s,3}(t)}{dt} = \sigma_2 X_{i,3,s,2} + \gamma_i X_{i,2,s,3} + X_{i,4,s,3} - u_{i,s} X_{i,3,2,3} + \delta_s X_{i,3,1,3} - (\sigma_3 + \delta_i + \varepsilon_i + \tau_i + l) X_{i,3,s,3}$$

$$\frac{dX_{i,3,s,4}(t)}{dt} = \sigma_3 X_{i,3,s,3} + \gamma_i X_{i,2,s,4} - u_{i,s} X_{i,3,2,4} + \delta_s X_{i,3,1,4} - (\sigma_4 + \delta_i + \varepsilon_i + \tau_i + l) X_{i,3,s,4}$$

$$\frac{dX_{i,3,s,5}(t)}{dt} = \sigma_4 X_{i,3,s,4} + \gamma_i X_{i,2,s,5} - u_{i,s} X_{i,3,2,5} + \delta_s X_{i,3,1,5} - (\sigma_5 + \delta_i + \varepsilon_i + \tau_i + l) X_{i,3,s,5}$$

Not recently incarcerated (>6 months ago)

$$\frac{dX_{i,4,s,1}(t)}{dt} = \kappa_i \gamma_{i,r} \omega_{i,s} \left[lN + \sum_i \tau_i N_i + \sum_{i,r,s,5} \sigma_5 X_{i,r,s,5} \right] - RR_{i,s}^{SC} RR_i^{NRInc} \lambda_i^{inj} X_{i,4,s,1} - \lambda_i^{sex} X_{i,4,s,1}$$

$$+\delta_i X_{i,3,s,1} - u_{i,s} X_{i,4,2,1} + \delta_s X_{i,4,1,1} - (\varepsilon_i + \tau_i + l) X_{i,4,s,1}$$

$$\frac{dX_{i,4,s,2}(t)}{dt} = RR_{i,s}^{SC} RR_i^{NRInc} \lambda_i^{inj} X_{i,4,s,1} + \lambda_i^{sex} X_{i,4,s,1} + \delta_i X_{i,3,s,2} - u_{i,s} X_{i,4,2,2} + \delta_s X_{i,4,1,2} - (\sigma_2 + \varepsilon_i + \tau_i + l) X_{i,4,s,2}$$

$$\frac{dX_{i,4,s,3}(t)}{dt} = \sigma_2 X_{i,4,s,2} + \delta_i X_{i,3,s,3} + X_{i,4,s,3} - u_{i,s} X_{i,4,2,3} + \delta_s X_{i,4,1,3} - (\sigma_3 + \varepsilon_i + \tau_i + l) X_{i,4,s,3}$$

$$\frac{dX_{i,4,s,4}(t)}{dt} = \sigma_3 X_{i,4,s,3} + \delta_i X_{i,3,s,4} - u_{i,s} X_{i,4,2,4} + \delta_s X_{i,4,1,4} - (\sigma_4 + \varepsilon_i + \tau_i + l) X_{i,4,s,4}$$

$$\frac{dX_{i,4,s,5}(t)}{dt} = \sigma_4 X_{i,4,s,4} + \delta_i X_{i,3,s,5} - u_{i,s} X_{i,4,2,5} + \delta_s X_{i,4,1,5} - (\sigma_5 + \varepsilon_i + \tau_i + l) X_{i,4,s,5}$$

κ_i, $\gamma_{i,r}$ and ω_s designate the distribution of individuals by sex i, by incarceration stage r for each sex i and by syringe confiscation exposure s at entry, respectively. σ is the rate of progression from each disease stage to the next. l is the average mortality rate assumed to be equal among men and women while τ_i is the rate at which individuals stop injecting

by sex. ς_i and ε_i represent the primary incarceration rate among never incarcerated PWID and the re-incarceration rate by sex, respectively. φ_i represents the rate at which individuals exit prison, by sex and δ is the rate at which recently incarcerated individuals progress to the "non-recently incarcerated" stage. $\upsilon_{i,s}$ is the rate at which men and women who inject drugs become exposed to syringe confiscation and δ_s is the rate at which they exit this state. $\upsilon_{i,s}$ is positive when s=2 (no exposure to syringe confiscation) and negative when s=1 (exposure to syringe confiscation) to represent movement between the two compartments. Equally, δ_s is positive when s=1 and negative when s=2.

Parenteral force of infection

Outside prison

$$Wp_i = \frac{b_2 \sum_{s,r=1,3,4} X_{i,r,s,2} + b_3 \sum_{s,r=1,3,4} X_{i,r,s,3} + b_4 \sum_{s,r=1,3,4} X_{i,r,s,4} + b_5 \sum_{s,r=1,3,4} X_{i,r,s,5}}{\sum_{s,r=1,3,4,h} X_{i,r,s,h}}$$

$$I_{i,j}^{inj} = C_i w_{i,j} Wp_j$$

$$I_{i,j}^{inj}(t) = \sum_j I_{i,j}^{inj}$$

In prison

$$Wp_i^{prison} = \frac{b_2 \sum_s X_{i,2,s,2} + b_3 \sum_s X_{i,2,s,3} + b_4 \sum_s X_{i,2,s,4} + b_5 \sum_s X_{i,2,s,5}}{\sum_{s,h} X_{i,2,s,h}}$$

$$I_i^{inj,prison}(t) = C_i w_{i,i} Wp_i^{prison}$$

Sexual force of infection outside and inside prison

$$Wp_i^* = \frac{\beta_2^* \sum_{s,r} X_{i,r,s,2} + \beta_3^* \sum_{s,r} X_{i,r,s,3} + \beta_4^* \sum_{s,r} X_{i,r,s,4} + \beta_5^* \sum_{s,r} X_{i,r,s,5}}{\sum_{s,r,h} X_{i,r,s,h}}$$

$$\lambda_1^{sex} = S_1^{stable} \varpi_{1,2} \left(1 - \left(1 - Wp_2^*\right)^{a^{stable}\left(1-k^{stable}\right)}\right) + S_1^{casual} \varpi_{1,2} \left(1 - \left(1 - Wp_2^*\right)^{a^{casual}\left(1-k^{casual}\right)}\right) + S_1^{com} \varpi_{1,2} \left(1 - \left(1 - Wp_2^*\right)^{a^{com}\left(1-k^{com}\right)}\right)$$
$$+ S_1^{stable}(1-\varpi_{1,2}) \left(1 - (1-P)^{a^{stable}\left(1-k^{stable}\right)}\right) + S_1^{casual}(1-\varpi_{1,1}) \left(1 - (1-P)^{a^{casual}\left(1-k^{casual}\right)}\right) + S_1^{com}(1-\varpi_{1,2}) \left(1 - (1-P)^{a^{com}\left(1-k^{com}\right)}\right)$$

$$\lambda_2^{sex} = S_2^{stable} \varpi_{2,1} \left(1 - \left(1 - Wp_1^*\right)^{a^{stable}\left(1-k^{stable}\right)}\right) + S_2^{casual} \varpi_{2,1} \left(1 - \left(1 - Wp_1^*\right)^{a^{casual}\left(1-k^{casual}\right)}\right) + S_2^{com} \varpi_{2,1} \left(1 - \left(1 - Wp_1^*\right)^{a^{com}\left(1-k^{com}\right)}\right)$$
$$+ S_2^{stable}(1-\varpi_{2,1}) \left(1 - (1-P)^{a^{stable}\left(1-k^{stable}\right)}\right) + S_2^{casual}(1-\varpi_{2,1}) \left(1 - (1-P)^{a^{casual}\left(1-k^{casual}\right)}\right) + S_2^{com}(1-\varpi_{2,1}) \left(1 - (1-P)^{a^{com}\left(1-k^{com}\right)}\right)$$

$I_i^{inj}(t)$ and $I_i^{inj,prison}(t)$ correspond to the rate of infection through parenteral transmission outside prison and in prison, respectively, by sex at time t. Outside prison parenteral transmission is modeled as a function of the number of receptive syringe sharing contacts by sex C_i (calculated as a function of the number of injections per month, the proportion who report any receptive sharing in the past 6 months and the proportion who report receptive sharing at last injection among never incarcerated and not exposed to syringe confiscation in the past 6 months), the proportion of sharing contacts from each sex, w_i , and the weighted HIV prevalence among syringe sharing partners by sex, Wp_i , which accounts for the

differential transmission probability by HIV stage b_s . In prison, we assume syringe sharing contacts are restricted to other PWID in prison and therefore of the same sex.

We model the rate of infection through sexual contact, I_i^{sex} , as a function of the number of sexual partners, S_i, sex acts per partner, a, frequency of condom use, k, with each of the different partner types (stable, casual and commercial) and of the HIV prevalence among sexual partners. A proportion of sexual partnerships happen between PWID, $\varpi_{i,j}$ and the rest happen with sexual partners who are not PWID. When estimating transmission from sexual partners who are PWID, the weighted HIV prevalence by sex, Wp_i^* , which accounts for the differential sexual transmission probability by HIV stage, β_s^* ,is used, and when estimating transmission from sexual partners who are not PWID, the overall HIV prevalence P and the baseline sexual transmission probability β_3^* are used. Sexual transmission is assumed to be exclusively heterosexual for simplicity.

$RR_{i,s}^{SC}$ represents the relative risk of HIV infection through injecting transmission by sex associated with syringe confiscation by the police. RR_i^{RInc} and RR_i^{NRInc} represent the relative risk of HIV infection through injecting transmission by sex associated with recent and non-recent incarceration respectively. There was no significant association between non-recent incarceration and syringe sharing and therefore the latter was set at 1.

Model calibration

We calibrate the model to available data on incarceration patterns and HIV epidemiology among PWID in Tijuana using a two-step process as detailed below.

3.4 Model calibration to prison demography

The primary incarceration rate (i.e. incarceration rate among never incarcerated PWID) and the proportion ever incarcerated among PWID before initiation of injecting were fitted using a simplified closed cohort model of PWID incarceration calibrated to the observed proportion of PWID ever incarcerated by duration of injection (disaggregated as 0-2, 2-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34 and >35 years) by sex as observed in El Cuete IV baseline data (**Figure S6**). This model disaggregated the population by sex and incarceration status (same categories as previously described but not representing HIV transmission or syringe confiscation and not allowing for new entries) and did not account for the differential in risk of HIV among ever and never incarcerated, but given the relatively low HIV prevalence in this population, it is not expected to impact the fitting results. Latin Hypercube Sampling (LHS)[19] was used to sample 10,000 times from the prior distribution of these parameters (determined through manual fitting), and fits within the 95% confidence intervals around the observed data on the proportion of PWID incarcerated by duration of infection were selected. The observed proportion ever incarcerated women who had injected for 30-34 years was low and inconsistent with the proportion ever incarcerated in other age groups, so its standard error was doubled for the fitting. The same was done for the proportion of men who had injected for >35 years. A total of 56 parameter sets fit the observed data, with the mean and 95% CI of the calibrated parameters shown in **Table S5**. These calibrated parameter sets were then used in the HIV transmission model detailed below.

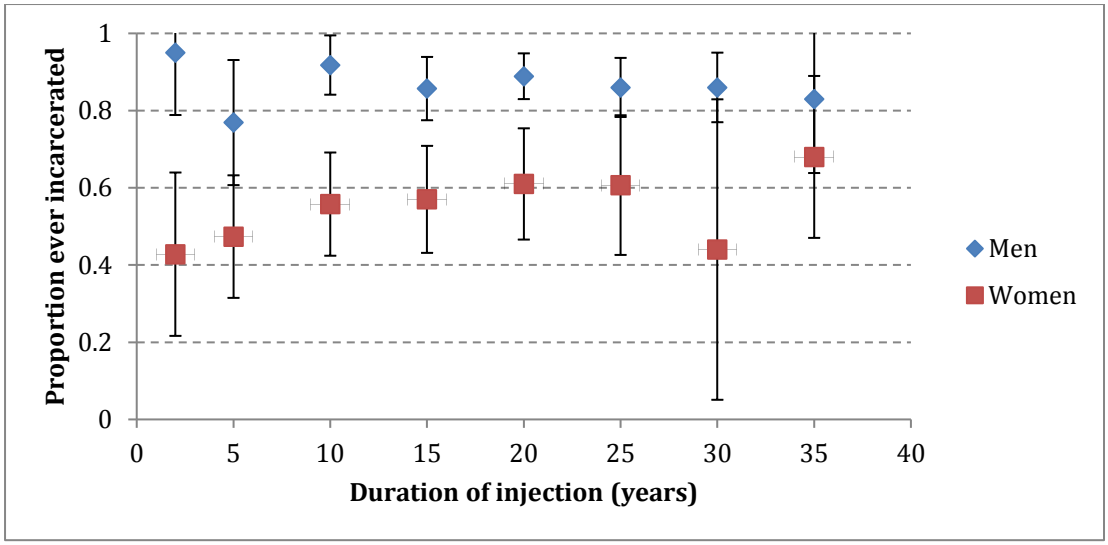

Figure S5. Proportion ever incarcerated among PWID in El Cuete IV cohort at baseline by duration of injection (in years) for men (blue diamonds) and women (red squares). Whiskers indicate the 95% CI of the data.

	Men Mean (95% CrI)	**Women** Mean (95% CrI)
Primary incarceration rate/yr	0·018 (0·0003-0·047)	0.034 (0·001-0·055)
Proportion ever incarcerated before starting injecting	82% (79%-92%)	33% (19%-61%)

Table S5. Incarceration parameters among PWID in Tijuana fitted from the cohort model. Table shows the mean and 95% credible intervals (95% CrI) of the parameters from the calibrated parameter sets.

3.5 Model calibration to HIV epidemiology

We used LHS to sample from the distribution of parameters in **Table S6** and the calibrated parameter sets from the incarceration fitting as detailed in the previous section. We used the beta and log normal distributions to sample values for proportions and relative risks respectively, to reflect their natural distribution; we used the uniform distribution to sample injecting and sexual behaviour parameters to reflect their wider uncertainty and we used the truncated normal distribution to sample incarceration parameters to reflect the data (point estimate and range). We ran 120,000 parameter sets to calibrate the model to HIV prevalence and incidence data from different phases of El Cuete and to the proportion of new infections attributable to sexual transmission in 2006 (as estimated using an HIV/Syphilis co-infection model described in section 2.6). Data used for the calibration are shown in **Table S7**. Exposure to incarceration and syringe confiscation were assumed to remain stable through time at their baseline level but the rates of exposure were allowed to vary in the fitting process to acknowledge uncertainty in the data. We selected runs that predicted an HIV prevalence among all PWID <80% in 2011 (corresponding to 18,668 runs) and we calculated the total log-likelihood as the sum log likelihoods for the proportion of PWID who are men in 2006, the total HIV prevalence in 2005, the HIV prevalence by sex in 2006, the HIV prevalence among ever incarcerated by sex in 2011, the relative HIV prevalence among never versus ever incarcerated by sex in 2011, HIV incidence by sex in 2013 and the proportion of new infections attributable to sexual transmission in 2006, using the beta distribution for the prevalence measures, the normal distribution for the relative prevalence and the contribution of sexual transmission measures and the Poisson distribution for the incidence measure. We resampled parameter sets that had a log likelihood above the 99th percentile and implemented the analyses on those 186 runs. The fit of these resampled runs to the data on HIV prevalence among all PWID, and among PWID by sex and incarceration status is shown in **Figures S6, S7,** and **S8**. The fit of the model to HIV incidence by sex is shown in **Figure S9.** The fit to the contribution of sexual transmission in 2006 is shown in **Figure S10**. The model has a tendency to overestimate HIV prevalence among never incarcerated women but for all other data points, the majority of runs are included in the 95% CI.

Parameters	Symbo	Point Estimate (Sampled Range) Men	Women	Sampling Distribution	Source
Demographic					
Size of PWID population	N	10,000			[20]
Proportion of PWID who are men at entry	κ	0·80 (0·7-0·9)		Beta	[21]
Mean duration of injecting among PWID (years)	τ	12-25	5-20	Uniform	[22]
Mean mortality rate among PWID (/year)	I	0·03			[21]
Rate of exposure to syringe confiscation (/year)	υ	0·26 (0·16-0·36)	0·23 (0·13-0·33)	Truncated normal	[22]
Rate of exiting syringe confiscation exposure (/year)	δ_s	2	2	Fixed	Model definition
Mean rate of exiting prison among PWID (/year)	1/φ	3·1 (0-7)	2·9 (0-7)	Truncated normal	[21]
Rate of exiting recent incarceration (/year)	δ_i	2	2	Fixed	Model definition
Proportion of PWID incarcerated before starting injecting	γ	82% (79%-92%)	33% (19%-61%)	Fitted values	Fitted to El Cuete data using cohort model
Primary incarceration rate (/year)	ς	0·018(0-0·047)	0·034 (0·001-0·055)	Fitted values	
Reincarceration rate (/year)	ε	0·27 (0·08-0·46)	0·2 (0·03-0·40)	Truncated normal	[22]
Behavioural					
Relative risk of receptive syringe sharing among recently released from prison vs not	RR^{RInc}	1·30 (1·15-1·46)		Lognormal	[22]
Relative risk of receptive syringe sharing among recently exposed vs not recently exposed to syringe confiscation by the police	RR^{SC}	1·16 (1·03-1·29)		Lognormal	[22]
Relative risk of receptive syringe sharing among PWID ever vs never exposed to CAP	RR^{InvT}	1·14 (1·00-1·30)		Lognormal	[22]
Relative risk of HIV infection among PWID on OAT	RR^{OAT}	0·46 (0·32%-0·67%)		Logormal	[23]
Rate of OAT cessation (/year)	ϖ	1			[24,25]
Number of sharing events in the past year among PWID baseline (/year)	C	10-472		Uniform	[26]
Number of stable sexual partners (/year)	s^{stable}	0·4-0·5	0·65-0·75	Uniform	[22]
Number of casual sexual partners (/year)	s^{casual}	0-4	0-8	Uniform	[22]
Number of commercial partners (/year)	s^{com}	0-0·5	0-20	Uniform	[22]
Number of sex acts per stable partner(/year)	a^{stable}	25-100		Uniform	[22]
Number of sex acts per casual partner(/year)	a^{casual}	1-25		Uniform	[22]
Number of sex acts per commercial partner(/year)	a^{com}	1-12		Uniform	[22]
Frequency of condom use with stable partner (proportion)	k^{stable}	0·04-0·12		Uniform	[22]
Frequency of condom use with casual partner(proportion)	k^{casual}	0·19-0·31		Uniform	[22]
Frequency of condom use with commercial partner(proportion)	k^{com}	0·24-0·38		Uniform	[22]
HIV prevalence among sexual partners	P	Linear increase to reach 0·5-1% in 2005, stable thereafter		Uniform	[27]

Table S6. Parameters informing the HIV transmission model among PWID in Tijuana.
Parameters in bold were allowed to vary in the model calibration
PWID: people who inject drugs; OAT: opioid agonist treatment

Parameters	Symbol	Point Estimate (Sampled Range) Men	Women	Sampling Distribution	Source
Biological					
Number of HIV positive PWID at the start of the epidemic	seed	4 (2-6)	2(0·5-4)	Truncated normal	Fitted
Average duration of acute HIV stage (months)	σ_2	2·9			[17]
Average duration of latent HIV stage (years)	σ_3	8			[17]
Average duration of pre-AIDS stage (months)	σ_4	9			[17]
Average duration of AIDS stage (months)	σ_5	10			[17]
HIV transmission probability through syringe sharing during the latent stage (/receptive sharing contact)	β_3	0·0001-0·024		Uniform	[28]
HIV transmission probability through sex during the latent stage(/sex act)	β_3^{sex}	0·0006-0·0017		Uniform	
Relative increase in HIV transmission probability compared to latent stage during the:					
Acute stage	RR^{h2}	3-26		Uniform	[17]
PreAIDS stage	RR^{h4}	1-7		Uniform	[17]
AIDS stage	RR^{h5}	0			[17]

Table S6 ctd. Parameters informing the HIV transmission model among PWID in Tijuana.
Parameters in bold were allowed to vary in the model calibration

	Men Point value (95% CI)	Women Point value (95%CI)	Distribution	Source
HIV prevalence among PWID in 2005	2·3% (1%-5·3%)		Beta	[29]
HIV prevalence among PWID in 2006	2·4% (1·3%-3·6%)	5·4% (1·5%-7·8%)	Beta	[21]
HIV prevalence among ever incarcerated PWID in 2011	3·5% (1·7%-5·4%)	5·2% (1·7%-8·8%)	Beta	[22]
Relative HIV prevalence among ever versus never incarcerated PWID in 2011	1·1 (0·3-4·7)	3·2 (0·7-15)	Normal	[22]
HIV incidence among PWID in 2014 (/100 pyar)	0·5 (0·06-0·9)	1·1 (0·3-1·8)	Poisson	[22]
Proportion of new infections attributable to sexual transmission in 2006	0·45 (0·3-0·6)		Normal	HIV/Syphilis model

Table S7. HIV prevalence and incidence data used to calibrate the HIV transmission model among PWID in Tijuana PWID: people who inject drugs; CI: confidence intervals

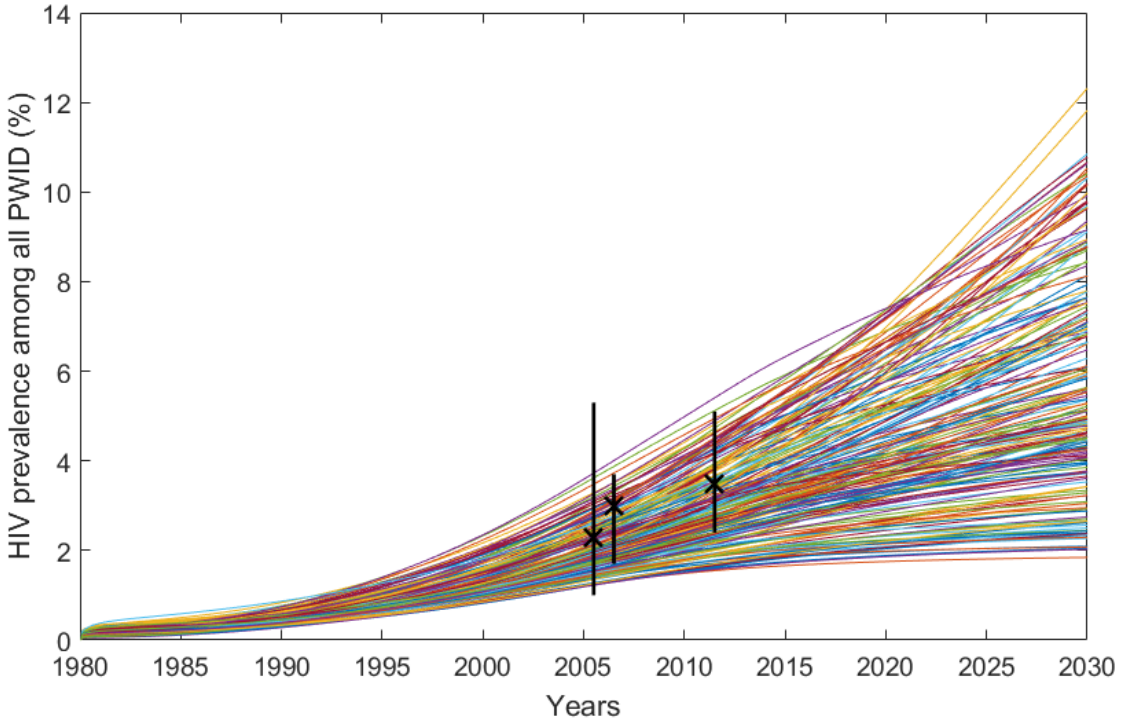

Figure S6. Model fits of HIV prevalence among all PWID compared to data from El Cuete II, III and IV (crosses represent the point estimate and whiskers the 95%CI)

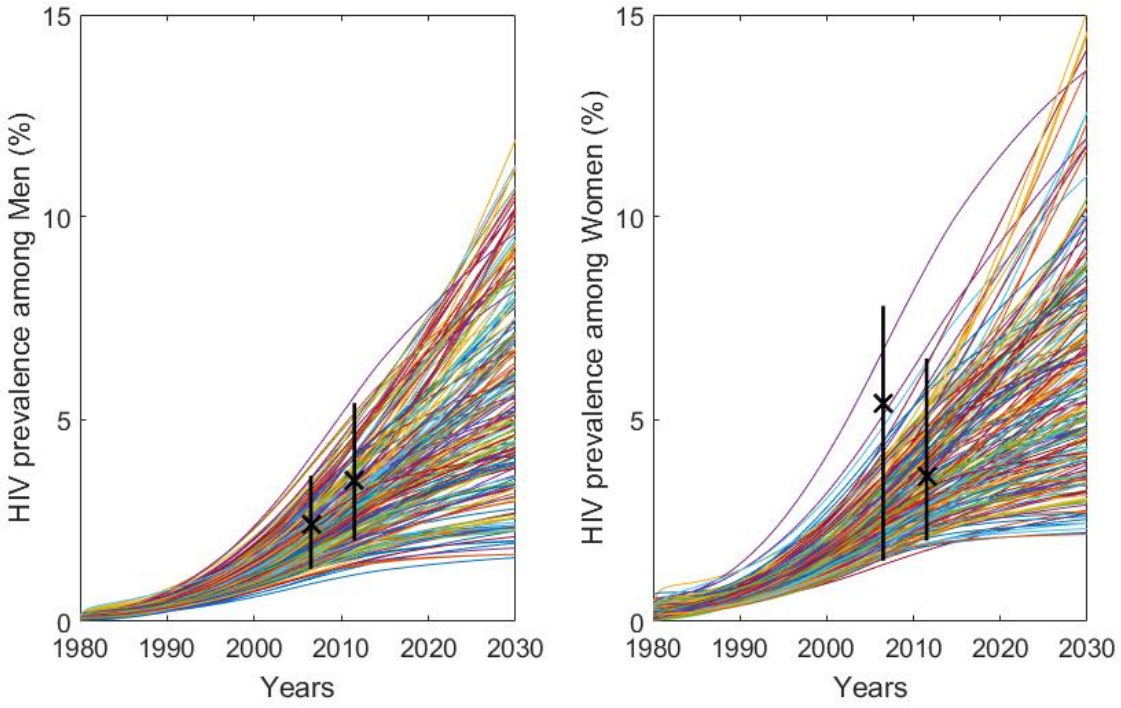

Figure S7. Model fits of HIV prevalence among men and women who inject drugs compared to data from El Cuete III and IV (crosses represent the point estimate and whiskers the 95%CI)

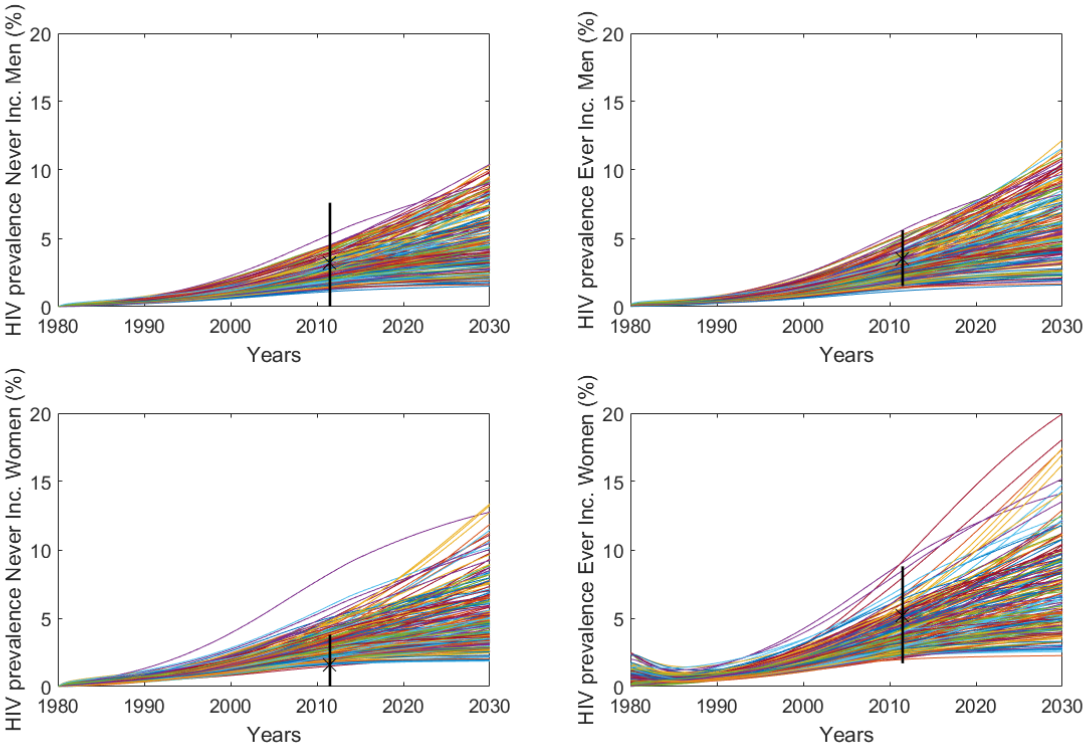

Figure S8. Model fits of HIV prevalence among never and ever incarcerated men and women who inject drugs compared to data from El Cuete IV (crosses represent the point estimate and whiskers the 95%CI)

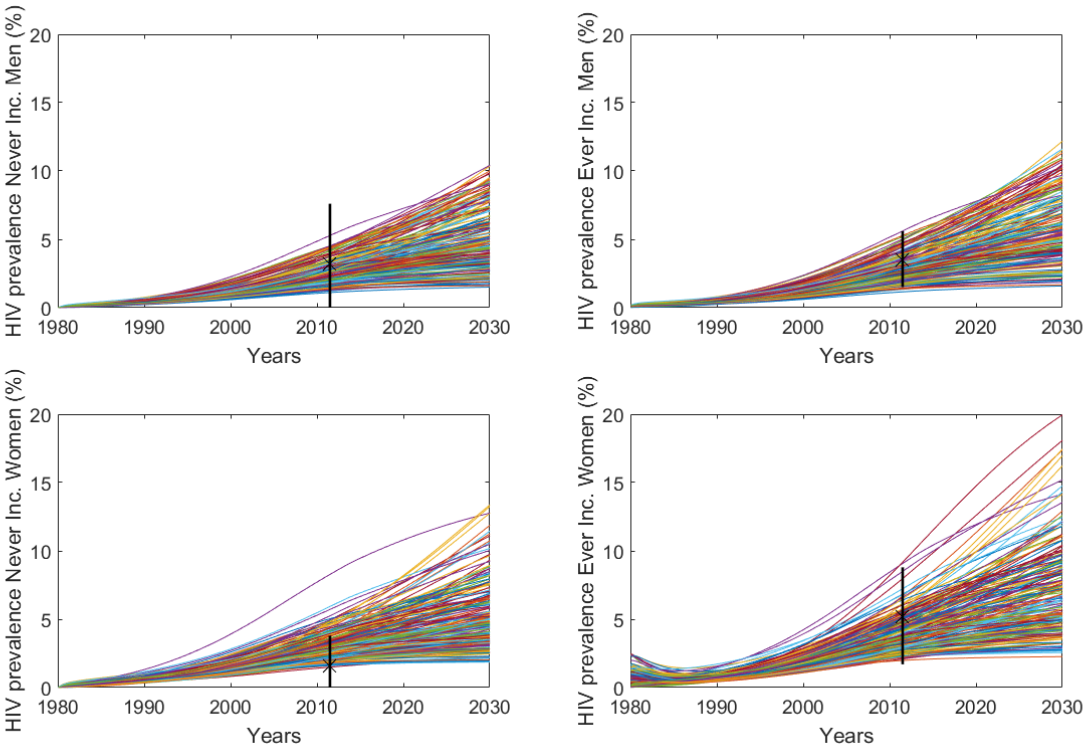

Figure S9. Model fits of HIV incidence among men and women who inject drugs compared to data from El Cuete IV (crosses represent the point estimate and whiskers the 95%CI). Incidence over 54 months is shown for the period's midpoint.

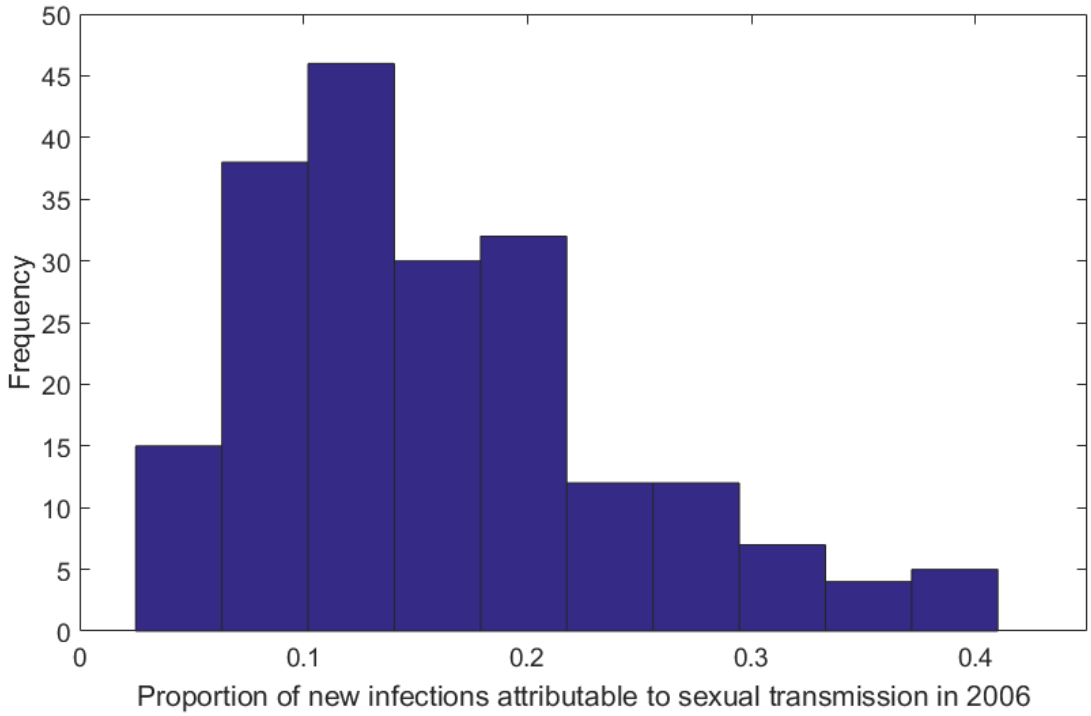

Figure S10. Histogram of the contribution of sexual transmission to incidence among PWID in 2006 for model fits.

3.6 Syphilis/HIV co-infection model to estimate the contribution of sexual transmission to the epidemic

To estimate the contribution of sexual transmission to the HIV epidemic among PWID, we utilized the data on HIV and syphilis co-infection from El Cuete to calibrate a joint co-infection model. As syphilis is sexually transmitted, and HIV is both sexually and parentally transmitted, a co-infection model allows us to estimate bounds on the likely contribution of sexual transmission to the HIV epidemic,[1,2] while the availability of syphilis/HIV co-infection data from the El Cuete cohort allows us to calibrate the model. The model allows for sexual transmission of syphilis and HIV between PWID and their PWID and non-PWID sexual contacts. The model also allows for injecting related transmission of HIV among PWID.

We developed a joint syphilis and HIV transmission model among PWID to reproduce the HIV and active and lifetime syphilis prevalence patterns observed among HIV positive and negative PWID by sex at baseline of El Cuete III study in 2006 (no syphilis testing was performed in El Cuete IV). To test for syphilis prevalence among participants, a rapid plasma reagin (RPR) test was conducted and positive samples were subjected to confirmatory testing using the *Treponema pallidum* particle agglutination assay (TPPA). A quantitative titre was obtained among those TPPA positive to classify their infection as active or lifetime and results are shown in **Table S8**. Respondent Driven Sampling (RDS) adjusted HIV prevalence among PWID in Tijuana in 2006 was 2.3% (95%CI: 1.3%-3.6%) among men, 5.4% (95%CI: 1.5%-7.8%) among women was calculated using the RDSAT software (RDS-I estimator) with further detail on the methods provided in Strathdee et al 2008.[21]

	Active syphilis		Lifetime syphilis	
	Raw Prevalence	**RDS Adjusted Prevalence (95% CI)**	**Raw Prevalence**	**RDS Adjusted Prevalence (95% CI)**
All PWID	79/1048=7·5%	0·053 (0·037, 0·072)	163/1053=15·5 %	0·101 (0·079, 0·128)
Men who inject drugs	54/895=6·0%	0·044 (0·029, 0·060)	106/876=11·8%	0·077 (0·057, 0·100)
Women who inject drugs	25/153=16·3%	0·090 (0·04, 0·185)	57/157=36·3%	0.199 (0·113, 0·342)
All HIV+ PWID	12/46=26·1%	0.286 (0·149, 0·483)	20/47=42·6%	0·380 (0·241, 0·606)
HIV+ men who inject drugs	7/30=23·3%	0.266 (0·083, 0·462)	9/31=29·0%	0·255 (0·09, 0·454)
HIV+ women who inject drugs	5/16=31·3%	0·347 (0·093, 0·780)	11/16=68·8%	0·649 (0·462, 1)

Table S8. Active and lifetime syphilis prevalence among men and women who inject drugs in 2006 disaggregated by HIV status.

The multi-step analysis plan was as follows:

- Step 1- Fit model to syphilis prevalence by sex and HIV status with sexual transmission only (injecting transmission off).
- Step 2-Turn on injecting transmission to calibrate model to HIV prevalence in all groups (and readjust sexual transmission to fit syphilis prevalence patterns among HIV-positive PWID as this group will be larger).
- Step 3-Turn off sexual transmission in 2006 (El Cuete III baseline) to estimate the contribution of sexual transmission to HIV incidence over a one-year period.

The model was disaggregated by sex, sexual activity level (low and high, defined by number of sexual contacts/year), HIV stage (susceptible, acute, latent, pre-AIDS, AIDS) and syphilis stage (susceptible, incubating, infectious (including primary and secondary syphilis), relapse, latent). The model diagram is provided in **Figure S11**. We did not differentiate those susceptible but previously infected in the model because individuals treated during the infectious period have no antibodies and individuals treated during the latent infection lose reactivity to non-treponemal tests (RPR) so would appear as negative in our sample.[30] We also did not differentiate between latent disease stages (early latent, late latent and tertiary infection) as no transmission is assumed during these stages.[31] A proportion of infected individuals relapse within one year of having gone through secondary infection and are infectious during this stage.[31] It was simplified here to follow straight from the infectious stage. High treatment rates among those in the latent stage had to be assumed in order to reproduce the relatively high prevalence of active syphilis. No immunity following treatment during the latent stage is assumed as there is high uncertainty around its development.[31]

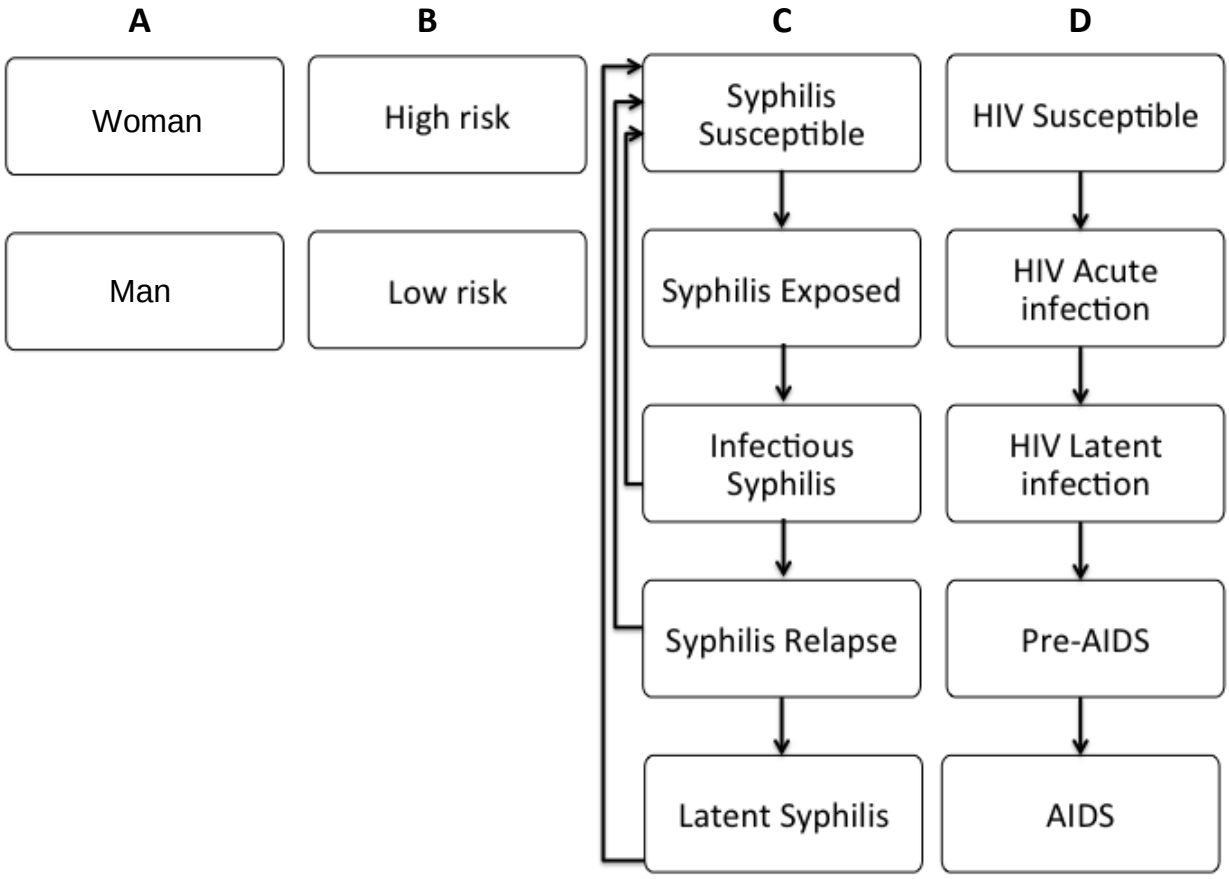

Figure S11. HIV/Syphilis co-infection model diagram showing the disaggregation of the PWID population by A) sex, B) sexual activity level (high risk, low risk), C) syphilis status and D) HIV status. The flows between states within each dimension are also represented. At each time step, individuals within any HIV or syphilis compartment may change compartment in either the HIV, syphilis or both dimensions.

HIV and syphilis transmission

Sexual mixing by sex between PWID was assumed to be exclusively heterosexual. As a relatively small proportion report having sex with other PWID (1·5% of men, 10% of women), in addition to the sexual transmission between PWID, an external force of infection was modeled to account for sexual transmission with non-PWID sexual partners. The prevalence of HIV among non-PWID sexual partners (0·5% to 1%) was based on estimates for Tijuana[27] while the syphilis prevalence (1·5%) was based on a national study.[32] Syphilis infection was assumed to increase the probability of HIV acquisition and transmission by a factor of 3 and 1·5, respectively.[33]

Few studies are available to estimate the syphilis transmission probability and all have limitations. The most rigorous estimate suggests the transmission probability per partnership is 65%[31]. However, no information on the duration of these partnerships and on the rate of sex acts among these partnerships is reported. If we assume that these partnerships lasted over the duration of the infectious period (5 months) we can infer the transmission probability per act. We assuming 8 sex acts per month, corresponding to 40 sex acts over 5 months and used the equation for the per partnership transmission probability to estimate the per act transmission probability X:

1-(1-X)^number of sex acts=65%, corresponding to 0·025/sex act.

In each scenario we varied the proportion of men and women who inject drugs in the high sexual activity group, the number of sexual partners and sex acts per partner in each of these groups to fit to the syphilis prevalence (active and lifetime by sex) and then varied the injecting transmission probability to fit to the observed HIV patterns (total HIV prevalence by sex and HIV prevalence among those with active and lifetime syphilis by sex). Once the model HIV prevalence estimates were within the 95% of the HIV prevalence data, we turned off sexual transmission and reran the model to compare the number of new infections in 2006 at baseline and with no sexual transmission. Model parameters are provided in **Table S9.** The population attributable fraction of sexual transmission was 19% in the scenario assuming

low HIV prevalence among non-PWID sexual partners (S1) and 72% in the scenario assuming high HIV prevalence among non-PWID sexual partners (S2).
Based on these findings, the contribution of sexual transmission to HIV incidence in 2006 was assumed to be normally distributed around 40% (95%CI: 20%-70%) to account for the fact that the explored scenarios are based on extreme assumptions for the HIV prevalence among non-PWID sexual partners.

	Men	Women	Source
Proportion PWID who are men	80%		ECIII
Duration injecting (years)	16·1	12·8	ECIII
Mortality rate (/year)	0·02	0·02	ECIII
Proportion in high sexual activity group (AG) (/year)	20% (S1, S2)	30% (S1, S2)	Fitted
Number of sexual partners in low sexual AG (/year)	1 (S1, S2)	1 (S1, S2)	Fitted
Number of sexual partners in high sexual AG (/year)	5 (S1,S2)	29 (S1, S2)	Fitted
Number of syringe sharing events in low sexual AG (/year)	300 (S1,S2)	360 (S1, S2)	Fitted
Number of sex acts per partner in low sexual AG (/year)	35 (S1), 40 (S2)	35 (S1), 40 (S2)	Fitted
Number of sex acts per partner in high sexual AG (/year)	50 (S1), 50 (S2)	50 (S1), 50 (S2)	Fitted
Proportion of sexual partnerships that are with other PWID	1·50%	Balanced	ECIII
HIV prevalence among non-PWID sexual partners	0·50%(S1), 1%(S2)		[27]
Infectious syphilis prevalence among non-PWID sexual partners	1·50%		[32,34]
HIV natural infection			
Average duration of acute HIV stage (years)	0·25		[17]
Average duration of latent HIV stage (years)	8		[17]
Average duration of pre-AIDS stage (years)	0·83		[17]
Average duration of AIDS stage (years)	1		[17]
HIV transmission probability through syringe sharing during the latent stage	0·0002 (S1), 0·0001(S2)		[28]
HIV transmission probability per sex act during the latent stage	0·1		[28,35]
Relative increase in HIV transmission probability compared to latent stage during:			
Acute stage	26		[17]
PreAIDS stage	7		[17]
AIDS stage	0		[17]
Syphilis natural infection			
Average duration of incubation stage (years)	0·08		[31]
Average duration of infectious stage (years)	0·42		[31]
Average duration of relapse stage (years)	0·30		[31]
Average duration of latent stage (years)	Lifelong		[31]
Proportion who relapse after the infectious period	0·25		[31]
Syphilis treatment rate in infectious stage (/year)	0·1		Fitted
Syphilis treatment rate in latent stage (/year)	1·3		Fitted
Syphilis transmission probability per sex act	0·025		Estimated
Relative risk of HIV transmission among syphilis positive in infectious and relapse stages	1·5		[33]
Relative risk of HIV acquisition among syphilis positive in infectious and relapse stages	3		[33]

Table S9. Syphilis-HIV co-infection model parameters.
S1 and S2 correspond to the scenarios assuming low and high HIV prevalence among sexual partners who are not PWID.
AG= Activity Group; PWID= people who inject drugs; ECIII= El Cuete III.

3.7 Estimating the contribution of incarceration and syringe confiscation and the potential impact of the implementation of the Narcomenudeo law

We modelled a series of scenarios as detailed below.

Assessing the contribution of incarceration and syringe confiscation on the HIV epidemic among PWID with no drug reform (2012-2030)

To estimate the contribution of incarceration and syringe confiscation to the epidemic from 2012 to 2030 we turned off the primary and re-incarceration rates and set the relative risks of infection associated with exposure to syringe

confiscation and history of incarceration to 1. To estimate the contribution of each factor in isolation, we only eliminated the risk associated with that specific factor in the counterfactual scenario by setting the relative risk associated with it to 1. We did not look at the contribution of risk in prison as we did not assume an increased risk of infection while incarcerated. We calculated the population attributable fraction of each factor (or group of factors F) PAF_F as follows:

$$PAF_F = \left({\left(I_B - I_F \right)} \Big/ {I_B} \right) \times 100$$

Where I_B corresponds to the number of new infections assuming no changes in incarceration or syringe confiscation between 2012-2030 and I_F corresponds to the number of new infections between 2012-2030 when eliminating the effect of factor F.

Potential interim impact of the limited enforcement of the Narcomenudeo reform to date (2012-2017)

To estimate the impact of the observed reductions in syringe confiscation between 2012 and 2017 we calculated the proportion of new infections averted under our baseline scenario, which reproduced the decline in syringe confiscation between 2012 and 2017 and compared to a counterfactual scenario in which no reduction in syringe confiscation occurred (using the same equation as shown above).

Potential impact of varied levels of future enforcement of the Narcomenudeo reform on the HIV epidemic among PWID (2018-2030)

To estimate the potential impact of the implementation of the Narcomenudeo reform including observed changes in syringe confiscation from 2018 to 2030, we compared different implementation scenarios to the baseline scenario in which no changes were assumed.

1) The first scenario assumed the observed reduction of syringe confiscation from 2012 to 0% in 2016 and continued elimination thereafter.
2) The second scenario assumed the elimination of syringe confiscation as described above and the reduction of incarceration among PWID by 80% from 2018 onwards. It is highly uncertain how much proper implementation of the Narcomenudeo will reduce incarceration rates for PWID. In addition to the direct reduction in incarceration relating to depenalisation of drug possession under specified threshold amounts, it is likely that proper implementation would also reduce incarceration for minor offenses. The "*Bando de Policía y Gobierno para el Municipio de Tijuana*" (or "*Bando de Policía*" for short) is the code of municipal ordinances that many officers consider central to their day-to-day enforcement. An entire spectrum of undesirable activities, such as sleeping in public, loitering, failure to produce identification, or engaging in public consumption of drugs or alcohol are proscribed, punishable by administrative sanction. In qualitative interviews among police in Tijuana, police realized that there is a contradiction between the Narcomenudeo's provisions on drugs and the local ordinance that prohibits public consumption or, ambiguously, any deviant behavior. Based on interviews, given the discretionary choice about which provisions to apply, police reported that the "*Bando de Policía*" presents itself as a much more familiar go-to legal toolkit. Given federal laws supersede state and municipal laws, proper enforcement of the Narcomenudeo reform, complete with clear operating procedures, should both reduce incarceration directly associated with drug possession but also reduce the enforcement of the "*Bando de Policía*" and associated minor infractions. Among participants in El Cuete IV who were incarcerated in the past 6 months in 2011, approximately 80% of them were charged with possessing drugs or minor infractions (such as trespassing public spaces and failure to produce identification) on their last arrest. Therefore, for this analysis we assume an 80% reduction in primary and re-incarceration rates.
3) The third scenario assumed the elimination of syringe confiscation and the diversion of ξ=80% of PWID who would have been incarcerated to OAT instead. In this scenario the CAP dimension was changed to represent current exposure to OAT (disaggregated into on and off OAT). In this way PWID were allowed to cycle on and off OAT, with a reduced risk of HIV while on OAT. Incarceration rates were reduced by 80%, with these individuals entering the "on OAT" compartment instead as shown in **Figure S12**. A yearly dropout rate from OAT was assumed. A 0·46% (95%CI: 0·32%-0·67%)[23] relative risk of infection through injecting was applied to those on OAT and the increased risk associated to recent and non-recent incarceration remained unchanged.

As such, previously incarcerated PWID who dropped out from OAT remained exposed to the same risk of infection as before entering OAT.

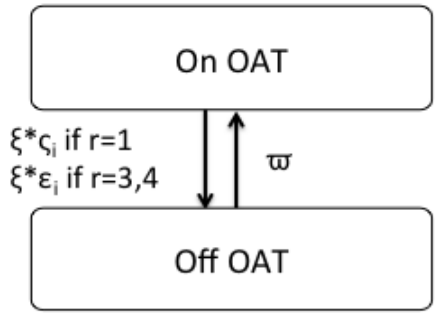

Figure S12. Schematic representation of the implementation of OAT in the HIV transmission model among PWID in Tijuana. OAT= opiate agonist treatment.

The proportion of new infections averted in each of these scenarios was calculated following the same method as described above.

4) The fourth scenario assumed the elimination of syringe confiscation and the referral of 80% of PWID who would have been incarcerated to CAP in a non-evidence based drug rehabilitation center. In this scenario, an additional dimension was added to the model to incorporate CAP in the community (disaggregated into never and ever exposed). PWID enter the model as never exposed to CAP. Incarceration rates were reduced by a factor ξ of 80%, with those who would have been incarcerated or re-incarcerated entering the "ever exposed to CAP" compartment as shown in **Figure S13**. In this way PWID entered CAP exposure instead of prison and remained in that state until they exited the population. A relative risk of 1·14 (95%CI: 1·00-1·30) was applied to men and women exposed to CAP and the increased risk associated with recent incarceration was eliminated among them to prevent from double counting effects.

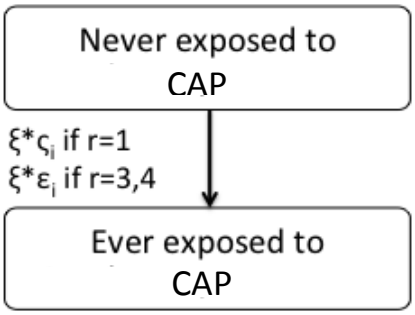

Figure S13. Schematic representation of the implementation of CAP in the HIV transmission model among PWID in Tijuana

3.8 Sensitivity analyses

We carried out sensitivity analyses investigating changes in two key assumptions determining the impact of the Narcomenudeo reform enforcement: the reduction in incarceration (50% instead of 80%) and the duration on OAT (0.5 and 2 years instead of 1 year.

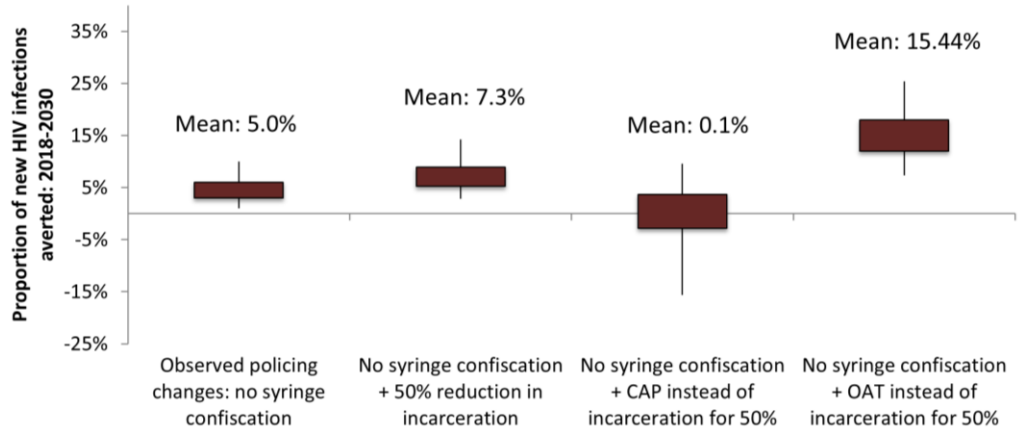

Figure S14. Sensitivity analysis exploring the impact of a lower reduction (50%) in incarceration (and associated CAP and OAT diversion) under the Narcomenudeo reform enforcement

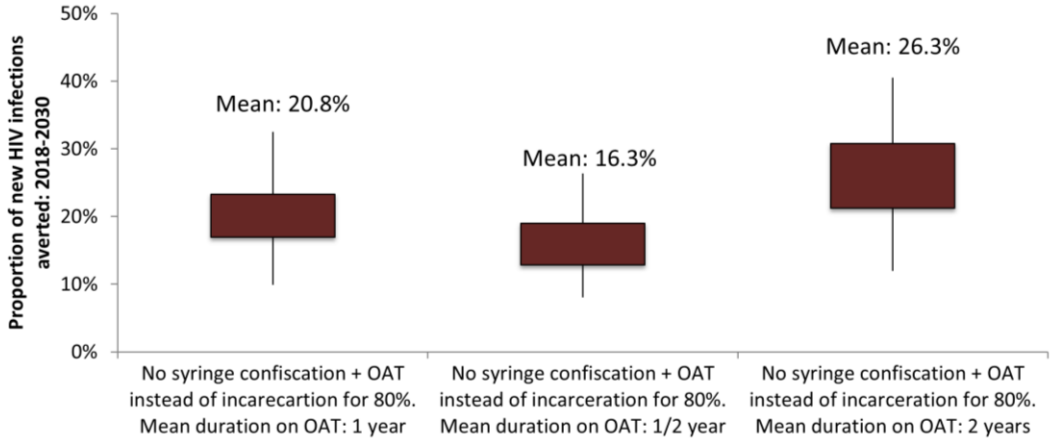

Figure S15. Sensitivity analysis exploring a shorter (6 months) and longer (2 years) duration

4. Qualitative study on experiences in compulsory abstinence based programmes among PWID participating to El Cuete IV study

Participants were purposively selected from El Cuete IV, [5] a cohort prospective study that has collected bi-annual data from 735 PWID since 2011 regarding their HIV risk behaviors, drug use and environmental context, as well as tested participants for HIV. A subsample of 25 participants, 15 women and 10 men were purposively selected and interviewed by C. Rafful between December 2015 and April 2016. [6] The main selection criterion was to have reported to have been taken involuntarily to treatment at the time of a policing program in Tijuana. Participants that agreed to be interviewed were asked to provide verbal consent, which was tape-recorded along with the interview. At the end of the interview, participants received a $20 USD compensation. Interviews were transcribed verbatim for thematic analysis in the language in which the interviews were performed (either English or Spanish).

BOX 1. Voices from PWID in Tijuana on compulsory abstinence based programmes

On the illegality of police forced referral to drug treatment:
R: My friend and I, we were the only women there [at the street]… They [police] took us first, they put [name] on the van and then they [police] tried to grab me and I fought them, I got crazy and I said "I don't want to go [to a treatment center], I am an adult and this is against the law… this is illegal deprivation [of freedom]". I was subdirector of a [treatment] center 3 years ago, and I know the law! (Woman, 29)

On human rights violations treatment centers:

I: Did you know of any punishments [while you were at the treatment center]?
R: One guy was punished because he was yelling, he was beaten up because he wouldn't stop [yelling], he kept saying that he was hungry, that he was hungry and that he needed more food… until they [the staff] entered and told him to stop and that he knew what would happen if he didn't. And they are Christians [Christian treatment center]. They are Christians and they hit him because he said he was hungry. They kicked him. They said that they were praying and that he was interrupting and that he shouldn't be screaming. (Woman, 37)

5. Qualitative study on attitudes and practices among police officers in Tijuana towards PWID carried out as part of the occupational training (ESCUDO)

A trained ethnographer, M. Morales, conducted a series of 20 interviews between May 2016 and June 2016. Written consent was obtained; an oral, closed-ended questionnaire was administered; and a semi-structured interview was conducted using a topic guide. Follow-up and probing questions were used to elucidate and expand on emerging themes after methodology described by Crabtree and Miller.[2] The interview process was pilot-tested with three police officers of the Tijuana Police Department. The final version of the interview guide and the study protocol were reviewed and approved by the Institutional Review Boards of UCSD and *Universidad de Xochicalco*, Tijuana. All of the respondents agreed to have the conversation audio-taped. Written notes were taken and used for the untaped interview. Audiotapes were professionally transcribed and the transcripts were verified against the audio record. Using a qualitative analysis software package (Atlas.ti), Escudo team analyzed and coded the transcripts. Emergent themes, trends, and frameworks were tallied by Escudo team using a grounded hermeneutic approach.[3,4] Identifying information for the department and the participants were changed to assure confidentiality.

BOX 2. Voices from police officers in Tijuana

On the lack of reconciliation between the Narcomenudeo reform and existing laws:
"No, no one had told us, no one had ever told us about amounts […] until now that we had the opportunity to take the workshop and…I'm being honest! That's just it, that is as far as it has got, what you told us, but there hasn't been any talk in which supervisors tell us this is what the law says about the permitted amounts, […]when you can disobey municipal laws in favor of state laws, because if a law is saying that one can possess that small amount of drug, but the *Bando de Policía* [Municipal ordinances] says that it is a sanction because a person cannot have traces [of drug] and because it says that [someone] cannot have on that small amount of drug, well then, there is a contradiction between the laws".

On the possibility to use discretion and apply principles of harm reduction:
"Of course you can use your judgment. If it is a person … that every day he ends up in jail for drug consumption … because it is someone that has a problem … I'm not going to arrest him every day because he is a drug user, that's … his problem … if I know that that person doesn't make any trouble, he is simply an addict, then I can let him go."

On the deleterious incentive based structure:
"[the] District Chief thinks that … because you stopped 1000 people today, you're doing your job. … Unfortunately, it's like…oh, I brought in 100, another district is like I brought in 200, and another brought in 50, oh, you're not working."

More information on policing among PWID in Tijuana and the police education program are available in:

Gaines TL, Werb D, Arredondo J, et al. The Spatial-Temporal Pattern of Policing Following a Drug Policy Reform: Triangulating Self-Reported Arrests With Official Crime Statistics. Subst Use Misuse (England), Jan 28 2017, 52(2) p214-222.

Wood EF, Werb D, Beletsky L, et al. Differential experiences of Mexican policing by people who inject drugs residing in Tijuana and San Diego. Int J Drug Policy (Netherlands), 03 2017, 41 p132-139.

Melo JS, Garfein RS, Hayashi K, et al. Do law enforcement interactions reduce the initiation of injection drug use? An investigation in three North American settings.Drug Alcohol Depend. 2018 Jan 1;182:67-73.

Mehta SR, Chaillon A, Gaines TL, et al. Impact of Public Safety Policies on Human Immunodeficiency Virus Transmission Dynamics in **Tijuana**, Mexico. Clin Infect Dis. 2018 Feb 10;66(5):758-764

Pinedo M, Beletsky L, Alamillo N, Ojeda VD. Health-damaging policing practices among persons who **inject** drugs in Mexico: Are deported migrants at greater risk? Int J Drug Policy. 2017 Aug;46:41-46.

Mittal ML, Beletsky L, Patiño E et al. Prevalence and correlates of needle-stick injuries among active duty police officers in **Tijuana**, Mexico. J Int AIDS Soc. 2016 Jul 18;19(4 Suppl 3):20874.

Harvey-Vera AY, González-Zúñiga P, Vargas-Ojeda AC, et al. Risk of violence in drug rehabilitation centers: perceptions of people who **inject** drugs in **Tijuana**, Mexico. Subst Abuse Treat Prev Policy. 2016 Jan 26;11:5.

Werb D, Wagner KD, Beletsky L, Gonzalez-Zuniga P, Rangel G, Strathdee SA.
Police bribery and access to methadone maintenance therapy within the context of drug policy reform in **Tijuana**, Mexico. Drug Alcohol Depend. 2015 Mar 1;148:221-5.

Gaines TL, Beletsky L, Arredondo J, Werb D, Rangel G, Vera A, Brouwer K. Examining the spatial distribution of law enforcement encounters among people who **inject** drugs after implementation of Mexico's drug policy reform. J Urban Health. 2015 Apr;92(2):338-51.

Volkmann T, Lozada R, Anderson CM, Patterson TL, Vera A, Strathdee SA. Factors associated with drug-related harms related to policing in **Tijuana**, Mexico. Harm Reduct J. 2011 Apr 8;8:7.

6. Health economic evaluation to inform and evaluate drug policy reform from a societal perspective

In addition to evidence of the public health benefits that may result from drug law reform, governments are increasingly reliant on estimates of expected budgetary impact and economic value of competing policy options. The Narcomenudeo reform in Mexico represents an opportunity to shift finances currently invested in law enforcement to the public health or other public safety sectors. As it stands, Mexico spends a significantly higher proportion of its GDP on the criminal justice sector (13% in 2013)[36] compared to the health sector (6·2% in 2012,[37] and only above Estonia and Turkey among OECD nations). Economic evaluations estimate the budgetary impact of drug law reform at multiple levels, and ultimately provide a comparison of the value of competing policy options. We outline the key aspects that need to be considered when conducting economic evaluations of drug policy reforms, and discuss the available data to evaluate the Narcomenudeo reform in Tijuana.

The decision problem

Drug policy reforms require multi-sectoral coordination to administer changes in law executed by police and the judicial system, as well as expand health services and social welfare programs. In light of this complexity, there can be varying levels of implementation within the security sector, and ideally, cross-jurisdictional legal reforms which coordinate complementary policy changes in other sectors. For instance, Portugal's decriminalization of small quantities of all psychoactive drugs in 2001 was successful because it de-stigmatized and encouraged drug treatment and thus was coupled with investments to expand treatment, prevention and reintegration programs.[38]

Written as state or federal laws, the target population of an economic evaluation of a drug law reform should necessarily be the population of the jurisdiction. While people who use drugs are the main focus, these policies affect the broader population through resulting changes in criminality and criminal victimization, as well as changes in population health through increased access to health care and reduced transmission of HIV and other blood borne infections.

The importance of a societal perspective

Even if drug law reforms are narrowly-defined or only partially implemented, their resulting costs and benefits will be multi-sectoral, affecting government expenditure in the security system, as well as the health care system and potentially other social services, and the individual, in the form of improving productivity and reducing criminal victimization. The use of a societal perspective strives to capture all relevant costs and benefits attributable to a policy change, breaking the silo-based mentality often adopted by specific government sectors.[39]

Prior studies on programs diverting non-violent drug offenders from prison to drug treatment have reported increases in opportunistic crimes,[40,41] associated costs of criminal victimization[42] and increased health expenditures on medications and outpatient care.[43-45] However, savings may accrue in a number of domains, including the security sector (e.g. law enforcement, processing and incarceration),[46,47] infectious diseases and treatment,[48] and workforce productivity. [49,50]

Analytical Strategy

A comprehensive model-based[51] economic evaluation of a drug policy reform would track the interactions of those affected with the health and criminal justice systems, and, particularly for one focusing on PWID, include transmission of relevant infections such as HIV, viral hepatitis, and tuberculosis (TB) to the broader population. Incorporating each of these elements necessitates a dynamic modelling framework (such as presented in the modelling section), incorporating changes in infectious disease transmission as well as prison and victimization effects, which captures both individual and population health benefits over an extended time horizon.[52,53] Also, explicitly quantifying uncertainty provides the requisite information to not only inform policy, but also inform decisions on where further data needs to be collected to reduce uncertainty in these decisions moving forward.[54]

Data requirements

Detailed data on the multi-sectoral costs and health benefits associated with the potential or enacted drug reform are required. For instance, linkage to existing health care data systems allows for analyses of health state costs, and partnerships with local security sector decision-makers could allow for the accounting of crime-specific statistics and the estimation of crime-specific costs attributable to the different sectors of the criminal justice system. Further work with local experts should also inform data collection. Tijuana offers a unique opportunity as much of the evidence required to project the effect of different degrees of implementations of the Narcomenudeo reform was found to be readily available. Data from diverse Mexican institutions at local and state levels as well as complementary data from the parallel cohorts provides the necessary information to estimate many of the components affected by the reform, and the cost data required for the economic evaluation. **Table S10** lists the components to be considered from the perspective of the healthcare sector, the security sector and the individual. It provides information on the expected direction of change for each of these resulting from reform enforcement. It describes costs and benefits associated with these changes and points to the data available and required to estimate them in Tijuana.

Implications

Health economic evaluation provides a valuable framework for synthesizing the relevant costs and benefits of drug law reform, and assessing value for money- a key piece of information for policymakers. However, it requires robust data on the multi-sector costs and benefits associated with reform. Nevertheless, where data is scarce or of poorer quality, explicitly quantifying uncertainty in each aspect of the analysis provides the requisite information to not only inform policy, but also inform decisions on where further data needs to be collected to reduce uncertainty in these decisions moving forward.[54]

Table S10. Aspects of costs and benefits attributable to drug policy reform, and specific data points available to plan and evaluate the Narcomenudeo reform

Attributable costs and benefits	Hypothesized direction, mechanism of effect	Available data for Tijuana	Additional required data, and proposed source(s) if applicable
Health care sector			
Opioid agonist treatment (OAT)	Increase in person-years on OAT.[55] OAT associated with reduction in drug-related mortality,[56,57] increased ART uptake and adherence, [58,59] reduction in HIV and HCV transmission,[23,60] and increased quality of life[61] among PWID.	Effect: Rate of OAT uptake among PWID estimated from El Cuete IV. Costs: Micro-costing estimation of OAT centers in Tijuana underway as part of Proyecto Futura.	N/A
Antiretroviral treatment (ART)	Increase in person-years on ART due to higher ART coverage among HIV-infected individuals, but reduced incidence of HIV partially offsets this increase.[62,63] ART associated with reduced HIV-related mortality[64] and reduced HIV transmission.[65-67]	Effect: Incidence/prevalence of HIV and ART uptake among PWID estimated from El Cuete IV. Costs: Average annual treatment costs available from Fondo de Gastos Catastróficos del Seguro Popular (FPCHE; Funds for Catastrophic Expenditures of the Seguro Popular).	Effect: ART uptake among other populations.
HIV-related care	Fewer HIV-related events requiring inpatient care as a result of increased ART and decreased HIV incidence.[62,68] Increase in number of HIV-infected people using outpatient care.[64,69,70]	Effect: Prevalence of HIV among PWID estimated from El Cuete IV. Costs (Inpatient and outpatient care, by CD4 strata): Derived from (i) literature,[71] or (ii) micro-costing from El Cuete IV using Costos Unitarios por Nivel de Atención Médica (Unitary Costs by Level of Medical Care), Instituto Mexicano del Seguro Social (IMSS; Mexican Institute of Social Security) 2015.	Effect: Prevalence of HIV among other populations. Costs (Inpatient and outpatient care, by CD4 strata): estimated using linkage of IMSS to Sistema de Administración y Logística de ARV (SALVAR; ART Management and Logistic System).
Care related to other infectious diseases	Decrease in incidence of infections such as HCV, HBV, TB, and other STIs and related events requiring inpatient care[72] or outpatient care.[69]	Costs: Micro-costing for El Cuete IV using Costos Unitarios por Nivel de Atención Médica, IMSS 2015.	Effect: Person-years of HCV, HBV, TB, and other STIs among PWID and other populations. Costs (per infection disease stage): estimated using linkage of IMSS to Sistema de Administración y Logística de ARV (SALVAR).
Opioid use disorder (OUD) related inpatient care	Decrease in OUD-related events requiring inpatient care,[73] increase in number of people using outpatient care.[55]	Effects: Rate of overdoses among PWID to be estimated from El Cuete IV Costs (outpatient care): estimated using: micro-costing from El Cuete IV using Costos Unitarios por Nivel de Atención Médica, IMSS 2015.	Costs (Inpatient care): estimated from Reports of the Sistema de Vigilancia Epidemiológica de las Adicciones (SISVEA; System of Epidemiological Surveillance of Addictions).
Security Sector			
Legal reform implementation education program(s)	Increase in cost of training per individuals employed in the security.[74,75]	Costs: Police education program (PEP).[74]	Costs: Other implementation costs,[48] to be determined in conjunction with Secretaría de Seguridad Pública Municipal de Tijuana (Secretariat of Public Security of the Municipality of Tijuana).

Policing for (i) drug possession; (ii) acquisitive crime; and (iii) violent crime	Police interactions: (i) Decrease related to drug possession; (ii) increase related to acquisitive crime;[40,41] (iii) decrease related to violent crimes.[40,55]	Effect: Exposure to police interactions among PWID from El Cuete IV. Costs, per incident: Average cost per reported criminal offense calculated using data from Secretaría de Seguridad Pública del Estado de Baja California and Ayuntamiento de Tijuana, Secretaría de Seguridad Pública Municipal.	Effect: Crime-specific rates in Tijuana. Costs: Crime-specific time and resource allocations determined in conjunction with Secretaría de Seguridad Pública Municipal de Tijuana.
Judicial processing	Ministerio Público (District Attorney) interactions: (i) Decrease in drug-related crime;[48] (ii) increase related to acquisitive crime; (iii) decrease related to violent crimes.	Costs, per proceeding: Average cost per case brought before the District Attorney calculated using Censo Nacional de Procuración de Justicia Estatal (National Census of State Justice Administration) with costs from Poder Judicial (Judiciary), Government of the State of Baja California.	Effect: Data for crime-specific proceedings in Tijuana. Costs: Crime-specific proceedings determined in conjunction with the Government of the State of Baja California.
Court proceedings, including prosecution and adjudication	Court proceedings: (i) Decrease in drug-related crime;[48] (ii) increase related to acquisitive crime; (iii) decrease related to violent crimes.	N/A	Costs: Number and length of prosecution time for crime-specific court cases as well as court budgets.
Incarceration	Decrease in person-years drug users are incarcerated, and decreased prison overcrowding.[48]	Effect: Incarceration rate, average duration of incarceration, and relative risk of sexual and/or injecting risk behaviour associated with incarceration, estimated among PWID from El Cuete IV. Costs: Average daily costs from Seguridad Pública y Sistema Penitenciario Estatales (Public Security and System of States' Prisons) 2015 (INEGI) and Política Criminológica Penitenciaria (Prison Criminology Policy), Government of the State of Baja California.	Effect: Relative risk of death and relative risk behaviour associated with prison overcrowding for all populations, number of prison inmates, and prison capacity.
Police harassment	Decrease in exposure to recent police harassment among drug users.	Effect: Relative risk of sexual and/or injecting risk behaviour (or incidence of infectious disease) associated with exposure to police harassment among PWID estimated from El Cuete IV.	N/A
Needle-stick injuries (NSI)	Decrease in NSI among police officers.[76-78]	Effect: Number of NSI to be estimated from the PEP evaluation Proyecto ESCUDO), and risk of BBI acquisition estimated from El Cuete IV. Cost: Microcosting using PEP data with Costos Unitarios por Nivel de Atención Médica, IMSS 2015.	N/A
Individual			
Workplace productivity	Increase in the number of person-years employed among drug users.[79]	Effect: Rate of employment among PWID estimated from El Cuete IV.	Effect: Rate of employment among NIDU. Costs: Net societal benefit to be estimated using the human capital method.[80]

Criminal victimization	Increase in acquisitive (usually opportunistic) crimes but decrease in pre-meditated and violent crimes reduces criminal victimization. [40,42]	Cost: estimated from ENVIPE 2015 derived using spending on security measures and losses because of crime (includes spending on household security, economic losses because of crime and health related spending).	Effect: Number of acquisitive and violent crimes.

LEGEND: †Assume frequency of acquisitive crimes not greater than combined decrease in frequency of drug and violent crimes
ART=antiretroviral treatment; BBI=blood borne infections; DALY=disability adjusted life year; MXN=Mexican pesos; OAT=opioid agonist treatment; OUD=opioid use disorder; PEP=police education program; PWID=people who inject drugs; SoC=standards of care; TBD=to be determined

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