HIV and related infections in prisoners 6

The perfect storm: incarceration and the high-risk environment perpetuating transmission of HIV, hepatitis C virus, and tuberculosis in Eastern Europe and Central Asia

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Despite global reductions in HIV incidence and mortality, the 15 UNAIDS-designated countries of Eastern Europe and Central Asia (EECA) that gained independence from the Soviet Union in 1991 constitute the only region where both continue to rise. HIV transmission in EECA is fuelled primarily by injection of opioids, with harsh criminalisation of drug use that has resulted in extraordinarily high levels of incarceration. Consequently, people who inject drugs, including those with HIV, hepatitis C virus, and tuberculosis, are concentrated within prisons. Evidence-based primary and secondary prevention of HIV using opioid agonist therapies such as methadone and buprenorphine is available in prisons in only a handful of EECA countries (methadone or buprenorphine in five countries and needle and syringe programmes in three countries), with none of them meeting recommended coverage levels. Similarly, antiretroviral therapy coverage, especially among people who inject drugs, is markedly under-scaled. Russia completely bans opioid agonist therapies and does not support needle and syringe programmes—with neither available in prisons—despite the country's high incarceration rate and having the largest burden of people with HIV who inject drugs in the region. Mathematical modelling for Ukraine suggests that high levels of incarceration in EECA countries facilitate HIV transmission among people who inject drugs, with 28–55% of all new HIV infections over the next 15 years predicted to be attributable to heightened HIV transmission risk among currently or previously incarcerated people who inject drugs. Scaling up of opioid agonist therapies within prisons and maintaining treatment after release would yield the greatest HIV transmission reduction in people who inject drugs. Additional analyses also suggest that at least 6% of all incident tuberculosis cases, and 75% of incident tuberculosis cases in people who inject drugs are due to incarceration. Interventions that reduce incarceration itself and effectively intervene with prisoners to screen, diagnose, and treat addiction and HIV, hepatitis C virus, and tuberculosis are urgently needed to stem the multiple overlapping epidemics concentrated in prisons.

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This is the sixth in a **Series** of six papers about HIV and related infections in prisoners

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Introduction

The negative and mutually reinforcing nature of incarceration, substance use disorders, and blood-borne viruses such as HIV, hepatitis C virus, and tuberculosis is especially problematic in the 15 UNAIDS-designated countries of Eastern Europe and Central Asia (EECA), and results in a concentration and deleterious interaction between these comorbid health and social conditions.[1,2] EECA is now the only region where the number of new HIV infections has increased annually, from 120 000 to 190 000 between 2010 and 2015, resulting in the number of people with HIV increasing from 1·0 million to 1·5 million in the same period.[3] Although new WHO guidelines recommend treatment for all people living with HIV irrespective of CD4 count, coverage with antiretroviral therapy in the region is less than 10%[4] and is compounded both by suboptimal screening for diseases and low coverage of evidence-based HIV prevention strategies (eg, opioid agonist therapies with methadone or buprenorphine, or needle and syringe programmes).[5,6]

In EECA, proscriptive policies that promote arrest of socially vulnerable individuals at increased risk of HIV, viral hepatitis, and tuberculosis (eg, people who inject drugs, men who have sex with men, and sex workers)

Search strategy and selection criteria

We conducted a comprehensive review of peer-reviewed publications and reports related to addiction, HIV, hepatitis C virus, and tuberculosis treatment and prevention in the criminal justice systems in the 15 countries of Eastern Europe and Asia (Armenia, Azerbaijan, Belarus, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Moldova, Russia, Tajikistan, Turkmenistan, Ukraine, and Uzbekistan). Keywords and MeSH headings related to incarceration (ie, "inmate", "prison", "prisoner", "detainee", "criminal justice", "pre-trial", "detention", "jail", "SIZO", "correctional") were cross-referenced with citations pertaining to each of the focus infectious diseases ("HIV", "AIDS", "HCV", "tuberculosis") or substance use disorders ("heroin", "opioids", "drug use", "methadone", "buprenorphine", "substance ab/use", "addiction"). We limited our search to articles that were published in English and Russian on PubMed and Google Scholar between Jan 1, 2012, and July 20, 2015. We retrieved and reviewed 1837 unique citations, and selected 449 for inclusion. Additional information from other sources was also included. We reviewed grey literature from websites in English, Ukrainian, and Russian, including government-reported health status of prisoners in each country.

Key messages

- Incarceration rates in Eastern Europe and Central Asia are among the highest in the world due to policies that concentrate people who inject or otherwise use drugs and others at high risk for HIV, viral hepatitis, and tuberculosis
- Due to policies within this region, the prevalence of HIV, hepatitis C virus, and tuberculosis infection is several times higher than in the surrounding community
- Analyses from Ukraine suggest that incarceration could be contributing to up to half of all new HIV infections among people who inject drugs, and scaling up of opioid agonist therapy within prisons and effectively maintaining them on treatment within the community after release would markedly reduce HIV transmission within this group
- Similarly, strategies that reduce incarceration of people who inject drugs in Ukraine would greatly reduce the number of new tuberculosis cases, especially among people who inject drugs, underscoring the importance of screening, treatment, and continuity of care for prisoners with or at risk for tuberculosis
- Armenia, Kyrgyzstan, and Moldova have successfully introduced all 15 of the HIV prevention strategies recommended by the UN, including provision of opioid agonist therapy with methadone and needle and syringe programmes—albeit inadequately scaled to need

result in a concentration of risk within prisons, which amplifies disease and leads to onwards transmission in the community after release.[7] These epidemics converge in the EECA region, where abrupt and far-reaching social, economic, and political transitions since the dissolution of the Soviet Union in 1991 have resulted in poor public health consequences. Where such negatively reinforcing comorbidities exist, effective HIV prevention and treatment must address all problems simultaneously to have a noticeable effect.[1] Yet, the HIV response remains inadequate as HIV incidence and mortality continue to increase in EECA, despite reductions worldwide.[3]

Although EECA countries are culturally and religiously distinct and have undergone different political, economic, and social trajectories since independence, they share sociopolitical, philosophical, and organisational vestiges of the former Soviet Union, which now shape the evolving synergistic epidemics (also known as syndemics) of mass incarceration, substance use disorders, HIV, hepatitis C virus, and tuberculosis. Aside from the high-income countries of Estonia, Lithuania, and Latvia, the 12 other EECA countries are low-income or middle-income countries. Following the Soviet Union's collapse, in this setting of political and economic instability, heroin entered through new trade routes from Afghanistan.[8,9] Use of injected heroin increased and led to explosive HIV transmission among people who inject drugs, where the epidemic remains mostly concentrated today. Harsh drug policies and criminalisation laws ensued targeting people who inject drugs, with resultant mass incarceration, prison overcrowding[10] and high incarceration rates (five of the highest ten globally).[11] The concentration of people who inject drugs, people living with HIV with compromised immune systems, and individuals with tuberculosis in criminal justice systems creates especially high-risk environments for HIV and tuberculosis transmission.[12–14] The unresponsive health authorities, unaccustomed to implementing HIV and tuberculosis prevention and treatment in prison settings, did not meet human rights recommendations.

Data have not, however, been comprehensively synthesised to understand how the criminal justice system contributes to the expanding HIV and related epidemics in EECA. In this Series paper, we apply the risk environment framework to describe how incarceration, HIV, hepatitis C virus, tuberculosis, and substance use disorders converge to produce drug-related harm and clarify how individual HIV risk behaviours are embedded within social processes, specifically incarceration within EECA.[15,16] Further, mathematical modelling and statistical analyses are used to estimate the degree to which incarceration contributes to HIV and tuberculosis transmission among people who inject drugs in Ukraine, and analyse the effectiveness of evidence-based HIV prevention strategies in reducing the harms of incarceration.

Methods

Analytical framework

In this comprehensive review, we aimed to review the historical features occurring during a devastating transitional period after the dissolution of the Soviet Union that now shape the concurrent epidemics of incarceration, HIV, viral hepatitis, and tuberculosis in EECA; present a theoretical framework—termed the "risk environment"—for understanding how the criminal justice system, including policing and incarceration practices, influences the evolving HIV and tuberculosis epidemics; provide an analysis of up-to-date legal, criminal justice, and epidemiological data from the 15 countries of EECA; use detailed data from Ukraine to estimate the degree to which incarceration contributes to HIV transmission among people who inject drugs (using dynamic mathematical modelling) and tuberculosis transmission among people who inject drugs and the general population (using statistical analyses); and recommend new directions for prevention, treatment, and research.

Here, we examine how the risk environment within the criminal justice system synergistically reinforces, concentrates, and amplifies the effect of several medical conditions (eg, HIV, hepatitis C virus, and tuberculosis). This is not only affected by social conditions (eg, incarceration, poverty) but also includes the policing practices that influence arrest and entry into the criminal justice system and the experiences within the prison environment itself, which result in the syndemic of social and medical comorbidities. The amplification of drug-related harm in prisons[17–19] is best understood using the risk environment framework.[15] This conceptual model

	Azerbaijan	Kazakhstan	Kyrgyzstan	Tajikistan	Turk-menistan	Uzbekistan	Russia	Ukraine	Belarus	Moldova	Lithuania	Latvia	Estonia	Armenia	Georgia
Prison population	16 500*	44 893	7961	9000*	30 568	42 000*	656 618	57 396	31 700	5329	6634	3276	2775	3894	9724
Estimated number of people who inject drugs															
Community	71 283	116 840	25 000	25 000	..	80 000	1·8 million	332 500	75 000	30 200	5403	10 034	9000	3310	45 000
Prison	31·9%	..	30·4%	..	..	..	..	48·7%	..	..	..	..	..	5·5%	..
Antiretroviral therapy coverage															
Community	14%	4639	13%	10%	..	24%	178 711	26%	21%	17%	542	1055	2998	16%	39%
Prison	63·2%	34·3%	69·9% of those registered	59·1%	..	..	5·0%	6·4%	..	63·1%	23·2%	19·3%	..	77·3%	87·5%
HIV prevalence															
Community	0·1%	0·2%	0·2%	0·4%	<0·2%	0·2%	1·1%	1·2%	0·5%	0·6%	0·1%	0·7%	1·0%	0·2%	0·3%
Prison	3·7%	3·9%	10·3%	2·4%	0	4·7%	6·5%	19·4%	..	2·6%	3·4%	20·4%	14·1%	2·4%	0·90%
Tuberculosis incidence or prevalence per 100 000															
Community	77	99	142	91	64	82	84	94	58	153	62	49	20	45	106
Prison	152	2110	145	162						184	58	69			56
Opioid-dependent individuals															
Community	1·5%	1·0%	0·80%	0·54%	..	0·80%	2·3%	0·91%	0·59%	..	0·24%	0·66%	..	0·16%	1·36%
Prison	32·5%	3·0%‡	13·7%	5·0%	..	..	..	44·3%	..	6·6%†	7·6%	30·0%	..	..	..
Number of opioid agonist therapy sites															
Community	2	10	23	6	..	..	..	169	19	3	23	10	9	10	21
Prison	..	..	7	..	..	..	..	..	..	9	..	9	4	9	2‡
Number of individuals receiving opioid agonist treatments															
Community	137	205	1227	677	..	..	..	8264	1066	392	930	424	919	430	2600
Prison	..	..	400	..	..	..	..	..	..	68	..	26	56	151	..

All values are from the survey administered for this study in collaboration with UNODC and refer to 2015, unless otherwise specified in the appendix. UNODC=United Nations Office on Drug Control. *Approximate number. †Present only as a pilot programme in SIZO (pre-trial detention) for detoxification and not for maintenance therapy. ‡Refers only those officially registered as opioid dependent with the National Narcological Registry.

Table 1: **Overview of prison populations in Eastern Europe and Central Asia**

	Azerbaijan	Kazakhstan	Kyrgyzstan	Tajikistan	Turkmenistan	Uzbekistan	Russia	Ukraine	Belarus	Moldova	Lithuania	Latvia	Estonia	Armenia	Georgia
Ministry overseeing prisoner health	Justice	Interior	Prison	Justice	Interior	Interior	Prison	Prison	Interior	Justice	Justice	Justice	Justice	Justice	Prison
Number of prisons	35	76	11	13	14	42	..	146	..	12	7	11	..	12	15
Male	16	69	10	12	12	39	..	131	..	10	6	10	..	11	11
Female	1	6	1	1	1	1	..	15	..	1	1	1	..	1	1
Number of prisoners	16 500*	44 893	7961	9000*	30 568	42 000*	656 618	57 396	31 700	5329	6643	3276	2775	3894	9724
Proportion female	2·8%†	7·7%	4·0%	3·3%	6·5%	3·0%	..	5·6%	..	6·6%	3·7%	7·4%	..	4·5%	3·3%
Incarceration rate‡	236	231	181	130	583	152	446	193	306	215	268	239	218	132	274
Occupancy	81·4%	71·8%	55·5%	61·5%	85·0%	80·0%	94·2%	120·24%	96·8%	102·9%	83·1%	59·5%	96·3%	89·3%	47·8%
Needle and syringe programmes in prison	No	No	Yes (2005)	Yes (2010)	No	No	..	No	..	Yes (1999)	No	No	..	Yes (2004)	No
Number of facilities	..	..	10	1	..	..	..	..	..	10	..	..	..	9	..
Opioid agonist therapy	No	No	Yes (2008)	No	No	No	..	No	..	Yes (2005)	No	Yes (2012)	..	Yes (2011)	No
Number of facilities	..	..	7	..	..	..	..	..	..	9	..	9	..	9	..
Number of patients	..	..	400	..	..	..	..	..	..	68	..	26	..	151	..
Detoxification with methadone or buprenorphine	No	No	No	No	No	No	..	No	..	Yes	No	No	..	No	Yes
Non-pharmacological detoxification	Yes	No	Yes	No	..	No	..	Yes	..	No	Yes	Yes	..	Yes	No
HIV testing and counselling (year)	Yes	Yes (1997)	Yes (2001)	Yes (2003)	Yes	Yes (2003)	..	Yes (2006)	..	Yes (2008)	Yes	Yes (1994)	..	Yes (2004)	Yes (2004)
Condom provision (year)	Yes (2011)	Yes (2002)	Yes (2005)	Yes (2003)	No	No	..	Yes (2008)	..	Yes (1999)	Yes (2004)	No	..	..	Yes (2004)
Antiretroviral therapy (year)	Yes (2007)	Yes (2005)	Yes	Yes (2007)	No	Yes (2008)	..	Yes (2008)	..	Yes (2004)	Yes	Yes (1998)	..	Yes (2005)	Yes (2005)
Tuberculosis fluorography (year)	Yes (1995)	Yes (1998)	Yes (1997)	Yes	Yes	Yes (1991)	..	Yes	..	Yes (1996)	Yes	Yes (2011)	..	Yes (2004)	Yes (1998)
TB treatment (year)	Yes (1995)	Yes	Yes (1998)	Yes	Yes§	Yes (2004)	..	Yes	..	Yes (1996)	Yes (1998)	Yes	..	Yes	Yes (1998)
HCV diagnostics (year)	Yes (2006)	Yes	Yes (2005)	Yes (2015)¶	..	Yes	..	No	..	Yes (2004)	Yes	Yes	..	No	Yes (2014)
Treatment of HCV	No	No	No	No	..	No	..	No	..	No	Yes (acute only)	No	..	No	Yes
HBV diagnostics	No	Yes	Yes	..	..	Yes	..	No	..	Yes	No	Yes	..	No	Yes

(Table 2 continues on next page)

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posits that individual decisions about disease prevention and treatment are rooted in structural risk such as spaces (in this case, prisons) that, while exogenous to the individual, independently contribute to risk-taking and health-seeking behaviours. Hierarchical social structures within the criminal justice system, interpersonal violence, and the lack of safety, stigma, privacy, and autonomy often limit decision making by prisoners, including choices about health-care engagement and drug use.[16,20] Access to prison-Wbased HIV and other health-care services (eg, opioid agonist therapy), and the capacity to reduce drug-related harm, is affected by these environmental factors at the social, economic, and political levels.[21]

Survey methods

In most EECA countries, access to accurate prison-related data and formal and informal operations of the penitentiary systems is limited. We therefore aimed to compile data about prisoner health and access to health services focusing on drug-related and comorbid conditions, and to compile supplemental survey information from prison medical departments with assistance from the United Nations Office on Drug Control (UNODC) using official governmental requests in each country. Among 15 surveys requested, 11 responded, with findings included in tables 1 and 2.

Modelling the contribution of incarceration to HIV and tuberculosis transmission

We conducted dynamic HIV transmission modelling to assess the long-term contribution of incarceration to HIV transmission among people who inject drugs in Ukraine, and assessed the impact of eliminating incarceration and scaling up of prison-based opioid agonist therapy. Additional statistical analyses were used to estimate the contribution of current or recent incarceration on yearly tuberculosis transmission both in people who inject drugs and in the general population in Ukraine. Modelling and epidemiological methods and results are described in the Ukraine case study, with further details and model equations included in boxes 1 and 2 and the appendix.

Historical framework, organisation of criminal justice, and its influence on EECA

Various governmental ministries other than the Ministry of Health administratively oversee the criminal justice system, including health-care delivery, in all EECA countries (figure 4, table 2). The Ministry of Interior oversees the police, including arrest and short-term detention in lock-up facilities. Health care in pre-trial detention and prisons falls under various ministries, although international organisations such as WHO and UNODC support the separation of oversight of investigations and prosecution from the execution and supervision of criminal sanctions. Although there are various organisational structures

	Azerbaijan	Kazakhstan	Kyrgyzstan	Tajikistan	Turkmenistan	Uzbekistan	Russia	Ukraine	Belarus	Moldova	Lithuania	Latvia	Estonia	Armenia	Georgia
(Continued from previous page)															
Treatment of HBV	No	No	No	..	..	Yes	..	No	..	No	No	Yes	..	No	No
HBV vaccination	No	No	No	..	..	No	..	No	..	No	No	No	..	No	No
Programmes on prevention of physical and sexual violence	Yes	Yes	No	..	..	Yes	..	No	..	No	..	No	..		Yes
Staff protection programme against HIV as an occupational hazard	No	Yes	Yes	..	..	Yes	..	Yes	..	Yes	Yes	Yes	..	No	Yes
Post-exposure prophylaxis	No	Yes	Yes (2010)	Yes	..	Yes	..	No	..	Yes	No	No	..	Yes	No
Diagnosis and treatment of sexually transmitted infections	Yes	Yes	Yes	..	..	Yes	..	Yes	..	Yes	..	Yes	..	Yes	Yes

All values are from the survey administered for this study in collaboration with UNODC and refer to 2015, unless otherwise specified. Start date is listed in brackets when available. HCV=hepatitis C virus. HBV=hepatitis B virus. UNODC=United Nations Office on Drug Control. *Approximate number. †Number of prisoners per 100 000 population. ‡People, treated, and tested refer to the total number of people receiving service in 2014. §Available only as a pilot project. ¶Women and juveniles housed in the same facility.

Table 2: **Policies and practices related to HIV infection and harm reduction services in prisons of Eastern Europe and Central Asia**

See **Online** for appendix

Box 1: Modelling the impact of incarceration and scale-up of opioid agonist therapies in prisons on HIV transmission among people who inject drugs in Ukraine

We developed a national, dynamic model of incarceration and HIV transmission through drug injection that stratified people who inject drugs by incarceration state (never, current, recently released within the past 12 months, and past incarceration more than 12 months ago), and HIV infection state (susceptible, initial acute and chronic HIV infection, and receiving antiretroviral therapy). Within a Bayesian framework,[22] the model was calibrated to detailed national data about the incarceration of people who inject drugs (appendix p 3),[23–25] and HIV prevalence (appendix p 4) among people who inject drugs who are never-incarcerated (11·9–13·6%), currently incarcerated (22·2–35·4%), and previously incarcerated (26·6–29·7%).[23,24,26] Based on the same national data, this calibration assumed elevated injection-related risk of HIV transmission among previously incarcerated people who inject drugs (relative risk 1·9–3·3 within 12 months after release and 1·4–2·0 thereafter; appendix p 5) compared with never-incarcerated individuals. Sensitivity analyses relaxed this assumption. Due to insufficient data, a non-informative prior was used for the transmission risk among incarcerated people who inject drugs.

To estimate the long-term population-attributable fraction (PAF) due to incarceration, the relative decrease in new HIV infections over 15 years was projected when the transmission risk among currently incarcerated and previously incarcerated people who inject drugs was set to the same as never-incarcerated individuals. A conservative PAF assumed the transmission risk among recently released individuals to be the same as previously incarcerated—but not recently incarcerated—people who inject drugs. We also examined how scale-up of opioid agonist therapy to 50% of incarcerated people who inject drugs, with 12-month continuity of opioid agonist therapy after release, could reduce HIV transmission. The appendix pp 1–7 provides more methodological details.

When assuming heightened HIV transmission risk in previously incarcerated individuals who inject drugs, the model (figures 1, 2) suggests that community HIV incidence and prevalence would decrease dramatically by 2030 (incidence by 75% [95% credibility interval (CrI) 64–87], prevalence by 56% [95% CrI 42–66]) if the HIV transmission risk among currently and previously incarcerated individuals were set equal to that of never-incarcerated individuals. Additionally, 55·1% (95% CrI 40·2–68·2) of new HIV infections would be prevented, mainly due to reduction in the heightened risk among recently-released people who inject drugs. Indeed, 28·2% (95% CrI 13·6–41·1) of HIV infections would be averted if this heightened risk was only partly reduced to the same as non-recently incarcerated individuals.

These findings were robust to less restrictive assumptions about the relative transmission risk among previously incarcerated individuals (appendix p 9). By contrast, if people who inject drugs had no new incarcerations after 2015, only 12·8% (95% CrI −4·7 to 24·6) of new HIV infections would be averted thereafter. If prison-based opioid agonist therapies were initiated in Ukraine, however, our modelled scenario suggests 19·8% (95% CrI 14·6–24·5) of HIV infections would be averted during 2015–30, and community coverage of opioid agonist therapy would increase by 8·3%. Much of this effect is due to benefits of retaining prisoners on opioid agonist therapies after release, with only 5·6% (95% CrI 1·6–8·3) of HIV infections being averted without continuation of opioid agonist therapy. Further projections suggest that community coverage levels of opioid agonist therapy (without prison-based opioid agonist therapies) of 28% (95% CrI 20–33), 48% (95% CrI 43–50), or 16% (95% CrI 12–21) would be required to achieve the same impact as scaling up of prison-based opioid agonist therapy, depending on whether this community therapy was untargeted or targeted to never-incarcerated or previously incarcerated individuals, respectively. Considering the prevention benefit per person of opioid agonist therapy, the scenario of prison-based opioid agonist therapy is as efficient as targeting opioid agonist therapy to previously incarcerated people who inject drugs in the community, but is 1·6 times more efficient than untargeted community opioid agonist therapy and 3·2 times more efficient than opioid agonist therapy targeted to never-incarcerated individuals.

These analyses suggest incarceration is a driver of HIV transmission among people who inject drugs in Ukraine, with 55·1% (95% CrI 40·2–68·2) of incident HIV infections possibly attributable to incarceration if we assume all the elevated risk among previously incarcerated people who inject drugs results from incarceration, or 28·2% (95% CrI 13·6–41·1) if we conservatively assume only the additional risk among recently released individuals is due to incarceration.

Importantly, increases in risk behaviours after incarceration fuel the HIV epidemic in Ukraine's injection drug users, highlighting the need to strategically target HIV prevention interventions to previously incarcerated individuals. Findings here, and confirmed elsewhere, suggest that expansion of prison-based opioid agonist therapy with effective community transition after release could be an effective strategy of achieving this.[27–30] Strategies that reduce incarceration, such as alternatives to incarceration (eg, probation, drug courts), community policing that promotes treatment over arrest, and changes in drug criminalisation policies should also be considered, although the HIV benefits may be less.

Our analyses have limitations (detailed in the appendix p 10), most specifically related to whether the elevated transmission risk among previously incarcerated people who inject drugs is due to incarceration or higher-risk individuals being incarcerated frequently; future studies should examine longitudinal changes in risk before, during, and after incarceration.

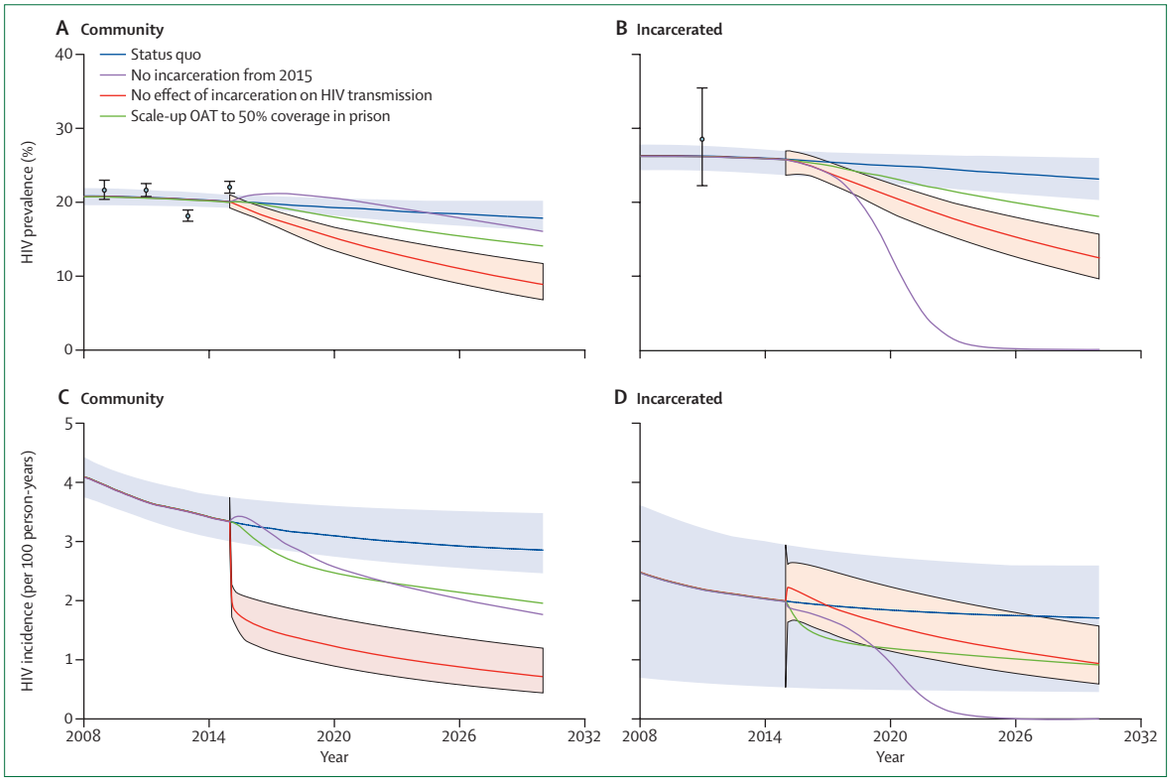

Figure 1: **Projected HIV trends among people who inject drugs in Ukraine**
Figure shows projected median trends for people who inject drugs. (A) HIV prevalence among individuals in the community (both never-incarcerated and previously incarcerated). (B) HIV prevalence among incarcerated individuals. (C) HIV incidence among individuals in the community (both never-incarcerated and previously incarcerated). (D) HIV incidence among incarcerated individuals. Scenarios shown are for the status quo, and if there was either: no effect of incarceration on transmission risk after 2015; no further incarceration after 2015; or initiation of opioid agonist therapy in prisons with 50% coverage among incarcerated people who have ever injected drugs who are maintained on therapy for a year after release. Data points with 95% CIs are shown for comparison and shading represents the 95% credibility intervals for the status quo projection (light blue shading) and if incarceration had no effect on transmission risk after 2015 (pink shading).

for prison health-care delivery across EECA countries, none comply with recommendations by the UN and WHO,[37] now known as the Mandela Rules, that stipulate that health care should be equal to that provided within the community and be continuous from prison to community. Some countries, however, have created separate ministries devoted specifically to specialised prisoner supervision.

The criminal justice system in all EECA countries (figure 4), derived from the Soviet system, includes pre-trial detention centres, similar to jails and referred to as SIZO, where detainees remain for up to 2 years while awaiting sentencing. After sentencing, treatment is interrupted by transitional supervision for up to 2 weeks in *etap*, while awaiting transportation to prison, which is overseen by the Ministry of Interior, followed by placement in penal colonies (including lower-security settlement colonies, and colonies for juvenile offenders) or prisons with cell blocks after sentencing. The separate ministries responsible for oversight at various stages within the criminal justice system, however, often have policies that conflict with each other (eg, regarding allowance or provision of various services). Table 1

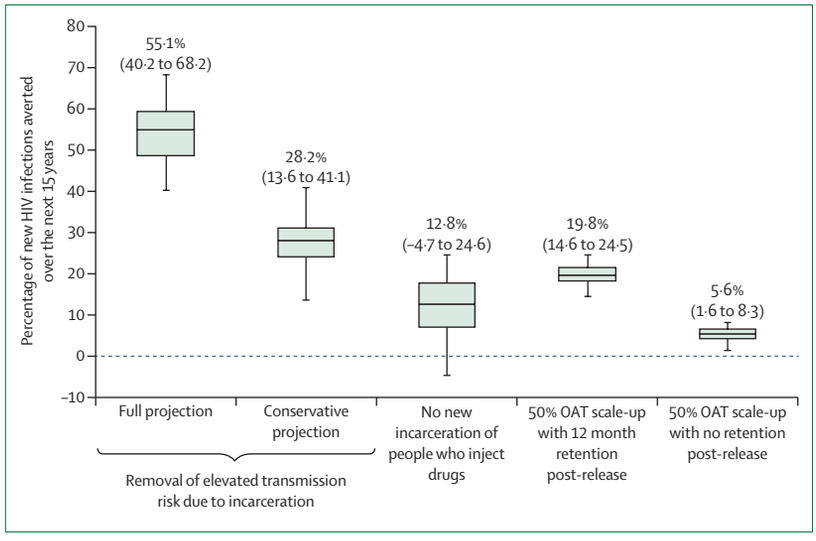

Figure 2: **Prevention of new HIV infections**
Figure shows percentage of new HIV infections that would be averted over 15 years (from 2015 and 2030) under the following scenarios: if incarceration no longer elevated transmission risk (full and conservative projections); if there was no further new incarceration of people who inject drugs; or if prison opioid agonist therapy was scaled up with or without retention after release. Bars show the median projections, while error bars show the 95% credibility intervals. Text above the error bars are the median projections and the corresponding 95% credibility interval. OAT=opioid agonist therapy.

Box 2: **Statistical analyses of the impact of incarceration on tuberculosis transmission in people who inject drugs and more broadly to the general population in Ukraine**

Statistical analyses were performed using national survey data to assess the short-term yearly contribution of incarceration to recent and lifetime tuberculosis transmission among both people who inject drugs and the general public in Ukraine. Detailed methods are provided in the appendix pp 12–13. Data sources included countrywide data from 1612 people who inject drugs in the 2015 ExMAT survey and 402 prisoners in the 2011 PUHLSE survey (appendix pp 12–13).[23,25] ExMAT provided individual-level data about incarceration (ever, total time), HIV status, drug injection duration, tuberculosis status in the past 12 months, and ever. PUHLSE provided individual-level data for age, total time incarcerated, HIV status, ever injected drugs, and ever tuberculosis status. Self-reported tuberculosis status was used for all analyses using a validated survey question.[31]

Using both datasets, linear regression models were firstly developed to evaluate the relationship between ever and recent tuberculosis status and ever being incarcerated or total duration of incarceration. Two survival models were then fitted to data for cumulative tuberculosis risk as a function of time in prison. Using the estimated hazard, an average tuberculosis incidence rate was estimated for each year of incarceration among prisoners (PUHLSE) or previously incarcerated people who inject drugs (ExMAT). The estimated incidence rate among prisoners (PUHLSE) and data for self-reported recent risk of tuberculosis (ExMAT) were then used to estimate the relative risk of tuberculosis among incarcerated people who inject drugs or prisoners overall compared with non-incarcerated individuals who inject drugs or the community as a whole,[32] and the population-attributable fraction (PAF) of incarceration to overall tuberculosis risk and tuberculosis risk among people who inject drugs was estimated using standard formula.

Our analyses consistently suggest that incarceration contributes substantially to tuberculosis transmission in Ukraine. After controlling for age, injecting duration, and other variables, we estimate that for every additional year of incarceration there is a 13% (95% CI 8–17) relative increase in tuberculosis prevalence among the overall population and a 6% (95% CI 3–10) relative increase in tuberculosis prevalence among people who inject drugs (figure 3).

Although only 0·5% of the adult population was incarcerated, we estimate that 6·2% (95% CI 2·2–13·4) of all incident tuberculosis cases result from incarceration. Conversely, among people who inject drugs this increases to 75% (95% CI 51–94) for HIV-infected people who inject drugs and 86% (95% CI 56–98) among HIV-negative people who inject drugs (appendix pp 13–14).

Our analyses from Ukraine indicate that the contribution of incarceration to tuberculosis in the general population was similar to findings from Russia,[33] and provides new insights that suggest a markedly higher PAF of incarceration to tuberculosis transmission among people who inject drugs. Although data suggest the importance of incarceration for tuberculosis,[12,33-35] there is a paucity of data surrounding the contribution of prison to tuberculosis incidence in low-income and middle-income countries, especially in EECA where tuberculosis incidence is high. Nevertheless, other studies and data presented here suggest that prisons contribute substantially to tuberculosis epidemics broadly, but especially in people who inject drugs in this region (panel 1). Although strategies that reduce incarceration for people who inject drugs would have the greatest impact, these findings also underscore the need to develop cost-effective interventions to diagnose, treat, and prevent tuberculosis transmission among incarcerated populations. Azerbaijan has emerged as a regional leader in implementing such programmes,[36] where the government has adopted tuberculosis prevention activities within prison (screening, early detection and treatment, case isolation, and preventive therapy for latent tuberculosis infection). Such strategies, especially if focused on people who inject drugs, should address the increased tuberculosis transmission risk associated with current or previous incarceration. Such strategies, including HIV prevention and treatment, are urgently needed to control the HIV and tuberculosis epidemics in Ukraine and other EECA settings.

compares the prevalence of infectious diseases and harm reduction coverage in prisons and communities in each country. Table 2 and its expanded version in the appendix provide an overview of criminal justice system facilities in each country based on our survey and published reports. Sentenced prisoners are generally divided into minimum-security, medium-security, and maximum-security facilities, which we collectively term "prisons". Prisoners with HIV are not segregated, but those with tuberculosis are isolated in specialised medical wards.

The legacy of Soviet-style addiction treatment, termed "narcology",[38] prevails in EECA countries and includes ineffective measures such as use of antidepressants, anxiolytics, antipsychotics, excessive physical exercise, neurosurgery, and kinesiotherapy to treat addiction. In Russia, the only criterion of successful addiction treatment is complete abstinence from any psychoactive substance, including from medically prescribed methadone and buprenorphine (which—despite being included on the WHO list of essential medications—remain banned throughout the country). These measures follow the Soviet-era models of repressive psychiatry, contrary to international standards,[39] and often amount to suffering, discrimination, and humiliation for drug-dependent people (panel 1). Consequently, prison staff often harbour negative attitudes towards opioid agonist therapy and consider drug dependence to be a social and moral problem that contributes to criminal behaviour, rather

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than a chronic, recurring illness.[40] Despite elevated HIV prevalence within prisons, the legal framework across EECA often falls short of human rights mandates for ensuring access to evidence-based services for addiction and HIV within the criminal justice system. Opioid agonist therapy with methadone or buprenorphine is internationally recognised as the most effective treatment for chronic opioid dependence, and is also among the most effective primary and secondary strategies for HIV prevention available.[1,41] Moreover, mathematical modelling suggests that expansion of opioid agonist therapy is the single most cost-effective means to control the HIV epidemic in EECA,[42] although when combined with antiretroviral therapy scale-up, is more effective but also more costly.[43] Regional policies (tables 1, 2) vary on whether opioid agonist therapy is provided throughout the entire incarceration (Moldova, Armenia, and Kyrgyzstan; panel 2), upon entry to police lock-up with supervised withdrawal from opioids (Georgia, Lithuania, Latvia, Estonia, and Ukraine), only in the community (Belarus, Azerbaijan, Tajikistan, and Kazakhstan), or not at all (Russia, Uzbekistan, and Turkmenistan). Moreover, contradictory legal mandates lead to an uneven distribution of care. In Ukraine, although national drug policies necessitate harm reduction programmes (including opioid agonist therapy and needle and syringe programmes) for all people who inject drugs, the medical guidelines require current signs of physical dependence, which are not always evident after a detainee completes withdrawal in police lock-up or in SIZO, disqualifying convicted prisoners from treatment.

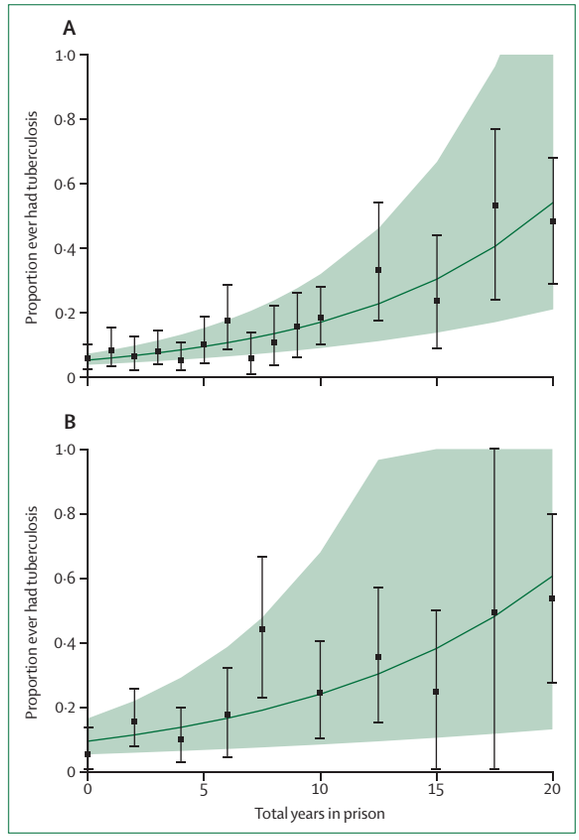

Figure 3: **Association between number of years incarcerated and prevalence of ever having tuberculosis among prisoners (A) and people who inject drugs in the community (B) in Ukraine**

The points are the mean proportion of prisoners or people who inject drugs in the community reporting ever having tuberculosis for different reported years in prison; the error bars are 95% bootstrapped CIs about the mean. The solid green line is the best logistic fit to the data, and the green shaded area is bounded by the best logistic fits to the lower and upper confidence bounds of the data. Data for prisoners are derived from a 2011 PUHLSE national prison survey.[23,24] Data for those in the community are derived from a multi-site ExMAT survey of people who inject drugs in Ukraine in 2015.[25]

The confluence of mass incarceration, substance use disorders, HIV, hepatitis C virus, and tuberculosis infections

Mass incarceration

The dramatic rise and inter-relationship between incarceration, HIV, hepatitis C virus, and tuberculosis in EECA is multifactorial.[49–52] The Soviet collapse gave rise to many factors that independently and collectively contributed to unprecedented mass incarceration in all EECA, partly as a result of decreasing industrial output, living standards, and life expectancy.[4] EECA, with 1·1 million prisoners, has some of the highest incarceration rates globally,[11] giving rise to the term "criminological transitions" for EECA countries.[53] Although incarceration rates have decreased modestly over the past decade, 13 of the 15 EECA countries still have rates that exceed the world average of 146 prisoners per 100 000 population, with ten exceeding 200: Turkmenistan (583), Russia (455), Belarus (335), Lithuania (315), Georgia (281), Kazakhstan (275), Latvia (264), Azerbaijan (236), Estonia (218), and Moldova (212); Ukraine recently plummeted from 324 to 195 due to regional conflicts.[11] This mass incarceration is the result of several intersecting factors, which have converged to result in some of the highest general-population prevalences of HIV,[54] hepatitis C virus,[55] and tuberculosis (including multidrug-resistant tuberculosis [MDR-TB])[12] in the world,[49,51] concentrated further within prisons where rates are substantially higher.

Substance use disorders

After 1991, injectable opioid use increased substantially due to changes in drug routes from Afghanistan and the contribution of economic collapse to a new drug economy.[8,56] Consequently, volatile opioid injection and HIV epidemics followed.[10] Many harsh criminal sanctions towards people who inject drugs ensued, resulting in escalating incarceration rates, especially of those who either had or were at high risk for HIV. Moreover, with the backdrop of economic instability and low wages for public servants such as police, these individuals became targets for bribes and other forms of corruption. Inability to pay resulted in arrest, detention, and imprisonment.[57,58]

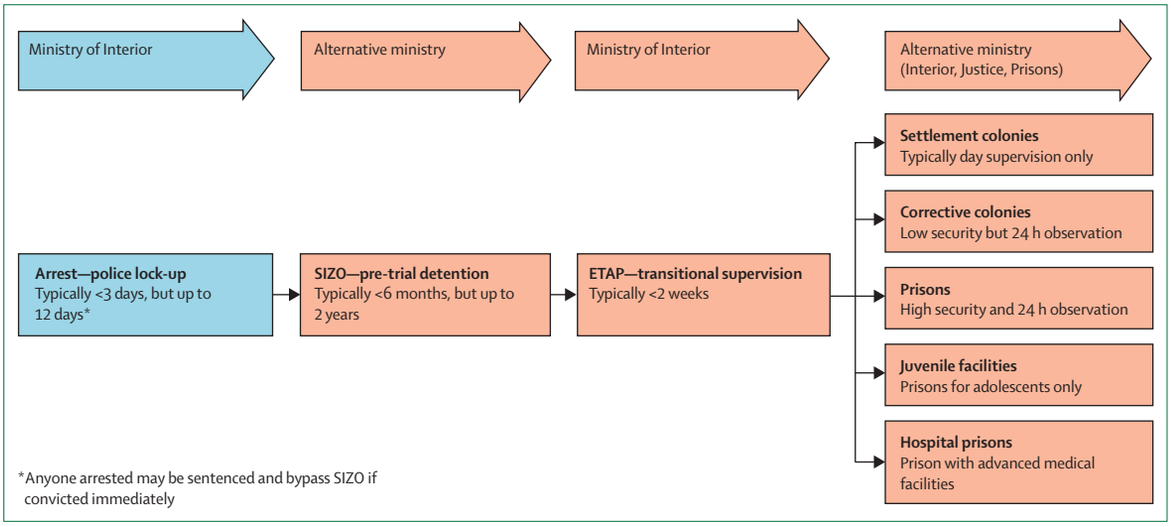

Figure 4: **An overview of the criminal justice system in Eastern Europe and Central Asia**
*Anyone arrested may be sentenced and bypass SIZO if convicted immediately.

Consequently, people who inject drugs represent more than a third of prisoners in EECA, but the level could be as high as 50–80% in some EECA countries.[23,59–61]

Explosive dynamics of HIV transmission accompanied the growing rates of injection drug use and incarceration in EECA, with HIV incidence and HIV-related mortality remaining volatile and increasing. Although HIV is concentrated among people who inject drugs and their sexual partners in EECA countries, there is also evidence of transmission among sex workers and men who have sex with men.[62] By the end of 2013, there were more than 1·4 million people living with HIV in EECA, with more than 85% of these residing in Russia and Ukraine.[63] Despite recent evidence of modestly expanded prevention programmes for HIV in some EECA countries, coverage with antiretroviral therapy (especially among those who inject drugs), opioid agonist therapy, and needle and syringe programmes remains low.[5,6] Additionally, extensive migration between and within some EECA countries results in lack of access to HIV prevention on the basis of citizenship or official registration for governmental health care.[59,62]

HIV infections

Prisons are structural risk environments for transmission of infectious diseases (figure 5) because of the high concentration of people who inject drugs, have HIV, or have hepatitis C virus.[54] HIV prevalence in prisoners is high throughout EECA. Although no reliable data exist for Turkmenistan and Belarus, HIV prevalence in prisons exceeds 10% in four countries—Latvia (20·4%), Ukraine (19·4%), Estonia (14·1%), and Kyrgyzstan (10·3%)—and remains markedly higher than in the community in Uzbekistan (4·7%), Lithuania (3·4%), Kazakhstan (3·9%), Azerbaijan (3·7%), Armenia (2·4%), Tajikistan (2·4%), Moldova (2·6%), and Georgia (0·9%). In nationally representative prison surveillance studies, HIV prevalence is 22 times, 19 times, and 34 times higher in prisons than in surrounding communities in Ukraine,[23,24] Azerbaijan,[59] and Kyrgyzstan,[60] respectively. Factors contributing to this increased concentration include harsh policies, laws, and policing targeted at people who inject drugs, and high levels of within-prison drug injection. In Russia, nearly all drug-related convictions are for drug use rather than drug trafficking.[64]

Estimates of the prevalence of within-prison drug injection range from 3% to 53%,[17,18,65,66] and have contributed to volatile HIV transmission within prisons in the region,[67] a sobering consequence of the over-representation of people who inject drugs and have untreated substance use disorders within prison. Evidence suggests that people who inject drugs do so more frequently within the community than they do within prisons, but HIV transmission risks are substantially elevated within prisons because injection equipment is scarce and results in more frequent sharing of contaminated injecting equipment.[18] This situation may, in part, contribute to findings that previous incarceration is independently associated with HIV among people who inject drugs in community settings,[68] which we also found in our Ukraine case study. Moreover, few studies have examined within-prison drug injection in EECA, but data from HIV-infected Ukrainian prisoners, the only individuals who can transmit HIV, showed extraordinarily high levels of injection drug use within prisons (54%), with many syringe-sharing partners.[17]

Effective HIV treatment with antiretroviral therapy is an effect method to prevent HIV transmission and must include prisoners,[69] many of whom are people who inject drugs.[70] Achieving the UNAIDS 90-90-90 targets of identifying 90% of people living with HIV, 90% of these

Panel 1: Sasha* and the ravages of incarceration

"Prisons here in Russia are places where people like me go to die. Though arrested often, I went there three times where I watched many people like me die. My first time occurred after police stopped me for a bribe. I had no money so he searched me, found a syringe he said contained heroin, and locked me up. When I got sick from withdrawal symptoms and was most vulnerable, they promised *shirka* [liquid poppy straw extract] if I admitted to stealing something that I didn't. I refused, spent a year in SIZO awaiting trial, but was finally convicted for 2 more years because drug users like me don't stand a chance. I was shocked to learn that drug injection in SIZO and prison was worse than on the streets of Gatchina, where I lived. The guards helped supply drugs and prison leaders made sure we remained addicted. Many of us paid with our lives. Some guys overdosed, others became HIV-infected like me and tuberculosis finished off the rest of us. Even though all of us were sick, seeing a doctor and getting care was nearly impossible. The bosses controlled everything. I swear the doctors were even worse than the guards. They just sent us back to our dorms to die."

"I was luckier than most and survived my first incarceration. I tried to be strong and avoid drugs. I cut back, but I had money and connections so I still used. I was weak and the prison bosses made sure I could get high and keep their pockets full. Within a week of release, I was back at it again. The police knew it too! They stayed on top of me, extracting their bribes, but once I ran out of money, I was arrested and back in SIZO and prison for another 3 years. This time, they sent me to a colony for seasoned criminals."

"I developed fevers and lost a lot of weight. I was sure I would die. My family had money and I was able to bribe my way and eventually saw a doctor. Without money, I would have died like everyone else. After 6 months of coughing and 15 pounds lost, my money bought me a fluorogram that was suggestive of tuberculosis, and I was shipped to a specialty tuberculosis colony. It seemed like everyone with tuberculosis also had HIV. I survived the scariest place I had ever been. We were 36 men in a closet with only 12 beds. We stood, coughed on each other, while others slept in shifts. Most guys, including me, would stop or dispose of our tuberculosis medications so that we could get sick and move from our closet to the infirmary where we'd get our own bed. Many who went to the infirmary never left except in a pine box because their medications didn't work anymore."

"I must be really strong. As soon as I got out, my parents took me to the local tuberculosis dispensary. Even though I told the doctors about what happened, they didn't believe me and I went through the entire process again of confirming tuberculosis. I received no medications for several months, developed fevers, drenching night sweats, and weight loss again before they would prescribe medications. I told them the medications had stopped working before, but they started me on the same ones I took before. It was no surprise that medications didn't work."

"I got sicker and my parents drove me to St Petersburg to a special hospital, and paid a lot of money for the doctors to find me a bed, prescribe new tuberculosis medications, and for the first time assessed my HIV with a CD4 count. Thankfully, my HIV was not a problem, but they said the tuberculosis might kill me. A doctor from the AIDS Centre said that he would bring me HIV medications if my parents would 'donate' some money for the convenience. I remained connected to an intravenous drip for 2 months and received many tuberculosis medications that my parents bought. The tuberculosis and HIV medications began to work. My cough and fevers went away, I gained weight, but I went home taking an entire cup of pills every day for almost 2 years."

"I know I almost died. Daily, I crave *shirka*! My mother knows me and never lets me out of her sight. Even when I try to make excuses to get some time alone, she never leaves my side. She knows me. I know me too! One minute alone and I know I will find *shirka*. If I do, I know I will get another free ticket to prison or to heaven. Either way, I am in prison. I prefer the prison in my house over the one where I know nobody cares."

*Sasha is not his real name.

initiating and remaining on antiretroviral therapy, and 90% achieving viral suppression, requires more effective HIV screening, treatment, and optimal medication adherence[71] in EECA countries, including in prisons. Despite National AIDS Centres in some countries reporting high coverage levels with antiretroviral therapy in prisoners who are diagnosed,[61,72] most people living with HIV within EECA prisons remain undiagnosed. Only half of people living with HIV in Ukrainian and Kyrgyz prisons are diagnosed before leaving prison.[23,24,60] In Ukraine, fewer than 12% of people living with HIV were aware of having HIV, with another 40% being diagnosed during incarceration, leaving almost half still not aware of their status.[24] In Azerbaijan, however, HIV diagnosis approaches 75% of cases.[59] Although both Azerbaijan and Kyrgyzstan provide high coverage of antiretroviral therapy for people living with HIV who are diagnosed within prison,[59,60] fewer than 4% of people living with HIV in Ukrainian prisons receive it.[23,24] No EECA country has data for antiretroviral therapy coverage after release, but even data from high-income countries suggest that the transition period from prison is one of heightened vulnerability, when antiretroviral therapy coverage falls precipitously and HIV risk is high,[73] especially for women.[74,75]

Hepatitis C virus infections

One review[55] reported hepatitis C virus prevalence among prisoners ranging from 3·1% to 38·0%, with the highest in central Asia.[76] Representative prison biosurveillance

Panel 2: Candles burning in the night

Despite its well documented efficacy in both prisons and communities, three countries in Eastern Europe and Central Asia (EECA)—Russia, Uzbekistan, and Turkmenistan—legislatively ban any type of opioid agonist therapy, while the remainder provide it in the community. Harsh criminalisation policies that result in high incarceration rates and large numbers of people who use drugs in EECA prisons—compounded by high levels of documented within-prison drug injection in the region—extraordinarily high levels of HIV, viral hepatitis, and tuberculosis and multidrug-resistant tuberculosis (MDR-TB) persist. Despite these poor prognostic indicators, a few countries have prevailed over the misaligned ideological policies espoused by Russia that favour punishment over rehabilitation and implemented internationally recognised evidence-based HIV prevention and treatment for prisoners. For example, small and financially vulnerable countries such as Kyrgyzstan, Moldova, and Armenia have introduced all 15 internationally recommended strategies for HIV prevention in prisons,[44] including both opioid agonist therapy and needle and syringe programmes. These three countries have emerged as welcomed beacons in the region because they have boldly overcome regional pressures to ban these HIV prevention strategies. Without international funding from international donors, however, such programmes would not exist, even though they remain suboptimally scaled. These successful programmes, however, may soon be jeopardised by anticipated loss of funding from international donors. Moreover, because Russia considers itself a leader in the EECA region and bans both opioid agonist therapies and does not fund needle and syringe exchange programmes, it continues to exert its pressure on other countries within the region by creating new political and trade alliances. By combining their ideological principles to ban HIV prevention programmes within both communities and prisons with financial support through these trade alliances, they could potentially undermine achievements made thus far by some countries in the EECA region that have aligned their HIV prevention strategies with those recommended by the UN based on public health and human rights mandates. It is conservatively estimated that a third of all prisoners in Kyrgyzstan, Moldova, and Armenia are people who use drugs (approximately 6900), mostly of opioids. However, only 802 (12%) individuals are prescribed opioid agonist therapy. Introduction and even scale-up of this therapy is minimally restricted by cost, since methadone is extremely inexpensive. Although its efficacy is well substantiated, policy around opioid agonist therapy is shaped more by ideology and prejudices than by scientific evidence.[45,46] Despite these ideological influences in the region, five countries (Armenia, Moldova, Kyrgyzstan, Latvia, and Estonia) have successfully introduced and expanded opioid agonist therapy throughout their criminal justice systems, including in pre-trial detention (table 2). Recent findings from Moldova, which may be emblematic of prison-based methadone problems in the region, suggest that myths about and prejudices towards opioid agonist therapy are amplified within prisons, resulting in bullying and ostracism of patients potentially undermining expansion efforts.[47] In nearby Ukraine, where opioid agonist therapy is not available within prison, extremely negative attitudes toward it prevail among prison personnel, although recent findings[40,48] suggest that provision of accurate information and training could partly overcome these myths. The within-prison risk environment is shaped by prisoners who use drugs, those who do not use drugs, prison personnel, and real and enacted policies for the setting; the next generation of efforts to expand opioid agonist therapies will therefore need to address multiple factors, including these myths and prejudices, and the within-prison drug economy, which probably propagates such myths to both incarcerated people who use drugs and to prison personnel who may view it as competition for the illicit drug trade. Continued support for opioid agonist therapy and needle and syringe programmes must therefore not only address service delivery itself, but also include strategies that combat misinformation and prejudices. Continued funding and provision of comprehensive prevention strategies are crucial for sustainability and should be coupled with shared best practices with other EECA countries that seek to align human rights and public health mandates in both community and criminal justice settings.

studies show hepatitis C prevalence to be substantially higher in Ukraine (60·2%),[23] Kyrgyzstan (49·7%),[60] and Azerbaijan (38·2%),[59] even though self-reported lifetime prevalence of injection drug use was substantially lower. These data suggest that drug injection is often under-reported in surveys. Hepatitis C infection in people living with HIV, when left untreated, complicates HIV treatment[1] and is associated with accelerated liver fibrosis.[77] New direct-acting antiviral treatments are costly, but have low toxicity, short treatment durations, and can cure hepatitis C virus in more than 90% of patients, irrespective of HIV status.[78] An internationally funded hepatitis C elimination strategy in Georgia has allowed prisoners to access this treatment, but it is not accessible elsewhere in EECA prisons due to cost constraints.[79]

Tuberculosis infections

Prisons generally, and especially in EECA, promote tuberculosis transmission (particularly drug-resistant strains), primarily because of crowding that increases contact between large numbers of high-risk individuals in poorly ventilated facilities over extended periods.[12,13] Furthermore, tuberculosis control is complicated by low cure rates due to delayed diagnosis, ineffective control policies (ie, screening, isolation, and treatment) in prisons, and perverse environmental disincentives to start or continue treatment (eg, better housing, treatment, or food, being excused from harsh work, and profiting from the sale of tuberculosis medications; panel 1).[80–82] Incarcerated individuals often have risk factors which increase their susceptibility to tuberculosis (eg, poverty, substance use

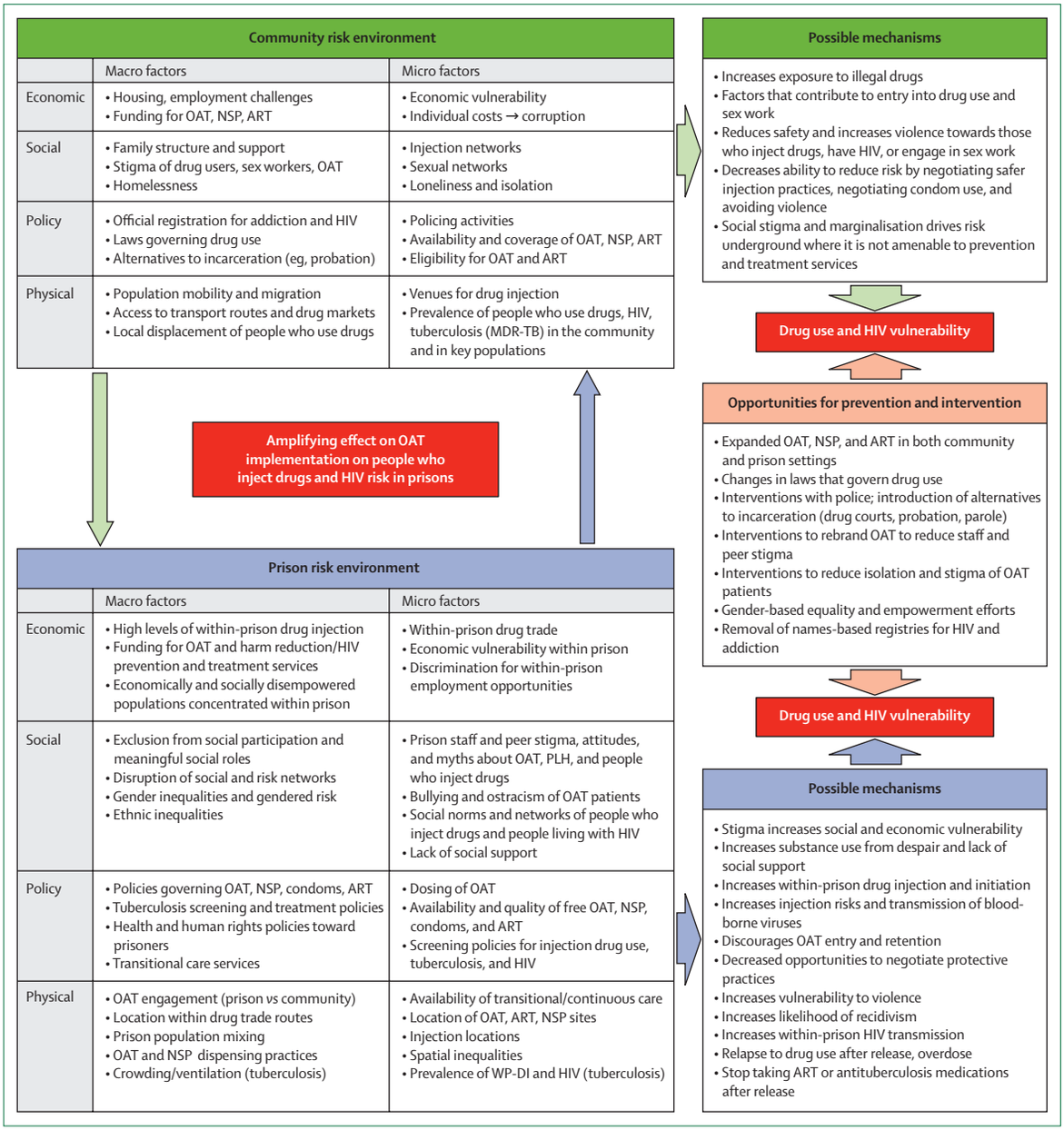

***Figure 5*: Relationship of the risk environment in community and criminal justice settings in Eastern Europe and Central Asia**
OAT=opioid agonist therapy. NSP=needle and syringe programmes. ART=antiretroviral therapy. MDR-TB=multidrug-resistant tuberculosis.

disorders, homelessness, malnutrition, and HIV infection) and are often released to the community before treatment completion, without effective transitional care.[12,83–85]

Factors contributing to tuberculosis transmission include overcrowding, high prisoner turnover, limited access to health-care services, delayed case detection and poor contact detection, lack of recommended rapid diagnostic methods such as Xpert MTB/RIF, and suboptimal treatment of infectious cases and implementation of tuberculosis infection control measures.[83–85] MDR-TB is disproportionately prevalent in EECA prisons[86,87] because of high prevalence in the community[88–91] and large numbers of HIV-infected people who inject drugs (who are more susceptible to tuberculosis due to being immunocompromised), and low treatment completion rates for tuberculosis.[92] The Ukraine case study illustrates the large degree to which incarceration contributes to tuberculosis transmission in EECA, with tuberculosis incidence rates directly correlated with increasing mass incarceration.[12] Additionally, MDR-TB incidence in EECA after independence was directly correlated with increasing mass incarceration.[12]

The Soviet Union collapse resulted in inadequate funding and supply of first-line tuberculosis regimens and extended confinement that facilitated transmission within prisons.[93] In Belarus, MDR-TB strains represent 35·3% of new and 76·5% of previously treated tuberculosis cases, meaning that half of all tuberculosis cases are MDR-TB.[87,94] Incarceration and HIV are independent contributors to the risk of patients having MDR-TB strains.[87] Remarkably high levels of MDR-TB also exist in Russia,[95,96] Lithuania and Latvia,[96] and Ukraine.[97] International guidance for tuberculosis screening and treatment[98] is inconsistently deployed in prisons throughout EECA, with resultant poor outcomes.[83,85] One notable exception is Azerbaijan, which reduced both tuberculosis and MDR-TB cases through the effective implementation of the WHO's Stop TB Strategy in the penitentiary sector, which involved routine screening, specialty tuberculosis hospitals, new infection control measures, rapid diagnostic testing, and training of prison personnel who now train prison staff elsewhere in EECA.[36]

Case study: evaluating the impact of HIV and tuberculosis transmission in Ukraine—a country in conflict

Ukraine, a middle-income country of 45 million people, is in the midst of conflict and has the highest prevalence of HIV in adults among EECA countries (1·2%), with tuberculosis and MDR-TB contributing the most to HIV-related mortality.[3] Before Russia's invasion of Crimea and the Donbas region, Ukraine's incarceration rate per 100 000 population was 324, but recently dropped to 195 per 100 000 in 2014 with large numbers of prisoners rapidly released to the community, increasing numbers of arrests and initiation of a new probation system that now supervises 70 000 people in the community. Incarceration among people who inject drugs in national surveys, however, does not appear to have decreased from 2011 to 2015.[99,100] HIV prevention services in Ukraine are under-scaled with only 2·7% of 310 000 people who inject drugs prescribed opioid agonist therapy and only 20% of people living with HIV prescribed antiretroviral therapy. Globally and within EECA, people who inject drugs experience high levels of incarceration (lifetime: 40–85%),[101,102] and current or previous incarceration is associated with heightened injecting risks and increased transmission of HIV and hepatitis C virus.[103–105] In Ukraine, at least 52% of people who inject drugs have been incarcerated,[25,26,106] with previously incarcerated people who inject drugs reporting an average of five incarcerations, each a year in duration.[23,25,26]

Data from three recent national surveys among people who inject drugs[25,26] and current prisoners[23] in Ukraine were used for the epidemiological analyses and HIV transmission modelling, described briefly in boxes 1 and 2 and further in the appendix. These data suggest that previously incarcerated people who inject drugs have a significantly higher HIV prevalence than never-incarcerated people who inject drugs (28% *vs* 13%; appendix figure p 25), even after controlling for injecting duration (adjusted odds ratio [aOR] 1·8, 95% CI 1·6–2·1). Additionally, they have heightened HIV risk behaviours, with previously incarcerated people who inject drugs reporting 3·9 (95% CI 2·8–5·0) more injections per month,[26] and a 1·5 times (95% CI 1·3–1·9) greater chance of sharing syringes[26] than never-incarcerated people who inject drugs, even after controlling for injecting duration. Recently released people who inject drugs (in the past year) had an even greater likelihood of syringe sharing (aOR 2·2, 95% CI 1·6–3·0).[26] Similarly, currently incarcerated people who inject drugs have more than twice the HIV prevalence of never-incarcerated people who inject drugs (28·5% *vs* 12·8%)[23,24,26] and high rates of syringe sharing.[17,57] Together, these data suggest that incarceration and the post-release period are important contributors to HIV transmission among people who inject drugs in Ukraine and forms the basis for our HIV modelling (box 1). This modelling suggests that incarceration, and specifically the heightened injecting risks after incarceration, could contribute 55% of new HIV infections among people who inject drugs in Ukraine over the next 15 years if we assume all this elevated risk is attributable to incarceration, or 28% if we conservatively assume that only the heightened risk among recently released people who inject drugs is due to incarceration. Conversely, reduced incarceration of people who inject drugs is unlikely to substantially decrease new HIV infections over the 15-year period because of the remaining elevated risk among previously incarcerated people who inject drugs. Scaling up and continuing prison-based opioid agonist therapy after release, however, could avert 19·8% of HIV infections over 15 years because it directly reduces the heightened post-release risk (figures 1, 2).

Tuberculosis incidence across EECA is high (nearly all more than 100 per 100 000 population), and is positively correlated with country-level incarceration rates,[12] highlighting the importance of within-prison tuberculosis transmission to the countrywide epidemics. An ecological analysis[12] estimated that across EECA, each percentage point increase in a country's incarceration rate corresponded to a 0·34% increase in tuberculosis incidence (95% CI 0·10–0·58). Findings from a systematic review[33] suggested that tuberculosis incidence in low-income and middle-income countries is ten to more than 30 times greater within prison than in the community. Few studies, however, have estimated the contribution of incarceration to the tuberculosis epidemic in EECA, with the systematic review estimating that between 5% and 17% of tuberculosis cases in Russia could be due to exposure within prison.[33] We therefore conducted in-depth statistical analyses with the datasets used for the HIV modelling[23,25,26] to evaluate the role of incarceration for increasing tuberculosis disease risk among the general population and in people who inject drugs in Ukraine (box 2). These analyses suggest that

incarceration is an important contributor to tuberculosis transmission (figure 3), and could be responsible for three-quarters of new yearly tuberculosis infections among people who inject drugs and 6·2% of all yearly tuberculosis infections in Ukraine.

Risk environment framework for criminal justice settings in the region

Overview

Figure 5 provides an overview of the risk environment factors in both the community and criminal justice system that contribute to onward disease transmission in EECA. The high prevalence of these infections in the community, coupled with both micro-level and macro-level factors embedded within the physical, social, economic, and policy and legal framework, result in the concentration of high-risk key populations such as those who inject drugs and sex workers in the criminal justice system. Incarceration, a physical factor, further amplifies these conditions by concentrating individuals with these infections. It also disrupts injection and social networks, a social factor, by creating new and riskier networks that develop as a survival tactic during incarceration.[107] HIV prevalence in Ukrainian prisons is high (19·4%),[23] but policy factors forbidding opioid agonist therapy or needle and syringe programmes, poor HIV detection, and low antiretroviral therapy coverage[24] facilitate frequent sharing of injecting equipment[17] and probably fuel HIV and hepatitis C virus transmission.[17,23,24,60] Similarly, individuals released from prison are highly stigmatised (social factor), relapse to drug use quickly (policy factor), develop new injection networks (social factor), and policing efforts target people who inject drugs and former prisoners due to registration of people who inject drugs in the community (policy factor).[57] Our analyses from our Ukraine case study suggest that the prison risk environment contributes to both HIV and tuberculosis transmission in people who inject drugs and tuberculosis transmission more generally to the community. Moreover, our findings suggest that introducing opioid agonist therapy to 50% of people who inject drugs within prison and retaining them in treatment for 12 months post-release would be the most effective strategy to reduce HIV incidence over the next 15 years, suggesting that this risk environment can be greatly influenced by the introduction of evidence-based addiction treatment with continuity into the community after release.

Drug-related policies

Key populations face many legal barriers that simultaneously contribute to incarceration and access to essential HIV programmes and services.[108,109] Drug policies vary considerably. In seven EECA countries (Russia, Uzbekistan, Ukraine, Belarus, Moldova, Lithuania, and Latvia) official names-based registration of people who inject drugs is required to receive treatment, including opioid agonist therapy. Registration, however, often results in restrictions in employment, loss of privileges (eg, driver's licence), and targeting by police.[57,110–112] Moreover, a passport and an official address is required for employment in Ukraine, undermining economic stability.[111] Collectively, these restrictions perpetuate re-incarceration,[113] especially given that alternatives to incarceration are uncommon in any EECA country. Addiction experts are required to report anyone accessing services, including for diagnosis confirmation, registration, and treatment. In most registries, there is little guidance or criteria to remove names from the registry or to define recovery from addiction. In Moldova and Uzbekistan, people who inject drugs are monitored for 3 years before removal from the registry is considered. In Uzbekistan, removal from the registry occurs upon incarceration. Otherwise, name-based registries persist for life.

Six countries have a mix of administrative and criminal penalties for drug possession. In Kazakhstan, administrative procedures can be deployed twice annually for drug possession, after which arrest and criminal sanctions ensue. In Kyrgyzstan, these penalties differ based on the quantity of illicit drugs found. Elsewhere, administrative procedures are used for individuals caught in possession of limited amounts for personal use, although the amount varies. In all countries, the criminal code defines the purchase of illicit drugs as an incarcerable criminal offence.

Punitive drug laws restrict access to HIV testing and treatment for people who inject drugs. Criminalisation of drug use and discriminatory practices restrict access to needle and syringe programmes and community agencies where these services are located. Harm reduction services are often legally restricted to adults. Police in some countries arrest people who inject drugs who access harm reduction services and confiscate drugs and syringes, or

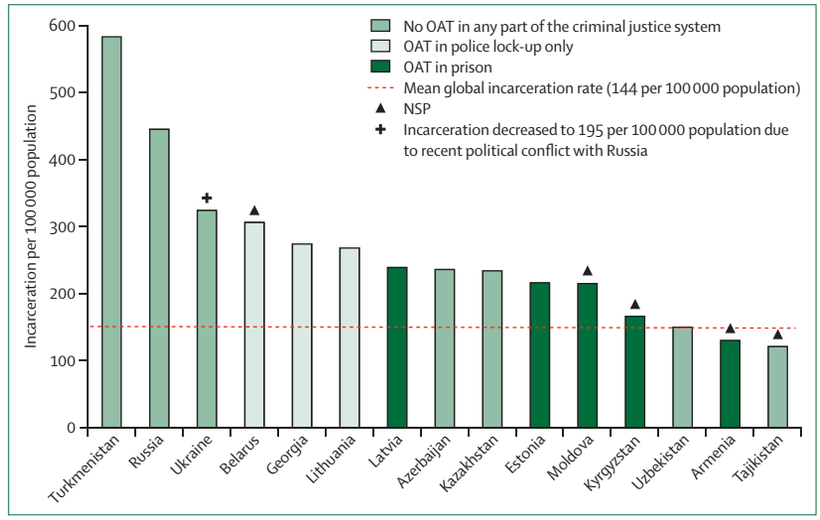

Figure 6: **Incarceration in EECA countries and availability of opioid agonist therapies and needle and syringe programmes**

EECA=Eastern Europe and Central Asia. OAT=opioid agonist therapy. NSP=needle and syringe programme.

Panel 3: Recommendations for prevention and treatment policies

Develop strategies to reduce incarceration rates in key populations

Laws and policies that criminalise personal drug use and sex work should be changed. New strategies should be developed that directly aim to reduce incarceration, especially to address tuberculosis transmission in people who use drugs. Modelling and statistical analyses here confirm the negative contributions of incarceration, especially on people who inject drugs, on perpetuating the HIV and tuberculosis epidemics. For example, current policing policies target high-risk individuals (ie, people who use drugs, registered drug users, sex workers, etc) and few provide community policing that focuses on engagement of drug users in evidence-based treatment for addition or harm reduction services in the community. Development of community policing efforts, pre-booking diversion programmes, alternatives to incarceration such as drug courts, or community supervision in probation that favours rehabilitation and treatment over incarceration are needed. Quality community supervision in probation that engages people living with or at risk for HIV in community settings where supportive social networks remain, and prevention and treatment is uninterrupted, is crucial.

Improve HIV testing and treatment strategies

In order to meet UNAIDS policies for 90% detection, coverage of antiretrovirals, and viral suppression (90-90-90), prisons in Eastern Europe and Central Asia (EECA) must improve HIV testing strategies because HIV identification falls far lower than UNAIDS targets. Although some countries meet mandates for antiretroviral therapy coverage, room for improvement remains. Identifying HIV and increasing antiretroviral therapy coverage within prisons must, however, be linked to continuity of therapy after release, including linkage to opioid agonist therapy.

Reduce gap between prison and community health-care services

Prisoners with comorbid conditions have a right to the same standard of prevention and treatment services as those in community settings.[122] Substance use disorders should be addressed as chronic, recurring health conditions, and should be screened for and treated in accordance with the UN Mandela Rules that support similar standards in both prisons and the community. Opioid agonist therapy programmes are substantially less expensive than imprisonment; modelling findings suggest that the most effective strategy to reduce HIV transition is to increase coverage of opioid agonist therapy to people who use drugs within prison and effectively transition them to opioid agonist therapy after release. When international donors fund HIV treatment and prevention (eg, Global Fund to Fight AIDS, Tuberculosis and Malaria; President's Emergency Plan for AIDS Relief), these agencies should stipulate that such prison-based programmes are both introduced and scaled-to-need as part of a national strategy as a requirement for continued funding.

Introduce and expand opioid agonist therapy, needle and syringe programmes, and antiretroviral therapy in the criminal justice system

Modelling of HIV transmission suggests that scaling up of opioid agonist therapy coverage to 50%, combined with retention after release during the heightened risk period, would reduce new infections in people who inject drugs the most. National guidelines for HIV prevention and treatment should specifically stipulate equivalence of treatment in the community and the criminal justice system. International agencies support 15 evidence-based practices in criminal justice systems. Where such stipulations exist, implementation and monitoring should specifically address criminal justice settings. Despite the existence of national guidelines, there is a failure to implement a comprehensive drug policy in prisons that includes psychological support, needle and syringe programmes, opioid agonist therapy, and antiretroviral therapy. Crucially, the scale-up of these interventions in criminal justice systems should coincide with improved continuity of care and prevention after release, which could have substantial benefits for HIV prevention.

Access to integrated care

Compared with individuals in the community, prisoners carry a higher burden of disease and often have multiple medical and social comorbidities—eg, HIV, hepatitis C virus, tuberculosis, and sexually transmitted infections, as well as psychiatric and substance use disorders—that require a comprehensive strategy to be addressed. Although policies that favour alternatives to incarceration are preferred, for those who do interface with the prison environment, such settings provide an opportunity to screen, treat, and provide continuity of care after release to individuals who have otherwise been missed by community prevention and treatment services.

(Continues on next page)

extract bribes for the possession of syringes or needles.[57,58,114,115] In one Russian survey of people who inject drugs, more than 60% had been arrested for needle possession or had drugs planted on them by the police.[116]

Sexual activity policies

Although many EECA countries have repealed laws prohibiting same-sex relationships, Uzbekistan and Turkmenistan continue to enforce them. Tajikistan, Uzbekistan, Ukraine, and Armenia have laws that criminalise sex acts between consenting adults of the same gender, sodomy, and cross-dressing or gender impersonation. Kyrgyzstan and Tajikistan have legislation where the age of consent differs for homosexual and heterosexual sex; Kyrgyzstan has laws or policing practices criminalising or preventing condom distribution

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(Panel 3 continued from previous page)

Align prisoner health with international HIV prevention and treatment goals

The 90-90-90 UNAIDS HIV prevention and treatment goal to diagnose, treat, and achieve viral suppression in 73% of all people living with HIV should be extended to prisoners where the HIV continuum of care in EECA is poorly characterised. To achieve this goal, innovations in HIV testing (eg, routine testing that has been successful in other settings where it was linked to treatment), provision of antiretroviral therapy to all people living with HIV, and achieving viral suppression through optimal adherence to antiretroviral therapy will require changes not only in prison-based services, but also in transitional programmes to the community. Our modelling suggests that transitional care, especially provision of opioid agonist therapy during incarceration and sustaining it after release, will be crucial to reduce HIV prevalence in the long run.

Continuity of care

Prison prevention and treatment should be embedded within a national framework for providing continuous care within SIZO and prison and after community release. Our modelling suggests that providing continuity of interventions such as opioid agonist therapy post-release is key to achieve large HIV prevention benefit among people who inject drugs. The criminal justice system is a crucial setting to provide treatment and prevention services where many diseases are concentrated, especially in people with comorbid conditions. Partnerships with non-governmental organisations should be encouraged to ensure that prevention and treatment services are maintained.

Education

To successfully implement evidence-based screening and treatment for substance use disorders, HIV, hepatitis C virus, and tuberculosis, continuing education is essential to directly address and reduce negative attitudes towards people with these conditions to reduce both stigma and discrimination. Such professional development should target not only medical personnel, but also custodial staff to better align efforts to engage to promote health and wellness in prisoners.

Implementation of organisational strategies

Administrators and staff within the criminal justice system need to understand that provision of health care, especially to people who use drugs, is the best strategy to reduce recidivism and improve public health. The success of many international efforts to expand harm reduction strategies has been accompanied with efforts to help staff understand the value of providing health care. This is a long-term strategy to better integration of health and safety policies.

yet supplies them within prison. Although transparent in its intent to target and stigmatise men who have sex with men, Russia's legislation prohibiting dissemination of "propaganda of non-traditional sexual relations [ie, LGBT] among minors" is ostensibly to protect so-called traditional family values. These laws result in arrest of individuals promoting HIV prevention for men who have sex with men. Similar but harsher legislation is being considered in Belarus, Kazakhstan, and Kyrgyzstan.[62]

All EECA countries prohibit sex work, but police enforce it variably and especially target sex workers who use drugs. Kyrgyzstan, Azerbaijan, and Uzbekistan have laws or policies allowing mandatory HIV testing of key populations. Some countries (Kyrgyzstan, Tajikistan, Uzbekistan, Ukraine, and Armenia) have laws that protect against human rights violations, but they are not specific to HIV or key populations.

Community supervision

Community sanctions such as probation or drug courts are not widely available, and probation is not generally linked to treatment. Several countries have limited community-based supervision, including Russia (supervision by former military or prison personnel), Ukraine (new in 2015), Moldova (started 2002), Latvia (started in 2005), Estonia (started in 1998 with expansion in 2013), Lithuania, Georgia, and Kazakhstan. Pilot projects are underway in Armenia to guide probation service initiation. Some probation programmes refer cases to drug treatment agencies or psychiatric hospitals. Many of the probation programmes emerged from the prison service and therefore reflect the prison culture. In most instances, probation is in its infancy.

Coverage with opioid agonist therapies

Many prisoners in EECA not only initiate drug injection within prison, but continue to share injecting equipment during incarceration[17,60] and especially after release.[17] Five countries (Armenia, Kyrgyzstan, Moldova, Latvia, and Estonia) have opioid agonist therapy in prisons, with coverage being extremely low. Georgia has a pilot programme in SIZO and four others offer it only in police lock-up (table 1, figure 6). Emblematic of the region, Ukraine's prison personnel have especially negative attitudes towards opioid agonist therapy, although this is improved when they are sufficiently knowledgeable about its benefits;[40] prisoners, meanwhile, often have high expectations about recovery that diminish after release in the absence of opioid agonist therapy.[48] In Moldova, opioid agonist therapy and needle and syringe programmes exist within communities and prisons, but treatment coverage is disproportionately lower in the community than in prisons, reducing access after release and necessitating many patients to discontinue therapy before release. In Moldova, prisoners receiving opioid agonist therapy are often ostracised by other prisoners, perhaps due to illicit drug economies within prisons that compete with opioid

agonist therapy.[40,47] Thus, effective and essential scale-up of opioid agonist therapies must coincide with education and motivation of both prisoners and prison personnel.

HIV diagnosis

The first step to achieving the UNAIDS 90-90-90 strategy is HIV testing.[71] Most EECA prisons deploy risk-based opt-in testing within prisons. One of the major challenges in EECA prisons is low HIV detection; more than half of HIV-infected prisoners do not know their HIV status.[23,24,60,61] For those that do, however, most are tested within prison.[23,24,59,60] Notable exceptions in which expanded HIV testing has greatly improved HIV diagnosis include Estonia[117] and Azerbaijan.[59] Required name-based HIV registries often undermine voluntary testing efforts and treatment engagement.[98,108] Officially reported HIV data therefore underestimate true prevalence,[118] with restriction of access to HIV treatment due to mandatory registration combined with stigma, discrimination, and criminalisation of key populations.[6,110,119] Similarly, patients receiving opioid agonist therapy must be officially registered before receiving it in all EECA countries, which can lead to restrictions on employment opportunities, limitations in housing, and revocation of drivers' licences, further compounding economic disparities.[119]

Conclusions

The 1990 United Nations Basic Principles for the Treatment of Prisoners state that prisoners "shall have access to the health services available in the country without discrimination on the grounds of their legal situation".[120] This basic principle has been expanded in the case of HIV to also include preventive services, but has been infrequently applied, especially in many EECA countries where prisoners derive less benefit from prevention and treatment services than other citizens.[121] Structural aspects of the criminal justice system in EECA concentrate most at-risk populations, which, taken together, probably contribute heavily to disease amplification and transmission within prison and to the community after release. These structural impediments also limit access to prevention and treatment services for HIV, hepatitis C virus, and tuberculosis. Our findings suggest that the high-risk prison environment, including the immediate period after release (for HIV), is an important contributor to HIV and tuberculosis transmission in people who inject drugs and more broadly for tuberculosis transmission in the general population. Strategies that reduce incarceration overall (especially for people who inject drugs) and greatly expand the availability of opioid agonist therapy within prison, ensuring effective continuation of this therapy after release, will probably have the greatest impact on HIV and tuberculosis transmission in people who inject drugs interfacing with the criminal justice system. Strategies that reduce incarceration for the entire population, but especially for people who inject drugs, are also likely to reduce tuberculosis cases. Not only are policy reforms necessary to abrogate this trajectory, but further epidemiological, qualitative, modelling, cost-effectiveness, and implementation science research are crucial to help ensure that both prisoner and public health are optimised and consistent with human rights mandates (panel 3). Such approaches could reduce the transmission of HIV, hepatitis C virus, and tuberculosis in these settings, especially if they also ensure continuity of care after release from prison.

Contributors

FLA, LA, JS, PV, NKM, EB-P, HS, SD, FST, PS, RB, NE-B, and KD contributed shared responsibility in developing initial drafts and writing this manuscript. LA, PS, and FLA analysed the initial Ukraine datasets. PV, NKM, JS, FLA, and EB-P performed the modelling and were responsible for initial and final drafts of the modelling sections and the development of figures. LA and FLA performed the initial literature search. FLA, LA, JS, PV, NKM, EB-P, HS, SD, FST, PS, RB, NE-B, and KD revised each draft of this work critically for important intellectual content. All authors made substantial contributions to the design and approach, and approve the final version to be published.

Declaration of interests

We declare no competing interests.

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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Online Appendix

Supplementary material for Box 1: Part 1

Title: Model projections of the role of incarceration for driving long-term HIV transmission among people who inject drugs in Ukraine

Model description

We developed a dynamic compartmental model of incarceration and HIV transmission among current people who inject drugs (PWID) to evaluate the impact of incarceration on HIV transmission among PWID in Ukraine. The PWID population was stratified by incarceration state (never incarcerated i=0, currently incarcerated i=1, previous recent incarceration (released in the last 12 months) i=2, and previous non-recent incarceration (> 12 months since release) i=3), OAT status (off OAT j=0, on OAT j=1) and HIV infection state (susceptible $S_{i,j}$, initial acute HIV infection $A_{i,j}$, chronic HIV infection $C_{i,j}$, and chronically infected and receiving ART $Z_{i,j}$; where $S_{i,j}, A_{i,j}, C_{i,j}$ and $Z_{i,j}$ represent the number of PWID in each state). The model schematics for the incarceration and HIV components of the model are in Figure S1.

PWID leave the model with rate μ either through death (non-HIV related) or permanent cessation of injecting, while chronically HIV-infected PWID not receiving ART experience an additional exit rate due to HIV-related death μ_C. The model is open, such that individuals continually enter through initiation of injecting drug use as susceptible (i.e. uninfected) PWID, with a proportion p_i of new PWID entering each incarceration compartment (never incarcerated, currently incarcerated and previously incarcerated), with the entry set to balance the exit of PWID due to cessation and non-HIV deaths, but not HIV deaths, hence giving a decreasing population size over time due to HIV-related morbidity and mortality. PWID within the model are assumed to be incarcerated and re-incarcerated at different fixed annual rates, γ and δ respectively, and are released from prison at a constant rate τ, independent of previous incarcerations.

All PWID can acquire and transmit HIV in their given setting, either community or in prison, with incarcerated PWID only being able transmit HIV to other incarcerated PWID. We do not distinguish between sexual and injection-related HIV transmission and do not stratify by gender, but just evaluate what overall level of HIV transmission is needed to fit the estimated HIV prevalence in each setting. Susceptible PWID are infected with a force of infection $\beta_{i,j}$, which is proportional to: a setting's dependent HIV transmission rate, the proportions of PWID in each stage of HIV infection in their setting (prison or the community), and the infectivity of each stage of infection (including ART status) relative to the chronic phase of HIV infection. We assume that never incarcerated PWID have a transmission risk of λ, and that community PWID with a history of recent or non-recent incarceration have different risks of HIV transmission ($\lambda\eta_1$ and $\lambda\eta_2$ respectively) than those who have never been incarcerated, and assume these groups mix proportionately relative to their overall transmission risk (product of transmission rate and size of sub-group). We also assume that currently incarcerated PWID have a different transmission risk ($\lambda\eta_3$) than never or previously incarcerated community PWID.

Following infection, individuals enter a short acute phase of infection, where they are assumed to be more infectious than in the subsequent chronic phase of infection (by a factor α_A)1 and progress from acute infection to chronic infection at a fixed rate ϕ. A proportion π of chronically infected PWID are enrolled onto ART each year, where they are less infectious than chronically infected PWID not receiving ART2,3 (by a factor α_Z), and experience a μ_Z factor lower HIV-related death rate than those not on ART.4 PWID receiving ART are lost to follow up at a rate θ, whereupon they return to the chronically infected PWID compartment that are not receiving ART. We assume these PWID can be re-enrolled onto ART at the same rate as ART-naïve chronically infected PWID.

PWID are enrolled onto OAT at a fixed rate ψ_i, which depends on their incarceration status. While on OAT, PWID are assumed to have a relative transmission risk of ζ compared to those not on OAT. A proportion, ω, of community PWID are maintained on OAT when incarcerated and both these PWID and those enrolled on OAT in prison, remain on OAT throughout their prison sentence. A proportion, χ, of PWID released from prison are maintained on OAT for 12 months following release. Similarly, PWID who are enrolled onto OAT in the community are assumed to remain on OAT for an average of 1 year.

Model equations

The full model equations are as follows, for never incarcerated PWID off OAT**,**

$$\frac{\partial S_{0,0}}{\partial t} = p_0\mu N - (\mu + \gamma + \beta_{0,0} + \psi_0)S_{0,0} + S_{0,1}$$

$$\frac{\partial A_{0,0}}{\partial t} = \beta_{0,0}S_{0,0} - (\mu + \gamma + \phi + \psi_0)A_{0,0} + A_{0,1}$$

$$\frac{\partial C_{0,0}}{\partial t} = \phi A_{0,0} - (\mu + \gamma + \mu_C + \pi + \psi_0)C_{0,0} + \theta Z_{0,0} + C_{0,1}$$
$$\frac{\partial Z_{0,0}}{\partial t} = \pi C_{0,0} - (\mu + \gamma + \mu_Z\mu_C + \theta + \psi_0)Z_{0,0} + Z_{0,1}$$

For currently incarcerated PWID off OAT

$$\frac{\partial S_{1,0}}{\partial t} = p_1\mu N + \gamma S_{0,0} + \delta\big(S_{2,0} + S_{3,0}\big) + (1-\omega)(\gamma S_{0,1} + \delta\big(S_{2,1} + S_{3,1}\big)) - \big(\mu + \tau + \beta_{1,0} + \psi_1\big)S_{1,0}$$
$$\frac{\partial A_{1,0}}{\partial t} = \beta_{1,0}S_{1,0} + \gamma A_{0,0} + \delta(A_{2,0} + A_{3,0}) + (1-\omega)(\gamma A_{0,1} + \delta\big(A_{2,1} + A_{3,1}\big)) - (\mu + \tau + \phi + \psi_1)A_{1,0}$$
$$\frac{\partial C_{1,0}}{\partial t} = \phi A_{1,0} + \gamma C_{0,0} + \delta(C_{2,0} + C_{3,0}) + (1-\omega)(\gamma C_{0,1} + \delta\big(C_{2,1} + C_{3,1}\big)) - (\mu + \tau + \mu_C + \pi + \psi_1)C_{1,0} + \theta Z_{1,0}$$
$$\frac{\partial Z_{1,0}}{\partial t} = \pi C_{1,0} + \gamma Z_{0,0} + \delta(Z_{2,0} + Z_{3,0}) + (1-\omega)(\gamma Z_{0,1} + \delta\big(Z_{2,1} + Z_{3,1}\big)) - (\mu + \tau + \mu_Z\mu_C + \theta + \psi_1)Z_{1,0}$$

For previously, recently incarcerated PWID (released in last year) off OAT

$$\frac{\partial S_{2,0}}{\partial t} = p_2\mu N + \tau S_{1,0} + (1-\chi)\big(\tau S_{1,1} + S_{2,1}\big) - \big(\mu + \delta + \beta_{2,0} + 1 + \psi_2\big)S_{2,0}$$
$$\frac{\partial A_{2,0}}{\partial t} = \beta_{2,0}S_{2,0} + \tau A_{1,0} + (1-\chi)(\tau A_{1,1} + A_{2,1}) - (\mu + \delta + \phi + 1 + \psi_2)A_{2,0}$$
$$\frac{\partial C_{2,0}}{\partial t} = \phi A_{2,0} + \tau C_{1,0} + (1-\chi)(\tau C_{1,1} + C_{2,1}) - (\mu + \delta + \mu_C + \pi + 1 + \psi_2)C_{2,0} + \theta Z_{2,0}$$
$$\frac{\partial Z_{2,0}}{\partial t} = \pi C_{2,0} + \tau Z_{1,0} + (1-\chi)(\tau Z_{1,1} + Z_{2,1}) - (\mu + \delta + \mu_Z\mu_C + 1 + \theta + \psi_2)Z_{2,0}$$

For previously, non-recently incarcerated PWID (released over a year ago) off OAT

$$\frac{\partial S_{3,0}}{\partial t} = p_3\mu N + S_{2,0} + \chi S_{2,1} - \big(\mu + \delta + \beta_{3,0} + \psi_3\big)S_{3,0} + S_{3,1}$$
$$\frac{\partial A_{3,0}}{\partial t} = \beta_{3,0}S_{3,0} + A_{2,0} + \chi A_{2,1} - (\mu + \delta + \phi + \psi_3)A_{3,0} + A_{3,1}$$
$$\frac{\partial C_{3,0}}{\partial t} = \phi A_{3,0} + C_{2,0} + \chi C_{2,1} - (\mu + \delta + \mu_C + \pi + \psi_3)C_{3,0} + \theta Z_{3,0} + C_{3,1}$$
$$\frac{\partial Z_{3,0}}{\partial t} = \pi C_{3,0} + Z_{2,0} + \chi Z_{2,1} - (\mu + \delta + \mu_Z\mu_C + \theta + \psi_3)Z_{3,0} + Z_{3,1}$$

For never incarcerated PWID on OAT

$$\frac{\partial S_{0,1}}{\partial t} = p_0\mu N - \big(\mu + \gamma + \zeta\beta_{0,1} + 1\big)S_{0,1} + \psi_0 S_{0,0}$$
$$\frac{\partial A_{0,1}}{\partial t} = \zeta\beta_{0,1}S_{0,1} - (\mu + \gamma + \phi + 1)A_{0,1} + \psi_0 A_{0,0}$$
$$\frac{\partial C_{0,1}}{\partial t} = \phi A_{0,1} - (\mu + \gamma + \mu_C + \pi + 1)C_{0,1} + \theta Z_{0,1} + \psi_0 C_{0,0}$$
$$\frac{\partial Z_{0,1}}{\partial t} = \pi C_{0,1} - (\mu + \gamma + \mu_Z\mu_C + \theta + 1)Z_{0,1} + \psi_0 Z_{0,0}$$

For currently incarcerated PWID on OAT

$$\frac{\partial S_{1,1}}{\partial t} = p_1\mu N + \omega(\gamma S_{0,1} + \delta\big(S_{2,1} + S_{3,1}\big)) - \big(\mu + \tau + \zeta\beta_{1,1}\big)S_{1,1} + \psi_1 S_{1,0}$$
$$\frac{\partial A_{1,1}}{\partial t} = \zeta\beta_{1,1}S_{1,1} + \omega(\gamma A_{0,1} + \delta\big(A_{2,1} + A_{3,1}\big)) - (\mu + \tau + \phi)A_{1,1} + \psi_1 A_{1,0}$$
$$\frac{\partial C_{1,1}}{\partial t} = \phi A_{1,1} + \omega(\gamma C_{0,1} + \delta\big(C_{2,1} + C_{3,1}\big)) - (\mu + \tau + \mu_C + \pi)C_{1,1} + \theta Z_{1,0} + \psi_1 C_{1,0}$$
$$\frac{\partial Z_{1,1}}{\partial t} = \pi C_{1,1} + \omega(\gamma Z_{0,1} + \delta\big(Z_{2,1} + Z_{3,1}\big)) - (\mu + \tau + \mu_Z\mu_C + \theta)Z_{1,1} + \psi_1 Z_{1,0}$$

For previously, recently incarcerated PWID (released in last year) on OAT

$$\frac{\partial S_{2,1}}{\partial t} = p_2\mu N + \chi\tau S_{1,1} - \big(\mu + \delta + \zeta\beta_{2,1} + 2 - \chi\big)S_{2,1} + \psi_2 S_{2,0}$$
$$\frac{\partial A_{2,1}}{\partial t} = \zeta\beta_{2,1}S_{2,1} + \chi\tau A_{1,1} - (\mu + \delta + \phi + 2 - \chi)A_{2,1} + \psi_2 A_{2,0}$$

$$\frac{\partial C_{2,1}}{\partial t} = \phi A_{2,0} + \chi\tau C_{1,1} - (\mu + \delta + \mu_C + \pi + 2 - \chi)C_{2,1} + \theta Z_{2,1} + \psi_2 C_{2,0}$$
$$\frac{\partial Z_{2,1}}{\partial t} = \pi C_{2,0} + \chi\tau Z_{1,1} - (\mu + \delta + \mu_Z\mu_C + 2 - \chi + \theta)Z_{2,1} + \psi_2 Z_{2,0}$$

For previously, non-recently incarcerated PWID (released over a year ago) on OAT

$$\frac{\partial S_{3,1}}{\partial t} = p_3\mu N + (1 - \chi)S_{2,1} - \big(\mu + \delta + \zeta\beta_{3,1} + 1\big)S_{3,1} + \psi_3 S_{3,0}$$
$$\frac{\partial A_{3,1}}{\partial t} = \zeta\beta_{3,1}S_{3,1} + (1 - \chi)A_{2,1} - (\mu + \delta + \phi + 1)A_{3,1} + \psi_3 A_{3,0}$$
$$\frac{\partial C_{3,1}}{\partial t} = \phi A_{3,1} + (1 - \chi)C_{2,1} - (\mu + \delta + \mu_C + \pi + 1)C_{3,1} + \theta Z_{3,1} + \psi_3 C_{3,0}$$
$$\frac{\partial Z_{3,1}}{\partial t} = \pi C_{3,1} + (1 - \chi)Z_{2,1} - (\mu + \delta + \mu_Z\mu_C + \theta + 1)Z_{3,1} + \psi_3 Z_{3,0}$$

Where the total population size $N = \sum_{\substack{i=0,1,2,3 \\ j=0,1}}(S_{i,j} + A_{i,j} + C_{i,j} + Z_{i,j})$

And $\beta_{0,0} = \lambda\frac{U}{L}$

$$\beta_{1,0} = \eta_1\lambda\frac{\big(\alpha_A A_{1,0} + C_{1,0} + \alpha_Z Z_{1,0}\big) + \zeta\big(\alpha_A A_{1,1} + C_{1,1} + \alpha_Z Z_{1,1}\big)}{\big(S_{1,0} + A_{1,0} + C_{1,0} + Z_{1,0}\big) + \zeta\big(S_{1,1} + A_{1,1} + C_{1,1} + Z_{1,1}\big)}$$

$\beta_{i,0} = \eta_i\lambda\frac{U}{L}$ for i=2,3

$\beta_{i,1} = \zeta\beta_{i,0}$ for i=0,12,3

where,

$$U = \big(\alpha_A A_{0,0} + C_{0,0} + \alpha_Z Z_{0,0}\big) + \zeta\big(\alpha_A A_{0,1} + C_{0,1} + \alpha_Z Z_{0,1}\big) + \sum_{i=2,3}(\eta_i\big(\alpha_A A_{i,0} + C_{i,0} + \alpha_Z Z_{i,0} + \zeta\big(\alpha_A A_{i,1} + C_{i,1} + \alpha_Z Z_{i,1}\big)\big)$$

$$L = \big(A_{0,0} + C_{0,0} + Z_{0,0}\big) + \zeta\big(A_{0,1} + C_{0,1} + Z_{0,1}\big) + \sum_{i=2,3}(\eta_i\big(A_{i,0} + C_{i,0} + Z_{i,0} + \zeta(A_{i,1} + C_{i,1} + Z_{i,1})\big)$$

Model parameterisation and calibration

The model was fit to detailed data from Ukraine. This was comprised of two steps. First, the incarceration component of the model was parameterised and calibrated to self-reported previous and current incarceration data, and then the HIV transmission component was parameterised and calibrated to HIV prevalence data for each incarceration state.

Tables S1 and S2 shows the incarceration parameter values and calibration data and Table S3 shows the HIV biological and transmission factors and HIV calibration data. In summary, most data used to parameterise and calibrate the models was obtained from three multi-site Ukrainian surveys; the National Prison Survey (PUHLSE survey) undertaken in 12 prisons during 2011 sampling 402 soon to be released prisoners (PWID and non-PWID[5]), the AIDS Alliance Integrated Bio-Behavioural Assessment (IBBA) survey which sampled 9502 PWID in 29 cities in 2013,[6] and the Expanding Medication-Assisted Therapy (ExMAT) bio-behavioural survey which sampled 1612 PWID in 5 cities in 2015.[7] The ExMAT survey was mainly used to provide data on PWID incarceration dynamics, including: the proportion ever incarcerated, the number of times incarcerated, and total time incarcerated, all stratified by duration of injecting when necessary. The PULHSE and ExMAT surveys were both used to estimate the average sentence length of a PWID. The PULHSE survey was also used to estimate the HIV prevalence among currently incarcerated PWID, whereas the AIDS Alliance IBBA survey was used to estimate the HIV prevalence among never and previously incarcerated PWID and the risk behaviour of these PWID.

Calibrating the model's incarceration dynamics

An incarceration dynamics sub-model was used to track a simulated closed cohort of 1000 PWID for 35 years from their onset of injecting. This model captured three stages of incarceration: PWID who had never been incarcerated, PWID currently incarcerated and PWID who had previously been incarcerated. The model was used to estimate the incarceration and re-incarceration rates, average time spent in prison, PWID exit rate (cessation and non-HIV deaths) and the proportion of new PWID initiating injecting in each incarceration state. This was done by calibrating the sub-model to data on the: (1) proportion of community PWID who have ever been incarcerated; and (2) mean number of times previously incarcerated community PWID report being incarcerated, both stratified by duration of injecting (Table S2 gives the data that the model was fit to). Although the incarceration sub model did not include HIV, it did assume an elevated HIV related death rate in each incarceration state to ensure the full model with HIV predicted the same proportion of PWID in each incarceration state. The additional HIV related death rate was

estimated by applying a HIV death rate to the observed HIV prevalence among never and previously incarcerated PWID in 2013,[7] and currently incarcerated PWID in 2011,[5] and adding that to the leaving rate for each incarceration subgroup. An Approximate Bayesian computation sequential Monte Carlo scheme[8] was used to obtain a sample of 1,000 incarceration-related parameter sets that fit the incarceration data sufficiently well such that the sum of the relative residual errors (ignoring whether errors are positive or negative) for each model fit was less than 30% (so that on average each of the 10 fitted points deviated by at most 3% from the corresponding data points). This tolerance was chosen to be approximately double the error (relative residual error: 14%) associated with an initial best fit to the data, which was fitted using a pattern search algorithm in Matlab. These parameter sets were then used directly to parameterise the incarceration dynamics of the full model, with the posterior ranges for these parameters given in Table S3. The fit of the model to the incarceration data in Table S2 can be seen in Figure S2.

Table S1: Prior and posterior model parameter ranges for the incarceration sub-model.

Parameter	Symbol	Posterior parameter range	Prior parameter range and distribution	Source/Comments
PWID leaving rate (1/duration of injecting + rate of non-HIV deaths) per year	μ	0.048-0.049	Non-HIV mortality rate per year: Uniform[0.0082-0.018] Years of injecting: Uniform [15-25]	Non-HIV mortality rate based on average among Eastern Europe.[9] Years of injecting based on ExMAT data.[7]
Percentage of PWID initiating injecting when:				
Never incarcerated	p_0	87.8-92.1%	Dirichlet distribution with parameters (17,1,1,1) which gives an expected value of 85% for p_0 and 5% for p_1, p_2 and p_3.	Our prior is based on 85% PWID having never been incarcerated prior to initiating injecting[7], but is uninformative as to where the remaining 15% PWID initiate injecting due to a lack of relevant data.
Incarcerated	p_1	0.3-8.0%		
Previously, recently Incarcerated	p_2	0.7-9.0%		
Previously, non-recently Incarcerated	p_3	0.7-9.0%		
Incarceration rate per year	γ	6.9-7.5%	Uninformative prior - Uniform [0,25%]	Both were estimated through fitting model to incarceration data.
Re-incarceration rate per year	δ	42.8-47.6%	Uninformative prior - Uniform [0,100%]	
Average time spent in prison per incarceration (months)	τ	13.3-14.2	Uniform [12.6,14.4]	Informed by data from ExMAT survey.[7]

Table S2: Incarceration data from the ExMAT survey[7] used to calibrate incarceration sub-model.

Duration of injecting	Proportion ever incarcerated (prison or pre-trial detention)	Mean number of times incarcerated (prison or pre-trial detention)
0-5 years	14.2% (25/176)	2.40 (95% CI 1.44-3.35)
6-10 years	33.2% (80/241)	2.43 (95% CI 2.03-2.83)
11-20 years	53.0% (344/649)	3.79 (95% CI 3.47-4.10)
21-30 years	67.5% (272/403)	5.94 (95% CI 5.44-6.44)
31-40 years	81.5% (110/135)	7.84 (95% CI 6.94-8.73)

Parameterising and calibrating the HIV transmission component of the model

Parameter ranges for the full model are shown in Tables S1 and S3. The HIV transmission aspect of the model was calibrated to the estimated HIV prevalence among never and previously incarcerated PWID in 2013, and currently incarcerated PWID in 2011 (see Table S3). Through the calibration process, the model was used to estimate the transmission risk among never incarcerated PWID, and the factor difference between this and the transmission risk among currently and previously incarcerated PWID. An Approximate Bayesian computation sequential Monte Carlo (ABC SMC) scheme[8] was used to obtain 1000 full parameter sets that fit the HIV prevalence among never and previously incarcerated PWID in 2013 and ART coverage in 2011 and 2015, with the sum of absolute errors of each fit having to be less than 9%. This tolerance was selected to allow for fitting to HIV prevalence among ever and never incarcerated PWID with a maximum total error of 4% (the approximate sum of the widths of the 95% confidence intervals), while the error in ART coverage for 2011 and 2015 was allowed to be 5% (the width of the widest confidence interval). In ABC SMC, a number of parameter values, sampled form their prior distributions, are propagated through intermediate distributions until they represent a target posterior distribution, fitting data to within a pre-specified tolerance.[8] A summary of the ABC SMC scheme is as follows. At each iteration of the ABC SMC scheme, the 1,000 incarceration parameter fits were randomly sampled and HIV biological parameters were randomly

sampled from their distributions in Table S3, derived from relevant literature. In the first iteration, a sample of 1000 transmission parameters were taken from the prior distributions. At subsequent iterations, the parameter sets from the previous iteration were sampled from with weights dependent upon the prior likelihood of the parameter set and the perturbation kernel (uniform in our SMC). The sampled parameter sets were perturbed, using a uniform perturbation kernel which could perturbate each parameter by at most +/- 2.5% of the prior range, so as to still be within the prior ranges, accepting those that gave model fits whose sum of absolute errors was less than a pre-determined tolerance, which decreased with each iteration, until a final sample of 1000 parameter sets were obtained which were all less than the desired tolerance, which we selected to be 9%. Twenty iterations of the ABC SMC were performed, with an initial tolerance of 40%, which decreased linearly on the logistic scale at each round to a final tolerance of 9%, with histograms of the parameter distributions of each iteration compared in order to check for convergence of the posterior distribution. Following the ABC SMC, parameter fits for the full model were accepted as full model fits if the HIV prevalence among never, currently and previously incarcerated PWID were within their respective 95% confidence intervals (Table S3).

For the baseline model, self-reported behaviour data were used to estimate prior ranges for the factor increase in risk among recently and non-recently incarcerated PWID compared to never incarcerated PWID (η_1 and η_2 respectively). These prior ranges were estimated from self-reported behavioural data on the frequency of injecting in the last month and proportion reporting syringe sharing in the last month among previously and never incarcerated PWID from the 2013 AIDS Alliance IBBA survey. The parameters were simultaneously sampled from the 95% confidence bounds for PWID that have previously (recently or not recently) or never been incarcerated, and the product of each pair of sampled parameters was calculated to give an estimate of the overall syringe sharing frequency. For each sample, the ratios of the syringe sharing frequency for previously incarcerated PWID (for both those that were released in last 12 months or greater than 12 months) compared to the never incarcerated PWID were calculated and used to construct a 95% confidence bound for the relative risks. Although this relative risk did not incorporate changes in sexual risk, data suggests that condom use among casual sexual partners (but not frequency of casual partners) also decreased similarly among previously incarcerated PWID, with the odds ratio of not using a condom among previously incarcerated PWID being 1.5 (1.2-1.8) after controlling for injecting duration in the 2013 AIDS Alliance IBBA dataset. Conversely, a non-informative prior, allowing both lower or greater transmission risk than never incarcerated PWID, was used for the relative transmission risk among incarcerated PWID (compared to never incarcerated PWID η_3) because of a lack of injecting frequency data to parameterise it.

Simultaneously, ART enrolment rates were also calibrated to the proportion of HIV-positive community PWID on ART while assuming a high ART LTFU rate of 10% as found among the Eastern European cohorts in the EuroSIDA collaboration.[10] ART was assumed to start in 2008, and then an ART enrolment rate was calibrated to give 14.6% coverage in 2011[11] and 19.5% coverage in 2015,[7] with ART coverage then allowed to increase beyond that with the same enrolment rate (increases to 28% coverage among HIV-positive PWID by 2030). No reduction in ART coverage was assumed among incarcerated PWID or previously incarcerated PWID as suggested by recent data from Ukraine.[6,12]

We assumed that the HIV epidemic was stable (in steady-state) up to 2008, prior to the introduction of ART, as suggested by the fairly stable HIV prevalence trends between 2008 to 2015 found in the AIDS Alliance IBBA surveys and other studies over that time period.[6,13,14]

During the HIV calibration process (and subsequently for model projections), the incarceration dynamics were initialised with all PWID having never been incarcerated and run to equilibrium prior to the introduction of HIV (approximately 39% never incarcerated; 22% currently incarcerated; 13% released in the last year; and 26% ever incarcerated but not released in the last year), which was seeded at 10% prevalence among all incarceration compartments, with 10% of infections being in the acute stage. The model was then run until the HIV prevalence among all incarceration subgroups (i.e. never, currently, recently and non-recently incarcerated) stabilized. The model was then run from this equilibrium point with the introduction of ART in 2008. The baseline model did not explicitly model community OAT because the coverage is still low (12% of PWID have ever been on OAT in 2013[6] and only 6% of PWID were currently on OAT in 2015), and instead assumed it was incorporated into the background force of infection. The scale-up of prison OAT, however, was modelled as one of the intervention scenarios (details as in section "**Model projections of scaling up OAT in prison")**.

Table S3: HIV Biological and Transmission Model Parameters

Parameter	Symbol	Posterior parameter range	Prior Range/Value and sampling distribution	Data Source
HIV-related natural history parameters				
HIV infectivity (relative to ART-naïve chronic infection) during				
Initial acute period of HIV infection	α_A	3.1 – 25.0	Uniform[3, 25]	[1]
While on ART	α_Z	0.06 – 0.57	Triangular 0.05-0.58, with peak 0.15	[2,3]
Duration of acute phase (months)	$12/\phi$	1.0 – 6.0	ϕ is sampled from Uniform[1,6]	[1,15]
HIV-related death rate per year for PWID with chronic HIV	$\mu_C = \frac{1}{\mu_1 + \mu_2}$	0.1 - 0.12	Years until progression to AIDs, $\mu_1$is sampled from Uniform[7.7,8.7], Years until death from AIDs, μ_2 is sampled from Triangular 0.96-1.07 with peak 1.05	[16,17]
Relative HIV death rate while on ART	μ_Z	0.2 - 0.5	Uniform[0.2, 0.5]	[4,18]
Loss to follow up rate on ART per year	θ	0.09 – 0.11	Normal(0.1,0.0068) truncated to the 95% CI [0.086,0.113]	[10]
HIV transmission parameters				
HIV transmission rate among never incarcerated PWID during chronic infection	λ	0.03 -0.11	Uninformative prior – Uniform[0,0.5]	
Relative HIV transmission rate compared to never incarcerated PWID:				
Currently incarcerated PWID	η_1	0.2 – 1.3	Uninformative prior – Uniform[0,5]	
PWID released in last 12 months	η_2	2.1 - 3.2	Uniform[1.9,3.3]	[6]
PWID released more than 12 months ago	η_3	1.5 – 2.0	Uniform[1.4,2.0]	[6]
HIV prevalence and ART data used for model calibration				
Never incarcerated community PWID (2013)		12.0-13.6%	11.9 – 13.6%	[6]
Previously incarcerated community PWID (2013)		26.9-29.7%	26.6 – 29.7%	
Currently incarcerated PWID (2011)		24.2-27.7%	22.2 – 35.4%	[5]
ART coverage among HIV+ PWID	Fit ART enrolment rate (π)	10.2-14.1%	14.6% for 2011	[11]
		16.8-23.4%	19.5% for 2015	[7]

Model Projections of the long-term PAF of incarceration for PWID HIV epidemic

To estimate the population attributable fraction (PAF) due to incarceration, the calibrated baseline model was used to project the degree to which the number of new HIV infections from 2015 to 2030 would be reduced if either (1) the transmission risk related to current and previously incarcerated PWID (recent and non-recent) were set to be the same (η_1, η_2 and η_3 = 1) as for never incarcerated PWID over this period (defined as '**15-year PAF**'), or more conservatively if (2) the transmission risk related to recently released PWID were set to be the same as the transmission risk among previously incarcerated but not recently released PWID over this period. We then assessed the impact of no further new incarceration of PWID from 2015 (γ and δ set to zero). The impact of these interventions on HIV prevalence and incidence in community and currently incarcerated PWID was also estimated.

Model projections for scaling up OAT in prison

We estimated the impact of scaling up OAT to 50% of incarcerated PWID, with and without retention of OAT for 1 year after release, assuming that OAT reduces an individual's HIV susceptibility and infectivity by 50% as suggested by a recent systematic review across different prospective studies[19]. Because these prospective studies estimated the effectiveness of OAT in populations where there was likely to be sexual and injecting HIV transmission among PWID, we assumed the same effectiveness would be achieved in Ukraine where there is also likely to be sexual and injecting related HIV transmission among PWID. It is likely that most HIV transmission (>80% of incident infections) among PWID, however, will be injection-related as has recently been estimated for St. Petersburg.[20,21] The model was also used to estimate the required OAT coverage among community PWID that would achieve the same impact (measured as proportion of new HIV infections averted between 2015 to 2030) as scaling-up prison OAT to 50% with retention for a year on release. This OAT scenario assumed no OAT in prison, as currently occurs in Ukraine, so when people enter prison they stop OAT and have to be recruited back on to OAT when they are released. We considered the required community coverage of OAT if OAT was scaled-up evenly among all community PWID, targeted specifically to never incarcerated PWID, or targeted to previously incarcerated PWID; and for all three scenarios assumed a one-year average duration on OAT. Table S4 shows the values of the OAT model parameters for each of the scenarios for scaling-up OAT in prison or the community.

Table S4: Summary of the model parameters for different OAT scale-up scenarios

Scenario	OAT Model parameters: OAT enrollment rates (ψ_i)	Proportion maintained on OAT at incarceration (ω)	Proportion maintained on OAT after release (χ)
Scale-up prison OAT			
with OAT maintained for a year after release	$\psi_0 = \psi_2 = \psi_3 = 0$; ψ_1 varied to give 50% OAT prison coverage	100%	100%
without OAT maintenance after release.	$\psi_0 = \psi_2 = \psi_3 = 0$; ψ_1 varied to give 50% OAT prison coverage	100%	0%
Scale-up community OAT			
Proportionately across all community PWID	$\psi_0 = \psi_2 = \psi_3$=x $\psi_1 = 0$ x varied to give OAT coverage with desired impact	0%	N/A
Targeted at never incarcerated PWID	$\psi_1 = \psi_2 = \psi_3$=0 ψ_0 varied to give OAT coverage with desired impact	0%	N/A
Targeted at previously incarcerated PWID	$\psi_0 = \psi_1$=0 $\psi_2 = \psi_3 = x$ x varied to give OAT coverage with desired impact	0%	N/A

Sensitivity and uncertainty analysis

To determine which parameter uncertainties are important for determining the uncertainty in our model projections, a linear regression analysis of covariance was performed on the estimated 15-year PAF of incarceration to the Ukraine PWID HIV epidemic. The proportion of the model outcome's sum-of-squares contributed by each parameter was calculated to estimate the importance of individual parameters to the overall uncertainty.

As described previously, the baseline model used self-reported injecting behaviour data to estimate a likely prior for the factor increase in transmission risk among previously incarcerated PWID (for PWID released in <12 months and >12 months) compared to never incarcerated PWID. Because there is always uncertainty around the reliability or accuracy of self-reported behaviour data, we undertook a sensitivity analysis to test the robustness of our results to assuming less informative priors for the relative HIV transmission risk among previously incarcerated PWID. Two alternative model calibration scenarios were considered. As for the baseline scenario, these additional scenarios used a non-informative prior (constrained to the range [0,10]) for the relative transmission risk among currently incarcerated PWID, but in contrast to the baseline scenario made less restrictive prior assumptions on the relative transmission risk in previously incarcerated PWID, either assuming that it is just greater than the transmission risk among never incarcerated PWID (constrained to the range [1,10]) or that it can be less than or greater than the transmission risk among never incarcerated PWID (non-informative prior constrained to the range [0,10] to ensure efficiency of the algorithm). Both these scenarios assumed no difference in transmission risk between recently and non-recently released PWID. For these two sensitivity analyses we re-estimated the main model outcomes and the impact of scaling up OAT in prison.

Results

Baseline model projections

The incarceration sub-model accurately mimicked the incarceration dynamics in Ukraine (Figure S2), and agreed with available data suggesting that about half of PWID have ever been incarcerated[7], and previously incarcerated PWID have been incarcerated about 5 times[7] with each sentence lasting about one year.[5,7] The model suggests that 22% of PWID are currently incarcerated, with PWID being initially incarcerated at a rate of 7.2% (95% CrI 6.9-7.4%) per year, but then re-incarcerated at a much higher rate of 45.0% (95% CrI 42.8-47.6%) per year. The model projections of the proportion of PWID that are currently incarcerated agrees well with independent projections derived by calculating the total number of PWID (0.95%[22] of Ukrainian adult population of 31,000,000[23]), and the number of current prisoners that are PWID (48.6%[5] of the current incarcerated population of 150,000[24]).

The baseline model also accurately fit the estimated HIV prevalence for each incarceration group (figure S3), and agreed with other community HIV prevalence data for 2008 to 2015 that was not used in the model fitting (Figure 3 in main text). A priori, this model assumed heightened transmission risk among previously incarcerated PWID (Table S3 gives their prior ranges), with the model posteriors for the relative transmission risk among recently released (RR range: 2.13-3.22) and non-recently released previously incarcerated PWID (RR range: 1.50-1.99) being slightly truncated compared to their prior distributions (Tables S3 and S5). In contrast, the model could not reliably determine whether there was increased or decreased transmission risk associated with being currently incarcerated (relative risk 0.89, 95% CrI 0.24-1.26) compared to never incarcerated PWID. The model estimated a HIV incidence of 4.1 per 100 person years (95% CrI 3.7-4.4) among community PWID in 2008, which in the status quo scenario decreases to 2.9 (95% CrI 2.5-3.5) by 2030 (Figure 3 in main text) due to the scale-up of ART to about 28% coverage of HIV-positive PWID by 2030. There exists uncertainty in the estimated HIV incidence among incarcerated PWID (Figure 3 in main text) due to uncertainty in their relative transmission risk, but it is also predicted to decrease by a similar degree over the next 15 years due to ART scale-up. No decrease in incidence is predicted without the scale-up of ART (results not shown).

Irrespective of the uncertainty in the transmission risk among currently incarcerated PWID, the baseline model strongly suggests that the overall level of HIV transmission will decrease dramatically if the HIV transmission risk among currently and previously incarcerated PWID were set to be the same as never incarcerated PWID over the period 2015 to 2030. Figure 3 in the main text suggests that the community incidence and prevalence would decrease by 79% (95% CrI 64-87%) and 56% (95% CrI 42-66%), respectively, whereas the number of new HIV infections would decrease by 55% (95% CrI 40-68% - Table S5) over this period. This is mainly due to the removal of the heightened risk among recently released PWID (41% (95%CrI 28-56%) of infections are averted if just this elevated risk is set to the same as never incarcerated PWID), because this state has a higher risk associated with it than for non-recently released PWID (Table S5) and 33.8% of a PWID's post incarceration time is spent in this state. In simpler terms, the reason that incarceration makes such a large contribution to the HIV epidemic in the baseline model is due to 33.5% of a PWID's injecting career being spent in the post incarceration state, and this being associated with on average a 2.7 or 1.7 fold increase in transmission for recently and non-recently release PWID (within the last 12 months or not), and so PWID in this state contribute 68% of a PWID population's instantaneous transmission potential for the baseline model.

Conversely, the model projected that the number of infections would increase by 3% (95% CrI -7-16%) if the transmission risk among currently incarcerated PWID was set to the same as never incarcerated PWID, reflecting the uncertainty in the relative transmission risk associated with current incarceration. The model also projected that 28% (95% CrI 14-41%) of new infections would be averted if the elevated risk in the 12 months after release were reduced to the same level of risk as among PWID with less recent incarceration and represents a conservative estimate for the degree to which incarceration elevates transmission risk.

In contrast, much less impact is predicted if no further incarceration of PWID occurred from 2015 (Figure 3 in main text). Initially this strategy will result in an increase in HIV incidence because previously incarcerated PWID will no longer be re-incarcerated, and so will remain in the previously incarcerated group, which has higher transmission risk than the currently incarcerated group. Our projections, however, show that incidence decreases below status quo levels by 2017, after sufficient numbers of previously incarcerated PWID have ceased injecting and left the PWID population.

Impact of scaling-up OAT in prison

Last, the scale-up of prison OAT with either methadone or buprenorphine to 50% of incarcerated PWID could have large impact if it is maintained for the first year post-release. The model projects that it could result in a 39% (95%CrI 23-49%) and 28% (95% CrI 18-36%) decrease in community incidence and prevalence, respectively, from 2015 to 2030 (Figure 3 in main text), and a 20% (95% CrI 15-25%) decrease in the number of new HIV infections over this period (Figure 4 in main text). This impact is primarily due to achieving retention on OAT upon release because it is covering the period of highest transmission risk immediately following prison release, with only 6% (95% CrI 2-8%) of new HIV infections being averted if there is no retention. This intervention results in an 8% increase in the coverage of OAT among community PWID, and results in much more impact than similar community only OAT interventions. For instance, assuming a one year average duration on OAT, additional model projections of the scaling-up of OAT among community PWID (without retention on incarceration) found that overall community OAT coverages of 28% (95% CrI 20-33%), 48% (95% CrI 43-50%) or 16% (95% CrI 12-21%) would be required to have the same impact on the number of new HIV infections as scaling-up prison OAT (with retention on release), depending on whether this scale-up was untargeted or was targeted to never incarcerated PWID or previously incarcerated PWID (both recently and non-recently), respectively.

Uncertainty and sensitivity analysis

ANCOVA analyses suggest that uncertainty in the relative transmission risks among previously incarcerated PWID (recently released transmission risk accounts for 47% of model uncertainty, whereas non-recently released transmission risk accounts for 11%) and currently incarcerated PWID (24% of uncertainty), the baseline HIV transmission rate (14%) and the relative infectivity while in the acute stage of HIV infection (2%) were the main factors that resulted in uncertainty in the population attributable fraction of incarceration to HIV transmission over 15 years, with no other factors contributing more than 0.7% to the uncertainty (Figure S4).

When two sensitivity analyses were undertaken to consider less informative priors for the level of transmission risk among previously incarcerated PWID, we find that the models could still accurately fit available HIV prevalence data (Figures S5 and S6). As with the baseline model, the new models predict on average a heightened transmission risk among previously incarcerated PWID (Table S5), although lower values are now possible and can be less than one for the scenario where we assume that the relative transmission risk among previously incarcerated PWID can either be greater than or less than the risk among never incarcerated PWID. As depicted in Figure S7, however, there is an inverse correlation between the relative transmission risk among currently and previously incarcerated PWID across the model fits, such that higher levels of transmission risk among currently incarcerated PWID are required for fits which have lower transmission risk among previously incarcerated PWID.

As presented in Figure S8, the distributions for the 15-year incarceration PAF differ between the baseline model and the sensitivity analyses, reflecting the wider prior ranges used in the sensitivity analyses, with the PAF estimates becoming more widely distributed as the priors become less restrictive. Although lower 15-year PAFs are predicted for the two sensitivity analyses than for the baseline model (Table S5), the median PAFs are still high (>30%), with there only being a small chance (8%) that incarceration plays a moderate to small role (PAF<20%) in driving HIV transmission (Table S5 and Figure S8). Importantly, all model fits for both sensitivity analyses suggest positive 15-year incarceration PAFs, even when the relative transmission risk in previously incarcerated PWID is less than one (occurs in 6% of the model fits in the second sensitivity analysis) contrary to what available risk behaviour data suggests.

Table S5: Summary of the model projections for the relative transmission risk for each calibration scenario, and the associated impact projections for different changes to the baseline model. Results are median projections with 95% credibility intervals.

	Posterior median and range of the relative transmission risk compared to never incarcerated PWID			**% of HIV infections averted over 15 years for different intervention scenarios**			
Model prior scenario	**Currently incarcerated PWID (β_1)**	**PWID released in <12 months (β_2)**	**Previously incarcerated PWID (β_3)[†]**	**No effect of incarceration on transmission risk (15-year PAF)**	**No further PWID incarceration**	**Scale-up of prison OAT with retention after release**	**Scale-up of prison OAT without retention after release**
Baseline model ($\beta_1 > 0$, $1.9 \leq \beta_2 \leq 3.3$, $1.4 \leq \beta_3 \leq 2.0$)	0.9 (0.2-1.3)	2.6 (2.1-3.2)	1.7 (1.5-1.9)	55.1 (40.2-68.2)	12.8 (-4.7-24.6)	19.8 (14.6-24.5)	5.6 (1.6-8.3)
Sens analysis 1 ($\beta_1 > 0$, $\beta_3 > 1$)	1.0 (0.1- 1.6)	Equal to β_3	1.6 (1.1-2.2)	41.1 (18.8-55.5)	-6.2 (-37.2-20.0)	15.0 (9.5-21.5)	7.7 (0.6-16.6)
Sens analysis 2 ($\beta_1 > 0$, $\beta_3 > 0$)	1.1 (0.1-1.8)	Equal to β_3	1.5 (0.5-2.3)	34.1 (6.8-56.9)	-2.2 (-27.7-45.2)	15.8 (9.7-34.1)	8.9 (0.6-32.0)

[†] For the baseline scenario this relates to PWID that have been released for over 12 months whereas for the other scenarios it relates to all previously incarcerated PWID.

The impact projections (% of infections averted from 2015 to 2030 – see Table S5) for the intervention scenario where no further incarceration of PWID occurs from 2015 are more uncertain for the two sensitivity analyses than they were for the baseline scenario, because of the less restrictive priors assumed in these sensitivity analyses. Importantly, negative impact is now generally achieved in the first sensitivity analysis because the intervention results in more PWID being in the post incarceration state, which normally (89% of fits) has more transmission risk than currently incarcerated PWID and there is no decrease in risk as PWID transition from recent to non-recent incarceration. This means no beneficial impact will be achieved until sufficient numbers of the previously incarcerated PWID have left the model. In the second sensitivity analysis, both a large positive or negative impact can be achieved, with a beneficial impact requiring the transmission risk in currently incarcerated PWID to be greater

than previously incarcerated PWID, which is the case in 56% of the fits, and a negative impact requiring the opposite scenario.

Last, slightly less impact of the prison OAT intervention scenario, in terms of proportion of infections averted (Table S5), is predicted in the sensitivity analyses as the baseline runs due to the baseline model incorporating a further elevated risk in the first 12 months following prison release, which is not captured in the sensitivity analyses where a constant risk among previously incarcerated PWID is assumed.

DISCUSSION

Limitations

Though robust, as with all modelling, there are limitations. First, our results and conclusions rely partly on the assumption of elevated transmission risk among previously incarcerated PWID. This assumption, however, was based on observed levels of elevated injecting and sharing frequency among previously incarcerated PWID compared to never incarcerated PWID, both among those that have been released within the past 12 months or more remotely. It is possible that this observation results from higher risk PWID being incarcerated more often. Due to the increased risk behaviour among recently released PWID compared to those released more than a year ago, however, we consider this reflects a true behavioural change following release. Our conservative model projections of the degree to which incarceration elevates transmission risk assumes this is the only heightened risk due to incarceration, but we also consider the implications of all the heightened risk among previously incarcerated PWID being due to the effect of imprisonment. It is important that future studies examine longitudinal changes in risk before, during and after incarceration to strengthen the evidence of causality between incarceration and subsequent increases in risk. Furthermore, in order to prevent this increased risk and the large proportions of new HIV infections that this risk contributes to, it is imperative to understand the causes of this increased risk.

Furthermore, although our model is calibrated to national incarceration and epidemiological data, it could not determine whether transmission risk differed between currently and never incarcerated PWID, even after relaxing the assumptions about the relative risk among previously incarcerated PWID. Again, longitudinal studies which follow PWID, both in the community and during and following periods of incarceration, would provide key risk behaviour and incidence data, that could resolve this issue, allowing for more stronger modelling projections in the future. Even despite this limitation concerning the level of risk in prison, however, our findings still suggest that incarceration could be an important driver of the HIV epidemic among PWID in Ukraine. Whilst our modelling was specific to Ukraine, the findings of high rates of incarceration and limited access to harm reduction in prisons found in the review of countries in Eastern Europe and Central Asia, suggest that this conclusion is likely to be applicable in many settings in the region. The contribution of prison, however, could possibly be greater in other settings within EECA if, unlike in our setting in Ukraine, incarceration also reduces the coverage of ART among previously incarcerated PWID. This should be considered in future modelling for other settings.

Our modelling of the effect of drug decriminalisation was limited by assuming it would remove all incarceration of PWID, where in reality it is likely that PWID will continue to be incarcerated for other reasons. Because our model projections failed to suggest that decriminalisation would have a quick beneficial impact, this limitation should not be a cause for concern because even less impact would be achieved if PWID continued to be incarcerated for other reasons. In addition, it is likely that decriminalisation would occur in parallel with improvements in harm reduction services for PWID, and that this combined approach would achieve greater impact than we projected.

Our modelling could also be limited because we used a relatively simple model structure that did not stratify by gender or other risk factors. The model, however, did include the crucial elements that enabled it to consider the question in hand, and was not over complicated by other additional detail that was not needed or could limit the degree to which the model could be accurately calibrated to the data that was available from Ukraine. Despite this, the fact that we did not stratify by gender means that we could not determine whether the effect of incarceration on elevating HIV transmission risk or ART coverage differs by gender. Indeed, because most PWID (75%) and prisoners (80%) are male it is likely that our results are weighted to what occurs among males. Further modelling needs to consider whether these effects differ by gender. Unlike other settings, though, where injection-related HIV risk among female PWID is markedly higher than among male PWID, data from Ukraine suggest that it is similar among male and female PWID. Other data also suggests that male and female PWID have similar uptake of NSP, OAT and ART.[25,26] We therefore were unable to fully model women and men separately, but as available data become available, future modelling should disentangle such differences.

Finally, our model and analysis is limited to HIV transmission among PWID only, and neglects transmission from PWID to the general population. It is possible that incarceration could result in more HIV transmission than we predict, given that HIV transmission among PWID could subsequently result in additional transmission among non-injecting sexual partners and then among the general population.

Comparisons with existing studies

To our knowledge, this is one of the first model analyses (other than parallel modeling analyses in this special issue) to evaluate the degree to which incarceration contributes to the wider HIV epidemic among PWID or any other population sub-group, and the possible impact of interventions to reduce that contribution. Other modelling studies have focused on the effectiveness of targeting HBV and HCV prevention interventions at incarcerated PWID, and suggest that scaling-up hepatitis B vaccination[27] and hepatitis C treatment with direct-acting antivirals[28-30] among incarcerated PWID can have substantial impact on the total epidemic. This work further suggests that scaling-up OAT in prisons, and maintaining PWID on OAT following release, could provide important HIV prevention benefits for PWID in the community.

Other recent modelling by our team showed that incarceration contributes significantly to the HCV epidemic among PWID in Scotland, despite low HCV incidence among incarcerated PWID (resulting from high coverage of within-prison OAT), due to elevated transmission risk in the six months following release[29]. Scenario modelling for other global settings also suggested that incarceration could contribute substantially to HCV transmission in other settings with higher HCV incidence in prison (due to lower coverage of prison OAT) or higher rates of incarceration, such as in Thailand.[31] This work further supports the assertion that incarceration can contribute significantly to the transmission of infectious diseases among community PWID and that interventions to control the spread of infectious diseases among PWID must focus on preventing the risk following release from prison as well as during periods of incarceration.

Last, modelling by other groups has considered the transmission of TB,[32-35] HIV, and sexually transmitted infections[36-38] in prison settings, as well as the impact and cost-effectiveness of different interventions, but have generally only included the transmission of infection and projected impact within the prison setting. One analysis has also considered how incarceration could result in increases in sexual behaviour due to dissolution of sexual partnerships,[39] but they did not include disease transmission within their model.

Supplementary material for Box 2: Part 2

Title: Contribution of incarceration to the TB burden in Ukraine and Eastern Europe

Background

Previous epidemiological analyses from multiple countries have shown that the number of incarcerations and total sentence length increase the risk of latent TB infection (LTBI) [40-44] and on-going active disease,[45] in addition to other factors such as population density in the prison[41,46] and whether they inject drugs and are HIV-infected.[45,47] These data, together with a systematic review from 2010 suggest the incidence of TB disease in lower or middle income countries (LMIC) can be 10 to over 30 times greater in prison than in the community.[48] Although data are not available for many countries including Ukraine, the systematic review also estimated that between 5 and 17% of TB cases in Russia could be due to exposure in prison, 3-6% in Brazil and 1.5% in Ivory Coast.[48]

TB incidence rates across Eastern Europe and Central Asia are high, and have been shown to be positively correlated with country-level incarceration rates,[49] highlighting the likely importance of within-prison transmission to the countrywide epidemic. Although such results are compelling, TB data from prisons in Ukraine is scarce and the individual-level risk associated with incarceration remains to be quantified in this setting. This analysis uses data from two surveys among prisoners and community PWID to evaluate the potential role that incarceration and other factors play in elevating TB risk in the general population and in PWID, and then the likely population attributable fraction (PAF) of incarceration to yearly TB risk among PWID and the overall general population.

Methods

Study data

We used data from two cross-sectional surveys in Ukraine.

1. The 2015 National Institute of Drug Abuse-funded Expanding Medication-Assisted Therapies (ExMAT) survey in Ukraine.[50] The 2015 ExMAT survey included 1,612 PWID sampled from 5 Ukrainian cities. Data were extracted on whether PWID were: ever incarcerated (yes or no), total time incarcerated within prison or sizo (pre-trial detention centre), documented HIV status (positive, negative, not known), duration of injecting drug use, and self-reported TB status in last 12 months ("Have you been told by a medical professional that you have had tuberculosis in the last 12 months?") and ever TB status ("Have you ever been told by a medical professional that you have had tuberculosis?"). The self-reported response is 90% accurate to identify patients who have ever been diagnosed with active TB disease.[51]

2. *The national prison survey (PUHLSE) from 2011.*[5,52] The 2011 PUHLSE surveyed 402 prisoners from all prison in Ukraine[11]. Data were extracted on prisoner age (years), total time incarcerated (prison or SIZO (pre-trial detention centre)), HIV status (positive, negative, not known), having ever injected drugs (defined by either self-reported usage or by verified HCV status), and self-reported TB status ("*Have you ever been told by a medical professional that you have had tuberculosis?*").

Analyses

The analyses of the PUHLSE and ExMAT data were undertaken in four stages:

1. Test the association between potential explanatory variables and TB risk using univariate regression models with binomial outcome.

We fitted univariate generalised linear models using the glm() function in the stats library of the R package. The outcome and explanatory variables ('*var*') for each model are given in Table S6. For each explanatory variable, the model was

$$glm(TB \sim var, family = binomial).$$

For each model, we calculated the Odds Ratio, 95% confidence interval, and the associated p-value.

2. Test the relationship between significant explanatory variables in a multivariate model.

The explanatory variables from the univariate model that had $p<0.05$ were included in the multivariate model with the same outcome variables (Table S6).

3. Use a survival model to estimate the increased hazard of reporting ever having had TB per year of time spent in prison or pre-trial detention.

Both PUHLSE and ExMAT data show a clear relationship between cumulative risk of reporting ever being diagnosed with TB and years of incarceration (Figure 5 in main text) after controlling for other potential explanatory variables. We fit a survival function, $h(t)$, to the probability of reporting TB as a function of time in prison, t, as

$$1 - h(t) = \exp(-\lambda t),$$

where λ is the rate of acquiring TB (self-reported) by people in prison per year of incarceration. As $h(t)$ is the cumulative increase in reporting TB, then $\frac{dh(t)}{dt} = \lambda \exp(-\lambda t)$ is the incidence rate. We estimated an average annual incidence rate, I_p, by weighting the incidence rate at *t* years in prison by the proportion of people who served *t* years. The mean rate of TB acquisition, $\hat{\lambda}$, was estimated by fitting a linear model to the log of the cumulative TB risk by time incarcerated using the R function lm() which fits via least squares. The 95% confidence intervals in the mean rate of TB acquisition were calculated from a t-distribution using the function confint().[53]

4. Estimate the Population Attributable Fraction (PAF) of TB due to incarceration using the estimated hazard.

The Population Attributable Fraction (PAF) of incarceration was estimated for the general population (from PUHLSE data) and among PWIDs (from ExMAT data) by estimating the relative risk of reporting TB disease if you have been incarcerated compared to if you have not. The PAF can be calculated using the formula:[54]

$$PAF = 100 \times \frac{p(r-1)}{p(r-1)+1} \quad (1)$$

where p is the proportion of the population (either the general population, or PWIDs) that had been in prison and r is the relative risk of having acquiring TB if they are or have been incarcerated compared to if they are not or have not been incarcerated. The relative risk of reporting TB was estimated using the average annual incidence rate, $r = I_p/I$, where I is the incidence in the population who have not been incarcerated.

The proportion of the general population in prison, p, was estimated at 0.47%-0.50%, based on assuming that between 145,000 and 154,000 individuals are in prison and pre-trial detention[55], and Ukraine has an adult population size of 31 million.[56] The TB incidence in the general population was taken from the WHO estimate of 105 (95% CI 87, 122) per 100,000 persons per year.[57]

The proportion of PWIDs that have been in prison was estimated using ExMAT data, where 805 out of 1,613 (52%) respondents reported having been previously incarcerated in prison or pre-trial detention. The relative risk of TB was estimated directly by comparing the proportion of PWIDs reporting TB in the past year among people who have previously been incarcerated and those that have never been incarcerated, either overall, or amongst those that are HIV infected and those that are not.

Results

Comparison of PUHLSE, ExMAT and WHO estimates

Among HIV negative PWID respondents who had not been to prison or pre-trial detention, 1 out of 544 ExMAT respondents reported having TB within the last 12 months, equating to 184 (95%CI 9.6, 1187) TB cases per 100,000 persons, which although uncertain is broadly consistent with the WHO population-wide estimate of 105 (95%CI 97, 114) cases per 100,000 persons in the general populatioin, despite the survey using self-reported TB status. Furthermore, the PUHLSE prison survey and EXMAT data also showed consistent results: 64 out of 398 (16.1%, 95%CI 12.7%, 20.1%) HIV-negative EXMAT respondents who had been to prison reported ever having TB, compared to 86 out of 527 (16.3%, 95%CI 13.3%, 19.8%) HIV-negative PWID PUHLSE respondents. The consistency across data sets and with WHO estimates suggested it was reasonable to combine multiple datasets to estimate the PAF due to incarceration.

Role of incarceration for TB transmission among PWID in Ukraine

In the Ex-MAT dataset, the univariate model suggested that ever being incarcerated was strongly associated with increased cumulative TB risk (OR 3.9, 95%CI 3.0-5.3) and increased risk of reporting TB in last year (OR 3.4, 95%CI 2.0-6.0) (See Table S7). This effect was maintained in the multivariate model when adjusting for age, number of years injecting and HIV infection status (Table S7). Number of years injecting (1.1 per year, 95%CI 1.0-1.1) and HIV infection (3.1, 95%CI 2.3-4.1) were significant covariates for cumulative TB risk in the multivariate model (Table S2). Importantly, as illustrated in Figure 5B in the main text, the number of years incarcerated was also strongly associated with cumulative TB risk (Table S8). Each year of incarceration increased an individual's cumulative TB risk in relative terms by 6% (95% CrI 3-10%).

Ex-MAT data suggests that 12 times more previously incarcerated PWID have been diagnosed with TB in the last year (5.0%) than never incarcerated PWID (0.4%). Assuming this difference largely resulted from being in prison (they are on average re-incarcerated within 2 years), this suggests that 93% (95% CrI 85-98%) of diagnosed TB infections in the last year were among PWID who have recently been in prison, and a relative risk of TB due to incarceration of 12.5. Therefore, the PAF of recent incarceration to TB transmission in community PWID was 85% (95% CrI 69-96%). Although some of this effect is due to the higher HIV prevalence (28% in previously incarcerated

PWID versus 13% in never incarcerated PWID) and associated TB prevalence in previously incarcerated PWID, lower but still very high PAFs were found for HIV-positive (75%, 95% CrI 51-94%) and HIV-negative PWID (86%, 95% CrI 56-98%).

Role of incarceration for overall TB transmission in Ukraine

The univariate analyes of the PUHLSE dataset showed that age, number of years in prison and injecting drug use were all significantly associated with cumulative TB risk (Table S9). HIV status was not significant. The multivariate model demonstrated that age and ever injecting drug use were correlated and age became not significant (Table S9). The regression model suggested each year of incarceration increased an individual's cumulative risk of TB in relative terms by 13% (95% CI 8-17%) (Table S9).

The survival model suggests that after an average period of 5 years of incarceration, an individual will have an 8.6% risk of ever having TB, and this increases to 15.3% or 54.3% risk after 10 or 20 years of incarceration, respectively (Figure 5A in the main text). The average incidence rate was 1.5% (95% CrI 0.6-3.4%) per year of incarceration, or an incidence of 1,500 per 100,000 persons per years in prison. This is 14 (95% CrI 6-32) times greater than the estimated 105 per 100,000 incidence rate of TB incidence in the general population. Assuming that between 145,000 and 154,000 individuals are in prison and pre-trial detention with an adult population size of 31 million[15] then this means the PAF of incarceration to current TB rates is 6.2% (95% CrI 2.2-13.4%), similar to previous estimates for Russia.[48]

Discussion

Despite our prison TB incidence projections being based on self-reported TB diagnosis data, which has been found to be highly reliable,[51] it may modestly underestimate real TB incidence and prevalence rates. Our analyses, however, consistently suggest that prison may be contributing significantly to TB transmission in Ukraine, with at least 6% of all incident TB cases possibly resulting from incarceration, and over 75% of TB cases among PWID. Although other studies have produced similar PAF estimates of prison to the overall TB epidemic in similar settings (Russia), no other study has suggested there may be a much higher PAF of incarceration to TB transmission among PWID. Avoiding incarceration of PWID altogether would likely reduce the likelihood of TB transmission among them, but nonetheless, harm reduction interventions for PWID should target TB screening strategies for PWID who have been recently incarcerated because they are likely to have a very high burden of TB disease.

Tables for supplementary material for Box 2

Table S6: The univariate and multivariate models explored for ExMAT and PUHLSE data.

Model	Survey	Outcome variable	Explanatory variables	Included participants
1	ExMAT	Ever reporting TB (binary)	age (continuous), duration of injecting drug use (continuous), HIV status (binary), ever been incarcerated in prison (binary) or sizo (binary),	All
2	ExMAT	Reporting TB in the previous 12 months (binary)	age (continuous), duration of injecting drug use (continuous), HIV status (binary), ever been incarcerated in prison (binary) or sizo (binary)	All
3	ExMAT	Ever reporting TB (binary)	age (continuous), duration of injecting drug use (continuous), HIV status (binary), years in prison or sizo (continuous)	People who have been to prison or sizo only
4	ExMAT	Reporting TB in the previous 12 months (binary)	age (continuous), duration of injecting drug use (continuous), HIV status (binary), years in prison or sizo (continuous)	People who have been to prison or sizo only
5	PUHLSE	Ever reporting TB (binary)	age (continuous), ever injected drugs (binary), HIV status (binary), years in prison or sizo (continuous)	All

Table S7: Results of univariate (OR) and multivariate (aOR) analyses using ExMAT data among PWID with outcomes i) ever reporting TB (model 1) and ii) reporting TB within the last 12 months (model 2).

	Model 1 outcome: Ever had TB				**Model 2 outcome: TB within last 12 months**			
	OR (95% CI)	**p-value**	**aOR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**	**aOR (95% CI)**	**p-value**
Age	1.09 (1.07, 1.10)	<0.0001	0.99 (0.96, 1.03)	0.76	1.06 (1.03, 1.09)	<0.0001	1.00 (.092, 1.07)	0.883
Ever in Sizo?	1.17 (0.81, 1.66)	0.4	-	-	1.9 (1.01, 3.39)	0.035	-	-
Ever in Prison?	3.96 (3.01, 5.25)	<0.0001	3.55 (2.52, 5.08)	<0.0001	3.41 (2.01, 5.95)	<0.0001	6.66 (3.01, 17.70)	<0.0001
Years injecting	1.09 (1.08, 1.11)	<0.0001	1.07 (1.04, 0.97)	<0.0001	1.07 (1.04, 1.10)	<0.0001	1.04 (0.97, 1.11)	0.303
HIV (ref negative)	4.13 (3.11, 5.53)	<0.0001	3.06 (2.27)	<0.0001	5.58 (3.09, 10.8)	<0.0001	4.01 (2.20, 7.84)	<0.0001

Table S8: Results of univariate (OR) and multivariate (aOR) analyses using ExMAT data for only those PWID that have been previously incarcerated, with outcomes i) ever reporting TB (model 3) and ii) reporting TB within the last 12 months (model 4).

	Model 3 outcome: Ever had TB				**Model 4 outcome: TB within last 12 months**			
	OR (95% CI)	**p-value**	**aOR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**	**aOR (95% CI)**	**p-value**
Age	1.06 (1.04, 1.08)	<0.0001	0.99 (0.94, 1.03)	0.566	1.03 (0.99, 1.07)	0.185	0.99 (0.91. 1.07)	0.770
Years in prison or sizo	1.09 (1.06, 1.12)	<0.0001	1.06 (1.03, 1.10)	<0.0001	1.02 (0.96, 1.08)	0.498	0.99 (0.94, 1.05)	0.827
Years injecting	1.07 (1.05, 1.09)	<0.0001	1.06 (1.01, 1.10)	0.013	1.03 (0.99, 1.07)	0.090	1.04 (0.97, 1.12)	0.292
HIV (ref negative)	3.06 (2.20, 4.30)	<0.0001	2.93 (2.07, 4.18)	<0.0001	3.46 (1.68, 7.84)	0.0014	3.55 (1.89, 7.17)	0.00017

Table S9: Results from univariate (OR) and multivariate (aOR) analyses using PUHLSE data among prisoners with outcome ever reporting TB (model 5).

	OR (95% CI)	**p-value**	**aOR (95% CI)**	**p-value**
Age	1.03 (1.01, 1.05)	0.0003	1.01 (0.98, 1.03)	0.624
Years in prison	1.15 (1.11, 1.19)	<0.001	1.13 (1.08, 1.17)	<0.0001
HIV (ref negative)	1.16 (0.65, 1.95)	0.593	1.05 (0.47, 2.23)	0.894
Ever injected drugs?	2.07 (1.45, 2.98)	<0.0001	2.08 (1.31, 3.36)	0.0023

Supplementary figures

Figure S1: Schematic of the (a) PWID incarceration and (b) HIV transmission components of the model.

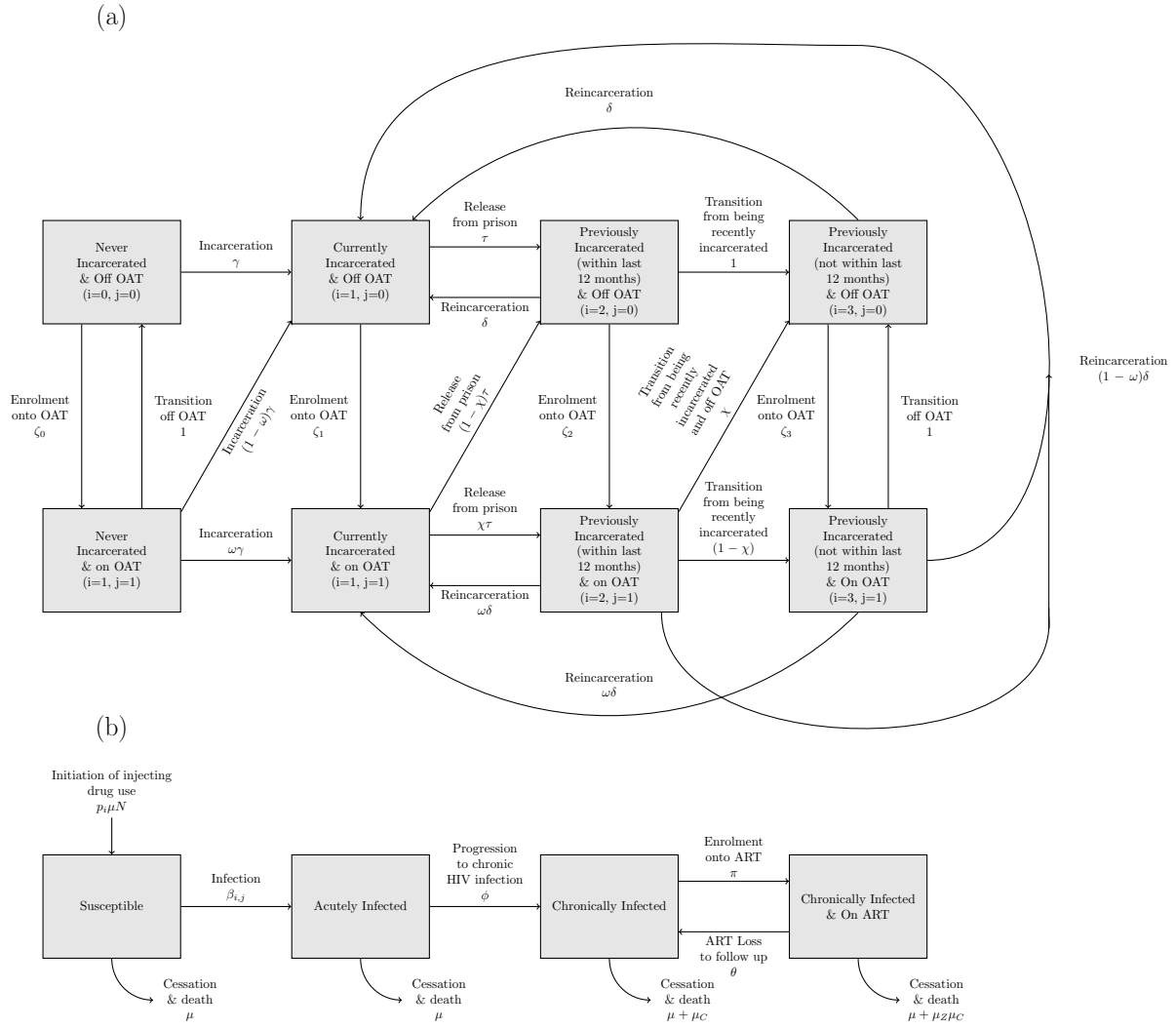


Figure S2: Model fits of the incarceration component of the model to (a) the proportion of community PWID previously incarcerated and (b) the mean number of incarcerations, by duration of injection. Lines represent the median of all fits, with the shaded area representing the range of the fits. Data points estimated from the ExMAT survey (circles), with their 95% confidence intervals (whiskers), used in the fitting procedure are shown for comparison.

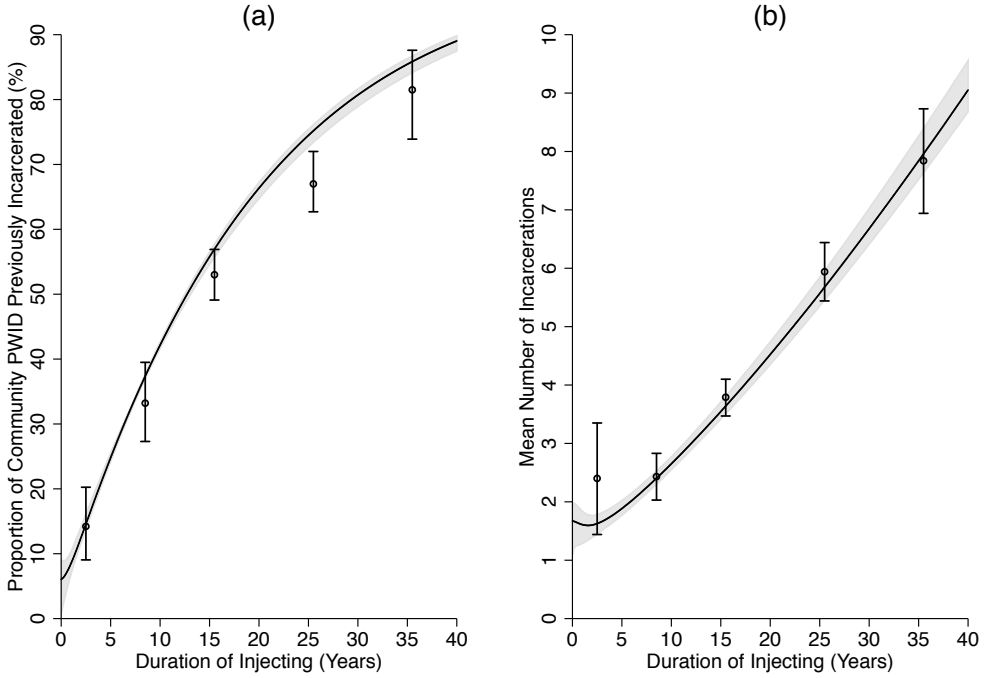


Figure S3: Baseline model projections of the HIV prevalence among (a) never incarcerated, (b) currently incarcerated and (c) previously incarcerated PWID for the status quo scenario, and if there was either: no effect of incarceration on transmission risk after 2015 (short dashed line); no further incarceration of PWID after 2015 (long dash-dot line); or 50% of incarcerated PWID were recruited on to OAT from 2015 and maintained on OAT for a year after release (short dash-dot line). Lines represent the median projections, with the shaded area representing the 95% credibility interval (CrI) for the status quo scenario. Data points with their 95% confidence intervals are shown for comparison.

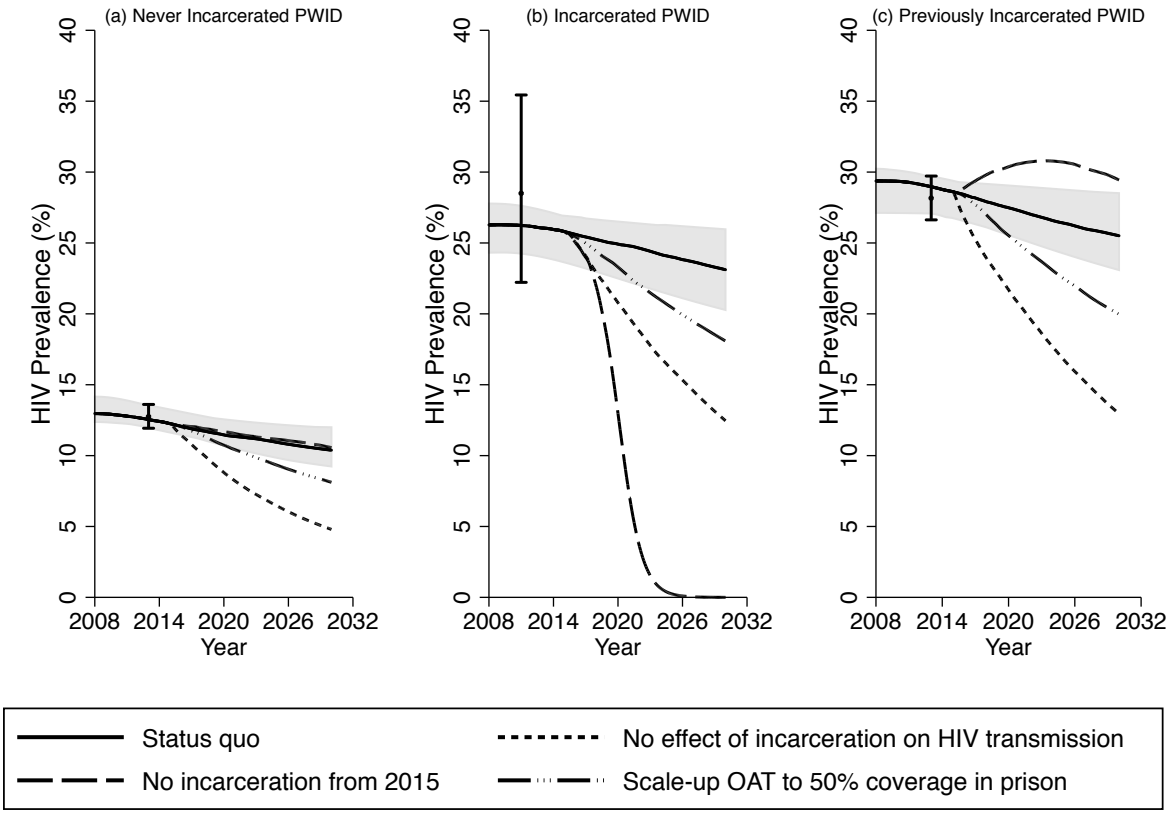


Figure S4: Results of the ANCOVA analysis detailing which model parameters' uncertainty contributes most to the uncertainty in the population attributable fraction of incarceration to HIV transmission over 15 years. The figure plots the proportion of the model outcome's sum-of-squares contributed by each parameter. Parameters contributing less than 0.2% of uncertainty are not shown.

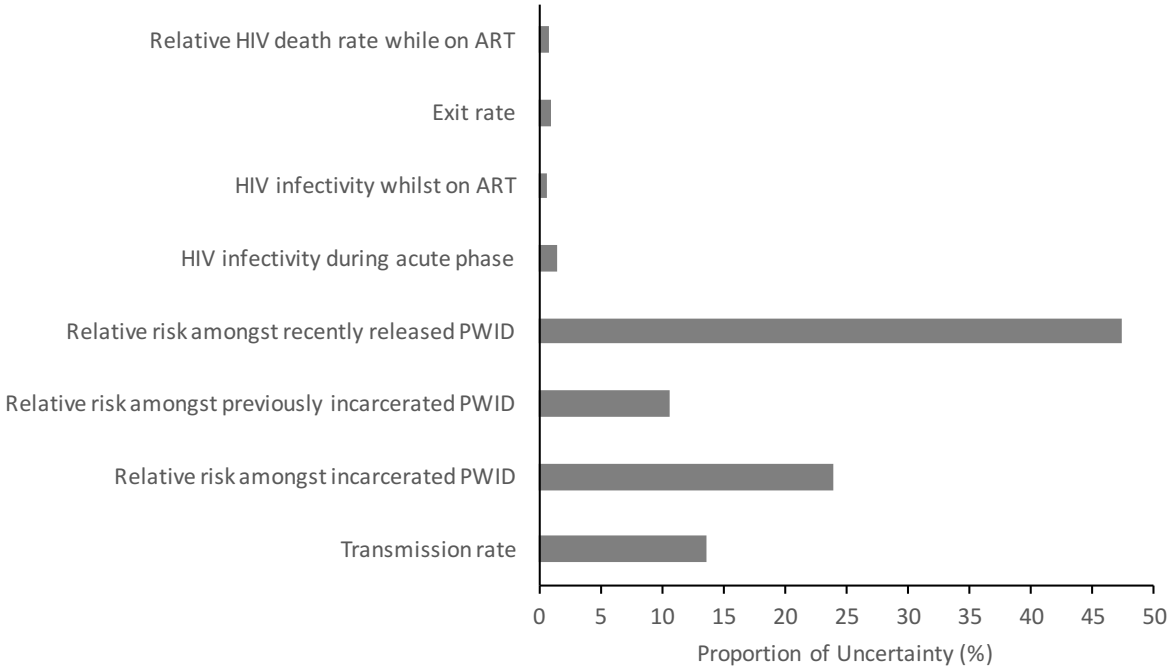
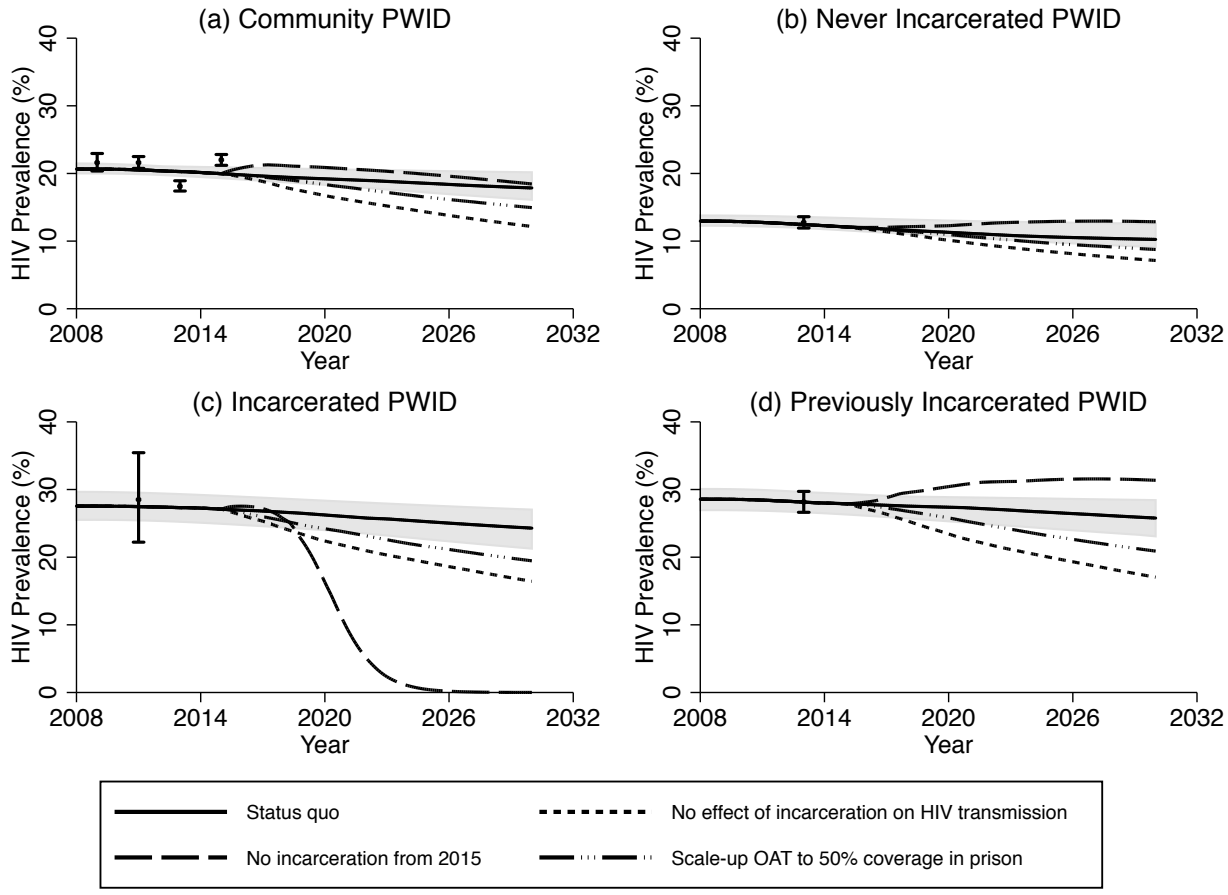


Figure S5: **Model projections, when imposing a less restrictive prior range [1,5] for the relative transmission risk among previously incarcerated PWID**, of the HIV prevalence among (a) community, (b) never incarcerated, (c) currently incarcerated, and (d) previously incarcerated PWID for the status quo scenario, and if there was either: no effect of incarceration on transmission risk after 2015 (short dashed line); no further incarceration of PWID after 2015 (long dash-dot line); or 50% of incarcerated PWID were recruited on to OAT from 2015 and maintained on OAT for a year after release (short dash-dot line). Lines represent the median projections, with the shaded area representing the 95% credibility interval (CrI) for the status quo scenario. Data points with their 95% confidence intervals are shown for comparison.



F**igure S6: Model projections, when imposing a less restrictive prior range [0,5] for the relative transmission risk among previously incarcerated PWID**, of the HIV prevalence among (a) community, (b) never incarcerated, (c) currently incarcerated, and (d) previously incarcerated PWID for the status quo scenario, and if there was either: no effect of incarceration on transmission risk after 2015 (short dashed line); no further incarceration of PWID after 2015 (long dash-dot line); or 50% of incarcerated PWID were recruited on to OAT from 2015 and maintained on OAT for a year after release (short dash-dot line). Lines represent the median projections, with the shaded area representing the 95% credibility interval (CrI) for the status quo scenario. Data points with their 95% confidence intervals are shown for comparison.

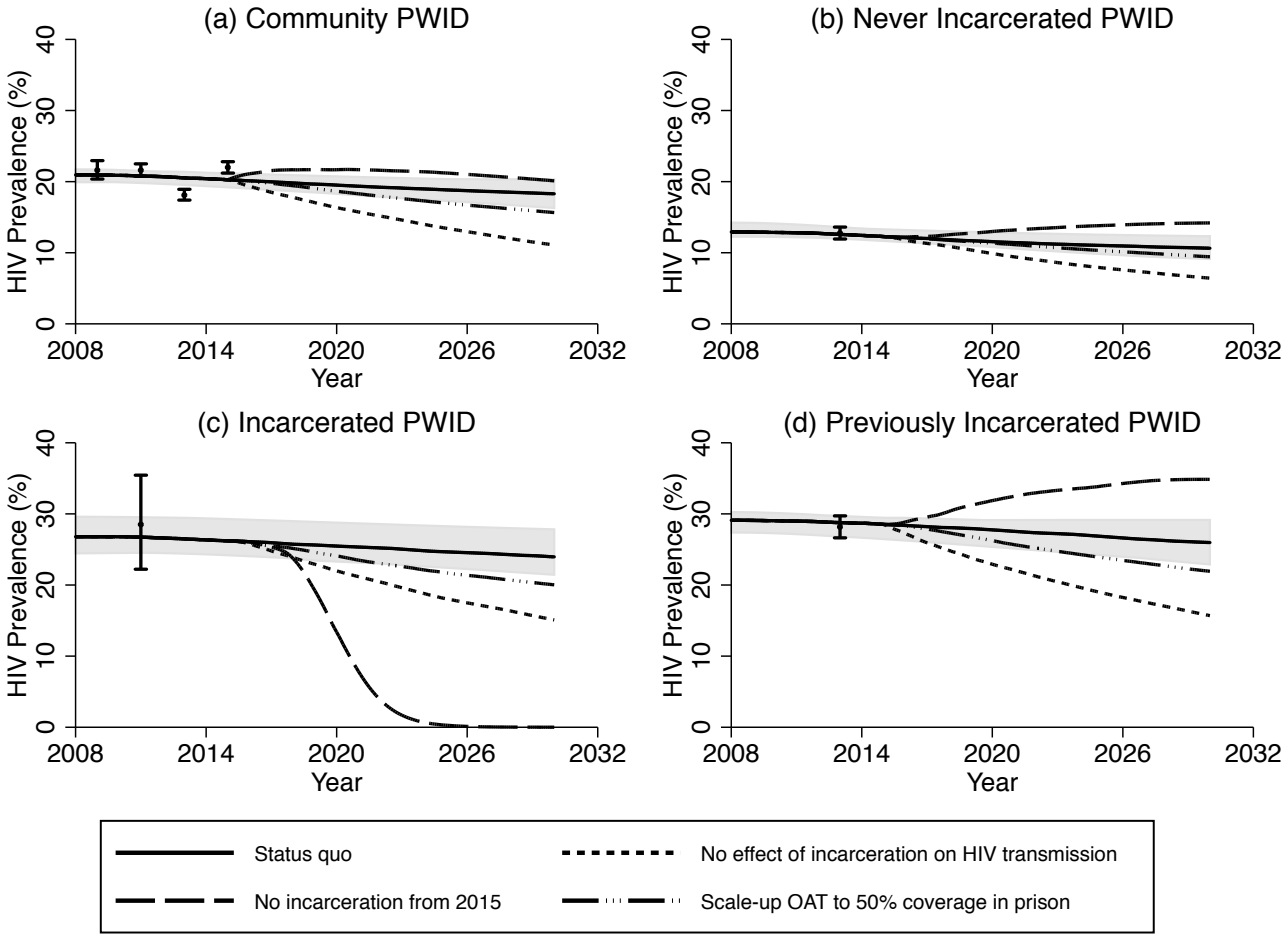


Figure S7: The relationship between the relative transmission risk among previously incarcerated and currently incarcerated PWID for each sensitivity analyses, with (a) presenting the projections for the sensitivity analysis where the relative transmission risk among previously incarcerated PWID was assumed >1, and (b) presenting the projections for the sensitivity analysis where there is no restriction on the relative transmission risk among previously incarcerated PWID (>0).

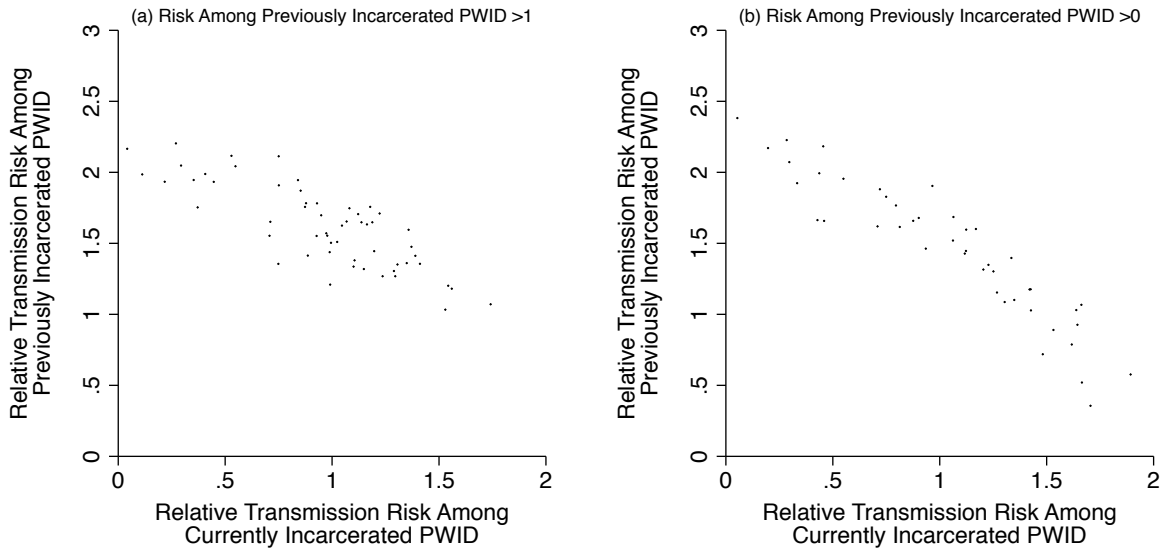


Figure S8: Distribution of the estimated 15-year population attributable fraction (PAF) of incarceration to the HIV epidemic among PWID for the baseline model fit and sensitivity analyses.

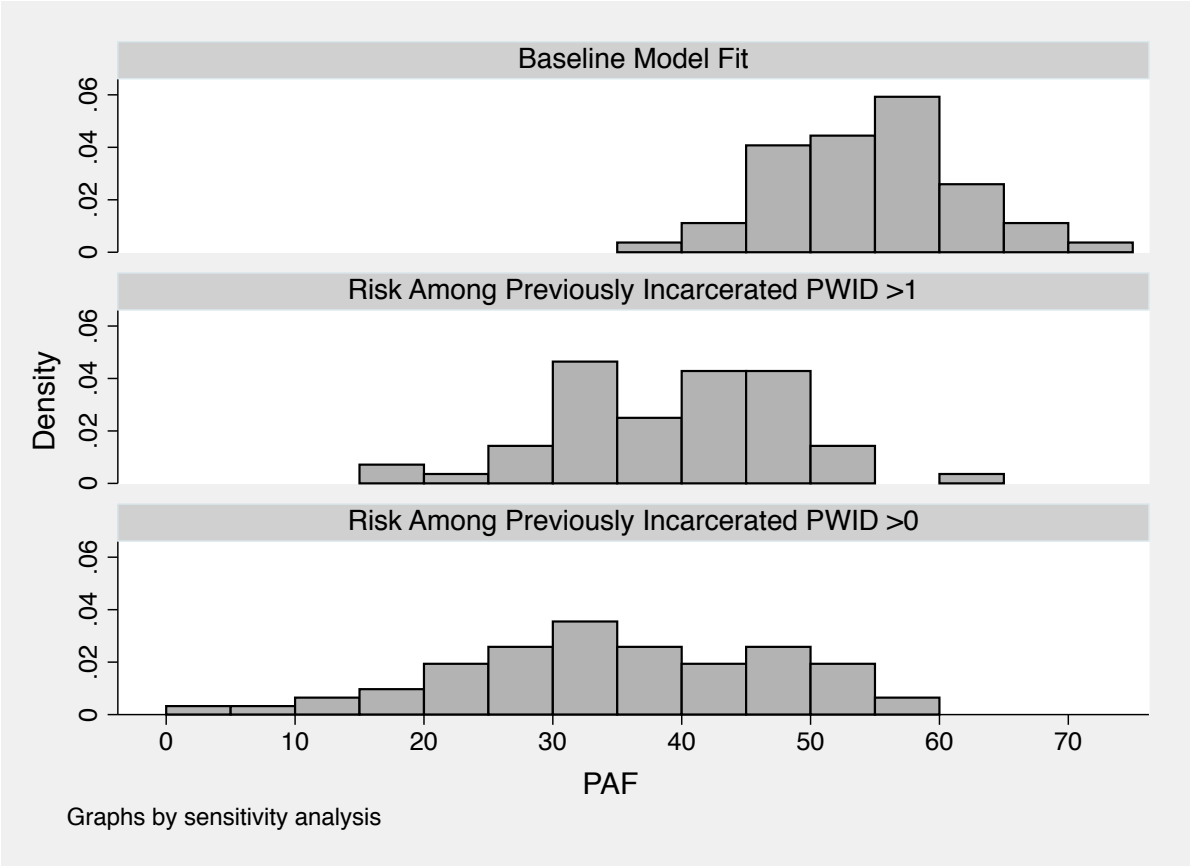
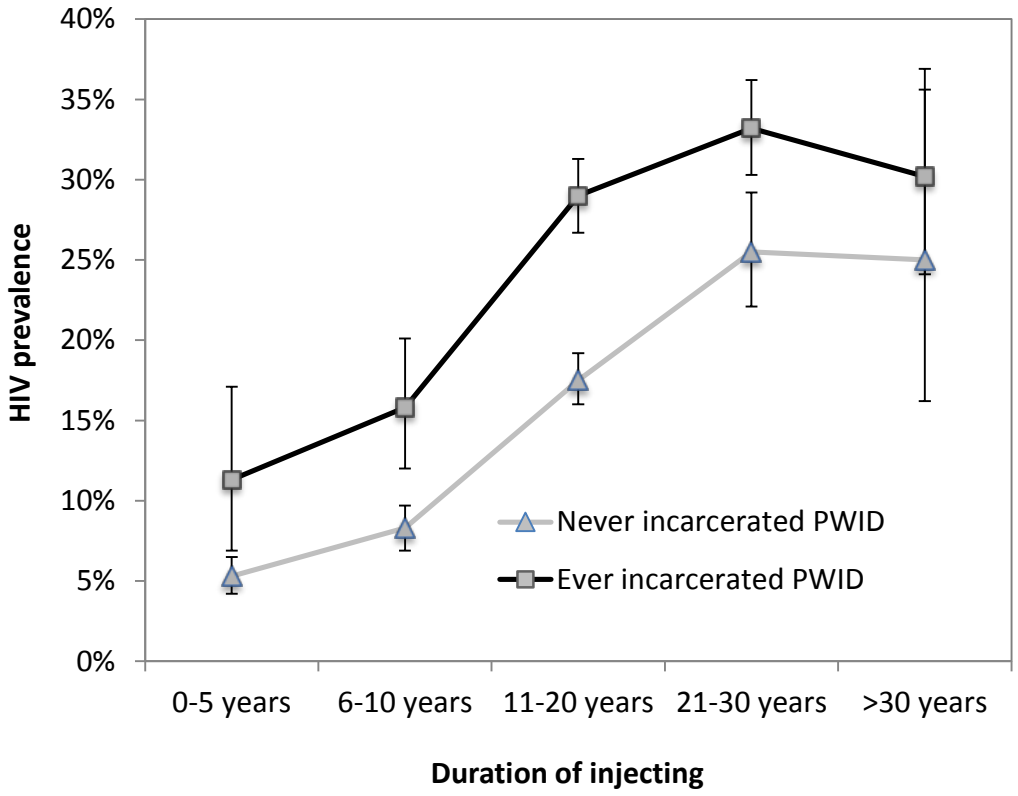


Figure S9: Comparison of HIV prevalence on people who inject drugs in the community in Ukraine, stratified by incarceration status



* Data are from the 2013 National AIDS Alliance Integrated bio-behavioural assessment (IBBA) among PWID with the whiskers denoting 95% confidence intervals