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Modelling the potential impact of implementing and scaling-up harm reduction and antiretroviral therapy on HIV and overdose deaths among people who inject drugs in two Russian cities

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Abstract

Background—Russia accounts for most new HIV infections among people who inject drugs (PWID) in Eastern Europe and Central Asia, and PWID have high overdose risk. Opioid agonist therapy (OAT) is prohibited, and coverage of needle/syringe programs (NSP) and antiretroviral therapy (ART) is limited. We assess scaled-up harm reduction and ART on HIV incidence and overdose among PWID in two settings in the Russian Ural and Siberian districts where HIV is surging.

Methods—We developed a dynamic deterministic model that incorporated injecting and sexual transmission of HIV among PWID that we calibrated to two Russian settings: Omsk (high but expanding HIV among PWID) and Ekaterinburg (very high but stable HIV). We model the impact of no intervention or combinations of scale-up of OAT, high coverage NSP, and/or ART (from

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Author contributions: CB, JC, and NM conceived the analysis. JC and NM wrote the first draft of the manuscript. JC conducted all modelling analyses in consultation with NM, PV, and AB. KE, AL, MS, and VO provided site specific data and provided interpretation of findings along with input from LB, MH, and CB. All authors critically reviewed and provided extensive feedback on all drafts of the manuscript.

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baseline of no harm reduction and 30% of HIV-positive PWID on ART) on HIV infections, HIV-mortality, and fatal overdoses averted from 2018–2028.

Findings—Without intervention, HIV prevalence among PWID in Omsk could rise to 34% in 2028 and remain high in Ekaterinburg (61% in 2028). OAT scale-up (to 50% coverage, 2 years duration) could prevent 35% and 19% of HIV infections and 19% and 10% of HIV-related deaths in Omsk and Ekaterinburg, respectively, and 33% of overdose deaths in 10 years. NSP+OAT scale-up to 50% and tripled ART recruitment (reaching ~65% of HIV-positive PWID) could prevent 58% and 38% of HIV infections and 45% and 32% of HIV-related deaths over 10 years in Omsk and Ekaterinburg, respectively.

Interpretation—Legalisation of OAT, and expansion of ART and NSP for PWID is urgently needed to prevent HIV and fatal overdose among PWID in Russia.

Keywords

Russia; modelling; injection drugs; harm reduction

Introduction

Despite global declines in HIV incidence, the epidemic in Eastern Europe and Central Asia (EECA) continues expanding, with Russia contributing most new HIV infections (80% in 2015).¹ HIV/AIDS is a leading cause of premature death in Russia², with HIV mortality reducing life expectancy.³ HIV prevalence is high (30% [18–43%]) among people who inject drugs (PWID) in Russia,⁴ who also experience high rates of fatal overdose (2.3 per 100 person-years(/100PY))⁵. The HIV epidemic is surging in the Ural and Siberian Federal districts, which experience high rates of new HIV diagnoses (>100 per 100,000 population), nearly half among PWID.⁶

Despite effective HIV treatment and harm reduction to improve health and prevent transmission access among PWID is low in Russia. Since Global Fund withdrawal in 2010, needle/syringe exchange programs (NSP) dwindled from 80 to 10–20 despite evidence demonstrating their effectiveness at preventing HIV by more than 50% in high-income settings.^{7–9} Although pharmacies sell syringes at low cost, they are prohibited from offering HIV testing¹⁰ and some PWID report police harassment and arrest outside.¹¹ Furthermore, opioid agonist therapy (OAT), such as methadone or buprenorphine, remains illegal in Russia despite evidence from meta-analyses documenting its effectiveness in reducing the risk of HIV transmission by 54%¹² and preventing overdose.¹³ Similar impact is seen for HCV, with combination NSP and OAT reducing HCV incidence by 74%.¹⁴

Naltrexone, an opioid antagonist, is legal in both oral and injectable forms, but its efficacy against HIV transmission is unclear, and cost remains a barrier to scale-up.¹⁵ HIV antiretroviral therapy (ART) is free for people living with HIV but coverage remains low overall (36% in 2017)⁶ and is likely low among PWID (estimated <1% among HIV-positive PWID in 2010).¹⁶ Although ART is legal among PWID, considerable heterogeneity in institutional policy and clinical practice has been documented with evidence of denial to active PWID in St. Petersburg in 2004.¹⁷ Russian clinical guidelines in 2017 recommend

immediate ART initiation, but stipulate possibly delaying initiation in patients with “severe drug addiction” without specifications for evaluation, which could prevent ART scale-up among PWID.¹⁸

A recent Lancet Commission on the Future of Global Health and the HIV Response¹⁹ discussed the potential impact of HIV service integration on HIV and other outcomes across different global settings. Due to the lack of HIV services among PWID in Russia, we use epidemic modelling to project the impact of introducing HIV services on reducing HIV and fatal overdose in two of the hardest hit areas of Russia. Only three analyses have modelled HIV epidemics in Russia, focused on St. Petersburg^{20–22}, a city socioeconomically distinct from other urban centers. We investigated the impact of policy changes facilitating expansion of harm reduction and/or ART for PWID on HIV incidence, HIV-related mortality, and fatal overdose among PWID in two urban centers in the Ural and Siberian regions.

Methods

Model design and settings

We modelled two major cities with differing epidemic profiles among PWID: Omsk, in the Siberian Federal District with a growing epidemic and Ekaterinburg, in the Ural Federal District with a high stable HIV prevalence. In Omsk (15,000–25,000 PWID), HIV prevalence among PWID increased from 9%²³ in 2009, to 17%²⁴ in 2011 and 19% by 2014²⁵ with increases in new HIV diagnoses (Supplementary appendix, page 11 Figure S1). In Ekaterinburg, HIV prevalence among PWID increased from 34% in 2001²⁶, stabilising at 59–65% from 2007 to 2014.²⁴ PWID population size in Ekaterinburg is uncertain, varying from 20,000–40,000. Heroin is primarily used in both settings, although use of bath salts has been increasing in Ekaterinburg since 2014.

We modelled the following intervention scenarios, based on coverage levels of OST, NSP and ART achieved in other global settings (>50% OST and high coverage NSP among PWID in Western Europe^{7,27}, and >60% ART among HIV+ PWID as reported by survey data in Estonia⁷) and WHO targets (>40% OST, 200 syringes/year).²⁸ We project HIV prevalence and incidence among PWID from 1996–2028, and estimated the proportion of new HIV infections, HIV-related deaths, and fatal overdoses averted over 2018–2028 comparing each scenario with the base case, presenting results as medians and 2.5–97.5 percentile intervals (95% I).

1. **No change (base case):** No scale-up of harm reduction or ART. No harm reduction at baseline, ART recruitment at current rates (26% of HIV-positive PWID on ART in 2014).
2. **ART expansion for PWID:** Tripled baseline ART recruitment rate from 2018, reaching ~65% coverage among HIV-positive PWID by 2028.
3. **50% OAT coverage, short duration (3 months).** Legal changes enabling OAT scale-up in 2018 to 50% coverage among PWID within 3 years. Because OAT duration varies by setting we explore very short duration on OAT (3 months) (see

supplementary appendix, page 6). as observed in some settings (and that may be expected for settings focusing on detoxification). OAT was assumed to increase ART recruitment and reduce ART attrition²⁹

4. **50% OAT coverage, long duration (2 years):** OAT scale-up as in scenario #3 but extend OAT duration to ~2 years based on data from low-middle income countries (see supplementary appendix, page 6).
5. **50% NSP coverage, long duration:** NSP scale-up in 2018 to 50% coverage among PWID within 3 years, assuming similar duration as scenario #4.
6. **50% NSP+OAT, long duration:** Scale-up of a singular NSP and OAT intervention from 2018 to 50% coverage among PWID within 3 years, assuming similar duration as scenario #4.
7. **50% NSP+OAT (long duration) + ART expansion for PWID.** Scale-up of a singular NSP+OAT intervention (as in scenario #6) plus tripled baseline ART recruitment rates (community and intervention) from 2018.

We developed a dynamic, deterministic model of HIV injecting and sexual transmission among PWID (details in the Supplementary appendix and Figure S2 and S3). Briefly, we stratified the model by HIV disease stage, ART stages, and harm reduction access (off/on). Based on multivariable log-binomial regression analyses of survey data from each site identifying factors associated with prevalent HIV (see Supplementary appendix, page 7–8, Tables S1 and S2), we also stratified the model by sex and risk (low/high defined by incarceration history), assuming proportional mixing. PWID can be recruited onto ART, which reduces HIV-related mortality, and HIV transmission risk (see Supplementary appendix, page 6). Individuals can drop-off ART, at a rate dependent on their intervention status.

The harm reduction scenarios explore scale-up of: high coverage needle/syringe programs (NSP) only (defined as receiving one or more sterile syringes per injection), OAT only, or a combined program delivering both NSP and OAT. Each harm reduction intervention is assumed to reduce an individual's risk of injecting HIV transmission. We incorporate synergistic effects of OAT on ART recruitment and retention and fatal opioid overdose prevention, but assume heightened risk of overdose in the first four weeks entering or leaving OAT (see Supplementary appendix, page 9, Table S3).

Model parameterisation and calibration

Model parameters with uncertainty bounds are presented in Table 1 and Supplementary Table S3. Apart from intervention effects, the model was parameterised mainly with setting-specific data, primarily behavioural and sociodemographic data from cross-sectional surveys conducted in 2009²³ in Omsk and 2007²³ and 2014 (unpublished) in Ekaterinburg (see Supplementary appendix, pages 7–8, Tables S1 and S2).

Self-reported data from Ekaterinburg revealed 26% of HIV-positive PWID were on ART in 2014. We assumed ART scale-up began in 2006 (see Supplementary appendix, page 1), to reach 26% among HIV-positive PWID by 2014. No ART data were available in Omsk, so

we assumed the same coverage as Ekaterinburg. As laws prohibit OAT, we assume no OAT at baseline. Data were unavailable on high coverage NSP access, but a systematic review from 2017 estimated 1–3 syringes/PWID/year provided by NSPs in Russia. No NSP is provided in Omsk. An NSP exists in Ekaterinburg, but in 2014 only 28% of PWID reported accessing an NSP in the past year, yet the number of syringes obtained were unavailable. Since the likely proportion receiving high coverage NSP is lower than these estimates, we assume no high coverage NSP in either setting.

Estimates and ranges for calibration data are in Table 2. We used Latin Hypercube Sampling to generate 500 parameter sets from uncertainty distributions, except for specific parameters used to calibrate the model. For each setting, the model was calibrated to multiple time-points of HIV prevalence among PWID (2009, 2011, 2014 for Omsk and in 2001, 2007, 2011, 2014 for Ekaterinburg), stratified by sex and incarceration status where available (2009 for Omsk and 2007 and 2014 for Ekaterinburg). We also calibrated to the ART coverage among HIV-positive PWID in 2014, the proportion of PWID high-risk (ever incarcerated in 2009 for Omsk and 2007 for Ekaterinburg), and the proportion of incident HIV infections due to sexual risk among PWID in 2009 in Omsk and 2007 for Ekaterinburg (additional details in Supplementary appendix). For each parameter set, we varied the following parameters to fit to this data: initial PWID population size in 1996, seed HIV prevalences among PWID in each group in 1996, sexual and injecting HIV transmission rates in the latent stage, ART recruitment rate from 2006, and the transition rate from low-risk to high-risk (never to ever incarcerated). The model was calibrated using a global optimisation solver (*fmincon* with *multistart* in MATLAB) by minimising the sum log-likelihood of the calibration points.

Sensitivity analyses

We performed sensitivity analyses to test the impact of assumptions such as harm reduction eligibility, preferential mixing by injecting risk, ART coverage in 2018, and injecting cessation rates on results for the combined NSP+OAT plus ART scale-up scenario. First, some PWID may not access harm reduction or would not benefit from OAT. For example, heroin is widely used by PWID in Russia (99% PWID in Omsk (2009) and Ekaterinburg (2007) reported recent heroin injection), but in 2014, 49% of PWID in Ekaterinburg reported exclusively injecting bath salts. We therefore performed an analysis where 49% never access OAT. Second, we model 50% preferential (like-with-like) mixing by injecting risk (versus fully proportional). Third, we model no ART at baseline in Omsk versus our baseline assumption of 26% in 2014. Fourth, we examined reduced injecting cessation in Omsk (to zero in 2009), due to uncertainty in trends in PWID population size (see Supplementary appendix). Fifth, we examined a worst-case sensitivity analysis utilising the lower bounds of the intervention effects for OAT, NSP, and ART on HIV transmission and overdose. Lastly, due to uncertainty in overdose parameters, we assess the impact of using the lower bound OAT overdose effect combined with varied overdose rates (0.5% or 3.5%/year, compared to 2% at baseline).

Role of the funding source

The funders had no role in the study design. The corresponding author had full access to all data and final responsibility to submit for publication.

Data sharing

Code for the modelling is available from the first author upon reasonable request.

Results

Model projections for HIV prevalence and incidence among PWID without intervention presented in the supplementary appendix show that the model fits the data well (see Supplementary appendix, pages 14–18, Figures S3–S8). Based on the calibrated ART coverage in 2014 (26%), the model projects 30% ART coverage by 2018, remaining stable thereafter (Supplementary appendix, page 18, Figure S8).

Without additional interventions, HIV prevalence among PWID in Omsk is predicted to increase from 30% (2.5–97.5 percentile interval [95%I] 20–36%) in 2018 to 36% (95%I: 22–52%) in 2028 (Figure 1A), with an HIV incidence of 9/100PY (6–14/100PY) in 2028 (Figure 1B). In Ekaterinburg, HIV prevalence and incidence among PWID remain high, at 60% (57–67%) and 23/100PY (13–34/100PY), respectively, in 2028 (Figures 1C–D).

Removal of structural barriers regarding harm reduction and expanding ART could have substantial impact. Increasing ART recruitment three-fold from 2018 (resulting in ART coverage of ~60% by 2028) could avert a median of 18% (95% intervals (95% I: 9–29%) and 6% (95% I: 2–14%) of new HIV infections in the next decade in Omsk and Ekaterinburg, respectively. Expanding NSP to 50% of PWID could avert 35% (95% I: 13–54%) and 22% (95% I: 7–33%) of new HIV infections in the next decade in Omsk and Ekaterinburg, respectively. Similarly, scaling up OAT to 50% coverage among PWID with long duration (~2 years) could avert 35% (95% I: 21–51%) and 20% (95% I: 11–29%) of HIV infections in Omsk and Ekaterinburg, respectively. The benefits of OAT on ART recruitment and retention leads to an increase in ART coverage (from 30% to ~40% by 2028). Similar HIV impact is achieved if OAT duration is shorter (3 months) but with the same overall coverage. Scaling up a combined OAT and NSP program at 50% coverage could avert 47% (95% I: 34–61%) and 31% (95% I: 20–40%) of HIV infections among PWID at 10 years in Omsk and Ekaterinburg, respectively. An integrated HIV prevention and care package incorporating harm reduction (OAT+NSP at 50% and tripled ART recruitment rates) could avert 58% (95% I: 46–69%) and 38% (95% I: 26–50%) of new HIV infections over the next decade in Omsk and Ekaterinburg, respectively. This would result in ART coverage of 65% by 2028, roughly 10% higher than if ART is scaled-up alone.

These interventions would have additional impact on mortality due to HIV and overdose (Figures 2B,C). In Omsk, tripling ART recruitment could avert 29% (95% I: 23–36%) of HIV-related deaths over the next decade, with small increases in overdose mortality (3% increase over 10 years) due to increased survival and competing risk of death from overdose. Scale-up of long-duration OAT to 50% coverage could reduce both HIV mortality (24% (95% I: 16–34%) in Omsk (similar with short duration) and overdose. The impact of OAT

on overdose mortality varied by duration of OAT; 3-month duration OAT (but equal coverage) would avert fewer deaths and could potentially increase mortality: 11% (95% I: -9–26%) fatal overdoses averted due to excess mortality within the first four weeks of initiation and discontinuation of OAT whereas OAT with an average duration of ~2 years could avert 33% (95% I: 25–38%) of overdose deaths in Omsk in the next decade. As with HIV incidence, an integrated harm reduction plus ART expansion strategy would have the most impact on HIV and overdose mortality, averting 45% (95% I: 36–54%) of HIV-deaths and 32% (95% I: 24–37%) of overdose deaths over a decade in Omsk. Roughly half the benefit on HIV-related mortality was observed in Ekaterinburg compared to Omsk due to differing epidemic characteristics, with similar overdose impact (Figure 2C).

Figure 3 presents sensitivity analyses with differing assumptions regarding preferential mixing by risk (50% preferential versus fully proportional), harm reduction access/eligibility (49% never accessing harm reduction, versus all), ART coverage in Omsk (0% in 2014 versus 26%), and injecting cessation in Omsk (reduced to zero from 2009 versus constant). Predictions for averted HIV infections, HIV deaths, and fatal overdoses were insensitive (<10% relative difference) to these variations (Figure 3a–c). The model was sensitive to intervention impact assumptions; using lower bound estimates for OST, NSP, and ART impact resulted in half the number of HIV infections averted compared to base-case. Estimates were less sensitive to overdose uncertainty; using the lower bound estimates of OAT impact on overdose, a median 8% and 18% fewer overdoses were averted in Omsk, assuming an annual overdose rate of 0.5% and 3.5%, respectively.

Discussion

Without urgent intervention, modelling indicates the burden of HIV among PWID in Russia will worsen, escalating in settings like Omsk and remaining endemically high in settings such as Ekaterinburg. Substantial impact on HIV incidence and mortality related to HIV and overdose among PWID could be achieved through policy and programme changes allowing OAT coupled with funding for NSP expansion and increased ART coverage among PWID. Over half of new infections and HIV-related deaths could be averted if harm reduction is scaled-up to 50% coverage and ART recruitment tripled in settings with expanding epidemics like Omsk. Further, over a third of new infections, HIV and overdose deaths could be averted in settings with high prevalence, like Ekaterinburg. Conversely, failure to scale-up harm reduction and solely scaling-up ART would have less impact on averting HIV incidence and overdose.

In settings with a high burden of HIV and overdose among PWID like Russia, harm reduction should be cornerstone prevention interventions. We project that high coverage OAT (either prolonged duration or high throughput short duration) can prevent HIV transmission and enhance ART benefits. However, only prolonged duration OAT, consistent with a chronic disease model of care as recommended by the WHO²⁸, is likely to substantially reduce overdose deaths. Conversely, short duration OAT could increase fatal overdoses, because OAT is associated with temporary increases in overdose at initiation and discontinuation.

To our knowledge this is the first study to explore the dual benefits of combination HIV prevention on both HIV and fatal overdose in Russia, which has one of the most rapidly growing HIV epidemics worldwide. We focused on two areas attracting international concern due to high rates of HIV diagnoses. It is unclear whether our findings will be generalisable, but other settings such as Irkutsk and St Petersburg exhibit stable high prevalence of HIV among PWID similar to Ekaterinburg, while there is evidence for expanding epidemics in Western Siberia, including the Altai Krai region, similar to Omsk.³⁰ Additionally, our work supports previous modelling highlighting the benefits of harm reduction and ART among PWID in St. Petersburg and in other global settings.²⁰ In contrast to recent modelling indicating the substantial value in integration of existing HIV with non-communicable diseases and STI services in settings like South Africa and India¹⁹, our work highlights the need for developing these basic services in Russia, ideally in an integrated manner.

Like all modelling studies, ours has several limitations. Firstly, there was parameter uncertainty, which we incorporated by sampling from wide distributions and propagating into the future. For example, due to minimal coverage of interventions among PWID in Russia, we utilised published intervention effect estimates from global meta-analyses incorporating uncertainty. Our sensitivity analyses indicate substantial intervention impact even using lower bound estimates for all interventions. One key area of uncertainty surrounds the impact of NSP, given that syringes can be obtained from pharmacies.¹¹ The proportion of PWID receiving full coverage (one sterile syringe per injection) from pharmacies is uncertain, so some proportion of PWID may not receive additional benefit from scaled-up NSP provision. Conversely, pharmacy provision may *enhance* NSP impact through providing another source for PWID to reach full coverage. Importantly, pharmacies do not provide many ancillary services recommended for NSPs by the WHO, such as HIV-testing, harm reduction education and counseling. Further research on pharmacy access, syringe coverage, and NSP preferences among PWID is needed. Additionally, we lacked site-specific overdose mortality data, and available data were of low quality and dated. More robust data are required on overdose mortality and impact of interventions in Russia. Furthermore, there is uncertainty regarding historic and future trends in the main drugs injected. In Ekaterinburg, we observed a shift from opioids to stimulants (e.g. bath salts), which may limit the relevance of OAT. We examined the effect of this in sensitivity analyses with the main results being robust to these variations. However, if opioid injecting becomes increasingly rare, then reaching high OAT may be unrealistic.

Second, our analysis considered only NSP, OAT, and ART, and neglected other interventions to prevent HIV and overdose. We note that although OAT is illegal, naltrexone (an opiate antagonist treatment) is available in oral and injectable forms. A recent U.S. study found that extended-release naltrexone improves viral suppression in prisoners³¹, but broad evidence for its effectiveness at preventing HIV is lacking so we did not consider it. Additionally, high costs (implants cost approximately 20,000 RUB (~300 USD), whereas the net average wage is \$620/month) provide a significant barrier to scale-up. The WHO recommends HIV pre-exposure prophylaxis (PrEP) for people at substantial risk of HIV, including PWID.³² However, given the low coverage of ART among HIV-positive individuals in Russia, and uncertainty of the cost-effectiveness of PrEP for PWID³³, we prioritised ART scale-up.

Finally, naloxone is effective at preventing fatal overdose and is cost-effective in Russia³⁴ but was not assessed as we chose interventions which prevent HIV.

Third, we focused solely on HIV transmission and overdose, and neglected additional benefits of harm reduction. For example, OAT and NSP reduce hepatitis C virus (HCV) acquisition¹⁴ which could yield substantial benefits as ~72% of PWID in Russia have a history of HCV infection. Additionally, OAT reduces drug-related criminal behaviour and could reduce incarceration and prison-associated infections.³⁵ We neglected any behaviour change resulting from HIV diagnosis, and might underestimate the impact of ART scale-up. Further, we found higher prevalence among those with a history of incarceration, as in other settings.³⁵ There is growing literature on the potential role of medications for opioid use disorder for increasing ART adherence among incarcerated populations³¹ and reducing the elevated risk of overdose associated with recent prison release, benefits we neglected. Although incarceration may disrupt HIV prevention, it could be an important point of contact for PWID where scaled-up HIV services in prison could have substantial community benefit.³⁵

Fourth, we do not address cost or cost-effectiveness. Given the paucity of HIV prevention services for PWID, the economic implications of the scenarios examined are uncertain, however we previously estimated scaling-up OAT and NSPs to half of the ~1.88 million PWID in Russia could cost \$333–521 million annually.¹⁹ Additionally, ART for PWID is cost-effective in Russia²¹, OAT is hypothetically cost-effective in Russia³⁶, and NSPs are cost-effective in Ukraine and Belarus.^{37,38}

In conclusion, there is a high concentration of HIV among PWID in Russia, yet harm reduction and HIV services for PWID reach few in need. Legalisation of OAT and support for expansion of NSP and ART is urgently required for PWID in Russia, which we find which could reduce HIV and fatal overdose among PWID in two Russian settings, among other potential benefits on infectious disease and incarceration.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Research in context

Eastern Europe and Central Asia (EECA) remains one of the few world regions where the HIV epidemic continues to expand, with a recent dramatic increase in infections in the Ural and Siberian Federal districts of Russia. In Russia, injecting drug use is the predominant mode of HIV transmission, and overdose rates among people who inject drugs (PWID) are high. Despite this, Russian laws prohibit opiate agonist therapy (OAT), and coverage of HIV antiretroviral treatment (ART) and needle and syringe programmes (NSP) among PWID is minimal. We searched PubMed on 2 April 2018 using the following MeSH terms (“modeling” or “modelling”) AND “HIV” AND (“harm reduction” OR “syringe exchange” OR “needle syringe program” OR “opioid substitution therapy” OR “medically assisted treatment”) AND (“treatment” OR “antiretroviral therapy”). We identified 5 studies that included dynamic epidemic models of HIV among PWID in EECA (three studies in Ukraine, one in Russia, one multi-country analysis of other former Soviet republics). The study from Russia assessed the coverage of harm reduction and ART needed to halve HIV incidence and prevalence in St. Petersburg. However, no modelling analyses have been conducted in other areas of Russia such as the Siberia and the Ural districts. Further, previous modelling studies from the EECA did not consider the dual outcomes of HIV and fatal overdose.

Implications of all available evidence

Current Russian drug policy is fueling the dual HIV and opioid overdose epidemics among PWID, with implications for the general population both nationally and regionally. Legalisation of OAT and expansion of NSP and ART coverage among PWID is critical to addressing mounting injection drug use-related morbidity and mortality. Failure to adopt evidence-based drug policies will be measured in Russian lives lost to HIV and overdose.

Added value of this study

To our knowledge, our study is the first to model the dual benefit of OAT on averting HIV incidence and fatal opioid overdose among PWID in Russia, where OAT is prohibited. Additionally, our study is the only modelling analysis in Russia outside of St. Petersburg, focusing on areas with the highest incidence of reported HIV cases. We show that without further intervention, HIV burden will rise to 36% of PWID by 2028 in Omsk, Russia, while it would remain high in Ekaterinburg, Russia (~60%). Legal changes allowing OAT would decrease both HIV incidence and fatal overdose among PWID, and increase ART coverage through increased recruitment/retention. Scaling-up harm reduction services (OAT +NSP to 50% coverage) and tripled ART recruitment could avert over one-half and one-third of HIV infections in Omsk and Ekaterinburg, respectively, while also averting one-third of fatal opioid overdoses in both settings over 10 years.

Figure 1. Model projections of HIV prevalence and incidence among PWID in Omsk, Russia (A: prevalence, B: incidence), and Ekaterinburg, Russia (C: prevalence, D: incidence) with various intervention scenarios

Solid lines represent median model projections. Dashed lines represent 2.5 – 97.5 percentile interval: of the base case scenario. OAT: opiate agonist therapy. NSP: high coverage needle and syringe programs. ART: Antiretroviral treatment.

Figure 2A

Figure 2B

Figure 2C

Figure 2. Proportion of (a) HIV cases and (B) HIV deaths in Omsk and Ekaterinburg from 2018–2028 (C) fatal overdoses averted in Omsk (results were nearly identical in Ekaterinburg) from 2018–2028

Box plots indicate the median (middle line) projections, 25–75% interquartile range (boxes), and 2.5–97.5 percentile interval (whiskers), and median estimates reported above box plots. OAT: opiate agonist therapy. NSP: needle and syringe programs. ART: Antiretroviral treatment.

(A) **(B)**

Figure 3. Results from sensitivity analyses presenting the percent relative median change in impact achieved at 10 years (averted HIV cases (A), HIV deaths (B), and fatal overdoses (C)) with the combined NSP+ OAT and ART scale-up scenario with different model assumptions White bars represent Omsk and grey bars represent Ekaterinburg.

Table 1
Intervention efficacy assumptions for the model and sampling distributions

OAT: opiate agonist therapy. NSP: high coverage needle and syringe programs. ART: Antiretroviral treatment. For references, please see Supplementary appendix, page 9, Table S3 in the supplementary information.

Intervention	Parameter	Mean and 95%CI of generated distribution	Sampling distribution and parameters
ART	Relative sexual-related transmissibility while on ART compared to latent phase (ω_{sex})	0.07 (0.02 – 0.21)	lognormal (mean= -2.66, sd=0.58)
	Relative injection-related transmissibility while on ART compared to latent phase (ω_{inj})	0.50 (0.26 – 0.74)	uniform (min=0.25, max=0.75)
	Cofactor reduction in HIV mortality rate if initiating ART in latent or pre-AIDS stage (ν)	0.27 (0.20 – 0.33)	uniform (min 0.2, max 0.33)
	Cofactor reduction in HIV mortality rate if initiating ART in AIDS stage (ρ)	0.51 (0.39 – 0.62)	uniform (min 0.38, max 0.63)
NSP	Relative HIV injection transmission risk if on NSP only compared to no NSP (RR_{NSP})	0.42 (0.21 – 0.81)	lognormal (mean=-0.42, sd=0.22)
OAT	Relative HIV injection transmission risk if on OAT only compared to no OAT (RR_{OAT})	0.46 (0.31 – 0.68)	lognormal (mean=-0.78, sd=0.19)
	Relative risk of ART discontinuation if on OAT compared to no OAT (Ψ_{OAT})	0.77 (0.63–0.95)	lognormal (mean=-0.26, sd=0.11)
	Relative increase in ART recruitment if on OAT compared to no OAT (χ_{OAT})	1.69 (1.32–2.14)	lognormal (mean=0.52, sd=0.12)
	Relative risk of fatal opioid overdose if on OAT compared to off OAT (Ψ_{OAT})	0.21 (0.12 – 0.35)	lognormal (mean=-1.57, sd=0.26)
	Relative risk of death within the first four weeks of entering OAT compared to on OAT ($RR_{odonOAT}$)	1.97 (0.93 – 4.00)	lognormal (mean=0.68, sd=0.37)
	Relative risk of death within the first four weeks of exiting OAT compared to off OAT ($RR_{odoffOAT}$)	2.38 (1.53 – 3.75)	lognormal (mean=0.87, sd=0.23)
NSP+OAT	Relative HIV injection transmission risk if on OAT +NSP compared to no OAT or NSP (RR_{BOTH})	Product of RR_{NSP} and RR_{OAT}	
	Relative risk of ART discontinuation, ART recruitment, fatal opioid overdose, and risks of death on entry/exit if on NSP+OAT compared to no NSP+OAT (Ψ_{BOTH} , χ_{BOTH} , Ψ_{BOTH} , $RR_{odonOAT}$, $RR_{odoffOAT}$)	Equal to OAT alone	

Table 2
Model calibration data and distributions for the log-likelihood calculation

95% confidence intervals are the computed Wald confidence limits from survey data. PWID: people who inject drugs.

	Omsk, Russia	Ekaterinburg, Russia	Distribution for the log-likelihood calculation	Reference
HIV prevalence among PWID in 2001		34% (95%CI: 23.7–44.6%)	beta	²⁶
HIV prevalence among PWID in 2007 by gender		Males: 60.6% (95%CI: 53.6–67.7%) Females: 70.5% (95%CI: 62.0–79.1%)	beta	²³ Survey data
HIV prevalence among PWID in 2009 by gender	Males: 8.5% (95%CI: 5.1–11.9%) Females: 9.0% (95%CI: 2.9–15.0%)		beta	²³ Survey data
HIV prevalence among PWID in 2009 by incarceration status	Ever Incarcerated: 12.7% (95%CI: 7.1–18.2%) Never Incarcerated: 5.8% (95%CI: 2.6–9.0%)		beta	²³ Survey data
HIV prevalence among PWID in 2011	16.7% (95%CI: 12.9–20.8%)	58.5% (95%CI: 53.4–63.8%)	beta	²⁴
HIV prevalence among PWID in 2014 by gender		Males: 58.2% (95%CI: 52.0–64.4%) Females: 77.9% (95%CI: 70.9–85.0%)	beta	Survey data (unpublished)
HIV prevalence among ever incarcerated PWID in 2014 by incarceration status		Ever Incarcerated: 70.3% (95%CI: 64.4–76.2%) Never Incarcerated: 56.6% (95%CI: 48.4–64.9%)	beta	Survey data (unpublished)
HIV prevalence among PWID in 2014	19.4%		beta	Survey data ²⁵
ART coverage among HIV positive PWID in 2014	26%	26%	beta	Data (unpublished) from Ekaterinburg but assumed similar coverage in Omsk
Proportion PWID with a history of incarceration	40.9% (95%CI: 35.7–46.0%) in 2009	37.7% (95%CI: 32.2–43.2%) in 2007	beta	²³ Survey data
Proportion of incident infections attributed to sexual transmission among PWID	8–28% in 2009	7–27% in 2007	uniform	Estimated from HIV/HCV coinfection survey data in each setting and published modelling (see Supplementary appendix, page 5 for details)