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HIV transmission from drug injectors to partners who do not inject, and beyond: Modelling the potential for a generalized heterosexual epidemic in St. Petersburg, Russia[☆]

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Abstract

Background—HIV infection is prevalent among drug injectors in St. Petersburg and their non-injecting heterosexual partners (PIDUs). There are fears that sexual transmission of HIV from IDUs to PIDUs may portend a self-sustaining, heterosexual epidemic in Russia.

Methods—Our model combines a network model of sexual partnerships of IDUs and non-IDUs to represent sexual transmission of HIV and a deterministic model for parenteral transmission among IDUs. Behavioural parameters were obtained from a survey of St. Petersburg IDUs and their sexual partners. We based our model fits on two scenarios for PIDU prevalence in 2006 (5.6% and 15.1%, calculated excluding and including HCV co-infected PIDUs respectively) and compared predictions for the general population HIV prevalence.

Results—Results indicate that sexual transmission could sustain a non-IDU HIV epidemic. The model indicates that general population prevalence may be greater than current estimates imply. Parenteral transmission drives the epidemic and the PIDU bridge population plays a crucial role transferring infection to non-IDUs. The model indicates that the high PIDU prevalence is improbable because of the high risk behaviour this implies; the lower prevalence is possible.

[☆]Supplementary materials for this article can be found by accessing the online version of this paper at <http://dx.doi.org/10.1016/j.drugalcdep.2013.04.028>. Please see Appendix A for more information.

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Contributors

HLM and EW designed the initial model, HLM wrote and ran the model and simulations. EW derived parameters from the SATHCAP dataset. CC, PV and RH advised on the model and analysis. PV and RH initiated the collaboration. All authors contributed to the paper text.

Conflict of interest

All authors declare that they have no conflicts of interest.

Conclusion—The model implies that transmission through PIDUs will sustain a heterosexual epidemic, if prevalence among IDUs and PIDUs is as high as survey data suggest. We postulate that current estimates of population prevalence underestimate the extent of the HIV epidemic because they are based on the number of registered cases only. Curtailing transmission among injectors and PIDUs will be vital in controlling heterosexual transmission.

Keywords

Injecting drug users; Mathematical model; Heterosexual transmission; Surveillance; Russia; Partners of IDUs

1. Introduction

Russia has one of the most rapidly growing HIV epidemics in the world (World Health Organization, 2008); an estimated 1% of its residents are infected (UNAIDS and the World Health Organization, 2010). St. Petersburg is Russia's second largest city and the one with the highest number of diagnosed HIV infections. As elsewhere in Russia, as much as 80% of HIV cases in St. Petersburg are among injecting drug users (IDUs) (Rhodes et al., 2004; Rakhmanova et al., 2007; Goliusov et al., 2008) who comprise nearly 2% of the adult population (Heimer and White, 2010). An estimated 45% of IDUs in St. Petersburg are infected based on data collected in 2006–08 (Niccolai et al., 2010); the majority are unaware of their infection (Grau et al., 2011). In a retrospective cohort analysis, estimated incidence among St. Petersburg IDUs was 14.1/100 person-years (95% CI 10.7–17.6); using corrected results of a BED enzyme-linked immunosorbant assay, estimated incidence was 23.9/100py (95% CI 17.8–30.1) (Niccolai et al., 2011).

The proportion of new HIV cases in Russia attributed to sexual transmission increased from 4.1% in 2001 to 35.8% in 2009 (for cases where mode of transmission was documented; Pokrovsky and Ladnaya, 2010). In a convenience sample of HIV-positive female clients of the St. Petersburg Municipal AIDS Center, 46% reported prior sexual contact with a male IDU (Toussova et al., 2009). Data indicate that sexual transmission of HIV from IDUs to their non-injecting sexual partners occurs relatively regularly in Russia; this has raised considerable concern regarding the potential for a generalized epidemic, in which HIV may be transmitted heterosexually independent of transmission from IDUs to non-IDUs (Doherty, 2011; Niccolai et al., 2010).

Much of the general work in this area is based on a large study of IDUs, men who have sex with men and their sexual partners conducted in St. Petersburg during 2005–2008 (Iguchi et al., 2009). The study, Sexual Acquisition and Transmission of HIV Cooperative Agreement Programme (SATHCAP), employed respondent-driven sampling (RDS). The IDUs were young (almost entirely between 20 and 45 years of age) and sexually active (84% reported sexual activity in the past 6 months; Niccolai et al., 2010). Of 157 HIV-infected, sexually active IDUs, unprotected sex in the prior six months was reported with 89 partners known not to be HIV infected (Grau et al., 2011). Given that HIV prevalence among IDUs in the sample was 44%, that 40% of IDU sex partners were reported to be non-injectors (PIDUs) and that unprotected sex occurred in 41% of last reported occasions of intercourse (Niccolai et al., 2009), it is not surprising that HIV prevalence among PIDUs is high. In a prior

analysis of SATHCAP data, HIV prevalence among 53 non-injecting partners of IDUs was 15% (Niccolai et al., 2009).

The core group in an epidemic is characterized by high connectivity and high prevalence of infection. Individuals outside the core group but who have contact with members of both the core and those outside the core are said to belong to a bridge population. In St. Petersburg, there is substantial potential for sexual HIV transmission from infected, non-injecting partners of IDUs, to their subsequent non-injecting sexual partners. Under SATHCAP, 68% of non-IDU partners of IDU reported multiple partnerships in the last six months and 57% reported unprotected sex with casual partners (Abdala et al., 2010). Additionally, 66% of non-IDU partners of IDUs reported new sex partners in the past 6 months (Niccolai et al., 2009).

In a separate study of clients of street-based female sex workers (FSW), most of whom are also IDUs in St. Petersburg (Aral et al., 2005), 58% were classified as active or potential bridgers, having both FSW and non-FSW partners and reporting inconsistent condom use with their non-FSW partners (Niccolai et al., 2012). Male clients of FSWs risk acquiring HIV from the FSW and may subsequently transmit HIV to others, including FSWs.

Behavioural data show the potential for non-injecting partners of IDUs to transmit HIV into the general population, but too few serological or partnership data exist to quantify that, and none are available to estimate whether such transmission could be sustained sexually, outside of and independent from the core groups of IDUs and men who have sex with men. However, data that do exist, from SATHCAP, other sources in the peer-reviewed literature, and technical reports, suffice to simulate likely scenarios for how HIV may or may not be transmitted from IDUs to their non-injecting partners and beyond. Thus, the purpose of this analysis is to examine the potential for HIV transmission to sustain itself through sexual transmission in St. Petersburg.

2. Methods

2.1. The transmission model

We create a model of HIV transmission informed by data from SATHCAP, technical reports on St. Petersburg and current literature. The model population is heterosexual and initially of two types: IDUs and non-IDUs. We connect them in a dynamic network with degrees and partnership durations determined by SATHCAP; non-IDUs have a slightly longer duration of partnerships than IDUs and different lifetime sexual degree distributions. Non-IDUs who form partnerships with IDUs are called PIDUs (non-injecting partners of IDUs); other non-IDUs are PPIDUs. Following current treatment and cessation rates in Russia, IDUs in our model do not cease injecting and female PIDUs may begin injecting while with a male IDU partner (Butler, 2003; Krupitsky et al., 2006; Torban et al., 2011). Full details of the network model are in Supplementary Material.

Transmission of HIV occurs by sexual and parenteral means. Our model focuses on the sexual transmission in the population so we use an individual based network to represent the sexual partnerships. Parenteral transmission is represented by a stochastic SI model. We

chose not to represent injecting contacts using an explicit network as a multi-network model of the population would require detailed data on correlations between contacts of different types and other complexities: this level of data is not available. Risk of infection by sexual transmission depends on the number of infected sexual partners, the number of risky acts per partnership and the probability of transmission; parenteral risk depends on the number of unsafe injecting acts and the HIV prevalence in the IDU population; further description is in the Supplementary Material. All behavioural parameters are informed by SATHCAP and biological parameters by current literature (see Table S1 in the Supplementary Material).

We model HIV with three stages: initial acute infection, stable viral state and increasing viral state, each with different probabilities of transmission and mortality (Pezzotti et al., 1999; Wawer et al., 2005). In our model only non-IDUs may receive treatment by ARVs, following current policy in St. Petersburg. Therefore, in the simulations non-IDUs take an HIV test on average 5 years following infection and will receive ARVs once diagnosed only if it has been at least 2.5 years since they were infected (the average time taken for CD4+ cell count to fall below the guideline limit of 350 cells/mm³) (World Health Organization, 2010; UK Collaborative HIV Cohort (CHIC) Study Steering Committee, 2007), see the Supplementary Material for more details. This reflects the most optimistic scenario offered by the treatment provided in St. Petersburg. Non-IDUs receiving ARVs have their infectivity reduced by 95%, following results of the HPTN052 trial (HIV Prevention Trials Network, 2006; Cohen et al., 2011; Anglemeyer et al., 2011). As IDUs do not receive ARVs, parenteral transmission is unaffected.

2.2. Model fitting

We have estimates for HIV prevalence among IDUs in St. Petersburg and estimates for prevalence in the general population for the time period 1999–2010, see Fig. 1 (World Health Organization, Global Health Observatory Data Repository; Ostrovskiy, 1999; Abdala et al., 2003; Shaboltas et al., 2006; Niccolai et al., 2011; Lyubimova et al., 2011). We note that the general population prevalence data likely underestimate the actual prevalence, because the methods used are based on the number of registered HIV infections and underestimate the number of individuals at risk (Feshbach and Galvin, 2005; Heimer and White, 2010; Kissin et al., 2011).

The estimated prevalence of HIV infection among PIDUs in the SATHCAP sample is 15.1%, however, excluding those PIDUs with HCV infection the prevalence is 5.6% [95% CI 0.7%–20.1%]. HCV infection is a strong indicator of injecting drug use and, as the cessation rate is thought to be negligible, it is logical to conclude that co-infected individuals who entered the SATHCAP sample as PIDUs might actually be IDUs. We therefore modelled a scenario based on a fit to the 5.6% PIDU prevalence obtained by excluding PIDUS with HCV infection. We also fitted the prevalence among IDUs in the model to the data from St. Petersburg for 1999–2009 (Fig. 1). We did this by scaling the number of sexual acts a month, the duration of partnerships and the number of risky injections a month (effectively altering the probability of transmitting HIV per partnership).

We model a population of size 10,000 with 20% IDU, 75% of IDUs are male and the rest female (agreeing with SATHCAP and other studies (Shaboltas et al., 2006)), non-IDUs have

an even proportion of each gender. We use an initial prevalence of 5% in the IDU population (Ostrovskiy, 1999). The simulation is run for 25 years, 1999–2024. For each fit we run 100 repeats of the stochastic model and average the results.

2.2.1. Latin hypercube sampling—We used Latin Hypercube Sampling (LHS) to determine the effect the parameters have on the simulation results (McKay et al., 1979). The confidence intervals for all parameters (biological and behavioural) are in Table S1 in the Supplementary Material. We tested all behavioural parameters within their 95% confidence interval range (keeping biological parameters constant). We focused our sensitivity analysis on the behavioural parameters, as these parameters are generally difficult to determine accurately and we were interested in their effect on the model. The sensitivity analysis comprised 20 repeats each of 100 different parameter combinations in a small population (size 1000). We used regression analysis on the results after 25 years to determine the parameters most strongly correlated with HIV prevalence.

2.3. Model analysis

Our model does not use the actual proportions of IDUs and non-IDUs in St. Petersburg as the numbers were unfeasible with an agent-based model. We want to estimate the population prevalence of the whole city, using the prevalences in each type (IDU, PIDU, PPIDU) in order to compare our model predictions to surveillance data. The surveillance data estimate the HIV prevalence of the 15–49 year olds in St. Petersburg. There are estimated 3.6 million individuals in this age range in St. Petersburg in 2010 (Nation Master, age distribution tables for Russia) and an estimated 83,118 IDUs (Heimer and White, 2010); therefore an estimated 2.3% of this age range are IDU. The proportion of PIDUs in St. Petersburg was calculated using the same ratio of IDUs to PIDUs as present in the model, at each time step. We adjust the prevalence in our model to the proportions of each type in the actual St. Petersburg population to get predicted prevalence for the general population (15–49 years old).

To determine whether sexual transmission could sustain a non-IDU epidemic we examine the prevalence of sexually transmitted HIV in each type (IDU, PIDU and PPIDU) and find in which partnership type (IDU–IDU, IDU–non-IDU etc.) the majority of sexual transmissions occurs. Finally, we ran the model with parenteral transmission removed from 2012 to determine whether the heterosexual non-IDU epidemic is sustained without the high IDU prevalence.

3. Results

We created a model of HIV transmission in St. Petersburg, informed by SATHCAP. Using regression analysis on the results of the Latin hypercube sampling of our model we found that HIV prevalence among IDUs was most sensitive to the mean number of injections a month per IDU (the majority of transmission in this population occurs over injecting pathways). Prevalence in non-IDUs was most sensitive to the mean number of sexual acts per partnership and PIDU prevalence was also correlated with IDU prevalence. The (adjusted) whole population HIV prevalence was most sensitive to changes in the mean number of injections a month. This indicates that transmission among IDUs is a key driver of incidence and that to control population prevalence the transmission of HIV over

injecting pathways must be limited by changing the behavioural risk patterns in this population and/or the structural determinants of risk that reduce access to and use of sterile syringes. The correlation with sexual behaviour indicates that reducing sexual risk among non-IDUs will also be important to reduce population prevalence.

We fit the model based on the prevalence among PIDUs in SATH-CAP who were not infected with HCV (5.6% in 2006). Fig. 2 shows the HIV prevalence among IDUs (note transmission is both sexual and parenteral). The fit nicely parallels the prevalence in IDUs in St. Petersburg, as estimated from cross sectional and point prevalence surveys.

Our model indicates that that if PIDU HIV prevalence and risk behaviours are as high as SATHCAP suggests, sexual transmission is likely to cause a substantial HIV epidemic among non-IDUs. Fig. 3A illustrates the prevalence in the different risk groups. The prevalence in PIDUs and PPIDUs increases steadily over the first 15 years. However, following the stabilising of the IDU epidemic, the rate of increase of prevalence among non-IDUs slows, eventually giving a stable prevalence.

Fig. 3B shows the model prediction for the general population prevalence of HIV in St. Petersburg after adjustment to the correct population proportions. The model prevalence initially matches the observed population prevalence (among 15–49 year olds) but continues to rise steadily, suggesting a much higher prevalence than is currently estimated and a growing epidemic.

The majority of transmission occurs from IDU to non-IDU throughout the simulation, see Fig. S7 in the Supplementary Material. Over time, as the prevalence increases, more transmission occurs within the non-IDU population. There is a small proportion of transmission from non-IDU to IDU.

For comparison, we also modelled a scenario based on the 15.1% PIDU point prevalence obtained when individuals infected with HCV were included; HCV infection is a strong indicator of injecting behaviour indicating that this estimate may include IDUs. In this scenario, the predicted general population prevalence is very high and conflicts with available surveillance data. The scenario is unrealistic given the high level of sexual activity required to maintain the PIDU prevalence, implying that the 5.6% prevalence scenario, which excludes the possible IDUs, is more realistic; more details and figures for the higher fit are in the Supplementary Material.

To determine whether the epidemic within the non-IDU population is sustainable, we ran the model again, with no parenteral transmission among IDUs from 2012 onwards, Fig. 4. On removing this force of infection IDU prevalence immediately declines, due to the reduction in new cases and deaths among IDUs who are denied ARVs. This confirms that prevalence among IDUs is maintained by parenteral transmission. Prevalence among PIDUs and PPIDUs continues to rise for a few years, then gradually declines. The predicted 2024 general population prevalence in both scenarios is lower than for those scenarios in the main model. The slow decline of general population prevalence indicates that without parenteral transmission, the non-IDU epidemic will be sustained for a considerable time (past 2050) but may eventually die out in the long term.

4. Discussion

Data were sufficient to create a realistic model of HIV transmission that reflected parameter values at the time they were taken. In our sensitivity analysis and results we have demonstrated outcomes that can reasonably be expected given known parameters and data. Our results indicate that HIV prevalence in the general population is higher than current surveillance data imply. Even at the lower estimated PIDU prevalence (5.6% in 2006, eliminating potential IDUs) our model predicts that the general population HIV prevalence may be double what current (2010) surveillance data imply. This seems to confirm the view that the general population prevalence data (for HIV prevalence among 15–49 year olds; World Health Organization Global Health Observatory Data Repository) underestimate the actual prevalence because of the imperfect methods of collecting surveillance data. As Feshbach and Galvin note (2005), HIV surveillance became suspect in 2003 due to decreases in the number of tests conducted and the venues for conducting testing, and shortly thereafter our model predictions begin to exceed the surveillance estimates (Fig. 3B). Additionally, as the addiction treatment system in Russia is ineffective, many IDUs have stopped using it (Lohman, 2008; Heimer et al., 2007). As IDUs no longer entered the surveillance system, it is likely that surveillance estimates do not reflect the course of the epidemic. This is confirmed by studies finding that many IDUs have not been tested (Niccolai et al., 2010).

We based our model fits on two scenarios of PIDU prevalence in 2006 (5.6%), obtained from SATHCAP by excluding those PIDUs infected with HCV. In the Supplementary Material we provide results of the model for the scenario with the higher PIDU prevalence (15.1%) obtained by including those HCV infected PIDUs. We believe that the model fit to the higher prevalence estimate among PIDUs is improbable since this requires very high rates of sexual transmission. HCV infection is a strong indicator of injecting activity, therefore those PIDUs infected with HCV may have been IDUs who concealed injecting from interviewers either to reduce the duration of the interview or because of socially desirable response bias. This has important implications for prevalence estimates in St. Petersburg; we stress the importance of careful examination of surveillance data to obtain reliable estimates of IDU and non-IDU prevalence.

Regardless, using the lower, 5.6%, prevalence estimate among PIDUs the outcomes of these simulations indicate that the transmission of HIV to PIDUs and onwards could cause an HIV epidemic among the general community outside injectors, even with the eventual 100% non-IDU treatment strategy that we assumed. Additionally, without parenteral transmission among IDUs the non-IDU epidemic may be sustained for some time, as shown in Fig. 4. Further, all realistic scenarios and the Latin hypercube sampling analysis show the prevalence in the general population of St. Petersburg to be strongly bound to the parenteral risk among IDUs. These findings collectively indicate that controlling parenteral transmission may eventually reduce heterosexual transmission of the virus, but sexual behavioural risk among non-IDUs (particularly the bridge population) should also be reduced in order to have a significant effect on general population prevalence.

Our model did not consider ageing because we did not have the longitudinal data required to adequately represent the effect of ageing on behaviour. Similarly, data were not available to represent parenteral transmission explicitly as a second network. We would need information on the correlations between sexual and parenteral partnerships and detailed information on the dynamics of parenteral partnerships. If complete data were available we could include these complexities; our model is as complex as possible given the data available. Additionally, as with all survey data, SATHCAP suffers from an element of recall bias which has limited our ability to accurately determine partnership durations and concurrency (discussed further in the Supplementary Material) and behavioural data, something we addressed in our sensitivity analysis of the behavioural parameters. The low number of PIDUs in the SATHCAP data limits the accuracy of the derived parameters for PIDUs; however, our presentation of two widely different scenarios (main text and Supplementary Material) and the sensitivity analysis acknowledge the large confidence intervals in this dataset and our conclusions hold throughout.

The HIV epidemic in Russia is concentrated in the IDU population; 80% of registered AIDS cases are among IDUs (World Health Organization, 2005; Golusov et al., 2008). Recent studies have found potential for HIV to transmit from core groups such as IDUs into the general population via a bridge population (Lowndes et al., 2003; Niccolai et al., 2009; Abdala et al., 2010). Modelling studies have investigated the impact this mechanism could have, (Grassly et al., 2003; Vickerman and Watts, 2003; Long et al., 2006; Nosova and Romanyukha, 2011) consistent with our result that transmission from IDUs to the general population will have a significant impact on the epidemic. However, the unique dual-risk factors of injecting and sexual risk behaviours among IDUs and the difficulty of determining the sexual behaviour of the adult population (both IDU and non-IDU) make the epidemic difficult to predict.

We have used an individual-based model, directly informed by the SATHCAP study, to show that the bridge population is crucially important in this epidemic and strongly influences HIV prevalence in the general population. We hypothesise that increasing the surveillance and targeting of these bridging individuals will be vital for the control of the epidemic. Treating IDUs has also been shown to be a cost effective way of controlling the epidemic among non-IDUs (Long et al., 2006); we show that transmission among IDUs is strongly linked to prevalence in the general population. Controlling parenteral transmission in St. Petersburg has proven challenging, and is constrained by a number of factors: opiate substitution therapy is unavailable, antiretroviral therapy for IDUs is rare and needle exchange has proven difficult to carry out in that city and is only now gaining acceptance among government officials. Further steps could be taken to prevent all transmission emanating from IDUs but given the scarcity of antiretroviral medications in Russia, HIV-infected IDUs are seen as a low priority population. Wider prescription to infected IDUs would likely curtail transmission both between IDUs and sexual transmission to non-IDU partners.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.drugalcdep.2013.04.028>.

Fig. 1. Observed HIV prevalence data: (Black) for adults aged 15–49 in Russia, from data on the number of registered infections (World Health Organization, Global Health Observatory Data Repository) and (grey) for IDUs in St. Petersburg, estimates from (Ostrovskiy, 1999; Abdala et al., 2003; Shaboltas et al., 2006; Niccolai et al., 2011; Lyubimova et al., 2011). 95% confidence intervals, where known, are plotted.

Fig. 2.

The prevalence in the IDU population in the model. We include the observed prevalence of HIV in IDUs in St. Petersburg with 95% confidence intervals (where known, detailed in Fig. 1).

Fig. 3.

The HIV prevalence in different risk groups split by type of transmission and the fit and prediction for the general population prevalence in St. Petersburg. (A) HIV prevalence in different risk groups. PIDUs maintain the highest sexually transmitted HIV prevalence. The IDU epidemic is maintained mainly by parenteral transmission. (B) The fit and prediction of the general population prevalence (scaled to the correct population proportions). The estimated population prevalences are shown with 95% confidence intervals (where known) (World Health Organization, Global Health Observatory Data Repository).

Fig. 4.

Model results when removing all parenteral transmission from 2012 onwards. (A) The HIV prevalence in different risk groups split by type of transmission. (B) The general population prevalence scaled to the correct population proportions. The prevalence surveillance data are shown with 95% confidence intervals (where known) (World Health Organization, Global Health Observatory Data Repository).