

Modelling emerging HIV epidemics: the role of injecting drug use and sexual transmission in the Russian Federation, China and India

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Received 16 August 2002; received in revised form 30 November 2002; accepted 2 December 2002

Abstract

Emerging epidemics of HIV in Russia, India and China will largely determine the future course of the HIV pandemic. Injecting drug use has been a major source of new infections in these countries. The evolving role of injecting drug use and sexual transmission in driving these emerging epidemics is investigated using a mathematical model. HIV prevalence projections based on behavioural data for urban Russia result in a wide range of possible outcomes, reflecting uncertainty in estimates of adult sexual behaviour. Surveys of adult sexual behaviour in all the three countries are limited, and represent a research priority if the futures of these emerging epidemics are to be better understood. Analysis of behavioural correlates with adult HIV prevalence reveal the central role of unsafe sex in driving HIV prevalence, even among injecting drug users. However, needle sharing can also play a very significant role, particularly when the potential for heterosexual transmission is limited. These emerging epidemics are more likely to cross higher prevalence thresholds when there is extensive sexual mixing between sex workers and the general population, and to a certain extent between injecting drug users and non-users. Both types of sexual mixing have been documented in Russia, India and China. © 2003 Elsevier Science B.V. All rights reserved.

Keywords: HIV; AIDS; Injecting drug use; Sex work; Mathematical model; Russia; India; China

Introduction

The future course of the HIV pandemic will be largely determined by the emerging epidemics in some of the most populous countries of the world, particularly Russia, China and India, where HIV transmission has recently been occurring at an increasing pace (UNAIDS, 2002). The epidemics in these countries have diverse initial foci and rates of growth, reflecting large populations, geographic dispersion and migration, cultural and economic differences. However, each of these countries have now reported HIV infections in nearly all administrative regions, provinces or states, with an estimated 700 000 people living with HIV/AIDS in Russia, 850 000 in China and 3.97 million in India at the end of 2001

(National AIDS Control Organisation, India 2002; UNAIDS, 2002).

A series of epidemics among vulnerable populations of injecting drug users (IDUs) in Russia and other countries of Eastern Europe and Central Asia has led to this region reporting faster growth in incidence of HIV infections than anywhere else in the world (UNAIDS, 2002). In China, injecting drug users currently account for 60–70% of reported infections, although the importance of heterosexual transmission has steadily increased to 7% (Zhang, Li, Li & Beck, 1999). In India the majority (85%) of new infections are due to heterosexual transmission, particularly among sex workers (SWs), their clients and the sexual contacts of their clients (Gangakhedkar et al., 1997; George et al., 1997; Mehendale et al., 1996; Panda et al., 2000). However, in north-east India and major cities such as Delhi, Chennai and Mumbai injecting drug use is a major source of new

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infections (Eicher, Crofts, Benjamin, Deutschmann & Rodger, 2000; Kumar, Mudaliar & Daniels, 1999; Kumar, Mudaliar, Thyagarajan, Kumar, Selvanayagam & Daniels, 2000; Dorabjee & Samson, 2000; National AIDS Control Organisation, India, 2002).

Other countries in South and South-East Asia have significant HIV epidemics associated with both sex work and injecting drug use (Crofts, Reid & Deany, 1998). The latter is of particular importance in the 'golden triangle' of Myanmar, PDR Lao and northern Thailand, where a quarter of the world's opium is produced (ODCCP, 2001), and along drug trafficking and distribution routes within and out of the region (Beyrer, Razak, Lisam, Chen, Lui & Yu, 2000).

The emerging HIV epidemics in these countries have, in many cases, been concurrent with observed increases in risk behaviours. In China and Russia reported rates of extra-marital sex have increased as age at first sex has declined (Chervyakov & Kon, 2000; Liu et al., 1998; Zhang et al., 1999). These increases in sexual risk behaviour, together with declines in quality and access to health care, have led to dramatic epidemics of sexually transmitted infections (STIs) in both these countries (Borisenko, Tichonova & Renton, 1999; Chen, Gong, Liang & Zhang, 2000; Tichonova, Borisenko, Ward, Gromyko & Renton, 1997). There has also been a dramatic growth in the extent of drug injecting in Russia, with recent transitions towards drug injecting coinciding with trends towards a decreasing age at first injection (Rhodes et al., 1999). This trend towards increased injection drug use is also seen in India, China and other Asian countries (ODCCP, 2001; Crofts et al., 1998; Reid & Crofts, 2000).

The potential for future spread of HIV in countries with emerging HIV epidemics remains unclear because future trends in risk behaviour are unknown, because of the lack of population-based quantitative surveys of sexual behaviour, and because of limitation of our ability to model the transmission dynamics of a disease that depends on highly stigmatised, private and complex behaviours. Extrapolation of trends using HIV prevalence data or case reports can be dangerous due to uncertainty in estimates of the size and turnover of high risk groups such as SWs and IDUs, and rates of secondary infection in the lower risk population. Despite the absence of behavioural data and uncertainty in estimates of the size of high risk groups, the demands of policy makers and the media often lead to speculative claims about the future scale of emerging HIV epidemics and their economic impact (National Intelligence Council, 2002; Eberstadt, 2002).

In this paper we examine the sources of uncertainty in estimating the potential size of emerging HIV epidemics, where injecting drug use and sex work are important, using a mathematical model of HIV transmission. We use behavioural data collected in Russia, and epidemio-

logic data collected via a literature review, to examine uncertainty about predictions of epidemic size for an urban area of Russia. We subsequently use the transmission model to examine the relative roles of transmission by sex or injecting drug use during the course of emerging HIV epidemics, such as those seen throughout China, India and Russia. A sensitivity analysis is used to reveal the major determinants of HIV prevalence both among IDU and in the non-IDU population. We also examine the impact of different patterns of sexual mixing between groups with different levels of sexual activity, and between IDUs and non-IDUs, on the likelihood of more widespread heterosexual epidemics. Behavioural surveillance data on patterns of sexual mixing are described for China, India and Russia. The implications of these analyses for prevention policy in countries with emerging HIV epidemics are discussed.

Methods

A mathematical model

Although many models of HIV transmission either through sex or injecting drug use exist, only a few have focused on the interaction of these transmission routes (Arcà, Perucci & Spadea, 1992; Blower, Hartel, Dowlatbadi, Anderson & May, 1991; Seitz & Mueller, 1994; Tan & Tang, 1993; Van Druuten et al., 1990; Vickerman & Watts, 2002; Williams & Anderson, 1994). Here we employ a novel deterministic model of HIV transmission that allows for heterogeneity in sexual and drug-injecting behaviour, different patterns of mixing among IDUs and the sexually active population, and the presence of a bacterial STI that can enhance HIV transmission (see Appendix A for a full description). In addition, a fraction of the female IDU population may be involved in sex work, associated with higher rates of sexual partner change but also increased condom usage. The model is not age-stratified and does not allow for geographic dispersion and migration. However, the demographic parameters of the model are defined to reflect best estimates of the dynamics of populations of both IDUs and the adult population as a whole. Further, we do not include male to male transmission through sex between men due to a lack of behavioural data and estimates of the size of this risk group in the region. This does not imply that male to male sexual transmission is not important (Pisani & Winitthama, 2001).

Behavioural data can be used to classify sexual activity into five levels, and drug injecting into six levels (including non-use). We fix the initial distribution of the population among these activity levels according to the data, but allow mean rates of change of sexual partners and rates of needle-sharing to vary. Parameterised in

this way, the model has 34 parameters, 14 describing the biology and transmission of HIV and a bacterial STI, seven describing the demography of the population, eight describing the sexual behaviour of the population and five describing the drug-injecting behaviour of the population (Table 1).

Projections of HIV prevalence using the model typically replicate the commonly observed pattern of rapid HIV spread among high risk groups such as IDUs who share unclean needles or sex workers, followed by more gradual spread in the lower risk adult population.

Table 1
Model parameters used in the uncertainty analysis of future HIV prevalence in Russia

Number	Parameter	Symbol	Estimate	Lowest value ^a	Highest value ^a	Distribution ^a
<i>Epidemiological parameters</i>						
1	Transmission probabilities per sex act by stage of infection	β_1 (primary)	0.002	0.0001	0.05	Triangular
2		β_2 (incubation)	0.001	0.0001	0.05	Triangular
3		β_3 (pre-AIDS)	0.001	0.0001	0.05	Triangular
4		β_4 (AIDS)	0.002	0.0001	0.05	Triangular
5	Enhancement of HIV transmission by a bacterial STI	ω_{sus}	2.5	2	26	Uniform
6		ω_{inf}	1.5	1.25	13	Uniform
7		ω_{susinf}	3	2.5	30	Uniform
8	Probability per sex act of STI transmission male to female	θ_{mfr}	0.3	0.02	0.5	Uniform
9	Probability per sex act of STI transmission female to male	θ_{ftm}	0.15	0.01	0.25	Uniform
10	STI recovery rate (per year)	σ	4	1	24	Uniform
11	Probability of HIV transmission from a contaminated needle per needle shared	α_1 (primary)	0.014	0.001	0.1	Triangular
12		α_2 (Incubation)	0.007	0.001	0.1	Triangular
13		α_3 (pre-AIDS)	0.007	0.001	0.1	Triangular
14		α_4 (AIDS)	0.014	0.001	0.1	Triangular
<i>Demography and behaviour</i>						
15	Crude adult mortality rate per year	μ_1 (non-IDUs)	0.0035	0.0015	0.0043	Uniform
16		$\mu_{>1}$ (IDUs)	0.035	0.0015	0.13	Triangular
17	Rate of becoming 50 (per year)	μ_1^{50} (non-IDUs)	0.022	0.019	0.029	Uniform
18		$\mu_{>1}^{50}$ (IDUs)	0.01	0.005	0.015	Uniform
19	Rate of entry to adult population (per year)	π	0.021	0.015	0.029	Uniform
20	Fraction of entrants becoming IDUs	$\Phi_{\cdot,i>1}$	0.02	0.01 (10^{-6})	0.1	Uniform
21	Fraction of IDUs who are men	$\Phi_{0,i>1}/\Phi_{1,i>1}$	0.8	0.5	0.9	Uniform
<i>Injecting behaviours</i>						
22	Proportion of IDUs reporting sharing	$\Phi_{\cdot,i>2}/\Phi_{\cdot,i>1}$	0.36	0.15 (0.09)	0.7 (0.95)	Triangular
23	Mean rate of acquisition of new sharing partners by those reporting sharing (per year)	κ	22	5 (1)	50	Triangular
24	Needle shared per partnership	Y	2.1	1	40	Triangular
25	Proportion of needles effectively cleaned	ν	0.57	0.2 (0.0)	0.67 (1.0)	Triangular
26	Mixing between different IDU categories	e_3	0.5	0.2 (0.0)	0.8 (0.8)	Uniform
<i>Sexual behaviour</i>						
27	Mean rate of partner change for all adults (per year)	c	2.5	1.2	3.5	Uniform
28	Sexual mixing by sex activity	e_1	0.1	0.0 (0.0)	0.5 (0.8)	Uniform
29	Sexual mixing by IDU activity	e_2	0.5	0.1 (0.0)	0.7 (0.8)	Uniform
30	Fraction of female IDUs in commercial sex work	$\Phi_{1..i>1}/\Phi_{1..i>1}$	0.43	0.2 (0.0)	0.6 (0.8)	Triangular
31	Rate of partner change of female IDU sex workers (per year)	$c_{1..i>1}$	432	50	800	Triangular
32	Number of unprotected sex acts per partnership	$a_{1..i=1,2...}$ (regular)	100	50 (10)	200 (500)	Uniform
33		$a_{2..i=3,4...}$ (non-regular)	19	1	50	Uniform
34		$a_{3..i=n=5...}$ (commercial)	0.14	0.1 (0)	1.0	Uniform

^a In the second sensitivity analysis of the model all parameters were varied over the range shown with a uniform probability distribution. In some cases the range was increased to reflect potential behaviours, rather than values that reflected a specific range recorded for Russia—these values are shown in brackets where applicable.

Behavioural and demographic data

We draw on behavioural data from a survey of HIV prevalence and risk behaviour conducted among a community-recruited sample of 426 injecting drug users in Togliatti City, Samara Region, Russia (Rhodes et al., 2002). The characteristics of the sample were broadly similar to those reported among samples of IDUs in other Russian cities (Grund et al., 2001; Rhodes et al., 1999): two thirds were male; over half were under 25 years; a fifth had commenced injecting within the last 2 years; over half had experience of using home-produced injectable drugs (including 'hanka' and 'vint'), and the currently most commonly injected drug was heroin. Togliatti City has a population of approximately 1 million and has witnessed the rapid diffusion of HIV since 1999, with over 90% of reported cases associated with injecting drug use and with HIV prevalence among IDUs estimated at 56% in 2001 (Rhodes et al., 2002).

Additional data on sexual and injecting behaviours of IDUs in Russia, used to assess the wider applicability of estimates from Togliatti city, were taken from surveys of IDUs in St. Petersburg (Carney and Heimer, Unpubl. Data; Abdala, Gleghorn, Carney & Heimer, 2001), and from rapid assessment studies completed in 61 Russian cities (Frost, Burrows & Bijl, 2000).

Parameters describing sexual behaviour in the 'general' adult population are based on results of a random-digit telephone survey carried out in St. Petersburg (Amirkhanian, Kelly & Issayev, 2001a). Recognition of the limits to self-reporting of stigmatised behaviour led to a broad range being placed around the mean rate of sexual partner change in the adult population.

The prevalence of injecting drug use in Russia is estimated at 1–3% of the adult (15–49-year-old) population, with increases in registered drug users suggesting significant growth in recent years (Dehne, Pokrovskiy, Kobyshcha & Schwartländer, 2000; Ministry of the Interior, 2000). Increase in the prevalence of injecting drug use is countered by increased mortality associated with overdose and other drug-related deaths (Bargagli, Sperati, Davoli, Forastiere & Perucci, 2001; Frischer, Goldberg, Rahman & Berney, 1997; Goedert, Fung, Felton, Battjes & Engels, 2001). The demography of the adult population is based on demographic rates derived from population estimates produced by the United Nations Population Division (United Nations, 1999). A detailed description of the derivation of model parameters from available behavioural and demographic data is given in Appendix B.

Epidemiologic data

There is good evidence that the probability of HIV transmission through sexual contact is augmented by higher viral loads (Chakraborty et al., 2001; de Vincenzi

& The European Study Group on Heterosexual Transmission of HIV, 1994; Fideli et al., 2001; Gray et al., 2001; Quinn et al., 2000), and by the presence of genital ulcer disease either in the infectious or susceptible individual (Deschamps, Pape, Hafner & Johnson, 1996; Gray et al., 1999; Hayes, Schulz & Plummer, 1995; Rottingen, Cameron & Garnett, 2001). We provide estimates of the probability of sexual transmission of HIV per sex act and enhancement by a bacterial STI based on this data (Table 1). The probability of HIV transmission during a single injection with an infected syringe, and the impact that cleaning with water can have on transmission are based on experiments in vitro and estimates from mathematical models (Abdala et al., 2001; Hudgens et al., 2001; Kaplan & Heimer, 1992). In agreement with models of HIV dynamics that suggest variability in the infectivity of syringes from an HIV positive IDU (Ianelli, Milner, Pugliese & Gonzo, 1997), we allow the infectivity of an infected syringe to change in proportion to the viral load of the infectious individual (Table 1). Further details about the derivation of the model epidemiological parameters from available experimental studies, models and observational data are given in Appendix A.

Uncertainty analysis

Using the behavioural, demographic and epidemiological data described above, the model of HIV transmission can be used to produce projections of HIV prevalence among different groups, and other outputs of interest, such as the proportion of incident HIV infections due to particular transmission routes or patterns of AIDS mortality. Model outputs can be considered to have three sources of uncertainty: parameter, structural and stochastic. The first is due to uncertainty about the values of the parameters describing the behaviour, demography and epidemiology of the population of interest. The second, structural uncertainty, is due to alternative ways of constructing the model to represent knowledge and assumptions. The third, stochastic uncertainty, reflects the inherent probabilistic nature of human encounters and HIV transmission. In this paper we investigate the parameter uncertainty of the HIV transmission model, with the assumption that this model is the best representation of current knowledge of sexual and drug-related transmission of HIV. As our understanding of sexual behaviour, injecting behaviour and HIV transmission improves, so too can the model. The size of the urban population which is represented by the model is such that stochastic uncertainty is likely to be relatively unimportant for the given model structure (cf. Tan & Tang, 1993).

Parameter uncertainty for prevalence projections in urban Russia was investigated by sampling from the parameter probability distribution functions (p.d.f.'s)

summarised in [Table 1](#) to produce 5000 sets of parameters. These p.d.f.'s for urban Russia are triangular where a meaningful best estimate exists, and uniform where only a range without a best estimate can be given (see [Appendix B](#) for further details). The model was then run with each of these parameter sets (i.e. 5000 times) to produce the outcome measures of interest. The sampling scheme used was based on the Latin Hypercube Sampling (LHS) algorithm. If model outcome is a monotonic function of input, LHS can give unbiased estimates of the mean and cumulative distribution function of model outcome, and ensure the full range of each parameter is sampled, with fewer model runs than point random sampling direct from the parameter p.d.f.'s ([Iman, Helton & Campbell, 1981a](#)). By holding all but one parameter constant, and plotting this parameter against model outcome, monotonicity of the transmission model can be confirmed (data not shown).

Sensitivity analysis

To examine which parameters correlate with HIV prevalence, multivariate regression analyses were performed with prevalence at a given time as the dependent variable, and the parameters as the independent variables. Two sensitivity analyses were performed: the first based on parameters estimated from urban Russian data; the second using the full range of potential parameter values (these ranges are presented in brackets in [Table 1](#)) with equiprobable distributions over these ranges. The former provided outcomes we believe are realistic in the Russian context whereas the latter explores the full range of uncertainty irrespective of place and hence illustrates the influence of a particular parameter in a wider context. In this way the sensitivity analysis addresses the question of which parameters are the key determinants of future HIV prevalence for emerging epidemics where injecting drug use is common, in addition to determining which parameters require further measurement to improve current projections for urban Russia. The full range of potential parameter values were based either on the natural limits of a parameter (e.g. fraction of needles effectively cleaned 0–100%), or on extreme values either observed or considered plausible in other countries (e.g. 0.0001–10% adults inject drugs).

The relationship between projected prevalence and individual parameters is monotonic but non-linear. To deal with non-linearity, standard multivariate linear regression can be performed on the rank transform of the dependent and independent variables ([Blower & Dowlatabadi, 1994](#); [Iman & Conover, 1979](#); [Iman & Helton, 1988](#); [Iman, Helton & Campbell, 1981b](#)). The rank transform converts the sensitivity measure from one of linearity to one of monotonicity. The relationship

between an individual parameter and the chosen outcome measure, controlling for variation in all other parameters, can be obtained by including all parameters in the regression. The strength of relationship is given by the size of the standardised rank regression coefficient (SRRC). Since the parameters are sampled such that they are independent, the fraction of the variance in model outcome explained by a given parameter is given by the square of the SRRC ([Hofer, 1999](#)).

Threshold sensitivity analyses were also performed to examine the relationship between measures of unsafe sex, injecting drug use and HIV prevalence under different assumptions about sexual mixing. All other parameters were set according to the best estimates given in [Table 1](#).

Results

Uncertainty analysis

Uncertainty in behavioural, demographic and epidemiologic parameters causes a large amount of uncertainty in projected HIV prevalence for an emerging epidemic in an urban Russian setting ([Fig. 1](#)). Five years after the introduction of HIV to the IDU community, prevalence is unlikely to remain at less than 19% among IDUs ($P < 0.05$), but could remain at less than 3% in the adult population for up to 7 years (at the 5% significance level). However, a significant fraction of the prevalence projections for the adult population fall in the range 0–60% after 5 years, and a large generalised epidemic in urban Russian populations cannot be excluded. As additional behavioural and epidemiologic data becomes available, the possible range of future prevalence outcomes will narrow. However, there is no reason to expect a narrowing towards the median outcome in [Fig. 1](#). Indeed, if higher mean rates of sexual partner change are excluded by improved population-based behavioural surveys, future prevalence projections would narrow to a value far below the current median. It is also possible that changes towards safer sexual behaviour in the future in response to prevention programmes, or the visible impact of HIV, could reduce projected HIV prevalence.

Sensitivity analysis

The first sensitivity analysis based on parameter distributions estimated for urban Russia reveals that most of the uncertainty in prevalence projections relates to adult sexual behaviour ([Table 2](#)). The large number of model runs implies that most parameters show a significant correlation with model outcome, but the strength of association is variable. We, therefore, present only those parameters that contribute to 1% or

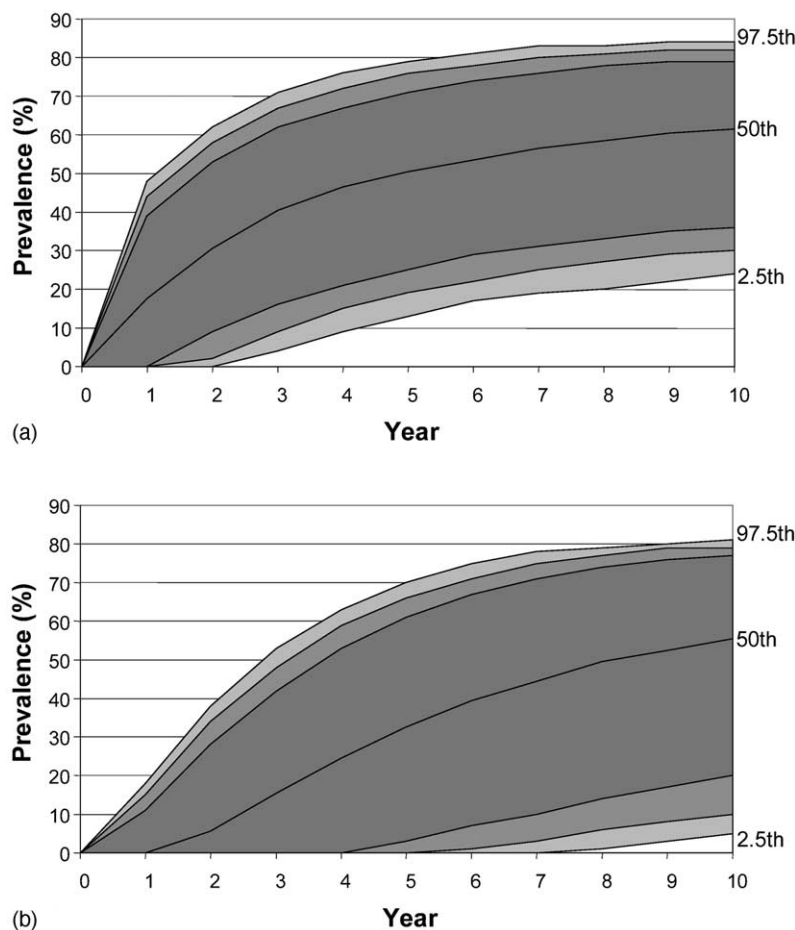


Fig. 1. Distributions of projected HIV prevalence outcomes for (a) IDUs and (b) all adults, plotted against time after the introduction of HIV to the IDU community in an urban Russian population. The 2.5th, 5th, 10th, 50th, 90th, 95th, and 97.5th fractiles of the cumulated distribution are shown. Prevalence outcomes that fall outside the 2.5th and 97.5th fractiles can be rejected at the 5% significance, given the model and current knowledge reflected by the behavioural, demographic and epidemiologic parameters. The 5th fractile of this distribution can be used in a one-tailed test to exclude certain low prevalence scenarios.

Table 2
Sensitivity analysis of projected Adult HIV prevalence 5 years after the introduction of HIV in urban Russia

Parameter	SRRC (95% CI)	Variance explained (%)
Mean rate of sexual partner change	0.600 (0.589, 0.611)	36.0
Transmission probability per sex act (incubation)	0.447 (0.437, 0.458)	20.0
STI recovery rate	-0.331 (-0.341, -0.320)	10.9
Number of unprotected sex acts in a non-regular partnership	0.289 (0.278, 0.299)	8.3
Transmission probability per sex act (primary)	0.163 (0.153, 0.174)	2.7
Number of unprotected sex acts in a commercial partnership	0.154 (0.144, 0.165)	2.4
Needles shared per partnership	0.100 (0.090, 0.111)	1.0

more of the variance in the model outcome ($SRRC^2 \geq 0.01$). Uncertainty in the mean rate of sexual partner change explains 36.0% of the variance in projected HIV prevalence 5 years after the introduction of HIV (of a total 85.5% variance explained by the regression model). Uncertainty in transmission probabilities per sex act explains 22.7% and frequency of unprotected sex an additional 10.7% of the variance. The behaviour of IDUs described by the number of needles shared per partnership also explains a small fraction (1.0%) of the uncertainty in the projected adult prevalence.

The second sensitivity analysis determines the key parameters driving any emerging HIV epidemic where injecting drug use occurs (Table 3). Results from this analysis are, therefore, of relevance to the emerging epidemics in China and north east and urban India, as well as Russia. This second sensitivity analysis again reveals the primacy of measures of sexual behaviour in the adult population, with the mean rate of sexual partner change explaining 40.9% of the variance in adult HIV prevalence 5 years after the introduction of HIV (of

Table 3
Sensitivity analysis of determinants of epidemic size

Parameter	SRRC (95% CI)	Variance explained (%)
Mean rate of sexual partner change	0.640 (0.627, 0.652)	40.9
Transmission probability per sex act (incubation)	0.320 (0.307, 0.332)	10.2
Number of unprotected sex acts in a non-regular partnership	0.289 (0.276, 0.301)	8.3
STI recovery rate	-0.260 (-0.272, -0.248)	6.7
Sexual mixing by sexual activity	-0.198 (-0.211, -0.186)	3.9
Number of unprotected sex acts in a commercial partnership	0.159 (0.147, 0.172)	2.5
Transmission probability per sex act (primary)	0.148 (0.136, 0.160)	2.2
Number of unprotected sex acts in a regular partnership	0.130 (0.118, 0.142)	1.7
Mean rate of acquisition of new sharing partners by those reporting needle sharing per year	0.089 (0.077, 0.102)	0.8

a total 81.4% variance explained by the regression model). They also reveal the importance of STI recovery/treatment in reducing HIV prevalence (variance explained = 6.7%). Sexual mixing between different sexual activity (risk) groups is also shown to play a role in determining adult HIV prevalence (variance explained = 3.9%). The negative SRRC indicates that as mixing becomes more assortative, growth in prevalence is restricted.

The fraction of IDUs who share needles can influence prevalence in the adult population (SRRC = 0.089; Table 3). This parameter also shows significant correlation ($P=0.008$) with prevalence among non-IDUs, indicating that risk behaviour and consequent HIV transmission among IDUs can promote HIV spread among non-IDUs. However, the strength of this correlation is weak (the fraction of IDUs who share needles explains 0.03% of the variance in non-IDU prevalence, and the mean rate of acquisition of new sharing partners 0.8% of the variance).

A clearer picture of the key determinants of HIV transmission is obtained if the SRRC in the second sensitivity analysis are calculated for prevalence outcomes through time (Fig. 2). In the first few years of the HIV epidemic, HIV prevalence in the adult population is determined by both injecting drug use and sexual risk behaviours (Fig. 2a). As the epidemic progresses sexual behaviour becomes of increasing importance, while the importance of injecting drug use declines. The importance of the rate of recovery from a treatable bacterial

STI also declines (although the decline is less substantial). This is because in the early stages of the epidemic, the STI and HIV are both concentrated in high risk groups, so the impact of a given STI prevalence on HIV transmission is larger. Among IDUs (Fig. 2b), injection-related risk behaviour remains a key determinant of HIV prevalence through the course of the epidemic, showing just a small decline. The importance of sexual risk behaviour (reflected by the mean rate of partner change) is initially small, but increases dramatically as the epidemic progresses. This reflects the increasing importance of sexual transmission, both among IDUs and between the IDU population and their non-IDU sex partners.

The relative role of sexual and injection-related transmission of HIV can be further elucidated by examining the incidence of HIV attributable to these different modes of transmission. Here we define the fraction of HIV infections attributable to a particular behaviour as the proportion of cases of infection occurring over the year which were acquired by a particular transmission route. For an urban Russian population where HIV prevalence remains at less than 1%, the number of new cases due to sexual transmission becomes greater than those due to needle-sharing after 4 years (Fig. 3a). Among IDUs, sexual transmission becomes of increasing importance as the epidemic progresses, while new infections due to needle sharing decline (Fig. 3b). This is the case, even for populations where rates of transition to injecting drug use are very high (Fig. 3c).

Threshold analysis reveals the role of sexual behaviour (c) and injecting behaviour (κ) in generating HIV epidemics of different sizes. Combinations of these parameters that result in greater than 0.1 and 5% adult HIV prevalence 10 years after the introduction of HIV are shown in Fig. 4. Increased sexual partner change is most likely to result in the 5% prevalence threshold being crossed (reflected in the independence of this threshold from changes in rates of needle sharing). Increased needle sharing will only cause this threshold to be crossed if sexual behaviour is in a very limited range. However, needle sharing can easily drive HIV prevalence over the 0.1% threshold. This threshold is curved, reflecting the influence of both needle-sharing and sexual partner change. If sexual mixing between groups with different levels of sexual activity increases, both thresholds shift to the left (Fig. 4a). Therefore, in populations with greater sexual mixing between individuals with different rates of acquiring new sex partners, HIV is more likely to spread widely. This is in agreement with the sensitivity analysis based on rank regression in Table 3.

Increased sexual mixing between IDUs and non-IDUs also makes a widespread epidemic more probable by shifting the prevalence thresholds to the left (Fig. 4b).

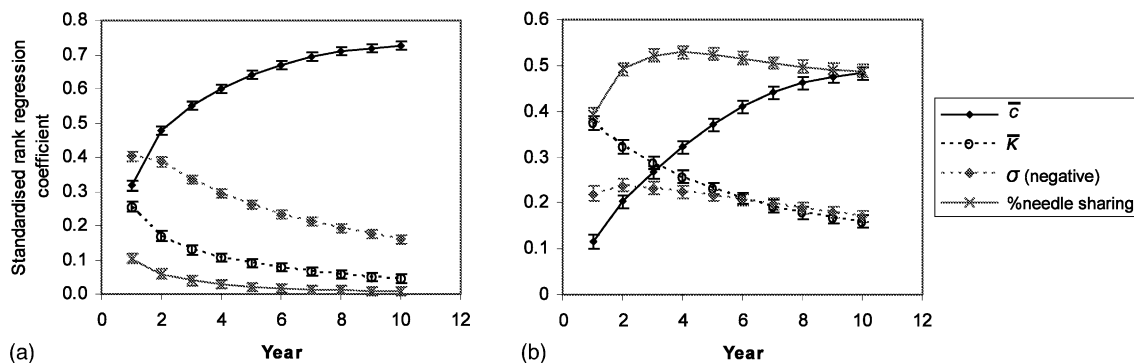


Fig. 2. The fraction of variation in HIV prevalence explained by each parameter as a function of age of epidemic based on a sensitivity analysis of the key determinants of HIV prevalence in an emerging epidemic where there is an IDU population. SRRC are calculated for different behavioural parameters with HIV prevalence in the (a) adult (including IDUs), and (b) IDU population up to 10 years after the initiation of the epidemic. The parameters are the mean rate of sexual partner change (\bar{c}), the mean rate of acquisition of new sharing partners by those reporting needle sharing (κ), the rate of STI recovery/treatment (σ) and the fraction of IDUs reporting needle sharing. The error bars show 95% confidence intervals. For ease of interpretation the negative SRRC for σ are plotted on the positive y -axis.

The shift is smaller than that caused by increased sexual mixing by sexual activity, and is more significant for epidemics driven mainly by injecting drug use (large κ). Curiously, when the potential for needle-borne and sexual transmission of HIV are both small, restricted sexual mixing between IDUs and non-IDUs results in a higher prevalence of HIV. However, if the epidemic is driven mostly by injecting drug use or mostly by sexual transmission, restricted mixing between IDUs and non-IDUs limits the size of the epidemic. Thus the 0.1% prevalence thresholds for random and assortative (restricted) sexual mixing cross in Fig. 4b. A similar pattern is seen for sexual mixing by sexual activity, but only when the mean rate of sexual partner change is very small (≤ 0.2 ; data not shown). This is in agreement with models of the transmission of STIs that suggest restricted sexual mixing can help sustain epidemics where the reproductive potential of the STI is small (Garnett & Anderson, 1993a).

Discussion

HIV transmission through sex or injecting drug use

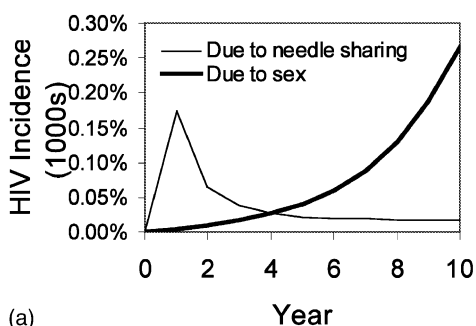
The future of emerging HIV epidemics in urban Russia is uncertain, mainly due to uncertainty about adult sexual behaviour. The upper bound on the prevalence projections (95th or 97.5th centile) after 10 years is extremely high, and reflects uncertainty about the upper limit of rates mean rates of acquisition of new sexual partners in the adult population. Whilst behavioural data is limited and unable to exclude such extreme scenarios, experience in other countries with generalised epidemics make such a scenario very unlikely. This highlights the importance of always interpreting model projections in the light of data from

similar situations, which cannot always be parameterised and included in a model.

Despite the uncertainty in predicting the future epidemic size for an urban Russian population, it is clear that sexual transmission of HIV becomes of increasing importance as epidemics among IDUs peak (Fig. 2). In Russia this has been reflected by an increase in the number of HIV case reports among individuals without identified injecting drug use (Ministry of Health, 2001). Even among IDUs, the model suggests sexual transmission rapidly becomes a key source of new infections. This is the case even if the rate of uptake of injecting drug use is very high (Fig. 3c), and is in agreement with cohort studies in the US that consistently find an association between sexual risk behaviour, including sex work, and seroconversion among IDUs (Kral, Bluthenthal, Lorvick, Gee, Bacchetti & Edlin, 2001; Strathdee et al., 2001). The increasing importance of sexual transmission among IDUs is mainly explained by the rapid saturation of HIV infection among individuals with risky injection practices, and subsequently more gradual spread of HIV through sexual transmission to IDUs who share needles less frequently. Sexual transmission tends to be slower due to lower transmission probabilities and a lower frequency of sex acts compared with needle sharing events. The results argue for a central role of safe sex messages and condom promotion in harm reduction programmes targeting drug users, as well as in the wider population. Although syringe and needle exchange are essential to reduce the primary role of injection risks, implemented without a safe sex component, they become increasingly less effective as an epidemic progresses.

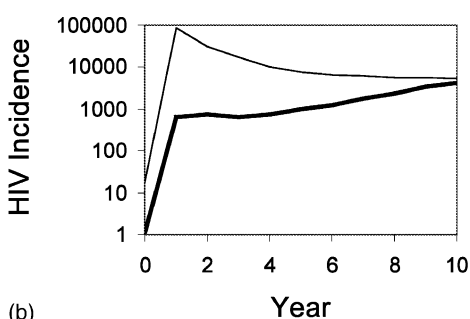
IDUs are especially vulnerable to HIV infection, and there is a need for effective harm reduction programmes. Furthermore, IDUs may have a role in promoting heterosexual HIV epidemics, though the impact of the unsafe injection practices of IDUs on HIV prevalence

All adults (prevalence <1%)



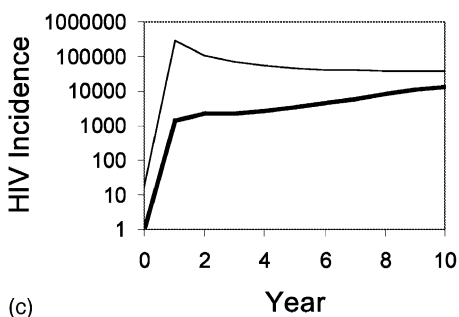
(a)

IDUs (constant number)



(b)

IDUs (high turnover)



(c)

Fig. 3. Incidence of HIV due to needle-sharing or sexual transmission over a 10-year period after the initiation of HIV in an (a) urban Russian adult population where prevalence remains less than 1%, (b) IDU population of constant size (~2 million), and (c) IDU population of initially 2 million with a high rate of uptake of injecting drug use. Note (b) and (c) plot absolute numbers of HIV infections on a logarithmic scale.

among non-IDUs is small in the model analyses presented here (Table 3). The limited impact reflects the predominant role of rates of unprotected sex with new sex partners in driving more widespread epidemics. However, if an epidemic remains at relatively low prevalence in the general population, the impact of the injecting behaviour of IDUs becomes relatively more important. For example, increased mixing between IDUs and non-IDUs generates a bigger increase in prevalence when sexual risk behaviour (c) is low, and

injection risks (κ) high (Fig. 4). In addition, in populations where the potential for heterosexual transmission is limited, the spread of HIV among IDUs due to needle sharing and sexual transmission, can trigger a heterosexual epidemic among non-IDUs, which otherwise would not have occurred or would have occurred much later. In these populations injecting drug use rapidly creates a large number of HIV infections, and subsequent sexual transmission is given a kick-start.

The model analyses also suggest the significant impact that improved diagnosis and treatment of other STIs can have on future HIV prevalence (Table 3). Although more significant early in the epidemic, due to co-occurrence of HIV in the same individuals and STIs, STI recovery rates remain a strong determinant of HIV prevalence throughout an epidemic, even after accounting for uncertainty in the degree of HIV transmission enhancement by the STI (Fig. 2; the presence of an STI is assumed to increase susceptibility by at least 100%, and infectiousness by at least 25% per sex act).

Forecasting epidemics

Surveys of sexual behaviour in India and China are as limited as those in Russia (Hawkes & Santhya, 2002; Jejeebhoy, 1998; Liu et al., 1998; Xenos et al., 2001), although a nationally representative survey of sexual behaviour of more than 3000 people in China has recently been completed (Yoosik Youm and William Parish, personal communication). Projections of HIV prevalence for populations from these countries where injecting drug use occurs will also be uncertain. However, even an adult prevalence of 2–3%, as seen in Thailand and Cambodia, would be equivalent to ~13 million people infected with HIV in India and ~18 million in China. This is more than half of the current global total, and strongly suggests an urgent preventive intervention. Recent conservative estimates suggest that in the absence of a global response to HIV/AIDS, South and South-East Asia will contribute 41% of all new infections over the period 2002–2010 (Stover et al., 2002).

Although adult sexual behaviour is the key determinant of widespread HIV transmission in countries with emerging HIV epidemics, representative surveys of sexual behaviour are extremely limited in number (Chervyakov & Kon, 2000; Jejeebhoy, 1998; Xenos et al., 2001). There are also significant problems with survey quality, and bias in respondents self-reporting of sexual behaviour. These problems are exacerbated in comparisons between countries and regions due to a lack of equivalence of behavioural indicators and differing bias in response to questions about stigmatised behaviour in different cultures. If future HIV prevalence and STI trends in countries with emerging epidemics are to be forecast more accurately, nationally representative

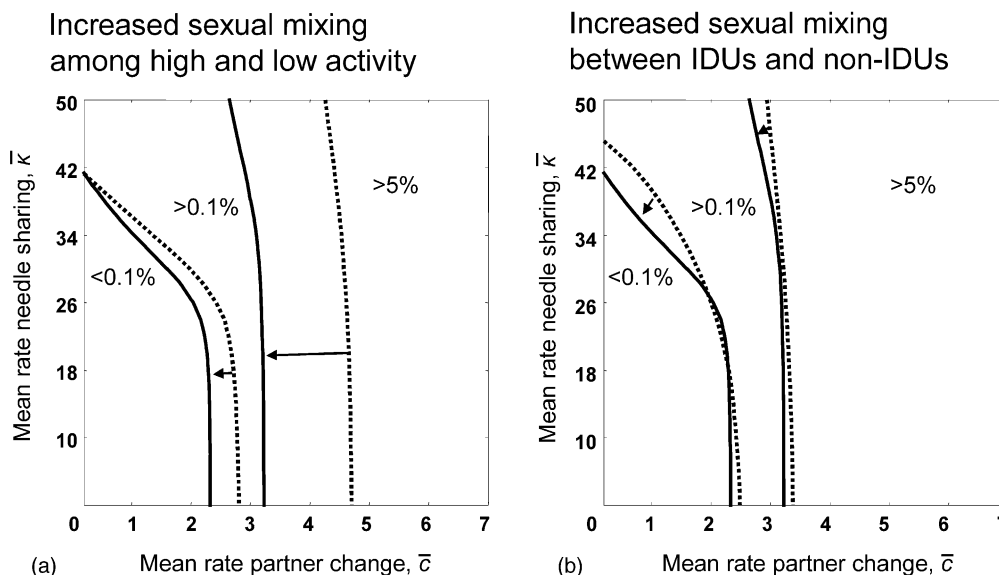


Fig. 4. Contour plot of HIV prevalence against the mean rate of needle sharing and mean rate of sexual partner change, showing 0.1 and 5% thresholds for adult HIV prevalence 10 years after the introduction of HIV. Increased sexual mixing between (a) individuals with different levels of sexual activity, and (b) IDUs and non-IDUs, can shift the thresholds to the left, making a widespread epidemic more likely. The solid lines correspond to sexual mixing parameters $\varepsilon_1 = \varepsilon_2 = 0.1$ (close to random), the dashed lines correspond to a) $\varepsilon_1 = \varepsilon_2 = 0.1$ (close to random), the dotted lines correspond to a) $\varepsilon_1 = 0.9$ (assortative), $\varepsilon_2 = 0.1$, and b) $\varepsilon_1 = 0.1, \varepsilon_2 = 0.9$.

and standardised surveys are required, that focus not only on high risk groups such as IDUs or sex workers.

Sexual mixing

The rate of acquiring new sex partners must cross a certain threshold for adult HIV prevalence to exceed 5% (Fig. 4). The rate required to cross this threshold is somewhat lower if injecting drug use and needle sharing occur. This threshold becomes substantially easier to cross when sexual mixing between high and low risk individuals is extensive, and to a certain extent where there is frequent sexual mixing between IDUs and non-IDUs. Greater sexual mixing implies higher adult prevalence for most scenarios. For some countries current estimates of HIV prevalence are based on estimates of the size of ‘risk groups’, such as MSM and IDUs, with a fixed multiplier used to account for transmission from these groups. The pattern of mixing will determine the appropriate ‘multiplier’ to apply to these high-risk populations in analyses that attempt to predict epidemic size from the size and saturation level of high-risk groups.

Sexual mixing is notoriously difficult to measure. However, surveys in Russia, India and China suggest significant sexual mixing both between high and low sexually active groups such as sex workers and their clients, and between IDUs and non-IDUs. In St. Petersburg, Russia, 7% of the adult population reported having had sex with a prostitute, or had sex for money, and half had done this more than once (Amirkhanian et al., 2001a). In the same city, 28% of female IDUs

reported receiving money or drugs for sex in the last month, indicating the significant overlap between sex work and drug use, and the link between IDUs and the adult population (John Carney, personal communication). In another Russian city, Togliatti, 43% of female IDUs reported current sex work, with an average of 36 new clients in the preceding 4 weeks (Lowndes, Renton, Alary, Rhodes, Pokrovsky & Stimson, 2002). Male IDUs rarely report selling sex for money or drugs (3% and 1% in St. Petersburg and Togliatti, respectively), although the impact of reporting bias is unclear. The regular sex partners of IDUs are also frequently non-IDUs. Half the IDUs in St. Petersburg and a third of those in Togliatti report that their regular sex partner does not inject drugs. This may be an important route of HIV transmission, since condom use is very low within these regular partnerships when compared with commercial sex. For example, in Togliatti 17% of male IDUs report condom use with their regular partner but 75% with sex workers.

In India the number of female sex workers is estimated to be about 2 million (range 1.0–16.2 million; Venkataramana & Sarada, 2001). In surveys of variable quality 19–78% of sexually active adolescents report ever visiting a sex worker (Jejeebhoy, 1998). Face-to-face interviews carried out in household surveys of Chennai and five districts of Uttar Pradesh found 0.5–7.0% of men reported ever paying for sex (Singh, Bloom & Tsui, 1998; Go et al., 2002). In lower-class urban Delhi, 1.1% of men report visiting a sex worker in the last year (Kumar, Mehra, Badhan & Gulati, 1997). Such survey methods may result in under-reporting of stig-

matised behaviours. Surveys of the clients of sex workers in several Indian states found that 11–48% reported non-commercial sex with a non-regular partner in the preceding 12 months (Pisani & Winitthama, 2001). Many of these men are also married, and transmission of HIV from HIV positive men to their wives is well-documented (Gangakhedkar et al., 1997; Newmann et al., 2000).

In the north-east of India, where injecting drug use is common, HIV transmission from male IDUs to their wives has been documented (Panda et al., 2000). In this region the link between injecting drug use and sex work is similar to that seen in Russia. In Manipur, two thirds of female IDUs reported sex in exchange for money or drugs (Panda et al., 2001), and in Calcutta, 71% of male IDUs reported sex with a sex worker (Panda, Chatterjee, Bhattacharjee, Saha & Bhattacharya, 1998).

In China, information on the extent and nature of sex work is limited, although in 1996 a public security estimate for the number of male and female sex workers was 3–4 million (Chinese Ministry of Health and the UN Theme Group on HIV/AIDS in China, 1997). The extent of mixing of sex workers with the general population is unclear and self-reported visits to sex workers are likely to be biased downwards. A figure of 2% of the population of three southern cities reporting ever visiting a sex worker is given by Pan (1995; cited in Zhang et al., 1999). Two thirds of reported HIV infections in China are among IDUs, and as in India, the transmission of HIV from male IDUs to their wives has been clearly documented (Zheng et al., 1994). The links between injecting drug use and sex work in China are less well-documented, although unofficial estimate in Guangxi province suggest 80% of female IDUs are involved in sex work (Reid & Costigan, 2002). The role of female IDUs in sex work is supported by cohort studies in Yunnan province, showing significantly higher prevalence of HIV among female compared with male IDUs (Zhang et al., 2002).

Future needs

The behaviours driving the emerging epidemics in Russia, India and China are poorly quantified, and comparability is hampered by the use of different indicators and survey methods. Standardisation would be a major advance, and the formation of a global database of relevant behavioural studies could aid policy formulation and understanding of HIV and STI dynamics. Despite the deficiencies in available behavioural data, the links between injecting drug use and sex work in these countries is clear. Substantial epidemics among these high risk groups are inevitable. The potential for more widespread transmission is unclear. This uncertainty indicates the need for extensive pre-emptive HIV

prevention programmes to reduce the risk of a global epidemic on a scale never seen before.

Acknowledgements

The authors would like to acknowledge the support of UNAIDS, the UK Department for International Development, the Royal Society and the Open Society Institute.

Appendix A: Mathematical model description

The number of individuals in a given category is denoted H_{kli}^s , where s denotes stage of HIV infection; b , bacterial STI status (0 = susceptible, 1 = infected) and k , gender. We use k' to denote the opposite gender. The subscript l denotes sexual activity class (1, 2, ... n), and i , IDU activity class (1, 2, ... r , class 1 implies no injecting drug use). Where an index is replaced by the symbol \bullet it indicates summation over all categories. For example $H_{k\bullet}^{01}$ refers to all HIV negative individuals infected with a bacterial STI irrespective of gender, sexual activity or drug injecting behavioural category.

The model is defined by the following set of ordinary differential equations:

$$H_{kli}^{00} = \pi \Phi_{kli} N + \sigma_{li} H_{kli}^{01} - \lambda_{kli}^{00} H_{kli}^{00} - \eta_{kli} H_{kli}^{00} - \varsigma_{ki} H_{kli}^{00} - (\mu_i + \mu_i^{50}) H_{kli}^{00} \quad (1)$$

$$H_{kli}^{01} = \eta_{kli} H_{kli}^{00} - \varsigma_{ki} H_{kli}^{01} - \lambda_{kli}^{01} H_{kli}^{01} - \sigma_{li} H_{kli}^{01} - (\mu_i + \mu_i^{50}) H_{kli}^{01} \quad (2)$$

$$H_{kli}^{10} = (\lambda_{kli}^{00} + \varsigma_{ki}) H_{kli}^{00} + \sigma_{li} H_{kli}^{11} - \eta_{kli} H_{kli}^{10} - \gamma^1 H_{kli}^{10} - (\mu_l + \mu_l^{50}) H_{kli}^{10} \quad (3)$$

$$H_{kli}^{11} = (\lambda_{kli}^{01} + \varsigma_{ki}) H_{kli}^{01} + \eta_{kli} H_{kli}^{10} - \sigma_{li} H_{kli}^{11} - \gamma^1 H_{kli}^{11} - (\mu_i + \mu_i^{50}) H_{kli}^{11} \quad (4)$$

and for $s > 1$:

$$H_{kli}^{s0} = \gamma^{s-1} H_{kli}^{s-10} + \sigma_{li} H_{kli}^{s1} - \eta_{kli} H_{kli}^{s0} - \gamma^s H_{kli}^{s0} - (\mu_i + \mu_i^{50}) H_{kli}^{s0} \quad (5)$$

$$H_{kli}^{s1} = \gamma^{s-1} H_{kli}^{s-11} + \eta_{kli} H_{kli}^{s0} - \sigma_{li} H_{kli}^{s1} - \gamma^s H_{kli}^{s1} - (\mu_i + \mu_i^{50}) H_{kli}^{s1} \quad (6)$$

where π , rate of entering the modelled population (determined by rate individuals become 15 years old) and Φ_{kli} is the proportion of people of gender k being recruited to sexual activity class l and IDU behavioural class i , μ_l is the crude mortality rate for drug using class l , μ_i^{50} is the rate of becoming 50 for drug using class i , σ_{li} is the STI treatment rate for sexual activity class l and drug using class i , and γ^s , the rate of progression from stage s to stage $s+1$.

The forces of HIV infection via sexual contact for different STI status are given by:

$$\lambda_{kli}^{00} = c_{kli} \sum_{m=1}^n \sum_{j=1}^r \sum_{s=1}^4 \rho_{klmij} \left((1 - (1 - \beta_{k's})^{a_{k'lm}}) \times \frac{H_{k'mj}^{s0}}{H_{k'mj}^{\dots}} + (1 - (1 - \omega_{\text{inf}} \beta_{k's})^{a_{k'lm}}) \frac{H_{k'mj}^{s1}}{H_{k'mj}^{\dots}} \right) \quad (7)$$

and

$$\lambda_{kli}^{01} = c_{kli} \sum_{m=1}^n \sum_{j=1}^r \sum_{s=1}^4 \rho_{klmij} \left((1 - (1 - \omega_{\text{sus}} \beta_{k's})^{a_{k'lm}}) \times \frac{H_{k'mj}^{s0}}{H_{k'mj}^{\dots}} + (1 - (1 - \omega_{\text{susinf}} \beta_{k's})^{a_{k'lm}}) \frac{H_{k'mj}^{s1}}{H_{k'mj}^{\dots}} \right) \quad (8)$$

where ρ_{klmij} denotes the probability that an individual of gender k , sexual activity class l , and drug using class i has sexual contact with an individual of the opposite gender in sexual activity class m , and drug using class j (the sexual mixing matrix), c_{kli} , the effective rate of acquisition of sexual partners per year by an individual of gender k in sexual activity class l and drug using class i (we assume $c_{kli} = c_{kl1}$ for $i > 1$), $\beta_{k's}$ is the per sex act transmission probability of HIV from an individual of HIV status s and gender k and $a_{k'lm}$ is the number of unprotected sex acts in a partnership between an individual of gender k and sexual activity class l and someone of the opposite gender in sexual activity class m . The enhancement of HIV transmission per sex act by an STI may be due to an increase in infectivity ω_{inf} , susceptibility ω_{sus} , or both ω_{susinf} .

The force of STI infection is given by:

$$\eta_{kli} = c_{kli} \sum_{m=1}^n \sum_{j=1}^r \rho_{klmij} (1 - (1 - \theta_{k'})^{a_{k'lm}}) \frac{H_{k'mj}^{*1}}{H_{k'mj}^{\dots}} \quad (9)$$

where $\theta_{k'}$, is the probability of transmission of a bacterial STI from an individual of gender k' per sex act.

The force of HIV infection via injecting drug use is given by:

$$\zeta_{ki} = \kappa_{ki} \sum_{j=1}^r \sum_{s=1}^4 \tau_{ij} \left((1 - (1 - \alpha)^{\nu(1-\nu)}) \frac{H_{i,j}^{\dots}}{H_{i,j}^{\dots}} \right) \quad (10)$$

where κ_{ki} the rate of acquisition of new needle-sharing partners by an individual of gender k and IDU behaviour class i ($\kappa_{ki} = 0$ for $i = 1$), τ_{ij} , the probability that an individual of drug using status i has a risky needle sharing partnership with another IDU of drug using status j (drug-use mixing matrix); α_s , the probability of HIV transmission by sharing a syringe with an individual in HIV stage s ; ν , the number of syringes received per drug injecting partnership, and ν , the proportion of shared needles that have been effectively cleaned.

Following the approach of Garnett and Anderson (1993b) the sexual mixing matrix can be defined as:

$$\rho_{klmij} = \left[\begin{array}{l} \varepsilon_1 \delta_{lm} + (1 - \varepsilon_1) \left(\frac{\sum_{u=1}^r c_{k'mu} H_{k'mu}^{\dots}}{\sum_{v=1}^n \sum_{u=1}^r c_{k'vu} H_{k'vu}^{\dots}} \right) \\ \varepsilon_2 \delta_{ij} + (1 - \varepsilon_2) \left(\frac{c_{k'mj} H_{k'mj}^{\dots}}{\sum_{u=1}^r c_{k'mu} H_{k'mu}^{\dots}} \right) \end{array} \right] \quad (11)$$

where ε_1 , is the degree of assortative sexual mixing within sexual activity class (0 = random, 1 = assortative), ε_2 , the degree of assortative sexual mixing within IDU activity class and δ_{lm} is the Dirac-delta function, which equals 1 when $l = m$, and 0 otherwise.

Rates of sexual partner change obey the rules of supply and demand, reflected in the constraint:

$$c_{kli} \rho_{klmij} H_{kli}^{\dots} = c_{k'mj} \rho_{k'mji} H_{k'mj}^{\dots} \quad (12)$$

Since AIDS results in differential mortality rates across sexual activity and drug using categories in a model of sexual HIV transmission it is necessary to continually balance the supply and demand of sexual partners across these categories. This is carried out using a partner balancing update rule.

If the discrepancy:

$$B_{lmij} = \frac{c_{k'mj} \rho_{k'mji} H_{k'mj}^{\dots}}{c_{kli} \rho_{klmij} H_{kli}^{\dots}} \quad (13)$$

then c is updated such that:

$$c_{k'mji}^* = c_{k'mj} B_{lmij}^{-(1-\nu)} \quad (14)$$

and the partner change rate in the reverse direction

$$c_{klmij}^* = c_{kli} B_{lmij}^{\nu} \quad (15)$$

where ν is the degree to which men or women alter their sexual behaviour (we assume $\nu = 0.5$; i.e. that they alter their behaviour equally).

A drug use mixing matrix can be defined in an analogous way:

$$\tau_{ij} = \varepsilon_3 \delta_{ij} + (1 - \varepsilon_3) \left(\frac{\sum_{u=1}^2 \kappa_{uj} H_{u,j}^{\dots}}{\sum_{v=1}^r \sum_{u=1}^2 \kappa_{uv} H_{u,v}^{\dots}} \right) \quad (16)$$

where ε_3 is the degree of assortative drug injecting within IDU activity class.

If the discrepancy:

$$D_{ij} = \frac{\tau_{ji} \sum_{u=1}^2 \kappa_{uj} H_u^{**}}{\tau_{ij} \sum_{u=1}^2 \kappa_{ui} H_u^{**}} \quad (17)$$

then κ is updated such that $\kappa_{k'ji}^* = \kappa_{k'j} D_{ij}^{-(1-\varpi)}$ and $\kappa_{kji}^* = \kappa_{kj} D_{ij}^{\varpi} = \kappa_{kj} D_{ij}^{-\varpi}$, where ϖ is the extent to which men or women change their drug use behaviour (we assume that $\varpi=0.5$; i.e. men and women alter their behaviour equally).

Appendix B: Derivation of model parameters for an urban Russian population

Epidemiological parameters

Stages of HIV infection and associated transmission parameters

We assume that HIV progression rates and disease stages are the same for IDUs and non-IDUs as shown for a cohort of IDUs in Amsterdam (Hendriks, Satten, van Ameijden, van Druuten, Coutinho & van Griensven, 1998). We assume four stages of infection: primary (3 months), incubation (8 years), pre-AIDS (9 months) and AIDS (1 year), associated with different mean plasma viral loads (500, 10, 50 and 100 thousand copies per ml, respectively) (Department of Health and Human Services (DHHS) and the Henry J. Kaiser Family Foundation, 2000; Mellors et al., 1997; Mellors, Rinaldo, Gupta, White, Todd & Kingsley, 1996). The probability of transmission of HIV per sex act has been estimated at between 0.0005 and 0.001 in US and European studies (Mastro & Kitayaporn, 1998; Royce, Sena, Cates & Cohen, 1997), 0.0011 in a study in sub-Saharan Africa (Gray et al., 2001) and up to 0.002 in Thai couples (Mastro, Satten, Nopkesorn, Sangkharomya & Logini, 1994). However, in studies in Thailand and Kenya the probability per sex act has been estimated at 0.056 and 0.1, respectively (Mastro & Kitayaporn, 1998; Mastro et al., 1994). This higher rate may reflect higher mean viral load, co-occurrence of other STIs or under-reporting of the number of sex acts. Correcting for the effect of viral load and genital ulcer disease in one study, together with cross-validation of reported numbers of sex acts gives an estimated transmission probability per sex act of 0.0012 from an individual with a viral load of 1700–12 499 copies per ml (Gray et al., 2001). The same study estimates the transmission probability per sex act as 0.0001 for viral loads of less than 1700 copies per ml. As viral load increases, so does the transmission probability (Chakraborty et al., 2001; de Vincenzi and The European Study Group on Heterosexual Transmission of

HIV, 1994; Fideli et al., 2001; Gray et al., 2001; Quinn et al., 2000). In line with these studies, we assume the transmission probability per sex act for incubation and AIDS stages is doubled. Evidence for a difference in the probability of male-to-female and female-to-male transmission is mixed, and we therefore assume equal rates (Fideli et al., 2001; Gray et al., 2001; Mastro & de Vincenzi 1996).

STIs and their impact on the sexual transmission of HIV

Both susceptibility to HIV and infectiousness can be enhanced by other STIs (Rottingen et al., 2001). It is difficult to measure the magnitude of these enhancement effects since STIs and HIV co-occur due to other behavioural or biological factors, such as a high level of sexual activity or lack of circumcision (Boily & Anderson, 1996; Korenromp, Vlas, Nagelkerke & Habbema, 2001). Recent estimates that attempt to account for these confounding factors, suggest per sex act HIV transmission probabilities should be multiplied three to 22 times if the susceptible female has genital ulcer disease (GUD) (Gray et al., 1999; Hayes et al., 1995; Korenromp et al., 2001). Estimates for enhanced male susceptibility are slightly higher (160 in one study (Hayes et al., 1995)), although these estimates are sensitive to assumptions about underlying transmission probabilities, and accurate reporting of numbers of sex acts. We, therefore, assume the magnitude of enhancement of susceptibility of men and women by a GUD is the same.

Only two studies have looked at the impact of STIs on HIV infectiousness (Deschamps et al., 1996; Gray et al., 1999). Both studies found the risk of seroconversion to be higher when the index case had GUD, but the relative risk was about half that seen when the susceptible individual alone had GUD. Only one study has looked at the combined effect of STIs on infectiousness and susceptibility, and this study suggests a less than additive effect, although confidence limits were large (Deschamps et al., 1996). Using this data best estimates and limits for the multiplier of per-sex-act HIV transmission probabilities in the presence of GUD were 4 (range 3–50) when the susceptible individual only has the STI, 2 (1.5–25), when the infectious individual has the STI, and 5 (4–60) when both are infected.

Since we are modelling a generic bacterial STI, that reflects general patterns seen for *Chlamydia*, syphilis or gonorrhoea we assume a transmission probability per sex act of 30% (range 2–50%) for male to female transmission and 15% (1–25%) for female to male transmission in line with available estimates (Garnett, 1997; Garnett, Mertz, Finelli, Levine & St Louis, 1999; Katz, 1992). The duration of infection is determined by treatment seeking behaviour and the natural history of the disease. Rates of treatment seeking in the Russian

Federation are currently unknown and undergoing significant changes due to changes in the delivery of health services. We currently assume a mean duration of infection of 3 months but explore a large range of estimates (0.5–12 months). The infected individual is assumed to be infectious at all times. Of those infected 50% are assumed to show symptoms of GUD, and hence enhancement of HIV transmission by the presence of an STI is assumed to be half that observed for the studies based on diagnosis of GUDs.

Probability of HIV transmission from a contaminated needle

The probability of transmission of HIV from a contaminated syringe during a single injection has been estimated at 0.0067–0.008 (Hudgens et al., 2001; Kaplan & Heimer, 1992). Although the probability of transmission from a contaminated syringe may depend on the viral load within the contaminating blood, no studies to date have determined transmission probabilities dependent upon viral load. Models suggest the infectivity of syringes from an HIV positive IDU must change over time to explain observed patterns of transmission (Ianneli et al., 1997). We, therefore, assume that the transmission probability from a contaminated syringe is 0.007, but that this doubles to 0.014 for primary infection and for AIDS cases (range 0.001–0.1 for all stages).

Demographic and behavioural parameters

Demography of IDUs

IDUs have a higher rate of mortality than non-IDUs even after accounting for AIDS-related deaths, due to overdose, other medical causes and 'external' causes such as suicide and homicide (Goedert et al., 2001). Increases in injecting drug use in Russia have been paralleled by increases in overdoses and other drug-related deaths (Ministry of the Interior, 2000). However, the excess rate of mortality among cohorts of IDUs in Russia has not been measured. Cohort studies from Europe and the USA estimate standardised mortality ratios for IDUs compared with non-IDUs of 4.3–22.0 (Bargagli et al., 2001; Frischer et al., 1997; Goedert et al., 2001). Differences in these ratios reflect not only differences in drug-injecting and other behaviour of the IDUs, but also differences in the age composition of the cohorts and the period of observation. For the Russian IDU population we assume a mortality rate ratio (mortality rate of IDUs/mortality rate of all adults) of 10 (range 1–30).

Using population figures from the United Nations (1999) the crude adult (15–49) mortality rate for Russia over the period 1950–1985 is estimated to remain roughly constant at 0.0035 (range 0.0015–0.0043). We,

therefore, estimate that the crude mortality rate of IDUs aged 15–49 years in Russia is 0.035 (range 0.0015–0.13). The rate of becoming 50 for the adult population over the period 1950–1985 is on average 0.022 (range 0.019–0.029), and we assume this rate applies for the period of interest. For IDUs this rate will be lower due to increased mortality at younger ages. Without an explicit age-structured model it is impossible to capture the change in the rate of becoming 50 for IDUs, and we therefore assume a mean rate of 0.01, but explore a range from 0.005 to 0.015.

The Russian population is expected to decline slightly from 148 million in 1990 to 137 million in 2010. We, therefore, assume the rate of entry to the modelled population (15–49 years) is 0.021 (range 0.015–0.029), which together with the adult mortality rate and rate of becoming 50 reproduces this decline. By specifying fairly broad ranges around these demographic parameters we are able to explore both expanding and declining IDU populations and the impact this has on the spread of HIV.

In Russia the number of people in treatment for drug use has increased from 155 971 in 1995 to 451 605 in 2000 (Ministry of the Interior, 2000). Of these about two thirds are thought to be injecting drug users (Dehne et al., 2000). The estimated total number of drug (other than alcohol and solvents) users in Russia at present varies from 600 000 to 3 million (Dehne et al., 2000; Ministry of the Interior, 2000). Assuming a total population size of approximately 80 million in the age range 15–49 years old (United Nations, 1999), this implies a prevalence of injecting drug use of 1–4%, although this will vary by locality. We explore a range of values for the fraction of youth who become injecting drug users at age 15 from 1 to 10% to reflect this uncertainty. The majority of IDUs in Russia are male (~80% (50–90%); Dehne et al., 2000).

Behavioural parameters

Drug injecting behaviour in the Russian Federation

We use a quantitative behavioural survey of community recruited injecting drug users from Togliatti, Samara oblast (Rhodes et al., 2002), to inform our model of injecting behaviours in the Russian Federation. Where additional information is available from other surveys we cross-validate our parameter estimates. Sharing needles in the 4 weeks preceding the survey was reported by 36% (95% CI: 31–40%) of IDUs. This is close to the figure of 40% recorded for IDUs attending a syringe exchange programme in St. Petersburg (Abdala et al., 2003), and consistent with a series of rapid assessments carried out in 61 Russian cities that found for the majority of cities 40–70% of IDUs reported sharing needles and syringes (Frost et al., 2000). The number of new IDUs with whom needles were shared

can be estimated from reports on the number of different people shared with in the 4 weeks preceding the survey (Appendix Table 1). For those sharing needles, this implies a mean rate of change of injecting partner of 22 per year (median = 1). We explore a range of values for this mean (5–50), whilst keeping the distribution of sharing frequency fixed.

For each sharing partnership, the mean number of needles shared is 2.1 (1–40). On average 85% of IDUs report consistently cleaning their syringes in the last 4 weeks, 84% using boiling water, 11% cold water and the rest a mixture of the two approaches. The tendency of IDUs to overestimate cleaning frequency and thoroughness is well documented (Gleghorn, Doherty, Vlahov, Celentano & Jones, 1994), and these figures should be viewed with some caution, particularly since HIV prevalence among IDUs in Togliatti has now reached 56% (Rhodes et al., 2002). A recent study found that cleaning a syringe after use for 5 s with cold water resulted in a loss of detectable HIV in 67% of syringes (compared with no loss in those untreated, Abdala et al., 2001). This effectiveness increased to 99.3% where undiluted bleach was used. Unfortunately no studies have looked at the use of boiling water, although effectiveness is likely to lie somewhere between these extremes. Given the problems with self-reported data on cleaning of syringes, and the unknown effect of using (self-reported) ‘boiling’ water, we use a wide range around the estimated fraction of needles cleaned (85% (30–100%)), but assume a fixed efficacy of 67%. In other words the proportion of needles effectively cleaned is assumed to be 57% (20–67%).

Of those IDUs who report sharing with more than three people in the last 4 weeks, 3% reported sharing with ‘infrequent’ drug users, whilst this increased to 13% for those who reported less frequent sharing. This suggests that sharing needles between different injecting frequency categories of IDU is mildly assortative ($\epsilon_3 = 0.5$ (0.2–0.8)).

Sexual behaviour in the Russian Federation

To assess the risk of HIV spread by heterosexual transmission in the general population it is necessary to have quantitative estimates of sexual behaviour in the Russian adult population. The Russian Federation, and the countries of the Newly Independent States, have undergone a ‘sexual revolution’ since Gorbachev’s *perestroika*, with rapid declines in the age at first sex during the 1990s (Chervyakov & Kon, 2000). The increased liberalisation of sexual behaviour among youth has been relatively well documented in school and university-based surveys (Amirkhanian, Tiunov & Kelly, 2001b; Denissenko, Zuanna & Guerra, 1999; Kalichman, Kelly, Sikkema, Koslov, Shaboltas & Granskaya, 2000). However, random surveys of sexual behaviour in the adult population in Russia are rare

(Valeriy Chervyakov, personal communication; Amirkhanian et al., 2001a). Furthermore, with one exception (Amirkhanian et al., 2001a), none of these surveys focus on AIDS risk issues in the general population (such as condom use). We, therefore, use this survey of sexual behaviour among 435 adults (36% men) aged 15–55 in St. Petersburg, conducted by a random digit telephone interview, to inform our modelling approach (Appendix Table 2).

This survey gives an estimated mean number of new partners in the last year of 2.5. If the 1.2% of the population reporting very high rates of partner change are excluded, the mean number of new partners drops to 1.3 (cf. 1.6 among 18–21-year-old university students in Moscow (Denissenko et al., 1999); and 1.7 among sexually experienced 15–17-year-old high school students in St. Petersburg (Amirkhanian et al., 2001b)). The existence of small but high risk ‘core’ groups can be important in fuelling STI and HIV epidemics (Wasserheit & Aral, 1996).

In recognition of the inherent problems with self-reporting of stigmatised behaviour (including sex), we explore a range of values for the mean rate of partner change of 2.5 (1.2–3.5). Sexual mixing amongst different sexual activity classes is assumed to be close to random ($\epsilon_1 = 0.1$ (0–0.50)), in agreement with other studies of sexual mixing (Garnett et al., 1999). Sexual mixing amongst IDU behavioural categories is assumed to be mildly assortative ($\epsilon_2 = 0.5$ (0.1–0.7)), since although only ~1–4% of the Russian population inject drugs, close to half of the IDUs interviewed in Togliatti city report their sex partner is also an IDU (Lowndes et al., 2002). Due to uncertainty in this parameter, a wide range is explored. It is assumed that men are as flexible as women in their rate of change of sexual partner when supply is limited ($v = 0.5$).

Commercial sex is associated with high rates of sexual partner change and can be important in determining the spread of HIV. In St. Petersburg 41% of 15–17-year-old girls at high school reported sexual experience, and of these 3.8% reported receiving money for sex (Amirkhanian et al., 2001b). In Saratov oblast, 2% of women and 1% of men aged 15–25 years old reported receiving money for sex (PSI, 2000). Amongst injecting drug users in Togliatti, Samara oblast, 43% of women reported being actively engaged in commercial sex (Lowndes et al., 2002). Among female IDUs attending a syringe exchange programme in St. Petersburg, 28% reported receiving money or drugs for sex (John Carney, personal communication). In Kaliningrad the only source of income for 82% of confirmed HIV positive female IDUs was commercial sex work (Mashkilleysen & Leinikki, 1999). In contrast only 1 and 3% of male IDUs in Togliatti and St. Petersburg, respectively, reported receiving money for sex (Carney, 2001; Lowndes et al., 2002). Although fewer male IDUs

sell sex for money, there is likely to be a significant underreporting of this behaviour due to its stigmatisation. Of those female IDUs reporting sex work in Togliatti, the mean number of new sex partners they reported in the last 4 weeks was 36 (Lowndes et al., 2002).

It is important to capture the overlap of injecting drug use and sex work when modelling the transmission of HIV. We, therefore, assume that 43% (20–60%) of female injecting drug users engage in commercial sex, with a high rate of partner change of 432 per year (50–800), based on the Togliatti data. We currently ignore sex work among men, due to the low reported rates and problems with reporting of this behaviour.

In the survey of sexual behaviour in the adult population of St. Petersburg, condom use was rare, with only 5.6% of respondents reporting consistent condom use (Amirkhanian et al., 2001a). The majority of this condom use is likely to be with casual sex partners rather than regular partners, and indeed female IDUs in Togliatti report 86% condom use for commercial sex (Lowndes et al., 2002). We assume commercial sex (50+ partners per year) involves a single sex act, regular partnerships (0–2 partners per year) at least 100 acts (at which point the per partnership transmission probability begins to saturate), and non-regular partnerships (3–49 partners per year) 20 acts. Assuming 0% condom use for regular partnerships, 5% for non-regular partnerships and 86% for commercial sex, best estimates of the number of unprotected sex acts for individuals from different sexual activity classes were obtained. The robustness of the model outcomes to changes in these assumptions was examined by providing a large range about these estimates (main text Table 1).

Appendix Table 1: Distribution of sharing frequencies among IDUs reporting sharing in Togliatti, Samara oblast, Russia (Data source: Rhodes et al., 2002)

Number of different people shared with in last 4 weeks	Mean number of new sharers per year*	Frequency (%)
1	1	52.1
2–3	16	27.5
4–9	50	13.4
10+	146	7.0

*We assume that one of those IDUs shared with in the last 4 weeks is a regular partner and does not change in order to estimate the rate of change per year, with the exception of those individuals reporting a single partner in the last 4 weeks, who we assume change partners once a year.

Appendix Table 2: Sexual behaviour among 435 adults aged 15–55 in St. Petersburg, Russia (modified from Amirkhanian et al., 2001a).

Reported number of different sexual partners in the last year	Inferred mean number of partners in last year*	Proportion of interviewees
0	0	7.9
1–2	0.6	78.8
3–5	3.0	8.2
6–9, 10–19, 20–29	15.4	3.9
50–99, 100+	100	1.2

*Assuming one of the reported partners in the last year is a lifetime sex partner, except in the case where 1–2 partners are reported, where approximately half of these are lifetime partners.

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