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The Cost-Effectiveness of Expanding Harm Reduction Activities for Injecting Drug Users in Odessa, Ukraine

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Objectives: **The objectives of this study were to estimate the cost-effectiveness of a harm reduction intervention among injecting drug users (IDUs) in Odessa, Ukraine; and to explore how the cost-effectiveness changes if the intervention were scaled up to 60% as recommended by WHO/UNAIDS.**

Study Design: **Economic providers' costs were estimated. A dynamic mathematical model, fitted to epidemiologic data, projected the intervention's impact. The cost per HIV infection averted for different intervention coverages was estimated.**

Results: **From September 1999 to August 2000, at the current coverage of between 20% to 38% and an injection drug user (IDU) HIV prevalence of 54%, projections suggest 792 HIV infections were averted, a 22% decrease in IDU HIV incidence, but a 1% increase in IDU HIV prevalence. Cost per HIV infection averted was $97. Scaling up the intervention to reach 60% of IDUs remains cost-effective and reduces HIV prevalence by 4% over 5 years.**

Conclusion: **At the current coverage, the harm reduction intervention in Odessa is cost-effective but is unlikely to reduce IDU HIV prevalence in the short-term. To reduce HIV prevalence, more resources are needed to increase coverage.**

EASTERN EUROPE IS EXPERIENCING ONE of the fastest-growing HIV epidemics in the world,[1] with injecting drug use (IDU) being the predominant mode of HIV transmission.[2] Over 100 harm reduction projects have been initiated in Eastern Europe, with over 20 being implemented across the Ukraine.[3] At present, there is only limited evidence that they are cost-effective[4] or have markedly decreased HIV transmission.[5] Indeed, current projects are estimated to reach less than 10% of IDUs in Eastern Europe,[6,7] much lower than the 60% coverage target recommended by UNAIDS/WHO.[8] There is an urgent need to estimate the cost-effectiveness of harm reduction projects in Eastern Europe and to estimate the resource requirements and potential impact of increasing the coverage of these projects.

This study uses economic analysis and mathematical modeling to estimate the cost-effectiveness of a harm reduction project in Odessa, Ukraine, and to project how the project's cost-effectiveness would have changed if it had reached a greater proportion of IDUs in Odessa (intervention coverage).

Materials and Methods

Economic analysis and dynamic mathematical modeling are used to consider the 1-year cost-effectiveness of a harm reduction project for IDUs in Odessa. A mathematical model is used to estimate the intervention's impact in terms of HIV infections averted, which is combined with the results of the cost analysis to estimate its cost-effectiveness. Additional modeling of the impact and costs are undertaken to explore how cost-effectiveness would vary for differing intervention coverages.

The methods for this analysis start with an overview of the study population and intervention. This is followed by a description of the mathematical model, discussion of the data used to parameterize the model, and the methods used to estimate intervention

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impact. The methods for the cost data collection and analysis, estimation of cost-effectiveness, and sensitivity analysis are then presented, and the section concludes with details of the modeling undertaken to explore the relationship between coverage and cost-effectiveness.

Study Site

The first HIV case in the Ukraine was registered in 1987, and since then there have been over 52,000 officially recorded HIV infections[9,10] and up to 200,000 unregistered HIV infections.[11] The spread of HIV has been mainly among IDU populations.[9,12–14]

Odessa is a city of over 1,000,000 people. It has been hard hit by the HIV epidemic, with 14,339 HIV cases registered between 1987 and 2001[15] and an IDU HIV prevalence of 64% in March 2000.[13,14]

Odessa Injection Drug User Intervention

The current harm reduction intervention in Odessa started in September 1999. The NGO “Faith, Hope, Love” administered the project, receiving technical and financial support from UNAIDS.

Three outreach points were established, 2 were stationary (at the Regional Narcological Clinic and a polyclinic) and the other was mobile. The project’s main activities involved promotion of safe drug use practices and sexual behavior through provision of condoms, syringes, and information materials. Peer education was also an important project component. The project undertook many information, education, and communication- (IEC) related activities, including a radio mass media component. IEC-related activities focused on harm reduction issues, specifically the risks of IDU and sharing syringes. This analysis focuses on the first year of the intervention, September 1999 to August 2000.

Over this period, the outreach points were attended by 7524 individual IDUs (each of which had a unique card for identification), and they distributed 71,273 syringes, 9843 condoms, and 528 bottles of bleach. Each IDU reached by the outreach points attended 4 times on average. At each visit, IDUs were counseled about routes of HIV/sexually transmitted infection (STI) transmission, diseases related to drug use, and methods of HIV and STI prevention. After counseling, each IDU received information materials, syringes, condoms, and bleach disinfectant. The information materials included life stories of HIV-positive IDUs, a newspaper dealing with issues important to IDUs, a pamphlet about the intervention including important phone numbers (such as a “help” hotline), and other literature. On average, each IDU in contact with the intervention received 10 syringes in their first year. In addition, they obtained cheap syringes (US $0.07–0.11 per syringe in pharmacies) from other sources. In the intervention’s first year, 29 peer educators were active with the project. Their role was to converse with IDUs about methods of safe drug use and safe sex.

In Odessa, data on the IDU population’s HIV prevalence was collected in 1995 and 1996 by testing IDUs registered at the narcology clinics and in 1998 and 2000 by testing used syringes collected by the mobile outreach point from IDUs in Odessa. The IDUs were required to submit only one syringe, used only for personal use, and were asked to complete a sentinel surveillance card incorporating demographic and behavioral questions. The prevalence of HIV in the syringes was used as an estimate for the IDU HIV prevalence. The estimated IDU HIV prevalence was 1.4% in January 1995, 13% in August 1995, 31% in January 1996,[12] 54% at the end of 1998 (n = 250),[16] and 64% in March 2000 (n = 293).[13] By analyzing the relationship between IDU HIV prevalence (from their syringes) and duration of injection,[17] the HIV incidence was estimated to be 20 infections per 100 susceptible IDU person-years in March 2000.

Model Description

A dynamic, deterministic mathematical model (IDU 2.4) was developed in Borland C++ (Inprise Corp., Scotts Valley, CA) and used to estimate the intervention’s impact on HIV transmission among IDUs and their sexual partners. The model simulates the patterns of HIV and STI transmission resulting from syringe-sharing and sexual contact between IDUs and their sexual partners. IDUs are divided into subgroups according to their level of syringe-sharing, sexual behavior, and condom use. The size of each subgroup is estimated from project data and behavioral surveys. The model includes the increased probability of HIV transmission during the initial high-viremia phase of infection,[18–20] the role STIs play in facilitating transmission,[21] the recruitment of new IDUs, and movement of IDUs out of the population (as a result of migration, overdose, or HIV-related morbidity). The model and its parameters are described elsewhere[5] and in Appendices 1 and 2.

Data Used to Parameterize Model

Since the start of the intervention, there have been 3 behavioral surveys among IDUs in Odessa, in October 1999 (n = 177), March 2000 (n = 293), and June 2001 (n = 97). For logistic reasons, the surveys did not involve the same cohort of IDUs or follow the same sampling procedure. However, the samples used for each survey seem to be comparable with no statistical difference ($P > 0.05$) between the proportion of male IDUs (68–75%), their mean age (27.5–28.9 years), or the mean duration of drug use (8.9–9.9 years). The first survey sampled IDUs from 51 different locations and was used to estimate the risk behavior of IDUs before the intervention. The March 2000 survey was undertaken at the mobile outreach point and was used to fill gaps in the behavioral data from the other 2 surveys. The June 2001 survey was undertaken at all 3 outreach points and was used to estimate the risk behavior of IDUs reached by the intervention. Key findings from the surveys include significant increases ($P < 0.05$) in the percentage of IDUs reporting: never shared a syringe (17% in March 2000 and 37% in June 2001), cleaning syringes with boiling water before reuse (6% in October 1999 and 49% in June 2001), and using condoms “all of the time” with casual partners (16% in October 1999 and 39% in June 2001).

The number of IDUs that attended the outreach points (7524) was used as a maximum estimate for the number of IDUs effectively reached by the project—those IDUs that changed their risk behavior as a result of intervention involvement. However, because some IDUs only attended the outreach points once, a range was used for the number effectively reached (5000–7524). Because of the hidden nature of IDU in Odessa, the size of the IDU population was estimated using a multiplier method,[22] using the number of IDUs registered at the narcology clinics in 2000 (6258) as a benchmark, and then estimating a multiplier from the proportion of IDUs that reported being registered in the behavioral surveys from October 1999 (26%) and June 2001 (32%). This method estimated the number of IDUs in Odessa to be between 19,556 and 24,069.

To produce bounds for the proportion of IDUs effectively reached by the intervention (intervention coverage), the low and high estimates of the number of IDUs effectively reached by the intervention were divided by the high and low estimates for the size of the Odessa IDU population, respectively. This estimated the intervention coverage was between 20% and 38%. However, this may underestimate the intervention’s coverage because one of the outreach points, being at a narcology clinic, may have led to more IDUs becoming registered, therefore leading to the IDU population being overestimated by the multiplier method.

Model Analysis

The behavioral, epidemiologic, and intervention specific data in Table 1 were used to parameterize the model. The model was run from January 1999, 9 months before the intervention, because there was HIV prevalence data for this time point (53.7% ± 6.5%).[16] From September 1999, the model was run with and without the intervention until June 2001, when the postintervention behavioral data were collected. Comparisons between these model simulations were used to estimate the intervention's impact on HIV transmission among IDUs and their sexual partners for September 1999 to August 2000. The impact of the intervention is estimated in terms of HIV infections averted compared with if no intervention had occurred.

The projections of intervention impact were complicated by uncertainty in the model's inputs. This related to the behavioral, epidemiologic, and intervention data from Odessa and uncertainty regarding inputs such as the risk of HIV transmission through syringe-sharing or unprotected sex. Because of such uncertainty, ranges for the inputs with greatest uncertainty were developed (Table 1), and 1000 parameter sets were randomly sampled from these ranges using Latin Hypercube sampling.[42] The sampling was undertaken using Crystal Ball software (Decisioneering, Inc., Denver, CO). The model was run with each parameter set, and the simulations that lay within the 95% confidence intervals of the IDU HIV prevalence and incidence for March 2000 were used to estimate the intervention's impact. The divergence between each simulation and the observed mean HIV prevalence and incidence for March 2000 was determined by calculating the sum of the squared difference between the data estimates and model predictions for the HIV incidence and prevalence at that time point. The model simulation that had the smallest divergence from the data for March 2000 (least-squared sum) was selected as the "best-fit" simulation to give a point estimate for the intervention's impact. The other simulations were used to produce a range around this estimate.

Cost Analysis

The intervention costs were analyzed for September 1999 to August 2000, including startup activities. Cost data were collected retrospectively following standard methods[43] using an ingredients methodology. Direct costs were estimated from the provider perspective of the NGO undertaking the intervention and do not include costs borne by IDUs.

A financial and economic costing of the project was made. Financial costs represent actual expenditure on goods and services purchased. Data on these costs were obtained from project documents, interviews, and observations. Economic costs include the estimated value of goods or services for which there are no financial transactions or the price of the good does not reflect the cost of using it elsewhere; this is the opportunity cost of the inputs. These costs were estimated from data obtained in interviews with the project coordinator and from observation of the resources used. For this cost-effectiveness analysis, economic costs were used.[44]

For the calculation of the financial and economic costs, an ingredients approach was used to identify all inputs. All buildings used by the intervention were provided free of charge to the NGO. An economic cost of this space was calculated based on the square footage used by the NGO (in its head office as well as stationary outreach points) and the prevailing market rental rates for this space. For space that had multiple uses, an allocation factor based on the IDU intervention's use of this space was applied to attribute the costs. Financial equipment costs were calculated using straight line depreciation, in which the item cost is divided by the expected life of the item and economic equipment costs calculated the opportunity cost of equipment based on the discount rate and length of life of each item. Startup activities included initial project training sessions for staff and development of IEC materials. These activities were treated as capital items, and the annual equivalent financial and economic cost was calculated as for the equipment. Financial personnel costs include only the cost paid by the project for each staff member. For each staff member, their total financial cost was multiplied by their time allocation on the project to attribute the specific amount to the IDU project. The full cost of employing staff (including benefits) was included. For many staff, the NGO only paid an honoria. The honorarium amount was included as part of the financial costs. To obtain their economic costs, their full salary cost was multiplied by their time allocation of the project. Financial costs were calculated based on the amount paid. Economic costs included a valuation of donated items such as condoms, syringes, and disinfections (based on a range of market rates; see sensitivity analysis subsequently).

A number of problems were encountered in collecting the cost data. There was no routine monitoring of actual spending so it was sometimes difficult to determine the difference between how funds were allocated in the budget and how they were actually spent. The intervention used radio air time to transmit mass media messages, which by law are donated for free. Unfortunately, the project did not monitor how many radio spots were used, so it was not possible to directly estimate an economic cost for this. Previous analysis has shown the inclusion of mass media could reduce cost-effectiveness ratios by half, or double them, depending on the extent to which commercial rates were used.[4] Lastly, time spent by volunteer peer educators was not systematically monitored and so was excluded from the costs. The influence of these uncertainties is explored in the sensitivity analysis.

All data were transformed into 1999 U.S. dollars and the average 1999 exchange rate of 4.5 Ukrainian Hryvnya to one U.S. dollar was used. A discount rate of 13%, reflecting the real national bank rate in 1999 was used. Project costs were classified as capital (buildings, equipment, startup training) and recurrent (staff, periodic training sessions, building maintenance).

Cost-Effectiveness

Cost-effectiveness is undertaken from the perspective of the provider. The additional costs for implementing the intervention (September 1999 and August 2000) were divided by the incremental effectiveness (estimated HIV infections averted for that period from the best-fit model simulation) to estimate the cost per HIV infection averted for the intervention, relative to the absence of an intervention, for the first year of intervention activity. Potential cost savings associated with averted infections (HIV and STI care) were excluded for 2 reasons. First, this approach evaluates the cost-effectiveness of the starting point (the do-nothing alternative).[45] Second, it is unclear to what extent treatment savings would be realized among this marginalized IDU population that has low levels of effective access to health systems. The confidence bounds reflect the uncertainty in the impact estimates, the low-end (best) cost-effectiveness ratio uses the highest impact projection, whereas the high-end estimate uses the lowest impact projection.

TABLE 1. Model Parameter Values for the Uncertainty Analysis to Estimate the Impact of the Odessa Injection Drug Users (IDU) Project (September 1999 to August 2000)

Types of Model Input	Definition of Model Input		Range for Model Inputs: Not Reached,	Reached	Data Sources for Model Input Values
Epidemiologic inputs	Initial HIV prevalence among IDUs		47–60%		16
	Average duration of high-viremia phase (months)		1.5 mo		18
	Average duration between HIV infection and morbidity		72–84 mo		Personal communication with Y. Kruglov, director of Ukrainian AIDS center
Transmission probabilities	Probability of HIV transmission per sex act (male to female)		0.001–0.003		23–27
	Ratio of probability of HIV transmission per sex act for female to male relative to male to female		0.5–1		
	Probability of HIV transmission per needle-sharing act		0.0029–0.0141		28, 29
	HIV transmission cofactor during high-viremia phase		7.6–18		18–20
	Condom efficacy per sex act		60–90%		30, 31
	Cleaning efficacy per sharing act		10–55%		32–40
Size of IDU population and intervention coverage	Proportion of IDUs that have injected for less than 1 year		4.9%	3.3%	IDU behavioral survey in Odessa, March 2000 and June 2001
	IDU mortality rate per 1000 person-years		40	40	Personal communication with Y. Kruglov, director of Ukrainian AIDS center
	Initial size of IDU population		19,400–24,400		6258 registered IDUs in Odessa in 2000; June 2001 survey found 32% of IDUs were registered and October 1999 survey found 26% of IDUs were registered
	Ratio of male to female IDU population		70% male		IDU behavioral survey in Odessa, October 1999 and June 2001
	Number of IDUs attending the IDU project		5000–7524		Project records state 7524 IDUs visited IDU project from September 1999 to August 2000 but many were infrequent attendees
Sexual behavior inputs	Definition of "low" and "high" number of sexual partners per 6 months (low) or month (high)	Low	1.65		IDU behavioral survey in Odessa, June 2001
		High	Male: 2.3, female: 13		
	Population distribution of male IDUs with respect to their level of sexual activity	None	21%		IDU behavioral survey in Odessa, October 1999 and June 2001
		Low	52%		
		High	27%		
	Population distribution of female IDUs with respect to their level of sexual activity	None	7%		IDU behavioral survey in Odessa, October 1999 and June 2001
		Low	18%		
		High	75%		
	Degree of assortative sexual mixing between individuals of different sexual activity (zero is random mixing and one is full assortative mixing)		Slightly assortative 0.15–0.35		Little data but reviews of data from elsewhere suggest sexual mixing is usually only weakly assortative[41]
	Proportion of reached IDUs' sexual partners that are IDUs for low and high sexual activity	Low	59%		IDU behavioral survey in Odessa, October 1999, March 2000, and June 2001
		High	70%		
Syringe-sharing behavior inputs	Average consistency of cleaning syringes		6%	49%	IDU behavioral survey in Odessa, October 1999 and June 2001
	Definition of "low" and "high" rate of needle-sharing partners in last month	Low	1		IDU behavioral survey in Odessa, June 2001
		High	3.0		
	Population distribution of IDUs with respect to their level of needle-sharing in last month	None	17–42%	56%	IDU behavioral survey in Odessa, March 2000 and June 2001
		Low	32–22%	17%	
		High	51–36%	27%	
	Degree of assortative mixing between individuals of different syringe-sharing behavior activity (zero is random mixing and one is full assortative mixing)		Slightly assortative 0.15–0.35		No data; assumed to be similar to sexual mixing
Condom use inputs	Consistency of condom use among stable partnerships		40%	44%	IDU behavioral survey in Odessa, October 1999 and June 2001
	Population distribution of condom use among casual sexual partnerships	None	33%	31%	IDU behavioral survey in Odessa, October 1999 and June 2001; none refers to using condoms in no sex acts, half refers to condom being used in 50% of sex acts, and all refers to condoms being using in all sex act
		Some	51%	33%	
		All	16%	30%	

Sensitivity Analysis

The cost-effectiveness of the IDU intervention is dependent on numerous context-specific factors, and so a sensitivity analysis was undertaken around key cost parameters and all model parameters.

To identify which model parameters have the greatest effect on the impact predictions, a multivariate sensitivity analysis using the best-fit model simulation was conducted. Each model parameter was given the same relative uncertainty bounds (±10%), and parameter sets were randomly sampled within these bounds using Latin Hypercube sampling in Crystal Ball. These parameter sets were used to produce different estimates for the HIV infections averted by the intervention over 1 year. The input and output of these simulations were used to undertake a multilinear regression to determine which parameters the model output is most sensitive to. Because of differences in the units of measurement for each parameter, the strength of the association between the model parameters and the projected HIV infections averted was determined by the degree to which the projected HIV infections averted fluctuates when the parameter is varied by ±10% in the regression model.

A sensitivity analysis around key cost parameters such as the discount rates and valuation of mass media and donated goods was also conducted. For this, the effect of decreasing the discount rate for capital items from 13% to 3% was explored. For donated supplies such as syringes, there were a number of donors. For the baseline economic analysis, prices specific to each donor were used to value these supplies. The sensitivity analysis looked at valuing donated supplies at the lowest and highest price for all suppliers. Although it was not possible to directly value mass media activities, a previous analysis found that valuing donated mass media can result in a substantial increase in costs.[4] In the sensitivity analysis, the likely impact of a mass media campaign on cost-effectiveness was explored. To estimate the costs for such a campaign, inputs from a campaign previously undertaken by the same organization were used. Low and high cost were estimated, reflecting the valuation of air time at concessional (rates for charitable organizations) and commercial market rates. Valuation of donated volunteer time was based on estimates from another costing of an IDU intervention in Kyiv where volunteers were paid.[46] The cost per volunteer was estimated and then applied to the number of peer educators in this project. Finally, the sensitivity analysis considered the highest cost scenario possible combining the high valuation of donated mass media and supplies and the volunteer time. When combined with the lowest impact projection, this scenario produces the most pessimistic cost-effectiveness ratio.

Cost-Effectiveness of Scaling Up the Intervention

The cost-effectiveness of the IDU intervention in Odessa is highly dependent on the proportion of IDUs effectively reached by the intervention—estimated to be between 20% and 38%. Using the best-fit model simulation and modeled costs for September 1999 to August 2000, the effect on the cost-effectiveness of changing the proportion of IDUs reached, from 10% to 80%, was estimated. For these calculations, the current coverage of the intervention was assumed to be the coverage estimate used in the best-fit simulation. The impact of increasing intervention coverage was estimated by assuming either the same patterns of behavior change occur among reached IDUs irrespective of coverage ("baseline impact" assumption) or the degree of behavior change diminishes among reached IDUs as coverage increases, by 15% at 60% coverage or more ("low-impact" assumption). The basis behind the second projection is that it may be harder to change the risk behavior of "harder-to-reach" IDUs. The costs associated with reaching more IDUs were also modeled using 2 methods to produce a low and high estimate. The low-cost method assumed the number of new outreach points could be tailored to different population sizes covered using the same proportions of each input as at the current coverage used in the best-fit simulation—a linear production process. The high-cost method allowed for indivisibilities and nonlinearities in the production process and that further expansion beyond the current coverage would require greater capital and semifixed factor investment.

Results

Intervention Costs

Table 2 presents the 1-year financial and economic costs for the project. The largest components of financial costs are supplies (29%),

TABLE 2. One-Year Costs of the Odessa Injection Drug User (IDU) Project, September 1999–August 2000, in 1999 U.S. Dollars*

	One-Year Costs			
Cost Category	Financial	Percent	Economic	Percent
Capital				
Startup activities	$2511	8%	$3518	4.6%
Buildings	$0	0%	$11,519	15%
Equipment	$0	0%	$258	0.3%
Total capital costs	$2511	8%	$15,296	20%
Recurrent				
Personnel	$4433	14%	$27,036	35%
Supplies	$9294	29%	$17,570	23%
Vehicle repair and maintenance	$1326	4%	$1326	2%
Building repair and maintenance	$881	3%	$3054	4%
Project management and training	$3305	10%	$3305	4%
Information, education, and communication materials	$2908	9%	$2908	4%
Other recurrent items	$6301	20%	$6301	8%
Total recurrent costs	$28,449	92%	$61,501	80%
Total costs US$	$30,960	100%	$76,797	100%
Average cost per IDU reached	$4.11		$10.21	

Note: Costs exclude valuation of donated mass media costs and volunteer time. The cost-effectiveness ratio uses the economic cost of the intervention.
*Percentages refer to the percent of total cost.

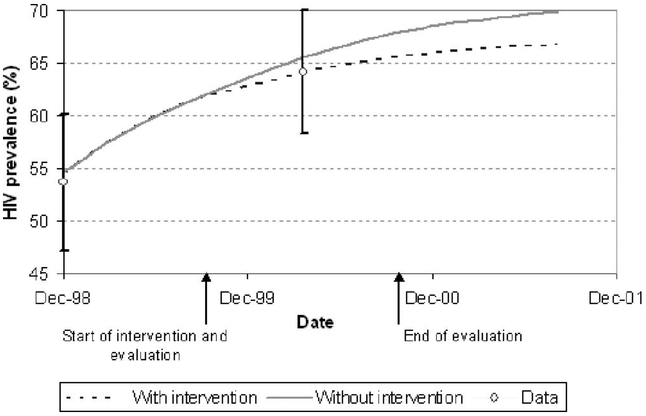

Fig. 1. Projected (best-fit model simulation) and observed trends in HIV prevalence among injection drug users with and without the intervention. Bounds on data points are 95% confidence intervals.

personnel costs (14%), and other recurrent items (20%). The "other recurrent items" category includes the initial rapid assessment research, sentinel surveillance, development of best practice materials, and per diems for travel. The largest components of economic costs are personnel (35%), supplies (23%), and buildings (15%). Economic costs were $45,837 (148%) higher than financial costs. The major difference between financial and economic costs was the inclusion of the full cost of employed staff, the market value for donated and discounted items such as syringes and condoms, and the rental value for donated building space. The financial cost includes only honoria payments for many staff, which the NGO made. The economic costs include a valuation of the staff time actually put into the project by these honoria staff and is the reason why their personnel economic costs are 6-fold higher.

Model Validation

From the uncertainty analysis, 186 model simulations lay within the 95% confidence intervals of the IDU HIV prevalence and incidence in March 2000. The best-fit model simulation and available IDU HIV prevalence data are presented in Figure 1.

Intervention Impact and Cost-Effectiveness

Over 1 year, the model projected the intervention reduced the IDU HIV incidence by 22% (95% confidence interval [CI], 12–25%), from 28 infections per 100 susceptible person-years without the intervention to 21 infections per 100 person-years with the intervention. This resulted in 792 HIV infections averted (95% CI, 422–1019) compared with no intervention, between September 1999 and August 2000, with 65% being averted among the IDUs. Despite this, the model projected the IDU HIV prevalence increased by 1.1% (95% CI, 0.1–1.8%) to 65.2% (95% CI, 59–67%) in August 2000, instead of 67.8% (95% CI, 60–69%) if no intervention had occurred. In addition, although 277 (95% CI, 184–395) HIV infections were averted among the IDUs' noninjecting sexual partners, this only accounted for 4% of the projected 6727 (95% CI, 5640–12,280) HIV infections that occurred in this subpopulation between September 1999 and August 2000. The cost-effectiveness of the project was $97 (range, $71–272) per HIV infection averted over 1 year.

Sensitivity Analysis

Table 3 shows the results of the multilinear regression analysis undertaken with the input and output of the sensitivity analysis. The adjusted R^2 value for the regression model was 0.980, indicating that it explained most of the variability of the model output. Table 3 shows the 10 model parameters that had the greatest effect on the HIV infections averted when adjusted by 10% in the regression model with their partial regression coefficients. The parameters are listed in order of their strength of association with the HIV infections averted in the regression model. Table 3 also shows the estimated HIV infections averted and cost-effectiveness (economic cost per HIV infection averted) when these parameters are adjusted by 10% in the regression model.

The initial IDU HIV prevalence and the factor increase in the HIV transmission probability during the initial high-viremia phase of infection (high-viremia cofactor) had the greatest effect on the projected HIV infections averted. The regression model estimated that a 10% increase in the initial HIV prevalence (from 54.9–60.4%) or the high-viremia cofactor (from 10.7–11.8) would result in a 17% increase in the cost per HIV infection averted, whereas a 10% reduction in either parameter would result in a 13% reduction. Indeed, both these parameters only have to increase by 35% for the cost per HIV infection averted to double in the regression model. The initial number of IDUs in Odessa and the percentage of IDUs effectively reached by the intervention also have a very strong affect on the cost-effectiveness projections. If either of these parameters increase by 57%, they result in a doubling of the cost per HIV infection averted in the regression model. Other model parameters that have a strong affect on the cost-effectiveness projections are the percentage of IDUs that share syringes frequently before the intervention, the percentage of highly sexually active reached IDUs that use condoms "always," the HIV transmission probability per sexual act from female to male, the condom efficacy per sex act, the HIV transmission probability per syringe-sharing incident, and the percentage of reached and not-reached female IDUs with high sex activity.

A sensitivity analysis was also undertaken around cost parameters. If the discount rate was decreased from 13% to 3%, then the cost-effectiveness decreased by 1%. If donated goods were valued at the lowest level ($3914), then the cost-effectiveness decreased by 6%, whereas if they were valued at the highest level ($17,061), it increased by 11%. Inclusion of mass media time increased the cost per HIV infection averted by 15% to 45% ($112–141) depending on whether mass media time is costed at a low ($11,737) or high rate ($38,055). Valuation of donated volunteer time increased costs and cost-effectiveness by 6%. The highest cost scenario with the inclusion of mass media time (high cost), donated supplies (high cost), and volunteer labor increases the costs and cost-effectiveness by 67%. If this is combined with the lowest impact projection from the model uncertainty analysis, the cost-effectiveness is increased to $304 per HIV infection averted. These represent likely upper bounds on the cost-effectiveness ratio.

Cost-Effectiveness of Scaling Up the Intervention

Using the best-fit model simulation, Figure 2A shows the "baseline impact" projections of the intervention's impact on HIV incidence for different coverage levels. At the current coverage used in the best-fit model simulation (27%), the intervention reduces the IDU HIV incidence to 21 infections per 100 susceptible person-years in the first year, but does not reduce the IDU HIV prevalence, with the HIV prevalence being 1.1% greater 1 year after the start of the intervention. If the coverage had been 60%, assuming the same patterns of behavior change, the intervention would have decreased HIV incidence by 42% (to 16 infections per 100 person-years) and prevalence by 0.7% and 4.1% after 1 and 5 years, respectively. However, if the degree of behavior change among reached IDUs diminishes by 15% at 60% coverage, then the decrease in incidence reduces to 39%, and the

TABLE 3. Sensitivity Analysis on the Model's Impact Projections and Cost-Effectiveness Ratio (cost per HIV infection averted) for September 1999 to August 2000[*]

Parameter (initial values used for the best-fit simulation in brackets)	Regression Coefficient Unstandardized	HIV Infections Averted From 10% Change in Model Input in Regression Fit (% change)		Cost-Effectiveness Ratio[†] From 10% Change in Model Input in Regression Fit (% change)	
		−10%	+10%	−10%	+10%
Model parameters					
Initial HIV prevalence among IDUs (55%)	−20.6	906 (+14%)	678 (−14%)	85 (−13%)	113 (+17%)
HIV transmission cofactor during high-viremia phase (10.7)	−106.5	906 (+14%)	678 (−14%)	85 (−13%)	113 (+17%)
Percentage of IDU reached by intervention (27%)	2,347.7	722 (−9%)	862 (+9%)	106 (+10%)	89 (−8%)
Initial IDU population (20,583)	0.034	723 (−9%)	861 (+9%)	106 (+10%)	89 (−8%)
Percentage of IDUs that share needles with high frequency at baseline (59%)	652.0	754 (−5%)	830 (+5%)	102 (+5%)	92 (−5%)
Percentage of the reached highly sexually active IDUs that use condoms "always" (39%)	1014.5	762 (−4%)	822 (+4%)	101 (4%)	93 (−4%)
The HIV transmission probability per sexual act from female to male (0.001)	286,407.6	763 (−4%)	821 (+4%)	101 (+4%)	94 (−4%)
Condom efficacy per sex act (87%)	307.9	765 (−3%)	819 (+3%)	100 (+3%)	94 (−3%)
HIV transmission probability per needle-sharing incident (0.013)	16,639.2	770 (−3%)	814 (+3%)	100 (+3%)	94 (−3%)
Percentage of reached and not reached female IDUs with high sex activity (75%)	266.2	772 (−3%)	812 (+3%)	99 (+3%)	95 (−2%)
Economic Parameters		Economic Costs (% change)		Cost-Effectiveness[†] (% change)	
Decrease discount rate applied to capital items from 13% to 3%		$75,871 (−1%)		$96 (−1%)	
Valuation of donated supplies	Low	$72,435 (−6%)		$91 (−6%)	
	High	$85,582 (+11%)		$108 (+11%)	
Inclusion of valuation for mass media					
	Low	$88,534 (+15%)		$112 (+15%)	
	High	$114,852 (+11%)		$145 (+50%)	
Inclusion of valuation of donated labor		$81,491 (+6%)		$103 (+6%)	
Highest cost scenario (inclusion of high valuation of mass media and supplies and valuation of donated labor)		$128,331 (+67%)		$162 (+67%)	

Note: HIV infections averted are in comparison to no program for IDUs. Positive figures for percentage change in cost-effectiveness mean that the cost-effectiveness ratios have increased and so overall cost-effectiveness has been reduced.

[*] The model parameters are ordered relative to their effect on the HIV infections averted in the regression fit (using the regression coefficient). A change in coverage will also change the costs of the intervention. This is analyzed in more detail elsewhere.

[†] Economic cost per HIV infection averted.

IDUs indicates injection drug users.

prevalence reduces by 3.0% after 5 years. The costs associated with achieving this coverage are uncertain and so low- and high-cost estimates were produced. For example, assuming a current coverage of 27%, the low- and high-cost estimates for reaching 60% of IDUs in Odessa are 233% ($179,193) and 266% ($204,792) of the current economic costs, respectively. Figure 2B uses these cost estimates and the "baseline impact" projections to estimate the cost-effectiveness ratio for the intervention reaching different numbers of IDUs. It suggests the cost-effectiveness worsens with increasing coverage. For example, at 60% coverage the lowest estimated cost per HIV infection averted (using the "baseline impact" assumption and low cost estimate) is 29% higher than for 27% coverage, whereas the highest estimate is 63% higher (using the "low-impact" assumption and high cost estimate), reflecting nonlinearities in the production process. The cost-effectiveness ratio may also be greater at low coverage depending on how costs are modeled.

Discussion

The analysis used economic analysis and mathematical modeling to estimate the cost-effectiveness of an IDU harm reduction intervention in Odessa. The results suggest that, despite the high IDU HIV prevalence, the intervention averted 792 HIV infections compared with no intervention, with a cost-effectiveness of $97 per HIV infection averted for September 1999 to August 2000. This cost-effectiveness ratio is 3-fold less than other harm reduction interventions in Russia[47] and Belarus.[4] Indeed, even the most pessimistic cost-effectiveness estimate ($304 per HIV infection

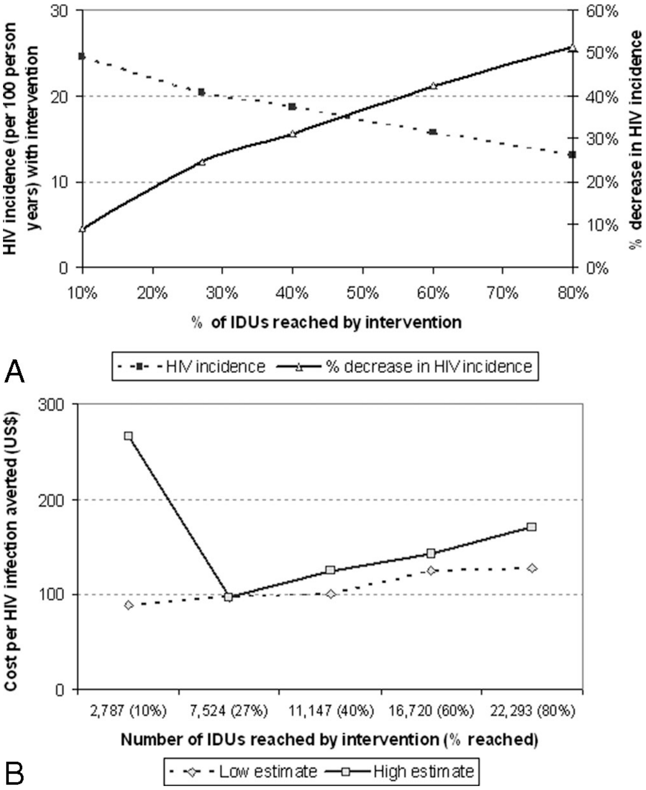

Fig. 2. The effect of increases in intervention coverage (number of injection drug users [IDUs] reached) on the HIV incidence in the Odessa IDU population and cost-effectiveness of the intervention (economic cost per HIV infection averted). The projections in Figure 2 use the best-fit model simulation that assumes the current coverage of the intervention is 27% of the IDU population in Odessa. (**A**) The projected decrease in HIV incidence for the Odessa IDU intervention reaching different numbers of IDUs. The figure only plots the "baseline impact" projections. (**B**) The projected range in the cost per HIV infection averted for the Odessa IDU intervention reaching different number of IDUs. The figure uses the "baseline impact" projections with low and high cost estimates for reaching different numbers of IDUs.

averted) is still less than the estimates from these interventions. This highlights the relative efficiency of the Odessa harm reduction project, especially considering the intervention from Belarus was found to be cost-effective when compared, using purchasing power parity factors to convert costs,[48] with other IDU interventions in North America and HIV prevention interventions in sub-Saharan Africa.[4]

A number of contextual factors contributed to the cost-effectiveness of this project. IDUs can easily acquire new syringes because it is legal to carry syringes and they are available inexpensively from pharmacies. This meant that although the intervention did not distribute many syringes per IDU, it did encourage and educate IDUs to obtain new syringes from other sources, therefore reducing syringe-sharing. Lastly, the project relied on donated resources, with the economic costs being 2.5-fold higher than financial costs. This highlights the importance of considering donated resources when planning the replication and scaling up of projects.

The findings are also context-specific about the epidemiologic setting and underlying risk behavior. The project's cost-effectiveness was very sensitive to the initial IDU HIV prevalence, with the cost-effectiveness being much improved if the HIV prevalence had been lower. This highlights that, although harm reduction interventions in high-prevalence settings such as Odessa can be cost-effective, it is more efficient to initiate them earlier in an HIV epidemic. In Odessa, 75% of female IDUs are commercial sex workers, with many clients being non-IDUs. This increased the sexual transmission of HIV to their noninjecting sexual partners, with an estimated 6000 HIV infections occurring in this group in 1 year. The intervention only decreased the HIV infections occurring in this subpopulation by 4%, primarily as a result of the modest increase in reported condom use among IDUs reached by the intervention. This result and the sensitivity analysis highlight the importance of promoting condom use and discouraging risky sexual behavior as part of harm reduction interventions to improve impact and reduce bridging infections to the general population. If this is not undertaken, these bridging infections could possibly maintain a generalized epidemic,[49] especially when IDU and sex work are closely linked.

Despite numerous HIV infections averted, the IDU HIV incidence is still high, comparable to other settings that have experienced explosive HIV epidemics.[12,50–53] Indeed, the results suggest the IDU HIV prevalence will continue increasing with the current level of intervention activity. The continued high HIV incidence is partially the result of the majority of IDUs (>60%) not being reached by the intervention. If the project had achieved similar behavior change among 60% of IDUs, as recommended by WHO/UNAIDS,[8] then our model simulations suggest the HIV incidence could have reduced dramatically (to 16 infections per 100 susceptible person-years with the best-fit simulation) and the IDU HIV prevalence would have started decreasing (by 4% after 5 years). For the intervention to reach these IDUs, greater resources are required. For example, if the current coverage is 27%, then the costs for increasing coverage to 60% are estimated to be $179,193 to $204,792 over 1 year. However, it will still be a worthwhile use of resources, because these cost estimates imply the cost-effectiveness ratio at 60% coverage will be at most 50% greater than at 27% coverage. The continued cost-effectiveness and increased impact attained at 60% coverage supports the coverage target recommended by UNAIDS/WHO and illustrates that high priority should be given to increasing the resources invested in the Odessa IDU intervention. However, for the intervention to decrease the HIV incidence to levels observed in low HIV prevalence settings (<5 infections per 100 person-years),[54–56] the intervention also needs to reduce IDU risk behavior to a greater extent, especially high-frequency syringe-sharing and condom use among highly sexually active IDUs (as highlighted by the sensitivity analysis). This is likely to entail an increase in project activity among the IDUs reached by the intervention.

The limitations of this analysis reflect the constraints of using routinely collected retrospective data to undertake cost-effectiveness analyses of interventions and the challenges of estimating intervention impact on an infectious disease. The model projections are dependent on the comparability of the samples of IDUs used in the behavioral surveys and the reliability of self-reported behavioral data. Because there was no control and the postintervention behavioral data were collected after the evaluation period, it is difficult to assess the attributability of the reductions in risk behavior to the intervention and the evaluation period. In addition, the method used to calculate the size of the IDU population could have overestimated the number of IDUs in Odessa and so may have underestimated the intervention's coverage and impact. To counteract this, key areas of uncertainty were factored into the analysis and the model projections were validated against available HIV epidemiologic data.

One important message from this work is the need for stronger and more systematic methods of data collection and monitoring, as encouraged by the World Health Organization.[57] This is essential for accurately estimating the cost-effectiveness of future projects. Projects need to document their activities, detailing resources used whether paid for or donated. Regular behavioral surveys need to be undertaken based on standardized methods, indicators, and sampling approaches, including control groups if possible. Lastly, projects should provide for cost-effectiveness analysis at the planning stage, including any additional resources required.

In summary, our analysis highlights that harm reduction interventions can be cost-effective in a high prevalence setting. However, for harm reduction interventions to substantially improve the epidemic situation, they need to increase their coverage to higher levels than were attained in Odessa. The cost of this is great but can be done at a low cost per HIV infection averted. If this investment is not made, and harm reduction interventions continue to have low to moderate coverage, then the HIV epidemic in places such as Odessa will continue progressing.

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APPENDIX 1: Technical Description of IDU Model

IDU 2.4 simulates the transmission of HIV resulting from syringe and needle sharing and heterosexual contact between 6 groups of male IDUs, 6 groups of female IDUs, and their non-IDU sexual partners. The heterosexual transmission of one STD between these subgroups is also simulated. The model is formulated in Borland C++ (Inprise Corp., Scotts Valley, CA), as a set of deterministic ordinary differential equations that describe the movement of IDUs between discrete subpopulations based upon their sex ($r = 0$ and $r = 1$ denotes males and females, respectively); injecting and sexual behavior; and HIV infection status. These are described in turn subsequently. A summary of the notation used is given in Appendix 2.

In the model, the IDU population is divided into 3 subgroups with different patterns of syringe-sharing behavior ($i = 0$, for those that do not share needles, $i = 1$ for those that "rarely" share needles with a low number of IDUs, and $i = 2$ for those that "frequently" share syringes with a larger number of IDUs). Each of these subgroups are further divided into 5 subgroups with different levels of sexual activity and condom use ($j = 0$, sexually inactive, $j = 1$, "low" number of sexual partners per month and a specified average consistency of condom use, $j = 2$–4 "high" number of sexual partners per month and have a low ("none" and $j = 2$), medium ("half" and $j = 3$) or high ("all" and $j = 4$) consistency of condom use[*]). We consider three levels of consistency of condom use among the IDU subgroup with the highest number of partners because variations in the distribution of condom use will have most effect on the overall patterns of HIV transmission.[†]

As with other HIV compartmental models, each behavioral subgroup of IDUs is divided into those that are susceptible to HIV infection (x), those that are recently HIV infected and in the initial high-viraemia phase (h), and those who have progressed into the low-viraemia phase (y). We assume that IDUs with late-stage HIV infection are chronically ill and stop being sexually active and sharing injecting equipment with others. New IDUs enter the susceptible population at a fixed per capita recruitment rate (Λ_r). Susceptible IDUs become infected with HIV at a per capita rate that is determined by the per capita risk associated with sharing needles or syringes with other IDUs (π_{idu}) and the per capita risk associated with their sexual behavior (π_{sex}). When a susceptible IDU becomes infected with HIV, they are initially highly infectious (for an average period $1/v$). They then enter a long period of low infectivity (average duration $1/\delta$). In the model, IDUs remain in the population until they stop injecting drugs (IDUs inject for an average period $1/\sigma_r$), or until they stop sharing needles as a result of chronic HIV-related illness (average duration $1/\delta$) or until they die from sepsis infection or drugs overdose (at a rate ψ_r). Equation 1 describes the HIV infection dynamics amongst the IDUs.[‡]

$$\frac{dx_{rij}}{dt} = n_{rij}\,\Lambda_r - x_{rij}\,(\pi_{idu} + \pi_{sex} + \psi_r + \sigma_r)$$

$$\frac{dh_{rij}}{dt} = x_{rij}\,(\pi_{idu} + \pi_{sex}) - h_{rij}\,(\psi_r + \sigma_r + v)$$

$$\frac{dy_{rij}}{dt} = vh_{rij} - y_{rij}\,(\psi_r + \sigma_r + \delta) \tag{1}$$

The probability that a susceptible IDU becomes HIV infected per unit time from needle sharing (π_{idu}) or unprotected sex (π_{sex}) is one minus the probability of not getting infected over this time. The probability of not becoming infected per unit time is the product of the probabilities of not being HIV infected from any

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[*] In general, the user can specify the number of sexual partners corresponding to "low" and "high", the average consistency of condom use for each subgroup, and the average number of sex acts per unit time for each subgroup.

[†] The notation for the behavioral subgroup that an IDU belongs to is given by *[r,i,j]*, except when we are referring to situations in which the sex of the IDU does not affect the probability of HIV transmission (such as the syringe-sharing partner of an IDU), in which case we use the notation *[i,j]*.

[‡] The subscripts, *r, i,* and *j* denote which behavior subgroup (denoted as *[r,i,j]*) a variable or parameter is associated with and n_{rij} denotes the total population of the subgroup *[r,i,j]*.

needle sharing or sexual act with partners from each behavioral subgroup. If we let c_i and d_{rj} denote the total number of syringe-sharing and sexual partners, respectively, that an IDU in subgroup *[r,i,j]* has per unit time, then mathematically, the probability that a susceptible IDU becomes HIV infected from a syringe-sharing (π_{idu}) or sexual partnership (π_{sex}) per unit time is given by:

$$\pi_{idu} = 1 - \prod_{\forall o,p} (1 - \varphi_{ijop})^{c_i \rho_{ijop}}$$

$$\pi_{sex} = 1 - \prod_{\forall o,p} (1 - \varphi_{rijop})^{d_{rj} \gamma_{rj} \rho_{rijop}} \qquad (2)$$

where γ_{rj} is the proportion of sexual partners that are IDUs for IDUs in sexual activity subgroup *j*. The functions φ_{ijop} and φ_{ijop} are defined as the probabilities that a susceptible IDU in behavioural subgroup *[r,i,j]* will become HIV infected per unit time from a particular syringe-sharing or sexual partnership with an IDU in behavioral subgroup *[r,o,p]* or *[r′,o,p]*§, respectively. The two functions, ρ_{ijop} and ρ_{rijop}, are defined to represent the extent to which IDUs within any behavioral subgroup form sharing and/or sexual partnerships with IDUs with different levels of syringe-sharing and/or sexual activity and have the following form:

$$\rho_{rijop} = (1 - A_2)\frac{d_{r'p} n_{r'op}}{\sum_{\forall k,l} d_{r'l} n_{r'kl}} + A_2 \delta_{jp}\, \rho_{ijop}$$

$$= (1 - A_1) c_o \sum_{\forall r,k,l} \left[\frac{n_{rop}}{c_k n_{rkl}}\right] + A_1 \delta_{io} \qquad (3)$$

Here, δ_{io} is the *dirac-delta* function and equals one if $i = 0$ and zero otherwise, and the parameters A_1 and A_2 determine how assortative the mixing is and can be varied from zero to one (one is complete like with like assortative mixing, and zero is random mixing). The form and derivation of ρ_{ijop} and ρ_{rijop} functions is described in full in a previous article by Garnett and Anderson.[1] The products $c_i \rho_{ijop}$ and $d_{rj} \rho_{rijop}$ then, respectively, give the total number of sharing and sexual partnerships an IDU from subgroup *[r,i,j]* forms with IDUs from subgroup *[r,o,p]* or *[r′,o,p]*.

Both φ_{ijop} and φ_{rijop} are the product of the probability that an IDU from that behavioral subgroup is infected and the probability that the infected partner transmits HIV to the susceptible IDU over that time period (defined as D_{ijop} for needle-sharing partnerships and D_{rijop} for sexual partnerships).

The probabilities of HIV transmission between a susceptible and an infected individual per unit time are derived from Weinstein et al.[2] The probability (D_{ijop}) that a susceptible IDU (from subgroup *[i,j]*) becomes HIV infected if they share injecting equipment with an HIV-infected IDU (from subgroup *[o,p]*) is dependent upon whether the needle and syringe are effectively disinfected, the per-injection HIV transmission probability when using a needle and syringe that has been recently used by an HIV-infected IDU (β_{idu}), and whether the infected partner in subgroup *[o,p]* is in the high or low viraemia phase (with high viraemia increasing the injecting transmission probability by a cofactor α_{idu}).

If we assume that a susceptible IDU from subgroup *[i, j]* shares syringes with an infected IDU from subgroup *[o,p]* on ε_{io} occasions per unit time, and we let θ denote the probability that bleach has been used to clear the syringe and *b* denote the probability that the syringe is effectively disinfected, then D_{ijop} can be written as follows:

$$D_{ijop} = 1 - \left[\frac{(y_{rop} + y_{r'op})\,(1 - \beta_{idu}\,(1 - b\theta))^{\varepsilon_{io}} + (h_{rop} + h_{r'op})\,(1 - \beta_{idu}\,\alpha_{idu}\,(1 - b\theta))^{\varepsilon_{io}}}{y_{rop} + y_{r'op} + h_{rop} + h_{r'op}}\right] \qquad (4)$$

The probability per unit time (D_{rijop}) that a susceptible IDU (in subgroup *[r, i, j]*) acquires HIV infection from having sex with an HIV-infected IDU (subgroup *[r′, o, p]*) can be calculated in a similar manner. If in each unit of time, an IDU in behavioral subgroup *[r, i, j]* has η_j sex acts with each sexual partner, f_j is the probability that a condom is used per sex act, *e* is the per sex act efficacy of the condom, β_r is the probability of HIV transmission per sex act from sex *r′* to sex *r*, and α_s is the extent to which STD coinfection of either partner increases the probability of HIV transmission, then D_{rijop} can be written:

$$D_{rijop} = 1 - \left[\left(1 - \frac{y^s_{r'op}}{n_{r'op}}\right) \times \left(1 - \frac{y^s_{rij}}{n_{rij}}\right)\frac{[\Gamma h_{r'op} + \Phi y_{r'op}]}{y_{r'op} + h_{r'op}} + \frac{[h_{r'op}\mathrm{H} + y_{r'op}\mathrm{E}]}{y_{r'op} + h_{r'op}} \times \left[1 - \left(1 - \frac{y^s_{r'op}}{n_{r'op}}\right)\left(1 - \frac{y^s_{rij}}{n_{rij}}\right)\right]\right]$$

where y^s is the number of IDUs infected with an STD for different subgroups *[r, i, j]*, and

$$\Phi = [1 - \beta_r (1 - f_j e)]^{\eta_j} \qquad \mathrm{E} = [1 - \alpha_s \beta_r (1 - f_j e)]^{\eta_j}$$
$$\mathrm{H} = [1 - \alpha_{sex} \alpha_s \beta_r (1 - f_j e)]^{\eta_j} \qquad \Gamma = [1 - \alpha_{sex} \beta_r (1 - f_j e)]^{\eta_j} \qquad (5)$$

Here the variables Φ, *E*, Γ, and *H* denote the probabilities that a susceptible person, who is having sex with an HIV-infected person, does not become HIV infected per unit time in the following different situations: Neither partner has an STD and the HIV infected partner is not in the high viraemia phase (Φ), at least one partner has an STD and the HIV-infected partner is not in the high viraemia phase (*E*), neither partner has an STD but the HIV-infected partner is in the high viraemia phase (Γ), at least one partner has an STD and the HIV infected partner is in the high viraemia phase (*H*).

In the model we assume that IDUs may form heterosexual partnerships with IDUs and non-IDUs, with the extent of non-IDU partnerships being determined by the reported proportion of IDU sexual partnerships that are with non-IDUs ($1-\gamma_{rj}$). For non-IDUs, we only consider their risk of HIV transmission from having sex with IDUs and only model the dynamics of HIV transmission from the IDUs to the non-IDU population (and not vice versa).

STD Infection Dynamics

The model simulates the transmission of one STD among IDUs and between IDUs and their non-IDU sexual partners. Both HIV-susceptible and HIV-infected IDUs can acquire an STD. The per capita probability of STD infection per unit time (π_s) is analogous to the per capita probability of HIV infection per unit time (π_{sex}) (Equation *2*). If the probability of STD transmission per sex act is β_{std}, and y^s is the number of IDUs infected with an STD, for each partnership with an IDU the probability that a susceptible IDU is infected with a STD per unit time (defined as D^s_{rijop}) is:

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§ *r′* denotes the opposite sex to *r,* i.e., if $r = 0$ (male), then $r' = 1$ (female).

$$D^{s}_{rijop} = \frac{y^{s}_{r'op}}{n_{r'op}} (1 - [1 - \beta_{std} (1 - f_j e)]^{\eta_j}) \qquad (6)$$

If we let x^s denote the number of IDUs susceptible to STD infection and y^s denote the number infected with an STD, the transmission dynamics of the STD among IDUs can be described using a set of deterministic differential equations (Equation 7). For this, we assume that IDUs remain infected for a fixed period of time ($1/\mu_r$) and then become susceptible to STD infection once more.

$$\frac{dx^{s}_{rij}}{dt} = n_{rij}\Lambda_r - x^{s}_{rij}\left(\pi_s + \psi_r + \sigma_r + \frac{\delta y_{rij}}{n_{rij}}\right) + \mu_r y^{s}_{rij}$$

$$\frac{dy^{s}_{rij}}{dt} = x^{s}_{rij}\pi_s - y^{s}_{rij}\left(\mu_r + \psi_r + \sigma_r + \frac{\delta y_{rij}}{n_{rij}}\right) \qquad (7)$$

IDU = injection drug user; STD = sexually transmitted disease.

APPENDIX 2. Model Parameters

Types of Model Input	Definition of Model Input		Model Parameter	Comments of References
Epidemiological inputs	Initial HIV prevalence among IDUs			Used to fit the model, which is thereafter used to model the HIV epidemic with and without the intervention
	Average duration of high viraemia phase (months)		$1/\nu$	3
	Average duration between HIV infection and morbidity		$1/\delta$	Use site-specific data if possible
Transmission probabilities	Probability of HIV transmission per sex act (male to female)		β_0	4–8
	Ratio of probability of HIV transmission per sex act for female to male relative to male to female		*Used to calculate* β_1	
	Probability of HIV transmission per needle-sharing act		β_{idu}	9, 10
	HIV transmission cofactor during high viraemia phase		α_{sex} and α_{idu}	3, 11, 12
	Condom efficacy per sex act		e	13, 14
	Cleaning efficacy per sharing act		b	15–23
Size of IDU population and intervention coverage	Proportion of IDUs that have injected for less than one year		Λ_r	Use site-specific data if possible
	IDU mortality rate per 1000 person-years		ψ_r	
	Initial size of IDU population		N_r*-used to calculate*	
	Ratio of male-to-female IDU population		n_{rij} *parameters*	
	Number of IDUs attending the NEPs			These individuals are given the 'reached' risk behavior
Sexual behavior inputs	Definition of "low" and "high" number of sexual partners per 6 months (low) or month (high)	Low	d_{rl}	
		High	$d_{rj}, j = 2–4$	
	Population distribution of male IDUs with respect to their level of sexual activity (%)	None	S_{00}	S_{rj} variables are used to calculate n_{rij}*
		Low	S_{01}	
		High	$S_{02} = S_{03} = S_{04}$	
	Population distribution of female IDUs with respect to their level of sexual activity (%)	None	S_{10}	
		Low	S_{11}	
		High	$S_{12} = S_{13} = S_{14}$	
	Degree of assortative sexual mixing between individuals of different sexual activity (0 is random mixing and 1 is full assortative mixing)		A_2	Little data but reviews of data from elsewhere suggest sexual mixing is usually only weakly assortative[24]
	Proportion of reached IDUs sexual partners that are IDUs for low and high sexual activity	Low	γ_{rl}	
		High	$\gamma_{rj}, j = 2–4$	
Syringe sharing behaviour inputs	Average consistency of cleaning syringes	θ		
	Definition of "low" and "high" rate of needle sharing partners in last month	Low	c_1	
		High	c_2	
	Population distribution of IDUs with respect to their level of needle sharing in last month	None	Z_{r0}	Z_{ri} variables are used to calculate n_{rij}*
		Low	Z_{r1}	
		High	Z_{r2}	
	Degree of assortative mixing between individuals of different syringe sharing behavior activity (0 is random mixing and 1 is full assortative mixing)		A_1	
Condom use inputs	Consistency of condom use amongst stable partnerships		f_1	Ω_{rj} variables are used to calculate n_{rij}. * None refers to using condoms in few sex acts (f_2 %), Half refers to condom being used in some (f_3 %) of sex acts, and All refers to condoms being using in nearly all of the sex acts (f_4 %)
	Population distribution of condom use amongst casual sexual partnerships	None	Ω_{r2}	
		Half	Ω_{r3}	
		All	Ω_{r4}	

IDU indicates injection drug user.

*These variables are used to calculate $n_{rij} = N_r S_{rj} Z_{ri} \Omega_{rj}$. When these variables are undefined for certain *r, i,* and *j,* they take the value 1.

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