

Effectiveness and cost-effectiveness of strategies to expand antiretroviral therapy in St. Petersburg, Russia

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Objective: To assess the effectiveness and cost-effectiveness of treating HIV-infected injection drug users (IDUs) and non-IDUs in Russia with highly active antiretroviral therapy HAART.

Design and methods: A dynamic HIV epidemic model was developed for a population of IDUs and non-IDUs. The location for the study was St. Petersburg, Russia. The adult population aged 15 to 49 years was subdivided on the basis of injection drug use and HIV status. HIV treatment targeted to IDUs and non-IDUs, and untargeted treatment interventions were considered. Health care costs and quality-adjusted life years (QALYs) experienced in the population were measured, and HIV prevalence, HIV infections averted, and incremental cost-effectiveness ratios of different HAART strategies were calculated.

Results: With no incremental HAART programs, HIV prevalence reached 64% among IDUs and 1.7% among non-IDUs after 20 years. If treatment were targeted to IDUs, over 40 000 infections would be prevented (75% among non-IDUs), adding 650 000 QALYs at a cost of US\$ 1501 per QALY gained. If treatment were targeted to non-IDUs, fewer than 10 000 infections would be prevented, adding 400 000 QALYs at a cost of US\$ 2572 per QALY gained. Untargeted strategies prevented the most infections, adding 950 000 QALYs at a cost of US\$ 1827 per QALY gained. Our results were sensitive to HIV transmission parameters.

Conclusions: Expanded use of antiretroviral therapy in St. Petersburg, Russia would generate enormous population-wide health benefits and be economically efficient. Exclusively treating non-IDUs provided the least health benefit, and was the least economically efficient. Our findings highlight the urgency of initiating HAART for *both* IDUs and non-IDUs in Russia.

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Introduction

Russia has experienced one of the fastest growing HIV epidemics in the world, with an estimated 90% of the country's HIV cases registered after 2000 [1,2]. In 2005, the official number of registered HIV cases in Russia exceeded 300 000; however, experts believe the number of HIV-infected individuals is closer to 860 000 (range:

420 000–1.4 million) [2–4]. The HIV epidemic in Russia has been fuelled largely by a dramatic rise in injection drug use over the last 15 years. The estimated 1.5–3 million injection drug users (IDUs) in Russia account for 70–85% of all registered HIV cases [1,3,5].

Virtually no active IDUs and only 5000 non-IDUs in Russia received highly active antiretroviral therapy

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(HAART) in 2005 [1,6]. By the end of 2005, approximately 139 000 individuals in Russia are expected to need HAART, although the number may be as high as 250 000 [1,7]. HAART dramatically reduces mortality from HIV infection. HAART also reduces HIV infectivity and may therefore provide substantial benefits from reduced transmission of HIV [7–10].

Although the HIV epidemic in Russia has been driven by injection drug use, current HIV treatment resources are targeted almost exclusively to non-IDUs, in part because of concerns about adherence with HAART among IDUs [11]. To understand whether such a strategy could be successful in slowing the HIV epidemic in Russia, we evaluated the effectiveness and cost-effectiveness of treatment strategies that target non-IDUs. We also evaluated treatment strategies that target IDUs, and untargeted strategies that provide HAART without regard to injection drug use status. Previous studies have evaluated the cost-effectiveness of HAART programs in the US [12,13] but no studies of the cost-effectiveness of HAART programs in Russia have appeared.

Methods

Overview

We developed a dynamic compartmental model of HIV transmission and progression in a population of IDUs and non-IDUs. Compartmental models have been used to evaluate the cost-effectiveness of a variety of HIV prevention and treatment programs [14–16]. Individuals transitioned between compartments according to rates defined by the dynamics of disease transmission and progression [7]. Additionally, individuals who began HAART transitioned from an untreated to a treated compartment. We implemented the model in Microsoft Excel 2003. Full details of the model are provided in the Appendix, available at www.stanford.edu/~brandeau/RussiaAIDSAppendix, or from the authors upon request.

We implemented the model using data for St. Petersburg, which has relatively high HIV prevalence, and conducted sensitivity analysis using data for Barnaul, a city with lower HIV prevalence [3,17–20]. Key parameter values and sources are summarized in Table 1; the Appendix (Table A2) shows additional data and sources, and values considered in sensitivity analysis.

Population groups

We considered the adult population of men and women aged 15 to 49 in St. Petersburg. The population was subdivided into 12 groups, based on injecting behavior (IDU or non-IDU), HIV status (uninfected, asymptomatic HIV, symptomatic HIV, or AIDS), and treatment status if HIV-infected (receiving HAART or not receiving HAART). We defined the stage of HIV infection

(asymptomatic HIV, symptomatic HIV, or AIDS) according to CD4 cell count (> 350 , $200\text{--}350$, or < 200 cells/ μl). We defined compartments to capture variations in key parameters (e.g., viral transmissibility and quality of life) across different health states. For these analyses, we assumed HIV-infected individuals have already been identified, either through screening programs or evaluation of symptoms.

In the base case, approximately 4% of adults aged 15 to 49 years were IDUs, and initial HIV prevalence was 35% among IDUs and 0.63% among non-IDUs, based on data from St. Petersburg (Table 1 and Appendix Table A2) [3–5,17–19]. In sensitivity analysis, we implemented the model using data from Barnaul, a smaller city (population, 600 000) in south-western Siberia where approximately 6.4% of adults were IDUs, and initial HIV prevalence was 1.7% among IDUs and 0.06% among non-IDUs (Table 1 and Appendix Table A2) [3,20].

Population dynamics

Individuals entered the population as a result of maturation (14-year-olds turn 15). All new entrants were assumed to be uninfected. Individuals exited the population as a result of maturation (49-year-olds turn 50) or death from HIV or other causes. We considered the adult population aged 15 to 49 years because the majority of HIV infections occur in this age group. The annual non-AIDS-related death rate for IDUs was significantly higher than for non-IDUs, due to the increased risk of mortality from drug overdose and other complications of injection drug use (Appendix Table A2). Based on data from St. Petersburg, the estimated total annual death rate exceeded the birth rate; thus, the population decreased over time (Appendix Table A2).

HIV transmission and progression

The model incorporated HIV transmission via needle-sharing and sexual partnerships. We estimated the average number of injections per year, the fraction of injections that were shared, and the probability of infection transmission to an uninfected individual per risky injection (i.e., an injection involving a needle previously used by an HIV-infected individual) (Table 1 and Appendix Table A2) [15–17,21–24]. The latter parameter varied across IDU compartments because injection transmissibility depended on viral load and whether the individual was undergoing HAART [7]. Estimates of needle-sharing behavior reflect common practice in Russia, which includes some needle-cleaning prior to injecting [25].

We modeled HIV transmission via sexual contact on a per partnership basis. All sexual partnerships resulted from random mixing, although we allowed for preferential mixing between IDUs and non-IDUs. We estimated the average number of new sexual partnerships per year, the average condom usage rate, condom effectiveness, and

Table 1. Model parameters and sources^a.

Parameter	Value	Range	Source
Demographic parameters			
HIV prevalence among IDUs			
St. Petersburg, Russia	35%	20–40%	[17–19]
Barnaul, Russia	1.67%	0.6–8.8%	[3,20]
HIV prevalence among non-IDUs			
St. Petersburg, Russia	0.63%	0.35–1%	[3–5]
Barnaul, Russia	0.06%	0.02–0.09%	Calculated [3,20]
Injection drug use parameters			
Number of injections per year	250	200–300	[15–17,21,22,24]
Proportion of injections that are shared			
St. Petersburg, Russia	15%	8–25%	[15–17,22,23]
Barnaul, Russia	8%	4–12%	[24]
Reduction in infectivity by injection drug use if on HAART	50%	10–90%	[7]
Sexual behavior parameters			
Number of sexual partnerships per year			
IDU	4.3	3.0–10.0	[15,16,25]
Non-IDU			
St. Petersburg, Russia	1.3	1.0–1.8	[15,16,25,26,28]
Barnaul, Russia	1.1	0.9–1.7	[15,16,24,26,28]
Proportion of IDUs sexual partnerships with another IDU	45%	20–50%	[17,23]
Proportion of sexual partnerships that involve condom use			
IDU	20%	10–30%	[15,16,27]
Non-IDU	30%	20–40%	[15,16,28]
Condom effectiveness	90%	85–95%	[15,16,29]
Reduction in infectivity by sexual contact if on HAART	90%	50–99%	[7–10]
Cost parameters			
Annual healthcare costs (non-HIV-related)	US\$ 115	US\$ 80–250	[36]
Annual HIV-related healthcare costs	US\$ 570	US\$ 450–1 000	[35]
Annual HAART costs	US\$ 1 700	US\$ 800–3 000	[33,34]
Annual counseling and adherence services costs	US\$ 250	US\$ 100–500	Estimated based on interviews with HIV prevention experts in Russia
Annual ancillary IDU services costs	US\$ 500	US\$ 300–1 000	Estimated based on interviews with HIV prevention experts in Russia

^aParameter values and ranges were estimated based on the sources listed. IDU, injection drug user.

the annual probability of infection transmission to an uninfected individual per unprotected sexual partnership (Table 1 and Appendix Table A2) [15,16,25–29]. The data reflect average sexual behavior practices in the non-IDU population, which may include high-risk individuals such as commercial sex workers.

We estimated the rate at which HIV-infected individuals progressed through disease states based on a detailed model of the natural history of HIV infection and the effect of HAART on disease progression (Appendix Table A2). We assumed that IDUs and non-IDUs experienced similar disease progression rates. For each compartment, we estimated the rate of death from HIV and other causes (Appendix Table A2).

Highly active antiretroviral therapy

Antiretroviral therapy for HIV includes the use of multiple antiretroviral drugs in combination, known as HAART, with the goal of completely suppressing HIV

viral replication. We assumed that HAART would be given according to current treatment guidelines, as specified by the US Department of Health and Human Services [7,30–32]. In our model, HIV-infected individuals with a CD4 cell count below 350 cells/ μ l (i.e., symptomatic HIV or AIDS) were eligible to receive HAART [7,30–32]. The primary advantages of HAART include a reduction in viral load – and thus, infectivity – and a delay in the progression of HIV infection [7,32]. We estimated that suppressive HAART reduced the annual probability of HIV transmission per sexual partnership by 90% (Table 1) [7–10]. The degree to which HAART reduces transmission from shared needle use is unknown; in our base-case analyses, we assumed the reduction was 50%, substantially less than for sexual transmission due to the probable higher efficiency of transmission from shared needles (Table 1) [7]. Based on a model of the natural history of HIV and the effectiveness of HAART, we estimated that HAART reduced the annual AIDS-related death rate by 20%, and led to a six-fold reduction in the

Table 2. Results for St. Petersburg^a.

St. Petersburg, Russia	Status quo	IDU targeted treatment strategy	Non-IDU targeted treatment strategy	Untargeted treatment strategy	Optimistic untargeted treatment strategy
Costs (US\$ 1000s)	9425985	10392885	10471769	10610477	11163471
QALYs (1000s)	75249	75893	75,656	75,880	76200
Incremental cost-effectiveness ratio	–	US\$ 1501	US\$ 2572	US\$ 1877	US\$ 1827
HIV prevalence after 20 years					
Among IDUs	63.6%	62.6%	63.4%	63.0%	62.3%
Among non-IDUs	1.7%	1.1%	2.1%	1.6%	1.4%
Number of people treated	636	50226	47030	57396	84100
HIV infections averted					
Among IDUs	– ^b	10830	45	6810	10934
Among non-IDUs	– ^b	29547	9418	23956	36544
Total	– ^b	40377	9463	30766	47478

IDU, injection drug user; QALYs, quality-adjusted life years.

^aThis table shows health and economic outcomes, using data for St. Petersburg, Russia. The incremental cost-effectiveness ratio for each strategy is relative to the status quo.

^bWith the status quo, a total of 212 704 HIV infections occurred over 20 years, including 110 172 among IDUs and 102 532 among non-IDUs.

progression rate from symptomatic HIV to AIDS (Appendix Table A2).

Interventions

In 2005, virtually no HIV-infected IDUs and approximately 1% of HIV-infected non-IDUs received HAART in Russia. We considered four incremental HAART programs: 80% of infected, treatment-eligible IDUs and 1% of infected, treatment-eligible non-IDUs receive HAART (IDU targeted treatment strategy); no infected IDUs and 80% of infected, treatment-eligible non-IDUs receive HAART (non-IDU targeted treatment strategy); 50% of all infected, treatment-eligible IDUs and non-IDUs receive HAART (untargeted treatment strategy); 80% of all infected, treatment-eligible IDUs and non-IDUs receive HAART (optimistic untargeted treatment strategy). In order to account for incomplete accessibility and imperfect adherence to HAART programs, we estimated that at most 80% of infected individuals could be treated with HAART.

Health outcomes and costs

For each intervention, we estimated quality-adjusted life years (QALYs) gained and costs incurred over a 20-year time horizon, as well as all future lifetime healthcare costs and QALYs, discounted to the present at 3% annually. For infected individuals, quality of life decreased with HIV disease progression (Appendix Table A2). We assumed that IDUs have a lower quality of life than non-IDUs by a (multiplicative) factor of 0.9 (Appendix Table A2).

We estimated the annual per person cost of HAART in St. Petersburg to be US\$ 1950, based on prices that have been recently negotiated in Russia [33,34]. For IDUs who received HAART, we included an additional annual cost of US\$ 500 for outreach, counseling, and adherence interventions. For all individuals with HIV, we estimated the annual non-HAART healthcare costs to be US\$ 570 [35]. All individuals, whether HIV infected or not, incurred an annual healthcare cost of US\$ 115 [36].

Results

HIV infections prevented

We estimated the resource requirements for each treatment strategy, measured by number of people treated over the 20-year time horizon, and calculated the (undiscounted) number of HIV infections prevented over the 20-year time horizon (Table 2; Fig. 1). The optimistic

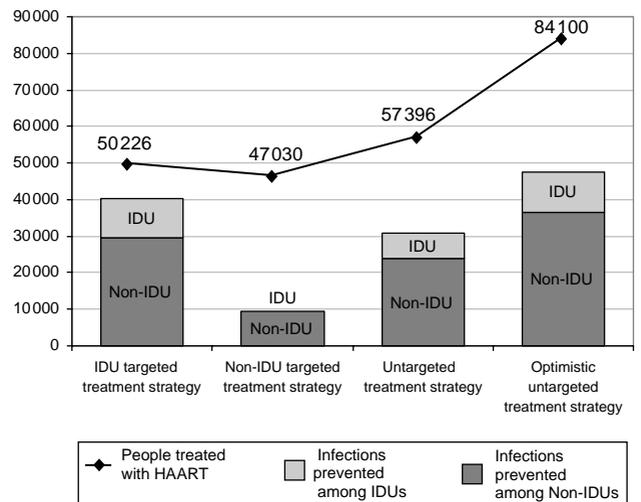


Fig. 1. Estimated number of people treated with HAART and estimated number of HIV infections prevented over 20 years among injection drug users (IDUs) and non-IDUs in St. Petersburg. This graph illustrates (a) the resource requirements for each treatment strategy, in terms of (undiscounted) number of people treated over 20 years, and (b) the net benefit to society for each treatment strategy, in terms of (undiscounted) number of infections prevented over 20 years. The line graph corresponds to the total number of IDUs and non-IDUs treated with HAART over 20 years for each treatment strategy. The light gray area corresponds to total HIV infections prevented among IDUs over 20 years, and the mid gray area corresponds to total HIV infections prevented among non-IDUs over 20 years.

untargeted treatment strategy treated the most people (84 100) and prevented the most infections (11 000 among IDUs and 36 500 among non-IDUs). The IDU targeted treatment strategy treated 50 200 people and prevented 40 000 infections, including 30 000 infections among *non-IDUs*, due to reduced sexual transmission from IDUs to non-IDUs. The untargeted treatment strategy treated 57 300 people and prevented 30 800 infections (6800 among IDUs and 24 000 among non-IDUs). The non-IDU targeted treatment strategy treated 47 000 people and prevented the fewest infections (9500), almost all among non-IDUs.

HIV prevalence

With no incremental HAART programs, we estimated that HIV prevalence among IDUs would reach 63.6% after 20 years (Fig. 2a). Strategies that included treatment of IDUs had only a modest effect on prevalence among IDUs: even though these strategies prevented many infections among IDUs, HIV-infected IDUs lived longer, which attenuated reductions in prevalence.

With no incremental HAART programs, we estimated HIV prevalence among non-IDUs to be 1.7% after 20 years (Fig. 2b). All treatment programs that included IDUs reduced HIV prevalence among non-IDUs (to 1.1% with the IDU targeted treatment strategy, to 1.6% with the untargeted treatment strategy, and to 1.4% with the optimistic untargeted treatment strategy) (Fig. 2b). If the non-IDU targeted treatment strategy were implemented, the prevalence of HIV after 20 years increased to 2.1%. This seemingly paradoxical result occurred because relatively few infections were prevented and each infected individual lived longer; the net effect was an increase in prevalence. Strategies that included treatment of IDUs reduced prevalence among non-IDUs because the reduction in prevalence from infections averted outweighed increases in prevalence due to infected individuals living longer.

We calibrated the results of our model by comparing the model's estimates of HIV prevalence with observed HIV prevalence in St. Petersburg. The number of registered HIV cases in Russia is thought to underestimate actual HIV prevalence, and estimates of prevalence vary substantially [2–4]. In addition, empirical evidence about longitudinal changes in prevalence in specific population groups is sparse. However, HIV prevalence as calculated by the model is consistent with estimated HIV prevalence in Russia and trends observed in IDUs and non-IDUs.

Cost-effectiveness

We evaluated the cost, effectiveness, and cost-effectiveness of each treatment strategy (Table 2 and Fig. 3). We report the cost-effectiveness ratios of each strategy relative to the status quo, rather than to the next best alternative, because some of the strategies may not be feasible or

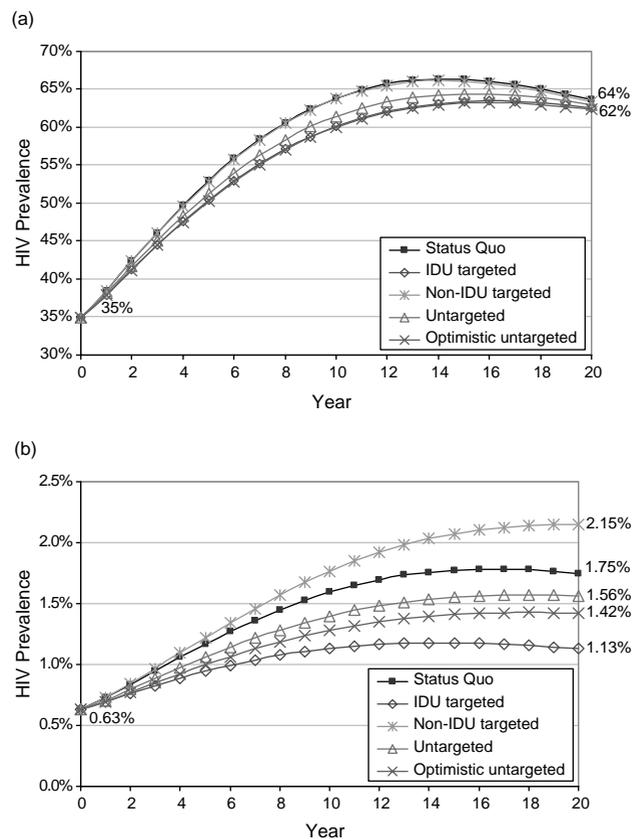


Fig. 2. Estimated HIV prevalence among (a) injection drug users (IDUs) and (b) non-IDUs in St. Petersburg for different treatment strategies. All strategies for IDUs have a starting HIV prevalence of 35% and all strategies for non-IDUs have a starting HIV prevalence of 0.63%. Under the status quo, no active IDUs and 1% of non-IDUs receive HAART. The IDU targeted treatment strategy corresponds to 80% of IDUs receiving HAART. The non-IDU targeted treatment strategy corresponds to 80% of non-IDUs receiving HAART. The untargeted treatment strategy corresponds to 50% of both IDUs and non-IDUs receiving HAART. The optimistic untargeted treatment strategy corresponds to 80% of both IDUs and non-IDUs receiving HAART.

considered appropriate (e.g., targeting resources exclusively to IDUs).

The least effective strategy was to target antiretroviral treatment only to non-IDUs. The most effective treatment was to treat as many HIV-infected people as possible (optimistic untargeted treatment strategy); this strategy was also the most expensive. The IDU targeted treatment strategy and the untargeted treatment strategy had similar effectiveness, but the IDU targeted treatment strategy cost substantially less. Of note, the IDU targeted treatment strategy was both more effective and less expensive than the non-IDU targeted treatment strategy.

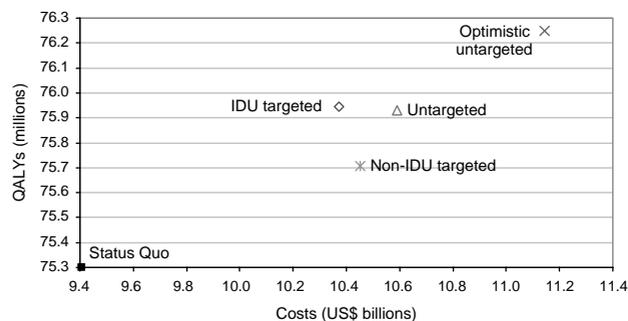


Fig. 3. Cost-effectiveness of treatment programs for St. Petersburg. Each point on the graph represents the costs and quality-adjusted life years (QALYs) incurred over a 20-year time horizon for the corresponding treatment strategy. Under the status quo, no active injection drug user (IDUs) and 1% of non-IDUs receive HAART. The IDU targeted treatment strategy corresponds to 80% of IDUs receiving HAART. The non-IDU targeted treatment strategy corresponds to 80% of non-IDUs receiving HAART. The untargeted treatment strategy corresponds to 50% of both IDUs and non-IDUs receiving HAART. The optimistic untargeted treatment strategy corresponds to 80% of both IDUs and non-IDUs receiving HAART.

The cost-effectiveness of expanded antiretroviral treatment relative to the current level of treatment ranged from US\$ 1500 to US\$ 2600 per QALY gained, depending on the strategy (Table 2, Fig. 3). Allocation of treatment resources to IDUs was the most cost-effective, and allocation of resources exclusively to non-IDUs was the least cost-effective. After eliminating the IDU targeted treatment strategy, which may be considered inappropriate, the incremental cost-effectiveness ratio of the best strategy (optimistic untargeted treatment strategy) to the next best strategy (untargeted treatment strategy) is US\$ 1729.

Sensitivity analyses

We performed sensitivity analysis over estimated data ranges for all parameters (Appendix Tables A2 and A3). The number of HIV infections averted over 20 years was sensitive to four key parameters: sexual transmission infectivity, HAART-related reductions in infectivity, risky injecting behavior, and risky sexual behavior (Appendix Table A3).

In our model, non-IDUs can only be infected via sexual contact. We evaluated the effect on infections averted if the annual probability of sexual transmission per partnership was moderately higher or lower. As in the base case, the IDU targeted treatment strategy prevented more HIV infections and was more cost-effective than was the non-IDU targeted treatment strategy.

We conducted sensitivity analysis on the effectiveness of HAART at reducing HIV transmission from injection drug use and sexual contact. If HAART reduced injection

infectivity by only 10% (instead of 50% as assumed in the base case), the IDU targeted treatment strategy prevented 30 114 infections, whereas the non-IDU targeted treatment strategy prevented 9463 infections. Conversely, if HAART reduced sexual infectivity by only 50% (instead of 90% as assumed in the base case), the IDU targeted treatment strategy prevented 18 691 infections, in comparison with 2732 infections prevented by the non-IDU targeted treatment strategy. If HAART was less effective at reducing both injection infectivity (10% reduction) and sexual infectivity (50% reduction), the IDU targeted treatment strategy prevented 9021 infections, more than three times the number of infections prevented by the non-IDU targeted treatment strategy. In all cases, the overall pattern of our findings remained unchanged: the IDU targeted treatment strategy was substantially more effective at preventing infections among both IDUs and non-IDUs than the non-IDU targeted treatment strategy. Additionally, the IDU targeted treatment strategy was more cost-effective than the non-IDU targeted treatment strategy, regardless of the effectiveness of HAART in reducing infectivity.

Comprehensive data on risky injecting and sexual behavior in Russia is very limited. We performed two-way sensitivity analysis on the annual number of injections per year and the fraction of injections that involve a shared needle. We also conducted sensitivity analysis on the annual number of sexual partnerships for IDUs and non-IDUs. Variations in risky injection behavior led to greater variation in infections prevented among IDUs; variations in risky sexual behavior led to greater variation in infections prevented among non-IDUs.

The cost of HAART is expected to decrease three-fold in Russia over the next 5 years, as Russian officials have negotiated lower prices from several drug manufacturers [1,34]. We estimated the incremental cost-effectiveness ratio if the annual cost of HAART, including counseling and adherence services, was significantly greater or less than assumed in the base case. In both cases, the IDU targeted treatment strategy was almost twice as cost-effective as the non-IDU targeted treatment strategy (Appendix Table A3).

Because St. Petersburg has relatively high HIV prevalence, we also estimated the effect of HAART programs in a low-prevalence region, using epidemiologic and behavioral data for the city of Barnaul. To ensure comparability with prior analyses, we assumed treatment levels similar to St. Petersburg, although actual treatment rates may be higher in Barnaul. The results for Barnaul (Appendix Table A4) are qualitatively similar to those for St. Petersburg and emphasize the benefits of providing IDUs and non-IDUs with access to HAART. The IDU targeted treatment strategy averted more infections and was more cost-effective than the other treatment strategies, and the IDU targeted treatment strategy

generated more QALYs at less total cost than did the non-IDU targeted treatment strategy.

Discussion

We developed an epidemic model of HIV in Russia to assess the health outcomes and costs associated with strategies to expand antiretroviral use. Our analysis indicated that expanded use of antiretroviral therapy, if appropriately implemented, could dramatically reduce HIV incidence among the general population in Russia, would result in enormous population-wide health benefits, and would be economically efficient. Our analysis also showed that the strategy of focusing treatment resources almost exclusively on non-IDUs, which is the current strategy in Russia, provided the least health benefit, was the least economically efficient, and will likely fail to slow the spread of HIV among IDUs or the general population.

We assessed strategies that focus on the IDU population to understand the significance of this mode of transmission in the overall epidemic. The importance of treatment for IDUs is highlighted by our finding that targeting HAART exclusively to IDUs prevented more HIV infections among non-IDUs than did targeting HAART exclusively to non-IDUs. Targeting treatment to IDUs prevented four times as many infections as treating only non-IDUs, and three-quarters of the prevented infections were among non-IDUs. Nonetheless, we neither advocate, nor consider appropriate, strategies that exclusively treat IDUs. Rather, our findings emphasize the critical need to include plans to treat both IDUs and non-IDUs as antiretroviral treatment is expanded in Russia.

A key question is whether providing antiretroviral treatment to IDUs in Russia is feasible, and whether adherence with treatment in these groups would be sufficient to obtain the benefits estimated in our analysis. Our analyses assumed that delivery of HAART to IDUs would require more intensive ancillary support, and we included an additional annual cost of US\$ 500 per IDU for services such as treatment for substance abuse, interventions to improve adherence, and social services. Treatment for substance abuse and harm reduction programs are important adjuncts to provision of HAART, and can include substitution therapy, needle exchange, and safer injection sites. Recent studies in other settings have found that both IDUs and non-IDUs who utilize counseling and support services exhibit similar adherence and drug resistance to all major antiretroviral treatment regimens [11,37]. In addition, substitution therapy can improve adherence and therapeutic response to HAART [38]. Experience with treatment and harm reduction programs in Russia is limited, so empirical evidence about their feasibility in Russia is lacking. Successful implementation of such programs would require changes in

national law regarding substitution therapy, and consistent regional implementation of recent changes in laws intended to increase access to harm reduction and treatment.

The cost-effectiveness of expanded use of antiretroviral therapy in Russia is favorable when judged by criteria developed by the World Health Organization (WHO) [39]. WHO criteria consider a health intervention cost-effective if it costs less than three times per capita gross domestic product (GDP). GDP in Russia was US\$ 9800 in 2004, and thus treatment with antiretroviral therapy meets WHO guidelines. However, interpretation of the cost-effectiveness of interventions in Russia is challenging because very few interventions have been evaluated with cost-effectiveness analysis [40]. The cost-effectiveness of all treatment strategies will improve substantially if the cost of antiretroviral therapy decreases further. Finally, the cost-effectiveness of a strategy should be viewed in the broader context of other important factors such as equity. Although therapy targeted to IDUs is the most cost-effective strategy, we consider it to fail the criterion of equity, leaving untargeted therapy as the most efficient approach.

The effect of expanded antiretroviral use on the course of the HIV epidemic depends on the degree to which HIV transmission by sex and injection drug use is reduced. This reduction depends on the reduction in viral load from HAART and on baseline sexual and needle-sharing behaviors. Reductions in sexual transmission from use of HAART have been well documented but a reduction from decreased transmission by needle sharing, although reasonable, is speculative [7–10]. However, even if we assumed that HAART reduced transmission via needle sharing by only 10%, the overall conclusions of our analysis remained unchanged.

The epidemiology of HIV varies substantially in different geographic locations within Russia. Our primary analyses used data from St. Petersburg, which has a relatively high HIV prevalence among IDUs and commercial sex workers. To understand whether our results could be generalized to other regions, we also evaluated the costs and benefits of expanded antiretroviral therapy in Barnaul. Although Barnaul has a substantial population of IDUs, HIV prevalence among IDUs remains less than 2%, for reasons that are not fully understood. The general pattern of our findings remained the same in Barnaul, with the exception that the IDU targeted treatment strategy averted the most infections.

In summary, our analyses demonstrated quantitatively that slowing the spread of HIV in St. Petersburg, Russia is inextricably linked to antiretroviral treatment for the IDU population. Successful provision of antiretroviral therapy will depend on concomitant treatment of substance abuse. Treatment of substance abuse in Russia presents

many challenges. Health care resources are highly constrained, harm reduction programs are uncommon, and substitution therapy with methadone is illegal. Plans to expand antiretroviral therapy in St. Petersburg provide the potential for enormous health benefits. However, if the full potential of this investment in health is to be realized, antiretroviral treatment must reach both the IDU and non-IDU populations.

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