HIV in Russia

Cost-effectiveness of Treating Injection Drug Users with Antiretroviral Therapy

Elisa F. Long, M.S.
Margaret L. Brandeau, Ph.D.
Tatyana Vinichenko, M.D., M.P.A.
Cristina M. Galvin, M.S.
Swati P. Tole, M.D.
Adam Schwartz
Gillian D. Sanders, Ph.D.
Douglas K. Owens, M.D., M.S.

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A global view of HIV infection:
38.6 million people living with HIV in 2005


IDUs are a key element of the global HIV epidemic

- Injection drug users comprise 10% of all HIV cases globally

- Outside sub-Saharan Africa, 1/3 of new HIV infections are due to injection drug use

- In many parts of Eastern Europe and Central and South Asia, needle-sharing is fueling the HIV epidemic

Russia is experiencing one of the fastest growing HIV epidemics in the world

- Official number of HIV cases exceeded 300,000 in 2005
- Experts believe actual number of HIV cases is closer to 1 million
- 90% of HIV infections occurred in the past 5 years
- Disproportionate effect on young people
  - Russia: 80% of infected individuals are under the age of 30
  - North America & Western Europe: 30% of infected individuals are under the age of 30
Injection drug use is a key driver of the HIV epidemic in Russia

• Estimated **1.5-3 million** IDUs in Russia

• IDUs account for **80-90%** of all HIV cases in Russia

• Few harm reduction programs exist
  – Only **2%** of IDUs have access to needle-exchange programs
  – Drug substitution therapy (methadone) is **illegal**
  – In Moscow, no needle-exchange programs exist, syringes cannot be purchased, and possession of a syringe with drug residue is a punishable offense
Access to HIV treatment is limited in Russia

- In 2005, virtually no IDUs and approximately 5,000 non-IDUs received highly active antiretroviral therapy (HAART)

- Estimated 139,000-250,000 people needed HAART at the end of 2005

- Russia has very limited resources for HIV prevention and treatment
Identifying relevant policy questions

• Interviewed local physicians, NGOs, and researchers in Russia to identify the key HIV policy questions

• Focus in developing countries:
  – Identification of key high-risk groups
  – Optimal resource allocation of HIV treatment and prevention
  – Implementation and delivery of intervention strategies
Research questions

1. What is the cost-effectiveness of alternative strategies to expand use of HAART in Russia?

2. How does expanded use of HAART in different risk groups affect the HIV epidemic in Russia?
Developed an epidemic and economic model of HIV in Russia

• Created dynamic compartmental model based on:
  – Injection drug use behavior
  – HIV status
  – Treatment status if infected

• Estimated health costs and benefits

• Simulated model over 20-year time horizon

• Considered 2 cities in Russia
  – St. Petersburg
  – Barnaul
Schematic diagram of HIV transmission model

HIV-

HIV+ Asymptomatic
CD4 >350 cells/mm³

HIV+ Symptomatic
CD4 200-350 cells/mm³

AIDS
CD4 <200 cells/mm³

IDUs

Untreated → Untreated → Untreated → Untreated → Untreated

Non-IDUs

Untreated → Untreated → Untreated → Untreated → Untreated
Transmission model details

• Developed system of simultaneous nonlinear differential equations
  – 1 equation for each compartment

• Used discrete-time approximations to continuous-time differential equations

• Performed simulation in Microsoft Excel

• Assumed deterministic parameter values and varied all parameters in sensitivity analysis
Transmission model equations

**IDU equations**

\[
\frac{dX_1(t)}{dt} = \rho_1 - X_1(t) \left[ \mu_1 + \delta_1 + \sum_{j=7}^{12} \lambda_{1,j}(t) \right]
\]

\[
\frac{dX_2(t)}{dt} = X_1(t) \left[ \sum_{j=2}^{7} \lambda_{1,j}(t) \right] - X_2(t) \left[ \mu_2 + \delta_2 + \alpha_2 + \theta_2 \right]
\]

\[
\frac{dX_3(t)}{dt} = X_5(t) \phi_{5,3} + X_2(t) \theta_3 - X_3(t) \left[ \phi_{3,5} + \mu_5 + \delta_5 + \alpha_5 + \theta_5 \right]
\]

\[
\frac{dX_4(t)}{dt} = X_6(t) \phi_{6,4} + X_3(t) \theta_3 - X_4(t) \left[ \phi_{4,6} + \mu_4 + \delta_4 + \alpha_4 \right]
\]

\[
\frac{dX_5(t)}{dt} = X_3(t) \phi_{3,5} - X_5(t) \left[ \phi_{5,3} + \mu_5 + \delta_5 + \alpha_5 + \theta_5 \right]
\]

\[
\frac{dX_6(t)}{dt} = X_4(t) \phi_{4,6} + X_3(t) \theta_3 - X_6(t) \left[ \phi_{6,4} + \mu_6 + \delta_6 + \alpha_6 \right]
\]

**Non-IDU equations**

\[
\frac{dX_7(t)}{dt} = \rho_7 - X_7(t) \left[ \mu_7 + \delta_7 + \sum_{j=2}^{12} \lambda_{7,j}(t) \right]
\]

\[
\frac{dX_8(t)}{dt} = X_7(t) \left[ \sum_{j=2}^{7} \lambda_{7,j}(t) \right] - X_8(t) \left[ \mu_8 + \delta_8 + \alpha_8 + \theta_8 \right]
\]

\[
\frac{dX_9(t)}{dt} = X_11(t) \phi_{11,9} + X_8(t) \theta_8 - X_9(t) \left[ \phi_{9,11} + \mu_9 + \delta_9 + \alpha_9 + \theta_9 \right]
\]

\[
\frac{dX_{10}(t)}{dt} = X_12(t) \phi_{12,10} + X_9(t) \theta_9 - X_{10}(t) \left[ \phi_{10,12} + \mu_{10} + \delta_{10} + \alpha_{10} \right]
\]

\[
\frac{dX_{11}(t)}{dt} = X_9(t) \phi_{9,11} - X_{11}(t) \left[ \phi_{11,9} + \mu_{11} + \delta_{11} + \alpha_{11} + \theta_{11} \right]
\]

\[
\frac{dX_{12}(t)}{dt} = X_{10}(t) \phi_{10,12} + X_{11}(t) \theta_{11} - X_{12}(t) \left[ \phi_{12,10} + \mu_{12} + \delta_{12} + \alpha_{12} \right]
\]
Example calculations

Rate of change in number of **uninfected IDUs**:

\[
\frac{dX_1(t)}{dt} = \rho_1 - X_1(t) \left[ \mu_1 + \delta_1 + \sum_{j=2}^{12} \lambda_{1,j}(t) \right]
\]

- **Entry rate into population**
- **Number of uninfected IDUs at time t**
- **Maturation rate out of population**
- **Non-AIDS death rate**
- **Total sufficient contact rate with all infected individuals**
Example calculations

Rate of change in number of **IDUs with AIDS (untreated)**:

\[
\frac{dX_4(t)}{dt} = X_6(t)\phi_{6,4} + X_3(t)\theta_3 - X_4(t)\left[\phi_{4,6} + \mu_4 + \delta_4 + \alpha_4\right]
\]

- **IDUs with AIDS who leave treatment**
- **IDUs with symptomatic HIV that progress to AIDS**
- Number of **IDUs with AIDS (untreated)** at time \(t\)
- **Entry rate into treatment**
- **Maturation rate out of population**
- **Non-AIDS death rate**
- **AIDS death rate**
Outcome measures

\[ IDU \text{ HIV Prevalence} = \left[ \frac{\sum_{i=2}^{6} X_i(t)}{\sum_{i=1}^{6} X_i(t)} \right] \]

\[ Non-IDU \text{ HIV Prevalence} = \left[ \frac{\sum_{i=8}^{12} X_i(t)}{\sum_{i=7}^{12} X_i(t)} \right] \]
Outcome measures

\[
\text{IDU New HIV Infections} = \int_0^T \sum_{j=2}^{12} \lambda_{1,j}(t) X_1(t) dt
\]

\[
\text{Non-IDU New HIV Infections} = \int_0^T \sum_{j=2}^{12} \lambda_{7,j}(t) X_7(t) dt
\]
Outcome measures

- Calculated discounted costs and quality-adjusted life years (QALYs) of all treatment strategies and the base case

\[
\text{Incremental Cost-Effectiveness Ratio} = \frac{\frac{\text{Costs}_{\text{Treatment Strategy}} - \text{Costs}_{\text{Base Case}}}{\text{QALYs}_{\text{Treatment Strategy}} - \text{QALYs}_{\text{Base Case}}}}
\]
Disease transmission assumptions

• Considered HIV transmission via needle-sharing and heterosexual contact

• Assumed homogeneous mixing within compartments

• Allowed for preferential mixing across compartments (between IDUs and non-IDUs)

• Did not distinguish males and females

• Did not consider harm reduction programs (IDUs may not enter non-IDU population)
Treatment assumptions

• HAART delays HIV progression and reduces AIDS-related mortality

• Suppressive HAART decreases viral load, which lowers infectivity
  – Sexual infectivity reduced by 90%
  – Injection infectivity reduced by 50%

• HAART does not change sexual or injection drug use behavior
Collected data from published studies, expert opinions, and interviews with physicians, policymakers and NGOs in Russia

Demographic parameters
- Population
- Proportion of IDUs
- HIV prevalence

Disease parameters
- HIV progression rates
- Death rates
- Quality-of-life factors

Sexual behavior parameters
- Number of sex partners
- Condom usage rate
- Transmission probability per sexual partnership

Injection drug use parameters
- Injection frequency
- Needle-sharing frequency
- Transmission probability per shared injection
Estimated annual cost parameters

- HAART: $1,700
- HIV Related Healthcare: $570
- Non-HIV Related Healthcare: $115
- Counseling & Adherence Services: $250
- Add'l IDU Services: $500
Evaluated four treatment strategies

<table>
<thead>
<tr>
<th>Treatment Strategy</th>
<th>% IDUs Receiving HAART</th>
<th>% Non-IDUs Receiving HAART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-IDU Targeted</td>
<td>0%</td>
<td>80%</td>
</tr>
<tr>
<td>IDU Targeted</td>
<td>80%</td>
<td>1%</td>
</tr>
<tr>
<td>Untargeted</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Optimistic Untargeted</td>
<td>80%</td>
<td>80%</td>
</tr>
</tbody>
</table>
St. Petersburg demographics

Non-IDU Population aged 15-49: 2.5 million
HIV Prevalence: x 0.6%
HIV+ Non-IDUs: 15,000

IDU Population aged 15-49: 100,000
HIV Prevalence: x 35%
HIV+ IDUs: 35,000
St. Petersburg results

Number of people treated with HAART over 20 years

- Non-IDU Targeted: 47,030
- IDU Targeted: 50,226
- Untargeted: 57,396
- Optimistic Untargeted: 84,100
St. Petersburg results

HIV infections prevented over 20 years

- Non-IDU
- IDU

Targeted

Untargeted

Optimistic

Non-IDU

IDU

Non-IDU

IDU
St. Petersburg results

Infections prevented per treated individual

- **Non-IDU Targeted**: 0.20
- **IDU Targeted**: 0.80
- **Untargeted**: 0.54
- **Optimistic Untargeted**: 0.57
St. Petersburg results

HIV Prevalence among IDUs

- Status Quo
- Optimistic
- Untargeted
- IDU Targeted
- Non-IDU Targeted

Year

35% 30% 40% 45% 50% 55% 60% 65% 70%

0 2 4 6 8 10 12 14 16 18 20

64% 62%
HIV Prevalence among Non-IDUs

- Status Quo
- Optimistic Untargeted
- IDU Targeted
- Non-IDU Targeted

- Untargeted

Year: 0 2 4 6 8 10 12 14 16 18 20

- 0.63%
- 1.13%
- 1.42%
- 1.75%
- 2.15%
- 1.0%
- 1.5%
- 2.0%
- 2.5%
Cost-effectiveness analysis

Costs

QALYs

Cost-Effectiveness Frontier

Increases QALYs
Saves Money

Decreases QALYs
Costs Money

Status Quo

Decreases QALYs
Costs Money
St. Petersburg results

- Optimistic Untargeted: $2,513
- Untargeted: $1,877
- Non-IDU Targeted: $2,572
- IDU Targeted: $1,501

Costs (billions)

- Status Quo
- QALYs (millions)
St. Petersburg results

Costs (billions)

QALYs (millions)

Optimistic Untargeted
$1,827

Untargeted
$1,877

Non-IDU Targeted
$2,572

Status Quo
Barnaul demographics

**Non-IDU** Population aged 15-49: 318,000
HIV Prevalence: x 0.06%
HIV+ Non-IDUs: 190

**IDU** Population aged 15-49: 22,000
HIV Prevalence: x 1.67%
HIV+ IDUs: 370
Barnaul results

HIV infections prevented over 20 years

- Non-IDU Targeted
- IDU Targeted
- Untargeted
- Optimistic Untargeted

HIV infections prevented over 20 years:
- Non-IDU: 200
- IDU: 400
- Total: 600
Barnaul results

- IDU Targeted: $931
- Optimistic Untargeted: $2,576
- Untargeted: $1,343
- Non-IDU Targeted: $2,684
- Status Quo
Barnaul results

QALYs (millions) vs Costs (billions)

- Status Quo
  - Untargeted: $1,343
  - Optimistic Untargeted: $1,278
- Non-IDU Targeted: $2,684
Conducted sensitivity analysis on uncertain parameters

• Treatment strategies **prevent fewer infections** if:
  – HAART is less effective at reducing infectivity

• Treatment strategies are **less cost-effective** if:
  – HAART is less effective at reducing infectivity
  – Baseline infectivity is lower than estimated
  – HAART is more expensive

• In all cases, ICER $\leq$ $3,500$ per QALY gained
Is HAART cost-effective in Russia?

- World Health Organization guidelines:
  Cost-effective interventions: \( \leq 3 \times \text{GDP per capita} \)
  Very cost-effective interventions: \( \leq \text{GDP per capita} \)

- Russia GDP per capita (PPP) in 2005: $11,000

- HAART is very cost-effective by WHO guidelines

- Limited cost-effectiveness studies for health interventions in Russia
Will IDUs be adherent to HAART regimens?

• Assumed treatment of IDUs requires more intensive support
  – Included additional $500 per IDU for substance abuse treatment, adherence support, and social services

• IDUs and non-IDUs who utilize support services have similar adherence and drug resistance

• Implementation of harm reduction programs in Russia requires changes in laws
Conclusions

- **Exclusive treatment of non-IDUs**
  - Averts fewest number of infections
  - Worsens HIV prevalence
  - Least cost-effective strategy

- **Exclusive treatment of IDUs**
  - Averts greater number of infections
  - Reduces HIV prevalence among non-IDUs
  - Very cost-effective (despite additional resources for treating IDUs)
  - May not be ethically acceptable
Conclusions

• Strategies to expand HAART in Russia
  – Provide enormous population-wide health benefit
  – Cost-effective
  – Should include treatment of both IDUs and non-IDUs
Policy implications

• Research goals
  – Disseminate our results to policymakers in Russia
  – Provide a transparent example of cost-effectiveness analysis for HIV interventions in Russia

• Research progress
  – Presented our findings at 2 U.S. conferences and 1 conference in St. Petersburg
  – Publication in November 2006 issue of AIDS
  – Intend to translate the publication into Russian and distribute to individuals in Russia
Possible future work

• Evaluate the cost-effectiveness of other HIV interventions in Russia
  – CEA of substitution therapy for IDUs
  – CEA of HIV screening
  – CEA of pre- or post-exposure prophylaxis among IDUs
Related work

• Developed transmission model of the HIV and tuberculosis (TB) co-epidemics in India
  – Evaluated the effects of HIV treatment, latent TB prophylaxis, and active TB treatment

• Currently developing HIV vaccine model
  – Evaluate the cost-effectiveness of vaccinating different risk groups (MSM, IDUs, heterosexual males and females) in the U.S.
  – Could apply model to regions outside the U.S.
Related work

• Develop resource allocation model to determine the optimal mix of HIV prevention and treatment
  – Allocation based on regional HIV epidemic
  – Include next-generation prevention programs:
    HIV vaccine
    Microbicides
    Circumcision
    Pre- or post-exposure prophylaxis
St. Basil’s Cathedral in Red Square
Moscow, Russia