

HIV incidence and factors associated with HIV acquisition among injection drug users in St Petersburg, Russia

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Background: The Russian HIV-1 epidemic has been driven by injection drug use.

Objective: To determine HIV incidence and identify demographic and behavioral correlates of infection to facilitate the development of longitudinal HIV prevention programs.

Methods: In 2002, a cohort of 520 injection drug users (IDU) in St Petersburg, Russia were recruited and tested and counseled for HIV-1. HIV-seronegative IDU were enrolled and reevaluated at 6 and 12 months. HIV testing was performed and sociodemographic and behavioral data were collected during each study visit. The relationship of sociodemographic and behavioral factors to HIV-1 incidence was assessed.

Results: Most enrolled subjects were young, male, living at home, educated, heroin users, and frequently shared needles and other injection paraphernalia. The retention rate at the 12 month follow-up was 80%. The HIV-1 incidence rate was 4.5/100 person-years. In univariate analysis, psychostimulant use, especially frequent use, three or more sex partners in the past 6 months, and females selling sex were associated with HIV seroconversion. In the multivariate analysis, psychostimulant use three or more times per week was the only factor still associated with HIV seroconversion.

Conclusions: The high incidence of HIV infection places St Petersburg among the worst IDU-concentrated epidemics in Europe. Interventions targeting psychostimulant and heroin users and their accompanying behaviors such as frequent injections and increased sexual activity are needed immediately. © 2006 Lippincott Williams & Wilkins

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Introduction

In the 1990s, injection drug use (IDU) grew rapidly in Russia, influenced by the multiple economic and social factors that accompanied the dissolution of the USSR [1–3]. This increase in IDU led to an epidemic of HIV-1

[4–6]. At the end of 2002, more than 75% of the officially registered HIV cases in Russia were associated with unsafe drug injection practices [4,5].

The prevalence of HIV infection among IDU in St Petersburg, estimated through cross-sectional convenience

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sampling, increased from 4% in 1999 to 12–19% in 2000 [7–9]. The prevalence of HIV infection among a National Institutes of Health-sponsored St Petersburg IDU cohort established in 2002 was 30% [10].

Similar to other European and Asian IDU epidemics, heroin and psychostimulants are the injected drugs of choice in Russia. Opium growing and processing is proliferating in former Soviet states, and heroin drug traffic is being routed along the Silk Road from Afghanistan [3]. In addition, many criminal groups in Russia have moved into psychostimulant drug production, including the production of amphetamines and derivatives of ephedrine [11,12].

The primary objective of this study was to determine the incidence of HIV-1 infection among IDU in St Petersburg and to describe the associations of demographic and behavioral characteristics with incident HIV infection.

Methods

Active IDU were recruited to enroll in the cohort if they met both the following criteria: (1) HIV seronegative at enrollment and (2) admitting to injecting drugs at least three times per week in the previous month or on at least three occasions in the previous 3 months used injection equipment after another person.

The Institutional Review Boards at the Biomedical Center in St Petersburg and the University of North Carolina at Chapel Hill approved the study. A community advisory board in St Petersburg was established to develop guidelines to protect the safety of the participants.

Participant recruitment and retention

Three strategies were used to locate and recruit potential participants: contacting patients at drug rehabilitation and detoxification facilities; recruiting from places where IDU congregate to sell/buy drugs or to socialize; and a social network approach where existing study participants were encouraged to bring or refer their IDU friends to the study site. In this method, the referring participants received non-monetary incentives when a new recruit identified them as their referral source. Data regarding the characteristic (drug, sex, etc.) of the relationship between these two participants was not elicited.

Data collection

At the research site, eligibility was confirmed and consent was obtained from eligible subjects. A questionnaire was administered to collect sociodemographic and behavioral information. HIV-1 testing was performed using an enzyme-linked immunoassay (Vironostica HIV-Uniform II plus 0; BioMerieux, Boxtel, the Netherlands)

with confirmatory Western Blot (NEW LAV BLOT 1; Bio-Rad Laboratories, France). Participants were instructed to return in 7–10 days for their test results. During the post-test visit, the HIV-negative subjects who gave consent were enrolled into the study. The HIV-positive subjects were counseled and referred for long-term care to physicians and psychologists working at the study site.

During follow-up visits at 6 and 12 months, participants completed an HIV risk assessment, received HIV pre-test and risk-reduction counseling, and underwent HIV antibody testing. HIV test results and post-test counseling was conducted 7–14 days following each visit. Subjects were encouraged to visit the study site at any time for drug counseling or primary healthcare services.

Statistical analysis

The target sample size was 500 to provide a half-width of 2.5% for the 95% confidence interval (CI) for HIV incidence based on a 12 month retention rate of 90% and a true HIV incidence rate of 8%. The nature of the distributions of screened participants sociodemographic and behavioral characteristics were summarized. Persons who enrolled or refused to enroll were compared using χ^2 -square tests for categorical variables and Wilcoxon rank sum tests for continuous variables.

Univariate and an adjusted multivariate analyses of the relationships of the sociodemographic and behavioral factors to incidence of HIV-1 infection were assessed using Cox proportional hazards models. To assess the potential interaction between sexual- and drug-risk behaviors, a model including an interaction term between psychostimulant use and number of sexual partners was used.

Results

Screening and enrollment

Between March and December 2002, approximately 5000 possible IDU were contacted regarding the study and 900 IDU who met the eligibility criteria and showed interest in the study gave consent. Of these 900, 680 (76.0%) were recruited and referred by another study participant. Of the 898 screened for HIV, 270 (30.1%) tested HIV positive. Of the 628 HIV-seronegative subjects, 520 (82.8%) enrolled in the longitudinal study. The demographic, drug-use and sexual behavior characteristics were similar for the HIV-uninfected subjects who did and did not enroll.

Baseline characteristics

The cohort was mostly male (365; 70.2%) single (349; 67.1%), with at least a secondary education (418; 80.4%), un- or underemployed (324; 62.4%), and lived with

parents or relatives (351; 67.5%). Median age was 24.3 years (range, 17.2–42.0). Men and women had similar demographic and behavioral characteristics. The participants' places of residence were well distributed around the city with 13 of 14 city districts and the surrounding Oblast (county) represented. No single district contained more than 16% of the 520 IDU cohort.

In the previous month, 497 (95.6%) injected heroin, and 315 (60.6%) used only heroin; 191 (36.7%) injected psychostimulants (ephedrine-based and/or amphetamines), but only 9 (1.7%) used psychostimulants alone. Sharing injection works (needles), rinse water, cookers, cotton, and using front/back-loaded syringes in the previous month was reported by 78.8, 91.9, 95.2, 89.2, and 80.2% of subjects, respectively. Sharing frequency or type of sharing did not differ by drug use type.

The median number of sexual partners reported in the past 6 months did not differ significantly by gender (two for women, three for men), but the reported selling of sex for money or drugs in the past 6 months did differ by gender. Among women, 50/155 (32.3%) reported such behavior, compared with 18/365 (4.9%) men. The median number of sex partners reported in the past 6 months for the 50 female sex workers was only 5.0 [interquartile range (IQR), 3–15]. Among these women, 47 (94%) used heroin, 23 (46%) used psychostimulants, and 20 (40%) used both. Overall, persons who injected psychostimulants had more sexual partners (median 3; IQR, 1–5) than those who did not (median 2; IQR, 1–4) ($P = 0.04$).

Retention

Of the 520 subjects, 417 (80.0%) had a 12 month visit or HIV seroconverted during the follow-up period. Among the 103 subjects lost to follow-up, 11 (10.7%) died, 31 (30.1%) were incarcerated, 3 (2.9%) were hospitalized, 3 (2.9%) stopped using drugs and refused participation, and 55 (53.4%) stopped participating for other or unknown reasons.

Incidence of HIV-1

During the 12 month follow-up period, 20/417 (4.8%) of retained subjects seroconverted. The 20 cases occurred over 443.5 person-years of risk (incidence rate, 4.5/100 person-years; 95% CI, 2.7–7.0). The univariate analyses identifying the sociodemographic/behavioral associations with HIV incidence are described in Table 1.

The HIV-1 incidence rate was similar by gender, age, marital status, employment status, housing, and recruitment method. Frequent psychostimulant use had a significant effect on incidence. Among the 28 subjects using psychostimulants more than three times per week, the incidence rate was 20.0/100 person-years. Of the 315 subjects who used heroin alone, the incidence rate was only 2.9/100 person-years. Although only 36.7% of the

entire cohort used psychostimulants, 13/20 (65.0%) of the incident cases were psychostimulant users. The hazard ratio for psychostimulant injectors was more than three times that of non-psychostimulant injectors. Seroconversion was not significantly associated with the self-reported frequency of sharing, the type of sharing, or the type of drug used while sharing.

Both reporting three or more sex partners and females selling sex for money or goods were associated with higher incidence. The incidence rate among the 50 female subjects who reported a history of selling or trading sex was 10.9/100 person-years, compared with 1.1/100 person-years for women without such history ($P = 0.017$).

In the multivariate analysis, subjects who used psychostimulants three or more times a week continued to be strongly associated with HIV incidence [hazard ratio (HR), 8.15; 95% CI, 2.43–27.34; $P = 0.0007$; Table 2]. However, after adjustment for psychostimulant use, both selling/trading sex and having three or more sex partners were no longer associated with HIV incidence.

In examining the relationship and interactions between selling/trading sex, having at least three sex partners, and frequent psychostimulant use, frequent psychostimulant use (three or more times a week) was strongly associated with HIV infection among persons with fewer than three sex partners in the past 6 months (HR, 33.82; 95% CI, 5.28–216.76; $P = 0.0002$), but not among persons with more than three sex partners (HR, 2.41; 95% CI, 0.51–11.46). Among persons with low or no psychostimulant use (two times per week or less), persons with three or more sex partners in the past 6 months were at greater risk of acquiring HIV infection (HR, 6.12; 95% CI, 1.33–28.08).

Discussion

With a prevalence of 30%, and an incidence of 4.5/100 person-years, the HIV epidemic among IDU in St Petersburg is among the most severe in Europe [13–15]. Frequent psychostimulant use (ephedrine-based and amphetamines) was strongly correlated with HIV seroconversion. Psychostimulant use, compared with heroin use, is associated with more frequent injection; binge injecting, involving more periodic but frequent sharing; and an increase in sexual activity [16–18]. Other HIV incident studies among IDU have also reported psychostimulant use as a correlate for seroconversion [19]. The majority of the psychostimulant users were also heroin users and did not have any unique demographic or social characteristics. The dual use of heroin and psychostimulants did not have an additive or synergistic effect on seroconversion. Heroin use alone did not have

Table 1. Behavioral characteristics associated with incident HIV infection in univariate analysis.

Characteristics	No.	Incident cases	Incidence/100 person-years (95% CI)	Hazard ratio (95% CI)	<i>P</i> value
Injection drug use					
Injecting heroin					
No	23	2	9.8 (1.2–35.2)	1	
Yes	497	18	4.3 (2.5–6.7)	0.44 (0.12–2.78)	0.236
Frequency if injecting heroin (times/week)					
≤ 2	169	6	4.2 (1.5–9.0)	1	
≥ 3	328	12	4.3 (2.2–7.5)	1.04 (0.39–2.99)	1.000
Injecting psychostimulant					
No	329	7	2.6 (1.0–5.3)	1	
Yes	191	13	7.7 (4.1–13.1)	3.00 (1.20–8.02)	0.020
Frequency if injecting psychostimulant (times/week)					
≤ 2	163	8	5.5 (2.4–10.9)	1	
≥ 3	28	5	20.0 (6.5–46.7)	3.61 (1.08–11.17)	0.032
Injecting heroin and psychostimulant					
No	348	9	3.1 (1.4–5.9)	1	
Yes	172	11	7.2 (3.6–12.9)	2.34 (0.96–5.87)	0.060
Sharing injection paraphernalia (in month prior to baseline)					
All injectors					
No	110	4	4.3 (1.2–11.1)	1	
Yes	410	16	4.6 (2.6–7.4)	1.05 (0.37–3.67)	1.000
Frequency if sharing (times/week)					
≤ 2	346	14	4.7 (2.6–7.9)	1	
≥ 3	55	1	2.2 (0.1–12.0)	0.45 (0.02–2.57)	0.512
Heroin injectors					
No	104	3	3.4 (0.7–10.1)	1	
Yes	393	15	4.5 (2.5–7.4)	1.29 (0.41–5.60)	0.782
Frequency if sharing (times/week)					
≤ 2	330	13	4.6 (2.5–7.9)	1	
≥ 3	54	1	2.2 (0.1–12.2)	0.48 (0.02–2.72)	0.708
Psychostimulant injectors					
No	40	3	8.8 (1.8–25.8)	1	
Yes	151	10	7.4 (3.5–13.6)	0.84 (0.24–3.78)	1.000
Frequency if sharing (times/week)					
≤ 2	122	8	7.4 (3.2–14.6)	1	
≥ 3	24	1	4.4 (0.1–24.8)	0.60 (0.03–3.75)	0.716
Sexual behavior					
Primary sex partner injects drugs					
No	153	5	3.8 (1.2–8.8)	1	1.000
Yes	179	6	4.0 (1.5–8.6)	1.06 (0.31–3.76)	
Sold sex for money or goods: males					
No	347	13	4.5 (2.4–7.7)	1	
Yes	18	1	6.1 (0.2–33.8)	1.34 (0.06–7.64)	1.000
Sold sex for money or goods: females					
No	105	1	1.1 (< 0.1–6.0)	1	
Yes	50	5	10.9 (3.5–25.4)	10.16 (1.41–241.83)	0.017
No. sex partners (6 months): all					
< 3	263	5	2.2 (0.7–5.1)	1	
≥ 3	257	15	6.9 (3.9–11.4)	3.15 (1.18–9.67)	0.024
No. sex partners (6 months): males					
< 3	179	4	2.6 (0.7–6.8)	1	
≥ 3	186	10	6.5 (3.1–12.0)	2.47 (0.79–9.08)	0.180
No. sex partners (6 months): females					
< 3	84	1	1.3 (< 0.1–7.3)	1	
≥ 3	71	5	7.9 (2.6–18.4)	5.98 (0.83–142.40)	0.099

CI, confidence interval.

the same relationship with HIV infection even though both heroin use and psychostimulant use involved unsafe sharing of injection equipment. This may be because of the small number of non-heroin users in the study or the small number of incident HIV infections and hence may not accurately portray differences in HIV infection risk. Additionally, there was no significant difference in HIV infection between those who did or did not share

injection paraphernalia. This may also be a consequence of the number of participants who did not report sharing, under-reporting of sharing, or HIV sexual transmission among the self-reported non-sharers.

Although our overall retention rate was an adequate 80%, we demonstrated the extreme risks of being an IDU in St Petersburg [20]: 8.1% (42/520) were jailed or dead,

Table 2. Behavioral factors associated with incident HIV infection by multivariate analysis.

Characteristic	Hazard ratio (95% CI)	P value
Psychostimulant use (times/week)		
None	1	
1–2	1.98 (0.70–5.57)	0.1955
≥ 3	8.15 (2.43–27.34)	0.0007
No. sex partners (6 months)		
< 3	1	
≥ 3	2.66 (0.91–7.79)	0.0733
Selling sex for money or goods (6 months, either gender)		
No	1	
Yes	1.86 (0.65–5.26)	0.24

CI, confidence interval.

and another 11.2% (58/520), despite Herculean efforts, were so lost to follow-up that we had no idea of their whereabouts or outcome.

The demographic and behavioral profile of the 520 IDU enrolled in this study was very similar to the profile that describes the IDU epidemic throughout Russia and Eastern Europe [13–15]. These broad-based characteristics, and the lack of significant focal geographic points for users, limits successful research recruitment and behavioral intervention options to social network constructs [21–22].

One third of the female subjects gave a history of selling sex for money or drugs. However, the median number of sex partners in the past 6 months for these 50 women was only five (IQR, 3–15). Therefore, most of these women do not appear to be daily sex workers but rather are occasionally selling sex for drugs or money to buy drugs when other monies are not available.

The relationship between sexual behavior, IDU, and HIV transmission is of particular interest and is generally considered the main bridging transmission activity between IDU and the general population [17]. In our cohort, reporting three or more sex partners in the past 6 months was associated with an increased risk of HIV-1 infection, especially among persons who did not use psychostimulants frequently. Frequent injection use of psychostimulants increased risk only slightly among those with a high number of sexual partners, but this risk increased dramatically among those without a high number of partners.

There were several limitations to this study. Because our inclusion criteria included sharing drug paraphernalia in the prior 3 months, over 90% of the cohort admitted to this sort of behavior in the previous month. Although the purpose of this requirement was an attempt to enroll those IDU at highest risk of seroconverting, the universality of this risk factor may have made it impossible to identify particular aspects of sharing as risks associated with HIV

seroconversion. In addition, although the baseline characteristics were similar, the 20% loss to follow-up may have obscured additional incident cases and important characteristics associated with seroconversion.

In conclusion, psychostimulant use, with and without the added injection of heroin, was the primary HIV acquisition correlate, with the increased rate of sexual activity associated with psychostimulant use a contributory factor. Further study and data collection regarding the social networks, geographic distribution, sexual mixing patterns, and additional details on injection practices of these psychostimulant and heroin users will be necessary before a coherent, directed intervention can be designed.

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