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HIV Risk Reduction in a Cohort of Injecting Drug Users in Bangkok, Thailand

*Kachit Choopanya, §Don C. Des Jarlais, *Suphak Vanichseni, ‡Philip A. Mock, †Dwip Kitayaporn, *Udomsak Sangkhum, *Boonrawd Prasithiphol, *Krit Hiranrus, ‡Frits van Griensven, ‡Jordan W. Tappero, and ‖Timothy D. Mastro

**Bangkok Metropolitan Administration, Bangkok, †Faculty of Tropical Medicine, Mahidol University, Bangkok, and ‡The Thailand Ministry of Public Health, U.S. Centers for Disease Control Collaboration, Nonthaburi, Thailand; and §Baron Edmond de Rothschild Chemical Dependency Institute, Beth Israel Medical Center, New York, New York, and ‖Centers for Disease Control and Prevention, Atlanta, Georgia*

Objective: To determine changes in risk behavior in relation to study participation among injecting drug users (IDUs) in Bangkok, Thailand.

Methods: During 1995–1996, 1,209 HIV-seronegative IDUs were recruited from Bangkok Metropolitan Administration drug abuse treatment programs to participate in a prospective cohort study. Study visits occurred every 4 months, at which the participants underwent an interview to assess risk behavior and HIV counseling and testing. Eight hundred nine of the IDUs were considered "long-term" participants, who remained in the study through at least the first four scheduled follow-up visits (16 months). Injection risk behavior at each study visit was measured on a four-point scale strongly associated with incident HIV infections in the cohort. Individual regression slopes were used to assess changes in injection risk behavior (risk increase, no change, or risk reduction).

Results: Of the 806 long-term study participants, 79% showed declines, 4% showed no change, and 17% showed increases in injection risk behavior. The percentage of participants in the highest-risk category (injecting daily or more frequently and sharing needles and syringes) declined from 42% at baseline to 3% at the final follow-up visit. Being in methadone maintenance treatment was associated with stable low rates of injection risk behavior, while recruitment from the 45-day detoxification treatment was associated with reductions in injection risk behavior. The risk reduction was independent of decline in risk behavior among IDUs in the community at large.

Conclusions: Participation in this cohort study was associated with substantial declines in injection risk behavior. This information is important in the evaluation of possible adverse behavioral effects of participation in future preventive HIV vaccine trials including IDUs, particularly in developing country settings.

Key Words: HIV—Risk reduction—Injecting drug users (IDUs)—Substance abuse—Bangkok, Thailand.

Longitudinal cohort studies are a standard method for studying incidence of HIV infection and for evaluating HIV preventive interventions, including HIV vaccines, among injecting drug users (IDUs) and other groups at risk for HIV infection. Such cohort studies typically involve multiple extensive risk behavior interviews and ongoing systematic episodes of HIV counseling and testing for all subjects. Participating in a cohort study, including an intervention trial, might lead to reductions in HIV risk behavior. The interviews may have an educational effect, and the HIV counseling and testing are

Address correspondence and reprint requests to Don C. Des Jarlais, Beth Israel Medical Center, 1st Avenue and 16th Street, New York, NY 10003. E-mail: Dcdesjarla@aol.com

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intended to reduce risk behavior. The special attention given to cohort study participants, including tracking for follow-up, may also lead to increased risk reduction.

A number of cohort studies of IDUs have described risk reduction among study subjects (1,2), including substantial risk reductions among subjects in the control arm of intervention studies. The United States National AIDS Demonstration Research/AIDS Targeted Outreach Model (3) studies may provide the most consistent evidence for a cohort study participation effect among IDUs. These studies were conducted at >60 different sites throughout the United States and typically involved random assignment of subjects into either experimental or control arms. At follow-up, large reductions from baseline levels of risk behavior were seen in almost all of the studies, but there were no statistically significant differences between experimental and control groups.

The long-term ALIVE cohort study has shown continuing reductions in both risk behavior and incidence of HIV infection, with incidence declining from 4.45 cases per 100 person-years in 1988–1990 to 1.84 cases per person-years in 1995–1998 (4). The long-term cohort study in Amsterdam appears to have reached a floor effect on risk behavior. Sharing of drug injection equipment in this cohort seems to have stabilized, with ≈30% of subjects reporting receptive sharing in the previous 6 months and a stable incidence rate of HIV infection of 3% to 4% per year (5). Although participation in cohort studies appears to lead to risk reduction, it clearly does not lead to risk elimination.

Because of the high incidence of HIV infection among IDUs, particularly in developing and transitional countries (6–9), this population has been proposed for the evaluation of preventive HIV vaccines (10). After several years of scientific and regulatory preparation (11–13), the first phase 3 trial of a preventive HIV vaccine (AIDSVAX B/E; VaxGen, Brisbane, CA) in a developing country was initiated in 1999; it included IDUs in Bangkok, Thailand (14).

Despite the impressive risk reduction seen in IDUs enrolled in longitudinal studies in developed countries, concern has been expressed that participation in an HIV vaccine trial may lead to an increase in risk behavior, due to perceptions about the efficacy of the vaccine (15,16). To evaluate such adverse behavioral effects of participation in an HIV vaccine trial, it is important to establish a baseline reference of behavioral change among participants in a nonvaccine cohort in the same setting. In this study, we evaluated behavioral changes among IDUs enrolled in the Bangkok Metropolitan Administration (BMA) HIV vaccine preparatory cohort study. This study, conducted from 1995 through 1998 among 1,209 attendees of 15 BMA drug treatment clinics, showed an annual incidence of HIV infection of 5.8 cases per 100 person-years, high rates of follow-up, and willingness to participate in HIV vaccine trials (12,17). HIV seroconversion in this study was primarily associated with the frequency of heroin injection and the sharing of injection equipment, especially related to incarceration (14,17). Sexual behavior was not associated with increased risk for HIV infection.

Some background information about the local context of the study will be helpful in understanding the methods and results. HIV spread rapidly among IDUs in Bangkok in 1987–1988 (18). AIDS education was provided through the BMA drug treatment clinics, and most IDUs responded by reducing risk behavior (18). Sterile syringes and needles are available at pharmacies and convenience stores throughout Bangkok without prescription for about 5 to 8 Thai baht (approximately US$0.20 to US$0.32 in 1996), although IDUs may be arrested on suspicion of drug use if they are found with narcotics paraphernalia.

MATERIALS AND METHODS

A full description of the methods of this study has been previously reported (19,20); therefore, an abbreviated description of the methods is presented here.

Subject Recruitment

Potential subjects were recruited from persons attending any of 15 BMA drug treatment clinics. The clinics provide both methadone-assisted detoxification and methadone maintenance treatment. The detoxification program includes a 45-day methadone-assisted detoxification followed by up to 1 year of drug abuse counseling. If continued drug use or relapse occurs, the patient may receive another round of detoxification. The average daily dose for maintenance patients is 60–70 mg. Informed consent was obtained, a blood sample for HIV testing was obtained, and a trained interviewer administered a brief standardized questionnaire. Note that for participants recruited from the detoxification program, the baseline risk behavior assessment (6 months prior to the interview) would have included the several months immediately prior to voluntarily entering the detoxification program. This is likely to be a period of very high drug use. After the HIV test result was known, each volunteer was counseled confidentially about his or her HIV status. HIV-seronegative persons were offered enrollment with informed consent into the prospective cohort study. On each study visit, participants received 200 Thai baht (approximately US$8 in 1996). Screening and enrollment were conducted during two periods: May through November 1995 and May through December 1996.

A second HIV test was administered to exclude persons who might have been in a seroconversion "window period" at the initial test. Participants were then asked to return for follow-up visits every 4 months. At each visit, participants were interviewed using a standard questionnaire, provided blood samples for serologic testing, and received HIV risk reduction counseling and health education. Bleach for cleaning injection equipment and male condoms were available at no

charge. As noted above, sterile injection equipment can be purchased without prescription in Bangkok.

Participants who became HIV seropositive during the study were offered follow-up enrollment under a separate study protocol in a clinical, immunologic, and virologic evaluation of HIV seroconverters (21). They received social and medical care according to BMA guidelines.

Management and Statistical Analyses

To examine potential long-term effects of participating in the cohort study, the analyses presented here were restricted to persons who participated in the cohort study through at least the first four scheduled follow-up visits (through 16 months after baseline). Participants who voluntarily withdrew or seroconverted or whose last study visit occurred before the fourth scheduled follow-up were excluded from these analyses. This strategy ensured that all participants in the analyses had an extended (16-month) participation in the cohort and that any reductions in group risk behavior during the first 16 months were not due to simple loss of high-risk subjects during that time. Not all of these long-term participants completed all of the first four scheduled follow-up visits, but adherence to study visits was quite high among these participants—81% attended all four visits, and an additional 16% missed only one of the first four visits.

There were 48 long-term participants who seroconverted after the fourth study visit and before the end of the study. Risk behavior data for these subjects prior to their seroconversion were included in the analyses. (We also repeated the analyses with these subjects excluded, and the results did not change.)

HIV Injection Risk Scale

We used a four-point scale to assess drug injection risk behavior during participation in the cohort study. Each subject was classified into one of the four categories for each 4-month follow-up period. The four points in the scale were as follows: not injecting; injecting less than daily; injecting daily or more frequently but not sharing needles and syringes; and injecting daily or more frequently and sharing needles and syringes.

This scale was developed as part of the previously reported analyses of seroconversion among cohort members (20) and has a strong positive relationship with incident HIV infection in the cohort. Incidences of HIV infection associated with the four scale values were as follows: 3.5, 4.9, 8.7, and 17.1 cases per 100 person-years at risk, respectively. The adjusted relative risks for the four scale points were 1.0 (referent), 1.5, 2.4, and 3.2, respectively. Thus, the relative risk of becoming infected with HIV increases by ≈50% with each one-point increase on the risk behavior scale.

Group trends over time in injection risk behavior were assessed using the distribution of participants on the risk behavior scale and the group means on the risk behavior scale for the baseline and each of the follow-up study visits.

The rate of change of HIV injection risk behavior was estimated for each subject by the slope from a linear regression over time on the four-point risk behavior scale described below. (A slope of zero represents no change in risk behavior for a participant, a positive slope represents increasing risk behavior, and a negative slope represents decreasing risk behavior.) A one-sample t test was used to analyze whether the overall mean slope was different from zero. The mean slopes associated with different subject characteristics were compared using one-way ANOVA or the nonparametric Kruskal–Wallis test. Adjusted comparisons for the factors that were significant ($p < .1$) in univariate analyses were conducted using linear regression.

χ^2 tests were used to investigate the relationship between possible predictors and four risk behavior groups: stable low-risk subjects, decreasing-risk subjects, increasing-risk subjects, and stable high-risk subjects. Polytomous logistic regression was used to assess multivariate predictors of the four change groups, and factors identified as significant ($p < .1$) in univariate analyses were included in the model.

We used Epi-Info (version 6.04c; Centers for Disease Control and Prevention, Atlanta, GA), SAS (version 6.12; SAS Institute, Cary, NC), and Stata (version 6; Stata Corporation, College Station, TX) for data management and analyses.

Ethics Review

The study protocols were approved by the Ethical Review of Research Committee, Ministry of Public Health (Nonthaburi, Thailand), the Institutional Review Board of the Centers for Disease Control and Prevention (Atlanta, GA), and the Global Program on AIDS, World Health Organization (Geneva, Switzerland).

RESULTS

Subject Characteristics

A total of 1,209 persons were enrolled in the study. Table 1 presents selected demographic and drug use history data for the 806 persons who participated in the cohort study through at least the first four follow-up visits (16 months). All participants were Thai; most were male and between ages 20 and 39 years, had some form of employment, and were injecting heroin.

Trends in Injection Risk Behavior Over Time

Tables 2A and 2B present the distribution of participants on the four-point injection risk behavior scale by study visit (Table 2A) and the group means on the scale by study visit (Table 2B). Baseline risk behavior data were missing for eight subjects (1%), but risk behavior data were then obtained at the next visit for these subjects. Not all of the long-term participants contributed data at each scheduled study visit. Thus, there was some change in the persons contributing data at each study visit. Despite the modest changes in persons contributing data at each study visit, there was a clear decline in risk behavior over time. The decline in the score distributions and the decline in the means were both highly significant. The decline was greatest for the period from baseline to the first follow-up, but it did continue after the follow-up visit. The decline appears to have halted after the eighth visit.

Individual-level regression equations for injection risk behavior scores over time were calculated. These regressions used all of the available data for each of the long-

TABLE 1. *Demographic and drug use characteristics among 806 injection drug users participating in the Bangkok Metropolitan Administration cohort study[1], Bangkok, Thailand, 1995–1998*

Characteristic	n*	%
Sex:		
Male	756	94
Female	50	6
Age:		
<25	174	22
25–30	151	19
31–39	329	41
40+	152	19
Education:		
Primary	353	44
Secondary	305	38
Post-secondary	147	18
Marital status:		
Single	273	34
Married/co-habiting	376	47
Separated/divorced	147	19
Income:		
>5,000 baht		
Yes	365	45
No	441	55
Methadone treatment program:		
Maintenance	168	22
45-day	608	78
Years since first injection drug use:		
<3	149	18
3–6	198	25
7–14	211	26
15+	248	31
Years since first treatment for injection drug use:		
<2	176	22
2–3	147	18
4–8	175	22
9+	308	38
Times incarcerated:		
0	258	32
1	175	22
2	140	17
3+	233	29
Heroin injection last 6 months:		
Yes	767	95
No	37	5
Shared equipment frequency:		
Never	523	65
Monthly	239	30
Weekly	14	2
Daily	28	3
Frequency of sex:		
Never	346	43
Rarely	134	17
Monthly	201	25
Weekly+	124	15
Casual sex:		
Never	718	89
Rarely	47	6
Monthly+	41	5

[1] Only those who had at least 4 or more follow-up visits.

IDU, injection drug user; BMA, Bangkok Metropolitan Administration.

* Total n may not equal 806 because of missing data.

TABLE 2A. *Distributions on the risk behavior scale at baseline and for up to 10 follow-up visits, among 806 injection drug users participating in the Bangkok Metropolitan Administration cohort study, Bangkok, Thailand, 1995–1998*

		Percentage at each scale score			
Follow-up visit	n	1	2	3	4
0 (baseline)	798	3.8	21.7	32.3	42.3
1	806	17.4	37.2	31.8	13.7
2	756	21.8	0.5	28.2	9.5
3	755	30.7	35.1	24.6	9.5
4	726	37.1	37.3	18.9	6.8
5	707	38.1	34.9	19.8	7.2
6	600	38.8	37.3	19.7	4.2
7	505	44.8	33.1	18.0	4.2
8	267	45.7	35.6	15.7	3.0
9	199	44.2	32.2	19.1	4.5
10	219	45.2	33.8	14.6	6.4

Chi-square test for a linear decline was 299.5 on 1 df, $p < .0001$, using a GEE longitudinal ordinal logistic regression model.

term cohort participants; there were from four to 11 data points for estimating the regression slope for each individual. The mean slope of the regression lines was –0.439 scale point per year (95% CI, –0.48 to –0.40; $p < .0001$). This corresponds to a mean of approximately one-point scale score reduction over a 2-year period. Of the 806 persons who participated for ≥16 months, 79% had a negative slope (indicating a reduction in injection risk behavior), 4% had a zero slope (indicating no trend toward change in risk behavior), and 17% had a positive slope (indicating an increase in risk behavior).

Baseline Values and Participant Characteristics Associated With Risk Reduction

Knowing which baseline characteristics predict changes in HIV risk can provide insight into factors driv-

TABLE 2B. *Mean and median score on the risk behavior scale, among 806 injection drug users participating in the Bangkok Metropolitan Administration cohort study, Bangkok, Thailand, 1995–1998*

Follow-up visit	n	Mean	Median
Baseline	798	3.13	3
1	806	2.42	2
2	756	2.25	2
3	755	2.12	2
4	726	1.96	2
5	707	1.96	2
6	600	1.89	2
7	505	1.89	2
8	267	1.76	2
9	199	1.84	2
10	219	1.82	2

Chi-square test for a decline (linear) was 321 on 1 df, $p < .0001$ using a GEE longitudinal linear regression model.

ing behavioral change. We used the individual regression slopes to identify characteristics of participants who were more versus less likely to reduce their injection risk behavior while participating in the cohort. Table 3 shows risk behavior at baseline (as the mean on the four-point scale) and the mean of the individual regression slopes among different groupings of study participants. Note that there was a consistent pattern of a higher baseline level of injection risk behavior associated with a greater likelihood of risk reduction while participating in the study, indicating a floor effect on risk reduction.

To further explore the relationship between the baseline injection risk score and the behavior change while participating in the cohort, we calculated the mean of the final visit risk scale scores for the participants with different baseline risk scores. For the 29 participants with a baseline score of 1 (the lowest possible score), the mean score at their last visit was 1.52. For the 169 participants with a baseline score of 2, the mean score on their final visit was 1.92. For the 247 participants with a baseline score of 3, the mean score on their final visit was 1.87. For the 336 participants with a baseline score of 4 (the highest score), the mean score on their final visit was 1.97. Thus, there was both convergence in the risk behavior scores during participation in the cohort and an overall trend toward risk reduction. Note that all of the means of the final scores were substantially below the mean of 3.13 at the baseline visit (see Table 2).

Injection Risk Behavior Change Groups

We also classified the long-term participants into four groups based on the pattern of injection risk behavior while participating in the cohort. We were able to classify 673 (83%) of 806 participants into one of the following four mutually exclusive groups:

1. Stable low-injection risk behavior, participants with an initial value of 1 or 2 on the risk scale who remained at those values throughout their participation in the study (n = 33, or 5% of classified long-term participants).
2. Declining-injection risk behavior, participants with individual regression slopes of less than −0.1 (n = 538, or 80% of classified long-term participants).
3. Increasing-injection risk behavior, participants with individual regression slopes of >0.1 (n = 85, or 13% of classified long-term participants).
4. Consistent high-injection risk behavior, participants with scale values of 3 or 4 on all of their study visits (n = 17, or 2% of classified long-term participants).

This risk behavior group classification shows the predominance of risk reduction over risk increase among cohort participants and that relatively few participants remained at either very low or very high risk levels during cohort participation. It is particularly noteworthy that while 75% of the long-term participants remained at risk

TABLE 3. *Baseline risk scale values and mean slope by selected characteristics among 806 injection drug users participating in the Bangkok Metropolitan Administration cohort study, Bangkok, Thailand, 1995–1998*

Factor	N	Mean	*p*-value	Univariate mean slope *p*-value	Multivariate *p*-value	
Age (y):						
<25	172	3.41		−0.67		
25–30	151	3.19		−0.45		
31–39	325	3.06		−0.37		
40+	150	2.92	<.001	−0.33	<0.001	0.02
Income >5,000 baht:						
Yes	437	3.07		−0.40		
No	361	3.20	0.04	−0.49	0.03	0.4
Single/marital status:						
No	526	3.09		−0.40		
Yes	272	3.20	0.09	−0.52	0.001	0.8
Treatment program:						
Maintenance	164	2.53		−0.18		
45-day	604	3.31	<.001	−0.52	<0.01	0.001
Years of injection drug use prior to enrollment:						
<4	147	3.35		−0.60		
4–6	196	3.25		−0.53		
7–14	210	3.10		−0.38		
15+	245	2.93	0.01	−0.32	0.01	0.5
Incarcerated prior to enrollment:						
Ever	543	3.12		−0.41		
Never	255	3.15	0.6	−0.50	0.02	0.4

P-values are *t*-test or one-way ANOVA *F* test checked with the non-parametric Wilcoxon or Kruskal-Wallis test, and multivariate *p*-value (adjusted) are via linear regression with robust variance.

scale values of 3 and 4 at baseline, only 3% remained at these values during the study. (An additional 5% of the long-term participants seroconverted.)

Table 4 shows the relationships between participant baseline characteristics and membership in the four risk behavior groups. The only significant association in the multivariate analysis was with the drug treatment program from which the participants were recruited. Participants recruited from methadone maintenance were much more likely to be in the stable low-risk group (group 1), while participants recruited from the 45-day detoxification program were more likely to be in the decreasing-risk behavior group (group 2). None of the participant baseline characteristics were associated with membership in the increasing-risk behavior group (group 3). With only 17 participants in the consistent high-risk group (group 4), there was not sufficient statistical power to identify predictors of membership in this group.

Potential Historical Change in Injection Risk Behavior

We considered the possibility that the decline in injection risk behavior reported by participants in the cohort might simply be a reflection of background declines in risk behavior among IDUs in Bangkok (i.e., historical change). To assess this possibility, we compared the baseline injection risk behavior of the participants enrolled in 1995 with the baseline injection risk behavior of the participants enrolled in 1996. On the injection risk scale, the 1995 enrollees had a mean of 3.0 and median of 3, and the 1996 enrollees had a slightly higher mean of 3.2 and median of 3 ($p < .001$ for t test of differences between means). The results of this comparison were in the opposite direction of a potential historical decline in risk behavior among IDUs in the community.

TABLE 4. *Percentage within each change group by baseline interview characteristics among 806 injection drug users participating in the Bangkok Metropolitan Administration cohort study, Bangkok, Thailand, 1995–1998*

Multivariate	N	Change group 1 %	2 %	3 %	4 %	Univariate *p*-value	*p*-value
Sex:							
Male	636	4	80	13	3		
Female	37	11	78	8	3	0.3	
Age:							
<25	157	2	87	10	1		
25–30	130	3	80	14	3		
31–39	264	5	78	14	3		
40+	122	11	74	12	3	0.04	0.7
Education:							
Primary	296	4	80	13	3		
Secondary	253	5	80	13	2		
Post high school	123	7	78	12	3	0.8	
Income >5,000 baht:							
Yes	365	5	80	12	3		
No	308	4	80	13	3	0.8	
Single:							
No	433	5	79	13	3		
Yes	240	4	82	12	2	0.8	
Treatment program:							
Maintenance	129	16	60	22	2		
45-day	521	1	86	10	3	<0.001	<0.001
Years of injection drug use prior to enrollment:							
3	128	2	88	7	3		
4–6	170	4	82	12	2		
7–14	180	3	78	17	2		
15	195	9	74	13	4	0.03	0.4
Incarcerated prior to enrollment:							
Never	213	4	85	10	1		
Ever	460	5	78	14	3	0.1	

Univariate *p*-value by chi-squared test and multivariate *p*-value from polytomous logistic regression.

Definition of the change groups: 806 injection drug users who made at least 4 visits including the first follow-up visit, were classified into four groups as follows: Group 1 = Stable low: started low (1, 2 on the risk behavior scale) and remained at 1 or 2 for all follow-up visits.

Group 2 = Decreased: an estimated regression slope of less than –0.1.

Group 3 = Increased: an estimated regression slope of greater than 0.1.

Group 4 = Stable high: started high (3, 4 on risk behavior scale) and never went to 1 or 2.

DISCUSSION

Our cohort study of Bangkok IDUs provides a unique opportunity to evaluate behavioral change as a result of long-term (16-month) study participation in a developing country. Our analyses showed considerable reductions in injection risk behavior (frequency of injection and sharing of equipment) over time, which could not be explained by a historical decline in HIV risk behavior in the community of IDUs at large. In these analyses, we used a four-point drug injection risk scale with high validity—it was strongly associated with HIV seroconversion while participating in the cohort study (14,17). Incidence of HIV infection also declined during the course of the study, from 7.0 cases per 100 person-years during the first year of follow-up to 5.9 cases per 100 person-years during the second year of follow-up to 3.6 cases per 100 person-years during the final 16 months of follow-up (16). Thus, the changes in reported injection risk behavior are likely to reflect real changes in behavior and not merely socially desirable reporting, although there is still a likelihood that some underreporting of risk behavior occurred.

The results of our study are important for evaluation of possible adverse behavioral effects of participation in future HIV vaccine trials among IDUs, particularly in developing countries. Our results suggest that participating in an actual vaccine efficacy trial should lead to reduction in injection risk behaviors. Failure to observe these reductions would be a signal that the participants may have substantial misunderstandings about the study design and/or unfounded perceptions about the efficacy of the vaccine (15,16). In 1999, a phase 3 trial of the protective efficacy of AIDSVAX B/E, ambivalent rgp120 HIV vaccine, was started among IDUs attending the same drug treatment clinics as our study participants (22). Whether the expected reductions in injection risk behaviors occur will be the subject of careful statistical analyses.

The reductions in injection risk behavior are similar to those reported in large cohort studies of IDUs in developed countries (4–9). The similarity of the reductions in injection risk behavior to findings of other studies supports the hypothesis that participation in an IDU cohort study should be associated with reduction of injection risk behavior. Power calculations for both vaccine and behavioral intervention trials should include consideration of likely risk reduction.

All of the participants in this study had access to voluntary methadone treatment. The detoxification program used a 45-day methadone-assisted detoxification schedule, followed by up to 1 year of additional drug abuse counseling. This extended detoxification program is likely to be considerably more effective than the shorter 7- to 28-day programs common in other areas. Methadone maintenance treatment has been shown to greatly reduce both heroin use and the likelihood of HIV infection (23). In addition to the availability of effective drug abuse treatment, the availability of inexpensive sterile injection equipment was probably important in the risk reduction in the cohort.

There was also considerable variation in risk behavior over time among the participants. Only 5% remained at stable low risk, and only 3% were at consistent high risk. This lack of stability/consistency may be seen as a function of drug addiction as a "chronic, relapsing condition" with cyclical patterns and suggests that risk behavior may be episodic, making prevention planning more difficult.

Researchers evaluating behavioral and biomedical interventions have a strong ethical obligation to make all reasonable efforts to reduce the risk of acquiring HIV infection in study participants. The data from this and other large cohort studies show that IDUs in developing and developed countries will reduce their injection risk behavior as part of study participation. This will need to be considered in the interpretation of data evaluating possible adverse effects of participation in preventive HIV vaccine trials.

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