Lack of increased HIV risk behavior among injection drug users participating in the AIDSVAX®B/E HIV vaccine trial in Bangkok, Thailand

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Objective: To determine whether HIV vaccine trial participation leads to increased risk behavior through beliefs about vaccine protection against infection.

Methods: Changes in risk behavior were evaluated among 2545 injection drug users participating in the AIDSVAX® B/E vaccine trial in Bangkok, enrolled from March 1999 to August 2000. Demographic characteristics, beliefs and risk behavior were assessed at baseline and every 6 months thereafter. Risk-reduction counseling was provided at every study visit. Generalized estimation–equation logistic regression analysis was used to study trends in risk behavior and associated factors.

Results: Participants were 93.4% male, their median age was 26 years, and 67.2% had at least secondary education. At baseline, 61.3% were receiving methadone detoxification and 20.9% were receiving methadone maintenance. From baseline to the 12-month follow-up visit, injection drug use decreased from 93.8% to 66.5% ($P < 0.001$) and needle sharing from 33.0% to 17.5% ($P < 0.001$). Multivariate analyses showed earlier follow-up time (at baseline and 6 months) and believing the vaccine to be efficacious associated with more-frequent injecting; younger age and lower education associated with less-frequent injecting. Earlier follow-up time (at baseline), younger age, and injection of methamphetamine and midazolam were associated with more-frequent needle sharing; methadone treatment and injecting less than weekly were associated with less-frequent needle sharing.

Conclusions: Injection drug use and needle sharing decreased during the first 12 months of the trial. No increases in risk behavior in relation to beliefs about vaccine protection against HIV infection could be identified.

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Introduction

Concern has been expressed that participation in preventive HIV-1 vaccine trials may lead to increases in HIV risk behavior [1,2]. Unfounded optimism among participants about the vaccine's efficacy is cited as the basis for these fears. In early phase I/II HIV vaccine studies in the United States, gay and bisexual

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white men reported increases in HIV risk behavior [3]. Some individuals reported that they joined these trials to seek protection from HIV infection, while others came forward because of a history of high-risk behavior [3]. An association between a history of high-risk behavior and increased willingness to participate in HIV vaccine trials has been reported from several studies [4–7]. In addition, participants may develop a sense of protection during the course of a trial if they remain HIV negative despite high-risk behavior, or they may think they have natural protection against HIV infection [8]. Several authors have questioned the possibility of conducting ethically sound HIV vaccine trials [1,2]. Nested behavioral interventions have been proposed to counteract a false sense of protection and increased risk behavior [2]. At a minimum, risk behavior monitoring and counseling, and access to condoms and methods to disinfect or obtain sterile injection equipment, should be part of a study visit [2].

Injection drug users (IDU), who have a high incidence of HIV infection, have been proposed for the evaluation of preventive HIV vaccines [9–12]. In March 1999, after several years of preparation [13–15] a phase III trial of a preventive HIV vaccine (AIDSVAX® B/E, VaxGen, Brisbane, California, USA) was initiated among IDU attending drug treatment clinics of the Bangkok Metropolitan Administration [16]. This trial provided a unique opportunity to investigate the impact of study participation on drug use and sexual risk behavior among IDU in a developing country setting. In this paper, we report on changes in HIV risk behaviors among trial participants in relation to demographic characteristics, drug-use history, and beliefs about study-arm assignment, vaccine efficacy and protection from HIV infection by participation. This analysis includes data collected at baseline and at 6 and 12 months after enrollment.

Methods

Study population and design

A description of the study design, recruitment, screening and enrollment of participants is presented in a separate paper in this issue [16]. Between March 1999 and August 2000, 2545 IDU were enrolled. Participants received AIDSVAX® B/E or placebo at months 0, 1, 6, 12, 18, 24, and 30. At baseline and every 6 months thereafter, a standardized questionnaire was administered to assess participants' demographic characteristics (baseline only), drug use, incarceration, sexual behavior and beliefs. Dichotomous answering categories assessed sexual and drug-use behaviors in the past 6 months (yes or no), followed by five-point frequency scales, for example 'How often did you use condoms during sexual intercourse: always, almost always, about half of the time, sometimes, or never?' At baseline, it was asked whether participants believed the vaccine would be efficacious (very, somewhat, or not at all) and whether they thought they had received vaccine or placebo. A single five-point item assessed protection motivation at the 6-month follow-up, for example 'I joined the vaccine trial because I may get some protection from HIV infection: strongly agree, agree, no opinion, disagree, strongly disagree'. Included in this analysis are 2545 study participants at baseline and 2485 (97.5%) and 2426 (94.3%) who returned for their 6- and 12-months follow-up visits.

Education and counseling

Education and risk-behavior counseling was provided at every study visit according to a standard operational protocol based on the client-centered model [17]. This direct, personalized and interactive form of counseling has proven to be more effective in reducing HIV risk behavior than other counseling approaches [17]. Male condoms and bleach to clean injection equipment were demonstrated and provided free of charge. Consistent with Thailand's HIV prevention policy, drug injection equipment is not exchanged at participating clinics, but sterile syringes and needles are widely available without prescription for 8 Thai baht (approximately US$0.20).

Statistical analysis

Analyses were adjusted for repeated within-subject measures and variables associated with injecting and needle sharing were evaluated independently using generalized estimating equation analysis for logistic model estimation with statistical inferences and 95% confidence intervals [18]. Variables significant in univariate analysis ($P < 0.05$) were evaluated in multivariate models to analyze injecting and needle sharing as a function of time and these covariates. Rates of reported sexual behaviors and drug-use practices while incarcerated were compared across assessments (at baseline and at 6 and 12 months) using chi-square tests.

Results

Demographics

Participants were predominantly male (93.4%) with a median age of 26 years (range, 20–59 years). Most (79%) had completed junior or secondary education, and 21.0% had completed tertiary school.

Beliefs

Almost half (47.3%) believed the vaccine would be somewhat efficacious, while 46.2% said they did not know. Few (3.6%) believed the vaccine would be very efficacious; fewer (3.0%) believed it would not be efficacious at all. Most (76.9%) said they did not know whether they had received vaccine or placebo, 13.9%

believed they had received placebo, and 9.2% believed they had received vaccine. Almost 80% of participants agreed that getting protection from HIV infection was a motivation to participate in the trial (Table 1).

Drug-use behavior at baseline

During the 6 months prior to enrollment, 93.8% reported injecting and 33.0% reported sharing; 61.3% reported methadone detoxification treatment, 20.9% reported methadone maintenance, and 17.9% reported no drug treatment. Heroin was the drug most commonly injected (98.5%), and 15.7% reported methamphetamine injection; midazolam, a fast-acting benzodiazepine, was injected by 12.2%. Daily drug injection was reported by 39.4% (Table 1).

No differences in reports of injection at baseline were seen by age, sex and educational level or by beliefs about vaccine efficacy, study arm assignment and protection motivation. Needle sharing was more often reported by those younger, those not in methadone treatment or receiving methadone detoxification, those injecting methamphetamine or midazolam, and those injecting more than weekly (all $P < 0.001$; Table 1).

Injecting and needle-sharing behavior over time

Over time, reports of injection during the past 6 months declined from 93.8% at baseline to 77.1 % at 6-month and 66.5% at 12-month follow-up. Among those who continued injecting, reports of sharing during the past 6 months declined from 33.0% at

Table 1. Injecting and needle sharing in the past 6 months among 2545 injection drug users participating in the AIDSVAX® B/E vaccine trial in Bangkok, Thailand, by characteristics and beliefs.

		Injecting			Sharing[b]		
Characteristic[a]	Total cohort	Baseline	6 months	12 months	Baseline	6 months	12 months
Total No. with any injecting/sharing (%)	2545 (100)[c]	2388 (93.8)	1915 (77.1)	1613 (66.5)	789 (33.0)	311 (16.2)	282 (17.5)
Age (years) (%)							
< 30	64.3	94.1	77.5	65.4	37.7*	17.5	20.5
30–90	21.0	92.5	80.4	71.9	27.7	14.8	14.3
40+	14.7	94.4	80.2	75.6	20.6	13.2	11.1
Sex (%)							
Male	93.4	94.0	78.7	68.2	33.0	16.4	17.7
Female	6.6	91.7	76.6	69.1	33.6	14.9	15.5
Education (%)							
Junior	32.8	92.5	77.0	65.2	32.0	16.4	17.9
Secondary	46.2	94.7	78.0	67.2	35.3	17.0	17.9
Tertiary	21.0	94.4	81.0	73.1	31.9	15.1	17.0
Methadone treatment[d,e] (%)							
Detoxification	61.3				34.7	17.2	20.0
Maintenance	20.9				24.2	13.4	11.8
None	17.9				40.3*	22.7	25.7
Drug injected[e] (%)							
Heroin	98.5				32.9*	16.4	17.6
Methamphetamine	15.7				45.2	28.8	28.1
Midazolam	12.2				45.2	24.3	30.1
Frequency of injection[e] (%)							
< Weekly	27.9				27.3*	15.4	13.8
> Weekly, but < daily	32.7				31.7	16.0	19.1
Daily	39.4				38.1	17.0	18.3
Vaccine efficacy (%)							
Very	3.6	94.5	80.7	71.5	32.7	16.4	16.9
Somewhat	47.3	94.5	80.7	71.5	32.7	16.4	16.9
None	3.0	93.1	77.0	65.6	33.1	15.8	18.8
Don't know	46.2	93.1	77.0	65.6	33.1	15.8	18.8
Assignment (%)							
Vaccine	9.2	95.1	76.6	68.1	32.7	18.3	17.1
Placebo	13.9	95.8	81.7	69.8	32.3	17.7	17.7
Don't know	76.9	93.4	78.3	68.6	32.8	15.5	17.5
Protection motivation[f] (%)							
Strongly agree	13.5	93.9	77.6	68.4	33.2	15.2	15.9
Agree	65.7	94.0	78.9	68.3	32.5	16.5	16.9
Not agree, not disagree	15.3	93.4	77.9	68.1	34.8	16.3	20.6
Disagree	5.3	93.4	77.9	68.1	34.8	16.3	20.6
Strongly disagree	0.2	93.4	77.9	68.1	34.8	16.3	20.6

[a] At baseline.
[b] Among those reporting injecting.
[c] Injecting during the past year.
[d] Detoxification with or without maintenance or in maintenance only.
[e] Association with injecting could not be evaluated because of similarity between predictor and outcome variables.
[f] Assessed at 6 month follow-up visit.
*$P < 0.001$.

baseline to 16.2% and 17.5% at 6- and 12-month follow-up, respectively (Table 1).

Univariate analysis showed earlier follow-up time (at baseline and 6 months versus 12 months of follow-up) and believing the vaccine to be very or somewhat efficacious (versus not efficacious or did not know how efficacious) to be significantly related to more-frequent reports of injecting. Lower education (junior versus tertiary school) and younger age were significantly related to less-frequent injection (Table 2). In multivariate analysis, earlier follow-up time and believing the vaccine to be very or somewhat efficacious were significantly and independently associated with more-frequent injecting, while younger age and lower education were associated with less-frequent injecting (Table 2).

Table 2. Results of univariate and multivariate analysis of injecting and needle sharing among 2545 injection drug users participating in the AIDSVAX® B/E vaccine trial in Bangkok, Thailand.

	Injecting		Sharing[b]	
Characteristic[a]	Univariate OR (95% CI)	Multivariate OR (95% CI)	Univariate OR (95% CI)	Multivariate OR (95% CI)
Time				
Baseline	7.0 (5.9–8.3)	6.9 (5.8–8.3)	2.3 (2.0–2.7)	2.5 (2.1–2.9)
6 months	1.7 (1.5–1.8)	1.7 (1.6–1.9)	0.9 (0.8–1.1)	0.9 (0.8–1.1)
12 months	1	1	1	1
Age (years)				
< 30	0.7 (0.6–0.9)	0.7 (0.6–0.9)	2.0 (1.6–2.5)	1.6 (1.3–2.1)
30–39	0.9 (0.7–1.2)	0.9 (0.7–1.2)	1.3 (1.0–1.8)	1.2 (0.9–1.5)
40+	1	1	1	1
Sex				
Male	1.0 (0.8–1.4)		1.0 (0.8–1.4)	
Female	1		1	
Education				
Junior	0.7 (0.6–0.9)	0.6 (0.5–0.8)	1.0 (0.9–1.3)	
Secondary	0.8 (0.7–1.0)	0.8 (0.6–1.0)	1.2 (1.0–1.4)	
Tertiary	1	1	1	
Methadone treatment[c,d]				
Detoxification			0.8 (0.6–0.9)	0.7 (0.6–0.9)
Maintenance			0.5 (0.4–0.6)	0.6 (0.5–0.7)
None			1	1
Drug injected[d]				
Heroin[e]			0.6 (0.3–1.1)	
Methamphetamine[f]			2.0 (1.6–2.4)	1.9 (1.6–2.2)
Midazolam[f]			1.9 (1.5–2.3)	1.7 (1.4–2.0)
Frequency of injection[d]				
< Weekly			0.7 (0.6–0.8)	0.8 (0.6–0.9)
> Weekly but < daily			0.8 (0.7–1.0)	0.9 (0.8–1.1)
Daily			1	1
Assignment				
Vaccine	1.0 (0.7–1.3)		1.1 (0.9–1.3)	
Placebo	1.2 (0.9–1.5)		1.0 (0.9–1.2)	
Don't know	1		1	
Vaccine efficacy				
Very/somewhat	1.3 (1.1–1.5)	1.3 (1.1–1.5)	1.0 (0.9–1.1)	
None/don't know	1	1	1	
Protection motivation[g]				
Strongly agree	1.0 (0.8–1.3)		0.9 (0.7–1.1)	
Agree	1.0 (0.9–1.3)		0.9 (0.7–1.1)	
Do not agree or do not disagree/disagree/ strongly disagree	1		1	

OR, odds ratio; CI, confidence interval.
[a]At baseline.
[b]Calculated among those injecting.
[c]Detoxification with or without maintenance or maintenance only.
[d]Association with injecting could not be evaluated because of similarity between predictor and outcome variables.
[e]Reference category is 'no heroin injection'.
[f]Reference category is 'heroin injection only'.
[g]Assessed at the 6-month follow-up visit.

Univariate analysis showed earlier follow-up time, younger age and injection of methamphetamine and midazolam to be associated with more-frequent sharing; being in methadone treatment and injecting less than weekly at baseline were related to less-frequent sharing (Table 2).

In multivariate analysis, earlier follow-up time, younger age and injection of methamphetamine and midazolam were significantly and independently associated with more-frequent sharing. Receiving methadone treatment and injecting less than weekly were associated with less-frequent sharing (Table 2).

The association between methadone treatment, type of drug injected, injection frequency and injecting could not be evaluated because of similarity between predictor and outcome variables.

Incarceration

At enrollment, 1996 (78.4%) participants reported a history of incarceration, of which 97.3% had ever been in a police holding cell, 64.0% had ever been in prison, and 61.3% had ever been in both. Of 446 (17.5%) who reported having been incarcerated during the 6 months before enrollment, 80.5% had been in a police holding cell, 42.2% in prison and 22.6% in both. At 6-month follow-up, 497 (20.0%) reported having been incarcerated during the past 6 months; of these, 92.2% had been in a police holding cell, 64.4% in prison and 56.5% in both. At 12-month follow-up, 623 (25.7%) reported having been incarcerated during the past 6 months; of these, 71.1% had been in a police holding cell, 74.8% in prison and 45.8% in both. Among those who were incarcerated during (part of) the 6 months prior to baseline or during (part of) the first 12 months of the trial, reports of injecting while incarcerated in police holding cells decreased from 12.0% at baseline to 9.2% and 8.4% at 6- and 12-month follow-up, respectively. This decrease was not significant. Reports of injecting while incarcerated in prison decreased from 11.2% at baseline to 1.6% and 2.6% at 6- and 12-month follow-up, respectively ($P < 0.001$).

Sexual behavior

Among the 860 (33.8%) participants who reported having a live-in sexual partner at baseline, 97.9% reported having had sexual intercourse with this partner during the past 6 months. Sexual intercourse with one or more casual sexual partners during the past 6 months was reported by 348 (13.7%) participants. The percentage having casual partner(s) declined significantly over time ($P < 0.001$; Table 3). Among those with a live-in partner, always using condoms during sexual intercourse with this partner increased from 7.4% at baseline to 10.4% and 9.8% at 6- and 12-month follow-up, respectively. This increase was not significant. Among those reporting casual partners, always using condoms during sexual intercourse with such partners increased from 46.0% at baseline to 53.1% and 55.0% at 6- and 12-month follow-up, respectively ($P < 0.001$; Table 3).

Table 3. Always using condoms among 2545 injection drug users participating in the AIDSVAX® B/E vaccine trial in Bangkok, Thailand, by partner type.

Partner type	Baseline [No. (%)]	6 months [No. (%)]	12 months [No. (%)]
Had live-in sexual partner	860 (33.8)	749 (30.1)	738 (30.4)
Always used condoms	62 (7.4)	81 (10.4)	70 (9.8)
Casual partners	348 (13.7)	288 (11.6)	255 (10.5)*
Always condom use	160 (46.0)	153 (53.1)	142 (55.0)*

*$P < 0.001$.

Discussion

During the first 12 months of the AIDSVAX® B/E trial among IDU in Bangkok, marked decreases in injection drug use and needle sharing were observed, in conjunction with increases in condom use, particularly with casual partners. Overall, no evidence was found for increased risk behavior in relation to optimism about the vaccine's efficacy or to beliefs about study-arm assignment and protection from HIV infection.

Increased risk behavior related to optimism about the vaccine's efficacy has been identified as an ethical challenge for the conduct of HIV vaccine trials, particularly in developing countries [1–3]. Even though almost 50% of our participants expressed optimistic beliefs about the vaccine's efficacy, substantial decreases in risk behavior were observed. Residual injection, but not sharing, was more often reported among those holding such optimistic beliefs. Our study results are in agreement with data presented from a clinical trial of AIDSVAX® B/B, a preventive HIV vaccine concurrently tested among 5109 gay men and 309 high-risk women in North America and Europe. During the first 12 months of this trial, similar reductions in HIV risk behavior were observed, although some interactions with perceived vaccine efficacy and assignment remained [19].

Risk behavior remaining after 12 months of follow-up may be more difficult to change. Total elimination of risk behavior, such as that associated with lack of access to and affordability of clean injection equipment, is in all likelihood beyond the reach of education and counseling, thereby emphasizing the need for an effective HIV vaccine. Residual risk behavior became apparent in the vaccine preparatory cohort study among Bangkok IDU, in which no further declines in injecting and sharing were reported after 32 months of follow-up (K. Choopanya, D. C. Des Jarlais and S.

Vanichseni S *et al.,* unpublished data). The reductions in risk behavior in this cohort were attributed to repeat HIV testing, counseling and interviewing. Similar behavioral changes have been observed in other cohorts of IDU [9,20,21]. These and our data suggest that increases in risk behavior among IDU participating in HIV vaccine trials are unlikely when studies include intensive education and counseling. Whether the observed reductions in the AIDSVAX® B/E trial are of a lesser or greater magnitude than could be expected from study participation and education and counseling alone is unknown. This should be the subject of careful future statistical analyses of the preparatory cohort and AIDSVAX® B/E trial data combined.

Our analyses identified age, education, methadone treatment, type of drug injected and frequency of injection as associated with injecting and sharing. Younger and less-educated participants who reported less-frequent injecting may have lower income and, therefore, reduced ability to buy injection drugs. However, younger participants reported more needle sharing, as did those who injected methamphetamine and midazolam. Younger participants may be more prone to risk taking, since sharing, and not injecting, is the main risk behavior for HIV transmission among IDU. Alternatively, older IDU who share needles may already be HIV infected and would not have been eligible for this trial. The lower levels of sharing among methadone recipients may be explained by their daily clinic attendance and exposure to preventive activities there. Injectors of methamphetamine and midazolam may be less prepared for injection (in terms of availability of clean injection equipment) than active heroin injectors, who attend methadone treatment and are exposed to preventive information on a daily basis.

Several studies among Thai IDU have identified incarceration as a risk factor for HIV infection [15,22,23]. Since clean injection equipment is not available in correctional facilities in Thailand, injecting while incarcerated usually implies sharing. The decline in injecting during incarceration among our participants is encouraging. However, most of this decline occurred in prisons (as opposed to police holding cells), where the risk for HIV infection from injecting appears to be lower. In Thailand, arrestees are initially detained in police holding cells before being transferred to prison or being released, depending on the outcome of judicial procedures. In a recently completed case–control study among Bangkok IDU [24], HIV-infected individuals were significantly more likely to have injected in police holding cells than in prisons. The absence of a significant decline in injecting in police holding cells is likely the result of efforts by IDU to alleviate acute withdrawal symptoms during this first stage of detention.

Incarceration during the past 6 months increased from 17.5% at baseline to 25.7% at the 12-month follow-up. This increase can be partially attributed to the fact that incarcerated IDU were not enrolled in this trial, whereas those who became incarcerated during follow-up were retained in the study. Another reason may be the Thai government's 'tough-on-drugs' policy, leading to more arrests, convictions and incarcerations [25]. Given the high risk and high frequency of incarceration among Bangkok IDU, the extension of methadone detoxification and HIV prevention methods into correctional facilities should receive serious consideration.

The reported increase in condom use with casual partners is positive. However, IDU in our study generally reported low sexual activity, and in previous analysis of risk factors for seroconversion among Bangkok IDU, sexual behaviors were not associated with HIV infection [15].

A limitation is that our study data consist of self-reports of stigmatized and illegal behavior, assessment of which has traditionally been problematic [26], and some underreporting of injecting and sharing is, therefore, likely. However, since the illegal and stigmatized nature of these behaviors did not change, rates of underreporting are likely to have been constant, allowing meaningful comparisons over time. Biological markers such as the incidence of HIV infection will help us to assess the completeness of behavioral self-reports. However, these data will only become available after the trial is completed and the blind is broken.

In conclusion, participants in the AIDSVAX® B/E trial reported significant reductions in drug-use risk behavior and increases in condom use, particularly with casual sex partners. No increases in risk behavior were found in relation to beliefs about vaccine efficacy, study-arm assignment and protection from HIV infection. Although this early decline in risk behavior provides reassurance that trial participation does not have an adverse behavioral effect, risk behavior may increase later for other reasons, including counseling fatigue, discontinuation of methadone treatment or availability of antiretroviral therapy. These factors will be closely monitored throughout the remainder of the trial and, if indicated, risk-reduction counseling and information for participants will be adjusted.

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