

## Willingness to Participate and Enroll in a Phase 3 Preventive HIV-1 Vaccine Trial

\*Jacqueline M. O'Connell, \*†Robert S. Hogg, \*Keith Chan, ‡Steffanie A. Strathdee,  
‖Nancy McLean, ¶Steve L. Martindale, #Brian Willoughby, and §Robert Remis

\*BC Centre for Excellence in HIV/AIDS, and †Department of Health Care and Epidemiology, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada; ‡Department of Epidemiology, Johns Hopkins School of Hygiene and Public Health, Baltimore, Maryland, USA; §Department of Public Health Sciences, University of Toronto, Toronto, Ontario, and ‖Vanvax—The Vancouver Vaccine Trial, and ¶The Vanguard Project, Vancouver, British Columbia; and #Spectrum Health Clinic, Vancouver, British Columbia, Canada

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**Objectives:** To assess the extent to which HIV-negative cohort study participants would be willing to participate (WTP) in future HIV vaccine trials, to explore enrollment into an ongoing phase 3 HIV vaccine trial, and to assess changing WTP in such trials over time.

**Methods:** The Vanguard Project is a prospective study of gay and bisexual men in the greater Vancouver region, British Columbia, Canada. Sociodemographic characteristics, sexual risk behavior, beliefs around HIV, and reasons for not participating in the AIDS-VAX B/B trial were collected from self-administered questionnaires. Contingency table analysis compared subjects who were WTP with subjects who were not WTP. Logistic regression analyses identified possible predictors of WTP. A subset analysis was conducted to assess changes in WTP in 2001 versus 1997.

**Results:** Of 440 respondents, 214 (48.6%) were WTP, and 97 (22.0%) were not WTP. Those WTP were disadvantaged, sexually risky, and had a high-perceived HIV risk (all  $p < .05$ ). Reasons for not participating in the AIDS-VAX B/B trial included fear of health problems and having missed the deadline for enrollment (all  $p < 0.05$ ). Multivariate analysis revealed that having had a regular sex partner (adjusted odds ratio, 0.48 [confidence interval, 0.25–0.92]) was a negative predictor whereas having a high-perceived HIV risk (adjusted odds ratio, 5.35 [confidence interval, 1.57–18.25]) was a positive predictor of WTP. Comparing WTP in 2001 with that in 1997, 24% of 100 participants who had been previously WTP were now not WTP.

**Conclusion:** Improving community and participant knowledge about preventive HIV vaccine trials may help ensure informed consent. However, whether informing potential participants will reverse or contribute to the declining trend in WTP observed in this cohort warrants further investigation.

**Key Words:** Preventive HIV vaccine—Phase 3 trial—AIDS-VAX B/B—Gay and bisexual men—Willingness to participate—Population-based cohort.

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Multiple preventive HIV candidate vaccines have entered phase 1 and 2 clinical trials, and the knowledge

gained in these trials has led to the first phase 3 HIV vaccine trial, which began in 1998 (1,2). With preliminary trials under way and with the introduction of other candidate vaccines on the horizon, a closer look at participant recruitment may help in planning future phase 3 clinical trials. Trials of preventive HIV vaccines require large populations among whom the incidence of HIV infection is high and individuals who are capable of ad-

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Address correspondence and reprint requests to Dr. Robert Hogg, Program Director, Division of Epidemiology and Population Health, BC Centre for Excellence in HIV/AIDS, 608–1081 Burrard Street, Vancouver, British Columbia V6Z 1Y6, Canada; e-mail: bobhogg@hivnet.ubc.ca

Manuscript received November 19, 2001; accepted August 12, 2002.

hering to study protocols and are willing to participate (WTP) (3–6). Other issues that need to be taken into account in study design include appropriate education about vaccine and trial concepts prior to enrollment and throughout the trial, optimizing recruitment and retention of high-risk individuals, and taking all reasonable actions to reduce risk behaviors in trial participants.

Characterizing high-risk populations who are WTP in HIV vaccine trials is important for assessing the feasibility of large-scale efficacy trials (3–8). Thus far, most studies of WTP in an HIV vaccine trial have measured WTP based on a hypothetical vaccine trial rather than any specific vaccine product or strategy. This is problematic, because self-reported willingness to enroll may not translate into actual enrollment into a trial once participants are presented with a specific vaccine product or opportunity for enrollment in a randomized clinical trial (9,10).

In this study, WTP in an HIV vaccine trial was examined among participants in an ongoing prospective study of HIV incidence and risk behaviors among young gay and bisexual men in Vancouver, British Columbia, Canada. We identified independent predictors of being WTP in an HIV vaccine trial and considered the implications of these findings for the design and implementation of phase 3 trials. In addition, we examined self-reported reasons for not participating in an ongoing phase 3 vaccine (AIDSVAX B/B; Vaxgen, Brisbane, CA, U.S.A.) trial. In a subanalysis, we examined WTP in the context of offering AIDSVAX B/B and a placebo-controlled trial as opposed to a theoretical trial by comparing our 2001 data with data from 1997 (5). In this subanalysis, we also assessed changing WTP from 1997 to 2001.

## METHODS

### Vanguard Project

Since May 1995, young gay and bisexual men have been recruited into an ongoing prospective study of HIV incidence and risk behaviors, as described previously (11). In brief, men are eligible to participate if they are between 15 and 30 years of age, live in the greater Vancouver region, and have not previously tested HIV-positive. Participants are recruited through outreach at gay community events, community health clinics or local physicians, and the gay and mainstream media. Eligible participants are referred to local HIV testing clinics, the study research nurse, or their physicians' offices, where they complete a confidential self-administered questionnaire and provide a blood sample for HIV testing. Follow-up visits are conducted annually.

### HIV Testing

Participants were provided with pre- and posttest HIV counseling by trained personnel at every visit. Reactive ELISA results were con-

firmed by western blotting according to standard procedures at the provincial laboratory of the British Columbia Centre for Disease Control. Participants were encouraged to return to their physician, clinic, or the study research nurse to receive their HIV test results. Referrals were provided for universal medical care, HIV/AIDS care, available drug and alcohol treatment, and counseling, where appropriate.

## Study Instruments

Information was collected on sociodemographic characteristics, sexual behaviors with men, and psychosocial variables using self-administered questionnaires. Data were collected on total numbers of male sexual partners in the previous year and lifetime, age at which respondents first engaged in sexual activity, and frequencies of specific sexual practices. Sexual behaviors were recorded for regular partners, defined as partners with whom respondents had sex on a regular basis (at least once a month on average), and for casual male partners, defined as partners with whom they had sex less than once a month on average (including "one-nighters").

The instrument included an abbreviated seven-item version of the Center for Epidemiological Study Depression Scale (12). Participant perceptions of HIV disease and HIV optimism—belief that new treatments will make HIV/AIDS a less serious threat—were collected from a series of 11 questions described elsewhere (13). In 1997, the following item was added to the Vanguard Project questionnaire that asked participants if they would be WTP in a future HIV vaccine trial: "If an HIV vaccine were tested in Canada on people who don't have HIV, would you be interested in participating in a study to see if it works?" The proportion of respondents who were WTP in HIV vaccine studies was calculated according to the range of possible responses to this question (absolutely, probably, don't know, probably not, no, and not eligible [e.g., HIV-positive or participating in the AIDSVAX B/B trial]). Subjects responding "absolutely" or "probably" were considered to be WTP. Similarly, subjects responding "probably not" and "no" were considered to be not WTP. To obtain the most conservative estimate of WTP, participants who reported being unsure were considered separately. Respondents already enrolled in the AIDSVAX B/B trial or who were HIV-positive were excluded from the analyses.

## AIDSVAX B/B Trial Participation

Self-reported participation in the ongoing phase 3 AIDSVAX B/B trial and reasons for not participating in this vaccine trial were collected from seven specific questions included in the Vanguard Project questionnaire since 1999. The AIDSVAX B/B trial is an international, double-blind, placebo-controlled study of the rgp120/HIV-1 vaccine (2). In this trial, subjects are randomized in a 2:1 ratio to receive either vaccine or placebo at months 0, 1, 6, 12, 18, 24, and 30. Participants were excluded if they had not engaged in anal intercourse with a male partner at least once in the previous year or if they were in monogamous relationships with the same seronegative male partner over the same time period. The questions were developed as a part of the Canadian Network for Vaccine and Immunotherapeutics Behavioral and Epidemiologic Aspects of HIV Vaccine Trials Initiative, a multicenter collaborative effort of the Montreal, Vancouver, and Toronto AIDSVAX B/B trial sites and the Vanguard Project (Vancouver) and Omega (Montreal) cohorts.

The Vanguard Project did not actively recruit participants into the AIDSVAX B/B trial; however, the participants were informed of the trial and educated about basic trial concepts using mailings, e-mails, and newsletters collected at the same time as questionnaires. These

covered a basic description of the AIDS VAX B/B, antibody production after receipt of the vaccine (including mention of the potential implications for indeterminate HIV test results after vaccination), eligibility for the trial, time commitment over trial participation, a brief description of what a placebo-controlled trial and blinding are, and clarification that there was no risk of being infected with HIV from the vaccine itself.

### Statistical Analysis

Participants were included in this analysis if they had completed a questionnaire between October 1999 and May 2001. The following variables were coded according to procedures defined a priori. Unstable housing was defined as living primarily in a hotel, boarding room, hostel, transition house, or jail or on the street (5). Center for Epidemiological Study Depression Scale scores were independently scored (e.g., never = 1; always = 5) and summed; higher scores indicated more depressive symptoms. Perceived threat of HIV infection was determined by an item that asked respondents' opinions about their likelihood of becoming infected with HIV. Persons who responded "much more likely" or "somewhat more likely" than present were considered to have a high-perceived HIV threat.

Contingency table analysis and Wilcoxon rank sum test were used to compare willing with unwilling subjects, according to the variables described above. Logistic regression models were also developed, whereby variables that attained a significance level of .05 in univariate analysis were offered into a multivariate model. In the multivariate model, all possible two-way interactions were examined.

Finally, based on a previous analysis of our cohort (5), we compared WTP in the context of the AIDS VAX B/B trial with a hypothetical trial, which corresponded to survey responses in 2001 versus those in 1997. In this subset analysis, we used the same definition of WTP in a vaccine trial (i.e., subjects responding "absolutely" or "probably" were considered to be WTP).  $\chi^2$  tests and the Breslow-Day test for homogeneity of odds ratios were used to compare the two waves of data. In this analysis, we also examined changing trends in WTP.

### RESULTS

A total of 474 Vanguard Project participants completed a questionnaire between October 1999 and May 2001. Eligible participants included 214 who were WTP and 97 who were not WTP. The 129 participants who were unsure of their WTP were considered separately. Participants ineligible for this study included 13 respondents who were HIV-positive and 21 who were already participating in the AIDS VAX B/B trial in Vancouver.

Compared with participants who were not WTP, those WTP were younger, more likely to live in unstable housing, and more likely to have injected drugs in the past year or in their lifetimes (Table 1). WTP was also associated with having had more sex partners in the past year, an increased likelihood of having had casual sex partners, and a decreased likelihood of having had regular sex partners. Participants WTP were more likely to report more unprotected receptive anal sex with casual partners, but they had a decreased likelihood of having

**TABLE 1.** Sociodemographic factors associated with willingness to participate (WTP) in an HIV vaccine trial

Variable	WTP (n = 214)	non-WTP (n = 97)	p value
Unstable housing			
Yes	35 (16.4%)	4 (4.3%)	.003
Ethnicity			
White	155 (74.2%)	69 (75.8%)	.100
Native	24 (11.5%)	4 (4.4%)	
Other	30 (14.3%)	18 (19.8%)	
Unemployed			
Yes	68 (32.1%)	22 (23.4%)	.125
High school education			
Yes	176 (83.4%)	80 (87.0%)	.433
Income $\leq$ \$10 000			
Yes	10 (6.9%)	3 (4.1%)	.406
Sex trade worker in the past year			
Yes	48 (22.4%)	14 (14.4%)	.102
History of injection drug use			
Yes	45 (21.0%)	9 (9.3%)	.011
Injection drug use in the past year			
Yes	35 (16.4%)	6 (6.2%)	.014
Median age (IQR)	27 (24–31)	29 (26–31)	.041

Column totals may not be equal to sample size due to missing values. IQR, interquartile range.

had insertive anal sex with casual partners (Table 2). There was no association between being WTP and ethnicity, involvement in the sex trade, education, income, sex with HIV-positive partners, or specific sexual behaviors with regular partners.

Compared with those not WTP, participants who were WTP were more likely to have depressive symptoms and were more likely to have a high-perceived threat of HIV infection (Table 3). However, participants who were WTP were more likely to report believing the following: new treatments for HIV infection will "take the worry out of sex," "a person with undetectable viral load cannot pass on the virus," and "because of new treatments, fewer people are becoming infected with HIV" (Table 3).

Less than one half of the respondents who reported having heard of AIDS VAX B/B were among the participants who were not WTP in a vaccine trial. No difference was found between participants WTP and those not WTP in beliefs surrounding risk behaviors due to the ongoing phase 3 trial (Table 4). Only 21 Vanguard Project participants reported having enrolled in the AIDS VAX B/B trial. Of those who provided reasons for not enrolling in the trial, participants not WTP were more likely to have cited fear of serious health problems, fear of the vaccine's potential to infect, and concern for being denied health insurance. Conversely, participants WTP were more likely to have cited missing the deadline for enrollment as a primary reason for not enrolling in the trial (Table 4).

**TABLE 2.** Associations between sexual risk taking and willingness to participate (WTP) in an HIV-vaccine trial

Variable	WTP (n = 214)	non-WTP (n = 97)	p value
Casual sex partners			
Yes	165 (81.7%)	67 (71.3%)	.043
Receptive anal sex with casual partners			
Yes	83 (50.3%)	32 (47.8%)	.726
Insertive anal sex with a casual partner <sup>a</sup>			
Yes	97 (58.8%)	50 (74.6%)	.023
Unprotected receptive anal sex with a casual partner <sup>a</sup>			
Yes	35 (42.1%)	7 (21.9%)	.043
Unprotected insertive anal sex with a casual partner <sup>a</sup>			
Yes	45 (46.4%)	18 (36.0%)	.228
Regular sex partners			
Yes	152 (73.8%)	80 (84.2%)	.046
Receptive anal sex with regular partner <sup>b</sup>			
Yes	110 (73.3%)	62 (77.5%)	.488
Insertive anal sex with a regular partner <sup>b</sup>			
Yes	117 (77.0%)	62 (77.5%)	.928
Unprotected receptive anal sex with a regular partner <sup>b</sup>			
Yes	77 (70.0%)	42 (67.7%)	.758
Unprotected insertive anal sex with a regular partner <sup>b</sup>			
Yes	80 (68.4%)	38 (61.3%)	.341
Sex with an HIV-positive partner			
Yes	36 (17.6%)	14 (14.9%)	.566
Unprotected sex with an HIV-positive partner			
Yes	10 (4.9%)	2 (2.1%)	.352
Median (IQR) number of male sex partners in the past year	4.5 (3–15)	3.5 (1–12)	.040
Median (IQR) number of male sex partners in lifetime	60 (12–300)	60 (12–70)	.106

Column totals may not be equal to sample size due to missing values.

<sup>a</sup> Among participants with casual partners.

<sup>b</sup> Among participants with regular partners.

In a multivariate logistic regression model, having had a regular sex partner was independently associated with being less likely to be WTP. Conversely, a high-perceived HIV threat was associated with being more WTP in a preventive HIV vaccine trial (Table 5).

Findings from questionnaires completed in 1997 in the context of a hypothetical trial were compared with our data from 2001 collected in the context of the AIDSVAX B/B trial. One hundred participants completed questionnaires in both 1997 and 2001. Overall, WTP responses remained the same for roughly three quarters (73%) of participants; however, one quarter (24%) of respondents who reported being WTP in 1997 were not WTP as recorded in 2001. Only 3% who were not WTP in 1997 changed their response to WTP when asked in 2001. For these 100 participants, there were no significant differences between participant characteristics and response consistency from 1997 to 2001.

Among participants who did not complete both questionnaires, a lower percentage of respondents were WTP when asked in 2001 (48.7%) than had been in 1997 (63.3%). Similarly, more people in 2001 were not WTP (22.1%) than had been in 1997 (11.8%). The percentage of people who reported being uncertain in 2001 versus

1997 did not change greatly (29.2% versus 24.8%, respectively). Interestingly, aboriginal (i.e., Native, First Nations, Métis, or Inuit) respondents were more likely to be WTP in 2001 than they had been in 1997 (90% vs. 60%, respectively), although sample sizes were small.

## DISCUSSION

Gay and bisexual men who expressed WTP in an HIV vaccine trial were more likely to be socioeconomically disadvantaged and sexually risky and to have a high-perceived risk of HIV infection. Reasons for not enrolling in the AIDSVAX B/B phase 3 trial in Vancouver included fear of infection, serious health problems, and being denied health insurance or having missed the deadline for enrollment. Comparing WTP in 1997 in the context of a hypothetical trial with WTP in 2001 in the context of the ongoing AIDSVAX B/B phase 3 trial, there is evidence of a decline in interest in vaccine trial participation since 1997.

In the present analysis, approximately one half of respondents reported being WTP in a future HIV vaccine trial. This value is slightly lower than those in other studies examining vaccine preparedness in cohorts of

**TABLE 3.** Social and emotional stability scores and perceived risk of HIV infection associated with willingness to participate (WTP) in an HIV-vaccine trial

Variable	WTP (n = 225)	non-WTP (n = 97)	p value
Median (IQR) CES-D score	7 (3–11)	5 (2–8)	.012
Median (IQR) Rosenberg score	31 (27–35)	33 (29–37)	.053
Median (IQR) number of HIV tests per year	2 (1–3)	1 (1–2)	.112
“A person with undetectable viral load cannot pass on the virus”			
Yes	31 (15.7%)	12 (13.8%)	.674
“I’m less worried about HIV infection than I used to be”			
Yes	79 (38.4%)	26 (28.0%)	.081
“New HIV treatments will take the worry out of sex”			
Yes	31 (15.1%)	6 (6.5%)	.035
“If every HIV-Positive person took the new treatments, the AIDS epidemic would be over”			
Yes	16 (7.9%)	1 (1.1%)	.021
“If a cure for AIDS were announced, I’d stop practicing safe sex”			
Yes	31 (14.9%)	18 (19.8%)	.295
“People with undetectable viral load don’t need to worry so much about infecting others with HIV”			
Yes	19 (9.3%)	2 (2.2%)	.027
“Until there is a complete cure for HIV/AIDS, prevention is still the best practice”			
Yes	189 (91.8%)	5 (5.4%)	.378
“HIV is less of a threat because the epidemic is on the decline”			
Yes	22 (10.8%)	7 (7.5%)	.330
“HIV/AIDS is a less serious threat than it used to be because of new treatments”			
Yes	41 (20.3%)	18 (19.8%)	.919
“It’s never safe to fuck without a condom regardless of viral load”			
Yes	179 (86.5%)	78 (83.9%)	.552
“Because of new treatments, fewer people are becoming infected with HIV”			
Yes	32 (16.0%)	13 (14.3%)	.708
“Possibly, probably, or most likely infected with HIV in the past year”			
Yes	31 (14.7%)	5 (5.3%)	.018

Column totals may not be equal to sample size due to missing values.

gay and bisexual men (4,7,14), including a previous analysis of our own cohort in 1997 (5). This difference may be attributable to study design, cohort selection factors, or the fact that the Vanguard Project questionnaire is self-administered (5). Our findings may also reflect a temporal decline in WTP in recent years.

A decline in WTP could be related to the availability and tone of vaccine trial information within a community and community characteristics overall (9). The Vanguard Project did not participate in active recruitment of participants to the AIDS VAX B/B trial; however, Vanguard Project mailings and newsletters disseminated information about the trial and about basic trial concepts. Thus, it is possible that the observed decline in willingness between a hypothetical trial in 1997 and a trial offered in the era of the ongoing AIDS VAX B/B phase 3 trial may actually be driven by an increase in awareness or understanding of vaccine trial concepts and potential consequences of participation in an actual trial. This hypothesis needs to be investigated more thoroughly in this cohort. Thus, because potential trial participants are likely to be exposed to confusing and changing information regarding risks, benefits, and other realities of trial participation, adopting an extended recruitment and intensive and community-wide education period will allow

participants the time to become informed about the risks and benefits of trial participation. This strategy will help ensure truly informed decisions and a lasting commitment to participate.

In our cohort, Aboriginal respondents were more likely to be WTP in 2001 than they were in 1997. Aboriginal men are at increased risk of antecedent risk factors for HIV infection including sexual abuse, poverty, poor mental health, and involvement in the sex trade (15). Because of small numbers, we are unable to examine this trend further; however, the increase in WTP in this population may reflect how hard hit this population is by HIV disease. As such, this population must be sufficiently represented in HIV vaccine trials.

Participants who were WTP were more likely to be younger and marginalized. For young participants, lack of experience with the AIDS epidemic (16) or a desire to escape the rigors and standards for a lifetime of safe sex (17) may help to explain ongoing sexual risk taking. Indeed, being young and disadvantaged (18) may increase the risk of HIV infection and, therefore, increase the likelihood of recruitment into a preventive HIV vaccine trial (4). However, younger men were shown to have greater difficulty understanding vaccine trial concepts (18). In addition, being younger, living in unstable

**TABLE 4.** Descriptive overview of beliefs surrounding and reasons for not participating in the AIDS-VAX B/B phase 3 HIV vaccine trial

Variable	WTP (n = 214)	non-WTP (n = 97)	p value
Ever heard of the AIDS-VAX B/B phase 3 trial			
Yes	80 (37.4%)	57 (59.4%)	<.001
Perceived likelihood that AIDS-VAX B/B trial will lead to engaging in unsafe sex			
For others <sup>a</sup>			
Much more likely	15 (19.0%)	6 (10.7%)	.115
Somewhat more likely	41 (51.9%)	25 (44.6%)	
Not more likely	18 (22.8%)	15 (26.8%)	
Unsure	5 (6.3%)	10 (17.9%)	
For self <sup>a</sup>			
Much more likely	3 (3.8%)	0 (0.0%)	.593
Somewhat more likely	6 (7.6%)	5 (8.9%)	
Not more likely	67 (84.8%)	47 (83.9%)	
Unsure	3 (3.8%)	4 (7.4%)	
Reasons for not enrolling in the AIDS-VAX B/B trial			
Might cause health problems	8 (10.1%)	27 (48.2%)	<.001
Can't be sure the vaccine won't infect	10 (12.7%)	25 (44.6%)	<.001
Not really at risk for HIV	14 (17.7%)	12 (21.4%)	.590
Worried about developing a false positive HIV test	9 (11.4%)	13 (23.2%)	.067
Plan to wait for a vaccine that will be more effective	13 (16.3%)	9 (16.1%)	.978
Missed the deadline for eligibility	26 (32.5%)	3 (5.4%)	<.001
Concern for being denied entry into other countries	6 (7.6%)	10 (17.9%)	.069
Concern for being denied health insurance	1 (1.3%)	7 (12.5%)	.009
Not eligible	7 (8.9%)	1 (1.8%)	.139
Vaccine probably does not work	5 (6.3%)	5 (8.9%)	.741
Other <sup>b</sup>	26 (32.9%)	14 (25.0%)	.321

<sup>a</sup> Column totals may not be equal to sample size due to missing values.

<sup>b</sup> Other category hand-written comments include (generally): not interested, not well enough informed, no time/inconvenient, boyfriend doesn't approve, monogamous relationship, not sexually active enough, travel/busy life, missed the enrollment deadline.

housing, and being an injection drug user were also associated with loss to follow-up in an HIV vaccine preparedness study (4) and are independent predictors of being lost to follow-up within the Vanguard Project cohort (19). Thus, recruitment of younger and marginalized participants may make informed consent and retention all the more challenging for vaccine trial investigators, and young men's reasons for being WTP in an HIV vaccine trial warrant further investigation in this cohort.

Individuals who engage in high-risk sexual behavior are desirable candidates for an HIV vaccine efficacy trial, and the present analysis supports the contention that persons more likely to engage in high-risk sexual behaviors are more likely to be WTP (7,9,14,15,20). Engaging in HIV risk behaviors and a desire for possible protection

from the vaccine are commonly associated with WTP (3,9,21). These motivations have not been confirmed for Vanguard Project participants; however, high-perceived threat of HIV infection was a strong and independent predictor of WTP in this cohort, and men with more depressive symptoms were more likely to be WTP. In previous studies, depression was associated with sexual risk taking in gay and bisexual men (11,22), and perceived HIV threat and depression were previously found to be predictive of WTP in the Vanguard Project (5) and elsewhere (18). Chesney et al. (15) described increased sexual risk taking in vaccine trial participants once the trial was under way, especially in participants who had engaged in risky behaviors prior to entry into the trial. Thus, direct measures may be needed to safeguard against increased risk taking in HIV vaccine trials, and the current study further highlights the importance of considering the psychologic health of potential participants and evaluating what threshold of distress should trigger exclusion from an HIV vaccine trial (5).

Having had regular sex partners was an independent predictor of being less likely to be WTP. This finding may simply be reflective of a low-perceived HIV risk or of perceived ineligibility, as vaccine trial design often

**TABLE 5.** Independent predictors of willingness to participate in an HIV vaccine trial

Variable	Odds ratio	Confidence intervals	p value
Have a regular sex partner	0.48	(0.25–0.92)	.027
“Possibly, probably, or most likely infected with HIV in the past year”	5.35	(1.57–18.25)	.007

stipulates exclusion of people in primary relationships because sexual behavior with primary partners is considered to be low risk. However, as has been reported elsewhere (23) and has recently been confirmed in the Vanguard Project cohort (unpublished data), young gay men are at risk for contracting HIV infection from a primary partner. Therefore, HIV vaccine trial design may consider targeting recruitment and education initiatives to promote the participation of men in primary relationships.

Most respondents in this study who were not WTP cited fear of serious health problems or fear of the vaccine's potential to infect as major reasons for not participating in the AIDS-VAX B/B trial. These responses support findings from other hypothetical vaccine preparedness studies (4,5,7-9,14,15), where common barriers to participation included safety concerns, vaccine-induced seropositivity, social risk, and doubts about the vaccine. Most of the willing participants who did not enroll cited having missed the deadline for enrollment. These findings again suggest a lack of community information about ongoing trials and about vaccines in general. In addition, most of the willing participants who did not enroll cited having missed the deadline for enrollment. Both of these findings support extending recruitment and education time for HIV vaccine trials.

Because of regional variations and because this cohort was based on a sample of convenience, these results may not be generalizable to other populations of gay and bisexual men in Vancouver or elsewhere. However, if future vaccine trials use the same strategies to recruit prospective HIV vaccine trial participants as are used to recruit participants into the Vanguard Project, these analyses may provide estimates of willing participant characteristics and risk behaviors and may also identify needed areas for targeted education that will benefit the design of efficacy trials in Vancouver.

In summary, our analysis identified a number of factors that are relevant in the design of phase 3 efficacy trials of HIV vaccines. Generally, sexually risky and socioeconomically disadvantaged men and men with a high-perceived HIV risk were more likely to be WTP. These men may represent a population who could be difficult to retain and may require careful monitoring and appropriate education and counseling at enrollment and throughout the trial to maximize safety for participants. Reasons for not enrolling in the AIDS-VAX B/B phase 3 trial in Vancouver included fear of serious health problems or having missed the deadline for enrollment, and there is evidence of a decline in interest in vaccine trial participation since 1997. We suspect that self-reported willingness to enroll in 1997 did not translate into actual enrollment into the AIDS-VAX B/B trial as measured in

2001, because of lack of complete or appropriate information on vaccine trial concepts. Thus, a comprehensive approach to educating communities and trial participants may help to improve community and participants' knowledge about preventive HIV vaccine trials—especially ongoing trials—and inform perceptions of trial-related risks and benefits (3,24). Whether this effort will help to reverse the declining trend in WTP observed in this cohort warrants further study. However, we suggest that a longer recruitment process may help ensure informed and considered consent. As knowledge of HIV vaccine trial concepts increases over time due to education and community input, perhaps self-reported WTP will more readily translate into a lasting commitment to vaccine trial participation.

**Acknowledgments:** This work was supported by the Canadian Network for Vaccines and Immunotherapeutics and by the Canadian Institutes of Health Research through an investigator award to R.H. The authors are indebted to the participants, physicians, nurses, and clinic staff of the Vanguard Project cohort and the Community Advisory Committee of the Vanguard Project. The authors thank Peter Vann for his administrative assistance.

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