Acceptability of HIV vaccine trials in high-risk heterosexual cohorts in Mombasa, Kenya

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Objectives: To ascertain the level of acceptance of a prophylactic HIV vaccine trial in high-risk HIV-seronegative heterosexual cohorts of men and women in Mombasa, Kenya, and to assess the anticipated effects of participation on risk behavior.

Methods: Standardized questionnaire administered to a convenience sample of commercial sex workers and trucking company employees enrolled in prospective cohort studies.

Results: Ninety-six per cent of respondents believed that HIV was a major problem in Kenya and 86% of men and 94% of women perceived themselves at risk. One hundred per cent of women and 84% of men expressed interest in participation in an HIV vaccine trial, after explanation of the experimental nature of the vaccine, double-blind placebo-controlled design, prolonged follow-up and potential change in serostatus. Seventeen per cent of men and 9% of women anticipated an increase in risk behavior as a result of participation.

Conclusion: The majority of individuals in two high-risk cohorts were interested in participating in Phase III efficacy trials of HIV vaccines. A significant minority anticipated an increase in risk behavior, which emphasizes the need for intensive counseling and education throughout a vaccine trial.

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Introduction

Since the first case of AIDS was reported in 1981, the HIV epidemic has spread throughout the world, often at an alarming pace. The World Health Organization estimates that at least 16 million infections had occurred worldwide by 1994, and projects an additional 14 million by the year 2000 [1]. The challenge to prevent transmission has been a difficult one. Although there have been some noteworthy successes in the developed world [e.g., the decreased HIV seroincidence among homosexual men as a result of safer sex practices [2], reduced acquisition of infection among intravenous drug users (IVDU) because of altered needle-sharing or cleaning practices [3], and the virtual elimination of HIV risk for recipients of blood products in many countries], the failure of current approaches to control the epidemic in many high-risk communities is obvious. Research demonstration projects have documented that HIV acquisition can be slowed among commercial sex workers (CSW), an important core group in many developing countries [4,5]. However, these programs have not been replicated on a large scale in most countries, and the number of infected individuals globally continues to climb rapidly. The explosive spread of HIV in Thailand, despite the accepted intervention tools of behavior mod-

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ification, condom promotion, and sexually transmitted disease (STD) control, was a humbling reminder of the limitations of existing control strategies [6].

The need for more effective interventions to control the current HIV-1 epidemic is clear, and a vaccine would hold the most promise for prevention of new infections. The ideal vaccine would be cheap, safe, highly efficacious, effective as a single dose, and associated with lifelong sterilizing immunity to all strain types of HIV. While the quest for a vaccine with these properties continues in many centers, preparation for safety and efficacy trials in human populations has been conducted simultaneously in many countries worldwide. As part of the Preparation for AIDS Vaccine Evaluation (PAVE) initiative, sponsored by the US National Institutes of Health, two cohorts of men and women at high risk of HIV infection were established in Mombasa, Kenya, for possible inclusion in Phase III vaccine efficacy trials. A survey was conducted to determine the likelihood of participation in such a trial under conditions likely to prevail: i.e., a randomized, placebo-controlled, double-blind trial of a vaccine of unknown efficacy and duration of effect, delivered by injection on more than one occasion.

Subjects and methods

Mombasa is a major East African port, with road and rail links throughout East–Central Africa, a popular international tourist resort, and a city of 600 000 people. Recruitment and follow-up of cohorts of female CSW at Ganjoni Municipal Clinic and male employees of trucking companies at the Mombasa trucking company terminals began in February 1993, as previously described [7]. After verbal informed consent was obtained, standardized interviews regarding demographic, occupational, medical, and sexual histories were completed at enrollment and follow-up visits as part of the PAVE project. Physical examinations and screening evaluations for STD were conducted at each visit. Sequential blood samples were obtained for HIV serologic assays. HIV/STD risk-reduction counseling, condoms and primary health-care services were provided to all study subjects.

Baseline HIV seroprevalence rates were 56% [8] among CSW and 17% [9] among male trucking company employees. As of May 1994, 463 seronegative women and 743 seronegative men were enrolled in the prospective cohort studies. The annual HIV seroincidence rates were 16% [27 in 167 person-years (PY) of follow-up] and 5% (18 in 337 PY) in the female and male cohorts, respectively; thus, establishing that these individuals were at high risk for HIV infection.

The vaccine acceptability questionnaire was administered to a convenience sample of 201 seronegative men and 206 seronegative women during a follow-up visit for the PAVE study between September 1993 and May 1994. No individual refused participation. The questions were developed in English, with a Flesch-Kincaid standardized readability formula educational grade level of 7.0 [10], translated into Kiswahili by Kenyan physicians and health educators, and finalized after holding focus group discussions with subjects at the clinics. The questionnaire was administered as a standardized interview, comprising four section: (1) general knowledge of prophylactic vaccines currently in use; (2) the magnitude of the HIV epidemic in Kenya and assessment of individual risk; (3) anticipated willingness to participate in an HIV vaccine trial; and (4) anticipated behavior change resulting from such participation.

Standardized information regarding the nature and limitations of prophylactic vaccines was given after questions in the vaccine knowledge section, in order to resolve basic misconceptions.

Results

The demographic and behavioral characteristics of respondents are described in Table 1. Sixty per cent of men were married: 58% reported two or more sex partners and 22% gave a history of unprotected sex with a CSW in the year prior to enrollment. The women reported a median number of sex partners of one per week (range, 0–5), median sexual frequency of twice per week (range, 0–7), and condom use with 64% of sexual partners. Ninety (44%) women and 145 (72%) men had completed primary education (8 years). The demographic and behavioral characteristics of the cohorts to which these subjects belong reported elsewhere [7]. The only statistically significant difference between the cohorts as a whole and the sample participating in the vaccine acceptability survey was in the percentage of truck drivers and their assistants, with these more mobile occupations making up 35% of the total male cohort, but only 20% of the sample surveyed ($P<0.001$).

Knowledge of respondents about vaccines currently in use in Kenya is shown in Table 2. At least 85% of men and women knew that vaccines are used to prevent disease and were able to name a vaccine-preventable disease. However, less than half knew that vaccines were not 100% efficacious and only one-third knew that vaccines could have adverse effects. There were no statistically significant differences in any of the responses by sex or educational level.

One hundred and ninety-one (95%) men and 202 (98%) women thought that HIV infection and AIDS was a major problem in Kenya. Only 29 (14%) men and 12 (6%) women felt at no personal risk of HIV infection.

Replies to questions regarding acceptance of a safe and efficacious HIV vaccine, the likely conditions of a vaccine trial, and participation in a vaccine trial are given in Table 3. Only 4% of men and 1% of women said they would refuse an HIV vaccine of known high safety and efficacy. The reasons given for refusal included the

Table 1. Demographic and behavioral characteristics of participants.

	Mean/median or proportion (%)
Male trucking company employees (n = 201)	
Mean age in years	30 (range, 17–54)
Kenyan nationality	199 (99)
Years of formal education	
None	3 (2)
0–7	53 (26)
≥ 8	145 (72)
Occupation	
Truck drivers or assistants	41 (20)
Mechanics	73 (36)
Ancillary workers	87 (43)
Religion	
Protestant	76 (38)
Catholic	66 (33)
Moslem	50 (25)
Marital status	
Married	121 (60)
Unmarried	75 (37)
Widowed or divorced	5 (3)
History of sex with a CSW	105 (52)
History of condom use	102 (51)
Sexual behavior in past year	
2–5 partners	95 (47)
≥ 5 partners	23 (11)
Unprotected sex with a CSW	44 (22)
Female commercial sex workers (n = 206)	
Mean age in years	29 (range, 17–46)
Kenyan nationality	193 (94)
Years of formal education	
None	25 (12)
0–7	91 (44)
≥ 8	90 (44)
Years as CSW (median)	3 (range, 0–24)
Religion	
Catholic	100 (49)
Protestant	79 (38)
Moslem	24 (12)
Marital status	
Married	4 (2)
Unmarried	89 (43)
Widowed or divorced	113 (55)
Sex partners per week (median)	1 (range, 0–5)
Sex frequency per week (median)	2 (range, 0–7)
Mean condom use (%)	64

CSW, Commercial sex worker.

Table 2. Participants knowledge of vaccines currently in use in Kenya.

	Men (%) (n = 201)	Women (%) (n = 206)
Knew vaccines are used to prevent disease	173 (86)	188 (91)
Able to name a vaccine-preventable disease	176 (88)	175 (85)
Knew vaccines are not 100% efficacious	98 (49)	92 (45)
Knew vaccines could have side-effects	58 (29)	68 (33)

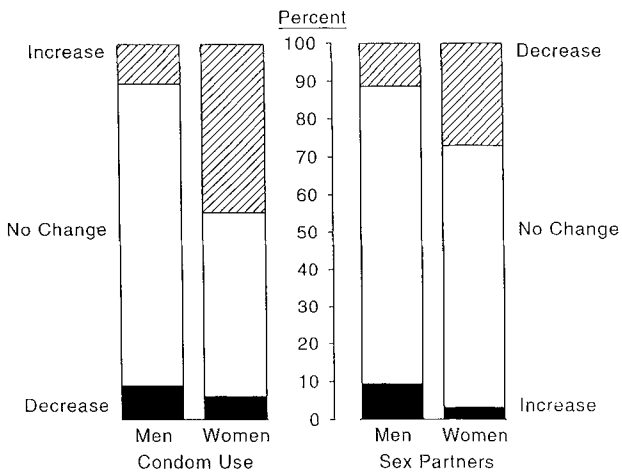

Fig. 1. Anticipated sexual behavior change as a result of participation in an HIV vaccine trial.

fear of acquiring HIV infection from the vaccine (seven men), no perceived risk of infection (two men, one woman) and fear of injections (one woman). Regarding the conditions of a prophylactic vaccine trial, acceptance of a double-blind, placebo-controlled design, prolonged follow-up, and change in serological status was consistently higher among women than men ($P < 0.001$ for each condition). Ninety-one per cent of women but only 67% of men said they would definitely agree to participate in a trial of a candidate HIV vaccine given the conditions specified, and an additional 9% of women and 18% of men said they would possibly participate. Concerns regarding participation included fear of a positive HIV blood test result (27 men, one woman), fear of HIV

Table 3. Acceptance of conditions of an HIV prophylactic vaccine trial.

	Men (%) (n = 201)			Women (%) (n = 206)		
	Yes	Perhaps	No	Yes	Perhaps	No
Would accept an HIV vaccine of known high safety and efficacy	186 (93)	8 (4)	7 (4)	191 (94)	11 (5)	2 (1)
Would accept a double-blind, placebo-controlled design	137 (68)	30 (15)	34 (17)	174 (85)	21 (10)	9 (4)
Would accept a follow-up of 3–5 years	129 (65)	34 (17)	34 (17)	183 (93)	14 (7)	0
Would accept a 'false-positive' HIV serologic result	132 (66)	34 (17)	33 (16)	173 (88)	23 (11)	1 (1)
Would participate in trial of a candidate HIV vaccine	133 (67)	35 (18)	32 (16)	181 (91)	8 (9)	0

infection from the vaccine (11 men, one woman), prolonged follow-up period (two men) and fear of injections (one man). There was no significant effect of educational level on vaccine trial acceptance among either men or women. There was, however, a highly significant sex difference in anticipated refusal to participate in a vaccine trial, with 16% of men and none of the women declaring no interest ($P<0.001$).

Anticipated sexual behavior changes as a result of participation in an HIV vaccine trial are shown in Fig. 1. Seventeen (9%) men said that they would decrease condom use, and 18 (9%) would increase numbers of sex partners. Two (1%) men stated that they would do both. Among the women, 6% anticipated decreased condom use and 3% anticipated an increased number of sex partners. Anticipated higher risk behavior was significantly associated with men ($P=0.02$) but not with age, years of education, history of unprotected sex with CSW among men, or years of prostitution, years of education, or current condom use among women.

Discussion

In this study of Kenyan trucking company employees and CSW, we have documented a high rate of willingness to participate in candidate prophylactic HIV vaccine trials. One hundred per cent of women and 84% of men indicated interest in participation. Of concern, however, were the disturbing anticipating behavior changes reported by a significant number of respondents. Seventeen per cent of men and 9% of women said they would increase sexual risk behavior if involved in a vaccine trial. This occurred despite an intensive individual HIV educational counseling program included in the PAVE cohort study, and having been informed in the context of the vaccine survey that half of trial participants would receive placebo and the other half a vaccine of unknown efficacy. This finding underscores the need for extensive education both before enrollment of individuals and throughout the duration of the trial.

The successful conduct of HIV vaccine efficacy trials requires the availability of cohorts with high seroincidence rates. A number of articles have addressed the ethical dilemma which confronts HIV vaccine investigators [11–19]. While a high HIV seroincidence permits a trial to be conducted with fewer subjects and shorter follow-up, the ethical principle of beneficence demands that the well being of participants be maximized by risk-reduction counseling aimed at reducing the likelihood of HIV acquisition. In the extreme case, if counseling were fully effective in inducing behavior change and the HIV seroincidence rate fell markedly, an HIV vaccine trial would not be feasible. Although the possibility that participation in a vaccine trial would result in reduced HIV seroincidence has been extensively discussed [11–16], less attention has been given to the converse. Our study suggests that participation in an HIV vaccine trial might be associated with increased risk-taking behavior and therefore possibly increased risk of HIV infection. In a study in Rwanda [20], women participating in focus group discussions expressed concern that their seropositive male partners may be less likely to use condoms if they knew that the woman was participating in a vaccine trial. Women may be particularly vulnerable because of the absence of a practical and effective female controlled means of avoiding infection during heterosexual intercourse.

Although the process of obtaining consent of participants has become standard for biomedical research involving human subjects, special care must be taken to ensure that individuals participating in HIV vaccine trials are fully informed of the implications of involvement. Counseling must be tailored to each community, directed by cultural and language considerations and the level of literacy of the cohort and the individual. The concept of a placebo-controlled, double-blind trial is not a simple one, particularly for poorly educated individuals from communities in which the scientific method does not have widespread acceptance.

Another difficult concept which must be conveyed during the consent process for HIV vaccine trials is the potential change in serostatus. In a US survey [21], 84% of seronegative IVDU initially said that they would participate in a Phase III vaccine trial, but this dropped to 41% once it was explained that they would test HIV-seropositive as a result of participation. In Bangkok [22], almost half of health-care providers surveyed were concerned about participation in a vaccine trial if HIV-antibody screening were a routine part of job or health insurance applications. Currently in Kenya, HIV-antibody tests are not often used for employment or acceptance for health-care insurance screening purposes in Kenya, although this may change in the future. Consequently, safeguards against potential discrimination for HIV vaccine trial participants would be required. In addition, the means of differentiating vaccine-induced seropositivity from HIV infection should ideally be accessible at the site of the vaccine trial, so that subjects can be informed promptly if they become infected.

The evaluation of candidate HIV vaccines will require multiple clinical trials in populations which differ according to mode of HIV acquisition, patterns of sexual behavior, exposure to STD and other transmission cofactors, viral strain type, and genetic and nutritional factors which may alter susceptibility. In addition, vaccine trials will require the participation of both men and women. Although the Mombasa PAVE study includes both male and female cohorts, it is noteworthy that there was a significant difference in anticipated acceptance of vaccine trial participation. This may reflect the different occupations and perceived levels of risk of the two groups, or greater familiarity of women with vaccines because of their children.

In summary, this study has documented that the majority of trucking company employees and CSW surveyed

were interested in participating in HIV vaccine trials. Combined with their high HIV seroincidence and compliance with follow-up, these appear to be ideal cohorts for vaccine or other intervention trials.

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