

Design, Implementation, and Evaluation at Entry of a Prospective Cohort Study of Homosexual and Bisexual HIV-1–Negative Men in Belo Horizonte, Brazil: Project Horizonte

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Background and Objectives: Project Horizonte, an open cohort of homosexual and bisexual HIV-1–negative men, is a component of the Minas Gerais AIDS Vaccine Program of the Federal University of Minas Gerais, Belo Horizonte, Brazil. Its objectives included the evaluation of seroincidence of HIV, to ascertain the role of counseling on behavior modification and to assess their willingness to participate in future HIV vaccine trials.

Methods: Various means of recruitment were used, including pamphlets, notices in community newspapers, radio, and television, at anonymous testing centers, and by word of mouth.

Results: From October 1994 to May 1999, 470 volunteers were enrolled. Their mean age was 26 years and over 70% of them had high school or college education. During the follow-up, they were seen every 6 months, when they received counseling and condoms, and when HIV testing was done. Eighteen seroconversions were observed, and the incidence rates estimates were 1.75 per 100 and 1.99 per 100 person-years, for 36 and 48 months of follow-up, respectively. During the entire period, 139 volunteers were lost to follow-up. Among them, 59 (42.4%) never returned after the initial visit and 51 (36.7) came only once after their initial visit. No losses were observed for those observed during follow-up for more than 3 years. At enrollment, 50% of participants said they would participate in a vaccine trial, and 30% said they might participate.

Conclusions: The results obtained up to this moment confirm the feasibility of following this type of cohort for an extended period, estimating HIV incidence rate, and evaluating counseling for safe sexual practices in preparation for clinical trials with candidate HIV vaccines in Brazil.

Key Words: HIV—HIV incidence—Homosexual and bisexual—Open cohort—Vaccines.

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In Brazil, 179,541 cases of AIDS have been reported to the Ministry of Health between 1980 and November 1999, a cumulative incidence of 124.2 cases per 100,000 inhabitants, ranging from 0.1 to 20.0 per 100,000 per

year. Homosexual and bisexual transmission represented 23.6% of all new adult cases reported in the last two years (1). The AIDS epidemic is still expanding in Brazil and no prospective studies to estimate HIV infection incidence rate and to identify risk factors were carried out prior to 1994.

To prepare for possible trials of preventive HIV vaccines in a population at high risk of infection, the Brazilian Ministry of Health established in October 1992 centers to participate in an HIV vaccine program. Among the center's objectives were the establishment and follow-up of an open cohort for the following purposes:

- To evaluate the feasibility of following such a cohort for extended period of time
- To determine the HIV infection incidence rate and to investigate risk factors for infection
- To evaluate the impact of preventive programs in the HIV incidence
- To ascertain the efficacy of counseling and of educational interventions in reducing HIV risk practices
- To evaluate the possibility of conducting clinical trials of preventive HIV candidate vaccines with volunteers recruited among cohort members
- To discuss ethical and technical aspects of clinical trials conducted with preventive HIV candidate vaccines

In April 1994, three vaccine centers were established in the States of Minas Gerais, Rio de Janeiro, and São Paulo, funded by the Ministry of Health and the United Nation's AIDS Control Program (UNAIDS). These centers initiated close collaboration in designing and implementing the study and following cohorts of HIV-negative homosexual and bisexual men, to conduct a similar investigation, including data collection and analysis, characterizing a multicenter study (2). During the first semester of 1994, the project teams developed the study protocol, data collection forms, and manuals. After a pilot test and data collection instruments' definition, each center began, in September of the same year, to recruit volunteers.

This paper describes the design and data collection methods of the Project Horizonte, which is located in Belo Horizonte, Minas Gerais State, including selected characteristics of participants at enrollment visit; HIV infection incidence rate during the first four and a half years of follow-up; an evaluation of losses to follow-up during the same period; and an appraisal of their willingness to participate in future vaccine trials.

METHODS

Study Protocol

The Project Horizonte proposal was submitted to and approved by the Committee on Human Research of the Universidade Federal de Minas Gerais.

The Project Horizonte site coordinated by the Universidade Federal de Minas Gerais (UFMG) is established at the Infectious and Parasitic Diseases Service (CTR DIP) and graduate program in tropical medicine in Belo Horizonte, Brazil.

The study protocol was divided in two phases: the selection process (recruitment and enrollment) and the follow-up. The objective of the recruitment phase was to identify HIV-1-negative homosexual or bisexual male, which would consent to participate in a cohort study. Eligibility criteria for enrollment included sexually active homosexual or bisexual men, aged between 18 and 59 years, consenting to do an HIV test and having a negative result for HIV-1 infection. Methods for recruitment were tailored to the resources of each study site and, as it was devised as an open cohort, recruitment was initially planned for 4 years. Various recruitment methods were used, including pamphlets, notices in community newspapers, radio, and television, at anonymous testing centers and by word of mouth.

The objective of the follow-up phase was to monitor the participants semiannually, to detect HIV incidence, to investigate risk factors for infection, and to counsel patients about how to reduce these risk factors. All negative volunteers were scheduled for 6-month visits, which included interview using the same psychosocial and epidemiologic form, blood collection for HIV and other laboratory tests, and clinical consultation. Preventive interventions implemented during the follow-up period included free condom distribution, HIV infection and AIDS information, opportunity to participate in discussion forums addressing questions as sexuality, HIV vaccine trials, safe sexual practices, and other subjects. Medical assistance was provided to all volunteers; those who became infected with HIV during follow-up received medical and psychological care, by the same health team, at the CTR DIP outpatient clinic.

Data Collection: Core Interview

A standardized form, given to all volunteers, was composed of five modules: 1) current demographic characteristics, 2) history of sexual behavior; 3) other risk factors for HIV infection; 4) knowledge about HIV/AIDS, and 5) knowledge about HIV vaccines and willingness to participate in future trials. The psychosocial team conducted a face-to-face interview, lasting around 1 hour, at each visit. Whenever possible the follow-up interviews were conducted by the same professionals who enrolled the volunteers. At each visit, participants were encouraged to schedule their next visit.

Blood Collection and Laboratory Tests

Two blood samples were obtained, the first for anti-HIV serologic tests, complete blood count, Venereal Diseases Research Laboratories tests and CD4/CD8 lymphocyte cells counts (flow cytometry) and the second to be stored at -20°C . A standardized clinical interview form was applied at each clinical visit. The volunteers were asked about their health status and current illnesses, including specific questions related to sexually transmitted diseases. A complete physical examination was performed and laboratory tests were done as necessary.

Statistical Methods

The sample size (500 participants) needed to estimate HIV incidence within 25% (relative precision) was calculated based on a 8 per 100 per year underlying seroconversion rate, obtained by backcalculation (3,4) based on 1987 to 1992 seroprevalence in UFMG's immunodeficiency clinic. Incidence rates were calculated using the person-time function method. To investigate whether the group of participants who came only once differed from those who remained in the project, they were compared (using demographic, social, and behavioral characteristics) using multivariate logistic regression (5).

RESULTS

The results presented here refer to volunteers recruited during the initial 4.5 years of Project Horizonte. Interim analysis of selected data has been presented elsewhere (6–13).

From October 1994 through May 1999, 567 volunteers were screened; 46 did not complete the initial protocol and 51 were considered ineligible (those who were not included had produced positive results when tested by enzyme-linked immunosorbent assay and Western blot at entry). The remaining 470 were included after signing the informed consent: 140 (30%) were recruited in the first year, 178 (38%) in the second year, 86 (18%) in the third year, and 66 (14%) in the last year and a half.

Word of mouth was the most frequent response given by the volunteers (52%) when asked "How did you find out about this study?" In this case, most reported that they received information from partners/friends or persons frequenting the same bars, restaurants, and saunas. Other responses included newspaper notes (advertisement in the personal add section), television and radio news (interviews given by members from the study team), and pamphlets (13.1 and 13.5%, respectively).

The demographic and behavioral characteristics at entry for the 470 enrolled men are shown in Table 1. The mean age was 27 years; 52% were mulattoes, 41% whites, and 7% blacks; 73.6% had either high school or college education, 77% were currently employed, and 52% received monthly more than three times the Brazilian minimum wage (i.e., the average for the region, or about \$250.00 U.S.). Approximately 60% reported practicing anal receptive intercourse and among those, 41% reported having anal intercourse with occasional partners without using condoms. Among the volunteers, 60% identified themselves as homosexuals and 40% as bisexuals.

Project Horizonte HIV Infection Incidence Rates

During the follow-up period, 18 seroconversions were observed, eight of them in the first 18 months of follow-

TABLE 1. Social demographics and behavioral characteristics of Project Horizonte HIV-negative recruited participants 1994–1999, Belo Horizonte, Minas Gerais, Brazil

Characteristics	N = 470 (%)
Mean age, y (SD)	26.9 (6.8)
Median age, y (IQR)	26.0 (21–31)
Race	
Mulatto	242 (51.8)
White	191 (40.9)
Black	34 (7.3)
Education	
Elementary school	123 (26.4)
High school	196 (42.1)
College	147 (31.5)
Currently employed	359 (76.9)
Monthly income (in BMW)	
<1	68 (14.7)
1–3	153 (33.1)
3–6	122 (26.4)
6–10	46 (10.0)
>10	73 (15.8)
Sexual identity	
Homosexual	276 (59.4)
Bisexual	189 (40.6)
Used alcohol in the last 6 months	368 (79.5)
Used drug in the last 6 months	81 (17.6)
Had oral sex	336 (72.1)
Had anal-receptive intercourse	265 (57.0)
Had anal intercourse without condom with occasional partners ^a	109 (41.3)
Reactive VDRL	17 (3.8)

Data for refusal, "not done," and "don't know" are not shown.

^a Only for those who reported anal intercourse.

SD, standard deviation; IQR, interquartile range; BMW, Brazilian minimum wage; VDRL; Venereal Disease Research Laboratories test.

up. The incidence rates estimated using the person-time function (95% confidence interval [CI]) were 1.34 (0.58–3.64), 1.75 (0.98–2.89) and 1.99 (1.18–3.14) per 100 person-years for 18, 36, and 48 months of follow-up, with 7167, 10,269, and 10,866 person-months denominators, respectively.

Losses to Follow-Up

During the entire study period, 139 volunteers were lost to follow-up. Among them, 59 (42.4%) never returned after the initial visit and 51 (36.7%) had only one interview. No losses were observed for those followed for more than 3 years.

Characteristics of Single-Visit Participants Versus Participants Who Continued With the Study

Table 2 shows the results obtained comparing participants who made only a single visit with those being observed on a long-term basis (at entry data). In univariate analysis, significant differences were observed for

TABLE 2. Baseline demographic and behavioral characteristics of Project Horizonte, 1994-1999

Characteristics	Those who came		Analysis		
	Only first visit (n = 59)	>One visit (n = 411)	OR Univariate (95% CI)	p Value	OR Multivariate ^a (95% CI)
Age ^b					
Mean (SD)	24.9 (5.2)	27.2 (7.0)		.008	
Median (IQR)	24 (21-29)	26 (22-31)		.028	1.1 (1.0-1.1)
Income (%)					
≤3 BMW	29 (50)	195 (48)			
>3 BMW	29 (50)	215 (52)	1.1 (0.6-1.9)	.728	
Currently employed (%)	46 (79)	314 (77)	1.2 (0.6-2.3)	.645	
Have health insurance (%)	39 (67)	331 (81)	0.5 (0.3-0.9)	.018	0.5 (0.3-0.9)
Sexual identity (%)					
Bisexual	23 (40)	94 (23)			
Homosexual	35 (60)	313 (77)	0.5 (0.3-0.8)	.008	0.4 (0.2-0.7)
Have knowledge about AIDS vaccine (%)	40 (69)	314 (77)	0.8 (0.5-1.5)	.053	
Willingness to participate in vaccine trials (%)					
Yes	23 (40)	201 (49)	1.0		
Maybe	16 (27)	121 (30)	1.1 (0.6-2.0)	.746	
No	19 (33)	86 (21)	0.5 (0.3-1.0)	.049	0.5 (0.3-0.9)

^a Final model.

^b Test for mean and median.

OR, odds ratio; CI, confidence interval; SD, standard deviation; IQR, interquartile range; BMW, Brazilian minimum wage.

age, having health insurance, sexual identity, knowledge about AIDS vaccine, and willingness to participate in vaccine trials. These variables, except for knowledge about AIDS vaccine, remained in the multivariate final model.

DISCUSSION

The decision to start an incidence cohort with men who have sex with men (MSM) and in a multicenter fashion was a sound one. The reasons for starting with MSM were multifold. Even with increasing prevalence of AIDS in other groups, the group still produces a considerable number of cases; MSM are usually more organized as a group and in certain ways more homogeneous. To do it as multicenter project (Belo Horizonte, Rio de Janeiro, and São Paulo) was necessary to grant the findings more power and reliability. In addition, the exchange of ideas and expertise helped in setting up other cohorts (e.g., women, commercial sex workers) by the same or other groups, using the acquired experience.

The main objective of the Project Horizonte was to evaluate the feasibility of implementing and maintaining a cohort of homosexual/bisexual HIV-negative men for an extended time and to appraise their willingness to participate in future HIV-vaccine trials.

The capability of the cohort team in recruiting participants can be analyzed by the proportion of volunteers yearly entering the study: 0.28, 0.36, 0.23, and 0.13, from the first to the fourth years, respectively. Budgetary constraints were undoubtedly responsible for the

smaller number of volunteers admitted in the last year and half. However, the initial goal of enrolling 500 volunteers was achieved and the capability of maintaining this open cohort for extended periods of time has been demonstrated.

Word of mouth was the most efficacious recruitment technique. Similar results were reported in other longitudinal studies on the natural history on HIV infection (14-16). Inasmuch as gay groups are not as well organized in Belo Horizonte as was previously expected, it was difficult to reach different segments of this population. This is reflected in the small number of transvestites and sex professionals who have been enrolled. In view of these considerations, the Project Horizonte participants, due to a possible selection bias, may not be representative of the wider Belo Horizonte homosexual/bisexual population. In addition, it was observed that a higher proportion of volunteers who remained in the Project were older, reported having health insurance, identified themselves as homosexuals, and were more willing to participating in future vaccine trials. Nonetheless, this group probably represents the population that would volunteer in future vaccine trials.

The results are encouraging in relation to the follow-up retention rates when considering those volunteers that returned for two or more visits; >80% of losses occurred in the first 12 months after enrollment. It should be noted that the characteristics of those who came only once to the Project revealed that a large proportion of them probably never had the intention of participating in the cohort; it is possible that the initial enrollment had to do

with the possibility of getting a free HIV test, because many of them did not have health insurance. If these volunteers are excluded, the retention rate achieved during this period was >90%. Similar results were reported from other studies; MACS retained 88.5% of participants after 9.5 years of follow-up and Project Praça Onze (Brazil) 97%, 91%, and 88% at 6, 12, and 18 months, respectively (17,18).

Despite the high level of counseling, condom distribution, and the participation in the discussion groups, a proportion of the volunteers continues to engage in high-risk practices; this is reflected by the 18 seroconversions that occurred in the 4 years of follow-up. A higher proportion of seroconversion happened among those observed <2 years (56%) when compared with those observed for longer than 2 years. It may be affirmed that even knowing the risks for infection, the observed changes in behavior were still unsatisfactory; as an example, they diminished the number of occasional partners and increased the usage of condoms, but the level of unsafe sexual practices continued at unacceptably high levels (19).

The HIV-infection incidence rate observed in this study were 1.34 (95% CI, 0.58–2.64), 1.75 (95% CI, 0.98–2.89), and 1.99 (95% CI, 1.18–3.14) per 100 person-years, for 18, 36, and 48 months of follow-up, respectively. These results are similar to incidence rates found in the USA MACS project (1.0–1.8/100 person-years from 1984–1989) and for homosexual men enrolled in a vaccine study in three U.S. cities, (2.3/100 person-years from 1993–1995) (20,21). The higher incidence (3.1/100 person-years) reported at the Project Praça Onze (18) was at least partially due to the inclusion of commercial sex workers in this cohort.

In relationship to the possibility of participating in future HIV vaccine trials, about 50% of participants at admission reported that they would enroll as volunteers and 30% said they were insecure and needed more information on the subject before reaching a definite decision. Our results were similar to Project Praça Onze, there were 69% of participants at admission who had reported their willingness to participate in a vaccine trial (18). Another cohort study conducted in the United States showed that at entry, 37% of the men reported that they would be definitely willing to participate in an HIV vaccine efficacy trial but this proportion dropped to 21% at 12 months and remained stable at 18 months (22).

In conclusion, the results presented here attest to the feasibility of following this type of cohort for extended periods of time, estimating HIV infection incidence and evaluating counseling for safer sexual practices. These volunteers will certainly be capable of autonomously de-

cide to participate in future HIV vaccine trials, although it will be necessary to discuss this issue with them further. Moreover, the research team is ready to engage in the implementation of a vaccine trial when a suitable candidate is available.

APPENDIX

Project Horizonte's members are A. C. Toledo Jr, U. Tupinambás, L. G. Machado, C. A. J. Pádua, F. A. Ribeiro, F. G. F. Ferreira, R. M. Ferraz, G. Câmara, W. Oliveira, M. A. Ribeiro, M. R. Oliveira, J. J. Fonseca, R. C. Dominguez, M. Matta-Machado, J. D. P. Nahass, M. J. D. Utsch, F. A. Cardoso, and L. Gouveia.

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