

Effects of a behavioural intervention to reduce acquisition of HIV infection among men who have sex with men: the EXPLORE randomised controlled study

The EXPLORE Study Team*

Summary

Background Effective interventions are needed to prevent acquisition of HIV infection in men who have sex with men. To date, no behavioural interventions specifically for this risk group have been tested with HIV infection as the primary outcome.

Methods This multisite two-group randomised controlled phase IIb trial tested the efficacy of a behavioural intervention in preventing HIV infection among 4295 men who have sex with men. The experimental intervention consisted of ten one-on-one counselling sessions followed by maintenance sessions every 3 months. The standard condition was twice-yearly Project RESPECT individual counselling. Twice-yearly follow-up visits included testing for HIV antibody and assessment of behavioural outcomes.

Findings The rate of acquisition of HIV infection was 18·2% (95% CI -4·7 to 36·0) lower in the intervention group than the standard group. Adjustment for baseline covariates attenuated the intervention effect to 15·7% (-8·4 to 34·4). The effect was more favourable in the first 12–18 months of follow-up. The occurrence of unprotected receptive anal intercourse with HIV-positive and unknown-status partners was 20·5% (10·9 to 29·0) lower in the intervention than in the standard group.

Interpretation The results from the primary analyses allow us to rule out that the experimental intervention is associated with a 35% lower rate of HIV acquisition than in the standard group. The overall estimate of a difference of 18·2%, more favourable estimates of effect in the first 12–18 months, and similar effects on risk behaviours suggest that prevention of HIV infection among men who have sex with men by a behavioural intervention is feasible. Further work should be done to develop more effective interventions.

Introduction

In 2002, men who have sex with men accounted for 44% of all new diagnoses of HIV infection and AIDS in the USA.¹ The need for interventions to prevent HIV infection with proven efficacy in this risk group is reinforced by the increase in HIV infection among this group during the past 7 years, in contrast to declining rates of risk behaviours and seroincidence observed in the 1980s and early 1990s.^{2–10} A recent meta-analysis of behavioural interventions for men who have sex with men showed that interventions focused on interpersonal skills related to risk reduction can reduce self-reported episodes of unprotected anal intercourse.¹¹ Previous publications also show that interventions should target use of alcohol and recreational drugs, social norms encouraging risk taking, enjoyment of risk-related sexual behaviour, and life events and environments that trigger risk taking.^{12,13} These components built into interventions individually tailored to assist a man to move toward risk reduction based on his own and his partners' serostatus, could have the greatest success in reducing risk of infection among men who have sex with men.¹⁴

The EXPLORE study was designed as a multisite two-group randomised controlled phase IIb or screening trial¹⁵ to test the effect of a behavioural intervention in

preventing acquisition of HIV infection among men who have sex with men in the USA. Until this trial, no behavioural interventions specifically for this risk group have been tested in a randomised controlled design with this outcome measure. We aimed to develop and test an intervention that incorporated the best information about effective strategies to address the many factors associated with acquisition of HIV infection among men who have sex with men. Furthermore, we assessed and documented the quality of the intervention delivery to ensure it was delivered according to protocol.

We report the primary study outcomes of the EXPLORE study.

Methods

This study was carried out in six US cities: Boston, MA; Chicago, IL; Denver, CO; New York, NY; San Francisco, CA; and Seattle, WA. Details of the baseline methods and intervention have been published elsewhere.^{14,16} Intervention and training manuals, the protocol, outcome measures, and interview details are available from the EXPLORE website (<http://www.explorestudy.org>). The study was approved by the institutional review boards at each of the participating institutions, and participants provided written informed consent.

Lancet 2004; 364: 41–50

*Participants and study organisation given at end of paper

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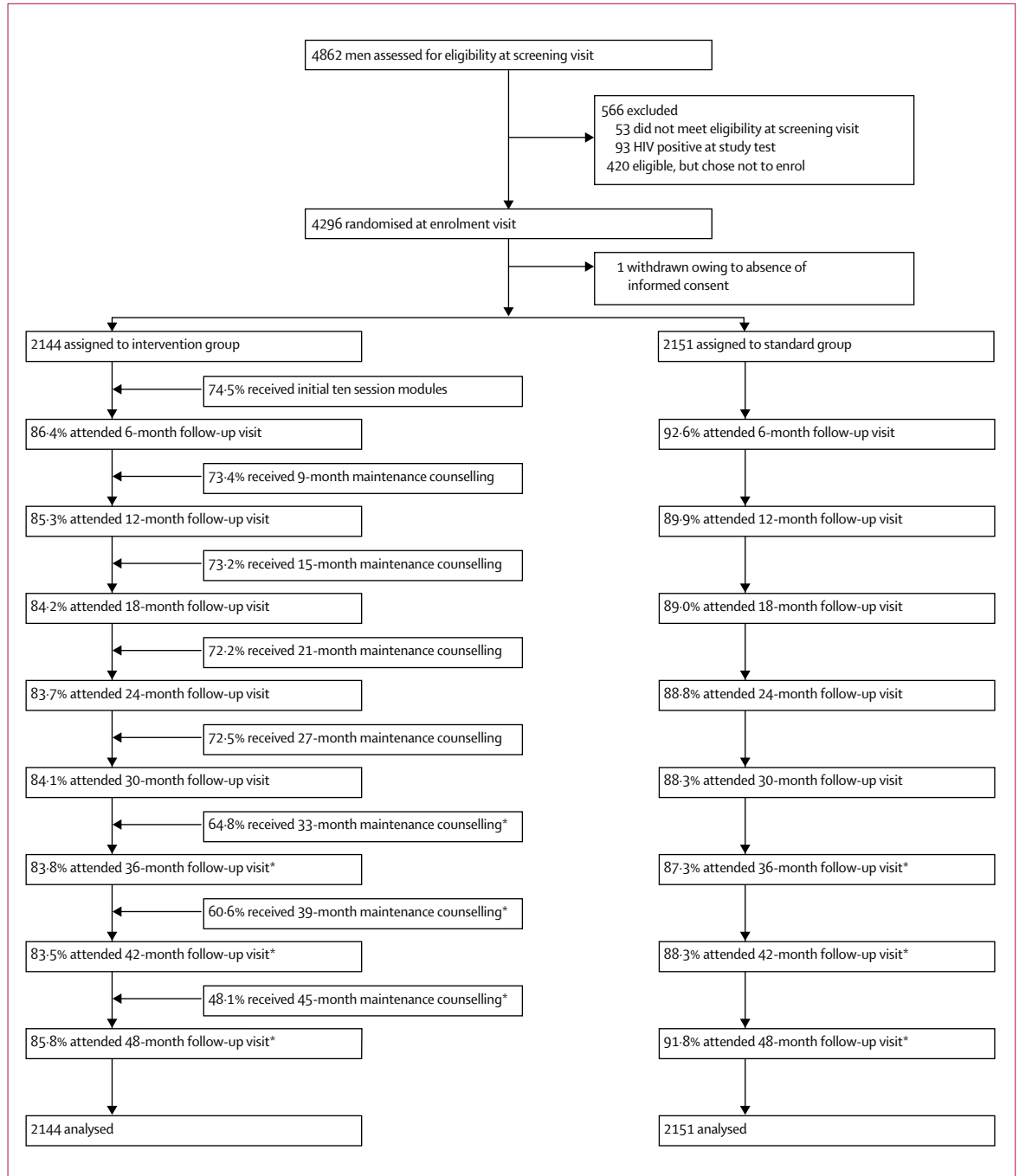


Figure 1: Trial profile

*Owing to the common close-out date, percentage is calculated on the basis of participants due at that visit.

Study population

Study participants were recruited at each site between January, 1999, and February, 2001. Recruitment strategies included outreach in streets, at dance clubs, bars, bathhouses, sex clubs, health clubs, and video arcades. Staff within each city also mounted public relations and advertising campaigns, with emphasis on the gay media. Participants also came to the study through internet sites,

community forums, community agencies, and referrals from other study participants and clinics. Men were eligible if they were negative for HIV antibodies, were aged 16 years or older, and reported having engaged in anal intercourse with one or more men in the previous year. Men were excluded if they reported a mutually monogamous relationship lasting 2 years or longer with a male partner known to be HIV seronegative.

Design and procedures

Baseline procedures have been described elsewhere.¹⁶ After informed consent had been given, trained interviewers collected information on respondents' demographic characteristics, reasons for participating in the study, history of sexually transmitted diseases, use of postexposure prophylaxis, and history of counselling and psychotherapy. Audio-computer-assisted self-interviewing (ACASI) technology was used to collect information on attitudes towards safer sex, social activities within the gay community, depression, alcohol and drug use, and sexual behaviours. Participants were asked about sexual behaviours in the previous 6 months with partners of each HIV-serostatus type (negative, positive, and unknown). After completing the interviews, participants received HIV pretest counselling, and blood samples were collected for HIV-antibody testing.

About 2 weeks after being screened, participants underwent post-test counselling after receiving the HIV test result. Those with a positive test result at baseline were referred to medical and social services. Men who had no detectable HIV antibodies at the baseline interview were asked to enrol in the trial. The EXPLORE statistical centre generated the allocation sequence to randomise participants to intervention or control conditions in a ratio of one to one (figure 1). Randomisation was stratified by study site and was blocked with random sequences of block sizes. Randomisation was obtained by a telephone call to a voice-prompted, interactive computer program at the statistical centre. Study staff answered questions about the participant's eligibility for randomisation, and the computer verified eligibility, then randomly assigned the participant to one of the two counselling groups.

The experimental intervention, described in detail elsewhere,¹⁴ consisted of ten core counselling modules delivered at one-on-one counselling sessions, typically with one module being delivered per session within 4–6 months of randomisation. For purposes of analysis, the variable "session modules" was defined as the maximum number of modules or sessions completed within 6 months of randomisation. After the initial ten modules, maintenance sessions were delivered every 3 months until the end of the study.

The intervention was designed to address individual, interpersonal, and situation-related factors associated with risk taking among men who have sex with men, such as greater pleasure in or enjoyment of risk-related sexual behaviour, negative mood states, communication difficulties, social norms encouraging misperceptions of risk and risk taking, use of alcohol or recreational drugs, and life events and environments that are catalysts for risk taking. An intervention manual detailed the materials to be covered at each of the ten core behavioural intervention modules. The first three modules established rapport between the counsellor and

participant and provided detailed personalised risk assessments to guide the future focus of the intervention sessions. The remaining sessions covered sexual communication, knowledge of personal and others' HIV serostatus in making sexual decisions, and alcohol and drug use in conjunction with risk behaviours. Modules were also offered on how unsafe sex could be triggered by meeting certain types of partners, by places or events related to selection of partners, and by cognitive or emotional cues associated with risk taking. Motivational interviewing was used to help participants make and sustain changes in knowledge, attitudes, beliefs, and behaviours.¹⁷

The standard condition was twice-yearly counselling on risk reduction based on the Centers for Disease Control and Prevention Project RESPECT model.¹⁸

Intervention and standard counselling sessions were carried out at the study sites by counsellors who had completed the required 40 h of training. Counsellors were trained to deliver both the standard and the interventional material. Several approaches were used to assess and ensure adherence to the intervention and standard protocols and to keep cross-contamination to a minimum. First, sessions were audio-taped and a planned 10% random sample of tapes (11.5%) were selected for review by raters at the intervention coordinating centre. The sessions were scored on many items specific to the session. The quality-assurance scores were percentages of the total possible score; sessions with scores above 80% were deemed to have followed the protocol and, therefore, to be acceptable. Another approach was to assess the duration of sessions; the intervention sessions were designed to be longer than the standard sessions. Finally, data on quality-assurance scores and duration of sessions were shared with study sites regularly, for monitoring and continuing training purposes, by the clinical coordinator at each site and the intervention coordinating centre.

Follow-up visits were scheduled every 6 months for participants assigned to both study groups. These visits consisted of behavioural surveys with both face-to-face interviews and the ACASI technology. All sexual-behaviour outcomes were collected by ACASI. To mitigate further against participants' under-reporting of risk behaviours owing to social desirability, no study staff had access to any ACASI risk-behaviour information for any participant, including during counselling sessions. Blood samples were collected for testing for HIV antibodies.

Antibodies to HIV were detected by ELISA. Serum samples shown to be reactive after a first test were retested in duplicate. Repeatedly reactive samples were confirmed by western-blot assay or immunofluorescence assay. Participants with a positive test result at any follow-up visit were referred to medical and social services.

| Characteristic | Number of participants | |
|--|------------------------|-------------------|
| | Intervention (n=2144) | Standard (n=2151) |
| Age, years | | |
| 16–19 | 43 (2.0%) | 50 (2.3%) |
| 20–25 | 359 (16.7%) | 362 (16.8%) |
| 26–30 | 450 (21.0%) | 463 (21.5%) |
| 31–35 | 458 (21.4%) | 452 (21.0%) |
| 36–40 | 376 (17.5%) | 379 (17.6%) |
| >40 | 458 (21.4%) | 445 (20.7%) |
| Race/ethnicity | | |
| White | 1559 (72.8%) | 1553 (72.2%) |
| Hispanic | 322 (15.0%) | 330 (15.3%) |
| African-American | 131 (6.1%) | 150 (7.0%) |
| Other | 131 (6.1%) | 118 (5.5%) |
| Education | | |
| High school or less | 198 (9.2%) | 209 (9.7%) |
| Some college | 557 (26.0%) | 572 (26.6%) |
| College | 761 (35.5%) | 773 (36.0%) |
| After college | 628 (29.3%) | 595 (27.7%) |
| Household annual income, US\$ | | |
| <12 000 | 280 (13.1%) | 282 (13.1%) |
| 12 000–29 999 | 579 (27.0%) | 587 (27.4%) |
| 30 000–59 999 | 839 (39.2%) | 817 (38.1%) |
| ≥60 000 | 444 (20.7%) | 460 (21.4%) |
| Currently a student | 338 (15.8%) | 362 (16.8%) |
| Employment status | | |
| Full time | 1623 (75.7%) | 1624 (75.5%) |
| Part time | 208 (9.7%) | 218 (10.1%) |
| Unemployed | 219 (10.2%) | 208 (9.7%) |
| Other | 94 (4.4%) | 101 (4.7%) |
| Number of male partners in previous 6 months | | |
| 0 | 25 (1.2%) | 17 (0.8%) |
| 1 | 142 (6.6%) | 164 (7.6%) |
| 2–5 | 678 (31.7%) | 704 (32.7%) |
| 6–9 | 393 (18.4%) | 357 (16.6%) |
| ≥10 | 904 (42.2%) | 908 (42.2%) |
| Female sex partner in previous 6 months | 86 (4.0%) | 92 (4.3%) |
| HIV-positive male partner in previous 6 months | 595 (27.8%) | 620 (28.9%) |
| Anal sex in previous 6 months | | |
| Any unprotected anal sex | 1442 (67.7%) | 1501 (70.4%) |
| Unprotected anal sex with positive or unknown-status partner | 999 (46.9%) | 1049 (49.0%) |
| Unprotected receptive anal sex with positive or unknown-status partner | 598 (28.0%) | 608 (28.5%) |
| Receptive anal sex | 1587 (74.2%) | 1597 (74.7%) |
| Unprotected receptive anal sex | 1011 (47.4%) | 1031 (48.5%) |
| Insertive anal sex | 1731 (80.9%) | 1760 (82.1%) |
| Unprotected insertive anal sex | 1135 (53.3%) | 1206 (56.5%) |
| Alcohol and drug use in previous 6 months | | |
| Heavy alcohol use* | 234 (11.0%) | 219 (10.2%) |
| Non-injection-drug use | 1392 (65.0%) | 1382 (64.4%) |
| Injection-drug use | 222 (10.4%) | 217 (10.1%) |
| Depression† | 1024 (47.8%) | 1006 (46.8%) |

Where totals do not reach 2144/2151, data were missing. *Four or more drinks every day or six or more drinks on a typical day when drinking in the last 6 months. †Based on a shortened version of the Center for Epidemiologic Studies depression scale.

Table: Baseline characteristics by study group

Statistical analysis

This screening or phase IIb trial was designed to have a high probability of establishing benefit for a highly effective intervention or of ruling out benefit for a totally ineffective intervention. Furthermore, for interventions with lower yet worthwhile efficacy (eg, 35% efficacy), the trial would have high probability of either establishing benefit or indicating plausible efficacy deserving of further study; in that instance, the trial would inform the development of future efficacy trials.

The EXPLORE study was designed so that the intervention strategy would be declared beneficial if the difference in the rate of acquisition of HIV infection between intervention and standard groups was significantly above 10% in favour of the intervention group (that is, that the lower limit of the 95% CI was above 10%). If not, and the difference was significantly below 35% (that is, the upper limit of the 95% CI was below 35%), the benefit of the intervention strategy would be ruled out. In case neither was true, the intervention would be judged plausibly effective with merit for

further evaluation, possibly with refinements. With the target sample size of 4350 and an expected rate of acquisition of HIV infection of 1.55 per 100 person-years in the standard group, if the true difference in the rate of HIV infection was 35% in favour of the intervention group, there would be a 3.0% chance of ruling out benefit, a 50.0% chance of declaring benefit, and a 46.9% chance of stating that the intervention had plausible efficacy. Furthermore, if the true difference in the rate of HIV infection was 0%, there would be a 75.0% chance of ruling out benefit.

By intention to treat, comparisons were made between the participants assigned to the intervention group and those assigned to the standard group, irrespective of the amount of counselling received. The primary analysis was to assess the intervention effect on rate of acquisition of HIV infection. A proportional-hazards model was adopted on the discrete timescale of twice-yearly visits, with the intervention-group indicator as the only covariate. The odds ratio of HIV infection was estimated and the intervention effect was defined as one minus the odds ratio (ie, the percentage of reduction in HIV infection). We assumed in the analysis that HIV serostatus was negative at a missing visit if there were no positive results at earlier visits and an assessment was made at a subsequent visit.

As secondary endpoints, serodiscordant (ie, with HIV-positive or status-unknown partner) unprotected receptive anal intercourse, serodiscordant unprotected anal intercourse, and unprotected anal intercourse were assessed at twice-yearly visits. For each endpoint, its occurrence during the 6 months before a visit was used and a logistic regression model was adopted with visit-independent intervention effect and visit-specific intercepts. The generalised estimating equations approach was used to account for within-participant correlation of repeated outcome measures, with an independent working correlation.

For both primary endpoint and secondary endpoints, additional analyses were done to adjust for baseline characteristics. Specifically, for rate of acquisition of HIV infection, in the proportional-hazards model, we added the following baseline variables as additional covariates: age, injection-drug use, sex with HIV-positive male partner, sex with HIV-positive female partner, unprotected receptive anal sex, and unprotected insertive anal sex, as well as site and race/ethnicity as stratification variables. This step was an attempt to account for imbalances in randomisation and loss to follow-up with respect to baseline characteristics. For serodiscordant unprotected receptive anal intercourse, its baseline measure was added to the logistic regression model as a visit-independent effect. The same approach was used in the adjusted analyses of serodiscordant unprotected anal intercourse and unprotected anal intercourse by adding their respective baseline measures to the regression models.

Before the final analyses, we identified three potential effect modifiers: alcohol use, non-injection-drug use, and depression. Alcohol use was classified as none, light, moderate, or heavy, and non-injection-drug use and depression as yes or no. Subgroup analyses were done for rate of acquisition of HIV infection and occurrence of unprotected anal intercourse, serodiscordant unprotected anal intercourse, and serodiscordant unprotected receptive anal intercourse for each potential effect modifier.

Role of funding sources

The study sponsors participated on the EXPLORE protocol team and provided review of the study design and implementation, including assurance of adherence to good clinical practice in data collection. The sponsors had no role in analysis or interpretation of data or in the writing of the report.

Results

Of the 4862 men screened for the study, 4296 enrolled and were randomly assigned to the two study groups (figure 1). The final analysis was based on 4295 participants; one participant was randomised in the absence of informed consent.

The mean age of the participants was 34.0 years (SD 9.4) and 19.0% were 25 years of age or younger. 72.5% of the participants were white, 15.2% were hispanic, and 6.5% were African-American. 35.8% had education less than a college degree, and 40.3%

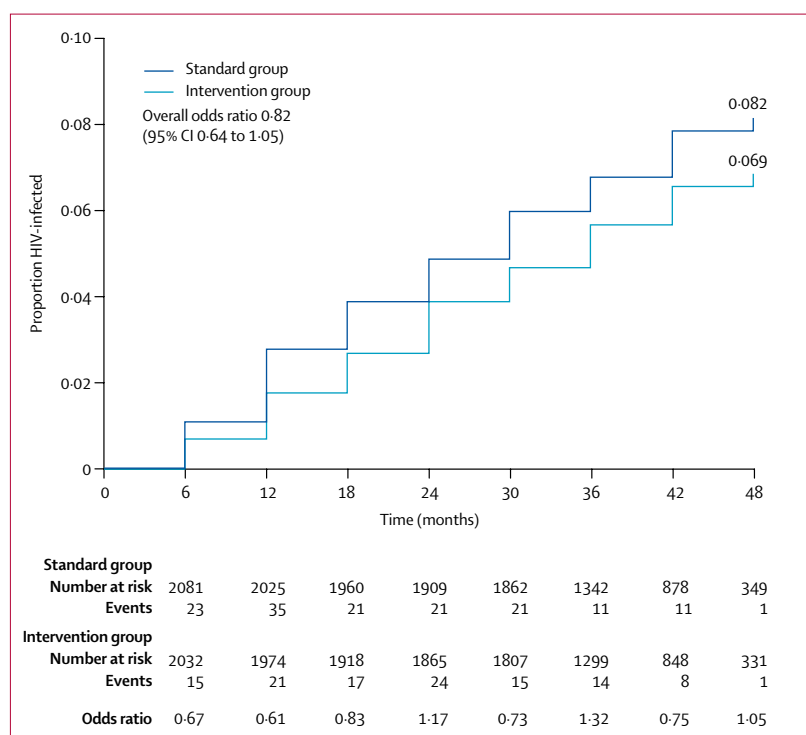


Figure 2: Kaplan-Meier curve of proportion of participants infected with HIV

had an annual household income of less than US\$30 000. The enrolled men reported a median of seven male sex partners in the 6 months before screening (IQR three to 18); however, 42.2% reported having ten or more male partners and 28.4% having an HIV-infected partner. 69.1% reported any unprotected anal intercourse, 48.0% reported unprotected receptive anal intercourse, and 54.9% reported unprotected insertive anal intercourse. 47.9% reported unprotected anal intercourse with an HIV-positive or unknown-status partner, and 28.2% reported unprotected receptive anal intercourse with an HIV-positive or unknown-status partner. Heavy alcohol use was reported by 11.0% of participants and any non-injection-drug use by 64.7%. At baseline, 47.3% of men had symptoms of depression as found by a shortened version of the Center for Epidemiologic Studies depression scale. Baseline characteristics were well balanced between the intervention and standard groups, with the exception of unprotected insertive anal intercourse (table).

Of the 2144 men assigned the intervention, 1598 (74.5%) completed all ten initial session-modules, 154 (7.2%) completed seven to nine, 105 (4.9%) completed four to six, 258 (12.0%) completed one to three, and 29 (1.4%) did not complete any. More than 70% of the men in the intervention group received maintenance sessions except at the 33-month, 39-month, and 45-month visits (figure 1).

Of the initial ten sessions, 1691 were reviewed and 83.3% met the quality-assurance criterion of a score of

80% or higher. 651 maintenance visits for the intervention group were also reviewed and 77.1% met this criterion. The proportion of the 6-monthly visits that met the quality-assurance criterion did not differ significantly between the intervention and standard groups (76.9% of 657 reviewed vs 80.7% of 841 reviewed, $p=0.0677$). The mean duration of the sessions at the 6-monthly visits was 16.1 min longer for intervention sessions than for standard sessions (37.9 [SD 20.4] vs 21.8 [11.1] min; $p<0.0001$).

Visit retention rates were above 83% in the intervention group and above 87% in the standard group during the follow-up period (figure 1). Retention was consistently higher in the standard group than in the intervention group. Lower retention, as defined by final-visit retention status, was significantly associated with minority-group status (89.5% white men retained vs 83.9% others), younger age (89.8% >25 years vs 80.0% <25 years), reporting of female sex partners at baseline (88.5% no female partners vs 74.2% one or more female partners), and reporting of unprotected receptive anal intercourse at baseline (89.0% no unprotected receptive anal intercourse vs 86.7% reporting unprotected receptive anal intercourse). In the intervention group, retention also was significantly associated with completion of the initial ten session-modules (92.2% for nine or ten session-modules vs 63.6% for less than nine session-modules).

The overall rate of acquisition of HIV infection in the study cohort was 2.1 per 100 person-years (95% CI 1.9 to 2.4). There were 6037 person-years of follow-up in the intervention group and 6203 in the standard group. 115 intervention-group participants and 144 standard-group participants became infected with HIV during the study. By intention-to-treat analysis, the odds ratio was 0.82 (95% CI 0.64 to 1.05) for the intervention group relative to the standard group (figure 2). Thus, the difference in the rate of acquisition of HIV infection was 18.2% (95% CI -4.7 to 36.0) in favour of the intervention group. The data suggest that the difference in acquisition of HIV infection was greatest in the first 12–18 months of the study (figure 2).

After adjustment for study site and baseline characteristics associated with retention and distributed differently in the two study groups, the estimated odds ratio for the intervention was 0.84 (0.66 to 1.08), translating to a 15.7% (-8.4 to 34.4) difference in HIV acquisition in favour of the intervention group. Subgroup analyses by baseline alcohol use, non-injection-drug use, and depression score were consistent with the overall results (data not shown).

The estimated odds ratios of reporting unprotected anal intercourse and serodiscordant unprotected anal intercourse in the intervention group relative to the standard group (figure 3) were 0.86 (0.79 to 0.94) and 0.85 (0.78 to 0.94). These odds ratios translate to differences in favour of the intervention group of 13.9%

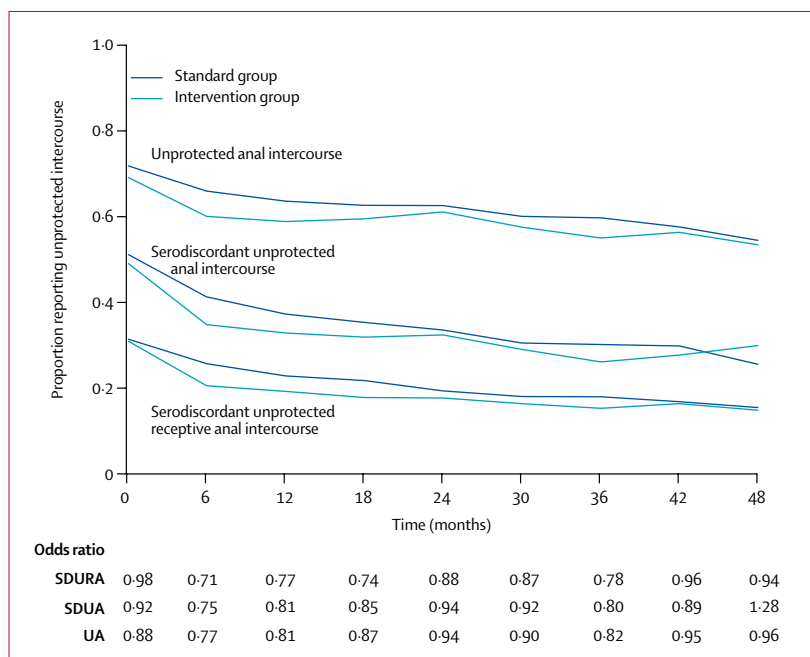


Figure 3: Proportions reporting unprotected intercourse by study group
SDURA=serodiscordant unprotected receptive anal intercourse; SDUA=serodiscordant unprotected anal intercourse; UA=unprotected anal intercourse.

(5.6 to 21.5) in unprotected anal intercourse and 14.8% (6.3 to 22.5) in serodiscordant unprotected anal intercourse. We also examined the highest risk behaviour, unprotected receptive anal sex with a partner positive for HIV or of unknown status; the estimated odds ratio was 0.80 (0.71 to 0.89), translating to a difference of 20.5% (10.9 to 29.0).

After adjustment for study site and baseline characteristics associated with retention and distributed differently in the two groups, the efficacy estimates for unprotected anal intercourse, serodiscordant unprotected anal intercourse, and serodiscordant unprotected receptive anal intercourse were 13.2% (4.8 to 20.9), 14.8% (6.5 to 22.4), and 22.5% (13.3 to 30.7). Subgroup analysis of the sexual behavioural outcomes showed similar results to overall results (data not shown).

Discussion

Challenges for trials of behavioural interventions have been completion of the intervention and retention of study participants over time.¹⁹ Most participants in the EXPLORE intervention group received all ten initial session-modules and maintenance sessions, and the sessions were delivered with high conformity with the protocol. Visit retention was above 87% in the standard group and above 83% in the intervention group over the 4-year study.

The primary analysis found that the intervention was associated with an 18.2% lower rate of acquisition of HIV infection; an analysis adjusted for baseline covariates attenuated the intervention effect to 15.7%. Analysis of the behavioural outcomes found that the intervention significantly affected the occurrence of the highest risk behaviour,²⁰ unprotected receptive anal intercourse with HIV-positive and unknown-status partners, as well as unprotected anal intercourse with HIV-positive and unknown-status partners, and unprotected anal intercourse.

The results from the primary analyses allow us to rule out that the experimental intervention lowers the rate of HIV acquisition relative to the standard group by 35%. The overall estimate of an 18.2% difference between the groups, together with more favourable estimates of effect in the first 12–18 months and similar changes in risk behaviours, suggests that a behavioural intervention can prevent HIV infection, not just reduce the frequency of self-reported risk behaviours. Further analyses of our data are under way with the aim of generating hypotheses to help develop more effective behavioural interventions. For example, are there subpopulations of men who have sex with men with demographic characteristics, baseline risk behaviours, or psychosocial measures for whom the behavioural intervention was more beneficial? With such evidence, more targeted behavioural interventions could be developed and tested. Furthermore, although over 70% of men completed the

ten-session intervention in this study, other designs of such interventions should be explored to improve the acceptability to different groups and facilitate implementation in community settings.

We are aware of only one other trial of an intervention to reduce HIV risk for men who have sex with men that involved a biological endpoint.²¹ In that study, the intervention was a 1-day workshop combining several models of behaviour change with motivational interviewing strategy. The primary infection outcome was a new sexually transmitted disease, as assessed from clinical and laboratory databases, and behavioural outcomes were collected by mailed questionnaire. Contrary to expectations, over 12 months of follow-up, a larger proportion of men in the intervention group than in the control group receiving standard care had a new sexually transmitted disease. Behavioural outcomes did not significantly differ between the groups.²¹

Two other large-scale trials of behavioural interventions with biological outcomes have been carried out in the USA among predominantly heterosexual populations. The Project RESPECT trial tested individually delivered interactive risk-reduction interventions delivered in either two or four sessions and found, over 12 months, a 20% lower rate of new sexually transmitted diseases than with people receiving didactic messages. The effect of the intervention was strongest early in follow-up.¹⁸ The National Institute of Mental Health Multisite HIV Prevention Trial of a seven-session small group intervention found no difference between study groups in overall rate of reinfection with sexually transmitted diseases over 12 months.²² Other smaller randomised trials of behavioural interventions have been done with sexually transmitted disease outcomes among women, patients with sexually transmitted diseases, and adolescents, with only one demonstrating a significant effect on rates of sexually transmitted disease.^{19,23} The lower rate of HIV acquisition with the intervention in the first 18 months of follow-up in EXPLORE was similar to that found with sexually transmitted diseases in Project RESPECT. Furthermore, the EXPLORE study found similar effects on risk behaviours over 12–18 months of follow-up to Project RESPECT and the meta-analysis of HIV intervention studies among men who have sex with men.¹¹

The EXPLORE trial had several limitations. First, the study sample recruited is not necessarily representative of men who have sex with men in the participating cities. Eligibility criteria were established to enrol a high-risk HIV-antibody-negative population for a trial with an HIV-infection endpoint. Furthermore, generalisability is limited since black and hispanic men, younger men, and those of lower socioeconomic status were less likely to enrol in the study, were more likely not to be eligible for the study owing to behavioural characteristics, and were more likely to be HIV infected¹⁶ and not retained in follow-up than white men in the study. However, the

population recruited was clearly at high risk as shown by the rate of acquisition of HIV infection and self-reported behaviours, which emphasises the need for prevention efforts to continue for many subpopulations of men who have sex with men. Second, the full effect of the intervention may have been muted for several reasons. The standard condition was based on the best available model, the Project RESPECT two-session behavioural intervention model, and decreases in sexual risk behaviours were observed in both study groups in the EXPLORE study. The amount of counselling in the standard group was probably more than that given in most public health settings and not equivalent to usual care, in which individuals would voluntarily seek anonymous counselling and testing in many cases, or to typical HIV counselling delivered in the community. In addition to the counselling, participants in both groups received much attention during the study, including repeat HIV-antibody testing, scheduling, and reminder letters or calls for all visits, newsletters, and other activities to maintain involvement and retention. Another possible reason for a muted intervention effect is cross-contamination if participants in the control group were in contact with others who were part of the intervention group. This effect, however, was likely to be negligible because only 13% of the men were enrolled as referrals from friends. Other community HIV-prevention efforts available to participants in both groups could also affect the results. Finally, the full effect of the intervention could have been dampened because not all intervention-group participants received the full initial ten session-modules or attended all maintenance visits. However, only 13% of the intervention-group participants received three or fewer of the initial session-modules.

A third limitation was a differential in retention between the study groups, with 90% and 86% retained at their final visit in the standard and intervention groups, respectively; those not retained tended to be from higher-risk subgroups. This higher rate of non-retention in the intervention group can be explained by the low retention rate in the participants who had lower adherence to the initial ten session-modules. Although the men in the intervention group who completed at least nine of the initial ten session-modules had a retention rate of 92%, close to that achieved in the control group, the remainder of the intervention group had only 64% retention. These data suggest that approaches are needed to improve the capture of longer-term outcome results, particularly among participants who have lower adherence to behavioural interventions.

Other research has shown that self-reported behavioural outcomes can overestimate the benefit of behavioural interventions and that the relation between the frequency of reported sexual behaviours and rate of HIV infection is probably complex and dependent on factors related to selection of partners and background

prevalence of HIV infection.^{19,21} The use of ACASI technology in our study might have helped to limit potential problems with the validity of self-reported behaviours.^{24,25}

The challenge for behavioural interventions has been maintenance of behaviour change over extended periods. The EXPLORE study was done during a period of substantial changes in the prevalence of risk behaviours and HIV incidence in communities of men who have sex with men, probably related to widespread use of highly active antiretroviral treatments and shifts in social norms.^{9,26,27} This trial provides encouragement that behavioural interventions can achieve reductions in risk in the short term. However, achievement of long-term effects is one of the most challenging features to face in design of effective behavioural interventions. In the long run, engagement of individuals at high risk in intensive interventions over a short period and delivery of periodic “boosters” may not be effective. A different model should be considered for long-term behavioural change, possibly combining improved, individualised interventions with community and structural changes to encourage and support behavioural change, particularly in relation to unprotected anal sex and disclosure of HIV serostatus.

Contributors

B Koblin, M Chesney, and T Coates conceived the study, oversaw all features of its implementation, and formed the writing committee. M Husnik, G Beauchamp, and Y Huang provided statistical expertise and did the data analyses. S Bozeman and M Madison were responsible for overall protocol implementation. S Buchbinder, C Celum, G Colfax, F Judson, B Koblin, K Mayer, and D McKirnan supervised study implementation at the individual research sites. M Chesney and T Coates supervised study activities at the study intervention coordinating centre. All other staff contributed to protocol implementation.

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Conflict of interest statement

None declared.

Acknowledgments

We thank the study participants for their contributions, and Thomas Fleming, Kendall Bryant, Rod Hoff, Monica Ruiz, and Michael Gross for scientific guidance. This work was supported by the HIV Network for Prevention Trials and sponsored by the US National Institute of Allergy and Infectious Diseases and the National Institute on Alcohol Abuse and Alcoholism through contract N01 AI35176 with Abt Associates Inc; contract N01 AI45200 with the Fred Hutchinson Cancer Research Center; and subcontracts with the Denver Department of Health and Hospitals, the Fenway Community Health Center, the

Howard Brown Health Center, the New York Blood Center, the Public Health Foundation Inc, and the University of Washington. In addition, this work was supported by the HIV Prevention Trials Network and sponsored by the National Institute of Allergy and Infectious Diseases, the National Institute of Child Health and Human Development, the National Institute on Drug Abuse, the National Institute of Mental Health, and the Office of AIDS Research through a cooperative agreement with Family Health International (cooperative agreement 5 U01 AI46749) with a subsequent subcontract to Abt Associates Inc with subcontracts to the Howard Brown Health Center and the Denver Department of Health and Hospitals; cooperative agreement U01 AI48040 to the Fenway Community Health Center, cooperative agreement U01 AI48016 to Columbia University (including a subagreement with the New York Blood Center); cooperative agreement U01 AI47981 to the University of Washington; cooperative agreement U01 AI47995 to the University of California, San Francisco.

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