NIMH Collaborative HIV/STD Prevention Trial

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Seth C. Kalichman

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Design and concepts of the NIMH Collaborative HIV/STD Prevention Trial

Frits van Griensven and Seth C. Kalichman

AIDS 2007, 21 (suppl 2):S1–S2

The scope of the AIDS pandemic demands a systematic approach to implementing multiple levels of prevention strategies to control the spread of HIV infection. On the individual level, voluntary counseling and testing (VCT) remains the frontline in HIV prevention. With effective HIV risk reduction counseling, there are clear preventive effects in conjunction with VCT [1], and risk reduction counseling can be effective independent of VCT [2]. Similarly, risk reduction interventions delivered to small groups of at-risk persons demonstrate significant preventive benefits in carefully controlled trials [3]. The greatest concern with implementing these effective individual-level behavioral interventions is that people who are counseled inevitably return to their unchanged social and risk environments where risk-taking practices are normative and socially reinforced. Interventions, such as microbicides, pre-exposure antiretroviral prophylaxis, diagnosis and treatment of sexually transmitted infections, and male circumcision may lead to population level reductions in HIV/AIDS risk, but their effects will be limited if compensating behaviors are not contained and exposure behaviors are kept at least constant [4]. Interventions that structurally alter the social context within which sexual and drug using behaviors occur are therefore necessary for facilitating, supporting, and maintaining HIV risk behavior change.

The NIMH Collaborative HIV/STD Prevention Trial is the first multi-site randomized community-level HIV prevention intervention study with behavioral and biological endpoints in international settings. The intervention under study is grounded in sound theories of disease prevention behavior change. Social Cognitive Theory [5] is the foundation for social and communication skills training that is conducted with community identified opinion leaders who are trained to become agents of change in their community. A critical mass of opinion leaders ultimately circulate in their community and through their conversations with peers, influence behavior change. The structural changes in social norms and perceptions occur through a systematic process detailed by the Theory of Diffusion of Innovations [6]. The tenants of Social Cognitive Theory and the Theory of Diffusion of Innovations are highly complementary and are actually unified in their approach [7]. The intervention being tested has been demonstrated effective in studies with diverse populations in the US [8–11]. The NIMH Trial is testing the intervention in China, India, Peru, Russia and Zimbabwe.

This Supplement issue of AIDS provides detailed reports on the design and concepts of the NIMH Trial. Papers in this volume offer important insights into the many facets of this complicated study. Each aspect of the study protocol is discussed in detail in these papers including the early formative and ethnographic studies, the adaptation of the intervention for use across cultures, behavioral and biological assessment protocols, and research ethics. This collection of articles describes the essential background and underpinnings of the trial. This volume is expected to serve as a resource to understand the trial design and to interpret the study outcomes when they are available. In addition, it is hoped that this volume and its papers will serve as an invaluable reference for the design and planning of future HIV prevention research.

References


Methodological overview of a five-country community-level HIV/sexually transmitted disease prevention trial

NIMH Collaborative HIV/STD Prevention Trial Group*

Objective: To provide an overview of the National Institute of Mental Health (NIMH) Collaborative HIV/STD Prevention Trial taking place in five populations at risk of HIV and sexually transmitted diseases in China, India, Peru, Russia, and Zimbabwe, including the rationale, study management, methods, and proposed data analyses.

Design: The Trial will scientifically evaluate the effectiveness of the community popular opinion leader (C-POL) community-level HIV prevention intervention that was adapted for use in the various cultures within the resource limitations faced by service providers in world regions threatened by high rates of HIV infection.

Methods: The study phases consist of an ethnographic study, pilot studies, an epidemiological study, and a community-randomized trial. The Trial uses the C-POL intervention, which researchers selected on the basis of research that shows the intervention’s success in populations vulnerable to HIV risk behavior in the United States, and has the potential to be applied in a variety of international settings.

Results: Trial results will be tabulated by and across country by randomization assignment. Results will include a careful review of data to substantiate original assumptions used in the study design. Data collection will not conclude until August 2007.

Conclusion: Although data collection is incomplete, researchers have learned lessons throughout the development of the study. These include the importance of preliminary epidemiological studies; the close monitoring of biological testing, follow-up rates and process measures at international sites; the tailoring of assessments and interventions to various cultures; regular communication; and a review of the timeline to accommodate Institutional Review Board clearances.

Introduction

The National Institute of Mental Health (NIMH) Collaborative HIV/STD Prevention Trial is the first multicountry randomized trial of a community-level HIV prevention intervention, and its scope spans four continents. The sites and populations selected for study within the countries represented in the Trial are among those in the world most imminently threatened by HIV infection [1]. The study is powered at a site level to detect change in either HIV/sexually transmitted disease (STD) risk behavior or disease incidence; it is powered at an overall trial level to detect change in both risk behavior and disease incidence. If successful, the Trial will validate an intervention urgently needed to reduce risk behavior in vulnerable high-risk populations in resource-poor countries, and governmental agencies and non-governmental organizations throughout the world can confidently add the intervention to their arsenal of weapons addressing the epidemic.

This paper provides an overview of the Trial, including the rationale, study management, methods, and proposed data analyses.

Background and significance

The HIV epidemic is a global catastrophe that had resulted in over 40 million active infections at the time the study was initiated [2]. At that time, more than 96% of the world’s infections were outside of north America, chiefly
in developing countries and world regions undergoing difficult social transitions. Therefore, the primary prevention of HIV disease was and still is one of the world’s most critical public health imperatives. Consequently, researchers urgently need to develop and scientifically evaluate the effectiveness of community-level interventions that target the populations most vulnerable to HIV, lend themselves to cross-cultural adaptation, and are practical within the resource limitations faced by service providers in world regions facing significant AIDS epidemics.

Community-focused behavioral HIV prevention interventions seek to reduce the prevalence and frequency of high-risk behaviors at a population level by reaching large numbers of vulnerable people with effective, culturally tailored, and theory-based HIV risk-reduction messages. Such programmes encourage behavior change among individual members of the risky population, and create and strengthen social norms to provide sustained peer support for making and maintaining these changes.

In research spanning more than 30 years, Rogers [3] and colleagues examined how technological and behavioral innovations became adopted, accepted, and normative within populations. This research has shown that a subset of population members, called community popular opinion leaders (C-POLs) for the Trial, often originates these innovations. They are the trusted trendsetters whose actions, attitudes, and views influence those of other population members, and they, therefore, are models who others naturally observe and emulate. The theory put forward by Rogers [3] considers opinion leaders to be effective innovators of new behavioral trends, because others like them, they are popular, and they can influence the social norm perceptions of others in the community. Kelly and colleagues [4,5], St Lawrence et al. [6], Kelly et al. [7] and Sikkema et al. [8] have reported several successful studies adapting the popular opinion leader intervention approach to reduce HIV risk behavior among vulnerable US populations.

Researchers selected the C-POL intervention model for evaluation in the Trial for several reasons. The first was the wide-scale potential applicability of this model across multiple countries, cultures, and populations. Second, this model addressed the urgent need to evaluate the effectiveness of community-level HIV prevention interventions that are feasible and cost-effective, and that can be implemented by governments (e.g. ministries of health, local health departments), non-governmental organizations, and others with limited resources.

One data coordinating center (DCC; RTI International) and five cooperating sets of US and international institutions [University of California, Los Angeles (UCLA)—Chinese Centers for Disease Control and Prevention (Chinese CDC), Beijing, China; Johns Hopkins University—Y.R. Gaitonde Centre for AIDS Research and Education (YRG CARE), Chennai, India; University of California, San Francisco (UCSF)—UCLA—Cayetano Heredia University, Lima, Peru; the Medical College of Wisconsin—St Petersburgh State University, St Petersburg, Russia; and Battelle Memorial Institute—University of Zimbabwe Medical School, Harare, Zimbabwe] were funded to develop a common cross-site protocol, develop common study procedures and supporting materials, engage in site preparation activities, conduct essential ethnographic and epidemiological studies, and implement and evaluate the impact of the common intervention using behavioral and biological outcomes. A data safety and monitoring board (DSMB) appointed by the NIMH has approved the entire protocol and, in many cases, has required substantial additions to the study scope of work and modifications to the protocol (see ‘Role of the Data Safety and Monitoring Board in an international trial’ [9]). The section on Trial organization describes the organization of the NIMH Collaborative HIV/STD Prevention Trial.

**Study phases and objectives**

The primary objective of this Trial was to adapt the C-POL intervention to five different cultures, and to test the efficacy of this community-level HIV prevention intervention in a variety of international settings. The Trial consists of a number of phases, each with its own activities and objectives. Specific activities and objectives for the ethnographic study, preparation activities, epidemiological study, and the community-randomized Trial are presented below. A schematic of the design of the Trial appears in Fig. 1.

Throughout the design and implementation of the Trial, investigators paid particular attention to ethical considerations related to conducting a behavioral intervention in the developing world. The translation of ethical principles into daily practice in international research trials is often not a transparent process. Therefore, researchers established a workgroup on protecting human participants during early deliberations. This workgroup included the top US and in-country investigator for each site, the principal investigator of the DCC, the NIMH staff collaborator, and selected consultants with expertise in international ethics deliberations. This group was charged with identifying and implementing optimal procedures for ensuring the ethical and equitable treatment of participants, and with making recommendations to minimize physical, psychological, and social harm to the participants. See ‘Ethical issues in the NIMH Collaborative HIV/STD Prevention Trial’ [10] for a further discussion of ethical considerations related to the Trial.
without contaminating the venues selected for the Trial. The purpose of these rapid ethnographic assessments was to identify and establish the demographics of risky populations in potential venues in the participating countries, elucidate sexual and other risk factors and nomenclature, develop procedures for identifying C-POLs in the study venues and microvenues (i.e., places within the venues where high-risk individuals socialize), determine the acceptability, content, and format of the C-POL intervention in the venues, and document social norms regarding outcome behaviors. Ethnographic supervisors were centrally trained by the DCC and other study investigators, and returned to their sites to train other local staff. Comprehensive quality control and quality assurance (QC/QA) plans were developed and implemented. QC/QA procedures included random observations of field teams by field supervisors, random checks of transcripts against tapes of interviews and group sessions, random checks of English-translated transcripts against local language transcripts, regular feedback to individual staff members by field supervisors, and regular conference calls between field supervisors and US-based staff. See ‘Design and integration of ethnography within an international behavior change HIV/sexually transmitted disease prevention trial’ [12] for additional information about the methodology of the ethnographic study.

Data from the ethnographic study informed the selection of venues, microvenues, and biological outcomes for the epidemiological study. Study ethnographers initially identified potential community venues with the following characteristics: (i) population expected to be relatively stable over 2 years; (ii) population believed to engage frequently in high-risk sexual behaviors and to have high STD prevalence; (iii) stakeholders or management supportive of the Trial; (iv) population density sufficient to ensure high exposure to the intervention; and (v) geographical and population separation sufficient to consider each venue independent of the other venues. The ethnographic study also built critical relationships with stakeholders, gatekeepers, key informants, nongovernmental organizations, and other service organizations in the venues and microvenues selected for study. See ‘Cross-site ethnographic findings that contributed to the design of the community popular opinion leader intervention in a five-country intervention study’ [13] for examples of the findings from the ethnography study and how those findings were used.

Preparatory activities
A number of specific preparatory activities occurred before beginning the epidemiological study and then the randomized trial. First, the steering committee developed and the sites implemented a feasibility study examining the acceptability of data collection using audio computer-assisted self-interviewing, in which a participant uses headphones to listen to interview questions and enters answers into the computer without interviewer assistance.

**Ethnographic study**
Before the formal ethnography study, an ethnography workgroup developed a common ethnography protocol that was adopted by the steering committee of the Trial and implemented across sites. The protocol: (i) defined the criteria for the selection of venues (individual geographically defined places in the community where members of a high-risk population gathered and could be accessed) for inclusion in the Trial (see ‘Selection of populations represented in the NIMH Collaborative HIV/STD Prevention Trial’ [11] for venue selection criteria); (ii) outlined standard ethnographic methodologies to be used across sites; (iii) described a list of key topic areas relevant to the objectives of the Trial, to be explored using these methodologies; and (iv) standardized techniques and tools for data collection to ensure quality and enable cross-site comparison. Subsequently, ethnographers conducted detailed interviews and focus groups mostly in the two or more resource venues selected in each site to provide access to target population members
A subsequent test–retest study compared data collected using audio computer-assisted self-interviewing with data collected using computer-assisted personal interviewing (CAPI), in which an interviewer reads questions from a computer screen and enters the participant’s answers into the computer. Although participants were generally not familiar with computer technology, both methods proved feasible in the populations studied. See ‘The feasibility of audio computer-assisted self-interviewing in international settings’ [14] for a complete description of these studies and their findings.

The sites also pilot tested various components of the assessment and intervention among populations that were similar to those in the venues but that were not going to be studied. Information gathered allowed site staff to tailor study procedures, assessment procedures, questionnaire items, and components of the intervention to the study populations while maintaining fidelity to the Trial protocols.

Supervisors of the assessment, laboratory, and intervention staffs received central training before these activities were initiated. Supervisors returned to the individual sites to train local staff. All staff were certified during site visits by personnel from the DCC.

**Epidemiological study**

Although each site believed that it had identified venues with sufficient risk, the DSMB required a large-scale epidemiological study in all venues, to ascertain that venue selection and sampling strategies within venues would yield stable populations of high-risk individuals and to provide intraclass correlation coefficients (ICC) for more precise power estimates. Therefore, before the Trial, large-scale epidemiological investigations were conducted in each of the five sites to confirm the prevalence of risky behaviors and STD in the venues identified by the ethnographers and to finalize the assessment and biological protocols, procedures, and questionnaire items. This study consisted of behavioral interviews with and testing biospecimens collected from 7150 individuals across the five international sites (see ‘Sexually transmitted disease and HIV prevalence and risk factors in concentrated and generalized HIV epidemic settings’ [15] for a description of this study and its findings). When data from two of the sites (India and Peru) demonstrated that the initial sampling strategy did not yield sufficient numbers of high-risk individuals, the DSMB required a second epidemiological study of 1358 individuals in India and 1205 individuals in Peru using a revised sampling methodology focusing on better-defined venues frequented by higher-risk populations. These new venues in India and Peru yielded populations at a much higher risk. The epidemiological studies also piloted the planned QC/QA procedures. This included shipping biological samples from each site to a reference laboratory (Johns Hopkins) to compare STD/HIV outcomes from a sample of participants.

The ethnographic and two epidemiological studies resulted in the selection of the following venues (and microvenues within venues) for the Trial: food markets with individually owned stalls in Fuzhou, China; clusters of wine shops in slums in Chennai, India; gathering points of young, high-risk people in barrios in Lima, Chiclayo, and Trujillo, Peru; trade school dormitories in St Petersburg, Russia; and retail establishments in business centers of growth points in rural Zimbabwe. See ‘Selection of populations represented in the NIMH Collaborative HIV/STD Prevention Trial’ [11] for a complete discussion of population and venue selection.

**Randomized trial**

The two-arm, phase III, community-randomized controlled trial involved between 20 and 40 independent community venues in each country where high-risk members of the target population could be accessed. Biological and behavioral baseline data were collected from a cohort of participants recruited in the venues (average number of participants eligible per venue in China, 98; India, 145; Peru, 148; Russia, 92; Zimbabwe, 185). Paired venues within a site were then randomly assigned by the DCC, one venue of each pair to the intervention and the other to the comparison condition. Participants in the cohort who had non-viral STDs on testing at baseline were treated. Although measurements were obtained on individual participants within each venue, the intervention was delivered to the target population in the venue. In comparison venues, access to HIV and STD educational materials and condoms was ensured. In intervention venues, these materials were available, and the C-POL intervention was undertaken. In intervention venues, staff observation, peer nominations, and gatekeeper (a person who controls access to the venue) nominations identified C-POLs from among the population members who frequented the venue. Between 15 and 20% of study population members regularly present in the venues were recruited and trained as C-POLs. Groups of C-POLs attended a series of four or five weekly sessions that provided training on how to communicate effective, theory-based, risk-reduction messages to friends and other acquaintances and guidance on having these conversations with others between sessions. The efforts of the C-POLs were supported with project logos and other ‘conversation starting’ tools. After their initial training, C-POLs attended reunion (booster) sessions six to nine times per year during the 2 years after the baseline assessment to reinforce and support continued conversation efforts. Both 12 months and 24 months after baseline data collection, behavioral interviews were repeated, and biospecimens for HIV/STD testing were
obtained from members of the cohort originally assessed at baseline. At both timepoints, cohort members were treated if they tested positive for non-viral STD.

Site staff transmitted all data to the DCC on an ongoing basis, and the steering committee monitored Trial progress biweekly. The DCC and the DSMB monitored all biological and behavioral data on an ongoing basis, but site investigators remained blind to study outcomes until the end of the Trial. The DCC was responsible for all data analysis and reports to the DSMB. In addition, the DCC worked with investigators to provide analyses for manuscripts approved by the steering committee as data were released.

Each site developed and implemented detailed strategies for retention and reassessment. QA procedures, implemented within and across sites, monitored the quality and fidelity of the assessments, intervention delivery, and adherence to ethical procedures and informed consent activities. The DCC coordinated the cross-site QA procedures for all assessment, laboratory, and intervention activities on an ongoing basis. Each site demonstrating protocol deviations implemented procedures to remediate processes as necessary.

Specific aspects of the randomized trial are provided in the following sections.

**Research questions**

The primary aims of the randomized trial are to test the hypotheses that, across all sites (countries), populations in venues that have received the C-POL intervention \( n = 69 \) venues \( n = 69 \) venues will: (i) have a lower overall observed incidence of STDs \( [\text{chlamydia, gonorrhea, syphilis, trichomonas (women only), HIV, and herpes simplex virus 2 (HSV-2)}] \) as detected by biological specimens collected at the 12 and 24-month follow-ups; and (ii) have fewer population members who report unprotected sexual acts with non-spousal partners during the 3 months before the 24-month follow-up point, measured as a change from baseline.

The secondary aims of the Trial are: (i) to test the hypothesis, across all sites, that populations in venues receiving the C-POL intervention, relative to comparison venues, will also report fewer unprotected sexual acts with non-spousal partners during the 3 months before the 12-month follow-up assessment; (ii) to test the hypotheses, separately within each country site, that populations in venues receiving the C-POL intervention, relative to comparison venues, will have either a lower overall observed incidence of STD as detected by biological specimens collected at the 12 and 24-month follow-ups, or will have fewer population members reporting unprotected sexual acts with non-spousal partners during the 3 months before the 24-month follow-up point, measured as a change from baseline; and (iii) to test the hypothesis, both within and across sites, that populations in venues receiving the C-POL intervention, relative to comparison venues, will, at 24 months’ follow-up, report greater exposure to HIV prevention messages, more STD treatment seeking, lower stigma regarding HIV and STD, and lower substance use associated with sexual behavior.

See ‘Challenges and process of selecting outcome measures for the NIMH Collaborative HIV/STD Prevention Trial’ [16] for further discussion of the outcomes chosen for the Trial.

**Study design**

*Randomization of venues*

Pairs of venues within a site were matched on the basis of site-specific characteristics (e.g. STD prevalence in Russia, city and STD prevalence in Peru, language and time of assessment in Zimbabwe). For each pair of venues, the DCC randomly assigned one venue to the intervention and the other to the comparison condition, immediately after baseline assessments were conducted for those venues.

*General considerations for sample size*

The data from the epidemiological studies were used to determine the sample size and to estimate power for detecting effects within and across sites using the following primary biological and behavioral endpoints: individuals with any new cases of chlamydia, gonorrhea, syphilis, trichomonas (women only), HIV, or HSV-2 at the 12 or 24-month follow-ups \( Y/N \), and individuals with unprotected sexual acts with non-spousal partners during the last 3 months before the second follow-up assessment \( Y/N \) measured as a change from baseline. In computing the sample sizes for each country site, the venue unit of randomization was taken into account, because a component of variation would be attributable to venues. Specific power calculations provided by Murray [17] for group-nested cohort designs were used to compute sample sizes (e.g. number of venues and number of participants per venue) for each site using the epidemiological study data. In addition, data from the epidemiological studies provided information on the degree of migration into and out of the venues that allowed follow-up rates to be estimated and provided information for the matching of venues for randomization.

In particular, the primary biological outcome assumed baseline treatment for any existing cases of chlamydia, gonorrhea, syphilis, and, for women, trichomonas. For sample size calculations, rates of new cases at the 12 and 24-month follow-ups of these four STDs were estimated in the comparison group as those observed on the epidemiological assessments. Furthermore, the percentage of all new cases of HIV or HSV-2 at the 12 or 24-month follow-ups was estimated in the comparison group as the
Cross-site statistical power

The cross-site intervention effect on the primary biological outcome can be detected using a type I error rate (two-sided) of 5%, with 97% power using at least 20 venues per site and 50 participants per venue, if there is a 33% lower STD incidence in the intervention venues versus the comparison venues within each site. This intervention effect translates into a common odds ratio (i.e. odds ratios computed for each site and averaged) of 0.63 using the data from the epidemiological studies to estimate the outcome rates in the comparison venues and 33% less to estimate the outcome rates in the intervention venues. Also, for this cross-site power analysis, the ICC was taken as the average of the ICC within sites from the epidemiological study data.

A cross-site intervention effect on the primary behavioral outcome can be detected using a type I error rate (two-sided) of 5%, with 99% power using at least 20 venues per site and 50 participants per venue, if there is an absolute difference of 10% in the change in high-risk sexual behavior between the intervention and comparison venues within each site. This intervention effect translates into a common odds ratio of 0.65 using the data from the epidemiological studies for India, Peru, and Russia to estimate the outcome rates in the comparison venues and 10 percentage units less to estimate the outcome rates in the intervention venues. Also, for this cross-site power analysis, the ICC was taken as the average of the ICC within sites from the epidemiological study data.

Within-site sample sizes

The study was initially designed so that each site would have at least 80% power to detect the relevant effect for either the primary biological or the primary behavioral endpoint (using the specific risk data for each site from the epidemiological studies) and operating with a type I error rate (two-sided) of 5%.

Table 1 summarizes the results of the within-site sample size calculations. These calculations use the epidemiological study data to provide estimates of the ICC, participation rates, and follow-up rates for each site and the proportion having sex in the past 6 months for Peru and China. The calculations assume that 20% of the study participants in the cohort are C-POLs and will be excluded from the primary analysis.

Recruiting, screening, and accessing a cohort in each venue

In each venue, staff met with stakeholders and gatekeepers in the community to gain support for the study and to gain access to the venue or to microvenues (specific areas or stores where members of the population gather) within it. The DCC worked with staff at each site to develop site-specific recruitment procedures based on the size of the population and the source of participants. Sometimes participants were approached as they entered one of the microvenues (e.g. a wine shop in India or a retail store in Zimbabwe) and recruited for the cohort. In other cases, a list was created (e.g. market stall owners and employees in China, dormitory rooms in Russia), and the DCC specified the order in which to approach those on the list for inclusion in the study. An average of between 92 and 185 eligible participants per venue were randomly or purposively selected from the population of all individuals present in the venue using the site-specific sampling protocol established by the DCC.

Eligibility

Generally, participants were eligible if they were between the ages of 18 and 30 years, although age ranges were expanded at some sites based on the STD and HIV epidemiology of the country (e.g. 18–49 years in China). Participants had to live, work, or socialize, as appropriate, in the selected venues or microvenues, and they had to plan to remain in the venue for at least the next year. In all sites, participants were excluded if they could not give informed consent or if they had a permanent disability (e.g. deaf, mental retardation). China excluded participants who reported no sex in the past 6 months and who did not have an STD at baseline. Peru excluded those who reported no sex in the past 6 months at baseline. Russia excluded students who were in their last year of school at the time of recruitment for the Trial. Zimbabwe excluded those who had lived in the venue for less than 2 years and those who lived in the venue for less than 9 months a year.

Table 1. Sample size requirements by country.

<table>
<thead>
<tr>
<th>Country</th>
<th>Powered on primary endpoint</th>
<th>Participation rate (%)</th>
<th>Follow-up rate (%)</th>
<th>No. of venues</th>
<th>No. of participants approached per venue</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>Biological</td>
<td>95</td>
<td>84</td>
<td>40</td>
<td>124</td>
</tr>
<tr>
<td>India</td>
<td>Behavioral</td>
<td>96</td>
<td>90</td>
<td>24</td>
<td>163</td>
</tr>
<tr>
<td>Peru</td>
<td>Biological</td>
<td>89</td>
<td>90</td>
<td>20</td>
<td>190</td>
</tr>
<tr>
<td>Russia</td>
<td>Behavioral</td>
<td>90</td>
<td>85</td>
<td>24</td>
<td>99</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>Biological</td>
<td>85</td>
<td>86</td>
<td>30</td>
<td>171</td>
</tr>
</tbody>
</table>

Slope coefficient from the linear regression of HIV/HSV-2 (Y/N) on age (× 2 years) using epidemiological study data. The ICC within each country for the primary biological outcome was taken as that for the composite of the four infections from the epidemiological data: chlamydia, gonorrhea, syphilis, or trichomonas (women only) without regard for HIV or HSV-2. No relevant incidence data were available on HIV or HSV-2 for China. The ICC within each country for the primary biological outcome was taken as the average of the ICC within these three sites from the epidemiological study data.
Informed consent
All sites had Institutional Review Board (IRB)-approved, culturally appropriate, informed consent procedures, including a signed consent form. In some sites, consent information was initially presented through a video. Both assessment participants and C-POLs always met individually with a staff member to review all study procedures, review the benefits and risks of participation, discuss the option to discontinue participation at any time without penalty, and receive methods to contact the investigator and the local IRB if questions about participation in the study arose. Finally, signed informed consent was obtained. Substantial ethnographic research informed the design of consent forms and procedures at the sites. In some sites, the behavioral risk assessment instrument was framed as a general health questionnaire in order to develop rapport with the research participant and reduce stigmatization.

Reimbursement
Study participants received modest reimbursements covering the time and expenses related to study participation. These reimbursements varied from country to country to reflect local economic conditions and the proximity of the assessment site to the venue. For the baseline assessment, reimbursement for time spent (in US dollars) was approximately $3 in China, $4 in India, $6 in Peru, $15 in Russia, and $6 in Zimbabwe. Transportation to the assessment site was generally provided, as was food if the assessment occurred during mealtime. Reimbursements were similar in scope at follow-up.

Baseline interview
The objectives of the assessment activities were to identify, recruit, and train assessment staff; to conduct a baseline assessment to document risk behaviors and HIV/STD prevalence in intervention and comparison venues before the intervention was initiated; to treat or refer positive cases of non-viral STDs; to refer cases of viral STDs on the basis of a site-specific plan; and to conduct outcome assessments 12 and 24 months after the baseline assessment to document the prevalence of risk behaviors and the incidence of HIV/STD in intervention and comparison venues after the intervention was initiated.

The behavioral assessment questionnaire was designed to take approximately 45 min to administer and included up to 300 questions. The following domains were assessed: demographic characteristics; mobility; self-reported sexual risk behavior; opportunities for social interaction; recognition of the project logo; exposure to HIV/STD prevention messages; general health and healthcare seeking behavior; HIV testing; substance use; and stigma. Interviewers administered the assessment using a CAPI program and a standard protocol to minimize variability within and across the five sites, as well as to reduce interviewer bias. Site staff used a decentering approach [18] to translate the assessment to local languages: Mandarin in China, Tamil in India, Spanish in Peru, Russian in Russia, and Shona and Ndebele in Zimbabwe. This approach focused on translation for meaning into language levels that participants could understand, and did not use a literal, word-for-word, translation process. The DCC arranged for backtranslation of the assessments, and discrepancies were resolved through discussions between DCC and site staffs. Staffs at both the DCC and study site tested the CAPI programs in the relevant language before they were finalized.

After completing the interview, participants received HIV pretest counseling following national guidelines and provided blood, urine and, for women, vaginal swab specimens. During this part of the evaluation, participants completed an STD symptoms questionnaire while talking with a health professional. If the responses indicated that STD symptoms were present, researchers provided syndromic treatment for participants with discharge or ulcers immediately after the biospecimens were collected, or these participants were referred to local clinics for treatment (depending on the country). Treatment procedures followed local, World Health Organization [19], or Centers for Disease Control and Prevention guidelines [20], as appropriate. Participants also received HIV/STD education when the biospecimens were collected.

Biospecimens were tested in study laboratories in each country following standardized laboratory protocols. Urine from men and vaginal swabs from women were tested for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* using polymerase chain reaction. HSV-2 testing was performed using enzyme immunoassay (EIA) or enzyme-linked immunosorbent assay (ELISA). HIV testing was performed using EIA or ELISA and repeated using a different EIA/ELISA. Positives were confirmed using Western blot, except in Zimbabwe where a positive result on both ELISA tests is considered confirmatory and a third ELISA or Western blot test was used only to confirm HIV status in the case of discordant results on the initial two. Syphilis testing was performed by rapid plasma reagin (RPR) and confirmed using the *Treponema pallidum* particle agglutination test. Vaginal swabs were cultured for *Trichomonas vaginalis* using the InPouch TV test.

Once local laboratory results were available, participants were given the opportunity to receive their test results and post-test counseling. If a result was positive and the participant had not been treated or referred for the disease on the basis of symptoms at the time of the assessment, the protocol specified that he or she was to be treated for non-viral STDs or referred for treatment by the study, treated for episodic HSV-2 in China, India and Zimbabwe, and, for positive HIV results, referred to local agencies for HIV counseling and treatment. In Zimbabwe, pregnant women who were HIV positive received vouchers to ease access to treatment near the time of delivery in order to reduce the chance of mother-to-child transmission.
Intervention and community popular opinion leaders

The primary objectives of the intervention activities were to identify, recruit, and train intervention staff; to identify or develop appropriate HIV/STD educational materials for distribution in the intervention and comparison venues at each site; to recruit, train, and deploy C-POLs in the intervention venues; to conduct between six and nine reunion sessions for C-POLs during each of the next 2 years; to assist C-POLs to co-facilitate reunion sessions during the second year of the study in order to enhance sustainability; and to conduct the C-POL intervention in comparison venues after the 24-month outcome assessment was completed.

The presence of certain core elements distinguishes the C-POL intervention from other types of general peer education approaches [21]. The following core elements reflect the theoretical base of the model implemented at the sites: (i) the intervention is directed to an identifiable target population in well-defined community venues where the population’s size can be estimated; (ii) techniques are systematically used to identify cadres of individuals, C-POLs, who are popular, well-liked, and trusted by others in their everyday social groups; (iii) over the life of the programme, at least 15% of the target population in the intervention venues are trained as C-POLs; (iv) the programme teaches C-POLs skills for sharing HIV risk-reduction messages with others in everyday conversations; (v) the training programme teaches C-POLs the characteristics of effective behavior-change messages targeting risk-related attitudes, norms, intentions, and self-efficacy, and teaches C-POLs personally to endorse the benefits of safer behavior and to recommend practical steps needed to implement change; (vi) small groups of C-POLs meet weekly in sessions that use instruction, facilitator modeling, and extensive role-play exercises to help C-POLs refine their skills and gain confidence in delivering effective HIV prevention messages; (vii) C-POLs set goals to engage in risk-reduction conversations with friends and acquaintances in the target population between the weekly training sessions; (viii) the conversational outcomes of C-POLs are reviewed, discussed, and reinforced at subsequent training sessions; and (ix) logos, symbols, or other devices are used as ‘conversation starters’ between C-POL and others.

C-POLs were initially identified by ethnographic and intervention staff observation, through interviews with key informants, and by self-nomination. Participants were recruited as C-POLs by emphasizing, in a culturally appropriate manner, how they were selected and how they could help their communities. C-POLs were informed of their ethical rights, provided voluntary informed consent, and were invited to attend four or five weekly training sessions, depending on site requirements. Reimbursements varied, were based on local economic conditions, and reflected the time involved in training at the local site (items worth the equivalent of US$1.45–$15 per session). C-POLs understood their commitment to provide social messages to social group members in their venues with the aim of preventing the spread of AIDS. Each C-POL training session lasted 90–150 min. Sessions were led by a team of two to three facilitators in a convenient location.

Groups of 10–20 C-POLs attended the four to five weekly training sessions. In the first session, C-POLs were introduced to the programme and were encouraged to think of themselves as an important vanguard in efforts to prevent HIV, STD, and AIDS in their community by talking with others about prevention. The threat of AIDS, national and local epidemiology, risk behaviors, and prevention steps were discussed. In the second session, C-POLs were taught how to correct myths and misconceptions held by friends about the disease, and began to learn the characteristics of effective health communication messages applied to HIV risk reduction. Because risk behavior reduction is a function not only of one’s knowledge about AIDS but also of attitudes, beliefs, intentions, skills, and peer norm perceptions, C-POLs were taught to develop and practice communication messages that focus on these determinants. Specific messages used in training were based on findings that emerged from the ethnography with each site’s populations. In subsequent sessions, C-POLs continued practicing conversations in the group. They also discussed and planned how, when, and where they would initiate conversations with other members of the target population, and they set goals at the end of each session to talk with a specified number of friends and acquaintances. Outcomes of the conversations were discussed and reinforced in the next group meeting, and any problems encountered and their potential solutions were discussed. The objective was for C-POLs to engage in increasing numbers of conversations with others each week.

Reunion sessions were held to build a sense of camaraderie and to enhance the perceptions of C-POLs that they are HIV/STD prevention leaders in order to sustain their delivery of prevention messages. In addition, the reunions provided support, reinforcement, and encouragement for C-POLs to continue in their HIV/STD prevention advocacy roles. See ‘The community popular opinion leader HIV prevention programme: conceptual basis and intervention procedures’ [22] for additional information about the intervention.

Assessment of outcome in the cohorts

All participants in the baseline cohort were followed, and those located were administered follow-up CAPI and STD symptoms interviews, and were asked to provide biospecimens for STD testing 12 and 24 months after the date when they completed the baseline measures. (India had difficulty maintaining IRB approval and completed its follow-up assessments at 18 and 30 months.) The
CAPI questionnaire measured the same domains as the baseline assessment, although some questions were modified to reflect the 12 months elapsed since the last study assessment. The plan for treatment of those with positive STD results was the same as at baseline. All sites used procedures developed in conjunction with the DCC that were designed to minimize attrition and the loss of participants at follow-up.

The Trial was powered assuming a greater than 80% follow-up rate across the 2 years. Each site aimed for a 90% follow-up rate. Staff would make at least eight attempts on different days and at different times of the day to locate each cohort member who was eligible for follow-up. In addition, once follow-up for a venue began, staff used up to 6 months to locate cohort members from that venue. After 6 months, cohort members who had not been located were considered lost to follow-up for that assessment round. In each site, participants who left the study area could be followed by telephone if they could be located, even if biospecimens were then not available. To ensure satisfactory retention rates, staff at all sites were trained to address participants’ concerns, obtain multiple types of locating information, and use reimbursements to compensate for participant’s time as appropriate.

**Implementation progress**

Figure 2 presents the number of participants who completed the baseline interview in each of the sites, indicates the subsequent randomization, and shows that the 12 and 24-month follow-up assessments are in process. Since the trial is in process and volunteers continue to be recruited and trained as C-POLs, we cannot, at this time, report the numbers of C-POLs successfully recruited and trained in each country.

**Quality control and quality assurance procedures**

QC for this Trial focused on developing procedures that ensured that data were collected in a standardized way, comparable measurements were valid, data were maintained in a secure and confidential manner, and the intervention was implemented in a similar fashion across sites. QA procedures addressed adherence to the study protocol and ensured that QC procedures were being implemented consistently across all participating sites, given the necessary country-specific tailoring.

The components of the QC/QA model adopted for this Trial were divided into three major categories: (i) manuals for the Trial (overall operation, assessment, biological specimen collection, intervention, data management system, laboratory management system, and laboratory procedures); (ii) personnel (including selection criteria, job descriptions, training, and certification procedures); and (iii) ongoing monitoring of adherence to study procedures including ethnographic activities, assessments, intervention training, and collection and analysis of biological specimens. Each site sent samples selected by the DCC to the reference laboratory at Johns Hopkins for QA. Specific activities for various areas appear below.

**Documentation**

Documentation of standard study procedures is one of the most important aspects of any trial. Documentation for this trial began with careful specification of the overall trial design and procedures in the study protocol. Once the protocol was fully specified, investigators began developing and pilot testing components of study

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**Fig. 2. Assessment implementation.** C, comparison; I, intervention; R, randomization within pairs of venues.
instruments, study procedures, training manuals, and other manuals documenting various study activities. Any instrument, procedure, or activity that needed to be implemented in the same manner across all sites was documented. When necessary, these documents were translated into the languages of the local countries, and elements were adjusted within protocol guidelines to reflect the content and procedural changes required to reflect the cultures and regulations of the five countries participating in the Trial.

In addition to the CAPI system that captured assessment data from individual participants, the DCC developed three intricate systems for monitoring the study: a data management system; a laboratory management system; and a process evaluation data collection and management system. The computerized data management system was designed to collect and monitor data from the assessment activities. This system monitored participant recruitment, assessment, and follow-up, including participant contacts and the accumulation of assessment and laboratory data other than the interview data collected via CAPI. The computerized laboratory management system monitored the location, testing, and results of biological samples obtained during the interviews. The process evaluation system collected and managed the data collected as part of the process evaluation. Each of these systems could easily produce reports that aided project staff in monitoring activities recorded in the system. Extensive manuals documented the purpose and use of each of these systems.

**Study personnel**

Selection criteria, job descriptions, and training procedures for study personnel were standardized across the sites. Selection criteria for each of the major study roles ensured that personnel with similar levels of training, experience, and ability were performing similar study functions across sites. The specific activities required in certain roles (e.g. assessment team members) could, however, be parsed among individuals in various ways. For example, in some sites, the same individual conducted the assessment interview, administered an STD symptoms questionnaire, and collected biological specimens, whereas in other sites, these activities were split among different team members.

Standardized job descriptions ensured that study personnel (e.g. project coordinators, assessors, facilitators, laboratory personnel) engaged in similar activities in a consistent manner across sites, except for local modifications approved by the steering committee. These formal job descriptions also ensured that certain functions could not be combined or overlap with other functions. For example, the duties of facilitators who trained the C-POLs could not be combined with those of the assessors, for this overlap could potentially bias the assessment of the effect of the intervention.

Central training for the local trainers of ethnographers, assessors, biospecimen collectors, laboratory personnel, and intervention facilitators also helped ensure the standardization of Trial procedures. Because of the travel expense required to bring staff from five countries to the United States and the differences in language and customs among those sites, a train-the-trainers model was used. Under this model, three or four senior staff in each area came to a central training session in the United States. The initial central training session also enabled the translation and tailoring of the training manuals, so that site staff implemented the principles and study procedures in a standard manner across all the sites. The trained supervisors then returned home, completed translating the training manual into the local language (or languages), and trained in-country staff. Bringing together senior personnel from the five sites had the added benefit of reinforcing the fact that they were key staff in an international, multisite trial and that common implementation of the elements of the protocol was critical to the success of the study.

Trainees who demonstrated competence were certified on the basis of a standard set of criteria for each function across the sites. Personnel who did not achieve certification were barred from undertaking the activity (e.g. collecting ethnographic data, administering the behavioral assessment, collecting or analysing biospecimens, training C-POLs) without additional training. Certification provided a strong motivation to meet required standards. This process also facilitated the rapid training of new staff.

Because the data and laboratory management systems were tailored to reflect nuances related to recruiting and maintaining the participants at each site and the correct installation of the systems was critical to their use, training in these systems was conducted at the sites during data management system site visits rather than centrally.

**Quality assurance for assessments**

Quality for all assessments was reinforced through five types of onsite and central monitoring procedures: (i) monitoring the behavioral risk assessment version and administration; (ii) monitoring biospecimen collection, storage, and analysis; (iii) monitoring data and laboratory management systems and operating procedures; (iv) monitoring IRB knowledge, procedures, and documentation; and (v) monitoring local laboratories. Annual visits to each site were conducted by QC/QA specialists from the DCC and the biological reference laboratory.

**Quality assurance for biospecimen testing**

The QA process for biospecimen testing was extensive. Senior laboratory staff from each country were trained at the reference laboratory to follow the protocols that specified standard biospecimen collection, storage, and
analysis procedures. Panels of approximately 200 samples were sent to site laboratories for analysis by appropriate assay, and annual site visits were conducted to review laboratory procedures. A 20% sample of specimens collected in each country and selected by the DCC, including all positive samples (if less than 10%, or a random sample of positives up to 10%) and a random sample of negatives, were shipped by the five site laboratories to the reference laboratory for retesting during the first year each laboratory operated. Once laboratories were certified through that procedure, the sampling rate for HIV, HSV-2, and syphilis dropped to 5%, whereas the rate for chlamydia and gonorrhea remained at 20%. All discordant results were initially checked for data entry or interpretation errors, and study data were corrected as needed. Remaining samples with discordant results were restested by the sites and reference laboratory, but study data were not changed on the basis of these results. Finally, panels (HIV, chlamydia and gonorrhea, HSV-2, and syphilis) assembled by the College of American Pathologists, were sent to the site laboratories several times per year for analysis.

**Quality assurance for the intervention**

The two sources of ongoing QA for the intervention were a process evaluation and central QA by a consultant experienced in the C-POL intervention model. These efforts are briefly described below.

The process evaluation was designed to provide feedback for intervention delivery, and document the reasons for intervention effects. The five specific objectives of the summative process evaluation are to assess: (i) the number and content of messages delivered by C-POLs; (ii) adherence to the training protocol; (iii) the spread of messages to the target population; (iv) community exposure to other sources of information related to outcomes; and (v) problems and challenges in the field related to the intervention/message or characteristics of a specific sub-population. The instruments developed to collect these data include: (i) a C-POL recruitment form that documents the number of people approached to be C-POLs, how they were identified, their basic demographics, and whether they agreed to participate; (ii) an attendance form that monitors which of the C-POLs attend training and reunion sessions, the number of conversations reported when homework is reviewed, and the number of those conversations that occurred in the venue; (iii) a C-POL demographic assessment that gathers basic demographic information about each C-POL; (iv) a generic C-POL session observation checklist, completed by a session observer, which is designed to assess fidelity to the training protocol, to improve the training sessions and to document what was covered during training; (v) a form to record facilitator notes documenting events during intervention delivery; (vi) a monthly log that records numbers of C-POL logos posted and worn in each venue and the number of other HIV/STD health education messages posted and worn in each venue; (vii) a form that documents other HIV/STD prevention messages and activities across a specific venue; (viii) a form that monitors other HIV/STD prevention messages and activities across the site; and (ix) process evaluation questions on the behavioral assessment that assess exposure to the project logo, participation in conversations on topics targeted by the intervention, and stigma related to HIV.

On an annual basis, the DCC consultant with expertise in implementation of the C-POL intervention visited each site, observed training and reunion sessions, interviewed each facilitator regarding the intervention protocol, and interviewed a selection of C-POLs in an intervention community when culturally appropriate. The monitor completed the ratings described in the site visit protocol and discussed areas in which improvement was possible with site supervisors and staff.

**Data analysis plans**

Data collection will not conclude until August of 2007. Therefore, plans for analysis are presented below.

**Analyses of baseline data**

Baseline results pertaining to primary and secondary outcome measures will be tabulated by and across venues by country, and compared by intervention assignment. In particular this will include: individuals with any case of chlamydia, gonorrhea, syphilis, trichomonas (women only), HIV, or HSV-2 (Y/N); individuals with any unprotected sexual act(s) with non-spousal partners during the past 3 months (Y/N); individuals with any case of chlamydia, gonorrhea, syphilis, or trichomonas (women only), (Y/N); the proportion of sexual acts with non-spousal partners by an individual during the past 3 months that were unprotected (with abstinence coded 0%); the number of unprotected sexual acts with non-spousal partners by an individual during the past 3 months; and the number of partners during the past 3 months. The prevalence of individual STD and HIV will also be analysed.

A careful study will be made of data to substantiate original assumptions used in the design. In particular, the following will be tabulated: participation rates for the assessment and collection of biospecimens by and across venues by country; the frequency of missing data for critical assessment questions by and across venues by country; the length of time until treatment for positive test results on chlamydia, gonorrhea, syphilis, and trichomonias by and across venues by country; the length of time between baseline assessment and implementation of study intervention by and across intervention venues by country; ICC estimates within country; and the HIV/HSV-2 rate of change with age. Finally, QC results for the laboratory data will be summarized.
Analysis of primary endpoints at follow-up

An intent-to-treat analytical approach will be used, in that any venue assigned to the intervention will be considered treated, whether or not the C-POLs were active in that venue. The intervention effect for the biological endpoint will be estimated as the difference between the percentage of intervention and comparison venues at the 12 and 24-month follow-ups. Cases (defined by a positive test result) of chlamydia, gonorrhea, syphilis, and TTR will be treated after each assessment. Existing baseline HIV and HSV-2 cannot be eliminated. An individual will thus be classified as a new case of any of the six infections at the 12 and 24-month follow-ups if there is a positive test at either of the follow-ups for chlamydia, gonorrhea, syphilis, TTR (if female), HIV (if not positive for HIV at baseline), or HSV-2 (if not positive for HSV-2 at baseline). To be considered a new case of syphilis if syphilis was documented at baseline, documentation will be required both that the syphilis at baseline was treated, and that the follow-up test at 12 months was negative. Otherwise, an individual who was positive at both baseline and 12-month follow-up and who has a fourfold or more RPR titer increase from baseline to 12-month follow-up and a fourfold or more RPR titer increase from the 12 to 24-month follow-up will be considered a new case. If the above conditions are not met for the six biological measures, the individual will be classified as negative for the composite outcome if at least two-thirds of the tests used in the individual's assessment provide definitive results (i.e. positive, negative, or indeterminate but not missing). For example, if the individual is a man, positive for HIV and negative for HSV-2 at baseline, the outcome assessment will be based on chlamydia, gonorrhea, syphilis, and HSV-2. At least three of the four test results must not be missing. If there are no new positive tests and more than a third of the individual's tests are missing, the composite variable will be set to missing. Prior to analysis, a panel of experts will meet to review laboratory and treatment data from selected cases to ensure that new cases are classified correctly.

The intervention effect for the behavioral endpoint will be measured as differences between intervention and comparison groups in the change scores from baseline to follow-up. Data will be gathered on the number of sexual acts during the past 3 months with non-spousal partners and the number of these occasions in which a condom was used, in order to compute indicators, numbers, and proportions of unprotected sexual acts with non-spousal partners. Individuals in the sample reporting no sexual acts with non-spousal partners will be assigned a proportion of 0%. See ‘Challenges and process of selecting outcome measures for the NIMH Collaborative HIV/STD Prevention Trial’ [16] for additional discussion of the outcome measures.

For the primary analyses, hypotheses regarding the study endpoints across countries will be evaluated using permutation tests (randomization tests) on unadjusted summary statistics (e.g. the difference between intervention and comparison venues on the percentage of participants with a new STD/HIV at the 12 and 24-month follow-ups). Permutation tests require far fewer assumptions than traditional model-based approaches, and seem appropriate for a trial with such diversity both within and across countries. The permutation tests will account for the fact that venues were randomly assigned and that this randomization involved pair-matching of venues in each country. For example, within a country with 10 matched pairs of venues (i.e. randomization to intervention and comparison within each of 10 pairs of venues), the permutation test for a specific endpoint involves computing the mean of the 10 pairwise differences between intervention and comparison venues calculated for each of the 210 (1024) ways that the intervention could have been randomly assigned to the 20 venues. The rank of the observed mean among the 1024 possible means will give the significance level. This same procedure will be used across countries. Test-based confidence intervals can be constructed on the basis of the permutation tests.

An advantage of the randomized assignment of intervention is that baseline covariates will be balanced on average (in expectation) between intervention and comparison groups. Any imbalances that occur by chance are accounted for by the significance test. The greater sample size for the primary analysis across all sites makes large chance differences unlikely. By performing adjusted analyses (particularly for site-specific analyses), however, the effect of chance imbalances can be investigated. In this regard, the DCC will examine the comparability between intervention and comparison venues for several baseline variables at all sites. Permutation tests on adjusted summary statistics will be used as secondary analyses. In general, the covariates used for adjustment may not be the same in each country because of the diversity of the study populations (e.g. Zimbabwe has little injection drug use, whereas injection drug use may be higher in other countries). Mixed-model regression analyses will be run as secondary analyses if these models prove to be reasonable.

As in the across-countries analyses, hypotheses regarding the within-country study endpoints will be evaluated using permutation tests on both unadjusted and adjusted summary statistics. In general, the unadjusted summary statistics will be the primary analyses, and the adjusted summary statistics (e.g. adjusted for baseline level of risk, age, sex) will be used as secondary analyses. Also, mixed-model regression analysis on each endpoint will be secondary analyses.

Statistical models

When using statistical models to analyse the study endpoints, the analysis must reflect the group-randomized design (e.g. nested cohort design). It is anticipated that
a mixed-model regression analysis on each behavioral outcome will be used to include fixed effects (e.g., as a result of intervention and time) and several random components of variation (e.g., as a result of venue nested within intervention and individual nested within venue). The interaction of intervention with time will assess the effectiveness of the intervention [7]. As distinguished by Murray and Hannan [23], the general nested cohort design will include a fixed effect for time that is crossed with intervention, venue and individual, and a random effect for individual that is nested within venue. For the biological endpoint, it is not appropriate to use this model, because the endpoint is a composite of new HIV/STD cases. In this case, the mixed model is a main effects model for intervention. For all of these models, additional levels of nesting may be specified, for example to combine results across countries (if it appears that using a statistical model across countries is feasible) and to take into account matching (e.g., pairing of venues within a country for randomization to intervention versus comparison). Regression adjustment for covariates may also be applied to account for baseline differences and to improve power. Before testing the hypotheses using mixed models, it will be necessary to determine if variable transformations are required. Experience in related studies has indicated that some of the self-reported behavioral outcomes (i.e., number or proportion of times) may be skewed. Box-Cox plots [24] will be generated to determine the most appropriate transformation. The SAS/STAT [25] MIXED procedures alone or in combination with the SAS macro GLIMMIX will be used to fit the mixed regression models. MIXED assumes a Gaussian error distribution for all random effects. The SAS macro GLIMMIX allows for different specifications of the residual error distribution [26]. Binary outcomes (e.g., the composite biological outcome) may be modeled with binomial error, whereas frequency of occurrence measurements (e.g., the number of unprotected acts) may require Poisson error or Gaussian error on a transformed scale. In addition to using the mixed regression models approach, it may be useful to explore a population-averaged approach via the generalized estimating equations methods of Liang and Zeger [27]. This method is more robust to misspecification of the covariance structure. The generalized estimating equations method is available in SAS/STAT GENMOD and the SUDAAN software product of Research Triangle Institute [28]. Each of these approaches will be explored for possible model-based analysis.

Other analyses
The primary results will probably need to be substantiated with a sensitivity analysis of the results to missing outcome data (e.g., losses to follow-up). To some degree, the need for a detailed sensitivity analysis will depend on the results of the primary analysis, the degree of loss to follow-up, and any intervention-dependent pattern to the missing data. A first step will be to look for patterns by comparing observed characteristics of participants who are lost to follow-up with those having complete data. Then, both non-parametric and parametric approaches will be undertaken to account for missing data. In the non-parametric approach, the participants will be stratified for characteristics thought to be related to outcome or the probability of missingness (e.g., venue, sex, age, intervention condition, and baseline and 12-month measures), and outcome values will be imputed within strata using the observed outcomes. This will be followed by a permutation test analysis. For the parametric approach, a mixed-effects model that includes covariates associated with outcome or the probability of missingness will be fit. The exact specifications will require investigation of the available data. Both approaches assume that the probability of missingness does not depend on the missing values, but only the observed data used appropriately in the stratification or modeling.

Additional analyses will be performed to explore the relationship of process measures to the magnitude of intervention effect. For example, to analyse a measure of extent of intervention in a venue, the correlation of this measure (recorded for each intervention venue) with the difference in outcome between the venues in each matched pair will be investigated. Regression models will be used to investigate the relationship of multiple process measures with outcome. This type of analysis can be performed both within and across countries. The interaction of process measures by country may be of interest. Process measures that can be used for this analysis include attendance at C-POL training sessions, the number of relevant conversations that C-POLs reported occurring during the 7 days before the training or reunion sessions, and the number of C-POL logos that are observed within each venue on one day each month.

Lessons learned from implementing this Trial
Many lessons have been learned from implementing this international, multisite HIV/STD prevention trial. These include the following.

Preliminary epidemiological studies are required to: (i) determine if the populations being studied are at risk; (ii) identify the STD/HIV and behavioral risk prevalences in each country; and (iii) provide preliminary data to use for sample size calculations.

Close monitoring and training of staff for biological testing in foreign laboratories is required including ensuring that they always have the proper equipment and supplies (e.g., test kits) available.

A sustained effort must be directed to meet the challenge of taking a common intervention and tailoring it to ensure cultural relevance across diverse cultures while still
ensuring that the same basic approach is being tested in all countries.

The intervention content must be tailored to multiple at-risk populations in different countries while ensuring adherence to core principles.

The implementation of a behavioral intervention must be carefully monitored through ongoing supervision, process measures, and periodic site visits to ensure that the intervention is comparable across sites.

Assessment measures must be carefully translated and adapted to maintain consistent meanings in multiple languages.

Be prepared to react to the loss of venues over time as a result of natural disasters, political upheaval, or business factors.

Each site must develop a plan for follow-up activities, monitor those activities, and be prepared to adjust the plan if retention rates are lower than anticipated.

Regular meetings and conference calls of the steering committee and workgroups are essential throughout the Trial.

The timeline must always reflect the extended time involved to obtain IRB clearances from multiple IRB for each site and the DCC.

In conclusion, this Trial provides an opportunity to test rigorously a behavioral intervention in five countries, which increases the generalizability of the results. The Trial will evaluate the efficacy of the C-POL community-level HIV prevention intervention that was adapted for use in the various cultures, within the resource limitations faced by service providers in world regions threatened by high rates of HIV infection. On the basis of data from ethnographic and epidemiological studies conducted preceding the randomized trial, investigators tailored both the assessment and the intervention to the diverse cultures while still ensuring that the same basic approach is being tested in all countries. Venues (and participants within venues) were selected on the basis of risk behaviors, thus permitting recruitment of a core age group, but still targeting those with high-risk behaviors in each country. For example, high-risk individuals in the Fuzhou markets in China included older individuals than the dormitories in Russia, and the age range was expanded to reflect this difference. The use of randomized allocation provides a valid comparison of intervention and comparison conditions, thus avoiding bias, providing balance (on average) in factors predictive of outcome, and providing a valid basis for statistical tests of significance. As is necessary for this type of community-level trial, the sample size and statistical power calculations, as well as the analysis plan, account for the randomization of clusters (venues). Efficacy will be assessed using both behavioral and biological outcome measures; the primary biological outcome is an innovative composite measure of the incidence of six STDs, providing a single measure that can be used across sites with variable burdens of different STDs. The results of the Trial will provide important information for addressing this major public health problem.

**Trial organization**

The NIMH Collaborative HIV/STD Prevention Trial was supported using the cooperative agreement mechanism. The National Institutes of Health use this mechanism to support large-scale, multisite, phase III randomized controlled studies when substantial resources are required and when the funding institute wants both to participate actively in the scientific development of the study and provide administrative oversight.

Figure 3 presents an organization chart for the Trial. The components of the organization are described below.

**National Institute of Mental Health**

The Division of Mental Disorders, Behavioral Research, and AIDS at the US NIMH funded the study. Division staff actively participated in all aspects of the study, with primary input provided by the NIMH senior scientist and the NIMH project officer.

The NIMH senior scientist had substantial scientific input, in collaboration with award recipients, both in planning and conducting the study, and was a voting member of the steering committee (see below). The senior scientist assumed a major role in developing the study protocols, specifying QC/QA procedures, informing data analysis and interpretation, and preparing publications.

The NIMH project officer had overall responsibility for budget negotiations and for monitoring the conduct and progress of the project. The project officer carried

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**Fig. 3. Organization chart.**
primary responsibility for periodic review, approval of the protocol in relation to stated objectives, and made recommendations regarding the continuation of the programme at critical decision points. The project officer oversaw the DCC, received all required reports, and determined that satisfactory progress was being made. The project officer sought advice from the DSMB on issues concerning the conduct and progress of the study.

Sites
Sites were located in China, India, Peru, Russia, and Zimbabwe. A site consists of a US institution and the foreign institution paired with it. The sites performed all of the research activities needed to implement the protocol, and were responsible for the daily conduct of the study at the foreign location. The sites participated in the design of study protocols, then implemented the ethnographic and epidemiological studies; adapted and translated the model intervention; trained staff; conducted baseline and follow-up assessments; selected, recruited, and trained the C-POLS; implemented on-site QC/QA procedures; helped interpret study results; and assisted in the preparation of reports and publications. The sites agreed to abide by the Trial design and policy recommendations developed by the steering committee and any requirements NIMH established in the terms and conditions of the cooperative agreement.

Data coordinating center
The DCC provided overall study coordination, including data management, data analysis, and training in common procedures, and ensured the distribution of necessary materials to all sites. It coordinated pilot testing of the protocol for assessment and full implementation of the Trial. DCC staff purchased and installed computer servers in each of the foreign sites, and the DCC retained a network manager to maintain these systems at each site. The DCC developed computer-assisted interviewing and other data capture programs to ensure efficient, accurate, cost-effective data collection. They developed and maintained a common data repository containing data files needed by many study participants. The DCC funded and monitored the activities of the core laboratory for the study. They arranged teleconferencing and other technical means (e.g. E-mail, a project web site) to facilitate rapid and easy communications among all staff from participating institutions. The DCC participated in QA activities, including site visits monitoring information technology, ethnography, behavioral and biological assessment, and intervention activities. The DCC conducted all data analyses required to prepare reports and manuscripts and participated in manuscript preparation. When requested, the DCC presented a written or oral progress report to the DSMB.

Steering committee
A steering committee provided scientific direction to the study and ultimately made decisions at the operational level. The steering committee was composed of the US and in-country principal investigators of each site, the principal investigator of the DCC, and the NIMH senior scientist. It had primary responsibility for developing the protocol, facilitating the conduct of the study, and reporting the study results to the project officer, the director of the NIMH Division of Mental Disorders, Behavioral Research, and AIDS, and the DSMB. The steering committee also developed policies on data sharing and on access to data and materials subject to NIMH review. The steering committee met on a regular basis to ensure that the Trial proceeded in a timely, systematic, and orderly fashion. The steering committee established workgroups to consider such topics as adoption/adaptation of the intervention, assessment measures, biological outcomes, ethnography, data collection and analysis, and protecting human respondents and ethical responsibility. Publications were written and authored according to procedures specified in the protocol and approved by the steering committee. The steering committee, working with the DCC, prepared reports for submission to the project officer, the director of the NIMH Division of Mental Disorders, Behavioral Research, and AIDS, and the DSMB.

Data and Safety Monitoring Board
The director of the NIMH Division of Mental Disorders, Behavioral Research, and AIDS and the project officer established a DSMB to serve as an independent and external board providing expert consultation to NIMH. The DSMB assisted NIMH in reviewing the final trial protocol and recommended modifications during the conduct of the study in order to meet scientific objectives. In addition, the DSMB monitored progress on the data and technical aspects and assisted the NIMH project officer in dealing with operational aspects of the study. Finally, the DSMB monitored safety issues related to the Trial.

References


Selection of populations represented in the NIMH Collaborative HIV/STD Prevention Trial

NIMH Collaborative HIV/STD Prevention Trial Group*

**Objective:** To identify venues with vulnerable populations suitable for testing the community popular opinion leader intervention in each of the five countries (China, India, Peru, Russia, and Zimbabwe) participating in the National Institute of Mental Health (NIMH) Collaborative HIV/STD Prevention Trial.

**Design:** HIV epidemiology and vulnerable populations differ considerably across the countries. Therefore, different community populations were targeted in the five countries.

**Methods:** Venues and populations were chosen on the basis of specific selection criteria (investigated during the Trial’s ethnographic research phase): the willingness of stakeholders and gatekeepers of the venues to cooperate; geographical boundaries defining each venue; population stability within venues; the independence of venues and non-overlap of population members across multiple venues; population size within each venue; social interaction opportunities; and either a high level of sexual risk behavior or a high prevalence of sexually transmitted diseases (STDs) or HIV.

**Results:** Venues and populations selected were food market stall owners and workers in China, male patrons of wine shops and at-risk women congregating near the shops in India, young men and women in social gathering points in neighborhoods in Peru, trade and vocational school dormitory residents in Russia, and people congregating in growth points in Zimbabwe.

**Conclusion:** Although the target populations differed across countries, they shared in common high behavioral or biological risk at baseline and suitability for a randomized trial of a community-level HIV/STD prevention behavioral intervention.

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Keywords: behavioral interventions, developing nations, epidemiological methods, epidemiology, intervention studies, risk factors, sexual behavior

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**Introduction**

Conduct of the National Institute of Mental Health (NIMH) Collaborative HIV/STD Prevention Trial (hereafter, the Trial) required the identification of vulnerable populations in each of the five countries (China, India, Peru, Russia, and Zimbabwe) represented in the Trial. HIV epidemiology differs considerably across the countries. Vulnerable populations also differ, and an objective of the trial was to determine the applicability of the community popular opinion leader (C-POL) intervention model across varied populations and cultures. For these reasons, different community populations were targeted in the five countries. The purpose of this article is to describe these populations, provide the rationale for the selection of each, and describe the community venues in which population members were assessed and intervention activities were conducted.

The target population selection process required each country site to identify at least 20 venues with similar populations, each of which would be randomly assigned to the experimental or comparison condition in the main outcome Trial. Venues were defined as geographically discrete places in which members of the site’s target population live or extensively socialize. The nature of the C-POL intervention, the Trial’s design, and the evaluation approach planned for the Trial required that venues be chosen with attention to a number of selection criteria. These criteria, which were the subject of investigation during the Trial’s formative ethnographic research, included the following:

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* See Appendix B for members of the NIMH Collaborative HIV/STD Prevention Trial Group.
Feasibility reflected the willingness of stakeholders and gatekeepers of the venues to cooperate with the research team in the conduct of assessment and intervention activities in the venue. These individuals included managers or owners of commercial venues, local officials, community leaders, and others whose cooperation was essential.

Boundaries were identified so that each venue became a geographically definable place. At some sites, a venue was a physical structure in which population members lived (Russia’s dormitories), drank alcohol and socialized (India’s wine shops), or worked (China’s food markets). At other sites, a venue was defined as a discrete, compact neighborhood setting, such as Peru’s barrios or Zimbabwe’s growth points, rather than a single building.

Stability of population members present within a venue was sought. As a community-level intervention that rests on the premise that population members know one another and must be present regularly in a venue to be adequately exposed to the ongoing intervention, site researchers identified venues characterized by stable, non-transient populations. Under ideal circumstances, a high proportion of the same people would be seen regularly in the venue during multiple observation periods. Such stability would be critical for successful long-term study cohort maintenance and follow-up. At all sites and venues, inclusion criteria for participants in the Trial assessment cohort thus required that prospective participants report plans to remain present for at least the next year.

Independence of venues and non-overlap of population members across multiple venues was sought to minimize contamination across experimental conditions after randomization. To the greatest extent possible, site researchers selected venues that had populations that did not socialize or interact extensively with individuals from other venues so as to lessen the likelihood of ‘cross contamination’ among population members in intervention and comparison venues.

Population size within a venue was an additional consideration. If venues were too large, it would be difficult to ensure adequate and sustained population member exposure to the intervention. Because the C-POL intervention model requires that at least 15% of population members be trained to deliver prevention messages, it was necessary to estimate the size of the population present in each venue to determine how many C-POLs would need to be trained. In general, sites attempted to select venues with estimated population sizes of between 150 and 500 individuals.

Social interaction opportunities within or near the venue were needed so that C-POLs could communicate HIV prevention messages to others in the venue during the course of everyday conversations. Most sites’ venues were social and had naturally occurring opportunities for conversation between C-POLs and others. In cases in which social interaction opportunities were limited, research staff stimulated opportunities by staging events that created social interactions between C-POLs and other population members in or near the venues.

A high level of sexual risk behavior or a high prevalence of sexually transmitted disease (STD)/HIV among individuals present in study venues was essential both to justify the need for intervention and to ensure that baseline risk indicators would be great enough for the Trial to detect changes in behavior or STD incidence after the intervention. Although potential venues were initially selected because of expected behavioral or disease risk, each site performed initial epidemiological studies in the planned venues to verify the presence of high levels of sexual risk behavior, high STD prevalence, or both. As we will discuss shortly in more detail, these epidemiological studies confirmed sufficient risk in the planned venues chosen by some country sites but not in others. In the latter situations, new, higher-risk population segments and venues were identified for the main Trial.

The process of target population identification and venue selection required extensive fieldwork, ethnography, and preliminary epidemiological research to identify relevant vulnerable populations in each country and select venues appropriate for the design and methods followed in the Trial. Individuals within a venue were excluded from participation if they could not give informed consent (e.g. were intoxicated) or if they had a permanent disability (e.g. deafness, serious mental illness, mental retardation). Site-specific inclusion and exclusion criteria are given within the description of each site’s target population.

In world regions with high HIV prevalence, high disease incidence and a high threat of HIV/AIDS, multiple community populations are vulnerable and could have been appropriately selected as Trial populations. At each country site, consideration was given early in the Trial to varied target populations, and epidemiological/formative studies were undertaken with multiple population segments at most sites. The final selection of a site’s target population was determined by evidence of its behavioral or biological risk and also by study design, venue characteristics, feasibility, population access, and other considerations. The population selected in a country was not the only one vulnerable to HIV/AIDS, and others might also have been chosen. The selection of five varied target populations in five different countries is a strength of the Trial design.

The following sections separately describe venue selection in each of the participating countries. The section for each country first describes the country’s ultimate target population, then describes the HIV epidemiology and
rationale for the target population selected as well as alternative populations considered but eliminated. Each section describes the rationale for the study venues and the initial epidemiological explorations that supported venue selection in that country.

China site study population

Description of the China site target population
In China, food market workers in Fuzhou were identified as an appropriate target population because they had the following characteristics: (i) a sufficient base rate of STD on the basis of the results of anonymous risk assessments; (ii) a relatively stable population that allowed for follow-up over an extended period of time; (iii) a sufficient number of venues of manageable size; (iv) stable social groups; (v) support of local gatekeepers and stakeholders for the intervention; (vi) organizational capacity in the local health department to mount the intervention; (vii) similar demographic profiles across potential venues; and (viii) sufficient distance separation between the venues to minimize contamination. Individuals 18–49 years of age who worked in a selected market were eligible for participation in the assessment cohort. Individuals were excluded if they reported having no sexual activity in the previous 6 months and if biological test results were also negative for STD and HIV at the baseline assessment.

HIV epidemiology in China and rationale for target population selection
Over the past 10 years, the incidence of STD and HIV infections in China has increased dramatically. The number of new STD reported in China increased from 13 in 1977 to over 460,000 in 1997 [1]. In 1997, the rate of reported STD increased 16% over the previous year, with further increases of 37% in 1998 and 42% in 1999 [2]. Simultaneously, HIV was identified in each of China’s 31 provinces [3], with estimates of at least one million individuals infected [4] when target population selection began.

The HIV epidemic in China affects different populations in different regions and through different modes of transmission. In central China, HIV outbreaks have primarily been among former plasma donors. In southwest China, the epidemic is mainly driven by injection drug use. On the eastern coast of China (including Fujian Province), the major mode of transmission is heterosexual intercourse, which accounts for more than 80% of total reported HIV infections. Therefore, Fuzhou, the capital city of Fujian Province, was selected as the China study site.

Ethnographic data were collected to identify the specific population at risk of STD that could be targeted with the intervention, and to determine how the intervention should be tailored for the target population and venues. Ethnographic methods used included participant observation, focus groups, interviews, and social mapping. Interviews with Chinese food market managers and a few market employees suggested that market workers might have high-risk sexual behaviors. Additional ethnographic data supported the applicability of the C-POL model in this population [5]. Moreover, a self-administered anonymous risk assessment questionnaire was implemented with 180 market employees during initial ethnographic studies. Sexual risk behaviors were high among market workers when sexual risk was defined as having multiple sexual partners in the past year.

Description of and rationale for study venues
The existing research literature in China identified five high-risk groups for HIV/STD: (i) sex workers and their clients [6,7]; (ii) injection drug users (IDU) and their sexual partners [8,9]; (iii) men who have sex with men (MSM) [10]; (iv) STD patients and their spouses [11]; and (v) migrants [12]. Each of these populations was investigated but eventually eliminated for a variety of reasons. Sex workers are very mobile, and it would not have been feasible to track a cohort over time. IDU engage in an illegal activity; identifying them as a high-risk population and tracking them over time in a highly visible study would be difficult and might result in incarceration and further stigmatization. MSM are not socially accepted in China; potential stigmatization would reduce the willingness to be identified and included in studies, particularly a longitudinal study. Individuals seeking treatment at STD clinics are also highly stigmatized; fewer than half of STD patients in China go to STD clinics [13,14]. Previous research suggests that no more than 50% of this population could be assessed and engaged to participate in the intervention, limiting the external validity of the sample. Migrants are at very high risk but are also highly mobile, preventing long-term tracking.

After examining and eliminating these five potential risk groups, the collaborative investigators conducted a series of interviews and focus groups with key informants that included public health officials, health education specialists, and HIV prevention researchers. These interviews suggested that food markets would satisfy the selection criteria for study venues. Food market workers in China are often stable migrants who live in the city on and off throughout their lives. Markets typically have 50–150 stalls, with a total of 100–300 stall owners and employees. Social activities for market workers usually center within a few blocks of the market because market workers usually live close by and socialize within the area. Maps have shown that karaoke bars and beauty parlors are often located near the markets. Fuzhou has approximately 150 food markets.

Initial epidemiological study findings that supported venue selection
The impression that food markets would be appropriate venues was confirmed during the epidemiological study.
when 81 out of 739 male (11.0%) and 194 out of 789 female (24.6%) market stall owners or employees had at least one of the following STDs on biological testing: chlamydia, gonorrhea, HIV, herpes simplex virus type 2 (HSV-2), syphilis, or trichomonas. The higher STD prevalence among women than men was because of greater chlamydia rates and because only women’s vaginal swabs were cultured for trichomonas. Although other groups from various geographical areas were considered, the risk characteristics of food market workers and the feasibility of food markets as study venues thus led to their selection as the China site population.

India site study population

Description of the India site target population

The India site target population was patrons of wine shops in Chennai, India, and the high-risk women who frequent the area near them. Wine shops serve mostly beer and distilled spirits of both local and international origin. A wine shop is usually a closed space approximately 28–56 square meters in size. In addition to selling liquor on a take-out basis, the shops cater to clients who want to sit down, order food, and drink. Seating areas are usually inside the wine shop or adjacent to it, and serve as a place of conversation and gathering. Wine shops are staffed by wine shop sellers (who sell liquor and receive cash) and by bar boys and bar help (who help serve food and snacks).

Wine shops are patronized primarily by men who may or may not be from nearby slum communities. Men commonly go with friends to a familiar wine shop where they drink and socialize in the attached bar. Women seldom drink in wine shops; they usually send a male friend to purchase liquor that they drink in private places such as homes. High-risk women, however, frequently meet men outside the wine shops. Typically, a small group of women will be found near a small cluster of wine shops. It is thus possible to link a group of women to a cluster of wine shops. As these women tend to frequent an area where they are known and know others, the likelihood of one of them meeting men from wine shops outside of a specific cluster is very low. A cluster of wine shops defined a venue for the Trial. Patrons aged 18–40 years who frequented the selected wine shops at least four times per week and the high-risk women associated with the cluster of wine shops were recruited to participate in the assessment cohort for the Trial.

HIV epidemiology in India and rationale for target population selection

The HIV epidemic is growing in India. Although HIV prevalence is less than 1% nationwide, India has a population of over one billion and the largest number of individuals living with HIV/AIDS outside of Africa. In India, HIV transmission is primarily through heterosexual intercourse. Studies suggest that intervening at the community level and targeting high-risk behaviors such as multiple sex partners and sex with sex workers is an important priority for HIV prevention [15].

An emerging factor of interest in HIV transmission is the role of alcohol use. Studies exploring the association between alcohol use and sexual risk, primarily conducted in the United States and other developed countries, have yielded mixed results. Some research on alcohol use and sexual risk behavior has been conducted in India. Early reports of the co-existence of alcohol use and risky sexual behaviors have, however, spurred calls for more research into the purported association. For example, 15.9% of truck drivers surveyed in northern India were HIV positive, whereas 60% reported alcohol consumption [16]. Evidence of alcohol dependency also exists among female sex workers; 81% of sex workers surveyed in Kolkata city in eastern India reported being dependent on alcohol [17]. Data from an alcohol rehabilitation center in south India suggest that over 70% of HIV-positive patients reportedly acquired HIV while under the influence of alcohol [18].

Description of and rationale for study venues

Four potential types of venues were initially explored for the Trial in India, industrial units, lodging houses called ‘mansions’, construction workers, and low-income public housing units called ‘slums’. Of these, only the slums appeared to meet all of the venue selection criteria. Site researchers were able to secure the permission of key community gatekeepers, which made the slums feasible venues. Preliminary ethnographic studies suggested high levels of sexual risk and other behaviors such as alcohol use and intimate partner violence that might increase an individual’s vulnerability to contracting HIV. Slum communities were also relatively stable. Most residents had lived there for a long time and anticipated living there through the time of the Trial. Finally, participation rates in the slums would be high because community stakeholders were keen to participate in the study. Upward of 700 slums existed in Chennai; therefore, it was possible to select the required number of slums in the size range specified by the Trial. As explained below, however, epidemiological study findings led the research team later to narrow the target population only to members of the slum population who frequented wine shops and the high-risk women near those shops.

Initial epidemiological study findings that supported venue selection

India site researchers first considered defining venues as entire slums, and conducted an epidemiological study of 1540 randomly selected slum residents to assess behavioral risk and the prevalence of HIV and other selected STDs. Only 0.7% of participants were HIV positive, and the frequency of multiple sex partnerships and other risk
behaviors was low. The prevalence of STD, including HIV, was under 10% in eight of 28 slum communities surveyed. On the other hand, over 20% of participants tested positive for an STD in seven communities. In the light of this evidence, the research team examined more closely the 10 slums with the highest STD rates. Ethnographic studies revealed that alcohol use was high in those venues, and that these slums were proximate to wine shops or alcohol outlets, places where sexual groups and alcohol users seemed to converge geographically. To test the effects of the intervention, the researchers selected 24 clusters of wine shops that conformed to the venue identification criteria. Each had four to five wine shops. A second epidemiological study of 1358 wine shop patrons was conducted. The findings revealed a high HIV prevalence (3.0%). Seventy-six per cent of wine shop patrons reported unprotected sex, and 43% of men reported that their most recent sexual partner was a female sex worker. These data, supported by in-depth ethnography findings, suggested that clusters of wine shops were appropriate venues for the Trial.

Peru site study population

Description of the Peru site target population
A barrio in Peru is a neighborhood with boundaries known to all inhabitants. The Trial venues in Peru were defined as sites composed of people within a lower socioeconomic barrio belonging to the following three subpopulations:

*Esquines*: young men who are permanently or primarily unemployed, who generally are not in school, who usually drink large amounts of alcohol at least once a week, who often use drugs (mainly cocaine paste and marijuana), and who have sex with girlfriends, with loose girls (*movidas*), and often (in exchange for compensation) with men seen as gay or transvestites. They represent 70% of Peru site participants.

*Movidas*: young women who are open to, and usually compensated for, having sex with men in their barrio and sometimes with men from outside the barrio. Most *movidas* are single mothers and most drink alcohol. They represent 10% of the site’s participants.

Homosexuals: men who are self-identified and locally regarded as gay or homosexual, including transvestites. These men often work as hairdressers or commercial sex workers in the barrio. They frequently offer young, unemployed men compensation, including free hair cuts, drinks, money, or presents, for having sex with them. They represent 20% of participants.

Within each venue, a cluster of two to four microvenues were identified. Microvenues are well-defined spaces, such as outdoor sports fields, hair salons, and cantinas, bars and *chicheriros*, where liquor is sold and people drink large amounts of alcohol. These are settings in which there are multiple opportunities for conversations and where people in the three subpopulations initiate risky behavior.

Eligible members of the assessment cohort in each venue included approximately 200 individuals 18–40 years of age who attended at least one microvenue in a venue at least twice a week and who lived within 30 min walking distance of the barrio. Individuals who reported that they had not engaged in sexual activity within the 6 months before the baseline were excluded.

HIV epidemiology in Peru and rationale for target population selection
The HIV/AIDS epidemic in Peru probably began in the early 1980s and evolved through the early 1990s, reaching a relatively stable level in the mid 1990s. The first cases of HIV infection occurred in MSM, and the epidemic became concentrated in that group early, reaching a prevalence of over 10%. The expansion of the epidemic to women resulted in a shift in the male:female ratio among reported AIDS cases from 18:1 in the mid-1980s to 3:1 in the mid-1990s. The overall HIV prevalence in male and female adults in urban centers has remained below 0.5%.

In a country with a high prevalence of bisexual behavior among men, HIV prevalence of over 5% in MSM and under 1% in all other groups can be explained by the rapid expansion of HIV within urban MSM sexual groups, which include female partners of MSM and their children. Because these women were for the most part monogamous and remained so, the epidemic did not generalize and remains largely driven by sex between men.

Description of and rationale for study venues
The Peru site first planned to work with young people from the general population in selected barrios. Barrios are home to local and community organizations and to an intense street life. People know each other and are related through diverse social groups. As a result of limited behavioral and biological risk found in an initial epidemiological study of a household probability sample of that population, site researchers used the ethnographic findings to identify three interrelated subpopulations in the same venues, and conducted a new epidemiological study that showed much higher behavioral and biological risks among these subpopulations.

Within barrios, researchers identified places where young people congregate, including hair salons, bars, street corners, pool halls, sports fields, and parks. Transvestites and self-identified gay men congregate around the volleyball courts and hair salons, whereas young
unemployed men and women congregate around the street corners, football fields, and at pool halls. All of these population segments interact in cantinas and hair salons. Young unemployed men go to street corners in the barrio to talk or play with their friends or be with their girlfriends, and go to cantinas or pool halls to see other friends and drink. They also go to hair salons for haircuts, and sometimes have sex with the male owner to pay for the haircut or to obtain money. Risky sexual interactions are common in these barrio subpopulations.

Initial epidemiological study findings that supported venue selection
The population targeted in the first epidemiological study of the general barrio population and the later epidemiological study of subpopulations in the high-risk venues (esquineros, movidas, homosexuals) subsequently chosen for the Trial differed in their sociodemographic profiles, the frequency of unprotected, non-spousal sex, and the prevalence of STD. Compared with the general population survey, participants from the high-risk subpopulations were predominantly male (90.9 versus 41.2%), were less likely to have finished high school (51.5 versus 76.6%), and were less likely to be in stable relationships (25.2 versus 35.5%; all $P < 0.001$). Their rate of unprotected sex outside of primary relationships in the previous 3 months was disproportionately higher than in the general barrio population (57.8 versus 2.4%; prevalence ratio 24.14; $P < 0.001$). They also had higher rates of HIV (1.5 versus 0.1%), HSV-2 (29.9 versus 14.8%) and syphilis (5.5 versus 0.8%; all $P < 0.001$). Members of the three high-risk subpopulations in the barrios were thus selected as the target population for the intervention.

Russia site study population
Description of the Russia site target population
The Trial’s Russia site is St Petersburg, the country’s second largest city, with approximately 5 million residents. The target population in St Petersburg consists of young adult men and women between 18 and 30 years of age, most unmarried, who attend vocational and technical training schools and institutes located throughout the city. Young people enter these 5-year training programmes after high school.

Each vocational or technical school operates a dormitory for the young people who attend its training programme. Dormitories provide housing for 140–800 young adults, many coming from outside the St Petersburg area. Most dormitories house both men and women. The Russia site study population consisted of residents of 24 vocational and trade school dormitories widely dispersed throughout the city. The Trial enrolled between 52 and 120 residents from each dormitory venue ($n = 2212$ participants) as the study cohort, with nearly equal numbers of men and women. Study participants were randomly selected from among the entire population of young people living in each dormitory, but excluded individuals in their final school year who would soon leave the dormitories and be unavailable for follow-up.

HIV epidemiology in Russia and rationale for target population selection
The HIV epidemic appeared later in Russia than in many other world areas, but has emerged quickly and grown explosively. During Soviet-era Russia, very few HIV infections were diagnosed; even as late as 1995, a cumulative total of fewer than 1100 cases had been detected in the country [19]. Beginning in 1996, the number of new infections recorded in Russia began doubling each year, and the epidemic accelerated in its pace. By 2004, approximately 300 000 infections were officially recorded [20], but the number of officially recorded cases is believed to underestimate the true number substantially. Most Russian and international public health authorities estimate the actual number of HIV infections to be between one and two million [21,22], most contracted during the past decade, making Russia’s HIV incidence rate one of the highest in the world.

Injection drug use, almost unknown during the Soviet era, became extremely common among young people after the breakup of socialist controls, and the large majority of HIV infections in Russia and other post-Soviet countries have been diagnosed among young IDU. Russia’s difficult cultural transitions have, however, resulted in the liberalization of sexual behavior values among young people, declining age at first sex, acceptance of multiple sexual partners, growing levels of prostitution, and the emergence of a wide-scale STD epidemic that has produced sharp increases in the rates of syphilis, gonorrhea, and other STDs among young people [23,24]. These enabling factors together have set the stage for efficient sexual HIV transmission, and the shift from a drug-related HIV epidemic to a sexual transmission epidemic has begun. Recent surveillance data indicate a decline in the percentage of new HIV infections attributable to injection drug use and an increase in cases attributable to sexual transmission. Some data suggest that half of all new HIV infections now occurring in Russia are the result of sexual exposure [25].

Several studies have examined patterns of sexual HIV risk behaviors in community samples of adolescents and young adults in Russia, especially in the major population centers of St Petersburg and Moscow. These studies have established that a high proportion of young people are sexually active, that multiple concurrent sexual partners or brief serial relationships are common, and that rates of consistent condom use are low [26,27]. These studies indicate that HIV/AIDS is widely perceived by the public to be a threat primarily to drug users and gay men,
knowledge about correct condom use is still limited, and condoms are seen as protection primarily against pregnancy rather than HIV/STD. Earlier research carried out specifically with vocational and trade school students established a high prevalence of sexual risk behavior [28]. Stopping the emerging sexual HIV epidemic in Russia requires that interventions to reduce high-risk behavior practices be directed towards sexually active young adults.

**Description of and rationale for study venues**

Vocational and trade school dormitories constitute urban environments appropriate for reaching a community population of young, at-risk adults. The dormitories are drab, overcrowded, and in disrepair, usually with large numbers of young people crowded together in small sleeping rooms. Most dormitories are surrounded by storefront cafes, drinking clubs, and socializing areas. Heavy alcohol use, marijuana use, and opiate smoking are widespread in the dormitories, although injection drug use is less common.

Dormitories constitute venues well-suited for a research trial of the C-POL intervention. The dormitories are residential and also social communities in which students know one another well. Young people who live in a given dormitory extensively socialize with others residing in the same building in common social areas at the dormitory and in adjacent ‘hangout’ areas. Because dormitory residents attend the same school and live and socialize together, popular opinion leaders influential with others could be readily identified. The dormitory populations are stable and non-transient. With the exception of the outmigration of young people finishing their final year and the in-immigration of new first-year students, population turnover in a given dormitory is minimal. Because of the compactness of the venues, the resident population size was known, the proportion of C-POLs to be trained could be accurately determined, and high intervention exposure could be ensured.

**Initial epidemiological study findings that supported venue selection**

Before finalizing the Russia site’s selection of 24 vocational or trade school dormitories as venues for the Trial, initial ethnographic studies were conducted in two other similar dormitories that served as locations for formative phase studies. In more extensive epidemiological research, risk behavior interviews and STD specimen collection were carried out with a sample of 1000 dormitory residents in 20 dormitories, equally divided between men and women, 90% unmarried, and averaging 20.2 years of age. Overall, 91% of students (96% of men and 87% of women) were sexually experienced, with a median of three lifetime sexual partners reported. At interview, 88% reported being sexually active during the past year, and 75% were sexually active during the past 3 months. The median number of sexual partners in the past year and in the past 3 months was one, although 47% reported two or more partners in the past year and 21% reported two or more partners in the past 3 months. Among the young people who had at least one sexual partner in the past 3 months, a median of 12 unprotected intercourse acts was reported, and 37% of students reported never using a condom during this period. On most indices related to sex with casual or non-spousal partners, Russia site men reported risk behaviors nearly twice as high as women. Biospecimen testing revealed that approximately 15% of students had an STD, predominantly chlamydia (8%) and HSV-2 (6.2%), with 1% or fewer diagnosed with syphilis, gonorrhea, HIV, or trichomonas. These data verified that the Russia dormitory resident sample is high in behavioral risk, and that vocational and trade school dormitories were appropriate venues for the Trial.

**Zimbabwe site study population**

**Description of the Zimbabwe site target population**

The site researchers chose to implement the C-POL intervention in ‘growth points’ in Zimbabwe. Growth points are designated sites in rural areas selected for economic and infrastructure development by the government. These areas are surrounded by villages and act as social and economic magnets for the surrounding community.

Individuals 18–30 years of age who patronized a growth point microvenues (e.g. a selected bottle store or market) at least twice a week were eligible to participate in the assessment cohort. Prospective participants were excluded if they had lived in the selected growth point for less than 2 years or if they lived in the area fewer than 9 out of 12 months of a year.

**HIV epidemiology in Zimbabwe and rationale for target population selection**

Zimbabwe is a landlocked country in southern Africa, bordered by Botswana on the west, South Africa on the south, Mozambique on the east, and Zambia on the north. With a population of approximately 11.6 million individuals [29], an estimated 1.4 million individuals in Zimbabwe are currently living with HIV/AIDS [30]. Approximately 58% of the population resides in rural areas, 32% in urban areas, and 10% in areas that are not classified as strictly urban or rural. Women constitute 51% of the population [29]. The first AIDS case was identified in Zimbabwe in 1985. AIDS case surveillance began in 1987, and sentinel surveillance of pregnant women receiving antenatal care services at public clinics has been ongoing since 1990. In 2005, the Zimbabwean Ministry of Health and Child Welfare (MOHCW) reported that the estimated HIV prevalence among adults 15–49 years of age in Zimbabwe was 20.1%, down from the 24.6% estimate in 2003 [30].
Zimbabwe has one of the highest adult HIV prevalence rates in the world, approximately 33.7% in 2001 [31,32]. Antenatal clinic sentinel survey results showed that HIV prevalence among pregnant women in Zimbabwe increased from approximately 25% in 1997 to 35% in 1999. Overall prevalence rates were 33% in 2000 and 27% in 2001 [33]. Modeling based on antenatal clinic surveillance data, reported by the MOHCW in 2003, estimated prevalence rates of approximately 25% in the population of 15–49 year olds [34]. Although these HIV estimates are based on antenatal clinic surveillance data, one nationally representative survey, the Young Adult Survey (which included HIV testing) was conducted in 2001–2002 with a randomly selected sample of 15–29 year olds by the MOHCW and the US Centers for Disease Control and Prevention Global AIDS Programme Zimbabwe office. That survey showed prevalence rates of 22% among 15–29 year old women and 10% among 15–29 year old men [35]. The country is experiencing a generalized HIV epidemic, with women having approximately twice the risk of men [35]. Mortality is high [36]. An estimated 3252 men, women, and children die each week from AIDS in Zimbabwe [30].

Although Zimbabwe has a generalized AIDS epidemic, Zimbabwean MOHCW data show that rates vary in different locales. In 2001, antenatal clinic surveillance data found that urban areas had an approximate prevalence of 30% compared with 20% prevalence in rural areas. Areas considered neither urban nor rural, however, such as commercial farming areas and growth points, had the highest estimated HIV prevalence, approximately 35% [30]. The Zimbabwean MOHCW and the National AIDS Council thus recommended those areas for intensified HIV prevention interventions.

**Description of and rationale for study venues**

Growth points are rural centers designated by the government in 1985 to facilitate commercial and industrial development. With such a designation, these centers received public investments in electrification, telephone installation, construction of water supply dams and waste disposal systems, administrative facilities, feeder roads, and banking facilities. The growth points consist of small commercial areas of shops and markets, and entertainment and other businesses, such as bottle stores (places that sell alcohol and provide centers of leisure, especially for men), beer halls, and night clubs. Small residential areas may be present at the growth points, and secondary schools and health centers are sometimes associated with them. Growth points have populations ranging from 2500 to 5000 people.

The growth points represent hubs of economic and population exchange because they usually have good transport connections and provide trading opportunities. This confluence of population and disposable income, against a background of rural poverty and limited job opportunities, presents a situation of high sexual risk. The preparatory ethnographic studies confirmed that drinking alcohol was a popular pastime for men (and some women), and that drinking took place in small groups of friends and relatives in bottle stores and beer halls. A distinguishing feature of growth points was the existence of a large number of bottle stores, some of which serve as night clubs later in the evenings. Sexual relations, including the exchange of sex for goods and money, often took place in association with drinking and night clubbing. Although men tended to socialize around bottle stores, socialization for women was more diffuse, often taking place in churches. The clustering of social groups for women was also found in markets and general dealers stores [37–39]. In some cases, market women by day sold sex by night. We thus selected growth points because they represented a high-risk population with distinct segments (men, women, and sex workers) and identifiable social groups in a relatively small population.

**Initial epidemiological study findings that supported venue selection**

An initial epidemiological study randomly selected residents of rural households in villages around 32 growth points to determine HIV/STD prevalence. It showed that overall HIV prevalence among randomly selected 16–30 year olds was 26%, over twice as high in women (33.9%) as in men (14.8%). Despite the high HIV rates, the prevalence of some STDs was relatively low, probably because of an STD control programme launched in the 1990s and based on a syndromic management approach and the provision of prenatal care services. Gonorrhea and chlamydia, previously relatively common infections, had prevalence rates less than 5%, and syphilis less than 2% [40,41]. HSV-2 prevalence was, however, approximately 45% [42], much greater among women (58.6%) than men (26.6%). Household residents’ reported number of sexual partners was relatively low (median one in the past year, with 22% reporting two or more partners), indicating a population whose recent behavior was not particularly risky against the background of a generalized HIV epidemic.

Because general residents of villages near growth points did not exhibit high current behavioral risk, and because the social groups and links to places of high risk were not clear, site researchers decided to focus on populations present in the specific microvenues of bottle stores, general dealers stores, and markets with growth points. These microvenues were selected through rapid ethnographic methods, which then confirmed their high risk. Another epidemiological study to assess HIV/STD prevalence was not performed with microvenues because sufficient biological risk existed in the village community and MOHCW data showed that growth points had among the highest HIV prevalence rates.

In conclusion, HIV epidemiology and the populations most imminently threatened vary throughout the world.
The objective of the Trial is to evaluate the C-POL intervention with different but high-risk populations at each country site. Although the target populations included in the Trial differed across countries, each was selected on the basis of a common set of criteria related to high behavioral or biological risk at baseline, venues for accessing high-risk community populations, and the suitability of these venues for a randomized trial of a community-level HIV/STD prevention intervention.

References


Challenges and processes of selecting outcome measures for the NIMH Collaborative HIV/STD Prevention Trial

NIMH Collaborative HIV/STD Prevention Trial Group*

Objective: To review the challenges of designing behavioral and biological outcome measures for the multinational NIMH Collaborative HIV/STD Prevention Trial and provide the rationale for selecting these measures.

Design: Although many different evidence-based prevention programmes have been developed, few have been evaluated in different countries, cultures, and populations. One issue in evaluating the generalized efficacy of any prevention approach is to identify a set of common outcome measures useful across diverse settings and peoples. The Trial is designed to evaluate whether the community popular opinion leader intervention can be adapted cross-nationally and cross-culturally for different populations and still retain its efficacy.

Methods: Literature reviews, investigator experience, ethnographic study, pilot studies, and epidemiological studies were used to select the endpoints for the Trial.

Results and conclusion: Both biological and behavioral data will be obtained at baseline and 12 and 24 months post-baseline. Communities that receive the intervention will be compared with matched control communities on two primary outcomes: (i) a change in self-reported unprotected sexual acts with non-spousal, non-live-in partners; and (ii) the incidence of sexually transmitted disease (STD), defined as a composite index of viral and bacterial STD.

Introduction

Identifying effective behavioral and social science interventions to reduce the incidence of sexually transmitted disease (STD) and HIV has taken on a new urgency in response to the global HIV pandemic. Although a number of HIV prevention programmes have been shown to be efficacious in well-defined risk populations in the United States, these programmes must be adapted to new cultures and tested before they can be implemented where they are desperately needed [1]. A significant barrier to effectively demonstrating intervention efficacy is the lack of evidence-based measures of reductions in sexual risk behaviors. In designing interventions that can be used across diverse settings, prevention researchers need to develop relevant, measurable, and common primary outcomes applicable across countries and risk populations to demonstrate to public health leaders and policymakers the success or failure of the behavioral intervention to promote behavior change and reduce the incidence of disease.

Evaluating the impact of a behavioral intervention to prevent the acquisition of STD, including HIV, requires measuring sexual risk behaviors targeted by the intervention. Because sexual risk behaviors are part of the STD acquisition causal pathway, a change in those behaviors needs to occur to decrease the subsequent acquisition of infection [2]. Collecting reliable information about sexual risk behaviors may, however, be difficult because this is a private, taboo subject. Whereas some researchers argue that self-reported behavior can provide valid and reliable outcome measures, others worry that participant self-reports do not always accurately reveal sensitive behaviors [3,4]. The measurement of sexual risk behaviors alone is thus often considered insufficient in the evaluation of interventions to prevent STD.

To impact an epidemic, an intervention needs to decrease the potential for acquisition of a disease. Whereas risky HIV-related behavior is linked to acquiring STD, the correspondence is not one-to-one [2,3]. Transmission models conceptualize the reproductive rate of an

* See Appendix B for members of the NIMH Collaborative HIV/STD Prevention Trial Group.
infectious disease as the product of three components: (i) the rate of contact between infected and susceptible individuals; (ii) the transmissibility of infection between partners; and (iii) the duration of infectiousness [5–7]. Each of these components can be influenced by behavioral factors, such as the number of sex partners in a given period, the correct use of condoms for every sex act, and the type and duration of every sex act, as well as by environmental factors, such as the extent and accessibility of population-level screenings and effective treatments.

Whether a reduction in risk behaviors results in a reduction in the incidence of infectious diseases depends on the epidemiological context in which the intervention is implemented [8]. Grassly et al. [8] proposed four indicators describing the epidemiological context that should be considered when evaluating the appropriateness of an intervention to prevent HIV infection: (i) the phase of the HIV epidemic; (ii) the co-occurrence of other STD; (iii) the mixing of the target population with other at-risk populations; and (iv) the sexual behavior of populations not targeted by the intervention. The relationship between risk behaviors and biological outcomes is thus complex, non-linear, and impacted by multiple social, cultural, and environmental factors [3,4,9,10].

The US National Institute of Mental Health (NIMH) Collaborative HIV/STD Prevention Trial (hereafter ‘the Trial’) was initiated to evaluate whether the popular opinion leader intervention [11] can be adapted in multiple countries with various vulnerable, at-risk populations and retain its efficacy. The community popular opinion leader (C-POL) intervention being evaluated in the Trial is the international adaptation of the popular opinion leader intervention, which was found to be effective in reducing behavioral risk among homosexual men, adolescents, and heterosexual women in housing developments in the United States [12–16].

The Trial is being conducted in five countries: China, India, Peru, Russia, and Zimbabwe. Using data from preliminary studies, vulnerable subpopulations were identified and targeted for the intervention in each country: food market stall owners and workers in China, male patrons of wine shops and at-risk women congregating near the shops in India, young men and women in social gathering points in neighborhoods in Peru, trade and vocational school dormitory residents in Russia, and individuals congregating in growth points in Zimbabwe. Whereas the age range of eligible participants in each country was based on the HIV/STD epidemiology in the country, all countries included a core group of young adults aged 18–30 years who are likely to be among the most sexually active and vulnerable in the population.

Given the complex dynamics between behavior and changes in HIV/STD incidence, the Trial researchers identified the need for both behavioral and biological indices to evaluate the efficacy of this intervention. Experts in behavioral interventions, STD transmission, behavioral assessment, and rapid ethnography formed workgroups that participated in designing different aspects of the Trial [see ‘Methodological overview of a five-country community-level HIV/sexually transmitted disease prevention trial’ in this issue [17]]. Intense review and debate occurred based on the results of both rapid ethnography and preliminary epidemiological studies of risky populations in each country that provided both behavioral and biological data. From this process, the two primary outcome measures for this collaborative community-randomized Trial were defined.

This paper presents the challenges and process of selecting an appropriate primary behavioral outcome and primary biological outcome for the Trial.

Defining the primary behavioral endpoint

Six principal challenges were encountered while developing a valid and reliable primary behavioral outcome: (i) the validity and reliability of self-report data; (ii) non-response to sensitive questions; (iii) interviewing strategy; (iv) recall window; (v) timing of the outcome assessment; and (vi) defining the primary behavioral outcome.

Validity and reliability of self-report data

The immediate goal of the Trial is to reduce sexual behaviors that potentially increase the risk of acquiring STD, including HIV. Of necessity, sexual behaviors must be self-reported. The validity of sexual behavior reports by individuals or aggregates of individuals depends on the willingness of the participants to respond to questions about their behavior honestly and their ability to recall specific behaviors accurately. The validity of the recorded information is influenced by many variables, including the memory of the participant, the context in which the information was elicited, the cultural mores of the social group to which the participant belongs, the level of social desirability bias, sex, the manner in which the information was obtained, and the participant’s confidence in the researchers and their staff [4]. Using a standard protocol and a common assessment modality to interview individuals of similar age across different cultures may favorably influence the comparability of self-reports across countries. The comparability of cross-cultural reporting, however, especially among countries in diverse areas of the world, may be greatly influenced by specific cultural norms. For example, in societies in which it is considered taboo to discuss sex, convincing people to reveal their sexual activities accurately is difficult. Furthermore, any disclosure of
sexual promiscuity or unacceptable practices may be unlikely unless the participant is convinced that the interview will be anonymous.

**Selection bias and non-response to sensitive questions**

The willingness of individuals to participate in behavioral studies or answer sensitive questions about private behaviors is influenced by the cultural setting in which they live. For example, in China it is considered impolite to discuss one’s sexual behavior, and any individual who does so would be considered ‘odd’ and likely be shunned by his or her peers. In other societies, such as India, it is acceptable for men to discuss their sexual activities, but it is unacceptable for women, as these discussions signal that a woman is immoral.

For these reasons, missing data may also be a problem for surveys in which sensitive information is elicited. Individuals who are willing to participate or answer specific sensitive questions may not be representative of the general population, and may include individuals who have low-risk behaviors and, thus, have less fear of disclosure. On the other hand, ‘macho’ individuals may be quite eager to participate and boast about their sexual prowess. In the trial, the wording of the consent form, the contextual statements preceding the sensitive questions, and the sensitive questions themselves were field-tested to ensure as high a response rate as possible.

**Interviewing strategy**

To increase the chance of collecting valid information about sexual behaviors, it is necessary to gain the participant’s confidence. Different interviewing methods have been used and compared to determine which strategies may best elicit sensitive information: (i) self-administration of a questionnaire; (ii) computer-assisted personal interviews (CAPI); or (iii) audio computer-assisted self-interviews (ACASI). No data had, however, been collected in these five countries on the effectiveness of these interviewing techniques. Therefore, before implementing the trial, two small pilot studies were conducted in each country to assess the feasibility and reliability of using CAPI and ACASI to administer the behavioral assessment questionnaire (see ‘The feasibility of audio computer-assisted self-interviewing in international settings’ in this issue [18]). These strategies were considered because participants do not have to be literate to respond to questions. In China, and to a lesser extent in India, self-reports of behavior appeared somewhat less reliable using ACASI compared with CAPI. Therefore, CAPI was selected for the trial in all five countries because the assessment administration must be standardized across sites.

**Recall window**

Participants who are able and willing to answer all questions honestly may nonetheless have difficulty accurately remembering activities that occurred over long, retrospective time frames. Most studies of sexual behavior attempt to use some strategy for estimating the frequency of sexual activity during a defined period in the past, introducing the possibility of recall bias. The extent of recall bias is influenced by the cognitive competence of the participant, which has been shown to be related to age, level of education, the consumption of alcohol and other drugs, and methods of eliciting the information [4]. In addition, recall ability may be affected by the frequency of the behavior and whether the activity was pleasant, unpleasant or neutral [19–21].

In a study comparing diary entries with sexual behaviors reported from interviews at one, 2, and 3 months after diary completion; recall bias was greater at 3 months compared with one month for one frequently occurring behavior, but not for other outcomes assessed [19]. Whereas long retrospective intervals (e.g. 12 months) may lead to unreliable data, low frequency behaviors may not occur during short recall windows. Three months has been suggested as a relatively reliable recall period [22]. Therefore, to limit recall bias in the Trial, participants are asked about behavior during the 3 months and 6 months before each assessment.

**Timing of outcome assessment**

Community-based interventions have been used across a range of health areas, including cardiovascular disease, HIV, and cancer, with varying results. Whereas many programmes aimed at HIV prevention appear to be effective, generally only modest effects have been seen for many studies in other programme areas. Reasons for the low impact achieved by many studies include methodological issues, such as low statistical power, the influence of naturally occurring changes in societal attitudes, and behavior that affects both control and intervention communities, smaller than anticipated effect sizes, an inadequate theoretical basis, and limitations of the intervention (e.g. insufficient dissemination throughout the community and length of the intervention) [23]. An ideal period in which change may be achieved and impact detected is not yet apparent. For example, researchers involved with the Community Intervention Trial for Smoking Cessation (COMMIT) speculated that 4 years was not enough to influence heavy smokers [24,25]. In contrast, several community-based HIV prevention studies have shown significant intervention effects on one or more outcomes after intervention periods lasting from one to 3 years [14,26,27].

On the basis of the data from these large trials and the performance of social diffusion interventions in the United States, data were collected at baseline and 12 and 24 months later to assess the behavioral and biological outcomes for the Trial.
Defining the primary behavioral outcome

During the ethnographic study conducted before beginning the Trial, qualitative interviewing supported the observation, also well supported in the literature, that sexual behavior in men and women varies substantially based on the perception of the type of partnership [28–30] [see 'Cross–site ethnographic findings that contributed to the design of the community popular opinion leader intervention in a five–country intervention study' in this issue [31] for a discussion of these differences among the Trial study populations]. Preliminary data indicated that the repertoire of behaviors was different with casual partners than with regular partners or spouses. In most of the Trial countries, women, especially married women, reported significantly fewer sex partners than men. On the basis of these ethnographic observations, we anticipated that we would not successfully change the sexual behaviors of partners within a marital relationship that had been well established for many years.

The primary behavioral outcome was established as a change in unprotected sex acts with non-spousal, non-live-in partners at 24 months. A change in condom use with non-spousal, non-live-in partners is, however, primarily a change in husbands’ behaviors, which has the potential to be reflected in the rates of STD among their wives. Whereas a secondary behavioral outcome will be the change in unprotected acts with non-spousal, non-live-in partners at 12 months, the primary behavioral outcome was defined at 24 months because of concerns that the intervention may take longer than one year to disseminate throughout the community and produce a community–wide effect.

Primary biological endpoint

Three challenges emerged while developing a valid and reliable primary biological outcome: (i) variation in STD across sites; (ii) defining incidence; and (iii) ensuring the successful treatment of STD at baseline.

Variation in sexually transmitted diseases across sites

When evaluating prevention programmes across multiple countries, it is necessary to recognize the variation in culture and demography within and between Trial populations and sites [32]. These variations can result in different risk populations and different prevalent STDs. For example, herpes simplex virus–2 (HSV–2) is the most common STD in Zimbabwe [33], and is commonly related to co-infection with trichomonas, HIV, and bacterial STD in young adults [34,35]. In China, chlamydia is one of the most prevalent STDs, and the rates of STDs are highest among middle and upper-class migrant Chinese in eastern coastal cities, such as the owners and staff in the Fuzhou markets [36–38].

Preliminary epidemiological surveys conducted before beginning the Trial [39] showed significant variations in the prevalence of specific STD across the subpopulations in the countries included (Table 1; see ‘Sexually transmitted disease and HIV prevalence and risk factors in concentrated and generalized HIV epidemic setting’ [40] in this issue for further discussion). Using data from the first epidemiological study in China, Russia, and Zimbabwe, and from the second epidemiological study in India and Peru, the percentage of HIV-positive participants in each venue in Zimbabwe was on average 26%, whereas the average was below 3% in each of the other four countries. HSV-2 was the most common STD in Zimbabwe, Peru, and India (average percentage positive 45, 30, and 24%, respectively), but prevalence was below 10% in most venues in China and Russia. For gonorrhea, chlamydia, and syphilis, the average percentage of positive participants in the venues was below 10% in all countries. Among women, the prevalence of trichomonas was highest in India, where the average percentage positive across venues was 22%.

A challenge was thus defining a primary biological outcome to which significant disease levels from all country sites could contribute. Although differences were found in the prevalence of specific STD across the

Table 1. Bacterial and viral sexually transmitted diseases reported by participants in China, India, Peru, Russia, and Zimbabwe.

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<th>China</th>
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<th>Russia</th>
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<td>Mean*</td>
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HSV-2, Herpes simplex virus type 2.

*Mean and range across venues for percentage of participants with each sexually transmitted disease from a sample of approximately 50 participants in each venue. (See ‘Selection of populations represented in the NIMH Collaborative HIV/STD Prevention Trial’ [40] in this issue for a description of venues in each country.) Data are from the first epidemiological study in China, Russia, and Zimbabwe, and from the second epidemiological study in India and Peru.
Defining incidence
In designing measures of disease incidence, the pathogenesis, treatment and transmission dynamics of each STD needs to be considered as well as the characteristics of the biological assays that define a new infection. Bacterial and protozoal STDs, such as gonorrhea, chlamydia, and trichomonas, are curable. Effective treatment reduces the period during which individuals with these diseases are infectious, while increasing the period during which they are susceptible to new infections. Syphilis can also be treated; and well-defined serological tests differentiate long-standing infection, treated or untreated, from newly acquired infection. Individuals infected with syphilis, unlike individuals infected with gonorrhea or chlamydia, may enter into a latent stage of disease 1–4 years after infection with relative immunity to re-infection and a lower risk of infecting a sex partner. Ignoring the differences in the biology of infections such as syphilis compared with diseases such as gonorrhea can lead to inaccurate assessments of the impact of a behavioral intervention [41].

In contrast, viral STDs such as HSV-2 or HIV cannot be cured, and although treatment may reduce infectiousness, both treated and untreated individuals may remain infectious and do not acquire a new infection with the same pathogen. Determining the incidence of viral infections is less problematical than for bacterial infections because the possibility of cure and re-infection is moot.

The combined biological STD endpoint provides a reliable method, adapted to the variations in disease prevalence in different countries, to identify the status (susceptible or infected) of each individual entering the Trial for each of six sexually transmitted infections (chlamydia, gonorrhea, HIV, HSV-2, syphilis and trichomonas). By repeating all of the biological measures at each study visit over 2 years, an incidence of STD may be calculated for each individual, community and country, as described in more detail below. The aggregate incidence of new STDs (percentage of new infections over time), and the comparison between intervention and comparison venues is presented as a ‘combined’ biological endpoint, less susceptible to reporting bias, and providing an accurate indication of a complex set of behaviors and interactions. Assessment of the prevalence of each infection in the target populations during the epidemiological studies before the start of the Trial contributed to estimates of the power of the Trial to measure statistically significant differences between intervention and comparison arms with regard to incident STD.

As described in the ‘Methodological overview of a five-country community level HIV/sexually transmitted disease prevention trial’ in this issue [17], an individual will be classified as a new case if they tested positive at either the 12 or 24-month follow-up for chlamydia, gonorrhea, syphilis (if negative at baseline), trichomonas (if female), HIV (if not positive for HIV at baseline), or HSV-2 (if not positive for HSV-2 at baseline). In addition, a person who tested positive for syphilis at both baseline and 24 months will be considered a new case if it can be demonstrated that the syphilis at baseline was treated, the follow-up test at 12 months was negative, and the 24-month result was positive. An individual who was positive for syphilis at baseline, 12 and 24-month follow up and who had a fourfold rapid plasma reagin titer decline from baseline to 12-month follow-up and a fourfold rapid plasma reagin titer increase from 12 to 24-month follow-up will be considered a new case. Table 2 characterizes the definition of a new case of syphilis for specific scenarios.

An individual will be classified as negative for the composite outcome if at least two-thirds of the tests used in the individual’s assessment are non-missing and all provide definitive negative results (i.e. negative or indeterminate). If there are no new positive tests and more than a third of the individual’s test results are missing, the composite variable will be set to missing.

Ensuring successful treatment of sexually transmitted diseases at baseline
Unique cultural and political factors impact healthcare-seeking behavior, the availability and acceptance of treatment, and the success of efforts to prevent re-infection and further transmission, including partner treatment or partner notification. For example, all STDs are reportable in Russia, even those discovered during conduct of a research project. Therefore, to measure a biological STD outcome in Russia it is necessary to assess the STD while concealing the identity of participants so that the research does not stigmatize an individual. The participant’s disease, but not name, may be reported as required. In contrast, people from India and China frequently seek treatment of STD at pharmacies that specialize in treatments using local herbal remedies. To assess STD reliably in India and China over time, it is necessary to ensure that participants receive treatment from healthcare providers who will treat the STD with recommended medicines. Treatment protocols were established for the Trial to increase the likelihood that
appropriate counseling and treatment were received by participants.

Treatment data are captured on a participant summary report and a symptom questionnaire. Both documents are completed at baseline and at each follow-up assessment. The Trial protocol requires that a participant summary report be completed for each participant who provides biospecimens at each visit. This report captures specific information such as whether laboratory test results were reported to the participant, the date those results were reported, and an explanation of why results were not reported if this is the case. More importantly, for participants who receive positive laboratory test results for any of the six STDs, the participant summary report indicates whether the participant received treatment, was referred for treatment to a medical facility, received education, or no action was taken.

The symptom questionnaire is administered to all participants who provide biological specimens at each assessment. The symptom questionnaire captures information regarding whether treatment for an STD was received in the past 12 months (China and Russia only), and whether the participant has experienced genital discharge, sharp/burning pain during urination, or genital sores in the past week. If the participant’s responses to the symptom questionnaire indicate that he or she has STD symptoms, free treatment or a referral for free treatment is given. Sites then record whether participants who presented with symptoms were referred for treatment or treated for an STD by project staff. The medications used for treatment are also captured on this form. During this interaction, counselors stress the importance of the participant returning for the results of the laboratory tests, even if treatment is received during the assessment. Counselors explain that many people who have an STD do not have symptoms or the symptoms reported do not identify the correct type of STD. Only by returning for test results can the participant receive an accurate diagnosis and additional treatment or referral, if necessary.

Data collected from the participant summary report and the symptom questionnaire, in conjunction with laboratory results, will determine if participants with positive laboratory results received treatment or referral for the correct disease(s). Review of treatment received, endpoints, and laboratory testing will help differentiate incident and prevalent cases of bacterial and protozoal infections.

Discussion

Many researchers have strong biases about the utility of behavioral versus biological endpoints in assessing the impact of interventions on public health [42]. Identifying a set of outcome measures that can be used across countries and with different populations is a complex issue not easily resolved. A reduction in STD incidence is potentially a valid and reliable endpoint that can be applied across a variety of settings. Even STD endpoints are influenced by social and cultural factors, such as sexual norms, healthcare-seeking behavior, knowledge about modes of transmission and the correct use of condoms, and the availability of treatment, and the use of individual STD endpoints may only be feasible in high-prevalence and incidence settings.

Behavioral outcomes are the immediate target of behavioral interventions, and may be used in low-prevalence countries. Behavioral measures, however, do not always predict incident STD, and may be subject to a different set of cultural influences causing bias. In addition, behavioral measures may not enable policymakers and those evaluating interventions to estimate the direct impacts of the interventions on HIV/STD incidence. Essentially, without knowing how many infections can be prevented, knowing the number of individuals necessary to treat in order to avert a certain number of infections, or having the ability to compare the impact of a variety of prevention interventions, studies of interventions without biological outcomes are of limited merit to decision-makers.
In addition, mathematical modeling of the epidemic can prove a powerful tool to overcome this problem by assessing both where the treatment and prevention funds should be spent and what kind of prevention programme designs will potentially avert the most cases of new infections. Multiple mathematical models of the dynamics of the HIV epidemic can be used in planning and designing HIV/STD prevention programmes for emerging epidemics in developing countries. For example, the NIMH/ASIST (AIDS Strategic Interventions Simulation Tool) was developed specifically to assess the impact of different behavioral intervention strategies on the incidence of HIV and STD [43].

In conclusion, a challenge in implementing the Trial was to develop behavioral and biological primary outcome measures that can be used to evaluate the effectiveness of the C-POL intervention implemented in diverse populations and settings in five countries. Researchers wanted to evaluate both the immediate outcome of the intervention on sexual behavior and provide a measure of impact that is biologically relevant and relatively resistant to self-disclosure bias. Accordingly, both behavioral and biological endpoints were defined: (i) a change in self-reported unprotected sex acts with non-spousal, non-live-in partners during the 3 months before the 24-month assessment measured as a change from baseline; and (ii) the incidence of STD defined as any new case of chlamydia, gonorrhea, syphilis, trichomonas (women), HSV-2, or HIV at 12 or 24 months. To evaluate the C-POL intervention, a behavioral outcome was thus developed that accounts for the relationship between sexual behavior and the type of partner by targeting the partnerships in which change is thought to be most likely, reducing the potential for recall bias by limiting the recall period to 3 months, and allowing 2 years for the effects of the intervention to be measured. Similarly, a combined biological endpoint was developed that can accommodate the variation in prevalence of individual STD across countries.

Because these measures provide different information, both behavioral and biological endpoints should be considered for the evaluation of a wide variety of intervention trials, including vaccine, microbicide, and peer-education. Although implementing the assessment of both behavioral and biological outcomes in this Trial is more complex, it permits a more complete assessment of the effects of the intervention, which provides clues about how to scale up the intervention effectively so that it can have the intended public health impact.

References


Design and integration of ethnography within an international behavior change HIV/sexually transmitted disease prevention trial

NIMH Collaborative HIV/STD Prevention Trial Group*

Objective: To use a common ethnographic study protocol across five countries to provide data to confirm social and risk settings and risk behaviors, develop the assessment instruments, tailor the intervention, design a process evaluation of the intervention, and design an understandable informed consent process.

Design: Methods determined best for capturing the core data elements were selected. Standards for data collection methods were established to enable comparable implementation of the ethnographic study across the five countries.

Methods: The methods selected were participant observation, focus groups, open-ended interviews, and social mapping. Standards included adhering to core data elements, number of participants, mode of data collection, type of data collection instrument, number of data collectors at each type of activity, duration of each type of activity, and type of informed consent administered. Sites had discretion in selecting which methods to use to obtain specific data.

Results: The ethnographic studies provided input to the Trial’s methods for data collection, described social groups in the target communities, depicted sexual practices, and determined core opinion leader characteristics; thus providing information that drove the adaptation of the intervention and facilitated the selection of venues, behavioral outcomes, and community popular opinion leaders (C-POLs).

Conclusion: The described rapid ethnographic approach worked well across the five countries, where findings allowed local adaptation of the intervention. When introducing the C-POL intervention in new areas, local non-governmental and governmental community and health workers can use this rapid ethnographic approach to identify the communities, social groups, messages, and C-POLs best suited for local implementation.

AIDS 2007, 21 (suppl 2):S37–S48

Keywords: Behavioral interventions, culture, developing nations, ethnography, qualitative data

Introduction

In November 1999, the US National Institute for Mental Health (NIMH) launched the NIMH Collaborative HIV/STD Prevention Trial (hereafter, the Trial), using an evidence-based community-level sexual behavior change HIV/sexually transmitted disease (STD) prevention intervention model adapted by Kelly and colleagues [1,2]. This model is based on the work of Rogers and colleagues [3,4], who examined and described how technological and behavioral innovations diffuse throughout a community, and how they are adopted, accepted, and become normative within populations. Rogers found that innovations are often first originated by a subset of community members who are its opinion leaders. These are the trusted trendsetters whose actions, attitudes, and views influence those of other community members. Expanding on the work of Rogers and colleagues [3,4], Kelly et al. [5], St Lawrence et al. [6] and Sikkema et al. [7] demonstrated the efficacy of such interventions with gay men, women, and adolescents in the United States.

Kelly [8] specified nine core elements that must be incorporated into a successful HIV/STD prevention programme on the basis of this diffusion of innovations model (for additional details, see *The community popular opinion leader HIV prevention programme*):

* See Appendix B for members of the NIMH Collaborative HIV/STD Prevention Trial Group.
conceptual basis and intervention procedures’ [9] in this issue). Ensuring fidelity to these core elements is critical when this evidence-based intervention is adapted and adopted in new settings. In addition, ongoing monitoring of implementation of the intervention is important to ensure that the integrity of these core elements is maintained.

Ethnography is the study of the social and cultural norms, mores, values, and beliefs of a group of people, using primarily qualitative research methods [10–13]. Ethnography traditionally has required immersion in cultures and an extended period of field-based research. In the 1980s, models for rapid or focused ethnographic assessment were developed and applied in various research areas [14–21]. In these settings, participant observational data were combined with open-ended qualitative interview data, which permitted an in-depth exploration of such sensitive topics as substance abuse and sexual behavior. These more focused ethnographic assessments have permitted formative research to be conducted more rapidly, which is useful when tailoring and implementing interventions in a short timeframe. Formative research allows community involvement in the design of prevention and clinical trial protocols [22], probably leading to greater community acceptance. In addition, advances in analytical software have allowed for more systematic analysis of the data collected [23–27].

The Trial used an integrated methods approach, starting with a formative research phase using qualitative methods, to provide input into the design of the quantitative assessment and intervention. Rapid ethnography was part of the process used to achieve culturally sensitive adaptation and implementation of the intervention. This paper describes how simultaneous, rapid ethnography in five countries enabled researchers to adapt and tailor the community popular opinion leader (C-POL) intervention [9] to each unique study site. Even though the site researchers had extensive experience with different populations in their countries, the implementation of this particular behavior change model had not been attempted. It was thus ill-advised to make assumptions about target populations without conducting formative research to help in the adaptation of the intervention. Site-specific ethnographic and epidemiological data were needed to identify the populations at risk of HIV and STD that should be targeted with the intervention [28], the specific venues where the Trial should be conducted [29], and how the intervention should be tailored given the characteristics and sexual practices of the target populations in the venues.

**Ethnographic study objectives**

This ethnographic study was designed to provide the dataset that was used to: (i) describe and confirm the social and risk settings and risk behaviors; (ii) develop the assessment instruments; (iii) tailor the intervention in the eight core topic areas described below; (iv) design a process evaluation of the intervention; and (v) design an understandable informed consent process. To standardize the ethnographic study across the five sites, a protocol including templates and a basic tool set was developed by Trial investigators representing each of the five country sites, the NIMH, and the data coordinating center (DCC). The protocol ensured that the components of the study, ethnographic methods, core topic areas and associated required elements, training materials and

The goals of the ethnographic study were to describe individuals’ sexual and HIV/STD knowledge as well as the sexual practices that put them at risk of HIV and STDs, healthcare practices and beliefs, health-seeking behavior, the social groups and interactions of individuals and settings where these interactions occur, characteristics of individuals who might make good popular opinion leaders, and suggestions for prevention messages. In addition, the ethnographic study provided a formative research opportunity to explore or assess specific issues as they arose during the conduct of the initial phases of the study. For example, one of the nine core elements defined by Kelly [8] is the identification of a venue that is a cohesive social setting in which opportunities to have social interactions are abundant, providing numerous occasions for risk-reduction conversations among an identified high-risk group of people. One contribution of the ethnographic study was input to the selection of these settings in each of the five country sites. The ethnography study thus identified community settings that were social gathering places, in each study country, using participant observation and focus groups or individual interviews. Study social settings selected and confirmed as study venues were: food markets with individually owned stalls in China; clusters of wine shops in slums in India; gathering points of young, high-risk people in barrios in Peru; vocational and trade school dormitories in Russia; and retail establishments in business centers of growth points in Zimbabwe (see ‘Selection of populations represented in the NIMH Collaborative HIV/STD Prevention Trial’ [29] for more detail on the site selection process and results).

Another critical element is the identification of natural leaders (innovators called ‘community popular opinion leaders’; C-POLS), whose opinions are valued by members of the community, to be trained to deliver the prevention messages. In each of the five international sites, the ethnographic studies established that popular individuals in communities, who were considered leaders, could be identified and recruited to participate in the intervention.
certification requirements, and data analysis plans, were implemented consistently at all study sites.

**Ethnographic methods**

Ethnographic methods and their associated standards were selected through input and consensus of a broad group consisting of both US and international representatives from each of the five country study sites, the NIMH, and the DCC. The ethnography protocol specified the definitions and procedures for the methods selected: participant observation, focus groups, interviews, social mapping, and archival data. Each of these dominant qualitative methods is associated with strengths and limitations, which vary among cultural groups. Some of the relevant strengths that we considered in selecting these methods for this Trial are:

Participant observation allows for the collection of behavioral data that people may take for granted so much that they find it difficult to explain in an interview. It also provides a basis from which to question, probe and clarify interview and focus group responses that contradict previous observations.

Focus groups are generally viewed as a method with strengths in eliciting normative data, and generating broad-sweep overviews of the issues of concern to the cultural groups or subgroups represented in the focus group.

Individual interviews are considered the optimal choice for collecting data on personal histories and experiences, particularly on sensitive topics.

Social mapping provides information about the names and relative locations of settings where members of the populations socialize and where conversations might be initiated. This information could be used to characterize risk and to develop realistic role play scenarios for each selected venue.

Archival or secondary document review provides insights into both basic facts about a cultural groups (e.g. age, sex, level of education), as well as information on a number of basic categories considered important by those who collect and maintain data on the group (e.g. who is considered to be a member of a household, what is considered as ‘income”).

Standards developed for each of the specified methods included: (i) the number and sampling of participants; (ii) the mode of data collection; (iii) the type of data collection instrument used; (iv) the number of data collectors present for each type of data collection activity; (v) the duration of each type of data collection activity; and (vi) the type of informed consent administered with the activity.

These data collection standards enabled comparable implementation of the ethnographic study across the five country sites. The data entry system included space for the researcher to indicate any variation from standard operating methods. Therefore, even though a focus group ideally included six to eight individuals, if fewer people attended, it was still possible to conduct the session and note the deviation in the number of participants. The data system also documented relevant information associated with the management of each source of data, such as the time when each task was performed and who conducted data translation, transcription, and coding.

Although standards were adopted for the specified methods, a method that may be a good choice in one cultural context may not elicit as much useful data in another, and, in any case, a researcher must always be alert to the fact that respondents are not always truthful and that simply asking questions may bias the response away from the truth [13]. For example, in many cultural contexts, sensitive information regarding individual sexual behavior is best collected using in-depth individual interviews with respondents, whereas information regarding sexual norms or mores is better gathered using focus groups, that is, holding group discussions among target group individuals or key informants and stakeholders. The ethnographic study was thus designed to include a core set of methods, but individual sites chose the appropriate methods to elicit specific elements of required information and each site’s ethnographic data collection plan specified the methods intended for use with different participant populations, focusing on different topics. For example, in focus group discussions in India, it was found that participants were reluctant to discuss sexual practices that were personal, but had lively discussions regarding sexual practices and mores when presented with scenarios or local stories describing characters in the community and their sexual practices [30]. Because different methods are associated with different strengths in different cultures, qualitative methods are often triangulated, a strategy in which data obtained from multiple sources and multiple methods on a similar topic are compared across methods. That practice was encouraged during this Trial. The standard methods agreed upon by the five study sites for the collection of data are described in greater detail below.

**Participant observation**

In the initial fieldwork, participant observation was used to describe where people congregated socially and how they behaved in social groups in different venues. Participant observation was an effective method for initially identifying the natural leaders in a group (the C-POL) who were later recruited and trained to deliver prevention messages to their friends and neighbors.
Behaviors of interest included how people reacted to each other, how they treated each other, which individuals seemed to be in charge or the center of attention, which individuals were greeted with respect, admiration or liking, and what happened when different members of the group left the venue. For example, when an individual entered a hair salon in Lima, and most of the people suspended what they were doing and focused on what that person was saying, and that person also knew the names of the people in the salon, that person was identified as a potential C-POL. In China, a person in the market stalls was identified as a potential C-POL when he or she walked around and visited with people in other stalls and seemed to have a lot of people dropping by his or her stall.

Participant observation was also useful for identifying opportunities for informal social interaction, one of Kelly’s core elements of the popular opinion leader intervention [8]. Using participant observation in Russia, study teams identified the specific times of day and places that students would meet informally. This confirmed that opportunities existed for C-POLs to deliver HIV/STD prevention messages to fellow students during implementation of the intervention.

**Interviews**

Open-ended, in-depth, or rapid assessment interviews were used to collect important data on the core topic areas. Key informants, gatekeepers, stakeholders, and potential target group members were asked some of the sample questions presented in Tables 1–8. Interviewers were able to tailor their questions to the interviewee; this approach thus yielded important information that would not have been elicited using close-ended questions. Key informants and stakeholders provided information not necessarily known to target group individuals. For example, in China, the ethnographers learned that doctors experienced an upsurge in patients in the STD clinics after International AIDS Day, indicating that the community’s awareness of STD or HIV was enhanced during certain events that resulted in additional health-seeking behavior by target group individuals (see Table 1 for example questions). In Zimbabwe, target group

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**Table 1. Core topic area: sexual health data.**

<table>
<thead>
<tr>
<th>Required elements</th>
</tr>
</thead>
<tbody>
<tr>
<td>STD knowledge, attitudes, beliefs</td>
</tr>
<tr>
<td>HIV knowledge, attitudes, beliefs</td>
</tr>
<tr>
<td>Health-seeking behavior</td>
</tr>
</tbody>
</table>

**Sample questions: STD knowledge, attitudes, beliefs**

Please name all the STDs that you know of (ask questions below for each STD):

- What are the different names for these STDs?
- What are the symptoms/manifestations of each of these?
- How are STDs transmitted? (Probe: Can STDs be transmitted through casual contact, e.g. touching, sharing food, kissing?)
- Are some people more vulnerable than others to STDs?
- Why?
- How are STDs treated?
- Are there things that people can do to treat their own STDs?
- Are there any STDs that are incurable?
- Do/how do STDs differ for men and women, in terms of symptoms, transmission, prevention, etc.?
- In this community, is there a stigma attached to having or being treated for an STD?
- How does one prevent getting STDs in the first place? (Probe for condom use, partner reduction, substance use-related gender, etc. issues)

**Sample questions: HIV knowledge, attitudes, beliefs**

What are the symptoms/manifestations of HIV/AIDS?

What terms are used to refer to HIV/AIDS?

How is HIV/AIDS transmitted?

Does having another STD affect your likelihood of acquiring HIV/AIDS?

How does one prevent getting AIDS in the first place? (Probe for condom use, partner reduction, substance use-related gender, etc. issues)

Does/how does AIDS differ for men and women, in terms of symptoms, transmission, prevention, etc.?

In this community, is there a stigma attached to having or being treated for HIV/AIDS?

Do you know anyone who has AIDS?

**Sample questions: Health-seeking behavior for STDs**

What STD symptoms lead people to seek care?

What providers are associated with STDs or reproductive tract infection care giving?

What are the factors associated with provider choice?

What are the barriers to seeking care (social, political, access, and gender-specific)?

What are the patterns of resort (self-treatment, self-medication, friends)?

**Sample questions: Health-seeking behavior for HIV**

How is HIV/AIDS treated (treatment-related questions)?

What can cure AIDS?

What symptoms lead people to seek care?

What providers are associated with HIV care giving?

What are the barriers to seeking care (social, political, access, and gender-specific)?

What are the patterns of resort (self-treatment, self-medication, friends)?

What are the factors associated with provider choice?

STD, Sexually transmitted disease.
members interviewed in open-ended interviews, revealed that, although the traditional lines of communication about sexual issues were via paternal aunts and uncles, most young adults currently learn about sex and sexual practices through discussions with their friends and peers (see Table 3 for example questions). Therefore, because conversations about sex now occurred more often among friends and peers, a C-POL approach was likely to be feasible if peers rather than aunts and uncles were trained in Zimbabwe. In addition to collecting information that would help tailor the intervention and assessment, interviews with gatekeepers and stakeholders determined

### Table 2. Core topic area: sexual practices and meanings.

<table>
<thead>
<tr>
<th>Required elements</th>
<th>Sample questions: Dominant sexual practices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dominant sexual practices</td>
<td>What are the different types of sexual practices?</td>
</tr>
<tr>
<td>Condom use</td>
<td>What terminology, safer/risker sex practices, partner definitions, disease definitions are used?</td>
</tr>
<tr>
<td>Sexual communication and negotiation</td>
<td>Describe the types of sexual and safer/risker sex practices that men and women like.</td>
</tr>
<tr>
<td></td>
<td>How do different types of relationships influence sexual and safer/risker sex practices?</td>
</tr>
<tr>
<td></td>
<td>What are the differences across different types of relationships (e.g., committed versus non-committed versus commercial; same versus opposite gender)</td>
</tr>
<tr>
<td>Sexual initiation</td>
<td>At what age do young men and women (in this venue) have their first sexual experience?</td>
</tr>
<tr>
<td></td>
<td>Are the first sexual experiences usually with a person of the same or different age? (Comment: Need to be sensitive to potential differences between normative perceptions and personal experiences)</td>
</tr>
</tbody>
</table>

### Table 3. Core topic area: healthcare delivery and beliefs.

<table>
<thead>
<tr>
<th>Required elements</th>
<th>Sample questions: Sexual health information sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexual health information sources</td>
<td>Where have you received your information about STD and AIDS? (Probe for IEC, governmental, community/NGO, or school-based programmes and mass media, social groups, religious, educational, marital/relational, familial, and other sources)</td>
</tr>
<tr>
<td>Prevention and care services for STD/RTI, HIV</td>
<td>Do you feel that this information is accurate? Understandable? Sufficient?</td>
</tr>
<tr>
<td>Access to condoms and STD information</td>
<td>What groups of people tend to rely on this source? (Probe for types of groups)</td>
</tr>
<tr>
<td></td>
<td>Are there any individuals who people tend to rely on for this kind of information? (Add to probe list for subsequent interviews)</td>
</tr>
</tbody>
</table>

Sample questions: Prevention and care services for STD/RTI

- Who provides STD services (doctors, quacks, pharmacists)?
- What is the system of referrals for STD/RTI at these facilities?
- What is the availability of diagnostics for STD/RTI?
- Are education and counseling services (including partner notification) available?
- Are these facilities accessible (cost, hours of operation, location, privacy)?
- Are condoms and/or STD medications available at these facilities?
- What is the quality of care and treatment in these facilities?

Sample questions: Access to condoms and STD information

- Who is supposed to have access to condoms? STD information (age restrictions)?
- Is the cost of condoms acceptable?
- Are condoms and STD information available at convenient hours?
- Is the location of condoms and STD information good?
- Is privacy an issue for people who seek condoms or STD information?

IEC, information, education, and counseling services; NGO, non-governmental organization; RTI, reproductive tract infection; STD, sexually transmitted disease.
the best methods to engage their support for the study and intervention. Study sites wanted to ensure that these key community members would not obstruct implementation of the intervention in the communities.

Focus groups
In each international site, focus groups were convened on specific topics, such as health behaviors, social groups, normative sexual practices and meanings, and C-POL characteristics. The groups were composed of six to eight members of the target population, and the discussion was guided by facilitators using probes that emerged from participant observation or interview data. This was an extremely potent technique for reaching consensus on a variety of topics. For example, not only was there consensus within focus groups at one site, but there was consensus across the five sites about many of the characteristics that contribute to someone being a natural leader and therefore a good C-POL. All sites agreed that natural leaders were respectful of traditions, yet open and good communicators. In addition, the ability to 'keep secrets', or ensure confidentiality during the discussion of sensitive issues, was seen as an important C-POL characteristic (see Table 5 for example questions).

Social mapping
Social mapping permitted examination of the social dynamics in the communities and the identification of suitable venues in which to conduct the study. Ethnography team members conducted social mapping by observation, as well as through discussion during focus groups and individual interviews. Locations in the community where people were observed to congregate or where they used services or initiated risky behaviors were indicated on a map by different symbols (e.g. bars, ball fields, coffee houses, cafes, markets, stores, clinics, hair salons). Locations were confirmed in study sites through interview or focus group data. Such knowledge
was important because this intervention requires the selection of venues with ample opportunities for informal conversations. These opportunities permit diffusion of the HIV/STD prevention messages delivered by the C-POL. Figure 1, a social map from Peru, shows different social settings (such as restaurants, sports fields, or other areas of congregation), sites that provide services (such as soup kitchens), and sites where risk behaviors occur (such as areas of prostitution). Such maps were used during intervention implementation to identify places to recruit C-POLs, conduct C-POL training, and place posters designed to stimulate conversations. In addition, social maps served as guides for process evaluation teams to conduct participant observation as part of the process evaluation, after the intervention had begun, to ensure that the C-POLs were having conversations, and to gauge community members’ reactions to the intervention and C-POL.

Archival data
In all study sites, archival data showing basic community demographics were collected. These data often came from official sources such as census data or, in the case of Russia, technical college enrollment data. These data

Table 5. Core topic area: community popular opinion leader characteristics.

<table>
<thead>
<tr>
<th>Required elements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual-level C-POL characteristics</td>
</tr>
<tr>
<td>Group-level characteristics</td>
</tr>
<tr>
<td>Group-level C-POL characteristics</td>
</tr>
</tbody>
</table>

Sample questions: Individual-level C-POL characteristics
(Ask questions for each name from C-POL probe list constructed from responses to questions in the social group core topic area)

Let’s talk a while about (name).
When you wish to discuss something with (name), do you go to her or him directly?
How do you get hold of (name) when you wish to discuss something?
Can most people go to (name) and talk to him or her directly? (Probe: Or do they need to go through someone else?)
Do you think many people consult with him or her?
Do you think (name) knows and talks with many people?

Sample questions: Group-level characteristics
(Ask questions for each group from group probe list)
We have talked about different groups of people, and some of the people who belong to these groups.
Who do you think are the most important members of (group name)?
Does (group name) have any relationship with (other group name)? What type?
Can someone in (group name) interact with someone in (other group name)? What type of interaction?
If someone is a member of (group name) and they want to get advice from (other group name), what do they have to do?
Do members of these groups tend to know one another and interact with one another? To what extent/frequency and on what topics?

Sample questions: C-POL characteristics
(Ask about each person from C-POL probe list)
What are (name)’s attitudes toward the (group name)?
How long has she or he been a member of (group name)?
How long has she or he lived in this community?
Do you know how she or he became a leader in this group? Please explain.
Is she or he knowledgeable about STD, HIV/AIDS? What are her or his beliefs about STD, HIV/AIDS?
If someone wanted to get a message out to people about how they might protect themselves from STD, HIV and AIDS, do you think she or he would be willing to help?
Is it easy for people to contact her or him? How do they go about it?
What does she or he do for a living?
How could I contact her or him?

C-POL, Community popular opinion leader; STD, sexually transmitted disease.

Table 6. Core topic area: appropriate reimbursements.

<table>
<thead>
<tr>
<th>Required elements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reimbursement experiences</td>
</tr>
<tr>
<td>Appropriate amount and type of reimbursement</td>
</tr>
<tr>
<td>Reimbursement delivery format</td>
</tr>
</tbody>
</table>

Sample questions
What is done in this community to show that something is appreciated?
Have there been any projects or studies conducted in this area in which people were asked to answer questions in an interview or meeting? If so, did they provide something to the people who answered questions to show their appreciation?
What would be considered an appropriate sign of appreciation when someone helps by answering questions?
Would it be better to offer money or a gift? What amount or type?
Who should provide the reimbursement and how should it be given?

STD, Sexually transmitted disease.

Table 7. Core topic area: prevention messages.

<table>
<thead>
<tr>
<th>Required elements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavior change experiences</td>
</tr>
<tr>
<td>Information sources for behavior change</td>
</tr>
<tr>
<td>Message types for behavior change</td>
</tr>
</tbody>
</table>

Sample questions: Behavior change experiences
When was the last time that you tried to change something you do in order to improve your health?
What did you do (stop smoking, drink less, change diet, etc.)?
What helped you to make the decision to change?
How do you think others could improve their health?

Sample questions: Information sources for behavior change
Who should provide information on how to improve your health?
Who should provide information on how to prevent STD?

Sample questions: Message types for behavior change
What types of messages do people think are the most believable?
included typical demographic information for the target communities, such as numbers of households, families, men and women, education, and socioeconomic status. In addition, STD and HIV data were collected from national or local health entities, such as ministries of health or from local clinics in study areas. These data were used to describe the community context.

**Table 8. Core topic area: population profile.**

<table>
<thead>
<tr>
<th>Required elements</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Note: This information will be provided primarily from secondary sources. The last section, on perspectives, may come from data collected from members of the community, including gatekeepers, stakeholders, key informants, and others)</td>
</tr>
<tr>
<td>Country and community-level sociodemographic data</td>
</tr>
<tr>
<td>Country-level HIV/AIDS and STD data</td>
</tr>
<tr>
<td>Healthcare service delivery system</td>
</tr>
<tr>
<td>Status of traditional and western medicine</td>
</tr>
<tr>
<td>Perspectives on HIV/AIDS and STDs</td>
</tr>
<tr>
<td>Sample questions: Country and community-level sociodemographic data elements</td>
</tr>
<tr>
<td>Population size by age and gender</td>
</tr>
<tr>
<td>Life expectancy</td>
</tr>
<tr>
<td>Literacy/education levels</td>
</tr>
<tr>
<td>Age of marriage</td>
</tr>
<tr>
<td>Age of sexual debut</td>
</tr>
<tr>
<td>Sample questions: Country-level HIV/AIDS and STD data</td>
</tr>
<tr>
<td>Sentinel data on HIV prevalence and STD prevalence</td>
</tr>
<tr>
<td>Age and gender distribution of reported AIDS cases</td>
</tr>
<tr>
<td>STD incidence</td>
</tr>
<tr>
<td>STD modes of transmission</td>
</tr>
<tr>
<td>Geographical distribution of HIV/AIDS infection</td>
</tr>
<tr>
<td>Sample questions: Community-level data</td>
</tr>
<tr>
<td>(Provide any of the above data that are available on city, village, and/or venue populations. Include available data on ethnic groups in venues, and specify groups)</td>
</tr>
<tr>
<td>Healthcare service delivery system</td>
</tr>
<tr>
<td>Status of traditional and western medicine</td>
</tr>
<tr>
<td>Percentage/relative share of public and private sources for healthcare</td>
</tr>
<tr>
<td>Physicians and nurses per capita</td>
</tr>
<tr>
<td>Structure of delivery system (level of centralization/decentralization)</td>
</tr>
<tr>
<td>Government per capita expenditure on healthcare</td>
</tr>
<tr>
<td>AIDS care costs (e.g. government health budget)</td>
</tr>
<tr>
<td>Perspectives on HIV/AIDS and STD (with additional emphasis on all ethnic groups within venues)</td>
</tr>
<tr>
<td>Sociocultural context</td>
</tr>
<tr>
<td>What social and cultural issues are known to have an effect on HIV/AIDS and STD transmission (e.g. circumcision, wife inheritance, dry sex)?</td>
</tr>
<tr>
<td>Political context</td>
</tr>
<tr>
<td>What has been the political response to HIV/AIDS in the country? STD?</td>
</tr>
<tr>
<td>Popular opinion: What has been the history of popular opinion about HIV/AIDS and STD?</td>
</tr>
<tr>
<td>Policy issues</td>
</tr>
<tr>
<td>What government policies address issues of HIV/AIDS and STD? What are the policies regulating access to contraceptives, including condoms?</td>
</tr>
<tr>
<td>Economic issues</td>
</tr>
<tr>
<td>What are seen as the economic costs of HIV/AIDS and STD? Are economic issues thought to influence risk behaviors?</td>
</tr>
<tr>
<td>Religious context</td>
</tr>
<tr>
<td>What are the dominant religious groups in the venues? What have these groups’ responses to HIV/AIDS and STD been? What is their position on condom use, sex education/family life education?</td>
</tr>
</tbody>
</table>

STD, Sexually transmitted disease.

**Sampling**

Sampling of participants for focus groups and individual interviews ranged from purposive, to snowball, to random. For example, the identification and recruitment of community stakeholders, or key informants, was done through a community entrée process conducted at each site, and included interviewing individuals from whom

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Fig. 1. Example social map of venue in Peru. Leisure places: ■ Sports field, ☐ Group kitchen, ● Game playing, ○ Restaurant/beer hall; Risky places, ▲ Prostitution, ★ Hang out for delinquents, ✸ Hang out for drug users.
Assessment instruments

To collect data on sexual risk behaviors and social groups, the ethnography workgroup developed eight core topic areas. Each international site was required to develop site-specific data collection guides that covered the eight core topic areas and their required elements. The data collection guides were designed to be appropriate for the intended population. For example, interviews administered to community members in the venues had a different tone, and possibly a different set of questions, than those administered to stakeholders. These data collection guides provided instructions to the field staff, specific questions to be posed, and probes to elicit additional information. At each site, trained ethnographers collected data about the core topic areas and required elements using methods selected from among those described above.

Core topic areas and required elements

To elicit the data required to develop an assessment instrument and adapt the intervention, Trial researchers developed eight core topic areas, each with three or more required data elements to be collected at all sites. Core topic areas and required elements were agreed upon by consensus among ethnographers from all sites. For the core topic area on sexual health data, STD and HIV knowledge, attitudes, and beliefs, and health-seeking behavior were required elements. For sexual practices and meanings, dominant sexual practices, and sexual communication and condom use were required. With healthcare delivery and belief questions, sexual health information sources, and medical services, as well as condom access were required. For social groups, the types and characteristics of community and personal groups were required. C-POL characteristics were designed to obtain information about personal and group-level characteristics. When exploring appropriate reimbursement for the time required for study activities, the teams asked about reimbursement for study activities, as well as the appropriate amount and type of reimbursement and delivery format. When focusing on prevention messages, ethnographers were required to ask about behavior change experiences, including information sources and message types that encourage behavior change. In addition, archival data were used to describe population profiles. These core topic areas and their associated required elements and sample questions appear in the tables. Each international site was required to collect ethnographic data on each of the core topic areas and their required elements using one of more of the methods listed previously to ensure culturally appropriate data collection for their site and target population(s).

Training and certification

To ensure systematic and rigorous collection of ethnographic data, a one-week, centralized train-the-trainers workshop was conducted. A participatory learning approach was used in the training, with didactic presentations, role plays, and group critiques. Training materials were developed in English (the central ethnography training manual is available from study researchers on request), and the central training was conducted in English. Each site sent two to four staff members for this central training. During the course of the training, these staff members were provisionally certified to conduct in-country training of their ethnographic field staff. The trainers then returned to their individual country sites, developed translations of the training materials, and conducted on-site training of local ethnography staff. To ensure staffing quality standards were uniform, staff from the Trial’s DCC conducted a site visit, during which locally trained staff were individually questioned about the study design, standards adopted for each data collection method, and the process and content of informed consent. Copies of their initial (in most cases, feasibility) data were reviewed. Trained individuals who met the criteria were certified as competent to collect data, whereas those who did not demonstrate a satisfactory understanding of the protocol were retrained or reassigned to other project activities.

Data analysis plans

The creation of core topic areas and associated required elements facilitated the development of a basic hierarchical coding system. Hierarchical approaches to data coding and analysis are appropriate for the basic content and summary analysis that was required for the study. The use of topic areas also facilitated access to the data by members of the other working groups, because the set of required elements and illustrative questions for each topic provided a standard format for results at each site. To
ensure some standardization and quality of data analysis among sites, an analysis plan requiring specific steps was developed at each site. These steps included basic data management, translation and transcription details, coding, and an assessment of intercoder agreement. The plan also specified who would conduct each step, the resources needed, and a timeline for the completion of all analyses.

The software used for data analysis varied among sites. Study sites chose software already available to them for the content analyses. Individual sites had quality control measures in place. Coders were trained extensively, using consensus to build coding validity. After coding of all interviews and focus group transcripts was conducted, subsamples were selected for double-coding. Coding discrepancies were resolved via consensus. In study sites where transcripts were translated, a subsample was selected for back-translation to verify meanings. The translation of summary results was required by all teams, but detailed coding in English for all sites was not. Study site needs for coded data were allowed to drive the level of coding and analysis. For example, data analysis needed within each site was more detailed than that needed across sites. For example, the risky behaviors of married men in India, Zimbabwe, and Peru were a major factor in HIV/STD transmission, but the Russian site had very few married men, thus study teams in the former list of countries had more detailed coding associated with these behaviors than Russia.

Data for cross-site comparisons were reported in English in summary format organized by core topic area and by required element within the core topic. The summaries were based on the individual site’s content analysis and were organized into matrices according to basic variables across sites. Each site used the software that the site researchers knew best, thus minimizing costs, time, and training needs for data analysis.

This standardized yet flexible approach resulted in the production of summary reports for cross-site comparisons, organized by core topic areas, and more detailed reports for use at each site. These reports constitute rich data repositories that have been accessed to answer questions emerging from different project activities.

Transcripts and coding structures were kept as part of the study record, such that summary data can be traced back to the coded data and further to the original data source (for example, transcription) as needed. Organizing the data in this way has enhanced the integration of ethnographic data within the Trial to meet the needs of the assessment and intervention workgroups, and help identify the process evaluation objectives. Details regarding the process evaluation are presented in ‘Methodological overview of a five-country community-level HIV/sexually transmitted disease prevention trial’ in this issue [32]. The ethnographic study was designed to inform different aspects of the Trial, but the data also have value as a source of information for health planners in the five countries.

### Use of ethnographic data to inform design and procedures of the Trial

This section describes in more detail how the ethnographic studies in the five countries provided input that described behavioral outcomes, social groups in the target communities, and C-POLs, and drove adaptation of the intervention and facilitated the selection of venues. In addition, this section describes how ethnographic data impacted on the methods of data collection and assessment of the intervention via the process evaluation. Ethnographic data were integrated into the Trial protocols and procedures through interactions of study members from different Trial workgroups.

**Ethnographic data used for selection of behavioral outcomes and tailoring the intervention**

Behavioral outcomes for the Trial were selected on the basis of ethnographic data on sexual practices and risks at all five international study sites. Consistent findings across all sites showed that both women and men highlighted the role of sex inequities driving intracouple dynamics and sexual practices. Although none of the local cultures at the study sites condoned premarital or extramarital sex, double standards were documented in all study sites except Russia. Extramarital and premarital sex are tolerated among men, but not among women. The sex inequities documented mean that women are particularly vulnerable to STDs, including HIV, for several reasons. Attitudes toward condoms were consistently negative in all study sites, particularly for steady or marital relationships. Sex inequities also provide women limited opportunities for negotiation about expectations of monogamy or the use of condoms in a relationship. In all countries, women reported often being pressured or coerced to have sex. In some countries, particularly India, sexual and physical violence against women was common. The consistency of the ethnographic results on sexual practices identified the main behavioral outcome for the Trial: unprotected sexual acts with non-spousal partners.

Another need for ethnographic data emerged when epidemiological study data indicated that some venues did not have sufficient HIV/STD-related behavioral or biological risk to assess this behavior change intervention in those locations with a feasible sample size [28]. For those sites, ethnographers worked with the site’s study team to identify new venues where higher levels of risk existed. They were able to provide information because
they had been collecting data on risk behavior, not only in the venues identified for probable inclusion in the Trial, but also in the larger community within which these venues were located. See ‘Selection of populations represented in the NIMH Collaborative HIV/STD Prevention Trial’ [29] for additional information on venue selection across the five international sites.

Ethnographic data were also used when adapting the intervention, including the selection of C-POLs and adaptation of the intervention training sessions by tailoring the training manual and curriculum. Cross-site ethnographic data established the following characteristics of an ideal C-POL: respectable, credible, life/sexual experience, trustworthy, empathetic, well-spoken, and self-confident. Ethnographic data also showed that, in all study sites, C-POLs could be identified and recruited to an HIV/STD prevention intervention. When tailoring the intervention manual and curriculum, ethnographic data helped to identify appropriate language for use in the manuals, helped with the choice of an intervention logo in each study site, identified social venues for the selection of C-POLs, and allowed the selection of C-POLs in intervention communities through participant observation and nomination. Ethnographic data allowed for site-specific tailoring in the selection of additional risk behaviors on which to focus prevention messages. Although all study sites focused on condom use with non-spousal partners, and on messages related to drinking and sexual risk, only some sites chose to include messages encouraging monogamy. Ethnographic data were also used to develop site-specific C-POL training, including examples of ways to initiate conversations and examples of C-POL conversations to promote targeted behaviors. Feedback from the ethnographic team showed that people at some study sites had lower levels of knowledge about HIV and STD, thus allowing tailoring of intervention C-POL training modules to include more information about HIV and STDs. Therefore, in Russia and India, an additional fifth training module included information about HIV and STDs, whereas four intervention training sessions were shown to be sufficient in China, Zimbabwe, and Peru.

**Ethnographic data used for study design and assessment methods**

In addition, ethnographic data provided information for a better design of the informed consent process, to select the final mode of data collection, and to flow into the process evaluation. An early, important decision facing the Trial was the possible use of audio computer-assisted self-interviewing (ACASI) as the mode of data collection [33]. An ACASI feasibility study was designed and implemented to compare ACASI with computer-assisted personal interviewing [34]. At the end of the study interviews, the ethnographers conducted exit interviews with study participants, using structured open and close-ended interview guides to probe for respondent comfort with and preference for the two interview modes. These cross-site data were analysed, summarized, and provided input when deciding which interview mode to use for the Trial. Similarly, when concerns arose about developing an informed consent process that was comprehensible in the five sites, the ethnography teams added questions to the exit interviews to assess comprehension of the informed consent process. Sites were able to use data from these exit interviews to improve their informed consent process.

Ethnographic methods were also used to implement the process evaluation that monitored implementation of the intervention. Observational data were collected regarding the logos and HIV/STD prevention messages displayed in communities, and whether or not C-POLs wore articles of clothing with the intervention logo, which were provided to them as part of the intervention to stimulate questions. In addition, process evaluation team members at some sites conducted brief intercept interviews to assess exposure to the intervention among community members and exposure to prevention messages, from both the identified C-POL and additional non-governmental or governmental agencies conducting HIV/AIDS or STD prevention programmes.

In conclusion, this study used a focused ethnography approach to collect data that were important in the overall design of the Trial and specifically in the design of the intervention and the assessment. Although the core topic areas, required elements, and specification of the methods to be used were standard across sites, each site was encouraged to tailor the data collection guides to meet the cultural characteristics of the local study population [35]. The ethnographic study used an iterative approach for data collection and analysis, which was well suited to collect data on the core topic areas and to respond to the emerging needs of the steering committee and other Trial workgroups for information needed to address issues related to the study design.

**Lessons learned**

An integrated, qualitative–quantitative approach is key to the successful adaptation of an intervention, especially when tailoring an intervention such as the C-POL model to new contexts. The rapid ethnographic approach described in this paper worked well, as results across the five country sites arrived at similar, yet distinctive, findings that allowed the local adaptation of the intervention. Data collected on sexual practices via the ethnography study were validated with epidemiological studies using quantitative computer-assisted methods for data collection (see ‘Sexually transmitted disease and HIV prevalence and risk factors in concentrated and generalized HIV epidemic settings’ in this issue [28]). Methods used in the ethnographic study to identify characteristics
of popular opinion leaders, and popular individuals were later used by the intervention teams in all study sites to identify and recruit C-POLS.

When introducing the C-POL intervention in new areas, it will be necessary to train local non-governmental and governmental health and community workers to use this rapid ethnographic approach, which can help focus intervention adaptation by identifying which communities, social groups, messages, and C-POLS are best suited for the intervention. This article presents a prototypical approach for identifying the domains in which the rapid collection of ethnographic data are needed to adapt the C-POL model to different contexts. Ethnographic data collected during a formative phase will feed into the adaptation of the intervention, and can also be used in designing evaluations of the C-POL intervention implementation.

References

The feasibility of audio computer-assisted self-interviewing in international settings

NIMH Collaborative HIV/STD Prevention Trial Group*

Objective: To determine the feasibility of using audio computer-assisted self-interviewing (ACASI) for data collection in developing countries, and to compare responses to questions eliciting sensitive information about sexual behavior using ACASI versus computer-assisted personal interviewing (CAPI) in five developing countries.

Design: A feasibility study determined whether ACASI could be used in populations in developing countries. A follow-up, randomized crossover study compared responses to questions eliciting sensitive information about sexual behavior using ACASI versus CAPI.

Methods: The NIMH Collaborative HIV/STD Prevention Trial conducted a feasibility study of ACASI in convenience samples in China, India, Peru, and Russia, then a randomized crossover ACASI versus CAPI study among volunteers in these countries plus Zimbabwe.

Results: Approximately equal numbers of men and women completed the feasibility study; the results suggested a high comfort level among participants. Married respondents in China and India appeared to give unreliable responses on sexual activity. In the crossover study, the pattern of responses to sensitive questions showed few differences. In China, higher rates of sexual risk were reported on CAPI. In Peru and Russia, differences by mode were found in the number of partners in the past year.

Conclusion: Despite variable computer experience and literacy, feasibility study participants reported ease in completing ACASI, and preferred a computer to an interviewer for answering sensitive questions, or had no preference. In the crossover study, most participants gave similar responses on both modes of survey administration. ACASI appears to be feasible in these settings, although low literacy may pose problems if participants cannot clarify questions.

Keywords: Developing nations, knowledge/attitude/practice studies, sexual behavior, survey methods

Introduction

The evaluation of HIV prevention programmes depends on the collection of reliable and valid reports of personal risk behaviors [1], particularly in heterosexual epidemics, in which unprotected sexual intercourse is the principal mode of transmission. Although it is critical that valid data be obtained to determine intervention programme effectiveness, it is also apparent that inaccurate reports of sexual behaviors occur in survey-based evaluations [2]. Survey researchers have responded to this problem by developing approaches to elicit accurate responses about highly stigmatized or sensitive behaviors (e.g. adolescent sexual activity, condom use, interpersonal sexual violence) by changing how surveys are conducted [3] and altering the mode of survey administration [4–7]. These approaches include the development of computerized assessments, notably computer-assisted personal interviewing (CAPI), conducted either face-to-face or by telephone [8], and audio computer-assisted self-interviewing (ACASI) [9,10].

A growing body of evidence indicates that increasing privacy during an interview can improve the completeness and accuracy of reporting of sensitive and illegal behaviors in population-based surveys [4,11,12]. Initially, the only way to afford privacy to interviewees was to use self-administered questionnaires, in which the respondent had only some degree of certainty that answers to sensitive questions would not be seen directly by another person. Unfortunately, subjects had to be able to read and navigate...
through questionnaires that often involved complex skip patterns. The reading skills of people at risk of HIV are often inadequate to complete self-administered forms, especially in many developing countries, where literacy may be an issue. Moreover, even people who can read well may have difficulty following data collection forms containing detailed questions and unfamiliar conventions defining complicated skip patterns [13]. Also, self-administered questionnaires are subject to respondent rumination, missing data, and changed responses, and bystander presence alone may influence responses [14]. Telephone surveys promised a high degree of anonymity [15], but increasingly low response rates in the 1990s rendered this approach infeasible for collecting survey sample data on sexual practices. The low coverage of telephones in many developing countries suggests that this mode of data collection may not prove feasible for widespread use as an evaluation approach.

In the late 1980s, computer-assisted interviewing was promoted to enhance face-to-face data collection. In CAPI, interviewers administer questionnaires using a computerized layout of the questionnaire, in which the questions and all possible responses are preprogrammed. This type of system enhances the accuracy and timeliness of data collection. It automatically executes skips and branching through complex questionnaires, conducts consistency and range checks, and produces a clean, machine-readable data file that requires no data entry, thereby reducing costs and maximizing reliability. This mode of data collection minimizes field editing and transmits accurate data quickly from the field.

The CAPI system is robust and can be used by interviewers in a broad range of settings using light-weight laptops, handheld computers, or even mobile telephones. Interviewers and respondents report few, if any, problems using this technology, and both parties frequently report a preference for CAPI to self-administered questionnaires. Because it is interviewer-administered, however, CAPI does not provide privacy, and sensitive and illegal behaviors may continue to be underreported by survey respondents because social desirability and impression management remain part of the interview process. In the 1990s, a new technology incorporated sound recording with CAPI technology, audio computer-assisted self-interviewing (ACASI). ACASI has all the advantages of CAPI, but instead of having an interviewer administer the interview, the respondent listens to an audio track recorded for, and linked to, each question. Respondents listen to the questions using a headset and move through the survey at their own pace. If illiterate, survey respondents can be instructed to push buttons on the touch screen that are color coded or have graphical representations of answer categories to indicate their response to each question.

The majority of the published studies comparing ACASI with other modes of data collection (including CAPI, self-administered questionnaire, interviewer-administered questionnaire, or telephone interviews) have focused on western countries [4,16,17]. Generally, higher rates of sensitive behavior are found on ACASI compared with interview [18–22] and self-administered questionnaire [23,24].

Interest in the use of these interviewing techniques in international settings has increased recently [25]. A study of 664 Thai college students found that ACASI led to higher reports of sexual activity compared with self-administered questionnaires, but the sample size was too limited to detect statistically significant differences [26]. A feasibility study of ACASI in Zimbabwe showed high acceptability, but the study reported on few sensitive behaviors [27]. A study of abortion in three groups of Mexican women showed the highest rates of reported abortion among women completing a randomized response approach, followed by self-administered questionnaires, with less frequent reports of abortion by women assigned to ACASI or interviewer-administered questionnaires [28]. Mensch et al. [29] examined self-reports of sexual activity from 4348 unmarried adolescent girls and boys in two communities in Kenya who were assessed using three interview modes: face-to-face interviewer-administered interviews; questionnaire self-administration; and ACASI. Results for girls were mixed and differed by community and mode of administration. Results for boys were somewhat more consistent, but had important, unexpected findings. The authors concluded that empirical research in developing countries to evaluate the interview mode is essential [30]. Although several randomized studies have evaluated whether sensitive behaviors are better elicited using ACASI in developing country settings, findings to date lack consistency and replication.

The NIMH Collaborative HIV/STD Prevention Trial (hereafter, the Trial) sought to determine the effectiveness of a community popular opinion leader approach to stimulating HIV risk reduction behavior change in developing countries. This study is a collaboration of diverse research groups, working in dramatically different cultural settings: food markets in southern China, urban slums in India, barrios in Peruvian coastal cities, vocational and trade school dormitories in Russia, and growth point rural villages in Zimbabwe. Before beginning the community-randomized, controlled trial of the community popular opinion leader approach, we first conducted a series of studies to help plan the Trial, including an ethnographic study, two small ACASI feasibility studies, and a series of epidemiological studies. The ACASI feasibility studies are the subject of this report.

Given the inconsistent findings in the literature on the feasibility and validity of ACASI in the developing world, we were interested in determining whether ACASI was feasible in the Trial’s diverse settings, where computer use has not been common until the past few years, and whether
we would obtain higher reports of sensitive behaviors using ACASI compared with interviewer-administered surveys, as has been shown in western countries. Therefore, we first conducted a feasibility study at four of the Trial sites to determine whether ACASI technology could be used in field conditions at these sites. The aims of this study were to: (i) develop and test a process for translating and programming the questionnaire to be administered by ACASI; (ii) evaluate the cultural acceptability of ACASI in collecting data on sensitive HIV risk behaviors; and (iii) identify and resolve logistical and technical issues associated with using computers in non-office settings. Next, a randomized crossover study comparing CAPI and ACASI was conducted at all five Trial sites to assess the relative validity of data collected on sensitive topics using these two different interview modes and to compare the amount of time required for survey administration for the two modes.

Methods

Audio computer-assisted self-interviewing feasibility study
In each country, a convenience sample, balanced by sex, of between 30 and 40 respondents was selected from areas similar to those selected for the planned epidemiological studies: markets in Fuzhou, China; slum communities in Chennai, India; barrios in Lima and Chiclayo, Peru; and vocational and trade school dormitories in St Petersburg, Russia. Zimbabwe joined the Trial too late to be included in the feasibility study. All participants gave informed consent, were given a description of the ACASI procedures and trained to use the computer, and completed the ACASI in their language of choice. The ACASI included approximately 80 questions dealing with demographics, residential stability, health, HIV and other sexually transmitted disease (STD) testing history, the use of alcohol and illicit drugs, sexual history, condom use, and other potentially sensitive topics. In addition, 11 feedback questions were included to assess participants’ comfort with the ACASI and preferences regarding interview mode. Participants were given headphones with which to listen to each question and the possible answers, and used touch-screens for data input. After completing the ACASI, selected participants were debriefed by a staff ethnographer about their experiences while completing the interview. Frequencies of responses to sensitive and non-sensitive questions were examined for each country, with particular attention to the feedback questions.

Crossover audio computer-assisted self-interviewing versus computer-assisted personal interviewing comparison study
A convenience sample of between 50 and 200 community volunteers, with approximately equal numbers of men and women, was recruited in each of the five countries from areas similar to those selected for the epidemiological studies and in the same age ranges: markets in Fuzhou, China, ages 18–40 years; slums in Chennai, India, ages 18–40 years; barrios in Lima and Trujillo, Peru, ages 18–30 years; dormitories in St Petersburg, Russia, ages 18–30 years; and the villages of Manhenga in Mashonaland Central province and Nkayi in Matabeleland North province in Zimbabwe, ages 16–30 years. Participants were randomly assigned to complete an assessment interview via CAPI or ACASI, after providing informed consent and being trained to use the ACASI computer (for those randomly assigned to the ACASI group). Two or 3 days later, participants returned and completed the same interview using the other interviewing method. The interview included approximately 90 questions covering demographics, health, STD history, alcohol and drug use, sexual activity and other sensitive topics. Many were questions that had been used for the ACASI feasibility study, although no respondent feedback questions were included.

Analyses were conducted separately for each country. Sex and age distributions were first compared between the two randomized groups, ACASI first, CAPI second (hereafter ACASI first) and CAPI first, ACASI second (hereafter CAPI first), to verify that imbalances did not occur by chance alone. Participant responses to the following 11 potentially sensitive questions were compared between the first and second interview:

‘Have you ever had a genital ulcer?’ yes/no

‘Have you ever had an abnormal urethral or vaginal discharge?’ yes/no

‘Have you ever had any (other) sexually transmitted diseases?’ yes/no

‘Have you ever been tested for HIV infection?’ yes/no

‘How often do you usually drink alcohol?’ (binary variable created with 1, drink at least once a week; 0, drink less than once a week/do not drink alcohol)

‘How often do you get drunk?’ (binary variable created with 1, get drunk at least once a week; 0, get drunk less than once a week/do not get drunk)

‘Have you ever exchanged money, goods, shelter, or anything else for sex?’ yes/no

‘Have you tried to obtain condoms in the past 3 months?’ yes/no

‘In the past 3 months, have you used drugs to get high?’ yes/no

‘Do you personally know or have you known someone with HIV or AIDS?’ yes/no
How likely is it that you will become infected with HIV? (binary variable created with 1, likely, somewhat likely, very likely, I am already infected with HIV; 0, unlikely, not likely at all, very unlikely, somewhat unlikely).

Sex behavior questions were also compared between the first and second interview, including 'Have you ever had sexual intercourse?', 'With how many different people have you had sexual intercourse during the past year?', and 'With how many different people have you had sexual intercourse during the past 3 months? The number of unprotected acts in the past 3 months was determined on the basis of the reported frequency of sex in the past 3 months and the number of times a condom was used. For participants who reported they had never had sex, the number of partners and the number of unprotected acts were coded as zero. The number of unprotected acts was also coded as zero for participants who reported no partners in the past 3 months.

For binary outcomes, the pattern of yes–no or 1–0 responses given by participants over time was examined (same response on each interview, 'no'/0 on the first interview but 'yes'/1 on the second, 'yes'/1 on the first interview but 'no'/0 on the second). Statistical significance for the null hypothesis of no difference in responses between the ACASI and CAPI methods was determined by Prescott’s test [31,32]. For continuous variables (e.g. unprotected acts, number of partners), the difference between the first and second interview period responses (ACASI minus CAPI or CAPI minus ACASI) was calculated for each individual. These period differences were then compared for the two groups (ACASI first versus CAPI first), with statistical significance for a difference in responses between the two groups determined by the Wilcoxon rank sum test [31,32]. Exact tests to determine statistical significance were used for all countries except China, where the normal approximation was used because of the larger sample size.

Results

Audio computer-assisted self-interviewing feasibility study

During the study period, August–October 2000, 30 market workers in Fuzhou, China, 40 residents from slum communities in Chennai, India, 30 young adults from barrios in Lima and Chiclayo, Peru, and 30 students from vocational and trade school dormitories in St Petersburg, Russia, participated in the ACASI feasibility study. Approximately equal numbers of men and women participated in each country (Table 1). Participants in China and India were older than those in Peru and Russia and more were married, reflecting the higher age range.

In general, those selected in China and India had little previous experience with computers, whereas the young, well-educated students in Russia had a high degree of computer literacy, and most participants in Peru had previous exposure to computers. The median time required to complete the same questionnaire translated into the local language was 17 min in Russia, 24 min in China, 25 min in Peru, and 35 min in India. This wide range may reflect differential ease in completing the interview, difficulties in understanding some questions at some sites, or cultural differences in the tendency to ponder questions or to take the interview seriously.

In each country, few questions had more than one ‘Don’t know’ or ‘Refuse’ response. In China and India, four to seven people responded ‘Don’t know’ on each of three questions related to STD testing (ever been tested for syphilis, gonorrhea, other STD), although the question ‘Have you ever been tested for HIV infection?’ was answered by all in India, and only one in China indicated ‘Don’t know’. Two participants from Russia answered ‘Don’t know’ to ‘Have you ever had sexual intercourse?’ perhaps reflecting ambiguity over whether the withdrawal method of contraception or oral sex constitute sex acts. Among those who said they had ever had sex, few refused to answer any of the potentially sensitive questions.

Table 1. Audio computer-assisted self-interviewing feasibility study: respondent characteristics.

<table>
<thead>
<tr>
<th></th>
<th>China</th>
<th>India</th>
<th>Peru</th>
<th>Russia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>30</td>
<td>40</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Time to complete ACASI (min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>24</td>
<td>35</td>
<td>25</td>
<td>17</td>
</tr>
<tr>
<td>Range</td>
<td>14–41</td>
<td>10–55</td>
<td>14–48</td>
<td>10–32</td>
</tr>
<tr>
<td>Male</td>
<td>15/30</td>
<td>50</td>
<td>21/40</td>
<td>53</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>29</td>
<td>27</td>
<td>22</td>
<td>19</td>
</tr>
<tr>
<td>Range</td>
<td>19–40</td>
<td>18–42</td>
<td>17–33</td>
<td>17–22</td>
</tr>
<tr>
<td>Married</td>
<td>20/30</td>
<td>67</td>
<td>29/40</td>
<td>73</td>
</tr>
<tr>
<td>Ever had sex ‘yes’</td>
<td>7/29*</td>
<td>24</td>
<td>22/40</td>
<td>55</td>
</tr>
<tr>
<td>Married, ever had sex ‘yes’</td>
<td>6/19</td>
<td>32</td>
<td>17/29</td>
<td>59</td>
</tr>
<tr>
<td>Married, ever had sex ‘yes’ (female)</td>
<td>2/8</td>
<td>25</td>
<td>7/15</td>
<td>47</td>
</tr>
</tbody>
</table>

ACASI, Audio computer-assisted self-interviewing.

*One participant from China, one from Peru, and two from Russia answered ‘Don’t know’.
about sexual history, including number of partners and condom use. No Refuse responses were given in China, and when they occurred in the other countries, typically no more than two people refused to answer a particular question. In China and India, however, participants appeared to give inconsistent responses to the question regarding sexual activity. Only a fraction of married respondents in these countries reported that they had ever had sex: 32% (6/19) in China and 59% (17/29) in India.

The majority of participants in each country reported a high level of comfort entering their answers into the computer (Table 2), ranging from 82% in India to 100% in Russia. When asked whether the computer ensures sufficient privacy, approximately 40% in China, India, and Peru, and only 23% in Russia responded Yes, absolutely. In China, Peru, and Russia, 60% or more of participants felt the computer provided more privacy in answering questions, would be better for getting honest answers to questions on topics such as sexual behavior and drug and alcohol use, and said they would prefer answering these types of questions with a computer compared with an interviewer. In India, although approximately 20–30% agreed, roughly 40–60% felt the computer and an interviewer gave the same amount of privacy, would result in equally honest answers, and did not have a preference for the interview mode. Most participants said they would prefer to hear a female voice, although in Peru approximately equal numbers said they did not have a preference. Between 67 and 77% of participants indicated that they had been Absolutely honest in answering the questions in the interview.

In response to findings in the ACASI feasibility study, we made several improvements to the ACASI computer program before the crossover study:

<table>
<thead>
<tr>
<th>Question</th>
<th>China N = 30</th>
<th>India N = 40</th>
<th>Peru N = 30</th>
<th>Russia N = 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>How easy was it for you to hear the questions?</td>
<td>Very easy or easy</td>
<td>23/30 (77%)</td>
<td>32/38 (84%)</td>
<td>29/30 (97%)</td>
</tr>
<tr>
<td>How easy was it to answer the questions using the computer?</td>
<td>Very easy or easy</td>
<td>25/30 (83%)</td>
<td>28/40 (70%)</td>
<td>29/30 (97%)</td>
</tr>
<tr>
<td>How comfortable did you feel entering your answers into the computer?</td>
<td>Very comfortable or comfortable</td>
<td>26/30 (87%)</td>
<td>31/38 (82%)</td>
<td>29/30 (97%)</td>
</tr>
<tr>
<td>Do you think that using the computer ensures sufficient privacy?</td>
<td>Yes, absolutely</td>
<td>11/29 (38%)</td>
<td>17/39 (44%)</td>
<td>13/30 (43%)</td>
</tr>
<tr>
<td></td>
<td>Perhaps</td>
<td>9/29 (31%)</td>
<td>9/39 (23%)</td>
<td>11/30 (37%)</td>
</tr>
<tr>
<td></td>
<td>It probably does</td>
<td>3/29 (10%)</td>
<td>9/38 (24%)</td>
<td>23/29 (79%)</td>
</tr>
<tr>
<td></td>
<td>No, absolutely not</td>
<td>10/30 (33%)</td>
<td>24/39 (62%)</td>
<td>6/29 (21%)</td>
</tr>
<tr>
<td>Which do you feel gives you more privacy in answering questions: a computer or an interviewer?</td>
<td>Computer</td>
<td>18/30 (60%)</td>
<td>9/36 (25%)</td>
<td>19/29 (66%)</td>
</tr>
<tr>
<td></td>
<td>Interviewer</td>
<td>4/30 (13%)</td>
<td>9/36 (25%)</td>
<td>3/29 (10%)</td>
</tr>
<tr>
<td>Answers are equally honest with both</td>
<td>Yes, absolutely</td>
<td>10/30 (33%)</td>
<td>19/37 (51%)</td>
<td>4/30 (13%)</td>
</tr>
<tr>
<td></td>
<td>It probably does</td>
<td>7/30 (23%)</td>
<td>7/36 (19%)</td>
<td>1/30 (3%)</td>
</tr>
<tr>
<td></td>
<td>No, absolutely not</td>
<td>13/30 (43%)</td>
<td>18/36 (50%)</td>
<td>7/29 (24%)</td>
</tr>
<tr>
<td>Which do you feel would be better for getting honest answers to questions topics like sexual behavior, and drug and alcohol use: a computer or an interviewer?</td>
<td>Computer</td>
<td>18/30 (60%)</td>
<td>8/39 (21%)</td>
<td>19/29 (66%)</td>
</tr>
<tr>
<td></td>
<td>Interviewer</td>
<td>3/30 (10%)</td>
<td>7/39 (18%)</td>
<td>0</td>
</tr>
<tr>
<td>I feel equally comfortable with both</td>
<td>Yes, absolutely</td>
<td>10/30 (33%)</td>
<td>24/39 (62%)</td>
<td>10/29 (34%)</td>
</tr>
<tr>
<td></td>
<td>It probably does</td>
<td>5/30 (17%)</td>
<td>21/39 (54%)</td>
<td>6/29 (21%)</td>
</tr>
<tr>
<td>Would you prefer to hear questions asked with a female voice or a male voice?</td>
<td>Female voice</td>
<td>19/30 (63%)</td>
<td>25/40 (63%)</td>
<td>13/30 (43%)</td>
</tr>
<tr>
<td></td>
<td>Male voice</td>
<td>1/30 (3%)</td>
<td>10/40 (25%)</td>
<td>5/30 (17%)</td>
</tr>
<tr>
<td>I do not have a preference</td>
<td>Yes, absolutely</td>
<td>10/30 (33%)</td>
<td>5/40 (13%)</td>
<td>12/30 (40%)</td>
</tr>
<tr>
<td>How honest have you been in answering the questions in this interview?</td>
<td>Absolutely honest</td>
<td>20/30 (67%)</td>
<td>26/39 (67%)</td>
<td>22/30 (73%)</td>
</tr>
<tr>
<td></td>
<td>Somewhat honest</td>
<td>7/30 (23%)</td>
<td>10/39 (26%)</td>
<td>7/30 (23%)</td>
</tr>
</tbody>
</table>

*All possible response choices are shown in brackets. Counts and percentages are not shown for all choices.
Participants were forced to enter a response (can include 0, Refuse, Don’t know) for questions requiring a numerical response or when error messages appeared. Previously, participants in the feasibility study could press ‘Enter’ without actually entering a numeric value and the system assigned a value of ‘0’.

Edit checks were included for questions to prevent an answer from being inconsistent with the response to the previous question (just before the current question). In the feasibility study, edit checks were not included; for example, individuals could indicate that they had had sex five times and used a condom 10 of those times.

Refuse/Don’t know answers in the feasibility study allowed the respondent to skip out as though the answer had been ‘No’. In the crossover study, participants were forced to answer subsequent related questions (in most cases).

A number box was added to the ACASI screen to allow participants to see the number they were entering for questions requiring a numerical response.

Several sites retranslated the questionnaire incorporating more colloquial language.

If a participant did not answer a question after approximately 60 s, the question was repeated.

Additional text was added before asking the first question on sex (ever had sexual intercourse) to provide a transition into the sensitive questions. If the participant took a long time to answer the sex questions, additional text appeared encouraging participants to answer these sensitive questions in a truthful manner.

The screen saver and monitor power-saver settings were disabled on the computer so that screens did not go blank when a participant took additional time to answer a question.

Crossover audio computer-assisted self-interviewing versus computer-assisted personal interviewing comparison study

Between December 2000 and May 2001, a total of 445 volunteers in five countries participated in the crossover study, with sample sizes ranging from 54 people in Zimbabwe to 199 in China. The two randomized groups (ACASI first and CAPI first) were similar with respect to sex and age, demonstrating the success of the local randomizations (Table 3).

The median time (minutes) required to complete the ACASI was longer than for the CAPI in all countries except Russia (ACASI versus CAPI, China: 18 versus 12, India: 32 versus 15, Peru: 20 versus 13, Russia: 11 for each, Zimbabwe: 25 versus 11). Notably, in India and Zimbabwe, the interviews took twice as long to complete on ACASI compared with CAPI. In Russia, investigators felt that the rapid completion time on both modes may suggest that insufficient attention was paid to the task or, alternatively, that the Russian students were more familiar with computer technology.

The pattern of participant response pairs on the ACASI and CAPI was examined for 11 potentially sensitive questions concerning STD history, alcohol and drug use, sex trade, the purchase of condoms, and the likelihood of becoming HIV infected (see Methods). The majority of respondents gave the same answer to these questions at both interviews. No statistically significant differences were found between the ACASI and CAPI responses to

<table>
<thead>
<tr>
<th>Country</th>
<th>Sex</th>
<th>Count</th>
<th>%</th>
<th>Count</th>
<th>%</th>
<th>P value*</th>
<th>Median</th>
<th>Range</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>China (N=199)</td>
<td>ACASI first</td>
<td>55/100</td>
<td>55</td>
<td>45/100</td>
<td>45</td>
<td>1.0</td>
<td>28</td>
<td>18-40</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>CAPI first</td>
<td>54/99</td>
<td>55</td>
<td>45/99</td>
<td>45</td>
<td></td>
<td>30</td>
<td>18-40</td>
<td></td>
</tr>
<tr>
<td>India (N=63)</td>
<td>ACASI first</td>
<td>13/29</td>
<td>45</td>
<td>17/29</td>
<td>55</td>
<td>0.8</td>
<td>29</td>
<td>18-40</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>CAPI first</td>
<td>17/34</td>
<td>50</td>
<td>16/34</td>
<td>50</td>
<td></td>
<td>28.5</td>
<td>20-40</td>
<td></td>
</tr>
<tr>
<td>Peru (N=69)</td>
<td>ACASI first</td>
<td>14/31</td>
<td>45</td>
<td>17/31</td>
<td>55</td>
<td>0.6</td>
<td>22</td>
<td>18-30</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>CAPI first</td>
<td>20/38</td>
<td>53</td>
<td>18/38</td>
<td>47</td>
<td></td>
<td>22</td>
<td>18-30</td>
<td></td>
</tr>
<tr>
<td>Russia (N=60)</td>
<td>ACASI first</td>
<td>16/30</td>
<td>53</td>
<td>14/30</td>
<td>47</td>
<td>0.8</td>
<td>20</td>
<td>18-24</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>CAPI first</td>
<td>14/30</td>
<td>47</td>
<td>16/30</td>
<td>53</td>
<td></td>
<td>19</td>
<td>18-24</td>
<td></td>
</tr>
<tr>
<td>Zimbabwe (N=54)</td>
<td>ACASI first</td>
<td>12/26</td>
<td>46</td>
<td>14/26</td>
<td>54</td>
<td>1.0</td>
<td>20</td>
<td>16-29</td>
<td>0.9</td>
</tr>
<tr>
<td></td>
<td>CAPI first</td>
<td>12/28</td>
<td>43</td>
<td>16/28</td>
<td>57</td>
<td></td>
<td>20</td>
<td>16-29</td>
<td></td>
</tr>
</tbody>
</table>

*P value for a difference between the audio computer-assisted self-interviewing (ACASI) first and computer-assisted personal interviewing (CAPI) first groups on sex by Fisher’s exact test; on age by the Wilcoxon rank sum test.
Table 4. Crossover audio computer-assisted self-interviewing versus computer-assisted personal interviewing comparison study: sex behavior outcomes by randomized group for China, India and Peru.

<table>
<thead>
<tr>
<th>Question</th>
<th>China</th>
<th></th>
<th></th>
<th>India</th>
<th></th>
<th></th>
<th>Peru</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes ACASI</td>
<td>Yes CAPI</td>
<td>Same on both</td>
<td>Yes ACASI</td>
<td>Yes CAPI</td>
<td>Same on both</td>
<td>Yes ACASI</td>
<td>Yes CAPI</td>
<td>Same on both</td>
</tr>
<tr>
<td>Ever had sex?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACASI first</td>
<td>3 (3%)</td>
<td>19 (19%)</td>
<td>78 (78%)**</td>
<td>1 (3%)</td>
<td>1 (3%)</td>
<td>47 (93%)</td>
<td>1 (3%)</td>
<td>1 (3%)</td>
<td>47 (85%)</td>
</tr>
<tr>
<td>CAPI first</td>
<td>2 (2%)</td>
<td>23 (23%)</td>
<td>73 (74%)</td>
<td>0</td>
<td>5 (15%)</td>
<td>29 (85%)</td>
<td>3 (8%)</td>
<td>0</td>
<td>35 (92%)</td>
</tr>
<tr>
<td>No. of partners in past year</td>
<td>Higher on ACASI</td>
<td>Higher on CAPI</td>
<td>Same on both</td>
<td>Higher on ACASI</td>
<td>Higher on CAPI</td>
<td>Same on both</td>
<td>Higher on ACASI</td>
<td>Higher on CAPI</td>
<td>Same on both</td>
</tr>
<tr>
<td>ACASI first</td>
<td>10 (10%)</td>
<td>20 (20%)</td>
<td>68 (69%)**</td>
<td>5 (19%)</td>
<td>3 (11%)</td>
<td>19 (70%)</td>
<td>6 (21%)</td>
<td>2 (7%)</td>
<td>21 (72%)**</td>
</tr>
<tr>
<td>CAPI first</td>
<td>5 (5%)</td>
<td>22 (22%)</td>
<td>71 (72%)</td>
<td>0</td>
<td>8 (26%)</td>
<td>23 (74%)</td>
<td>5 (13%)</td>
<td>0</td>
<td>33 (87%)</td>
</tr>
<tr>
<td>No. of partners in past 3 months</td>
<td>Higher on ACASI</td>
<td>Higher on CAPI</td>
<td>Same on both</td>
<td>Higher on ACASI</td>
<td>Higher on CAPI</td>
<td>Same on both</td>
<td>Higher on ACASI</td>
<td>Higher on CAPI</td>
<td>Same on both</td>
</tr>
<tr>
<td>ACASI first</td>
<td>2 (2%)</td>
<td>18 (18%)</td>
<td>79 (80%)**</td>
<td>0</td>
<td>1 (4%)</td>
<td>24 (96%)</td>
<td>5 (17%)</td>
<td>7 (24%)</td>
<td>17 (59%)</td>
</tr>
<tr>
<td>CAPI first</td>
<td>5 (5%)</td>
<td>23 (23%)</td>
<td>70 (71%)</td>
<td>4 (13%)</td>
<td>6 (19%)</td>
<td>21 (68%)</td>
<td>7 (19%)</td>
<td>1 (3%)</td>
<td>29 (78%)</td>
</tr>
<tr>
<td>No. of unprotected acts in past 3 months</td>
<td>Higher on ACASI</td>
<td>Higher on CAPI</td>
<td>Same on both</td>
<td>Higher on ACASI</td>
<td>Higher on CAPI</td>
<td>Same on both</td>
<td>Higher on ACASI</td>
<td>Higher on CAPI</td>
<td>Same on both</td>
</tr>
<tr>
<td>ACASI first</td>
<td>16 (18%)</td>
<td>31 (35%)</td>
<td>42 (47%)**</td>
<td>7 (33%)</td>
<td>2 (10%)</td>
<td>12 (57%)</td>
<td>8 (28%)</td>
<td>2 (7%)</td>
<td>23 (70%)</td>
</tr>
<tr>
<td>CAPI first</td>
<td>15 (16%)</td>
<td>27 (29%)</td>
<td>51 (55%)</td>
<td>5 (20%)</td>
<td>6 (24%)</td>
<td>14 (56%)</td>
<td>6 (18%)</td>
<td>4 (12%)</td>
<td>23 (70%)</td>
</tr>
</tbody>
</table>

*Individuals lacking a response to the same question on one or both interviews could not be included in the counts for that question. Therefore, the total number of participants in each group does not always add up to the number randomized.

*Response was ‘yes’ on the audio computer-assisted self-interviewing (ACASI) and ‘no’ on the computer-assisted personal interviewing (CAPI).

*Response was ‘yes’ on the CAPI and ‘no’ on the ACASI.

*P ≤ 0.05 for a difference between ACASI and CAPI responses by the Wilcoxon rank sum test.

**P ≤ 0.01 for a difference between ACASI and CAPI responses by Prescott’s test (Ever had sex) or the Wilcoxon rank sum test.
any of these questions in any country except for one question in Peru. For example, in response to ‘Have you ever been tested for HIV infection?’ most people said ‘No’ on both interviews or ‘Yes’ on both interviews, with only one to four people (depending on the country) saying ‘No’ on one interview and ‘Yes’ on the other. In Peru, in response to ‘How likely is it that you will become HIV infected?’ six participants said ‘likely’ with CAPI but ‘unlikely’ with ACASI ($P = 0.04$).

ACASI and CAPI responses to ‘Have you ever had sex?’ and three other sexual behavior outcomes were compared for each study site (Table 4 and Table 5). Consistent differences in responses by interview mode occurred only in China, where more participants reported ever having sex, a greater number of partners in the past year and in the past 3 months, and a greater number of unprotected sex acts in the past 3 months on CAPI than they did on ACASI ($P < 0.01$ for each). In most cases when a difference in the number of partners was reported, only one more partner was reported on the CAPI compared with the ACASI.

No significant differences were found between ACASI and CAPI responses on any of the four sexual behavior outcomes in India or Zimbabwe. Most people said ‘Yes’ on both interviews or ‘No’ on both interviews to ‘Have you ever had sex?’ and for most, the same number of partners and unprotected acts were reported on each interview. In Peru, a statistically significant difference between interview methods was found for the number of partners in the past year ($P = 0.02$). Among the participants whose responses changed from one interview to the next, a larger number of partners was reported at ACASI than at CAPI, although in most cases only one more partner was reported. Although not statistically significant, there was a trend to report more unprotected acts in the past 3 months on ACASI compared with CAPI ($P = 0.06$). Differences were not found in Peru on the other two sexual behavior outcomes. All Russian participants reported the same response on both of their interviews to ‘Have you ever had sex?’, and no differences were found by interview mode on the number of partners or the number of unprotected acts in the past 3 months. In Peru, in response to ‘Have you ever had sex?’, six participants said ‘likely’ with CAPI but ‘unlikely’ with ACASI ($P = 0.04$).

**Table 5.** Crossover audio computer-assisted self-interviewing versus computer-assisted personal interviewing comparison study: sex behavior outcomes by randomized group for Russia and Zimbabwe.

<table>
<thead>
<tr>
<th>Question†</th>
<th>Russia</th>
<th></th>
<th></th>
<th></th>
<th>Zimbabwe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes ACASI No CAPI$^a$</td>
<td>Yes ACASI No ACASI</td>
<td>Same on both</td>
<td>Yes ACASI No CAPI</td>
<td>Yes ACASI No ACASI</td>
</tr>
<tr>
<td>Ever had sex?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACASI first</td>
<td>0</td>
<td>0</td>
<td>30 (100%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CAPI first</td>
<td>0</td>
<td>0</td>
<td>28 (100%)</td>
<td>1 (4%)</td>
<td>0</td>
</tr>
<tr>
<td>No. of partners in past year</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACASI first</td>
<td>2 (7%)</td>
<td>7 (23%)</td>
<td>21 (70%)$^*$</td>
<td>2 (8%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>CAPI first</td>
<td>2 (7%)</td>
<td>5 (18%)</td>
<td>21 (75%)</td>
<td>3 (11%)</td>
<td>0</td>
</tr>
<tr>
<td>No. of partners in past 3 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACASI first</td>
<td>2 (7%)</td>
<td>3 (11%)</td>
<td>23 (82%)</td>
<td>2 (8%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>CAPI first</td>
<td>6 (21%)</td>
<td>2 (7%)</td>
<td>20 (71%)</td>
<td>2 (7%)</td>
<td>0</td>
</tr>
<tr>
<td>No. of unprotected acts in past 3 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACASI first</td>
<td>3 (12%)</td>
<td>5 (20%)</td>
<td>17 (68%)</td>
<td>0</td>
<td>2 (9%)</td>
</tr>
<tr>
<td>CAPI first</td>
<td>2 (9%)</td>
<td>1 (4%)</td>
<td>20 (87%)</td>
<td>7 (27%)</td>
<td>3 (12%)</td>
</tr>
</tbody>
</table>

$^a$Individuals lacking a response to the same question on one or both interviews could not be included in the counts for that question. Therefore, the total number of participants in each group does not always add up to the number randomized.

$^b$Response was ‘yes’ on the audio computer-assisted self-interviewing (ACASI) and ‘no’ on the computer-assisted personal interviewing (CAPI).

$^c$Response was ‘yes’ on the ACASI and ‘no’ on the CAPI.

$^*P \leq 0.05$ for a difference between ACASI and CAPI responses by the Wilcoxon rank sum test.

**Discussion**

We conducted a feasibility study to determine whether ACASI could be used successfully to conduct interviews containing potentially sensitive questions in diverse settings in China, India, Peru, and Russia, and a randomized crossover study to compare results obtained by ACASI versus CAPI in the same four countries plus Zimbabwe. Despite the varying levels of literacy and exposure to computers by country, most feasibility study
participants reported that it was easy to enter their answers into the computer, that they felt comfortable doing so, and that they preferred the computer rather than an interviewer for answering questions about topics such as sexual behavior and drug and alcohol use, or had no preference. In the crossover study, most participants gave the same responses on both their ACASI and CAPI. Only in China did responses on sexual behavior outcomes differ consistently by interview mode, with more people reporting sexual activity and a greater number of partners at CAPI.

Both studies indicated that it was possible to use ACASI in the settings selected in each of the five countries. ACASI is a more standardized method of assessment because with CAPI interviewers may use probes beyond the standard set even though they are instructed not to do so. ACASI may, however, present problems for people with low educational levels if they cannot clarify a question that they do not understand. Nevertheless, both ACASI and CAPI can be used with people who are not literate, and both interview modes simplify response input over self-administered questionnaires because data are entered in real time and do not require remote data entry at a later time. Accordingly, both ACASI and CAPI lead to fewer data entry errors because the skip patterns are programmed into the computer and are executed as the interview is administered. Although ACASI provides a more private experience for participants, and less staff time is required to administer ACASI questionnaires because they are self-administered, ACASI generally takes longer to administer than CAPI. We found this in all research sites with the exception of Russia, where the participants had more exposure to technology and, as they were students, were of a younger age. Alternatively, the Russian students may have paid less attention to the task; it is not known what reason accounts for the similar time in responding to the surveys.

On the basis of our results, the Trial leadership decided to use ACASI for the first epidemiological study in Peru, Russia, and Zimbabwe and use CAPI in China and India. To ensure a common method of administration of assessments during the Trial, however, investigators adopted CAPI as the standard for all subsequent assessments. This was largely driven by the inconsistent findings in China, and the longer duration of the interviews in most countries for ACASI compared with CAPI. It should be noted that the number of people who participated in the crossover study was approximately three times as large in China as in the other countries, which may have increased our ability to detect interview mode differences in that country. Even without considering statistical test results, a difference by mode appears more consistent across the four sexual behavior outcomes in China, and statistical test results were not considered when making the decision to use CAPI during the Trial. Most importantly, few differences in responses were found in general between the two methods in the other countries, and in all countries we did not find the consistently higher reporting rates of sensitive sexual behaviors on ACASI that had been anticipated. This lack of differential in reporting among participants in the other countries was important in our selection of CAPI for the Trial.

References


The community popular opinion leader HIV prevention programme: conceptual basis and intervention procedures

The NIMH Collaborative HIV/STD Prevention Trial Group*

Objective: To describe the community popular opinion leader (C-POL) intervention employed in the NIMH Collaborative HIV/STD Prevention Trial, including its theoretical, conceptual, and empirical basis, intervention procedures and methods, core elements, and how its content was culturally tailored to address the needs of varied populations.

Design: The programme is designed to identify, recruit, train, and intensively engage C-POLs of a target population to convey HIV risk reduction messages to people in their communities, with the intention of reducing high-risk behavior at a population level.

Methods: Based on the diffusion of innovation theory, the intervention identified, trained, and engaged C-POL within a high-risk community population to advocate, recommend, and endorse the importance of safer behavior to other members of the same population. Nine core elements of the intervention are discussed. Data collected during rapid ethnography were used to adapt the content of the intervention for food market owners and workers in China, male patrons of wine shops and at-risk women congregating nearby in India, young people in social gathering venues in Peruvian barrios, dormitory students in Russia, and people congregating in commercial areas of growth points in Zimbabwe.

Results: The C-POL intervention model taps into community strengths, altruism, and people’s desire to do something to help fight against AIDS. With few exceptions, C-POLs participated enthusiastically in the training sessions and reported having conversations in the community.

Conclusion: Rapid ethnography can be used to tailor an intervention to diverse settings while maintaining fidelity to the core elements of the intervention.

Introduction

The NIMH Collaborative HIV/STD Prevention Trial (hereafter the Trial) is a two-arm randomized outcome study evaluating the impact of a common community-level risk reduction intervention implemented in vulnerable target populations in five countries: China, India, Peru, Russia, and Zimbabwe. The community populations included in the Trial were: (i) food market stall owners and workers in China; (ii) male patrons of wine shops and at-risk women congregating near the shops in India; (iii) young men and women in social gathering points in barrios (neighborhoods) in Peru; (iv) trade and vocational school students living in slumlike dormitories in Russia; and (v) people congregating in commercial areas of growth points in Zimbabwe. Intensive ethnographic and epidemiological formative studies established high levels of unprotected sex with non-spousal partners, frequent exchange of sex for valuables, high rates of sexually transmitted diseases (STDs), and high vulnerability to HIV infection in these target populations, and led to their selection for the Trial [1–3]. The Trial’s objective was to determine the effects of a community-level HIV prevention intervention on two primary endpoints: STD incidence and the percentage of population members who report engaging in unprotected sexual acts with non-spousal partners [4].

The purpose of this article is to describe the intervention employed in the Trial, including its theoretical, conceptual, and empirical basis, intervention procedures and methods, core elements, and how its content was culturally tailored to address the needs of varied populations.
conceptual, and empirical basis, intervention procedures and methods, core or essential elements of the intervention, and how certain aspects of the intervention were culturally tailored to address the needs of varied populations. Although the study spanned five countries on four continents, it was unique in that a common intervention model was tested across all sites. The intervention identified, recruited, trained, and intensively engaged cadres of community popular opinion leaders (C-POLs) of a target population to convey HIV risk reduction messages to people in their communities with the intention of reducing high-risk behavior at a population level.

**Theoretical and conceptual basis of the community popular opinion leader intervention model**

Initially, peer-based HIV prevention interventions focused on disseminating information rather than on using social influence to promote behavior change. Research suggests that information alone often does not result in behavior change. The principles of the C-POL intervention are grounded in the ‘diffusion of innovation theory’, a conceptual framework developed by Rogers [5] and used for more than 30 years as a model to explain how new technological and behavioral innovations are initiated and become adopted, accepted, and normative within community populations. In a variety of marketing, agricultural, social, community, and economic development contexts, Rogers [5] found that innovations often originate with the subset of population members who are its opinion leaders: trusted trendsetters whose actions, attitudes, and views influence those of other members through interactions in existing social relationships. In this sense, C-POLs are therefore models whose views are naturally observed and emulated. In the theory of Rogers [5], opinion leaders are considered to be effective innovators of behavioral trends because they are naturally and widely liked, are perceived as similar, and therefore are able to influence normative perceptions of the population. His studies established that new trends originally adopted by opinion leaders first influence those population members most open to innovation (termed ‘early adopters’) and then, over time, the innovation gradually diffuses to influence and shift the actions of larger proportions of the population. As this takes place, the formerly new and innovative behavior becomes widely normative.

Various factors can influence the speed and efficiency of innovation diffusion. These factors include whether the opinion leaders’ adoption of the innovative behavior can be readily observed, whether the innovation becomes adopted across multiple population segments, the extent and nature of social communication patterns among population members, and the expected consequences of adopting the innovation. The theory of Rogers [5] suggests that new behavioral trends are most efficiently established after a ‘critical mass’ of opinion leaders has adopted the innovation. Approximately 15% of a population are usually opinion leaders and early adopters, suggesting that this critical mass creates optimal circumstances for the adoption of an innovation by others.

Diffusion of innovation was first applied to HIV prevention in a series of community-level outcome trials conducted by Kelly and colleagues [6–8] and Sikkema et al. [9] in the United States over the past 15 years. Within a population vulnerable to HIV/AIDS that is presently characterized by high levels of unsafe sexual behavior, the behavioral innovations that one seeks to encourage are reductions in high-risk sexual practices and increases in protective behavior among those who are sexually active. On the basis of a diffusion theory model, this trend can become established and will become normative if enough opinion leaders in the presently at-risk population are known by others to endorse and support the value of risk reduction behavior change. Initial tests of this approach were first carried out in gay communities in three small southern cities [7,8], and the model was later rigorously evaluated in a randomized community-level intervention outcome trial undertaken in eight small US cities [6]. In each of these studies, the baseline prevalence of high-risk sexual behavior practices in large community samples of men who have sex with men was determined by surveying all men entering all gay bars in all of the study cities. These surveys revealed that risky practices initially were both common and frequent in the community target populations. The intervention implemented in these studies first identified which members of the target population of men in the clubs were its popular opinion leaders. Observations and nominations made by club bartenders and key informants directly knowledgeable about individuals frequenting the bars, ethnographic observations made by field staff, and the recommendations of known opinion leaders were used to identify popular opinion leaders. Study staff then recruited successive waves of popular opinion leaders to attend a series of five weekly group sessions that provided training, guidance, and inspiration to deliver sustained HIV prevention messages to friends, acquaintances, and others during everyday conversations.

Although diffusion theory provides a framework for conceptualizing the process by which population behavior and norm change can be instigated by the opinion leaders of a community population, it does not directly address the question of what the opinion leaders should say to influence others, especially about making changes in sexual behaviors that are private and are not directly observable. Both social cognitive theory [10] and the theory of reasoned action [11] have shown that constructs such as...
knowledge, attitudes, beliefs, intentions, normative perceptions, skills, and perceived self-efficacy predict individuals’ adoption of AIDS-preventive behavior changes. Consequently, popular opinion leaders in the gay bar studies were trained to deliver conversational messages that personally recommended and endorsed the value of making risk reduction behavior changes in their communications with others. Across this set of studies, follow-up surveys of all men patronizing intervention city bars revealed significant population-level increases in condom use, and reductions in both the prevalence and frequency of high-risk sexual behavior, usually at a magnitude of approximately 30% change from baseline. Evidence of these effects was present 12 months post-intervention [6] and continued to be observed even 3 years later [12].

Positive effects of HIV prevention interventions based on the popular opinion leader model have also been found in controlled trials with other populations in the United States. Sikkema et al. [9] conducted an outcome study with 690 impoverished inner-city women who lived in 18 low-income housing developments, nine of which received only standard HIV educational materials and nine of which received an intervention that, in addition to other components, identified and trained opinion leaders among its residents to deliver AIDS preventive messages in conversations with neighbors. At a 12-month follow-up, risk-assessment surveys of women living in all 18 of the housing developments showed, for women in intervention developments, large reductions in the proportion who had any unprotected intercourse and in their frequency of unprotected sex, and an increased use of condoms. These results, together with findings of a similar intervention among male commercial sex workers in New York [13], have collectively established the efficacy of HIV risk reduction interventions based on the popular opinion leader model with at-risk populations in the United States.

**Rationale for the community popular opinion leader model for HIV prevention in developing and transitional countries**

Ninety-six per cent of the world’s HIV infections have occurred outside of north America, primarily in impoverished developing countries and in countries undergoing difficult social and structural transitions [14]. Large segments of the population in these regions are at imminent risk of contracting HIV, and intervention programmes that can reach vulnerable population segments are especially critical. HIV prevention and service resources in these areas are, however, often limited. A recent study of major HIV service provider non-governmental organizations (NGO) in the capitals or largest cities of countries in Africa, central/eastern Europe, Latin America, and the Caribbean, including many countries hard hit by AIDS, revealed that the median budget for NGO HIV prevention programmes was less than US$46,000 per year [15]. Although this underscores the need to provide better funding for international HIV prevention efforts, it also argues for the development of community-level interventions that are not only cost-effective but also feasible given the limited resources of NGO and other community service providers.

The C-POL intervention does not require technological resources or high levels of healthcare professional staffing, is capable of reaching, in their natural social settings, community members who may not be willing or motivated to seek out risk reduction counseling, does not require literacy, and is relatively inexpensive to conduct [16]. Moreover, the model is adaptable across cultures. Although countries and vulnerable communities differ markedly in their languages, risk patterns, behaviors, and values, the notion that certain people in any community population are its opinion leaders and that these individuals can influence the norms and behavior of others through their words and actions is culturally transcendent. The intervention being tested in the Trial mobilizes existing community social resources and ‘people power’ in efforts to prevent HIV/AIDS. An aim of the Trial is to evaluate an intervention model that: (i) can later be disseminated to NGO and other service providers on a global scale; (ii) will be feasible and practical for implementation with diverse communities at risk of HIV and other STDs; and (iii) adds breadth to the repertoire of HIV prevention approaches urgently needed in international public health efforts to prevent these diseases.

**Core elements of the community popular opinion leader intervention model**

The conceptual underpinnings of the C-POL intervention, and the premise that popular opinion leaders of a community can be engaged to communicate HIV prevention messages and thereby reduce the risk levels in their social circles, make common sense and have intuitive appeal. Successful implementation of the intervention, however, requires careful preparatory ethnographic fieldwork, the selection of contained community settings characterized by sustained social interaction, and sufficient resources to sustain intervention activities over a considerable period. The model’s theoretical basis, research studies that have tested the approach, and practical experience gained in previous field implementations collectively indicate that certain core or essential elements must also be present for the C-POL intervention to have significant impact. HIV prevention interventions that have been implemented with fidelity to these core elements
Table 1. Core elements of the community popular opinion leader model.

<table>
<thead>
<tr>
<th>Developing momentum, exposure, and repetition</th>
</tr>
</thead>
<tbody>
<tr>
<td>The intervention is directed to an identifiable target population in well-defined community venues where the population's size can be estimated.</td>
</tr>
<tr>
<td>Ethnographic techniques are systematically used to identify segments of the target population and to identify those individuals who are most popular, well-liked, and trusted by others in each population segment.</td>
</tr>
<tr>
<td>Over the life of the programme, 15% of the target population in the intervention venues is trained as C-POL.</td>
</tr>
<tr>
<td>Delivering effective, theory-based HIV prevention messages</td>
</tr>
<tr>
<td>The programme teaches C-POL skills for initiating HIV risk reduction messages to friends and acquaintances during everyday conversations.</td>
</tr>
<tr>
<td>The training programme teaches C-POL the characteristics of effective behavior-change messages targeting risk-related attitudes, norms, intentions, and self-efficacy. In conversations, C-POL personally endorse the benefits of safer behavior and recommend practical steps needed to implement change.</td>
</tr>
<tr>
<td>Groups of C-POL meet weekly in sessions that use instruction, facilitator modeling, and extensive role play exercises to help them to refine their skills and gain confidence in delivering effective HIV prevention messages. Groups are small enough to provide extensive practice opportunities for all C-POL to shape their communication skills and create comfort in delivering conversational messages.</td>
</tr>
<tr>
<td>Initiating and sustaining risk reduction conversations</td>
</tr>
<tr>
<td>C-POL set goals to engage in risk reduction conversations with friends and acquaintances in the target population between weekly sessions.</td>
</tr>
<tr>
<td>The conversational outcomes of the C-POL are reviewed, discussed, and reinforced at subsequent training sessions. Logos, symbols, or other devices are used as ‘conversation starters’ between C-POL and others.</td>
</tr>
</tbody>
</table>

C-POL, Community popular opinion leader.

have been successful; however, more generic and lower-intensity peer education programmes that incorporated some but not all of the core elements did not produce robust effects [17–19]. For this reason, the intervention for the Trial was designed to incorporate all C-POL core elements, which are shown in Table 1 and have been described elsewhere in greater detail [20].

Developing momentum, exposure, and repetition

The first three C-POL core elements shown in Table 1 reflect factors necessary to ensure broad and continued impact of the intervention: (i) achieving momentum; (ii) ensuring high intervention exposure; and (iii) delivering repeated prevention messages to a high proportion of population members. This intervention targets an identifiable, stable, and non-transient population that can be reached in well-defined community social venues. Because the intervention model requires that a 'critical mass' of the target population's opinion leaders be engaged to diffuse safer behavior innovation messages to others in the same target population, one must first be able to estimate the size of the target population in the community venues, and then recruit 15% of this total population size to function as behavior change advocates. The model attempts to create a community social movement against AIDS that is led by cadres of opinion leaders. If too few leaders are enrolled, trained, and engaged, the intervention is unlikely to achieve critical momentum. To ensure that a sufficient number of C-POLs would be trained and that the 15% threshold would be reached, ethnographers at each site estimated the number of unique individuals present in a study venue over a one-week period, and used that number as the denominator term for determining the size of the required C-POL cadre.

Equally important with respect to model fidelity is selecting, as the 15% to be disseminators of behavior change messages, people who really are the natural community opinion leaders (C-POLs) within the population being targeted. Characteristics that can define individuals as C-POLs include their observed frequency of positive social interactions with other members of the target population (e.g. how often they greet or are greeted by others in a venue and are the ‘center of positive attention’ among others [21]), their reputation as sources of trusted advice to others, their informal social leadership roles with others, their sociometric standing among peers, and the extent to which others are likely to emulate their actions. Sites used up to four methods to identify C-POLs. Field observations made by project staff were used to observe individuals present in a venue who most often and most positively interacted with others and appeared to be sought out by them. Stakeholder or gatekeeper nominations of individuals they knew to be influential with others were sought from those directly familiar, firsthand, with the venue’s population. Population member nominations were also used to identify C-POLs through surveys or questions directed by study staff to individuals present in the venue to determine who the population members considered to be most popular and influential. Finally, individuals could self-nominate to participate provided that field staff concurred that the self-nominated individual met the popularity criteria for being a C-POL.

Even in a single gathering point social venue, populations are likely to be composed of multiple social segments or strata that may be distinguished on the basis of sex, age, ethnicity, race, social affiliation patterns, sexual orientation, social class, and characteristics such as being purchasers of sex, sellers of sex, or other dimensions. Different social segments, groups, or strata often have different opinion leaders. Ethnography was used to identify the multiple social segments present in venues so that opinion leaders were identified and could be drawn proportionately from all segments of the target population. This was accomplished by training field staff to carry out observations in venues to characterize the different population segments present and to observe who the potential C-POLs in each segment were. This process ensured that each population segment was reached through the involvement of a sufficient number of its opinion leaders.
Opinion leaders of a target population are the individuals most liked, trusted, perceived as similar, and popular within their social circles. They are not necessarily safe in their own behavior and may not be viewed as ‘exemplary responsible citizens’ to traditional outsiders. The highest-risk social segments of a community population, those most in need of HIV prevention, would probably be missed by the intervention unless people who are popular and well-liked within very risky segments are fully engaged in the programme.

**Delivering effective, theory-based HIV prevention messages**

Core elements 4, 5, and 6 in Table 1 pertain to the training of C-POLs to communicate effective, theory-based HIV prevention messages. The ‘active ingredient’ responsible for the success of the C-POL model is not just changing the views, knowledge, or behavior of opinion leaders; rather, it is engaging those C-POLs to diffuse effective HIV prevention messages actively, frequently, and skillfully to other members of the target population in the course of everyday conversations. Unlike behavioral innovations that are public and readily observable, sexual risk reduction involves private activities, and opinion leaders can diffuse the endorsement of safer behavior such as the use of condoms and the avoidance of high-risk behaviors primarily by talking about these topics with friends and acquaintances.

Explicit discussion about HIV prevention topics does not necessarily arise during everyday conversation, and the topics may be uncomfortable to discuss. This presents two challenges: helping C-POLs gain motivation and comfort in initiating discussions about sexual risk reduction behavior changes, and the skills needed to communicate those prevention messages in an effective manner that will have a positive impact on the behavior of others.

In the C-POL intervention, groups of opinion leaders met in weekly sessions that were intended first to inspire participants to take on roles as AIDS prevention advocates in their community and then to train and guide the leaders in delivering ongoing, effective risk reduction messages. As in other forms of behavioral and social skills training, accomplishing these goals is best achieved by bringing participants together over multiple group sessions, using interaction, discussion, modeling, and role play interactive techniques to help participants practice and refine their behavioral skills for comfortably delivering HIV prevention messages, and guiding opinion leaders in having real-life conversations with friends, acquaintances, and others between group meetings. Repeated and multiple training sessions afford an opportunity for C-POLs to practice new skills and conversational approaches, discuss in the next group meeting the outcomes of real-life conversations that took place, problem-solve barriers encountered, and both plan and be reinforced for having still more conversations before the next session. Such opportunities would be lost if training took place in a single session, or if ongoing training and follow-up sessions were not well spaced and regular. In order to ensure that all C-POLs have the opportunity for behavioral practice, role playing, skills development, and interactive discussion, sessions had at least two facilitators and not more than 20 C-POLs as attendees.

The potential impact of this intervention approach also rests on what opinion leaders are taught to communicate with others about AIDS—prevention steps and behavior change. In contrast to traditional peer education, in which the messages given are primarily factual and educational, C-POLs were trained during group sessions to introduce prevention endorsement messages into everyday conversations with friends and acquaintances and to convey messages that target the recipient’s AIDS-related knowledge, skills, norms, attitudes, intentions, and self-efficacy. Table 2 lists examples of conversational statements that illustrate each of these domains.

<table>
<thead>
<tr>
<th>Table 2. Examples of conversational statements made by community popular opinion leaders to target psychosocial determinants of risk behavior.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AIDS-related knowledge</strong></td>
</tr>
<tr>
<td>‘AIDS is a serious problem even here’.</td>
</tr>
<tr>
<td>‘No-one can tell by looking if someone has the virus that causes AIDS. Most people with the virus look completely healthy’.</td>
</tr>
<tr>
<td>‘The two ways to avoid AIDS are refraining from sex or using a condom when you have sex’.</td>
</tr>
<tr>
<td><strong>Risk reduction skills</strong></td>
</tr>
<tr>
<td>‘It’s OK to say no to sex when you aren’t sure’.</td>
</tr>
<tr>
<td>‘I always carry condoms with me so they are right there if I need them’.</td>
</tr>
<tr>
<td>‘I always have a little talk with someone ahead of time to be sure they are willing to use condoms’.</td>
</tr>
<tr>
<td><strong>Norms</strong></td>
</tr>
<tr>
<td>‘Everyone I know is taking AIDS more seriously and using condoms’.</td>
</tr>
<tr>
<td>‘I thought it would be hard to bring up using condoms with my partner, but when I did, my partner was relieved, so we used them’.</td>
</tr>
<tr>
<td>‘Everyone is saying that condoms are the new way to show someone that you care about them and that you care about yourself’.</td>
</tr>
<tr>
<td>‘Smart people are expecting even their boyfriends (girlfriends) to use condoms’.</td>
</tr>
<tr>
<td><strong>Attitudes</strong></td>
</tr>
<tr>
<td>‘Condoms make sex better because they take away worry’.</td>
</tr>
<tr>
<td>‘Staying faithful to your one partner makes life a lot easier and protects against AIDS as long as your partner is faithful, too’.</td>
</tr>
<tr>
<td>‘People who use condoms are smart’.</td>
</tr>
<tr>
<td><strong>Intentions</strong></td>
</tr>
<tr>
<td>‘Everyone’s done a lot of foolish things in the past. Being safer in the future is what is important’.</td>
</tr>
<tr>
<td>‘I plan to use condoms from now on, even with a regular partner’.</td>
</tr>
<tr>
<td>‘I will try to stay away from sex if I am drinking too much’.</td>
</tr>
<tr>
<td><strong>Self-efficacy</strong></td>
</tr>
<tr>
<td>‘At first, condoms seem unusual. But, they become the natural, normal thing when I used them regularly’.</td>
</tr>
<tr>
<td>‘It is possible to leave a situation when things seem to get too sexual’.</td>
</tr>
<tr>
<td>‘I thought it would be difficult to buy a condom. But when I went to the pharmacy to get one, they were right there on the shelf, and I could buy it without becoming embarrassed’.</td>
</tr>
</tbody>
</table>
Opinion leaders were also taught to adopt an interaction style in which they offered practical advice to friends about how to make risk reduction behavior changes, to endorse the benefits of safer behavior personally, and to use ‘I’ statements (rather than ‘you should . . .’) to reinforce their personal endorsement of behavior change further when communicating with others. Although C-POL were taught about the characteristics of effective health communication messages, they were encouraged to talk with others in their own natural style, using language with which they were comfortable, framing messages in their own words.

Initiating and sustaining risk reduction conversations

Core elements 7, 8, and 9 shown in Table 1 all pertain to strategies for helping C-POLs carry out risk reduction conversations with others, especially with members of the community target population with whom C-POL are popular and influential. After C-POLs gained proficiency and comfort in delivering theory-based HIV prevention messages during role play practice in the group training sessions, each was asked to establish the goal of talking with a specified number of friends or acquaintances before the next group meeting. (The number of assigned risk reduction conversations increased over the course of C-POL training.) Group facilitators encouraged each C-POL to make these goals concrete by specifying with whom conversations would take place, how they would be initiated, and when or where they would occur. C-POLs monitored their risk reduction endorsement conversations and discussed the outcomes of these conversations during the next group meeting. Facilitators reinforced the successful efforts of C-POLs and problem solved any difficulties encountered. During each subsequent session, C-POLs set goals for talking with more of their friends, acquaintances, and even strangers, reviewed conversational outcomes, and were encouraged to think of themselves as being in the vanguard of HIV prevention efforts in their community.

Even popular and socially skilled individuals may find it difficult or awkward to initiate explicit conversations about AIDS, sexual behavior, risk reduction, and safer sex. Beyond extensive training and guidance in how to do this, the C-POL model used poster logos placed noticeably in venues where the intervention took place. Logos consisted of memorable but ambiguous visual images without text or reference to AIDS, and were meant to create population curiosity about its meaning. As C-POLs began to have conversations, they were asked to wear buttons, t-shirts, or other items with the same ambiguous logo that appeared earlier on the posters in the venues. These items usually stimulated many questions to the C-POL about the logo’s meaning, and the C-POL used the questions as openings for initiating risk reduction endorsement conversations. As the meaning of the logo gradually became known, the C-POL, who were themselves selected because they were the most popular members of the target population, became visibly identified as endorsers or proponents of safer behavior.

In summary, the C-POL intervention model identified, trained, and engaged popular opinion leaders within a high-risk community population to advocate, recommend, and endorse the importance of safer behavior to other members of the same population. C-POLs did this by learning how to deliver theory-based risk reduction communications during their day-to-day conversations with others, and by being guided to have specified and increasing numbers of conversations between group meetings. The intervention’s ‘active ingredient’ was the repeated, sustained exposure of population members to HIV prevention endorsement messages coming from C-POLs who were popular, well liked, and personally known. High levels of sustained population member exposure were produced by holding frequent reunion sessions with cadres of already-trained C-POLs to maintain their ongoing efforts and also by enrolling multiple or successive waves of C-POLs who proceeded through the same training and reinforced the messages of earlier waves. The intervention enhanced the social identities of C-POLs as HIV prevention advocates, and diffused behavior change through natural social roles among members of the community. By training at least 15% of the target population, the intervention could achieve the momentum necessary to ensure that most target population members would hear multiple, sustained risk reduction messages from individuals known and credible to them.

Implementation of the community popular opinion leader intervention with high-risk populations in five countries

Implementation of the C-POL intervention at research sites in five countries posed considerable challenges because of the coexisting needs to implement the same intervention at all sites, ensure that all sites’ intervention activities adhered to core elements of the model, but also to tailor intervention content to different cultures and to the different risk circumstances characterizing multiple target populations. This section briefly discusses how those issues were addressed in the development of the intervention protocol for the Trial.

Venue selection

Table 3 identifies the target population at each country site and describes venues where the population was accessed and intervention activities occurred. Because the Trial design required the identification, location, and randomization of 20–40 similar venues within each
country to intervention or comparison condition, we needed to locate relatively large numbers of separate venues in each country. Several considerations influenced population and venue selection [3]. Preliminary epidemiological studies conducted with samples of population members present in potential venues had to ensure the high prevalence of HIV risk behavior or the high prevalence of STD. We also took into account structural and social characteristics of the potential venues. Because a critical determinant of intervention impact is a high level of population member exposure to C-POL messages, each country site used extensive preparatory ethnography to select venues that were compact, geographically well defined, and social in nature, provided opportunities for C-POL conversations, and had relatively stable and non-transient populations regularly present.

Venues within a country were randomly assigned to the intervention or comparison condition, so it was necessary to ensure the independence of venues. The potential for contamination was reduced by selecting venues widely separated from one another. An individual venue in the Trial generally consisted of a well-defined place (or places) where a stable group of between 50 and 500 target population members regularly congregated. Determining the population size present in a venue provided a critical denominator for ascertainment of the number of C-POLs who needed to be recruited and trained to reach the 15% minimum threshold. For example, a Chinese market consisting of 100 workers would require a cadre of at least 15 trained C-POLs; a Russian dormitory with 400 residents would require engaging at least 60 of those residents as C-POLs.

**Identifying community popular opinion leaders within experimental condition venues**

Ethnography field teams spent a considerable time in each of the venues identifying different social segments in the population and planning strategies for identifying the opinion leaders within each segment. In Russian dormitories, for example, identifiable segments were differentiated on the basis of sex and on the floor or wing of residence in the dormitory building. C-POLs needed to be recruited from among men, women, and people on different floors within each intervention dormitory. In Peru, the social gathering points within venues were attended by at least three distinct population segments: heterosexual and primarily unemployed young men, young women who were open to, and usually compensated for, having sex with men in their barrio and sometimes with men from outside the barrio, and men who were self-identified and locally regarded as gay or homosexual, including transvestites. These different social segments often had different opinion leaders, and cadres of C-POLs had to be identified from within each segment.

To identify C-POLs, all study sites relied on direct observations made by the field staff and ethnographers in the venues and the nominations or reports of population members themselves when asked to identify who, among other individuals present in a venue, they most liked or trusted for advice. Some sites also used nominations made by gatekeepers familiar with crowds in the venue to identify who was most popular, whereas other sites accepted population members who volunteered for the training after their status as opinion leaders was verified by study field staff. Once identified, C-POLs were approached, informed that they were known to be liked and trusted by others with whom they socialized, and told that their help was needed to implement a new HIV/AIDS prevention programme that had the potential to save lives in their own community. These approaches emphasized the important and special role that each identified individual could play in helping to protect and educate others, stressed that the individual was being invited specifically because she or he was well-liked and trusted.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>China</th>
<th>India</th>
<th>Peru</th>
<th>Russia</th>
<th>Zimbabwe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Venues</strong></td>
<td>Retail food markets in Fuzhou</td>
<td>Wine shops and adjacent areas in Chennai</td>
<td>Cantinas, sports fields, and other gathering points in barrios in Lima, Trujillo, and Chiclayo</td>
<td>Dormitories attended by trade and vocational school students in St Petersburg</td>
<td>Social meeting places in growth points throughout the country</td>
</tr>
<tr>
<td>No. of venues</td>
<td>40</td>
<td>24</td>
<td>20</td>
<td>24</td>
<td>30</td>
</tr>
<tr>
<td>C-POL identification strategies:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Field observations</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>Population member nominations</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>Stakeholder/gatekeeper nominations</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>Self-nomination with field staff approval</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>Number of C-POL training sessions</td>
<td>4</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Duration of C-POL training sessions (hours)</td>
<td>2.0–2.5</td>
<td>1.5</td>
<td>2.0–2.5</td>
<td>1.5–2.0</td>
<td>1.5–2.5</td>
</tr>
<tr>
<td>Number of reunion sessions per year</td>
<td>6</td>
<td>6–9</td>
<td>9</td>
<td>6–9</td>
<td>6</td>
</tr>
<tr>
<td>Reimbursement for C-POL attendance at training and reunion sessions (US$ equivalent)</td>
<td>6.00</td>
<td>7.00</td>
<td>1.45</td>
<td>15.00</td>
<td>6.00</td>
</tr>
</tbody>
</table>

C-POL, Community popular opinion leader.
among friends, and framed the programme as one that would emphasize positive approaches regarding how to help others. More than 80% of C-POLs who were approached agreed to participate and attended intervention sessions.

**Community popular opinion leader training sessions**

The C-POL intervention in each country site was delivered in a series of four or five group training sessions, each lasting between 1.5 and 2.5 h, with sessions occurring approximately weekly. This 4–5-week main training phase was followed by reunion or booster sessions that brought C-POL groups back together to reinforce and sustain their efforts on an ongoing basis. Between six and nine reunion sessions were held per year for the 2 years after the main training phase. C-POL training sessions were held in meeting areas convenient to the venues, and each group consisted of two to four facilitators and between 10 and 20 C-POLs. Participants received payments valued at between US$1.45 and 15, depending on local economic circumstances, to reimburse their transportation and childcare costs, and to compensate for time attending training or reunion sessions. They did not receive any reimbursements for time spent having conversations in the community.

C-POL training sessions followed a standard intervention protocol manual, and intervention supervisors from all sites were centrally trained to conduct the training sessions using the same procedures. On-site facilitator training, monitoring, and supervision were conducted regularly, and annual quality assurance/quality control visits ensured that the intervention was carried out with procedural fidelity to the core elements of the C-POL model and to the procedures specified in the common intervention manual [22].

As implemented at all sites in the Trial, the first training session introduced C-POLs to the programme and explained how and why participants were selected to attend; it urged all members of the group to think of themselves as being in the vanguard of important efforts to prevent HIV/AIDS and STD in their community by talking with others about prevention. The threat of AIDS, national and local HIV epidemiology, risk behaviors, and prevention steps were discussed.

In the second training session, C-POLs were taught how to correct myths and misconceptions held by others about the disease and the characteristics of effective health communication messages applied to HIV risk reduction. Because risk-behavior reduction is a function not only of one’s knowledge about AIDS but also of one’s attitudes, beliefs, intentions, skills, and peer norm perceptions, C-POLs were taught to compose and practice communication messages that focused on these determinants (see Table 2).

In subsequent training sessions, C-POLs continued refining the types of prevention messages they would deliver. They also discussed and planned how, when, and where they would initiate these conversations, especially with other members of the target population present in the study venues, and set goals at the end of each meeting to talk with a specified number of friends, acquaintances, and strangers before the next meeting. Beginning with the third group session, considerable time was spent reviewing the outcomes of each member’s conversations during the preceding week, reinforcing those efforts, problem-solving any difficulties, role playing new conversational skill styles, and planning still more conversations for the week ahead. All sessions employed a range of interactive techniques for teaching behavioral skills, including group discussion, interactive exercises, facilitator modeling of effective conversation examples, role play practice, and goal setting. With no more than 20 participants, C-POL groups were small enough to allow the group to be divided into pairs or triads for role playing so that each participant had an opportunity to practice examples of conversations that incorporated elements such as those shown in Table 2, receive feedback from the group’s facilitators, practice further, and refine his or her communication skills.

Some Trial sites with larger venues trained multiple C-POL groups concurrently (such as on different meeting days of each week), whereas other sites trained first one group followed by subsequent waves until they achieved the 15% minimum number of C-POLs trained from an intervention venue. Reunion sessions were held monthly to bimonthly after the main C-POL training phase to reinforce, support, and maintain ongoing conversations by the entire cadre of C-POLs. Some Trial sites reunited only the group of C-POLs trained together from a single venue; other sites brought together groups of C-POLs from multiple venues to strengthen the feeling that a widespread social movement against AIDS was being created.

**Tailoring of the community popular opinion leader intervention across sites and populations**

The conduct of a common behavioral intervention across diverse countries, populations, and cultures requires not only standardization but also tailoring. If completely different intervention procedures were used in each country, the overall project would consist of five independent and separate studies rather than a unified trial. On the other hand, important cultural differences in initial AIDS awareness, styles of communication, and situations or relationships that confer risk must be recognized. If the same intervention content were used across all sites, the content or examples relevant in one country site might be culturally inappropriate in another. To balance the need for commonality with the need to tailor, the intervention used the same C-POL training procedures across sites, but adapted and tailored certain aspects of the...
intervention content, training examples, risk situations being targeted, and communication style taught to C-POLs. This created across-site procedural commonality and also allowed tailoring to ensure cultural appropriateness.

Although the intervention’s framework and procedures were implemented consistently across country sites, C-POL messages and communication approaches had to be tailored to the needs, issues, and culture of the population. In Zimbabwe, AIDS is well known, and most opinion leaders are knowledgeable about it. By contrast, knowledge about AIDS is lower in China and misconceptions about the disease were widespread. Consequently, more time was spent during C-POL training sessions to ensure that C-POLs had a foundation of accurate information to share with others.

The balance of attention across topics covered in the C-POL training differed across sites depending upon the initial levels of knowledge, misconceptions, beliefs, and attitudes of the target population found in preparatory ethnography at the site. The Trial’s preparatory ethnography also identified the type and context of risk behavior among members of the target population in each country, the language and terms that would or would not be acceptable to use in messages, and the types of sexual relationships in which risky behavior took place [2,23]. For example, Russian dormitory residents were primarily unmarried, and most risk behavior occurred in the context of either casual or serial dating relationships. In India, men visiting wine shops often had sex with casual or commercial sex partners. In both countries, risky behavior was often associated with heavy alcohol use. At other sites, men were often married but also had sex with casual, commercial, or side partners. The primary goals of the intervention and prevention messages were to reduce unprotected sex behavior and to encourage condom use during sex with any non-spousal partner. The types and content of messages delivered by C-POLs were, however, tailored across sites and informed by each site’s earlier ethnography study, the nature of relationships and practices that conferred risk in the site’s population, and social HIV epidemiology.

We observed differences across site populations in how individuals discussed sex and aspects of behavior that confer risk of HIV and STD. Men were more explicit in their talk than women. Particularly in China, there was a general reluctance to discuss sexual practices, and intervention content was tailored to remain culturally consistent with participant values and language preferences. There was also variability across sites in the availability of low-cost condoms and community medical services for STD treatment. Because population-level behavior change requires access to the means needed to act on change, all sites ensured that population members had access to free or inexpensive condoms and STD treatment.

Lessons learned

The outcomes of the Trial will be known when final follow-up assessments are conducted with large, longitudinally followed cohorts in intervention and comparison venues in each country site. In addition to behavioral and biological outcomes at a population level, intervention process data were collected to analyse key aspects of intervention delivery at each site, including fidelity to the protocol, the number of C-POLs trained, the number of conversations C-POLs had with others, population exposure to the intervention, and other dimensions.

Some conclusions about participant reaction to the intervention can, however, already be drawn. First, because more than 80% of C-POLs who were approached in the community agreed to attend the training, it is evident that the intervention model used in the Trial tapped into community strengths, altruism, and people’s desire to do something to help in the fight against AIDS. Second, although adverse event monitoring protocols were in place at all sites, no serious adverse events related to the intervention have been reported to date in any country. Third, we were not certain in advance about the willingness of intervention participants to discuss sensitive aspects of sexual behavior openly, especially in cultures in which these topics are not typically discussed. With few exceptions, attendees at C-POL training sessions became eager and comfortable talking openly about sexual health issues, and a challenge to facilitators was keeping session durations to the parameters planned in the protocol, given the participant enthusiasm and the amount of material to be covered during each session. We believe this phenomenon occurred because many cultures offer few opportunities for individuals to discuss AIDS-related concerns, sexual health, and the role that ordinary people can play in protecting their community from AIDS openly. Finally, although process data are not yet analysed, feedback from the sites has confirmed that most C-POLs took on the challenge of disseminating HIV prevention messages with enthusiasm, energy, and dedication. The outcomes of the Trial will determine the effects of these efforts.

References


Ethical issues in the NIMH Collaborative HIV/STD Prevention Trial

NIMH Collaborative HIV/STD Prevention Trial Group*

Objective: To develop decision rules regarding key ethical dimensions in scientific protocols for the National Institute for Mental Health (NIMH) Collaborative HIV/STD Prevention Trial taking place in five countries (China, India, Peru, Russia, and Zimbabwe).

Design: Countries had HIV rates from 27 to 0.1%, the standard of care varied from access to antiretroviral drugs to no availability, and the reporting of sexually transmitted diseases (STD) to government agencies was mandatory in some countries and not in others. These variations presented challenges when developing decision rules that could be uniformly adopted across countries and simultaneously follow the ethical principles of beneficence, respect, and justice.

Methods: We used several strategies to identify and resolve ethical dilemmas for this international HIV prevention trial. First, we identified key principles, especially those derived for clinical therapeutic, biomedical preventive, or device trials. We convened a ‘workgroup on protecting human participants’ and charged them with identifying and implementing optimal procedures for ensuring the ethical and equitable treatment of participants and making recommendations to minimize physical, psychological, and social harm to the participants. Each site had a community advisory board, essential in identifying local ethical issues and possible resolutions to them. The NIMH established a data safety and monitoring board with ultimate responsibility for adjudicating ethical dilemmas and decisions. The protocols were deliberated thoroughly by the Trial steering committee, and approved by nine United States and five in-country institutional review boards.

Results: We summarize the decision rules adopted to resolve the ethical dilemmas identified. Especially important were the translation of clinical trials principles for a behavioral intervention trial, strategies for ensuring confidentiality and informed consent, dilemmas relating to partner notification of sexually transmitted infections including HIV, minimizing the risks of social harm, establishing community partnerships, ensuring equity among United States and in-country principal investigators, and building capacity for additional research.

Conclusion: We document our processes and decisions, and their underlying rationales, and hope they contribute to the development of further thinking and practice regarding the ethics of social and behavioral HIV and STD prevention trials in resource-poor settings.

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Keywords: AIDS, behavioral intervention, HIV, international ethics

Introduction

The ethical conduct of HIV prevention research, especially in less-resourced countries, continues to evolve rapidly [1–5]. Its evolution is marked by major differences of opinion [6–8], trials being held up or halted [9,10], and attempts to design and conduct trials to benefit participants and the communities and countries in which they reside [11,12]. Hopefully, the results of these trials will have broad application to protect others at risk of HIV infection [13]. This paper focuses on the ethical issues identified and resolved from 2000 to 2003 while designing the National Institute of Mental Health (NIMH) Collaborative HIV/STD Prevention Trial (‘the Trial’), which is assessing the efficacy of an international, community-level, social diffusion HIV prevention

* See Appendix B for members of the NIMH Collaborative HIV/STD Prevention Trial Group.
intervention designed to influence both behavioral and biological endpoints. Our goal in writing this paper is to document our processes and decisions, and their underlying rationales, and thus contribute to the further development of this important area of thinking and practice regarding the ethics of prevention trials in resource-poor settings. Some may disagree with the decisions that we made; others may argue that our decisions are outdated, superseded by subsequent research findings. Our goal is to articulate what we did and why, so that others may discuss and follow or change our procedures if their reading of ethical principles leads them to different conclusions or compelling new evidence leads to new practices.

The Trial’s steering committee established a workgroup on protecting human participants and ethical responsibility to ensure the highest level of protection of human participants during this Trial and to provide a forum for resolving issues related to ethical responsibility. The workgroup was composed of the steering committee (highest ranking US and host country investigators for the five sites; the principal investigator of the data coordinating center; and the NIMH senior scientist) augmented with experts on the ethics of conducting international prevention and biomedical trials.

The workgroup was charged with identifying and implementing optimal procedures for ensuring the ethical and equitable treatment of participants and with making recommendations to minimize physical, psychological, and social harm to the participants. The workgroup reviewed all informed consent procedures, assessed the risks and benefits associated with participation, and established procedures for fairness in the selection of participants. In addition, the workgroup identified ethical dilemmas, addressed in this paper, which arose or reasonably could be expected to arise during the course of the Trial. Because of the ethical imperative of equity for all study participants, the intervention is being delivered in the comparison venues once the final follow-up endpoint data are collected. Expansion of the intervention to the comparison venues will permit, in some sites, an evaluation of technology transfer to governmental and non-governmental organizations capable of continuing this effort after the conclusion of the Trial. If results indicate that the intervention is successful, researchers will encourage local organizations to sustain it in the sites.

We convened a series of consultations to ensure that ethical standards for this research adhered to evolving international standards relevant to the conduct of a behavioral trial. The most extensive of these was a workshop involving international leaders in the ethical conduct of HIV trials in London in September 2000. In addition, ethical consultations were sought and received from other developed and developing-country experts. We were guided in these deliberations by the findings of the US National Bioethics Advisory Commission [14].

The NIMH also established a data safety and monitoring board [15], which not only monitored the safety of individual participants but also raised larger ethical questions about the responsibilities of US investigators undertaking international research. In addition, the protocols were reviewed and approved by nine institutional review boards (IRB) in the United States and one IRB in each of the participating countries (a total of five more).

It should be noted that the local IRB were in place before the start of the study. Furthermore, it should be noted that gaining consensus among so many different regulatory bodies for a large-scale multisite trial is not an easy task. We had to take into account both the judgements of the US institutions, including the funding agency and the body acting on behalf of the participants (the data safety and monitoring board), but also the in-country IRB and regulatory bodies. In the latter case, although all bodies wanted to adhere to the highest standards of clinical research, the local IRB were also clear that it was important that we not impose standards for research that contravened local laws or regulations, or that skewed local best practices in order to provide undue inducement to participate in the research study. These issues are discussed below, especially in relation to the provision of antiretroviral therapy for individuals with HIV and partner notification or contact tracing.

Ethical standards for behavioral research

The fundamental principles guiding the conduct of all clinical trials were followed during the Trial. The first code of ethics, the Nuremberg Code, emerged from the Nuremberg trials in 1946 in response to the abuses of human research subjects during World War II. The World Medical Association’s Declaration of Helsinki followed this in 1964. The Declaration of Helsinki has been revised many times over the past 40 years, most recently to include a provision that ‘medical research is only appropriate if there is a reasonable likelihood that the populations in which research is carried out stand to benefit from the results of the research’ [16]. Applied to the Trial, this required that the interventions being tested could be implemented reasonably and cost-effectively, and would benefit the participants and countries involved in the investigation both during and after the Trial.

Regulations governing the standards for all research involving human participants in the United States have evolved over time. Following the disclosure of the Tuskegee experiments in 1972, the US Congress amended the Public Health Service Act to require the Secretary of Health, Education and Welfare to develop standards for research involving human participants. The first regulations, issued in 1974, established the US Office
for Protection from Research Risk. Consequently, the Ethical Conduct of Research with Human Participants, the Belmont Report [17], was developed in 1979. The Belmont Report outlined the principles, respect for persons, non-malfeasance, beneficence, and justice, by which federally funded research is conducted in the United States. These principles became the basis for federal regulations, which have been revised several times over the years, most recently in 2000 with the establishment of the US Department of Health and Human Services’ Office for Human Research Protections (OHRP). The OHRP directly oversees all human research funded by the National Institutes of Health (NIH), including international collaborative research involving US institutions.

**Drug trials versus behavioral trials**

Although different ethical dilemmas may arise during behavioral research trials than during medical intervention trials, the ethical principles governing medical trials still apply. Namely, such research must ensure adequate informed consent, a favorable risk–benefit ratio, and the just distribution of the benefits and burdens of the research. Whereas the focus in medical intervention trials is primarily on protecting participants from physical harm, the focus in behavioral trials is largely on protecting participants from psychological or social harm. Groups deliberating ethical standards, such as the US National Bioethics Advisory Commission, have focused predominantly on medical intervention trials [3,5]. The development of ethical principles guiding international social and behavioral HIV/sexually transmitted disease (STD) prevention research has thus lagged somewhat behind the principles governing international trials of drugs or devices. Our efforts were designed not only to guide this specific trial, but also to foster the evolution of the principles for social and behavioral HIV/STD prevention efforts more generally. We also believe that issues related to psychological and social harm can and should apply to medical intervention trials, but are often not considered in the development of research and ethics protocols for those studies.

Ethical standards for behavioral research developed as a result of public attention focusing on controversial research conducted in the 1960s. In 1971, the American Psychological Association (APA) promulgated ‘Standards for the conduct of research with human participants’ [18]. This document was based on a content analysis of ethical dilemmas encountered by APA members when conducting behavioral research. Other professional associations, such as those for sociology, anthropology, social work, and psychiatry, have developed similar guidelines. The guidelines governing behavioral research have focused primarily on protecting participants from deception and potential social harms that may result from a breach of confidentiality. Such social harms might include embarrassment (e.g. being questioned about sexual behavior), stigma and discrimination (e.g. being identified with an AIDS or STD-related study) [19], disruption of family (e.g. detection of infidelity) [19], suspicion of being a commercial sex worker [20], injection drug user [21], or blood donor [22,23], loss of employment (e.g. if illegal drug use becomes known to an employer), and legal exposure (e.g. if HIV status becomes known in the context of an arrest or court case) [24]. All of these issues were relevant to our study.

The APA continues to review its ethical guidelines as new dilemmas arise. The latest example is developing guidelines addressing the conduct of research using the Internet [25].

**Standard responsibilities of trial investigators**

The principles regulating research with human participants require that the dignity of all participants and communities be respected, equality be promoted among participants, vulnerable populations not be unfairly burdened, and risks be minimized. These principles translate into the need for the strict protection of confidentiality, an appropriate risk–benefit ratio, clear strategies for minimizing risk, close attention to informed consent processes and procedures, and training and monitoring for staff involved in the study.

**Confidentiality**

We collected information on HIV/STD knowledge, attitudes, and risk behaviors, i.e. self-reported sexual risk, including the number and types of partners (regular partner/spouse, casual partners, and commercial partners), the use of alcohol and drugs, and condom use, in a cohort at baseline and 12 and 24 months later. We also obtained biological specimens for the assessment of chlamydia, gonorrhea, HIV, herpes simplex virus 2 (HSV-2), and syphilis in all participants, and trichomonas in female participants only.

Participants in the Trial faced the risk of social harm if behavioral data or biological test results were inadvertently revealed to others. Therefore, a number of traditional measures were taken to protect confidentiality. These included assigning a unique participant code to data rather than using names or other common identifiers, ensuring secure storage of research data, limiting the number of individuals in the study staff with access to sensitive information, and requiring that all participant counseling take place in private settings. Under US
Potential risk could have been eliminated completely had the samples and data been analysed with no identifiers (unlinked data), but we decided against this for various reasons. The investigators believed that it was unethical to identify HIV and STD in voluntary participants without informing the participants of test results and treating the bacterial STD. Linked results allowed individual counseling for all participants and treatment or referral for positive results. Moreover, linked data allowed researchers to measure the incidence of HIV, HSV-2, and syphilis in the study cohort because baseline test status and treatment can be linked to data for the same participant 12 and 24 months later. Third, linked data allowed the identification of the types of individuals who were influenced by the persuasive messages and the types who were not (intervention effect).

The Trial faced potential consequences if STD could not be tracked by individuals and if treatment was not provided to those who tested positive at recruitment for bacterial STD. Without these steps, it would not be possible to know whether infections were new incidences or if bacterial STD were untreated from the time of recruitment to 12 or 24 months later. Substantial arrangements were thus made to ensure that participants could access their results. In Russia, participants in the Trial had to contact the researchers to be informed about their HIV status by accessing a personalized, confidential number known only to each participant, and were provided access to cell phones to make these calls at their convenience. The clinic staff never had the names of the participants, only matched identifying numbers informed the research staff of the Russian sample's STD results. This system allowed participants to learn of their bacterial STD through their own initiation via a numbered system and to receive free treatment while the study tracked incident bacterial and viral STD infections over time, without the clinic knowing the status of any specific participant and requiring the reporting of incident STD by participant name to the state.

The HIV and STD testing conducted by the study was thus confidential. These laboratory tests, with pre and posttest counseling, were offered to all participants and to partners of participants with positive laboratory results. All test results were made available at no cost to participants and their partners. Although participants were strongly encouraged to return for test results, no attempts were made to contact individuals in a way that might be stigmatizing. Participants were encouraged to notify their partners of results, and they were offered couples counseling by the study or by referral at the study's expense. Also, participants were given basic counseling and education when results were returned; if more extensive counseling was required, an appropriate referral was made at the study's expense.

Pregnant women identified as HIV positive through this screening programme were referred for appropriate counseling and prophylaxis to prevent vertical transmission. The rationale on whether the study was to provide prophylactic regimes to pregnant women is outlined more fully below under the topic of antiretroviral and antibiotic prophylaxis.

**Partner notification**

Previous studies of HIV transmission and prevention [26], have been criticized for failing to notify uninfected individuals of their sexual partner's infection. We did not engage in partner notification in this study, for two reasons. First, even in the United States, where sexually transmitted infections might be reportable and public health authorities need to engage in contact tracing, the confidentiality of the infected individual is always respected and people cannot be contacted if the infected individual does not reveal names [27,28]. Second, not all of the countries where the study was being implemented require the reporting of infections, and the places that do require reporting do not necessarily require name reporting. Some countries have specific laws against breaking participant confidentiality, and not all countries allow partner notification nor do they necessarily have the resources to do it. Therefore, we concluded that the most ethical strategy, and one that would not have us run foul of local laws and regulations, was to follow in-country laws and regulations, the country-specific standard of medical practice established by the country's Ministry of Health, and the standard established for other HIV/STD prevention studies in that country. This is consistent with the Joint United Nations Program on AIDS and World Health Organization guidelines [29]. We encouraged disclosure when appropriate, and also encouraged infected individuals to refer their partners for testing, counseling, and treatment or referral at the study's expense if needed.

Treatment for bacterial STD was provided to partners of study participants for free. In China, where all medical treatment is fee based, single dose treatment for all bacterial infections except syphilis was provided to the participant for their partners at the time of receiving the assessment results. If syphilis was identified, a coupon for free treatment was provided to the Chinese participants for their partners, as well as themselves. In other countries
these procedures varied, depending on the availability of treatment in the local environment. In some countries, we documented a high rate of reinfection for some STD [30], suggesting that this strategy was not completely successful. Future studies might examine additional strategies to enhance partners’ awareness and treatment, while respecting participant confidentiality [30–39].

Assessing the risk–benefit ratio

One of the guiding ethical principles in the protection of human research participants is the requirement that the research be justified on the basis of a favorable risk–benefit ratio (US CFR 45). Therefore, IRB and scientific reviewers are asked to judge whether the risks to study participants are outweighed by the potential benefit to the individual participant and the importance of the knowledge to be gained from the study (i.e. the ‘Trial’s ‘social benefit’).

Many research studies, such as phase I drug trials, offer no direct benefit to participants while at the same time posing more than minimal risk. Such studies are, however, deemed to have a favorable risk–benefit ratio if the importance of the knowledge to be gained from that trial may provide significant social benefits. In addition, substantial evidence indicates that assessing their own behavior benefits many participants. An old public health adage states that ‘the quickest way to stop an epidemic is to study it’. Across studies, the behaviors being addressed in the assessment improve by 15–30%, presumably because of the repeated examination of one’s own behavior. Also, participants frequently comment that they found the study very helpful, even when they were enrolled in the control group and received no intervention.

Beyond the benefits of repeated assessments, the NIMH Collaborative HIV/STD Prevention Trial is testing the efficacy of a social diffusion intervention in reducing the number of new HIV infections and STD in various international contexts. If successful, the social benefit would be enormous because this intervention is inexpensive, could be adopted widely, and could limit the further spread of the epidemic. We expect this intervention to be effective, cost effective, sustainable, and easily disseminated in international settings. The primary risk to participants is social harm associated with HIV and STD testing: disruption of family (e.g. breakup of couples after HIV/STD detection or the revelation of infidelity); stigma and discrimination (e.g. being associated with a morally or socially disqualifying condition, with a consequent loss of employment or status in community); physical harm (e.g. acts of physical violence directed at individuals who have been diagnosed with HIV); or embarrassment and distress as a result of being questioned about sexual behavior.

Strategies for minimizing risk

Although almost all research involves some risk to participants, protocols should be judged on the basis of the overall risk–benefit ratio and the extent to which research-related risk is minimized. Obtaining individual informed consent, maintaining strict standards for confidentiality, and providing appropriate referral services may minimize the previously described risks to participants. In this protocol, we made a special effort to ensure that risks of social harm were explained as clearly as possible to potential participants during the informed consent process. Many of these same concerns were addressed in pretest counseling, when the participant’s motivation for testing and preparedness for a positive test result were explored. The training of counselors for both pre and posttest counseling included confidential assessment and direct referral for crisis services. Counselors were trained to seek immediate consultation with a second counselor in any problematical situation. The intervention in this protocol also involved providing information regarding where participants could receive posttest referral services through the existing health system.

Informed consent

Informed consent is an essential part of minimizing risk to potential participants [40]. IRB accept differences among sites in informed consent procedures as long as the required information is conveyed and the differences are necessary to conform to local laws, regulations, or customs. The countries participating in this study have adopted a requirement for informed consent procedures at various times in the past, although some do not have a well-established tradition in this regard. The social meaning of consent depends on local cultures and traditions, and public perceptions about what is good or fair (particularly in a balance between individual and community) vary across cultures. Furthermore, conflict exists in some places about who can give consent. According to the OHRP guidelines for research on adults, only the research participant himself or herself can give consent to participate in the research. Permission to participate may sometimes be needed from the prospective participant’s head of household or others in the community. Study implementation thus required extensive discussions about how to ensure that the ethical guidelines adopted reflected a multicultural understanding, rather than an imposition from one culture to others where a study commonly must first be endorsed by other members of the household or by local officials. Work with community advisory boards and others was required to ensure that communities accepted the requirements of informed consent, and understood the differences between permission, assent, and informed consent. Informed consent procedures and forms were validated in each country to ensure that they accomplished similar goals in each setting.

The language of consent forms often appears to be complex, legalistic, and difficult to understand for all populations, but especially for vulnerable populations in
international settings. Potential research participants may be very suspicious of any document that looks formal to them. Also, written, signed, informed consent forms may be impractical in sites where: (i) literacy levels are low (e.g. signing with ‘X’ or a thumb print is common); (ii) documents may symbolize undesired bureaucratic interference; (iii) even signing one’s name to a consent document might pose a risk to confidentiality; or (iv) the content of the form itself may disclose important information such as serostatus [4,41]. The most important aspect of the informed consent process is not the signed document itself, but that the field staff honors the principles of respectful and protective treatment of study participants, and that the individual clearly understands the study and has agreed to participate in the research effort. The participant must feel free to refuse participation based on an understanding of what he or she is being asked to do and know that there are no implied or actual negative consequences of refusal.

Because we were concerned that individuals might feel coerced into participating, especially in countries with authoritarian histories, the Trial protocol required that the consent process involve a face-to-face discussion between the research participant and the field staff member obtaining informed consent. In some countries, videotapes were made locally demonstrating the procedures and activities that would follow and outlining the responsibilities and potential benefits and costs to participants (e.g. in China). Even when videotape orientations were used, a one-on-one meeting with a research interviewer was held. The study procedures and the risks and benefits of participation were explained carefully to the potential participant in simple language, and the individual had the opportunity to have any questions answered. Every effort was made to make the information conveyed clear and easy to understand, and not so long that parts of it were forgotten before the form was signed or so long that it overwhelmed potential participants. Participants were provided with contact information for in-country personnel who could answer any questions that arose in the future. Individuals were assured that their participation was entirely voluntary. We made every effort to ensure that no authority, in the markets in China, in the wine shops in India, in the barrios in Peru, in the dormitories in Russia, or in the growth point villages in Zimbabwe, was involved in recruiting individuals into the study or obtaining consent from them. No one except study personnel and the individual knew who did and who did not agree to participate.

Informed consent for the collection of biological specimens for HIV and STD testing must include a statement of the potential risks of such testing to participants. The following elements describing this risk were used in the consent forms adopted by each site: (i) HIV and STD tests may cause anxiety regardless of the test results; (ii) a positive HIV result means that the individual has been infected with HIV, but other tests will be necessary to determine the extent to which the disease has progressed; (iii) it may be possible to treat an STD identified through laboratory testing; (iv) receiving a positive HIV or STD test result may cause psychological distress (e.g. anxiety and depression) and may affect partner relationships; (v) if other people learn about an individual’s positive test result, it could affect the way family and friends treat the individual; and (vi) if the individual’s test is negative, it is still possible that the individual could become infected with HIV or another STD in the future.

Improving confidentiality through staff training
The NIH requires education on the protection of human research participants for all investigators and their key personnel (both national and international staff), including all personnel who have responsibility for the design and conduct of the study or direct contact with human participants. The Trial went further, however, by requiring that all personnel supported by project funding be certified on the protection of participant confidentiality before data collection began. Certification involved participation in a workshop on ethical principles and their application and signing an agreement through which staff agreed to abide by the international principles for the protection of human participants adopted by this study. This included receptionists, drivers, and clerical workers to ensure that they maintained the confidentiality of those participating in the study.

Because of the major harm that staff could do in small communities by inadvertently revealing personal information about research participants, extra steps were taken to ensure confidentiality. In addition to certification, sites developed and adopted procedures to ensure adherence to ethical principles by interviewers and other personnel involved in research contact with participants. Mechanisms included proficiency testing, field supervision, group discussions, and other appropriate techniques to ensure adherence to all protocols, including those involving human participants. Finally, the ongoing quality assurance procedures implemented by each site, and the external monitoring system, provided additional oversight and assurance that participant protection procedures were being followed. For example, on a random basis, supervisors in each site would visit recruitment venues and check that all procedural guidelines to assure informed consent were being followed. Case vignettes were generated across countries and project staff had the opportunity to discuss ethical dilemmas experienced by other country teams, examples that helped teams proactively to address potential problems. For example, the study resources to health examinations were considered so valuable in some countries that a few participants encouraged their friends to impersonate them to get free services. Protocols to protect both the
participant's confidentiality and the study's integrity were constantly updated as such new obstacles were encountered.

Challenges unique to international collaborative research

The challenge of collaborative research
The NIMH Collaborative HIV/STD Prevention Trial was established as collaborations between US academic institutions and host country counterparts. Such collaborative research between international and US researchers has the potential to benefit both parties. Research in host countries that is sponsored by a resource-rich country has the potential to exploit vulnerable international populations, and has thus been the subject of extensive recent debate [14]. Lo and Bayer [2] have further challenged investigators conducting research in host countries to meet certain guidelines for collaboration, including the following: (i) research must be responsive to the needs of the host nations and consistent with their priorities for healthcare; (ii) lower standards of care offered in host countries, compared with standards of care normally offered in the United States, need a special ethical review; (iii) reasonable efforts need to be made to secure access to experimental interventions proved effective after the Trial is over; and (iv) sponsors and researchers from the United States should build capacity for clinical trials and ethical review of research in host countries.

The collaborative research teams addressed each of these concerns a priori, anticipating the issues within the protocol that would be impacted by these guidelines. We have detailed below the domains in which these principles were most apparent.

Establishing community partnerships
Lo and Bayer [2] challenged investigators conducting research in host countries to develop partnerships with researchers, government agencies, and community leaders at all stages of trial conduct. This increases the chances that the research meets the needs of host and sponsoring nations and can be carried out successfully. Such partnerships are also essential to ensure that participants’ concerns are understood, informed consent is appropriate and understood, and risks are minimized and benefits maximized.

The request for applications (RFA) for this Trial asked teams of US and host country investigators to respond with applications that identified both members of the partnership and described the functions and contributions of both partners. The Trial is governed by a steering committee including both the US and host country principal investigators. All of the Trial working groups (e.g. intervention, assessment, biological outcomes, ethics, ethnography) are composed of US and host country investigators and staff. Serious efforts were made to establish horizontal working relations between US and host country teams, although it was recognized that even a lack of English language proficiency might pose obstacles to equity. It is difficult for anyone to work and write in a second language. Added to that is the fact that scientists in the United States have first-hand knowledge of the NIH and its systems and regulations, and also ways of interacting in scientific settings that individuals elsewhere might consider abrupt, abrasive, or impolite. Therefore, the Trial team worked hard to ensure that all steering committee members had opportunities to speak and to question, to participate in all deliberations, and to have their voices heard as the study procedures were articulated.

All Trial sites developed ongoing relationships with in-country health officials and established community advisory boards to comment on all aspects of study design and implementation. Ethnographic studies conducted in advance of the Trial revealed major community stakeholders and leaders and important constituencies, which have been consulted for advice on all aspects of the study.

To ensure that we addressed the needs of the host country, each team led by the in-country and US leaders engaged in an active search for the risk population most likely to benefit from the Trial. In several countries, identification of appropriate populations and venues took many attempts. In China, the team conducted brief surveys and qualitative studies with sex workers, truck drivers, factory workers, and construction workers in many provinces in order to identify a suitable in-country population. Two sites, India and Peru, had to modify their risk populations from the initial choices in order to identify an appropriate study population. Similarly, Zimbabwe chose village populations in economic transition sites, increasing the team’s work to maintain the cohort, but ensuring that a population at high risk would be addressed.

Establishing an acceptable standard of care
This is perhaps the most difficult of all issues, given that the standards of care are evolving and changing because of advocacy and programmes such as the Global Fund to Fight AIDS, Tuberculosis and Malaria [42] and the President’s Emergency Program for AIDS Relief [43]. We agreed that all participants should receive counseling equal to Project RESPECT, which found that even brief counseling reduced incident STD [44]. This was also the standard adopted in Project EXPLORE, which tested the efficacy of an individualized intensive intervention in reducing HIV acquisition [45].
Demonstration of disease prevention and reductions in behavioral risk are the primary goals of this phase III prevention trial [46,47]. Therefore, STD diagnostic tests established baselines and were used as the Trial endpoint, despite concerns that this might constrain the Trial. All sites agreed that bacterial STDs should be treated with regimens adopted by the host country and confirmed to be efficacious. We agreed, for ethical and Trial protocol purposes, that individuals would be treated initially according to syndromic management protocols, and treated again if they received positive laboratory results that had not been treated through the syndromic approach.

Difficulties arose with regard to the treatment of HIV, because none of the countries in which the Trial was conducted had easy access to antiretroviral treatment at the beginning of the Trial. After consultation, we decided that individuals diagnosed with HIV during the course of the Trial would be referred to the nearest treatment centers, and that study personnel would work hard to ensure that these participants had access to those centers. The issue of research sponsors providing treatment for HIV during or after the Trial has been a contentious one, but the generally agreed upon principle is the following: ‘The issue of whether Trial sponsors should guarantee lifetime antiretroviral therapy led contentious debates in vaccine research. The present outcome of this debate is that trials rely on publicly funded programs in the host countries to provide antiretroviral treatment to infected Trial participants. This outcome reflects both financial and ethical considerations: a lifelong guarantee of treatment could exhaust limited research resources and does nothing for those who elect not to participate in research’ [9].

Although it is important to work with host countries to provide access for research participants, it would not be ethical to provide antiretroviral drugs in a way that produces undue inducement or incentive to participate in the Trial. We thus had to seek a balance between inducement and reasonable access to care. We could not guarantee access to antiretroviral drugs after the end of the Trial. It would not be ethical to start individuals on antiretroviral drugs, and then stop treatment once the Trial was completed. This Trial was supported by the National Institute of Mental Health of the US NIH. The resources were allocated for prevention research, not treatment. Although some have argued that prevention research may carry the requirement for providing treatment for those diagnosed with HIV, the NIH and other groups such as the Bill and Melinda Gates Foundation have argued that such a requirement would place an undue burden on prevention trials, and even deplete already sparse funds further, and perhaps limit the number and quality of trials that might be conducted.

The question arises, then, is it ethical to test for HIV when antiretroviral treatments are not available? Because the vast majority of individuals who need HAART in the areas where we were working lacked access to the treatment at the beginning of our work, this and other HIV prevention trials involving HIV testing raised ethical questions related to diagnosing HIV without providing treatment. Although providing HAART is not required under the Joint United Nations Program on AIDS Guidance on Ethical Considerations in HIV Preventive AIDS Vaccine Research [48], treatment advocates in the United States and other countries are concerned about these issues. Therefore, we engaged in vigorous discussion and consulted ethical experts about the responsibility of the Trial to provide HIV treatment to individuals identified as HIV infected during assessment procedures.

Even without treatment, the benefits of knowing one’s serostatus accrue to both the individual and the community. Individuals can take better care of their health, even without access to antiretroviral drugs, and can help stop the epidemic by reducing their transmission behaviors. Evidence indicates that globally approximately half to two-thirds of HIV-positive individuals reduce their transmission acts on learning their serostatus. This is a huge prevention benefit for local communities coping with the virus.

As leaders in the research community, the steering committee agreed on the social responsibility to advocate for better healthcare infrastructure and HIV specialty care in each of the five countries where the Trial was implemented. Investigators were optimistic that considerable progress would be made in terms of access to treatment, hopefully at the level of international standards being developed by multilateral agencies. Several steps have been taken towards this goal since the Trial started (e.g. the United Nations General Assembly Special Session on HIV/AIDS ‘Declaration of Commitment on HIV/AIDS’, in which prevention and care are linked [49], ‘The framework document of the Global Fund to Fight AIDS, Tuberculosis and Malaria’ [42], the 3 by 5 initiative of the World Health Organization [50], and the President’s Emergency Program for AIDS Relief [43]). Several of the countries participating in the Trial were planning to initiate an HIV treatment programme, but these programmes were initially limited to certain areas and to specific populations. The prevailing view of the group was that the researchers have the responsibility to conduct this prevention study and report their findings as soon as possible to both the government and the local community. Recognizing that many countries have significant competing social priorities, each government is ultimately responsible for facilitating access to treatment for HIV when it is diagnosed. The hope is that the results of this research will assist communities and countries in making the case to their governments for increased access to treatment as part of a broad prevention plan.
The difficult ethical question at this point, in this and similar prevention trials that involve screening for HIV and STDs in host countries, is: do the risks outweigh the benefits of voluntary HIV counseling and testing (VCT) and STD screening in resource-poor settings without current access to antiretroviral therapies and with high levels of stigma within local communities? In other words, are the ethical principles of not doing harm (non-maleficiance) and doing good (beneficence) being properly respected?

This study involved counseling and testing for several bacterial and viral STDs in blood and urine and, in women, vaginal swabs. Although the collection of urine does not pose risks, and the risks of venipuncture are minimal, obtaining self-collected vaginal swabs from women may pose challenges to women unaccustomed to touching their genitals, or, particularly, to women with no previous sexual experience.

When a non-viral STD was identified on the basis of laboratory results, treatment meeting acceptable international standards (such as those developed by the Centers for Disease Control and Prevention) was provided at the study’s expense [51]. Participants were informed at the time of biological specimen collection that their STD results would be available within an estimated time period. Information was provided on specified times and locations for receiving test results. Results were provided in-person and privately to each participant, and every effort was made to ensure that participants received their results whether they were positive or negative. Although multiple opportunities to receive results were arranged, along with strong motivational messages to return for results, sites did not directly contact individuals. Free treatment for non-viral STDs was made available either at the study site or through referral at the expense of the study for participants and their regular sexual partners. One ethical dilemma did arise in one of the study countries because the treatment recommended by the investigators for an STD was in conflict with the health policy of a country that wanted to reserve that drug for more serious ailments; consequently, in that situation, the Trial offered treatment that would have been considered less than optimal in the United States, but was locally appropriate. Another ethical dilemma arose when HSV-2 proved highly prevalent, but was treated episodically if at all, even though this infection is observationally associated with HIV acquisition [52–55]. The benefits of treatment to suppress HSV-2 to reduce HIV transmission have not yet been demonstrated [13,53]; if such a benefit is demonstrated in the future, studies may need to consider adding treatment to suppress HSV-2 to the standard HIV prevention protocol. A similar argument might be made for male circumcision, now that the Kenya and Uganda clinical trials have replicated the findings of the South African Orange Farm study [56].

As an HIV/STD prevention trial, the Trial was responsible for trying to prevent infections through known methods. Therefore, sites offered condoms at the time of interview and when laboratory results were reported to the participant. Sites also offered health education (discussion, pamphlets, etc.) at time of interview and when the HIV/STD results were provided. Study counseling included referral to existing testing, counseling, and treatment resources in the area, and encouraged participants to bring in their partners for syndromic treatment in several of the study sites.

One of the most effective methods for preventing HIV transmission involves administering antiretroviral medications to HIV-positive pregnant women to reduce transmission to infants. Before the Trial, this had been demonstrated in studies in the United States, Europe, and the developing world [57]. We had debates within the Trial with regard to providing this care in this study context, especially in Zimbabwe where HIV prevalence is high, the epidemic is a generalized one, and mother-to-child transmission is frequent. After considerable consultation and discussion, investigators decided to counsel pregnant women about the options for preventing transmission during the birthing process, and to provide referral to Ministry of Health-identified local district, provincial or mission hospitals that offer nevirapine for the prevention of mother-to-child transmission. Women were provided with transportation vouchers to reach these hospitals during labor. Therefore, although we decided that providing antiretroviral treatment was not its obligation, the cost-effective feasibility of being able to prevent mother-to-child transmission led the research team to provide access to nevirapine as an antiretroviral prophylactic regime to pregnant women. This decision was not without controversy: is it better to provide nevirapine to the pregnant mother, knowing that the child is likely to be orphaned? Despite the controversy, we provided access to mother-to-child transmission prophylaxis at the birth of the child. We also provided access to prophylactic antibiotics for participants living with HIV. Given the current scale-up of prevention and treatment activities in the developing world, these interventions appeared likely to be sustainable before the Trial ended in the local communities. Furthermore, it was highly likely that the capacity existed or could be built to sustain these interventions. Finally, these decisions were consistent with in-country policies.

Regarding the benefits of VCT in a situation without general access to treatment, our experience has been that most individuals enrolled in the study wanted to know their HIV status so that they could plan for the future, particularly in terms of family responsibilities [58,59]. Individuals also mentioned the opportunity to live more positive lives in terms of taking better care of themselves and adopting behaviors that could prevent further
transmission [60,61]. In many countries, individuals who wish to know their HIV status face barriers that are often logistical or cost related, and this study design removed many of these barriers. Offering VCT as part of the study to individuals eligible to participate in the Trial provided a significant potential benefit to these individuals.

The other issue to consider regarding the potential risk or benefit to individuals is their alternatives. VCT outside of this study may be difficult to access at some sites because of logistical issues (location and expense), but testing may be available in private clinics or government-sponsored programmes. Pre and post test counseling is rarely offered in private doctor’s offices, and the quality of the counseling at public VCT sites is frequently inadequate compared with protocol standards. Post test support services are also limited outside the study protocol, suggesting that the potential for social harm from the research study may be lower than for testing conducted outside of the Trial.

Finally, it should be noted that the most affected countries would receive the most direct benefit of this research. This intervention has already proved efficacious in the United States, and the purpose of this Trial is to prove such efficacy in less resourced countries, with the advantage of its low cost and its being based on a simple concept: social communication. This Trial also responds to the ethical principle of justice, the group experiencing the research risk can potentially receive the greatest benefit from the research.

**Ensuring that prevention can be achieved in the international context**

One major advantage of the Trial is that the intervention, if it proves to be efficacious, can be implemented at low cost in a variety of settings. Furthermore, developing the intervention for the study resulted in treatment and training manuals in host country languages, adapted to local cultures as a result of extensive ethnography and pilot testing, and these manuals can be adapted for wider dissemination once the study is over.

**Providing the experimental intervention to comparison communities and participants**

For many reasons, the steering committee decided to offer the experimental intervention to the comparison communities and participants after data collection concluded in a particular area but before unblinding occurred at the end of the Trial. First, the steering committee decided that comparison participants should have access to the experimental intervention if they chose to participate in it. Second, waiting until the Trial was unblinded to offer the intervention to comparison communities would not have been feasible because the study will not have funding after unblinding in 2008. Finally, implementing the intervention in the comparison communities provided the opportunity for a variety of experiments to determine ways to adapt and implement the intervention in real-world settings. In a very real sense, it allowed the investigative teams to take the first step in adapting the intervention and training manuals for use by non-governmental organizations, ministries of health, local health authorities, and others.

**Additional Trial responsibilities**

The investigators in this Trial also adopted, consistent with Lo and Bayer [2], two additional principles of operation as they designed and implemented the Trial. The investigators in this study felt strongly that it was important to leave behind the capacity and ability to conduct further prevention trials. This translated into specific strategies for building local capacity and translating the findings into policy and practice.

**Building capacity**

Capacity was built in several important ways. In the first years of the Trial, the Fogarty International Center of the NIH provided US$50,000 to each US and international country pair for training purposes. Each of the sites used these funds in different ways, but all provided training in research skills for international staff. Because the study was powered partially on STD and HIV endpoints, laboratories in each country had to be developed or enhanced so that they could reliably and validly conduct the necessary assays. This required training laboratory personnel, providing or upgrading equipment, and certifying staff and laboratories through the core laboratory at the Johns Hopkins University School of Medicine. Information technology capacity was developed for data storage, management, and transfer to the data coordinating center at RTI International in North Carolina. Investments were made in equipment, laptops, secure broadband data lines, and the personnel necessary to meet this requirement. Capacity was also built among staff participating in all of the Trial workgroups. Each workgroup was composed of US and international scientists and staff, working together to understand theory and translate theory into operations. Training manuals and programmes were developed in each of the host country languages, and staffs were taught how to train and supervise others in programme implementation and evaluation. Staffs in all sites were trained in research ethics, and quality assurance checks and monitoring provided further opportunities for ethics training.

The US institutions participating in the Trial expanded their repertoire of skills and capacities for conducting research in the developing world. Important working relationships between host country and US scientists were deepened, and all sites worked to develop additional projects for the benefit of the host country. The US
researchers had the opportunity to learn about the cultural adaptation of interventions in general, and site-specific needs for intervention adaptation and adoption through their improved knowledge of diverse realities. Successful strategies for ensuring timely and accurate accounting and money transfers were developed, as were the requirements for specimen transfer and validation checks.

**Moving research into policy and practice**

The final ethical requirement laid out by Lo and Bayer [2] stipulated that trial investigators should attempt to find ways to ensure that trial strategies are available to affected communities once the trial is over. This implies more than making materials and manuals available, and more than providing training to non-governmental organizations and Ministry of Health personnel. The steering committee for the Trial interpreted this requirement to mean that it was essential to advocate for prevention, especially for cost-effective strategies, and keep host country governmental personnel abreast of Trial implementation, feasibility, and outcomes. Each site is developing materials that can be used in-country for the diffusion of the intervention throughout the host countries.

In conclusion, using a rigorous clinical trials design, this study developed, adapted, and evaluated the efficacy of a behavioral intervention for reducing HIV and STD transmission in resource-limited settings. The challenges in conducting such a study were enormous, but the need is even more enormous. An HIV vaccine is still years away, and biomedical preventive strategies, although promising, will always need to be provided together with behavioral strategies [13,62]. We have outlined here the ethical challenges we faced and the strategies we used to resolve them. We presented them in this paper to document the issues encountered, our decisions regarding their resolution, and to contribute to the overall development of ethical standards for HIV prevention trials in the developing world. We hope that others benefit from our thinking, take our deliberations forward, and continue these important discussions.

**References**

Sexually transmitted disease and HIV prevalence and risk factors in concentrated and generalized HIV epidemic settings

NIMH Collaborative HIV/STD Prevention Trial Group*

Background: In many developing countries, the threat of nascent HIV epidemics expanding rapidly requires immediate and appropriate HIV prevention activities. Inexpensive and sustainable interventions are especially relevant in resource-constrained environments. In 2001, we assessed the prevalence and behavioral risk of sexually transmitted disease (STD) and HIV among at-risk populations in five developing countries in preparation for a community-randomized controlled trial, the NIMH Collaborative HIV/STD Prevention Trial.

Methods: Using a standardized protocol, more than 1000 participants in each country (China, India, Peru, Russia, and Zimbabwe) were selected by random sampling methods, completed a behavioral risk assessment, and provided biological specimens using a common laboratory protocol. Sample characteristics were studied within each country, and risk factors for HIV/STD acquisition were evaluated using logistic regression models.

Results: HIV rates were low (<1%) in China, India, Peru, and Russia but were high (26%) in rural Zimbabwe. STDs were generally twice as common in women as men, and serological evidence of herpes simplex virus type 2 infection was the most frequently detected STD. Behavioral data showed high rates of multiple partners in the Russian sample, and very low condom use rates in India and China. Among participants who reported ever having sex, female sex and having two or more sex partners were the factors most frequently associated with an increased risk of prevalent STD.

Conclusion: Behavioral or biological risks were of sufficient magnitude in the locations selected in China, Russia, and Zimbabwe to implement the community-based randomized trial. Higher-risk subsets of community residents in India and Peru were identified before beginning the Trial.

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Introduction

The HIV epidemic has continued to unfold in developing countries more than two decades after HIV was first detected. Global estimates indicate that nearly 25 million deaths over the past 20 years can be attributed to HIV/AIDS and that 42 million individuals are currently infected [1]. Although some successes have been noted in the control of the HIV pandemic, particularly in Thailand, Uganda, Senegal, and Brazil, epidemics continue unabated in many resource-poor countries [1]. Countries at different stages in the HIV epidemic require different types of preventive interventions [2]. Those in the concentrated (or nascent) stage, where the epidemic still affects less than 1% of the general population, are often characterized as having HIV confined to limited, high-risk (often mobile) populations. With sufficient mixing between high-risk individuals and the general population, referred to as epidemiological ‘bridging’, the epidemic may become more generalized and expand rapidly [3]. In concentrated epidemics, HIV prevention is most efficient when it addresses so-called ‘core groups’ [4]. In generalized epidemics, prevention focused on the general population is more efficient, given the widespread prevalence of the local HIV epidemic. Depending on the local situation, prevention efforts might thus entail making HIV voluntary counseling and testing easily accessible to core groups or to the general population, providing or promoting sexually transmitted disease

* See Appendix B for members of the NIMH Collaborative HIV/STD Prevention Trial Group.
(STD) diagnosis and treatment to core or general target populations, and promoting condom use and peer intervention to appropriate populations [5].

An HIV prevention strategy using a popular opinion leader approach initiated by Kelly and colleagues [6] demonstrated efficacy in multiple settings with multiple populations in the United States [6–8]. Adapting this intervention using community popular opinion leaders is an ideal HIV/STD prevention programme for international low-resource settings because procedures for conducting such a programme already exist, it may be cost effective [9,10] depending on the local context, and because it relies on word-of-mouth and social influence the intervention can be easily implemented in low-literacy settings.

One of the principal approaches to HIV prevention in developing-country settings has been the control of sexually transmitted infections through interventions aimed at treatment as well as those aimed at prevention through behavior change (risk reduction) and condom promotion. To date, the effects of community randomized trials aimed at reducing HIV incidence through the treatment of STDs in these settings have been inconclusive [11,12], as have behavioral interventions [13]. There is widespread agreement, however, that effective behavior change can lead to a reduction in disease acquisition [14].

The NIMH Collaborative HIV/STD Prevention Trial (‘the Trial’) seeks to determine the effectiveness of a community popular opinion leader intervention approach to stimulating HIV risk reduction in developing countries. Before implementing this large, community-randomized controlled trial for HIV/STD prevention in China, India, Peru, Russia, and Zimbabwe, an epidemiological study was conducted in these countries to assist with planning of the Trial. The objectives of the epidemiological study were to assess STD and HIV prevalence and behavioral risk in each country and to field test HIV/STD sampling procedures, laboratory assays, and reference laboratory procedures. Findings from this study are the subject of this article.

Methods

Study design
During the study period, February–September 2001, approximately 20–30 locations for study implementation (venues) were identified in each country using standardized criteria, although different types of places were selected in the individual countries, described briefly under Study sites below and more completely in ‘Selection of populations represented in the NIMH Collaborative HIV/STD Prevention Trial’ [15]. In each country, simple probability sampling after enumeration was used to select 50 or more participants in each venue to ensure that the final sample provided behavioral risk data and biological specimens for at least 50 participants. Because behavioral risk factors and the epidemiology of STDs were expected to vary by site, the age range of participants varied, but all countries sampled a core group of 18–30 year-olds. All participants verified that they lived or worked in the selected venue, planned to remain in their neighborhood for the next year, were able to give informed consent, and did not have any condition (deafness, serious mental illness, or mental retardation) that would preclude obtaining informed consent and thus participating in the study.

Identification of venues
Venues and at-risk populations were identified in each country. Extensive ethnographic studies [16,17] were used to assess sexual behavior and HIV/STD risk factors to help ensure that appropriate venues and populations were selected. These studies also identified characteristics of natural leaders in the venues, provided the formative data necessary to design the final intervention strategy, and identified high-risk behaviors.

Study sites

China
Thirty food markets were selected, based on size and geographical location, from among 95 commercial food markets in five districts in Fuzhou city in the Fujian Province in southern China. Each market was an identifiable venue located in a separate physical structure. Most markets had 50–150 independent stores or stalls, with a total of approximately 150–300 employees. A sample of workers, aged 18–40 years, was drawn at each of the 30 markets by first selecting a random sample of stalls and then selecting one person at random among those aged 18–40 years in each selected stall. Participants were accompanied to a local community health center where they provided biological samples and were interviewed.

India
Participants were selected from low-income neighborhoods called ‘slums’ (government-designated low-income housing communities scheduled for the construction of subsidized housing blocks), in Chennai, the capital of Tamil Nadu State in southern India. The selection of slums was based on ethnographic evidence of low condom use and anticipated high HIV prevalence. The 28 geographically separated slums used for the study, with 100–300 families each, were enumerated. A simple random sample of households, and then a random sample of adults aged 18–40 years within households, was drawn in each slum. The residents selected in each slum were asked to participate in the confidential interview and to give biological specimens when they attended a 1-day ‘health camp’. All slum residents were invited to the camps, where physical examinations were conducted, health education provided, medications given free of
charge, and appropriate referrals made. Over 90% of eligible participants invited to the health camps attended.

Peru
Residential areas (barrios, or neighborhoods) were selected in the capital city of Lima, and in Chiclayo and Trujillo, coastal cities north of Lima. Geographically separate communities were selected to reflect the sociodemographic structure of low to low middle-income populations and to be homogeneous with regard to values of an indicator of poverty widely used in the country (the score of unmet basic needs). Within the barrios, core clusters of between eight and 16 contiguous blocks with resident populations of between 800 and 1600 were selected as study venues. A random sample of residents aged 18–30 years was drawn from each of 30 venues, and all selected residents were invited to a storefront location in the community, where study procedures were conducted.

Russia
Participants were selected from among young adults aged 18–30 years living in vocational, technical, or trade school dormitories in St Petersburg. Earlier studies with similar populations in Russia suggested high rates of sexual risk behavior, substance use, and STDs. Approximately equal numbers of men and women lived in the dormitories, with an average of 400 residents per dormitory. From residential rosters, residents were randomly selected in each of the 20 dormitories with at least 200 residents. At a health station nearby, participating residents responded to interviews and provided biological samples.

Zimbabwe
Thirty-two rural villages across eight rural districts were purposely selected as venues from communities designated by the government in 1985 as ‘growth points’ to receive aid for the development of local area rural economies. With populations ranging from 2500 to 15000, these villages have small commercial areas, usually consisting of a few stores and markets, other services, and bottle stores, beer halls, or nightclubs. Primary, and occasionally secondary, schools and a health clinic were occasionally part of these communities. Participants, aged 16–30 years, were randomly selected from among inhabitants in randomly selected households in each of the 32 villages. All data collection took place in households where privacy was assured.

Data collection
A behavioral risk assessment instrument was used to collect data systematically on the participants’ demographics, residential stability, health status, drug and alcohol use, sexual behavior, and condom use. Participants in Peru, Russia, and Zimbabwe entered their responses themselves directly into computers using audio computer-assisted self-interviewing (ACASI). In China and India, interviewers used computer-assisted personal interviewing (CAPI) to administer the questionnaire to participants in privacy and enter their responses into computers. ACASI was not used in these countries because preliminary studies showed that it took considerably longer to administer, and it appeared that participants in China and India may have been more forthright when CAPI was used [18]. All assessments were conducted in the languages of the country: Mandarin and Fuzhou dialect in China, Tamil in India, Spanish in Peru, Russian in Russia, and Shona and Ndebele in Zimbabwe. All translations were independently back-translated into English to assess meaning and fidelity to the original questions. The interviews took 15–35 min to complete, depending on reported sexual and drug use behaviors. After completing the interview, participants received HIV pretest counseling and provided blood and urine specimens and self or clinician-collected vaginal swabs to test for the following STDs: HIV, herpes simplex virus type 2 (HSV-2), syphilis, trichomonas (women only), gonorrhea, and chlamydia.

Specimens were tested in study laboratories in each country, following standardized laboratory protocols developed by a team of STD and laboratory experts. HIV testing was performed using HIV enzyme-linked immunosorbent assay (ELISA), and it was repeated using a second approved ELISA kit. Positives and discordants were confirmed using Western blot, except in Zimbabwe, where a positive result on duplicate ELISA tests was considered confirmatory, and a third ELISA test or a Western blot was used to confirm HIV status in the case of discordant results on the previous two. As a result of the anticipated high prevalence of HIV in Zimbabwe, triplicate ELISA testing was allowed to minimize study costs. HSV-2 testing was performed using Herpeselect 2 enzyme immunoassay (MRK, Focus Technologies, Los Angeles, California, USA). Those with index values of 1.1 or greater were considered positive for HSV-2. The Trial’s biological workgroup is evaluating the HSV-2 index value cutoff values for the study populations in light of recent scientific data regarding the variability in confirmed HSV-2 seropositive results using the US Food and Drug Administration-cleared manufacturer’s instructions for the focus Technologies Herpeselect enzyme immunoassay. This workgroup will make recommendations regarding cutoff values for the main Trial. Syphilis testing was performed by rapid plasma reagin and confirmed using the Treponema pallidum particle agglutination test. Vaginal swabs were cultured for Trichomonas vaginalis using the InPouch TV 20 test kit (Biomed, San Jose, California, USA). Urine from men and vaginal swabs from women were tested for chlamydia and gonorrhoea DNA using Amplicor CT/NG polymerase chain reaction (Roche, Branchburg, New Jersey, USA). Individuals with non-viral STDs were treated according to US Centers for Disease Control and Prevention STD treatment guidelines [19] or World Health Organization...
STD treatment guidelines [20], or were referred to local centers for treatment based on national best practices guidelines. People testing positive for HIV were referred to existing local treatment centers. All participants were offered their HIV and STD test results and post-test counseling within 4 weeks of the initial visit. Over 85% of participants either received on-site treatment or referrals.

Quality assessment
Interviewers were trained centrally, and site visits were conducted by the data coordinating center to ensure that the ACASI and CAPI programmes were functioning correctly and that data were recorded accurately. Procedures for drawing samples of participants in each venue were developed centrally and overseen locally.

The quality assurance process for biological specimen testing was extensive. Senior laboratory staff from each site were trained at the Johns Hopkins University international STD reference laboratory. Protocols were developed to specify standard biological specimen collection, storage, and analysis procedures. The reference laboratory prepared panels of approximately 200 known samples and sent them to site laboratories for analysis by appropriate assay, and site visits were conducted to review laboratory procedures. The five site laboratories shipped to the reference laboratory for retesting a 20% sample of specimens collected in each site, including all positive samples (if less than 10%) or a random sample of positives (up to 10%) and a random sample of negatives. All discordant results were initially checked for data entry or interpretation errors, and study data were corrected as needed.

Statistical analysis
Data were analysed using SAS software [21]. The percentage of participants who tested positive for HIV and each STD (chlamydia, gonorrhea, syphilis, trichomonas, HSV-2) was determined separately for men and women. A binary variable (Any STD) was created to indicate participants who tested positive for any of these STDs including HIV, but was not calculated for individuals with three or more missing results (3% of those with at least one test). A second composite binary variable (Any non-viral STD) was created to indicate participants who tested positive for chlamydia, gonorrhea, syphilis, or trichomonas, STDs treatable with simple pharmacological regimens. This variable was not calculated for people with two or more missing results (9% of participants tested).

Unadjusted comparisons of demographic characteristics between men and women were made using Fisher’s exact or Wilcoxon tests. The risk of prevalent STD was studied among the subset of participants who reported ever having sex. Possible risk factors were evaluated for each country separately using logistic regression models fit to the Any STD outcome with statistical significance of covariates determined by Wald chi-square tests. We also considered risk factors for Any Viral STD and Any non-viral STD, but as the results were similar, we report here only the results for Any STD (results for the previous two outcomes are available from the authors). First, a stepwise procedure was used to select, from the following, the behavioral variable with the strongest association with the outcome after adjusting for sex: number of sexual partners in the past year (two or more, one, or none), the number of sexual partners in the past 3 months (two or more, one, or none), and the frequency of condom use in the past 3 months (<100% of the time, 100%, no sex in the past 3 months). The number of sexual partners in the past year or in the past 3 months was selected for all countries.

Models that were fit included the behavioral variable as well as venue, sex, marital status, age (≤24, 25–30, 31–40 years), education (high school or not), the frequency of alcohol use (weekly or more, less than weekly, no use), any illegal drug use in the past 3 months, ever exchanged sex for money or goods, attempted to obtain condoms in the past 3 months, and perceived likelihood of HIV infection (somewhat or very likely or already infected versus unlikely). All two-way interactions with sex were first included to test for differences by sex. No significant interactions were detected except in Zimbabwe. Therefore, models were refit with main effects only, as well as with non-significant interactions removed for Zimbabwe. Adjusted odds ratios (OR) and 95% confidence intervals from these models are reported.

Results

Population
Between 1000 and 1600 people participated in each country. Slightly less than half of the participants in each country were men (Table 1). Participation response rates varied from 77 to 89% of those selected, depending on site. No information was available from Russia on the number of people selected who refused to participate. Participants in Peru, Russia, and Zimbabwe were younger than those in China and India (by design), and were more likely to be unmarried and to have at least a high school degree. Female participants in all countries were more likely than men to be married. Significantly more men than women had high school degrees in China, India, and Zimbabwe but not in Peru. All Russian participants had completed high school. In China, India, and Zimbabwe, more female than male participants reported ever having had sex. In Russia more male participants reported having had sex, and no difference was found among participants in Peru.

Prevalence of HIV and sexually transmitted diseases
Refusal rates for STD testing were extremely low, and virtually all participants were tested for at least one
STD: in China, 1537 (99.7%); in India, 1513 (98.2%); in Peru, 1446 (98.9%); in Russia, 998 (99.8%); and in Zimbabwe, 1596 (99.4%). With few exceptions, more women than men in all countries tested positive for each STD (Table 2). STD prevalence rates varied widely by specific pathogen and by sex. Overall, serological evidence revealed that HSV-2 infection was the most prevalent STD, with rates in women generally two to three times as high as rates in men. HSV-2 antibody prevalence was lowest in Russia (3.2% in men and 9.1% in women), intermediate in China (5.8% in men and 11.3% in women), India (10.3% in men and 16.4% in women), and Peru (7.1% in men and 20.2% in women); and highest in Zimbabwe, where 27% of men and 59% of women tested positive. HIV prevalence was generally under or very close to 1% in all countries except Zimbabwe, where 15% of men and 34% of women in this sample of young adults tested positive for HIV. More than 30% of Zimbabwe men and 66% of Zimbabwean women were positive for at least one of the six STDs.

Chlamydia prevalence ranged from 0.1% among women in India to a high of 12% among women in China. In all countries except India, women had somewhat higher rates of chlamydia than men. Gonorrhea and syphilis were infrequent in all countries, with small differences between men and women. Finally, the prevalence of trichomonas ranged from 0.5% among women in Russia to 15% among those in Zimbabwe.

Behavioral risks
More than 80% of participants in each country reported ever having had sex (Table 3). Most participants reported having one sexual partner in the year preceding the interview, except in Russia, where 47% reported having two or more sexual partners. Between 49 and 79% of participants reported having had sex at least once during the 3 months before the interview. Among those who reported having sex in the past 3 months, most participants in China (87%), India (93%), and Peru (60%) reported never using condoms, whereas approximately half (53%) in Zimbabwe and a minority (37%) in Russia reported never using condoms. The percentage of participants who said they had ever exchanged money, goods, shelter, or anything else for sex ranged from 4% in India to 15% in Zimbabwe. Attempts to seek condoms correlated strongly with reports of the frequency of condom use: less than 10% of participants in China and India had attempted to obtain condoms, compared with 17% in Peru, 30% in Zimbabwe, and 51% in Russia.

Reported alcohol use was highest among Russian participants and lowest among those in India and Zimbabwe. In Zimbabwe, however, among those who drank alcohol (mostly men), 48% reported getting drunk at least once per week; less than 10% of those reporting alcohol use in all other sites reported frequent drunkenness. Illegal drug use was reported by 6% or less of participants in China, India, and Peru but by 17% in Russia and Zimbabwe.
When asked how likely they were to become HIV infected, most participants in each site thought that it was unlikely. Of note is the fact that only four people in Zimbabwe responded that they knew they were already HIV infected, whereas 408 (26%) tested positive among the 1594 tested for HIV. Because in-country antenatal clinic monitoring surveys of HIV status are conducted anonymously, many women who have been tested may not be aware of their serostatus.

In each site, some participants who indicated that they had never had sex tested positive for at least one STD. That percentage was similar for women and men in China (6% for women and 5% for men), India (3% for both), and Russia (5% for both) but higher for women in Peru (10% for women and 1% for men) and Zimbabwe (23% for women and 11% for men). The most common infection among this group was serological evidence of HSV-2 infection. In Zimbabwe, with the highest rates of HSV-2, some HSV-2 infections are likely to have been acquired perinatally. Inferences based on our results must take this into account.

### Risk-factor analysis

In the subset of participants in each country that reported ever having had sex, we evaluated possible risk factors for acquiring at least one of the six STDs. Female sex was significantly associated with increased odds of STD in Russia (OR 3.3) and Zimbabwe (OR 5.5), but not among men who had multiple partners (OR 1.1). Other factors were less frequently associated with increased odds of STD.

In India, Peru, and Zimbabwe, younger participants were at a significantly reduced risk of STD compared with older participants. The odds of having an STD were reduced by half for those with at least a high school education compared with those with less education in Peru (OR 0.5) and among women in Zimbabwe (OR 0.5), but no association with education was found among Zimbabwean men (OR 0.9).

### Discussion

Few international comparative studies of HIV risk in defined populations have used standardized sampling approaches, common behavioral assessments, and

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Table 2. Prevalence of selected sexually transmitted diseases by sex and study site.

<table>
<thead>
<tr>
<th>STD</th>
<th>China</th>
<th>India</th>
<th>Peru</th>
<th>Russia</th>
<th>Zimbabwe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>n (%)</td>
<td>N</td>
<td>n (%)</td>
<td>N</td>
</tr>
<tr>
<td>Chlamydia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>732</td>
<td>33 (4.5)</td>
<td>709</td>
<td>3 (0.4)</td>
<td>533</td>
</tr>
<tr>
<td>Women</td>
<td>746</td>
<td>91 (12.2)</td>
<td>722</td>
<td>1 (0.1)</td>
<td>812</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>739</td>
<td>5 (0.7)</td>
<td>699</td>
<td>1 (0.1)</td>
<td>536</td>
</tr>
<tr>
<td>Women</td>
<td>746</td>
<td>8 (1.1)</td>
<td>719</td>
<td>2 (0.3)</td>
<td>716</td>
</tr>
<tr>
<td>HSV-2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>741</td>
<td>43 (5.8)</td>
<td>716</td>
<td>74 (10.3)</td>
<td>537</td>
</tr>
<tr>
<td>Women</td>
<td>788</td>
<td>89 (11.3)</td>
<td>782</td>
<td>128 (16.4)</td>
<td>769</td>
</tr>
<tr>
<td>Trichomonas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>671</td>
<td>46 (6.9)</td>
<td>628</td>
<td>45 (7.2)</td>
<td>853</td>
</tr>
<tr>
<td>Syphilis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>735</td>
<td>12 (1.6)</td>
<td>698</td>
<td>6 (1.2)</td>
<td>573</td>
</tr>
<tr>
<td>Women</td>
<td>785</td>
<td>13 (1.7)</td>
<td>765</td>
<td>6 (0.8)</td>
<td>824</td>
</tr>
<tr>
<td>HIV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>739</td>
<td>0 (0)</td>
<td>717</td>
<td>8 (1.1)</td>
<td>584</td>
</tr>
<tr>
<td>Women</td>
<td>790</td>
<td>0 (0)</td>
<td>778</td>
<td>2 (0.3)</td>
<td>851</td>
</tr>
<tr>
<td>Any STDa</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>739</td>
<td>81 (11.0)</td>
<td>709</td>
<td>87 (12.3)</td>
<td>586</td>
</tr>
<tr>
<td>Women</td>
<td>789</td>
<td>194 (24.6)</td>
<td>766</td>
<td>163 (21.3)</td>
<td>851</td>
</tr>
<tr>
<td>Any non-viral STDb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>721</td>
<td>46 (6.4)</td>
<td>671</td>
<td>11 (1.6)</td>
<td>538</td>
</tr>
<tr>
<td>Women</td>
<td>756</td>
<td>132 (17.5)</td>
<td>712</td>
<td>51 (7.2)</td>
<td>787</td>
</tr>
</tbody>
</table>

HSV-2, Herpes simplex virus type 2; STD, sexually transmitted disease.

aAny positive test for chlamydia, gonorrhea, HSV-2, trichomona, syphilis, or HIV. Variable was calculated if at least four test results were non-missing.

bAny positive test for chlamydia, gonorrhea, trichomona, or syphilis. Variable was calculated if at least three test results were non-missing.
standardized protocols for laboratory assays. Other comparative studies generally have not included both behavioral and biological outcomes. Combining individual self-reports of behavioral risk with biological outcomes adds strength to the findings of this study.

As anticipated, the overall HIV prevalence was very low in four of the five countries in our study. These sites were selected purposely because they have many of the factors that can fuel an HIV epidemic [22], and they offer good prospects for primary prevention. Although India had approximately 5.7 million HIV cases in 2005 [23], these results indicate that HIV had not yet unduly affected the urban general population considered to be at highest risk, inner-city slum dwellers. Nevertheless, if slum residents were to mix sexually with high-risk individuals (e.g. sex workers or drug users), the opportunity exists for the rapid expansion of an HIV epidemic. The current situation in Fujian Province, China, is more reassuring, for HIV infection does not yet appear to have reached the heterosexual working population in Fuzhou, despite recent reports of a potentially explosive HIV epidemic [24,25]. This is also true for Peru and Russia, where concentrated epidemics exist, most commonly associated with men who have sex with men in Peru and injection drug use in Russia. As was known, Zimbabwe has a very well established, generalized epidemic.

The type and level of STD burden showed some important variation across sites. Gonorrhea and syphilis were consistently low and showed little variation by sex. Chlamydia, however, was more common among women

### Table 3. Behavioral risks for sexually transmitted disease acquisition in participants by study site.

<table>
<thead>
<tr>
<th>Behavioral risk</th>
<th>China n (%)</th>
<th>India n (%)</th>
<th>Peru n (%)</th>
<th>Russia n (%)</th>
<th>Zimbabwe n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever had sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1322 (86)</td>
<td>1286 (84)</td>
<td>1242 (85)</td>
<td>908 (91)</td>
<td>1308 (82)</td>
</tr>
<tr>
<td>No</td>
<td>220 (14)</td>
<td>254 (16)</td>
<td>214 (15)</td>
<td>87 (9)</td>
<td>296 (18)</td>
</tr>
<tr>
<td>Missing</td>
<td>–</td>
<td>–</td>
<td>6</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Married</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever had sex, Yes</td>
<td>1200 (99.7)</td>
<td>1101 (99.7)</td>
<td>513 (98.8)</td>
<td>99 (100)</td>
<td>643 (99.2)</td>
</tr>
<tr>
<td>Ever had sex, No</td>
<td>4 (0.3)</td>
<td>3 (0.3)</td>
<td>6 (1.2)</td>
<td>0</td>
<td>5 (0.8)</td>
</tr>
<tr>
<td>Not married</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever had sex, Yes</td>
<td>122 (36)</td>
<td>185 (42)</td>
<td>728 (78)</td>
<td>808 (90)</td>
<td>664 (70)</td>
</tr>
<tr>
<td>Ever had sex, No</td>
<td>216 (64)</td>
<td>251 (58)</td>
<td>208 (22)</td>
<td>87 (10)</td>
<td>291 (30)</td>
</tr>
<tr>
<td>Missing</td>
<td>–</td>
<td>–</td>
<td>7</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>No. of partners in past year</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>254 (17)</td>
<td>403 (26)</td>
<td>399 (28)</td>
<td>122 (13)</td>
<td>440 (28)</td>
</tr>
<tr>
<td>1</td>
<td>1203 (78)</td>
<td>1053 (68)</td>
<td>763 (53)</td>
<td>399 (41)</td>
<td>801 (51)</td>
</tr>
<tr>
<td>2–5</td>
<td>42 (5)</td>
<td>73 (5)</td>
<td>245 (17)</td>
<td>385 (39)</td>
<td>288 (18)</td>
</tr>
<tr>
<td>&gt;5</td>
<td>9 (&lt;1)</td>
<td>10 (1)</td>
<td>22 (2)</td>
<td>71 (7)</td>
<td>57 (4)</td>
</tr>
<tr>
<td>Missing</td>
<td>4</td>
<td>1</td>
<td>7</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>No. of times had sex in past 3 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>322 (21)</td>
<td>526 (35)</td>
<td>691 (51)</td>
<td>266 (31)</td>
<td>710 (51)</td>
</tr>
<tr>
<td>1</td>
<td>1205 (79)</td>
<td>990 (65)</td>
<td>654 (49)</td>
<td>596 (69)</td>
<td>682 (49)</td>
</tr>
<tr>
<td>Missing</td>
<td>15</td>
<td>24</td>
<td>117</td>
<td>138</td>
<td>214</td>
</tr>
<tr>
<td>Frequency of condom usea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1043 (87)</td>
<td>914 (93)</td>
<td>378 (60)</td>
<td>209 (37)</td>
<td>336 (53)</td>
</tr>
<tr>
<td>1–50% of the time</td>
<td>32 (3)</td>
<td>22 (2)</td>
<td>83 (13)</td>
<td>107 (19)</td>
<td>84 (13)</td>
</tr>
<tr>
<td>51–100% of the time</td>
<td>14 (1)</td>
<td>2 (&lt;1)</td>
<td>29 (5)</td>
<td>60 (11)</td>
<td>43 (7)</td>
</tr>
<tr>
<td>Every time</td>
<td>115 (10)</td>
<td>42 (4)</td>
<td>138 (22)</td>
<td>186 (33)</td>
<td>175 (27)</td>
</tr>
<tr>
<td>Missing</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>23</td>
<td>20</td>
</tr>
<tr>
<td>Frequency of alcohol use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>587 (38)</td>
<td>1012 (66)</td>
<td>429 (29)</td>
<td>26 (3)</td>
<td>1098 (68)</td>
</tr>
<tr>
<td>Less than weekly</td>
<td>618 (40)</td>
<td>222 (14)</td>
<td>838 (57)</td>
<td>516 (52)</td>
<td>216 (13)</td>
</tr>
<tr>
<td>Weekly</td>
<td>192 (13)</td>
<td>184 (12)</td>
<td>190 (13)</td>
<td>430 (43)</td>
<td>227 (14)</td>
</tr>
<tr>
<td>Daily</td>
<td>145 (9)</td>
<td>121 (8)</td>
<td>2 (&lt;1)</td>
<td>23 (2)</td>
<td>65 (4)</td>
</tr>
<tr>
<td>Missing</td>
<td>–</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>–</td>
</tr>
<tr>
<td>Frequency of drunkennessb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weekly or more often</td>
<td>2 (&lt;1)</td>
<td>30 (6)</td>
<td>95 (9)</td>
<td>53 (6)</td>
<td>244 (48)</td>
</tr>
<tr>
<td>Ever exchanged sex for material goods</td>
<td>85 (6)</td>
<td>57 (4)</td>
<td>109 (9)</td>
<td>66 (7)</td>
<td>194 (15)</td>
</tr>
<tr>
<td>Tried to obtain condoms in past 3 months</td>
<td>133 (9)</td>
<td>97 (6)</td>
<td>244 (17)</td>
<td>512 (51)</td>
<td>481 (30)</td>
</tr>
<tr>
<td>Drug use in past 3 months</td>
<td>133 (9)</td>
<td>97 (6)</td>
<td>244 (17)</td>
<td>512 (51)</td>
<td>481 (30)</td>
</tr>
<tr>
<td>Perceived likelihood of becoming HIV infected</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Already infected</td>
<td>0 (0)</td>
<td>3 (&lt;1)</td>
<td>5 (&lt;1)</td>
<td>0 (0)</td>
<td>4 (&lt;1)</td>
</tr>
<tr>
<td>Somewhat/very likely</td>
<td>20 (1)</td>
<td>54 (4)</td>
<td>152 (12)</td>
<td>58 (6)</td>
<td>527 (33)</td>
</tr>
<tr>
<td>Unlikely</td>
<td>1513 (99)</td>
<td>1397 (96)</td>
<td>1160 (88)</td>
<td>907 (94)</td>
<td>1058 (67)</td>
</tr>
<tr>
<td>Missing</td>
<td>9</td>
<td>86</td>
<td>145</td>
<td>35</td>
<td>17</td>
</tr>
</tbody>
</table>

*aAmong participants who reported having sex in the past 3 months.

*bAmong participants who reported drinking alcohol.

*cAmong participants who reported ever having had sex.
Table 4. Participant characteristics and risk of any sexually transmitted disease among people who reported ever having had sex.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>China N = 1310</th>
<th>India N = 1236</th>
<th>Peru N = 1222</th>
<th>Russia N = 898</th>
<th>Zimbabwe N = 1192</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%) with any STD</td>
<td>Adjusted OR (95% CI)</td>
<td>n (%) with any STD</td>
<td>Adjusted OR (95% CI)</td>
<td>n (%) with any STD</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>188 (27)</td>
<td>3.9 (2.6–5.9)*</td>
<td>161 (23)</td>
<td>4.2 (2.1–8.1)*</td>
<td>206 (29)</td>
</tr>
<tr>
<td>Male</td>
<td>75 (12)</td>
<td>1.0</td>
<td>82 (15)</td>
<td>1.0</td>
<td>61 (12)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>239 (20)</td>
<td>0.7 (0.3–1.3)</td>
<td>203 (19)</td>
<td>0.7 (0.4–1.1)</td>
<td>135 (27)</td>
</tr>
<tr>
<td>Unmarried</td>
<td>24 (20)</td>
<td>1.0</td>
<td>40 (23)</td>
<td>1.0</td>
<td>132 (19)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 24</td>
<td>16 (13)</td>
<td>0.5 (0.3–1.3)</td>
<td>31 (12)</td>
<td>0.3 (0.2–0.5)*</td>
<td>132 (18)</td>
</tr>
<tr>
<td>25–30</td>
<td>85 (20)</td>
<td>1.0 (0.7–1.4)</td>
<td>70 (15)</td>
<td>0.4 (0.3–0.6)*</td>
<td>135 (28)</td>
</tr>
<tr>
<td>31–40</td>
<td>162 (21)</td>
<td>1.0</td>
<td>142 (27)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school plus</td>
<td>25 (17)</td>
<td>0.8 (0.5–1.3)</td>
<td>40 (12)</td>
<td>0.7 (0.5–1.1)</td>
<td>175 (19)</td>
</tr>
<tr>
<td>Less than high school</td>
<td>238 (21)</td>
<td>1.0</td>
<td>203 (23)</td>
<td>1.0</td>
<td>92 (30)</td>
</tr>
<tr>
<td>Number of partnersc</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2+</td>
<td>23 (28)</td>
<td>3.4 (1.0–11.7)</td>
<td>12 (36)</td>
<td>2.6 (1.0–6.8)</td>
<td>65 (25)</td>
</tr>
<tr>
<td>1</td>
<td>233 (20)</td>
<td>1.2 (0.4–3.5)</td>
<td>185 (19)</td>
<td>1.1 (0.7–1.7)</td>
<td>164 (22)</td>
</tr>
<tr>
<td>0</td>
<td>6 (19)</td>
<td>1.0</td>
<td>46 (19)</td>
<td>1.0</td>
<td>31 (17)</td>
</tr>
<tr>
<td>Alcohol use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weekly plus</td>
<td>42 (14)</td>
<td>1.2 (0.7–2.1)</td>
<td>47 (17)</td>
<td>1.6 (0.8–3.2)</td>
<td>37 (22)</td>
</tr>
<tr>
<td>Less than weekly</td>
<td>101 (21)</td>
<td>1.3 (0.9–1.8)</td>
<td>25 (15)</td>
<td>2.0 (0.9–4.2)</td>
<td>150 (21)</td>
</tr>
<tr>
<td>Don’t drink</td>
<td>120 (23)</td>
<td>1.0</td>
<td>171 (21)</td>
<td>1.0</td>
<td>80 (24)</td>
</tr>
<tr>
<td>Illegal drug use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>NA*</td>
<td>32 (35)</td>
<td>2.2 (1.3–4.0)</td>
<td>13 (25)</td>
<td>2.1 (0.9–4.7)</td>
</tr>
<tr>
<td>No</td>
<td>211 (18)</td>
<td>1.0</td>
<td>250 (22)</td>
<td>1.0</td>
<td>120 (17)</td>
</tr>
<tr>
<td>Exchanged sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>21 (25)</td>
<td>1.5 (0.7–3.1)</td>
<td>16 (29)</td>
<td>2.3 (1.0–4.9)*</td>
<td>25 (24)</td>
</tr>
<tr>
<td>No</td>
<td>242 (20)</td>
<td>1.0</td>
<td>227 (19)</td>
<td>1.0</td>
<td>242 (22)</td>
</tr>
<tr>
<td>Tried to obtain condoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>24 (18)</td>
<td>0.9 (0.5–1.4)</td>
<td>14 (15)</td>
<td>0.8 (0.4–1.6)</td>
<td>40 (18)</td>
</tr>
<tr>
<td>No</td>
<td>239 (20)</td>
<td>1.0</td>
<td>229 (20)</td>
<td>1.0</td>
<td>226 (23)</td>
</tr>
<tr>
<td>Likelihood of HIV infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Some/very likely/already</td>
<td>4 (24)</td>
<td>0.8 (0.2–2.9)</td>
<td>13 (27)</td>
<td>1.9 (0.9–4.0)</td>
<td>37 (27)</td>
</tr>
<tr>
<td>Unlikely</td>
<td>256 (20)</td>
<td>1.0</td>
<td>211 (19)</td>
<td>1.0</td>
<td>212 (22)</td>
</tr>
</tbody>
</table>

CI, confidence interval; OR, odds ratio; STD, sexually transmitted disease. Any STD means a positive result for chlamydia, gonorrhea, herpes simplex virus type 2, trichomonas, syphilis, or HIV. This outcome was calculated if at least four test results were non-missing. People for whom any STD could not be calculated were excluded: 12 in China, 50 in India, 20 in Peru, 10 in Russia, and 116 in Zimbabwe. The numbers shown for each country thus differ by these amounts from the number of people who reported ever having had sex in Table 4. Odds ratios for any STD (95% CI) from logistic regression models that included all variables shown as well as venue are reported. Separate models were fit for each country.

All participants from Russia had completed high school.

Among men, 104 out of 277 (38%) with and 65 out of 162 (40%) without a high school degree had an STD; adjusted OR 0.9 (0.5–1.4), P = 0.6.

Number of sexual partners in the past year for China, Peru, and Zimbabwe; number of partners in the past 3 months for India and Russia.

Among men, 97 out of 213 (45%) with two or more sexual partners in the past year, 50 out of 157 (32%) with one, and 18 out of 60 (30%) who reported no sexual partners in the past year had an STD; adjusted OR for two or more compared with no partners 1.1 (0.6–2.3), P = 0.7; adjusted OR for one compared with no partners 0.8 (0.4–1.6), P = 0.4.

Only one person from China reported illegal drug use.

P ≤ 0.001;

P ≤ 0.01;

P ≤ 0.05.
than men, except in India, and was most prevalent in China and Russia, where virtually no HIV was detected. India and Zimbabwe showed very low rates of chlamydia among women. However, HSV-2 antibody prevalence was much more common and positive test results occurred approximately twice as often among women as men, ranging from 9 to 20% among women in all countries except Zimbabwe, where the prevalence among women was 59%. This has important implications for the future prominence of HIV epidemics, because herpes virus has been implicated as an important STD risk factor for HIV seroconversion in several recent epidemiological studies [26,27]. When the six STDs were combined, all sites showed prevalence above 10% for both sexes, and women consistently had an STD burden double that of their male counterparts. When restricted to the four non–viral STDs evaluated, the male rates were all below 10%, although the female prevalence continued to be 10% or above for all sites but India.

Our study found important differences by site in the behavioral risks evaluated. In Russia, there were very high rates of multiple sexual partnerships compared with the other four countries. Almost half of the Russian participants reported a history of multiple partners in the past year, and 7% reported having more than five. This reflects the young age and single status of these students compared with participants in the other countries. In the two Asian sites, unmarried participants reported lower rates of sexual experience than in the other three sites. This finding may be partly the result of socially desirable responses among participants in these countries; discussions about sex in public settings are considered taboo, and premarital sex, at least for women, is considered culturally unacceptable. Behavioral risk, whether measured by the number of partners [28], partner selection practices [29], or condom use [30], may be independent of STD prevalence [28]. Therefore, to be effective, prevention efforts for HIV acquisition must focus on both risk reduction and STD control, along with appropriate AIDS care [31,32], using established and cost–effective measures [33].

The feasibility of obtaining biological specimens in these settings outside of a medical encounter was initially of some concern, because few previous studies had obtained blood and urine specimens and vaginal swabs as part of random population STD/HIV assessments in developing countries. Although the sites used different strategies to select and approach potential participants, overall response rates to requests for biological specimens were equally high across sites. In particular, our ability to obtain self or clinician collected vaginal swabs for trichomonas testing was quite high, as has been demonstrated in other studies [34–38].

In conclusion, on the basis of these results, the data safety and monitoring board of the Trial determined that there was sufficient behavioral and biological risk in three of the sites (China, Russia, and Zimbabwe) to warrant moving ahead with the community–randomized controlled trial. Study personnel in India and Peru conducted a second survey of approximately equal size to identify higher–risk populations. In India, the focus shifted to the recruitment of men who were frequent patrons of ‘wine shops’, establishments selling beer and distilled spirits by the drink or bottle. These venues were the principal locations for non–brothel female sex workers in Chennai, and the behavioral and STD risks there were significantly higher than in the general population sample originally tested. In Peru, the focus shifted to higher–risk young adults, particularly men who had sex with men, young unemployed men, and women with multiple partners. The risks in these second cross–sectional surveys approximated those seen in China, Russia, and Zimbabwe during the initial surveys.

Baseline data collection for the Trial began in September–October 2002 in China and Russia and in May–October 2003 in India, Peru, and Zimbabwe. Behavioral interviews and biological specimen collection will be repeated at 12 and 24 months after baseline. The incidence of STD and behavioral outcomes (principally unprotected sex with non–spousal partners) will be compared between intervention venues, which will receive a community popular opinion leader intervention along with STD/HIV educational materials and easy access to condoms, and comparison venues that will receive only the STD/HIV educational materials and easy access to condoms. Results of the intervention Trial are expected to be available in 2008.

References

Formative study conducted in five countries to adapt the community popular opinion leader intervention

NIMH Collaborative HIV/STD Prevention Trial Group*

**Objective:** To obtain information about the social and cultural factors related to health behaviors influencing HIV/sexually transmitted disease (STD) transmission in study communities in China, India, Peru, Russia, and Zimbabwe so that the assessment and intervention of the National Institute for Mental Health (NIMH) Collaborative HIV/STD Prevention Trial could be adapted appropriately.

**Methods:** Field observations, focus groups, in-depth interviews with key informants, and an observation of community social dynamics were conducted as part of a rapid ethnographic assessment.

**Results:** All five sites reported a power dynamic tilted towards men, which rendered women particularly vulnerable to HIV and other STDs. Women’s relative lack of power was exemplified by a double standard for extramarital sex, women’s limited ability to negotiate sex or condom use, and sexual and physical violence against women. In all sites except Russia, extramarital sex is tolerated for men but proscribed for women. In Peru, power dynamics between men who have sex with men were tilted towards men who self-identified as heterosexual. Condom use (reported to be low across all sites) was often linked to having sex with only those perceived as high-risk partners. Regardless of site or study population, participants agreed on the following characteristics of an ideal community popular opinion leader (C-POL): respectable, credible, experienced (life and sexual), trustworthy, empathetic, well-spoken, and self-confident.

**Conclusion:** The ethnographic studies provided critical information that enabled the study teams to adapt elements of the Trial in culturally appropriate ways in diverse international settings.

*See Appendix B for members of the NIMH Collaborative HIV/STD Prevention Trial Group.*

**AIDS 2007, 21** (suppl 2):S91–S98

**Keywords:** Behavioral interventions, culture, ethnography, low-resource countries, qualitative data, risk factors, sexual behavior

**Introduction**

Researchers appreciate the need to understand the social and cultural factors related to health and illness in diverse settings because of the direct and indirect impact of these factors on exposure and vulnerability to disease, risk-taking and health promotion behaviors, and access to quality healthcare [1]. Ethnographic methods, including field observations, in-depth interviews, focus groups, and social mapping, provide an important set of tools for understanding the contextual features that elicit behaviors that are protective or damaging. Rapid ethnographic assessment is regularly applied in behavioral intervention research and programme evaluation [2–6]. In-depth interviews are particularly useful for exploring sensitive topics, such as sexual practices, sexual norms, and HIV-related risk behaviors, and providing explanations for quantitative findings [7,8].

To ensure that the intervention, the community popular opinion leader (C-POL), and assessment measures were culturally appropriate and acceptable, a rapid ethnographic assessment [2] was conducted before final protocol development for this five-country (China, India, Peru, Russia, and Zimbabwe) study. Using a standard set of methods, with operational definitions specified in the protocol, each research site collected data on the following core topic areas: (i) sexual health data; (ii) sexual practices and meanings; (iii) healthcare delivery and beliefs; (iv) social groups; (v) characteristics of C-POL (natural
leaders in a community); (vi) appropriate incentives; (vii) prevention messages; and (viii) population profiles. See ‘Design and integration of ethnography within an international behavior change HIV/STD prevention trial’ [9] for a description of the core topic areas, the required elements within each core topic area for this study, and the suggested probes. Whereas the research teams in all five countries were required to adhere to the protocol, the strength of the approach was the flexibility in how each country would meet these expectations. Each team collected data on all core topic areas and implemented the methods according to the stated procedures, but each team used an iterative process in applying the methods and tailoring the appropriate questions based on the demands of each sociocultural context and in-vivo field experience about how best to access the required data.

The culture, language, setting, and risk populations were different across the five countries, and therefore it was especially important to adhere to the procedures meticulously described in the protocol. This is an unusual and challenging approach because most studies that use rapid ethnographic assessment work in a single site with a specific population.

In this paper, we briefly discuss the rapid ethnographic assessment conducted in the five countries, the preliminary selection and description of venues and high-risk populations in each country, and the findings on two core topic areas from the rapid ethnographic assessment to demonstrate the relevance of ethnographic findings to developing effective HIV/sexually transmitted disease (STD) prevention messages, selecting appropriate C-POLs, and tailoring assessment instruments.

Methodology

Rapid ethnographic assessment

Although a full discussion of the ethnographic methods used in this multisite, multipopulation Trial is beyond the scope of this paper, we will summarize the methods used to collect the data upon which this paper is based. Ethnographers conducted field observations and social mapping within the venues. In-depth interviews and focus groups were conducted in the local language (Mandarin and Fuzhou dialect in China, Tamil in India, Spanish in Peru, Russian in Russia, and Shona or Ndebele in Zimbabwe), audio tape recorded, transcribed, and translated into English as necessary for analysis. Site-specific ethnography teams reviewed all data for emergent themes and patterns. To facilitate cross-site analysis, each site was required to code transcripts using the core topic areas and to sub-code using the required elements within each core topic area, organizing the data with a pre-approved qualitative analysis software package (e.g. NUDIST, nVivo, ATLAS.ti, EthnoNotes). Each site prepared an executive summary and a full report triangulating the data from field observations, in-depth interviews, focus groups, and social mapping by core topic area, and including specific quotations from in-depth interviews and focus groups. The scientific teams used these reports to tailor various aspects of the Trial at each site according to protocol guidelines. These reports provide the basis for this paper. For a more complete discussion of the protocol for the rapid ethnographic assessment, please see ‘Design and integration of ethnography within an international behavior change HIV/sexually transmitted disease prevention trial’ [9].

We focused on the two core topic areas selected for discussion in this paper, sexual practices and meanings and the characteristics of C-POLs, because they were particularly critical to the process of designing and tailoring the intervention and assessment. The C-POL intervention consists of training natural leaders in the community, who are known as ‘community popular opinion leaders’ (C-POLs), to deliver HIV prevention messages to their peers and friends through regular conversations in the venues described below. The intervention model is defined by nine required core elements, which must be implemented at each site. The C-POLs are trained by facilitators, who are staff on the study, using a common manual developed by the study and tailored to the needs of each site. A critical part of the training is to help the C-POL develop and learn to deliver HIV-related prevention messages using language tailored to community sexual practices and meaning. Therefore, the success of the intervention relies on selecting appropriate C-POLs who are natural leaders, and on crafting salient and relevant HIV-related prevention messages that can be delivered to their friends and neighbors as part of daily conversation. The theory of diffusion [10], on which this intervention is based, posits that members of a community will adopt the recommendations and behaviors of their natural leaders, and this will result in a shift in the social norms regarding acceptable behavior. A baseline structured assessment, which included a personal interview on sexual risk taking and other health behaviors and tested for HIV/STDs, was administered to a randomly selected cohort from each venue. The intervention was then initiated in half of the venues in each country. Follow-up assessments were conducted 12 and 24 months after the baseline assessment. If the C-POLs have been effective in delivering the intervention, intervention venues should show a greater improvement in HIV-related risk behavior and the incidence of HIV/STD than comparison venues at the time of the 24-month assessment. The intervention is described elsewhere. See ‘Methodological overview of a five-country community-level HIV/sexually transmitted disease prevention trial’ [11] for an overview of the methodology for all aspects of the study and ‘The community popular opinion leader HIV prevention
programme: conceptual basis and intervention procedures [12] to learn more about the intervention and how the intervention core elements were tailored across the five countries.

**Venues and populations studied**

One of the nine core elements of the C-POL intervention mentioned above is the selection of a venue that has clearly defined physical or social boundaries (e.g., housing project, bar, dormitory, etc.) with an identifiable target population where multiple informal conversations occur frequently [13]. Within or near those venues, the target populations must engage in high-risk sexual behavior and have a high prevalence of sexually transmitted disease (STD). On the basis of the rapid ethnographic assessment in each country, venues and target populations that met the criteria specified in the protocol were selected to implement the National Institute for Mental Health (NIMH) Collaborative HIV/STD Prevention Trial (the Trial) [14]. The appropriateness of the venues and populations were confirmed by epidemiological studies that collected both behavioral and biological data [15]. We will briefly describe the venues and populations selected in the five countries to provide a context for the ethnographic data collected on the two core topic areas: (i) sexual practices and meaning; and (ii) characteristics of C-POLs.

In China, venues were food stalls in markets, each with between 50 and 150 independent owners and employees, who formed our study population. The ethnographic study included 43 in-depth interviews (22 women, 21 men) focused on broad aspects of risk behavior; another 52 semi-structured interviews (31 women, 21 men) focused on knowledge, attitudes, and beliefs about HIV/STDs; one focus group with market workers (four women, six men) covered a variety of intervention-specific issues; and six field observations of market activities. In-depth interview respondents included market workers, female sex workers employed near a market, STD clinic patients, one market manager, and one public hospital physician.

The original venues selected for study in India were slums (housing projects). ‘Slum’ is the local term for public housing units or a housing project in Chennai, India. Housing allotment, construction, and oversight are managed by a government agency called the Tamil Nadu Slum Clearance Board. The link to their web site is http://www.tn.gov.in/citizen/tsnsc.htm. The name for these venues reflects the local term used by residents and government and is not intended to be pejorative. Because of the low HIV/STD risk in the overall population in these areas, the final venues selected for study were clusters of wine shops in and near these communities. The study populations in India are men who are regular customers of the selected wine shops and the high-risk women who frequent the area near these shops. Key informant interviews with community leaders and healthcare providers, field observations, and social mapping exercises were conducted to facilitate the recruitment and implementation of the ethnographic interviews and focus groups. A total of 62 in-depth interviews and 24 focus group discussions were conducted with married and unmarried men and women in several slum areas. In addition, staff made field observations to understand locations where communication and sexual liaisons occur.

The venues selected in three cities in Peru (Lima, Trujillo, and Chiclayo) were lower socioeconomic neighborhoods and the high-risk populations selected were young heterosexually identified men who do not work or study, young women with multiple male sexual partners, and self-identified homosexual men. The ethnographic study included field observation, social mapping, 108 in-depth interviews (59 heterosexually identified men, 40 women, and nine men self-identified as homosexual), 17 focus groups (eight groups of heterosexual men, seven of women, and two of homosexual men), and 70 semi-structured interviews with gatekeepers, stakeholders, and key informants who were respected leaders and members of the target population in the community.

Dormitories at vocational trade schools in Russia were selected as the venues, and the student residents were the high-risk study population. A total of six focus groups and 20 in-depth interviews were conducted with residents in these venues. All participants were students living in the selected dormitories. Focus groups were conducted separately for male and female participants (three groups each). In addition, in-depth interviews were conducted with 30 key informants and providers, including administration and technical personnel of the dormitories, student committee members, doctors, and café and bar owners. Field observations and social mapping were also conducted.

Thirty-two of the 56 villages identified by the Zimbabwe government as growth points for economic development were selected as the venues and, specifically, within the growth point villages, the bottle stores, markets and general dealer stores were selected as the points of contact. In conjunction with field observations and social mapping, a total of 49 focus group discussions (25 with women) and 55 key informant interviews (24 with women) were conducted. In-depth, 2–3 hour interviews were held with 15 participants, with approximately equal numbers of men and women. A total of 176 rapid assessment interviews were also held with target community members.

In summary, the venues in each country support frequent informal conversations among friends, neighbors, and co-workers, which provide the C-POL with multiple opportunities to deliver HIV/STD prevention messages designed to shift the social norms towards HIV-related
risk reduction. The core age range of the high-risk populations was between 18 and 30 years. In some countries, however, the range was adjusted to reflect the ages with the highest risk behaviors and prevalence of HIV/STD in the venue. For example, in China, older men in the markets had the resources to engage in rituals associated with sex outside of marriage. Therefore, on the basis of ethnographic and epidemiological findings, the upper age range of the population was extended to 40 years in India and Peru and to 49 years in China.

Both men and women were selected in all countries, although the populations were not always balanced. In India and Peru, only approximately 10% of each population was female. In India, only men drink in wine shops because of cultural mores, but the high-risk women who congregate near the shops and often meet with those men as they leave the shops were included in the population. In Peru, approximately 80% of the members of the population were high-risk heterosexual men, but young women with multiple partners and homosexual men each made up approximately 10% of the population because they engaged in high-risk sex within the venue. In China, all workers in the markets were vulnerable to HIV, so both male and female market stall owners and employees were included in the population. Similarly, in Russia, both men and women engaged in HIV risk behaviors in the dormitories and tended to have serially monogamous relationships without using condoms, so all dormitory residents over the age of 18 years who were not going to graduate within a year were included in the population. In Zimbabwe, primarily men engaged in sex with multiple partners, but women were vulnerable to HIV and STD because they did not tend to use condoms with their sexual partners, whom they were likely to see as steady. Therefore, both men and women had high HIV and STD rates, and all members of the venue who attended the selected bottle stores, general dealers, etc., at least twice a week were selected as members of the study population. The selected C-POLs interact with these high-risk populations and received training about how to deliver effective HIV/STD prevention messages. In the next section, we discuss how the rapid ethnographic assessment contributed to the identification of C-POLs and the basis for messages.

**Discussion of two core topic areas**

Across the core topic areas investigated, findings related to sexual practices and meanings, and C-POL characteristics were most instrumental in shaping the implementation of the C-POL intervention in the five countries. The collected ethnographic information was central to decisions in all sites about those aspects of the socio-cultural context and HIV-related risk behaviors most open to influence and who would be most effective in delivering HIV/STD prevention messages. Examples from the findings in each country illustrate that despite the common C-POL intervention model being applied, economic and sociocultural variations required site-specific tailoring of each of the required core elements of the C-POL intervention.

**Sexual practices and meanings**

Across countries, a number of prevention-related themes emerged from field observations, focus groups and in-depth interviews related to sexual practices and meanings.

**Sex imbalances**

The overarching issue across sites was the power imbalance between men and women, which was reflected in their sexual practices. Reports from all five countries described power dynamics tilted toward men, most dramatically in China, India, and Peru, which rendered women particularly vulnerable to HIV and other STDs. Both women and men highlighted the role of sex inequities in shaping intracouple dynamics and sexual practices. Women’s relative lack of power also manifested itself in sexual and physical violence against them in all sites except for China, especially when they were resisting having sex with a husband or partner. Similarly, in Peru, power dynamics between men who have sex with men were tilted towards men who self-identify as homosexual, with limited ability for the men who self-identified as homosexual to negotiate safer sex.

Another manifestation of the power imbalance was the low condom use across sites despite the high prevalence of STDs or HIV in the populations selected in the venues [15]. Women were frequently unable to refuse sex or to negotiate condom use. Most men and women explained that a wife is expected to respond to her husband’s sexual urges in a way that satisfies him. In addition to the inability of women to protect themselves as a result of men’s entitlement is the implied accusation of infidelity when a woman attempts to suggest condom use. Respondents across the sites did report that condoms are used for preventing HIV/STDs primarily when men have sex with prostitutes or others they consider ‘high’ risk. In Peru, condom use is limited and both men and women reported that it does not feel the same to use a condom; furthermore, condoms were believed potentially to break, be too small, or be ineffective. If a man suggested using condoms, a woman would be offended, believing that he was unfaithful or distrusted her. In Russia, steady couples refuse to use condoms and instead use contraceptive pills to prevent an unwanted pregnancy, even though one or both members of the couple may have had a similar relationship with someone else only a month or two earlier.

In addition to limiting women’s choices in sexual practices, sex inequities were evident in the acceptability of premarital and extramarital affairs, which resulted in a double standard for men and women in four of the sites. Only Russia accepted premarital and extramarital affairs for both men and women. In the other four countries,
these behaviors were only tolerated (and frequently encouraged) for men. In those sites, husbands reported that wives may be displeased with their extramarital affairs, but the women had no recourse. In Peru, extramarital sex is prohibited among ‘decent’ women, but men may release their sexual tensions with ‘promiscuous’ women, who have multiple male partners and are marginalized within the population. Among the low-income men and women interviewed in India, cultural norms strongly prohibit women from engaging in premarital or extramarital sex, whereas norms sanction a variety of sexual behaviors for men [16]. Reports indicate that a strong sexual drive for young Indian men is natural and expected. This attitude justifies both premarital and extramarital affairs for married and unmarried low-income men in urban India, and contributes to their high risk of HIV/STD infection and, secondarily, to a high risk for their wives and girlfriends.

**Types of partners and risk behaviors**

Across the sites, ethnographers found similarities and differences in the types of sexual partners and associated sexual risk. Men and women cited trust and knowing a partner’s behavior as the most common reasons for choosing a steady partner. Both men and women used a visual assessment that reassured them that the potential partner was healthy and therefore no condom was required during sex. Except for commercial sex workers, fewer women compared with men were described as engaging in sex with a variety of different partners. Distinctions were made between ‘regular’ partners or ‘good’ girls and ‘casual’ partners or ‘fast’ girls. Many unmarried men described their sexual relationships with their regular girlfriends in romantic terms because ‘love is involved’, whereas in casual relationships or with prostitutes or sex workers ‘it’s only sex’. Having a steady partner was also described as a means by which to avoid HIV/STD infection and a justifiable reason for not using condoms. Culturally, premarital sex for men remains acceptable in all five countries, so men who desire sexual experiences with multiple partners before marriage have multiple opportunities.

In China, expressions of sexuality and media exposure to sex have, until recently, been culturally and politically suppressed [17]. As these norms change, they also reflect changing types of sexual partners and opportunities for sexual risk and early sexual initiation. Both married and unmarried men frequent clubs, saunas, and dance halls or bars, where alcohol is consumed and sexual liaisons and interactions occur with waitresses, bar girls, massage girls, and sex workers. These casual sexual partners may be labeled as ‘fast women’. In contrast, sexual initiation for young men in India may result from sexual partners known as ‘aunties’ (an older, often married relative or family friend), with other men [18], or with a prostitute, which may involve a group of young men visiting a venue where sex workers are available. In both China and India, alcohol consumption in groups frequently precedes sexual experiences to help the men gain the ‘courage’ needed for the visit but does not result in steady partnerships.

In Peru, men distinguished between ‘fast girls’ (movidas) and ‘decent girls’ (tranquilas), and described different kinds of sex acts that are permissible with them. Gang rape, associated with getting a fast girl drunk, was a practice reported often. Young, single, unemployed Peruvian men reported infrequent sex with prostitutes because of the cost. Instead, they reported going to parties and chicken cookouts to look for fast girls. Another strategy to have sex was to approach homosexual men from the same neighborhoods, because young, inexperienced heterosexual men think it is easier than having sex with a woman; it is free, and they perceived that the homosexual men are always available for sex. In those situations, heterosexual men mostly performed the insertive role with homosexual men. Although knowledge of HIV/STD among homosexual men in Peru was relatively higher than among heterosexual men and women of that country, their capacity to negotiate safer sex and condom use was limited.

Data collected from young Russian male and female students residing in dormitories also indicated different types of sexual partners, although sex influenced the interpretation of the types. ‘Permanent’ and ‘incidental’ partners reflect the categories of ‘regular’ and ‘casual’ that were evident in the other countries. Respondents reported that ‘incidental’ acquaintances and liaisons are usually found in clubs, discotheques, and bars, and are accompanied by high levels of alcohol consumption. These sexual relationships are for the most part unprotected because of the low use of condoms among the students. Participants reported that the majority of students have little or no sexual experience before moving into the Russian dormitories. Many students considered partnerships lasting one month or more to be steady, stable, and permanent. Female students, however, often interpreted this steady relationship (frequently the only relationship for the female during a defined period of time) as a civil marriage (usually not registered or formalized, or even verbalized between the partners). By contrast, young men consider themselves free even in the presence of a steady partner (of whom there could be several at one time), until they declare their intention to marry.

In Zimbabwe, several different types of sexual partners are recognized. A man may have multiple wives as part of the practice of polygamy. A man who moves to another place for employment often has a wife in the rural area and a regular girlfriend for whom he is paying the ‘lobola’ (bride price) at the site where he found work. Men described having sex with concurrent relationships,
usually a steady partner or wife and also other partners. If men had sex with casual partners or commercial sex workers, they often declared that they used condoms. Both men and women, however, mentioned that condom use in steady or marital relationships was ‘not the done thing’. Women were much less likely to have multiple partners, and although acknowledging that their steady partner often had other partners, they felt that they could not discuss or expect a commitment or monogamy from their husbands or steady partners.

This more complete understanding of sexual practices and meanings was critical to the development of HIV/STD prevention messages delivered by the C-POL, particularly messages that recognize sex inequities in practising safer sex with different sexual partners.

Characteristics of community popular opinion leaders

Across sites, members of study populations reported many similarities regarding the characteristics of natural leaders who would be able to deliver effective health messages to their social networks. Regardless of the subpopulation within the country (e.g. married men, married women, men who have sex with men), informants converged on the following characteristics of an ideal C-POL: respectable, credible, experienced (life and sexual), trustworthy, empathetic, well-spoken, and self-confident. Within study populations in all countries, however, the characteristics that made for a natural leader varied by subpopulation. Again, country-specific descriptions illustrate the variety of characteristics that emerged in the data regarding the selection of C-POL candidates that would best fit the unique sociocultural circumstances.

Recognizing the need to emphasize female-focused HIV/STD prevention messages, married and unmarried Chinese and Indian women identified older, married, sexually experienced, empathetic, persuasive, non-judgmental, and bold women who were uninhibited about discussing sensitive topics as ideal C-POLs. Both married and unmarried women at the two sites agreed that an unmarried woman may be too shy and inexperienced to be an effective C-POL.

In Peru and Russia, somewhat younger populations were targeted, and C-POL characteristics included skills in getting along with everyone, having social prestige, and being a little older and therefore having more life experience than the youngest members of the population. Targeting a student population, the Russian participants described optimal C-POLs as individuals with a depth of knowledge on relevant topics, who possessed good communication skills, and who had an interesting personality. According to Russian students, C-POLs should be peers who are extroverts, are involved in a variety of school activities, frequently offer to help, provide good advice to fellow students, and have lived in the dormitory for at least 2 years. Some groups of male students completely rejected the concept of a leader, as leadership was equated with subordination of the masses.

In Zimbabwe, men and women tended to identify more formal leaders as potential C-POLs, although, in addition, popular individuals who were seen as leaders were also identified. Village chiefs, headmen, kraalheads (leaders of a rural village, typically consisting of huts surrounded by a stockade), village elders, and health workers were widely considered the most appropriate people to deliver health messages, given their experience and training and the respect that they hold in the community. Both popular men and women who were not necessarily part of the formal leadership network were also identified as C-POLs. Both men and women in Zimbabwe agreed that desirable C-POL characteristics included honesty, sensibility, eloquence in speech, ability to provide good advice and keep confidences, and being a behavioral role model. Being a hard worker, religiously faithful, easily approachable, intelligent, and active in the community were offered as admirable characteristics.

Conclusion

A major challenge for this study was to adapt a single community-based C-POL intervention to prevent HIV/STD transmission to five diverse international settings (China, India, Peru, Russia, and Zimbabwe). A rapid ethnographic assessment was conducted to tailor the assessment and intervention design and implementation. Although a detailed protocol was developed to standardize methods and assessment tools, the teams had latitude in matching the method used to elicit the required data to the sociocultural context and high-risk population. During the conduct of the Trial, the ethnographers communicated across the sites frequently through meetings, conference calls, and E-mail in order to prevent protocol drift. The success of the implementation of the C-POL intervention in such diverse cultural situations with different high-risk populations was a result of the important data collected by the ethnographers.

Several patterns emerged when examining data across sites for two core topic areas: sexual practices and meanings and C-POL characteristics. First, cultural norms of sex inequity, sex relations that favor men, and sanctioning of men’s premarital and extramarital sexual behavior played an important role in increasing sexual risk for both men and women. Women, whether married or unmarried, younger or older, understood their vulnerability to HIV/STD infection related to a partner’s sexual behavior and their limited ability to protect themselves by negotiating condom use or insisting on a partner’s fidelity.
In all sites except China, the narrative data contained explicit discussion by both men and women about the use of violence in sexual relationships. This violence took the form of forced sex, often between married partners, in addition to other kinds of sexual relationships, beatings, and individual or gang rape. The prevailing viewpoint in Zimbabwe was that a man has a right to have sex with his wife, and the wife must acquiesce; thus pressure or coercion exists, although physical violence was only rarely mentioned. In India, where violence toward women is prevalent in daily life, women are likely to submit to sex to avoid harm to themselves [16,19–21]. In all of the sites, alcohol played a key role in sexual risk-taking because alcohol consumption increased the likelihood of unprotected sex with partners who may be at high risk of the transmission of HIV/STD.

In China and India, where the HIV/AIDS epidemic was at a relatively early yet rapidly growing stage, stigma associated with disclosure of infection was evident. For example, in China, having an STD marked an individual’s failure to adhere to sexuality norms, prompted negative emotions (e.g. shame, fear, and embarrassment), devalued the infected individual’s social roles, and reduced his or her status. Strategies that informants reported using to avoid stigmatization included avoiding HIV/STD knowledge, avoiding seeking healthcare professionals, particularly in public settings, and conforming to community norms of shunning those suspected of risky behaviors [17]. In Peru, however, having an STD was a sign of ‘manliness’ and proof that the man had multiple partners and sexual prowess.

This formative multisite ethnographic study was instrumental in identifying the social and cultural factors related to health behaviors important to HIV and STD transmission that were to be considered during the design and development of the assessment and the HIV prevention intervention. For example, the behavioral assessment was designed with core questions that were asked at all sites and with optional and unique questions that were used to tailor the assessment at individual sites, a necessarily flexible application of a systematic approach. In China, some of the optional questions were used to introduce the assessment as a broader health questionnaire rather than a sexual behavior questionnaire to increase its acceptance by the target population. In other countries, additional questions focusing on mediators identified during the ethnographic activities, such as injection drug use or violence, were included as unique questions in the assessment.

Each site culturally tailored the HIV/STD prevention messages to address the local social and cultural context and sexual practices and meanings. For example, Russian students tend to be single and have serial relationships. Accordingly, messages were developed to encourage students to use a condom every time they have sex. In China, many of the study participants were married. Therefore, messages encouraged all members of the population to have routine checkups to detect asymptomatic HIV/STDs and receive treatment when needed. Messages also encouraged married people to use condoms outside of the marriage and encouraged single people to use condoms for every sexual act. Across the sites, C-POLs encouraged their friends and neighbors to initiate conversations about sexual health with all sexual partners.

This paper illustrates how ethnographic formative research provided critical information that enabled the study teams to adapt components of the Trial in culturally appropriate ways in diverse international settings. The attention paid to both standardization and tailoring of the C-POL intervention and assessment based on a comprehensive rapid ethnographic assessment strengthened the ability of this Trial to evaluate the efficacy of this community-based intervention.

References


Role of the data safety and monitoring board in an international trial

NIMH Collaborative HIV/STD Prevention Trial*

Objective: To describe the composition and role of the data safety and monitoring board (DSMB) for the National Institute of Mental Health (NIMH) Collaborative HIV/STD Prevention Trial.

Design: NIMH appointed to the DSMB nine members representing the following areas of expertise: prevention science, ethnography, infectious diseases (especially HIV and sexually transmitted diseases), laboratory diagnostics, clinical practice, methodology, international trial experience, statistics, and ethics.

Methods: The DSMB assessed the overall study for any concern about plans or implementation and reviewed cumulative study data to evaluate the safety of study participants, the ongoing conduct of the study, and the scientific validity and integrity of the Trial. Because of the Trial’s international scope, the DSMB examined the effects of cultural differences on study implementation and fidelity.

Results: Among the DSMB recommendations that strengthened the Trial was one to conduct initial epidemiological studies of the venues selected for the intervention to verify risk and to establish intraclass correlation coefficients that could be used to calculate appropriate sample sizes.

Conclusions: The DSMB played a critical role in this Trial. Because members have the expertise required to monitor the Trial, are not involved in the daily management of the Trial, and can review interim analyses and adverse event reports, they are in an excellent position to provide expert advice to ensure that the Trial’s goals are achieved and that NIH funds are well invested.

Keywords: community popular opinion leader, data safety and monitoring board, sexually transmitted diseases, HIV

Introduction

In June 1998, the US National Institutes of Health (NIH) issued a policy for data and safety monitoring, which stated ‘It is the policy of the NIH that each Institute and Center (IC) should have a system for the appropriate oversight and monitoring of the conduct of clinical trials to ensure the safety of participants and the validity and integrity of data for all NIH–supported or conducted clinical trials.’ The policy provides flexibility so that data and safety monitoring can be implemented in the manner appropriate for different clinical research activities. Monitoring exists in a continuum from ongoing review by the principal investigator or NIH programme staff in a small phase I study to the establishment of an independent data safety and monitoring board (DSMB) for a large phase III clinical trial.

Although studies may be monitored by a variety of mechanisms and methods, the NIH has mandated that every randomized clinical trial must have an independent DSMB. This short report describes the composition and role of the DSMB for the NIMH Collaborative HIV/STD Prevention Trial.

Components of data safety and monitoring

Data and safety monitoring includes the following four important components:

The principal investigator of each study must include a data and safety monitoring plan in each new protocol.

The institutional review board must approve the plan and determine what types of safety monitoring processes are required (e.g. principal investigator monitoring only, a single independent monitor, a group appointed by the principal investigator or an independent DSMB).

* See Appendix B for members of the NIMH Collaborative HIV/STD Prevention Trial Group.
The NIH Institute or Center is responsible for appointing an independent monitor or convening a DSMB.

The study principal investigator is responsible for providing all required data to the individual monitor or to the DSMB and for acting on the findings of any monitor or the DSMB.

This Trial has engaged in all four of these components.

Membership of the data safety and monitoring board

The first step in establishing the DSMB for this Trial was to identify the areas of expertise needed to monitor all aspects of the Trial effectively. The following expertise was deemed critical: prevention science, ethnography, infectious diseases (especially HIV and sexually transmitted diseases), laboratory diagnostics, clinical practice, methodology, international trial experience, statistics, and ethics.

National Institute of Mental Health (NIMH) staff identified and appointed to the DSMB members who represent the areas of expertise listed above. Some members have expertise in more than one of the areas, and no member of the DSMB has direct involvement in the study or any conflict of interest with the investigators. The nine members of the DSMB are acknowledged in this issue.

Role of the data safety and monitoring board

As specified by NIH policy, the DSMB assessed the overall study, including the protocol and the performance of the staff implementing the protocol, for any concern about plans or implementation. The DSMB also reviewed cumulative study data to evaluate the safety of study participants, the ongoing conduct of the study, and the scientific validity and integrity of the Trial. Because the Trial was international in scope, the DSMB was especially concerned with the effects of cultural differences on study implementation and fidelity.

The members of the DSMB closely reviewed the quality assurance of the biospecimens (from the collection of the specimens to analysis), the reporting of results to participants, and the treatment of participants with positive laboratory results. As is common in international studies, this was of special importance because some of the sites where laboratory capacity was not available were establishing or upgrading laboratories for the Trial. Also, members realized that, in addition to the normal delays encountered with domestic shipments, shipping specimens halfway round the world for quality assurance involves special difficulties related to distance, various customs clearances, and permission for shipping from foreign governments.

In particular, the DSMB reviewed: Trial protocols for appropriateness in achieving goals, including sample size assumptions and randomization procedures; epidemiological data to verify the selection of appropriate study populations and venues; adherence to the Trial protocol; data for evidence of study-related adverse events; data for evidence of efficacy in accordance with the approved statistical plan; data quality, completeness, and timeliness; quality assurance data that might identify problems with Trial procedures; and factors that might compromise the confidentiality of the Trial data.

As the Trial progressed, the data coordinating center (DCC) provided data to the DSMB in the following categories: epidemiological data; baseline data; 12-month follow-up data; 24-month follow-up data; process data; adverse events; and hypothesis testing (interim and final). See Table 1 for a description of the types of data that were presented over time. These data were used by the DSMB to evaluate the likelihood of the trial having significant results on the basis of the recruitment and retention rates and the data safety procedures.

The safety of the research subjects was evaluated by multiple methods and multiple groups including site staff, the Trial steering committee, the DSMB, and institutional review boards. The DSMB evaluated safety by carefully evaluating the protocol that described every planned activity in detail. This group also had access to the reports from the central quality assurance monitors from the DCC that evaluated each component of the Trial (human subjects, data collection and assessment, biological specimen collection, intervention) using structured evaluation forms during periodic site visits. Finally, the DSMB had access to listings of both protocol violations and reported adverse events. Of the eight adverse events reported to date, four involved robbery of a field office or a staff member, two involved incorrectly giving test results to participants, and two involved research participants being harassed or assaulted.

Meetings of the data safety and monitoring board

Based on progress of the Trial, the frequency of the DSMB meetings varied. The DSMB first met shortly after the first draft of the protocol was available. While pilot studies were being conducted and the Trial protocol was being revised, the DSMB met approximately three times a year to provide timely feedback. Once the Trial
One interim analysis after most 12-month follow-up data were collected. Final analysis before releasing to public.

protocol was approved and the study was in the field, the DSMB met approximately once a year, sometimes by conference call.

Table 1. Types of interim data provided by the data center to the data safety and monitoring board.

<table>
<thead>
<tr>
<th>Epidemiological study data</th>
<th>12-month follow-up</th>
<th>24-month follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics (e.g., age, sex, marital status)</td>
<td>Demographics</td>
<td>Demographics</td>
</tr>
<tr>
<td>Behavioral risk data</td>
<td>Follow-up retention rates</td>
<td>Follow-up retention rates</td>
</tr>
<tr>
<td>HIV/STD prevalence</td>
<td>Behavioral risk data</td>
<td>Behavioral risk data</td>
</tr>
<tr>
<td>Protocol implementation</td>
<td>HIV/STD prevalence data</td>
<td>HIV/STD prevalence data</td>
</tr>
<tr>
<td>Time between collecting biological samples and reporting test results</td>
<td>Assessment questions regarding whether they have seen the logo</td>
<td>Treatment and/or referral data for positive STD – time to treatment</td>
</tr>
<tr>
<td>Time between assessment and beginning of intervention by venue</td>
<td>QA data</td>
<td>QA data</td>
</tr>
<tr>
<td>Treatment and/or referral data for positive STD – time to treatment</td>
<td>Results of initial panel prepared by core lab and sent to sites</td>
<td>Results of CAP testing</td>
</tr>
<tr>
<td>QA data</td>
<td>Results for sample drawn by DCC and sent to reference lab for confirmation</td>
<td>Results for sample drawn by DCC and sent to reference lab for confirmation</td>
</tr>
<tr>
<td>Results of CAP testing</td>
<td>QA data</td>
<td>QA data</td>
</tr>
<tr>
<td>Results for sample drawn by DCC and sent to reference lab for confirmation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Process data</td>
<td>C-POL recruitment information</td>
<td>C-POL recruitment information</td>
</tr>
<tr>
<td>Training session attendance information</td>
<td>Number of relevant conversations held</td>
<td>Number of relevant conversations held</td>
</tr>
<tr>
<td>Presence of logos and posters in venues</td>
<td>Adverse events at intervals</td>
<td>Adverse events at intervals</td>
</tr>
<tr>
<td>Hypothesis testing (interim and final)</td>
<td>Hypothesis testing (interim and final)</td>
<td>Hypothesis testing (interim and final)</td>
</tr>
<tr>
<td>Compare intervention and comparison venues on primary endpoints at 12 and 24 months (unadjusted and adjusted for baseline covariates)*</td>
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</table>

*One interim analysis after most 12-month follow-up data were collected. Final analysis before releasing to public.

Table 2. Questions for consideration by the data safety and monitoring board on 17 March 2000.

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
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<tbody>
<tr>
<td>Is the protocol for implementing the study an appropriate plan for this Trial, given the aims in the RFA?</td>
<td>Yes</td>
</tr>
<tr>
<td>Are the scientific criteria and methodology that have been developed appropriate for venue identification and verification?</td>
<td>Yes</td>
</tr>
<tr>
<td>Are the site venues proposed by the PI appropriate for conducting a C-POL intervention Trial?</td>
<td>Yes</td>
</tr>
<tr>
<td>Are the plans appropriate for conducting the epidemiological HIV/STD study?</td>
<td>Yes</td>
</tr>
<tr>
<td>Are the initial plans appropriate for overall data collection, monitoring, and analysis?</td>
<td>Yes</td>
</tr>
<tr>
<td>What are the critical points for the DSMB to meet to review protocol development, progress, data, and make recommendations about the conduct of the Trial?</td>
<td>Yes</td>
</tr>
</tbody>
</table>

C-POL, Community popular opinion leader; DSMB, data safety and monitoring board; PI, principal investigators; RFA, Request for Assistance; STD, sexually transmitted disease.

In advance of each meeting or call, the NIMH staff in consultation with the DSMB chair prepared a set of questions to be addressed. The specific questions being addressed varied depending on the phase of the study being evaluated. As an example, the questions contemplated during the DSMB meeting that reviewed the full protocol on 17 March 2000 are presented in Table 2.

The DSMB meetings generally lasted approximately a day and included both closed and open sessions within the day. Materials required for the discussion were provided to the members of the DSMB approximately a week before the meeting. Meetings began with a closed session attended by the DSMB members and NIMH staff not involved in the study. During this portion of the meeting, the members discussed major areas of concern and developed the questions they wanted to ask members of the trial steering committee.

This closed session was often followed by an open session during which members of the steering committee met with the DSMB, in person or by telephone, to make brief presentations or to respond to questions. Finally, the DSMB reconvened in a closed session to review both the interim data provided by the DCC and information provided by the steering committee and to formulate a report to the NIMH. Confidential study documents were collected from members at the end of the meeting and were subsequently destroyed.

Confidentiality was an important aspect of these meetings. Voting members of the DSMB viewed interim analyses and individual adverse event data. Therefore, discussions from the meeting were not revealed outside of the meeting room.
Reports of the data safety and monitoring board

After each meeting, the DSMB provided the NIMH with a written report responding to the questions posed and recommending whether the study should continue without change, be modified, or be terminated. Recommendations regarding design modification and study conduct were forwarded to the Trial steering committee, which carefully considered each recommendation, made necessary modifications to the protocol, and provided a written response to the NIMH and the DSMB describing how each issue had been addressed.

In the course of these reports, the DSMB made a number of recommendations that strengthened the Trial. One of the most striking was the recommendation to conduct initial epidemiological studies of the venues selected for the intervention to verify risk and to establish intraclass correlation coefficients that could be used to calculate appropriate sample sizes for the Trial. Although ethnographic findings had indicated that each of the sites had initially identified risky populations and venues in which to conduct the Trial, the epidemiological study results indicated that the venues and populations initially selected in India and Peru did not have the characteristics required for the study. The DSMB required these two countries to refine their choice of venues and populations and conduct a second epidemiological study before beginning the Trial. The implementation of this recommendation from the DSMB greatly strengthened the Trial and enabled sample size calculations to be based on reliable data.

In conclusion, DSMB play a critical role in the conduct of phase III clinical trials sponsored or conducted by the US NIH. Because members of the DSMB have the expertise required to monitor the Trial, are not involved in the daily management of the Trial, and can review interim analyses and adverse event reports, they are in an excellent position to provide expert advice that will ensure that the goals of the Trial are achieved and that NIH funds are well invested. DSMB review and recommendations for this Trial strengthened both the study design and the procedures used for specific activities.

National Institutes of Health policy statements

The NIH has published a number of policy statements related to data and safety monitoring in the NIH guide. These statements guided the formation and operation of the DSMB for this Trial and provide useful suggestions for studies funded through other sources. The most recent of these documents are available on the Web. See Table 3 for the Web addresses of relevant documents.

<table>
<thead>
<tr>
<th>Table 3. National Institutes of Health websites for policy statements on data safety and monitoring boards.</th>
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<tr>
<td>NIH policy for data and safety monitoring (1998)</td>
</tr>
<tr>
<td>Guidance on reporting adverse events to institutional review</td>
</tr>
<tr>
<td>boards for NIH-supported multicenter clinical trials (1999)</td>
</tr>
<tr>
<td>Further guidance on a data and safety monitoring for phase I and phase II trials (2000)</td>
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APPENDIX A: Acknowledgements

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A Data Safety and Monitoring Board, appointed by NIMH, advised NIMH on study design and monitored participant safety during this trial. Members of this board are: Susan Allen, M.D., M.P.H. (University of Alabama - Birmingham); Floyd E. Bloom, M.D. (Scripps Clinic and Research Foundation); Robert Johnson, Ph.D. (UMDNJ - New Jersey Medical School); Charles Judd, Ph.D. (University of Colorado); David Murray, Ph.D. (Ohio State University); Ina Roy, M.D., Ph.D. (Plan A Inc.); Julius Schachter, Ph.D. (University of California San Francisco); Robert T. Trotter, II, Ph.D. (Northern Arizona University); Judith Wasserheit, M.D. (Fred Hutchinson Cancer Research Center)

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Dedication: This volume is dedicated to the memory of Louis H. Steinberg, Ed.D., who served as the National Institute of Mental Health Project Officer for this study until his sudden and untimely death in December 2005. Dr. Steinberg served in the United States Federal Government for more than 40 years, holding positions in the Veterans Administration, the U.S. Department of Health and Human Services Bureau of Health Manpower, the Health Resources Administration, the National Institute of Neurological Disorders and Stroke, and most recently with the National Institute of Mental Health for more than 17 years. Dr. Steinberg’s scientific knowledge, professional wisdom, political savvy, and personal charm will be deeply missed by his colleagues, friends, and family.
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1 RTI International is a trade name for Research Triangle Institute.