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BRIEF REPORT

Preventive Misconception as a Motivation for Participation and Adherence in Microbicide Trials: Evidence from Female Participants and Male Partners in Malawi and Zimbabwe

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Abstract This paper presents empirical data on motivation to join an HIV prevention trial of vaginal microbicide gels in Malawi and Zimbabwe, and participant assumption of a preventive misconception. Interviews were conducted with women participating in the trial and their male partners. Most of the female participants were able to adequately describe basic aspects of the trial design. HIV counseling and testing were primary reasons motivating women's participation, and male partners' support of the trial. 29% of women and 20% of men also provided indications of a preventive misconception, attributing gel use and trial participation to avoiding HIV infection.

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Introduction

Clinical trials of HIV prevention technologies usually require a change in behavior for participants. For example, participants may be expected to put something in their vagina, take a pill every day, use condoms, use contraceptives, avoid using vaginal products other than those provided by the trial, etc. Additionally, participants are asked to come to a research center regularly, answer questions about their sexual activity, give blood for regular HIV testing and listen to HIV counseling. All study requirements must be explained clearly to participants before they enroll, so they can make an autonomous decision about participation, and international ethics bodies provide guidance on what must be communicated.

Although ethics bodies specify certain information that must be provided to participants during the informed consent process, and further state that researchers must demonstrate that participants understand this information, researchers are not required to assess why participants join their studies, or why they stay in. Motivation to participate in research has been studied primarily for practical purposes, e.g., developing recruitment strategies. Motivation to participate is also of ethical interest, for this information can help assess comprehension of informed consent and signal possible undue inducement as well as therapeutic or preventive misconceptions. This paper presents empirical data on motivations to join an HIV prevention trial of vaginal microbicide gels in Malawi and Zimbabwe, and motivations to adhere to use of trial products as required by the protocol.

Background

Informed consent is meant to be a process of information exchange that results in an agreement between research investigator and participant, which is documented and maintained throughout the research period. This information exchange is particularly challenging for health research that is conducted in multi-national settings amongst disadvantaged populations, and focuses on prevention yet provides limited treatment for some conditions [1]. Participants of HIV prevention research who do not understand basic research concepts may place undue faith in the protective effects of the intervention or technology under study, possibly changing their behavior such that their risk of infection is increased.

Changes in risk behavior have been monitored in HIV vaccine and treatment research, and male circumcision studies [2, 3]. Although most microbicide trials have observed a decrease in incidence amongst participants, researchers express concern that participants in microbicide trials may mistakenly assume they are using an effective product, and discontinue condom use or otherwise increase their risk [4]. Simon and Sugarman [5] observe a "preventive misconception," which they define as "the overestimate in probability or level of personal protection that is afforded by being enrolled in a trial of a preventive intervention" (p. 371). They assert that preventive misconceptions could indicate inadequate informed consent. We are concerned that a preventive misconception could also contribute to an increase in risk behavior.

The potential for preventive misconception can be explored by examining the range of participant motivations to enroll in HIV prevention trials. In high HIV prevalence research settings, where many people have been affected by the disease, altruistic motivations for participation are common and do not generally raise ethical concerns. Although the standard of care for trial participants is often higher than what is easily available to the friends, neighbors and family members of non-participants, it has been argued that care offered to research participants generally does not constitute an undue inducement and thus inappropriate motivation to participate [6]. In international research, money given to participants is generally meant to reimburse expenses to come for study visits, yet researchers often express concern that participants are motivated to join trials to gain access to this cash. Another motivation to join HIV prevention trials is a belief that the trial will provide protection from infection.

Microbicide trials present an important opportunity to investigate these interlinking ethics issues, since most large trials to-date have been conducted among women in African countries, where motivation to participate may easily span the range of altruism, access to higher standards of care and assumption of a preventive misconception. In the study reported here, participants were asked about their knowledge of HIV prevention methods, their understanding of the microbicide trial's requirements, and their motivation to participate in (or support their partner to participate in) the trial.

Research Methods

Study Setting and Participants

This study is ancillary to HPTN 035, a Phase II/IIb double-blind randomized controlled trial of two candidate microbicide gels, (BufferGel® and 0.5% PRO 2000 Gel) with a placebo gel control arm and a no-gel (condom-only) control arm. Condoms and risk reduction counseling were provided to all participants. HPTN 035 included 3,099 women at multiple sites in Malawi, South Africa, the United States, Zambia and Zimbabwe, for an average of 20 months to evaluate the safety, efficacy and acceptability of the candidate gels. The trial demonstrated that PRO 2000 Gel was 30% effective in reducing women's risk of HIV; this was a promising trend yet not statistically significant [7].

Our study, called HPTN 035A, was conducted at the trial sites in Lilongwe, Malawi and Harare, Zimbabwe, which were located on the compounds of public health care facilities. At these sites, most of the 1,083 clinical trial participants enrolled were in stable sexual relationships with men, and resided in urban or peri-urban settings. In this paper we refer to HPTN 035 as the "trial," and HPTN035A as the "study." This paper reports findings from individual interviews administered to 66 women in the gel ($n = 47$) and no-gel ($n = 19$) arms of the trial, and 40 male partners (27 gel arm, 13 no-gel arm).

Individual interviews were conducted in two waves at each site, and individuals participated in only one wave of data collection. The sample size for each wave of individual interviews at each site was based on the expected number to reach saturation for qualitative data collection (10 per category). Approximately twice as many gel-users and partners of gel users were recruited, since use-experience was of primary importance to the study. Female study participants were recruited weekly from the trial population as they came in for their regular monthly visit until the sample size for each category (gel, no-gel) of interview was reached. All interviews took place while women were enrolled in the trial, and none of the women declined to participate. Male partners were recruited by asking trial participants for permission to contact their partner, and then recruiting those who gave permission, or by directly recruiting men at the end of male partner information

sessions convened by the clinical trial. We assume that the men who agreed to be interviewed were favourable to the clinical trial and the trial gels, which may have biased their responses. Ethics approval for our study was obtained from the five ethics committees associated with the research groups engaged in the study.

Data Collection and Analysis

The semi-structured interview guides included open-ended questions with required and optional probes. The study was staffed with experienced interviewers trained on-site on the study protocol and data collection instruments by the Principal Investigator and Study Coordinator, who are anthropologists experienced in qualitative research methods. Data were collected in the local language by persons of the same gender as participants. Interviews were audio-recorded, transcribed and translated into English, using a standardized transcription protocol. Data were coded at the local sites and in the US using NVIVO software. Initial codes were based on the study's conceptual framework [8] and the codebook was modified and further developed following the first round of data review. Inter-coder agreement was achieved by having staff independently code the same transcripts, discuss discrepancies, clarify the codebook and code additional transcripts until 85% or greater agreement was reached. Agreement was checked every ten transcripts, and never dropped below 82%. Descriptive analytic codes were applied and linked to transcript data, and the coded data were then summarized and, when appropriate, quantified for this paper.

Findings

General Understanding About the Trial Design

Women were asked a set of questions that probed about the information provided to them during the trial's informed consent process. They were asked to briefly describe the trial. They were then asked specific questions about each of the following details, if they had not spontaneously mentioned them: trial duration, trial requirements, eligibility requirements, the inclusion of different gel products, blinding and condom use requirements.

All (100%) women accurately reported at least some aspects of the trial purpose and requirements. The most common trial requirements mentioned were gel and condom use, HIV testing, and regular trial visits. Study duration was accurately reported by 90% (59) of the women, and most of those who could not correctly identify duration said simply that they planned to remain in the trial until it ended. All knew some of the trial's eligibility criteria; the criteria most often mentioned were that women must not be HIV-positive, nor pregnant.

When asked if different types of gels were being tested in the trial, 94% (62) answered correctly. Comprehension dropped slightly when aspects of blinding and condom use were questioned. Women were asked if those randomized to a gel arm could stop using condoms, and 88% (58) said that all trial participants were expected to use condoms. When asked if women could tell which gel they were using, 86% (57) responded that women could not discern this. Women were not asked specifically if the trial was testing gel efficacy, but in their responses to questions about the study design and/or motivation to join the study, 50% (33) of the women mentioned that the study was testing gel efficacy.

Motivations to Join the Trial

Women were asked their reasons for joining the trial, and men were asked why they were motivated to support their partner's participation. Most provided more than one reason. For women and men, the primary motivation was HIV testing and counseling for the woman (71% (47) women; 43% (17) men). Some female and male participants further explained that they valued the repeated quarterly testing that the trial required of participants.

The second most commonly cited motivation for joining the trial (60% (40) women), or supporting their partners (38% (15) men) was statements that joining the trial would help them remain uninfected, and many further elaborated that they valued gaining (or their partners gaining) access to information and counseling services about prevention. Altruism was another commonly reported motivator 27% women (18), 30% men (12). In addition to reporting a general sense of helping address the AIDS problem in their country, women spoke of doing something to help "us women." A number of women (17% (11)) and men (25% (10)) mentioned access to health services, which included treatment for STIs, other vaginal infections, and family planning, as a motivation to participate in the trial.

Preventive Misconception

When conducting our analysis of comprehension of informed consent data and motivation to participate in the trial, it became apparent that many women and men associated trial participation with maintenance of their HIV-negative status, which raised our concerns about a preventive misconception. Simon and Sugarman's [5] seminal work on preventive misconception considered responses to questions about (1) the purpose of the trial and (2) perceived benefits of participation. We considered similar questions in our exploration of preventive

misconception. As described above, general knowledge of the purpose of the trial and its requirements was high. However, evidence of preventive misconception was observed for 29% (19) of women, and 20% (8) of men. There was no observed association between knowledge about the trial and preventive misconception.

Although most women stated that they were motivated to join the microbicide trial in order to receive HIV testing, many also made statements about joining the microbicide trial in order to "prevent HIV infection," or "protect myself." Some clarified that they would receive counseling on how to prevent HIV infection, and thus would be protected. However, since no participant, female or male, spoke of changing their behavior as a result of the counseling received in the trial, it is not clear if participants recognized their role in obtaining the protective benefit they sought. Participants who said that the trial was trying to determine if gels prevent HIV, and did not further indicate that they personally felt some measure of protection through their participation were not considered to have a preventive misconception. We take a conservative position that a preventive misconception was assumed by participants who said they were motivated to join the trial because they wanted to be protected.

Examples of the preventive misconception assumed by female participants are included below in statements about why they joined the microbicide trial:

> The main reason was that the study is about the gel, which protects against acquisition of HIV, so to be protected I decided to join. (Malawi female)
> I was able to get something [microbicide gel] so that I continue protecting my health in my flesh. (Zimbabwe female)

Examples are also found in data from the male partner interviews.

> Because the gel will prevent her from contracting HIV as well as pregnancy. When I considered all these, I decided to encourage her to continue using the gel. (Malawi male)
> What made me support her joining is the need for us to be protected from the disease. (Zimbabwe male)

For cases where participant's motivation to participate statements were unclear, their statements about HIV prevention methods were consulted for further evidence. At the beginning of each interview, participants were asked about their understanding of HIV and how it can be prevented. Knowledge was quite high, and 100% of female and male participants reported at least one effective prevention method (e.g., abstinence, be faithful, condom use). However, some participants included microbicide gels in their list of prevention methods. If a participant said that microbicide gels can prevent HIV infection, and if their motivation to participate response included general statements about joining the trial to prevent HIV infection, these participants were considered to have a preventive misconception. The statements below are examples of responses to the question how HIV can be prevented.

> It is prevented by using the methods that we are using, the use of microbicide gels and condoms. (Zimbabwe female)
> It can be prevented by using condoms and using the gel. (Malawi male)

Logical Preventive Misconception

We observed a "logical preventive misconception," among 12% (8) of the 66 female participants. A logical preventive misconception is participants' articulation that if the trial drug is proven effective, they will have been protected while they were in the trial. We consider this a preventive misconception because none of these participants explained that such protection would only be obtained if they were randomized into an effective product arm. A few illustrative quotes are provided below, again from responses to the question about why participants joined the microbicide clinical trial.

> I saw that if I try… these gels and if they are proven to work, it will be an advantage to me. I will be one person, one of the people who would have already protected herself. (Zimbabwe female)
> When I got into the gel group I felt very happy, because if they are said to be effective, I am able to protect myself from sexually transmitted diseases and the HIV disease (Zimbabwe female).

Perhaps a Logical Preventive Misconception is simply wishful thinking, and it is possible that upon further probing participants might have clarified that they would be protected only if they were in an arm using a product that was proven effective. Nevertheless, we again take a conservative position that participants expressing these beliefs did not fully realize the implications of three gel use arms, including a placebo arm.

Discussion

The informed consent information for the clinical trial appears to have been largely retained by trial participants. Most female participants were able to provide accurate responses to questions about the basic design elements of the microbicide trial. Female participants understood that

active and placebo gels were being tested in the trial, and most said that all participants were expected to use condoms for HIV prevention while in the trial.

Female and male participants valued the microbicide trial primarily for HIV testing and the counseling that provided information on how to prevent infection. All of the female and male participants knew at least one effective behavioral method of HIV prevention. Unfortunately, as the HIV epidemic has demonstrated, awareness of behavioral causes of HIV infection, and exposure to HIV prevention counseling messages does not necessarily result in adoption of HIV prevention behavior. A negative HIV test is not preventive, nor is counseling or education, unless acted upon.

No study participant made an explicit connection between HIV counseling and adoption of HIV risk reduction behaviors. Rather, there appeared to be some conflation of knowledge and protection. A decreased incidence of infection was observed during the clinical trial, but it cannot be determined how much of this is due to behavioral changes adopted by participants. Furthermore, it is not known if participants acted on risk reduction knowledge after the trial ended and support for condom use was no longer provided in a monthly counseling session.

Conclusion

Research participants will likely form their own meanings about research experiences that may be different from what they have been told by the research team. For example, STI treatment is routinely provided in microbicide trials, and it is not unreasonable for women to attribute therapeutic properties to microbicide products that are applied directly to the body at the location where itching, discharge, rashes, etc. occurs. Papers from three different microbicide efficacy trials describe such occurrences. Mantel et al. [9] observe that African women in one microbicide trial believed that spent microbicide gels were cleansing HIV and other harmful substances from their bodies. In another efficacy trial Stadler and Saeth [10] report women ascribing therapeutic properties to microbicide gels rather than the STI treatment they received. Green et al. [11] note that half of their female participants believed the trial gel protected them from HIV and other infections. In all these trials, women were told about unknown efficacy, they were given condoms and risk reduction counseling, and those who received treatment for STIs were given pharmaceutical products, not more trial gel. Nevertheless, they attributed vaginal health to the gels they were using in the trial.

Assumption of a preventive misconception could result in behaviors that increase risk for HIV infection. For example, female microbicide trial participants might stop using condoms (or stop asking their partners to), or increase the number of sex partners. Male partners of women in a microbicide trial might also assume a preventive misconception and increase their own risky behavior, thereby increasing that of the trial participant. These disturbing possibilities add to the increasingly recognized need to inform male partners about microbicide trials in which their steady partners are enrolled. Counseling partners about the unknown efficacy of trial products and the use of placebos could help dispel a preventive misconception.

Another disturbing and intriguing issue lies in HIV prevention trial results that show higher levels of efficacy correlated with increased reported adherence [7, 12]. If participants believe a product is effective, they might be more likely to adhere to product use. Such a preventive misconception can be perversely advantageous to clinical trials, but it is anathema to the ethical protection of research participants. It is difficult to know what else can be done to convincingly explain to participants about the unknown efficacy of trial products. Since it is likely that future microbicide gel trials will use a partially effective gel, rather than a placebo gel as a comparator, unambiguous explanations about partial efficacy must be developed. It is clear that efforts to improve the informed consent process, and provide culturally appropriate risk reduction counseling, must be strengthened.

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