

Women's Willingness to Participate in Microbicide Trials in Northern Thailand

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Summary: To assess women's interests and concerns regarding participation in trials of microbicides in Chiang Rai, Thailand, we administered structured questionnaires. Before answering the questionnaire, women attended an educational session on microbicides and clinical trials. Of 370 participants, 82% correctly answered 8 or more of the 11 overall comprehension questions, indicating an adequate knowledge base among the women from which to answer questions about attitudes toward microbicide trials. The most common motivations for participating in a trial were "getting tested for HIV" and "doing something good for women's health." The greatest barrier to participation was women's fear that if they proposed use of a microbicide, their husbands might feel protected and thereby have more sex partners. Overall, 6.2% said they would be "definitely willing to participate," and 66.8% said they wanted to participate but wanted to think about it. Most women previously unacquainted with the concept of microbicides or clinical trial design displayed adequate knowledge of these subjects after the short educational session. If women's initial reactions are validated by actual willingness, surveys could prove valuable for selecting sites for microbicide trials, estimating enrollment rates, and tailoring trials to make them most acceptable to women. **Key Words:** Vaginal microbicides—Clinical trials—Willingness to participate—Thailand.

Vaginal microbicides—products such as gels, creams, or other formulations designed to prevent sexually transmitted infections when applied vaginally before intercourse—offer a promising new approach for expanding women's HIV prevention options. All effectiveness trials of candidate microbicides have been completed among sex workers, however, which presents several problems. For instance, mucosal irritation that is related to extremely high coital frequency might negate the benefits

of an otherwise effective candidate microbicide. These considerations raise the possibility that future trials should be conducted among women more representative of the general population. An ideal trial population would consist of sexually active women who perceive themselves to be at some risk for HIV infection and are informed and willing to participate in potentially lengthy trials of a new and as yet unproven product.

Epidemiologic data indicate that for many women in Thailand, the greatest risk factor for HIV infection is sexual transmission from their husband or regular partner (1,2). Although recent promotional programs have successfully increased condom use in brothels in northern Thailand, condom use among regular partners in the gen-

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Manuscript received March 26, 2001; accepted July 23, 2001.

eral population remains low (1,3). This suggests that women recruited from the general population may be appropriate participants in microbicide effectiveness clinical trials.

We assessed women's interests and concerns regarding participation in clinical trials of new vaginal microbicides and estimated the proportion of clients at antenatal care and family planning clinics who were potentially willing to enroll in a clinical trial. We selected Chiang Rai, the northernmost province of Thailand, as the research site because of its high rates of HIV infection. In the 1990s, HIV infection prevalence peaked at 17% among 21-year-old military conscripts and at 11% among young primigravida women (3). After a multisectoral response, including public education and the Thai government's "100% condom use" campaign begun in 1991, AIDS awareness reached a high level, and infection rates declined dramatically. We present the findings from structured surveys carried out in May 1998. Findings from a series of focus group discussions and in-depth interviews of women and men in Chiang Rai focusing on perception of risk of HIV, norms surrounding abstinence during the peripartum period, and prospects for the evaluation and use of vaginal microbicides provided the foundation for this survey and are described elsewhere (K. Tharawan et al., unpublished data).

METHODS

Using structured questionnaires, we interviewed 370 women. Of these women, 276 were recruited from the Chiang Rai Hospital antenatal clinic, which provides antenatal care to about 1000 women per year, and 94 were recruited from Chiang Rai Municipal (Tesaban) Clinic family planning clinic, which has about 1200 visits per year. These facilities are the largest single providers of antenatal and family planning care, respectively, in the province. During study recruitment, all women attending the clinics were offered enrollment. Written informed consent was obtained from each study participant. The study protocol was approved by the Ethical Review Committee of the Thai Ministry of Public Health and by an Institutional Review Board of the U.S. Centers for Disease Control and Prevention. Before being given the structured questionnaire, participants attended a 30- to 45-minute group educational session on microbicides and the characteristics of clinical trials. Of the 46 questions, which covered all portions of the survey, 11 "comprehension questions" asked about issues covered during the educational session, including microbicide development and the nature of clinical trials. The remaining 35 questions asked about willingness to participate in a trial, about the roles of husbands and community in microbicide development, and about potential barriers to trial participation. The questionnaire was developed based on other studies of willingness to participate in HIV prevention research trials and on findings from the focus group discussions and in-depth interviews. Research instruments were pretested and revised before actual use.

We entered survey responses in a computer database using the software EpiInfo version 6.0 (CDC, Atlanta, GA, U.S.A.). We used SPSS version 6.1 for Windows (SPSS, Chicago, IL, U.S.A.) for all analyses.

We compared and tabulated demographic characteristics of survey participants. We calculated differences in means using *t* tests and differences in the distribution of categorical variables using a χ^2 test and, where appropriate (because cell sizes were small), the Fisher exact test. We also calculated correlation between motivating factors and barriers to participation in a microbicides trial as well as actual willingness to participate in the trial.

RESULTS

Selected demographic characteristics of survey respondents appear in Table 1. Of note, more than two thirds of the participants had attended only primary school (6 years). Most women had had only one sex partner during their lifetime, and none were commercial sex workers. Fewer than 25% of women believed that their husbands would always use a condom if asked; substantially fewer (13.5%) believed that their husbands would never use a condom if asked.

After presenting the educational session, we asked respondents 11 questions as part of the same questionnaire about their comprehension of microbicides and the characteristics of effectiveness trials. The proportion that answered each question correctly is shown in Table 2. Eighty-two percent answered 8 or more questions correctly, and only 10% answered 5 or more questions incorrectly. The median number of correct responses was nine. For 9 of the 11 questions, more than 90% of respondents answered either correctly or "I don't know."

We found that the number of correct responses was not correlated with age but was positively correlated with years of education, with no significant difference between the antenatal care versus family planning groups of women (Spearman rank correlation coefficient = 0.29, $p < .0001$).

The level of importance of 13 potential motivations for joining a trial appears in Table 3. The motivation cited most often as "very important" was getting tested for HIV during their participation in the trial (82%). Women also believed that HIV testing for their partners was "very important." Reimbursement for travel was least likely to be considered "very important" but was rated by half of the women as "somewhat important." Confidentiality and approval by the Thai Ministry of Public Health Ethical Review Board were also "very important" factors for deciding whether to join a trial. When asked which single motivation was most important in deciding whether to join the trial, "doing something good for women's health" was most often cited.

Table 4 shows women's responses to 19 potential barriers to participation in a microbicides trial. The barrier most often cited as a "major problem" was that if they proposed use of a microbicide, this might lead the wom-

TABLE 1. Selected demographic and reproductive health characteristics of northern Thai women by recruiting location

Characteristic	Family planning clinic clients (n = 94)	Antenatal care clinic clients (n = 276)	Total (n = 370)
Demographic			
Mean age, years (SD)	29.4 (6.6)	26.1 (6.6)	26.9 (6.7)
Mean education, years (SD)	8.2 (3.8)	8.3 (5.9)	8.3 (5.4)
Occupation (%)			
Housewife	23.4	33.7	31.1
Unskilled laborer (i.e., daily-paid worker)	9.6	8.7	8.9
Farmer, gardener	5.3	27.2	21.6
Street vendor, seller at market	12.8	8.3	9.5
Unskilled employee (i.e., hair dresser, cleaner)	26.6	9.4	13.8
Semiskilled employee (i.e., clerk, cashier)	7.4	3.6	4.6
Small business owner (i.e., beauty salon owner, tailor)	9.6	2.9	4.6
Civil servant	5.3	4.0	4.3
Student	0.0	1.1	0.8
Skilled freelancer (i.e., tour guide, insurance salesperson)	0.0	0.7	0.5
Reproductive			
Number of pregnancies (%)			
0	9.6	0.0	2.4
1	39.4	43.1	42.2
2	30.9	40.9	38.4
3	17.0	12.3	13.5
4-7	3.2	3.7	3.6
Number of children at home (%)			
0	13.8	51.1	41.6
1	50.0	43.5	45.1
2	29.8	4.7	11.1
3-4	6.4	0.7	2.2
Mean duration of current marriage or relationship, years			
Percentage of women who have had 1-10 partners	8.6 (5.6)	5.6 (6.5)	6.4 (6.4)
1	89.4	86.6	87.3
2	8.5	9.8	9.5
3	1.1	1.4	1.4
4-10	1.1	1.1	1.8
Partner's presumed willingness to use a condom when asked (%)			
Always	29.8	22.5	24.3
Sometimes	38.3	29.7	31.9
Never	12.8	13.8	13.5
Don't know	19.1	33.7	30.3

en's husbands to feel protected and consequently to have more sexual partners. Fewer than half of women, however, saw this as a "major problem." More than 60% of women did not consider the need for regular follow-up as a problem at all, and most (67%) were not afraid to get their HIV results.

When asked what was the single most important reason they would not participate in a trial, the fact that the "long-term side effects of a microbicide are not known" was most often (27%) cited by all respondents (see Table 4). The second most frequently cited barrier to participation was that "the product is not registered and available on the market" (8.9%), followed by "husband disagrees with participation" (8.4%).

Responses about willingness to participate in the trial described to them appear in Table 5. Fewer than 3% of women were "not at all willing to participate," and 6.2% were "definitely willing." About two thirds of women

said they thought that they would be willing to participate, although they wanted to think about it.

Willingness to participate did not correlate with age, years of education, duration of current relationship, or whether one's partner would use a condom when asked. Willingness also did not correlate with the number of correct responses to the comprehension questions. Family planning clinic attendees were slightly more inclined to participate than were their antenatal counterparts (Pearson χ^2 statistic = 15.65, $p < .001$).

DISCUSSION

We found that a short (30-45 minute) educational session was sufficiently informative to answer questions in a population of women previously unacquainted with the concept of microbicides or clinical trial design in this setting in northern Thailand. Few clinical trials had been

TABLE 2. Northern Thai women's responses to questions testing comprehension of trial information (n = 370)

Question (correct answer)	Response		
	Correct response (%)	Incorrect response (%)	"Don't know" (%)
In order to participate in a microbicide efficacy trial, women need to be tested for HIV. (True)	97.3	1.1	1.6
Women must come for regular follow-up visits if they participate in the trial. (True)	96.2	1.9	1.9
A microbicide to prevent STDs and HIV is under development, and the trial discussed today is to test the effectiveness of the microbicide in preventing HIV in women. (True)	93.2	2.2	4.6
A microbicide is a preventive, not a curative method. (True)	92.7	3.2	4.1
It is possible that some women may experience some side effects when using a microbicide. (True)	89.2	1.6	9.2
A microbicide could be available as a foaming tablet, gel, suppository, or other preparation. (True)	88.1	2.7	9.2
Like drawing a lottery, some women will be assigned to receive microbicide and some will be assigned to receive placebo. (True)	84.3	5.4	10.3
To prevent HIV infection, using a condom with a microbicide would be more effective than using a microbicide alone. (True)	82.7	6.8	10.5
A microbicide is applied vaginally after each act of intercourse. (False)	78.1	15.4	6.5
The study clinic staff will know which women will be getting microbicide and placebo. (False)	51.9	29.7	18.4
A microbicide prevents HIV infection 100% at every use and for every user. (False)	50.5	11.9	37.6

STD, sexually transmitted disease.

performed in this population, but after the educational session, women were able to correctly answer most questions; only a few questions were answered incorrectly by 10% or more of the women. A response of "I don't know" is clearly less problematic than an incorrect answer, as it would likely lead to further discussion of the issue rather than to misinformation about participation in a trial.

Of the three "true/false" questions answered incorrectly by at least 10% of the women, the one most commonly answered incorrectly concerned whether the study would be blinded. This misunderstanding would have no practical effect on a woman's ability to follow instructions and participate in the trial and would therefore not

cause her any harm resulting from potential misuse of the study product. The question incorrectly answered second most often, "a microbicide is applied vaginally after each act of intercourse," combined multiple ideas, which may have led to confusion. Even so, only 15% answered it incorrectly. Finally, the third most confusing question, "a microbicide prevents HIV infection at every use and for every user," highlights an important issue regarding participation in microbicide trials and identifies an important area for improvement.

MacQueen et al. (4) have documented similar results regarding comprehension of vaccine trial information among a cohort of injection drug users in Bangkok. In that study, comprehension improved at a follow-up visit 1 week after the initial presentation once participants could review a brochure and discuss the trial with family members. Written materials and the opportunity for discussion of the details of a study may thus lead to a more informed decision regarding participation.

Although results from this study indicate considerable potential interest in trial participation, many issues have to be addressed before successful trial enrollment can be ensured. Clearly, women need to understand the research process better, including concepts such as placebo use, randomization, and blinding. In particular, less-educated women need special help in comprehending these concepts. Study design should also consider the potential roles of the male partners. Roughly half of the women indicated that uncertainty about their husband's willingness to consent to their participation in a clinical trial was a major concern.

The percentage of women reporting that they were definitely willing to participate (6.2%) in a microbicides trial was much lower than the percentage willing to participate in the Bangkok vaccine trial study (51% indicated willingness at baseline and 54% indicated willingness at follow-up) and lower than other reports of willingness to participate in vaccine trials in northern Thailand (5) and the United States (6,7). Perhaps, compared with vaccines, microbicides represent a concept that is more unfamiliar and difficult to comprehend, or perhaps women at family planning or antenatal clinics are less likely to participate in studies than are intravenous drug users or other populations recruited for HIV vaccine trials. Other possibilities might be that women want to consult their husbands before making a decision on trial participation, because the husband is involved in the sex act and therefore potentially exposed to the microbicide, and that microbicides are self-administered and therefore require skill and commitment for application. Finally, women may perceive a microbicide to be potentially less effective than a vaccine at preventing

TABLE 3. Northern Thai women's relative importance of motivations to join a microbicide trial (n = 370)

Motivation	Very important (%)	Somewhat important (%)	Not at all important (%)	Single most important motivation (%)
You will get HIV tests during your participation in the trial.	82.2	15.9	1.9	2
Your partner will also receive HIV testing during the time of the trial.	81.9	16.5	1.6	3
The trial guarantees the confidentiality of your HIV test results.	75.9	17.6	6.5	2
The efficacy trial is approved by the Thai MOPH Ethical Review Committee.	75.7	22.2	1.9	19
The trial offers free physical checkups.	73.2	24.1	2.4	3
Information about the trial will be available and disseminated in trial communities so that the local people can understand the trial.	73.0	22.7	4.3	6
By participating, you will feel you are doing something good for women's health.	72.2	25.4	2.4	35
A counseling service is provided for trial participants during the trial period.	70.3	27.6	2.2	10
The appointment of each clinic visit would be scheduled at a time that is convenient for you.	68.9	28.6	2.4	5
You and your partner will be provided free condoms throughout the whole trial period.	64.1	31.1	4.6	1
The clinic is not too far from you, for example, in Amphur Muang, Chiang Rai.	59.2	33.5	7.0	1
A microbicide is a method that you, not your husband, will use.	54.1	42.7	3.0	12
For each clinic visit, you will be reimbursed for your travel cost (not loss of time) up to, for example, 300 baht. ^a	34.1	49.2	16.5	1

^a At the time of the study, \$1 US = 40 Baht. MOPH, Ministry of Public Health.

HIV infection and therefore may be less interested in participating in a clinical trial.

Implications

We conclude that a microbicide trial seems reasonably attractive to family planning and antenatal clinic clients in northern Thailand. A single educational session on microbicide development and clinical trials resulted in a high level of understanding among potential participants. Written information about the development and testing of microbicides may also help to foster understanding among those populations most at risk for infection.

The two most important barriers to participation involved male partners. Although the most frequently cited barrier, fear that the husband would take other partners if the threat of spreading infection in his family were removed, is not amenable to changes in study design, the role of the husbands can be considered in other ways.

The barrier second most often cited as a "major problem" for participation was "deciding to participate without husband's consent." Education for husbands would therefore certainly help to enable women to discuss potential trial participation with their husbands. Special educational outreaches to married men or men in regular partnerships might also be useful.

The public should be regularly consulted about the educational materials developed for the trial. Such consultation will help to ensure that women are informed and feel supported by the community for participating in trials. It will also help to identify special efforts (e.g., outreach to husbands) needed to make the trial maximally appealing to otherwise interested women. In addition, it will be important to plan occasional meetings among interested persons to further advocate for women-controlled methods to prevent HIV transmission. Such meetings would help to educate women's health advocates about the development of microbicides.

TABLE 4. Barriers for northern Thai women to participation in a microbicides trial (n = 370)

Barrier	Major problem (%)	Small problem (%)	Not a problem (%)	Most important (%)
If you suggest using a microbicide, your husband may feel protected and have more sexual partners.	45.9	33.0	21.1	8
Deciding to participate in the trial without your husband's consent would be a problem for you.	42.2	38.9	18.6	3
Product is not yet registered and available in the market.	37.0	44.9	17.8	9
The long-term side effects of a microbicide are not known.	35.4	50.3	14.1	27
In case of an adverse event resulting from using the product being tested, the trial offers medical care to you only up to a certain period of time.	35.4	37.0	27.3	7
If you suggest using a microbicide, your husband may not agree to use condoms.	33.2	47.3	19.5	4
Husband may think it a bad idea to participate in the trial.	33.0	48.9	18.1	8
You might develop some side effects after use.	31.4	57.6	11.1	7
You may be given a placebo, not the microbicide.	31.1	48.1	20.8	4
The trial offers medical care to you but not your husband.	19.7	40.0	40.3	2
The product is produced in a foreign country but tested in Thai people.	17.0	45.1	37.8	3
A microbicide may be noticeable during sex, and your husband may not like it.	15.7	60.8	23.5	2
You are afraid of having pain from the needle used to draw blood at follow-up visits.	15.1	32.4	52.2	1
A microbicide is difficult to use (i.e., it must be inserted into your vagina every time before sex).	14.9	55.1	30.0	1
You are afraid to get an HIV test because you do not want to know if you have HIV infection.	13.0	20.3	66.8	0
You do not feel yourself at risk for HIV infection.	12.4	40.5	46.8	3
A microbicide may be only partially effective in preventing HIV infection.	10.0	67.0	23.0	5
Your neighbors might gossip if you participate in the trial.	9.5	32.2	58.4	1
Regular follow-up is not convenient for you.	4.6	34.9	60.5	2

As emphasis in the microbicides research community shifts toward conducting trials among women drawn from the general population, it is reassuring to learn that many women are willing to participate. We plan to vali-

date our assessment of willingness by surveying women who do join our upcoming microbicide phase II expanded safety trial, which will be conducted among the same population of women. This information could prove valuable for selecting future sites for microbicide trials, estimating enrollment rates, and tailoring trials to best meet women's needs.

TABLE 5. Willingness of northern Thai women to participate in microbicides trial by recruiting location

Willingness	Family planning clients (%; n = 94)	Antenatal care clients (%; n = 276)	All respondents (%; n = 370)
I am definitely willing to participate.	10.6	4.7	6.2
I want to participate, but let me think about it.	76.6	63.4	66.8
I do not want to participate but would think about it.	10.6	29.0	24.3
I am not at all willing to participate.	2.1	2.9	2.7

Pearson χ^2 statistic = 15.65, $p < .001$.

Acknowledgments: The authors acknowledge the important assistance of the staff of the Chiang Rai Health Club, the Chiang Rai Hospital, and the Chiang Rai Municipal Health Office. They also thank Kritaya Archavanitkul for consultation on this study.

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