

**Prevention, Partners, and Power Imbalances:
Women’s views on how male partners affected their adherence to vaginal microbicide
gels during HIV prevention trials in Africa**

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Abstract**Background**

Low adherence has contributed to disappointing results for trials testing vaginal microbicides for HIV prevention. This study engaged former gel trial participants to understand the reasons behind low adherence and seek suggestions on how to improve products and adherence to microbicides. This analysis examines the impact of participant perceptions of male partners on participant adherence and suggestions on how to address those issues.

Methods

Eight focus group discussion workshops were conducted with 46 former microbicide trial participants in South Africa and Tanzania. Participants provided feedback on why women join trials, barriers to using gels and reporting adherence accurately, and how adherence and adherence reporting can be improved.

Results

Participants reported that male partners can affect women's ability to use gels. For some, the lubricating effects caused relationship conflicts due to suspicion of male partners about infidelity. Needing to provide sex to partners on demand was a barrier to gel use. Participants suggested a gel formulation which was thicker and less noticeable, and explicit male partner engagement to enhance understanding of the purpose of the gels.

Conclusion

The imbalance of power in intimate relationships affects the ability of women to use microbicides as directed. To improve adherence to HIV prevention methods within trials and for successful rollout of proven HIV prevention methods in populations, it is important that the complicated dynamics of sex and relationships be taken into greater consideration and that women receive targeted support to navigate product use and communication within the context of these gender dynamics.

Abstract Word count: 250

INTRODUCTION

The impetus for vaginal microbicide research for HIV prevention arose over two decades ago out of the need for women to protect themselves from HIV without having to rely on male cooperation to use condoms. HIV disproportionately affects women, who often do not have a choice about how and when they have sex. Structural factors perpetuate environments where women have less autonomy than men.¹⁻⁵ A range of HIV prevention methods which women can use themselves is still urgently needed. Multiple clinical trials, largely conducted in Africa, have tested the effectiveness of candidate microbicide gels, with disappointing results.⁶⁻¹⁸ Low adherence has likely played an important role in many of these trials being unable to accurately characterise the biological efficacy of the candidate products.¹⁹⁻²⁴ With 1% tenofovir gel, the link between suboptimal adherence and the lack of demonstrated efficacy has been shown in VOICE⁹ and FACTS001²⁵. As adequate adherence has been a challenge during trials, the field has shifted focus towards methods which do not require daily or coitally dependent adherence such as vaginal rings, and long-acting injectable pre-exposure prophylaxis (PrEP).

Despite the challenges of adherence in microbicide trials, analyses from CAPRISA004 and VOICE suggest that when vaginal gels of 1% tenofovir are used regularly, they can reduce the risk of HIV infection.^{9,26-28} The need for on-demand and topical products is important from a public health perspective and support for these methods exists among researchers and community stakeholders.^{29,30} A range of effective products which meet the different needs of users and the needs of users at different times in their lives will support optimal public health benefit for HIV prevention.

This small qualitative study sought to engage former vaginal microbicide gel trial participants in two African countries to better understand the reasons behind low adherence and seek their suggestions on how to improve future products and adherence to these products. This research was grounded in the principles of community engagement^{31,32}: as the field continues to design and implement trials to identify HIV prevention options and rolls out proven methods into communities, it is critical to understand the context of the lives of women and how gender dynamics affect their adherence to products.

METHODS

Former microbicide gel trial participants from the Microbicides Development Programme 301 (MDP301)⁸ and the Vaginal and Oral Interventions to Control the Epidemic (VOICE)³³ clinical trials, participated in 8 focus group discussion workshops (FGDWs), a novel method which combines focus group discussions with participatory activities, in Tongaat, South Africa and Mwanza, Tanzania in 2014. MDP301 was a randomised, double-blind, placebo-controlled phase III clinical trial of a coitally dependent regimen of PRO2000 gel, conducted in South Africa, Tanzania, Uganda, and Zambia and completed in 2009.⁸ VOICE was a randomized, double-blind, placebo-controlled phase IIB trial of a daily use regimen of 1% Tenofovir gel (as well as oral pre-exposure prophylaxis--PrEP), conducted in South Africa, Uganda, and Zimbabwe and completed in 2012.³³

Recruitment Procedures

In Tongaat, a randomised list of trial participants was used to contact former MDP 301 and VOICE gel participants via mobile phone. In Mwanza mobile phone numbers were not available; former MDP301 participants were traced by car and then by foot using locator narratives, by geographical areas alternating between urban and peri-urban areas. Former participants interested in participating were booked for a FGDW session.

Focus Group Discussion Workshops (FGDWs)

Four FGDWs were conducted in each location. In Tongaat two FGDWs were held with former MDP301 participants, and two were held with former VOICE gel participants. In Mwanza all four FGDWs were held with MDP 301 participants, because no other microbicide trial had been conducted in Mwanza. FGDWs were organised by trial, and then by general age categories. FGDWs ranged from 2-9 participants each, with an average of about 6.

FGDWs began with a discussion, using a simple diagram, about how microbicide trials compare HIV incidence in trial arms to identify potentially efficacious products. How low adherence can prevent interpretation of trial results was discussed using the Carraguard trial as an example, which included a picture of dye-stained applicators.^{15,34,35} This was provided so that participants could understand the importance of adherence and offer meaningful recommendations. FGDWs included discussions and participatory activities addressing motivations for participation, trial experiences, gel use and its reporting, feelings and needs of participants, perceptions about trial staff and trial beneficiaries, options for different prevention technologies and trial designs, and an activity where participants designed future hypothetical microbicide trials to include their recommendations for improving adherence and its reporting. Participatory activities included activities such as role plays, group work, brainstorming, and sorting activities. FGDWs lasted approximately 2-4 hours. Modifications to the FGDWs were made in real time to adjust to each group's dynamic. FGDWs were conducted in Swahili in Mwanza and in isiZulu in Tongaat.

Due to the length and intensity of the FGDWs, each workshop was facilitated by two trained individuals: one who led the discussions and one who led the participatory activities. All FGDWs were audio recorded and contemporaneous written notes were taken.

Data Processing and Analysis

Each FGDW was followed by a debriefing session with staff to discuss what was said or not said, what worked, and what might need to be modified for the next day's FGDW. Debriefing sessions began the initial analysis of the data with respect to participant perspectives.

Audio recordings were transcribed verbatim by a trained individual and then reviewed. Transcripts were then translated by native speakers and reviewed for accuracy. Transcripts were coded inductively (using NVivo 10) for themes which emerged from the data, by the principal investigator who was present at each FGDW.³⁶ Analytic memos were used to reflect on the meaning of quotations, relationships between themes, differences between groups, and

identification of overarching themes. After codes were harmonized and organized, 100% of the transcripts were coded a second time for quality assurance.

This analysis focuses on participant perspectives of how male partners influenced their adherence and suggestions from participants on how to improve adherence with regard to male partners. Perception of male partner influence emerged from participants as an important theme and had not been included in the semi-structured FGDW guides. Themes presented below cover the vulnerability of women due to male partner infidelity, participant report of male partners as a barrier to gel use, participant report of male partner reaction to vaginal differences during sex, and participant suggestions to address barriers to adherence related to male partners.

A separate analysis examines the underlying needs of participants and how those needs intersect with the assumptions and objectives of microbicide trials, and will be published elsewhere.

Ethical review

This study was approved by the Tanzania Lake Zone Institutional Review Board, the Tanzanian National Institute for Medical Research, the South African Medical Research Council Ethics Committee, and the London School of Hygiene & Tropical Medicine Ethics Committee. All participants provided written informed consent.

RESULTS

Participants

A total of 46 participants participated in this study (Table 1). In Tongaat, 188 former MDP301 participants were called; of those, 26 were reached, 20 expressed interest in attending, and 14 participated in a FGDW. In Mwanza, 128 former MDP301 participants were traced in person; 31 expressed interested in attending, 10 former participants who were encountered by chance or through invitation of a fellow participant expressed interest, and 27 women participated in the present study. In Tongaat, 124 former VOICE gel participants were called; 26 were reached, 18 expressed interest in attending, and 5 participated in a FGDW.

Participants ranged in age from 24-73 years (Table 1). Most were not formally employed. Most participants in Tongaat had completed or had some secondary education. Most participants in Mwanza had completed or had some primary education.

Male partner infidelity and vulnerability of women

Participants discussed how HIV has affected women more than men, and how they feel at risk in their relationships due to male partners having multiple sexual partners. They discussed how men often refuse to use condoms and that leaves them with no way to protect themselves. This reality motivated some women to join microbicide trials so they could have access to a potential HIV prevention method they could use on their own.

...really a woman's life is always at risk he [a husband] can go somewhere for a job like [a far location] and not come back. I do not know with whom he is sleeping with wherever he is--he may come back with something and infect me with it.

33, Tongaat Participant 1

I had a problem that my baby's father did not want us to go there into using a condom. I did not trust him saying he does not eat a sweet in a paper.

28, Tongaat Participant 2

The man may have had sex outside there with three or even four women, he will just force you to have sex with him; therefore when you get the gel, maybe a little gel, you will at least be trusting yourself.

54, Mwanza Participant 10

Even though participants understood they might receive either the active gel or the placebo gel, some participants were hopeful that the gel might prevent them from getting HIV, as they had no other means to protect themselves.

Male partners as a barrier to gel use

Despite interest of some participants in using the gel, they discussed the reality of the power imbalances they experienced in their relationships with men. Some women found that their male partners did not want them using the gel, and that affected their ability to adhere to protocol instructions for gel use.

It is true that you can be pressed by the man that you shouldn't use many gels...Now you find many gels remaining unused...

42, Mwanza Participant 11

He did not like the condom and the gel as well. He did not like both.

28, Tongaat Participant 2

For some participants, the need to be ready for sex as soon as their male partners demanded it prevented them from inserting the gel before sex and thus impacted their consistent use of gel during the trial.

When you have hidden the gel, and your husband needs you [wants sex], it means you don't have time to prepare as you will be late, so you just have to go ahead, and you haven't inserted the gel.

42, Mwanza Participant 11

This was particularly the case when male partners had not been informed about the gel, when trial participants' homes had outside latrines, and when their partners demanded sex late at night or early in the morning. Participants who discussed this problem noted that they had to be ready when their partner "needed" sex, and that they were not in a position to make him wait, as he would not be understanding if she was not able to provide sex at the time that he wanted it. In those instances, the participants stated they were unable to use the gel, despite wanting to.

One participant noted that the combination of needing to insert the gel secretly in an outside latrine, and needing to provide sex to her partner on demand meant she was not able to use the gel as she had hoped:

...the surroundings where most of us are living are difficult... you go to wash [for post-coital cleansing]...when you return your partner wants [sex] again, and you don't have that time of evading him, he will demand. It is already two or three o'clock, to go outside again...Really it was difficult. It is those surroundings which make us fail to get time ...to insert the gel again.
42, Mwanza Participant 12

Male partner reaction to vaginal differences during sex

Many participants noted that the gel, once inserted into the vagina, made a noticeable difference that could be detected by their partners. For some, this increased lubrication was not a positive attribute and raised suspicion about her fidelity with their male partners. This was in particular noted by participants in Mwanza.

... if he finds that it is watery he starts questioning you that 'what is wrong with you, why were you not like this on other days?' That is the problem which is there.
32, Mwanza Participant 13

This increased lubrication was reported to create conflict in some relationships in Mwanza. Male partners noticed the difference in their female partners and, in some cases, associated this increased lubrication with infidelity, at times to the point of accusing some trial participants of being unfaithful.

... he will tell you that maybe you have had sex with other men because he will find that there is a difference...they were saying that it [the gel] was bringing them problems; they were using it but quarrels and problems never ended inside the house.

32, Mwanza Participant 13

Some participants explained that partners disapproved of them using the gel and when they chose to use the gel, it created conflict in the relationship. Some participants who had been in this situation had to make a choice between using the gel, which they hoped would protect them, and not using the gel, to avoid further discord with their partners. Other participants chose to discuss the gel with their partners and found resolution.

...personally I used the gel like it was directed and at the beginning -- it brought some arguments at home until I came to ask the doctor why does my husband complain when I insert the gel, he says that I have become watery; what is wrong with me and what should I do? The doctor told me 'go and involve him, you should show him.' In fact I did so. I went to involve him that I have these medicines [gels], therefore you shouldn't worry. When he knew that I was using that thing [gel] there was no quarrel again.

60, Mwanza Participant 14

Participant suggestions to address adherence barriers related to male partners

Improved formulation of gel

Mwanza participants had recommendations about the gel formulation. These participants recommended that it should have a less-watery consistency, less volume, not be as highly lubricating, and have a warming sensation upon application; packaging could also be more discrete (Table 2). Some thought that vaginal capsules might solve this problem or that the microbicide should be available in both formats, capsules and gel. Some acknowledged that different bodies are different, thus what works for one person might not work for another. Mwanza participants spoke of the importance of making these changes so that the microbicide could be used covertly, which was important for some, and so that microbicide use would not be surprising for the male partners who might notice a difference during sex and then accuse the trial participants of having sex with other men.

My suggestions are ...[the] medicine [gel] should continue being improved so that it should be warm, I mean that gel should not be light [liquidy], it should be heavy [thick].

40, Mwanza Participant 15

So that when you bring it here at least it should have some certain warmth to make the man also get the desire when she inserts it inside the vagina.

39, Mwanza Participant 16

Explicitly include male partner engagement into trial design

While some participants chose not to disclose gel use to their partners, others thought it was important to let long term partners know about the gel. Some participants who wanted to include their partners expressed concern about their lack of confidence or skills to effectively engage their partners. Participants advocated for better inclusion of male partners in the research process. Many agreed that if there were more support in the trials to engage and educate male partners, it would be extremely helpful. They thought that male partners would likely be supportive of the gel and the research, thus improving a trial participant's ability to adhere to the study protocol and use the gel as directed.

...men should be given education on how to protect themselves against HIV infections, they should be educated about the gel; the participants are not supposed to be women only, and young men too need education.

30, Mwanza Participant 17

...when this project starts it should involve men and women and there shouldn't be something like a secret; if her partner doesn't like it, it's better she quits, if her partner will be ready then she should agree; particularly those with husbands...

... if you involve him, he will understand... We have said that education should be given openly to both sexes.

60, Mwanza Participant 14

Participants suggested that male partners should be included from the beginning of the process and that there should be opportunities for them to receive counselling on HIV, health, the research, and the gel. Participants thought this education should be detailed and complete, so that trial participants and their partners would not be left with doubts. Participants also noted that better education would help the trial participants themselves to have courage and strength to tell their male partners about the details of the trial. Participants thought that once male partners were involved and understood the purpose of the study, they would be supportive. For a coitally dependent regimen, this support could translate into, for example, male partners being willing to wait for participants to insert the gel just before sex, thereby increasing adherence.

Hopefulness and desire for gel

The purpose of this qualitative study was to ask former microbicide trial participants about the reasons for low adherence in past microbicide trials and hear their suggestions for how to improve adherence. Therefore, the results reported here focus on barriers. Despite these discussions during the FGDWs, there was a strong sense of appreciation for the trials that was spontaneously expressed by participants. This included deep interest in the gels and optimism that microbicide gels would be an important HIV prevention technology, if found to be safe and effective.

...for example, for us barmaids, we were seeing that it was helping us...we were using the gel every time; now I mean for the others, maybe they were using it occasionally, but for us, we were working at places where there were many people, in fact it was helping us very much.

40, Mwanza Participant 15

Although many challenges were discussed, especially around managing gender dynamics in the relationships, participants remained hopeful that these challenges could be addressed. This optimism was grounded in their strongly expressed need to have prevention methods to protect themselves from HIV.

DISCUSSION

While the microbicides field has endeavoured to discover a female-controlled product women can use to prevent sexual transmission of HIV, ironically, the field has learned through the process of conducting microbicide trials that male partners, and women's perceptions of their reactions, are important factors in determining female trial participants' ability to adhere to the study regimens.³⁷⁻³⁹ Participants reported that women who desired to use the study gels as directed were sometimes not able to do so due to imbalances in gender norms and factors related to their male partners. In some cases, male partners did not like the lubricating effect of

the gel, or forbade their female partners to use the gel. In other cases, trial participants feared using the gel because their male partners had accused them of being unfaithful, due to the increased lubrication. In yet other cases, the need to be ready for sex exactly at the time their partner demanded it meant there was no time for insertion of the gel. The experiences of these trial participants highlight the need for women to have more control over their own health and additional means to protect themselves from HIV infection.

An important aspect of male partner influence on participant adherence was related to gel attributes. As discussed by some participants in Mwanza, the gel consistency made it difficult to use covertly, was not always liked by male partners, and put some women at risk for being accused of infidelity, thereby causing discord within trial participants' intimate relationships. There were participants in this study who also mentioned positive effects of the gel, consistent with previous studies.³⁹⁻⁴⁵ Participants were supportive of the idea of a gel for HIV prevention and thought that negative aspects could be addressed with improved formulation. Some lubrication was seen by some as positive, but not so much that the gel could not be used covertly. Vaginal suppositories or a dissolving film would provide an on-demand form of protection but potentially with less obvious lubrication.

The effect of male partners, or perceptions about male partners, on product use has also been observed in trials with products that are arguably more easy to use covertly, such as vaginal rings and oral PrEP.^{46,47} In the ASPIRE vaginal ring study, having an unsupportive male partner, as reported by female participants, was associated with lower ring adherence.⁴⁶ Research has also shown that a proportion of women experience social harms within HIV prevention trials including gel and pill users in VOICE, and vaginal ring users in the Ring Study, and ASPIRE.⁴⁸ Women in the Partners PrEP study (oral PrEP) and ASPIRE studies who reported social harms had lower adherence than women who did not report such social harms.^{49,50} Research is increasingly demonstrating that when women use any HIV prevention option, due to societal gender dynamics, they will need to navigate informing their longer-term partners^{37,38,51-56} or anticipate partner discovery, and that those circumstances can impact product adherence.

In the present study, participants longed for greater support to engage their male partners, and believed that such support would result in more partner agreement for product use. More robust provision of HIV and health information to both partners, joint orientation to the trial, and tours of the laboratory and clinic facilities are examples of strategies which were not available to MDP301 participants in Mwanza, who were most vocal about the need to support male engagement. However, male clinic attendance was observed to be low (12.9%) in the ASPIRE study when this was offered.⁴⁶ Participants also thought that support for male engagement could be in the form of helping women to better understand the research and products, and to better communicate with their male partners. Participants lacked confidence about the best ways to engage their partners and requested assistance to better communicate with their partners.

The growing body of evidence from HIV prevention trials shows that consideration of gender dynamics is not only an important issue for successful adherence in trials, but will be key for real-world settings where women want to or need to negotiate their product use for any HIV prevention method with male partners. Therefore, a successful HIV prevention approach includes not only identifying effective HIV prevention tools, but developing strategies to roll out these methods in ways which empower women to negotiate the gender dynamics and communicate with their partners successfully. A cluster randomised HIV prevention intervention in South Africa which sought to engage male partners to improve power, communication, and relationship conflict saw modest improvements with both gender-separate and couples-based

interventions.⁵⁷ More research is needed to determine how best to empower women to effectively engage male partner support around adherence to HIV prevention methods.

This was a small qualitative study which asked former participants to recall their participation in past microbicide trials. For most, considerable time had passed, which could affect their ability to remember. The majority of participants represented MDP301. Two contrasting locations and cultures were selected. Due to small sample size, group differences between the locations and trials did not emerge, with the exception of concern for gel consistency by Mwanza participants. The unique format of FGDWs included discussion and participatory activities, addressing research questions from several angles. As participants were asked about adherence, they may have used their partners as an excuse for their own low adherence. The FGDW format, where women were not directly asked about their own adherence, and could speak about others, attempted to minimise this effect. This study was independent of the initial trials-- this, together with the time elapsed since trial participation, may have supported participants to speak more candidly. While this study is not representative of all microbicide trial participants, views reported here add to the body of understanding of trial experiences. This was the first participatory qualitative study conducted to engage microbicide trial participants in explicitly thinking about the design of microbicide trials to address the challenge of suboptimal adherence.

Conclusion

Results of this research have shown that the imbalance of power in intimate relationships affects the ability of women to use vaginal gels with good adherence. The impact of gender dynamics on adherence has been identified in HIV prevention trials of different modalities. For optimal trial design and programmatic rollout of HIV prevention methods, it is important that donors, sponsors, researchers, and implementers understand the complicated nature of sex and intimate relationships, within the context of a world that provides fewer freedoms and opportunities for women than it does for men. Women want and need a range of HIV prevention options which can empower them to protect their lives. Women also need support to have greater self-efficacy to talk to their male partners and negotiate use of these tools in their relationships.

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Dedication

We dedicate this manuscript to our dear Prof. Gita Ramjee, co-author, mentor, and friend. Gita passed away unexpectedly of COVID-19 complications in March, 2020, while this paper was being finalised. We are deeply saddened by Prof. Ramjee's untimely death. She was an inspirational role model and an international renowned scientist. Gita dedicated herself tirelessly to find methods that empower women to take control of their HIV prevention and reproductive health rights through informed choices. Her death is a loss to women in Africa, to the scientific community, and to the world. Dear Gita, your work lives on through the many researchers you have touched. We miss you.

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Table 1: Participant Characteristics

	Tongaat	Mwanza
Total Number of Participants	19	27
Number of Participants MDP 301 <i>(clinical trial completed in 2009)</i>	14	27
Number of Participants VOICE <i>(clinical trial completed in 2014)</i>	5	N/A
Age range at time of FGDW	27-51	24-73
Education level at time of trial participation		
Some/completed secondary education	15	1
Some/completed primary education	3	20
Illiterate	1	6
Employment at time of trial participation		
No work	16	4
Employed	3	0
Informal vendor	0	17
Hotel worker	0	6
Relationship status at time of trial participation		
In relationship	18	26
Single	1	1

Table 2: Suggestions from Mwanza participants on how to improve gel formulation and packaging

Suggestions for improved gel formulation and use	
1	Less watery consistency
2	Less volume
3	Warming sensation/ lack of "cold" feeling upon insertion
4	Greater ability to use covertly, should not be obvious to a partner that a highly lubricating product is being used
5	Gel applicators and boxes should be smaller and more discreet
