

Low Adherence in Vaginal Microbicide Gel Trials?

Opinions of Former Trial Participants on Improving Adherence



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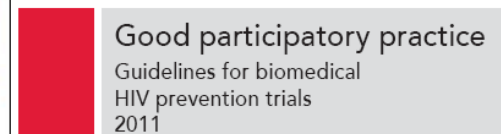
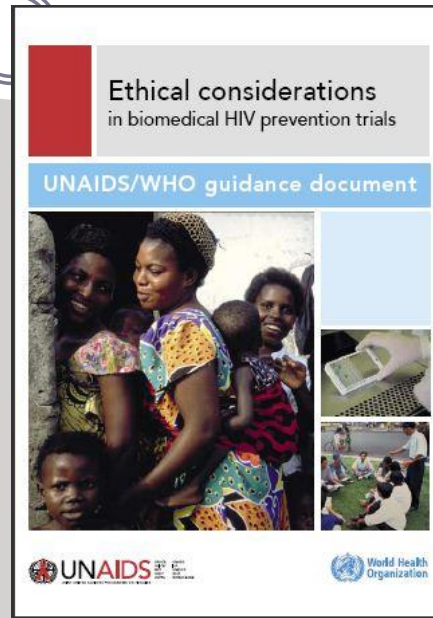
Background



- We need a coitally dependent vaginal microbicide
- Low adherence is a problem in vaginal microbicide trials
- While trial teams have tried to improve adherence using a number of methods, microbicide trial design has largely stayed the same

Background: Guidance Documents

- UNAIDS guidance states the importance of stakeholder involvement in trial design to ensure its ethical and scientific quality, and successful implementation
- Ethical Considerations in biomedical HIV prevention trials (Guidance Point 2)
- Good Participatory Practice Guidelines for biomedical HIV prevention trials



Study Objectives



If low adherence is a problem in these trials, why not ask former microbicide trial participants what they think about:

- How to **improve adherence** in future trials
- How to **improve adherence reporting** in future trials

Methods



- Qualitative study which engaged former **gel** trial participants from
 - MDP 301: Phase III trial of PRO2000, conducted between 2006-2009
 - VOICE: Phase IIB trial of 1% tenofovir gel (plus oral PrEP), conducted between 2009-2012
- Conducted in October and December, 2014
 - Tongaat, Durban, South Africa
 - Mwanza, Tanzania

Methods: Focus Group Discussion Workshops (FGDWs)



- Former participants were recruited through trial participant lists
- Study format: Focus Group Discussion Workshops (FGDWs), which included discussions and participatory activities
- 8 FGDWs held in total, 4 in each location; 2-4 hours each
- Data were analyzed by coding transcripts inductively for themes

Methods: Focus Group Discussion Workshops (FGDWs)



Unlike typical focus group discussions...

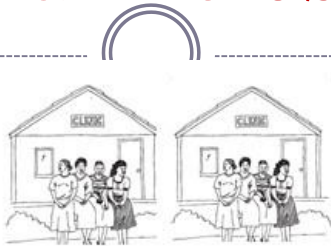
Methods: Focus Group Discussion Workshops (FGDWs)



- FGDWs started with a background orientation so participants would understand trial design basics and could provide meaningful recommendations
 - How do microbicide trials answer their research questions?
 - Demonstration of why adherence is necessary in microbicide trials, using the Carraguard trial as an example

Methods: Focus Group Discussion Workshops

Anatomy of a Microbicide Trial



HIV Negative Women

Active Gel Arm



Placebo Gel Arm



HIV Positive



HIV Negative



HIV Positive



HIV Negative

FGDWs: Why Adherence is important

Carraguard Example



- Overall, adherence via self report was 96% at last sex act
- Adherence estimates using an applicator stain assay indicated coverage for about 42% of the sex acts
- Carraguard gel did not significantly decrease HIV incidence, thus was discarded from the HIV microbicide product development pipeline



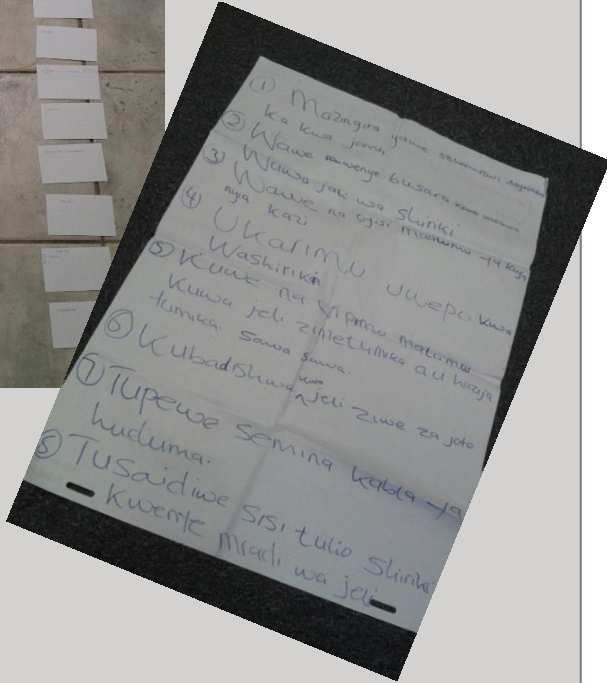
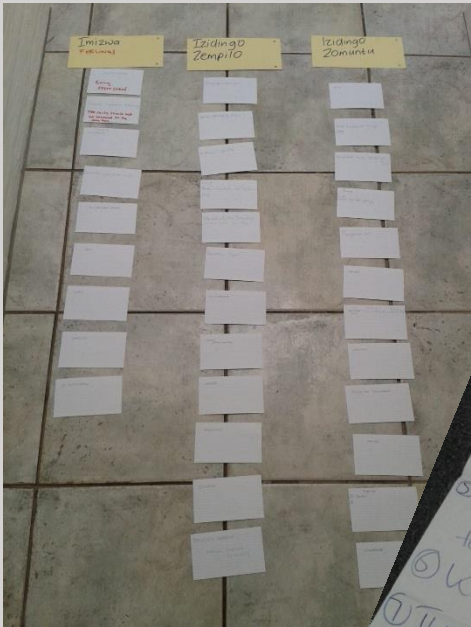
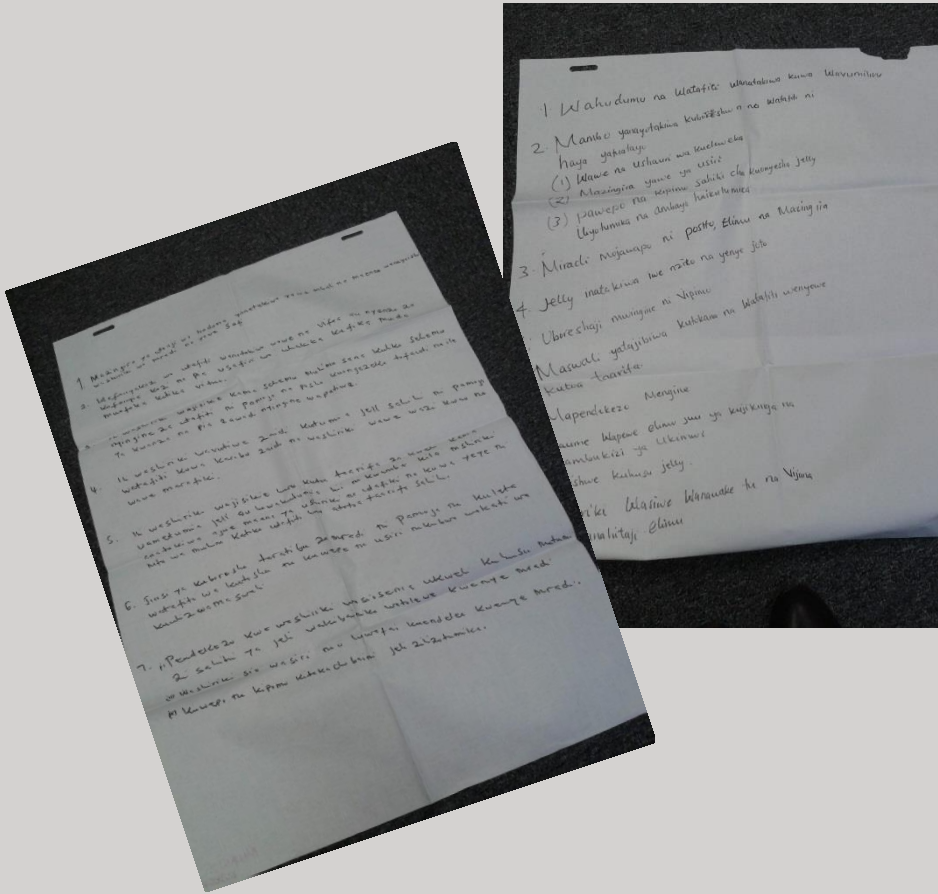
Then

Methods: Focus Group Discussion Workshops (FGDWs)



- Discussion and participatory activities included the following topics
 - Motivations for participation, trial experiences
 - Perceptions about the trial, staff, trial beneficiaries
 - A hypothetical 3 arm trial design with one non-randomized, no-gel arm
 - “Design Your Own Trial” activity
 - ✦ Participants worked in groups to design future microbicide trials with regards to their recommendations

Methods: Focus Group Discussion Workshops (FGDWs)



Some Results...

Results: Participant Characteristics

	Tongaat		Mwanza		Total	
Number of participants	19		27		46	
Trials						
MDP 301	14		27		41	
VOICE	5		N/A		5	
Current age range	27-51		24-73		24-73	
Education level	15 (80%) Some/completed secondary education		20 (74%) Some/completed primary education		23 (50%) Some/completed primary education	
	3 Some/completed primary education		6 Illiterate		16 (35%) Some/completed secondary education	
	1 Illiterate		1 Completed secondary education		7 (15%) Illiterate	
Employment at time of study participation	16 (84%) No work 3 Employed		17 (63%) Informal vendor 6 Hotel worker 4 No work		20 (40%) No work 17 (37%) Informal vendor 6 (13%) Hotel worker 3 (7%) Employed	
Relationship status at time of study participation	18 (95%) In relationship 1 Single		26 (96%) In relationship 1 Single		44 (96%) In relationship 2 (4%) Single	

Reasons for Joining and Staying in Trials



- **Need for HIV and STI protection**
 - Male partners often refuse condoms
 - Male partner infidelity

Reasons for Joining and Staying in Trials



- **Health benefits**
 - Free, confidential, high quality health care and treatment
 - Ongoing knowledge of their own health status
 - Health education
 - Learned to care for themselves and this persisted over the years

Reasons for Joining and Staying in Trials



“... knowing my status was also encouraging... how to behave because things are bad outside. I like it most because they were checking for diseases on us...It also encouraged us not to have unplanned babies...I liked it because I found friends even when you came with a problem you would be able to discuss with people. You can see that, you will leave with no problem. I also liked money, money is part and parcel (laughs).”

Tongaat participant, 42

Reasons for Joining and Staying in Trials



- Financial benefits: Reimbursement provided a type of income for some women

“Mainly this project tempted us to check our health, it attracted us to get that little income and to make us start our businesses, therefore we profited health wise and economically...”

Mwanza participant, 60

Adherence



- Some participants thought certain groups were more likely to use the gel such as barmaids, older participants and those who didn't trust their partners
- Overall, many participants thought gel use was low in the trials
- Key reasons for low use
 - Lack of trust of an investigational product
 - Pressure or refusal from male partner
 - Lack of ability to use gel logistically, when partner demands sex

Adherence



“I can say that some were not using it [gel] saying that they are scared that they are going to get sick, they are going to have diseases in the [womb], they do not know what it does when stuck in there, yes only a few using it.”

Tongaat participant, 38

Adherence



“They are going to check it on us fools, why are they not checking it on themselves?”

Tongaat participant

Adherence Reporting



- Participants noted it was difficult to be truthful in reporting adherence
- The primary reason given was fear of removal from study and thus loss of benefits

Adherence Reporting



“...if she will say the truth she will be chased away and she will not get that money, therefore she tells lies.”

Mwanza participant, 27

Why not develop a clinical trial design that could better meet the needs of women in these settings and trialists?

Hypothetical 3 Arm Microbicide Trial



- Participants were presented with an alternative trial design
- 3 arms in a hypothetical microbicide gel trial
 - Prospective participants choose if they would like to use gel or not
 - If they choose to use the gel, then they are randomized to the placebo or active arm
 - If they choose no gel, they stay in the study in this non-randomized arm
 - All participants (gel and no gel) attend regular study visits

3 Arm Microbicide Gel Trial Design



Women **choose** if they want to be in the gel using group or no-gel group

No gel group

Gel using group



Active
Gel

Placebo
Gel



Reactions to 3 Arm Trial Design



- Many participants, due to orientation provided earlier in the workshops, noted that women in the no-gel arm would not contribute data to answer the research question

- Overall participants liked the idea of this trial design

Reasons given were:

- Many women don't want to use the investigational gel in these trials
- It is better for women to choose themselves if they use the gel or not
- This will prevent women from taking the gel and then throwing it away
- Women will not have to lie about adherence
- This will help answer the trial's research question as women who aren't interested in using the gel won't be in the gel arms

Reactions to 3 Arm Trial Design



“It is better like this... At least it is better because there is a group that will never use it [gel]...it is better not to take it than to take and throw it away.”

Tongaat participant, 28

Reactions to 3 Arm Trial Design



- A few participants did not like this design because
 - Women joining the no-gel arm would not contribute to answering the research question, thus they weren't "helping"
 - They thought most women would join the no-gel arm

Reactions to 3 arm Trial Design



“...If you say that they should choose, most of them will go where there is no gel.”

Mwanza participant, 32

Discussion



- Low adherence and inaccurate reporting are driven by the reality that many women in communities where microbicide trials are conducted participate in trials for a number of important reasons which are not related to interest in the **investigational** gel
- Thus there is a fundamental difference in the objectives of many women agreeing to participate in a microbicide trial and the research objectives of trial implementers

Discussion



- For many participants, trials provided
 - Free, high quality health services
 - Income via reimbursements
- Given these different objectives, it is important for trial design to take this reality into consideration in order to improve adherence

Discussion



- A 3 arm trial with a non-randomized, no-gel arm may help address the fact that many women in communities where microbicide trials are conducted do not join trials to use the investigational gel
- This trial design was acceptable to many participants, and mentioned as a recommendation to improve adherence

Discussion



- While this 3 arm design would be more expensive, as more participants would need to be enrolled, it may result in increased adherence in the randomized gel arms, decreasing the chance of finding a null result
- As each microbicide trial is expensive (~\$40-80 million), repetitive trials with poor adherence and null results are also an expensive endeavor

Conclusions



- This was the first study to engage former microbicide trial participants in explicitly thinking about trial design
- Given the difference in objectives of participants and trial implementers, it is worth exploring innovative trial designs which take this reality into account
- Trialists can work more closely with former participants to consider innovative trial designs that can help improve adherence and adherence reporting in future microbicide trials

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