COMMUNITY INVOLVEMENT IN HIV PREVENTION RESEARCH

Experiences and perceptions of communities participating in the MDP 301 microbicide trial in Masaka, Uganda

November 2010

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However, the information, facts and opinions presented in this report – unless otherwise explicitly stated – are not necessarily those of the individuals and organisations mentioned or not mentioned in this section. The author takes full responsibility for all the errors and omissions that may emerge from the text of this report.

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Executive Summary

The MDP 301 microbicide trial site in Masaka registered many successes in community engagement at the Masaka site: the trial worked with a broad range of stakeholders; took advantage of opportunities presented by stakeholder forums to provide information; responded to issues that arose from the community; and established a network of community-level contact persons through whom information was channelled to and from the host community. Future trials should adopt these strategies, and do better on aspects that did not work well in the MDP 301 trial. For instance, some sections of the community still felt left out of the trial process; not all volunteers received trial results promptly; some key stakeholders at the national level seemed left out of the results preparation activities; and the community found it difficult to come to terms with a flat result. The concept of the CAB needs rethinking to clarify and define its size, composition, selection criteria, functions, mandate and funding.

Background

This work was conceived as part of the author's AVAC HIV Prevention Research Advocacy Fellowship. The objective of this survey was to document community experiences and perceptions related to the MDP 301 clinical trial of PRO 2000 candidate microbicide in Masaka, Uganda, as a case study of community engagement around large clinical trials in Uganda. The MDP 301 was a multi-site, phase III trial conducted in Masaka district, Uganda, and at five other sites in Tanzania, Zambia and South Africa. It started enrolment in September 2005 and ended in September 2009. The final results of this trial, in which a total of 9,385 women volunteers participated, were released in December 2009, showing that PRO 2000 (0.5%) was safe but not effective in preventing HIV infection in women.

Methods

This survey employed a qualitative process that collected data using in-depth personal interviews with about 35 respondents in Masaka and Kampala. One information-sharing meeting was held with 28 trial and community stakeholders. The dissemination of trial results was monitored in results dissemination meetings, other stakeholder meetings, and media reports. This survey also reviewed official documents and Internet resources. The MDP Programme Liaison Group approved the concept and methods for this survey, and the information gathering and analysis took place between December 2009 and April 2010.

Knowledge and awareness of the trial results

All former trial participants, except one, and all CAB members this project interacted with knew the trial results. For some respondents who were not directly involved with the trial, knowledge and awareness of the trial results was relatively lower. Among this category of respondents, a majority of those who were aware of the results reported that the media was the first, and in some cases the only source of the information. A few of the respondents who reported hearing about the results had little or no knowledge of the key messages, while in a couple of cases, the information respondents had about the key messages was incorrect. Public debate of the results in the community was limited.

From the interviews, it appears that a small section of the community stakeholders, particularly the participants and members of CAB seemed not well prepared for a flat result. The reaction of trial participants seemed influenced by their experience with the trial and whether they considered themselves safe from HIV-infection or not. Respondents among the trial team, participants and community stakeholders, expressed relief that the trial product was found safe.

Understanding and interpretation of key messages in the trial results

There were seven key messages the trial team used to communicate the trial outcome. The most important message – that PRO 2000 (0.5%) was found not to be effective in reducing the risk of HIV infection in women – was fairly well understood among stakeholders. Responses from those interviewed indicated that the second key message that the gel was acceptable was fairly understood by a majority of the respondents in the community. The key message on safety of the gel seemed better understood among former trial participants and CAB members than among other community stakeholders.

The message that seemed least understood was that the trial was 'successful'. Among some few respondents, there was difficulty in understanding the difference between safety and efficacy. Among community respondents who were not directly involved with the trial, the logic of using condoms was not apparent, and was one of the least understood messages.

Key recommendations

- Trials/investigators should engage and create partnerships with stakeholder groups within the host community as well as with those at the national level, and build their capacity to understand and engage meaningfully with the research process

- Trials/investigators and global/international advocacy groups should work together in future trials to identify grassroots-level contact persons who they should nurture early in the trial process into community advocates to promote awareness, mobilise the community, monitor trial progress, and provide feedback from the community

- Civil society groups and advocates should build their capacity in biomedical HIV prevention research advocacy through networking and sharing information with research institutions and global advocacy organisations so they can better engage with the research process and advocate for changes or actions deemed important

- The media should take initiative to build their own capacity in reporting on biomedical HIV prevention research clinical trials by seeking and sharing information and networking with trial investigators and advocates

- Local leaders, politicians and opinion leaders should invest time and resources in understanding trial processes, and seek partnerships with trial investigators and advocates in their communities

- Future trials should consider broadcasting and publishing an official public statement of research results in the mass media, with a clear and full explanation of the key messages

Abbreviations and Acronyms

ART	Anti-retroviral treatment/therapy
AVAC	AVAC: Global Advocacy for HIV Prevention
CAB	Community Advisory Board
CRF	Case record form
CSO	Civil society organisation
DHO	District Health Officer
DFID	Department for International Development
DSMC	Data and safety monitoring committee
FIDA	Federation of Uganda Women Lawyers
GCM	Global Campaign for Microbicides
HC	Health centre
HEPS	Coalition for Health Promotion and Social Development
HPTN	HIV Prevention Trials Network
HSD	Health sub-district
IAVI	International AIDS Vaccine Initiative
JCRC	Joint Clinical Research Centre
LC	Local Council
MADNASO	Masaka District Network of AIDS Service Organizations
MDP	Microbicides Development Programme
MRC	Medical Research Council
MUJHU	Makerere University-John Hopkins University Research Collaboration
PEAP	Poverty Eradication Action Plan
PMTCT	Prevention of mother-to-child transmission (of HIV)
PNFP	Private-not-for-profit (health service providers)
PrEP	Pre-exposure prophylaxis
SOBUJA	Southern Buganda Journalist Association
STI	Sexually transmitted infections
TASO	The AIDS Support Organisation
TSC	Trial steering committee
VCT	Voluntary counselling and testing
HCT	Village Health Team
UAC	Uganda AIDS Commission
UNAIDS	Joint United Nations Program for HIV/AIDS
UNCST	Uganda National Council for Science and Technology
UVRI	Uganda Virus Research Institute
UWESO	Uganda Women Efforts to Save Orphans

1. Background

Involving local leaders, civil society groups, the media and other influential individuals and groups in communities where HIV prevention clinical trials are conducted contributes to the success of the research, its relevance and the rapid dissemination of and actions based on the research findings.[1] National and international guidelines[2] encourage researchers to use multiple community engagement strategies, such as a community advisory board (CAB), an information desk or a toll-free number, and community meetings, among others.

(Notes)

1 International Council of AIDS Service Organisations (ICASO), 2006: "Community involvement in HIV vaccine research: Making it work". Available at www.icaso.org

2 "Good participatory practice: Guidelines for biomedical HIV prevention trials", published by UNAIDS and AVAC in 2007; and "Uganda Guidelines for AIDS Vaccine Research: A Guide for Vaccine Research, Development and Evaluation", published by Uganda AIDS Commission in 2001.

1.1 Community Involvement in HIV Prevention Research

As described in the Good Participatory Practice Guidelines for HIV Prevention Trials (2007), the term "community" has different meanings. In basic use, it refers to the separate and overlapping groups of people who share a common identity on the basis of location, ethnicity, occupation, sexual orientation/behaviour, or common interest or activity (UNAIDS and AVAC, 2007; HPTN, n.d.).[1] In the context of research, a community is the group of people who will participate in or are likely to be affected by or have an influence on the conduct of a study.[2] It includes the different sectors of society with a stake in biomedical HIV prevention trial and its outcomes. It is also used to describe the specific location for research where key populations live or congregate and from which research participants are recruited (UNAIDS and AVAC, 2007).

In the case of this survey, therefore, the community refers to the district of Masaka as a geographical area from where participants in the MDP 301 trial were recruited. It also refers to the district's entire social structure, the general populace and the individuals and groups with influence, including community and local political leaders, opinion leaders, community-based groups (CBOs), the civil society organisations (CSOs), professionals, healthcare providers and workers, and the media. It is also used in the broader context to include national-level civil society advocates and the media based in the country's capital Kampala.

Engaging such a wide range of stakeholders as active and informed partners in decision-making about the research and its implementation enhances both the scientific validity and ethical integrity of clinical trials (GCM, n.d.)[3], even when it is a complicated, time-consuming and expensive undertaking to do well. Studies have shown that clinical research is more likely to succeed when all community members affected - investigators, government and non-governmental entities, product manufacturers as well as community members - regard the research as relevant and the process as collaborative (HPTN, n.d.). Participatory management, a fundamental principle of good participatory practices, benefits all parties; helps ensure smooth trial functioning; and builds community capacity to understand and inform the research process, raise concerns, and help address to unexpected issues that may emerge once the trial is underway(UNAIDS and AVAC, 2007).

The Joint United Nations Programme on HIV/AIDS (UNAIDS) emphasizes the value of involving communities "in an early and sustained manner in the design, development, implementation, monitoring and distribution of results of biomedical HIV prevention trials" (UNAIDS and AVAC, 2007: pp. 11). The Uganda Guidelines for AIDS Vaccine Research require trial planners to involve the community in trial planning and implementation. Trial sites are encouraged to pursue multiple community engagement strategies: a community advisory board (CAB); an information desk, or a toll-free number; and community meetings, roundtables and focus group discussions for both trial participants and the broader community (Uganda AIDS Commission, 2001: pp.11-12).

Over time, HIV prevention research trials have increasingly adopted a community engagement approach (UNAIDS and AVAC, 2007). However, while community involvement has become an established requirement in the field of HIV prevention research, the approaches, depth and the community stakeholders engaged has varied across trials, research sites and research institutions. Research sites often have elaborate mechanisms of educating communities before the actual commencement of trials and for disseminating results with trial participants and host

[1] http://www.hptn.org/community_program/CommunityFAQs.htm [Viewed 22 June 2010]
[2] HPTN, http://www.hptn.org/community_program/CommunityFAQs.htm [Viewed 22 June 2010]
[3] GCM, Community Involvement, http://www.global-campaign.org/comm-involvement.htm [Viewed 10 April 2010]

communities at the end of a trial. This may not always be the case with other stakeholders, including volunteers' spouses/partners, relatives, local leaders, civil society and the broader community. And yet, effective engagement and support of both the immediate and broader community during the entire life-cycle of a biomedical HIV prevention trial, and beyond, through genuine, transparent, meaningful participatory processes enhances both the quality and outcome of research (UNAIDS and AVAC, 2007).

1.2 Objectives of the survey

How the various sections of the community are engaged before, during and after trials determines their contribution and support for ongoing and future trials. This research project was designed to document experiences with, and perceptions of community members and groups about the MDP 301 microbicide trial.

This survey sought to answer the following questions:

1) How did the MDP 301 microbicide trial engage with the various stakeholders in the host and broader communities?
2) How did the MDP 301 trial prepare community stakeholders for the trial results?
3) Do selected community members know the trial results? How did they learn of them?
4) How did stakeholders in the host and broader community react to, understand and interpret the key messages in the trial results?
5) What do the community stakeholders think about their engagement with the trial and the trial process?
6) What lessons does this case study provide on community engagement around HIV prevention clinical trials in Uganda?

1.3 Methods

The research project employed a qualitative process that collected data using in-depth personal interviews with investigators and key staff of the MDP 301 trial, and of staff involved in other trials in Uganda; members of the MDP 301 Community Advisory Board (CAB); former participants; regulators; and civil society leaders.

One information-sharing meeting was held with the trials staff and community members, including the civil society representatives, local leaders, and media practitioners. The information-sharing meeting was held in Masaka town on Tuesday, April 27, 2010 and had 28 participants.

The results of the MDP 301 trial were released in Uganda on December 14, 2009. This project surveyed some stakeholders, monitored media coverage and followed the release, dissemination and debate around the results in results dissemination meetings organised and/or addressed by the trial staff.

Information was also gathered through a review of the study protocol, press releases as well as of relevant literature and Internet resources.

The information gathering and analysis process took place between December 2009 and April 2010 and with approval of methods and processes by MDP Programme Liaison Group.

Figure 1: Personal interview respondents (N = 35)

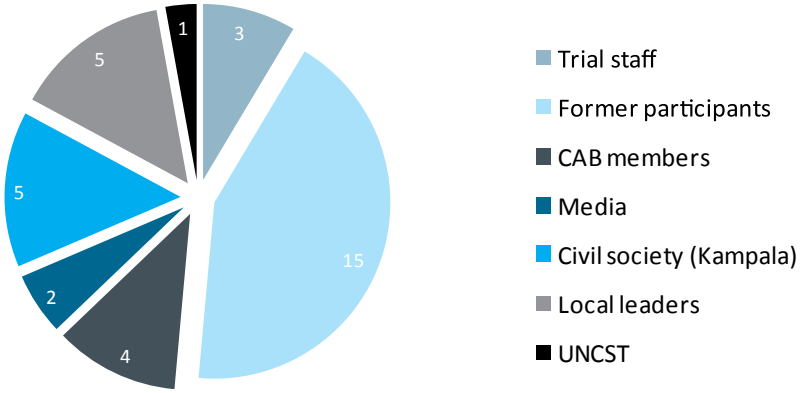
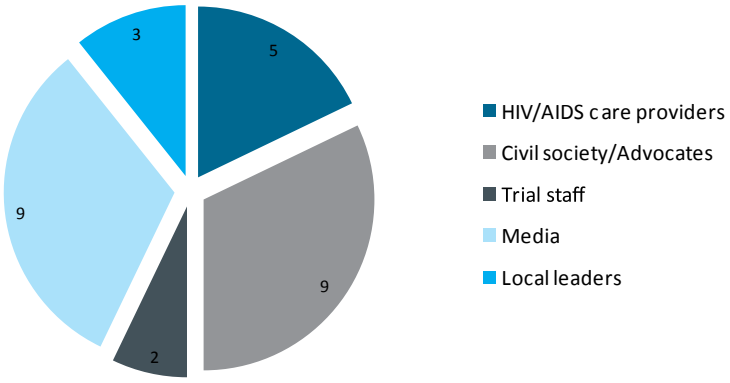


Figure 2: Participant categories at the information-sharing meeting (N = 28)



1.4 Limitations

This work represents a civil society advocate's perspective of community engagement with the MDP 301 microbicide trial at the MDP site at the Medical Research Council (MRC)/Uganda Virus Research Institute (UVRI) in Masaka, Uganda. The trial staff of MDP 301 and MRC/UVRI were not involved in authoring this report, but the trial staff made comments on the initial drafts. The information presented and discussed here does not in any way represent an audit of the trial process or records. The author has relied on information collected and analysed using the methods outlined in the methods section. This survey was not able to access official documents of interest, notably the community advisory charter, media engagement and communication strategy, trial results dissemination field reports, and community information feedback reports.

2. The Trial Process and the Participants

Working with couples, where both the male and female are involved, may make it easier for women in communities where men are the decision makers to participate in HIV prevention research. It minimises the suspicion with which sometimes men in such male-dominated communities view their partners' intentions to participate in a clinical trial. Trials designed to recruit couples as participants call for hard work and multiple approaches to secure informed consent from both partners. However, once recruited, couples make follow-up easier and retention higher. With consistent counselling, they share information more easily, support each other in keeping appointments and in allaying fears and misconceptions that may be circulating about the trial product or procedures done in the trial. In addition, couple recruitment facilitates conversation about sexuality in homes where, in some instances, they may have never before discussed condom use and safe sex. The MDP 301 trial has also demonstrated that involving men in reproductive health issues improves uptake of services.

2.1 Recruitment and enrolment process

The MDP 301 trial tested the efficacy of an experimental microbicide, PRO 2000. The trial targeted high-risk HIV-negative women. The Medical Research Council (MRC)/MDP Masaka research site specifically HIV-negative women whose sexual partners were HIV-positive. The site enrolled and followed up about 840 couples between September 2005 and August 2009.

There were challenges in getting the target number of discordant couples as they were a "hard-to-find" population and also needed to consent as a couple.

> *"It is easier to recruit individuals if you have a criterion that you are recruiting HIV negative people, you would have a big sample size. And it's the way you bring out information which actually matters in a way to get them, if you define the inclusion and exclusion criteria very well. With couples, it is a little bit different. These are already a hard to find population."*
> – Member of trial staff

The Masaka site employed various strategies to raise the required number of volunteers. The target area spanned the entire district, where couples were recruited through three approaches: office-based voluntary counselling and testing (VCT); field outreach sensitisation, education and VCT; and by referral from HIV/AIDS care providers.

> *"If you are dealing with the participants in a clinical trial, as a researcher or a support staff to researchers, you need patience; you need to allow people time to understand the information. Sometimes it is not something they can understand immediately. But with time, science can be made simple by the same people you target. If you want people to appreciate, they need time to synthesize; the results can be amazing."*
> – Member of the trial staff 2

The study is one of the few that have recruited a substantial proportion of participants directly from the community rather than from health centres. A team of community mobilisers, counsellors and health workers worked together to move throughout the district, and succeeded in completing recruitment in time.[4] The trial staff made their initial entry through community leaders, who helped mobilize people for community meetings where the trial team met and sensitised them about the importance of testing, sero-discordance and the microbicide trial. VCT services were provided within the communities where sensitisation took place.

Women who tested HIV-negative and their spouses positive were invited to attend the screening visit. Potential volunteers who agreed to be screened were provided with general information about microbicides and the MDP 301 trial, study procedures; offered safe sex counselling, voluntary counselling and testing (VCT), and before being requested to give informed consent.[5],[6]

> *"You cannot manufacture discordance. You will need to go and find out if it does exist in the communities and to get them, you need a good approach to the community to get the community understand the concept and importance of the trial. It was clearly explained during community meetings. Because of the good explanation, we had a big number of people turning up for testing. We eventually got a good number required to answer the research question with support from the community."*- Member of trial staff 1

[4] Interview with member of the trial staff
[5] MDP 301 trial protocol, version 2.1
[6] Interview with member of trial staff

Negative sentiments in the community around MDP 301 trial reflected the common misconceptions and myths related to the lack of information on trial design and ethical and regulatory safeguards. This work has noted that some HIV-discordant couples that were referred to the trial were at the time of referral made to understand that MRC provides "support" (care) to discordant couples. The general perception of MRC as a care provider for HIV discordant couples, rather than as a research institution, was also noticeable among respondents from the broader community in Masaka, particularly the local leaders. This perception, reinforced by the fact that the trial provided participants with better medical and clinical care than was available in the general health care system, may have contributed to high hopes of gel efficacy and complicated the management of community expectations. It is important to provide clear information to potential participants and their communities about the trial and its objectives, the trial product, potential benefits and risks, and the roles, rights and responsibilities of the different stakeholders. Clear information will generate a volunteer spirit and avoid cases where people may be motivated by expectations of product efficacy, medical care, or financial gain.

The trial also worked closely with organisations providing HIV care services, such as The AIDS Support Organisation (TASO), Uganda Cares, government health units, and private-not-for-profit (PNFP) hospitals that are providing HIV services in the district. The trial team reached out to them at the beginning of the trial and explained the study to the staff, informing them about the target population and requesting them to support the participant recruitment process. The service providers supported the trial's recruitment effort by referring the discordant couples they had among their clients to MRC.[7]

2.2 Motivation of trial participants

As part of this project, a survey tool was developed to use when talking with former trial participants to explore their motivation in joining and remaining in the trial. The trial staff were also asked what they thought was the biggest motivating factor for participants. The responses from both sides suggested the community was desperate for a solution to the HIV problem. They however, differed on the other key motivators, with the participants emphasizing their expectation of assistance, including the hope that the microbicide would work, the health care that came with trial participation, and the reimbursements. The trial staff looked at the participants more as heroes who offered to volunteer in order to contribute a solution to a public health problem.

> *"I think the biggest credit I give them is what I would call enthusiasm; the willingness of people (to contribute to) community benefit, for public health benefit… I think that was the big motivating factor for these participants and to get a cure or a product to help others benefit from in preventing them acquiring HIV. I think this motivated them and (even in) accepting all the visits till the end... It was an advantage for the men; those who are positive to get access to care."*
> – Member of the trial staff 1

The female participants benefited from examination and treatment for sexually transmitted infections (STIs) and other minor illnesses and all needs related to their reproductive care. Some couples had STIs and had a chance to get them diagnosed and treated. Many respondents among former trial participants cited this kind of health care as their biggest benefit from the trial. Availability of free health care could have contributed to the high retention rates.

> *"What motivated me most was that my husband was found HIV positive and I was found negative, and I had been told they (the trial) assist couples that are discordant in the way they handle you, counsel you to help you live together without the positive person infecting you. So I expected to remain with my husband without him infecting me."*
> – Former participant in Masaka Municipality

> *"We expected to get something good from the process that might help us avoid infection (from one partner to the other). In my mind, I thought the gel might help me avoid infection since they told us it has the ability to stop HIV."*
> – Former participant in Masaka municipality

> *"I thought may be it would work and help us avoid being infected... Later, (I had) hope that the trial would get something that would help... I don't think anybody (else) knew (about our participation in the trial) but some relatives knew. After we tested and found that we were discordant, we told them some organisation gave us medicine to use. It was easy to tell*

[7] Interviews with trial staff, TASO and Uganda Cares

relatives because we did not expect them to go rumour-mongering about us (the way) the neighbours (would).
– Former participant in Kimaanya

2.3 Participant understanding of key trial messages

The women participating in the trial were followed up for a period of 12 to 24 months. The first follow-up visit came after one month of enrolment, and subsequent ones on a monthly basis. Each woman made at least nine visits for regular genital examinations, blood tests, urine pregnancy tests, and for questioning about their sexual activity, among other clinical procedures. About 140 of the women also attended detailed interviews and focus group discussions as participants in the social science component over the course of the follow-up.[8]

Before enrolment, trial staff discussed gel use with volunteers, and the potential risks associated with the gel and study procedures before seeking consent from potential participants. The study protocol highlights four critical points that volunteers had to comprehend prior to enrolment:

(1) that the primary reason for doing the trial was to test whether PRO 2000 would prevent HIV, and that at the moment the researchers did not know;
(2) that there was a 50% chance that a participant would receive a dummy product (placebo) and no-one, including the trial staff, knew which product any of the participants was using;
(3) that participants should use the gel during all episodes of sexual intercourse during the study, and, because it is not known if the gels prevent HIV, it was best that condoms are used with gel whenever possible;
(4) that screening includes sensitive questions about sexual activity and an HIV test, and that they would need to know their HIV result if they were to join the trial.

The study staff tried to ensure that the participant understood before seeking their informed consent to participate; that it was not known if any of the gels prevent HIV and it is known that condoms do prevent HIV if used consistently and correctly, before every sex act. The trial team indeed reported that participants were duly provided with all information, emphasizing the fact that they did not know whether the gel works or not, and that they were conducting research to find out the answer.

"We discussed all through with the participants (informing them that) if this product does not go through such a big trial and it is brought on market people would think it works. The mere fact that it went through a trial where we had these participants giving in their time to participate and it comes out that it does not work in preventing HIV, they have a very big contribution in saving many people who would have used this product which does not work and would probably get infected." – Member of the trial staff 1

Before enrolment, participants underwent HIV pre-test counselling which included promotion of safe sex practices and a demonstration of how to use a condom. They were also given an opportunity to have their questions answered by a member of the trial team in private. Throughout the course of the trial, all participants were given male condoms free of charge and asked to use them. Participants were "asked to use the gel during all episodes of sexual intercourse during the study, and, because it is not known if the gels prevent HIV transmission, it is required that condoms are used with gel."[9]

[8] Interviews with two trial staff
[9] MDP 301 study protocol, version 2.1, May 2008, pp.25

This message helped overall to improve condom use among participants than before the trial, and this survey found that some participants clearly understood this message and its rationale, and reported they would never stop using condoms until there was a proven, effective alternative. The final study results indicated that, while participants improved their use of condoms overall, the frequency of condom use was lower than gel use.

However, there was at least one participant who seemed not to have understood the rationale of using condoms together with the gel, and a few participating women who reported that the men did not want to use condoms. Among the broader community, the majority of respondents indicated they did not understand the logic of using condoms together with the gel when the research objective was to find out if the gel prevents HIV.

> *"Using the gel together with the condom? Why condoms? I thought the objective is to find out if the gel works or not... How could they find out if it works when they are telling people to use condoms? I don't think if you gave people the gel they would use condoms; people don't want condoms."*
> – Local leader in Bukulula

Clinical follow-up procedures in phase III microbicide trials require that women regularly undergo genital examinations and STI screening, among other assessments. One of the key points that trial staff pointed out to volunteers at screening was that participation in the trial would include regular genital examinations, blood tests, urine pregnancy tests and sensitive questions about their sexual activity. The feasibility study for this trial found that men and women preferred female health workers for performing genital examination on women[10], and this approach was applied during the trial. It helped make genital examination acceptable for women. Overall, the trial participants interviewed were happy with the examinations, except at least one who expressed discomfort with the procedures of examination.

The trial staff had an opportunity to meet the participants after the trial had ended – during the dissemination of results. While unblinding[11] the participants from the trial arm and informing them that the gel was not effective in preventing transmission, the trial staff took the chance to reinforce the message that the proven methods of preventing HIV remain abstinence, faithfulness and condoms.

[10] Kasse, et al.

[11] The process of informing the participant whether they used a product with the active ingredient being tested or one without the active ingredient (placebo)

Some participants also reported that their neighbours came to learn about their participation in the trial after seeing MRC-branded vehicles visiting their homes on several occasions. Those who reported this said it did not affect their decision to stay in the study. However, given that the trial targeted couples where one partner was HIV-positive, this inadvertent breach of confidentiality potentially exposed such participants to social stigmatisation. This may have raised the social costs of participation for such volunteers. There were reports of finger pointing and bad mouthing of trial participants in village talk because HIV-related stigma is still high in Masaka. Investigators and advocates need to reach out to the wider community from which these participants are likely to be drawn and sensitize all stakeholders about the need to support HIV prevention research.

2.4 Confidentiality, trial-related stigma and effect of the trial on the Masaka community

Trial staff have an ethical obligation to protect the identity of trial participants and ensure confidentiality of their medical records that are generated as part of the research process, to protect them from the social stigma related to inclusion or exclusion from the trial, their HIV status, and adverse events that could emerge in the course of the trial (UNCST, 2007).

Respondents in this project's survey suggested that, in general, HIV-related stigma has reduced over time in Masaka due to the long history of HIV in the area and the fact that most people in the district have either been infected or affected by HIV/AIDS. Nevertheless, it was apparent that it remains an important concern to people living with HIV. HIV-related stigma was an issue for the trial because the site mainly enrolled sero-discordant couples in which the woman was HIV- negative and the man HIV-positive. This meant that the community was bound to conclude that any couple that was enrolled in study had the male partner living with HIV. This was fully anticipated by the investigators, who decided to include some sero-concordant HIV-negative couples in the trial.

While the inclusion of some HIV-negative couples may have reduced the tendency of the community to automatically associate trial participation with discordance and HIV prevalence in a household, responses from community informants and former trial participants indicated that it was not completely eliminated. Most of the former participants interviewed in this survey reported having deliberately kept their participation in the study unknown to neighbours, friends and in some cases, even relatives. One MDP301 investigator reported that at least two men requested the investigators not to visit their homes, but that this was at the beginning of the trial. Some participants tried to keep their participation a secret for the reason that the rest of the community would make conclusions about their HIV status, while others just did not wish to be associated with the research.

Not all participants who tried to keep their participation in the trial confidential succeeded in doing so. For some, the surrounding community realised over time that they were in the trial, as MRC-branded vehicles kept visiting their homes, though respondents noted denied that this did not have any effect on their retention and adherence.

Another important effect that the MDP 301 clinical trial had on the community was to highlight it as an area still with high HIV-prevalence. It happens that Masaka and the neighbouring Rakai districts were the first regions in Uganda to be devastated by the HIV epidemic in the 1990's, which resulted in the emergence of the much-publicized child-headed households phenomenon and the once vibrant transit town of Lukaya in Masaka turning into a ghost town in the early 2000s. That infamous reputation however seemed to level off as HIV became a generalized epidemic and as other "red zones" emerged in other parts of the country. In this survey, some respondents outside Masaka expressed surprise that the trial was able to find such a big number of discordant couples, suggesting that within the country, the trial may have inadvertently reminded the country that the district is still one of the worst affected by HIV.

3. Community Engagement Goals, Tasks and Mechanisms

Community involvement, which refers to efforts to engage a wide range of stakeholders in decision-making about the research and its implementation, is considered crucial for practical and ethical implementation of clinical research (UNAIDS and AVAC, 2007). Supporting a community voice in the research process improves the likelihood that the research will be accurate, acceptable, and ethical. Given the devastating impact of HIV/AIDS on the communities that are usually selected for HIV prevention research, HIV-related studies tend to attract high levels of concern, expectations, and hopes, all of which need to be managed to create a conducive environment for research. On the other hand, each community has unique values, norms and practices that investigators should understand and consider in the design and implementation of clinical trials to ensure successful outcomes (UNAIDS and AVAC, 2007).

3.1 Goals of engaging the community in the MDP 301 trial

As HIV prevention research trials are being planned or begin in communities all around the world, it is important for researchers to work with existing community structures to convey accurate information about the study.[12] Explanations of medical procedures can be confusing and difficult to explain to participants and the broader community. Experience has shown that communities are willing to participate in trials, but they must understand the broader questions of *why* and *how*. Thus, sustained, meaningful community engagement can be the foundation for ensuring that trials are successful (GCM, 2004).

Researchers involve the host community mainly to gain community entry and participants; promote exchange of knowledge and information; maintain the scientific validity and ethical integrity of the trial; and to contribute to community capacity and development. On the other hand, communities look at involvement in trials as a way of increasing the relevance, transparency, and accountability of the research to the community; maximizing the benefits and decreasing the risks of the research to the community; and leveraging auxiliary benefits to the community. Creating meaningful community involvement and partnership involves integrating the goals of community involvement from the perspective of the researchers as well as from the perspective of the community members (GCM, 2004).

Community involvement was a key component in preparation for the MDP 301 trial at the sites, with the aim of promoting community participation and involvement in the research process (Mutemwa et al, 2006). The MDP 301 trial was conducted in partnership with the community (trial staff 2, interview). The aim of seeking community support was to demonstrate that there was a shared concern about HIV's impact on Uganda, to the researchers as well as the host communities.

> *"If you come as a researcher, people will think that it is your problem and that you have the answers. But our partnership (with the community) means jointly working together to achieve a given set of objectives and in this case it was how do we prepare and implement the MDP 301 trial together with the communities. Without their participation, would there be a trial? So the support I am talking about is, can we work together to identify the potential trial participants; can we work together to achieve the trial objectives? It is the support I am talking about, and this support is not from one source, not from one category of people; it is the entire community of Masaka in our case."* – trial staff 2

3.2 Mechanisms of community engagement

The MDP 301 trial had an elaborate community engagement mechanism with formal structures. The Masaka site had a community liaison officer to oversee the information provided to local stakeholders and the target population, and to capture and catalogue feedback; a Community Advisory Board to act in as advisory role to the trial team; a network of community-level participant (peer) leaders; and a written media strategy to engage the mass media. These mechanisms were used to prepare the communities for the trial, to monitor its progress, highlight any misconceptions about the clinical trial objectives and procedures, and act as an "early warning" system for the investigators.[13] Due to the absence of a "gold standard" for community activities

[12] Global Campaign for Microbicides (2009), "Community issues and concerns" http://www.hivpreventionresearch.org/Articles/GetCoursePagePopUp/courseId/6/moduleId/9/linkId/85/user/Default.aspx [Viewed Monday, March 22, 2010]

[13] MDP 301 study protocol, version 2.1

in clinical trials and the lack of defined competencies for clinical trial community liaison officers, the MDP's policy was to work with rather than replace existing systems (Mutemwa, 2005).

3.2.1 Community liaison officer

The position and role of a community liaison officer has been widely recognised in the field of biomedical HIV prevention research, and has become a requirement in almost all publicly-funded research networks. As such, the MDP 301 trial had a community liaison officer at each of the six participating sites. In Masaka, the community liaison officer had previously worked with MRC as a condom promoter and participated in MDP 301's pre-trial feasibility study. In engaging with various categories of stakeholders, the trial team shared the responsibilities of engaging with the different stakeholders. For example, the Principal Investigator liaised with the Ministry of Health and the MRC Clinical Trials Unit in UK; the trial coordinator liaised with regulatory authorities and day-to-day working with the study participants and the MRC Clinical Trials Unit; and the community liaisons worked with the various stakeholders within the host community and the rest of the country as well as community liaison persons at other MDP 301 research sites.

At the Masaka site, the role of the community liaison officer was generally to sensitize the Masaka community about biomedical research. He spearheaded the preparation of Masaka community for the trial and managed all initiatives to engage various stakeholders in the trial. The community liaison officer was in charge of the general community sensitisation effort, which was done through community meetings and VCT sessions.

> *"My role as a community liaisons officer begins with the community sensitisation, then liaison with key stakeholders in the study areas, identification of partners in the struggle against HIV, sensitization of potential study participants. I am saying study participants because we start from a wider level, sensitizing the community, target the women, in this case of the MDP trial and we narrow down to the actual target population which in our case were the discordant couples. Mainly, that's how I could summarize my role."*
> – Member of trial staff 2

Beyond Masaka, the role of the community liaison officer was also to link with different key stakeholders in the country, such as Makerere University-John Hopkins University Research Collaboration (MUJHU), Makerere Walter Reed Project (MUWRP), the UVRI-IAVI HIV Vaccine Program and other HIV prevention research institutions. He shared this role with the trial coordinator and the Principal Investigator (PI) and engagement was done at different levels. The community liaison officer also linked with liaison officers at MDP 301 trial sites in Zambia, Tanzania, and South Africa. He also liaised with other structures like the media, religious leaders and other community 'gate keepers'.

3.2.2 The Community Advisory Board

The concept of a community advisory board (CAB) or community advisory group (CAG) was first developed in the United States in the early days of activist involvement in HIV treatment trials. It has over time developed into a model for community involvement, although recently, research networks are questioning whether the CAB model is the best or only approach to developing partnership with communities in biomedical HIV prevention research (GCM, 2004).

Structure of the CAB

The MDP Masaka site had a 14-member CAB constituted from the different stakeholders they worked with, as Table 1 shows. The CAB membership consisted of volunteers, selected by the constituency or stakeholder organisation. The trial staff constituted this CAB by going to an identified stakeholder and explaining the need for their support and the need for them to have a representative on the CAB, as well as the CAB's role in the conduct of the trial, including its role in linking the trial team with the relevant stakeholders.

The CAB had terms of reference and a two-year, renewable term. It was chaired by the district health officer (DHO), one of the representatives of the medical professionals in the district. Over the course of the trial, the CAB remained largely unchanged, as only three out of 14 members changed. Thus, the rate of attrition was low.[14]

Table 1: Composition of the CAB

	Constituency	No. of representatives
1	District political leadership	2
2	District technical leadership	2
3	Medical professionals	2
4	HIV/AIDS care providers	2
5	Religious leaders	3
6	Community leaders (LC III)	2
7	Media	1
	Total	14

Under Uganda's decentralised system of governance, the governance structure consists of layers of authority where the district functions as a local government (Local Council V or LC V) and the most influential authority after the central government. It oversees the lower levels of administration at the sub-county (LC III) and the village (LC I). LC III and LC V consist of elected executive committees and pseudo-legislatures with elected representatives headed by a "speaker".

This structure of administration was well-recognised in constituting the MRC CAB, with representation from the elected political leadership at the district (LC V), who are elected by adult suffrage to oversee how services in the district are handled; the technical leaders who manage central administration in the district; the district health office that oversees health service delivery in the district by the health personnel (medical professionals); and the sub-county level (LC III), which represents the community-level leadership. At the time of the trial, there were 27 sub-counties (LC III) in Masaka, which were represented on the CAB by one LC III chairperson and one LC III secretary for women affairs.

Another important constituency in Masaka consisted of the organisations providing HIV/AIDS care service, such as TASO, Uganda Cares, Kitovu Mobile, and others. At the start of the trial, there were seven prominent organisations providing HIV/AIDS treatment and care services in the district. The trial team had a meeting with them and shared with them its vision of the CAB and requested them to nominate two individuals to represent that constituency. This stakeholder constituency was allocated two slots because it was considered large (trial staff 2, interview).

[14] Interview with member of trial staff

The MDP 301 trial's experience with the participants and CAB members has shown that, if simplified and clearly explained, scientific information will be understood by anyone regardless of their academic background and their literacy level. The members of the CAB for instance, had different levels of education and the majority did not have training in science, but were able to support the investigators to translate communication materials, seek informed consent, and address issues that emerged in the course of the trial. Through focus group discussions, the trial participants who took part in the social science component of the trial, came up with appropriate translations of terms related to sexuality and sexual practices. These experiences demonstrated that, when empowered with information and given sufficient time to digest it and understand the cause, lay community stakeholders will support and contribute to the success of HIV prevention clinical trials.

The other key constituency in Masaka consists of the three dominant religious denominations: Catholic Church; Church of Uganda (Anglican/Protestants); and Muslims. The Catholicism is the dominant faith in the district, but it was allocated one slot on the CAB, just as the Protestants and the Muslims were.

The media fraternity in Masaka has an umbrella organisation called Southern Buganda Journalist Association (SOBUJA). The representation on the CAB for the media came from this umbrella organisation. Over the course of the CAB, three journalists have represented the media in succession.[15]

In choosing CAB members, the trial team tended to deal directly with organisations or institutions that they thought were essential to the course of the research and its likely outcome. As a result, it turned out that some CAB members were defined to represent one category by the research team, when sometimes CAB members felt they represented a different category. For instance, some individuals selected as representatives of the NGOs saw themselves as actually representing the clients of the selected NGOs.

Some respondents in this survey had issues with the procedures used to select the CAB members. One respondent in the civil society thought the trial team should have targeted established networks or umbrella organisations [such as Masaka District Network of AIDS Service Organisations (MADNASO) for HIV service organisations], and not by writing to individual organisations to nominate. As a result, it was not easy even the CAB members to know who exactly they represented. For instance, while the TASO and Uganda Cares were selected by the trial team to represent service providers/civil society, one felt that they represented civil society while the other felt they represented their clients (people living with HIV).

On the other hand, respondents of different categories did not know about the existence of the CAB, who represents them, and how that representative was selected. A respondent from the civil society in Masaka, on the other hand, felt that the civil society was not represented on the CAB and during the information-sharing meeting, recommended that it (civil society) should be represented on the CAB. The 27 subcounties in Masaka district were represented on the CAB by two people, but one LC III who participated in the interview did not know about the existence of the CAB, the members who represent the lower local governments or how they were selected.

The role of the CAB in the implementation of the trial

The CAB met on a quarterly basis. During such meetings, the CAB helped the investigators in translating scientific concepts into easy-to-understand language. The investigators would explain to members of the CAB what the scientific concept was that they were trying to explain, and then the CAB would brainstorm and come up with appropriate translations or interpretations in the local language. This made it possible to translate key concepts like randomization, double blinded, and other scientific, clinical concepts.

> *"We would spend a day discussing that and at the end of the day you would find it a lot easier with their input, and then you would have an appropriate interpretation."*
> – Member of the trial staff 2

Members of the CAB were involved in getting the message about the trial shared with their

[15] From interviews with trial staff, media and trial staff presentations at an information sharing meeting

Good community participatory principles require investigators to build capacities within communities by building and nurturing a group of advocates who understand the design of biomedical HIV prevention trials.[1] The MDP 301 trial team in Masaka reached out to and attempted to work with all major community stakeholders. The effort from the community to take the initiative and engage with the trial team was limited. This survey noted one case in which women from UWESO, sought information from the trial team about the misinformation that was circulating in the community following the stopping of the cellulose sulphate study. This project did not find any evidence that the trial had built and nurtured a group of advocates in the civil society or the community that was actively following developments within the trial and enriching its implementation. The trial made good strides in developing community strengths in Masaka through research literacy and engagement however this was lacking at the larger national level. There is therefore still need for innovative mechanisms to act on this important principle of biomedical HIV prevention research.

[1] UNAIDS and AVAC (2007), Good participatory practice guidelines for biomedical HIV prevention trials, pp.30

respective constituencies. The regular, quarterly CAB meetings were used to share information between the CAB members and the trial staff, during which feedback from the community as well as new developments in the study were shared and discussed. Members of the CAB in turn, subsequently passed the information onto their constituents.

An important innovation in ensuring that the CAB effectively links the investigators to the general community was when the trial staff at the Masaka site worked with members of the CAB to arrange meetings with their constituents to have the trial staff address them directly. In some instances, the meetings were arranged as part of a CAB members' routine work and trial staff were allocated a slot on the meeting agenda alongside other items that concerned the routine work of the relevant institution.

This was the case with the district council meetings, where the district representative arranged with the district speaker to include the trial staff on the agenda during the quarterly district council meetings, during which the trial staff would address the members of the council, which consists of elected representatives of sub-counties. The Church of Uganda Masaka Archdeaconry convened meetings that brought together the clergy from central Buganda; while the Masaka Sheikh arranged meetings for Imams from all over the district.

Other meetings were arranged purposely to be addressed by the trial staff, as was the case when the trial staff worked with the CAB member representing the media to arrange media briefings on a quarterly basis, and also the press conference where the trial results were announced in Masaka. Other members of the CAB, such as those from the HIV/AIDS care providers, addressed their colleagues in staff meetings and addressed their clients who came to attend clinics.

Sometimes the information went in stages. The CAB worked well in linking the trial team to their constituents, who in turn linked the team to the wider communities they serve. Meetings with the Muslim community convened Imams, who the trial staff addressed, and in turn asked to pass the information on to their congregations. The same happened with the other CAB constituencies such as; the Church of Uganda and Catholic church, where the trial staff addressed priests from all over the arch-deaconry (which includes Masaka and three other neighbouring districts). The system worked in a similar way with politicians in the district council, where the trial staff addressed councillors and requested them to pass the information to their respective constituents. Over the course of the trial, the research team was able to address the district council about nine times.[16]

This system enabled key community leaders to get first hand information, directly from the trial staff. However, the investigators did not have a system of ensuring that the information given to the community leaders actually reached the general community. And, sometimes the agenda in such meetings, typically in the case of the district council, turned out too tight and the item for the trial information was cancelled (trial staff 2, interview). For this reason, the trial team did not address the district council as often as they had hoped and planned to or as frequently as they were included on the agenda.

[16] Interview with member of trial staff

Good community participatory practices call for autonomy of the different players, particularly the CAB and the media. The experience of the MDP 301 trial brought to fore concerns about the independence and capacity of these two important structures in shaping trial design and implementation. The key question is whether a CAB that is selected and funded by the trial will not feel obligated to give their allegiance to the trial team rather than to the community they represent. How can a CAB constituted after the trial protocol has been approved by the regulatory authorities shape the design of a clinical trial? In the case of the media, the issues of concern were its presence on the CAB, the influence of the media CAB member over other journalists, and the fact that the media only relied on the trial team for capacity building and all the information they needed. How best can the autonomy and independence of the CAB and the media be achieved, while also fostering their partnership with investigators?

Challenges with the CAB

The first challenge of the trial staff working with the CAB stemmed from the fact that CAB members were volunteers yet sometimes the work the members were expected to do was demanding and time consuming. Virtually all the members of the CAB were people with full time jobs and, except the politicians and those from the district health office, the trial was ideally not a direct concern in their day-to-day duties. The approach the trail took in using the CAB to reach the wider community called for CAB members to put in substantial time, effort and resources.

> *"Sometimes you feel you are asking a little bit too much from them. These are people you are inviting for quarterly meetings, but they have their own offices and responsibilities. So sometimes you really see your engagement being a bit too much on them in terms of time."* –trial staff 2

While CAB members were called on to do critical mobilisation, such work also called for financial support. Convening meetings to be addressed by the researchers meant that the respective CAB members had to be supported to mobilise for such meetings. In the course of preparation for such meetings, the CAB member might need to make a series of visits to the trial office, and in the process need transport support at each of the visits, since they were doing work for the trial. At each visit, action points may arise, and may also call for financial facilitation. In the end, it is likely that a CAB member will begin to look at or conduct the CAB responsibilities as some kind of gainful employment, and thus, lose the independent advisory focus.

> *"If you are not very careful, you might end up turning this advisory service into some sort of gainful employment of some sort. Because you need to agree with them, for me I find this as a bit of a challenge: you can find a CAB member coming to you, 'I have brought a report'. What that would mean sometimes is that (let us) discuss the report, give me a daily allowance and also refund my transport. That can be a challenge because you will wonder whether someone is doing it voluntarily or for an economic gain. I am not saying this exactly happened to me but I have shared a lot about other CABs. When the roles and responsibilities are not clearly defined, there is always a likelihood of conflict of interest."* –trial staff 2

The other challenge that arose was in relation to the boundaries of the CAB responsibilities *vis-a-vis* their expectations. Some CAB members wished to be involved in the actual mobilisation and recruitment of the participants, so they could follow them up for feedback and to help with enhancing retention.

> *"Sometimes I find myself useless; these are people selected (from my constituency) but I don't know them or those participating in the trial. Given the confidentiality ethics and the double blind design, (I realised they were entitled to confidentiality) so I would talk to all whether they were participants or not... It becomes a challenge because I cannot get in touch with specific persons to encourage them; sometimes you are forced to wonder if certain information is relevant for that congregation."* – CAB member

On the other hand, the research team would not allow them to get directly involved with the trial participants for ethical reasons, as this would breach the confidentiality of the participants and also compromise the independence of the CAB.

The concept of the CAB needs rethinking to clarify and define its size, composition, selection criteria, functions, mandate and funding. The community has many constituencies from which trials constitute the CAB. The wider the representation, the wider the range of skills and perspectives, and the more relevant and suited the trial will be relevant to the host community and its given socio-cultural setting. Since a CAB is meant to have diverse representation, it is made up of medical professionals, academicians, politicians, religious leaders and opinion leaders and people with influence in a community, it represents the different facets of the social spectrum of the community in which the trial is taking place and a mechanism that investigators can use to promote community ownership and involvement in the trial. It is therefore important that members of the CAB are selected fairly and transparently, and the CAB's role and membership communicated and promoted widely for the general community to feel that it represents their interests and to support its work.

"I remember this coming up, not with the CAB but with the participants. The participants would always ask, 'You tell us our participation is confidential, do you sometimes share this with the CAB members?' then the answer would be no, because CAB members are advisors, they do not have any access to the medical records. If you have a CAB and you don't specify what their roles are in the trial they might assume they should have access to everything which is against medical ethics." – Member of trial staff2

"While CAB members want to go into every aspect of the trial, in terms of community mobilization, to the level of recruitment, we always act with restraint. We would want their role to be advisory; 'tell us what you hear from the community, tell us how we can deal with this concern… when it comes to actual recruitment, leave it to trial staff.' Sometimes the members might feel that you are over restricting them; their enthusiasm is greater than what you are asking them to do. And some of the members do not have the time to do the little you are asking them to do. You need to take care of all these issues when you draft your charter: be very simple, let their roles and responsibilities be spelt out clearly. Where they start and where they stop in supporting the work of the researchers." – Member of the trial staff2

Finally, another challenge was in getting information to the community. There was no mechanism of ensuring that information to the grassroots leaders, such as Imams and priests reached the grassroots communities. As already mentioned, some opportunities to address the district council were not utilised in cases where the item was cancelled from the agenda. Thus, the HIV prevention research was yet to gain priority status in community discussions.

"The problem with my congregation is that I meet the clergy first, they are my immediate people and I disseminate the information which I expect them in turn to disseminate to the community… There is no effective mechanism to know that the clergy is disseminating this information." – CAB member

3.2.3 Trial participant leaders

The trial participant leaders were a form of community-level peer leaders who filled a gap that the trial team later realized the CAB members could not cover. This structure came later in the course of the trial, after the researchers realized that while the CAB was useful in linking them with key stakeholder groups, its ability to go to the grassroots at the community level was limited because its members were "*groomed from a higher level*" (trial staff 2, interview). In order to facilitate grassroots acceptance of the trial and to have a mechanism that allowed investigators to identify and respond rapidly to concerns from the community, the trial team established a network of "participant leaders" throughout the localities where they had participants.

The participant leaders were trial participants themselves and were selected at parish level, where they supported the day-to-day interaction between the investigators, the trial participants and other community structures on an ongoing basis. The participant leaders were at the parish level to minimize the distance covered, and also to ensure that each participant had access to them.

The process of identifying the participant leaders involved asking the trial participants from each community to nominate one male and one female trial participant on the basis of a given criterion and guidance from the trial staff to be their participant leaders. The requirement was that participants nominate a leader, from amongst themselves, who was active and based in the community full time in order to be accessible. Once identified, the participant leaders were trained in communication and mobilization skills.

It is through these participant leaders that the investigators would engage the trial participants at the community level. Using templates provided by the researchers, participant leaders collected feedback from the participants and the general community, particularly the community-based organisations (CBO's) with which the trial staff worked with during community education. The participant leaders were volunteers, but were supported financially to carry out tasks.

> *"We always introduced our participant leaders to any structure that would identify as a potential support structure. So, because we knew that… I give you an example, one of the villages is about 55km from here. So if you ask those people to send in their feedback, sometimes you would never get it. So what we did was to introduce the nearest participant leader as our contact person in that particular community. If any group had an issue, whether written or verbal, they would pass it to the participant leader... We developed a template, which would log in all the feedback reports and send to our central coordinator, Richard Mutemwa. "* – trial staff 2

3.2.4 The MDP 301 trial and the media

The researchers recognised the role of the media as an important avenue for the dissemination of trial-related information. After meeting the leaders of the different media institutions in Masaka, including the print and electronic media, the trial staff drew up a media engagement strategy.

Media engagement strategy

The trial staff reported that the media strategy provided for regular sessions with the media, organised on a quarterly basis, to provide trial-related information and updates. They pointed out that there were cases where researchers wanted to pass information to the public, and considered radio to be the most appropriate mechanism to disseminate the information, and arrangements were made to secure airtime for a team to go to a radio station and communicate the information. They also cited instances when there were new developments in the field of microbicides, as was the case when the cellulose sulphate trial was stopped, when the trial staff called the media and informed them about the development and how it related to the MDP 301 trial.

> *"We would have a meeting with the media where we would share with them trial progress and challenges in the communication of the trial, especially in relation to the different media reports and other related trials, then we would also give a chance for the media to ask their questions and the trial team would answer and this was at the level of Masaka. Actually we can say the trial had a written media plan."* – trial staff 2

The trial staff also reported they monitored the media and made an initiative to respond to reports that required clarification, correction or additional facts. This research project was not able to access press cuttings, audio/video clips or other documentation on responses to inaccurate media reports. They reported that every after a meeting with the media they would keep their *"eyes and ears open"* to see what had come out and how the journalists had reported. The community liaison office was in charge of monitoring the media for reports that were relevant to the trial and to circulate them amongst the research team.

Capacity building for journalists

Being attached to Uganda Virus Research Institute (UVRI), MRC undertook its capacity building activities for journalists under that umbrella, in partnership with the Uganda Virus Research Institute-International AIDS Vaccine Initiative (UVRI-IAVI) HIV Vaccine Programme. The trainings were organised by UVRI-IAVI, and MRC took the opportunity to sponsor some journalists based in Masaka to attend. In addition, the trial staff reported that they took advantage of the quarterly media sessions to sensitise journalists about reporting on prevention research, including the role of the media and how the media could help in the dissemination of information related to biomedical HIV prevention research.

According to the trial staff, these capacity building initiatives "*tremendously had a positive impact*" on the quality of media reports that were published/broadcast.

> "*I remember when we started engaging the media, they were so sceptical about HIV related clinical trials and their main concerns were safety, which were really genuine concerns... My personal judgment, my opinion is that there was a tremendous change. When we started with the media, the kind of reporting was I would say 50% accurate or 50% false, reflecting the common misconceptions, myths and rumours on biomedical research, but with time we had a case where some journalists cross-checked their facts with us before they wrote articles or aired out. This was positive and it reflected on how they handled the final trial results."* –trial staff 2

While the investigators were by and large impressed by the quality of reporting, particularly of the trial results, they also pointed out areas where they should have done better with the media. They recognised that the scope of information shared with the media should have been wider, to educate journalists about developments in the entire HIV prevention research field. And because this was not sufficiently done, media reports tended to use the terms microbicides and vaccines interchangeably. The trial staff thought this could have resulted from limited knowledge among journalists about the various approaches for HIV prevention that are being explored. Journalists should know that microbicides are part of the very wide spectrum of interventions being looked at and evaluated in the prevention of HIV. The trial staff reported that they tried to educate journalists about the various options to some extent but admitted when given another chance they could do more.

The second area that needed more work with the media was the need to engage more the top leadership of the media, including editors, managers and proprietors, who determine how the information a journalist has submitted comes out. It may happen that the journalist submits a well-written, accurate draft, but if the copy editor is not as informed as the reporter, they might try to simplify the language by substituting terms or trying to fit headlines in the available space or to summarise the article, and in the process end up distorting the facts or the message. The trial staff in Masaka reported recommending to the cross-CAB network forum (which brings together CABs from other research sites in Uganda) that editors be included in capacity building initiatives for the media, and said at least one session was held in the course of the trial with editors at the national level. UVRI-IAVI and MRC jointly organised the session with MUWRP and MUJHU, both of which are also involved in HIV prevention research.

By the end of the MDP 301 trial, the engagement activities had changed the media substantially for the better.[17] The trial made helped interested journalists to better understand the importance

17 From interviews with trial staff, media and CAB member

of biomedical research in the fight against HIV. The trial served to narrow the gap between the medical sector and the media, as the working relationship between them greatly improved with time. The trial staff learnt that, when given the time and shown the cause to support research, the media will be supportive.

The media representative on the CAB was a very active journalist and bureau chief for southern Buganda of a regional radio station based in Kampala. He played a key role in linking the media and the investigators. He initiated most of the meetings the investigators had with the media fraternity. He gave feedback to the investigators and asked them to clear misinformation. He had an arrangement with journalists based in Masaka where he "proofread" their drafts before they were submitted to their respective media articles.

> *"Before any journalist wrote an article on HIV, he was to go through me as we agreed in the first meeting. What I had not told you is that before I joined the CAB there was a big gap between the research team and journalists. So I tried to bridge the gap."* – CAB member

The trial staff denied being behind the arrangement, which some respondents from the media disapproved as it being tantamount to censorship and a failure on the part of the trial team to build the requisite capacity in individual journalists to have the confidence and ability to report independently.

> *"I came to learn of (it) later, because of the need for accuracy in reporting, they would go to him to review the information they got but that arrangement was not endorsed by MRC. At a later stage, when we shared the results and thanked them for their good reporting and support they gave us, it was then that they told us how they came to the good reports."* – Member of the trial staff

Some of the journalists interviewed in this survey indicated that it was difficult for them to follow-up issues about the trial when the trial had ended and site closed and so researchers were not available to answer questions on issues that might emerge after the trial closed.

The presence of the media on the CAB also raised other ethical issues, particularly in terms of the potential conflict of interest. The media representative on the CAB admitted the challenge but reported he was able to fight it.

> *"So I fought that conflict in this way, knowing that being a CAB member who accesses all updates did not mean that I could publish it. There were interesting information, like we went to a fishing site where MRC was carrying out a research related to the lifestyle of these people, it would be an interesting story but I thought that if I wrote about it,it may scare the people involved because I came to learn that some of these people were not sensitized about what a trial is, many thought it was a proven thing just like the male circumcision in Rakai. So given that I thought I did not have to write the article that could scare away those who had already joined the trial."* – CAB member

The media felt that the trial staff were not releasing sufficient information.

> *"As journalists our food is news and before we come up with a story we needed to research. I would say a challenge (we faced as journalists was) of inadequate information, when you want to write about HIV research, the research team was so cautious, not giving information or when you go confirming what you could have read from a newspaper. I*

would even request them to come up with press releases periodically, because when you are informed you can inform correctly." – Journalist in Masaka

3.3 Engagement with other stakeholders

3.3.1 The populace

The populace and its socio-cultural structure – including community groups, cultural institutions and leadership, political leadership, elders and opinion leaders and social groups – determine how a community will receive and influence a trial. In turn, a community's structure, norms, beliefs and practices will be influenced by the way a trial is conducted and its outcomes. Researchers need to study and adjust to the prevailing cultural structures, traditions and sensitivities in order to have the best out of its engagement efforts with a community.

Working with community structures

It matters who represents the study staff before the community and how they do it. Physical safety is one of the most important concerns that may arise during HIV prevention clinical trials, but the possibility of social harms – harm caused by the social stigma associated with HIV and HIV research, misunderstandings by family and friends regarding the purpose of the study, problems with partner relationships – are also issues of concern for the community during HIV prevention studies.[18]

Apart from the CAB, community leaders were used as point of entry to the community, to inform and mobilise their communities for sensitisation meetings with the researchers. Local leaders were also invited to trial results dissemination meetings.

"We got two seminars at the sub county. We were invited as community leaders, and explained how the gel was going to be used and we asked questions. They told us the research would start and they had selected a category and they would use some gel one which was a placebo and the other had medicine (active ingredient), and promise to come to inform us about the progress.," – Local leader in Bukulula

Capacity building for community systems

One of the recognised goals of community engagement is to build capacity within the community for mobilisation, awareness and addressing community problems and concerns, and strengthening structures that serve the community. The trial contributed to building a skills base in Masaka. The investigators, the support staff, field mobilisers and trial staff in various capacities engaged with community members and gained valuable experience at their different levels that will remain in the community. For instance, up to 100 people, most of them recruited from within the district, were involved in community education and VCT which took place as part of the process of preparing the community for the research as well as recruitment of volunteers. The senior trial staff have undertaken or were undertaking courses in various skills, including academic advancement.

"I really appreciate the experience working with trial participants and other stakeholders involved, it is actually a classroom to participate in clinical trial and also I have benefited personally in that my capacity has been built." –trial staff 1

[18] GCM, Microbicide Essentials Course text

"The MDP 301 was the first clinical trial I participated in, and like any other clinical trial we had to do a lot of training before we embarked on the trial related community activities. I had to do a lot of GCP [training] and I also had to do community mobilisation related training. I also got the opportunity of learning more about clinical trials in general and the MDP clinical trial in particular. So basically my scope of understanding what it takes when we talk about drug development, drug testing and so forth and so on widened a lot, and this was a result of formal trainings the interactions with senior scientists and community liaison officers from the other sites." –trial staff 2

There was also a transfer of skills when the trial staff worked with the mainstream health system during mobile clinics to health centres where MDP/MRC doctors and nurses worked with the nurses and doctors at the government health units. MDP/MRC also helped renovate health centres that they selected to see the participants from, and also constructed a children's ward at one of the public health centres in the district.

Contribution to public health

Although the trial targeted a cohort of discordant couples, the surrounding community also gained access to information on HIV/AIDS. Other than that information on HIV/AIDS, the communities were sensitized on primary health care, particularly during outbreaks of diarrhoea and cholera.[19] The fact that this trial provides opportunity to give health education, treat STIs, refer people for care is a big contribution to public health.

The trial has added to the progress made by previous Ministry of Health condom promotion programmes. Condoms have come to be generally accepted as a reliable method of HIV prevention, given the long history of HIV/AIDS in the district. What was new about condom use in the case of the MDP 301 trial was for them to be used in stable marriages, where it all went back to the issue of HIV prevention, because the couples in the trial were HIV-discordant.

The trial raised the issue of discordance as a reality within the Masaka community. It provided the first opportunity for so many people to test for HIV, know their HIV status and that of their partners, decide on condom use, and to discuss their sexuality with their partners. The counselling provided helped many couples that would have broken up to stay together safely, there by promoting social stability and reducing HIV-related stigma.[20]

"People are informed about HIV/AIDS, people understand that discordance can exist, and people have accepted that they can use condoms to avoid HIV infection in a couple relationship. Also, the trial has made couple communicate about their sexuality. It also opened up tolerance among couples and sense of appreciating research." –trial staff 1

Research literacy

From the interviews with community representatives, it appears that by the end of the MDP 301 clinical trial in Masaka, much of the host community and its various stakeholders had a better understanding of what happens in research involving human beings as research participants. The general community education and sensitization campaign in Masaka as well as the engagement with the various stakeholders in meetings and capacity building activities helped

[19] Interview with member of the trial staff
[20] Interview with member of trial staff

to ensure that they were in a better position to appreciate and understand clinical trials, and are still willing to participate and support research if given another chance.

> *"I learnt that the researchers are very patient people, imagine toiling that entire long and the results comes out it's not working!"* – CAB member

3.3.2 Health service providers

Trial staff worked closely with organisations providing HIV/AIDS treatment and care services in Masaka for various reasons: they were working in the same field and were useful in sharing information; they were referral points for the male participants in the study and the few women who sero-converted during the study; and they were already caring for discordant couples amongst their clientele who were the target population for the trial.

Working with HIV care providers

The investigators worked with five of the seven prominent HIV/AIDS treatment and care provider organisations: Masaka government hospital, Kitovu hospital, TASO, Uganda Cares, and Kitovu Mobile. The investigators made their entry by arranging meetings in which they explained the research to the staff of these organisations, telling them the population they were targeting. The good relationship with these HIV service organisations was important in the trial's quest to raise sufficient numbers of discordant couples (trial staff 2, interview).

Also, having participated in recruiting trial participants themselves, HIV/AIDS service organisations were more willing to provide services to participants who were referred to them for care by the trial. Referral forms were written in such a way that participants were referred to centres that were easily accessible to them.

> *"We kept them (HIV care providers) abreast about the trial and every time we got news, we shared it, like when the Cellulose Sulphate closed we shared with them; HPTN results were release we shared with them; when we closed one arm of the trial, we shared with them; another thing was there are always shortages of drugs, especially in government health units, and we always supplied drugs to health units, especially drugs for sexually transmitted infections."* – trial staff 2

Successes and challenges with the referral system

The MDP 301 operated an onsite clinic and provided treatment for STI's and other health complaints during the clinic days at the health centres where they arranged appointments with the trial participants. Even then, they had an enormous referral responsibility. During community education, sensitization and VCT, there were many people who had never tested for HIV before who were found HIV-positive during the pre-trial community VCT and had to be referred to treatment and care providers, even though they would not be part of the trial. In addition, the majority of men who were recruited in the trial as couples with their HIV-negative female partners were HIV- positive, and had never received care. Almost all of them were to be referred for treatment and care services. There were also trial participants who sero-converted during the trial, though not that many, and the investigators had to refer them.

In the course of the trial, all these cases were referred to about five institutions where the investigators referred people screened out of the study and study participants for HIV/AIDS treatment and care services. Then there were other medical complicated cases which needed

referral either to hospitals away from the district or for investigations that the referral centres don not ordinarily provide.

The feedback mechanism was two-way: by the investigators talking to the participants about the care a participant received at the referral point, whether she had accessed the service and how the service was; and from information received directly from the referral point.

On the other hand, the trial complemented the work of the HIV/AIDS treatment and care institutions by providing counselling and referring clients who had already undergone the requisite tests and diagnoses and knew what they needed. The trial supplied the referral facilities with major treatment drugs especially for treatment of STIs. The MDP also undertook repairs for health units, and constructed a paediatric unit at one health centre.

There were however, some challenges with the participant expectations of the quality of care in the referral centres. Responses from participants as well as the trial staff indicated that some participants preferred to access care at the MDP/MRC clinic that from health facilities close to them. One service provider this survey interviewed indicated that they had challenges in managing the quality expectations of participants after the trial ended and they were referred to them for treatment and care.

> *"When clients are in trials they would receive good care, (but) when the trial ends they are referred to the health units where they don't get what they are used to. I think these people should be told that during the trial they would get some of these things and when the trial ends it would be different. And the government should make sure such care is in the health centres. I think this is a problem."* – HIV care provider in Masaka

3.3.3 Engagement with the civil society

Good community participatory practice guidelines encourage HIV prevention research to nurture local advocates from the civil society sector to partner with the investigators in the conduct of research. In engaging the civil society, the MDP 301 researchers in Masaka aimed at making local advocates understand what the trial was about, given that they shared/worked in the same community. The researchers realised that they needed partners working on related issues who could recommend the trial to the community when asked, given that the community in Masaka tended to refer to all people talking about health issues in the community as "*basawo*" (health workers or doctors). The community needed to hear from people other than the trial staff; it is better if other players tell them that they know about the trial. In addition, the trial staff needed the civil society to support the trials with community mobilisation for sensitisation and VCT.

The trial staff arranged information-sharing sessions with structures like the district AIDS committee, where the civil society is represented, to engage with the civil society as need arose. Trial staff used opportunities such as the annual World AIDS Day to engage in public events with the civil society. Another opportunity was when the lower local governments, the LC III, were debating their budgets, to engage with local leadership. There were also opportunities during workshops and meetings arranged by the civil society when they invited the trial staff to give HIV-related talks to participants.

On a few occasions, civil society advocates took the initiative to engage the researchers. A case in point is when the Cellulose Sulphate trial was stopped, and some members of the public thought it was the MDP 301 trial or that the product was the same. A group of women from UWESO went to MRC and sought to know why it was stopped and whether information

that was circulating in the community was true.

> *"Their fear was, may be it was our study that was stopped. Some did not know that the products were different. Because (they had) safety concerns... After we explained to them, they strongly advised us to (go out and) explain to the community why the arm was stopped. Their concern was if the rumours spreading were not corrected, they would jeopardize the progress of the trial."*- trial staff 2

Overall however, this survey did not find evidence that the civil society was invited to contribute to the design of the trial and its contribution to the trial conduct appeared to have been minimal. At the time of the trial, Masaka district did not have a wide civil society sector that engaged in advocacy work around HIV prevention research. There were prominent organisations in other areas of advocacy, such as gender, domestic violence and human rights, such as UWESO, the Federation of Women Lawyers (FIDA), and others. These were not necessarily focused on HIV/AIDS or HIV prevention, let alone prevention research. The civil society organisations (CSOs) in HIV/AIDS field that stood out in the district were the ones engaged in HIV treatment and care. These were organised under MADNASO. This is the framework that researchers used to engage with the civil society.

> *"At this point I would not say that UWESO, TASO or FIDA went out and said this or that about the outcome, but there are some organisations who closely worked with us in our in recruitment drive of participants. They would give information about the trial and refer discordant couples to us for further information, screening and if possible recruitment."* –trial staff 2

Besides formal, established CSOs, the researchers also reached out to community-level groups and organisations. The trial staff reported making an effort to identify every possible community structure during community mobilisation outreach activities that could help reach the wider communities.

> *"We worked closely with women groups, women groups that ranged from the "munno mukabi" (a friend in need) women groups. These are groups of people who support one another when a member loses a dear one; they contribute food, firewood, etc for the funeral. They are very active, and are almost in every village in Masaka. We also worked with groups that were initiated by World Vision, which was doing agricultural development work in most of the communities where we worked. So we would go to the leaders of these groups, and ask them to help us access their members. The same applies to post-test clubs formed and supported by TASO."* –trial staff 2

The researchers worked with the community groups to make them aware of the trial and its objectives and to provide feedback. The researchers were interested in getting feedback from wherever they delivered messages about the trial.

> *"Whenever they went and talked to people, we were interested in hearing the issues raised and so that we can determine how best they could be handled. If something was raised during their own meetings, then they were in the best position to advise how best to deal with it."* –trial staff 2

4. MDP 301 Trial Results: Preparation, Dissemination and Interpretation

The extent and depth of activities trials implement in preparation for the final trial results has an influence on how participants, CAB members and the broader community get to know the results, and how they receive, react to and interpret them. People within and outside the trial need multiple opportunities to hear and discuss the implications and benefits of each possible scenario, and to share views and engage in an informal public debate and exchange of opinions around the conduct of the trial prior to the release of the final trial results. This process may be useful in preparing participants and other stakeholders mentally for whatever results come out, and in managing expectations. A written trial results preparation plan that is discussed and designed with input from the CAB can be a useful starting point.

4.1 Preparation of stakeholders for the trial results

4.1.1 Preparation of participants

The trial team at the Masaka site reported that the preparation of participants for the trial results was a continuous process, starting right from recruitment right through follow-up. Responses from the trial participants interviewed in this survey showed that they were informed about the objectives of the trial and that the results could turn out either way.

> *"We didn't wait until the trial ended to start talking about results; it was right away from recruitment. We talked to them about the likely outcome of the results: one, it could be safe or not safe, though preliminary information showed that it was safe; and it could work or not work. So, it was a continuous process to talk to the participants that the outcome of this trial could be this (or that)... We had told them all through their clinical visits, we organised couple workshops reviewing with them the aims and objectives of the trial... So it is something which was continuous."* – trial staff 2

In addition to the continuous review of the trial objectives and possible results, the last visit that trial participants made during clinical follow-up offered the trial staff a strategic timing to further prepare them for the final trial results. The MDP 301 trial protocol recommended a list of procedures and assessments for the final visit, but did not explicitly provide for a message that would prepare the participant for the trial results. In relation to results, it only required investigators to check contact details and to seek consent to contact participants at a later date when the results of the trial were available for dissemination, and to share information about future microbicide trials.

Responses from the trial staff and the trial participants this survey interacted with indicated that information was provided to exiting trial participants on when they should expect to get the trial results.

> *"By the time I finished the research, some people were still using the gel. The doctors told me that after every one had finished using the gel here in Masaka and in other places, they would put together everything and call us to tell us the outcome. They told us that it might work or it might not work; I hoped that it would work"* – Former participant in Masaka Municipality

Depending on when they enrolled and how they fared along the way, participants exited the trial at varying times, over a period that exceeded a year. For some participants, therefore, information on the trial results came many months after they had stopped gel use and clinical follow-up. While information on when to expect the trial result was important, discussions and counselling on all the possible scenarios on this last clinical follow-up visit would have likely put the trial participants in an appropriate frame for the flat result that eventually came out.

> *"I was so scared when they told us that some of our colleagues had been infected; it is a pity that some of us did not take the doctors' instructions seriously."* – Former trial participant in Masaka municipality

4.1.2 Preparation of the CAB members

The trial staff reported that they used the regular, quarterly meetings of the CAB to inform members about the possible outcomes. The final pre-result quarterly CAB meeting was held a week before the final trial results were released. The investigators used this meeting to inform the CAB members that the results were to be released the following week. In this meeting, the CAB and the trial staff agreed that the results be communicated to the CAB first and that a work plan be drawn on how to go about disseminating the results to the different community stakeholders. As one outcome of this, a session was scheduled for the CAB to receive the results on the same day they were released internationally.

However, respondents from CAB reported they did not have an opportunity to discuss the dissemination plan for the results before the results were released.

> *"The CAB members should have done some work in preparing their constituencies for the trial results but I don't recall anything like that happening... The trial staff informed us how they intended to disseminate the results but that was on the day of the results. I think it would have been better to go through it earlier so that I can know where I fit. If you intend to come to my constituency, isn't it fair that you inform me in time?"* – CAB member

4.1.3 Preparation of community stakeholders

In preparation for the release of the PRO 2000 MDP 301 results, the trial staff reported that they drew up a plan shortly after the last follow-up visits and embarked on an outreach campaign in the trial communities, telling general public that recruitment for the trial and the follow-up had ended, and that they were awaiting results. During this campaign, they reported answering questions on the given scenarios; what they should expect; and promised return to share the final results. Information on when this pubic campaign started and ended and how widely it went was not available.

The trial team also reported that activities to disseminate results from the previously ended HPTN 035 trial, which had an arm testing for safety and efficacy of 0.5% PRO 2000 and released its results in February 2009, also served to prepare the communities for the MDP 301 results. Although not significant, the HPTN results indicated a positive trend towards 0.5% PRO 2000 possibly preventing HIV infection by 30%.[21] After these results were released, the trial staff drew a plan to share them and how they related to the MDP 301 study with the different partners in Masaka.

> *"We thought it was important for people to know that these results came from a product that was being tested in our community and needed to be understood. We thought that if people took it that the product had already been proven effective, they would wonder why this trial should continue. We wanted our stakeholders to know that these were preliminary results that needed to be confirmed by a larger trial,"* – Member of the trial staff

It is notable, however, that community stakeholders outside Masaka seemed to have been left out of the activities that were organised to prepare the community for the MDP 301 trial results, including the outreach sessions. This survey talked with stakeholders from Uganda National Council for Science and Technology (the regulatory authority), national-level HIV/AIDS civil society based in Kampala, and one other HIV prevention research institutions. None of

[21] Microbicide Trials Network (MTN), Press Release, "Trial finds microbicide promising as HIV prevention method for women", 9 February 2009, Montreal, accessed 18 June 2010 at http://www.hptn.org/web%20documents/HPTN035/MTN%20release%20%20HPTN%20035%20results.pdf

these respondents recalled attending a session or meeting, or receiving information about the MDP 301 results *before* they were officially released.

> *"I have personally not attended or seen an invitation for a meeting from MRC to talk about their results... we all heard (MDP 301 results) from the media. Trial results are usually disseminated by the trial sponsors, so in their case I think it was done by MDP, and they determine how best to disseminate them. For medical (male) circumcision, we attended some meetings, may be because it had a positive outcome,"* – Member of staff, MUJHU[22]

4.2 The trial results dissemination process

The trial staff drew up a comprehensive plan to disseminate the MDP 301 trial results widely to the participants, the CAB as well as to the broader community of stakeholders in Masaka and at the national level. The objective was to disseminate the results promptly and widely. Two teams were set up to implement the dissemination plan: one led by the site principal investigator to disseminate results to stakeholders at the national level; and the other by the trial coordinator to disseminate results to the participants and other stakeholders at the district level in Masaka. The trial results were disseminated mainly through the media, meetings and visits to participants' homes.

4.2.1 Results dissemination to trial participants

The trial staff communicated the trial results to the trial participants through meetings convened at the nearest health centres where they used to go for clinical follow-up visits. The participants were mobilised to attend the results dissemination meetings by the trial's community outreach staff and their respective trial participant leaders. The invitations were verbal, communicated through visits to participants' homes because most of them reportedly did not have telephone contacts. The participant results dissemination meetings started after the trial results were released, but not all could be covered at once.

During the meetings, the trial staff read out a statement of the trial results prepared in Luganda, the local language, followed by a question-answer session before the trial participants were invited in separate rooms one-at-time for unblinding and written acknowledge of receipt of the trial results.

Getting results to the participants in a timely manner was a big challenge. The participants were scattered all over the district and each of them had to be reached in person to be mobilised for dissemination meetings or to be given the results individually. Participants who did not make it to the dissemination meetings were subsequently reached through visits to their homes over a period stretching just over a month.

Most of the participants did not have telephone contacts, and some had to be tracked down after shifting from the locations they were by the last follow-up visit. Some of trial participants this survey talked with indicated that they first heard about the trial results through the media. At least one case was reported of a trial participant who declined an invitation to a results dissemination meeting because she had already heard the trial results from the media.

[22] This interview took place on 22 April 2010, before MUJHU convened a stakeholder meeting on 11 May 2010 during which MDP 301 trial staff from MRC/UVRI made a presentation on the MDP 301 results

The power and influence of the mass media needs to be harnessed to disseminate and communicate the key messages in trial results. The MDP 301 trial issued press releases and held press conferences to communicate the trial results, and the media published the news. A number of respondents in this survey, including participants, first heard of the trials from the media. This suggests that to optimise the role of the media in the dissemination of trial results, specific preparatory activities need to target the journalists to set the stage for media debate of the final results. The experience of the MDP 301 trial has shown that even seemingly simple messages can be misunderstood or difficult to understand for not just the lay people in community but also journalists. In addition, to promote a clear understanding and interpretation of the trial results, trials should in future consider paying for space and airtime for official statements to explain the key messages in the trial results. Even then, trial participants should not first hear the news from the media; they should get results before other stakeholders do.

4.2.2 Dissemination of trial results to CAB members

The MDP 301 Masaka site held a CAB session to share the findings on the afternoon of 14th December 2009, the same day the results were released internationally. The meeting was held at the MRC offices in Masaka. Nine of the 14 members of the CAB were present. The meeting discussed the trial results and how best to communicate them to participants and the general public. The meeting then went through and edited a translated statement of results to be used to communicate the trial results to the trial participants. The trial team also presented its plans to share results with the various stakeholders. A copy of the translated Luganda statement was given to the members of the CAB to use in disseminating the results to their constituents.

Respondents reported that some CAB members invited the trial staff to address their constituents directly about the trial results. However, there were some of the members of the CAB who felt that they had not been fully utilised in disseminating the trial results. All CAB members had the information but some could not mobilise their constituencies due to lack of resources or skill. There were CAB members who were considered not to be articulate, yet dissemination of results came with the need to answer many questions from the community.[23]

4.2.3 Release of trial results to the media

The investigators held two press conferences to announce the results: one in Kampala on the day the results were released and another in Masaka a few days later. The trial results were well covered in the local and national media. In general, the trial staff judged the media reports to have given a "*very good interpretation of the results"*, saying most of the newspapers reported relatively accurately.

> *"I cannot rule out a few inaccuracies; in whole, it was much better than when we started. I remember when the cellulose trial was closed what came out was irresponsible reporting. We had to go to several radios to tell Ugandans that the MDP 301 trial was still going on because there was some confusion like someone would say that all the research sites dealing with microbicide research have been closed because of the harm of the product and other myths that surrounded the stoppage of the sulphate trial."* – trial staff 2

4.2.4 Results dissemination to other stakeholders at district and national levels

At the national level, the trial staff targeted the international audience attending the (AAVP) forum in Kampala, the national media, the Ministry of Health, and the regulatory authorities. At the district level, the dissemination plan targeted the trial participants, CAB members and their constituents, Masaka-based journalists, local leaders, health professionals, civil society and the general public in Masaka.

At the national level, the principal investigator made a presentation at the 2009 African AIDS Vaccine Programme (AAVP) forum in Kampala 14th December 2009, the same day the results were released. The PI also addressed a press conference, together with the Director General of Uganda AIDS Commission (UAC), and the Minister of Health. The press conference was held on the sidelines of the AAVP forum and was attended by journalists working for the Kampala-based national media as well as international journalists attending the AAVP forum. The Masaka press conference was co-addressed by the District Health Officer and the investigators.

The trial staff also took advantage of meetings organised by partner organisations to share the trial results with the broader community. For instance, they willingly agreed to participate

[23] Opinion expressed by one CAB member during a personal interview

in a civil society HIV prevention research information sharing meeting organised 27 April 2010 as part of the data collection process for this research project. During the meeting, the trial staff made presentations on the trial process and results and responded to questions from the meeting participants, who included civil society advocates, Masaka-based journalists, HIV care providers, and local leaders. The trial staff were also represented at MUJHU stakeholder meeting in Kampala 11 May 2010, where they presented the results of the MDP 301 trial and participated in the implications of the results for the recruitment process for the VOICE[24] trial, which was at the time enrolling participants.

4.3 Knowledge, understanding and interpretation of key messages in the trial results

4.3.1 Awareness, knowledge and discussion of trial results

Local and national electronic and print media widely covered the release of the MDP 301 trial results. As a result, most people who were interviewed in this survey reported that the media was the first, and sometimes only, source they first heard the news of the results. Most of the trial participants and the CAB members this project interacted with knew the outcome of the trial. Some local leaders confirmed that they had attended meetings MRC convened to inform them the outcome of the research.

> *"I first heard (the results) from MRC. They invited us as leaders and told us. That meeting was attended by LCs and people who were involved in community education and sensitization and requested us to disseminate the outcome,"* – Local leader in Mukungwe subcounty

Much as the trial staff disseminated the trial results as widely as possible, knowledge of the results was neither widespread at the district level nor at the national level. At least one of the former trial participants said she had never received or known the trial results, more than three months after the official release. There were a few more respondents within the communities, particularly the community leaders, who were not even aware that the trial had ended. Some local leaders reported that they were not aware of any meetings in their areas of jurisdiction that had been convened to announce or discuss the results.

The debate of the results in the community was limited. Some respondents partly blamed the high degree of confidentiality that was involved. Some respondents suggested that the limited knowledge of the results was due to the extreme confidentiality of the participation in the trial and the fact that the product in question concerned women, which according to them, stifled community discussions and debate around the final results.

> *"I think it (the research) was not done in the open, people did not know about it as it was taking place. Even when you came up with a story, it was better understood by the participants. People have heard about 'ekizigo' (the gel), they knew the purpose of the research but they did not understand why the gel did not work. I think the attitude is like 'it has ended it has ended'. And given the closure of CBS radio station which the biggest (proportion of the) population relied on for information... Some of the radio stations don't relay messages that the community want to hear, like there is a radio station that runs a program from 10am to 1pm teaching people how to fall in love so even when there is some serious news people will not consider it from that station,"* – Journalist

[24] MUJHU is one of the sites for the MTN 003 or "Vaginal and Oral Interventions to Control the Epidemic" (VOICE) trial of ARVs Tenofovir and Truvada as oral pre-exposure prophylaxis (PrEP) and a vaginal microbicide gel

"I heard only heard one person talk about it (the results); it was one of those people I had taken to MRC. She was wondering why so many people had become infected yet we had been told the gel works. I tried to explain to her that the gel was to be used with the condom... She had gotten it wrong because she was in shock." – Former participant in Kimaanya

"Since that gel was for women and women issues are not discussed in public… Women are usually shy and men are usually concerned about issues (that concern them, such as male) condoms. It was similar to the female condoms that came earlier and vanished; men are concerned with issues that directly concern them," local leader

4.3.2 Reaction to trial results among trial and community stakeholders

From the interviews, it appears that in spite of the effort that the trial team invested in preparing the various stakeholders for the results, some of the community stakeholders, particularly those directly involved with the trial – the participants and members of CAB – seemed not well prepared for a flat result. Knowledge of the challenges of research was found to be low, and people seemed to hope for or expect immediate results. People needed to have been told and to understand that flat results are part of the long research processes, and that even a negative result adds to the existing knowledge. Some volunteers and members of the CAB had strong hope that PRO 2000 would work, and in the end, they had challenges coming to terms with a flat result.

The reaction of trial participants to the news of the results seemed to be influenced by their experience with the trial and whether they considered themselves safe from HIV or not. A former participant in Kalungu subcounty reported that she got worried when she heard the news of the results because she had never tested again ever since she exited the trial and she feared she might have been infected. Others who used condoms throughout the study sighed with relief and seemed less worried.

"I did not take it badly but I was sad that some of us had become infected; that made me sad because they had counselled us on how to protect ourselves and yet in the end it emerged most people did not use condoms. I was sad because many people didn't take the doctors' advice seriously; I was not happy. On my side, I was not affected because the message was clear that we should use both the gel and condom, and I knew if I never used the condom the chances of getting the infection was high." – Former participant in Masaka Municipality

One former participant who happened to have become pregnant during the trial (evidence that she did not use condoms at some point), said that she did not know the trial result by the time of the interview (slightly more than three months after they were released) and expressed shock when told that the gel was found not to have worked.

"If that is what it is, then I have a question mark... I am worried if it did not work; I might have got infected. I have a reason why I am saying that. Because ever since I delivered I have never tested again. I realize there has been some change in my life; I get rashes and irritations. Sometimes I worry that the earlier tests were not accurate enough." former trial participant in Kitabaazi, Masaka Municipality

The expectations of the participants and members of the CAB appeared to have been raised by two key developments that came in the course of the trial. The first was the February 2008 discontinuation of the 2% dosage for futility, which to some of the informants in this survey seemed to suggest that the 0.5% dosage which was left to continue had shown signs of effectiveness. The second was the HPTN 035 results which had shown a modest though insignificant effectiveness of PRO 2000 0.5% of about 30%. This raised the hopes of not only the communities participating in the MDP 301 trial but also those of the investigators and the entire field of HIV prevention research.

In addition, expectations were raised by the publicity surrounding the trial, as a result of a well-conducted trial, given that the women were using the gel and the entire trial was well-organised and handled by a research team with trusted members.

> *"In preparation for the results, we were told that whenever there is a research or study we were to expect a yes or no answer, and according to the (series of) developments we were actually expecting a yes answer. They took us through the positive results. I was shocked by the results at the end of the day... Apart from what they told us that it could be a yes or a no, I was not prepared for a negative answer; I knew we were progressing steadily so I did not hope for a no."* – CAB member

> *"We were very disappointed in the results that it was found ineffective; most people had a high expectation, and it was hard for us to communicate to the people that it didn't work and they don't need to depend on it but should keep their hopes because the researchers are still working."* – CAB member

After hearing that the trial result was flat, community stakeholders were more interested in the way forward. The trial team did well in informing the community that research was still ongoing to pursue other ideas and products. Many demonstrated a good memory of the options that were being explored with the use of ARVs in prevention, in microbicides and in pre-exposure ARV oral prophylaxis.

> *"Not all understood the results, others came thanking me for the information given and asking for the way forward which I replied the struggle continues, the researchers are working and that this has given us a clue, it is not 100% failure, and it was a lesson we learnt that it did not work, from there the researchers can build on to find what works."* – CAB member

The investigators however, took the results in a positive light, given that the trial had been able to answer the research question and also to provide lessons for future work.

> *"Of course everyone would prefer to come up with a result saying 'yes, it prevents HIV', but I look at it from a positive point of view... The biggest benefit for me from this result is that PRO 2000 does not protect against HIV. If this product had been given to people thinking it protects and yet it does not, we would have had more people dying. So I look at the result from a positive point of view."* – trial staff 1

Respondents among the trial team, participants and community stakeholders, expressed relief that the trial product was found safe.

> *"We were informed that it really worked well for women and men except that it was not effective. In the beginning of course there were fears among women about its safety. If it was safe, then it means they should continue with research so that it can work."* – Local leader in Mukungwe subcounty

4.3.3 Understanding and interpretation of key messages in the trial results

In drafting the statements that were used to communicate the trial results to the participants, the media and other community stakeholders, the trial staff emphasized several key messages. The key messages were:

- PRO 2000 (0.5%) was found not to be effective in reducing the risk of HIV infection in women
- the gel was safe to use
- the trial was successful
- the trial has provided good lessons that will inform future research
- there is need to continue supporting research into microbicides
- a prevention package (free condoms, counselling for safer sex negotiation and sexual health) was provided to participants throughout the trial
- the gel was acceptable

In order to gauge the community's understanding of the results, this research project explored the respondents' comprehension and interpretation of the key messages that the trial staff emphasized during the dissemination of the trial results.

4.3.3.1 Key messages that were fairly well-understood across community stakeholders

The most important message – that PRO 2000 (0.5%) was found not to be effective in reducing the risk of HIV infection in women – was fairly well understood among stakeholders, including those at the grassroots community level. Most respondents indicated that the message meant that the gel "did not help" the women who used it, to prevent them from getting infected by their partners.

The second key message was that the gel was acceptable. Responses indicated that this message was fairly understood by a majority of the respondents in the community. The final trial results showed that women used the gel more than they used the gel with condoms or the condoms alone. Respondents in this survey were asked for their opinion on this finding. Responses ranged from the suggestion that women and men had confidence in the gel and had the false illusion that it should be effective, to the perception that it made sex more pleasurable.

> *"Whenever I would insert the gel it would help with lubrication and it would help in preventing the condom from bursting... My opinion is that they should have allowed us continue using the gel since they said it was safe, so that it would continue to help making the condom slippery (lubricated)."* – Former participant in Kimaanya

Others suggested that the men did not want to use the condoms claiming that they did not enjoy sex when they used them; that condoms inconvenience and require a lot of patience in wearing and removal, which process they said is "painful"; and that couples may have just gotten tired of using them after using them for a long time. There was one suggestion that some men may have actually tried to deliberately infect their partners.

> *"The biggest problem is that men don't want to use condoms. Whenever time came and he forced you, you would use the gel with the hope that it would protect you. Most men according to my female colleagues I talked to did not want to use condoms, yet they (it was agreeable to them) to use the gel."* – Former participant in Kimaanya

> *"I understand some were scared of the condoms; other times it is the men who refused to use them. They say they don't enjoy (sex when they use a condom). Our husbands felt that the God who has always kept us (discordant) should be the one to continue helping us (to remain so),"* – Former participant in Kasanje

Among community respondents who were not directly involved with the trial, the logic of using condoms was not apparent, and was one of the least understood messages. One local leader asserted, *"Since it is research, and condoms prevent HIV, it would be inappropriate to use condoms, so that your research yields results."* Another quizzed, *"Using the gel together with the condom? I find that hard... I don't understand why."*

There was only one response from former participants that suggested the possibility of a false illusion that the gel was effective.

> *"I think people took it from the research perspective and really wanted to find out if it works. People wondered how they would find out if they used the condom which protects and the gel. What I think is both the gel and the condom were protective and if used both we would never really get to know the truth. The men preferred the gel than to use the condom saying that if they gave us the gel why do we still use the condom?"* – Former participant in Kitabaazi

The key message on safety of the gel seemed better understood among former trial participants and CAB members than among other community stakeholders who were not directly involved with the trial. Responses from former participants and CAB members demonstrated a clear understanding of the difference between efficacy and safety. They understood that not being effective meant that the gel did not prevent women from acquiring HIV, while being safe meant that it did not harm the people who used it and cited the absence of rashes, irritations and the like.

Key messages that were not widely well-understood

The understanding of other key messages however, seemed more problematic. The trial ran its full course, was well-conducted and answered the research question; it demonstrated that a safe, effective gel could be accepted and used by women for HIV prevention; many couples started talking about issues of sexuality and many more knew their HIV status, accessed diagnosis and treatment for STI they even never knew they had, and significantly reduced their chances of acquiring HIV; and the trial did not deliberately expose women to HIV, since it provided counselling about safe sex and provided free condoms. These messages, which could have facilitated the understanding of the final results, were apparently detached from the text of the statements that the trial staff used to disseminate the results.

The message that the trial was successful was not well-understood by most of the respondents, including journalists who covered the news of the trial results. For instance, a headline in a national newspaper on 15 December 2009 read, *"Anti-HIV trials on vaginal microbicide fail"*, although the text of the article was generally accurate in quoting the MDP statement.

About the notion that the trial was a success, a former trial participant in Masaka Municipality, said, *"I did not understand it well, but the trial was not successful because we did not benefit."* Another stated, *"I did not understand because when they say it was successful, yet people were infected, may be only for those who followed the instructions (on condom use)."*

A local leader in Mukungwe subcounty, retorted, *"Our concern was that it might harm people; (if the trial was successful then) it means it did not harm people. And on the other hand, it should have prevented HIV transmission but since it could not prevent HIV then the trial was not successful."*

A few respondents had totally wrong information about the trial results. For instance, asked if he had heard about the outcome of the trial of the gel, one local leader replied that he had heard about it on two occasions, at the subcounty headquarters and at Uganda Cares. However, probed for what he had heard about whether the gel was effective or not, he said, *"It was effective, but it has not widely circulated among people… many people would love to use it but need to know where to find it."* Later in the interview, when asked what he understood from the main message in the results which stated that the gel was found not to be effective in protecting women from HIV, he said, *"I was not aware of that."*

In another case, a news anchor on a Kampala-based FM radio station during the 6.00 o'clock Luganda news bulletin on 14 December 2009 stated, "*The research that has been investigating whether gels can help in preventing HIV has been* **stopped** *after* **most** *of the women were infected…"* This was obviously incorrect because the trial was not "stopped", as it ran its full course; and infection was not in "most of the women".

Key messages considered confusing by some community stakeholders

Among some respondents in the community and media, however, there appeared to be difficulty in understanding the difference between safety and efficacy. The message that the gel was safe but not effective seemed contradictory to some respondents. The trial team also reported receiving many questions from participants who did not seem to understand why a product that was safe could not also prevent HIV.

Key messages that were misunderstood or misinterpreted

While the message on the lack of efficacy seemed clear and well-understood by the respondents in this research project, there was a tendency within the community to infer conclusions that were not accurate. Some respondents within the community seemed to wrongly take it that since the gel was not effective, then *all* the participants were infected during the trial. Some respondents among former trial participants reported that rumours were circulating within their communities that they (participants) were infected because the gel did not work.

This research project noted reports of village talk teasing trial participants about the flat trial result: *"Why then did you participate?"*, "*So what have you gained?*", and the like. A few participants were made to feel that they had in fact wasted their time. This research project noted some few cases where some trial participants, also considered the gel's lack of efficacy to mean that whoever did not use condoms was most likely infected.

During an information-sharing meeting organised as part of the data collection process in this research project, one journalist asked the trial staff what they were doing to protect the general population from the people who had participated in the trial and "*might be out there infecting unsuspecting members of the public!*" This question suggests that the journalist believed that the gel's lack of efficacy meant that every participant was infected.

5. Recommendations and Conclusion

Trials have long, complex processes that call for commitment from many different stakeholders. It takes the commitment of all stakeholders to make a trial successful. In this case, the trial participants gave their time for the study to be conducted and volunteered personal and sensitive information; the CAB members volunteered their time and effort to learn and understand the study and took their valuable time to explain the study to their constituent groups; the regulatory authorities and the ethics committee did not just sit and approve the protocol but took the time to understand it and weigh potential benefits against potential risks and the safety provisions in place. All these stakeholders contributed to the success of the MDP 301 trial.

5.1 Recommendations

To clinical trial staff, research institutions and trial sponsors

- Trials should provide clear, accurate, simplified information on the trial, the trial product and the trial objectives to potential participants and their communities, and the media in order to avoid doubts, suspicions, misinformation, false expectations and wrong perceptions about the potential benefits and risks of the trial. Trials should adopt participatory approaches to simplifying and translating scientific terms necessary in understanding trial processes and key messages in trial results

- Trials should engage and create partnerships with stakeholder groups within the host community as well as with those at the national level, and build their capacity to understand and engage meaningfully with the research process

- Given the limitations of CABs, there is need to use multiple approaches to reach to different community stakeholders. Trials/investigators and global/international advocacy groups should work together in future trials to identify grassroots-level contact persons who they should nurture early in the trial process into community advocates to promote awareness, mobilise the community, monitor trial progress, and provide feedback from the community. These should be empowered to document and report any emerging concerns, myths and misinformation

- Design and implement a proactive and ongoing media engagement plan that targets both journalists and editors for capacity building in biomedical HIV prevention research literacy and ethical issues; regular updates through official statements and meetings; and dedicated media communications personnel

To civil society groups and advocates

- Civil society groups and advocates should partner with global advocacy organisations and build their capacity in biomedical HIV prevention research advocacy through networking and sharing information with Ugandan research institutions and global advocacy organisations (such as AVAC, GCM, AMAG, IAVI, IRMA, and others) in order to enable them follow and implement interventions within the host as well as the wider community in countries where biomedical HIV prevention research is ongoing or planned. They should partner with global advocacy organisations to develop and implement research literacy programmes that enhance community ownership, willingness to support future trials, and promote new prevention options when they become available.

- Civil society groups should undertake continuous mobilisation of communities within which they work to promote the known HIV prevention strategies such as abstinence, faithfulness, male and female condoms, prevention of mother-to-child HIV transmission, and promote the hope research offers for additional new tools for the tomorrow. The civil society is best suited to be the alternative source of information about ongoing trials for communities, the media and other community stakeholders.

- CSOs in Uganda should network to facilitate the sharing of information, put up a joint voice, and facilitate dialogue around HIV prevention research, and become proactive in engaging researchers.

To the media

- The media are the eyes and ears of society, and should take initiative to build their own capacity in reporting on biomedical HIV prevention research clinical trials by seeking and sharing information and networking with trial investigators and advocates. Taking the initiative will enable them maintain their independence and ethical standards while engaging with trials and providing their professional duties of informing, educating and monitoring trials in the community

To local leaders and their communities

- Local leaders, politicians and opinion leaders should invest time and resources in understanding trial processes. They should seek partnerships with trial investigators in their communities. They should use their influence to ensure that community interests are represented in the design and implementation of clinical trials through a transparent and participatory selection of capable community representatives to an independent, autonomous CAB. They should work toward other community representation mechanisms intended to build and strengthen the capacity and relevance community structures and systems.

5.3 Conclusion

The MDP 301 registered many successes in community engagement: it attempted to work with a wide range of community stakeholders; used the CAB well in community mobilisation; came up with creative ways of engaging with the community; and took advantage of several opportunities to work more closely with community stakeholders.

In spite of all these and other commendable efforts, some sections of the community still felt left out of the trial process, trial results were not received promptly and some stakeholders were not well-prepared for a flat result. Some key messages were not well understood or well interpreted by some community stakeholders.

Communities that have been affected by HIV understand the value of a new, effective prevention option in the fight against HIV/AIDS, and the outcome of this feedback supports the development of community engagement plans that broaden the range of target

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THE AVAC/GCM HIV PREVENTION RESEARCH ADVOCACY FELLOWSHIP PROGRAMME

Effective, sustainable advocacy grows out of work that reflects organisational and individual interests and priorities. This research project was conceived as part of the "AVAC-GCM HIV Prevention Research Advocacy Fellowship" programme, which provides support to emerging and mid-career advocates to design and implement advocacy projects of their interest related to biomedical HIV prevention research activities in their countries and communities. The overall goal of the fellowship programme is to expand the capacity of civil society advocates and organisations to monitor, support, and help shape biomedical HIV prevention research worldwide.

The 2009/10 fellows are hosted at local host organisations that they identified. This fellowship project was hosted and implemented in partnership with the Coalition for Health Promotion and Social Development (HEPS-Uganda), a national health rights advocacy organisation in Uganda.

The fellowship project aimed to:

(1) To document community experiences and perceptions, and lessons to:-
   - α) contribute to a better understanding of the effects of closure of HIV prevention clinical trials on communities
   - β) identify best practices that should be emulated in future trials
   - χ) highlight areas that need further work and advocacy

(2) To contribute to a better understanding and appreciation of biomedical HIV prevention research and advocacy within the trial community and the broader community of civil society

DEMOGRAPHIC CHARACTERISTICS OF MASAKA DISTRICT

Map of Uganda showing the location of Masaka district

Masaka district is located in central Uganda. Masaka town, the district headquarters, is located 130 km southwest of the capital Kampala. The district has a rich diversity of ethnicities. The majority of the people (approx. 972,500.[1] in 2010) are Baganda and the majority of the people in the district speak Luganda and practice Buganda culture. Other sizeable ethnic groups are Banyankole, Banyarwanda and Banyoro.

The majority of people in Masaka are peasants and are poor. The major economic activities in the district include the cultivation of the staple food 'matooke', sweet potatoes and cassava. The major sources of income for the population are: coffee, cattle-keeping and fishing.

Masaka district is run by a district local government, headed by a district (local council V) chairperson. In administrative terms, it consists of four counties; 23 subcounties; 127 parishes; and 1,331 villages (Masaka district information portal). The main administrative structures are at the district level (local council V or LC V); subcounty level (LC III); and at village level (LC I), (www.masaka.go.ug: 8 April 2010).

Health structure, access and status

The health structure in Masaka district consists of a total of 84 health facilities, consisting of three hospitals, eight HC IVs, 22 HC IIIs, and 50 HC IIs (Masaka District Administration, 2009). Access

[1] http://en.wikipedia.org/wiki/Masaka_District#cite_note-0

to health care[2] to the population of the district was estimated at 68% by June 2009 (Masaka District Administration, 2009).

Masaka Hospital serves as a regional referral hospital serving five districts – Masaka, Rakai, Sembabule, Kalangala and Lyantonde. With a bed capacity of just 330 beds, it serves a catchment population of more than two million people. It directly provides anti-retroviral treatment (ART) to over 5000 clients and provides comprehensive care (non-ART) to over 10,000 (June 2009 statistics). The hospital experiences a shortage of professional staff, infrastructure and supplies, particularly medicines. In 2009, for instance, the hospital had a total establishment of 322, far less than the estimated requirement of 540.

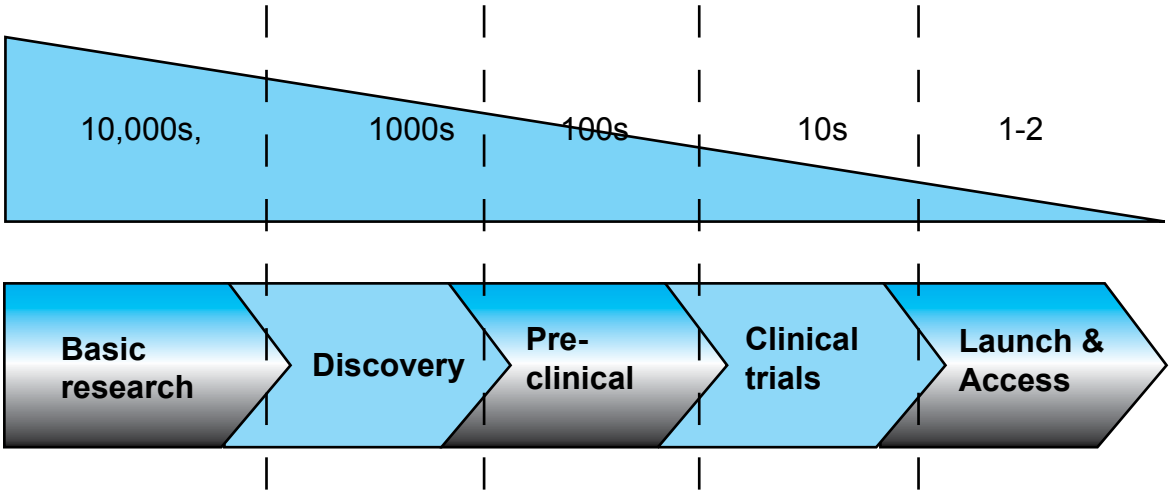
Masaka and the HIV/AIDS problem

Masaka is one of the districts where the first cases of HIV in Uganda were diagnosed in the early 1980s, and by the time of this survey, was one of the districts that had experienced the most devastating effects of the HIV/AIDS epidemic. Since then, the Uganda AIDS Commission (UAC) reports that cumulatively, an estimated 2.6 million Ugandans have been infected and 1.6 million have lost their lives to HIV and AIDS-related illnesses. Development partners, donors, aid organisations and the Uganda government have made sizeable investment in HIV prevention and treatment programmes in Masaka over the past 20 years. These interventions have reduced the HIV infection rate from a peak prevalence rate of about 23% during the 1990s.

Nevertheless, HIV prevalence, estimated at about 12%, is still far above the national average of about 6.4% (Sullivan, 2008). It is notable however, that in spite of such high prevalence, HIV/AIDS is not among the top 10 diagnosed illnesses in the district. HIV/AIDS does not appear on the list of top causes of ill health in the district possibly because HIV/AIDS is rarely presented as a health complaint and/or that AIDS is not ordinarily diagnosed as such in medical records. It is therefore represented by the various illnesses that are part of the symptoms of AIDS.

[2] Geographical access is defined by the Uganda government to be a radius of 5km from a health facility

BIOMEDICAL HIV PREVENTION RESEARCH PROCESS



HIV prevention resesarch is a long and complex process, and only a small fraction of the ideas for new prevention strategies make it through all these stages.

1. Basic science

Basic science research investigates how HIV infection happens, the life cycle of the virus, and how the virus affects the immune system. These questions are at the core of some of the scientific challenges confronting the biomedical HIV prevention research field.[1]

2. Discovery

Laboratory scientists work to identify molecules or ingredients that may be active against HIV. The scientists who initially develop the idea for these experimental products may be independent individuals or they may work for scientific institutions, not-for-profit organisations, pharmaceutical companies, or university laboratories. The molecules are put into a testable form. Once a promising candidate microbicide has been identified, research teams formulate it into a usable substance for application.[2]

3. Preclinical research

In preclinical research, scientists test their formulations of new biomedical prevention strategies in laboratory experiments and in animals.

4. Clinical trials

Candidate strategies that pass the preclinical research move into clinical trials in humans. Clinical trials enroll human participants to evaluate scientific or medical interventions like drugs or vaccines. Clinical trials are conducted in stages or phases.

Phase I trials are the first stage of testing an experimental product in human participants. They evaluate the candidate's safety in humans. These trials typically involve several dozen healthy participants.

Phase II trials are usually larger than Phase I studies and may involve a more diverse group of participants. Phase II studies can enroll anywhere from a few dozen to several hundred participants. These studies gather more information about safety.

Phase IIb studies are also known as "proof-of-concept". The goal is to get an early indication of whether a given strategy might be effective at reducing the risk of HIV infection or transmission.

Phase III trials are large-scale studies that examine whether an experimental product can reduce the risk of HIV infection. They often involve thousands of participants and also gather additional data about safety.

5. Launch and access

Once a product proves that it can prevent HIV infection, through Phase III and confirmatory studies, it is presented for regulatory approval and licensing, pilot projects or pre-introductory studies and operations research (Phase IV studies), before general access.

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[1] http://www.avac.org/ht/d/sp/i/296/pid/296

[2] http://www.hivpreventionresearch.org/Course/GetCoursePage/courseId/6/moduleId/9/pageId/3/user/Default.aspx

THE MDP 301 PRO 2000 EXPERIMENTAL MICROBICIDE CLINICAL TRIAL

The MDP 301 was a multi-site trial of vaginal candidate microbicide PRO 2000 conducted in Masaka district, Uganda, and at five other sites in Tanzania, Zambia and South Africa. It was the largest international clinical trial to date of a microbicide. It started recruitment in September 2005 and ended in September 2009 and was carried out by the Microbicides Development Programme (MDP), a not-for-profit partnership of 16 African and European research institutions. It was funded by the UK Department for International Development (DFID) and the UK Medical Research Council (MRC).

The multi-centre, randomised, double-blind, placebo-controlled trial enrolled a total of 9,385 women volunteers as participants. It was a three-arm study, which was initially testing for efficacy and safety of two concentrations of PRO 2000 (0.5% and 2%) against a placebo in preventing vaginally acquired HIV infection. In early February 2008, the trial arm testing 2% gel was stopped after the data and safety monitoring committee (DSMC) and trial steering committee (TSC) found that that concentration had very little chance of showing effectiveness.

The trial also included a major social science component that investigated sexual behaviour and adherence, as well as factors which encourage or inhibit condom use.

In Masaka, HIV sero-discordant couples (and some sero-concordant couples to maintain blinding of sero-status) recruited in the Masaka district of Uganda from either office based voluntary counselling and testing services or following census and sero-survey. Women aged 16 years and above were enrolled in Masaka and were followed up for 24 months.[3]

The final results, released on 14 December 2009 internationally, in Uganda and at all sites, showed that 0.5% PRO 2000 gel was found not effective in protecting women against vaginally acquired HIV infection. There were 130 HIV infections out of 3,156 women who were given 0.5% PRO 2000 gel, and 123 HIV infections out of 3,112 given the placebo gel in the main analysis. The rates of HIV infection were very similar in both groups: 4.5 per hundred women years in the 0.5% PRO 2000 group, and 4.3 in the placebo group. Thus 0.5% PRO 2000 gel did not reduce the risk of HIV infection. However, the gel was found safe (MDP, 2009).

[3] MDP 301 study protocol, and MDP press release issued 14 December 2009

About HEPS-Uganda

HEPS-Uganda is a health rights advocacy organisation that focuses on access to essential medicines, especially for the poor and marginalised sections of society in Uganda

About AVAC

Founded in 1995, AVAC is an international, non-profit organization that uses education, policy analysis, advocacy and community mobilization to accelerate the ethical development and eventual global delivery of AIDS vaccines and other new HIV prevention options as part of a comprehensive response to the pandemic.