Feasibility of Telephonic Unblinding as part of a Randomized Controlled Trial Results Dissemination Plan in the South African Context

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Candidates Declaration

I, Bonnie Jeanne Saxon, declare that this research report is my original work. It is submitted in partial fulfilment of the requirements for the degree of Master of Public Health, in the field of Social and Behaviour Change Communications, in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination to this or any other university.

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Abstract

Introduction The Good Participatory Practice Guidelines recommend that research results are made available to a broad range of stakeholders, including policy makers and trial participants, yet there is little guidance on how this may be achieved. The Microbicides Development Programme (MDP301 trial) was a large scale clinical trial that took place at thirteen clinics in South Africa, Tanzania, Uganda and Zambia between 2004 and 2009. The results of this trial were released in late 2009 and a comprehensive, multi-method results dissemination plan was implemented to communicate the research findings to policy makers, key stakeholders, research staff, Community Advisory Boards and trial participants between December 2009 and November 2010. This study was a retrospective analysis which included a process evaluation (and costing) of the implementation of the results dissemination plan for the MDP301 trial and an analysis of how the incorporation of telephonic unblinding potentially benefited the research community.

Materials and methods Data were collected for all planned results dissemination activities to assess whether each activity was implemented as planned. The study involved two components to answer the specific study objectives with different study designs. The first component was a process evaluation of the implementation of the results dissemination plan using a retrospective record review. The process data were collected on the number of activities held, the number of people reached through each activity, responses to those events and the resources (cost) required to implement the plan. The process evaluation framework included context, recruitment, dose delivered, dose received, reach, fidelity and resources. The second component was a cross-sectional survey design (n=1707) which included quantitative and qualitative responses from participants.

Results The results were delivered to the broader public via press release, radio and television interviews and peer-reviewed journal and to key stakeholders via telephone, email and meeting. The results were delivered to CAB and research staff by meeting and to participants via SMS, meetings and individual dissemination and unblinding calls. There were different numbers of participants reached through each activity and the total number of people reached through all dissemination activities was not available. The overall cost of implementing the results dissemination plan was R76 788.88, or approximately R30.73 per MDP301 participant (n=2499). Finally, 87.50% of the dissemination plan was implemented as planned.

412 (24.14%) MDP301 participants with up-to-date locator information on record at the time of the unblinding were contacted for individualized results dissemination and unblinding. Of the 412 participants who were unblinded, Soweto had a greater response rate with 281 (68%) unblinded, while only 131 (32%) were from Orange Farm. Of those who were unblinded, 55% had previously heard the results, primarily through planned dissemination activities and 88% had disclosed their trial participation to their partner while they were in the study.

Conclusions

The results of this study demonstrate that the MDP301 dissemination plan was implemented successfully with minor deviations. The dissemination plan was feasible in terms of cost and time required for implementation. Despite the active, multi-level, multi-method dissemination process that was implemented for the communication of the MDP301 results, the reach of the dissemination activities was suboptimal and the dose received was unclear. Only about half of the participants were reached but not all participants who were reached actually understood the results without dialogue. The MDP301 unblinding experience has proven that telephonic unblinding is feasible in the African setting and adds additional benefit to the research community by building trust and research literacy, ensuring that all participants fully understood the results.

Recommendations

Future HIV prevention researchers must ensure that a trial communications plan incorporates the on-going communication with the trial participant between the time she/ he finishes the study and the time that the results are released. Further research is required to better understand the stakeholder acceptability of receiving the results by phone, email or meeting and the participant acceptability and experience of telephonic unblinding in this setting. Better monitoring systems should be set up before the dissemination process commences to ensure that all indicators are captured. Finally, more explicit links are needed between research results dissemination and the policy to practice interface.

Dedication

I dedicate this work to my family, who inspired me to pursue a career in public health. With you, I witnessed how a suboptimal health care system can irreversibly change the life course of the people I love most. You taught me to be hard working, resilient and never to quit. Without these traits, I could never have made it through this Master of Public Health degree.

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List of Abbreviations

CAB	Community Advisory Board
CLO	Community Liaison Officer
DOH	Department of Health
GPP	Good Participatory Practice
HIV	Human Immuno-deficiency Virus
HPTN	HIV Prevention Trials Network
HREC	Human research ethics committee
MCC	Medicines Control Council
MEC	Member of executive committee
MDP	Microbicide Development Programme
OR	Odds ratio
RCT	Randomised controlled trial
SES	Socioeconomic status
SMS	Short message service
SRH	Sexual and reproductive health
STI	Sexually transmitted infection
WRHI	Wits Reproductive Health & HIV Institute

Definition of Terms

Community Advisory Board: "A board composed of individuals or stakeholder representatives that act as an independent advisory voice and facilitate community stakeholder participation and involvement in the research process. They meet regularly with research team representatives, inform community stakeholders about proposed and on-going research, and provide feedback to research teams about local norms and beliefs, as well as local views and concerns that arise in specific trials" (pg. 70) [1].

Microbicides: "A range of products that could be used vaginally or rectally (such as gel, cream, ring, film, suppository or sponge) that are being tested to determine if they reduce or prevent the transmission of HIV and other disease-causing organisms during vaginal and anal intercourse" (pg. 73) [1].

Process evaluation: A process evaluation is used to monitor and document program implementation and to understand which components of a program lead to different outcomes [2]. A process evaluation framework includes seven components: context, reach, dose delivered, dose received, fidelity, implementation and recruitment [3].

Randomised Controlled Trial (RCT): Randomised controlled trials are massive and costly undertakings that involve a large number of human participants. RCT have an experimental design and are typically used to test new interventions for major health problems of public health importance [4].

Unblinding: In a randomised controlled trial, the term blinding "refers to keeping trial participants, investigators (usually healthcare providers), or assessors (those collecting outcome data) unaware of an assigned intervention, so that they are not influenced by that knowledge. Blinding prevents bias at several stages of a trial, although its relevance varies according to circumstance" (pg. 696) [5].

Unblinding or unmasking is the act of providing the trial participants, investigators and/or assessors with the blinding information or randomisation allocation information for each participant [6].

CHAPTER 1

INTRODUCTION, LITERATURE REVIEW, AIMS & OBJECTIVES

1.1 Introduction

Randomised controlled trials (RCT) are massive and costly undertakings that involve a large number of human participants [4]. RCT have an experimental design and are typically used to test new interventions for major health problems of public health importance [4]. While South Africa has seen success with HIV treatment, it is still necessary to slow the tide of new HIV infections [7]. In South Africa, several RCT have been designed to identify safe and effective methods for HIV prevention [8, 9]. In the last ten years, there has been a growth in the number of HIV prevention RCT in South Africa, including several trials with limited success in the field of microbicides [9, 10].[1]

Because RCT are designed to answer such critical questions, it is essential that people, including policy makers, community and trial participants, understand the results with minimal delay so that effective interventions are rapidly adopted as policy, and implemented in programmes [11]. If the RCT shows that an intervention is futile, it is important to minimize the impact of findings on future research endeavours. However, RCT are complex and often require some level of understanding of the scientific method. It is necessary to communicate research findings to policy makers and the trial community in the most effective terms using methods that are feasible in *that* research setting [10, 11]. Ideally (and according to the 2011 *Good Participatory Practice*

[1] Microbicides are a new type of product being developed that people could use vaginally or rectally to protect themselves from HIV and possibly other sexually transmitted infections.

Guidelines for biomedical HIV prevention trials), a results dissemination plan should be drafted and budgeted for when the study commences [1].

A results dissemination plan may include a press release, stakeholder and participant meetings, local media, mobile phone text communication and more recently, individualized face-to-face or telephonic contact with trial participants. By explaining the research results to the individual participant, researchers have the opportunity to personalize the research findings while disclosing the participant's randomization arm while they were in the study [12]. This may be referred to as "unblinding" the participant to their randomization allocation, which is a relatively new phenomenon in the field of HIV prevention and more generally [1, 10, 13]. Unblinding participants to their randomization allocation and disclosing the study results on an individual basis may build on good participatory practice in research and create a better sense of trust with participants and the research community [1, 10].

This study was a retrospective analysis from the researcher perspective which included a process evaluation (and costing) of the implementation of the results dissemination plan for the Microbicide Development Programme (MDP) 301[2] trial and an analysis of how the incorporation of telephonic unblinding added benefit to the research community.

[2] MDP301 was a phase 3, randomised, double-blind, parallel group trial that took place at thirteen clinics in South Africa, Tanzania, Uganda and Zambia between 2004 and 2009.

1.2 Background

1.2.1 History of microbicide research

South Africa has witnessed the history of microbicides development clinical trials for over a decade. Between 1996 and 2000, a product called nonoxynol-9 (N9) was tested among sex worker populations in several African countries, including South Africa [9]. The results of this study suggested that the N9 microbicide may have actually increased the risk of HIV acquisition among women and no further large-scale trials were conducted [9, 14]. Between 2004 and 2007, a different microbicide, Carraguard, was tested in three centres in South Africa with approximately 6000 women [14]. While this product was found to be safe, it did not demonstrate any effect on the acquisition of HIV [14]. The next trial conducted between 2005 and 2007 in several sites in Africa (including South Africa), which was looking at a cellulose sulphate (CS) microbicide, was actually stopped prematurely because an interim analysis suggested that the product was likely to increase the risk of HIV among trial participants [9, 15]. This finding conflicted with several earlier safety trials on the same product which had not revealed any safety concerns and another CS trial in Nigeria that also found no evidence of increased risk [16]. These conflicting findings led to subsequent debates and negative perceptions in the public and policy realms of microbicides development.

The HIV Prevention Trials Network (HPTN) 035, conducted in seven sites in Africa (including South Africa), was the first RCT that had optimistic results. The HPTN035 was looking at the safety and effectiveness of the vaginal microbicides 0.5% PRO 2000 gel and BufferGel for preventing vaginally acquired HIV-1 infection. The study was

conducted between February 2005 and September 2008 and included 3099 sexually active HIV-negative women. The HPTN035 study found that PRO 2000 gel was safe and reduced the risk of HIV by 30 per cent. This finding was encouraging, but a larger trial was needed to confirm whether or not the results were accurate. [9, 17]

The MDP301 was a large trial that took place between October 2005 and August 2009 and included 9385 women at six clinical research sites, with three in South Africa. The MDP301 trial was testing the safety and efficacy of 2% and 0.5% PRO2000 gel compared with placebo. Of the 9385 enrolled women, 2501 (26.6%) were from the Johannesburg and Orange Farm sites. In February 2008, the 2% arm was discontinued when a Data Monitoring Committee found that it was not effective in reducing the risk of HIV acquisition and continuing the trial was futile. The study continued with the 0.5% PRO 2000 and placebo arms and completed in mid-2009. Despite the promising results of the HPTN035 study, in late 2009, the MDP301trial found that the microbicide being tested (PRO2000) was safe but not efficacious against vaginal HIV-1 infection. [9, 18]

While having witnessed the microbicide research history in South Africa and also conducting the MDP301 amongst other HIV and sexually transmitted infection (STI) prevention trials, the Wits Reproductive Health & HIV Institute (WRHI)[3] has had in-depth experience with disseminating trial results. For a series of smaller trials that looked at the potential role of herpes treatment for HIV prevention, the WRHI made a concerted effort to communicate the results, yet the process and methods used were not

[3] The Wits Reproductive Health and HIV Institute (WRHI), formerly known as the Reproductive Health & HIV Research Unit (RHRU) and ECHO, is a leading African academic research institution working in the fields of reproductive health, HIV, and broader arenas of infectious diseases.

implemented systematically [10]. Although the WRHI was not a HPTN035 trial site, the research team communicated these trial results to the MDP301 trial communities, participants and site staff. The research team also closed the 2% arm of the MDP301 trial and did their best to ensure that the communication of the discontinuation was prompt and transparent to the research staff, trial participants and trial communities.

The dissemination and communication experiences above taught the WRHI team to view research as a two-way dialogue and communication endeavour rather than something to be imposed upon a community without consultation [10, 19]. Including individualized results dissemination and unblinding in the MDP301 results dissemination plan was one opportunity to provide that two-way dialogue and communication, and to clarify whether participants had heard the results and understood them. The experience taught WRHI that face-to-face unblinding of such a large cohort of trial participants was not feasible within budget and timeframe available at the end of a trial. This led the researchers to explore alternative options, such as telephonic communication, to meet the obligation of unblinding participants to their randomization allocation. With the accumulation of these experiences, the WRHI had developed an approach to results dissemination which had not been formally evaluated. Through this analysis, we wanted to formally conduct a process evaluation of the implementation of this approach, particularly given the GPP recommendations and the results of the MDP301 trial.

While South Africa witnessed developments in the field of microbicides and the WRHI developed an approach to communicating trial results, the GPP guidelines were

developed in response to the premature and controversial closure of other biomedical HIV prevention trials in Cameroon and Cambodia in 2005 [1]. The GPP guidelines were developed by UNAIDS and AVAC in collaboration with research entities around the globe with the hope of preventing such early trial closures from happening again in the future. The guidelines were meant to "provide trial funders, sponsors, and implementers with systematic guidance on how to effectively engage with stakeholders in the design and conduct of biomedical HIV prevention trials" (pg. 5) [1]. The guidelines provided step by step guidance on how to effectively engage all levels of stakeholders (from trial participant and research community to global funders) effectively throughout the research cycle, from trial inception to results dissemination and post-trial access to an effective product or procedure. [1]

1.2.2 MDP301 results dissemination activities

In mid-2009, a results dissemination plan (Appendix 1) was created by MDP301 site staff. As per the dissemination plan, the results were disseminated to four target groups: regulatory authorities and the Department of Health (DOH), media and other key stakeholders, the CAB and finally the trial participants. The results were disseminated to some groups and stakeholders prior to when the press embargo on the results was lifted while others were told at or after the embargo was lifted. The results were disseminated to the regulatory authorities and the DOH in a face-to-face meeting or by telephone and summarized by email prior to the lifting of the press embargo. The media was informed via international and local press releases and radio and television interviews at the time that the press embargo was lifted. Other key stakeholders (e.g. other research

organisations, research donors and sponsors, scientists, collaborating universities, etc.) were informed of the results via email after the press embargo was lifted.

The CAB and site research staff was informed through face-to-face meetings just before the press embargo was lifted. The CAB and staff meetings included preparation for difficult questions from the media, the research communities, friends and families by going through mock questions and answers that were facilitated by trained communications staff.

The participants were informed of the results through community radio, SMS, participant meetings and telephonic unblinding after the press embargo was lifted. The participants were invited to the results dissemination meetings via SMS and telephone calls made on the day of and days just after the public press release. The WRHI had a weekly radio program that included a thirty minute slot on Jozi FM community radio station. WRHI had an annual contract with Jozi FM that included the cost for the weekly slot, advertisements and promotions over an eleven month period. The MDP301 results dissemination plan included pre-written scripts about the results before and after the results was released.

The SMS were sent to participants through an online bulk SMS system (www.opennetworkscrm.co.za) [20]. For each SMS sent, a report was generated which confirmed how many SMS were ‘sent confirmed’ and how many replies were received. The bulk SMS system used to disseminate the results allowed for 160 characters and

therefore messages were written in abbreviation and with slang terminology. Some example SMS messages included:

> Researchers are reviewing MDP301 trial data of PRO 2000 gel. Letting u know of results is important. Plz reply with 'Yes' if you want to receive SMS with results
> *(Sent to all MDP301 Orange Farm and Soweto participants)*

> PRO 2000 gel: Participant events abt trial results: 15, 17, 18 Dec. in Soweto & Orange Farm. Call 0119899200 for more info or reply to this SMS with: Plz call me
> *(Sent to all MDP301 Orange Farm and Soweto participants)*

> MDP301 trial results show that PRO 2000 gel is safe but does not reduce the risk of HIV transmission. Plz call 011 989 9200 or reply with 'Plz call me'
> *(Sent to all MDP301 Orange Farm and Soweto participants)*

> MDP301 PRO 2000 gel: If u want to know more about the results & which study product u were using, respond with 'Plz call me' or call 072 752 8949
> *(Sent to all MDP301 Orange Farm and Soweto participants)*

All responses to the SMS sent were communicated to the appropriate research staff who would then respond to each participant on an individual basis.

The unblinding was conducted telephonically, though women were given the option to be unblinded in person. This is described in detail in the methods section of Chapter 2.

1.3 Literature review

In the research realm, there are two levels of practice which are both expected and ethical, which include the dissemination of the research results to policy makers, clinical trial communities and participants, and the diffusion of the intervention, solution or programme if found to be effective [21-24]. This section focuses on the dissemination of research results, which is only one step in the research to policy and practice interface [11]. The task of disseminating trial results may be underestimated in the time and resources required. A well planned study should ideally include a results dissemination plan and have resources allocated from the protocol development stage [25]. It is necessary and important that efficacious, negative and futile trial results are communicated to both policy-makers and trial participants. The available literature about communicating trial results to both stakeholder groups is reviewed below.

Research to policy and practice

Recently, there has been a growing interest in both the uptake and engagement in research. This interest is driven by several factors, the first of which is the ethical imperative of using the best research available to influence policy and practice in

resource poor contexts where there are high levels morbidity and mortality associated with HIV and sexual and reproductive health (SRH). This interest is also driven by the fact that research funders are keen to show the weight of 'research impact' on grant proposal assessments. With this increased interest, "there is a need for increased reflection and experimentation with research communication techniques to enable academics and communication specialists to be more strategic about the tools and approaches they use to target particular audiences" (pg. 2) [11].

The tools and approaches used may also vary with the political context in which the research has been conducted [10]. While some tools and approaches may be appropriate to communicate research to policy-makers and trial funders, different approaches are necessary for the trial community and research participants. Also, it is important to understand the objectives of the communication itself, which would assist with the identification of the most appropriate communication approach [10].

For example, while mass media is an important communication tool, it is sometimes more important to engage with the process of developing clear and appropriate messages in the media by increasing research literacy among journalists through workshops and training [26]. Another objective of communicating research may be advocacy to influence perceptions towards sexual health and the need for HIV and STI prevention research. This level of advocacy and communication may assist with creating a more enabling environment for future research [10]. The priority audiences for creating a more

enabling environment for future research might be the trial community and potential participants [10, 27].

Communication of research results to participants

The prompt dissemination of research results to trial participants is an ethical imperative that is suggested by the 2002 International Ethical Guidelines for Biomedical Research Involving Human Subjects (guideline 5, article 7) [21, 22, 28, 29]. Clear guidance, specifically for biomedical HIV prevention trials, on results dissemination is also outlined in the 2011 GPP guidelines [1]. The act of disseminating research results to participants demonstrates a greater respect for research participants and acknowledges their central role in study completion [28]. Despite being an ethical obligation to researchers, there are also potential benefits to disclosing study results such as expressing appreciation to participants, improving the participant and public perception of research by allowing for a transparent understanding of their contribution towards science, and having a potential positive impact on the future health of study participants [28].

The published work on results dissemination is almost entirely set in North America and Europe and focuses on treatment trials rather than prevention trials [27]. The available literature reviews participant desire to receive trial results; individual and personalised communication of results versus aggregate and group or public communication of results; the available and preferred methods for communicating results; as well as the impact of results dissemination on both the participant and the researcher.

In a paper which reviewed 28 empirical studies around communicating research results, studies which looked at reported desire to receive the results found that the large majority of participants wished to receive the results [27]. Another common finding was that participants with more education were more likely to have heard the results and more likely to opt for receiving the trial results (if given the option) [27]. The desire to receive research results was driven by the clinical significance of the results, the participant's right to receive the results and raising awareness of research in general [27]. As noted by Shalowitz, et al., "Participants' desires do not necessarily determine policy, but respect for participants requires taking their preferences seriously" (pg. 0717) [27]. While participant's in several studies were satisfied and generally appreciative of receiving aggregate and impersonal study results, the preferred trend was for individual and personalised communication of results [22, 25, 27, 28]. This finding was also dependent on the outcome of the trial and the implications for the individual if they suffered any adverse reaction or negative impact while participating in the trial [25, 27].

The available and published methods of communicating trial results most commonly included publications, conference presentations, the media, postal mail (with helpline or research team contact details included for queries), telephone call by research staff or invitation to a group meeting [19, 22, 27, 30]. The participant's preferred method of receiving the research results was also dependent on whether the findings were negative, positive or null, as well as his/ her personal experience in the study [27]. For example, if the study had positive or neutral results, participants generally preferred to receive results

via email or letter, while if the results had negative implications, the participants preferred in person communication [27].

Publications in peer-reviewed journals are generally aimed at the scientific and research communities and are not written for the lay population. Conference attendees are also generally scientists, researchers and specialists in the field and only include a limited number, if any, community representatives. In one study which looked at communicating trial results to the participants, the researchers distributed copies of the publication to the participants [22]. There was no evaluation to determine whether or not the participants understood and appreciated receiving the publication [22].

While media is typically used as a first method of communication through a press release of study results, one study that conducted a postal survey with participants from a RCT on Huntington's disease, found that media (e.g. newspaper, television, radio and the Web) were uncommon sources of information about the trial results [19]. No participants in this study reported that they initially heard the trial results from the media and a majority of participants were generally not satisfied with hearing the study results from a media source [19]. In another study, the researchers warned that communicating results via the media may cause confusion to the participant and leave the researcher with the responsibility of interpreting the results and mitigating any confusion: "Results of high profile trials often fall under the media spotlight ahead of any adequate peer review. Dissemination of results by the media and the 'spin' put on them in popular press may be

misinterpreted by trial participants…" (p. 38) [30]. This may suggest that media is only a sufficient method of communicating results if combined with other methods.

Studies that used postal mail as the method for communicating results sometimes included a letter stating that the results would soon be released at which time they would receive further postal correspondence or a telephone call from the research staff, while other studies included an information leaflet which summarized the aggregate study results and listed a helpline for any additional queries [19, 21, 27, 30]. In a study which evaluated how participants (who during the study were pregnant women receiving antibiotics for preterm labour and preterm rupture) responded to receiving a summary of trial results via post, found that while the participants received and read the leaflet summary of the results, some found the leaflet complicated and difficult to understand [25 , 31]. In the same study, participants expressed that a benefit of receiving results by post allowed them to reread the results several times while if they had received the results by telephone, they may not have remembered everything that was explained by the research staff [25]. Finally, women in this study were disappointed with the lack of personalized research results as they were hoping to learn their randomization allocation when the results were released [25]. This was especially true for women who had adverse reactions or experiences during their pregnancy or gave birth to a child with health problems [25].

In a study which included 1431 breast cancer patients, researchers provided the participants (via letter) three options for receiving the trials results along with the

advantages and disadvantages of each option [30]. The options included the results posted in the mail once available, a letter stating that results were available with a phone number to call for a copy of the results and finally results provided at their next hospital visit [30]. Most participants wanted the results posted when available or given to them at their next hospital visit [30]. Only 13% of the participants preferred the second option which required a phone call to a national helpline [30].

In a different study that was looking at a new treatment for Huntington disease, a three-pronged communication plan was implemented which included a media release, a telephone call to research participants and a joint telephone conference for investigators, sponsors and study participants [19]. Participants in this study were sent a letter in the post to inform them that the results would soon be released [19]. The media release was provided by investigators within one day after the sponsor-issued press release with a subsequent call to study participants [19]. The conference call was two weeks after the original press release. In this study, the participants expressed high or complete satisfaction with the telephone call as it allowed for customized communication [19]. Meanwhile, in another study which was stopped early due to futility, participants were sent a lay summary of the findings, the implications of the findings and had the option to receive the results via mail, in person or via phone [21]. In this study, only 2% of the participants opted to receive the results via phone [21].

Finally, one study looked at the explicit use of group presentations to communicate research results. This study offered two participant meetings, of which took place

between two and nine months after the results were released. Both meetings had very low attendance by the study participants. The researchers in this study attributed the low attendance to the likelihood of participants' preference not to learn study results. In general, the participants were satisfied with the group presentation and engaged in discourse with fellow participants and research staff. Criticisms of the group presentations included the fact that some people may not have been comfortable in the group setting and that more participant meetings should have been made available for those with scheduling problems. In addition, this study provided each participant with their randomization allocation after study closeout without giving participants the choice to opt out of receiving this information. No further description of this unblinding experience was provided. [22]

In the studies described above, only one study described an explicit and comprehensive results communication plan while the others described and evaluated the use of one communication method [19]. Also, several of the studies listed the lapse in time between trial closure and results dissemination as a major limitation and cause for the low participant response rate to dissemination activities [22, 25, 30]. Finally, some studies merely mentioned that they provided participants with their randomization allocation and other studies stated that participant's wished to know their randomization allocation but it was not provided [22, 25]. This was attributed to the cost, human resource time required and psychological impact on the participant if unblinded [22, 32]. While the literature on unblinding participants to their study arm is limited, the available literature is reviewed below.

Participant Unblinding

Over the last 60 years there have been significant changes in science and in the research field on a global level. In particular, ethics of research involving human subjects have undergone review and revision since the Second World War. From the Nuremburg Code (1947) and the Declaration of Helsinki (1964), to the Belmont Report (1979), researchers have spent the past few decades outlining ethical principles which are meant to prevent unethical research such as that conducted during World War II [33]. While the rest of the world saw these changes, South Africa has only seen similar changes over the last 16 years (since democracy). Prior to this human rights framework, Black South Africans faced human rights violations and colonial exploitation which made them vulnerable targets of unethical research [34-36]. South African research institutions and the current government have responded to this history of exploitation by establishing a number of guidelines for conducting ethical research, such as *The Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa* [37]. South African research projects have also needed to build a relationship of trust with communities where research is conducted and increasingly established community advisory boards (CAB) to provide the links with the community [38]. A CAB such as this is typically composed of individuals or stakeholder groups who serve as an independent advisory voice for the research community [1]. The CAB members would meet regularly and provide feedback to researchers about the community norms and beliefs [1]. They also provide feedback to their fellow community members about proposed and on-going

research [1]. CAB member roles and responsibilities are often defined by a 'constitution' or 'terms of reference' [1].

While South Africa entered the post-apartheid era and grappled with implementing ethical guidelines for research using human subjects, there were key developments internationally that were shaping ethical guidelines. The research world faced the early closure of several HIV prevention trials which led to the creation of the *Ethical considerations in biomedical HIV prevention trials* and the *Good participatory practice (GPP) guidelines for biomedical HIV prevention research* [1, 39]. While the 2007 GPP guidelines strongly recommended the planning and implementation of a results dissemination strategy, it did not mention unblinding as a component of the strategy [40]. It was only in the 2011 version of the GPP guidelines where it was stipulated that a dissemination plan should include "how and when participants will be informed of their group assignment" (p. 63) [1]. Several studies have looked at different strategies for results dissemination, including group versus individual results dissemination; dissemination via post, telephone or in-person appointments, though none of these studies address unblinding as a component of results dissemination [28, 29].

There are papers which discuss the success or failure of blinding participants to their randomization allocation during the trial and methods of measuring the success; participants' perception of randomization allocation, why they have this perception and how their perception affected their drug product adherence; and finally the incorporation of unblinding into a results dissemination plan [12, 41, 42].

In a review which looked at the methods used to assess the success of blinding in RCT, the authors reviewed who was assessed (e.g. care giver, participant, outcome assessor), timing of assessment and whether or not the participants were asked to guess their randomization allocation [42]. This review found that the methods of assessing the success of blinding, the analysis and reporting the results were inconsistent and questionable [42]. Meanwhile, two other papers which looked at participants' guess of randomization allocation found similar findings for the reasons for their perceptions, including intervention-related factors (e.g. physical characteristics of the study product) and outcome related factors (e.g. participant's health, side effects, etc.) [6, 13].

There was only one study which looked at unblinding participants to their randomization allocation as part of a broader results dissemination plan. The PROSPER study, which took place in Scotland and was looking at the use of a cholesterol lowering drug in an elderly population, planned to offer participants their treatment allocation at the close of the study from the initial planning process of the trial [12]. The objectives of the PROSPER unblinding process were to provide participants with their treatment allocation and cholesterol levels, to provide the information with support of counselling, and to respect those participants who did not wish to be unblinded [12].

In the PROSPER unblinding process, participants were mailed a summary of the results and were offered the option to be advised on their treatment allocation via appointment with or telephone call from a study nurse. Although the initial response from participants

included 41% to be unblinded by appointment and 26% to be unblinded telephonically, the majority of participants were telephonically unblinded due to scheduling difficulties and room availability in the research site. The outcomes of this unblinding experience suggested that dissemination of results and treatment allocation should be an integral part of the research process; procedures for unblinding should be developed in the early phases of the trial; timing of research results dissemination and unblinding should be optimized; accurate contact information for participants should be kept up to date; and telephone unblinding should be considered as the initial option for unblinding participants. More importantly, participants who were unblinded were grateful for the personal communication [12].

Theory for Dissemination Research

Research results dissemination can be informed by theory. This section will explore some of the theoretical perspectives applied to dissemination research. While this report focuses on the dissemination of research results to various target audiences, the term ‘dissemination’ is also used interchangeably with ‘diffusion’ in the literature around dissemination research [43, 44]. A review of the literature suggests that the dissemination of research results may be thought of through the lens of the diffusion of innovations theory and/or the theory of change for public will campaigns.

Despite the current guidelines and recommendations for dissemination activities for clinical trial results, there is no clear set of guidelines for the dissemination and diffusion of evidence-based public health interventions [44]. Though the terms ‘dissemination’ and

'diffusion' have been used interchangeably in the dissemination research literature, some have published about the difference between the two. According to Owen, et al., "Dissemination is the planned process of creating awareness of the program or intervention among the targeted population, informing stakeholders about the innovation, and persuading them to try it" while "Diffusion (the outcome of dissemination efforts) involves three main stages: adoption (the decision to commit to a program or innovation); implementation (actually carrying out the program); and institutionalization (integration and sustainability of the program over the long-term, through policy and practice)" (p. S36, 2006) [45].

The diffusion of innovations theory was derived from the work of sociologists and anthropologists who tried to understand the adoption or rejection of new ideas or innovations [46]. An innovation is "an idea, practice, or object that is perceived as new by an individual or other unit of adoption" (p. 11) [46]. In the dissemination of research findings, the innovation is the study result. Diffusion is defined as "the process by which an innovation is communicated through certain channels over time among the members of a social system" (p. 314) [46, 47]. From the 1950s moving forward, diffusion theory was applied to understanding the uptake of public health interventions [47]. For example, in an efficacy trial, the Pool Cool skin cancer prevention program was found to have significant positive effects on sun safety environments at swimming pools and later progressed into a diffusion trial, incorporating constructs from the diffusion of innovations theory, to better understand and document the spread and adoption of the Pool Cool intervention [48]. Two other interventions, SPARK (Sports, Play and Active

Recreation for Kids) and CATCH (Coordinated Approach to Child Health), which looked at school-based physical education programs were also found to be effective and constructs from the diffusion of innovations theory were applied retrospectively to describe the dissemination of the interventions [45].

While diffusion of innovations theory is typically considered for the dissemination of effective or positive innovations and for group or community-wide behaviour change, it is important to consider this for futile or negative findings from a clinical trial. Results dissemination can be done through "active diffusion" in that there is a systematic and intentional process to diffuse the results to the target groups or through "passive diffusion" which is often a slow, uncoordinated and insufficiently capitalized process, which tends to be ineffective for influencing policy or practice [24, 49]. Active diffusion of research results may include communication "by targeting and tailoring the findings and the message to a particular audience" (p. 26) [49].

According to Rogers, "The essence of the diffusion is the information exchange through which one individual communicates a new idea to one or several others" (pp.17-18, 1995) [46]. The information exchange may take place through various channels including mass media, interpersonal and electronic communications [47]. While mass media is useful to communicate broad messaging to broad audiences, interpersonal communication is best for communicating complex issues like trial findings [47]. Accessing mass media through media advocacy using strategies such as a press release,

participation in community radio shows and working with journalists to increase news coverage, are typically used to reach segments of the general public and policy makers [30, 47]. Interpersonal communication strategies such as participant meetings, SMS and telephonic unblinding have been used to communicate trial results to participants [50]. It is important to note that a mix of both mass media and interpersonal channels may be used to reach various segments of the target audience(s) when necessary or appropriate.

It is important to apply systematic and targeted diffusion theory to disseminating research results to increase scientific literacy, to build trust within the research community and to create an enabling environment for future research [10]. Ultimately, this may "modify the social and policy environment that affects health behaviours" which is often the intention of theory of change public will campaigns (p. 8) [51].

Frameworks for Process Evaluation of Dissemination Research

In order to better understand the link between the theoretical constructs described above and the success of diffusion and dissemination efforts, there are frameworks which may be applied. The RE-AIM (reach, efficacy/ effectiveness, adoption, implementation and maintenance) framework by Glasgow, et al., is complimentary to the diffusion of innovations theory in that the "impact of an intervention is determined not only by its 'reach' multiplied by 'efficacy,' but impact also depends on the extent to which the intervention is adopted, implemented as intended and can be maintained at both systems and individual levels" (p. S36, 2006) [45, 52, 53]. The RE-AIM framework has been used

as an evaluation framework for several studies which looked at the dissemination and diffusion of effective evidence-based public health interventions [53, 54].

Other dissemination, diffusion and communication interventions have been evaluated through various components of a process evaluation framework. Process evaluation has evolved since the 1960s to assess the success or failure of a program in order to understand why and how a program worked or did not work [3]. In the early 1980s and 1990s, there were studies that were attempting to evaluate community-based public health interventions using different approaches to assess and describe the program activities, including what activity, for whom the activity was for and how much of the activity was delivered (by whom) and received by the program participants [3]. The investigators of these studies soon realized the importance of developing a consistent approach to assess the dose of the intervention delivered and dose of the intervention received by the target audience [3]. This stemmed from the realization that interventions were being delivered but not necessarily received. For example, programs or interventions were scheduled or offered but attendance was low. This experience emphasized the importance of recognizing when a program was not delivered optimally and when corrective actions needed to be taken [3].

During these decades, the components of the process evaluation evolved and by 2000, there were eleven major components (e.g. recruitment, maintenance, context, resources, implementation, research, barriers, exposure, initial use, continued use and

contamination) of which different studies used only selected components to fit their process evaluation [3, 55]. For example, in a study that tried to understand the effectiveness of peer education for health promotion around sexual health, HIV and drugs, the researchers used an interactive process evaluation that only looked at recruitment and context [56]. In 2002, Linnan & Steckler, further refined the key components of the process evaluation to include context, reach, dose delivered, dose received, fidelity, implementation and recruitment [3]. One paper reviewed gave a "How-to Guide" on developing a process evaluation plan to assess health promotion program implementation with the example of the implementation of a school-based program designed to decrease adolescent risk behaviours via media messaging that was based on Bandura's Social Cognitive Theory [57]. This guide used the 2002 Linnan & Steckler's refined components to guide their process evaluation development [3, 58].

The Communications Consortium Media Center has offered different guidelines for evaluating non-profit communications efforts in 2004 [51]. These guidelines described how the purpose of the communication efforts (such as the dissemination of the MDP301 results) can determine the focus of the evaluation, with process evaluation as one option for evaluation [51]. While these guidelines do not specify the process evaluation components to be included, they suggest that the purpose of a process evaluation for communications efforts is to "measure effort and the direct outputs of campaigns- what and how much was accomplished and to examine the campaign's implementation and how the activities involved are working" (p. 10, 2004) [51].

In order to evaluate whether the MDP301 dissemination plan was diffused according to the actual plan, and to determine whether the results were communicated in a way that could ultimately increase future community and policy maker support towards clinical research, the implementation of the plan needed to be assessed through a (retrospective) summative process evaluation framework.

1.4 Statement of the problem

The MDP301 results dissemination plan was created in mid-2009 to ensure GPP recommendations were followed and policy makers, policy influencers, all trial participants, trial communities and stakeholders were informed of the null research findings. The WRHI had developed an approach to communicating research results and wanted to formally conduct a process evaluation of this approach, especially given the GPP guidelines. Given the size of the MDP301 cohort, face-to-face unblinding was not feasible within timeframe and budget. An analysis was necessary to understand the feasibility and process of implementing such a complex dissemination plan to multiple target audiences, and the additional benefit of incorporating telephonic unblinding to the research community.

1.5 Justification for the study

As described in the literature review, there are many methods for disseminating research results. While some researchers have used postal services to send participants information

about study results and their randomization allocation, it is not an option in the South African setting where many people do not have mailing addresses or the resources to respond. Written results also require high levels of literacy which are often not found in low resources settings (such as South Africa). Various results dissemination methods require financial resources from both the researcher and the participant (if they are expected to phone, mail or visit the study clinic) which is also a limitation in low resource settings.

The literature reviewed does not provide a clear message around results dissemination to multiple audiences but alludes to the understanding that results dissemination is not a 'one size fits all' approach and must be context specific. While the experience of communicating research results has been discussed elsewhere in various contexts, no literature touches upon the cost and time required to do so [10]. It is important to understand the context-specific cost of various dissemination methods and the reach of each method. This is necessary to inform future planning and research proposals.

The GPP guidelines (2007 & 2011) and the *Communications Handbook for Clinical Trials* (2010) firmly outline the minimum package of dissemination activities, but they do not specify any means of measuring or evaluating the implementation of the dissemination plan [1, 39, 59]. Though the WRHI as an institution has had experience with communicating trial results, there has never been a formal evaluation of the results dissemination plan that has been developed and implemented. Finally, there is a need to

better understand the challenges of disseminating futile research findings and both the community and policy implications of the null finding.

The concept of personalized communication with trial participants, including results dissemination and unblinding participants to their randomization allocation is also new in the HIV prevention field and was only recommended in the 2011 version of the GPP guidelines. Yet no guidance exists on how to follow these recommendations effectively for large cohorts of participants. Although the literature has shown a successful example of telephonic unblinding, there is no documented work on telephonically unblinding trial participants as part of a broader dissemination plan in the African context or in HIV prevention research trials.

1.6 Aims and objectives

This study aimed to evaluate the process of implementing the MDP301 results dissemination plan; to document reach and how the results were received; and to assess the feasibility and additional benefit of telephonic unblinding as part of the broader dissemination plan. The study also aimed to determine the costs of implementing the entire MDP301 dissemination plan to determine the feasibility of implementing such a plan in the African setting. The specific objectives were:

1. a) To conduct a process evaluation of the implementation of the MDP301results dissemination plan.

   b) To calculate the cost of the MDP301 results dissemination plan.

2. To determine the additional benefit of telephonic unblinding from the researcher perspective as part of a broader dissemination plan. The sub-objectives were:
    a. To describe the proportion of trial participants reached through unblinding who were aware of the study results and factors associated with their awareness (e.g. age, sex, education level, employment status, religion, housing type, etc.).
    b. To explore women's beliefs around their trial participation and factors associated with their beliefs (e.g. age, sex, education level, employment status, religion, housing type, etc.).
    c. To assess the association between partner disclosure of trial participation and beliefs around randomization allocation.

1.7 Summary of chapter

Results dissemination for RCT is not only an ethical imperative, but provides an opportunity to create an enabling environment for future research which aids the research to policy interface. Telephonic unblinding as part of a broader results dissemination plan is new in the field of HIV prevention research and in the African context. It is important to understand the process and feasibility of the MDP301 results dissemination plan for future research proposals and to understand how the incorporation of telephonic unblinding potentially benefited the research community.

CHAPTER 2

STUDY METHODS & MATERIALS

This chapter gives a detailed overview of the research methodology applied to this study. The study site and population for the MDP301 trial are described and the variables used and generated for the study are explained. The data analysis and management plan is explained and the ethical considerations for this study are provided.

2.1 Study design

The study involved two components to answer the specific study objectives with different study designs. One component was a process evaluation using a retrospective record review and the other was a cross-sectional survey design. The MDP301 results dissemination plan was developed and implemented between November 2009 and January 2010. Data was collected for all planned activities to assess whether each activity was implemented as planned.

Process evaluation: The first component was a process evaluation of the implementation of the MDP301 results dissemination plan in both Orange Farm and Soweto using a retrospective record review. The process data were collected on the number of activities held, the number of people reached through each activity and responses to those events. The process evaluation framework in this study included context, recruitment, dose delivered, dose received, reach, fidelity, resources (e.g. cost).

Telephonic unblinding: The second component was a cross-sectional survey design which included quantitative and qualitative responses from participants. This data was collected from July through October 2010.

2.2 Study site

Soweto and Orange Farm are located to the south west of Johannesburg, approximately twenty kilometres apart. These sites were chosen for the MDP301 trial because of the high HIV prevalence in these areas [60].[4] Under the apartheid administration, these highly planned townships were reserved for Black South Africans [61]. Soweto is significantly larger than Orange Farm with 1.2 million inhabitants compared to Orange Farm's 170,000 [62]. While Soweto is an urban area where residents have access to water, electricity, paved streets and public transport, Orange Farm is more peri-urban and few residents have access to potable water. The people of Orange Farm and Soweto come from a wide range of social classes and ethnic identities.

2.3 Study population and sample

Process Evaluation: The results dissemination plan targeted four groups including the research staff, CAB, other key stakeholders (e.g. regulatory authorities, policy makers, donors, researchers, the Department of Health) and Orange Farm and Soweto MDP301 trial participants. In order to reach these target groups, there were a series of activities. All records from these activities were reviewed for the process evaluation.

[4] More information about the MDP301 trial sites and study population may be found in the main MDP301 paper.

Records from the meeting with the MDP301 research staff included attendance registers and social science field notes. Records from the two CAB meetings held included meeting minutes, attendance registers and social science field notes. The 41 Soweto and Orange Farm CAB members at the time of the study were invited to attend these meetings and included men and women who were representing local organisations or were otherwise individual community representatives. The CAB members were above 18 years of age and had served on their respective CAB from one to six years.

A senior MDP301 staff member kept records from dissemination to other stakeholders such as media, regulatory authorities, the South African Department of Health, donors, sponsors, other researchers and the South African National AIDS Council (SANAC). These records included summary notes from the engagement with the different stakeholders.

Records from the six participant meetings included meeting minutes, attendance registers, field notes from study staff and social science field notes. The 2501 women who were enrolled in the MDP301 trial, located at the Orange Farm and Soweto sites, were volunteers who were 18 years or older; did not have HIV-1 infection at screening; were likely to be sexually active; and were willing to be tested for HIV-1 infection and receive the result; have regular speculum examinations and urinary pregnancy tests; use gel as instructed; receive health education about condoms; and give informed consent.

The costing data included all records from which cost data was collected from the dissemination activities that took place from November 2009-November 2010.

Telephonic Unblinding:

At the start of the MDP301trial, there were three arms in the study (n=2499)[5] including a 0.5% gel (867 women), a 2% gel (764 women) and a placebo gel (868 women). In 2008, the 2% arm was discontinued after a review committee confirmed that the gel was not efficacious and it was futile to continue [18]. Women receiving the 2% gel were immediately unblinded to their randomization allocation and discontinued from the trial [18].

All women in the 0.5% and placebo arms who participated in the MDP301 Orange Farm and Soweto sites (n=1735) were eligible for inclusion in the unblinding process. Of those who were eligible, those with listed and up-to-date contact information (including name, address and phone numbers) were included for unblinding (n=1707).

2.4 Data Collection

Process Evaluation

The data on dissemination activities targeting regulatory authorities, DOH, the media and other stakeholders was collected through a record review of all documentation completed during the dissemination process.

[5] The final number of participants used for all MDP301 analysis was 2499 after removing those participants who had co-enrolled in the trial.

All attempted, failed and successful calls made to recruit participants to the participant meetings were logged by the Community Liaison Officers (CLO) in an Excel spread sheet. All SMS data to recruit participants to meetings, to call or visit the research clinic for more information or for unblinding and to provide the study results were retrospectively collected from the online bulk SMS system. The staff who were involved with sending out the SMS to participants were provided a two hour training on the bulk SMS system prior to the results dissemination.

There were no records of the calls made or email sent to invite the research staff and CAB members to results dissemination meetings. The staff, CAB and participant meetings were documented in reports (Microsoft Word format) that were written by the CLO who facilitated the meetings, along with field notes from social scientists who also attended the meetings and had one-on-one conversations with some stakeholders. During the one-on-one conversations with CAB members and participant meetings, the trained social scientists used a pre-scripted interview guide (Appendix 2). Attendance registers for participant, CAB and staff meetings were also used to collect data on the number of people reached through each activity.

Costing information was collected between May and June 2011 through a record review by the researcher. All data was collected using a costing table (Appendix 3).

Telephonic Unblinding:

In early 2010, an unblinding script was developed by the researcher based on a similar script from a sub-study on adherence from the HPTN 039 trial [41]. The unblinding questionnaire included both closed and open-ended questions (Appendix 4).

The unblinding script was pilot tested and minor changes were made before it was translated and back translated to local language. The final translated versions of the script were then submitted to and approved by the Wits Human Research Ethics Committee (HREC). The questionnaire was then administered telephonically between July through November 2010 by a trained research nurse. Four attempts were made to contact each trial participant. After the fourth attempt, it was documented that the participant was unable to be contacted. The women who were unblinded were required to confirm their identification by providing their name, date of birth, address and the name of the last clinician or counsellor that they saw at the study clinic. Women were also given the option to visit the clinic for face-to-face unblinding. Once the participant had confirmed her identity, the research nurse gave a short background of the MDP301 trial and what the trial involved. Once they were done explaining the trial, the participant was given the opportunity to ask questions and was then asked whether or not they had heard the results and how. From there, she was then given the option to receive her randomization allocation.

All data from the telephonic unblinding was captured in an Access database by the research nurse who facilitated the unblinding calls.

2.5 Data Measurement

Process evaluation: The implementation of the MDP301 dissemination plan was measured through the key components and indicators of a process evaluation which are outlined in the table below:

Table 1: Process evaluation components measured

Component	*Definition	Indicators
Context	*'Aspects of the larger social, political and economic environment that may influence intervention implementation.'* (pg. 12, 2002) [3].	See background section
Recruitment	*'Procedures used to approach and attract participants. Recruitment often occurs at the individual and organisational/ community levels.'* (pg. 12, 2002) [3]. This includes all procedures and activities aimed at attracting CAB members and participants to the CAB and participant meetings; to invite participants to the research clinic to learn about the trial results; to contact participants for telephonic unblinding.	- # of SMS confirmed/ # of SMS sent to invite participants to meetings - # of SMS sent confirmed/ # of SMS sent to invite participants to call or visit the clinic for more information about the results - # of SMS sent confirmed / # of SMS sent to invite participants to SMS, call or visit the clinic if they wanted to learn their randomization allocation - # of participants who confirmed their intention to attend results meeting/ # of calls made to invite participants to meetings - # of posters hung in Soweto & Orange Farm inviting participants to call or visit the clinic for more information about the results** - # of community radio shows aired to invite participants to meetings
Dose delivered	*'The number or amount of intended units of each intervention or each component delivered or provided. Dose delivered is a function of efforts of the intervention providers.'* (pg. 12, 2002) [3]. This includes all efforts that the MDP301 research team made to inform all target audiences about the results before and after they were released.	- # of SMS sent confirmed/ # of SMS sent to participants with the results - # of community radio interviews about the results** - # of commercial radio interviews about the results** - # of CAB meetings held** - # of participant meetings held** - # of stakeholder meetings held** - # of emails sent to stakeholders** - # of phone calls made to stakeholders** - # of publications in peer-reviewed journals** - # of television interviews about the results**
Dose received	*'The extent to which participants actively engage with, interact with, are receptive to, and/or use materials or recommended resources. Dose received is a characteristic of the target audience and it assesses the extent of engagement of participants with the intervention.'* (pg. 12, 2002) [3].	- #of unblinded participants who had previously heard the results/ total # of unblinded participants - # of SMS sent confirmed/ # of SMS sent to participants with the results - # of staff who attended results meeting / total # of

Component	*Definition	Indicators
	This includes all data on the extent which the dissemination efforts were received by the target audiences.	research staff - # of Soweto CAB members who attended results meeting / total # of Soweto CAB members - # of Orange Farm CAB members who attended results meeting / total # of Orange Farm CAB members - # of Soweto participants who attended results meetings/ total # of Soweto participants who had confirmed to attend - # of Orange Farm participants who attended results meetings/ total # of Orange Farm participants who had confirmed to attend - # of people who attended results meetings/ total # of people invited/ confirmed to attend meetings - # of times a participant had previously heard the results*** - # of sources that the participant had previously heard the results*** - # of listeners of the community radio shows aired*** - # of emails sent confirmed to stakeholders/ # of emails sent
Reach	*'The proportion of intended target audience that participates in an intervention. If there are multiple interventions, then it is the proportion that participates in each intervention or component. It is often measured by attendance. Reach is a characteristic of the target audience.'* (pg. 12, 2002) [3]. This includes the actual number of each target audience that was reached through the dissemination efforts.	- # of research staff reached via meeting/ total # of research staff - # of CAB members reached via meeting/ total # of CAB members - # of participants reached via SMS/ total # of participant mobile numbers on bulk SMS database - # of participants reached via meeting/ total # of MDP301 participants - # of participants unblinded/ total # of participants eligible for unblinding - # of stakeholders reached via phone** - # of stakeholders reached via email** - All qualitative data from staff, CAB and participant meetings
Resources (cost)	*'The materials or characteristics of agencies, implementers, or participants necessary to attain project goals.' (pg. 8, 2002) [3]*	- Cost per radio show aired on weekly programme * total # of shows about the MDP301 results

Component	*Definition	Indicators
	For the purpose of this study, this only includes the cost data for all dissemination efforts.	- Cost per SMS sent * total # of SMS sent - Cost per venue rental for CAB meeting * total # of CAB meetings - Cost per CAB members reimbursement * total # of CAB members who attended meetings - Cost per refreshments for CAB meetings * total # of CAB meetings - Cost per venue rental for participant meetings * total # of participant meetings - Cost per participant reimbursement * total # of participants who attended meetings - Cost per refreshments for participant meetings * total # of participant meetings - Cost per minute for unblinding calls * total minutes for all unblinding calls - Cost per hour of staff time for unblinding calls * total hours of staff time for unblinding
Fidelity	*'The extent to which the intervention was delivered as planned. It represents the quality and integrity of the intervention as conceived by the developers. Fidelity is a function of the intervention providers.'* (pg. 12, 2002) [3]. This includes a qualitative assessment of whether or not the MDP301 results dissemination plan was delivered as intended and whether or not efforts deviated from the actual plan.	- Qualitative data and perceptions on whether or not the dissemination plan was followed accordingly or if there were any deviations.

** No denominator available for indicator.

*** Not measured/ no data available.

Telephonic Unblinding:

Data from unblinding was merged with the MDP301 trial dataset to include baseline demographics (Appendix 5), baseline sexual history (Appendix 6) and sexual behaviour at the final study visit (Appendix 7) for all participants who were unblinded.[6] The data was categorized into three sections, as described below. This is followed by a detailed description of the variables.

1. *Socio-demographic factors*- examined factors such as age, education level, employment status, religion, housing type and socioeconomic status.

2. *Sexual history factors*- assessed the participant's sexual history at baseline. This questionnaire included items about condom usage at last sex act, number and type of sexual partner(s) and history of sexually transmitted infections (STI).

3. *Telephonic results dissemination and unblinding*- dealt with all items included in the unblinding questionnaire. This included whether or not the participant had heard the results, how they heard the results, their belief about which arm of the trial they were on, why they believed this, whether or not they disclosed their trial participation to their partner(s) and lastly whether or not they wished to be contacted for future research clinical trials.

2.6 Data Management

Process evaluation: All dissemination activity records were stored electronically.

Telephonic unblinding: The unblinding data was cleaned before analysis and imported into Stata 10. Any data entered with no available unblinding envelope was dropped from the analysis because it was not possible to link the participant randomization arm with the correct socio-demographic data.

[6] The baseline demographics, baseline sexual history and sexual behaviour at the final study visit data were collected by either a trained and qualified counsellor or a trained research nurse. The methodology for the data collection of the main MDP301 study is documented elsewhere.

The documented questionnaire results along with the demographic and sexual history data[7] were then merged and recoded for analysis.

2.7 Data Analysis

2.7.1 Description of variables

1. *Socio-demographic factors:*

- Age was originally captured as a numeric variable and was later categorized into three age groups (18-24, 25-34, and 35+). The categories were made to determine whether there were differences in awareness of trial results in different age groups. The distribution of the data was used to determine the cut points.

- Educational attainment was originally an eight level question that was dichotomized into *"completed high school"* and *"did not complete high school."* This question was dichotomized because there were too few responses in some of the original categories, resulting in small cell sizes. The two categories also allowed for meaningful comparison by educational attainment.

- Religion was originally a thirteen level question that was sub-categorized into *"Christian," "None"* and *"Other."* This question was sub-categorized because there were too few responses in some of the original categories, resulting in small cell sizes.

- Socioeconomic status (SES) was assessed with two questions. The first question included a proxy asset indicator with ten items that the participant could own. A low score (0) was defined as having a low SES while a high score (10) was defined as having a high SES. This score was used as a continuous variable in the analysis. The second SES question asked

[7] The demographic and sexual history data were collected at the baseline visit for each MDP301 study participant. This database was merged with the unblinding database.

participants, *"If a person became ill in your home and R100 was needed to pay for treatment or medicines, how easy would it be for you to find the money?"* The original question included a five level response which was dichotomized into *"Easy"* and *"Difficult."* This question was dichotomized because there were too few responses in of the original categories, resulting in small cell sizes.

- The housing type question was originally a thirteen level response that was later sub-categorized into four groups including *"municipal house," "private house," "room"* and *"shack."* This question was sub-categorized because there were too few responses in some of the original categories to be an independent category for analysis.

- Lastly, employment status was originally a nine level response that was later dichotomized into *"employed"* and *"unemployed."* This question was dichotomized because there were too few responses in some of the original categories, resulting in small cell sizes.

2. *Sexual history factors*

- At the enrolment visit, participants were tested (laboratory diagnostics) for six STI, including bacterial vaginosis, herpes simplex virus type-1, gonorrhoea, chlamydia, syphilis and trichomonas. These results were dichotomized into *"ever had an STI"* which included a positive diagnosis of any one of the six STI at the baseline study visit and *"never had an STI"* which included all women who had negative results for all six STI (at the baseline study visit). This question was dichotomized because we were not looking at prevalence of individual STIs but rather trying to understand whether or not they ever had any STI at baseline.

- At the enrolment visit, participants were asked whether or not they had used a condom at their last sex act. The responses were dichotomized into *"yes"* and *"no."*

- At study completion (final visit), participants were asked if at any time during the study they had had multiple and concurrent sexual partners. The responses were again dichotomized into *"yes"* and *"no."*

3. *Telephonic results dissemination and unblinding*

- The participants' open-ended responses to the question "Do you have any questions?" were post-coded into the following themes: *"Results:"* when the participant merely asked for the results of the study; *"New study:"* for when the participant asked if there was a new study they could join; *"Is MDP301 still going on;" "Is gel available;" "Health care/ screening:"* which captured participants' questions about where they can obtain health care or screening now that the MDP301 is over; *"Arm:"* when the participant wanted to know which arm of the trial they were in; and *"other."*

- Once their questions were responded to, the participants were asked whether or not they had heard the results and how. The original question which asked how they heard the results included a ten level response (e.g. radio, SMS, CAB member, etc.). A new variable was generated called *"results_source"* and these responses were post-coded and sub-categorized into *"word of mouth"* which included friends, a CAB member or another participant, *"dissemination strategy"* which included all deliberate dissemination strategies (e.g. radio, posters, SMS, call or letter from study staff), and multiple sources which included participants who had heard from both *"word of mouth"* and *"dissemination strategy."* This question was sub-categorized because there were too few questions in some of the original categories, resulting in small cell sizes. The new categories were meaningful according to the literature.

- The next questions asked about the participant's belief of which study arm they were in and what led them to believe their response. The optional responses for study arm included

"0.5%," "2%," "not sure" and *"placebo."* Although the 2% arm participants were not included in the unblinding exercise because they had been unblinded previously, the 2% gel was given as an option because this question was around the participant's belief and some may not have understood that the discontinuation of the 2% arm meant that they were not on that arm. For the purpose of this analysis, the *"0.5%"* and *"2%"* were later categorized into *"active arm."* This question was dichotomized because the researcher wanted to understand whether or not they thought they were receiving placebo or active gel and the concentration was not relevant. The reasons for their belief included a five level response (e.g. *"appearance of the gel," "how the gel felt in my body," "information from study staff," "discussions with other MDP301 participants,"* and *"other, specify"*) that was later sub-categorized and post-coded into *"Characteristics of the gel"* (e.g. smell, appearance, etc.) *"Study related"* (e.g. was not on 2% arm, gel applicator box, study staff), *"No side effects"* and *"Random guess."* The *"other, specify"* responses were post-coded to fit into the new sub-categories. These responses were recoded and responses to 'other, specify' were post-coded and had listed reasons that were better suited to the new categories.

- The participant was then asked whether or not they disclosed their study participation to their partner and if yes, how their partner felt about using the gel. The participants' open-ended responses were post-coded into nine categories: *"No problem/ no partner opposition," "Liked/ supportive," "Did not like," "Partner opinion changed after using gel or learning more information," "Did not know how partner felt," "Partner did not understand," "Partner had no choice, "Partner persisted on condom usage"* and *"Partner questioned side effects."* The responses to this question were post-coded and recoded because there were limited responses in some of the original categories, resulting in small cell sizes.

- If the participant did not disclose their study participation to their partner, they were asked why not and their responses were post-coded into six categories: *"To avoid conflict/ partner opposition," "No reason," "Casual sex partner," "Partner does not believe in research," "Fear of no condom usage,"* and *"No partner."* The responses to this question were post-coded and later recoded since there were few responses in some of the original categories, resulting in small cell sizes.

- The participant was asked whether or not they wished to be contacted for future research. This was followed with an open-ended question asking "If yes, what were the benefits of participating in the previous study or why do you want to participate in upcoming studies?" These responses were post-coded into *"Reimbursement," "HIV/ STI Screening," "Social reasons," "Altruism,"* and *"other."*

2.7.2 Statistical analysis

Process evaluation: The process evaluation data was analysed in terms of the framework outlined in Table 1.0 in the data measurement section above. Indicators for recruitment, dose delivered, dose received and reach were analysed using descriptive statistics (e.g. counts).

Qualitative meeting reports and field notes were analysed using manual thematic analysis (no software was used). For the resources required for the dissemination plan, the unit costs and frequency of each activity were summed for all dissemination activities, including unblinding. From there, the dissemination cost per person reached was calculated.

Telephonic unblinding: All data was checked for completeness and Stata 10.0 was used to perform all quantitative analysis. Descriptive statistics were used to describe each variable. For the continuous variables, counts, medians and ranges were used to describe the data. For categorical

variable, frequencies were tabulated. Chi-square testing was used to test the association between the proportions of responses to the categorical variables in the bivariate analysis. A student's t-test was performed for the analysis of the socioeconomic status as it was the only continuous variable and allowed for the comparison of SES between two groups. For variables where there were fewer than 10 responses in some categories, a fisher's exact test was used.

If the p-value for the bivariate analysis was less than 0.2, the variable was included in the logistic regression. All candidate variables were then included in the base model and were then eliminated one by one until a parsimonious model was achieved where only the variables which explained the outcome remained. The results are presented as odds ratios with a 95% confidence interval and significance was set at 0.05%.

2.8 Ethics

This study including the process evaluation and the analysis of the unblinding data was approved by the Wits HREC, (Appendix 8, Reference No: M110482). Additionally, the unblinding questionnaire and telephone script was approved by Wits HREC in April 2010 as an addition to the MDP301 trial (Appendix 9, Reference No: 050810).

All participants in this study were at least 18 years of age. All participants gave verbal consent to participate in the unblinding call. All women who agreed to participate in the call were asked to confirm their identity giving their name, date of birth, address and the name of the last clinician or counsellor seen at the clinic. If a woman was not able to provide this information, the call was stopped. All data collected from the unblinding process is kept confidentially and stored electronically under password protection. Also, permission to utilize the MDP301results

dissemination and unblinding data was granted by the Principle Investigator of the MDP301trial (Appendix 10).

2.9 Summary of the chapter

This study included a process evaluation of the MDP301 dissemination plan and a cross-sectional survey design for the telephonic unblinding data. The study sites included Orange Farm and Soweto and the participants of the study included the MDP301 trial participants, the trial staff, CAB members and other key stakeholders. The process evaluation data was analysed through a framework which included seven components with clear indicators. The unblinding data was analysed using Stata 10.0. The study describes descriptive data and logistic regression for the variables associated with awareness of the trial results, one's belief of randomization allocation and partner disclosure of study participation. Ethical approval was obtained from the University of the Witwatersrand and permission to use the data was granted by the Principle Investigator of the MDP301 trial.

CHAPTER 3

RESULTS

3.1 Introduction

This chapter presents the main results of this study in terms of the study objectives. The results dissemination activities and the process of implementation are discussed through the process evaluation framework components described in the methods chapter. The individual telephonic results dissemination and unblinding questionnaire are described. Factors associated with awareness of the study results; beliefs of randomization allocation and partner disclosure of trial participation are explored.

3.2 Process evaluation

The results of each process evaluation component, including recruitment, dose delivered, dose received, reach, resources and fidelity, are reported below.

3.2.1 Recruitment to results dissemination activities

SMS was the primary method used to invite participants to the participant meetings and to SMS, call or visit the research clinic for more information about the results. At the time of the results dissemination, there were 986 (56.83%; n=1735) participant mobile phone numbers in the bulk SMS database. The percentage of SMS that were ‘sent confirmed’ ranged between 97.26 and 99.80%. The participant response rate (please call me or SMS reply) to the SMS sent was low and ranged between 0.20 (to find out study arm allocation) and 2.92% (to attend a results dissemination meeting).

Table 2: SMS sent recruiting participants to hear the trial results

Indicator: SMS sent to participants		No. of SMS Sent	No. of SMS Delivered	% (n=986)	No. of Replies	%
To invite them to participant meetings with phone number to call for more information	1	986	959	97.26	28	2.92
	2	986	967	98.07	19	1.96
	3	986	977	99.09	9	0.92
To invite them to call or visit the clinic for more information about the results	1	986	982	99.59	3	0.31
To invite them to SMS, call or visit the clinic if they wanted to learn their randomization allocation	1	986	984	99.80	2	0.20
	2	986	974	98.78	19	1.95
	3	986	984	99.80	3	0.30
	4	986	965	97.87	21	2.18

In a final attempt to invite participants to the participant meetings, 1051 calls were made and 448 (42.63%) participants verbally agreed to attend one of the six participant meetings. Posters in English and in local language (Appendix 11) inviting participants to call or SMS for more information about the results were also posted at various public locations in Soweto and Orange Farm. Also, in two weekly community radio shows, the presenters invited participants to the results dissemination meetings. There is no data available on how many people called, sent SMS or visited the research clinic as a result of the posters or the community radio programme.

Table 3: Calls made to participants recruiting them to attend dissemination meetings

Indicator	No. of calls made	No. of participants who answered and confirmed attendance	%
Calls made to invite Soweto participants to participant meetings	532	208	39.09
Calls made to invite Orange Farm participants to participant meetings	519	240	46.24
Total	1051	448	42.63

Each CAB member was recruited to attend the dissemination meetings via phone calls from the respective CLO for each site. There is no record of these recruitment calls. The research staff was invited to attend the results dissemination meeting via email and word of mouth. Again, there is no record of this recruitment.

3.2.2 Dissemination of trial results: dose delivered/ dose received

One SMS was sent to the trial participants about the actual trial result. Of the SMS sent, 99.49% were 'sent confirmed' and 5 (0.51%) of the participants replied.

Table 4: SMS sent with actual results

Indicator		No. of SMS sent	No. of SMS delivered	%	No. of replies	%
SMS sent to participants with actual results	1	986	981	99.49	5	0.51

There were a series of meetings held to disseminate the results to the research staff, the CAB members and the trial participants. There was a joint meeting held with both the Orange Farm and Soweto research staff where 96.55% of the staff attended and received the results. There were two CAB meetings held, one with each site CAB in Soweto and Orange Farm where 77.27% and 63.16% of the members attended. There were six meetings available for participants to attend, three at each site on three separate days immediately following the public release of the results. Of the 448 participants who had confirmed that they intended to attend one of the meetings, only 177 (39.51%) actually attended. Three Orange Farm participants attended two of the three Orange Farm results dissemination meetings.

Table 5: Results dissemination meetings

Indicator	Site	Meeting	No. of ppl invited/ confirmed	No. of ppl attended	% attended
Research staff results meeting	Orange Farm/ Soweto	1	29	28	96.55
CAB results meetings (2)	Soweto	1	22	17	77.27
	Orange Farm	1	19	12	63.16
Participant results meetings (6)	Soweto	1	163*	51	31.29
		2	30*	17	56.67
		3	15*	21	140.00
	Orange Farm	1	229*	63	27.51
		2	14*	11**	78.57
		3	7*	14	200.00
Total # of people reached through results meetings	-------	-----	518	231***	44.59

*Total # of participants who confirmed via phone that they would be attending the meeting.
**Of these 11 participants, three had also attended the first meeting.
*** With the 3 participants who attended more than one meeting, 231 people actually attended the results dissemination meetings.

The results were otherwise disseminated to stakeholders and the broader public via email, phone, a peer-reviewed journal and the internet. A general media briefing (on the status of the HIV prevention research field in South Africa) a few weeks prior to the results being released and the national press release resulted in community and commercial radio coverage, as well as a television interview and newspaper articles. The count data on dose delivered of each dissemination method is included in Table 6.0 below. There is no dose received data available for these dissemination activities.

Table 6: Dose delivered for all other dissemination activities

Indicator	Count
# of stakeholders recipients of email communication	27 sent (27 delivered)
# of community radio interviews about the results	3
# of commercial radio interviews about the results	3
# of phone calls made to stakeholders	4
# of publications in peer-reviewed journal	1
# of press releases posted on the internet	2
# of television interviews about the results	1
# of features in newspapers, magazines, other similar publications and media **in response to requests** for such articles	9
# of infomedia websites that provided link to research programme	1

3.2.3 Reach of actual trial results

While there are reach data for each dissemination activity, it was not possible to calculate the total number of people reached through all dissemination activities. For the dissemination meetings, 96.55% of research staff and 70.73% of CAB members were reached with the results while only 7.08% of the participants were reached via this activity. The bulk SMS with the results reached 39.36% the 2499 MDP301participants and the unblinding reached 24.14% of the 1707 participants who were eligible for unblinding. The total number of participants reached could not be calculated as some participants may have received the results through multiple sources and this overlap was not captured. With all data on record, approximately 31 stakeholders were reached with the results via phone or email. There was a face-to-face meeting with members of the Medicines Control Council (MCC) prior to the press embargo being lifted but there were no records of this meeting.

Table 7: People reached through each dissemination activity

Indicator	Total No. of ppl in group	No. of ppl reached	% reached
# of research staff reached with results via meeting	29	28	96.55
# of CAB members reached with results via meeting	41	29	70.73
# of participants reached with results via SMS	2499*	981	39.26
# of participants reached with results via meeting	2499*	177	7.08
# of participants reached with results via unblinding	1707**	412	24.14
# of stakeholders reached with results via phone	----	4	----
# of stakeholders reached with results via email	----	27	----

*Total # of participants (who may have heard about meetings via call, SMS or community radio).
**Total # of 0.5% and placebo arm participants with up-to-date locator information on file who were included for unblinding.

At the time of the results dissemination, there were 986 participant mobile phone numbers in the bulk SMS database. Of the 986 participants with mobile numbers on the database, 99.49% (981) received the results SMS (confirmed sent delivered).

All qualitative reception data from the staff, CAB and participant meetings are reported on in the sections below.

3.2.3.1 Study staff reception of trial results

The MDP301 study coordinator and clinicians explained the results to the MDP301 staff. The MDP301 staff entered the room excited and energetic yet the mood changed drastically once the results were described with staff looking bored and sad. They were disappointed with the results: *"I am very disappointed about the results. I worked on this trial for so many years hoping for a better result (Female, Soweto Staff)."* The staff responses to the results were similar to the response from the participants. Staff expressed the benefits that both the participants and the research staff received by being a part of the study:

> *"This is an achievement, a trial of this size in developing countries, and it is beneficial in the field of microbicides research as well as the communities. Many women received voluntary counselling and testing as well as treatment for STI and counselling on condom use. They also received regular medical examinations and care while in the trial. The research staff have acquired more skills than before through training and working in the trial."* (Staff member)

Despite the fact that staff had on-going comprehensive training about the possible outcomes of the trial, several staff required clarification about the efficacy of the PRO2000 gel (even after a presentation was given and visual aids were used): *"What was the level of efficacy of the MDP301 results?"* and *"So the rate of HIV infection of 4.5 per 100 women years in the 0.5% arm and 4.3 in the placebo arm means that the effectiveness is zero as they were not different?"* The clinicians had to explain again that there were the same number of seroconverters[8] in both the placebo and active arms of the trial.

[8] A seroconverter is someone who had a HIV-negative status and became HIV-positive while they were participating in the study.

The staff also had questions about other uses for the PRO2000 gel such as a lubricant, contraception or the prevention of STI. Although the secondary objectives of the MDP301 trial examined the effect of PRO2000 on STI acquisition, there was no effect. The message was reinforced that PRO2000 was not efficacious in preventing HIV or other STI.

3.2.3.2 CAB member reception of trial results

Prior to disseminating the results to the MDP301 participants, each CAB met to hear the results confidentially in preparation for the public dissemination. Each CAB meeting started with an overview of the trial which was followed by the results. The results were presented by one of the MDP301 clinicians while other MDP301 staff and WRHI communications staff were present to answer questions and to prepare the CAB members for the public reaction to the results.

While the Soweto CAB was disappointed with the results, the Orange Farm CAB members reacted more dramatically and actually required a few minutes to calm down before asking further questions. The Orange Farm CAB members commented: *"We need a minute, it is disappointing;" "I feel empty…our hopes were high;"* and *"Our hopes are dented."* Another member commented, *"We all felt so low, the morale was high when we came in because we expected good results. There is nothing that we can do; we just have to accept the results and pick up the pieces and move on."* Members from both the Orange Farm and Soweto CAB expressed confusion and disappointment that was created by the optimistic results of the HPTN035 study (as described in the background section above). One member said, *"You see we expected that since the HPTN results showed 30% effectiveness maybe MDP was going to show 60%."* Another member expressed similar disappointment stemmed by the HPTN results.

> *"Honestly my spirit went down after I heard that the gel cannot prevent HIV. I was hoping that because the HPTN results were promising therefore the MDP301 with many*

participants would show better results. We were expecting to gain from the participation of so many women from our community but now we are disappointed." (CAB member)

Several of the CAB members were concerned about the participants' reaction to the results. Others were concerned about participants' partners' reaction to the results. They questioned whether the participants and their partners would feel that they had been exposed to greater risks since the gel did not work.

"Are you ready to give news to participants because I think they had hope that the gel would work and they also participated fully as some had lost their loved ones to HIV; they wanted something that could prevent this illness. What strategies do you have to deal with the disappointment they may feel when they hear the results?" (CAB member)

All questions and concerns were responded to by the study clinician and supporting staff who explained that all participants went through the informed consent process. The communications staff then went through mock interviews with the CAB to prepare them for unplanned media interviews and questions from the public. These mock interviews included questions about community myths and rumours and how to respond to them as well as 'underdog' stories in the media. One CAB member commented that there is a rumour in the community that WRHI was paying people for their blood:

"On Monday I heard two women saying that women are being paid for selling their blood at Dr. Gwala[9] *surgery. So I decided to join them and told them that the information that they had was incorrect."* This CAB member then rehearsed a well thought out response to such a rumour to explain that this was not true.

[9] The MDP301 research clinic in Orange Farm was located in the building of a former surgeon. The building was referred to as the "Dr. Gwala surgery" building.

The CAB members also had positive feedback about how the MDP301 trial educated their respective communities about the research process and made research a more normal and familiar term in community households. CAB members also inquired about whether or not there were any new research studies taking place in their respective communities.

3.2.3.3 Participant reception of trial results

Approximately 7.08% (177) of the MDP301 participants attended one of the six participant dissemination meetings. Participants were asked if they had received and understood an SMS with the trial results. Most participants expressed that they had received the results by SMS but did not understand them.

While all of the participants expressed disappointment after hearing an explanation of the results, they were all well-versed in the research process and understood that MDP301 was a study. Several of the participants found other benefits to their participation, including knowing their HIV status, their health status (e.g. blood pressure, anaemia) and receiving general reproductive health education.

> *"This was not a waste of time as we have answered the question we were asking. Also, we benefited as we know our status and were checked and treated for different STI and diseases…"* (No identifying information available)

Each group (research staff, CAB, participant) also required some clarification of the results with extensive explanations about what it meant to have the same number of seroconverters in both the placebo and active arms of the study. Once the participants understood what this meant, there was a general concern about the safety of the participants who became HIV positive during the trial. There was obvious concern that these participants would be more upset and affected by the null results: *"What about those participants who got HIV while they were involved with the study?"* Another

CAB member commented, *"Won't the participants feel like they were exposed to greater risk since the gel did not work?"*

Some participants were interested to know whether the gel would be available as a lubricant for sexual pleasure. Others were interested to know if the gel was effective in preventing other STI and pregnancy. Again, it was explained that the gel was ineffective in preventing any other STI and was not tested for anything other than vaginally acquired HIV or other STI and therefore it would not be available for any use. One participant's reaction to the results was to blame herself and others for non-adherence to the study product: *"I think we have ourselves to blame as some of us were not honest to the study and did not use the gel as prescribed."*

Lastly, nearly all participant meetings concluded with a discussion about future HIV prevention research. This allowed the research staff to explain the next microbicide study, MTN VOICE 003.[10] The explanation of this new study led to discussions around the use of ARVs for prevention and possible challenges with this new research.

3.2.4 Resources: costing of the dissemination activities

A total cost of R76 788.38 was spent on the implementation of the MDP301 results dissemination plan. This amounts to R30.73 per MDP301 participant (n=2499).

[10] MTN VOICE 003 is a HIV prevention study looking at the use of oral ARV tablets and a microbicide containing ARVs in HIV-negative and sexually active women.

Table 8: Resources required for the implementation of the MDP301 results dissemination plan

Activity	Sub-activity expenses	Outcome	Unit	Cost per unit	Total Cost per activity
Slots on the weekly radio program	NA	7 slots aired	Cost per radio slot	Approximately R5250 per show	36 750.00
SMS to research staff, CAB members, trial participants	NA	11,018 SMS sent to 1114 people	Cost per SMS	R0.29 per SMS	3 195.22
CAB meetings	Venue	2 meetings held	Cost per venue rental	R450 per rental	900.00
	CAB member reimbursement	29 CAB members met	Cost per participant reimbursement	R50 per participant	1450.00
	Refreshments	Refreshments provided at each (2) CAB meeting	Total cost per refreshments per meeting	R300 per meeting	600.00
Participant meetings	Venue	6 meetings held	Cost per venue rental	R500 per rental	3000.00
	Participant reimbursement	177 participants projected	Cost per participant reimbursement	R15 per participant	2655.00
	Refreshments	Tea & Biscuits	Total cost of refreshments per meeting	R400 per meeting	2400.00
Research staff meeting	NA	1 meeting was held with research staff	NA	NA	0.00
Unblinding	Calls	366* calls made (average 20 minutes per call)	Total minutes for unblinding calls (7320 minutes)	0.65 per minute	4758.00
	Staff time	412 participants unblinded (average 20 minutes per unblinding session)	Total hours for unblinding calls and face-to-face sessions (137.33 hours)	153.50 per staff time hour	21080.16

Activity	Sub-activity expenses	Outcome	Unit	Cost per unit	Total Cost per activity
Meetings with key stakeholders	NA	Meetings were held with MCC, MEC and HREC after the results were released	NA	NA	0.00
Total					76 788.38

*All other participants were unblinded in-person at the research clinic.

3.2.5 Fidelity to the dissemination plan

The MDP301 dissemination plan (Appendix 1) included 24 specific activities including 10 before the results were released publicly and 14 activities after the results were released. Of these 24 activities, 21 (87.50%) were carried out as planned. Of the three (12.50%) activities which were not implemented as planned, Table 9 describes the deviations and explanations for the deviations.

Table 9: Deviations from the MDP301 results dissemination plan

Planned Activity	Outcome/ Deviation
A 'hotline' to be set up before the results were released.	The 'hotline' was never set up due to logistical complications. These included the process and cost implications expense of diverting calls from the general mobile phone line to the MDP301 administrator line and an unregistered SIM card with RICA[11].
Briefings to be conducted with key partners in each community after Christmas break.	There was a strategic decision not to conduct these briefings after the negative government reaction to the results in Zambia.
Regional multi-site meeting planned for February 2010 with key stakeholders.	This meeting never took place because the MDP301 site in Zambia faced extreme criticism from the Zambian government which would have major implications for the future of HIV prevention research in Zambia. Attention and media coverage that would have been generated by the regional meeting was deemed to be potentially detrimental.

[11] The Regulation of Interception of Communications and Provision of Communication-Related Information Act (RICA), requires compulsory registration of all SIM cards in use, and came into effect on 1 July 2009, only months before the MDP301 results were released.

3.3 Unblinding of trial participants

Among the 1707 MDP301 participants with up-to-date locator information on record at the time of the unblinding, 24.14% (412) were contacted for individualized results dissemination and unblinding. While there were originally 416 participants included in the unblinding database, the cleaning process reduced the analysable data to 412 unblinded participants as a result of missing identifiers or unblinding envelopes. Each participant who was contacted telephonically was given the option to come into the clinic for face-to-face unblinding; 46 (11%) of the unblinded participants chose this option. Each individual unblinding interview ranged between 10 and 30 minutes in duration. Of the 412 participants who were unblinded, Soweto had a greater response rate with 281 (68%) unblinded, while only 131 (32%) were from Orange Farm. The social and demographic characteristics of the participants are described below.

3.3.1 Socio-demographics and sexual history

Table 10 compares the demographics characteristics of those MDP301 participants who were unblinded and those who were not. Differences were noted in educational attainment and socioeconomic status. Participants who were unblinded were more likely to have completed high school ($p<0.001$). Fifty-one per cent of those who were unblinded lived in a municipal house while those who were not unblinded typically lived in a shack or a room. Those who were unblinded found it easier to obtain money if a person in their home became ill and needed to pay for treatment or medicine. There were no statistically significant differences in the employment status, religion or sexual history of participants who were unblinded and those who were not.

Table 10: Demographic characteristics of those who were unblinded and those who were not

Descriptive Variable	Not unblinded	%	Unblinded	%	p-value
Trial Site	n=2098		n=412		
Soweto	968	46.14	281	68.20	0.000
Orange Farm	1130	53.86	131	31.80	
Socio-demographic factors					
Age in years	n=2098		n=412		
18-24	1091	52.00	184	44.66	0.000
25-34	616	29.36	164	39.81	
35>	391	18.64	64	15.53	
Education Level	n=2094		n=412		
Completed high school	862	41.17	236	57.28	0.000
Employment Status	n=2086		n=412		
Employed	281	13.47	64	15.53	0.267
Religion	n=2098		n=412		
None	261	12.44	53	12.86	0.825
Christian	1775	84.60	349	84.71	
Other	62	2.96	10	2.43	
Housing Type	n=2086		n=412		
Private house	837	40.12	126	30.58	0.000
Municipal House	768	36.82	211	51.21	
Shack	409	19.61	51	12.38	
Room	72	3.45	24	5.83	
Ease Money	n=2097		n=412		
Easy	781	37.24	193	46.84	0.001
SES score (mean)	4.382409		4.805825		0.000
Sexual history at baseline factors					
Multiple partners	n=1771		n=381		
Yes	127	7.17	21	5.51	0.246
Condom use at last sex act	n=2071		n=411		
Yes	1471	71.03	286	69.59	0.678
STI present at lab screening	n=1984		n=393		
Yes	1488	75.00	285	72.52	0.302

Nearly half (44.66%) of participants who were unblinded were between the ages of 18-34. Approximately 84% of the unblinded participants were not employed and labelled themselves as Christian.

3.3.2 Awareness of study results

Approximately half (55.31%; n=224) of the participants who were unblinded had previously heard the MDP301 trial results. The results were heard most commonly (51%) through planned dissemination activities (e.g. radio, phone call from trial staff, participant meetings).

Table 11: Participant awareness of study results

Participant awareness	n	%
Heard the results	n=405	
Yes	224	55.31
No	181	44.69
Source of hearing results	n=405	
Word of mouth	16	3.95
Dissemination strategy	208	51.36

3.3.2.1 Factors associated with awareness of study results

Table 12 shows the demographic factors associated with awareness of the trial results. Among those who had heard the results, there was a significant association with age and education level. Participants in the 18-24 and 25-34 age categories were more likely to have heard the results (p=0.062). Participants who had completed high school were also more likely to have heard the results (p=0.001). Employment status, religion, condom use at last sex act and history of STI were not associated with having heard the results.

Table 12: Factors associated with awareness of trial results (p-values were calculated with Pearson's chi unless otherwise specified)

Explanatory Variable	Outcome Did not hear the results	%	Variable Heard the results	%	p-value
Trial Site	n=181		n=224		
Soweto	116	64.09	159	70.98	0.140
Orange Farm	65	35.91	65	29.02	
Age in years	n=181		n=224		
18-24	87	48.07	95	42.41	0.062
25-34	61	33.70	100	44.64	
35>	33	18.23	29	12.95	
Education Level	n=181		n=224		
Completed high school	87	48.07	145	64.73	0.001
Employment Status	n=181		n=224		
Employed	28	15.47	36	16.07	0.869
Religion	n=181		n=224		
None	24	13.26	29	12.95	--------*
Christian	153	84.53	189	84.38	
Other	4	2.21	6	2.68	
Housing Type	n=181		n=224		
Private house	62	34.25	65	29.02	0.349*
Municipal House	89	49.17	115	51.34	
Shack	23	12.71	27	12.05	
Room	7	3.87	17	7.59	

Explanatory Variable	Outcome Did not hear the results	%	Variable Heard the results	%	p-value
Ease Money	n=181		n=223		
Easy	74	40.88	112	50.00	0.063*
SES score (Mean)	4.701657		4.848214		0.319
Sexual history at baseline factors					
Multiple partners	n=164		n=210		
Yes	12	7.32	9	4.29	0.259*
Condom use at last sex act	n=181		n=223		
Yes	127	70.17	154	69.06	0.810
STI present at lab screening					
Yes	125	72.25	153	71.83	0.927

*These p-values were calculated by a Fisher's exact test.

Table 13 shows the results of a multivariate model of factors that predict awareness of trial results. Women aged between 25 and 34 years had increased odds of 1.71 and those who had completed high school were nearly twice as likely to be aware of the trial results (OR 2.06; 95% CI: 1.31-3.24).

Table 13: Logistic regression model for factors associated with awareness of results

		Adjusted		
Explanatory variable	Unadjusted OR	OR	95% CI	p-value
Clinic				
Soweto	*Ref*	*Ref*	*ref*	*ref*
Orange Farm	0.73	0.87	0.54-1.41	0.573
Age				
18-24	*Ref*	*Ref*	*ref*	*ref*
25-34	1.50	1.71	1.08-2.72	0.023
35>	0.80	1.07	0.56-2.04	0.842
Education level				
Completed high school	1.98	2.06	1.31-3.24	0.002
Did not complete high school	*Ref*	*Ref*	*ref*	*Ref*
Ease Money				
Easy	*Ref*	*Ref*	*ref*	*ref*
Difficult	0.70	0.95	0.60-1.48	0.807
Multiple Partners				
Yes	0.57	0.49	0.19-1.25	0.137
No	*Ref*	*Ref*	*ref*	*ref*

3.3.3 Women's belief of study arm

Of the 412 women who were unblinded, 404 (98.06%) wanted to know whether they had received the placebo gel or active gel. Of these women, 70.79% (286) were not sure which study arm they were in, while 19.31% (78) believed they received the active gel (0.5% or 2%) and 9.90% (40) believed they had received the placebo gel. When asked why they believed they were in that arm, 26.98% (109[12]) of the participants gave an explanation. Of these, 42.20% (46) attributed their belief to characteristics of the gel while 25.69% (28) made assumptions based on study related information that they had heard or received. Characteristics of the gel that influenced women to believe that they were receiving the active gel included: *'from the smell of the gel'* and *'gel smelled like it was medicated.'* Study related information that influenced the beliefs of study arm allocation included: *'because I was not on the 2% arm,' 'I think that is what they told me at the clinic'* (However, all clinic staff was blinded in during the trial), and *'It was written on the carton.'*

Table 14: Women's belief of study arm and why

Study arm belief	n	%
Gel type	n=404	
0.5% Gel	59	14.60
2% Gel	19	4.70
Placebo	40	9.90
Not sure	286	70.79
Why belief	n=109	
Characteristics of the gel	46	42.20
Study related	28	25.69
No side effects	12	11.01
Random guess	23	21.10

As seen in Table 15 below, there were no statistically significant factors associated with the women's belief of their study arm.

[12] Nine of the 118 participants who guessed their randomization arm did not provide a response when asked why they believed they were in that arm.

Table 15: Factors associated with women's belief of study arm (p-values were calculated using a Pearson's chi unless otherwise specified)

	Gel Type						
Explanatory Variable	**Active Gel**	**%**	**Not Sure**	**%**	**Placebo**	**%**	**p-value**
Socio-demographic factors							
Age in years	n=78		n=286		n=40		
18-24	36	46.15	126	44.06	20	50.00	0.441*
25-34	35	44.87	111	38.81	15	37.50	
35>	7	8.97	49	17.13	5	12.50	
Education Level	n=78		n=286		n=40		0.675
Completed high school	48	61.54	160	55.94	23	57.50	
Employment Status	n=78		n=286		n=40		
Employed	13	16.67	45	15.73	6	15.00	0.975*
Religion	n=78		n=286		n=40		
None	11	14.10	36	12.59	6	15.00	0.787*
Christian	64	82.05	244	85.31	33	82.50	
Other	3	3.85	6	2.10	1	2.50	
Housing Type	n=78		n=286		n=40		
Private house	19	24.36	98	34.27	10	25.00	0.608*
Municipal House	44	56.41	139	48.60	21	52.50	
Shack	11	14.10	33	11.54	6	15.00	
Room	4	5.13	16	5.59	3	7.50	
Ease Money	n=77		n=286		n=40		
Easy	44	56.41	126	44.06	17	42.50	0.072
Sexual history at baseline factors							
Multiple partners	n=78		n=261		n=35		0.363*
Yes	2	2.56	18	6.90	1	2.86	
Condom use at last sex act	n=78		n=285		n=40		
Yes	56	71.79	194	68.07	30	75.00	0.595
STI present at lab screening	n=75		n=270		n=40		
Yes	54	72.00	196	72.59	27	67.50	0.799

*These p-values were calculated by a Fisher's exact test.

3.3.4 Participant disclosure of trial participation to their partner

Of the 412 women who were contacted telephonically, 362 (87.86%) had disclosed their study participation to their partner. As seen in Table 16 below, Christian participants were more likely to disclose their participation to their partner (p= 0.003).

Table 16: Factors associated with partner disclosure of trial participation (p-values were calculated using Pearson's chi unless otherwise specified)

Explanatory Variable	Outcome Did not disclose	%	Variable Disclosed	%	p-value
Socio-demographic factors					
Age in years	n=35		n=362		
18-24	16	45.71	163	45.03	0.888*
25-34	13	37.14	145	40.06	
35>	6	17.14	54	14.92	
Education Level	n=35		n=362		
Completed high school	23	65.71	203	56.08	0.272
Employment Status	n=35		n=362		
Employed	2	5.71	59	16.30	0.138*
Religion	n=35		n=362		
None	9	25.71	44	12.15	0.004*
Christian	23	65.71	311	85.91	
Other	3	8.57	7	1.93	
Housing Type	n=35		n=362		
Private house	18	51.43	106	29.28	0.062*
Municipal House	13	37.14	188	51.93	
Shack	2	5.71	47	12.98	
Room	2	5.71	21	5.80	
Ease Money	n=35		n=362		
Easy	18	51.43	165	45.58	0.772
Sexual history at baseline factors					
Multiple partners	n=28		n=340		
Yes	2	7.14	19	5.59	0.668*
Condom use at last sex act	n=34		n=362		
Yes	24	70.59	254	70.17	0.959
STI present at lab screening	n=32		n=346		
Yes	22	68.75	251	72.54	0.647

*These p-values were calculated by a Fisher's exact test.

The multivariate model (Table 17) shows that women who identified as Christian and lived in a municipal house were nearly three times more likely to disclose their study participation to partners. The overall model was marginally significant (p=0.0734).

Table 17: Logistic regression for factors associated with partner disclosure

Explanatory variable	Unadjusted OR	Adjusted OR	95% CI	p-value
Employment Status				
Employed	*Ref*	*Ref*	*ref*	*Ref*
Unemployed	0.31	0.34	0 .08 - 1.47	0.149
Religion				
None	*Ref*	*Ref*	*ref*	*Ref*
Christian	2.77	2.65	1.19 - 6.18	0.024
Other	0.48	0.66	0.13 - 3.21	0.605
Housing Type				
Private house	*Ref*	*ref*	*ref*	*Ref*
Municipal House	2.46	2.82	1.05 - 4.95	0.036
Shack	3.99	3.29	0.72 – 15.06	0.125
Room	1.78	1.52	0.32 – 7.21	0.602

If the participant had disclosed their study participation to their partner, they were asked how their partner felt about their participation. The responses are categorized below in Table 18 below. While most partners (n=201) were reported to have no problem with women participating in the study, there were some (n=46) who were not supportive.

Table 18: Partner opinions about trial participation

Category	No. of participants	% of participants (n=362*)
No problem/ no opposition/ partner ok with gel	201	55.52
Liked/ supportive	83	22.93
Did not like	46	12.71
Partner changed opinion after using gel and/or learning more	15	4.14
Partner persisted with using condom	7	1.93
Did not know how partner felt	4	1.10
Partner did not understand	3	0.83
Partner questioned side effects (e.g. thrush)	3	0.83
Partner had no choice	2	0.55

*Total number of participants who disclosed their trial participation to their partner.

For those who did not disclose their trial participation to their partner(s), they were asked why they did not disclose. Their reasons given are categorized in Table 19 below.

Table 19: Reasons for not disclosing trial participation to partner

Category	No. of participants	% of participants (n=35*)
To avoid conflict/ partner opposition	17	48.57
No reason	8	22.86
Partner does not believe in research	3	8.57
Casual sex partner	3	8.57
Fear of no condoms	1	2.86
No partner	1	2.86

*Total number of participants who clearly stated that they did not disclose their participation to their partner

3.3.5 General responses from participants

At the beginning of each unblinding call, participants were asked if they had any questions. Of the 412 participants who were contacted, 33 had questions which are categorized in Table 20 below. Eleven participants wanted more information about the trial results while five inquired about whether or not there were any new studies for them to take part in. Four participants wanted to know if the MDP301 trial was still going on. Lastly, five participants asked "other" questions. For example: 'Other' questions and comments included: *"I'm not happy that I did not receive a t-shirt and cap."*

Table 20: Participant question themes

Category	No. of times question asked	% of times asked (n=33*)
Results	11	33.33
New study	5	15.15
Is MDP301 still going on?	4	12.12
Is the gel available	3	9.09
Health care/ screening	3	9.09
Arm	2	6.06
Other	5	15.15

* Total number of questions asked.

3.4 Summary of the chapter

SMS, calls, posters and community radio were the methods used to recruit participants to the participant meetings and to SMS, call or visit the research clinic for the results and to learn their

randomization allocation. Despite these efforts, the response rate in SMS replies, participant meeting attendance and unblinding was low. While the results were delivered to different stakeholder groups through multiple activities, there was no data collected on dose received. Also, the data on the total number of participants reached through dissemination activities was unclear considering that some participants may have received a SMS, attended a meeting and have been unblinded. Of the planned dissemination activities, 87.50% were implemented as planned.

Of those who were unblinded, 55% had previously heard the results, primarily through planned dissemination activities and 88% had disclosed their trial participation to their partner at the time. Of those who disclosed their participation to their partner, their partners tended to have no problem with or were supportive of their trial participation. The women who did not disclose their participation to their partners chose not to, mostly to avoid conflict with their partner.

CHAPTER 4

DISCUSSION

4.1 Introduction

This study aimed to evaluate the dissemination process to determine whether the targets of the MDP301 results dissemination plan were reached, how the results were received and to determine the resources required to implement the MDP301 dissemination plan. Lastly, the study aimed to assess the feasibility and additional benefit of the telephonic unblinding as part of the broader dissemination plan.

4.2 MDP301 results dissemination: What have we learned from the process evaluation?

Overall, 87.50% of the dissemination plan was implemented as per the original plan and all stakeholder groups were reached. The MDP301 results dissemination plan included a comprehensive strategy to deliver the results to the different stakeholder groups through multiple methods and channels. It was apparent that two-way, interpersonal communication or a combination of channels that included interpersonal communication was more effective in reaching the specific target groups. It allowed for dialogue on the results ensuring that the relevant stakeholders understood them clearly.

This dialogue was especially important for the null findings of the MDP301 trial to ensure that the results were fully understood and not misinterpreted. Though this study does not document the MDP301 Zambia site results dissemination activities, the public and negative Zambian government reaction to the MDP301 results demonstrates a misinterpretation of the results which had a catastrophic outcome for the country [63]. Upon learning the results, the Ministry of Health banned all microbicide clinical trials in Zambia and further reports in the media printed inaccurate information about the MDP301 trial, including that it was ‘unethical’ [63-65]. This was the primary

reason for cancelling the multi-site meeting that was part of the original WRHI MDP301 results dissemination plan.

This exemplifies the imperative to create an enabling environment for future HIV prevention and microbicide research by building a positive and transparent relationship between the researchers and policy makers, research communities and the trial participants. Having learned from the previous microbicide history in South Africa, the WRHI research team understood that the results needed to be communicated in a more personal and proactive way (via meeting, phone or email) in addition to the broader dissemination channels, to key stakeholders and actors in the policy to practice interface, such as the MCC, HREC, MEC and research sponsors [10, 27]. Although there was no systematic documentation of the stakeholders' reaction to, or acceptability of, receiving the results in this manner, there was a general sentiment of appreciation for receiving the results before the results were released publicly.

At the local stakeholder level, and as demonstrated by the rumours reported by CAB members during the dissemination meetings, transparency is required to mitigate the on-going community suspicion around research. This is especially important in the South African research context where the apartheid regime left a legacy of mistrust with evidence of unethical research [10]. Additionally, due to the poor education system in some areas of South Africa, science knowledge is limited [66]. This limited knowledge of scientific principles can increase suspicion about research. The dramatic reactions to the results by the research staff and CAB members indicate the importance of on-going community-based activities using both mass media and interpersonal communication to increase research literacy around trial outcomes in future studies. The CAB and participants are members of the community and as such are influenced by the beliefs and social norms of the community in which they live. This was and is the primary reason for the weekly

WRHI community radio programme, upon which the results were disseminated to the broader research communities.

Despite the multiple channels used to deliver the results to the trial participants, the reach of these efforts was suboptimal and unclear. From the researcher perspective, it is important to understand the reach and reception of the various dissemination activities to better understand the value and benefit of each activity for future dissemination research. SMS was the best method to deliver the results to every participant with an up-to-date phone number on the database immediately upon the press release embargo being lifted. While it was a useful tool for delivering the results, it was not an optimal method for allowing interpersonal, two-way communication between the participants and study staff.

During the informal interviews with participants at the dissemination meetings, it was clearly expressed that while the participants had received the results, they did not necessarily understand what they meant until they came to the face-to-face meeting. Additionally, SMS allows for generating a message with very few characters (usually 160). Results needed to be abbreviated and shortened and detailed explanations are not possible. Even though there was an expressed need for further explanation of the results by those who attended the dissemination meetings, there was a low response rate (1.3%) to the results SMS that was sent. This indicates that SMS should be used in combination with other dissemination methods whenever possible. Although a phone line was available and advertised via poster, community radio and SMS for participants to call for more information, there were few calls. The low number of SMS responses and phone calls may be attributed to the cost barrier which is especially present in this research setting where there is a generally low SES [67]. Aside from the cost barrier, contact by mobile phones is difficult in South Africa where people often have more than one phone or may share their phones with friends, family

or partners. This may have led to the fact that the participant phone number database was not up-to-date and/or the participant may have changed their phone number since they exited the study.

Though group dissemination of results has been recommended by others, only 7.08% of the MDP301 participants actually attended these meetings [27]. In consideration of other researchers' suggestions to have more than one meeting available for participants to attend, there were three meeting dates available at each site [27]. Despite this effort, the attendance at the MDP301 participant meetings was still low. This may have been partly attributed to the time of year, as the results were made available just before the December holidays; a time when the majority of South Africans travel to their home land. The low turnout to the participant meetings and the low response rate to the SMS may also be ascribed to the futile research findings of the MDP301 trial which could have led to participant apathy [21, 22, 25]. If there was a positive result, there may have been more interest from the participants and the community to understand the results and some urgency to know which study arm they were randomised to [21]. The low response rate to dissemination activities indicate that while there were high retention rates of participants during the trial, there is a need to maintain contact and actively follow-up with participants from the time they exit the study to the time that the trial results are released [30]. For the MDP301 trial, some women had exited the study one to two years prior to the results dissemination. SMS may be considered as one method to remain in contact with trial participants and to invite them to site meetings or events during this lull of research activity.

4.3 Resources required for the implementation of a results dissemination plan

Other dissemination studies have cited cost and time involved as perceived barriers to individualised results dissemination and rather opted for group or media dissemination efforts [12, 22]. Such studies have recommended that future studies assess the cost of dissemination activities,

including individual unblinding. The implementation of the MDP301 results dissemination plan, including telephonic unblinding, demonstrates that the cost is relatively small, at less than ZAR 32 per participant, in the context of RCT budgets which usually cost millions of dollars [27].

Although staff time was the largest expense required for the unblinding activity, the cost was curtailed by having one person do the unblinding over an extended period of time rather than employing many people to do the unblinding simultaneously. Also, this provided an opportunity to keep a MDP301 staff member employed during the lull between the MDP301 closure and other studies commencing. While SMS was successful in reaching large numbers and the cost was fairly low, it is important for future researchers to ensure that SMS is only the first step in communicating the results and that follow-on activities are in-place or available to ensure that the SMS message is fully understood. It is also important to consider including the cost of participant sent SMS in the study budget which may increase the overall cost of dissemination activities and potentially improve participant engagement with the trial results. Participants benefitted from the unblinding calls and the meetings where there was an opportunity to have a dialogue with study staff about the research results.

4.4 Unblinding

4.4.1 Demographics of unblinded participants and awareness of study results

Descriptive analysis of the study cohort showed considerable differences in the demographic variables of those who were unblinded and those who were not. As found in other studies (based in the United States and Europe), the majority of participants accepted to be unblinded telephonically (89%), while only 11% opted for face-to-face unblinding [68]. The participants who were unblinded were more educated and had a higher socioeconomic status. This suggests that those participants who were unblinded may have been those participants who were already well-informed and more

likely to have heard the results, while those participants who were more vulnerable (due to their low SES and low education level) were less likely to be connected with such information. For example, a participant with a lower SES may not have had a cell phone or may have lived in a shack where they were less likely to own a radio (where they could have heard the results or learned about the unblinding calls).

Of the 24.14% of participants (n= 412) who were unblinded, 55% were aware of the MDP301 results and had most commonly heard through planned dissemination activities. A study that evaluated the effectiveness of a communications plan for an RCT looking at Huntington disease also found that the majority of participants had heard the trial results through planned dissemination activities [19]. While it was only a very small number of women (4%) who heard the trial results through word of mouth, this shows that people were talking about results. Women from Soweto between the ages of 18-34 and who had completed high school were more likely to have heard the results. Similarly, another study that assessed whether or not participants wanted to receive null trial results found that those who chose to learn the results were more educated than those who were not [21]. In the South African context, this age group included women who were born or raised in the post-apartheid era and may have had different views of research than those who lived through or remember the apartheid regime.

4.4.2 Belief around randomization allocation

Of the women who were unblinded, the large majority were “not sure” whether they had received the active gel or the placebo gel. While the “not sure” response may suggest that blinding was maintained in the trial, it may not necessarily represent successful blinding [6]. Findings from other

studies have suggested that "forced guesses" rather than giving a "not sure" option may be justified and useful in future unblinding exercises [6].[13]

As found in other unblinding studies, women who guessed that they had been randomized to receive "active" or "placebo," stated that the number one reason for their guess was the physical characteristics of the study product. These characteristics included smell, taste or feeling of the gel itself. Though, it was not clearly understood from the participant whether these physical characteristics were based on knowledge or assumption [69, 70].

The other reasons for randomization arm belief were study related including that the product they received had no side effects (i.e. they assumed no side effects meant that they were receiving the placebo gel). This is similar to other unblinding studies which found that study product side effects may act as unblinding factors [13]. This is otherwise known as the "uncontrolled placebo effect" [13]. Meanwhile, some of the participants were certain that the randomization allocation (e.g. "Placebo" or "PRO2000") was specified on the study product packaging. For MDP301 all study products were in the same packaging which said "Active gel OR placebo." A similar result was found in a study that was looking at the use of acyclovir/ placebo for the prevention of HIV acquisition [10]. During the unblinding interviews in the result dissemination phase of this study, participants were certain that the drug bottle was labelled "acyclovir" when actually it was labelled "acyclovir/ placebo 400mg" [10].

All three reasons for women's belief around their randomization allocation demonstrate that trial participants do try to guess their randomization allocation while participating in the study. This is important for the researcher to note in order to ensure continuous education and counselling around

[13] This study was not aimed at measuring the success of blinding in the trial but rather to explore women's perceptions in relation to other variables.

the study blinding. It is also important for product development in future clinical trials to ensure that the placebo and active products do not have any side effects and share all of the same characteristics, especially to ensure that blinding is maintained [6, 10].

4.4.3 Partner disclosure

There was no association between partner disclosure of trial participation and the participant's belief around randomization allocation. The analysis of other factors associated with partner disclosure, found that if a participant self-identified as a Christian and lived in a municipal house; she was more likely to have disclosed her trial participation to her partner. However, the questionnaire did not include questions about the participant's partner. There may be partner or relationship characteristics that influenced disclosure of trial participation, such as who is the breadwinner or home owner. The responses to the open-ended items about why women did or did not disclose could inform the development of future questionnaires used to collect data during the unblinding process.

4.4.4 Benefit of unblinding for the research community

The low response rate to SMS (and the lack of understanding of the results via SMS), the invitation to phone for results and the participant meetings, made the individualised results dissemination and unblinding calls (and visits) even more important. The telephonic unblinding activity allowed the research team to have a more personal interaction with the trial participant where a better understanding of the woman's beliefs and practices around her trial participation was gained. Unblinding provided an opportunity to collect data to investigate women's experiences of participating in a clinical trial, which can inform future HIV prevention trials. For example, understanding which socio-demographic factors were associated with awareness and comprehension of trial results could inform a tailored dissemination plan where activities are

segmented according to age group or education level. It also allowed the researchers to assess the reach of the other dissemination activities.

Participants need to hear the results repeatedly and in a personalized manner before they truly understand the implications of the results. During these calls, the researchers were also able to pave the way for future studies and gained buy-in from the participants. Other studies have also found that by communicating the study results on a personal level, the participant is more likely to advise others to join future research and "may bolster public opinion of investigators and the research they conduct" (pg. 0719) [27].

4.5 Diffusion and communications theory: a convergence model for RCT results dissemination

There are several examples in the literature where the diffusion of effective interventions or innovations are retrospectively described through the lens of communication theory, yet there are hardly any examples in the literature where a diffusion plan is prospectively developed based on theory [45, 48]. This may be due in part to the fact that the dissemination or exchange of information, more specifically about clinical trial results, is ultimately about communication which necessitates dialogue between the researcher and the various target groups. Yet the diffusion model (a product of the diffusion of innovations theory) is limited as it only describes the vertical transfer of information with the assumption that information provides knowledge which would change one's attitude and in turn change their practice or desired behaviour. The MDP301 results dissemination process evaluation indicates the need for a participatory model which describes a horizontal process of information exchange that involves participation and dialogue through individual or group interaction [71].

The qualitative data from the participant meetings, where participants stated that they did receive the SMS communication, but still did not understand the results, demonstrates that diffusion strategies were not enough and that participants needed to engage and have dialogue about the results. Null findings where a product is found to be safe, but not efficacious are difficult to understand without dialogue and the participants seemed to understand better when they had the opportunity to ask questions. The qualitative data also suggests that the participants understood the results better than the CAB members, which may be due to their experience in the research process. Participants had the opportunity to engage with and discuss the research process at each monthly trial visit, while CAB members were on the outside of the trial and only met monthly to receive trial updates. These findings suggest that a convergence model, which includes the diffusion model with participatory or dialogic activities, for trial results dissemination may be the best approach, especially in the South African context where it is important to continuously build an enabling environment for future research [71].

4.6 Limitations

One of the greatest limitations of this study was that the broader stakeholder, local stakeholder and participant acceptability or experience of the different dissemination activities, including the telephonic unblinding, was not measured. There were no questions that assessed how the stakeholder or participant felt about the dissemination activities and how hearing the results benefited their lives or views towards clinical trial research.

Despite all efforts made to reach the target groups, it was not possible to thoroughly measure the dose received by each group. For example, there were no means to measure dose received or reach through the broader public dissemination channels, including the peer-reviewed journal publication,

press release, radio and television interviews and newspaper articles. This was due, in part, to a lack of monitoring of these dissemination efforts. While using mass media can reach the intended broader audience, there is an element of uncertainty about whether the relevant people were exposed to the key study results.

A limitation of the qualitative findings was that there was no identifying information about the participants (e.g. gender, age, etc.). We are uncertain about the range of voices and opinions reflected in the qualitative data, yet we know that the qualitative data only captures the opinions of those who made the effort to attend the meetings and not those who were less likely to be connected and aware of the results.

Also, the unblinding questionnaire was created and implemented without an analysis plan in place and the objectives of this study were retrospectively fitted for the dissemination plan and unblinding process. As mentioned previously, the lapse in time between women exiting the study and the results being released, as well as the lapse in time between results being released and the unblinding exercise were also a major limitation in this study as they resulted in participants being lost to follow-up.

Finally, the demographic data on those women who were unblinded and those who were not suggest that the women who were unblinded were more likely to be those who are already engaged and well informed of news and current affairs. They also seemed like those who were more likely to have a phone or ability to obtain the results or contact from the researchers. This indicates a limitation of the results dissemination plan in reaching more vulnerable women who are at a greater risk for HIV. In future trials, we must work harder to reach these women who are less likely to be engaged or informed.

4.7 Summary of the chapter

The analysis of the MDP301 dissemination plan and unblinding showed that data from this study was similar to that of other dissemination and unblinding studies. The findings emphasize the value of providing on-going research literacy training to research communities and trial participants. Individualized results dissemination and unblinding is necessary and feasible to ensure that participants fully understand the implications of the research results and to pave the way for future clinical trials.

CHAPTER 5

CONCLUSION & RECOMMENDATIONS

This chapter summarises the key findings and discusses possible recommendations.

5.1 Conclusions

The results of this study demonstrate that the MDP301 dissemination plan was implemented successfully with minor deviations. The dissemination plan was feasible in terms of cost and time required for implementation. Despite the active, multi-level, multi-method dissemination process that was implemented for the MDP301 results, the reach of the dissemination activities was suboptimal and the dose received was unclear. Only about half of the participants were reached but not all participants who were reached actually understood the results without dialogue. While CAB may be a good mechanism or 'professional communicator' for trial results, it is still limited and the extent to which CAB members initiate dialogue within the community needs to be more structured and measurable through clear indicators [72]. There is also a need for continued research literacy enhancement within the CAB and the community more broadly. This highlights the added value of the telephonic unblinding and personalised results dissemination.

As recommended in the 2011 UNAIDS/AVAC GPP guidelines, future biomedical HIV prevention trials should include unblinding as part of the broader dissemination plan[1]. The MDP301 unblinding experience has proven that telephonic unblinding is feasible in the African setting and adds additional benefit (to the researcher) by building trust and research literacy, ensuring that all participants fully understood the results. Telephonic unblinding also allowed the researcher to pave a smooth and transparent path for future trials. In addition, talking with participants provided an opportunity to get feedback about their experiences of participating in the trial, which may improve research management and conduct in future trials.

5.2 Recommendations

5.2.1 Current & future HIV prevention trials

Future HIV prevention researchers must ensure that a trial communications plan incorporates the on-going communication with the trial participant between the time she/ he finishes the study and the time that the results are released. This should go beyond keeping up-to-date locator information on file, but rather sustaining meaningful engagement with the participants around their health, sexual behaviour and research more generally. In addition, both national and local level stakeholders require continuous research literacy training to bolster their support for and understanding of HIV prevention research. Similarly, researchers require on-going training on both vernal and interpersonal communication skills to ensure quality communication with both participant and non-participant stakeholders.

Future HIV prevention trial results dissemination plans should be flexible to accommodate the different potential result scenarios (e.g. product is futile vs. efficacious). The result of the study may have implications on how the researcher prioritizes when (and how) the different stakeholder groups are informed. For example, policy makers and regulatory authorities should be prioritized when the result is negative or futile to ensure that they fully understand what effect this may have on the participant, the research community, future trials and policy. Similarly, the participant may be prioritized if the result is positive or the product is found to be efficacious as it is an ethical imperative to make the product affordable and accessible to this group and their community [1].

Current and future studies should include dissemination activities in their budget cost per trial participant to ensure that adequate resources are allocated for a broad range of dissemination activities. Also, the next version of the Good Participatory Practice guidelines should further

elaborate on the practical steps required for planning and implementing a results dissemination plan which includes unblinding in low resource settings.

5.2.2 Practical lessons learnt

A process evaluation framework should be designed when the results dissemination plan is being written with clear objectives and indicators of success. Better monitoring systems should be set up before the dissemination process commences to ensure that all indicators are captured. This will ensure that there is comprehensive data available to measure dose delivered, reach and reception of every dissemination method, including those used to reach the broader public.

Two-way, personalized communication is the most optimal method for results dissemination to both key stakeholders and trial participants. While some methods like SMS are useful, it is best to use a combination of methods, including interpersonal communication to ensure that target groups receive *and* understand trial results. Although the 2011 GPP Guidelines recommend that there is a results dissemination plan in place at the protocol development stage which includes a plan for unblinding, the next version of the guidelines should include more detailed and practical recommendations such as those provided from this study.

5.2.3 Telephonic unblinding

Telephonic unblinding is recommended as a feasible and affordable method in the South African context. Future telephonic unblinding scripts should be drafted with clear objectives for what information is useful to obtain for *that* study. It is recommended that unblinding scripts include more questions around adherence and randomization allocation belief; partner disclosure and

factors associated with partner disclosure; and participant acceptability of learning the results and randomization allocation telephonically.

5.2.4 Further research needed

Further research is required to better understand the stakeholder acceptability of receiving the results by phone, email or meeting and the participant acceptability and experience of telephonic unblinding in this setting. More research is needed to understand the benefit of proactively applying constructs from behavioural and communications theory to the design of a results dissemination plan. This may assist with understanding how to reach participants who are often from marginalized populations.

References

1. UNAIDS/AVAC, *Good Participatory Practice Guidelines for Biomedical HIV Prevention Trials* 2011, UNAIDS: Geneva.
2. Saunders, R.P., Evans, M.H., Joshi, P., *Developing a Process- Evaluation Plan for Assessing Health Promotion Program Implementation: A How-To Guide.* Health Promotion Practice, 2005. **6**(134): p. 134-147.
3. Linnan, L., Steckler, A., *Process Evaluation for Public Health Interventions and Research: An Overview*, in *Process Evaluation for Public Health Interventions and Research*, A. Steckler, Linnan, L., Editor. 2002, Jossey-Bass: San Francisco. p. 1-23.
4. Sibbald, B. and M. Roland, *Understanding controlled trials. Why are randomised controlled trials important?* BMJ, 1998. **316**(7126): p. 201.
5. Schulz, K.F. and D.A. Grimes, *Blinding in randomised trials: hiding who got what.* Lancet, 2002. **359**(9307): p. 696-700.
6. Rees, J.R., et al., *Changes in beliefs identify unblinding in randomized controlled trials: a method to meet CONSORT guidelines.* Contemp Clin Trials, 2005. **26**(1): p. 25-37.
7. South African National AIDS Council, *South Africa HIV Epidemic, Response and Policy Synthesis- Getting to Success: Improving HIV Prevention Efforts in South Africa*, T.W.B. UNAIDS, Human Science Research Council, Health and Development Africa, Centre for the Governance of AIDS in Africa and the South African Centre of Epidemiological and Modelling and Analysis, Editors. 2011.
8. Orner, P., et al., *Challenges to microbicide introduction in South Africa.* Soc Sci Med, 2006. **63**(4): p. 968-78.
9. Ramjee, G., A. Kamali, and S. McCormack, *The last decade of microbicide clinical trials in Africa: from hypothesis to facts.* Aids, 2010. **24 Suppl 4**: p. S40-9.
10. Delany-Moretlwe, S., et al., *Investing in the future: lessons learnt from communicating the results of HSV/ HIV intervention trials in South Africa.* Health Res Policy Syst, 2011. **9 Suppl 1**: p. S8.
11. Theobald, S., et al., *Strengthening the research to policy and practice interface: exploring strategies used by research organisations working on sexual and reproductive health and HIV/AIDS.* Health Res Policy Syst, 2011. **9 Suppl 1**: p. S2.
12. Dinnett, E.M., et al., *Unblinding of trial participants to their treatment allocation: lessons from the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER).* Clin Trials, 2005. **2**(3): p. 254-9.
13. Moscucci, M., et al., *Blinding, unblinding, and the placebo effect: an analysis of patients' guesses of treatment assignment in a double-blind clinical trial.* Clin Pharmacol Ther, 1987. **41**(3): p. 259-65.
14. Skoler-Karpoff, S., et al., *Efficacy of Carraguard for prevention of HIV infection in women in South Africa: a randomised, double-blind, placebo-controlled trial.* Lancet, 2008. **372**(9654): p. 1977-87.
15. Van Damme, L., Govinden, R., Mirembe, F.M., Guedou, F., Solomon, S., Becker, M.L., Pradeep, B.S., Krishnan, A.K., Alary, M., Pande, B., Ramjee, G., Deese, J., Crucitti, T., Taylor, D., , *Lack of Effectiveness of Cellulose Sulfate Gel for the Prevention of Vaginal HIV Transmission.* The New England Journal of Medicine, 2008. **359**(5): p. 463-472.
16. Global Campaign for Microbicides. *Cellulose Sulphate*. 2007 21 September 2007 [cited 2012 18 January]; Available from: http://www.global-campaign.org/Cellulose-Sulfate.htm.
17. Microbicide Trials Network. *What Happens Next: Understanding the Results of HPTN035 and MDP301 and the Promise of ARVs for HIV Prevention*. 2009 14 December 2009 [cited 2011 27 September]; Available from: http://www.mtnstopshiv.org/node/1594.

18. McCormack, S., et al., *PRO2000 vaginal gel for prevention of HIV-1 infection (Microbicides Development Programme 301): a phase 3, randomised, double-blind, parallel-group trial.* Lancet. **376**(9749): p. 1329-37.
19. Dorsey, E.R., et al., *Communicating clinical trial results to research participants.* Arch Neurol, 2008. **65**(12): p. 1590-5.
20. OpenNetworks. *CRM Database*. 2010 [cited; Available from: www.opennetworkscrm.co.za
21. Partridge, A.H., et al., *Offering participants results of a clinical trial: sharing results of a negative study.* Lancet, 2005. **365**(9463): p. 963-4.
22. Avins, A.L., Bent, S., Padula, A., Staccone, S., Badua, E., Goldberg, H., , *Initial experience with a group presentation of study results to research participants.* Trials, 2008. **9**(16).
23. Oldenburg, B.F., et al., *Health promotion research and the diffusion and institutionalization of interventions.* Health Educ Res, 1999. **14**(1): p. 121-30.
24. Kerner, J., Rimer, B., Emmons, K., , *Dissemination Research and Research Dissemination: How Can We Close the Gap?* Health Psychology, 2005. **24**(5): p. 443-446.
25. Dixon-Woods, M., et al., *Receiving a summary of the results of a trial: qualitative study of participants' views.* BMJ, 2006. **332**(7535): p. 206-10.
26. Oronje, R.N., et al., *Engaging media in communicating research on sexual and reproductive health and rights in sub-Saharan Africa: experiences and lessons learned.* Health Res Policy Syst, 2011. **9 Suppl 1**: p. S7.
27. Shalowitz, D.I. and F.G. Miller, *Communicating the results of clinical research to participants: attitudes, practices, and future directions.* PLoS Med, 2008. **5**(5): p. e91.
28. MacNeil, S.D. and C.V. Fernandez, *Offering results to research participants.* BMJ, 2006. **332**(7535): p. 188-9.
29. Miller, F.A., Giacomini. M., Ahern, C., Robert, J.S., de Laat, S. , *When research seems like clinical care: a qualitative study of the communication of individual cancer genetic research results.* . BMC Medical Ethics, 2008. **9**(4).
30. Johnson, L., et al., *How do patients want to learn of results of clinical trials? A survey of 1431 breast cancer patients.* Br J Cancer, 2008. **98**(1): p. 34-8.
31. Snowdon, C., Garcia, J., Elbourne, D., *Reactions of participants to the results of a randomised controlled trial: Exploratory study* BMJ, 1998. **317**: p. 21-26.
32. Miller, F.A., Giacomini, M., Ahern, C., Robert, J.S., de Laat, S., *When research seems like clinical care: a qualitative study of the communication of individual cancer genetic research results.* BMC Medical Ethics, 2008. **9**(4).
33. Angell, M., *The ethics of clinical research in the Third World.* N Engl J Med, 1997. **337**(12): p. 847-9.
34. Baldwin-Ragaven, L., de Gruchy, J., London, L., *An ambulance of the wrong colour: Health professionals, human rights and ethics in South Africa.* . 1999, Cape Town: University of Cape Town Press.
35. Fassin, D., *The embodiment of inequality. AIDS as a social condition and the historical experience in South Africa.* EMBO Rep, 2003. **4 Spec No**: p. S4-9.
36. Fassin, D. and H. Schneider, *The politics of AIDS in South Africa: beyond the controversies.* BMJ, 2003. **326**(7387): p. 495-7.
37. *The Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa*, D.o. Health, Editor. 2000.
38. Jewkes, R. and A. Murcott, *Community representatives: representing the "community"?* Soc Sci Med, 1998. **46**(7): p. 843-58.
39. AVAC, U., *Good participatory practice guidelines for biomedical HIV prevention research*. 2007, UNAIDS: Geneva.

40. UNAIDS/AVAC, *Good participatory practice guidelines for biomedical HIV prevention trials* 2007, UNAIDS: Geneva
41. Jacob, S.T., Baeten, J.M., Hughs, J.P., Peinado, J., Wang, J., Sanchez, J., Reid, S.E., Delany-Moretlwe, S., Cowan, F., Fuchs, J., Koblin, B., Griffith, S., Wald, A., Celum, C. for the HPTN 039 Protocol Team, , *A post-trial assessment of factors influencing study drug adherence in a randomized biomedical HIV-1 prevention trial.* AIDS Behav., 2011. **15**(5): p. 897-904.
42. Boutron, I., C. Estellat, and P. Ravaud, *A review of blinding in randomized controlled trials found results inconsistent and questionable.* J Clin Epidemiol, 2005. **58**(12): p. 1220-6.
43. Dearing, J.W., *Evolution of Diffusion and Dissemination Theory.* Journal of Public Health Management Practice, 2008. **14**(2): p. 99-108.
44. Kerner, J., B. Rimer, and K. Emmons, *Introduction to the special section on dissemination: dissemination research and research dissemination: how can we close the gap?* Health Psychol, 2005. **24**(5): p. 443-6.
45. Owen, N., Glanz, K., Sallis, J.F., Kelder, S.H., *Evidence-Based Approaches to Dissemination and Diffusion of Physical Activity Interventions.* Am J Prev Med, 2006. **31**(4S): p. S35-S44.
46. Rogers, E.M., *Diffusion of Innovations*. 4th ed. 1995, New York: Free Press.
47. Oldenburg, B., Glanz, K., , *Diffusion of Innovations,* in *Health Behavior and Health Education: Theory, Research, and Practice,* K. Glanz, Rimer, B.K., Viswanath, K.,, Editor. 2008, Jossey-Bass.
48. Glanz, K., et al., *Diffusion of an effective skin cancer prevention program: design, theoretical foundations, and first-year implementation.* Health Psychol, 2005. **24**(5): p. 477-87.
49. Gagnon, M.L., *Moving knowledge to action through dissemination and exchange.* J Clin Epidemiol. **64**(1): p. 25-31.
50. Valente, T.W., Rice, R.E., *Evaluating communication campaigns,* in *Public communication campaigns,* R.E.A. Rice, C.K., Editor. 2001, Sage: Thousand Oaks, C.A. p. 105–124.
51. Communications Consortium Media Center, *Guidelines for Evaluating Nonprofit Communications Efforts*. 2004, Communications Consortium Media Center: Washington, D.C.
52. Glasgow, R.E., Vogt, T.M., Boles, S.M.,, *Evaluating the public health impact of health promotion interventions: the RE-AIM framework.* Am J Prev Med, 1999. **89**(1): p. 1322-1327.
53. Lorig, K.R., Hurwicz, M, Sobel, D., Hobbs, M., Ritter, P.L., *A national disemination of an evidence-based self-management program: a process evaluation study.* Patient Educ Couns, 2005. **59**: p. 69-79.
54. Dzewaltowski, D.A., Estabrooks, P.A., Klesges, L.M., Bull, S., Glasgow, R.E., *Behavior change intervention research in communtiy settings: how generalizable are the results?* Health Promot Int, 2004. **19**(2): p. 235-245.
55. Baranowski, T., Stables, G., *Process Evaluation of the 5-a-Day Projects.* Health Education and Behavior, 2000. **27**(2): p. 157-166.
56. Backett-Milburn, K., Wilson, S., *Understanding peer education: insights from a process evaluation.* Health Education Research, 2000. **15**(1): p. 85-96.
57. Saunders, R.P., Evans, M.H., Joshi, P., *Developing a Process-Evaluaiton Plan for Assessing Health Promotion Program Implementation: A How-to Guide.* Health Promotion Practice, 2005. **6**(2): p. 134-147.
58. Braun, V. and N. Gavey, *'With the best of reasons': cervical cancer prevention policy and the suppression of sexual risk factor information.* Soc Sci Med, 1999. **48**(10): p. 1463-74.

59. Robinson. E.T., B., D., Heise, L.L., Moffett, J., Harlan, S. , *Communications Handbook for Clinical Trials*. 2010, Washington DC: Global Campaign for Microbicides, PATH, Family Health International
60. McCormack, S., et al., *PRO2000 vaginal gel for prevention of HIV-1 infection (Microbicides Development Programme 301): a phase 3, randomised, double-blind, parallel-group trial.* Lancet, 2010. **376**(9749): p. 1329-37.
61. Seekings, J., *"Social ordering and control in the African townships of South Africa: an historical overview of extra state initiatives from the 1940s to the 1990s"*, in *The Other Law: Non-state Ordering in South Africa*, W. Scharf, Nina, D., Editor. 2001, Juta: Cape Town. p. 71-97.
62. Morris, A., *Change and continuity: A survey of Soweto in the late 1990s.* , B. Bozzoli, Cook, J., Crankshaw, O., Gilbert, L., Lehutso-Phooko, L., Posel, d., Tshandu, Z., Van Huysteen, E., Editor. 1999, University of Witwatersrand Johannesburg.
63. Chibulu, H., *MoH bans microbicide clinical trials*, in *The Post Newspapers*. 2010: Mazabuka, Zambia.
64. Mapara, E.M., *Oh Happy Day?! Zambia Bans All Microbicide Clinical Trials*, in *UKZambians*. 2010.
65. Zanis. *Zambia: No more Microbicide clinical trials on women – Mazabuka Central MP*. Lusaka Times 2009 [cited 2012 5 January]; Available from: http://www.lusakatimes.com/2009/12/29/no-more-microbicide-clinical-trials-on-women-mazabuka-central-mp/.
66. Webb, P., *Science education and literacy: imperatives for the developed and developing world.* Science, 2010. **328**(5977): p. 448-50.
67. Morris, A., *Change and continuity: A survey of Soweto in the late 1990s.*, B. Bozzoli, Cock, J., Crankshaw, O., Gilbert, L., Pose, D., Tshandu, Z., van Huyssteen, E. , Editor. 1999, University of Witwatersrand: Johannesburg.
68. Dinnett, E.M., et al., *Offering results to research participants.* BMJ, 2006. **332**(7540): p. 549-50.
69. Desbiens, N.A., *In randomized controlled trials, should subjects in both placebo and drug groups be expected to guess that they are taking drug 50% of the time?* Med Hypotheses, 2002. **59**(3): p. 227-32.
70. Ney, P.G., C. Collins, and C. Spensor, *Double blind: double talk or are there ways to do better research.* Med Hypotheses, 1986. **21**(2): p. 119-26.
71. Morris, N., *A Comparative Analysis of the Diffusion and Participatory Models in Development Communication.* Communication Theory, 2003. **13**(2): p. 225-248.
72. Ascroft, J., Agunga, R., , *Diffusion theory and participatory decision-making.*, in *Participatory communication: Working for change and development*, S.A. White, Nair, K.S., Ascroft, J., , Editor. 1994, Sage: New Delhi. p. 295-311.

Appendices

1. Results Communication Plan for RHRU, Johannesburg
2. Interview guide for CAB and participant results dissemination meetings
3. Costing table
4. MDP301Unblinding Script (English)
5. Demographics questionnaire
6. Sexual behaviour questionnaire at enrolment
7. Sexual behaviour questionnaire at final study visit
8. Ethics approval for process evaluation and retrospective analysis
9. Ethics approval for unblinding script
10. Permission to use data
11. Posters inviting participants to call or SMS for more information about the results

Appendix 1: Results Communication Plan for RHRU, Johannesburg

MDP301trial

RESULTS COMMUNICATIONS PLAN FOR RHRU, JOHANNESBURG

The MDP301trial is a multi-centre trial involving 3 sites in South Africa, namely RHRU, Medical Research Council (MRC), and the Africa Centre (AC). Results reporting to national stake-holders will be coordinated by the MRC with support from the other two sites.

Site description and key considerations

There is a trial site in Soweto based at Chris Hani Baragwanath Hospital. RHRU has not had experience of disseminating research results in this community directly. The area is large, densely populated and participants living here have been challenging to track and retain. Jozi FM is located in this area and has been an important partner for communicating about the research to participants and community over the years. Other trials like MIRA were conducted in this site by PHRU. Orange Farm is about 30 km from the Soweto Office. We have had experience with communicating research results to this community. Thetha FM broadcasts in this area. We have worked with Thetha FM. Both sites have CABs.

Planned activities at a national level

A meeting with the MCC is planned for 7 December.
Joint press release is planned with all South African sites on 11 or 14 December.

Planned activities at a local level

A. Prior to the Press Release

The purpose of this communication is to give advance warning of results to programs or institutions that would be accessed by the media for comment or would need to respond with programmatic implications. On the MDP301RDP version XXX see details of those to be contacted prior to the press release.

1) Wits Human Research Ethics Committee:

Prior to the press release an email will be sent by the PI/Site investigators notifying the Chairperson of the pending release of the results. Documents summarizing the trial will be sent with this email. A confidentiality agreement will be sent with this email. In the week prior to the press release, PI/Site investigator will either meet or contact chairperson telephonically to inform of the results (as per preference of the REC). (SD)

2) Community Advisory Groups:

A meeting will be held with the CAB in Orange Farm and Soweto to go through the potential trial outcomes. Prior to the press release, a meeting will be held with both CABs to present the results. This event will be used to coach CAB members in responding to questions about the trial. Confidentiality agreements will be issued and signed at this meeting. One person from the CAB will have attended the MDP media training in Durban. (PM/GF)

3) Participants

On the morning of the press release a message will be sent via bulk SMS to participants with confirmed cell phone numbers and who agree to receive SMS announcing the results. The message will need to be approved by the REC and translated into SeSotho and isiZulu. Prior to

this, a test message will be sent out the week before announcing that the results will be available and requesting confirmation that participant would like to receive results by sms. The message will include a note that results are confidential. Between now and the results release we will use the weekly radio shows to encourage participants to contact the clinic to confirm their contact information and receive there results. A "hotline" will be set up which will be used to manage questions from participants about results. This will be staffed by research clinicians or junior project coordinators from each site. A script will be developed to assist with answering questions. (BS/TP/SD)

4) MEC

Prior to the press release an email will be sent by the PI/Site investigators notifying the MEC of the pending release of the results. Documents summarizing the trial will be sent with this email. A confidentiality agreement will be sent with this email. In the week prior to the press release, PI/Site investigator will meet with/phone the contact MEC to inform of the results. (SC/HR)

5) Site research team

Site staff will be asked to sign confidentiality agreements. As soon as results are available they will be informed during a face-to-face meeting. This meeting will be used to confirm key messages as well as plans for dissemination. (TP)

6) Other key stake-holders

Other key stake-holders will be sent a group email announcing that the results will be released and providing background information on the trial.(SD/SC/HR)

Materials needed during this stage

- Confidentiality agreements (TP/SD)
- MDP background document (MDP)
- Results key messages (currently in draft) (MDP)
- Approved & translated SMS notification (SD)
- Updated contact information of participants, key-stakeholders (TP)
- Song (JonS)
- Radio primers (JonS)

B. Press release

Consider simultaneous press release in Johannesburg on day of national press release. Work with Communications Department on this. Notify Wits Press Office as well. RHRU staff will be trained in media handling prior to this event. Consider training reception staff to handle all incoming enquiries. Update RHRU website with press release plus RHRU specific information.

Participants

1) Site staff (Thes, MAS, SN, CLO, JonS)
2) CAB, participant representative

Materials required

- Contact list of media persons (Will M)
- RHRU specific press release (SD/Will M/HR)
- FAQ/Key message documents for staff (SD/Will M/TP)
- Media handling guidelines for staff (SD/Will)
- Updated RHRU website (Will)

C. After the Press Release

1. Participants:

A results workshop will be held at each site over a period of 3 days up until 16 December. At this event, the results will be presented in local languages with an opportunity for questions and answers. All questions will be documented so that these issues are addressed in subsequent sessions. Participants will be provided with a written document which summarises the key results. Ideally, this should be translated into Zulu and Sotho. (GF/PM)

Participants will be advised that if they wish to know their treatment allocation that they should indicate their interest in this at the meeting. They will be contacted telephonically with this information. A telephone service will be set up to offer unblinding information telephonically. (TP/SD)

An SMS line will be set up for participants to SMS for standard messages about the trial results. (BS)

The song will be played at these events (JS).

2. Community and local stake-holders

We will use the shows on Jozi FM to provide information about the trial results.
The song will be aired on these shows (JS).
Briefings can be conducted with key partners in each community after the Christmas break.
At all events, questions will be documented and used to improve future presentations.

3. RHRU staff
Results will be communicated via bulk sms to all RHRU staff.
A item will be included in the next newsletter about the results.
RHRU staff will be invited to the dissemination event in February.
An item will be prepared for the FHS newsletter as well.
The press release will be posted on the RHRU website

4. Other stake-holders
A group email will be sent to other identified RHRU stake-holders with a covering letter from the PI and the press release.

A meeting is planned to take place in early February 2010 to discuss the results. CAB, participants, academics and department of health officials will be invited to this meeting.

The song will be played at this meeting.

Potential Problems/Post-Results Activities

- There is likely to be a lot of media interest in the results given the previous history of some trials in the area. All staff will receive training in how to respond to media questions, including reception staff.
- The timing around the Christmas break is not ideal and means that we will have to rush to get information out to key partners but will not be available to respond to questions after the 16th – we will identify key staff who will have to respond to questions

Resources

Here are some resources, that could be helpful for specific audiences, that will be provided:

- Backgrounder (for public)
- Frequently Asked Questions (for study staff and the public)

- Internal Questions and Answers (for use by the PI)
- Key Messages (for use by the PI)
- Press Release (for public)
- Slide Presentation of Results (for scientific audience)
- Participant Unblinding script (for sites)

□ What, if any, additional documents/resources do you need to communicate the results?
  - SMS messages announcing plan to release results
  - SMS message announcing results
  - SMS line to access standard message about results after the trial
  - Radio show primers for pre-release messages and post-release message
  - Local press release for RHRU
  - Newsletter item for staff, FHS
  - SMS for staff
  - Song

□ If you plan on translating any of these documents into local languages please describe in this section.

Any other activities

Monitoring and evaluation

We will track responses via the following mechanisms

Media coverage – Will
SMS responses – BS
Radio phone in – BS/JS
Listener clubs – BS/JonS
Community – social science team, community team
Participants – social science team, community team
RHRU reception – National office

Appendix 2: Interview guide for CAB and participant results dissemination meetings

1. How do you feel about the results?
2. Were the results what you expected?
3. Had you heard the results before coming to the meeting today?
4. If yes to Q3 (via SMS): Did you understand the results when you received the SMS?
5. Do you think this study was a waste of time?
6. What do you understand of the results?
7. Who are you going to tell first about the results?

Appendix 3: Costing Table

Activity	Sub-activity expenses	Outcome	Unit	Cost per unit	Total Cost per activity
Slots on the weekly radio program					
SMS to research staff, CAB members, trial participants					
CAB meetings	Venue				
	Participant reimbursement				
	Refreshments				
Participant meetings	Venue				
	Participant reimbursement				
	Refreshments				
Research staff meeting					
Telephonic unblinding	Calls				
	Staff time				
Meetings with key stakeholders					
Total					

Appendix 4: MDP301Unblinding Script (English)

MDP301Unblinding Script

PTID: | |

Hi, can I please speak to _____.

My name is (name) and I am calling from the RHRU Tshireletso Clinic.
I would like to please ask for 5 minutes of your time to share some information with you.

Are you able to talk freely now?

□ Yes No

If no, is there a more convenient time I can call you at?

_____

_____

Before I tell you about the study results, I will need to confirm your identity.

Can you please tell me your name? | |

Can you please tell me your DOB? | |

Can you please tell me your address?

And lastly, do you remember the name of the clinician or counselor that you last saw at Tshireletso Clinic? | |

[If unable to confirm participant identity, ask them to visit the clinic for a face to face discussion and to bring proof of identity with them]

I am calling with regards to the results of MDP301PRO 2000 gel trial.

This call may be recorded for quality control purposes. Is this ok with you?

□ Yes No

Are you comfortable with English or would you prefer I talk in Zulu or Sesotho?

□ English □ Zulu □ Sesotho

I would like to take some time to thank you for your participation in this study. By taking part, you have made an important contribution to the fight against HIV/AIDS and of making research more acceptable in our community.

[Recap on the MDP301study]

Let's briefly discuss what you remember about the project,

- MDP301was a Phase III trial evaluating the safety and effectiveness of the vaginal microbicide PRO 2000 for reducing the risk of HIV infection in women.
- All women were asked to attend 15 visits and were counseled and tested for HIV at each visit. They were also provided with gel, condoms and further counseling at each visit.
- Participants were originally randomised in approximately equal numbers to one of three study groups: PRO 2000 gel 0.5% dose, PRO 2000 gel 2% dose and placebo (gel with inactive ingredient).
- By randomized, I mean that people were placed into one of these study groups by chance without the nurse, clinician or counselor even knowing which group the woman would be in.
- In February 2008, an independent monitoring committee recommended that no more women should be allocated to 2% PRO 2000 gel as there was little chance that it would prove effective. The trial promptly stopped dispensing the 2% gel to all women who had been allocated to it but these women continued to be followed up. All women enrolling after that were randomly put into one of the other two study groups: placebo or 0.5% PRO 2000.
- As a participant, you will recall that all participants were informed about the trial before they enrolled. All trial participants gave written informed consent to participate. The study was conducted in compliance with South African Good Clinical Practice, the protocol and study standard operating procedures.

Do you have any questions about what I've just told you?

1. Have you heard the study results of MDP301?

□ Yes No [skip to question 3]

2. How did you hear about the study results? (*mark all that apply*)

□ Radio
□ SMS
□ CAG member
□ Another participant
□ Poster
□ Newspaper
□ Phone Call/Letter from Study Site

□ Dissemination meeting arranged by the study clinics in December
□ Online (i.e., through the internet)
□ Other_____

3. During MDP301, did you think you were using the active 0.5% PRO 2000 gel or the placebo (non-active) gel?
□ Placebo 0.5% gel Not sure

***Comment: Remember the 2% gel arm ppts would have had gel retracted so the list when calling needs to highlight this so this question is not asked of them**

4. What led you to believe that you were taking either 0.5% or placebo?
□ Appearance of the gel
□ How the gel felt in my body
□ Information from study staff
□ Discussions with other MDP301participants
□ Other, specify:

5. Would you like to know which arm of the study you were in OR which gel you received?

□ Yes No Not sure

6. If yes:

[You were randomized to the (placebo or 0.5% PRO 2000) arm. This means that you were not (were) using the active product (gel) during the study.]

t did

Section B: Disclose study results (if they don't already know)

In this study, the 0.5% PRO 2000 gel used at every sex act has not shown reduction in preventing HIV infection.

- The 0.5% PRO 2000 gel that was used in MDP301showed no side effects or adverse reactions. There are no known risks for the use of this gel.
- The results support that using a vaginal gel for HIV prevention is acceptable by women and their partners.

Did you disclose to your partner that you were using the gel?

□ Yes No

If yes, how did he feel about the gel use?

If no, why did you not disclose?

-We look forward to the results of trials of new microbicides made from antiretroviral drugs that are expected to be more potent.
We will soon be starting a new study in Hillbrow on ARV containing microbicides and you can contact us on <<<<<<<<<<<<<<< for more information is you want to participate. Alternatively, if you want us to contact you with more info, please let me know and a study staff member will call you closer to the time we aim to start the new study

With the growing number of HIV infections among women worldwide, this research into developing an effective vaginal microbicide remains vital.

We would like to give you information on places where you can go for different types of services now that you will not be coming here for regular study visits.

→ For primary healthcare in Soweto:
→ For family planning and other reproductive health care:

→ For primary healthcare in Orange Farm:
→ For family planning and other reproductive health care:

Section C: Close

Thank you for participating in the study; it is through your participation that we now have an answer/ results.

Do you have any questions about these results? (Record questions)

Last, we may want to contact you regarding participation in future studies for which you may be eligible. May we contact you when another study takes place?

□ Yes No

Thank you again for your time and participation in the MDP301trial. It has been a great pleasure to work with you.

Appendix 5: MDP301 Screening Demographics Questionnaire

MDP301– SCREENING – DEMOGRAPHICS CRF – D1 Version 1 September2005

Site name: Joburg - South Africa		Date of visit: DD /MM/YYYY
Screening number: ☐☐☐☐☐☐☐	Initials: ☐☐☐	☐☐/☐☐/☐☐☐☐

Interviewer: read the questions to the volunteers verbatim and allocate the correct answer from the selection, unless it is indicated that you read out each answer to the volunteer as well. Boxed type is instructions to the interviewer. Type in italics is to be read to the volunteer.

Section 1: Personal details

1 Date of birth ☐☐/☐☐/☐☐☐☐ Or age (if DOB not known) ☐☐

DD / MM / YYYY

2 _____

What language do you speak at home?

3 What religion do you belong to?

Christian (protestant)	☐	Christian (unspecified)	☐
Christian (catholic)	☐	Traditional African	☐
Seventh day adventist	☐	Born again Christian	☐
Muslim	☐	Hindu	☐
Zionist	☐	Shembe	☐
Jehovah's witness	☐	None	☐
Other	☐	Specify_____	

Section 2: Education and sources of income

"I am now going to ask you some questions about your level of education and what sources of income there are coming into your household. This information will not be used for any other reason than to contribute to the results of the study. We want to see if people taking part in the study in this country are similar to people taking part in other countries."

4 What is the highest level of education you gained?

None	☐		
Went to school but did not complete primary	☐	Completed primary	☐
Incomplete secondary	☐	Completed secondary	☐
Incomplete tertiary	☐	Completed tertiary	☐
Refused to answer	☐	Incomplete secondary but some vocational training	☐

5a How would you define your employment status?

- ☐ Employed full time →Q. 5c
- ☐ Employed part time →Q. 5c
- ☐ Student/scholar
- ☐ Work seeker
- ☐ Declined to answer
- ☐ Unemployed
- ☐ Housewife
- ☐ Retired
- ☐ Other Specify_____

5b During the past year did you do any kind of work?

- ☐ Yes
- ☐ No →Q. 6

5c Describe briefly the main type of work or job that you do/did. ***Interviewer tick the answer most relevant to the description - make sure to only tick 'other' if the participant's work does not fit into any of the categories***

- ☐ Unskilled manual
- ☐ Sales/services
- ☐ Crop farming
- ☐ Household/domestic
- ☐ Fishing
- ☐ Livestock rearing
- ☐ Office
- ☐ Manufacturing
- ☐ Other Specify_____

5d Which of the following best describes your employment?

- ☐ Regular paid
- ☐ Self-employed
- ☐ Casual labourer
- ☐ Paid per piece
- ☐ Unpaid
- ☐ Other(specify_____)

5e Where did/does this work take place? [tick all that apply]

- ☐ Family's dwelling
- ☐ Employer's house
- ☐ On the street
- ☐ Shop/market/kiosk
- ☐ Industry/factory
- ☐ Plantation/farm/garden
- ☐ Construction/mine/ quarrying sites
- ☐ Other(specify_____)

Section 3: Housing and household

"I am now going to ask you some questions relating to your household. By household we mean the physical and social unit in which you live (either by yourself of with family and relatives). This could be a house or a compound consisting of different buildings that belong together, even though they may not be very close together. A household consists of a group of people, usually relatives, who share resources and regularly share meals."

6 Who would you say is the head of your household?

- Self ☐ →Q. 8
- Partner ☐
- Sibling ☐ →Q. 7
- Child ☐
- Daughter/Son in law ☐ →Q. 7
- Parent ☐
- Mother/Father in law ☐ →Q. 7
- Other relative ☐
- Niece/Nephew ☐ →Q. 7
- Other ☐ Specify_____ →Q. 7

We would like to ask you some questions about the head of the household you have just identified

7a How would you define the head of household's employment status?

- Employed full time ☐ →Q. 7c
- Employed part time ☐ →Q. 7c
- Student/scholar ☐
- Work seeker ☐
- Declined to answer ☐
- Unemployed ☐
- Housewife ☐
- Retired ☐
- Don't know ☐
- Other ☐ Specify_____

7b During the past year did the head of household do any kind of work?

- Yes ☐
- No ☐ →Q. 8
- Don't know ☐ →Q. 8

7c Describe briefly the main type of work or job the head of household does/did. ***Interviewer tick the answer most relevant to the description - make sure to only tick 'other' if the work does not fit into any of the categories***

		Unskilled manual	☐	Sales/services	☐
		Crop farming	☐	Household/domestic	☐
		Fishing	☐	Livestock rearing	☐
		Office	☐	Manufacturing	☐
		Don't know	☐		
		Other	☐	Specify_____	
7d	Which of the following best describes the head of household's employment?	Regular paid	☐	Self-employed	☐
		Casual labourer	☐	Paid per piece	☐
		Unpaid	☐	Don't know	☐
		Other	☐	Specify_____	
7e	Where did/does this work take place? [tick all that apply]	Family's dwelling	☐	Employer's house	☐
		On the street	☐	Shop/market/kiosk	☐
		Industry/factory	☐	Plantation/farm/garden	☐
		Construction/mine/ quarrying sites	☐	Don't know	☐
		Other	☐	Specify_____	
8	How many rooms in your household are used for sleeping?			List number	☐☐
				or tick if declined to answer	☐
9	How many people usually sleep in your household?			List number	☐☐
				or tick if declined to answer	☐
10	What type of housing do you stay in?			RDP house	☐
		Municipal house	☐	Train house	☐
		Double house	☐	Hostel	☐
		Room inside	☐	Hostel family unit	☐
		Flat	☐	Town House	☐
		New house (bonded house)	☐	Shack	☐
		Other	☐	Specify_____	

11	Who owns the house/place that you live in?	Partner	☐	Self	☐
		Private landlord	☐	Sibling	☐
		Parent/parent-in-law	☐	Government/council	☐
		Other relative	☐	Declined to answer	☐
		Company	☐		
		Other	☐	Specify_____	

12	Does your household have: [tick one answer for each item]				
		Electricity	Yes ☐	No	☐
		A radio	Yes ☐	No	☐
		A television	Yes ☐	No	☐
		A telephone	Yes ☐	No	☐
		A refrigerator	Yes ☐	No	☐
		A personal computer	Yes ☐	No	☐
		A washing machine	Yes ☐	No	☐

13	Does any member of you household own: [tick one answer for each item]				
		A bicycle	Yes ☐	No	☐
		A motorcycle or motor scooter	Yes ☐	No	☐
		A car	Yes ☐	No	☐
		A donkey or horse	Yes ☐	No	☐
		Sheep or cattle	Yes ☐	No	☐

Section 4 – Access to resources

14	If a person became ill in your home and R100 was needed to pay for treatment or medicines, how easy would it be for you to find the money?	Very easy	☐
		Easy	☐
		Quite difficult	☐
		Very difficult	☐
		Declined to answer	☐

15	What proportion of the household expenses does your partner contribute	N/A ☐ Nothing ☐ One third ☐ Half ☐ Three quarters ☐ All ☐

Appendix 6: Sexual Behaviour Questionnaire at Enrolment

MDP 301– ENROLMENT – SEXUAL BEHAVIOUR CRF – SB2 Version 1 September 2005

Site name: ------site name pre-printed---------	Date of visit: DD /MM / YYYY □□/□□/□□□□

Section 1: Family planning

1	Are you currently using any method of family planning?	Yes No	□ □	→ Q. 1a → Q. 1b

1a	If yes, which of the following methods are you using? [tick all that apply]			Natural/rhythm	□	→ Q. 2
	Pills	□		Foam/jelly/spermicide	□	→ Q. 2
	Diaphragm	□		Injectable Nur-Isterate	□	→ Q. 2
	Injectable Depo-Provera	□		Injectable other (specify below if possible)	□	→ Q. 2
	IUCD	□				
	Condom (male or female)	□		Norplant implant		→ Q. 2
	Traditional oral			Traditional vaginal		→ Q. 2
	Sterilisation			Traditional other (specify below if possible)		→ Q. 2
	Other			Specify_____ _____ ____		→ Q. 2 → Q. 2

1b	If no, why are you not using any method of family planning?			Breastfeeding	□
	Wanting to become pregnant	□		Not sexually active	□
	Menopause	□		Sterilised (participant or partner)	
	Other			Specify_____ __	

2	How many days ago was the first day of your last menstrual period? [List number, 99 if more than 3 months or 00 if menstruating now]	□□

2a	Was this period when you expected it to be?	Yes	☐
		No	☐

Section 2: Sexual activity and condom use

Interviewer: please spend some time ensuring that the volunteer understands what is termed by a sex act: one sex act is "penetrative vaginal sex that may or may not end with ejaculation".
Also – don't forget to probe for EXACT NUMBERS

"I am now going to ask you about your sexual activity and condom use. Please answer accurately as the responses are very important to the study results."

3	How many days ago did you last have sex?	1 (includes yesterday, last night and today)	☐	2 (the day before yesterday)	☐	→ Q. 4
		3	☐	4	☐	→ Q. 4
		5	☐	6	☐	→ Q. 4
		7				→ Q. 4
				1-4 weeks		→ Q. 7
				More than 4 weeks	☐	→ Q. 9
4	How many times have you had sex in the last week?	[list number of times or 77 if unsure]				☐☐
5	How many different people have you had sex with in the last week?	[list number or 77 if unsure]				☐☐

Ensure that the volunteer understands what we mean by each category of partner.
1) Long-term stable partners include some/most of the following characteristics: official marriage, traditional marriage, bride price paid, man known to and accepted by woman's family, have children together, live together, long-term relationship, man provides regular financial/material support, may be cohabiting or non-cohabiting.
2) Other partners includes all partners who do not fit into the first category above.

5a	How many of these partners were:	Long term stable partners	☐☐
		Other types of partner	☐☐

Interviewer: check that the total of the answers given in question 5a is the same as the answer given in question 5 and rectify if necessary.

Interviewer: only fill this table in with participants who HAVE had sex in the last 1 week.

6. "Now I am going to ask you some more detailed questions about your condom use each time you had sex in the last week."

Interviewer: each question (row) refers to a particular sex act. Go through all columns for the individual sex act before moving on to the next row. Write the number corresponding to the answer code for each column in the box in each cell. Remind the participant about the definition of a 'sex act' and allow enough time for the participant to carefully consider each answer.

Sex acts	Partner	Condom
Sex acts in the last week	What type of partner was this act with?	Did you use a condom during this sex act?
Codes	1=long-term stable relationship 2= other type of partner, 8=don't remember	1=yes 2=no 8=don't remember
1 last sex act	□	□
2 sex act before that	□	□
3 sex act before that	□	□
4 etc.	□	□
5	□	□
6	□	□
7	□	□
8	□	□
9	□	□
10	□	□

Interviewer: only fill this table in with participants who have NOT have sex in the last 1 week but who HAVE had sex in the last 4 weeks. You should only fill in one table for each respondent: either 6 or 7

7. “Now I am going to ask you some more detailed questions about your condom use each time you had sex in the last 4 weeks. Please answer the questions for each time you had sex.”

Interviewer: each question (row) refers to a particular sex act. Go through all columns for the individual sex act before moving on to the next row. Write the number corresponding to the answer code for each column in the box in each cell. Remind the participant about the definition of a ‘sex act’ and allow enough time for the participant to carefully consider each answer.

Sex acts	Partner	Condom
Sex acts in the last 4 weeks	What type of partner was this act with?	Did you use a condom during this sex act?
Codes	1=long-term sexual relationship, 2= other type of partner, 8=don’t remember	1=yes 2=no 8=don’t remember
1 last sex act	□	□
2 sex act before that	□	□
3 sex act before that	□	□
4 etc.	□	□
5	□	□
6	□	□
7	□	□
8	□	□
9	□	□
10	□	□

8 In the last 4 weeks have you had sex whilst you were menstruating? Yes □

No □

Section 3: Other products and practices

“Some women insert products into their vaginas for a variety of reasons, such as cleaning inside the vagina, or drying or lubricating the vagina before sex. The next questions are about this”.

9	In the last week have you inserted anything (excluding water/fingers) into your vagina?			Yes ☐ No ☐	→ Q. 10
9a	Why did you insert this other thing? [tick all that apply]	To clean the vagina ☐ To dry the vagina ☐ Other ☐		To lubricate the vagina ☐ Specify_____ ☐	
9b	If yes, how many times did you do this?				
	More than once per day ☐		Once per day ☐		
	Less than once per day but more than once in the week ☐		Once in the week ☐		
			Don't remember ☐		
9c	What time of day did you normally do this? [tick all that apply]	Morning ☐	Afternoon ☐		
	Evening ☐				
9d	When in relation to sex did you normally do this? [tick all that apply]	After sex ☐	Before sex ☐		
			Some other time ☐		
9e	PROBE FOR MULTIPLE ANSWERS What did you insert?	Disinfectant ☐	Creams ☐		
	Vaseline ☐		Dry cloth ☐		
	Herbs ☐		Wet cloth ☐		
			Lemon ☐		
	Other ☐		Specify:		

"Some women have anal sex. The next question refers to this practice".
Interviewer: spend some time making sure the participant understands what anal sex is: "penetrative anal sex that may or may not end with ejaculation".

10	Have you had anal sex in the last 4 weeks?	Yes ☐ No ☐	→ Q. 11

10a	Did you use a condom?	Always	□	Most of the time	□
		Sometimes	□	Never	□

Section 4: Pregnancy test

11	Has urine sample been collected for pregnancy test?	Yes	□
		No	□
11a	Why not? [volunteer must not be enrolled until a negative urine pregnancy test has been obtained]	Not possible to obtain urine specimen	□
		Other (specify_____ ___)	□

Interviewer code □□□

Comments

_____
_____
_____
_____
_____
_____
_____
_____

Appendix 7: Sexual Behaviour Questionnaire at Final Visit

MDP 301– Final Visit – SEXUAL BEHAVIOUR CRF – SB5 Version 1.2 February 2007

Site name:		Date of visit: □□/□□/□□□□ DD/MM/YYYY
Screening number: □□□□□□□	Initials: □□□	Trial number □□□□□□

WEEK 52 □ final visit □

Interviewer: read the questions to the volunteers verbatim and allocate the correct answer from the selection, unless it is indicated that you read out each answer to the volunteer as well. Boxed type is instructions to the interviewer. Type in italics is to be read to the volunteer.

Please try to answer these questions accurately as the answers to them are very important to the outcome of the study. Remember that the information you give us is confidential and will only be used for the purposes of this study.

1.	What are you most afraid of in your daily life? Please rank in the order of importance	Tick all that apply [maximum 3]	Order of Importance (1, 2 etc)
		□□	□□
	Crime	□□	□□
		□□	□□
	Poverty	□□	□□
	HIV		
	Other diseases		
	Rape/domestic violence		
	Loss of partner		
	Witchcraft		
	Other (Specify)_____		

2.	How likely do you think it is that you might get infected with HIV?

Very Likely □□
□

Not Very Likely

Impossible

3. If you think you might get infected with HIV, what can you yourself do to reduce this likelihood?

Nothing □□

Use condoms □□

Abstain □□

Be faithful □

Use gel

Reduce partners

Partner choice

4. During the trial you have been asked questions about the following topics: Gel use, Vaginal washing and inserting substances, Condom use , Casual partners, Numbers of sex acts ,Anal sex Which questions would people find the most sensitive? [Tick all that apply- Maximum 3]

Gel use □□

Vaginal washing and inserting □□

Condom use □□

Casual partners

Numbers of sex acts

Anal sex

5. Which topics would most people have difficulty remembering? [Tick all that apply- Maximum 3]

Gel use □□

Vaginal washing and inserting □□

Condom use □□

Casual partners

Numbers of sex acts

Anal sex

6. How often did you forget the number of sex acts when you were asked in the CRF interview?

Often □□

Occasionally □

Never

7. How often did you use gel but then forget to report it in the interview?

		□□
	Often	□
	Occasionally	
	Never	
8.	How often did you use a condom but then forget to report it during the interview?	
		□□
	Often	□
	Occasionally	
	Never	
9.	Did you talk to other women in the trial about the gel?	
		□□
	Yes	
	No	→11
10 b	If yes was this useful?	□□
	Yes	
	No	
11.	Was it easy to predict when you may need to insert gel?	
		□□
	Yes	
	No	
12.	Do you think that most women in the trial would find it difficult to admit they hadn't used the gel when they were asked in the interview?	

□□

Yes □

No

Don't know

13. How often did you report using the gel during the interview when in fact you had not used it?

□□

Often □

Occasionally

Never

14. Did you ever use the gel for anything other than sex?

□□

Yes

No →15

14a If yes, what for?

□□□

Cleaning inside the vagina/womb □□□

Treating STIs

Skin cream/moisturising

Sex aid

Pain relief

Other (Specify)_____

15. How often did you share gel with other women?

□□

Sometimes

Never

16. If a microbicide gel was available to buy, where would you prefer to get it?

Shop	□□
Clinic or other medical facility	□□
Chemist	□□
A box or machine	□
A woman of my own age that I don't know	
Counsellor	
Other (Specify)_____	

17 Has using gel made it easier for you to talk about sex with your partner?

Yes	□□
No	

18. Has being in the trial made it easier for you to talk about sex with your partner?

Yes	□□
No	

19. What did your partner think of the gel?

Didn't know I was using □□

Liked □□

Neutral □

Disliked

Don't know

20. Did the gel affect how much your partner enjoyed sex?

Didn't know I was using □□

Made no difference □□

Made sex less enjoyable □

Made sex more enjoyable

Don't know

21. What does your partner think of condoms?

Likes □□

Neutral □

Disliked

22. Has using gel made it easier for you to talk about condoms with your partner?

Yes □□

No

23. Do you think that most women in the trial would find it difficult to admit they hadn't used a condom when they were asked in the interview? □□

Yes

No

24. How often did you report using a condom when you hadn't? □□

Often □

Occasionally

Never

25 During the trial, did you use a condom more or less compared to before the trial? □□

More □

Same

Less

26 How likely do you think women are to honestly report having had casual partners? □□

Likely

Not Likely

27 Did you have any casual partners during the trial? □□

Yes

No

28	You were told not to wash inside your vagina for at least one hour after sex. Was this a problem?	□□
	Always	□
	Sometimes	
	Never	
29	Do you think that most women would answer honestly if they were asked whether they had ever had anal sex?	□□
	Yes	
	No	
30	Did you ever have anal sex before the trial?	□□
	Yes	
	No	
31	During the trial, how often did you have anal sex?	□□
	Often	□
	Occasionally	
	Never	
32	What is the main reason for you deciding to join this study?	

Gel protects □□

Try the gel □□

Money □□

Help others □□

To get pregnant □□

Get tests/treatment/improve health □□

Nothing else to do with my time □□

HIV test □□

33 If we show that this microbicide halves women's risk of getting HIV:

a How likely do you think it would be that you would want to regularly use the gel? Would you say: □□

very likely □

somewhat likely

or not likely

---

b Would you encourage or discourage your friends to use the gel? □□

Encourage

Discourage

c	If this microbicide was available, what is the highest price it could be for you to still want to buy it, ?	[local currency unit]_____ __
d	Would you be willing to pay (price of soc.mark condom) for a microbicide that reduces your risk of getting HIV by half? Yes No	□□
e	Would you be willing to pay (50% price of soc.mark condom) for a microbicide that reduces your risk of getting HIV by half? Yes No	□□
f	Would you be willing to pay (200% price of soc.mark condom) for a microbicide that reduces your risk of getting HIV by half? Yes No	□□

Interviewer code □□□

Appendix 8: HREC Approval for process evaluation and retrospective analysis

M110482

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Ms BonnieJeanne Saxon

CLEARANCE CERTIFICATE	**M110482**
PROJECT	Feasibility of Telephonic Unblinding as Part of a RCT Results Dissemination Plan in the South African Context
INVESTIGATORS	Ms BonnieJeanne Saxon.
DEPARTMENT	School of Public Health
DATE CONSIDERED	06/05/2011
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 06/05/2011 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Nicola Christofides

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

Appendix 9: Ethics Approval for Unblinding Script

University of the Witwatersrand, Johannesburg

Human Research Ethics Committee: (Medical)
FWA Registered No IRB 00001223

SECRETARIAT: Suite 189, Private Bag x2600, Houghton 2041, South Africa Tel: +27-11-274 9200 Fax: +27-11-274 9281

Prof Helen Rees,

Executive Director (RHRU) - 12th Floor Room 12o
Reproductive Health and HIV Research Unit
P O Box 10474
Hillbrow
Johannesburg
2038

Fax: 011 358 5301

FAXED & COURIE

01 April 2010

Dear Prof Rees,

PROTOCOL: MDP301 SUB STUDY 01 HPV - SUB-STUDY TO AN INTERNATIONAL MULTI-CENTRE, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL TO EVALUATE THE EFFICACY AND SAFETY OF 0.5% AND 2% PRO 2000/5 GELS FOR THE PREVENTION OF VAGINALLY ACQUIRED HPV INFECTION

ETHICS REFERENCE NO: 060810

RE : APPROVAL FOR UNBLINDING SCRIPT FOR USE WITH MDP 301 TRIAL PARTICIPANTS

We acknowledge receipt of your letter dated 29 March 2010 with the following documentation pertaining to the above-captioned trial.

Amendment Date:	18-Mar-10	Amendment Version:	Version: 4.0
Amendment Number:		Received Date:	29-Mar-10

The following has been approved by the Wits Human Research Ethics Committee: (Medical)

* MDP 301 Unblinding Script / English, Version 4.0 dated 18 March 2010

Noted: The above trial was completed in September 2009. The trial results were released globally in December 2009 and shared with HREC at the time of release. Despite the results indicating that the investigational product (0.5% PRO 2000/5 gel) was safe but not effective in HIV prevention, it is essential that the sites make efforts to inform trial participants which arm of the randomization scheme they were allocated to for the course of the trial.

In line with this responsibility, a site specific unblinding script has been developed for use with participants who were enrolled in the MDP 301 trial at the RHRU sites in Soweto and Orange Farm. The script will be translated into Zulu and Sesotho and administered telephonically using study staff who were part of the implementation teams at those sites.

On completion of translations, the Zulu and Sesotho versions will be submitted for HREC approval along with their matched Back-translations for verification purposes.

Ethics Approval Date: 01 April 2010

The above has been noted for the Ethics Committee information and records.

KINDLY FORWARD TO THE RELEVANT INVESTIGATORS / CRA / STUDY CO-ORDINATORS

Regards,

PROF PETER CLEATON-JONES
For and on behalf of the Human Research Ethics Committee: (Medical)

Appendix 10: Permission to use data

Wits Institute for Reproductive Health & HIV
Hugh Solomon Building
Esselen Street, cnr Klein St.
Hillbrow, 2001

2 March 2011

Re: Bonnie Jeanne Saxon, research project, 'Experiences of Implementing a Results Dissemination Plan with a focus on personalized messages for trial participants'

Dear Ethics Committee,

This letter is a confirmation that Bonnie Jeanne Saxon will be given access to the data from the MDP 301 dissemination and unblinding dataset for analysis for this research project. This is a dataset belonging to the Wits Institute for Reproductive Health & HIV and I am the Principal Investigator.

Kind Regards,

Professor Helen Rees
Principle Investigator MDP 301

Appendix 11: Poster inviting participants to call or SMS for more information about the trial results

RHRU
Reproductive Health & HIV Research Unit
of the University of the Witwatersrand, South Africa.

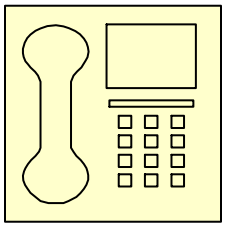
MDP
Microbicides Development Programme

Tshireletso MDP 301 Research Study

1. Did you take part in the Microbicide Development Programme (MDP) P301 Trial that took place at RHRU Tshireletso Clinic at Orange Farm, Ext 3 behind Dr Gwala's surgery?

2. Are you aware that the results of this trial have been released?

To learn more about the study results and which product you received (active or placebo gel), please contact:



Mandisa at 011 358 5490

OR

Keneuoe at 011 358 5489

OR

SMS: 'Please call me' to 072 725 8949