UNIVERSITY OF PRETORIA

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PARTICIPANTS' VOLUNTARINESS AND UNDERSTANDING OF A FEASIBILITY STUDY TO ASSESS POTENTIAL COHORT SUITABILITY FOR FUTURE MICROBICIDE TRIALS IN NORTH WESTERN TANZANIA

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This research project is an original work and has not been used for other degrees or diplomas in the past.

This research was approved by Institutional Review Boards of University of Pretoria, South Africa and The National Institute of Medical Research, Tanzania on 27th October 2010 and 29th October 2010 respectively.

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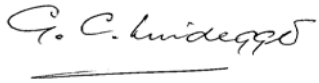
Student's signature.



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Supervisor's signature.

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ACRONYMS AND DEFINITIONS

ACRONYMS

HIV	Human Immunodeficiency Virus
STI	Sexually Transmitted Infection
VCT	Vocational Counselling and Testing
PPFO	Perceived Pressure From Others
PVOD	Personal Voluntariness Of a Decision

DEFINITIONS

Mama Lishe	Women selling traditional street food in busy neighbourhoods such as bus stands and construction sites,
Pombe Shop	Local brew bar

ACKNOWLEDGEMENT

This is the part of the thesis in which the student typically claims that no one writes a thesis by himself and then proceeds to mention all the people who presumably wrote the thesis for him. Well, I wrote the thesis myself, but not without enormous support from SARETI executive. It would have been quite enough to sponsor my MPH and provide academic support during my stay in South Africa. Yet, the SARETI executive has been patient and encouraging as I struggled to complete the MPH program back home. It is their faith in me and research ethics review framework in Africa that has provided the much needed momentum. In all honesty, I do not presume I could have done this without them.

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ABSTRACT

This informed consent study was conducted as an adjunct to a feasibility study designed to assess cohort suitability for future microbicide trials in North Western Tanzania. The general objective was to assess adequacy of understanding of the HIV/STI feasibility study and extent of voluntariness of participation including possible factors which had impinged on voluntariness.

A semi-structured interview was conducted with 122 of the 987 women who had participated in the parent study. The first part of questionnaire covered understanding of 6 concepts: research awareness, benefits, risks, study procedures, freedom to participate and withdraw, and confidentiality. The second part of questionnaire asked open-ended questions on how decisions to participate were made. These descriptions were later scored using a Likert scale of voluntariness as developed by Manafa *et al*, which was in two categories: Perceived Pressure From Others (PPFO) and Personal Perception of Voluntariness of Decision (PVOD)

The group as a whole had inadequate understanding of the research (51.7%). The best understood concepts were study procedures (94.4%) and confidentiality (62.2%). Least understood concepts were research awareness (20%) and research risks (20%). 50.8% of the study group had talked to someone before joining the study. 56.4% of those who talked to someone made the decision to participate independently i.e. they were not pressured or threatened to participate. On personal perception of voluntariness, 66.4% of the study participants perceived that they had a choice regarding their participation and that benefits provided by the study had not impinged on their choice to refuse. Participants' understanding was significantly related to age ($p = 0.041$) and education ($p = 0.006$) but not to type of facility, job at facility, marital status, spouse's education or spouse's occupation. Perceived pressure from others (PPFO) was significantly related to marital status ($p = 0.001$) but not to other demographic variables. Also, Personal Perception of Voluntariness over a Decision (PVOD) was significantly related to level of education ($p =0.017$) but not to the remaining variables.

Though challenges of illiteracy, poverty, and alien culture prevail, participants can be empowered to give valid informed consent.

1. INTRODUCTION

1.1. Background

Respect for human dignity and autonomy compels us to seek meaningful and voluntary informed consent from those who participate in research, as all people have a perfect right to determine their own goals and follow their own beliefs [1].

Gone are days when we used to think of informed consent mainly as a document that has to be authorized in order to secure participation. While it might be an easier task to obtain a signature on a piece of paper to relieve researchers of legal indemnities, it is a daunting task to achieve participants' understanding in particular cultural contexts [2]. Even when adequate understanding is claimed to be achieved upon disclosure, it is another milestone to ensure that participants have agreed to the study voluntarily. Further, even as understanding may be complicated by culture and belief systems that do not explain health and disease in the terms of modern medicine and technology, voluntariness may be undermined by incentives like medical care and compensation[3] alongside cultural practices that require the prospective participant to relinquish power to significant others [2,4,5]. Even more, socio-economic differences between different communities may influence the understanding, such as when the informed consent process and methods are not appropriately contextualized to the prevailing literacy levels [2, 6]. All three elements -- disclosure, understanding and voluntariness -- are essential in the process of formal informed consent.

To establish new cohorts for future HIV/STI preventative trials, researchers must study procedures and obtain information on key indicators to develop future trial protocols. Recognized as preparedness studies, researchers are not only supposed to test characteristics associated with completeness of follow up and clinical and socio-behavioral issues related to infections [7, 8] but also legal and ethical issues that have a bearing on protection of human subjects and validity of results [5].

Apart from ensuring that human participants' rights are protected, adequate informed consent can improve study retention and completeness of follow-up over long study duration. If participants are well informed of relevant aspects of their participation and have agreed voluntarily, they are likely to respond accurately to questions and keep their scheduled visits. As such, informed consent

becomes a defence against false or negative information that sometimes comes out of research-naive communities. This is important because participants lost during follow-up can also potentially bias the results because of differences between those who are lost and those who continue to participate [7].

1.2. Study Objectives

The aim of the study was to assess participants' understanding of key concepts of informed consent and the extent of perceived voluntariness of their participation. Specifically, the study sought to assess the adequacy of understanding and voluntariness, the factors associated with both of these, and the process by which participants made decisions regarding their participation. Relationships between understanding and voluntariness were examined in addition to the influence of demographic factors such as age, level of education, marital status, and specific job at the facility.

1.3. Hypotheses

1) Participants adequately understood the concepts of the study to make an informed choice about participation.
2) Participants' choice to participate was made freely without pressure or coercion from family members and friends.
3) Understanding was significantly related to age and education level.
4) Voluntariness was significantly related to age, marital status, educational level of the participant and educational level of the spouse.
5) Understanding was significantly related to voluntariness

2. LITERATURE REVIEW

2.1 THE PRACTICE OF INFORMED CONSENT

2.1.1 Background

Stemming from atrocities of Nazi Germany, a person's right to accept or refuse participation in medical research is unanimously recognized as one of the benchmarks of ethical research [9]. Enshrined in the Nuremberg Code[10] and the Universal Declaration of Human Rights (UDHR, 1949)[11], these rights feature strongly in every declaration, report, set of guidelines and code pertaining to research ethics today.

While the significance of informed consent is not debatable, its realization in specific communities is difficult and complex [2, 12]. A number of critical questions have been raised, including: whether consent is affected by different belief systems [2, 13], whether it is culturally bound or universal, whether individual informed consent is insufficient for participation in studies [4, 9] and whether the difficult concepts in some of the studies can be understood by individuals with little formal education [14].

Even so, it is important to find ways that may lead to attainment of adequate informed consent in communities where such challenges prevail [15]. More often than not these communities need interventions that ethical research can bring and therefore must be involved in a manner that enables adequate informed consent [16].

2.1.2. Informed Consent and HIV/STI Trials

The difficulty in obtaining adequate informed consent increases with the number and severity of risks carried by the research in question. HIV/STI trials are very high-risk [17]. Participants in HIV vaccine research are vulnerable to: rapidly progressing infection if they are later exposed to HIV, serious infection if they had an undetected infection during vaccination, immune tolerance that may preclude future immunization by more effective vaccines, vaccine-induced seropositivity, repeated injections, and associated pain [17, 18]. Most of these ethical concerns have been elaborated upon in microbicide research, proving that HIV has changed the way we morally think about research. Microbicide trials are fraught with safety concerns due to repeated exposure of both partners to the

product and unknown effects of the product upon unborn children [19, 20]. Moreover, early trials have paradoxically demonstrated an increased risk of contracting HIV [21].

Psychosocial risks include: inconvenience and fatigue associated with lengthy research, anxiety provoked by repeated HIV testing and possible stigmatization, discrimination due to perceived high risk of HIV infection, vaccine induced seropositivity and possible stigma, stress caused by exposure to foreign medical/research concepts, raised expectations of attaining protection from the deadly infection and gaining speedy access to the approved product, a false sense of protection leading to increased risky behaviour and stress between partners as a result of the participation of one partner [8,17,22].

Risks pertaining to the community include: possible stigma to the community from which participants are drawn, and vulnerability to exploitation by foreign and local researchers due to prevailing conditions such as poverty, inadequate health systems and ignorance of scientific methods [17].

Owing to potential social and physical harms, it has been proposed that certain information should always be imparted to prospective participants. Allowing for some overlap, the mandatory components are: Trial aims, Eligibility to participate, False positivity in conventional HIV tests, Inability to donate blood or get insurance in HIV vaccine trials, Wrong sense of protection, Explanation of methodology such as randomization, placebo and blinding, Compensation for research–related injury, Right to withdraw, The investigational product not being the cause of HIV infection, Exclusion of persons who are pregnant and/or infected with HIV[23 ,24, 25, 26].

Though the investigational product cannot be the direct cause of HIV infection, recent research has established that recipients of vaccines and microbicides may be at increased risk of HIV acquisition when exposed to the virus through unsafe sex or other pathways due to biologic or other confounding factors [21]. Hence, the inclusion of this information in newer HIV Trials Protocols [21].

2.1.3. Women, Gender, and Participation in HIV/STI Studies

In Africa, most HIV infections are due to heterosexual transmission and three times more women are infected than men [27]. A combination of biological, social, cultural and economic factors contribute to women's increased vulnerability.

In order to enrol and retain women in clinical studies, researchers need to consider societal definitions of what women can and cannot do [28]. In a setting where women do not assert power over their own lives, participation may be impossible without spousal or family approval [4]. Moreover, even if women could be allowed to decide freely, many are burdened by housework or other income-generating activities to the point of not being able to participate. For those whose homes are far away, the trial needs to think of ways to facilitate travel since women are not privileged with simple modes of transportation like bicycles. Odds are increasingly being withdrawn from these women when the studies require that pregnancy or breast-feeding be avoided in cultures that put high stakes on women's fertility. In HIV vaccine trials in Kenya, some women had reservations about using contraception for fear of giving their husbands licence to look for other women with whom to bear children [28]. Indeed, being unable to decide on matters that affect their own lives not only hinders their participation in research but may affect their economic well-being to the extent of risking their own lives by engaging in commercial sex.

Studies indicate that multi-partner sex, paid sex, and STIs are important risk factors fuelling the HIV epidemic [29, 30, 31]. Not diminishing the impact of other categories in the acquisition of HIV/STI, women selling alcohol in trading settlements along the major highways are considered to be one of the highest risk groups for infection with HIV and STI in Tanzania, as well as other parts of Africa [31, 32].

People at high risk for HIV infection such as commercial sex workers must be recruited for efficacy trials to find preventive interventions [33]. Moreover, these interventions need to be targeted to specific populations that bear the brunt of the disease in a specific setting. Beyond the long-established imperative to include women in medical research, women of Sub-Saharan Africa need preventive methods that they can use to protect themselves [34]. In the context of commercial sex, women are often totally dependent on the generosity of their client, and are not always able to negotiate consistent condom use, proven to offer effective protection from heterosexually acquired

HIV. Vaginal microbicides are being developed in response to this prevalent need for methods that women can control.

Given the failure of earlier microbicide products to demonstrate efficacy, larger study populations will be needed to evaluate new products that are coming through the development pipeline [35]. Considering that the trials may need to compare new products or product combinations with earlier products rather than with a placebo group, many new cohorts must be prepared for future interventions [15]. However, researchers must also maintain rigorous ethical standards as they react to the urgency of the HIV/AIDS burden by simultaneously conducting studies in this area. Informed consent surveys may help researchers understand how to morally involve research-naive participants in the quest for interventions that may better their own health.

2.1.4. Elements of Informed Consent

We can identify five components of informed consent from the literature: (1) competence, (2) disclosure, (3) understanding, (4) voluntariness, and (5) consent [1, 18, 36]. Accordingly, one gives informed consent to participate in research if one is competent to make the decision about participation, receives relevant information, comprehends the disclosed information, acts voluntarily, and formally consents to participate [1].

A person consenting to research participation must be one whose capacity is not diminished on account of age or physical or mental condition, and they must be legally regarded as competent [36]. Upon establishing capacity e.g. that the person is over eighteen years of age, and mentally healthy, the participant must be informed that they are participating in research. The competent participant must not be asked for a decision without having first received a comprehensive information package which includes: purpose of the research, study duration and procedures, risks and benefits, right to refuse or withdraw, alternative procedures that might be advantageous, safeguards of privacy, and compensation [15, 36]. The purpose of the disclosure is to achieve understanding, which is difficult to ascertain, especially when lay people are confronted with complex and scientific information.

One appropriate way of establishing understanding is by engaging in discussions where the prospective participants are actively encouraged to ask questions [13]. After establishing

understanding, the participant must voluntarily and freely decide to take part in the research. Intimidation, manipulation, and undue influence are factors that may invalidate informed consent. Inducements may also impair voluntariness [37]. The issue of benefits and compensation, if appropriate, should therefore be peer reviewed and later discussed with the participant lest they form the basis on which participants give and authorize consent [38].

2.1.5. Ethical and Legal Aspects of Informed Consent

Faden and Beauchamp[39] shed light upon the issue of informed consent by distinguishing two different ways to approach it: the *legal* approach which focuses on responsibilities of the researcher towards a set of regulations versus the *ethical* approach which focuses on rights of the subject or participant.

Similarly, the topic of this study can be conceptualized and analyzed in two different ways. In one sense, “informed consent” is an autonomous action by a subject that authorizes a researcher to involve the subject in research or medical intervention [39]. In the other sense, “informed consent” refers to institutionally or legally effective authorization that satisfies rules and requirements defined by specific institutional practices.

In autonomous authorization, one gives informed consent if one: (a) has adequate understanding of relevant information, (b) is not under substantial control by others and (c) intentionally (d) authorizes a researcher or a physician [1, 39]. In authorizing, the subject is responsible for what is authorized and transferred to another person for implementation [39]. A person must understand the responsibility of authorization and must intend to warrant another to proceed. This form of authorization fosters due respect for self-determination and has been coined by some ethicists as ‘ethical aspect of informed consent’ [13].

By contrast, legal aspect of informed consent is policy-oriented and does not totally originate from the analyses of autonomy and authorization. Legality refers to effective authorization from a participant that has been achieved through procedures in compliance with rules and requirements defined by specific institutions [13, 39]. Conformity to regulations and rules of the practice of informed consent is a necessary and often sufficient condition. Such regulations often focus on monitoring the behaviour of the professional and on setting up procedures and norms for the context of the

consent rather than autonomy of giving consent. Because legal aspect of informed consent focuses on those requirements of professional conduct and procedures that are observable and enforceable, it is by no accident that legal aspect of informed consent has been more concerned with disclosures than understanding. Legal systems require applicable mechanisms that courts can use to readily and fairly assess injury and responsibility. Typically, physicians confronted with negligence action are called upon by the courts not to prove that the patient understood them, but rather they did not withhold any material information from the patient [21, 37].

Contrary to this, the moral aspect of informed consent is based on sharing of information that enables patients or participants to exercise their rights as autonomous agents capable of self-determination [13]. It does not seek to indemnify the physician and the researcher as an end in itself but focuses on voluntary decision-making that is centered on adequate understanding of the disclosure. Given different beliefs and background, the researcher provides the information in a way that makes sense to the participant and checks if he has been understood before asking for consent. On the other hand, the participant checks if he has understood the information by asking questions and gives consent based on his own personal goals and beliefs.

At the heart of the ethical aspect of informed consent is the quality of interaction between the researcher and participant and not just the disclosure or documentation of the consent [40]. The procuring of the consent is regarded as a process that continues even after the participant has provided written documentation. If during the course of the ongoing trial, new information emerges that may affect the already procured consent , the participant must be informed in a manner that involves satisfaction of the five elements mentioned above.

In concluding, these two notions are not mutually exclusive. Informed consent should adhere and be scrutinized to both constructs [39]. Policies and regulations that govern informed consent in the legal sense should be made to conform to standards of autonomous authorization. That is, they should aim to maximize the likelihood of attainment of informed consent that satisfies the conditions of autonomous authorization.

2.1.6. Historical Shift from Disclosure

Following the Second World War, the Nuremberg Code was formulated as a set of standards that not only served to judge the perpetrators but also functioned as a guideline for physicians doing human experimentation [10, 37]. This code paved the way for many later codes designed to assure that human research is done in an ethical manner. Primarily, these codes largely served as conventions or rules that made it socially or legally acceptable to use a person in medical experimentation as long as measures were taken to prevent harm [37]. For example, informed consent was largely a complicated legal document that needed an authorization by a signature or a mark from a volunteer. It was one-way communication and a one-time event that was rarely repeated once the document was signed and filed. With time, however, informed consent came to be regarded as a tangible expression of respect for individuals as autonomous agents. Later codes such as Declaration of Helsinki (DoH) and International Ethical Guidelines by the Council for International Organization of Medical Sciences (CIOMS) [15] outlined key considerations of informed consent and autonomous decision-making. Even so, many discussions thereafter were more focused on the researcher and how he could present study information than the participant who needed to understand in order to make an informed choice. Only recently, the attention has shifted to participant and understanding, with focus on communal sessions, person-to-person discussions, innovations in the testing of understanding and continued reinforcement of information in subsequent visits [12, 24,].

2.2. UNDERSTANDING

2.2.1 Adequate vs. Complete Understanding

Aware that actions can never be completely informed, Beauchamp and Childress argue that persons can be said to understand if they have received pertinent information and have considered the nature and consequences of their actions against relevant beliefs [1]. Such understanding, they argue, is possible even for patients who have narrow knowledge bases. The physicians must communicate complex information in language and concepts fitting to the local context in addition to drawing analogies with locally relevant practices. In such settings, the physicians or researchers will have to ensure that they do not give too much or too little information [18]. They must use appropriate techniques that will enable patients and participants to appreciate the positive and

negative aspects of their participation in acceptable proportions. Understanding is not an easy task.

All over the world, informed consent research reveals that although research participants often do not understand and retain information that is considered important to the studies they are participating in, the outcome is reversed when researchers use local language and concepts in addition to incorporating locally relevant traditions and customs. [12, 25, 41]. Many studies are experimenting with different ways to present study information -- from the amount and nature of information, to language and format, to supplementing with video or Power Point presentations, to directly engaging the participant in discussions of the consent document [12]. With cultural differences between sponsors and researchers further compounding the informed consent process [2], many ethical guidelines like the Nuffield Report [5] have focused on prescribed procedures for volunteers in developing nations, including communal meetings, person-to-person dialogues, procedures for checking understanding, and continued reinforcement of information on subsequent visits [2, 5, 12, 15, 23]. Naturally, the guidelines and scholars do not always agree but they do insist, across the board, on achieving the goal of adequate understanding, however difficult it is. Understanding is so crucial to the participant's right to autonomy that no complexity justifies dispensing with it or relegating it to formality.

2.2.2 Understanding of Information in Consent Process

Research participants in developed and developing world alike have been found to lack adequate understanding of informed consent. Apart from novel research concepts such as randomization, placebo allocation and blinding [42], participants have been found to lack understanding of more mundane issues such as experimentation, risks and benefits, voluntariness, and confidentiality [40, 43, 44].

We limit ourselves, here, to common concepts that cut across different types of medical research. These are research awareness, benefits and risks, freedom to participate and withdraw, study procedures and confidentiality.

One of the key concepts that participants must understand is the fact that they are participating in research and not merely receiving medical care [15]. Indeed, attempts to maximize benefits for

participants have added to the confusion [45]. In South Africa, one study of participants in microbicide trials found a widespread belief that the gel provided prophylaxis against HIV even though they had been informed of the experimental nature of the study [22]. Correspondingly, in an informed consent study on patients participating in a placebo-controlled HIV Antiretroviral study in Nigeria, some participants (15%) believed that they were receiving free treatment for HIV with a small number strongly expressing their conviction about the therapeutic efficacy of the treatment [40]. Partly contributing to this confusion is the lack of local terminology for describing research as a separate process from other laboratory or clinical investigations that seek to confirm or rule out a certain diagnosis. Molyneux et al, in studying community notions of informed consent practice in Kenya found a need to better explain "utafiti" or "uchunguzi" as a separate process from widely understood clinical investigation [46]. Such observation was also shared by researchers in Mwanza, Tanzania where participants' association of research with individual therapy was compounded by hailing the research as "health project" [47].

Participants are likely to be motivated more by indirect or collateral benefits such as free medical care and referrals, than by perceived collective or societal value of research [36]. Inclusion of the statement of research in research protocols, as required by most ethical guidelines, serves to remind participants of unknown risks involved in their participation. Still, opportunity to access free services is a dominant feature in studies of understanding in resource poor settings. In addition, such appreciation of benefits does not go hand in hand with understanding of risks. In an antiretroviral clinical trial in Nigeria, 70% of participants mentioned free tests and checkups but only 26% identified at least one risk owing to their participation [40]. Probably due to the benefits involved, participants tended to devalue the risks such as drug side effects, and this suggests a clouding of judgment instilled by the program itself.

One of the main informed consent safeguards is the understanding that participation is voluntary and withdrawal from the study is permissible. Studies indicate that participants understand better the voluntariness of signing on than the freedom to withdraw [43]. In a Kenyan study, participants were adamant about maintaining "happy moment(s)" [i] with the health professionals, not only on joining but throughout the study, despite being informed that their refusals would not carry any repercussions [46]. A similar result was noted in another study where one participant with tertiary

education decided to participate because doing otherwise would have indicated he had not understood [44].

While *privacy* is "the freedom of the individual to pick and choose for (her)self the time and circumstances under which, and most importantly, the extent to which (her) attitudes, beliefs, behaviour and opinions are to be shared with or withheld from others" [ii], *confidentiality* refers to a mode of management of private and personal information [48]. Given the association of HIV/STI with illicit sex trade and drug/alcohol abuse, privacy and confidentiality is of paramount importance to ensuring that participants do not shun clinical care because of the fear of stigmatization. Although total confidentiality cannot be guaranteed in research, participants need to understand the safeguards put in place to ensure they are not personally linked to the data they have volunteered. In addition, it may be important to disclose the circumstances under which their identified or de-identified data may be provided to those not directly associated with the research [49]. Unfortunately, studies do indicate that participants are not aware how their study records will be stored or the manner in which their information or specimen will be used [40,43,44,50]. 85.8% of participants in oral health studies in Nigeria did not know how their records would be kept and as few as 37% of those participating in a prospective cohort study of malaria recalled being told that their data would be kept confidential [44].

On the other hand, several studies have been able to demonstrate that participants do understand and remember technical information such as procedures involved in trials or their duration [40, 42, 43, ,44, 51] . Koelch *et al* [51] found that while children with psychiatric disorders, and their parents, often failed to understand that the primary objective of the clinical trial was research, they showed sound understanding of study procedures, such as study visits, blood drawing, being sober and taking medication. Likewise, women in feasibility studies for microbicide trials have been found to be acutely aware of procedures such as HIV testing and speculum examination which is generally not well received [22]. These procedures are easily recalled and remembered because they are done routinely in the course of preventative studies.

2.2.3 Recall and Understanding

Differentiating between recall and understanding is a daunting task in informed consent research [43, 50, 52]. This is because recall is affected by the timing of the test of understanding and also by the severity or importance of the disease [1.] Many studies claim to measure understanding but are actually measuring short term recall, whereby participants are challenged to recall and repeat the information in the manner delivered. By focusing on what participants later remember, these studies cannot adequately reflect what participants understood at the time they made up their minds to participate or not. Since we know that memories deteriorate with time [53, 54, 55], some ethicists have argued that remembering everything is not important as long as the information is understood at the time of consent and the salient facts of the study are recalled. While it is true that at times information need not be remembered for a long time after consent is obtained, at various times the study's moral legitimacy relies on continued understanding and recall of critical information [56]. For example, it is crucially important that participants continue to remember that they received an investigational product since forgetting this could unleash risky sexual behaviour and lead to actual infection.

Studies show that there are many psychological processes involved in memory and understanding with no simple or clear-cut relationship between the two [54]. That said, it can be argued that adequate understanding facilitates recall of given information [13]. Understanding enables us to know where to place new information in context of previously learned experiences or what is already valued or believed. It is the association between the new and old information that facilitates recall of information over a long duration. Contrary to short-term memory, long-term memory indefinitely stores seemingly unlimited information owing to connections between different pieces of information [53]. To overcome limitations of short-term memory and store the information for longer, information must be rehearsed repeatedly – by articulating loudly or mentally simulating such articulation. Nonetheless, such rote memorization is no more than a learned response that does not help participants apply the information to make thoughtful decisions about their participation [13].

While it is conceivable that one may have adequate recall with inadequate understanding [57], long-term recall probably depends more on understanding than does short-term recall [13, 53]. Long – term memory may rely on how much the researchers tailored the concepts to fit the participants' personal and cultural values [23] and to the extent they availed attitudes, feelings and emotional

factors as “hooks” to new study information. By power of association or correlation, new information is likely to be understood and remembered if it is meaningfully “hooked” to what is already known, valued or believed [53]; association being equated to a mental hook from which one may fish facts out of one’s mind. And if recall is influenced by subjective value systems in addition to objective study information, it stands to reason that participants will recall more if both systems are incorporated in the informed consent process [13].

In most evaluations of understanding of study information, it is difficult to separate recall from understanding. A few studies have unpacked the concepts by relating *recall* to the selection of correct answers from checklists; and *understanding* to correct interpretation of statements provided [50]. Others have eliminated the effect of recall by allowing participants to refer to their informed consent documents when answering questions in the tests of understanding [58]. In the latter, *comprehension* was defined as “the measurement of performance as it might provide the best estimate of what is known at the time when informed consent was obtained.” [iii]

2.2.4 Testing Understanding

After an informed consent discussion, it is not enough simply to ask, “do you understand the study information?” HIV trials protocol insists on checks of understanding, usually in the form of a checklist where one agrees or disagrees with a series of study statements [14]. Still, it can be argued that closed-ended methods such as checklists do not provide true gauge of understanding because they may encourage rote repetition of important information. In such situations, participants increasingly ‘learn’ what is anticipated and score excellently in later tests. Moreover, *potential* participants may ‘learn’ required responses from their enrolled colleagues before attending their informed consent sessions and falsely demonstrate understanding. This concern is valid for sex workers who often live or work in groups. Accordingly, open-ended methods of assessing understanding such as narratives and vignettes may need to be applied so as not to reduce informed consent to a legal formality [23].

In light of the above, some have argued [23] that narratives and vignettes are the gold standard of tests of understanding because they invite participants to contextualize study information in light of their own concerns and situations in life, forcing them to engage their thought processes to reflect on consequences and implications of their participation [23]. By associating what is new to what is

already believed and lived, participants are likely to experience enduring impressions as opposed to short-term recall of disclosure. Thus, open-ended methods allow researchers and participants to explore not only technical facts related to the study but also subjective aspects related to values, motivation, and needs, which are probably more important. Being more conversational and closer to what people are used to, open-ended methods fall into line with Emanuel *et al* [12] findings that one-on-one prolonged discussions significantly and consistently improved understanding more than any other intervention. Correspondingly, in a South African study designed to compare four measuring instruments, two open-ended and two closed-ended, narratives and vignettes revealed gaps in understanding more than self–report and forced choice checklists [23]. Also, open-ended methods showed more agreement between themselves than closed-ended methods, suggesting that the latter were using different aspects of multi-dimensional construct.

It is true that open-ended methods may involve additional costs, take up much time, require more highly skilled staff, and may not be as quantifiable as the checklist method. Still, open-ended methods should be availed to assess understanding when there is potential risk related to poor understanding. Specifically, issues like therapeutic misconception must be tested by using resource-intensive open-ended methods. If researchers must employ closed-ended methods to discover gaps in understanding, the checklist should be availed for talking points in subsequent one-on-one discussions.

2.3 VOLUNTARINESS

2.3.1 Background and Definition

True Informed consent does not end with adequate understanding upon disclosure. After all is said and done, participation must be voluntary and free from coercion. Following a blatant abuse of human free will during the middle third of the twentieth century, all policies on human experimental subjects now stipulate that participants must not only be able to appreciate the risks of research, but also their freedom to participate or not. These guidelines are particularly significant for communities where certain vulnerabilities exist due to internal or situational factors such as women involved in commercial sex [5]. Sex workers may be considered a vulnerable group to the extent they are driven by economic hardship [59], limited educational attainment, social stigmatization, morbid health problems (e.g. AIDS), alcohol and drug abuse, and legal involvement.

We shall discuss voluntariness under primary notions of influence and control drawing from analysis by Nelson and colleagues [60].

2.3.2. Coercion, Persuasion and Manipulation

Although external influences such as offers of payment or medical care, threats, deceit, and emotional appeals exist, they only become morally problematic when they control action [61]. If a physician enrols a patient into a study through a threat of abandonment, the physician's influence controls the participant's action. But if he rationally persuades the patient in the process of informed consent, he only influences but does not control the patient's choice [38]. On the other hand, if the physician's threats have no effect on a participant, no coercion has occurred. Such is also the case if the patient perceives a threat, although no threat has been issued [60]. True coercion, therefore, only happens when plausible and intended threats from another person upset a person's chosen course of action.

Manipulation is a distinct form of influence that is different from persuasion and coercion. It entails the use of non-persuasive means such as withholding/exaggerating information or offering benefits to make the person do as the agent of influence intends [60, 62]. Virtually all forms of information manipulation are morally problematic. Falsehoods, withholding information, exaggeration -- all hinder voluntary decision–making. Offers of money and health care by researchers may compromise voluntariness when the prospective participant's lack of options renders the offer highly attractive.

In discussing control through coercion, persuasion or manipulation by another person, it is important to consider the degree of relationship between a person and others. There are two extremes of decision-making: *independent voluntariness* where a person decides without any help or influence from anyone else and *involuntariness* where other people make decisions for the person against their will. As opposed to imposing one's will on someone, an action is regarded as "nonvoluntary" when the consent of the person is unavailable due to circumstances e.g. debilitating illness. In the continuum between these extremes, there exists a third option – *cooperative decision making* [63]*.* Based on the idea of relational autonomy, cooperative decision-making may facilitate a voluntary decision, although it may be difficult to pinpoint at what degree of influence

cooperation ceases and the decision becomes externally controlled. Cooperative decision-making is congruent with the communitarian ethos of African culture where the spirit of collectivism is held to be embedded in individuals [64, 65, 66].

Frimpong-Mansoh [65] argues that communal culture in Africa does not have to be in opposition with the original conception of informed consent where one must make personal decisions about participation. At odds with the notion of community consent, where community leaders or family heads decide for participants whether to participate or not, Frimpong-Mansoh maintains that community culture can be used to better inform potential participants in the process of informed consent. From the standpoint of "a person is a complete person only through humane dealing [interaction and communication] with other people" [iv], it is appropriate to allow for consultation with the family and community as long as the final decision remains with the participant. After all, participants may well be able to make informed decisions within the framework of community debates and discussions. Arriving at a decision to participate or not by the participant should thus be regarded as a multi-step decision-making process that involves community discussions, and may serve to foster an informed and voluntary choice in addition to safeguarding the welfare of the participant. Through consultation with community members, participants can deal with doubts about the research and confirm whether participation is congruent with their own personal beliefs. As a result, participants are better positioned to understand and contribute to the later interaction with the research staff.

Although consultations are acceptable and encouraged, community and family members should not make decisions for potential participants. It is morally problematic when participants seek permission or approval from family or community members instead of a counsel that may help thrash out personal motivations. Unjustly, such approval or consent from the family heads to participate is more required for women who bear a bigger disease burden owing to biological and social factors [67]. In most African settings, men are essentially "protectors" of their families and are responsible for making crucial decisions even on personal matters that should be in women's domain. Correspondingly, in a survey to test the effect of relationships on decision-making in Harare, Zimbabwe, 87.6% of women were prepared to consult their husband about joining a study, but only 58.6% were prepared to act against the views of their spouses regarding their participation

[66]. These findings are congruent with other research involving study participants, where similar patterns were found [66].

Some people regard sex workers as social rebels that do not need permission to do anything they would like to do. However, this is hardly true. These women are often under the authority of a manager or a brothel keeper and may have to do what their bosses say. Even if their manager allows them to participate in a study, women, especially those who sell sex "on the side" may need to consult with or request permission from a partner or even significant family members [28].

2.3.3. Constraining Situations

As opposed to coercive situations, constraining situations are *nonintentional* in nature and are not, by design, controlled by another person [38, 61]. A person may feel controlled by circumstances or situations such as illness, lack of resources, or receiving an offer, and hence be in a position of making decisions divorced from personal goals. Nonetheless, lack of options does not make choice nonvoluntary although such situations may lead to "deprivations of voluntariness that are morally problematic" [v]. One such problem is undue influence [60]. Inducements and incentives trigger ethical concern when they distort people's judgment, encouraging them to participate in activities they would have deemed harmful in the absence of incentives. Defined by some ethicists as "an offer too good to refuse" [vi] or a benefit greater than the cost [68], inducements are hard to avoid in the context of research where study procedures such as costly gynaecological examinations and testing for STI/HIV are means whereby hypotheses are accepted or rejected. Inducements may also colour the participant's responses, causing them to deny potentially meaningful information that could later compromise their safety and/or the validity of the study.

Although there has been a debate on standard of care that should be made available to participants in trials, many assert that "effective established" services and interventions should be provided in default to participants who are exposing themselves to research risks [3, 69, 70, 71]. To them, inducements only become problematic when the offers are highly attractive, when risks are increased, or the person's current situation, e.g. financial hardship is worsened.

Most debates about undue inducements hinge on notions of autonomy. However, when risks, inducements or economic disadvantage are elevated above morally acceptable standards, it becomes necessary to view the problem in terms of exploitation.[38, 61, 60].

Acknowledging the confusion between different notions, Emmanuel Ezekiel rejects the standpoint of reducing benefits under the guise of reducing exploitation [61]. Instead, he proposes permission of reasonable benefits that go hand in hand with reduction of risks and adequate informed consent. To be valid, claims of exploitation require the presence of serious risks, proponents argue [60, 61.] Indeed, an irresistibly attractive offer is only a necessary condition for undue inducement but not exploitation or involuntariness. It may be manipulative and probably unjustifiable but not exploitative in absence of serious risk. All in all, the trend nowadays is providing benefits while putting measures in place to ensure that participants understand the nature of their participation and are not exposed to serious risks [69].

2.3.4. The Agent of Action and Voluntariness

Regarding voluntariness of decision, the agent of control is also important. The agent's control of his own deeds essentially serves as a means of attaining what he regards as good [1]. He not only controls his deeds but wants to control them in view of such attainment. Over and above the freedom of an action, the generic purposiveness of an action is also a necessary good [72]. If the agent acts according to specific purposes he regards as good, he also regards as good an increase in his level of purpose-fulfilment. We act purposely or intentionally when our actions or deeds are at par with our plans or wishes [60]. Our capacity for intentional action is questioned when we act in opposition to our desires e.g. an alcoholic who wants to quit drinking but cannot. Intending an action is not the only condition for voluntariness. Essentially, there must be no influences or desires that control the choice.

However, a person's subjective experiences of voluntariness may not be captured by the notions of intentional action or external factors. Participants are likely to have various subjective responses to multiple potentially constraining political, cultural, economic and social factors, many of which are beyond researcher's ability to control [40, 63]. In addition, participants may feel that they are unable to make voluntary decisions given the disparity of power and education between participants and researchers even when there is no objective evidence of control by researchers [73]. In such a

situation, participants may authorize their participation out of fear of nonexistent consequences. Also, participants living in a culture that puts emphasis on politeness may automatically say “yes” rather than “no” from the want of creating a favourable impression. To capture these notions, researchers must conduct qualitative evaluations to learn participants’ motivations for participating in research; subjective effects of factors such as benefits on their decision-making process and if they were able to decide freely or not. Also, internal conditions may curb voluntariness to a greater degree than expected as when external persons and control are internally contextualized [63]. Memory of a comparable but different incident with a partner, for example, could pressure a woman not to participate in a study because she imagines her partner will react negatively, based on the previous incident.

2.3.5. Testing Voluntariness

Of the three essential components in formal informed consent: disclosure, understanding and voluntariness, voluntariness has received comparably poor attention [74]. Literature search on reliable and valid measures of this construct leads to few results in the field of research ethics [58, 75]. Cognizant of the paucity of such measures, Miller *et al* describes a multifaceted approach that eventually leads to measurement of voluntariness across all fields [75]. After defining voluntariness as “the degree to which an individual controls a decision,” and linking the notion of control to “the individual’s resistance to influence” [vii], the group settled on the individual’s subjective perception as the basis of an assessment. This is because we only know that a certain influence is controlling a decision by assessing the individual’s subjective perceptions. The mere presence of an influence is not enough [75]. The study group availed instruments existing in different fields, discarding all items that had no relevance to the construct, and selecting the few that not only indicated the perception of voluntariness but also attended to issues of clarity and content validity. Of significance to developing countries where participants are said to have no options, this group, using a matrix approach, also differentiated between *voluntariness* and *perception of options*, leading to a conclusion that it is possible to make voluntary decisions, yet with only one option.

As opposed to noncontrol, which can be measured in terms of degrees of the ability to take control, intentional actions can only be declared as present or absent [60]. Miller et al, in their study to assess the perceived voluntariness of parents making decisions for their children, assumed intentionality when the parent indicated that he or she had made a decision [77]. Perception of noncontrol, on the

other hand, was on a continuous scale that allowed for fractions of perception of control over a decision. To measure the degree of perceived noncontrol, they developed a “Decision Making Control Instrument (DMCI)” that required participants to either indicate on a Likert scale or mark a forced checklist when they felt situations such as financial incentives and referrals were controlling. The instrument also allows for exploration of family’s involvement in decision-making: whether it undermines or supports a participant’s voluntary choice.

Manafa *et al* [40] assessed voluntariness by interviewing participants in an antiretroviral clinical trial. Participants not only described how they decided to participate but also who and what were involved in the decision-making. They also detailed influences and motivations as well as their feelings about their participation. Were they hesitant at any point? How did they resolve the uncertainties they had? How did they feel about someone making decisions for them? Later, researchers assessed and rated participant’s narratives by using Likert scales on two categories: pressure from others (husband, family etc.) and personal feeling of having a choice or no choice in the participation. To test the reliability of scoring, two separate researchers ranked narratives from forty volunteers at different times. The resulting agreement rate between researchers was more than 81%. Contrary to DMCI, the Likert method can be used on illiterate participants without modification.

2.4 CRITICAL CONCLUSIONS

Until effective preventative interventions for HIV/STI are discovered, there are likely to be increasing numbers of HIV/STI studies and trials. In responding to the urgency, researchers will also need to attend to ethical issues in research, especially in research-naive or vulnerable communities. Informed consent is one of the ethical challenges requiring particular attention in such communities, as it may be complicated by illiteracy, cultural norms and expectations, gender inequalities, and abject poverty, all of which may exacerbate the realization of adequate informed consent.

While it may be easier to satisfy the legal requirements for informed consent such as a signature on a consent form, it is far more challenging to satisfy the higher ethical demands for informed consent. We are ethically bound to ensure that autonomous authorization is obtained from potential participants. Autonomous authorization is given when “participants with substantial

understanding and in substantial absence of control by others intentionally" authorize a researcher to carry out an intervention [39]. Two of the most challenging requirements for informed consent are understanding of information and voluntariness.

Apart from understanding methodological considerations such as randomization, participants must be able to understand the personal implications of increased risks associated with HIV/STI trials. However, such understanding has been difficult to achieve. Indeed, participants have been found to lack understanding of basic concepts such as the difference between research and medical care, risks of trial participation, right to withdraw, and confidentiality. Further, studies that examine understanding may have been confounded by measuring recall instead of understanding. Of significance to understanding is the long-term memory that is achieved by associating new information to what is already known. To achieve long-term memory and deeper understanding, researchers must tailor the concepts to fit the participant's personal life situation and cultural values and must avail attitudes, feelings and emotional factors as links to new study information. The currently used closed-ended tests of understanding, such as checklists, apparently do not lead to understanding the personal implications of trials, nor do they assess this personal understanding as well as open-ended methods such as narratives. They rather encourage rote repetition by participants and may elicit well learned responses rather than genuine understanding.

True informed consent does not end at adequate understanding. Participation must be voluntary and free from control by others. Though external influences such as threats or emotional appeals exist, they only become problematic when they control the decisions and actions of potential trial participants. Influences and communications that help one to make decisions through discussions and debates are appropriate and may facilitate voluntary decisions, but those that lead to decisions contrary to what the participant would otherwise pursue are disapproved. Apart from controlling relationships, constraining situations such as inducements may also hinder voluntariness. Inducements trigger ethical concern because they may distort people's judgment and encourage them to participate in activities they would otherwise have preferred not to participate in or may have deemed harmful. They are especially problematic when they are highly attractive, or the research is irrationally risky, or when the person's current situation is worsened by the research.

Over and above external factors of control, the factors relevant to agent of control are important. One must act intentionally, where one's actions are at par with one's wishes. Nonetheless, intentional action and external factors may not capture the person's subjective experience or personal perception of voluntariness, since participants are likely to have various subjective responses to numerous potentially constraining political, cultural, economic and social factors, many of which are beyond researcher's ability to control. To capture these notions, participants' subjective perceptions must be assessed.

Only when substantial understanding and voluntariness have been achieved, can it be said that genuine informed consent has been obtained.

2.5. RATIONALE OF THE STUDY

As new study sites are reviewed for feasibility of future HIV/STI preventative trials, informed consent studies should be run concurrently to uncover factors that may impinge on understanding and voluntariness in a particular context. Such understanding has a bearing towards fine-tuning of prevalent informed consent practices and establishing community liaison systems that work.

Beyond adding to the scanty knowledge of informed consent practices in Tanzania, this study explored the characteristics of high risk female cohorts as a group, with attention to comprehension levels and voluntariness. The level and relationship between understanding and socio-demographic characteristics such as age and education level are not only relevant to the targeted group, but can be extrapolated to other study populations within the country, and in Africa. Likewise, perceived voluntariness in research participation and its relationship with characteristics such as marital status will inform researchers of decision-making processes in environments where health care options are limited and communal decision-making is the norm, and often a male prerogative.

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Cognisant of the need to ensure that the number of HIV/STI preventative trials is commensurate with the burden of the disease, researchers must move forward carefully, walking a difficult line between two imperatives: reacting to the urgency of the HIV pandemic and maintaining rigorous ethical standards.

3. METHODOLOGY

3.1. Study Population & Study Sites:

The study invited 134 women out of 987 participants in a preparedness study to assess the cohort suitability for future microbicide trials. Nine (9) invitees declined, three (3) did not agree to the study after informed consent and 122 participants agreed to participation in this study. Participants working in bars, guesthouses, hotels and other food recreational facilities were sourced from all three sites of the ongoing feasibility study in Geita, Shinyanga and Kahama Districts. These establishments are located in gold-mining settlements, and towns and villages along truck stops in Mwanza and neighbouring regions.

3.2. Demographic Characteristics

The mean age of participants was 32.3 (range 19 – 46, SD. 6.7). 21.3% of respondents had never gone to school and 90.2% had not gone past primary level education. The majority were either working in hotels (31.4%) or as Mama Lishe (28.9%) -- women selling traditional street food in busy neighbourhoods such as bus stands and construction sites. 35.8% of participants were working as waitresses and 29.2% were working as Mama Lishe. 32.8% and 12.3% of participants were married as one wife, and as more than one wife; and 35% were divorced. As for husbands of married women, 5.4% had never gone to school and more than 50% had achieved at least secondary level education.

Table 1: Demographic characteristics of respondents

Demographic characteristics		Freq.	%	Cumulative %
Site (District)	Geita	46	37.7	37.7
	Shinyanga	45	36.9	74.6
	Kahama	31	25.4	100.0
Age (Yrs)	18 – 24	18	14.8	14.8
	25 – 29	34	27.9	42.7
	30 – 34	21	17.2	59.9
	35 – 39	28	23.0	82.9
	40 – 44	21	17.2	100.0

Education	None	26	21.3	21.3
	Primary	84	68.9	90.2
	Secondary	12	9.8	100.0
Facility	Guest House	17	14.1	14.1
	Hotel/Café	37	31.4	45.5
	Bar Only	24	19.8	65.3
	Grocery/Pombe Shop	7	5.8	71.1
	Mama Lishe	35	28.9	100.0
Job at Facility	Waitress	43	35.8	35.8
	Cook/Cleaner/Receptionist	27	22.5	58.3
	Manager	15	12.5	70.8
	Mama Lishe	35	29.2	100
Marital Status	Not married	17	13.9	13.9
	Married	40	32.8	46.7
	Married (More than one wife)	15	12.3	59.0
	Widowed	7	5.7	64.7
	Divorced	43	35.3	100.00
Husband Education	None	3	5.4	5.4
	Primary	24	42.9	48.3
	Secondary	26	46.4	94.7
	Post Secondary	3	5.4	100
Husband Job	Not employed/Peasant	7	12.5	12.5
	Civil Servant	11	19.6	32.1
	Trader	15	26.8	584.9
	Artisan	12	21.4	80.3
	Driver	5	8.9	89.2
	Mine worker	6	10.7	100.0

3.3. Ethical Considerations

This study will add knowledge to the practice of informed consent in Tanzania. Although several studies have been conducted to date, there is a paucity of literature on voluntariness of research participation and understanding of informed consent. Acquainted with this knowledge, Research Ethics Committees and researchers will be more capable of contextualizing ethical requirements to prevailing situations on the ground. On the issue of reliability and scientific validity, this study availed the standard methods of testing understanding and assessed voluntariness using established methods, the scarcity of literature notwithstanding. To enhance reliability of narrative data, two trained researchers independently scored the data using pre-determined criteria following which comparisons of two score sets were made.

Participants volunteering the data were a subset of women who had participated in the preparedness study, all of whom were invited if they had not since relocated. No woman was denied participation after giving informed consent. The study was described as a method of helping researchers test participants' understanding of the study and how they had made decisions about their participation. Participants were informed about the social value of the research and potential risks involved, particularly the unlikely possibility of confidentiality breach pertaining to recorded sounds. No one except the informed consent team would have access to the recorded interviews. No names were written on questionnaires. Participants were free to refrain from answering any question that made them uncomfortable, and they could stop the interview at any time without giving any reason. Participants were not paid for the interviews but the study facilitated transportation for those who specifically attended for this activity.

Prior to any study procedure, ethical approval was obtained from Ethical Review Boards of the University of Pretoria, School of Health Systems and Public Health, and National Institute of Medical Research, Dar es Salaam. Study results will be shared with participants who are still retained for future studies as well as the research institution and the public.

3.4. Study Procedures

This study was open to all participants (n=987) participating in the Feasibility study. The interviews were conducted during a 2–week period in each of the respective study sites, commencing at the end of the 2–year study. Interviewing took place within the study clinic grounds at all three sites. Apart from writing down answers on the questionnaire, the two interviewers digitally recorded and timed all the interviews.

3.5. Study Instruments

The Interviewer-Administered Questionnaire (Appendix A) comprising of closed and open ended questions was used to test understanding and perceived voluntariness of women participating in a feasibility study. In addition, the instrument assessed Willingness To Participate (WTP) in future microbicide or vaccine trials. The translated instrument was pre-tested on 11 participants, after which, confusing and ambiguous terms were reworded. Open ended questions were treated as narrative text to be scored. The scoring methodology is explained in Section 3.5.1 below.

3.5.1. UNDERSTANDING

A total of 12 questions were asked in this section. The questionnaires were interviewer-administered, given the considerable illiteracy of participants. Upon asking the closed-ended question and understanding the response, interviewers chose from a list of options such as YES, NO or I DON'T KNOW. If the response was not on the list, the interviewer was instructed to write the response in the space provided. Some questions on research awareness were open-ended, and if such was the case, the interviewer was to write the responses as delivered if the response was short and paraphrase if lengthy. Prompting was done if the question, as written in the questionnaire, was not understood.

The questions in this section assessed six concepts, four of which had also been assessed previously by means of a quiz at the beginning of the parent study after informed consent at screening and enrolment. All concepts had featured in the informed consent document given to participants. The six concepts are:

- Knowledge of the research and its purpose.
- Understanding of risks,
- Understanding of benefits,

- Understanding the right to refuse participation and right to withdraw from the study,
- Understanding of confidentiality,
- Understanding of practical procedures of the research.

Scoring

- Content analysis of narratives and descriptions (Research Awareness):

  Interviewers developed criteria according to what they would consider to be poor through excellent understanding. Then, they separately scored (11) eleven participants accordingly, compared the scores and updated the scoring criteria. Later, using the new scoring criteria, each interviewer, in a one-month interval, ranked responses from 50 participants. The accounts or descriptions were ranked from 1 – 5, 5 being excellent understanding. Inter-rater reliability on the knowledge questions was 86%

- Scoring of multiple choice questions:

  Scoring was based on the number of correct responses mentioned. For example, participants who mentioned none of the laid out options were assigned the lowest score (1). If they mentioned all the options, they received the highest score (5). Only one correct response was applicable in forced-choice questions. Later, an overall score for each of the measured concepts was obtained by adding up individual scores in each concept.

Maximum score for each concept was 5, making a total Maximum score of 30. After ranking, a total score for each participant was calculated and the following cut-offs were used: a high score of 75% and above signified excellent understanding, 60% - 74% good understanding, 50% - 59% moderate, 30% - 49% poor understanding and 0% - 29% extremely poor understanding. We defined adequate understanding as having at least good understanding i.e. ≥ 60%. These cut-offs are based on the study by Manafa *et al* [40] whereby scores above 60% and 74% signified good and excellent understanding respectively.

3.5.2. VOLUNTARINESS

Participants were asked to share the story of how they decided to participate, who and what was involved in this decision, and how other people influenced their participation. Perceptions of voluntariness were assessed from the details of these stories. A Likert scale of voluntariness

developed by Manafa *et al* [40] was used, upon permission, to assess and score each subject's description of how they decided to participate and who they consulted. In addition, participants were asked about their motivation to participate, if they were uncertain at any point, and how their uncertainty was resolved.

The scorings were in two categories:

1. Pressure from others to participate; spouses, family, friends, facility owners and researchers (PPFO).
2. Personal perception of having a choice or no choice about participation (PVOD).

To test the reliability of scoring, two separate researchers rated narratives from 0 – 5 and 0 – 3. The agreement rate between researchers was 81% and 84% respectively. One rater had 6 years experience in research and 12 months intensive training in research ethics. The other had 2 years experience in research with frequent GCP courses. Fifty participants were used to assess inter-rater reliability, with scoring for these participants done by both raters, one month apart.

The Likert scale for scoring is as follows:

Likert scale of pressure from others: spouse, manager, family and friends.

5 Participant reports extreme pressure from others to participate with threats for non-participation.

4 Participant reports strong pressure from others to participate, but no threats.

3 Participant reports mild pressure from others to participate e.g. hopeful expectation of a spouse, manager, family or researchers.

2 Participant reports strong encouragement to participate, but no pressure.

1 Participant reports mild encouragement to participate, with no pressure

0 Participant reports no pressure or encouragement.

On this scale, involuntariness was assumed if pressure from others was reported. Participant was assumed to act voluntarily if she herself had made a decision with or without encouragement to

participate. Voluntariness of the cohort group was assumed to be adequate if ≥ 60% of the women made the decision to participate themselves i.e. they were not pressured or threatened to participate

Likert scale of personal perception of voluntariness of decision

3 Participant feels that they have no other choices, therefore have to participate because of benefits, e.g. free reproductive health services, but would have preferred not to participate.

2 Participant feels that it would be an advantage to them to participate, given little or no choice, e.g. having a chronic Pelvic Inflammatory Disease (PID)

1 Participant feels that it would be an advantage to them to participate because of the benefits, even though there are other choices, e.g. they can access the reproductive health services elsewhere.

0 Participant feels no great advantage to participation, and free choice about participation.

Participants were assumed to be voluntary if they perceived having a choice regarding their participation despite provided benefits. Voluntariness of the study population was assumed to be adequate if ≥ 60% of women participated while perceiving no great personal advantages or having other choices.

3.6. DATA ANALYSIS

Upon scoring, the data was analysed using STATA 11 statistical package. To test hypothesis 1 that participants adequately understood the key concepts of the study disclosed to them in the consent process, total scores of understanding were calculated for each participant and later for all participants. These scores were considered against the predetermined cut-off of 60% for adequate understanding. To test hypothesis 2 that participation was voluntary, individual and overall scores were obtained for the two Likert scales designed to measure voluntariness. To test hypothesis 3 that understanding was significantly related to demographic variables the following analyses were performed: A Spearman rank correlation to test relationship between understanding and age. A One-way ANOVA was used to test relationships between understanding and all remaining

variables. To test hypothesis 4 that voluntariness was directly related to demographic variables the following analyses were made: A Spearman rank correlation to test relationship between voluntariness and age, and One-way ANOVA to test relationships between voluntariness and all remaining variables; and the Student t test to test relationships between (collapsed) binary variables and voluntariness. To Test hypothesis 5 that understanding was directly related to voluntariness, levels of understanding were cross-tabulated against two Likert scale of voluntariness and a Chi-square test was conducted to determine if there were significant differences in degrees of voluntariness.

Also, levels of understanding and voluntariness were separately cross-tabulated against willingness to participate in future microbicide trials. A Chi-square test was performed to determine if understanding and voluntariness had any bearing on the participants' willingness to participate in future trials. Similarly, levels of understanding and voluntariness were cross-tabulated against previous participation in research.

4. RESULTS

4.1. UNDERSTANDING

4.1.1. Mean Understanding of the Study Concepts

Table 2: Mean Understanding/Knowledge of the Study Concepts by Respondents

Understanding	Range	Mean Score	SD	% Underst.
Research Awareness	1 - 5	1.25	0.47	20
Benefits	1 – 5	2.35	0.65	47
Risks	1 – 5	1.25	0.47	20
Study Procedures	1 – 5	4.72	0.65	94.4
Freedom to Participate and Withdraw	1 – 5	2.84	1.41	56.8
Confidentiality	1 – 5	3.11	1.81	62.2
TOTAL SCORE	1 – 30	15.56	3.37	51.7

Scores equal to 3 or above were regarded as adequate understanding i.e.3/5×100=60%. To assess if total understanding was equal to or above 60%, i.e. good or excellent understanding, the % of maximum score was calculated – 15.56/30×100=51.7%. Our overall findings show that participants' understanding was inadequate i.e. < 60%. On relative levels of understanding of different concepts, study procedures (94.4%) and confidentiality (62.2%) were adequately understood while research awareness (20%) and research risks (20%) were least understood.

4.1.2. Research Awareness

Most participants (88.5%) had never participated in research before. Nonetheless, the majority (82%) of participants said that the program they were participating in was a research. On the aim(s) of the research, 86% mentioned testing for HIV and 75% mentioned getting treatment for STI. Almost two-thirds (65%) of participants cited both testing for HIV and getting treatment for STI as aims of research. Only 5% of participants mentioned the correct aim: To determine whether areas in north-west Tanzania are suitable for future studies of microbicide gel. Of those who said they were not participating in research (n=22), 86.4% were there to test for HIV and 77.3% to get

treated for STIs. 72.7% mentioned both. As to why they were invited into the program, 71.3% of all participants said they were at risk of contracting STIs/HIV.

Descriptions given by participants were scored to assess understanding of research. The Score was from 1 – 5, with 1 signifying extremely poor understanding and 5 excellent understanding. Almost three quarters (74.6%) of participants scored 1 (Mean = 1.4, SD = 0.9). When asked to mention the differences between procedures at the research clinic and the district hospital, most participants replied: “There is no difference except that we are getting quicker HIV tests than other VCT centres in addition to getting thorough STI investigations and free treatment”, “The clinic runs laboratory tests even when we are not sick in order to find hidden infections”, and “The only difference is *that* special test (gynaecological examination by speculum) which I hadn’t received in my whole life.”

Table 3: Understanding of research

Understanding	Score	Frequency	%	Cum.
Extremely Poor	1	91	74.6	74.6
Poor	2	10	8.2	82.8
Moderate	3	17	13.9	96.7
Good	4	2	1.6	98.3
Excellent	5	2	1.6	100.00

4.1.3. Research Benefits.

92.6% of participants correctly reported that there were benefits involved in research. Finding out one’s HIV status, getting access to treatment for STI, and having access to counselling were cited as benefits by most participants. More than two fifths (43.4%) of participants mentioned both finding out their HIV status and getting access to treatment for STI as benefits. In addition, about one third (29.2%) of participants mentioned getting access to treatment for other minor elements as a benefit. Very few participants identified with the societal or collective value of research: helping to determine if the area is suitable for future studies of microbicide gel (0.9%) and helping to understand why there is a high rate of HIV/STI transmission in the area (2.7%).

Table 4: Research Benefits

Benefit	No	%
Knowing my HIV status	79	69.9
Being treated for STI	74	65.5
Learning from HIV/STI counselling	63	55.8
Helping to determine if the area is suitable for future studies of microbicide gel	1	0.9
Helping to understand why there is a high rate of HIV/STI transmission in the area	3	2.7
Receiving treatment for minor ailments	33	29.2
Receiving family planning services	2	1.8
Will help me not get HIV	13	11.5
Getting money for meal and transport	10	8.8

4.1.4. Research Risks

Only 23.8% of participants reported that research involved risks and discomforts. Becoming anxious while waiting for HIV/STI results (41.4%) and pain/discomfort during gynaecological examination (41.4%) featured more than risks such as discomfiture/embarrassment of discussing sexual practices (6.9%) and confidentiality breach (10.3%).

However, participants tended to report risks in comparison or in reference to benefits received. Upon mentioning confidentiality breach and discomfiture in disclosure as risks, one participant added: "...but these are not risks. I think when you receive expert services [gynaecological examination and laboratory tests] which you would have paid for dearly, and without much fuss, you have to thank God." Clearly, this participant appreciated the risks but regarded them worth taking because of free services provided promptly.

4.1.5. Study Procedures

When asked to describe study procedures, a majority (82.3%) of participants mentioned three procedures or more. 89.3% mentioned both gynaecological examinations and drawing of blood for

testing. About half (45.1%) of the participants reported being asked general and private questions about their lives and sexual behaviour. Furthermore, 86.9% of participants knew the duration of the study and 97.5% understood how often they were supposed to attend scheduled visits.

4.1.6. Freedom to Participate or Withdraw

While more than two thirds (68.9%) of respondents correctly understood they could refuse to join the study, fewer participants (59.9%) understood they could withdraw from the study after joining. When asked what would happen if they decided to withdraw, more participants (37%) identified with losing the benefits associated with the study than with suffering no consequences at all (32.8%). 18% of all participants responded that they did not know what would happen to them. Making research staff unhappy was less frequently mentioned as a consequence (8.2%).

4.1.7. Confidentiality

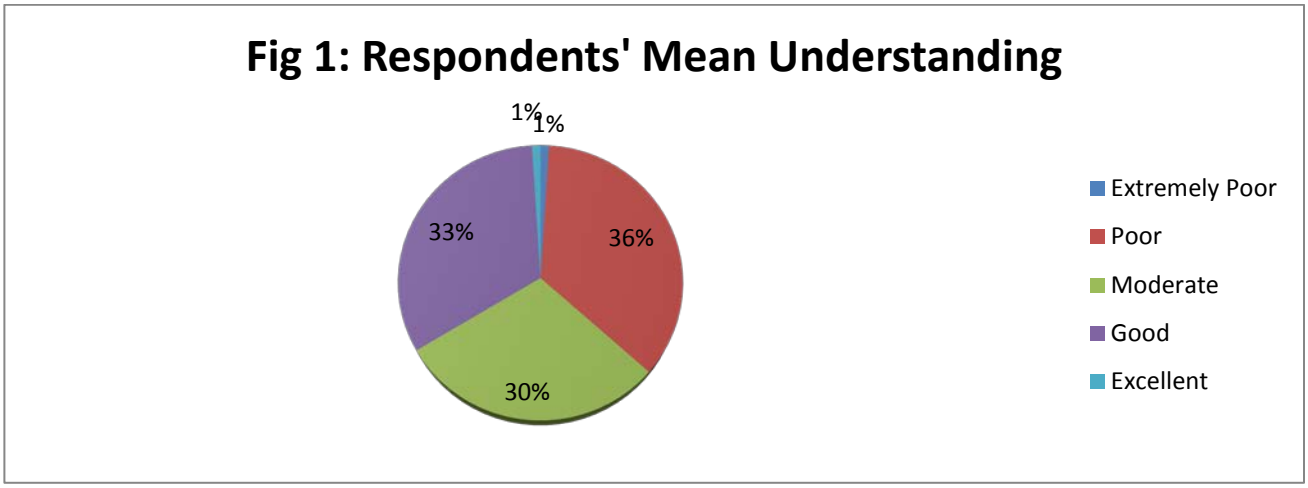
About a third (22.6%) of participants incorrectly reported that their names would be included in future publications. Nearly the same number (27%) of participants incorrectly reported that the samples taken from them were accompanied by their names. 64.9% of respondents correctly answered that their samples would be kept anonymous while only 59.4% correctly reported that associated publications would not include their names. More participants were uncertain (responded I don't know) about being named in publications (18%) than were unsure about the anonymity of their samples (8%).

4.1.8. Cohort Study participants' total understanding.

The maximum score of understanding was 30. The mean participant's understanding was 15.56 (range 1 – 30) with a standard deviation of 3.37. Very few participants (n=1) scored in the extreme categories: extremely poor understanding or excellent understanding. The majority were more or less uniformly distributed between the three intermediate categories: poor understanding(36%), moderate understanding (30%), and good understanding (33%). Overall, participants had moderate understanding of their study participation.

Thus Hypothesis 1 that participants adequately understood the study information is rejected.

Fig 1: Respondents' Average Understanding



4.1.9. Relationship between the level of understanding and demographic variables

Finally, the level of understanding was related to demographic characteristics of the respondents. Spearman's rank correlation shows a direct relationship between understanding and age, ($p = 0.041$ rho = 0.186). One-way ANOVA revealed a significant difference between three education levels when understanding was related to education levels ($F = 5.36$, $p = 0.006$). To determine where the variance lay, the Bonferroni post-hoc multiple comparison test was conducted. This showed that women with no education scored significantly lower in understanding than those with primary education ($p = 0.029$). Likewise, women with no education scored significantly lower than women with secondary education ($p = 0.01$). No significant difference was found between primary education and secondary education ($p = 0.435$). Analysis by One-way ANOVA showed no association between understanding and type of employment facility ($F = 0.19$, $p = 0.944$), understanding and job at facility ($F = 0.31$, $p = 0.817$), understanding and marital status ($F = 0.77$, $p = 0.549$), understanding and spouse's education ($F = 1.64$, $p = 0.191$), and understanding and spouse's occupation ($F = 0.77$, $p = 0.577$).

Given these results, hypothesis 3 that understanding was significantly related to age and education level is accepted.

Understanding was cross-tabulated against previous participation in research and a Chi-square test was conducted to establish whether there were significant differences in levels of understanding given previous participation. Participants who had participated in research prior to the feasibility study scored significantly higher in levels of understanding than those who had not (Pearson chi2(4) = 12.89, p = 0.012). Cross-tabulation between understanding and willingness to participate in future microbicide trials did not reveal a significant difference in levels of understanding (Pearson chi2(8) = 12.92, p = 0.115).

Table 5: Relationship between understanding and level of education

Understanding	**None**	**Primary**	**Secondary +**	**Total**
	No (%)	No (%)	No (%)	No (%)
Extremely Poor	1 (7.7)	0 (0.0)	0 (0.0)	1 (1)
Poor	7 (53.9)	35 (36.1)	2 (16.7)	44 (36)
Moderate	5 (38.46)	27 (27.8)	4 (33.3)	36 (30)
Good	0 (0.0)	35 (36.1)	5 (41.7)	40 (33)
Excellent	0 (0.0)	0 (0.0)	1 (8.3)	1 (1)
Total	**13 (10.7)**	**97 (79.5)**	**12 (9.8)**	**122 (100)**

4.2. VOLUNTARINESS OF PARTICIPATION

4.2.1. Decision to Participate

Regarding decisions to participate, 50.8% of the study group said they had talked to someone before joining the study. Spouse (43.5%) was the category most frequently mentioned by those who consulted other people. Other important categories were relatives (25.8%) and co-workers (24.2%). Most participants were encouraged rather than discouraged to participate by those they shared the study information with - spouse (88.8%), relatives (87.5%) and co-workers (73.3%). Out of all married women (n = 55), 45.5% discussed with their husband about their participation. 23.6% discussed with other people but not their husband. 31.0% did not discuss their participation with anyone. None of the widowed (n=7) discussed their participation with anyone.

Friends (36.4%) and co-workers (36.4%) were the ones most often reported as discouraging participation. Predictably, they were the most likely source of pressure to withdraw from the study upon joining (71.4%). Only one respondent reported being discouraged from participating by her husband. Most participants (75%) dealt with the discouragement by discussing the issues with the study staff. Spouses (37.5%) were more likely to leave it to their partners to participate or not than any other category.

49.1% of participants did not consult anyone before deciding to participate, reasoning that since they were the direct beneficiaries and HIV is a stigmatizing disease, there was no need to talk to others about their participation. One participant responded, “It is my life. I do not need to discuss with anyone. If people know about your condition (infected with HIV), they are going to talk about instead of helping you”.

4.2.2. Voluntariness of Participation

Respondents were asked several questions inviting them to disclose how voluntary their participation was. Most of these questions were in the open-ended format.

PRESSURE FROM OTHERS

Respondents indicated that some of the advice they received helped in making up their mind about their participation. The varying degrees of pressure perceived by women from advice they received from others is shown in Table 6. The scores in the table are derived from the adapted Likert scale.

Table 6: Likert scale (1) on perceived pressure from others to participate (PPFO)

Degree of Pressure perceived	**Frequency**	**%**	**Cum %**
No pressure or encouragement	11	17.7	17.7
Mild encouragement	11	17.7	35.4
Strong encouragement	13	21.0	56.4
Mild pressure	19	30.6	87.0
Strong pressure	8	12.9	100.0
Extreme pressure	0	0.0	100.0
TOTAL	62	100	100

Of those who consulted others, 12.9% saw the advice given as strong pressure. More participants (30.6%) perceived the advice given as mild pressure. None perceived the advice given as extreme pressure. 56.4% of those who talked to someone made the decision to participate themselves i.e. they were not pressured or threatened to participate.

Considering that 49.1% of total population did not consult anyone and 56.4% of those who talked to someone made the decision to participate themselves, we can calculate that 77.9% of the total population participated independently and thus accept hypothesis 2 that women participated freely without pressure or coercion from others.

Spouses were the most likely group of significant others to pressure women to participate. One woman said: "...he said that I should come to participate because women have many diseases and it would be good for him to know". Another said: "...my husband said that it was a chance of lifetime....and he was the one keeping track of my scheduled visits and reminding me." Nonetheless, there were some who said that their husbands discouraged them because they thought "researchers would spoil (their) uteri" and hence reducing the chances of bearing children. Most of those who perceived the advice of others as neither pressure nor encouragement reported that their family members had left it up to them to decide since it was their own health.

PERCEPTION OF PERSONAL CHOICE ABOUT PARTICIPATION.

16.4% of respondents reported having experienced personal doubts about participating when they were first invited to join the study. The rest did not experience any hesitation. Through open-ended questions, participants' feelings of having a choice regarding their participation were assessed from their accounts on how they resolved their doubts and on why they felt so sure about participating. Results are shown in the Likert scale on personal feelings of pressure to participate (Table 7).

Table 7: Likert scale on perceived personal voluntariness of a decision (PVOD)

PERCEIVED VOLUNTARINESS OF A DECISION	Freq	%	Cum %
No great advantage to participate	24	19.7	19.7
Participation to my advantage	57	46.7	66.4
Wise to participate	36	29.5	95.9
Have no other choice	5	4.1	100
TOTAL	122	100	100

The largest group (46.7%) felt that it was a personal advantage to participate even though they had other choices. About one fifth (19.7%) of respondents indicated there was no great advantage in participation. About two thirds (66.4%) of the study population perceived either no great advantages to participation or had other means of attaining the perceived benefits.

Thus, the hypothesis that women demonstrated adequate levels of voluntariness as regards to personal perception of voluntariness of decision is accepted.

Only 4.1% of respondents indicated that they had no choice i.e. participating only because of benefits. One of those who would not have participated if she had other choices said: “I have been suffering from foul-smelling discharge and lower abdominal pain for several years....going to health centre and traditional healers had not helped. So I had to participate because I would not have had full attention if I refused.”

4.2.3. Willingness To Participate in the Future Microbicide Research

Majority (78.7%) said they would participate in the future microbicide research if invited. One tenth (10.7%) of respondents said they would not participate and another one tenth did not know.

Of those who said they would participate, more than half (53.1%) believed that the microbicide gel would protect them. A quarter (25.0%) stated they would join because of benefits associated with their participation, namely free services such as HIV tests and treatment of minor illnesses. 20.8% said they would participate but could not say why, even upon probing. Of those who would not participate, 53.8% and 38.5% respectively would not do so because of unknown risks and refusal from spouses.

4.2.4. Relationship between voluntariness and demographic characteristics

Analysis was performed on the two Likert scales of voluntariness, as shown in table 6 and 7: *perceived pressure from others (PPFO)* and *perception of voluntariness of a decision (PVOD)*. Spearman's rank correlation showed a non-significant relationship between *perceived pressure from others (PPFO)* and age (p = 0.889, rho = 0.011). One-way ANOVA revealed a significant difference by marital status in *perceived pressure from others* (F = 8.62, p = 0.001. In order to establish where the variance lay, the Bonferroni post-hoc multiple comparison test was conducted. This test determined that, in terms of perceived pressure from others, women married as one wife scored significantly higher than unmarried women (p = 0.019), women married as one wife scored higher than widowed women (p = 0.003), and women married as one wife scored higher than divorced women (p = 0.001). No other significant differences were found for marital status: between unmarried women and married as more than one wife (p = 1.000), married as one wife and married as more than one wife (p = 0.429), unmarried and widowed (p = 1.000), married as more than one wife and widowed (p = 0.477), unmarried and divorced (p = 1.000), married as more than one wife and divorced (p = 0.743), or widowed and divorced (p = 1.000).

Upon collapsing the categories into married and unmarried, analysis by Student's unpaired t test also revealed that unmarried women scored higher in voluntariness than married women (t = 5.255, degrees of freedom = 20, p = 0.001). However, using one-way ANOVA, no significant relationship was found between perceived pressure from others [PPFO] and education (F = 0.57, p = 0.5652), PPFO and type of facility (F = 0.07, p = 0.991), PPFO and type of job at facility (F = 0.51, p = 0.676), PPFO and spouse's education (F = 0.90, p = 0.446), or PPFO and spouse's job (F = 2.01, p = 0.093).

Thus, the hypothesis that voluntariness was related to age and educational level of a spouse is rejected. However, the hypothesis that voluntariness is related to marital status is accepted.

On *perception of voluntariness of a decision (PVOD)*, no significant relationship was found between PVOD and age using Spearman's rank correlation (p = 0.591, rho = 0.049). However, one-way ANOVA revealed a significant difference between PVOD and level of education (F = 4.21, p = 0.017). When the Bonferroni post-hoc test was performed, it was established that

women with no formal education scored significantly higher than women who had completed primary education (p = 0.091) and women who had completed secondary education (p = 0.022). No significant difference was found between primary education and secondary education (p = 0.410). Moreover, no significant relationship was found between PVOD and type of facility (F = 1.38, p = 0.247), PVOD and type of job at facility (F = 1.32, p = 0.271), PVOD and marital status (F = 0.25, p = 0.907), PVOD and spouse's level of education (F = 0.79, p = 0.505), or PVOD and spouse's job (F = 0.76, p = 0.583).

Thus, the hypothesis that voluntariness is related to age, marital status, and educational level of a spouse is rejected. Nonetheless, the hypothesis that voluntariness is related to participant's education is accepted.

Voluntariness was cross-tabulated against previous participation in research and a Chi-square test was performed to establish if previous participation significantly affects perceived pressure from others (PPFO) and personal voluntariness of a decision (PVOD). The Chi-square results showed no significant differences in levels of voluntariness for either of the Likert scales: PPFO – (Pearson's chi2(4) = 3.12, p = 0.538, PVOD – (Pearson's chi2(3) = 3.54, p = 0.315. Likewise, cross-tabulation against willingness to participate in future microbicide trials did not show any differences in level of voluntariness in the Likert scales: PPFO – (Pearson's chi2(8) = 8.58, p = 0.379, PVOD – (Pearson's chi2(6) = 3.70, p = 0.718.

4.3.5. Relationship between Understanding and Voluntariness

To relate understanding and voluntariness, levels of understanding were cross-tabulated against two Likert scales of voluntariness and Chi-square test was conducted to determine if there were differences in degrees of voluntariness. Participants with high levels of understanding scored significantly lower on personal perception of voluntariness over a decision (PVOD) than those with low levels of understanding (Pearson's chi2(12) = 32.31, p = 0.001). Cross-tabulation between understanding and the Likert scale on pressure from others (PPFO) did not reveal significant differences in degrees of voluntariness (Pearson chi2(8) = 12.92, p = 0.115).

As regards to personal perception of voluntariness over a decision (PVOD), the hypothesis that understanding is related to voluntariness is accepted**.**

5. DISCUSSION

The testing of newer investigational products after the failure of preceding trials often requires recruitment of additional newer study populations. Before such interventions studies, researchers recruit new cohorts in order to study procedures and obtain information on key indicators that will help refine or develop future protocols. Our study utilizes experienced cohorts from one such preparedness study to inform the debate surrounding informed consent which has become a concern for ethicists. Apart from ensuring that rights and well being of research participants are protected, ethical norms in research promote research aims, foster values crucial to collaborative work and make researchers accountable to the public, whose support researchers often need.

In recent years, as attested by the Nuffield Report [5], research ethicists have taken an interest in the unique conditions on the ground for developing world participants. Different belief systems and illiteracy have made it difficult to achieve understanding whilst constraining situations such as poverty and limited access to health care have arguably made standard study procedures such as physical examination and laboratory tests the basis on which some participants make decisions regarding their participation. Free examinations and tests trigger ethical concerns because they can distort people's judgment, inducing them to participate in activities they would not have done otherwise. This study examined understanding of informed consent material and perceived voluntariness of participation of participants who had participated in a preparedness study for future microbicide trials in North-Western Tanzania.

5.1. STUDY PARTICIPANTS' UNDERSTANDING OF INFORMATION GIVEN

5.1.1. Overall Understanding of Study Information

The overall understanding was inadequate. Very few (one respondent) fell into the margins of Extremely poor and Excellent understanding. Although participants scored well in areas of procedures and confidentiality, their understanding of research and risks/discomfort was poor. Such modest understanding in participants prepared for future trials could be due to low literacy rates and different beliefs system that made research concepts difficult to comprehend. Moreover, participants in the environment with limited health care options could have focused on the free medical care and disregarded other information in the whole package. In studying the informed

consent documents, we found them to be standard texts, with proper emphasis on research, risks, right to participate, and right to withdraw. More troubling was the finding that most participants did not take the documents home, suggesting that the counsellor's role was integral to the informed consent process while the role of significant others was limited. Perhaps if participants had consulted with relatives, they would have been better positioned to understand concepts alien to their beliefs and to contribute meaningfully in later interactions with research staff.

5.1.2. Research Awareness

Our results show that participants were not research aware. When initially asked if they were participating in research, majority replied in the affirmative but when interviewers probed further it was obvious that research often meant provision of expert services to women at risk rather than testing of developed hypotheses. Although participants had passed tests of understanding after the informed consent process at the screening and enrolment, very few participants mentioned the correct aim of research: to determine whether areas in the north-west of Tanzania are suitable for future studies of microbicide gel.

Many studies have reported on the concept of therapeutic misconception where trial participants express convictions that the investigational product will meet their medical needs despite being informed of the experimental nature of the study [12, 15, 22]. In our preparedness study, although the participants helped researchers to complete questionnaires that sought to understand risk factors related to STI infections, no investigational product was provided. Accordingly, it is reasonable to assume that participants in our study would demonstrate a lower level of understanding of research processes than participants in other studies since our procedures, such as close monitoring of symptoms, psychosocial counselling and health education are more similar to activities that typically take place in a clinical setting. Furthermore, two of the study sites were within district hospital compounds and the other was in close vicinity of a hospital, facts that could have augmented the notion of treatment and individualized care.

Even when we probed for details of research knowledge, participants' understanding was not more than treatment. For most participants, the study clinics meant better care than district hospitals. In contrast, Sumathipala *et al* found that most participants in the lay public had a solid understanding of research when exploring public and professional views of research [78]. The difference could be

explained by different characteristics of the study populations. Whereas the latter was comprised of diverse population groups , our population was limited to women working in bars and hotels, most of whom had never been exposed to research or achieved more than basic primary education. Indeed high illiteracy rates as well as language and cultural barriers have been associated with therapeutic misconception together with risk factors such as extreme poverty, lack of access to health care, gender disparity and an enhanced *doctor-knows-best* viewpoint [79].

Informed consent literature and advertising materials often use words such as “treatment” in preference to “intervention” and “doctor” instead of “researcher” as well as terms with dual meaning such as “investigation”, which could mean either “laboratory tests” or “research process” in Kiswahili [80]. This sloppy use of language can influence participants’ understanding of research, and is a preventable obstacle to the aim of actualizing informed consent. In our survey, participants had difficulty with the concept that laboratory tests were not only to manage their infections but also to answer research questions. Dubbing the feasibility study “Women’s Health Project” as a way of reducing stigma may have contributed to this confusion, along with addressing research staff as “doctor” and “counsellor”, terms which tend to suggest clinical practise.

As expected, most participants said they would participate in a microbicide trial in the future if invited because of benefits associated with the research and protective nature of the gel. Only one tenth declined participation in future research and this was for reasons of unknown risks and spousal refusal.

Further, the low understanding could partly be explained by failure to recall provided information given the 1- year interval between the enrolment and our study. If the study had been done a few weeks or months after the enrolment, we probably would have witnessed more research- aware participants. While acknowledging that recall is not equal to or necessarily indicative of understanding, we feel that the failure of our participants to recall that STI management involves research is a singularly important finding, contradicting the general objective of the feasibility study: *to prepare new cohorts for future microbicide trials.* Considering the lower educational attainment and potentially critical consequences for a misinformed participant, research staff will need to do better in laying groundwork for participants’ understanding of the complex study information that is anticipated in the future.

5.1.3. Risks and Benefits

Mimicking other studies, our study revealed significant differences between the number of respondents who understood benefits compared with those who comprehended risks. This is probably because the risks were deemed too minimal to be important and the benefits were deemed too beneficial to pass up. Blood draws, completing the questionnaire, and undergoing gynaecological examination, however discomfiting, might have been a small price to pay compared to free diagnosis and management of minor ailments for one year. The most cited risks were anxiety while waiting for HIV/STI results and pain/discomfort during examination. Interestingly, these are the same risks that a patient would expect if she went for management of HIV/STIs. On the issue of social desirability, participants might have been predisposed to mentioning benefits rather than risks and discomforts given the established relationships with research staff over one year.

Probably due to limited understanding of research, very few participants identified the society and general public as beneficiaries of research. Majority believed that "Women's Health Project" was there to improve their individual lives by providing HIV testing, treating STI and minor ailments, as well as giving education through counselling. In Sumathipala's study [78] in which participants had more understanding of research, most participants identified society and the general public as beneficiaries in addition to personal benefits for the respondent. This suggests that where people are aware of research as an inquiry, identification of societal benefits is likely to be witnessed, though risks for the participant may not be appreciated.

While it is generally acceptable that participants may join a study for their own personal benefit provided they have understood the study, it is morally problematic when participants do not appreciate the potential risks involved with their participation. Their right to safeguard their physical and mental integrity is compromised if they do not comprehend the risks involved and thus, researchers must ensure that benefits do not sway participants' appreciation of risks.

5.1.4. Study Procedures

Of all the concepts we tested, study procedures were best understood. More than four-fifths of participants mentioned three procedures or more. Gynaecological examinations and drawing of blood were recalled most often, probably because they are concrete, practical, and also sensitive

procedures. Since study procedures were done routinely in all five visits the participants had to make, they were probably more easily recalled than other concepts such as research awareness and right to withdraw, which largely depend on verbal communication with the researcher. Moreover, researchers are likely to emphasize research procedures over knowledge because it is through the procedures that research questions are answered. Indeed, good understanding of procedures has been demonstrated by other studies that assessed understanding of given information [40, 42, 44].

5.1.5. Freedom to Participate or Withdraw

Like participants of informed consent studies in Northern Ghana and Kenya [43, 46], women in this study understood better the voluntariness of signing on than the freedom to withdraw. Whereas participants in the Kenyan study were keen on maintaining "happy moments" with the researchers, few respondents in our study expressed this kind of desire. This is probably because high-risk women, given the nature of their job, are probably more assertive and could not just continue to participate in order to please someone. Women who sell sex on the side likely view their participation in terms of a contract where each party is expected to look after their own best interests. We submit that our population probably stayed in the program as a means of ensuring the continuation of perceived and actual benefits. Indeed, retention was an issue to the research staff since some women were likely not to attend after the first visit if the tests revealed no infection. Once given the result they least expected, a clean bill of sexual health, they could not understand the value of more tests or continuing to participate.

Though a good percentage of participants understood their rights to withdraw from the study, and very few would continue to participate just to maintain an amicable relationship, many would continue so as not to lose the benefits. It is possible they understood that they would not lose any benefits if they withdrew but found it implausible that the research staff would continue to cater for their needs while researchers' goals were not met. This incorrect interpretation of study information due to nonacceptance or false belief has been described by Beauchamp and Childress, who propose that it may be permissible to attempt to dispute false beliefs when such beliefs are demonstrably false [1].

5.1.6. Confidentiality

Confidentiality scored next to procedures in terms of good understanding. Although some participants incorrectly thought that their names would be included in future publications or attached to the samples taken from them, majority had good understanding of the safeguards in place. More participants were uncertain (responded I don't know) about the anonymity in publications than the anonymity in laboratory investigations. Less understanding of confidentiality was found by Taiwo and Kass [44] in assessment of subjects' understanding of informed consent in oral research in Nigeria where 85.8% of participants did not know how their records would be kept. The difference in our survey could be due to the sensitiveness associated with sexual relations and HIV infection. During recruitment, most high-risk women participated on condition that the study would take pains to ensure their spouses and relatives did not know of their participation and that their workmates, with whom they were recruited, did not know of their results. Some participants did not want to be followed up at their homes and refused to give their home addresses. Those who agreed indicated what time the staff could arrive and not with a project car. As to why participants would be more uncertain about their anonymity in publications than in laboratory tests, we speculate that the latter is more familiar to respondents' experience, and more readily calls to mind their fear of repercussions should confidentiality be breached. The great importance of the laboratory work to respondent's well being precludes a major focus upon and understanding of laboratory work to the exclusion of other things such as publications.

5.1.7. Relationship between the level of understanding and demographic variables

Whereas other researchers have found better understanding in younger participants over older participants[81], our survey showed opposite results. Understanding varied proportionally with age. We postulate that older women have acquired sophistication by virtue of being in the business for a longer period of time. Though sex is a unique commodity, it must obey market principles of supply and demand. Sex workers have to maintain their worth by buying hip clothes and caring for their hair without immediate returns; they have to find ways to outsmart the competition in order to secure as many proceeds as possible to cover the expenses incurred, which often include middleman's fees. Also, more than younger women, older women probably have better understanding of the world through associations with different clients and people with whom they have to exercise their people and negotiation skills. Moreover, women gain ingenuity and resourcefulness as they constantly deal with run-ins with the law and work to justify their sexual

practices against the societal norms, in addition to safeguarding against diseases from partners who could care less.

Association of understanding with education level has been documented in previous studies. Manafa *et al* [40] found that level of education was in direct relation with level of understanding. Like Manafa's study and several others, we found that education of participant had an impact on the level of understanding of the participant. Nonetheless, the significance of education decreased after primary education, implying it is possible to correct for lack of formal education. For example, researchers could use concepts and language fitting to the social context and could incorporate relevant traditions into informed consent, such as story-telling to check understanding. The quality of interactions between the researcher and participant is at the very heart of the ethical aspect of informed consent.

5.2. VOLUNTARINESS OF STUDY PARTICIPATION

5.2.1. Decision to participate

While it has been reported that collectivist culture is dominant in Africa, implying that decisions are normally made in collaboration with others, about half of women reported that they did not discuss their participation with any family member. This could be due to stigma around HIV and STIs in addition to noncompliance to cultural norms likely to be typical of women at higher risk of acquiring HIV/AIDS. Out of all participants who shared their participation, married women were most likely to discuss with relatives and husbands. We know that traditionally family consultation has been more required from women than men and even more-so from married women, who are expected to seek approvals from their husbands or even mother-in-laws. In that vein, a survey to test the effect of relationships on decision-making processes in Zimbabwean women by Nyika and Wassenaar [66] found that although most women were prepared to consult their husbands in the context of *hypothetica*l participation in research study, married women were less prepared to act against their husbands' wishes than women who were single or divorced *at the time*. In our study, husbands were reported to encourage or pressure rather than discourage their wives to participate because it was "through (women) that they could know if they had been infected with HIV and other STIs". It was not uncommon to see husbands check in at the clinic to "confirm" the negative HIV test when their wives had sent them "good news". On the other hand, friends and co-workers were mostly

discouraging. In the recruitment phase, the study information was presented to groups of facility workers and it was common to find some group members reacting negatively, and also influencing other potential cohorts. In contrast, spouses received the information from their wives, who were already considering participation.

On the whole, researchers will need to recognize that participants' decision to join the study is not necessarily independent of the opinions of immediate family members and friends, and for some, this level of involvement with significant others is a way of life. In this circumstance, it is wrong for researchers to downplay ongoing family or community consultations as this would deprive some participants of their support system.

In this cohort, the idea of relational autonomy plays itself out in marital relationships rather than the general study population, emphasizing the impact of spouses and other family members in decision-making. Nonetheless, since about half of our study population clearly do not subscribe to communitarianism, when conducting research with a similar cohort, there is a need for adaptability of the research design to encompass the range of decision-making styles; from cooperative decision-making to independent decision-making.

5.2.2. Voluntary Participation

We were able to use participants' descriptions and perceptions of feedback received from spouses, relatives and friends as a measure of voluntariness. The results suggest that family and friends do influence research participation ranging from encouragement to pressure. In our survey, more participants reported mild pressure and strong encouragement to participate than other categories on the extremes of the continuous scale. No participant reported extreme pressure or threats. Comparing our results with the Nigerian study where some HIV patients perceived extreme pressure from relatives to participate [40], we speculate that participants in our study were not in as dire a situation. Their lives did not depend on medication to be provided and by and large they seemed healthy. In contrast, participants in Nigeria were already diagnosed of HIV infection and did not have access to the then expensive and unavailable medication. Thus, it is logical to assume that caring relatives would coerce or threaten patients to participate as this might be the only means of access to antiretroviral drugs.

Usually, an individual position in the family is a determining factor of coercive relationships. If one is dependent on the other for livelihood, one is likely to feel the pressure to follow the other's wishes. In addition, patriarchal communities are less likely to respect women's rights to self determination. Referring to our results, we speculate that those who reported mild to strong pressure were more dependent in their relationships than those who reported encouragement or discouragement. As a counter measure, research teams should search for interventions that women can better control, such as vaginal gel, which will reduce their dependence on methods that men control. A woman should not be compelled to depend on her partner's willingness to use condoms, and she does not have to if given the option to take that control upon herself, The purpose is not to undermine relational decision making, or to deprive men, but to support women by bringing new and better options into her existing framework. In the best case scenario, women will take the lead in the fight against the spread of AIDS and other venereal diseases. Indeed, the concept of perceived voluntariness of the female participant must be achieved in the real world with all its flaws such as the patriarchal society, the notion that women are property, illiteracy, poverty, and lack of other available health options.

An important force in the subjective feeling of pressure to participate is the matter of lack of treatment options in face of sexually transmitted infections. Whereas 29.5% of participants felt that participation was to their advantage given their lack of other available health care options, fewer (4.1%) participated despite not wanting to. We cannot say that those who had no or few health care options (29.5%) did not act voluntarily because lack of options does not automatically render choice involuntary. We can only concur with Nelson and colleagues that lack of choices may lead to "deprivations of voluntariness that are (ethically) problematic". Nonetheless, we can justify involvement of women in the unfortunate background by availing other principles such as justice, beneficence, and nonmaleficence.

It is worthwhile to note that 46.7% of all participants felt it was an advantage to participate even though they had other health care options and 19.7% of participants consented despite perceiving no great advantage to participation. This differs greatly from Manafa's study [40] where participation involved the provision of free antiretroviral drugs. Only 11.4% of the Manafa cohort felt they had other options and only 8% perceived they had free choice regarding their participation. 55.6% had participated only because they had no other choice. The difference could be attributed to the

differing natures of the study populations. The former consisted generally of healthy participants while the latter were sick patients requiring care and drugs for survival. Moreover, our participants might have been focusing on one service e.g. HIV testing, to the exclusion of the other services in the total 'package' offered by researchers. Whatever the case, the results imply that researchers' beliefs regarding benefits might be at odds with participants' perceptions.

5.2.3. Relationship between voluntariness, understanding and demographic variables.

Our study showed that married women were less likely to perceive their decisions as voluntary than single women, i.e. to report pressure to participate (Likert scale 1 – Perceived Pressure from Others). Men may have pressured women to participate because it was a way of knowing their own health status and ensuring their own reproductive/sexual health. The counter-intuitive relationship between perceived voluntariness of decision (PVOD) and education could be due to awareness of the complexities of decision making by educated women. Unlike less educated women, these women were more likely to think that other people and multiple factors were involved in decision-making and hence the lower perceived voluntariness of their own decision. *Perceived* voluntariness is based on the individual's subjective perception and is not the same as voluntariness. Much as different people have different interpretations of the same situation, voluntariness can be perceived or defined in different ways. This idea relates to the earlier discussion that perceiving a threat does not necessarily mean that a threat has been issued. Likewise, a valid threat does not necessarily impinge on voluntariness since the threat could be ignored although we might choose to define voluntariness by the mere presence of the threat.

Also, the inverse relationship between education and perceived voluntariness of decision (PVOD) could probably be explained by more appreciation of laboratory investigations by educated women. Whether healthy or not, educated women probably understood that the opportunity to scan for the majority of sexually transmitted infections was hard to come by and hence they perceived little or no choice but to participate. In actual fact, laboratory investigation of sexually transmitted infections is not routine procedure in a majority of hospitals in Tanzania. Most STI's are managed by symptoms using *National Guidelines of Syndromic Management* rather than routine tests. Routine screening is only done for pregnant women and only for syphilis infection. Additionally, the inverse relationship between perception of voluntariness over a decision (PVOD) and education could be compared with the direct relationship between understanding and age, which is

inconsistent with findings from other studies [40, 50, 78, 81]. Like education, age was an important factor in understanding. Much as age could have made participants wiser as regards to unavailability of laboratory tests, we probably could say that education made participants more appreciative of the importance of such tests in addition to their unavailability.

The inverse relationship between understanding and voluntariness on the Likert scale, perception of voluntariness over a decision (PVOD) could be explained along the same lines, that women with higher levels of understanding could better appreciate the opportunity for scanning for the majority of STI's than those with lower levels of understanding.

5.3. Study Limitations

As we used convenience sampling, it is possible that those who participated may represent a biased sub-sample of the total population of the cohort study. Further, our sample was limited to participants of the feasibility study, i.e. invitees who accepted enrolment; it would have been interesting to analyze the motivations of those invitees who declined participation in the feasibility study; however, the knowledge sections of the questionnaire could not have been applied to this group.

Given that all participants had completed their scheduled visits when this survey was done, it is difficult to establish if the demonstrated inadequate understanding is not, in part, a result of memory loss over a period of one year. As well, participants may have forgotten other details such as who they consulted, what the response was, if they felt resistant, and how they resolved the conflict. Also, one time collection of data does not reflect changes of understanding and opinions over time. A longitudinal design could have allowed for detection of changes regarding understanding and voluntariness over time.

As voluntariness has not been well researched, there were few studies to compare our results with and no standardized instruments designed to test the concept. As a result, very few comparisons were made. Moreover, lack of a standardized instrument hindered meaningful comparisons between our survey and other studies.

More conclusions on quality and quantity of information could have been drawn. However, we did not observe the informed consent process when it was being conducted during enrolment and screening nor did we interview any of the trial study's counsellors.

5.4. Summary and Conclusion

The principal aim of this study was to assess this cohort's understanding of the study information provided during informed consent process and to determine the perceived voluntariness of their participation. The cohort comprised of women working in recreational facilities who are regarded to be most at risk of acquiring sexually transmitted infections including Human Immunodeficiency Virus (HIV).

The participants' overall understanding of the information provided through the course of the trials was inadequate. Among the concepts least understood was research awareness. Most participants failed to understand that the major aim of *Women's Health Project* was to know the extent of sexually transmitted infections and factors associated with such infections. Interestingly, most participants had responded in the affirmative when initially asked if they were participating in research or not. Only by asking open-ended questions, were the researchers able to gauge participants' understanding. In associating understanding with socio-demographic variables, total understanding varied in direct relation with age and education. Congruent with other studies on informed consent, this study found that the impact of education level on understanding started to disappear after primary education. In contrast to other studies, older rather than younger participants in this study had better understanding of general study information.

On perceived voluntariness, more participants than in other compared studies reported to have made the decision to participate themselves, without being pressured or coerced by friends and families with whom they discussed their participation. Married women who shared their participation with family and relatives reported more pressure to participate than unmarried women. About half of the study population did not discuss their participation with anyone. On perceived l voluntariness of the decision to participate, more than two thirds of the population participated despite having other choices or perceiving no great advantages in participation. Of note, education was found to negatively impact on perceivedl voluntariness of decision. Women with higher

education tended to join the trials in order to satisfy unmet health needs or to receive benefits associated with participation, whereas women with lower education were less constrained in their reasons for joining.

While these findings show that low literacy levels and poverty make it more complex to uphold the ethical obligation of clinical research, it is necessary and possible to ethically involve these populations in the quest of interventions that will better their own health. We must focus on adapting the universal models of research to local customs, beliefs and literacy levels whilst recognizing and correcting for the use of local languages. We must also ensure that participants have understood complex information by looking at ways of facilitating understanding as well as availing tests that provide an adequate gauge of understanding, and checks that help participants think of study information in terms of stories. These should be provided frequently in studies to ensure that participants understand and retain information. Regarding voluntariness, it could be important to know *how* participants make decisions about joining research in order to understand possible pressures in them which limit voluntariness. This understanding could empower researchers and other stakeholders to come up with better means for fostering voluntariness in the decisions of participants.

Needless to say, research ethics committees and government institutions must be active players in the advancement of ethics. Whereas anthropologists in government institutions could help uncover the structural realities on the ground, ethics committees, on the other hand, could ensure that informed consent documents are fittingly contextualized and adequately understood. Rigorous ethical standards must always be maintained as we all react to the urgency of HIV pandemic.

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APPENDICES

APPENDIX A

PATIENT/PARTICIPANT'S INFORMATION LEAFLET & INFORMED CONSENT FOR ANONYMOUS QUESTIONNAIRE

Dear Participant

You are invited to volunteer to participate in our research project on:

PARTICIPANTS' VOLUNTARINESS AND UNDERSTANDING OF A FEASIBILITY STUDY TO ASSESS POTENTIAL COHORT SUITABILITY FOR FUTURE MICROBICIDE TRIALS IN NORTH WESTERN TANZANIA

This letter gives information to help you to decide if you want to take part in this study. Before you agree you should fully understand what is involved. If you do not understand the information or have any other questions, do not hesitate to ask us. You should not agree to take part unless you are completely happy about what we expect of you.

The purpose of the study is to test ourselves on how we have explained informed consent on the **Feasibility Study** to you by assessing your present understanding of your rights as a volunteer. We would like you to help us complete a questionnaire by responding to the questions we ask you. I am going to start with few questions about the project. Some questions require you to provide a brief explanation. Others are Yes-No questions. Later, you'll get a chance to discuss what the project means to you in greater detail. This interview will also be recorded on a voice recorder and will take about 40 minutes. Your name will not be written anywhere on the questionnaire and it will be kept in a safe place,

along with the recordings to ensure confidentiality. No one related to this survey will have any access to the recordings.

The Research Ethics Committees of National Institute of Medical Research, Tanzania and University of Pretoria, Faculty of Health Sciences have granted written approval for this study. Your participation in this study is voluntary. You are free to refrain from answering any question that makes you uncomfortable and you can stop the interview at any time without giving any reason. As you do not write your name on the questionnaire and don't mention your name during the interview, you give us the information anonymously. Once you have given the questionnaire back to us, you cannot recall your consent. We may not be able to trace your information. Therefore, you will also not be identified as a participant in any publication that comes from this study.

We sincerely appreciate your help.

Yours truly,

……

x

UNDERSTANDING

Read out the question and Circle the correct answer(s)

Research Awareness

1. Are/Were you participating in a research study?

    a) YES
        i. So what is the purpose of this research?
            1. To determine whether areas in the north-west of Tanzania are suitable for future studies of microbicide gel.
            2. To test microbicide.
            3. To test people for HIV.
            4. To provide treatment for STI.
            5. To counsel people
            6. To reduce the spread of HIV
            7. To empower women.
            8. Other.
                Specify:……

    b) NO.
        i. Why are you here?
            1. To be tested for HIV.
            2. To get treatment for STI.
            3. To be counseled.
            4. To reduce the spread of HIV.
            5. To be empowered as a woman.
            6. Other reasons
                Indicate:……..

2. Have you participated in a research study before?
    1. YES
    2. NO

3. What does the word “research” mean to you? Please, explain in your own words.-
    ……
    ……
    ……

4. What is the difference between the services that are provided here and those provided at district hospital or any other health centre?
    ……
    ……
    ……

5. Why were you invited to participate in this project?
    a) To get tested for HIV
    b) Because I am at risk
    c) Other reasons:
        (Indicate)……..

Risks and Benefits

6. Are there any benefits for participants in this project?
    a) YES
        i. What do you think are the possible benefits?
            1. Knowing my HIV status
            2. Being treated for STI
            3. Learning from HIV/STI counseling
            4. Helping to determine if this area is suitable for future studies of microbicide gel
            5. Helping us to understand why there is a high rate of HIV/STI transmission in our area
            6. Receiving treatment for minor ailments
            7. Receiving family planning services
            8. Will help us not get HIV
            9. Other
                Specify:……...

    b) NO

    c) I DON'T KNOW

7. Are there any risks/discomforts for you taking part in the research?

    a) YES
        i. What do you think are the possible risks of taking part in this project?
            1. Feeling uncomfortable, worried or embarrassed about discussing my sexual practices, and ways to protect against HIV and other infections during sex.
            2. Becoming anxious while waiting for HIV/STI results.
            3. Losing a lot of blood.
            4. Pain and discomfort during the blood collection.
            5. Pain and discomfort during the gynecological examination and taking of the samples.
            6. Confidentiality breach.
            7. Spending too much time at the clinic.
            8. Other
                Specify:…….

    b) NO

c) I DON'T KNOW

Study Procedures

8. How long did/will the study take to complete?
    a) Three months
    b) Six months
    c) One year
    d) Two years
    e) I don't know
    f) Other
        Specify:……

9. How often are/were you supposed to attend the clinic for a check-up for STIs?
    a) Three months
    b) Six months
    c) One year
    d) I don't know
    e) Other
        Specify:……

10. What does your participation in this project involve?
    a) General and private questions about me, my family and my sexual behavior.
    b) Physical examinations.
    c) Gynecological examinations and collection of genital samples.
    d) Drawing of blood for testing HIV and other STIs, including Syphilis.
    e) Providing urine samples for Pregnancy testing.
    f) Receiving counseling.
    g) Other
        Specify:……

Freedom to Participate and Withdraw

11. Could you refuse to participate in this project?
    a) YES
    b) NO
    c) I DON'T KNOW

12. Can/Could you withdraw from this project?
    a) YES
    b) NO
    c) I DON'T KNOW

13. What would happen if you withdrew?
    a) I would not receive/have received services provided at this clinic
    b) Clinic staff would not be happy.
    c) Nothing would happen to me.
    d) I don't know.
    e) Other
        Specify:……

Confidentiality

14. Will your name be used in any publication or reports produced from this study?
    a) YES
    b) NO
    c) I DON'T KNOW

15. Will your samples be linked to your name?
    a) YES
    b) NO
    c) I DON'T KNOW

VOLUNTARINESS

Now I want to ask you about the decision to participate in this research.

16. Did you talk to anyone about the study before agreeing to participate?

    a) NO → Proceed with Number 17

    b) YES
        i. Who did you talk to ?
            1. My spouse
            2. My partner
            3. Friends
            4. Co-workers
            5. Facility owner
            6. Neighbors
            7. Other (Specify):……

        ii. Did your spouse/partner/co-workers/friends/employer/other (repeat the question for each class of acquaintance named in 16b) encourage, discourage or leave you to decide for yourself?

1. They encouraged me

a. What did they say or think?

Specify relationship:……

Explanation:……..

……

……

Specify relationship:……

Explanation:……..

……

……

[Use Attached Extra pages when necessary]

b. Would you say they helped you to decide, or would you say they made the decision for you?

Specify relationship:……

Explanation:……..

……

……...

Specify relationship:……

Explanation:……..

……

……

2. They discouraged me

a. What did they say or think?

Specify relationship:……

Explanation:……..

……

……

Specify relationship:……

Explanation:……

……

……...

b. How did you decide to take part in the study, given their discouragement

……

……

……

3. They left it for me to decide

a. What did they say or think?

Specify relationship:……

Explanation:……..

……

……

Specify relationship:……

Explanation:……

……...

.....

b. How did you feel?
……

……

17. Did you ever consider refusing?

a) YES
   i. What made you feel hesitant?
   ……

   ……

   ii. How did you resolve the uncertainty or conflict?
   ……

   ……...

b) NO
   i. What made you feel so sure?
   ……

   ……...

18. While in the study, have/did you experienced/experience any pressure to withdraw?\

a) NO → Proceed with Number 16

b) YES
   i. From whom?
      1. My spouse
      2. My partner
      3. Friends
      4. Co-workers
      5. Facility owner
      6. Neighbors
      7. Other (Specify):……

ii. What did they say or think

Specify relationship:…….

Explanation:…….

……..

Specify relationship:……..

Explanation:…….

……

iii. Why have you continued in spite of that pressure?

……

……...

19. Would you participate in Microbicide Trials if invited in the future?

a) YES

i. Why?

……

……

b) NO

i. Why?

……

……

c) I DON'T KNOW

i. Why?

……

……

DEMOGRAPHIC INFORMATION

1.	Age (years)	.....
2.	Level of Education	1. None 2. Primary Incomplete 3. Primary Complete 4. Form I -IV 5. Form V -VI 6. Post Secondary 7. Other Specify:……
3	What main service is provided at your facility?	1. Guest House 2. Hotel 3. Bar Only 4. Night Club/Discotheque 5. Grocery (Small beer shop 6. Pombe Shop (Local brew Pub) 7. Café 8. Mama Lishe (Food vendors in make-shift huts)
4	What is your main job at the facility?	1.Waitress 2. Cook 3. Cleaner 4. Receptionist 5. Manager 6. MamaLishe

		7. Other Specify:……
5	Are you married?	1. Not married 2. Married (One wife) 3. Married (More than one wife) 4. Widowed 5. Divorced 6. Other Specify:……..

6	If Married: What is the highest level of education your spouse completed?	1. None 2. Primary Incomplete 3. Primary Complete 4. Form I -IV 5. Form V -VI 6. Post Secondary
7	What kind of work does your spouse do?	1. Civil servant 2. Trader 3. Artisan 4. Teacher 5. Driver 6. Mineworker 7. Other. Specify:.....