Workshop On

SOCIO-BEHAVIOURAL ASPECTS OF MICROBICIDE TRIALS FOR HIV PREVENTION

New Delhi, December 5-6, 2005

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Proceedings of the workshop on
"Socio-Behavioural Aspects of Microbicide Trials for HIV Prevention"
Organised jointly by
Indian Council of Medical Research, New Delhi
and Microbicides Development Programme, UK
New Delhi, India December 5-6, 2005

CONTENTS

FOREWORD 6

PREFACE 7

EXECUTIVE SUMMARY 8

OPENING SESSION 10

SCIENTIFIC SESSION I 11

THE SOCIAL CONTEXT OF HIV IN INDIA: DEMOGRAPHIC INFORMATION ABOUT THE POPULATION FERTILITY CONTEXT AND AIDS KNOWLEDGE 11

Women and HIV/AIDS in India 12

Dr. Saseendaran Pallikadavath and Dr. William Stones

Information gained from the Indian Behavioural Surveillance Survey (BSS) 14

Dr.Arvind Pandey

SCIENTIFIC SESSION II 17

ETHICAL CHALLENGES IN HIV PREVENTION RESEARCH 17

Overview of research ethics in HIV prevention trials 18

Dr.(Ms) V.Muthuswamy

Standard of care and lessons learnt from recent clinical trials 21

Dr. Alan Stone

Need for understanding the concerns of women participating in a trial: Perspectives of women participating in AZT feasibility study 24

Dr. (Ms) Nita Mawar

SCIENTIFIC SESSION III 29

METHODOLOGIES FOR STUDYING SEXUAL BEHAVIOUR; HOW TO OBTAIN RELIABLE AND VALID INFORMATION 29

How many participants are needed for clinical trials and how long does the study need to be? 30

Dr. Andrew J. Nunn

Increasing the accuracy of sexual behaviour and adherence data 33

Dr.Robert Pool

Experience of computer assisted data collection (ACASI) 37

Dr. Mdu Mntambo and Dr. Jonathan Stadler

Understanding EMIC perspectives 38

Dr. R.K. Mutatkar

CONTENTS

SCIENTIFIC SESSION IV 41

COMMUNITY PREPAREDNESS AND MOBILIZATION STRATEGIES FOR HIV PREVENTION 41

Overview of community liaison processes 42

Dr. Richard Mutemwa

Community involvement and education in Phase I AIDS vaccine clinical trial 44

Dr. (Ms) S. Sahay

Acceptability of microbicides: Experience from India 47

Dr. (Ms) Sethulakshmi J

SCIENTIFIC SESSION V 49

STRATEGIES AND MODELS FOR RECRUITMENT AND RETENTION OF STUDY VOLUNTEERS FOR CLINICAL TRIALS ADDRESSING HIV PREVENTION 49

Working with participants in a rural setting 50

Dr.Mitzy Gafos

Recruiting volunteers in Phase I and II vaginal microbicide trials in India 53

Dr. S. M. Mehendale

Behavioural and Social Science Research in Support of Phase III Microbicide 57

Dr. Betsy Tolley

RECOMMENDATIONS SESSION 61

Acknowledgements 64

LIST OF PARTICIPANTS 65

FOREWORD

The threat of the HIV/AIDS epidemic has highlighted the need for socio-behavioural research to understand various issues related to human sexuality and high-risk human behaviour. This includes gender-power relations and sexual dynamics. It is now generally agreed that at least in the forseeable future, behaviour modification leading to safer sexual practices and improved utilization of available technologies such as condoms at present and microbicides in the coming years, would be the main tools to prevent the disastrous spread of HIV with its associated burden of disease and social misery. The capacity to undertake good social sciences research utilizing valid and updated methodologies, has been relatively weak in India as well as in several other countries.

In order to sensitize the social scientists engaged in sexual health and HIV related research, it was therefore decided to organize a workshop on the socio-behavioural aspects of microbicides clinical trials, as a first joint collaborative effort between the Indian Council of Medical Research, New Delhi and the Microbicides Development Programme, a consortium of international partners led by the Medical Research Council of UK and Imperial College London. It is hoped that the Proceedings of this workshop would be helpful in strengthening the capabilities for undertaking socio-behavioural research, in order to contribute to the fight against the spread of the epidemic in India and other countries.

Prof. N.K. Ganguly
Director General
Indian Council of Medical Research
New Delhi

PREFACE

The pandemic of HIV/AIDS has highlighted research on sexuality and sexual behaviour as a critical priority, so as to characterize risky behaviour and identify those population sub-groups who are at greater risk of infection. It is now understood that merely increasing the awareness of the community about the risk factors for infection is not good enough successfully to fight the epidemic of HIV/AIDS. It is necessary to provide correct information through effective communication strategies so as to ranslate awareness into behavioural change, especially in terms of safer sexual practices. Furthermore, in the context of gender relations typically dominated by men, with complex patterns and dynamics amongst different population sub-groups in a diverse country like India, women are generally powerless to negotiate for safer sexual behaviour and practices. There is an urgent need for a deeper understanding of the decision-making processes and sexual dynamics within the family, community and society at large; specifically, the sexual behaviour of men, women and young people, and particularly adolescents.

It is also now increasingly realised that for the forseeable future, behaviour change towards safer sexual practices and utilisation of preventive methods such as condoms and microbicidal products would be the only effective tools available for preventing HIV/AIDS. This has become especially important as the availability of effective vaccines against HIV and many non-HIV STIs is probably a few decades away. The availability of detailed reliable information on sexuality and sexual behaviour is the sine qua non for our ability to plan and implement effective, evidence–based ntervention strategies for the prevention of HIV/AIDS among different vulnerable population sub-groups. It has become essential to integrate the qualitative methods of social science research with the quantitative methods of demographic surveys and epidemiological studies, so as to obtain reliable and valid data. In undertaking studies related to sexuality and sexual behaviour and related clinical trials of barrier methods and microbicidal products, it is essential to adopt high ethical standards and to rigorously handle the issues of confidentiality and informed consent for study participants. It is also imperative to engage with the wider society to foster a climate supportive of research on these very sensitive subjects.

Both the research capabilities and capacities for studying sexuality and sexual behaviour have been limited in India. The immense value both of using integrated multidisciplinary approaches (i.e. social sciences, anthropology, demography and epidemiology) and of combining the efforts of scientific or academic institutions with those of grass roots non-governmental organizations (NGOs) are widely acknowledged by the research workers in India. Therefore, in view of the proposed collaboration in the field of Microbicides research between the Indian Council of Medical Research (ICMR) New Delhi and the Microbicide Development Programme (MDP), it was decided to organize a "Joint Workshop on the Socio-Behavioural Aspects of Microbicide Trials for HIV Prevention" in New Delhi on December 5-6, 2005. It was felt that this workshop would provide a platform for sharing experiences by the concerned scientists from India, Africa, UK and USA engaged in HIV prevention research, and would help to identify the priority areas for research in the field of sexuality and sexual behaviour. It was decided to disseminate the information shared at the workshop in the form of 'Proceedings'–written in a brief and easy-to-understand format, catering to the needs of the concerned policy makers, NGOs and research workers from universities and scientific institutions. We hope that the resultant publication of the Proceedings of the Workshop has achieved this aim.

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EXECUTIVE SUMMARY

The pandemic of HIV /AIDS has highlighted the importance of research on sexuality and sexual behaviour as a means of characterising risk behaviour and identifying those population sub-groups who are a greater risk of HIV infection. Behavioural change towards safe sexual practices and utilization of preventive barrier methods like condoms and microbicides are the only effective tools available in a forseeable future, since anti-HIV vaccines are unfortunately a few decades away. Reliable information on sexuality and sexual behaviour would be essential to plan and implement evidence-based interventions for HIV prevention. This type of data collection would require an integration of the qualitative approaches of social science research with the quantitative methods of demographic surveys and epidemiological studies.

Both the research capabilities as well as the capacities for carrying out socio-behavioural research on sexuality and sexual behaviour are limited in India as well as in several other countries. A workshop was organized as a joint initiative of the Indian Council of Medical Research (ICMR) New Delhi and the Microbicides Development Programme (MDP) of the UK Medical Research Council (MRC), with the following key points for consideration: (i) the importance of forming close links with communities, based on an effective sharing of knowledge; (ii) the need for a profound understanding of the social context of sexual behaviour and (iii) the challenges inherent in obtaining reliable information about sexual practices in specific contexts. Scientists from India, Africa, UK and USA, representing the socio-behavioural sciences and various other disciplines, took part in the workshop. Besides individual scientific presentations and discussions, working group sessions were also held during the workshop to debate specific issues.

Some of the highlights of the workshop are summarized below

It was observed that for a vastly diverse country like India with low HIV prevalence, obtaining reliable HIV incidence data is very difficult. Furthermore except in the state of Tamil Nadu, there are no Behavioural Surveillance Systems (BSS) in place for collecting data on a regular basis on the sexual behaviour and sexual practices either at the national or at the state level.

The major lessons from several recent intervention trials, such as the trial to evaluate oral Tenofovir as a prophylactic regimen–indicated that besides maintaining the highest ethical and scientific standards, it is essential to work closely with the community through various flexible mechanisms such as Community Advisory Boards (CAB) and local Ethical Review Boards. These mechanisms ebanble the growth of trusting partnerships between researchers and the community, necessary for the successful conduct of clinical trials. Microbicide clinical trials are complex as well as expensive. Various ways to reduce the costs were suggested such as: **(a)** evaluate more than one active agent within a trial rather than conducting individual separate trials; **(b)** enrol a larger number of study participants and shorten the duration of follow-up; and **(c)** collect concurrently sexual behaviour data for better understanding of the results. Increasing the accuracy of sexual behaviour and adherence data is necessary for a better understanding of the significance of effectiveness findings from vaginal microbicide trials. Various approaches for this purpose included the multi-method data collection strategy and triangulating the results. It was stressed that there was no absolute truth about sexual behaviour. It was also pointed out that while clinical trials were conducted within a cultural setting, they do not entirely replicate that culture. As the trials themselves create certain expectations about the availability and accessibility of the test product, it is necessary to continue to monitor the community's expectations and concerns. Some major challenges of conducting Phase III microbicide clinical trials include–recruitment, retention, adherence, ethical considerations and post-trial product acceptability.

Research priorities: recommendations of three working groups

Working Group 1: Understanding sexual behaviour and norms

(a) Conduct studies of sexual behaviour of different population sub-groups.
(b) Undertake socio-behavioural studies of HIV discordant couples.
(c) Review published and unpublished Indian studies on sexuality and sexual behaviour.
(d) Investigate utility of multi-method strategy and triangulation for studying sexual behaviour.
(e) Foster networking among Indian government institutions and NGOs.
(f) Arrange visits of Indian scientists to microbicide clinical trial sites in Africa and elsewhere.

Working Group 2: Community preparedness and moblizations

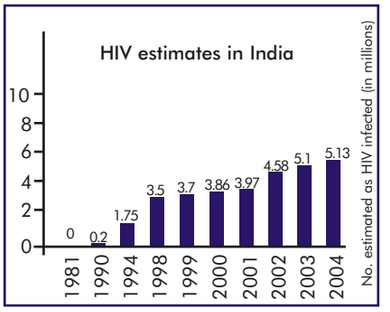
(a) Assess the suitability of potential clinical trial sites by using available local data on HIV/STI prevalence/incidence and by carrying out formative research on sexual behaviour, gender relation, men's employment, transport and migration.
(b) Assess the usefulness various community consultative mechanisms like CAB and Panchayati Raj System (local self-government)

Working Group 3: Acceptability and utlization of microbicides

(a) Investigate determinants of acceptability of microbicides.
(b) Determine the optimal positioning and social marketing of microbicides among various communities and specific risk-groups.
(c) Investigate community attitudes towards the acceptance of microbicides and their utilization in different populations groups, including as the general population and sex workers.

OPENING SESSION

Professor N.K.Ganguly, ICMR Direector General welcomed the international and national participants to the workshop. He said that microbicides research was the topmost priority for research and development efforts, since it represented the most important tool to fight and prevent HIV epidemics in different parts of the world including India. This area of research has become most urgent since development of an HIV vaccine was going to take considerably more time. Owing to the prevailing socio-cultural context where women are not empowered to negotiate and ensure safe sex, it would be necessary to have woman-initiated HIV prevention options such as microbicides. In order to successfully fight the epidemic of HIV, it would be necessary to ensure the accessibility, availability and affordability of microbicidal products–specially to the socio-economically poor and vulnerable population sub groups including the adolescents. Dr. Ganguly highlighted his views about the priority areas for consideration by socio-behavioural researchers. These were, firstly, assessing the needs of the community and creating demand for microbicides, secondly to assess the likely impact of the widespread availability of microbicides on sexual behaviour, and thirdly to consider ways of ensuring the ethics, equity and transparency of research in this field, to the community and related stakeholders, in clinical trials of microbicides.



Dr. William Stones welcomed the participants on behalf of Professor Jonathan Weber, who had been unable to attend the meeting. Dr. Stones introduced the MDP as a partnership between a number of stakeholders, including UK researchers led by the Medical Research Council and Imperial College, African partners at six sites (Reproductive Health and HIV Research Unit, Johannesburg, Medical Research Council Durban, Africa Centre KwaZulu Natal, MRC Uganda, University Teaching Hospital Zambia and AMREF/NIMR Mwanza, Tanzania in partnership with the London School of Hygiene and Tropical Medicine), industrial and non-profit civil society organizations. He said that the emphasis in the present workshop would be to share the experiences of African partners involved in the MDP programmes with the Indian scientists and civil society representatives present at the meeting, especially the work leading up to the current Phase 3 trial of Pro 2000/5 gel (Indevus) versus placebo.

Dr.Nomita Chandhiok informed the participants about the estimated 5.13 million HIV infections in India with an overall prevalence of 0.9 %. She briefed the participants about ICMR's Microbicides Research Initiative that had a wide mandate ranging from product discovery and development; clinical studies; capacity building; acceptability and community preparedness; clarifying regulatory review; and advocacy and policy work among both non-governmental and government organizations. The current focus was on conducting clinical trials of products developed inside or outside India as well as epidemiological and socio-behavioural research. She highlighted the clinical trial challenges and the need to partner clinical, social and behavioural research in order to advance our understanding of microbicide use. Dr. Chandhiok re-iterated the views of Dr Ganguly for urgently having women-initiated HIV prevention options as well as ensuring the accessibility and availability of microbicidal products at an affordable price.

Socio-behavioural Resrach

- Clinical trials provide a unique opportunity to learn from women who are actually using a microbicide
- Imperative to partner clinical, social and behavioural resarch in order to further advance our understanding of microbicide use.
- Social behavioural issues in clinical trials
  - Informed consent
  - Understanding sexual behaviour and norms
  - Community preparedness and mobilization
  - Acceptability and continued utilization

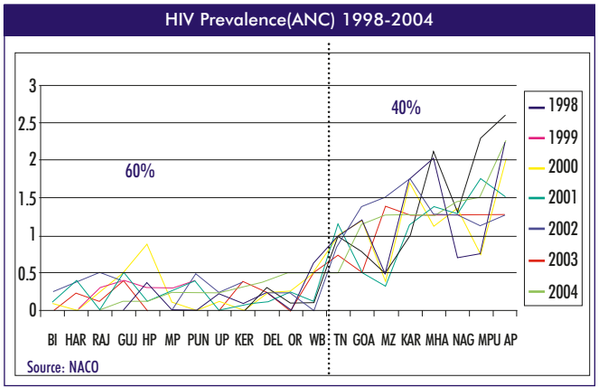
SCIENTIFIC SESSION –1

THE SOCIAL CONTEXT OF HIV IN INDIA: DEMOGRAPHIC INFORMATION ABOUT THE POPULATION FERTILITY CONTEXT AND AIDS KNOWLEDGE

WOMEN AND HIV/AIDS IN INDIA

Saseendaran Pallikadavath and William Stones, Centre for AIDS Research, University of Southampton, UK.

The National AIDS Control Organisation (NACO) estimates the total number of HIV cases in India at 5.13 million in 2004. There are possible errors that could underestimate the HIV prevalence in India. Among others, there could be errors due to non-representativeness of women attending antenatal clinics to the general population, one of the assumptions used in the estimation of HIV cases. The risk of HIV could be different for various women population sub-groups, non-attendees of antenatal clinics and sterilised women for example. There is a substantial proportion of women not attending antenatal clines in north India, and there is a huge proportion of sterilised women in southern India. Research is required to examine the risk of HIV infection among various women sub-groups. While obtaining correct number of HIV infected population in difficult in a low prevalence setting, obtaining the number close to reality is vital in planning and monitoring treatment, care and prevention programmes. As the epidemic is progressing in India there is clear evidence of increase in AIDS patients and paediatric HIV cases.



The 2004 NACO surveillance data shows no serious upsurge in HIV prevalence, although difficult to conclude the trend, among women attending antenatal clinics in India. Nearly 60 per cent of the Indian population i.e., about 600 million people still live in states where HIV prevalence among antenatal population is less than 0.5 per cent. On the negative side, nearly 400 million people live in states where the HIV prevalence among antenatal women is between 0.5-2.5 per cent. Further, there are significant inter-state variations in HIV prevalence in India. The mode of HIV transmission in India is diverse sexual route in northern India, sexual and IDU in southern India and IDU route in north-eastern India. Diversity of the epidemic is an important dimension of the HIV epidemic in India. Reaching diverse population groups with different epidemic levels, cultural practices, and sexual behaviour for HIV related service is a challenge.

An increasing proportion of younger women with HIV is reported in India. In 2005 nearly 40 per cent of the AIDS cases in the age group 15-29 years were women compared to 28 per cent in 2001. Increasing the proportion of women with HIV has serious implications for the vertical transmission of the disease and the overall welfare of women and their families. Recent studies have indicated the spread of HIV among married women in rural India suggesting the urgent need to prevent the infection of otherwise low risk groups through effective interventions.

In India, like other developing countries, rural women are the hardest hit by HIV/AIDS. The chronology of the infection, husband receiving the virus first and transmitting it to the wife, poses much greater threat to the women's overall welfare, particularly after the demise of the husband. In patriarchal cultural settings men spend most of the family resources for their treatment leaving very little for the women or children who will eventually become AIDS patients. Studies have shown that often in-laws send the widow of HIV positive men to their natal homes with their HIV positive children. Such patients eventually become destitute. Thus, the impact of HIV on women and children could be devastating. Mitigation of the impact of HIV through appropriate legislative measures is urgently required to protect

women's and children's rights over property.

Among women correct knowledge about HIV infection is low in low HIV prevalence states in the north compared to higher HIV prevalence states in the south. Knowledge about AIDS seems to have followed the epidemic rather than preceding it, this has to be reversed. There seems to be more facilitating factors for women's access to awareness of AIDS knowledge. However, there are only few facilitators for imparting detailed knowledge about HIV infection. Thus, imparting correct knowledge about HIV to women is much more difficult compared to creating awareness about HIV. Further, awareness of HIV should not be considered as the same as correct knowledge about HIV. Imparting correct knowledge about HIV to women require focused, locally relevant and culturally sensitive approaches. Imparting correct knowledge about HIV infection to women is low HIV prevalence states is urgently required.

Research indicates that in the northern states, older, poor, less educated, not having access to TV, and non-users of family planning methods are the most vulnerable women population to HIV infection primarily due to their lack of AIDS knowledge. In the high prevalence southern India, less educated, not working, not having access to TV, not visited by a family planning worker, never users of family planning and no access to modern electronic media are highly vulnerable to HIV infection. Reaching AIDS message to these women groups require innovative approach as the existing IEC approaches are less likely to reach them.

There is a need to review mass media efforts to educate rural women about AIDS as the electronic media may not achieve 100 per cent AIDS knowledge among women. The electronic media seems to be missing a critical population sub-group 'the media underclass' from its outreach. Research indicates that best methods to utilise highly effective low-cost channels such as community workers, health workers, and friendship networks must be explored to reach hard-to-reach population sub-groups including the 'media underclass'. A multi-media approach should continue, but must have other programmes directly aiming to the 'media underclass'.

The Indian rural health care system is capable of reaching potential family planning users while have no direct access to those out of reproductive career either through sterilisation, menopause or in-fecundity. Using family planning workers to impart correct knowledge about HIV is a cost-effective way of reaching rural women. Considering the high workload of health workers integrating limited HIV services in the reproductive health package needs to be tested for feasibility for wider use.

Finally, as knowledge alone will not allow women who are less powerful in conjugal relationships to demand condom use for HIV prevention there is perhaps hope in making vaginal microbicides available to women to protect from possible HIV infection from their husbands or partners. Thus, women's choice of methods to protect them form HIV infection is likely to increase protection from HIV infection.

Suggested bibliographic material for further reading

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INFORMATION GAINED FROM THE INDIAN BEHAVIOURAL SURVEILLANCE SURVEY (BSS)

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In India, most of the documented evidence on behaviour pertains to use of contraceptive services among married women. The behaviour studies since independence and pre-ICPD(1995) was related to utilization of various family planning products and reasons of non-use. Over emphasis on permanent methods especially female sterilization and low acceptance of couples were some of the reasons of low utilization of other family planning products such as condom, oral pills (OP), diaphragm, jelly etc. The other reasons were socio-cultural factors and lack of easy access to these products near home. Social marketing of condom is a recent phenomenon in context of family planning in India. Not many studies have examined the sexual practices among couples in the use of non-permanent methods. Indirect data interpretation reveals that couples do not prefer condoms as they find it difficult to use it for every sex act.

Community's perception on spacing methods is undergoing changes as documented evidence shows increase in utilization of spacing methods post ICPD (comparison of NHFS-1 and NFHS-2 data). In Rajasthan, one-third of women in the age group 15-19 years had not heard of condom and those who had heard about it did not use it. Less than 3% of surveyed women used condom in the past. The current use of OP is 3 percent and that too among women aged 20-29 years. Rhythm methods were not known in all age groups. Few knew withdrawal method and knowledge about other traditional methods (Baseline Survey Report of Chayan Project in Rajasthan, 2003). Chemists in urban areas were the major source of obtaining OP, while in rural areas it is AWWs/ANMs. Counselling on methods was very poor (only 18% users reported receiving counselling). Even for condom the major source seems to be chemist though in rural areas other key sources are ANMs and AWWS. The behaviour change communication for family planning was therefore geared towards motivating married couples to accept family planning methods, avoid unwanted pregnancies, postponing births, services of safer pregnancies and delivery and immunization. However, not much was discussed on sexuality and sexual factors that affect use of family planning methods. Reproductive health is a new term that gave credence to have studies on sexual relationships. With the advent of HIV/AIDS as an epidemic there has been increasing discussion on sexuality–multiple partners, condom use, age at initiation of sex, pre-marital sex, extra-marital liaisons etc.

Every society has convention/norms that govern sexual behaviour. They are often based on religious principles and power relations. Pre-marital sex is a taboo especially for women. It is a topic/area that is most difficult to get information on unlike FP surveys and research on sexuality is not well developed because researchers grope with the best ways to ask intimate questions about sex and respondents level of comfort. It is difficult to encourage condour. Unlike FP research, which is characterized by large sample population, power of reliability and validity, studies on sexual practices are small and often not representative of general population. The definition related to sex is usually not straight. Therefore it is difficult to obtain accurate data.

Following are some data that gives glimpses of views on sex among some sections of the population:

- In rural Gujarat, evidence shows changes in sexual behaviour, social taboos or sanctions against sex outside wedlock have weakened and some have started accepting it as normal behaviour as an emerging social reality. One-fifth of rural men above age 18 felt that sex was important for men before marriage (Khan et al., 1997). One-

third stated that both young men and women could have sex before marriage. This view was opined more by young men than older men (Khan et al., 1997).

- 36% of boys and 19% of girls from university students in Baroda believe that pre-martial sex is acceptable to both the partners (SORT, 1997; Barge and Khanna, 1998). In Rajasthan, 42% of boys and 31% girls agreed that these days before marriage boys are sexually active (Baseline survey report of Chayan, 2003).
- 15% of boys and 7% of girls from colleges in Mumbai had already exposed to coital sex. 40% of boys had first coitus before 18 years (Verma and Rangaiyan, 1997). Students from class 10-12 in Lucknow reported experience of sexual intercourse. 16% of students reported at least one of their close friends had this experience (CORT, 1997).
- Street children aged 8-14 years worked as sex workers and their regular clients included police inspectors, municipal ward representatives and students living in hostels. They were forced initially to have sex by close friends and rest by peers for pleasure.
- Is the family or community influences sexual decision-making among married couples or among unmarried couples? Few studies show the power relations in the household that determine women's vulnerability:
  - 2/3 of rural Gujarat men believe that only men should initiate sex.
  - 1/3 and above felt that it would be shameful for a women o express a desire for sex.
  - 1/3 believe that men can have sex with their wives whenever they want to even if she is not interested. (Khan, Khan and Mukherjee, 1997b)
  - Men in UP believe that men can go ahead even if she refuses (Khan, Townsend, Sinha and Lakhanpal. 1996).

The baseline for the CHARCA districts revealed that a considerable proportion of women (single and married women aged 15-24 years) have reported that spouse/partner do not give regards to their unwillingness to have sex (2005). The other interesting feature was that..."Condom use at last sexual encounter is consistently low. Also a sizeable proportion of women (20-40 percent) reported to have faced mistreatment in Aizwal. Kanpur and Kishanganj admitted to have mistreatment followed by & while this proportion is low in Guntur and Bellari.

Mother in law/mother and Husband's friends meet further mistreatment out to them. There are instances that men coerce their spouses into sexual relation for economic reasons. This makes women more vulnerable to STI/HIV infections (Women's Vulnerability to STI/HIV in India CHARCA Baseline Survey, 2005).

For understanding the epidemic in India, we have

- HIV sentinel surveillance
- Management Information System (MIS)
- Behavioural Surveillance Surbey (BSS)
  - Wider Population Coverage
  - High-risk, bridge population including/migratory and general population
- Gender sensitive with focus on Pregnant Women, Adolescents and Children
- Programme coordination: NACO
- Research and development: ICMR

The recent spurt of studies in the area of behavioural surveillance owes to HIV/AIDS. These studies at national or state level are limited as no continuous mechanism is inbuilt to continuously collect such data except to AIDS programme in Tamil Nadu. The first national baseline for general population BSS was done in 2001 for major states, followed by sex workers (including street based and brothel based), clients of sex workers, youth population, IUD users etc. The AIDS control society in some states does carry out BSS studies. The available information is elucidated below:

BSS General Population (2001)

12% males and 2 % females reported sex with non-regular partner in last 12 month recall period. Large inter-state variation occurs–lowest 2.5% in Manipur to 23.4 % in Maharashtra among urban males and from 0.1% among females in Orissa to 15% in Maharashtra.

One-third of males and a fourth of females reported consistent condom use in the country. Lowest condom use among males is in Orissa (10.7%) while highest in Goa (80%). While lowest condom use was reported among females in Orissa (0.0%), highest was report in Punjab (55.7%). Access to condom was found to be very poor in rural areas (more than 30 minutes travel to procure the same).

BSS General Population

Coverage and Methodology

- 35 states/UTs
- total respondents 3832 (15-49 yrs.)
- Urban-Rural settings (equal proportion)
- Sampling procedure-a three-stage Cluster sampling

Data

- Knowledge of HIV,
- Heard of STD
- Linkage between STD and HIV,
- Awareness on common symptoms

BSS data Gujarat ((1999)

The study sample was drawn from sub population groups that ranged from those with known high-risk behaviour such as female sex workers (FSW) and male clients of female sex workers (MC), Male Diamond Industry Workers (MDIW), Male Slum Dwellers (MSD), and Working Female Slum Dwellers (WFMSD). The BSS sampling universe consisted of areas in the state where major concentrations of the above groups were located. The seven places where the survey was implemented covered cities as well as purposefully selected districts. The sample sizes were chosen based on the estimated level of key risk behaviour and the degree of confidence (95%) required detecting a significant change (15%) in behaviour over time.

Ninety six percent, 75%, 16% and 8% sex workers had reported having sexual intercourse with a one time client, regular client, spouse or cohabiting partner and non-paying partner respectively in the preceding month. The study indicated that the reported consistent condom use was lower than the reported condom use during the last sexual intercourse. Consistent condom use with one-time clients in preceding 12 months was reported to be 73%, which was lower than that with regular clients (78%). The proportion of FSWs who had never used a condom in the preceding 12 months (4%) was lower with one-time clients than with regular clients (6%).

The reported condom use during last sexual intercourse with a female non-regular partner was low. It was 32% among diamond industry workers and 16% among male clients. Condom use was lowest among male slum dwellers (11%). A larger proportion of the university students (58%) had said that they had used condoms during their last sex with a female non-regular partner. The difference between condom use with a FSW and non-regular partner was least among the university students at 13% and was highest among clients of sex workers at 72%. Only the clients of sex workers had reported condom use (20%) during the last sexual intercourse with a male partner.

The BSS in Orissa had included few different target groups than that covered by Gujarat–i.e. Female Sex Worker (FSW) Male Clients of FSW (MC), Male Miners (MM)and Women in the Marine/Fishing Industry (WF). The reported condom use during last sexual intercourse for all subpopulation groups with female sex worker and female non-regular partners (range: 28% to 73%) were relatively higher than consistent condom (range: 12% to 31%). Female sex workers had reported lower use of condom during last sex as well as consistent condom use with non-paying partners (21% and 9%) than with paying partners (71% and 51%). Other than female sex workers (76%) and their clients (83%), awareness about HIV/AIDS was lower among other groups (range from 44% to 56%). Between 40% and 59% of all sub population groups were aware that diseases could be transmitted sexually. While 70% of the women in fishing industry were from Orissa, 30% were from Andhra Pradesh. Of the male migrants, 33% had migrated to Gujarat, 13% to Maharashtra and 10% to Andhra Pradesh. Inter personal communication and TV was cited as the most common sources of information on HIV/AIDS.

In summary, behavioural surveillance studies has helped to clarify and bring to consensus the risks of several population segments, for example in the state of Tamil Nadu. More emphasis was on knowledge of HIV/AIDS and ways of the prevention of the same and condom use. However, the large scale behavioural studies do not reveal whether the women can negotiate a safe sex with their partner–either husband or the client. Are women really powerful to participate in any decision making? For example–would they be really involved in decision making for becoming part of microbicide trials and/or their consistent use when the product becomes available for general use in future? What are the ethical issues to be dealt in country where the vulnerable are poor-below the poverty line? These questions can only be answered with further studies on the subject.

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SCIENTIFIC SESSION-II

ETHICAL CHALLENGES IN HIV PREVENTION RESEARCH

OVERVIEW OF RESEARCH ETHICS IN HIV PREVENTION TRIALS

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Ethical issues have gained attention since the Second World War when biomedical research experiments conducted by Nazi physicians on unsuspecting, helpless prisoners of war in the concentration camps came to light. Subsequently the Nuremberg trial held against these physicians resulted in the enunciation of Nuremberg Code in 1947, which clearly spells ten principles for the ethical conduct of any research on human subjects. Later in 1964, the World Medical Associate released the Helsinki Declaration which elaborated on the basic requirements for any therapeutic and non-therapeutic research undertaken by physicians. The basic principles guiding these fundamental documents of research ethics including the subsequent national and international guidelines developed by various countries and funding agencies are autonomy of individuals in providing informed consent to participate in research, a careful risk benefit analysis derived out of the principles of beneficence and non-maleficence and the concept of distributive justice taking care that the burden and benefit of research is equitably distributed. In spite of these guiding documents, unethical studies were conducted in many countries and in the last quarter of this century a spate of guidelines have been issued on various aspects of medical research. The 'Belmont Report' of USA released in 1979 and the 'Policy Statement on Ethical Consideration for Research on Human Subjects' from Indian Council of Medical Research in 1980 were the earliest of these followed by other countries and international agencies.Subsequently large number of special guidelines have evolved on different aspects of clinical research including clinical trials, human genetics, transplantation, assisted reproductive technologies, behavioural and social science research, use of human tissues, international collaboration etc.

BASIC TENETS OF ETHICS

AUTONOMY JUSTICE BENEFECIENCE NON-MALEFECIENCE

The advent of HIV/AIDS in the global scenario in the early 80s has not only presented unique health care challenges to population but also raised a host of ethical and moral issues related to human rights and human dignity. The disease has affected mostly the vulnerable groups of the population often leading to stigma and discrimination. The high cost of the therapeutic interventions has brought into the forefront the issues related to accessibility, affordability and availability of the appropriate health care to the affected individuals and the communities. HIV/AIDS has affected several nations by knocking down decades of development and widening the gap between poor and rich nations by pushing the vulnerable populations to the margins of society. According to the latest UNAIDS report an estimated 39.4 million people are living in the world with HIV of which 90 per cent are in developing countries and 64 per cent being in Sub-Saharan Africa. The most vulnerable groups of the populations women, children, young adults, sexual minorities are the worst affected with 47 per cent being infected women in general while 76 per cent women are from Sub-Saharan Africa. The extent of vulnerability is directly proportional to the magnitude of the risk of HIV and access to affordable health care and prevention strategies. Currently available treatments can only slow the progress of the disease but does not offer complete cure or eradication. The most effective of all is anti-retroviral therapy (ART) which is complicated to administer, requires close medical supervision, causes significant adverse effects and above all is extremely costly. The most needy population in developing countries lacks

access to therapy in spite of the availability effective drugs in the developed world. Hence, WHO has declared the lack of access to ART to HIV/AIDS as a 'global health emergency' in September 2003. Following this many countries around the world have come out with different policies to facilitate availability of drugs to affected populations as well as promotion of R&D to develop new drugs for HIV/AIDS.

In the meantime there is growing interest in promoting major efforts towards preventive strategies apart from therapeutics to find appropriate vaccines, vaginal/rectal microbicides or strategy for preventing perinatal transmission of infection to the neonate from the mother. The UNAIDS guidance document for "Ethical considerations in HIV preventive vaccine research" of 2000 calls upon countries and agencies involved in development of vaccines to foster early and ethical development of effective vaccines. Clinical trials with different drug regimens and varied protocols are also being conducted in many countries for the prevention of perinatal transmission of HIV/AIDS to the offspring. However, the main HIV prevention tools-Condoms, reducing the number of sexual partners, treatment of reproductive tract infections etc are not feasible for most women. After two decades of male condom promotion, though there is considerable increase in the absolute number of male condoms used, consistent condom use still remains difficult to achieve specially with the persistent resistance to condom use in some settings such as privacy, regular partnerships. Further there is limitation to condom use due to social, cultural and economic gender inequalities. In some countries, female condoms has increased options for protection against HIV to some extent, but problems remain with its long term acceptability and female condoms requiring co-operation of men for using the same.

Therefore, there is an urgent need to extend the range of prevention methods and specifically for the women to control. Microbicides potentially offer an important, valuable protective tool for individuals and couples who are unable or unwilling to use condoms. These have the double advantage of protection .against HIV as well as host of bacterial and viral sexually transmitted infections apart from unwanted pregnancy. These may be in the forms of gels, creams or suppositories and may or may not be spermicidal. These can be used alone or in combination with other barrier methods. By reducing the risk of HIV infection in women, microbicides may also contribute to a reduction of mother to child transmission. They prevent transmission from women to their male partners and re-infection in women who are already HIV positive. These can also be used in rectum during anal sex. Development of novel microbicides is one of the most rapidly expanding areas of HIV prevention research and it is estimated that currently over 50 products are in the pipeline undergoing various phases of preclinical and clinical studies. Generating strategies is essential so as to reduce the extent of infection in women and young girls which is essential if AIDS is to be brought under control. Hence large number of women have to be subjected to clinical trials thereby bringing to the forefront various ethical issues related to such trials.

Some Ethical Challenges

- What are acceptable standards of care?
- What are researchers responsibilities for moving research into policy & practice?
- How should stigma be dealt with?
- When are placebo controlled trials justified?
- How can informed concent be assured?
- Is research on new interventions ethical if existing knowledge is not being used?
- Partner Notification
- Empowerment of women

Ethical Issues and Microbicidal Trials

- Availability-Safety & Efficacy data
- Only microbicidal, anti-HIV, Contraceptive
- Teratogenicity, Mutagencity data
- Risk-Benefit Analysis
- Informed Consent-Women, Partners
- Privacy & Confidentiality
- Affordability, Access issues-Post trial benefits
- Community consultation

Microbicide trials include high risk women as well as monogamous women with single partners who perceive themselves at low risk. The trials require use of condoms in both arms with microbicides or placebo and should involve women of all state of society with cooperation of men. In these studies social scientists play a critical role in designing behavioural interventions and collecting sexual behaviour data. Laboratory and clinical research on microbicides are complemented by social science and market research to achieve harm reduction, dual protection strategies and potential market. Hence, informed consent from women and their partners are essential along with appropriate counselling. Though there is a directed need for the overall prevention and management of sexually transmitted infections amongst women, specially in developing and resource-poor countries, more targeting preventive means are required which women can use to protect themselves. For women participating in these trials, post trial availability and access to effective

products is a major issue for consideration by the sponsors, researchers and the policy-makers. All the stakeholders to be thoroughly educated on the role of microbicides in the prevention prorgrammes and the ethical issues in the conduct of such trials. The HPTN guidance documents developed by the Ethics Working Group (EWG) of the HIV prevention Trial Network of the Family Health International (FHI) of USA emphasizes protection of vulnerable from exploitation, promotion of equality through non-discriminating access to the benefits of research and minimization of research related medical, psychological, social and economic harms. Whenever possible, the HPTN researchers are directed to seek ways to improve local access to care rather than contribute to the creation of dual standard that privileges research participants and the potential for undue inducement. The guidance document stresses the desirability of seeking resources and building capacity locally so that care and access to drugs can be sustained after the research is completed. Women in general and high risk groups such as sex workers and sexual minorities, children and adolescents constitute the vulnerable segment of the population and hence measures are to be in place to protect their human rights in all prevention trials. The HPTN guidance document for prevention research is a compilation of best practices, accepted standards and emerging consensus for the ethical conduct of HIV prevention research developed by participants from many countries with the goal of ensuring ethical decision making of highest quality along with the best scientific approach.

Increased and sustained international collaboration in this area is the need of the day so that one can bring out the most acceptable and effective microbicide products in the shortest possible time. Although, these collaborations have assumed a reasonable proportions in the recent years thus necessitating intense ethical debates all over the globe, certain ground rules are to be kept in mind so that there is no scope for exploitation of any vulnerable population. The need of the host country before trials are conducted is to be examined and strategies are to be adopted to build capacity in the local communities so that meaningful participation as equal partners in the conduct of any research including clinical trials can be achieved. The social contexts and the cultural specificities of the host communities should be given due consideration to protect the dignity, safety and well being of the trial participants. The burden and benefit of trials should be shared by the collaborating countries. Guidelines, rules and regulations of both countries should be respected and followed. All issues related to intellectual property rights, exchange of biological materials, data transfer security issues and protection of confidentiality are to be given due consideration.

In India, clinical trials with vaginal microbicides are ongoing with both international funding and indigenously developed products. While this is a method to empower the women to protect themselves, consent of partner and maintaining privacy and confidentiality are major issues, which may be difficult to accomplish in all cases. A strong programme of counselling for both partners is to be in place if these trials are to be ethically conducted. Provision of ART to those become HIV positive during the trial is another major issues requiring prior agreements. While conducting trials in India, the Ethical Guidelines for Research involving Human Subjects released by ICMR in 2000 and Indian GCP guidelines released by CDSCO in 2002 are to be followed in addition to the Helsinki Declaration.

Like any other area of HIV/AIDS research microbicides trials pose specific challenges to researchers and policy makers. In recent years, attitudes towards microbicides have become positive in spite of the inherent barriers. A strong public private partnership is needed to make microbicides available as early as possible to the women who need them. Ethically conducted clinical trials with appropriate safety of the participants play a major role in achieving these objectives.

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STANDARD OF CARE AND LESSONS LEARNT FROM RECENT CLINICAL TRIALS

Alan Stone, International Working Group on Microbicides (IWGM), London, UK

Whoever is conducting a clinical trial will always have to deal with some difficult challenges: practical, financial, regulatory and ethical, and to make matters worse these all impinge on each other. In trials involving vulnerable individuals in resource-poor settings the ethical problems are amplified, and this is perhaps especially true for trials concerned with the prevention of infection with a deadly virus like HIV.

It is easy to define what is meant by ethics in this context. We mean the measures that have to be taken to protect and promote the safety and well-being of trial participants and of the community more broadly: their physical, emotional and societal well-being. Trialists nowadays fully recognize the importance of this and take all reasonable steps to run their trials accordingly. But recent adverse publicity–largely unwarranted-about a particular clinical trial of oral HIV prophylaxis with the antiretroviral drug tenofovir has dragged the issue of trial ethics under a harsh spotlight.

This is a multi-site trial to determine whether participants at high risk of acquiring HIV can be protected by taking one 300 mg tablet of tenofovir every day. This trial has been the subject of an astonishing campaign of criticism by local and international activists. And these criticisms have been widely reported in the media, including the lay press, scientific journals and internet websites. Some of these criticisms highlighted aspects of the study that needed to be looked at more closely, but for the most part these attacks were based on inadequate information, misunderstandings and sheer ignorance.

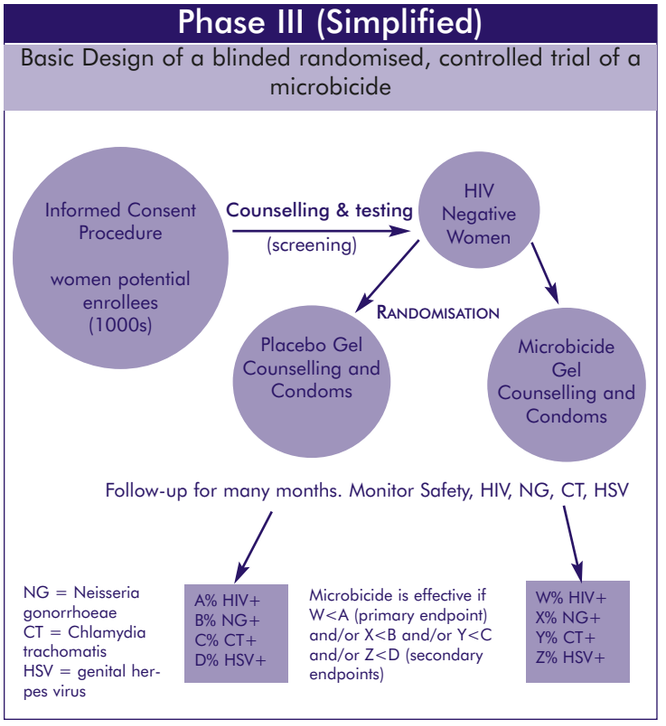
Nevertheless, this propaganda and its knock-on effects caused the governments in Cambodia and Cameroon terminating the trials in these important sites. There were also plans to expand the trial into sites in Malawi but the government there recently decided to withdraw their approval. However, the reason for that is different: they are planning to introduce tenofovir as part of the second-line treatment regimen for HIV+ people who fail on the first–line regimen and are concerned that the trial will result in tenofovir-resistant strains emerging in the community. There is no indication that this decision has been influenced by activism as in Cambodia or Cameroon.

But overall, the evaluation of a promising preventive technology has been delayed, a technology which is potentially able to save the lives of millions of people at risk of HIV infection. What we should be worried about is that similar activism could disrupt other important trials of HIV interventions in the future, whether of oral prophylaxis, microbicides, vaccines or other technologies. So it is important to try to understand how this situation came about and to consider what can be done to reduce the chances of its happening again.

In the case of Cambodia, the activists argued that it was unacceptable for Western interests to exploit commercial sex workers in a poor country like Cambodia for experimental drug testing and asked why the trial could not be carried out in high-risk US and European populations. They even accused the researchers of providing inadequate HIV prevention counseling so that sufficient study end-points would be achieved. The use of placebo pills was either misunderstood or misrepresented and the researchers were accused of giving some women “dummy pills”. They had also demanded 30-40 years’ medical insurance cover for trial-related injuries. Finally, they drew attention to insufficient community involvement in planning the study, and indeed this is one area that would have benefited by a more active effort on the part of the researchers.

In the case of Cameroon, the criticisms included inadequate access to care for seroconverters, the provision of participants with insufficient information about risks, inadequate numbers of study staff and an unethical study design in which participants "were being used as guinea pigs to promote the interest of the drug's manufacturers". Once again, the inadequate involvement of the community was highlighted.

Several lessons can be drawn from this experience. First, those responsible for clinical trials must ensure that they are designed, implemented and monitored to the highest standards. Second, researchers should work together with the community to make certain that adequate measures are being taken to promote the well-being of trial participants and ensure that these measures are being scrupulously maintained and records kept. Third, it is increasingly clear that bad politics can override good science. To counteract this there need to make prior preparations aimed at minimizing the risk that false, misleading and potentially damaging reports will be circulated; a strategy should be in place for enabling a swift and effective response should such reports nevertheless appear. Fourth, the development of a trusting partnership between researchers and community is pivotal to achieving these aims.



In engaging with the community, it should be made clear to all concerned that women who volunteer for a microbicide trial will be randomized to receive either the microbicide or the placebo; that they will be asked questions about their sexual behaviour; that they will be expected to undergo regular counseling sessions; that they will have blood samples taken for HIV and STI testing and must be willing to hear and accept their test results. These points also need to be made as part of the informed consent procedure. Experience has shown that it is not an easy matter to ensure that people understand some of the concepts to which they are exposed during this procedure. There are often cultural and linguistic challenges, and here again assistance from the community is important. Abstruse concepts like randomization and placebo–ideas that may not even exist in the local culture and language -will need to be explained very carefully. It can be particularly difficult to get the right message across about "equipoise", on which the ethical authority of the trial is founded, viz: at the time of the trial, there is no good reason to believe that the microbicide provides more benefit and less risk to the user than the placebo, or vice versa; the judgements either way are balanced.

Clearly, there also needs to be clear information and agreement with the community about the standard of care that can be expected: what will be provided and what will not; to whom will it be provided (trial participants, their partners, their family, the community more generally?), and for how long (for the duration of the trial, for longer, in perpetuity?), and who will pay (the trial sponsors, local or national services, bilateral or multilateral programmes?). Specific areas for discussion include the provision of VCT and condoms, the treatment of STIs and OIs, the provision of ARVs for seroconverters and/or for those found positive at screening, arrangements for avoiding stigma, and expectations regarding the continued provision of microbicide after the trial's completion should it be successful.

It is important that the care offered, and anything else, eg financial compensation, should not constitute undue inducement to participate in the trial. This can be defined as an inducement strong enough to encourage participation in the trial despite an awareness of risks that would otherwise have acted as a deterrent. It is also crucial to avoid creating a situation in which the community could become dependent on temporary arrangements for providing care during the trial which may not remain after the trial finishes. Indeed, investigators and their sponsors should regard a clinical trial as an opportunity to improve local services and standards of care in ways which will be sustainable after the trial has been completed.

There are a number of mechanisms for facilitating dialogue with the community on these issues. It is usual to establish a Community Advisory Board (CAB) with representatives from the researchers and from the community. The CAB's main role is to be aware of and discuss all aspects of the trials and to serve as a bridge for two-way communication between researchers and the community more broadly. The CAB, together with the local Ethical Review Board, is able to address trial issues as they emerge, whether they be rumours, complaints, SAEs etc. Community networks can facilitate the exchange of views within the community and the transmission of queries and concerns to researchers and the CAB. Strategic partnerships can be set up between researchers and community members to address specific issues, such as arrangements for consenting, counseling, the provision of drugs etc. This is not an exclusive catalogue of arrangements to improve dialogue and others may be set up as appropriate to the circumstances. Social scientists and advocates can of course be very helpful in creating these mechanisms. All such arrangements should form part of the trial protocol and should be reviewed as part of the regulatory approval process for the trial.

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NEED FOR UNDERSTANDING THE CONCERNS OF WOMEN PARTICIPATING IN A TRIAL: PERSPECTIVES OF WOMEN PARTICIPATING IN AZT FEASIBILITY STUDY

Nita Mawar, National AIDS Research Institute (NARI), Pune

"For much of my life I have felt that the struggle of gender inequality is the toughest struggle on the face of the earth. And never have I felt it more keenly than in the battle against HIV/AIDS,.... ....I ask all of you that you see microbicides not merely as one of the great scientific pursuits of the age, but as a significant emancipation for women, whose cultural, social and economic inheritance puts them so greatly at risk."

Stephen Lewis, UN Special Envoy at meeting in London

It is well documented that AIDS is as much a social and behavioural problem as it is medical problem. The organized global sector responded to the HIV/AIDS epidemic in eighties and since then there has been a serious concern about how the epidemic would impact the community. As defined by Mann, the HIV epidemic exists in three phases. In the first phase, the epidemic enters a community silently and develops over many years without being widely perceived or understood. The second phase is the epidemic that can occur after a delay of number of years. The third phase revolves around the social, cultural and political issues which are central to the global AIDS challenge. We are now in the third phase where these aspects need to be understood from community perspective in their social and cultural milieu.

With nearly 87% of infections contracted sexually, a focus on behaviour change and prevention intervention seems to be crucial. Preventive interventions need to be addressed to both men and women, especially considering the latter's vulnerable situation to negotiate safer sex behaviour. It is also seen that women with no reported risk behaviour of their own get an HIV infection from their husbands. This reflects women's vulnerability, while these women in traditional societies are considered to be the "breeders, feeders and producers' of goods yet they are not able to decide about their own health matters.

Most of the women around the world are powerless to control sexual relations, thereby, creating an urgent need for a women controlled prevention technology. Experience with contraceptives has demonstrated that women controlled methods have been used far more effectively. At present, an effective microbicide is not available while trials are being undertaken. These technologies may prove useful to answer the everyday challenges that women face like their lack of autonomy and decision making to manage their reproductive and sexual lives.

Research Concerns: It may be pertinent to recognize that while understanding biological diversities in the laboratory or testing of a product through trials, it is as much significant to understand the cultural diversities where these products would be used. This requires an approach that is multidisciplinary where bio-medical sciences and social sciences partnership is to be based on equality to ensure good quality research. These approaches would also ensure keeping concerns for the individual and the community where studied along with the product that is being tested. The concerns of women and their significant others must always be in the forefront as we work to develop a safe, accessible,

and effective microbicide and these have to be kept in mind while a product is planned, being tested, or available for the community.

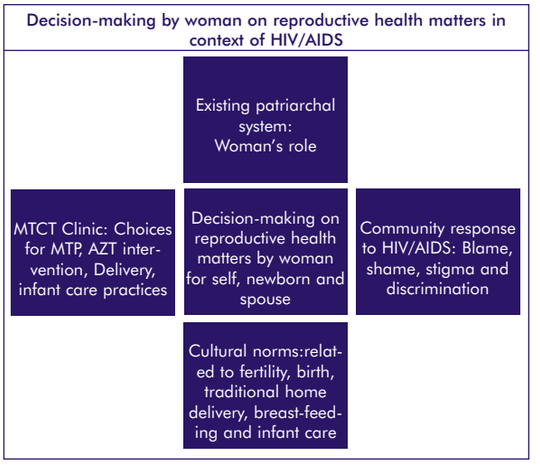
Methodological concerns: Understanding context of behaviour for preventive technologies like microbicide requires an "emic perspective" (insiders view) within which the normal population is at risk. There would be an impetus to get insights of sexuality issues, gender sensitivity, ethical issues around acceptance of a product (even a hypothetical product), reproductive health and sexual behaviour for planning appropriate prevention programs for bringing sustainable behaviour changes. The emic perspectives in the studies would be required prior to clinical trials to understand attitudes and concepts of men and women, through the preparatory studies, hypothetical/actual user preference, parallel to clinical trials for acceptability and attitudes, in conjunction with clinical trials like product use dynamics during trials and how best to educate trial participants on microbicide and after clinical trials have been completed on product use dynamics with experiences and changing attitudes. The issues from the insiders perspective would enable in understanding the context where these behaviours take place and how best they can be sustained e.g. issues around decision making to use a microbicide by a discordant couple to prevent HIV/STD transmission, yet have a child would require perspectives at several levels.

Ethical Concerns: The third phase of HIV/AIDS epidemic has gone beyond traditional realms of medicine with societal impact related to an individual's basic needs/instincts: sexual behaviour and motherhood. In this context ethics of HIV/AIDS is also related to basic rights and responsibilities of the dyad of researcher and those being researched. These are based on the ethical principles which are a set of principles of right conduct governed by well-being/ beneficence that leads to no harm; equity and distributive justice that does not discriminate; the respect for autonomy, dignity, rights through informed consent and confidentiality; and shares the solidarity and mutuality-with the greater involvement of people living with HIV/AIDS (GIPA). While following the ethical principles it is important to take up research to learn more about values, attitudes, desires, expectations of the population so that the decisions we study and contemplate will apply to the women within a community setting.

Ethical concerns are important and should be addressed as part of a research process. This envisages a need for more research on ethical issues and related concerns from the trial sites and includes considerations like what does ethical mean in context of research, who is to be protected and how? is it the researcher, the institution's, the community one works with, the host country and donor country and the mechanisms of guaranteeing ethics in research. These would be required at a formal level like safe-guaranteeing anonymity, maintaining confidentiality, informed consent and also at nformal levels through safeguarding trust and rapport with Community Advisory Board, establishing culturally appropriate research tools and sharing and feeding back information to participants.

It may be pertinent to learn lessons from a Zidovudine (AZT) intervention feasibility study on pregnant women to prevent mother to child transmission so that the concerns of women are kept in future during trials.

In India, more than three fourths of the HIV infections are due to the heterosexual route where women are often the innocent victims of being infected through the risky behaviour of the partners. This concern eventually paved way for a short-term AZT intervention programme to prevent mother to child transmission on an urgent basis at eleven sites with successful results. The findings of this study aimed to understand the women's perspectives while participating in the study and how it changed during the study. The study used qualitative methods used to understand this intervention from emic and etic perspective. (Using in depth interviews). The women at



antenatal clinics could access HIV/AIDS information and avail of the AZT intervention, their main consideration being preventing transmission to their new born. A SWOT analysis in table highlights the strengths, weaknesses, opportunities and threats of the intervention.

In summary, the pregnant women who were enrolled for an AZT intervention study to reduce the HIV transmission to their newborn evinced interest in participating in this study. However, these women were not clear at understanding the long-term implications of participating in this short term AZT intervention feasibility study during pregnancy to reduce the HIV transmission. This included the fear of being stigmatized by the family members on revealing her HIV status, especially by participating in the study entailing several visits to the clinic. Thus, monitoring women's comprehension during follow up visits with provision of psychosocial support is essential.

The major recommendations arising from the study were: that the project is useful but should help women through networking them and form self-help groups.

Women's confidentiality should be maintained even during delivery, follow-ups and making referrals; options of breast-feeding and top-feeding should be left up to women, considering her family background, and where required some options for a subsidy for top-feeding be given to women; ongoing training for the staff of the unit and other related staff should be conducted to emphasize options; the main objective of the study and comprehension of the trial by women backed with counselling at varied stages is required to enable women take appropriate decision; this should be incorporated through understanding women's comprehension of the trial as an ongoing strategy and support provided accordingly. This is an ethical responsibility at this stage to enable realistic planning for up scaling of programme. This has now been translated into a major intervention programme at Government Hospitals where Nevirapine is given to HIV infected mothers to avoid transmission to the newborn.

Lessons learned: the experience of this study underscores the need to involve the community when women controlled technologies are planned as part of an intervention. This be planned through the discussions through the Community Advisory Board (CAB) on issues related to the beneficiaries of the study, risks taken by whom, the public health importance of the trial, benefit beyond the trial, building up capacity for future development, the methodology of the study, the selection of participants, the treatment/participation risks. The CAB works as a surrogate of the community. The closer they are to the community the better would they be represented where the members should represent community, both genders, age, socio-economic representation, GIPA, their understanding of the protocol be clear as they are like the gate keepers.

Their participation in the protocol begins from the very start of its development, especially on methodology, selection of participants, the procedures for the dissemination of the study results at various stages of the research and enhancing informed participation through researcher–community participation. This process begins with community consultation that culminates in establishment of a community advisory board as seen in South Africa and India.

Thus, HIV/AIDS prevention efforts should be addressed through a framework based on well-being, justice and autonomy and mutual solidarity to maintain ethical standards using least intrusive measures. It is pertinent to remember that women represent nearly half of our population and are the harbingers for change and development in traditional societies and keeping their concerns would contribute in preventing HIV from further spread would pose no ethical problems if their concerns are kept, how so ever challenging they may seem to be. As a reminder the following words would keep us moving ahead.

> *"Those who decide not to conduct research, take care of sick or avoid prevention measures on controversial issues would have failed in their responsibilities to the persons who might have benefited from their experience"*
>
> **Primm**

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SCIENTIFIC SESSION III

METHODOLOGIES FOR STUDYING SEXUAL BEHAVIOUR; HOW TO OBTAIN RELIABLE AND VALID INFORMATION

HOW MANY PARTICIPANTS ARE NEEDED FOR CLINICAL TRIALS ANDHOW LONG DOES THE STUDY NEED TO BE?

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Several candidate microbicides are currently being assessed in Phase III trials but at the present time there is no microbicide with demonstrated effectiveness. The aim of the research community is to develop a microbicide which is effective, affordable and acceptable but we must begin by demonstrating proof of efficacy. Is the concept possible in reality?

To achieve proof of efficacy it is essential that we design our trials so as to maximise the possibility of showing that a potential product works. This requirement will influence our choice of design.

How many control arms?

A fundamental question concerns the nature of the control arm. What is the comparator to be? An obvious choice would be a matching placebo gel which could not be distinguished from the test product. Unfortunately it is not always possible to get a good match and some placebos may have a protective effect of their own. For this reason there has been considerable discussion and debate about the possibility of using a no gel, condom only arm as a second placebo. The condom represents the best available means of protection, it is highly effective if correctly and consistently used but unfortunately in many vulnerable populations its use is not an option for many women.

The no gel arm control would at first seem to be an attractive option. It represents real life and overcomes any possible problems about a placebo gel which might offer some protection itself. However, there are significant potential disadvantages. These relate to behaviour and follow-up.

It is well known that behaviour of participants within a trial is often different to that of those not enrolled. Within a trial the level of supervision and contact with medical and paramedical staff is likely to be much greater than in real life. In these circumstances adherence to medication is usually better. Differences from real life don't matter so much in a placebo controlled investigation as they will be independent of the treatment to which a participant has been allocated. If, however, a no gel arm is included in the study the participants will be at least partially unblinded; those not receiving gel will know it. This would almost certainly result in behaviour change. However hard we try to ensure that participants receiving gel don't behave as though the gel will protect them it is almost inevitable that some of them will assume that it does. In contrast those without gel maybe more diligent in attempting to protect themselves by using condoms if they can. There is also a real possibility that those with gel will share it with those without. This is most likely to be a problem among those living in the same accommodation or closely related.

Can we correct for these behavioural changes? We could try, but obtaining accurate sexual behaviour data is not easy and we could never be sure that our corrections had been effective.

Then there is also the problem of follow-up. Retaining women in the trial who are receiving only condoms is likely to be particularly difficult. Most women will have consented to join the study in the hope or even expectation of receiving gel, and in many cases in the belief that the gel will protect them. Why should those receiving only condoms bother to continue to come for follow-up if all they are going to get is free condoms? Differential follow-up rates coupled with differential

behaviour change are likely to make the findings from the trial at best difficult to interpret and at worst misleading.

Collecting behavioural data

Having said it is difficult it is important to obtain behavioural data (Robert Pool discusses different approaches to this in his talk). Behavioural and acceptability data may be necessary to understand the differences in outcome that may occur at different trial sites. Such differences could, for example, be explained by condom migration women who, were using condoms reducing their use in favour of using gel. A gel could appear to be more effective at one site than another due to greater acceptability, or because of a greater prevalence of anal sex.

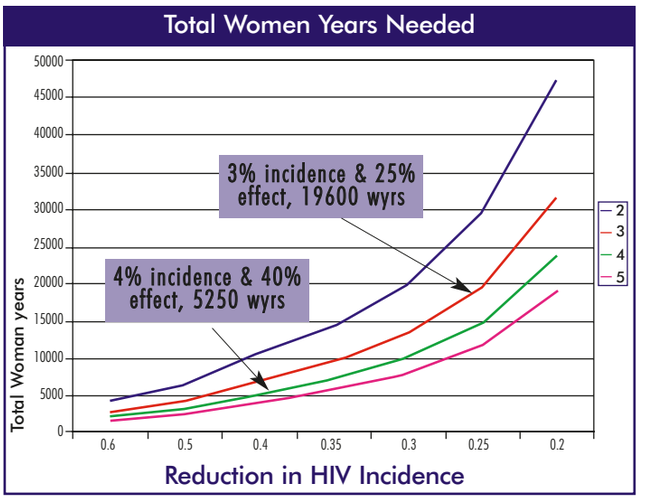
How many participants?

As with any clinical trial the size of the study population required will be determined by a number of factors, the number of study arms, the HIV-incidence rate, the expected effectiveness of the active product, the significance level and the power. Loss to follow-up rates and product adherence rates over time are also likely to be very important factors. Table 1 gives numbers of women years required in a two arm study with 90% power and 5% significance for varying incidence rates and effect sizes.

Table 1: Total number of women Years required in a two arm study to demonstrate varying reduction in HIV-incidence rates.

Incidence per 100 women years	Total Woman for varying effect sizes					
	0.5	0.45	0.4	0.35	0.3	0.25
2	4083	6300	10500	14143	19833	29400
3	2722	4200	7000	9429	13222	19600
4	2042	3150	5250	7071	9917	14700
5	1633	2520	4200	5657	7933	11760

It is apparent that as the effect size and incidence rate declines the number of woman years increases dramatically. An incidence of 4 per 100 years and a 45% reduction in incidence requires 3150 woman years of data. To demonstrate a 30% reduction with the same incidence rate requires more than three times as many woman years. These numbers do not take into account losses to follow-up or protocol withdrawals for pregnancy.



A target of 5000 women years can be accumulated in various ways, for example (if we assume no loss to follow-up) we could follow 2500 women for two years or 10,000 women for six months. We can expect follow-up rates to decrease with time as more women decide to drop out, or become pregnant. It is also likely that adherence rates will decline with time, women may use the product less with an accompanying decline in effectiveness.

If we assume a 3% increase in loss of women years every three months and a reduction in overall effectiveness from 50% at three months to 42.5% by 12 months then the total number of women years required if the incidence in the control arm is 4 per 100 woman years would be 3248 in a three month study compared with 5203 if participants are followed for a year, an increase of 73%. The three month follow-up requires fewer women years but the total number of women that would need to be enrolled would, however be over 12,000. In the context of a high HIV-prevalence among women expressing interest in the trial, as in some South African sites, this could require over 25,000 women to be screened.

Power of MDP301 Phase III trial

There was considerable discussion about the length of follow-up in the MDP301 trial funded by DFID. This is a three arm trial in which two doses of PRO2000 are compared. The study team eventually opted for a nine month follow-up but the FDA indicated that all women should be followed for a minimum of 12 months. We opted to follow all women to 12 months but retain nine months as the primary endpoint. We plan to recruit 9673 women; Table 2 gives the power of the study to detect different effect sizes at different time points for different incidence and effect sizes and assuming progressive loss of women years over time due to drop-out or pregnancy.

Table 2: Power of MDP301 to detect different effect sizes at different time points for an HIV-incidence of 4 or 5 per 100 women years in the control group.

HIV incidence in control arm/100 woman years	Follow-up in months	Evaluable women years	Effect size: reduction in HIV incidence rate 0.5	0.45	0.4	0.35
	12	7738	99	96	89	79
4/100 w-yrs	9	6166	96	91	82	70
	6	4352	87	79	67	55
	3	2297	62	52	42	33
	12	7738	100	98	95	87
5/100 w-yrs	9	6166	99	91	82	70
	6	4352	94	87	77	64
	3	2297	71	61	50	39

Assumes 5% loss of women years by 3 months, 10% by 6 months, 15% by 9 months and 20% by one year.

Incidence rates observed in the MDP feasibility studies varied from 3.5 to 12.6 per 100 women years, a weighted average of 6.2 according to the numbers of women expected to be enrolled in the trial. By powering the study for an incidence of 4 per 100 woman years we have allowed for the possibility that rates may decline during the study or that the full intake will not be achieved.

Conclusion

Microbicide trials are complex and costly. Costs can be reduced by including more than one active agent rather than conducting separate trials. To maximise the chance of demonstrating an effect it is probably better to enrol large numbers for a relatively short duration of follow-up. Collecting sensitive sexual behaviour data is essential to understanding the results.

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INCREASING THE ACCURACY OF SEXUAL BEHAVIOUR AND ADHERENCE DATA

Robert Pool, London School of Hygiene & Tropical Medicine, UK

In order to determine the effectiveness of vaginal microbicides it is necessary to have accurate data on product adherence (whether and how women used the product), sexual practices (frequency of sex, condom use, anal sex, dry sex), and vaginal practices (douching, insertion of various products into the vagina).

Methods for studying sexual behaviour

Information on these topics is collected largely through various forms of self-reporting. Survey style questionnaires with fixed questions and multiple-choice answer options are by far the most common. It is widely accepted, however, that questionnaires are not the ideal method for collecting data on sensitive topics, and various other forms of self-reporting are being increasingly used.

One of these involves attempting to reduce the distance between researcher and participant by developing rapport through the use of open in-depth interviews. The relative intimacy of this method may put the respondent at ease and thereby facilitate the discussion of personal and sensitive topics. On the other hand, it may also result in desirability effect bias, with the respondent trying to please the interviewer by giving the answers that he or she thinks the interviewer wants to hear, or it may inhibit the respondent from revealing behaviours considered to be socially undesirable.

MDP strategy

- Choose a range of methods
  - face-to-face & self assessment
  - qualitative & quantitative
  - partners
  - participants observation
- Short recall periods
- Compare same time period for indivual women
- Terminology
- Compare results during the study
- Continuous dialogue with participants
- Training

To reduce these biases attempts have also been made to increase the distance between researcher and participant through the use of various forms of self-assessment tool. These include computer assisted interviewing such as ACASI, ballot boxes and coital diaries. These methods offer respondents the opportunity to reveal undesirable or potentially stigmatising behaviour without the fear of disapproval or discovery.

Various other methods that do not rely on self-reporting have been used. Participant observation, a method derived from anthropology, and the subject of jokes when mentioned in this context, has also been used to collect data on sexual behaviour that would otherwise have remained hidden [1,2]. Other methods, that could perhaps be seen as a more indirect form of participant observation, have also been used: the collection of condom wrappers, the counting of used condoms, or the collection of used applicators in vaginal microbicide research. Finally there are the "hard" biological indicators: STI incidence and the presence of sperm in the vagina can reveal the occurrence of unprotected intercourse and assays can reveal whether or not a woman has inserted a microbicide gel applicator into her vagina.

Although all of these methods have advantages, they also all have their weaknesses when it comes to collecting accurate data on sexual behaviour. Self-reporting can reveal the details of what people do and think, but it may be unreliable. Participant observation and the collection of condoms and applicators are not adequate in themselves, and

they are also not always feasible. Biological markers, though perhaps more reliable than self-reporting, only provide limited information and are also by themselves often insufficient. For example, testing applicators for the presence of vaginal mucous will not tell you whose vagina it was and whether or not the woman had sex, and the presence of an STI will reveal unprotected sex, but cannot tell us how often the person had unprotected sex, why or with whom.

Triangulation

The solution: multi-method triangulation?

- In surveying: find position by getting bearings on different landmarks
- Methodological: Use several approcahes so the biases of one are cancelled out by the others
- Outcome asumed to be a single fixed point

Kinds of triangulation?

- Different time or place
- Different sources (partners, gossip)
- Different investigators
- Different methods
  - Often qual/quant, with qual confirming and giving more depth to quant
  - or inteviewer/self-administered
- Internal comparison
- Member validation

How can we overcome the disadvantages of the various methods and increase the accuracy of out data? One way is to make use of a multi-method data collection strategy and then triangulate results. The idea of triangulation is derived from surveying and navigation and refers to finding ones position by getting bearings on different landmarks. methodological triangulation similarly refers to using several methods so biases of any one method are cancelled out by the others. As with surveying and navigational triangulation, this assumes single fixed reality about which we can obtain objective information [3, 4]. In social research various types of data can be triangulated:

- Data collected at different times and places (e.g. interviewing the same person in a clinic setting and then later at home)
- Data from different sources (e.g. comparing data from both partners, or what respondents say with what others say)
- Data collected from the same participant by different researchers
- Data collected by using different methods (e.g. qualitative and quantitative, or self-administered vs researcher administered)
- Internal comparison of different aspects of the same set of data (e.g. looking for contradictions in individual interviews)
- Member validation (asking the participants how accurate they thought the data they provided is).

Multi-method studies of sexual behaviour

Various studies have used combinations of methods to study sexual behaviour. The table contains a summary of some of these.

There are many such studies, using different methods and carried out in different settings, but the results are mixed, and they often do not reach the fixed point. There are various reasons for this, both practical (e.g. the difficulty of ensuring that different methods cover the same time period, and the ambiguity of sexual terminology) and philosophical (perhaps there is no fixed point). We will not enter into a detailed discussion of these issues here, suffice it to say that innovative and relevant as many of these studies have been, they have tended to reveal the problems rather than solve them. So what needs to be done? First, we must try and understand the reasons for inconsistencies in sexual behaviour reporting. These are often not a result of participants trying to mislead researchers, but are caused by various other factors: the difficulty in accurately recalling details of sexual behaviour, misunderstanding of research questions, ambiguous terminology (most of the key terms relating to sexual behaviour are ambiguous, especially when translated in research settings), and ambiguous acts (it is not always easy to define the behaviours we are trying to measure in sexual behaviour research). Second, we must address these issues before and during studies, rather than simply identifying them afterwards. We can do this by helping participants to remember (e.g. by using short recall periods, aide

Table 3: Summary of selected multi-method studies of sexual behaviour		
Padian et al 1995 [5]	Concordance between partners' reporting of sexual histories	Couples, general population & STD clinic attenders', US
Zenilman et al 1995[6]	Self-reported condom use unreliable when compared to STD incidence	Urban men & women STD clinic attenders, US
Orr et al1997[7]	Self-reporting reliable when compared to STD incidence	Adolescent women & STD clinic attenders', US
De Boer 1998[8]	Agreement on contraception, common sexual practices & frequency, less on condom, anal & oral sex.	Couples, men HIV+ blood donors, Thailand
Lagarde et al 1995[9]	Reports of frequency in short term reliable; less so in longer term. Over-reporting of frequency in retrospective vs weekly reports, esp. among men.	Couples, Senegal
Allen et al 2003[10]	Biological markers (sperm, STDs) provided evidence of under-reporting of unprotected sex	Couples, VCT centre, Zambia
Hewett et al 2004[11]	ACASI appears more accurate than face-to-face interviews	Adolescent girls, Kenya
Plummer et al 2004[1]	Self reports inconsistent compared to biomarkers In-depth interviews better than self-completion questionnaire. Participant observation better for understanding sexual behaviour	Adolescents, Tanzania

memoires), by understanding vernacular terminologies relating to sex, and by confronting inconsistencies directly during the research process.

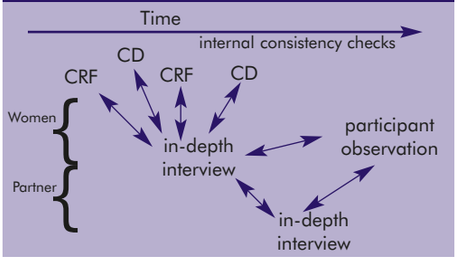
In this process we must make a number of assumptions. First, we must assume that study participants are basically honest, and that there are often have good reasons for nconsistencies, and we must ask for them. Second, we must assume that participants do not necessarily feel threatened when confronted with inconsistencies in their own reporting. My experience with this is that they often welcome the opportunity to correct misunderstandings or inaccuracies that inadvertently crept into their reports. Finally, we must accept that there is no absolute truth about sexual behaviour.

MDP301

In the MDP301 trial we have adopted the following strategy:

- Use a wide range of methods, combining different approaches: face-to-face (interview) and self- assessment (coital diaries), qualitative (in-depth interview) and quantitative (CRF questionnaire).
- Interview partners and compare with participants answers
- Use short recall periods (sex in the last week)
- Collect data through CRF, in-depth interview and coital diary for the same week
- Preliminary study of local terminologies across different sites and languages inorder to select the most accurate and comparable terminologies
- Compare results during the study and conduct a continuous dialogue with participants, going back and asking them, explicitly, about apparent inconsistencies in their reporting
- Training of field staff to use the right vocabulary and probe inconsistencies

MDP Triangulation process



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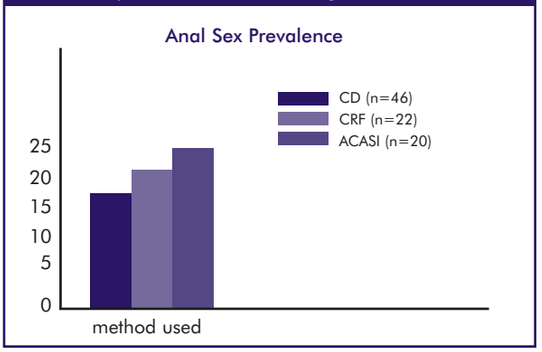
EXPERIENCE OF COMPUTER ASSISTED DATA COLLECTION (ACASI)

Mdu Mntambo and Jonathan Stadler, Reproductive Health Research Unit, Johannesburg, South Africa.

During the Microbicide feasibility study participants were regularly interviewed by a community health worker at clinic visits using a questionnaire called the Case Record Form (CRF). This interview included questions on sexual behaviour, including anal sex. According to these interviews less than 2% reported having had anal sex. Some concerns were expressed regarding the accuracy of the data collected using the CRF. Sexual behaviour questionnaires have limitations when it comes to collecting sensitive questionnaire data. It was therefore necessary to validate these data and to collect qualitative data on the perceptions and experiences of Soweto residents regarding anal sex so as to understand whether or not anal sex poses a significant risk to women who would be recruited into the microbicide trial.

Focus group discussions were held with 25 enrolled female participants in the microbicide feasibility study. An additional group discussion was held with seven male university students. In these discussions participants were asked to talk about what they knew about anal sex in Soweto. Forty six enrolled women completed pictorial coital logs which depicted anal sex, vaginal sex, oral sex and condom use. These same women were interviewed using the CRF questionnaire either by an interviewer or using ACASI. The intention was to validate the reported sexual behaviors from the CRF questionnaires.

Self reported anal sex according to method used



Feasibility Study results covered 589 woman years of follow up. The HIV prevalence at screening was 23% and the incidence at 12 months was 3.4%. The retention rate of participants was 93% and 60% reported condom use for the last sex act. Of the forty six women who completed the coital logs, ten (21%) reported having had anal sex. Four (18.1%) of the 22 women who were interviewed by an interviewer reported having had anal sex, while five (25%) of the 20 who did the ACASI reported having had anal sex. Anal sex appeared to be a relatively well known practice in Soweto. Women had been exposed to visual images of anal sex in pornographic films and on television. This was seen as an important source of awareness as well as curiosity about anal sex. Focus groups revealed that women often talked about anal sex amongst themselves with friends. Some who were very open about their sexual preferences spoke openly about having had anal sex. Some women did anal sex because they thought it strengthens the relationship. Anal sex has at times been seen as a substitute for vaginal sex to prevent pregnancy when men refused to use condoms. Many respondents recognized the dangers of anal sex as a means of transmitting HIV.

Participants spoke freely and openly about anal sex in the discussions. They told us different names that are used locally to refer to anal sex and circumstances under which anal sex happens. A number of challenges were encountered with the ACASI method. These ranged from technical to respondent's level of computer literacy.

UNDERSTANDING EMIC PERSPECTIVES

R.K. Mutatkar, Maharashtra Association of Anthropological Sciences & School of Health Sciences, University of Pune, Pune.

Human beings share the biological instinct of sex with other animals and more so with the primates. In human society, sex is institutionalized in marriage and is governed by rules of endogamy, exogamy, monogamy, polygamy, hypergamy and such other coping mechanisms as levirate and sororate. Sexuality is thus socially constructed. A majority of human societies are patriarchal, giving rise to issues of gender. In the evolution of human society, man woman relationships have been conceptualized differently in pastoral and agricultural communities. In Mahabharat times, society would permit insemination of a woman, if she could not conceive from her husband, a practice called "Niyog". Choice of male was an issue since seed was considered more important than the field.

The technical interventions either to prevent conception or to prevent morbidity in the context of STD and HIV infection have raised other behavioural issues. It is a cultural practice to provide for privacy in sex to young married couples, to promote fertility as early as possible after marriage. Even in the hard core Hindi speaking patriarchal belt, six months of privacy is provided by the parental generation whatever may be the housing patterns and gender specific locations of sleeping.

Enough information is available about the non-use of condoms among emotionally or socially accepted hetero-sexual partnerships. Even relationships between CSWs and their frequent clients preclude the use of condoms in the relationships. In the patriarchal society there are double standards of permitted and tolerated sex behaviour for men and women. If a woman uses any method for preventing fertility or morbidity without the knowledge of the male partner, a needle of suspicion is directed to woman about infidelity. The use of condoms continues to be associated with deviant sexual relationship. In tribal communities where pre-marital sexual relations are not uncommon and are permitted, the pregnancy consequences are not denied and could culminate in socially approved marriage. The idea about sex in tribal societies differs from that of the caste peasant society. In tribal society, adultery is frowned upon since the divorce and re-marriage are relatively easy and approved with social and economic procedures.

The issue is about understanding the cultural and opportunistic context in which sexual interactions formally take place. The quantitative methods of data collection such as survey methods provide the information about 'how many' and 'how much' prevalence. The qualitative methods can provide the information in the context and provide explanations about the variety of behavioural patterns. Administration of intervention programmes usually take into account the requirements for success of technology and would strive to promote the acceptance of technology by the people. Peoples' response to the technology is based on their attitudes or personalities which are shaped by the process of enculturation and socialization and by their experience. To transform the awareness of new technology into acceptance at the individual level depends upon social acceptance and approval of the use of technology. As compared to the use of technology in such visible areas as agriculture which are soft aspects of culture, technologies dealing with human biology and more particularly sexual behaviour are in the realm of belief system which forms hard core culture. It is therefore necessary to understand the ideas and practices from the perspectives of the subject (Emic) in contrast with the

EMIC - ETIC

EMIC-Information that reflects point of view of local people including vocabulary

ETIC-Data, categaories and language of the researchers or 'Outside' biomedical ways of conceptualizing knowledge

Problem oriented research; combination of Emic-Etic and combination of qualitative and quantitative methods desirable.

'Going Native' is the dictum in Anthropological Research. Preference for Observation. Informal Interview, Life History and Case Study.

perceptions of the researchers and administrators. "The concept Emic refers to information that reflects the point of view of local people in the study population, including their vocabulary and their categories for understanding sexual behaviours and other information. The concept Emic is used as a contrast to Etic data (and categories), which present the language and categories of the researchers, or the 'outside' biomedical ways of conceptualizing knowledge" (Pelto, 2005: 40). Unless we have good understanding of 'what is', we cannot take successful steps to market 'what should be'. Awareness and acceptance are polar types and there are several steps in between.

The informal interview is the best method for getting sensitive information. Focus group discussions could be useful in getting to know the range of behavioural patterns in a particular homogenous group, of the same age group, caste and socio-economic levels. It would also be desirable to have such group discussions among young men to get their perspective about sexual relationships. We have also seen the dilemma of more rural boys claiming pre-martial sex experiences as compared to the girls. The dilemma could be resolved through an explanation that only a few women who were vulnerable due to poverty, desertion, widowhood or absence of husband for a long time, could provide pre-marital sex experiences to young boys through plural episodes of sex.

One of the dark areas in legitimate relationships between husband and wife relates to locations of sleeping, which would prohibit privacy of sex. The only privacy women could have could be a bathing place or a place where she could ease out. The more complicated issue pertains to knowledge and approval of the husband. One of the crucial issue pertains to free and frank communication between husband and wife about sex, and risk involved in case of opportunistic deviant behaviour. It has been seen that Self Help Groups of women in India have facilitated better inter-spouse communication in general.

The best suitable methods for microbicides studies would be the in-depth interviews of women of various age groups, class groups and from tribal, rural and urban communities. The insistence by CSWs of the use of condom by clients is fairly successful since the clients are now aware about the potential risks. For the same reason, the use of condoms is not favoured between married couples. The migrant youth from rural areas around Pune who work at Pune as rickshaw drivers, hotel workers and as labour have started using condoms in relation to CSWs, but would not use them in their relationship with village girls. The 17 field based studies carried out at the School of Health Sciences, University of Pune, funded by Ford Foundation under small grants awards, are all based on qualitative research techniques. These have been grouped under five themes (1) Construction of Sexuality and Gender (2) Sexual Behaviour (3) Reproductive Health Issues (4) Decision and Utilization of Contraceptives (5) Connectivity, Information and Language.

These themes include studies on male and female adolescent behaviour in the tribal, rural and urban settings. The studies on migrant youth and the adolescent girls in the slums and the hotel worker have brought out the practices and perspective of youth about sexuality. The studies on commercial sex workers in Rajasthan and in the red light areas at Pune have provided ethnographic evidence of sexual relationships. The couple of studies on reproductive health and morbidity among slum dwelling adolescent girls and women in rural area enlighten us about the degree of ignorance of women about menstruation and white discharge.

The information about microbicide trials would require knowledge about the logistics of sexual contact in the general population in the rural and urban setting. In view of the absence of concept of bedroom privacy and well demarcated bathroom privacy for the women, it is necessary to get the emic information about the use of gels. Although women are aware about the double standards of men in sexual behaviour and even tolerate it in a patrilocal setting, the matters cannot be discussed openly between the spouses. The community and in some cases the parents do perceive the risk in certain occupational groups which keep the men away from homes for long duration and in the urban setting where there are temptations, peer group pressure and easy available money to indulge in risky sex behaviour. However it has been possible to unravel the behavioural patterns of these groups through informal open ended indepth interviews by developing a good rapport with the subjects. Multicentric studies are required in India to understand the emic perspectives about sexual behaviour and practices.

Methods of data collection	Subjects; Indivuals and Groups
Group discussion (Focused)	Groups of young women and men of similar age group, caste, self help groups, specific groups such as migrants
Key Informant Interview	Mother-in-law, TBA, ANM, female school teachers, CSWs
Expert Interview	Folk & traditional medicine practitioners
Indepth Informal Interview	Lay women: whose husband are constantly touring or visit them occasionally, with morbidity symptoms, mobile and migrant youth
Social mapping	Sleeping locations of men and women in different age groups in urban, rural, tribal setting in different climatic season, privacy: bath, lavatory-toilet
Life history	Older women from joint and nuclear families: document sexual and reproductive history
Case study	Women with STD and reproductive mobidity
Secondary data	Peak months of child birth

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SCIENTIFIC SESSION IV

COMMUNITY PREPAREDNESS AND MOBILIZATION STRATEGIES FOR HIV PREVENTION

OVERVIEW OF COMMUNITY LIAISON PROCESSES

Richard Mutemwa, Centre for AIDS Research, University of Southampton, UK

The major observations made by Dr. Mutemwa during his presentation about the strategy adopted for the community involvement in the MDP trial are summarised below. The "community" is not a monolithic or homogenous entity as it consists of several sub-groups such as women of reproductive age, male partners, trial participants, community leaders, private and public stakeholders. Each sub-group could be seen to have an interest in its own"comparative advantage"

Elements of the community mobilization strategy in MDP were community liaison entities like community advisory boards (CABs), community advisory group (CAGs), and community advisory consultants (CACs). There was a need for communication materials and media including inter-personal activities, for involvement in health talks by counselors and clinic staff, and finally a critical role of health service providers and quality of care as perceived by the community.

The community involvement strategy was designed as a phased activity reflecting the progress of the trial.

Four key elements aspects were a dedicated community liaison officer, formation of a community advisory board (at all but one of the six MDP sites), communication channels of various types depending upon their local availability, and a monitoring system to capture both the positive and negative feedback from the community about the study.

BASIC PRINCIPLES

- **Community is not a monolithic homogeneous entity**
  - Women of reproductive age
  - Public/Private stakeholders
  - Men/Partners
  - Community leaders
  - trial participants
  - Others - social networks/opinion consultants
- **Differentiated participation: comparative advantage**
- **Communication-centred**
  - liaison (CABs,CAGs,CACs)
  - Communication materials/media
  - Clinical Process counsellors, reception
  - Service: Services provided, quality of service
  - Communication centred
- **Phased: entry-middle-next**

LESSONS

- **What attracts women to the study?**
  - 'Familiarity' of the CLO: enrolled women do help too
  - Clear, simple messages in local language: purpose, safety, other relevant clinical services, compensation
  - Continuous feedback loop, concerns addressed
  - Hope–in case the drug works for her!!
- **What keeps women on the study?**
  - Continuous feedback loop, concerns addressed –otherwise explained why not
  - Sustained hope
  - Consistency in messaging and sustained communication
  - Demonstrated, consistent confidentiality
- **What makes women leave the study?**
  - Rumour, stigma
  - Perceived lack of confidentiality
  - Partner hostility
  - Issues about compensation: did you consult?
  - Other priorities: education, work, household economy, migration, marriage, health, pregnancy, sexually inactive, etc.

Lessons learned include appreciation of factors that attract participants, encourage them to keep in follow up, or might cause them to drop out.

In undertaking liaison work it is important to appreciate that each site has its own unique socio-political features. Every member of the community should be able to speak directly to the researchers, and the community grows in experience as the trial progresses, thus trusting relationships are necessary between the researchers and trial participants. Finally, actions speak louder than words, so little acts of compassion by trial staff mean a lot more to local people.

Major challenges include explaining clinical trial terminologies such as "randomisation" and "placebo" in a local vocabulary. There can be complexities arising from the legacy of previous trials in the area, and from expectations raised by new developments such as wider availability of antiretroviral therapy. In some settings the quantum of remuneration for participants can become a problem, if this is a substantial sum in relation to normal family income.

SOME CHALLENGES

- **Social Marketing: Selling a clinical trial (research) Vs selling boreholes**
  - Will I have the drug free later?'
  - 'Okay. But, then, why don't you just give the product to everybody, we start using it, and then you see if it works!'
- **Understanding of Research/Trial**
  - 'Random-ization? What's that?'
  - 'Placebo–do you mean it's `fake`?'
- **"Trial Rush" & "The Legacy Effect":**
  - 'They said that they don't care about us. Prove to us that you're different'
  - 'They gave us everything we asked for. We don't understand why you are so reluctant'
- **Bottom-line: Is a common front for all trialists / researchers achievable?**
  - How about possibility of overarching GLP guidelines (in the lines of GCP)?
  - for ethical & informed consent purposes

COMMUNITY INVOLVEMENT AND EDUCATION IN PHASE -I AIDS VACCINE CLINICAL TRIAL

S. Sahay, National AIDS Research Institute, Pune

Pune is an industrial city with a population of nearly 3 million, situated in the higher HIV prevalence state of Maharashtra in India. Baseline feasibility studies on high-risk cohort (Sexually Transmitted Infections (STI) clinic attendees, sex workers) in Pune have reported high HIV prevalence (18-26%) and provided information on the associated biological and behavioural risk factors in the study population [Mehendal et al, 1995]. HIV-1 C is the most common subtype [Gadkari et al, 1998]. The sentinel surveillance among pregnant women attending Government clinics in Pune city indicated HIV prevalence ranging from 2.5% to 3.7% [Unpublished data from National AIDS Research Institute, Pune, India] and that in the rural areas around Pune was 1.2% [Kunte et al, 1999]. National AIDS Research Institute started epidemiological research in Pune city in 1993 and over the last decade the research focus has changed from descriptive epidemiology to prevention research and clinical trials. Naturally transition has occurred from clinic based to community centred research and involvement of community became critical for conducting various clinical trials of microbicides, vaccine and anti-retroviral drugs at NARI. Community involvement strategies were designed initially for microbicide trials that later transitioned to the vaccine trial also. This presentation examines the experiences and lessons learned through involving community for the first AIDS vaccine trial in India.

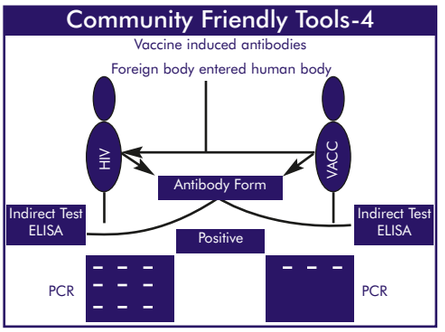
We faced a major challenge of making the community understand the complexities of various phases of clinical trials, meaning of participation in such trials, AIDS vaccines and the test vaccine. Explaining vaccine induced antibodies, risks, placebo and randomization in community-friendly language is difficult. The purpose of involving community in the vaccine trial was as follows:

- Inform, facilitate and guide the development of a community centred, relevant, utilitarian and ethical research agenda
- Bridge the gap between research participants and their communities and the researchers
- Proactively identify challenges and provide formalised mechanisms for dialogue that will provide ethical and scientific rigour aimed at effectively reducing the number of new infections
- Conducting community preparedness study to understand and then formalise all the above mentioned issues.

Community Preparedness Studies: In order to understand the actual needs of the community that would eventually use a preventive AIDS vaccine, a study was conducted with high-risk group of STD clinic attendees at NARI clinics in Pune. A 22 item structured instrument was used to assess willingness to participate in hypothetical AIDS vaccine trial, concerns and fear pertaining to such participation. The study indicated nearly 64% willingness to participate where knowledge of current effort on AIDS vaccines significantly related with willingness to participate in HIV vaccine trial (Sahay et al, 2005). Individuals who were concerned about serious adverse event were less likely to be willing to participate. Barriers to participate emerged like fear, couple disharmony, stigma, and misconceptions. During interim analysis of this study in 2003-2004, these concerns were becoming important indicators for the need to involve community and understand the concerns of the general population as India was getting ready for its first phse-1 AIDS vaccine trial.

Expanded Informed Consent Approach: A qualitative study was conducted with representatives of nearly all direct and indirect stake holders. Informed consent forms were developed by consultative process jointly by the trial team, the sponsors and the community representatives through a series of meetings. Care and support issues, transparency, informed consent, long term safety emerged out to be the major concerns of the community (Mehendale et al, 2004; Sahay et al, 2004). Based on these findings, informed consent and IEC materials were developed and recruitment plan was designed.

Community Advisory Board (CAB): The CAB was already assisting us on several on-going projects, including preparedness study for microbicide trials, discordant couples' study and other national and international studies being



conducted at the institute. From the very initial stages our goal was to build the capacity of the CAB members through orientation workshops, participation in international ethics training and providing platform at international investigators meetings. CAB is involved in the research process from the beginning of the protocol development. We explained phase-1 clinical trials, vulnerable group concept and special design related features in the context of clinical trials to CAB members. CAB has not only shown solidarity with the community to which they belong, but they have also helped in bridging the gap between researchers and the community by attending forums like National Bioethics Conference; participating in huge public activities like marathons & rallies and writing in the news papers. CAB members also assisted us in developing community friendly education material for the vaccine trial and assisted in formulating forms in colloquial language. They also helped us in designing recruitment plan by involving communities at grass-root level through partnership arrangements with the NGOs and CBOs. We have developed a parallel NGO partnership plan too.

CAB has given us socio-culturally relevant inputs for study implementation like advising us to involve partners for married volunteers during recruitment process and family involvement in case of unmarried youth. We have adhered to these recommendations in our recruitment strategy. A four member CAB team was involved in development of informed consent. Some of the tangible contributions of the CAB are development of community friendly IC forms and information material, facilitating recruitment meetings for vaccine trial, setting examples for the community by getting themselves enrolled. One CAB member is on editorial board of 'Sankalp', a news bulletin of IAVI on AIDS vaccine.

Community Involvement at Grass-Roots Level: Two exploratory meetings were conducted with various NGOs working in Pune city to assess their interest in collaborating with NARI by assisting NARI to conduct ethical and community sensitive biomedical research. Subsequently, six NGOs drew memorandum of understanding with the NARI. The basic understanding was that NGOs would facilitate community support to the institute and the institute will help in providing technical resource and capacity building of these NGOs. Six grass-root level social workers of these partner NGOs were trained on the following issues: HIV/AIDS as a public health issue, Role of community in HIV/AIDS research, Research v/s treatment Ethics in human subject research, Vaccine as a biological intervention, Scientific Information about vaccine, Eligibility of prospective volunteers in the Vaccine trials, Risks and benefits.

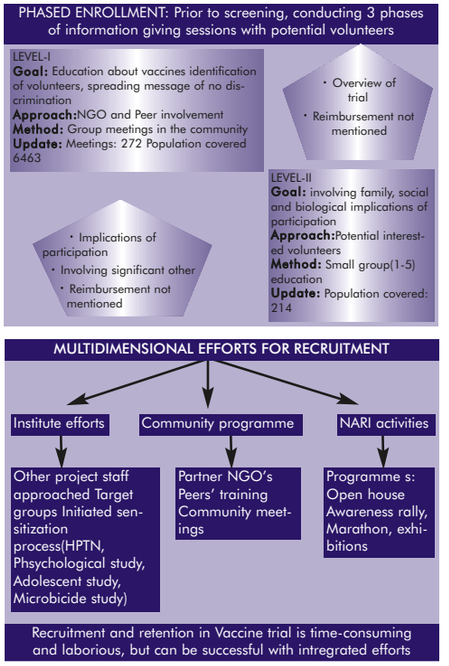
These were the training supervisors who identified approximately 20 individuals directly from the community in which they were working [peers]. The goal was to build a team of community peers who could articulate the voice and concerns of the community by taking it to the researchers. A majority of the peers were housewives, anganwadi workers/ teachers, elderly citizens and young men. Peers were imparted a training of sixty hours spaced over 2 months on all above issues. Emphasis was laid on developing communication skills, avoiding power relationship and maintaining confidentiality. We have nearly 150 trained peers in the community who endeavor towards AIDS free world by supporting biomedical research.

Peers are direct link to the community. They sensitise the community through group education and door-to-door approach. They belong to the community, facilitate community meetings, collect information on health and disease, alleviate rumours, guide the study volunteers to research facilities and they themselves participate in trials to set an example.

Recruitment process for AIDS Vaccine trial:

Target identification: NGO peers and CAB were consulted to identify potential volunteer groups. Response for participation varied between various groups. We got low response from government offices staff, research organizations, housing societies, family courts and medical interns. A fair response was seen when we approached banks, hospitals, nurses associations, colleges, school teachers and women's associations. We got positive support and large participation from NGOs, CBOs, peers, CAB members, HIV affected families and industries.

Recruitment process: A phased enrolment process was designed wherein information was given to the community in three phased manner so that technical aspects of the trial and participation expectations became clear to the potential



volunteers. This process ensured transparency about risks and also dealt with the responsibilities of the trial participants. Sensitization of almost 6500 individuals through group meetings led to enrolment of 20 individuals in low and high dose level categories in the vaccine trial.

IEC innovations: It was important that the community education be imparted by the scientists. Community friendly tools to educate community about dose escalation, randomization, placebo, and vaccine induced antibodies were devised as per the needs and level of understanding of the target audience. A constant innovation in communication techniques was considered important to support the informed consent process that started in the community as information giving session to the masses, narrowing down to potential interested group of people some of whom proceed finally to enrolment.

Lessons learned from ongoing AIDS Vaccine trial: taking these experiences to microbicide trials: Community involvement can help in building trust for biomedical research even in developing nations with high level of illiteracy, poverty and lack of empowerment. It is important to mitigate the fear of being used as 'guinea pigs'. Trial design and implementation through community consultative process might help to build a sense of community ownership in research studies and clinical trials. A phased enrolment process might be a slow process of recruitment but it is a sure way to maintain transparency, gain the community trust and arriving at high retention rates. Experiences gained during the first vaccine trial in the country might be very useful in designing appropriate trategies for the upcoming microbicide trials.

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ACCEPTABILITY OF MICROBICIDES: EXPERIENCE FROM INDIA

Sethulakshmi J., YRG Care, Chennai

A topical microbicide is any cream, gel, or foam that can be applied to the vagina or rectum and that can kill or disable disease-causing organisms such as viruses or bacteria. A microbicide can work by covering the surface of the vagina, thus preventing the virus from entering the body, it can attack the virus itself and finally, it can stop the virus from adhering to cells. Some of the characteristics of an ideal microbicide are that it should be safe to use, should be fast-acting, long-lasting, non-irritating, and most importantly, it should be effective against multiple STD's including HIV/AIDS. The need for a microbicide arose primarily because women are becoming increasingly vulnerable to HIV with 50% of new infections being detected in women. This is because most infections are spread by unprotected sex with the male condom being under the control of men. Thus a need arose to develop a product that will allow women to take complete control of their lives. However, some of the challenges in using a microbicide are domestic violence, substance abuse, acceptability to both men and women, cultural issues, cost, and disposal of applicators. A study conducted on 1969 women found that the most important cause for domestic violence was alcoholism (95.7%) while women's refusal to have sex and women initiated condom use accounted for 78.5% & 55.7% respectively.

THE IDEAL MICROBIOCIDE

- Colourless and Odourless
- Inexpensive to manufacture and purchase
- Safe to use more than once a day and for long period of time
- Effective against multiple STD's, including HIV/AIDS
- Fast-acting, long-lasting and non-irriating
- Undetectable to either partner
- Available in contraceptive and non-contraceptive forms
- Available without a prescription

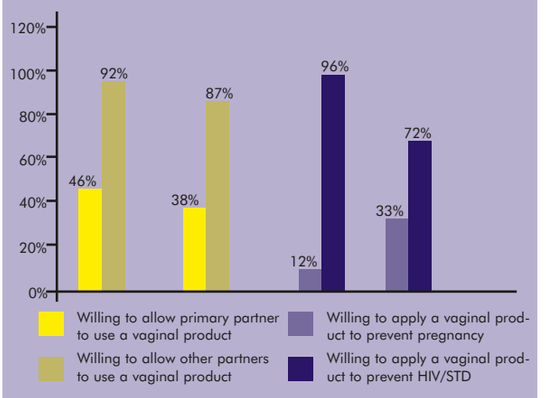
Age at which had First Sexual Experience?

Description	Men Low Risk	%	Women Low risk	%	Men High Risk	%	Women high risk	%
less than18	172	29.30%	191	44.84%	173	24.93%	282	75.60%
18-21	164	27.94%	180	42.25%	239	34.44%	81	21.72%
22-25	166	28.28%	48	11.27%	187	26.95%	10	2.68%
26-29	58	9.88%	4	0.94%	65	9.37%		
30-33	20	3.41%	3	0.70%	18	2.59%		
34-37	4	0.68%			7	1.01%		
DK					5	0.72%		
No Answer	3	0.51%						
Total	587	100.00%	426	100.00%	694	100.00%	373	100.00%

Use of condom during Vaginal sex

Description	Men Low Risk	%	Women Low Risk	%	Men High Risk	%	Women High Risk	%
No	432	73.59%	381	89.44%	484	69.74%	42	11.26%
Rarely	72	13.46%	13	3.05%	77	11.10%	9	2.41%
Sometimes	22	3.75%	2	0.47%	59	8.50%	13	3.49%
Always	29	4.94%	13	3.05%	63	9.08%	299	80.16%

Microbicide Willingness



96% of FSW and 72% of housewives were willing to use them to prevent STD/HIV

Study on acceptability of vaginal microbicides:

The study population included a total of 1243 men and 829 women and 8 Hijras. The study showed that 75.6% of high risk and 44.8% low risk women and 29.3% low risk men had their first sexual experience when they were younger than 18. 68% of the general population (men) versus 6% women had more than 1 partner. Except for women at high risk, all other groups reported minimal condom use during vaginal sex. A total of 68% claimed not to have been infected with any STD's and the risk perception of "no chance" or "small chance" was reported by 96% of

RISK Perception				
HIV Risk Perception	Men High Risk	Men low Risk	Women Risk	Women Risk
Participant's perception of personal risk in past, ever	85 (4%)	188 (29%)	202 (58%)	65 (14%)
Participant's perception of personal risk in last 6 months	47 (8%)	92 (5%)	139 (40%)	38 (8%)
Participant's perception of personal partner risk in past ever	90 (18%)	98 (16%)	105 (42%)	329 (73%)
"no chance" to 'small chance'	548 (96%)	607 (98%)	221 (64%)	419 (91%)
"likely" to 'absolutely'	24 (4%)	15 (2%)	122 (36%)	40 (9%)

high risk men and 91% high risk women although 96% FSWs and 72% housewives reported that they were willing to use microbicides to prevent STD/HIV.

The most crucial question that the study posed was, "Would people use microbicides if majority continues to believe that they are not at risk of HIV?" Some of the barrier issues in using microbicides are fertility pressures, marriage, forced abstinence etc and this data was collected among 2408 couples of which 1154 were concordant and 1254 were discordant of which 1132 men were positive and 122 women were reported HIV positive.

SCIENTIFIC SESSION –V

STRATEGIES AND MODELS FOR RECRUITMENT AND RETENTION OF STUDY VOLUNTEERS FOR CLINICAL TRIALS ADDRESSING HIV PREVENTION.

WORKING WITH PARTICIPANTS IN A RURAL SETTING

Mitzy Gafos, Africa Centre for Health and Population Studies,
KwaZulu Natal, South Africa

The Africa Centre for Health and Population Studies is located in the rural Umkhanyakude District of KwaZulu Natal, South Africa. The centre was established as a Demographic Surveillance Site (DSS) and commenced data collection in January 2000. The Microbicides Development Programme (MDP) study is hosted by the Africa Centre, but is not confined to the Demographic Surveillance Area (DSA). The MDP feasibility study was conducted in the area from July 2003 to December 2004 to assess the feasibility of conducting a microbicide clinical trial in the area. The study demonstrated the sites ability to recruit and retain female participants up to 12 months, the acceptability of collecting sexual behaviour data, and conducting regular genital examinations and HIV tests. In the feasibility study, 79% of the 883 women screened were from the DSA, with an average age of 28 years (SD:9.19, range: 16-55). Only 20% of the women were married, 70% had at least high school education, 69% were unemployed, and 53% were using a modern method of contraception (50% of those using Depo-Provera). 50% of women screened for the study were HIV positive, and this resulted in a need to screen 3 women for every 1 women enrolled. From July to October 2005 the Africa Centre conducted the MDP pilot study to optimise study procedures and access acceptability of using a placebo gel vaginally before sex. The pilot study showed acceptability of the gel and assisted in refining study procedures, and the centre is now preparing to start the clinical trial in early 2006.

Africa Centre for Health & Population Studies

- Africa Centre Demographic Surveillance System (ACDIS)
- 1st January 2000
- Area of 435 km
- 12,000 homesteads
- 85,000 members
- 25% members non-resident in DSA.

Feasibility Study

- 79% of women screened for the feasibility study were members of DSA households
- Average age: 28 (SD:9.19, range: 16-55)
- Marital status: 20% married (DSS: 50% 40-44yrs never married)
- Highest education level achieved
  - Less than High School: 30%
  - High School: 43% (DSS: 55%)
  - Standard 10 and above: 27% (DSS: 23%)
- Employed:
  - No – 69% (DSS: 60% but 36% not eco active)
  - Yes FT – 16% (DSS: 37% Y – 34% FT)
  - Yes PT – 15%
- High levels of female mobility:
  - 70 internal movements per 1000 women at mid-year pop
  - 124 out-migrations per 1000 women at mid-year pop
- Sanitation & Water
  - Piped water 38%; 20% river water
  - Pit latrines 50%; 38% no toilet facilities
  - Electricity grid 50%
- Contraceptive Use
  - 53% of women using contraceptives
    - 50% of those use Depo-Provera
- Sexual history from DSS
  - Av. age first sex: 17.7 years
  - Av. age first child: 19.3 years
  - Av. age first use of modern contraception: 22.5 years

Community Engagement Strategies for the Microbicide Clinical Trial

Community Engagement Strategies have multiple purposes within the study. They are designed to disseminate information about the study, assess the acceptability of the study in the community, to refine study procedures, to inform the dissemination of messages, to identify misconceptions in order to enable the team to correct them, to feed back results to the community hence keeping them informed, and to support the recruitment and retention process. There are multiple community engagement strategies in place in preparation for the microbicide clinical trial:

- **Department of Health:** Agreements are in place with the local hospital enabling the study team to present information about the study across the 13 local district clinics and the mobile clinics which service the most remote areas. This includes putting posters in the clinics, disseminating leaflets and giving talks about the study to people in

the clinic waiting rooms. Agreements have also been reached regarding the referral of HIV positive participants screened out of the study, into the government ARV programme, with the study teams providing CD4 tests and completing referral documentation. The team will provide six monthly updates to the hospital management meeting on the progress of the study and respond to any questions raised by the hospital.

Strategies 1

- Monthly Community meetings
  - Via traditional ward counsellor & Induna's
- Community Advisory Board(CAB)
- Participant "Representatives"
  - Open Days
- Monthly grant collection points
- Hospital Management meetings and ad hoc events (i.e. World AIDS Day event)
- Municipality Health Meetings and ad hoc events (i.e. Agricultural shows)
- Community Road-Shows
- Opening of new centres (i.e. HIV counsellors)

• **Department of Social Welfare:** It has been agreed that the study team can introduce the study to people congregating at the monthly grant collection points throughout the area and respond to queries.

• **Municipalities:** The area is covered by 2 municipalities and discussions are ongoing regarding utilising municipality meetings and events to introduce the study to the community, such as at agricultural days. The team will provide six monthly updates to the municipalities on the study.

• **Community Advisory Board (CAB):** The CAB comprises elected representatives from each area inside and surrounding the DSA as well as representatives from the main government and traditional structures. The CAB advise the study team of the appropriateness of the study protocol prior to its introduction to the community. CAB members are informed about all Africa Centre studies at monthly CAB meetings, they disseminate this information at monthly community meetings to their communities, and feedback comments and concerns at the CAB meetings. CAB members can be approached at any time by their community, but given the complexity of the trial there is a nominated 'expert' CAB member to advise other CAB members and all community members as necessary.

• **Community Meetings:** CAB members, Induna (traditional leaders), and the community liaison officer attend community meetings throughout the area regularly to facilitate ongoing discussions about the study.

• **Road Shows:** The Africa Centre presents monthly 'road-shows' in the community in collaboration with the local Indunas to present information to the community in an interactive manner. Various entertainment is organised to attract the youth such as music, football games, and traditional dancing. Information is presented to the community and then they are given prizes for answering questions about the information correctly. We are planning to have T-shirts, caps, badges and umbrellas printed with the Microbicide logo for dissemination at these events. The road-shows are well attended and provide an excellent discussion forum for the microbicide study.

• **Community Radio shows:** For the trial we are planning regular slots on a community radio station to disseminate health information and inform the community of where they can find out more about the study. The team has developed a Microbicide jingle that will be used on the radio shows.

• **Opening of new HIV counselling centres:** The microbicide study is presented at launch events of new counselling centres throughout the area.

• **Participant Representatives and open days:** We will identify former study participants to serve as 'representatives' or facilitators for existing and potential participants. The facilitators will hold regular open days when female participants will be welcome to attend to ask questions, raise concerns or complaints, and discuss common challenges. This will inform the development of study specific resources such as frequently asked question sheets. We will also have open days for any men in the community to approach the study team and participant facilitators in order to find out about the study.

Challenges

- Explain Concepts
  -Trial, randomised, double-blind, placebo controlled.
- Manage expections
  -Efficacy & licensing
- Avoid condom migration
- Avoid undue incentive (MCC reimbursement policy)
- Retain women for 12 months
- Engaging men & gaining acceptance from men
- Avoid stigmatisation
- Do not over burden ARV clinics
  -Offer CD4 & deliver training
- Maintain relationships
  -Politicized and often complex!
- Establish structures for effective "participant representation"
- Coordinate with other microbicide studies in the area

• **DSS fieldworkers & DSS HIV counsellors:** collectively the fieldworks and counsellors have contact with over 12,000 homesteads and every women in the DSA aged between 15 to 49 annually. These Africa Centre staff will be trained to provide information about the microbicide study and supplied with leaflets for dissemination. The counsellors will be able to directly refer women into the study.

• **Posters:** posters are being designed locally and will be displayed at clinics, mobile clinics, shops, post offices, banks, in taxis etc. Snowballing: participants will be encouraged to tell their family and friends about the study and given leaflets to disseminate.

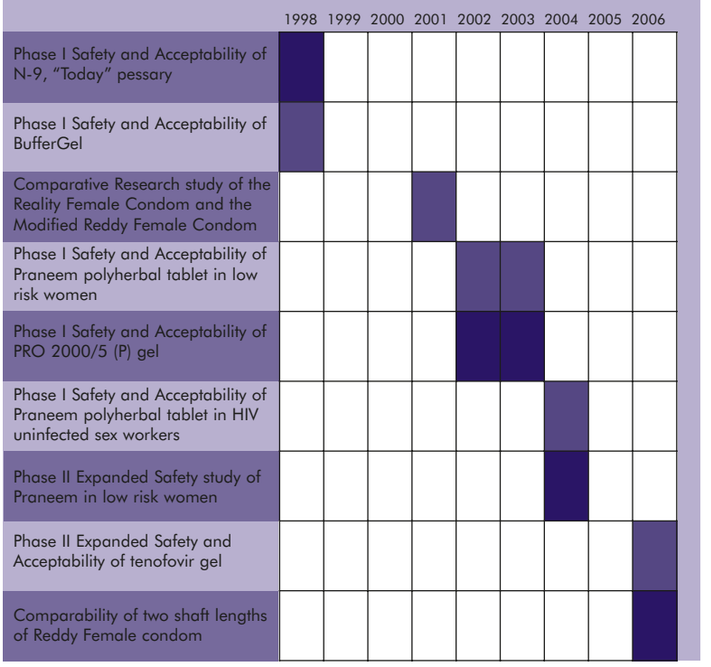
There are many challenges that lie ahead of us as we plan for the trial, not least explaining the concepts of a multi-centre, double-blind, randomised, placebo controlled clinical trial. To have any hope of ensuring that we protect the participants of the trial at all times by supporting the informed consent process, we require the support and help of the many community structures in order to get the messages right and monitor responses to the study. In other words, we need to work hand in hand with the community at all times.

RECRUITING VOLUNTEERS IN PHASE- I AND II VAGINAL MICROBICIDE TRIALS IN INDIA

S. M. Mehendale, National AIDS Research Institute, Pune

With an estimated over 5.2 million HIV infections and adult population prevalence of 0.8 to 1 per cent, HIV/ AIDS is an important public health problem. There are reports of spread of HIV among married monogamous women in India primarily due to risk behaviour of their husbands. Thus research on female controlled options assumes great significance and both National AIDS Research Institute [NARI], Pune and Indian Council of Medical Research have a significant focus on research on vaginal microbicides.

Studies at NARI on female controlled options for prevention of sexually transmitted infections



Participation by healthy adult women is essential in the conduct of Phase I and II clinical trials of vaginal microbicides. It is important to identify women with no/ low risk of HIV, who are apparently healthy with normal reproductive history and are able to give informed consent to voluntarily participate in research. For accurate assessment of study end points good adherence to study regimen and satisfactory follow-up is essential. Better assessment of acceptability is possible among women with some level of literacy.

For a variety of reasons, the role of men is considered important in microbicide trials in India. They are the primary decision makers and have to cooperate with their partners to enable them study participation. Also, acceptability among men might affect future acceptance of microbicides. In our experience, women in stable and harmonious married relationships find it easy to participate due to better understanding about the expectations about the study procedures among the partners, better adherence to coitally dependant product use and this can ensure better retention during the entire study period. Therefore, we always try approaching couples rather than individuals whenever possible.

Investigators' have concerns about recruitment of participation being driven by social desirability rather than individual motivation or peer pressure and inducement by the study benefits offered. Participants have a variety of concerns. They are concerned about long term side effects and follow-up medical care and investigators responsibility therein. The study procedures like physical examinations & blood draws, time required to be spent and possibility of

stigmatization due to study participation are considered as problems. Some are worried about compensation in case of serious and lasting injuries. Participants are also concerned about the authenticity of the research and competence of the researchers and such notions can affect recruitment. This is because vaginal products are not commonly used in India and vaginal microbicide is a new concept. The concept of research is not completely understood by many and some have questions about authenticity of research and the research team.

Participants' concerns that may affect recruitment

- Long term side effects and follow-up medical care
- Investigators responsibility for the side effects
- Questions regarding compensation
- Concerns about physical examinations & blood draws
- Stigma related to participation
- Time required for participation: house hold responsibilites

Strategies to address participants' concerns

The real motivation for participants results from properly educating the community, building in investigation and care support and appropriate facilities for free HIV testing and counseling. We conduct detailed discussions about participation in research studies with the help of pictorial education material and pelvic models. We provide examples of studies done in other countries. If necessary we offer additional individual discussion sessions and clinic visits. Assuring and re-assuring confidentiality is very important and it is equally important to offering adequate and long-term care and treatment.

Addressing participants' concerns ...

Discussions about participation in research studies

- Pictorial education material and pelvic model
- Providing examples of studies done in other countries.
- Offering additional individual discussion sessions and visits.
- Assuring and re-assuring confidentiality
- Offering adequate and long-term care and treatment

Ways to educate the community about research and the researchers

- By keeping complete transparency about the research: explaining the methods and procedures in great details
- By speaking about various approvals required for the study at length
- By speaking about the institute, different ongoing studies and other activities
- By stressing their important role in research and development

We explain and discuss the methods and procedures in great details with all the participants and speak about various approvals required for the study at length. We talk about different ongoing studies, other activities and the approval mechanisms involved. The basic principle is to screen and enroll participants only when the research team is completely convinced that the individual wants to participate and is ready to participate. Additionally the study investigators' active involvement in community education and engagement efforts and imparting the research related information in a phased manner is useful. We appreciate and acknowledge the positive and altruistic attitudes of potential motivated volunteers and discuss some role-models.

Approaches for participant recruitment

1. Community Involvement Programme

We have involved and engaged six Non-Governmental Organizations [NGOs] in the community work of NARI by formalizing the work and cooperation plan. The basic approach is to train two trainers from each NGO and with their help identify and train up to 20 peers per NGO for involvement in the community program.

	Activity	Outcome
NGO Peers	Individual contacts	Innumerable women were individually contacted
NARI investigators and NGO peers	Group Meetings with women	104 group meetings conducted, 892 women participated
NGO peers & NARI investigators	Follow up with the women indicating interest	142 women screened
NARI investigators	Follow up with partners of the participants	100 women enrolled

Community involvement through NGO partners

Our experience with community involvement through NGO partners has been satisfactory. The advantages of this approach are the possibility to reach large numbers of participants, quick resolution of many questions and rapid decision making due to peer support. However, the disadvantages include difficulties in preventing attendance by ineligible participants, restricted discussions in the group environment and issues related to confidentiality.

2. Community Advisory Board

NARI established a CAB nearly 8 years ago and it has evolved into an active and vibrant body. CAB members speak to the potential participants about the study and facilitate conduct of meetings with potential participants. Involvement of CAB helps to reduce any element of distrust in the minds of people. CAB members do play a role in clearing misconceptions and rumors. In the Phase I PRO2000 study, 18 out of 42 participants were referred from the NGO of a CAB member.

3. Snow ball approach

We encourage participants to refer other individuals to the study clinic. Some participants help us by arranging women's group meetings in their areas. In all, 35 women were referred by the participants in Phase II study of 'Praneem polyherbal tablet'. This approach has the advantage of less inputs in the field, very little chance of misconceptions and better clarity regarding study procedures among the referred women. Other approaches like NGO programmes and newspaper articles are sporadically used.

Scaling up for phase III trials

Eventually, we will have to move towards conduct of Phase III trials in India and the main issues that we will be required to deal with include the large sample size as recruitment of many thousands of women will be necessary; multi-center recruitment while establishing and employing uniform recruitment strategies; finding truly high-risk populations that will yield high HIV incidence rates in groups such as sex workers, STD patients, partners of HIV infected men, spouses of HIV infected IDUs. It will also be necessary to find populations able to commit to long term follow-up, and involve the mass media.

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BEHAVIOURAL AND SOCIAL SCIENCE RESEARCH IN SUPPORT OF PHASE- III MICROBICIDE TRIALS

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Phase III Microbicide trials face several daunting challenges. In each clinical trial site, staff must recruit a sufficient number of trial participants who correspond to eligibility criteria within a limited recruitment period. Once enrolled, participants must remain in the trial for a period of six months or longer. During the trial, participants are expected to comply with a number of behavioural expectations, including frequent clinic visits, gel, condom and sometimes contraceptive use. As difficulties within several recent microbicide trials have demonstrated, concerns within the immediate geographic community, as well as national or international health policy and advocacy communities, can bring clinical trials to a standstill. Therefore, increased attention should be given to monitoring community expectations and concerns. Finally, although clinical trials are conducted within cultural settings, they do not entirely replicate the culture. Nevertheless, the trials themselves tend to set in place certain expectations–about the product, how it should be delivered and to whom–that can have long term effects.

In the remainder of this paper I will discuss each of the five above challenges related to recruitment, retention, adherence, ethical considerations, and post-trial microbicide acceptability. For each challenge, I will present some preparedness and microbicide acceptability research conducted by FHI in support of two microbicide trials: CONRAD's multi-country phase III microbicide clinical trial of 6% Cellulose Sulfate and the HPTN phase II trial of Tenofovir Gel conducted in collaboration with the National AIDS Research Institute (NARI) in Pune, India.

Recruitment

In addition to the estimated effectiveness level of the experimental gel, sample size calculations for a microbicide effectiveness trial are driven by the estimated incidence rates within a target population and expectations about trial participants' retention in the trial and adherence to gel use. Holding all else equal, the higher the incidence levels in the population from which trial participants are drawn, the smaller the study sample needed. For this reason, several trials have aimed recruitment efforts towards high-risk women with multiple sex partners, who are oftentimes professional or non-professional sex workers. Nevertheless, identifying groups of women who are HIV-negative but at risk of HIV is less straight forward than it might first appear. In part, this is because HIV prevalence is not always a clear indication of HIV incidence. Prevalence rates are likely to be much higher than rates of new incident infections in mature epidemics or within certain sub-groups. For example, prevalence rates from 50-70% have been estimated among sex workers in Mumbai (Shankaran 2002) We might imagine that longer-term sex workers are either HIV-positive (and thus excluded from clinical trial participation) or have avoided HIV infection through consistent condom use (thus, lowering their risk of future infection). More incident infections are likely to occur in younger women or those new to sex work. However, these women may be less visible and consequently more difficult to recruit.

HIV-negative BUT at risk

- Prevalence may not indicate incidence
  -Easily identified risk groups may be saturated
- HIV risk factors may not be known
  -vary by relationship, rather than individual
- Stigma of sexual risk behaviour impedes recruitment
  -Some high risk groups will be hard to reach
  -Others will not recognize risk

Couple Characterstics Influence Risk Perception and Behaviour

- Cluster analysis of 150 couples' data produced 3 groups
- Low variation between groups of socio-demographic variables
- Significant differences in couple harmony, perceived partner identity, HIV risk perception and AIDS fatalism

There is some indication that the HIV epidemic is spreading into the general population of married women in India. However, HIV risk indicators are not well understood in this population. FHI and NARI conducted some formative research in Pune among married men and women from middle to low income urban communities to develop psychometric scales measuring potential predictors of microbicide acceptability related to couple harmony, HIV risk perception, and sexual power. Using cluster analysis procedures on survey data from 150 married couples, we identified three types of couples with significantly different couple mean scores on scales measuring couple harmony, HIV risk perception, AIDS fatalism and Protection Efficacy. One of the couple clusters reported high levels of marital harmony and protection efficacy, as well as the lowest levels of HIV risk perception and AIDS fatalism of the three groups. Such couples might make compliant trial participants, but are likely to be least at risk of HIV and ultimately least likely to use a microbicide. A second group reported very low marital harmony, high perceived partner infidelity, HIV risk perception and AIDS fatalism. They also scored low on Protection Efficacy, a scale measuring the ability to protect oneself from HIV. A third group scored almost as high on couple harmony as the first group, but higher on HIV risk perception and AIDS fatalism than Group 1, and reported levels of protection efficacy as low as group 2. While HIV risk perception is not synonymous with risk, it does lead us to wonder whether it would be possible to identify couple characteristics within this more generalized population of married women (like risk perception or AIDS fatalism) that indicate higher risk levels. And, if so, how can we encourage such women to participate in microbicide trials?

Approaches: In the CONRAD trial, ethnographic research is being conducted to identify and conduct interviews with women from high risk groups and others in the community who might influence their participation in the trial. Activities generally include observational field work to identify geographic locations where high risk sexual behaviour takes place (night clubs and bars, brothels) and then interviews with opinion leaders (owners, managers) and potential participants. Interviews with opinion leaders assess interest in or resistance to the trial and are aimed at gaining access to women to inform them about the study. Interviews with potential participants focus on understanding women's motivations and disincentives for trial participation, including their concerns about HIV testing, gynecological exams or other trial procedures, concerns about stigmatization associated with the trial, and attitudes towards gel use.

Retention and Adherence

A successful clinical trial must avoid losing large numbers of participants to follow up. In addition, it must recruit and retain women who are willing and able to comply with a number of clinical trial conditions. These conditions include willingness to: learn about the study and provide signed (or marked) informed consent; have repeated HIV tests and learn their results; return regularly to the clinic and submit to gynecological exams and questions related to sexual behaviour; and use study gel, condoms and sometimes another contraceptive method as described in the protocol. Regardless of women's initial intentions, experiences during a trial can reduce retention and adherence. They include fear or experience of side effects related to gel or contraceptive use, trouble with sexual partners related to the trial, or just difficulty related to making regular study visits to the clinic.

Accurate measurement is another issue related to trial adherence. The effectiveness of HIV prevention interventions, like the use of a topical microbicide, cannot be tested unless participants actually use the product and are exposed to HIV. Therefore, accurate measurement of sexual behaviour, as well as both microbicide and condom use within the trial is essential.

Approaches: Prior to clinical trial initiation, BSS research with potential participants may identify and/or explore a range of issues related to trial retention and adherence, including the existence of seasonal patterns of travel; acceptable systems for contacting women about missed appointments; the potential for differential use of the study gel and condoms with different kinds of sexual partners or local language terminology for sexual behaviour that differ

greatly from more technical terms. Having identified such issues, BSS staff can assist the clinical trial team in developing appropriate strategies to address them.

Retention / Adherence Strategies

At the clinic:
- Assist in follow-up efforts:
  - Generating missed visit reports
  - Accompanying outreach workers
  - Monitoring clinic waiting times
- Document retention and adherence problems noticed by CT staff and develop strategies

Trial Participants
- Obtain feedback on positive and/or negative experiences with participants who have missed visits

One BSS approach to maintaining high retention rates within a trial would be to assess participants' attitudes towards the trial in an on-going fashion. However, clinical trial researchers may worry that such activities might increase the burden of participants or lead to contradictory information (for example, related to adverse events or to adherence data.) In the CONRAD trial, BSS staff will monitor participants' attitudes indirectly, by regularly polling clinical trial doctors, counselors or outreach staff about problems or concerns raised by trial participants, and documenting such issues in order to identify any common problems that should be addressed within the trial. In addition, a BSS team member may accompany an outreach worker to follow up women who have missed visits in order to get a more in-depth understanding of her reasons for missing visit(s) and to determine whether there is a way to help her remain in the trial.

Ethical Issues

Given the potential of HIV sero-conversion during trial participation, a whole host of ethical issues may plague the trial. They include ensuring that participants understand the experimental nature of the trial (that product effectiveness is not known and that participants may be assigned either an active or non-active/placebo product to use); determining what kind of care and support should be undertaken for participants who seroconvert during the trial; and how to explain the potential risks and benefits of the trial to community members.

Approaches: During the CONRAD trial, BSS teams will identify a range of individuals (government officials, medical personnel or others) and organizations at local, state and national levels who might take interest in the trial and influence trial implementation, either positively or negatively. In consultation with the international and local investigators, the team will develop a plan as to the best way to inform such individuals/organizations about the trial and maintain on-going monitoring as the study progresses. The team will try to identify a small number of well-informed, articulate and supportive individuals outside the clinical trial who can help advocate for the trial.

Post-Trial Microbicide Acceptability

As a final note, we should at least keep in mind that decisions we make about clinical trial design are likely to have lingering effects on microbicide acceptability outside and post-trial. For example, although microbicide acceptability research suggests that products with both contraceptive and non-contraceptive effects are desired, a uniform requirement that women use "an effective" contraceptive method during a microbicide trial will lead some to construe that microbicides are for HIV prevention only. For others, it will provoke fear (not entirely unfounded) that microbicides might impair fertility or cause harm to unborn fetuses. We will need to develop messages to counteract the more extreme reactions. Other topics that will require rapid adaptation post-trial include how to frame information about (partial) microbicide effectiveness (versus unknown effectiveness) and how to address microbicide introduction strategies to a more diverse population of women than those participating in the trial.

Challenges: How do we...
- Identify high-risk without stigmatizing
- Reconcile contradictory safety or adherence data
- Maintain participant and staff confidentiality
- Translate descriptive data into effective strategies
- Ensure rapid follow-up of community concerns

Post-Trial Microbicide Acceptability
- Perception of efficacy
- Perception of condom and contraceptive use requirements and desire for contraceptive, as well as non-contraceptive products
- Who should use product and how information and product should be made available

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RECOMMENDATIONS SESSION

Three working groups discussed issues arising from the presentations and considered priorities for capacity strengthening and research to underpin microbicides development in the Indian setting. Highlights from the three groups were as follows.

Group I–Understanding Sexual Behaviour and Norms

There was a strong basis of research on sexuality and sexual behaviour in the Indian setting on which to build for future microbicides research. For example, rhe range of work on sexual behaviour already undertaken is described in detail in Dr Mutatkar's recent book "Sexuality and Sexual Behaviour: Social Science Perspective".

Priorities for new research on sexual behaviour were discussed. Given the diversity and complexity of Indian society there was thought to be a need for studies of sexual behaviour patterns among a range of different population sub-groups. Setting this agenda would also require special consideration of groups especially at risk, including men who have sex with men and their heterosexual partners. Similarly, commercial sex workers with non-commercial partners were thought to be another group where greater understanding of behavioural dynamics was needed. Noting the relatively low incidence of HIV infection in India discussed during the workshop, HIV serodiscordant couples are a potentially key group who might wish to become involved in microbicides studies, and thus they should be a priority group for socio-behavioural research.

As well as considering specific population sub-groups with respect to the research agenda, the importance of gaining detailed knowledge of sexual preferences and norms was emphasised. As indicated in Dr Mehendale's presentation there are no norms relating to vaginal products in the Indian population at large, and information about this in specific sub-groups is lacking. Similarly, there is a dearth of information on such highly sensitive topics as anal sex.

Up until recently there has been something of a separation between social science and biomedical research in terms of research culture, funding streams and publication channels so that bringing to bear the multidisciplinary perspectives that are needed for microbicides development has not been straightforward. One consequence is that much useful material on topics such as sexual behaviour is not readily available. The group therefore considered that reviews of literature, both published and unpublished would be particularly useful so as to ensure that work that has been done in India is fully disseminated to the research community across the range of disciplines.

As well as review and dissemination of research findings, there was also thought to be considerable potential in sharing experience of methods and tools used at other microbicide clinical trial sites and modifying these according to local conditions and needs. As made clear in Dr Pool's presentation, "we must accept that there is no absolute truth about sexual behaviour" and the way forward is to use different but complementary methods of assessment.

Capacity building with regard to methodological approaches was considered to be of future value to Indian researchers. This might include visits to clinical trial sites in Africa and also fostering of networking among research institutions and NGOs, both nationally and internationally.

Group II–Community Preparedness and Mobilisation

It is problematic to approach communities without knowing whether a particular location or population will turn out to be suitable for a particular study. The group highlighted the importance of microbicides researchers having the flexibility of organizational arrangements and funding to conduct formative research at potential sites. An initial step

might be to undertake a mapping exercise based on data available from existing voluntary counselling and testing facilities. The next step would be to pursue limited scale formative research. Key points for rapid assessment would be the local prevalence of HIV and other STIs, available information on incidence (while recognising that a formal feasibility study of a cohort over at least one year would be needed to obtain reliable information on incidence), the local context of sexual behaviour and gender relations, and factors such as men's employment, transport and migration that are known heavily to influence risk.

Having moved forward to site selection based on the above formative steps, site preparation should be maxially inclusive along the lines described by Dr Gafos in her description of the approach taken at the Africa Centre and the Indian experience from NARI, involving NGO partners and linking up with local health authorities. Key challenges include coming to agreements with local authorities and communities on standards of care for research participants and infrastructure development, covering capacity to undertake information, education and communication activities, clinics, setting up of laboratories, training of staff and deploying counsellors.

A recruitment plan is needed for setting up formal consultative systems such as Community Advisory Boards (CAB) and other mechanisms. This plan will need to address issues of inclusivity and representativeness and the capacity of the individuals concerned effectively to review and comment on the proposed study including the ethical aspects. Appropriate honoraria for such community participants will require careful consideration as will the building up of a range of other channels of contact with communities, as discussed by Dr Mutemwa in his presentation. The current policy emphasis on 'Panchayati Raj' in India provides an opportunity for local communities to align the various administrative and local governance processes in support of a shared objective.

Group III- Acceptability and Continued Utilization of Microbicides

The group considered that it was necessary to address basic questions in the Indian context about whether and why someone would want to use microbicide products, and how reactions to the concept might vary in different contexts and subgroups. More specific information would be required about determinants of acceptability such as product characteristics, use within sexual relationships, and socio-cultural factors. It was emphasised that these factors may be associated differentially with initial acceptance and consistent or continued use.

The manner in which microbicides are promoted is likely to influence acceptability: for example there are different social marketing options such as emphasis on microbicides as a hygiene product or a product aiming to provide for better sexual health, or a product primarily for HIV prevention. The "pleasure" aspect of microbicide use could inform marketing messages. At present an important gap in knowledge relates to other vaginal product use in the Indian setting. What products are used? By whom? For what purpose? Do we know male perspectives on these products?

As discussed above in relation to methods for studying sexual behaviour, there is a need to share experience of scales and other tools that can be used for microbicide acceptability research. Even in the absence of an actual product it is possible to ascertain the reactions of women and men to hypothetical use scenarios: naturally, such studies are enhanced when actual products are available for people to try.

While clinical trial site selection requires very specific local conditions to be fulfilled, acceptability of microbicides to the wider population is a pressing topic for research given that if they prove to be effective there will be a strong impetus to make suitable products widely available. There are trade-offs with regard to cost and logistics versus generalisability when considering the type and settings for this type of research. Hard choices may need to be made between social science research on acceptability in wider populations, or more narrowly to support particular clinical trials, but clearly both are needed.

Research priorities identified in this group session included specific research within various communities to understand attitudes towards microbicide use (including interest in different formulations for different groups of

women), research on how to communicate about partial effectiveness, and contraceptive versus non-contraceptive future potential products.

Acceptability research was considered necessary in all phases of clinical research, but the composition of data collection methods may vary depending on the circumstances. While undertaking such work it is necessary to be clear on how "acceptability" is assessed, considering that this term is really a shorthand for a number of different aspects such as the level of consistent use, changes in consistency over time, interest in microbicide use outside the clinical trial setting, for example if it became commercially available.

With regard to research methods, qualitative, quantitative and participatory approaches have different strengths and weaknesses in this context. Designs such as cross-over studies could be informative, as could comparative studies of different groups such as sex workers versus the general population.

ACKNOWLEDGEMENTS

We are thankful to DFID Sexual Health Resource Centre, New Delhi for funding the international participants and printing this report for wider dissemination.

The organizers are extremely grateful to the MDP Principal Investigator partners at RHRU, Johannesburg and the Africa Centre, KwaZulu Natal for facilitating the participation of the social scientists at these sites for this workshop

Our special thanks to Dr. Badri N. Saxena for compiling this summary report and for providing continued guidance in the conduct of the workshop.

We thank all the international and national participants who spared their valuable time and came from long distances to attend the workshop. Their constructive inputs not only contributed immensely to the success of the workshop but would also effectively move the microbicide research agenda forward.

The contribution of our scientific and administrative colleagues from the Division of Reproductive Health, ICMR are duly acknowledged for their technical support and for providing the logistics for this workshop.

ICMR-MDP WORKSHOP ON SOCIO BEHAVIOURAL ASPECTS OF MICROBICIDE TRIALS FOR HIV PREVENTION

5-6th December, 2005

Conference Room No. 301, ICMR Hqrs., New Delhi

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ICMR-MDP WORKSHOP ON

Supported by RCSHA with financial assistance from DFID

The Studio, D-4/4232, Vasant Kunj.