

**DIVISION OF
EPIDEMIOLOGY AND BIostatISTICS**

Division Of Epidemiology And Biostatistics

Major projects undertaken by the Division of Epidemiology and Biostatistics in the period of reporting included IBBA survey, cervical cancer screening study among HIV infected women, mutli-country clinical trial on HIV prevention among HIV discordant couples and studies on HIV prevention among women. The first AIDS vaccine trial was successfully completed and the Division led NARI's team in monitoring and supervision of Annual HIV Sentinel Surveillance [HSS] program that is implemented by the National AIDS Control Organization [NACO] in India for the year 2007.

The most significant contributions by the Division in the HSS 2007 program were publication of "User's Manual" and preparation of the "Training Modules" for the trainers as well as program functionaries. This effort was greatly appreciated by NACO. The first AIDS vaccine trial using HIV-1 subtype C based AAV candidate was completed in December 2006, the data was unblinded, analysed and disseminated. This vaccine candidate is not likely to move into Phase II trials in spite of good safety because it was found to be a poor immunogen. The planning for the Prime-Boost trial with DNA and MVA vaccines is underway.

After the wrap up of the first round of IBBA, the reports were finalized and disseminated in various national forums. State-wise reports were prepared and discussed in the state level meetings. Preparations for the second round of the survey to be initiated in 2009 are ongoing. Following successful completion of the cross-sectional study to evaluate visual inspection of uterine cervix with acetic acid to identify early cancers among HIV infected individuals; nearly 300 women were enrolled in a study involving other investigations like PAP smears and HPV testing [clinic collected and self-collected swabs]. Following very encouraging results, an application was sent for the Indo-US Administrative Supplementary Grant to do a prospective evaluation of the enrolled cohorts and establish 3 additional centers: KEM Hospital Pune rural field practice station at Vadu in Pune district, JN Medical College, Belgaum and National Institute of Epidemiology, Chennai. The project has been approved for funding. Another flagship study of the Division of Epidemiology and Biostatistics is HPTN 052 study, which is HIV prevention among HIV discordant couples. With a target of enrolling nearly 250 HIV discordant couples, massive community work has been undertaken in the year of reporting. The Division continued to work on vaginal microbicides and completed the Phase II HPTN 059 study on 1% Tenofovir gel. The data is being analyzed. Other smaller studies that were completed in this area include CONRAD funded comparability study of 2 shaft lengths of Reddy's female condoms and study on intermenstrual bleeding.

A. HIV Sentinel Surveillance 2007

[Team leaders: Dr. S. M. Mehendale, Dr. A. R. Risbud and Dr. S. V. Godbole]

As in 2006, NARI in the capacity of 'Regional Institute' was responsible for supervision and monitoring of the HIV sentinel surveillance programme for the year 2008 in the western states of India [HSS 2008] which is conducted annually by the National AIDS Control Organization.

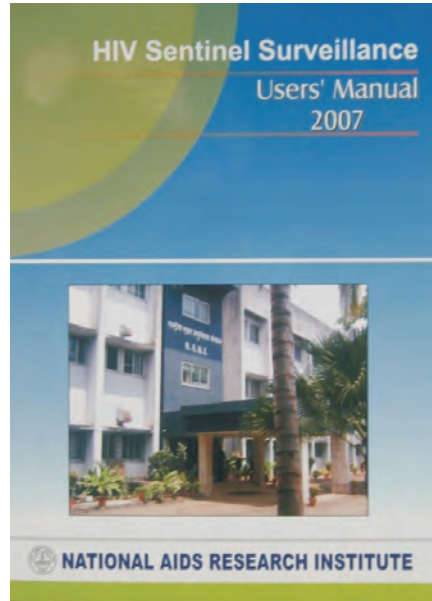
Major contributions of NARI in HSS 2007

States supervised by NARI



States covered: Daman-Diu, Dadra Nagar Haveli, Goa, Gujarat, Madhya Pradesh, Maharashtra, Mumbai, Rajasthan

User' Manual



1. HIV Sentinel Surveillance User's Manual 2007:

In the previous year, it was noted that the state AIDS control societies had been preparing their own guidelines for each year's surveillance leading to non-uniformity in procedures across states at times. NARI felt that all the states should follow uniform procedures and guidelines and a common manual should be used by all. It was also realized that a user's manual with pictures and flowcharts outlining the standard operative procedures for every aspect of the surveillance would be useful in maintaining quality in surveillance. A key achievement in 2007 was the development of a **'User's Manual'** for HIV Sentinel Surveillance. This manual is a pictorial guide with a significant practical guidance and was based on the 2007- 'Guidelines for HIV Sentinel Surveillance' of the National Institute of Health and Family welfare (NIHFW) and NACO. This manual was distributed to all the sentinel sites, SACs testing centers and state core teams.

The manual was appreciated by the sites and testing centers. Based on the feedback and experiences, we have planned to develop smaller individual manuals for all the functionaries like site-in-charges, nurses, counselors and laboratory technicians during HSS 2008.

2. Training modules:

In order to minimize discrepancies and differences in the training process across all the states assigned to NARI, a standard set of training modules was developed with the intent of standardization of sentinel surveillance related training procedures. Separate modules were developed for trainers and for the site/ testing center staff. The modules were distributed to the state-level core team members and trainers and they were advised to use the same to maintain uniformity while training the sites and testing centers in their states.

3. State-wise trainings conducted by NARI before the start of HSS 07 round

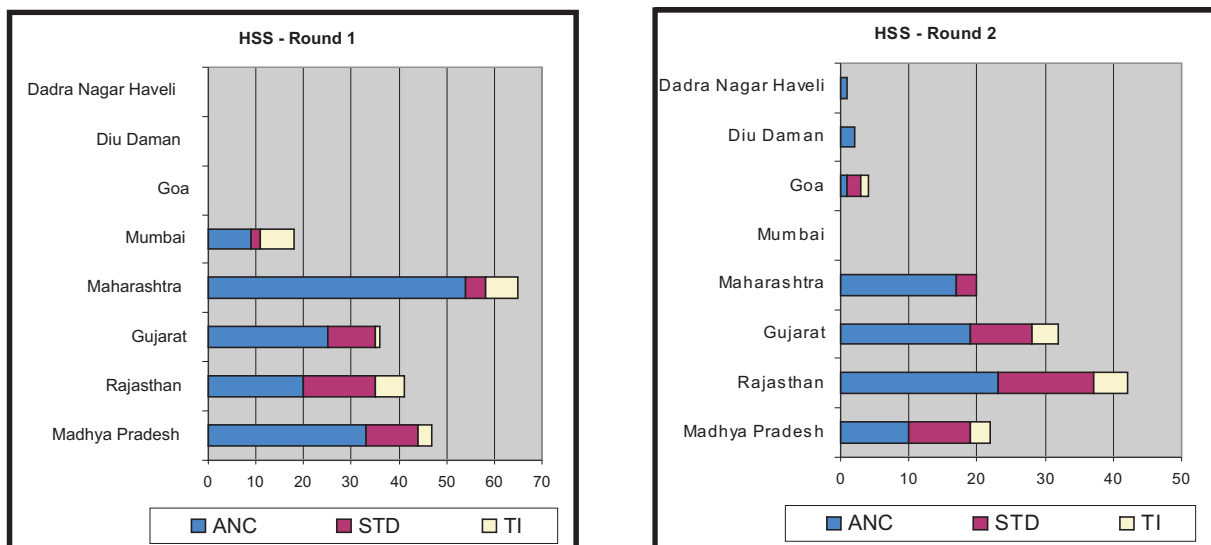
During this year NARI conducted day-long Training of Trainers (TOT), in each state using the newly developed manual and modules. A total of four Training of Trainers [TOT] Programmes were conducted by NARI for the HSS 07 round. TOTs were followed by the zonal trainings in respective states and in all 14 (4 in Maharashtra, 6 in Rajasthan, 2 in Gujarat and 2 in Madhya Pradesh) trainings each of one day duration were attended by one member from NARI as an observer.

4. Monitoring visits:

In HSS 2007 round, there were a total of 254 sentinel sites (Madhya Pradesh - 52, Maharashtra - 87, Gujarat - 41, Rajasthan - 48, Mumbai - 18, Goa - 5, Daman-Diu - 2 and Dadra Nagar-Haveli - 1) in the States allotted to NARI. During this round of surveillance, two rounds of extensive monitoring visits to the sentinel sites and testing centers, were conducted. The first round of monitoring was conducted very early, immediately after the initiation of the surveillance. An effort was made to cover approximately 95% of the sites/testing centers during the first round of monitoring visits. This was useful in identifying and handling various deficiencies very early so that the rest of the surveillance could be conducted better.

The second round of monitoring visits targeted the sites identified as problematic in the first monitoring visits as well as those that were performing poorly in terms of sample collection, or had not been visited in the round I.

Figure 1.1: State-wise monitoring of sentinel sites: Number of sites visited



Key findings of HSS 2007 in the western states supervised by NARI:

NARI and the state epidemiologists conducted an in-depth investigation of the sites showing high HIV prevalence or unusual findings. A detailed report of the findings was sent to NACO for necessary action.

a) Newly Identified Districts with ANC HIV Prevalence >1%: In Western states of India there were a total of 5 ANC sites (3 in Gujarat and 2 in Rajasthan) that were newly identified districts with HIV prevalence >1%.

b) District with ANC HIV Prevalence >3%: One ANC site in Maharashtra showed a HIV prevalence of >3%

c) Districts with STD HIV Prevalence >15%: There were total of 4 STD sites (2 in Maharashtra, 1 in Gujarat) that showed a HIV prevalence of >15%. Data from one STD site in Maharashtra was not considered.

d) Districts with HIV Prevalence >15% among High Risk Groups: Eight targeted intervention sites (7 in Maharashtra, 1 in Gujarat) with HIV prevalence of >15% were identified in HSS 07 round.

5. Quality Control:

NARI is the National Reference Laboratory (NRL) for HIV testing for 5 States (Maharashtra, Gujarat, Goa, Daman-Diu and Dadra Nagar-Haveli) out of 8 States in western region. A total of 3692 (1307 HIV positive and 2385 HIV negative) samples were received from these states in batches for quality control and HIV testing. All the samples were tested for HIV and 12 samples were found to be discordant. Reports were sent to the respective State Reference Laboratory (SRLs) at regular intervals.

B. Mapping, Size Estimation And Integrated Behavioral And Biological Assessment (IBBA) In High HIV Prevalence Setting In India

[Principal Investigator: Dr. R. S. Paranjape]

Collaborating Partners: NIE, NIMS, NIN, RMRC-NE and KHPT, FHI

Bill & Melinda Gates Foundation (BMGF) started The India AIDS Initiative, Avahan in India in 2003 with the aim of slowing down the HIV epidemic through focused, integrated, large-scale prevention programs complementing other HIV prevention service providers to achieve “saturated” (over 90%) coverage of high-risk populations. The focus of Avahan is on FSWs and their clients, high-risk MSM, Hijras (transgendered persons), and IDUs in 83 districts in six high prevalence states in India (Andhra Pradesh, Karnataka, Maharashtra, Tamil Nadu, Nagaland and Manipur) and in 17 sites along the National Highways (NH 1 9).

Bill and Melinda Gates foundation has commissioned Integrated Behavioural and Biological Assessment Survey with the objectives,

- To measure the major outcomes and impacts of the interventions funded by Avahan under the India AIDS Initiative;
- To make available data for estimating sizes of populations targeted by the Avahan project; and
- To make information available to a partner organization under Avahan for modeling the impact of the intervention.

The study has been implemented by National AIDS Research Institute in collaboration with four other ICMR Institutes, Regional Medical Research Center-North East, Dibrugarh, National Institute of Epidemiology, Chennai, National Institute of Nutrition, Hyderabad and National Institute of Medical Statistics, Delhi. The study is unique in that it involves coordination between ICMR Institutes, Family Health International, professional research agencies, Avahan, lead partner NGOs in the states, State AIDS Control Societies and other state agencies.

The study involved the mapping of the persons with high risk behavior, development of sampling frame, enrolling the participants for behavioural questionnaire and biological samples, data analysis and dissemination to the stake holders. The study involved collection of behavioural data worth more than 150 variables, seven biological tests from 25500 participants spanning six states and national highways.

This year saw the completion of the first round. While the final report of Round I is getting ready, an interim report was published and released by the Hon Union Minister of Health and Family Welfare Dr. Ambumani Ramdoss on 5th December 2007 in Delhi during inaugural function of the Department of Health Research.

In the first round of IBBA, 29 districts from six states, viz., Andhra Pradesh, Karnataka, Maharashtra, Tamil Nadu, Manipur and Nagaland were covered. Field work was carried out by reputed research agencies.

IBBA procedures:

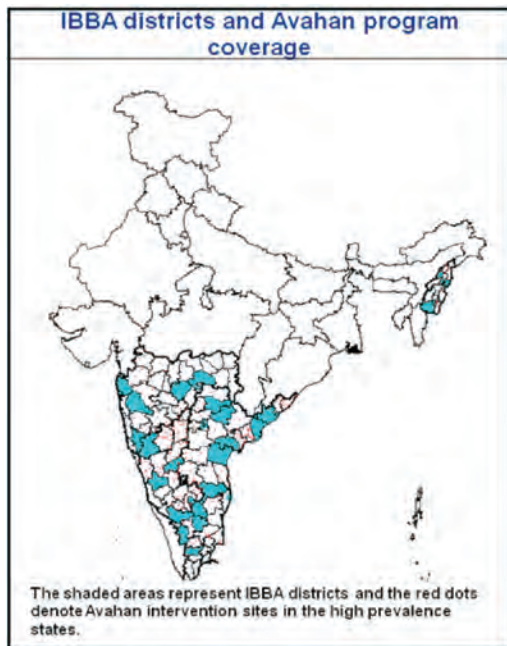
The IBBA was initiated in the selected districts with mapping of the sub populations followed by sampling frame development. Simultaneously Community Advisory Boards (CAB) and Community Monitoring Boards (CMB) were established as a part of harm minimization protocol for protecting participants' rights in each district.

Behavioral Domains of IBBA	Biological Domains of IBBA
Number and types of sexual partners	All participants:
Condom use with different types of partners	Syphilis serology
Practices related to condom use and safe sex	N. gonorrhoeae NAT
Knowledge of STIs and STI care-seeking behaviors	C. trachomatis NAT
Knowledge and attitudes toward HIV/AIDS	Herpes simplex virus type 2 (HSV-2) serology (10% sample)
Drug and substance use	HIV serology
Mobility and migration patterns influencing risk	BED assay for early HIV infection
Perception of HIV and STI risk	IDUs only:
Exposure to Avahan and other HIV Interventions	Hepatitis B virus (HBV) surface antigen
	Hepatitis C virus (HCV) antibody

Sampling approaches employed and Sample size
400 sample size for per group
Probability sampling method for all groups in all districts
Conventional Cluster Sampling (CCS)
Time Location Cluster Sampling (TLC)
Respondent Driven Sampling (RDS)
Take-all

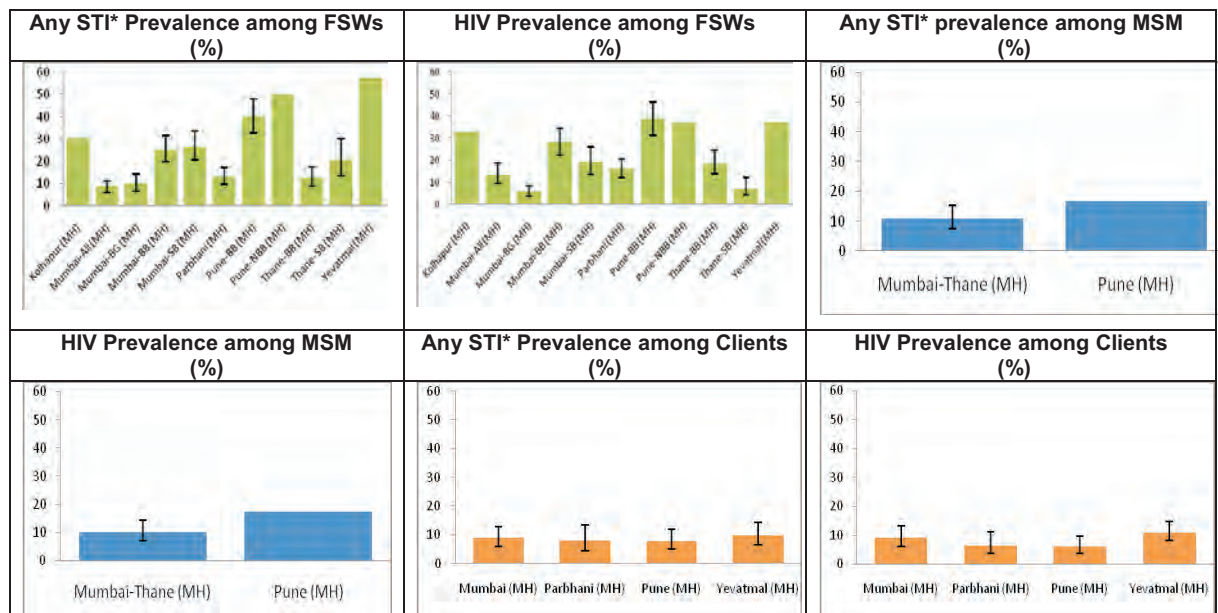
Survey details:

First FSW survey was piloted in Karimnagar, Andhra Pradesh in October 2005 followed by the surveys among IDUs, MSM, Clients of FSWs and the long distance truck drivers. The average time spent in completing one survey group was 6 weeks. The first round was completed in November 2007 with completion of Bar Girl Survey in Mumbai.



States	Districts	Survey groups	Sample achieved
Andhra Pradesh	8	17	6912
Karnataka	5	6	2560
Maharashtra	6	19	6230
Tamil Nadu	5	13	5260
Nagaland	3	3	1286
Manipur	2	2	839
National Highway	4 (NH routes)	4	2075
Total			25162

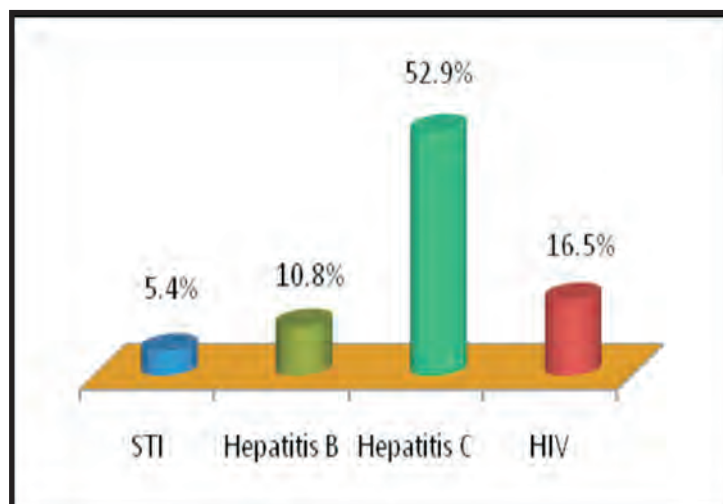
Figure 1.2: Prevalence of HIV / STIs Maharashtra



Any STI* = Any STI testing positive for any one or more of Syphilis, N. gonorrhoeae or C. trachomatis

Salient findings among FSW:

- The proportion of FSWs who could read and write varied from 14% in Hyderabad to 61% in Dimapur.
- Consistent condom use with regular clients was observed lowest in Dimapur (5%) and highest in Thane BB FSWs (97%) whereas, consistent condom use with occasional clients was reported to be lowest in Dimapur (11%) and highest in Thane BB FSWs (99%).
- Consistent condom use with non-commercial partners was low in Chitoor and Prakasam (1%) and highest in Thane BB (58%).
- In Andhra Pradesh the reported proportion of FSWs receiving any services ranged from 45% to 95% in different districts. For Karnataka it was 55% to 91% and Maharashtra 17% to 86% and for Tamilnadu it was 30% to 79%.
- The STI prevalence among FSWs in Andhra Pradesh districts, ranged from a low of 7.6% in Prakasam to a high of 24.1% in Hyderabad. The prevalence ranged from 9.5% to 20.6% Shimoga and Bangalore respectively in Karnataka. In Maharashtra, Thane had the lowest prevalence of 12.7% and highest in Pune and Yavatmal ie. more than 40%. In Tamilnadu, it ranged from 10.8% to 14.5% in Salem and Coimbatore respectively.
- HIV prevalence was also high in many districts, with Maharashtra having the highest prevalence rates (highest in Pune BB FSW 38.7% and lowest in Mumbai bar girls 5.9%).
- HIV prevalence was by and large low in Tamil Nadu highest of 12.5 % in Salem and lowest in Chennai (2.2%).

Prevalence among IDUs (%)**Salient findings among MSM:**

- The proportion of MSM who could read and write was high in all the IBBA districts from 58% in Guntur to 91% in Pune.

- In Andhra Pradesh, the reported proportion of MSM receiving any services ranged from 4% to 95%. In Maharashtra and Tamil Nadu, it was 6% to 60% and 55% to 78% respectively. In Karnataka, it ranged from 48% to 67%.
- MSM reported low levels of condom use for anal sex with their regular sexual partner in all districts ranging from lowest in Visakhapatnam (2%) to highest in Bangalore (73%).
- The STI prevalence ranged from lowest 5.3% (Guntur) to 18.8% (Madurai).
- Chennai had the lowest HIV prevalence (4.8%) and the highest was reported prevalence was in Hyderabad (24.7%).

Salient findings among IDUs:

- Exposure of IDUs to the various intervention programs was around 50% in the districts surveyed.
- A majority of the IDUs reported that their usual place of injecting drug use was their own home or the home of their injecting partner.
- Heroin was the most commonly injected drug among almost all IDUs.
- A large proportion of IDUs from Wokha (86%) reported starting of first drug use at age of 20 yrs or below whereas it was seen much less in Maharashtra (55%).
- Similarly, first injecting drug use at the age of 16 yrs or below was reported by 5% IDUs from Maharashtra and 15% in Phek.
- A large proportion of IDUs in Manipur (70%) reported using brand new needles and syringes the last time they injected.

Only a very small proportion of IDUs reported having commercial female sex partners in the past one year (2% in Phek and 27% in Mumbai-Thane).

The STI prevalence was low in Churachandpur (3%) and high in Wokha (29.7%).

The HIV prevalence was found very low in Phek (1.1%) and high in Churachandpur (32.2%)

Clients of FSW:

The data on behavioural as well as Biological indicators among the Clients of Sex workers in the Indian context is very scanty. Pilot exercises were undertaken to identify the appropriate sampling approach that would lead to the best participation rates. Finally a time-location cluster sampling approach at female sex worker's solicitation sites was used. For the identification of the potential clients brothel owners, FSWs, Community Liaison person and other key informants were involved.

- Overall, response rate was low in client groups across the states.
- Many of the clients reported low consistent condom use with female sex workers. With occasional FSWs it was reported low in Hyderabad and Warangal (19%) and high in

Parbhani (64%). Whereas, consistent condom use with regular FSWs was reported low in Salem (15%) and high in Pune (68%).

- Consistent condom use with regular female partners was reported very low among all the districts ranging from 0% (Guntur and Hyderabad) to 14% (Madurai).
- In Andhra Pradesh, lowest HIV prevalence was seen in Hyderabad (2.4%) and highest in East Godavari (8.3%).
- In Maharashtra it was lowest in Pune (6%) and highest in Yavatmal (10.9%). Similarly, in Tamil Nadu Chennai reported lowest (2%) and Salem highest HIV prevalence (4.2%).
- A state level Dissemination of IBBA results for all the surveyed groups in Maharashtra was conducted for the government health officials of Maharashtra and key stake holders on January 2, 2008 in Mumbai.



C. Cervical Cancer Screening for HIV-infected Women in India

[Principal Investigator: Dr. S. M. Mehendale]

HIV-infected women are at heightened risk for cervical intraepithelial neoplasia (CIN) and invasive cervical cancer. Increasing numbers of HIV-infected women in resource limited settings including India are living longer due to access to affordable antiretroviral therapy and ART roll out programme of Government of India. While life-spans of HIV-infected women are increasing, access to cervical cancer screening and treatment services is limited; hence women continue to present in advanced stages of cervical cancer.

Screening using visual inspection with acetic acid (VIA) is a cost-effective alternative to cytology-based screening programs in developing countries. This simple, inexpensive procedure can be performed by non-physician health workers and allows linking of screening and treatment in the same clinic visit. VIA-based screening programs nested within the context of antiretroviral therapy programs or HIV counseling and testing programs can allow early detection of cervical cancer in high-risk HIV-infected women in a cost-effective way. This also allows opportunities for beginning to provide broader gynecologic care for women with HIV. VIA-based screening programs could be eventually integrated with low-cost, rapid diagnostics for Human papillomavirus (HPV), the causative agent for ICC in 99.7% cases. This approach could increase programmatic efficiency in resource constrained settings and can be a scalable intervention that can reach out to all women regardless of HIV status.

Table 1.1: Analysis of predictors of disease prevalence for outcomes > CIN1

Predictor variables	Outcome: >CIN1	
	OR (95% CI)	'p'
Unit (1-year) increase in age (e.g., 28 vs. 27 years)	1.04 (0.99, 1.08)	0.13
No/some primary education (vs. ≥high school)	1.70 (1.02, 2.84)	0.04
Cohabiting with husband/spouse (vs. ≥widowed/separated)	1.17 (0.70, 1.96)	0.56
Family income <1,000 INR/month/person (vs. ≥ 1,000)	0.86 (0.51, 1.46)	0.58
Employed/Professional (vs. unemployed/housewife)	0.80 (0.48, 1.36)	0.42
Unit (1-yr) increase in age at first sex (e.g., 18 vs. 17 yrs)	0.94 (0.87, 1.03)	0.19
Unit (1-yr) increase in age at menarche (e.g., 13 vs. 12 yrs)	1.03 (0.85, 1.25)	0.76
≥2 lifetime sexual partners (vs. single lifetime partner)	2.33 (1.15, 4.74)	0.02
HIV-infected spouse (vs. no HIV-infected spouse)	1.22 (0.71, 2.09)	0.48
No/inconsistent condom use (vs. consistent use)	0.79 (0.35, 1.79)	0.57
History of presence of STI (vs. no STI)	1.14 (0.66, 1.95)	0.64
Ever used tobacco products (vs. never users)	0.85 (0.50, 1.42)	0.53
Hormonal contraceptive ≥1 year (vs. not used/used <1 yr)	1.27 (0.53, 3.07)	0.59
Unit increase in number of births (e.g., 3 vs. 2 births)	1.04 (0.85, 1.28)	0.68
Unit incr. in months since HIV detection (e.g., 13 vs. 12)	0.94 (0.78, 1.14)	0.54
Presence of gynecological symptoms (vs. no symptoms)	0.81 (0.46, 1.42)	0.46
Unit increase in BMI (e.g., 20 vs. 19)	0.99 (0.91, 1.08)	0.82
100 unit increase in CD4+ count (/μL) (e.g., 350 vs. 250)	0.92 (0.81, 1.04)	0.19
WHO Stage III/IV (vs. WHO Stage I/II)	1.11 (0.54, 2.30)	0.77
Currently taking ART (vs. ART-naïve)	2.38 (1.33, 4.26)	0.004

NARI in collaboration with Vanderbilt University, with funding from the National Cancer Institute (NCI, grant# R21CA113465) of the U.S. National Institutes of Health (NIH), has recruited a cohort of three hundred HIV-infected women. The study participants were enrolled in a cross sectional study in the “VIA study clinic” located in the Gynaecology Outpatient Clinic at Sassoon General Hospital (SGH). This is the first study in India that evaluated CIN disease prevalence in HIV-infected women with confirmatory colposcopic-histopathological assessment. The study revealed a very high prevalence of advanced cervical neoplasia (>CIN1: 27.7% and >CIN2: 16.6%), prompting a call to action for implementing cervical cancer screening as part of routine care services for HIV-infected women accessing antiretroviral therapy. VIA had better estimates of accuracy for detecting CIN than cytology or HPV testing in HIV-infected women and can be utilized in 'screen-and-treat' cervical cancer prevention programs targeting HIV-infected women in developing countries.

Building on the “VIA study” collaboration, NARI is now serving as a central coordinating agency for the “HIV-Cervical Cancer Prevention Research Program in India”, a joint Indo-US venture funded by the National Institutes of Health (NIH) of the US government [through National Cancer Institute (NCI) Fogarty International Center (FIC) and Vanderbilt University (VU)] with matching funding from Indian Council of Medical Research (ICMR). The new consortium seeks to

continue the follow-up of this cohort of HIV-infected women at the Pune site to study the progression or regression of CIN. It will also allow the development of site capacity in three new sites covering three of the four high-HIV prevalent states in peninsular India (Maharashtra, Karnataka, and Tamil Nadu). The proposed site expansion will help development of recruitment and retention strategies for enrolling and following-up HIV-infected women and generalizing the findings of the VIA study in Pune. Information from this research will guide the development of evidence-based guidelines for cervical cancer prevention in HIV-infected women residing in resource-limited settings.

D. A Randomized Trial to Evaluate the Effectiveness of Antiretroviral Therapy plus HIV Primary Care versus HIV Primary Care Alone to Prevent the Sexual Transmission of HIV-1 in Serodiscordant Couples .[HPTN 052 study]

[Lead Investigators: Dr. S. M. Mehendale, Dr. S. V. Godbole and Dr. S. Sahay]

The study has been conducted in two phases: Run in Phase and Full study. Date of commencement of Full study: 14th June 2007. During run-in phase, 22 screening and 10 enrollments were done. During the full study, 108 Screenings and 45 enrollments were done as of 31 March 2008. Thus, a total of 130 screenings and 55 enrollments were done.

Table 1.2: Screening, Enrollment and follow-up status of sero-discordant couples for full study (28.6.2007 to 31.3.2008)

Screening	Enrollment	Retention rate	Patients on ART
108	45	100%	30

Community Mobilization for Recruitment for HPTN 052 study

HPTN 052 full study recruitment began in June 2007. Core community involvement plan was found inadequate to identify potentially eligible HIV discordant couples.

In order to recruit discordant couples in HPTN 052 study five pronged strategy was developed in the reporting period. Each strategy was evaluated as follows:

Strategy 1: Community meetings:

Peer educators visit house to house in their community sub area; disseminate information about NARI research and HIV/AIDS. Group meetings are convened by them from these household visits.

Strategy 2: Promoting referrals from private practitioners



Doctors' meetings as a part of recruitment promotion activities

Recruitment team conducts sensitization meetings with private practitioners and their associations. Monthly follow up contacts are made and referral cards are distributed to them to facilitate referrals. Meetings were conducted with 11 associations involving over 600 private practitioners since May 2007 to March 2008. The challenge with this strategy is that it is an expensive strategy, people with low CD4 counts are identified and many felt that they will not be able to refer their patient to NARI due to stigma; hence they are concerned about loss of patient / practice. Another challenge is the logistic challenge. All meetings are conducted during late hours at night till early morning beyond mid night to ensure attendance by practicing physicians.

Strategy 3: Involving State AIDS Control Program and Integrated Counseling and Testing Centers (ICTC)



Maharashtra State AIDS Control Society (MSACS) has a network of 42 ICTCs in Pune rural and urban areas. This program was initiated with sensitization meetings with ICTC counselors and in-charges. Presently, NARI has established partnership with 29 ICTCs in urban and peri-urban area. The referral and tracking mechanism at each VCTC has been established. All VCTCs refer potential participants through NARI care cards. Monthly follow up visits are made to these ICTCs.

Strategy 4: Linkages with non partner NGOs

Some NGOs are also interested in associating with NARI. A sensitization meeting was held with such NGOs and they were followed up on monthly basis. Discordant couples are also identified through this strategy.

Strategy 5: Linkages with PLHA care and support program

The community program is dynamic and an evolving program. Evaluation becomes important to revisit the existing programs and develop new strategies. Recruitment targets for HPTN 052 are still not met with all the above mentioned strategies hence Core CIP team evolved a new strategy for forming linkage with PLHA self help groups.

Series of meetings were held with the Director of PLHA organization 'Network of Maharashtra People living with HIV/AIDS' (NPP). The activity was initiated in February 2008 and since then two NARI counselors are deputed at the 'Positive Living Center' [PLC] of the organization. NARI counselor provides counseling services and the PLC staff help in tracking their clients who are in HIV discordant relationship. Potentially eligible couples are referred to NARI clinics. Out of total seven couples found eligible, five have been screened and one enrolled in the study.

Outcome Evaluation of the recruitment program

NARI has a system of tracking referrals. The tool used is care card. The methodology has been described during the last reporting period. The following graph shows strategy wise distribution of referrals received in NARI clinics as couples from April 2007 to March 2008.

Table 1.3: Number of 'Couples' and 'Individuals' referred to the study clinics through the different recruitment strategies [April 2007 to March 2008]

Referred number	CIP-Peers	Health care provider	VCTC/ICTC	Other*
Couples	188	18	26	6
Individuals	459	69	58	16

*Other category includes non CIP NGOs, self help groups and savings group.

E. Studies on female controlled options for prevention of HIV transmission

E.1. Phase II Expanded Safety and Acceptability Study of the Vaginal Microbicide 1% Tenofovir Gel [HPTN 059 study]

[Principal Investigator: Dr. S. N. Joshi]

This was a multi-centric study [HPTN 059 study] with other sites being University of Alabama and Bronx Lebanon Hospital Center in the United States of America. The total sample size was 200 with 100 enrolments in the US and 100 at NARI, Pune India. The study was initiated in August 2006 at NARI and enrolment of 100 participants was completed in March 2007. The study was completed with 100% retention at NARI and >95% retention at the international sites. The product was safe (local as well as systemic safety) when used daily or with each act of sex when compared to the placebo. There was no difference in the safety laboratory parameters such as Complete Blood Count, Liver Function Tests and Renal Function Tests in the product and the placebo group at 4, 12 and 24 weeks. Adherence to product use was 80% in the coitally dependent arm and 83% in the daily use arm. Both the treatment groups (daily use Vs coitally dependent use) were well acceptable and acceptability about product characteristics and future

use are being analysed. Other parameters such as absorption of Tenofovir gel and effect of Tenofovir gel on viral load in Hepatitis B infected patients are being analysed.

E.2. Sustained Acceptability of Tenofovir Microbicide Gel: Male and Female perspectives in Pune

[Lead Investigators: Dr. S. M. Mehendale, Dr. R. Kohli]

The purpose of this acceptability study is to increase our understanding of factors associated with the initial acceptance and longer-term patterns of microbicide use and/or condom use.

Data Collection: Structured interviews are administered at baseline and follow-up visits at 8, 16 and 24 weeks. Baseline questions included socio-demographic information, description of household composition, resources and space, and initial measures of psychometric scales. Follow-up interviews assessed consistency of microbicide and/or condom use, HIV risk perception, sexual self-efficacy or control, couple harmony, and perception of product characteristics. In addition, structured questionnaire with the cohort participating in the HPTN 059 Clinical Trial study explored motivation for clinical trial participation and the importance of counseling and other interactions with staff to microbicide or condom use acceptance.

Qualitative data collection through in-depth interviews: A small cohort of couples also participated in qualitative studies by participating in interviews conducted at 12 and 20 weeks after joining the study. A subset of ten couples (five per cohort) and ten women without a partner in the study (five per cohort) were interviewed about their experiences using microbicides and/or condoms. These interviews explored the same factors as those measured by the psychometric acceptability scales. Additionally 5 in depth interviews of Clinical Trial providers were conducted.

Progress: After initiating the enrollment in September 2006, the data collection phase has been completed during the period of reporting.

Gender of respondents	Clinical trial participants	Non clinical trial participants
Female	100	100
Male partners/ spouses	53	56

E.3. Reddy Female Condom study: Evaluation of Two Condom Shaft Lengths in India.

[Principal Investigator: Dr. S. Joshi]

The objective of the study was to assess the functional performance and fit, safety and acceptability of the Reddy female condom with two shaft lengths and to determine the optimal shaft length. It was a Phase I study with a crossover design at the single site at NARI, Pune , India. Screening was initiated in March 07 and the study was completed in July 07. A total of 26 couples were screened to enroll 25 couples. All 25 couples completed two follow-ups and retention rate of the study was 100%. There were no serious adverse events reported by study participants. The adverse events reported by the study participants were minor and transient and these include irritation, burning, itching, rash and pain.

Comparison of the Reddy Version 6-120 and Version 6-90 Female Condoms in terms of the functional performance

Total clinical failure was significantly greater with the Reddy Version 6-90 mm condom than the Reddy Version 6-120 mm condom. This was largely due to more slippage and invagination observed with the shorter condom. The California study results were similar to ours although the difference in the total clinical failure was not statistically significant. There was no safety concern associated with the use of Reddy Version 6-90mm as well as Reddy Version 6-120mm condom. There were no unanticipated adverse events reported over the course of the study. All the adverse events were of transient in nature, resolved completely and only one AE of genital itching required medical intervention. Condom acceptability was somewhat difficult to interpret. The Reddy condom with 90 mm shaft length received slightly better acceptability scores than the 120mm shaft length.

E.4. Assessing the vascular changes occurring in the cervix in relation to the hormonal levels and menstrual cycle

[Principal Investigator: Dr. S. Joshi]

In order to detect possible effects of vaginal products on the genital tract, the baseline findings of vagina and cervix must be understood. A study was initiated to assess colposcopically observed vascular changes occurring in the cervix in relation to cyclical hormonal variation (serum oestradiol and progesterone) in normal healthy sexually abstinent women having regular menstrual cycles.

Thirty women between the ages of 18 and 45, with regular menstrual cycles and willing to remain sexually abstinent during a menstrual cycle were enrolled. Colposcopy was performed during the peak of the oestrogen level and the peak of the progesterone level. The main outcome measures included color of the cervix, hypertrophy and friability of the columnar epithelium; prominence, density, clarity of outline of blood vessels, and diameter of the largest visible blood vessel on the cervix; cytokine and chemokine estimation in cervicovaginal lavage specimens during the oestrogenic and the progestogenic phase of the menstrual cycle. The major findings of the study show that physiological changes of increased vascularity of the cervix observed colposcopically during the progestogenic phase are normal. If such changes do not correspond to the menstrual cycle phase in women using vaginal microbicides in early phase clinical trials, presence of inflammatory markers should be evaluated. Elevated IL-8 during the oestrogenic phase needs further evaluation.